

1917 2026

RHODE ISLAND MEDICAL JOURNAL



Mary Edwards Walker, MD:
Civil War Physician and Advocate for Women's Rights,
age 33 in 1865, and age 79 in 1911

See Heritage, page 67

A healthcare worker with dark hair and a light blue surgical mask is looking down at a tablet. A patient with blonde hair and a blue surgical mask is also looking at the tablet. The background is a blurred indoor setting.

Are insurance costs affecting your bottom line?

As record setting malpractice verdicts occur with increasing frequency, insurance premiums for medical practices will continue to rise. It's critical to partner with an experienced insurance broker who can advocate on your behalf to secure the best coverage at the best price.

HUB can help. Our insurance and risk management specialists work with you to develop a strategy to manage your insurance costs — so you can continue to focus on patient care.

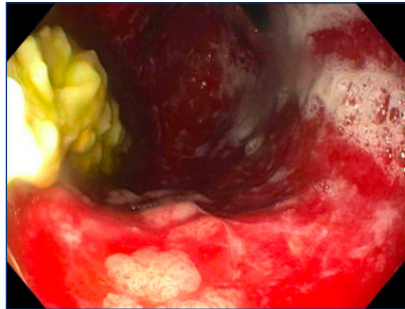
hubinternational.com/rimed

Put our resources to work for you.

Patrick Marra ○ 978-661-6203 ○ patrick.marra@hubinternational.com



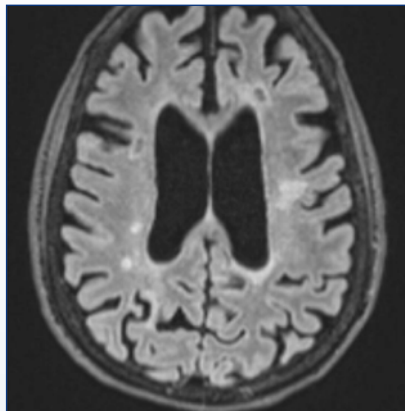
Risk & Insurance | Employee Benefits | Retirement & Private Wealth



IMAGES IN MEDICINE

- 7** Phlegmonous Gastritis Refractory to Antibiotics with Subsequent Improvement on Empiric Quadruple Therapy

ADITYA SHARMA, MD;
 SANGINI TOLIA, MD;
 SARVANI SURAPANENI, MD;
 MARJAN HAIDER, MD;
 KEVIN PLATT, MD;
 MARC PIPER, MD;
 EMILY TOMMOLINO, MD



CASE REPORTS

- 11** Recognition and Treatment of Concurrent Amyotrophic Lateral Sclerosis and Multiple Sclerosis

NGA YING ENG, MD;
 SYED RIZVI, MD;
 VINCENT LABARBERA, MD



- 15** Resolution of Phlegmasia Cerulea Dolens in a Patient with Metastatic Cancer and an Inferior Vena Cava Filter

MARIE NICOLE HAMEL, BS;
 JOHN J. LEE, MD;
 SUN HO AHN, MD, FSIR

- 18** Mucinous Adenocarcinoma Arising in a Mature Ovarian Teratoma

TANIN ZADEH, DO;
 KOMEIL MIRZAEI BABOLI, MD;
 SARA SALEHIAZAR, MD;
 TRUC TRAN, MD

- 23** Factor V Deficiency and Mechanical Valve Replacement: Challenges in Perioperative Hemostasis and Anticoagulation

DANIEL IDOATE DOMENCH, MD;
 ROBIN REID, MD;
 DUA AZIM, MD;
 SYED EHSANULLAH, MD;
 ADITYA SANJEEVI, MD;
 ANIKET RAO, MD



- 27** Atypical Bullous Sweet Syndrome

JONATHAN LONDON, MD;
 JOHN PATRESAN, MD;
 ALEXANDER BELKIN, MD;
 RADOWAN ELNAIR, MD

PUBLISHER

RHODE ISLAND MEDICAL SOCIETY

PRESIDENT

MARIAH H. STUMP, MD, MPH

PRESIDENT-ELECT

CHRISTOPHER DIMARCO, MD

VICE PRESIDENT

TANUJA GANDHI, MD

SECRETARY

STEVEN SCHECHTER, MD

TREASURER

MATTHEW J. SMITH, MD, MHL

CHIEF EXECUTIVE OFFICER

STACY PATERNO

EDITOR-IN-CHIEF

WILLIAM BINDER, MD

ASSOCIATE EDITORS

PHILIP CHAN, MD

**SENIOR EDITOR FOR RESEARCH
AND DEVELOPMENT**

ROY K. AARON, MD

EDITORS EMERITUS

JOSEPH H. FRIEDMAN, MD

EDITORIAL ADVISORY BOARD

JANETTE BAIRD, PhD

ERIC M. COHEN, MD

MAYA COHEN, MD

STACI FISCHER, MD

ANDREW HSU, MD

EDWARD HULTEN, MD, MPH

STEVE KWON, MD, MPH

ADAM LEWKOWITZ, MD, MPH

LESLIE ROTH, MD

ALESSANDRA J. SAX, MD

OLIVER J. WISCO, DO

PUBLICATION STAFF

MANAGING EDITOR

MARY KORR

mkorr@rimed.org

GRAPHIC DESIGNER

MARIANNE MIGLIORI

RHODE ISLAND MEDICAL JOURNAL (USPS 464-820), a monthly publication, is owned and published by the Rhode Island Medical Society, 225 Dyer Street, 2nd Floor, Providence RI 02903, 401-331-3207. All rights reserved. ISSN 2327-2228. Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society, unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society.

© COPYRIGHT 2013–2026, RHODE ISLAND MEDICAL SOCIETY, ALL RIGHTS RESERVED.

RHODE ISLAND MEDICAL JOURNAL



RESEARCH STUDIES

30 Decreasing Ghost Scanning in Point-of-Care Ultrasound: Impact of a Visual Prompt to Save Images

ROBERT BRADSHAW, MD; CURTIS XU, MD; DAVID CANNATA, MD; TRENT SHE, MD; ZACHARY BOIVIN, MD

35 Evaluating the Reliability, Accuracy, and Readability of ChatGPT-3.5 and GPT-4 in Providing Patient Education Related to Glenohumeral Joint Osteoarthritis

MOHAMAD Y. FARES, MD; TARISHI PARMAR, BSc; PETER BOUFADEL, MD; MOHAMMAD DAHER, MD; JONATHAN BERG, BSc; ADAM Z. KHAN, MD; BRIAN W. HILL, MD; JOHN G. HORNEFF, MD; JOSEPH A. ABBODD, MD

RESEARCH REPORT

41 Transitioning Young Adult Patients from Pediatric to Adult Rheumatology Practices in Rhode Island

VICTORIA KOENIGSBERGER, BA; MEGHAN GEARY, MD; ALI YALCINDAG, MD; MADELEINE WARD, MD

RESEARCH REVIEWS

47 Screening for Celiac Disease in Children: Practical Guidance for Primary Care Providers

PRERANA BARANWAL, MD

50 Metabolic Dysfunction-Associated Steatotic Liver Disease: A Review and Cases Regarding Liver Transplantation

KIMBERLY HO, MD; PAIGE MCLEAN DIAZ, MD

56 Intensity of Healthcare Utilization Among Pediatric Hospice Patients Receiving Concurrent Care

JACKIE LEE, MD; HAL EDMONSON, MD, MDiv; TESSA CENTRACCHIO, MSN; REBECCA E. MACDONELL-YILMAZ, MD, MPH

PUBLIC HEALTH

60 Vital Statistics

ZUHEIL AMORESE, DEPUTY STATE REGISTRAR

RHODE ISLAND MEDICAL JOURNAL

COMMENTARY

- 64** From Classroom to Community: Medical Students Address Women's Health Literacy through Community Education

NADINE NAJAH, BA;
FATINE OLIVEIRA, BSc;
BRIAN VU, BA;
MALIA PERALES, BA;
SANJANA KONDA, BSc;
ODINAKA ANYANWU, MD;
SRILAKSHMI MITTA, MD

HERITAGE

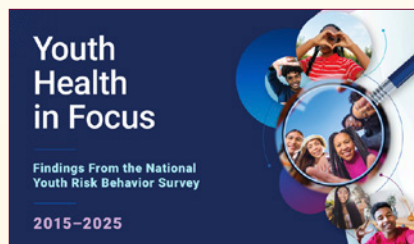
- 67** Mary Edwards Walker, MD: Civil War Physician and Advocate for Women's Rights
MARY KORR

IN THE NEWS

- 70** Progress against lung cancer drives down cancer mortality
CDC data show encouraging progress in youth health
- 71** Starr Foundation \$37M investment will create alliance to advance breakthroughs in aging research, clinical care
RI gets \$1M federal grant to strengthen 988 Suicide and Crisis Lifeline
- 72** Providence College Athletics, University Orthopedics announce new partnership focused on student-athlete care
- 73** VA awards \$8,720,113 in grants to fight Veteran homelessness



Women's Community Health Fair exhibitor
Urban Perinatal Education Center



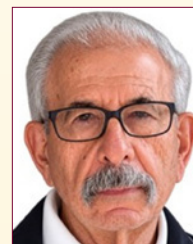
CDC's National Youth Risk Behavior Survey



G.R. Nicastri, MD



B. del Pozo, PhD



O. Basile, MD

PEOPLE/PLACES

- 75** Guy R. Nicastri, MD, FACS, appointed Chief Quality Officer at CharterCARE Health

Brandon del Pozo, PhD, receives 2026 Bruce M. Selya Award for Excellence in Research

- 76** Brown University Health's Cancer Institute Stem Cell Transplant Program earns national accreditation for quality and safety

Fatima Hospital, Roger Williams laboratories earn CAP accreditation

OBITUARY

- 77** Orazio Basile, MD

- 73** RIDOH launches new men's mental health campaign

- 74** Newport Hospital first in RI to implement da Vinci 5 Surgical System

Saint Anne's Hospital receives state approval for EP lab



Rhode Island's Medical Staffing Experts

Favorite Healthcare Staffing provides a comprehensive range of staffing services at preferred pricing to RIMS members. Call today to see why we are the favorite choice of healthcare professionals and physician practices across the US!



401.354.7115



MedicalStaffing@FavoriteStaffing.com



Favorite Healthcare Staffing is a Valued
Sponsor of the Rhode Island Medical Society

Phlegmonous Gastritis Refractory to Antibiotics with Subsequent Improvement on Empiric Quadruple Therapy

ADITYA SHARMA, MD; SANGINI TOLIA, MD; SARVANI SURAPANENI, MD; MARJAN HAIDER, MD; KEVIN PLATT, MD; MARC PIPER, MD; EMILY TOMMOLINO, MD

ABSTRACT

Phlegmonous gastritis is a rare infection of the gastric wall that presents with nonspecific symptoms and can rapidly progress with high mortality. We report a 59-year-old woman with two days of intractable nausea, vomiting, and inability to tolerate oral intake while on chronic proton-pump inhibitor therapy. She had leukocytosis, diffuse gastric wall thickening on computed tomography, and severe gastric mucosal abnormalities with antral sparing on endoscopy. Biopsy showed acute purulent gastritis but was negative for *Helicobacter pylori*. Given the unclear etiology and incomplete response to initial broad-spectrum antibiotics, empiric *H. pylori* quadruple therapy was initiated. The patient subsequently demonstrated clinical improvement without requiring surgical intervention.

KEYWORDS: Phlegmonous Gastritis; *Helicobacter pylori*; Endoscopy

INTRODUCTION

Phlegmonous gastritis (PG), also known as purulent gastritis, is a rare but potentially life-threatening bacterial infection of the gastric wall, marked by localized or diffuse suppurative inflammation of the submucosa and muscularis layers. Without prompt treatment, it can rapidly progress to necrosis, perforation, or septic shock.¹ PG typically presents with nonspecific symptoms, including epigastric pain, fever, nausea, and systemic signs of infection. Endoscopy, imaging, and histopathology remain the mainstay of diagnosis, while treatment consists of broad-spectrum intravenous antibiotics, with surgery reserved for severe or refractory cases.² Risk factors include mucosal injury (e.g., endoscopic procedures, peptic ulcer disease), immunosuppression, malignancy, and chronic alcohol use.²⁻⁴ *Streptococcus* spp. are the most common causative organisms. Although rare, *Helicobacter pylori*-associated PG has also been documented.^{5,6} We present a case of acute PG initially unresponsive to broad-spectrum antibiotics that improved following empiric quadruple therapy, with *H. pylori* considered a possible but unconfirmed contributing factor.

CASE DESCRIPTION

A 57-year-old woman presented to the hospital with two days of intractable nausea, vomiting, left-sided abdominal pain, and inability to tolerate oral intake. Her past medical history was significant for relapsing-remitting multiple sclerosis, for which she was not receiving disease-modifying therapy, and generalized anxiety disorder. She had no significant family history. Her home medications included a daily proton pump inhibitor (PPI). She endorsed chronic constipation and denied diarrhea, fever, chills, sick contacts, or change in her dietary habits, including any unusual food items.

On presentation, she was tachycardic with heart rates up to 127 beats per minute. Laboratory evaluation revealed leukocytosis with a white blood cell count of $20.2 \times 10^9/L$ (reference range $4-10 \times 10^9/L$) and an elevated lactate level of 2.1 mmol/L. Computed tomography (CT) of the abdomen demonstrated diffuse wall thickening of the gastric body, suggestive of gastritis [Figure 1].

The patient underwent Esophagogastroduodenoscopy (EGD) on hospital day 2, which revealed severe, unusual-appearing gastric mucosa with antral sparing [Figures 2A,B].

Figure 1. Contrast-enhanced computed tomography (CT) of the abdomen and pelvis demonstrating diffuse wall thickening and edema of the gastric body (yellow arrow).



Figure 2A. Initial esophagogastroduodenoscopy demonstrating diffuse severe erythema of the gastric body.

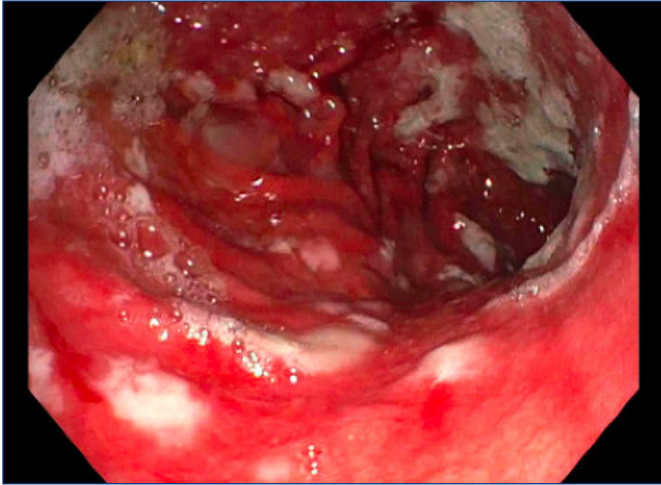
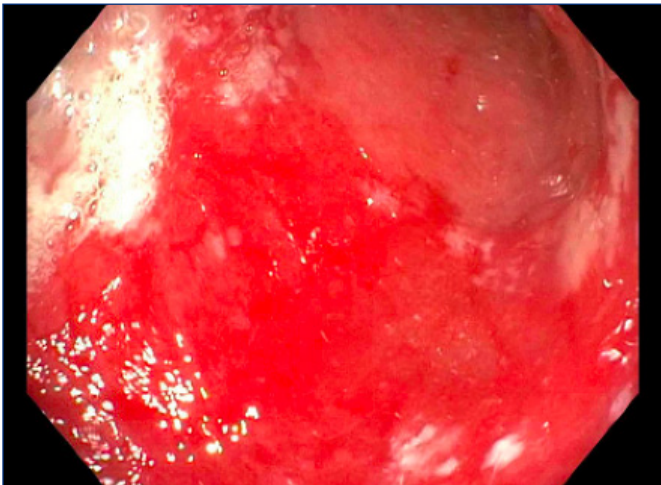


Figure 2B. Initial esophagogastroduodenoscopy demonstrating overlying inflammatory exudates within the gastric body mucosa.



Histopathologic examination of biopsy specimens showed diffuse acute purulent gastritis with surface ulceration and erosion, crypt abscesses, and dense neutrophilic infiltration. Special stains were negative for *H. pylori*, fungal organisms, viral inclusions, and malignant cells. Blood cultures remained negative. She was initially treated with intravenous ceftriaxone 2g every 24 hours, intravenous metronidazole 500mg every 8 hours, intravenous pantoprazole 40mg twice daily, and intravenous famotidine 40mg nightly.

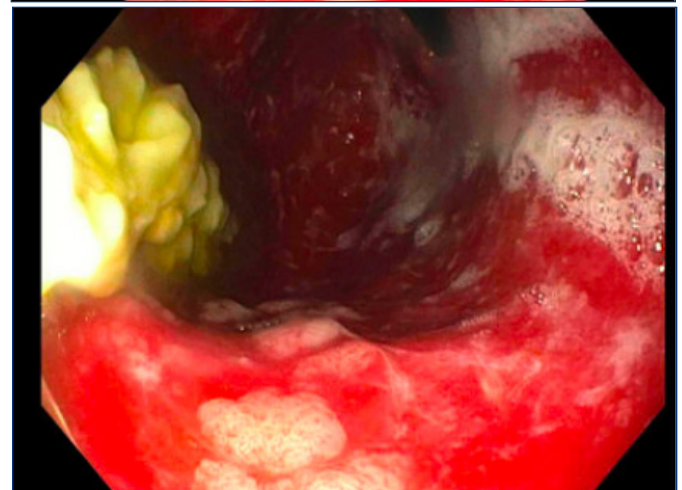
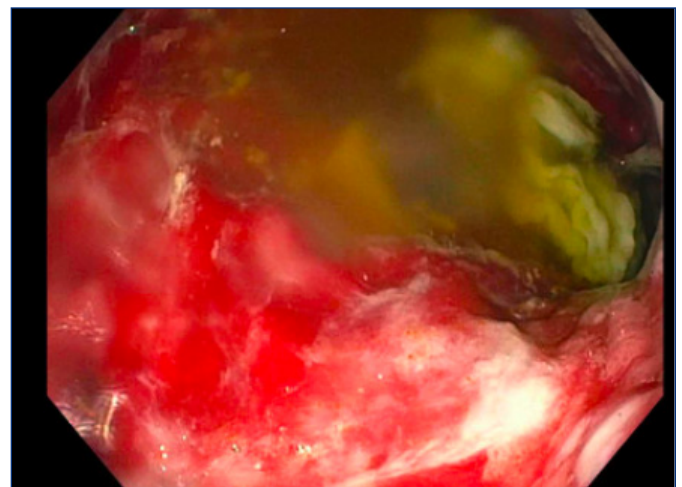
Given her prior use of a PPI, the possibility of a false-negative *H. pylori* result was considered. On hospital day 6, she was empirically started on quadruple therapy, consisting of clarithromycin, metronidazole, amoxicillin, and a PPI for a planned duration of 14 days, and ceftriaxone was discontinued. A stool antigen test for *H. pylori* subsequently returned negative.

Despite treatment, the patient continued to experience abdominal pain requiring opioid analgesia, along with persistent leukocytosis and tachycardia. A repeat EGD was performed on hospital day 8, demonstrating persistent acute gastritis characterized by intense erythema and exudates involving the gastric fundus and body, with an abrupt transition to normal-appearing mucosa in the antrum [Figures 3A,B]. Repeat biopsy specimens were again negative for *H. pylori*, viral inclusions, and malignancy. Sucralfate was initiated on hospital day 8 for additional symptom management.

By hospital day 13, the patient's white blood cell count had normalized to $9.7 \times 10^9/L$, and she was tolerating an oral diet. She was subsequently discharged home.

At outpatient follow-up approximately two weeks later, she had completed the full course of empiric *H. pylori* therapy. She reported persistent but mild nausea and epigastric discomfort, rated as 2 out of 10 in severity, for which she was advised to resume sucralfate as needed. A repeat outpatient EGD was planned for 2–3 months to assess for endoscopic resolution. However, the patient was lost to follow-up.

Figures 3A and 3B. Repeat esophagogastroduodenoscopy demonstrating persistent erythema and inflammation of the gastric body.



DISCUSSION

PG is an elusive diagnosis that can rapidly progress to clinical deterioration if not recognized early. Although only several thousand cases have been documented worldwide, it remains a rare but highly fatal condition, and this case attempts to fill the current void in literature on this rare diagnosis.⁷ Historically, mortality rates approached 90% but have declined to below 50% with antimicrobial therapy.^{6,8,9}

The pathophysiology of PG involves bacterial infiltration of the gastric wall, typically beginning in the submucosa via direct mucosal invasion, hematogenous or lymphatic spread, or ingestion of pathogenic organisms.^{10,11} Once established, infection can rapidly extend through the gastric wall, including the serosa. Based on the extent of involvement, PG is classified as either localized or diffuse, with the diffuse form associated with significantly higher mortality rates.¹² In this case, endoscopic findings were most consistent with the diffuse pattern.

Streptococcus spp. are the most common causative organisms, though polymicrobial infections involving gram-negative bacilli and anaerobes have also been reported.¹³⁻¹⁵ Although rare, *H. pylori*-associated PG has also been documented.^{5,6}

Our case presents with classic features as reported in the literature, including acute abdominal pain, systemic inflammatory response, and marked leukocytosis.^{6,10,16} Our patient was relatively young, without significant comorbidities or immunosuppression, and demonstrated clinical improvement following empiric *H. pylori*-directed therapy in addition to initial broad-spectrum antibiotics, thereby avoiding the need for surgical intervention. Although mucosal injury is a recognized risk factor, endoscopy remains essential for definitive diagnosis and longitudinal disease assessment.

Given the rarity of PG and the lack of standardized treatment guidelines, management is often individualized. Among the two documented cases of possible *H. pylori*-associated PG, one case from Portugal progressed to refractory shock with multiorgan dysfunction and resulted in death,⁶ while the other was successfully treated with medical therapy alone.⁵ In cases refractory to initial broad-spectrum antibiotic therapy, empiric 14-day quadruple therapy may be considered, particularly when *H. pylori* cannot be reliably excluded and diagnostic uncertainty persists. While this regimen primarily targets *H. pylori* and includes agents with activity against some anaerobic and gram-positive organisms, it does not provide comprehensive coverage for typical pathogens implicated in PG. Its use in this setting may be considered an adjunctive or alternative empiric approach when response to standard therapy is inadequate. This may be particularly relevant in patients receiving acid suppression, where diagnostic testing for *H. pylori* may be less reliable.

This case reinforces the critical role of early diagnosis and endoscopic evaluation in the management of this highly

morbid condition. It also suggests a possible role for *H. pylori* in select cases, although causality remains unproven. A broad infectious differential should be maintained. Unfortunately, the patient was lost to follow-up, underscoring loss of outpatient continuity as a significant barrier to care, and emphasizing the need for coordinated transitions between inpatient management and outpatient primary care and gastroenterology follow-up to ensure complete disease resolution and organism identification.¹⁷

Our case has several limitations that preclude establishing *H. pylori* as the definitive cause of PG. Histopathologic staining and stool antigen testing were negative, arguing against active infection, and although chronic PPI use may reduce diagnostic sensitivity, this does not provide confirmatory evidence. The absence of microbiologic confirmation further limits identification of the causative pathogen, and alternative etiologies such as *Streptococcus* species or a polymicrobial process remain plausible. In addition, the temporal association between initiation of quadruple therapy and clinical improvement does not establish causality and may reflect a delayed response to prior antibiotics, cumulative antimicrobial coverage, or mucosal healing with acid suppression. Finally, loss to follow-up precluded serologic evaluation and repeat testing, which may have provided further clarification of infection status. These limitations highlight the diagnostic challenges of PG and support maintaining a broad infectious differential even when a specific organism is suspected.

References

1. Saeed S, Alothman S, Saeed K, Ahmed L, Gray S. Phlegmonous Gastritis in a Bariatric Patient After Sleeve Gastrectomy. *Cureus*. 2019;11(10):e5898. doi:10.7759/cureus.5898
2. Park CW, Kim A, Cha SW, et al. A case of phlegmonous gastritis associated with marked gastric distension. *Gut Liver*. 2010;4(3):415-418. doi:10.5009/gnl.2010.4.3.415
3. Matsuura K, Hiramatsu S, Taketani R, et al. Medical Treatment of Postendoscopic Submucosal Dissection Phlegmonous Gastritis in an Elderly Diabetic Woman with Myelodysplastic Syndrome. *Case Rep Gastrointest Med*. 2018;2018:8046817. doi:10.1155/2018/8046817
4. Modares M, Tabari M. Phlegmonous gastritis complicated by abdominal compartment syndrome: a case report. *BMC Surg*. 2021;21(1):5. doi:10.1186/s12893-020-00999-y
5. Czapka MT, Schrantz SJ. Phlegmonous gastritis: Evolving from surgical to medical disease. *IDCases*. 2023;32:e01777. doi:10.1016/j.idcr.2023.e01777
6. Costa C, Antunes I, Lalande R, et al. An Under-Recognised Rapidly Fatal Condition: Phlegmonous Gastritis. *Eur J Case Rep Intern Med*. 2025;12(3):005175. doi:10.12890/2025_005175
7. Yang H, Yan Z, Chen J, Xie H, Wang H, Wang Q. Diagnosis and treatment of acute phlegmonous gastritis. *Medicine (Baltimore)*. 2018;97(18):e0629. doi:10.1097/MD.00000000000010629
8. Fan JQ, Liu DR, Li C, Chen G. Phlegmonous gastritis after esophagectomy: a case report. *World J Gastroenterol*. 2013;19(8):1330-1332. doi:10.3748/wjg.v19.i8.1330
9. Rada-Palomino A, Muñoz-Duyos A, Pérez-Romero N, et al. Phlegmonous gastritis: A rare entity as a differential diagnostic of an acute abdomen. Description of a case and a bibliographic review. *Rev Esp Enferm Dig*. 2014;106(6):418-424.

10. Taniguchi H, Aimi M, Matsushita H, Shimazaki G. A case of phlegmonous gastritis after acute pharyngitis. *Clin J Gastroenterol*. 2021;14(2):500-505. doi:10.1007/s12328-021-01345-2
11. Ramon C, Shay N, Malka A, Daniel E. Phlegmonous gastritis: Review of the pathophysiology. *Am J Med Sci*. 2024;367(4):274-277. doi:10.1016/j.amjms.2024.01.019
12. Shaik KS, Khatib MY, George S, et al. A case of phlegmonous gastritis complicated by stomach necrosis requiring gastrectomy. *Gastroenterol Endosc*. 2024;2(1):38-41. doi:10.1016/j.gande.2024.01.001
13. Kim GY, Ward J, Hennessey B, et al. Phlegmonous gastritis: case report and review. *Gastrointest Endosc*. 2005;61(1):168-174. doi:10.1016/s0016-5107(04)02217-5
14. Yang H, Yan Z, Chen J, Xie H, Wang H, Wang Q. Diagnosis and treatment of acute phlegmonous gastritis: A case report. *Medicine (Baltimore)*. 2018;97(18):e0629. doi:10.1097/MD.00000000000010629
15. Yakami Y, Yagyu T, Bando T. Phlegmonous gastritis: a case series. *J Med Case Reports*. 2021;15(1):445. doi:10.1186/s13256-021-02999-9
16. DeCino A, Gonzalez Martinez JL, Wright R. Phlegmonous Gastritis: A Case Report of Successful Early Antibiotic Treatment. *Cureus*. 2021;13(2):e13359. doi:10.7759/cureus.13359
17. Amat M, Duralde E, Masutani R, Glassman R, Shen C, Graham KL. Patient Lost to Follow-up: Opportunities and Challenges in Delivering Primary Care in Academic Medical Centers. *J Gen Intern Med*. 2022;37(11):2678-2683. doi:10.1007/s11606-021-07216-3

Authors

Aditya Sharma, MD, Department of Internal Medicine, Wayne State University School of Medicine, Detroit, Michigan.

Sangini Tolia, MD, Department of Internal Medicine, Trinity Health Ann Arbor Hospital, Ann Arbor, Michigan.

Sarvani Surapaneni, MD, Division of Gastroenterology and Hepatology, Trinity Health Ann Arbor Hospital, Ann Arbor, Michigan.

Marjan Haider, MD, Division of Gastroenterology and Hepatology, Trinity Health Ann Arbor Hospital, Ann Arbor, Michigan.

Kevin Platt, MD, Huron Gastroenterology, Ann Arbor, Michigan.

Marc Piper, MD, Division of Gastroenterology and Hepatology, Trinity Health Ann Arbor Hospital, Ann Arbor, Michigan.

Emily Tommolino, MD, Huron Gastroenterology, Ann Arbor, Michigan.

Disclosures

Financial disclosure: None reported

Use of Artificial Intelligence: All parts of the study, including idea generation, literature review, and manuscript preparation were completed by our research team. The manuscript reflects our original work and thought process. ChatGPT (OpenAI) was used only for grammar correction and to improve text readability. No scientific content, analysis, or interpretation was generated by Artificial Intelligence.

Conflicts of interest statement: The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed.

Prior Presentation: This case was previously presented at the Annual Scientific Meeting of the American College of Gastroenterology (ACG) 2024, held in Philadelphia, Pennsylvania, USA, on October 28, 2024. <https://acg2024.eventscribe.net/fsPopup.asp?PosterID=683656&mode=posterInfo>

Patient Consent Statement: Repeated and documented attempts were made to contact the patient and the patient's designated emergency contact to obtain written informed consent for publication. Despite exhaustive efforts to reach the patient, next of kin, and/or parent or guardian, informed consent could not be obtained, as the patient was lost to follow-up. No directly or indirectly identifiable patient information is included in this manuscript. In accordance with ethical standards, the authors believe that publication of this case poses minimal risk to patient privacy. This case also underscores the clinical importance of robust follow-up mechanisms to reduce loss to follow-up in routine medical care.

Correspondence

Aditya Sharma, MD
313-221-6393
Fax 315-291-6111
drasharma5@gmail.com
hw8777@wayne.edu

Recognition and Treatment of Concurrent Amyotrophic Lateral Sclerosis and Multiple Sclerosis

NGA YING ENG, MD; SYED RIZVI, MD; VINCENT LABARBERA, MD

ABSTRACT

Amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) are neurological disorders with different underlying pathophysiology but can share similar clinical features. Co-occurrence of both diseases is extremely rare with only 46 documented cases in literature to our knowledge. This case report relays the diagnosis of ALS in a patient with a decades'-long history of MS, and illustrates the importance of expanding the differential diagnosis and pursuing additional workup in a patient with overlapping progressive symptoms that can be caused by an alternate neurological etiology.

KEYWORDS: Amyotrophic lateral sclerosis; multiple sclerosis; co-morbidities

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) are both progressive neurological disorders that lead to a spectrum of motor, bulbar, and cognitive impairments despite having different pathophysiology.¹ ALS is a neurodegenerative disease affecting both upper and lower motor neurons, resulting in a progressive and insidious loss of motor function.² MS is an autoimmune disease characterized by inflammation and demyelinating plaques in the central nervous system and is one of the most common causes of neurologic disability within the young adult population.³ This case reports upon the rare and unfortunate co-occurrence of MS and ALS in a middle-aged woman, to our knowledge, representing only the 47th reporting of such a case in the literature.⁴

CASE REPORT

A 58-year-old woman with a history of secondary progressive MS (SPMS) and gastric bypass for obesity presented to her primary neurologist for

worsening weakness. The patient was initially diagnosed with relapsing and remitting MS (RRMS) at the age of 36, when she developed abnormal eye movements and facial paresthesia. She was started on interferon beta 1b and later transitioned to natalizumab. The patient remained on natalizumab for many years until further disease progression which manifested as dysmetria and worsening gait, approximately two years prior to current presentation, prompting a transition to ocrelizumab.

Following disease stability for the subsequent two years, the patient returned to clinic with a new, but gradual, distal left leg weakness. This was documented as Medical Research Council (MRC) 2 out of 5 strength in the proximal left leg, with 1 out of 5 strength in the distal left leg. She had 3+ patellar reflexes bilaterally. This was then followed by distal right leg weakness, over months, in a similar pattern. Magnetic Resonance Imaging (MRI) of the brain and spine with and without contrast was obtained to evaluate for MS progression but did not demonstrate corticospinal tractopathy, discrete enhancing lesions affecting the corticospinal tract, or new demyelinating lesions compared to prior MRIs [Figure 1]. Over the course of months, the patient developed worsened weakness at the distal left foot, now to MRC 0 out of 5, with marked hyperreflexia, including 4+ reflexes at the

Figure 1. MRI T2 FLAIR imaging [A] demonstrated global atrophy of the cerebral cortex and significant white matter lesions, and [B] T1 imaging with hypointense foci. No active contrast enhancement was observed (not pictured).

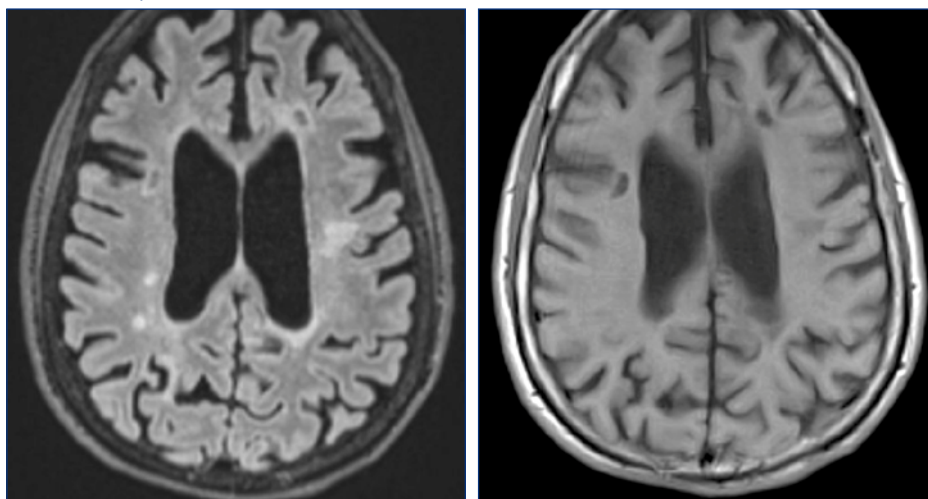


Figure 2. Nerve conduction studies [A,B] demonstrated an axonal motor-predominant neuropathy, and electromyogram [C] demonstrated marked ongoing denervation with chronic reinnervation changes in three bodily segments.

Sensory NCS									
Nerve / Sites	Rec. Site	Peak Lat ms	NP Amp μ V	PP Amp μ V	Segments	Distance cm	Velocity m/s	Temp C	
L Median - Digit II Ortho									
Digit II	Wrist	4.08	4.9	5.2	Digit II - Wrist	13	38.8		32
Ref.		3.50	10.0	10.0	Ref.				
L Ulnar - Digit V Ortho									
Digit V	Wrist	2.88	6.0	9.5	Digit V - Wrist	11	48.0		
Ref.		2.90	5.0	5.0	Ref.				
L Sural - Lat Mall									
Calf	Lat Mall	2.73	7.7	7.2	Calf - Lat Mall	14	67.2		
Ref.		4.20	5.0	5.0	Ref.				
R Sural - Lat Mall									
Calf	Lat Mall	2.79	8.8	10.9	Calf - Lat Mall	14	65.9		
Ref.		4.20	5.0	5.0	Ref.				

Motor NCS									
Nerve / Sites	Rec. Site	Lat ms	Amp mV	Rel Amp %	Segments	Dist cm	Velocity m/s	Area mVms	
L Median - APB									
Wrist	APB	5.38	3.5	100	Wrist - APB	6.5		13.3	
Ref.		4.40	4.2		Ref.				
Elbow		9.19	2.6	72.6	Elbow - Wrist	18.5	48.5	10.1	
Ref.			4.2		Ref.		49.0		
L Ulnar - ADM									
Wrist	ADM	2.65	7.3	100	Wrist - ADM	6.5		24.6	
Ref.		3.50	5.6		Ref.				
Below Elbow		5.54	7.1	96.5	Below Elbow - Wrist	18.5	63.9	23.7	
Ref.			5.6		Ref.		49.0		
Above Elbow		7.38	6.7	91.5	Above Elbow - Wrist	27.5	58.1	23.3	
Ref.			5.6		Ref.		49.0		
L Peroneal - EDB									
Ankle	EDB	4.25	0.2	100	Ankle - EDB	7.5		0.6	
Ref.		5.70	2.0		Ref.				
Fib Head		10.38	0.2	110	Fib Head - Ankle	29.5	48.2	0.8	
Ref.			2.0		Ref.		41.0		
Knee		11.92	0.2	111	Knee - Ankle	36	47.0	0.7	
Ref.			2.0		Ref.		41.0		
L Tibial - AH									
Ankle	AH	5.10	1.0	100	Ankle - AH	7.5		3.2	
Ref.		5.70	2.8		Ref.				
Knee		13.40	0.7	69.6	Knee - Ankle	37.5	45.2	4.3	
Ref.			2.8		Ref.		41.0		
L Peroneal - TA									
Fib Head	TA	4.06	0.4	100	Fib Head - TA	11.5		1.6	
Ref.			3.5		Ref.				
Knee		5.21	0.4	101	Knee - Fib Head	6.5	56.7	2.8	
Ref.			3.5		Ref.		41.0		
R Tibial - AH									
Ankle	AH	4.17	4.2	100	Ankle - AH	7.5		11.3	
Ref.		5.70	2.8		Ref.				
Knee		13.25	2.8	65.6	Knee - Ankle	39	42.9	6.2	
Ref.			2.8		Ref.		41.0		
R Peroneal - TA									
Fib Head	TA	4.96	1.8	100	Fib Head - TA	15		13.7	
Ref.			3.5		Ref.				
Knee		6.83	1.6	88	Knee - Fib Head	9.5	50.7	11.6	
Ref.			3.5		Ref.		41.0		

EMG Summary Table											
Muscle	Nerve	Roots	Spontaneous				H.F. / Other	MUAP			Recruitment Pattern
			IA	Fib	PSW	Fasc		Amp	Dur.	PPP	
L. Deltoid	Axillary	C5-C6	N	None	None	2+	None	1+	1+	N	Reduced
L. Biceps brachii	Musculocutaneous	C5-C6	N	None	None	1+	None	1+	1+	N	Reduced
L. Triceps brachii	Radial	C6-C8	N	None	None	1+	None	1+	1+	N	Reduced
L. First dorsal interosseous	Ulnar	C8-T1	N	None	None	1+	None	1+	1+	N	Reduced
L. Cervical paraspinals	Spinal	C4-C8	2+	2+	2+	None	None	1+	1+	N	Reduced
L. Vastus lateralis	Femoral	L2-L4	3+	3+	None	None	None	1+	1+	Incomplete activation.	
L. Tibialis anterior	Deep peroneal (Fibular)	L4-L5	3+	3+	3+	None	None	No motor unit potentials observed.			
L. Gastrocnemius (Medial head)	Tibial	S1-S2	3+	3+	3+	None	None	No motor unit potentials observed.			
L. Tensor fasciae latae	Superior gluteal	L4-S1	3+	3+	3+	None	None	1+	1+	N	Reduced
L. Lumbar paraspinals	Spinal	L1-L5	3+	3+	3+	None	None	1+	1+	1+	Reduced
L. Thoracic paraspinals	Spinal	T1-T12	3+	3+	3+	None	None	1+	1+	N	Reduced

multifocal leukoencephalopathy (PML). An inpatient nerve conduction study and electromyogram (NCS/EMG) was performed, and widespread active denervation in the cervical, lumbar, and thoracic segments, as well as a superimposed axonal sensorimotor neuropathy, was observed [Figure 2]. Based on the electrodiagnostic testing, she was diagnosed with ALS, meeting El Escorial Revised Criteria for definite ALS, with secondary diagnosis of axonal sensorimotor polyneuropathy due to malnutrition. Riluzole was initiated, but she did not meet candidacy criteria for edaravone, due to advanced ALS-Functional Rating Scale-Revised (ALS-FRS-R). Although she denied a family history of motor neuron diseases, genetic testing was offered and ultimately resulted negative for the most common genetic causes of ALS including C9orf72. Following diagnosis, weakness and bulbar symptoms progressed, now inclusive of significant neck extensor weakness (MRC 3 out of 5) and proximal arm weakness (MRC 4- out of 5) and the patient became wheelchair-dependent, aphonic, and markedly dysphagic. Seven months after development of foot drop, tongue fasciculations were observed with a present pathologic jaw jerk reflex. Ocrelizumab was discontinued in the interim due to malnutrition and the development of additional co-morbidities. Palliatively, she was treated with methylphenidate for her excess fatigue, baclofen for spasticity, and botulinum toxin for sialorrhea. She was eventually transitioned to hospice care and died approximately 27 months following onset of symptoms attributable to ALS, and 13 months after diagnosis.

DISCUSSION

Concomitance of ALS and MS, although previously documented, remains an extraordinarily rare finding, with this case possibly representing only the 47th documented case of co-occurrence. To date, no definitive genetic or mechanistic association has been identified between the two diseases,

left biceps with present Hoffman's sign, and upgoing plantar reflex (Babinski sign) on the right. Additionally, progressive dysphagia and burgeoning spastic dysarthria with limited word output, without frank tongue atrophy or fasciculations, was observed. Progressive dysphagia, in the context of her history of gastric bypass, led to severe protein calorie malnutrition requiring temporary total parenteral nutrition.

The patient was eventually admitted to the hospital for an expedited neurologic workup, as outpatient imaging did not support increasing MS disease burden or central nervous system (CNS) infection, such as progressive

though a combination of environmental and genetic factors, as well as inflammatory pathways have been explored.^{4,8} Although genetic testing was not always completed in previous cohorts with concurrent ALS and MS, only 5 of 33 reported cases in a literature review were found to carry a C9orf72 gene abnormality.⁵ Our patient had neither a family history of ALS, nor a de novo mutation in the most common ALS-causing genes.⁶ Some studies suggest a geographical north-south gradient of disease mortality in the ALS population, similar to that as seen in MS.⁸ In some cohorts, patients with ALS and MS patients had a higher frequency of PPMS compared to the standard MS population, and inaugural MS (i.e., MS presenting prior to ALS) appears to be the order in the majority of cases.^{4,5}

Most cases of MS present as RRMS, in which relapses are followed by gradual, and at times incomplete recovery.³ RRMS will classically develop into SPMS 10–15 years after initial onset and is characterized by a progression of disability without definitive clinical relapse, as was the case in our patient.³ Resumption of progression after initial stabilization on disease-modifying therapy in secondary progressive MS (SPMS) is not well-quantified but appears to occur with some frequency, reflecting the modest and variable treatment effects seen in this population. SPMS trials show only 20-25% relative reductions in disability progression, meaning most patients continue to progress, and treatment benefits are greatest in those with ongoing inflammatory activity that may diminish over time. In our case, a two-year period of stability followed by resumed progression likely reflects the exhaustion of the inflammatory component responsive to therapy with the non-inflammatory neurodegenerative mechanisms of SPMS becoming dominant; natural disease variability (as SPMS progression is not linear); or the modest treatment effect being overwhelmed by ongoing pathological processes not adequately addressed by current immunomodulatory therapies.

As demyelinating plaques often involve the brainstem and spinal cord, it is possible that clinical symptoms of SPMS can mask an underlying upper motor neuron-predominant neurodegenerative disorder. Of note, both conditions may result in corticospinal tractopathy, with MRI in ALS demonstrating a FLAIR hyperintense “Lateral Corticospinal Tract Sign” in the brain or spinal cord,⁹ whereas corticospinal tract lesions in MS tend to be discrete inflammatory lesions. Using diffusion tensor imaging (DTI) to determine characteristics of white matter tractopathies in these two disorders is a burgeoning field in radiologic research. Furthermore, given the chronic use of a B-cell suppressive agent, a CNS infection such as PML, or a process with positive mass effect (either tumefactive MS or neoplastic process) must be considered and ruled out.¹⁰

In this case, the patient was diagnosed with SPMS for over two decades prior to the onset of ALS based on imaging and clinical findings. ALS and SPMS can both present

as an insidious progression of upper motor neuron findings on examination (e.g., progressive hypertonicity, pathologic hyperreflexia, spastic weakness and gait dysfunction, particularly if corticospinal tract involvement is prominent); however, progressive sensory findings would not be expected in ALS, and marked lower motor neuron features such as ongoing and active denervation seen on EMG testing would not be expected in SPMS. Re-imaging, particularly with MRI with gadolinium contrast, and NCS/EMG testing, was critical in this patient to distinguish SPMS disease progression from ALS, as disease trajectory and treatment vary greatly. In this patient’s case, palliative treatments, such as anti-spasticity treatments and treatments against fatigue, can be shared between the two conditions. However, discovery of co-occurrence led to changes in management of the disease-modifying treatments, with discontinuation of the immunosuppressive MS medication ocrelizumab, and addition of the life-prolonging medication of riluzole. A unifying pathophysiologic principle such as a defined genetic basis or pertinent environmental trigger was not identified in this case, most likely indicating a random coincidence of disorders. Regardless, the rarity of this co-occurrence bears the importance of reporting.

CONCLUSION

In conclusion, as both SPMS and ALS may demonstrate similar clinical findings, a high index of suspicion for an alternative corticospinal tractopathy, such as ALS, is suggested, especially if new and insidiously progressive motor and bulbar features appear in a patient with SPMS. Prudence in re-assessing the diagnosis, and avoidance of anchoring on SPMS is advised, as treatment options and prognostic counseling, for both patient and family members, may change.

References

1. Guennoc AM, Pallix-Guyot M, Le Page E, Le Port D, Daryabin M, Hergesheimer R, et al. Co-occurrence of MS and ALS: a clue in favor of common pathophysiological findings? *Amyotroph Lateral Scler Frontotemporal Degener*. 2018 Nov;19(7-8):500-505. doi: 10.1080/21678421.2018.1476547. Epub 2018 Sep 3. PMID: 30175630.
2. Menge S, Decker L, Freischmidt A. Genetics of ALS - genes and modifier. *Curr Opin Neurol*. 2025 Oct 1;38(5):568-573. doi: 10.1097/WCO.0000000000001416. Epub 2025 Aug 7. PMID: 40772638; PMCID: PMC12419016.
3. Dobson R, Giovannoni G. Multiple sclerosis - a review. *Eur J Neurol*. 2019 Jan;26(1):27-40. doi: 10.1111/ene.13819. Epub 2018 Nov 18. PMID: 30300457.
4. Jellinger KA. Co-occurrence of amyotrophic lateral sclerosis and multiple sclerosis: a rare but interesting association. *J Neural Transm (Vienna)*. 2026 Jan;133(1):1-13. doi: 10.1007/s00702-025-02975-3. Epub 2025 Jun 28. PMID: 40580315.
5. Aljthali R, Albalawi R, Alyahya A, Alhathloul R, Alhashemi M. Multiple sclerosis and amyotrophic lateral sclerosis: is there an association or a red flag? A case report and literature review. *BMC Neurol*. 2024 Aug 31;24(1):307. doi: 10.1186/s12883-024-03821-x. PMID: 39217293; PMCID: PMC11365120.

6. Ismail A, Cooper-Knock J, Highley JR, Milano A, Kirby J, Goodall E, et al. Concurrence of multiple sclerosis and amyotrophic lateral sclerosis in patients with hexanucleotide repeat expansions of C9ORF72. *J Neurol Neurosurg Psychiatry*. 2013 Jan;84(1):79-87. doi: 10.1136/jnnp-2012-303326. Epub 2012 Oct 20. PMID: 23085936.
7. Li G, Esiri MM, Ansorge O, DeLuca GC. Concurrent multiple sclerosis and amyotrophic lateral sclerosis: where inflammation and neurodegeneration meet? *J Neuroinflammation*. 2012 Jan 24;9:20. doi: 10.1186/1742-2094-9-20. PMID: 22269588; PMCID: PMC3308920.
8. Schilling MA. The geographic association of multiple sclerosis and amyotrophic lateral sclerosis. *Sci Rep*. 2025 Oct 14;15(1): 34665. doi: 10.1038/s41598-025-18755-8. PMID: 41087397; PMCID: PMC12521557.
9. Desai AB, Agarwal A, Mohamed AS, Mohamed KH, Middlebrooks EH, Bhatt AA, et al. Motor Neuron Diseases and Central Nervous System Tractopathies: Clinical-Radiologic Correlation and Diagnostic Approach. *Radiographics*. 2025 Jan;45(1):e240067. doi: 10.1148/rg.240067. PMID: 39636751.
10. Sharma K, Tolaymat S, Yu H, Elkhooly M, Jaiswal S, Jena A, et al. Progressive multifocal leukoencephalopathy in anti-CD20 and other monoclonal antibody (mAb) therapies used in multiple sclerosis: A review. *J Neurol Sci*. 2022 Dec 15;443:120459. doi: 10.1016/j.jns.2022.120459. Epub 2022 Oct 14. PMID: 36283150.

Authors

Nga Ying Eng, MD, Department of Neurology, Warren Alpert Medical School of Brown University, Providence, RI.

Syed Rizvi, MD, Department of Neurology, Warren Alpert Medical School of Brown University, Providence, RI.

Vincent LaBarbera, MD, Department of Neurology, Warren Alpert Medical School of Brown University, Providence, RI.

Disclosures

The authors have no financial or personal disclosures.

Acknowledgment: We thank the patient and her loving sisters who were instrumental in providing the inspiration for this article. The patient provided literature to the authors prior to her passing, regarding the rarity of her condition, which served as the foundation for this article in her honor.

Correspondence

Vincent LaBarbera, MD

vincent_labarbera@brown.edu

Resolution of Phlegmasia Cerulea Dolens in a Patient with Metastatic Cancer and an Inferior Vena Cava Filter

MARIE NICOLE HAMEL, BS; JOHN J. LEE, MD; SUN HO AHN, MD, FSIR

ABSTRACT

Phlegmasia cerulea dolens (PCD) is a rare but serious complication of extensive venous thromboembolism (VTE) that can lead to limb ischemia and significant morbidity if not treated promptly. We describe a 69-year-old man with metastatic non-small cell lung cancer and hemorrhagic brain metastases who developed rapidly progressive PCD despite recent negative imaging and an existing inferior vena cava filter. He presented with bilateral lower extremity discoloration, absent Doppler signals, and signs of end-organ involvement. The patient underwent urgent mechanical thrombectomy with rapid clinical improvement and restoration of venous flow. This case highlights how quickly PCD can develop in high-risk patients and supports thrombectomy as a useful option for the resolution of extensive VTE and PCD.

KEYWORDS: phlegmasia cerulea dolens; deep vein thrombosis; thrombectomy; cancer-associated thrombosis; inferior vena cava filter; brain metastases

INTRODUCTION

Phlegmasia cerulea dolens (PCD) is a rare but limb-threatening manifestation of extensive venous thromboembolism, characterized by near-total venous outflow obstruction, severe limb edema, and compromised arterial inflow that can rapidly progress to venous gangrene. It most commonly arises in the setting of massive iliofemoral deep vein thrombosis and carries a high risk of limb loss and mortality if not promptly recognized and treated.

Venous thromboembolism (VTE) is a well-documented complication in patients with malignancy, particularly those with non-small cell lung cancer (NSCLC).¹ The risk of VTE and PCD is further amplified in older patients in the setting of metastatic disease, prior thromboembolic events, and the presence of an inferior vena cava (IVC) filter.^{2,3,6} Management of PCD is especially challenging in patients with brain metastases, where the elevated risk of intracranial hemorrhage limits the use of systemic anticoagulation.⁴ Acute decompensation from extensive thrombosis and PCD can result in hemodynamic instability and multiorgan dysfunction, necessitating urgent intervention.

Mechanical thrombectomy is a highly effective treatment option in such cases, offering immediate clot burden reduction and symptom resolution.⁵ This case highlights the complexities of managing extensive venous thromboembolism resulting in phlegmasia cerulea dolens in a patient with metastatic NSCLC and hemorrhagic brain lesions, underscoring the need for timely recognition and interdisciplinary coordination to optimize outcomes.

CASE PRESENTATION

A 69-year-old male with a history of hypertension, type 2 diabetes mellitus, chronic obstructive pulmonary disease, prior NSCLC treated in 2013, and PE/DVT with an IVC filter placed in 2012 presented to the emergency department for lightheadedness and new right-sided weakness. CT panscan revealed a frontal brain mass and two cerebellar masses as well as a right apical lung mass, concerning for recurrence of NSCLC. There was no evidence of VTE on CT panscan. He was admitted to the hospital for neurosurgical intervention scheduled for the following week.

Five days after admission, the patient acutely decompensated while ambulating, with hypotension (83/59 mmHg) and tachycardia (heart rate 120 bpm). Bilateral lower extremities appeared mottled and cyanotic and pulses were unable to be obtained using doppler, consistent with PCD [Figure 1].

An emergent CTA of the abdomen revealed extensive VTE involving bilateral common femoral, external iliac, common iliac veins and IVC that extended superiorly to the level of the IVC filter that had been placed during his previous treatment for NSCLC [Figure 2].

The venous congestion resulted in bladder hematuria and congestion of the left kidney. The patient was not on anticoagulation at home, and at this time, blood work showed a lactate of 5.2 and a pH of 7.18 on venous blood gas.

Heparin was started after a conversation with the patient's family regarding the risk of bleeding given the hemorrhagic brain metastases. The family consented to treatment with heparin. Interventional radiology was consulted and the patient was taken for VTE thrombectomy. Access was achieved through bilateral popliteal veins with a 16 French sheath. Endovascular thrombectomy was performed using the Penumbra Lightning Flash device. Afterwards, a venogram demonstrated no significant residual stenosis or filling

Figure 1. Presence of PCD in bilateral extremities**Figure 3.** Resolution of PCD in bilateral extremities**Figure 2.** Evidence of VTE up to the level of IVC filter on CT

defects. After the procedure, bilateral lower extremity pulses returned and PCD resolved [Figure 3].

Lactate levels decreased to 1.3, and the hematuria resolved. The patient was wrapped with ACE bandages from toes to upper thighs and was encouraged to ambulate and

use the sequential compression devices (SCDs) as much as possible to prevent future clot formation. The decision was made after communicating with the primary care team and the neurosurgery team to keep the IVC filter in place until after the neurosurgery.

DISCUSSION

This case underscores the importance of rapid diagnosis and intervention in patients presenting with PCD, especially in the context of metastatic cancer. PCD requires evidence of four cardinal signs and symptoms: pain, edema, bluish discoloration, and severe venous obstruction. All of these signs were present in our patient on exam. The characteristic bluish discoloration of PCD indicates severe, often fatal, venous obstruction that can quickly lead to venous gangrene, shock, and death.⁷ Endovascular thrombectomy provided a safe and effective means of restoring venous flow and reversing end-organ congestion, including renal and bladder involvement, without exacerbating intracranial hemorrhage risk. The patient's hemodynamic stabilization and rapid symptom improvement illustrate the value of early interventional radiology involvement.

One striking feature of this case is the rapidity of thrombus formation, with no evidence of VTE on imaging five days prior, followed by the development of extensive thrombosis. This underscores the importance of preventative measures such as ambulation and SCDs in the hospital to prevent blood stasis and the subsequent prevention of VTE. Pharmacological anticoagulation would also be appropriate had the patient not been diagnosed with hemorrhaging

brain metastases. Additionally, the presence of an indwelling IVC filter may have contributed to thrombus propagation, highlighting an important consideration in patients with recurrent or extensive thrombosis.

Despite the unfortunate development of this patient's condition, the patient's care team responded swiftly and appropriately to provide life-saving care. In patients with cancer-associated thrombosis and complicating factors such as brain metastases, a multidisciplinary approach remains essential to balance bleeding risk with thrombotic burden and optimize patient outcomes.

CONCLUSION

In the setting of metastatic cancer and immobilization in the hospital, phlegmasia cerulea dolens can develop rapidly and represent a limb- and life-threatening vascular emergency, even in the presence of recent negative imaging. This case is notable for extensive thrombosis occurring despite an indwelling IVC filter and in the context of contraindication to anticoagulation due to hemorrhagic brain metastases, with associated end-organ dysfunction, including renal congestion and hematuria. Urgent endovascular thrombectomy enabled rapid restoration of venous outflow while minimizing bleeding risk, demonstrating the critical role of endovascular intervention in complex, cancer-related thrombosis. Early recognition and prompt consultation with interventional radiology are essential in similar high-risk scenarios to optimize patient outcomes.

References

1. Albalawi MA. Phlegmasia cerulea dolens as an initial presentation of ovarian cancer. *J Appl Hematol*. 2025;16(4):402-406. doi:10.4103/joah.joah_88_25
2. Lyman GH, Bohlke K, Khorana AA, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol*. 2015;33(6):654-656. doi:10.1200/JCO.2014.59.7351
3. Secemsky EA, Rosenfield K, Kennedy KF, et al. Contemporary management of inferior vena cava filters. *JACC Cardiovasc Interv*. 2020;13(7):873-882.
4. Saba N, McBride A, Jillella AP, et al. Anticoagulation therapy in patients with cancer and central nervous system metastases. *J Natl Compr Canc Netw*. 2018;16(11):1337-1345.
5. Shammash NW. Role of percutaneous mechanical thrombectomy in management of deep vein thrombosis and pulmonary embolism. *Vasc Health Risk Manag*. 2013;9:439-446.
6. Fürbringer-Schwarz A, Janscak M, Jeanneret-Gris CR. Outcome after bilateral deep vein thrombosis. *Vasa*. 2022;51(6):372-376. doi:10.1024/0301-1526/a001030
7. Mumoli N, Invernizzi C, Luschi R, Carmignani G, Camaiti A, Cei M. Phlegmasia cerulea dolens. *Circulation*. 2012;125(8):1056-1057. doi:10.1161/CIRCULATIONAHA.111.051912

Authors

Marie Nicole Hamel, BS, The Warren Alpert Medical School of Brown University, Providence, RI.

John J. Lee, MD, The Warren Alpert Medical School of Brown University, Providence, RI.

Sun Ho Ahn, MD, FSIR, The Warren Alpert Medical School of Brown University, Providence, RI.

Disclosures

Funding: This study was not supported by any funding.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethical approval: For this type of study formal consent is not required.

Informed Consent: For this type of study informed consent is not required.

Consent for publication: Consent for publication was obtained for every individual person's data included in the study.

Availability of data and materials: There is no associated data for this case report.

Correspondence

Marie Nicole Hamel, BS
mhamel117@gmail.com

Mucinous Adenocarcinoma Arising in a Mature Ovarian Teratoma

TANIN ZADEH, DO; KOMEIL MIRZAEI BABOLI, MD; SARA SALEHIAZAR, MD; TRUC TRAN, MD

ABSTRACT

Malignant transformation of a mature cystic teratoma (MCT) is rare, with mucinous adenocarcinoma being an even more uncommon subtype. Accurate diagnosis requires distinction from metastatic gastrointestinal tumors. A woman in her 30s presented with a 19 cm right ovarian mass. She underwent exploratory laparotomy with right salpingo-oophorectomy, left ovarian cystectomy, omentectomy, peritoneal biopsies, and bilateral pelvic and para-aortic lymphadenectomy with intraoperative rupture of the mass. Frozen section suggested immature teratoma, but final pathology revealed mucinous adenocarcinoma arising within a mature teratoma. The tumor showed CK20, CDX2, SATB2 positivity, patchy CK7, and loss of PAX8. All lymph nodes and staging biopsies were negative for carcinoma. Final stage: FIGO IC1. This case highlights the diagnostic and staging challenges in malignant transformation (MT) of a MCT. Thorough sampling, immunohistochemistry (IHC), and clinical correlation are critical to differentiate primary ovarian neoplasms from metastatic disease. Accurate classification is essential to guide appropriate management.

KEYWORDS: Mature cystic teratoma; mucinous adenocarcinoma; ovarian neoplasm; malignant transformation; immunohistochemistry

INTRODUCTION

Mature cystic teratomas are among the most common ovarian germ cell tumors and are generally benign. Malignant transformation occurs in approximately 1–3% of cases, with squamous cell carcinoma being the most frequent malignancy. Transformation into mucinous adenocarcinoma is much rarer, accounting for approximately 5–8% of MTs.¹ Mucinous tumors arising in MCTs often demonstrate gastrointestinal-type differentiation, including positive immunoreactivity for CK20, CDX2, and SATB2, and variable PAX-8 and CK7.^{2–4} This immunochemical profile can mimic metastasis from the gastrointestinal (GI) tract, making integration of histology, immunohistochemistry, clinical findings, and imaging studies essential for accurate diagnosis.

Due to their rarity and overlapping histologic features with metastatic GI tumors, mucinous carcinomas arising

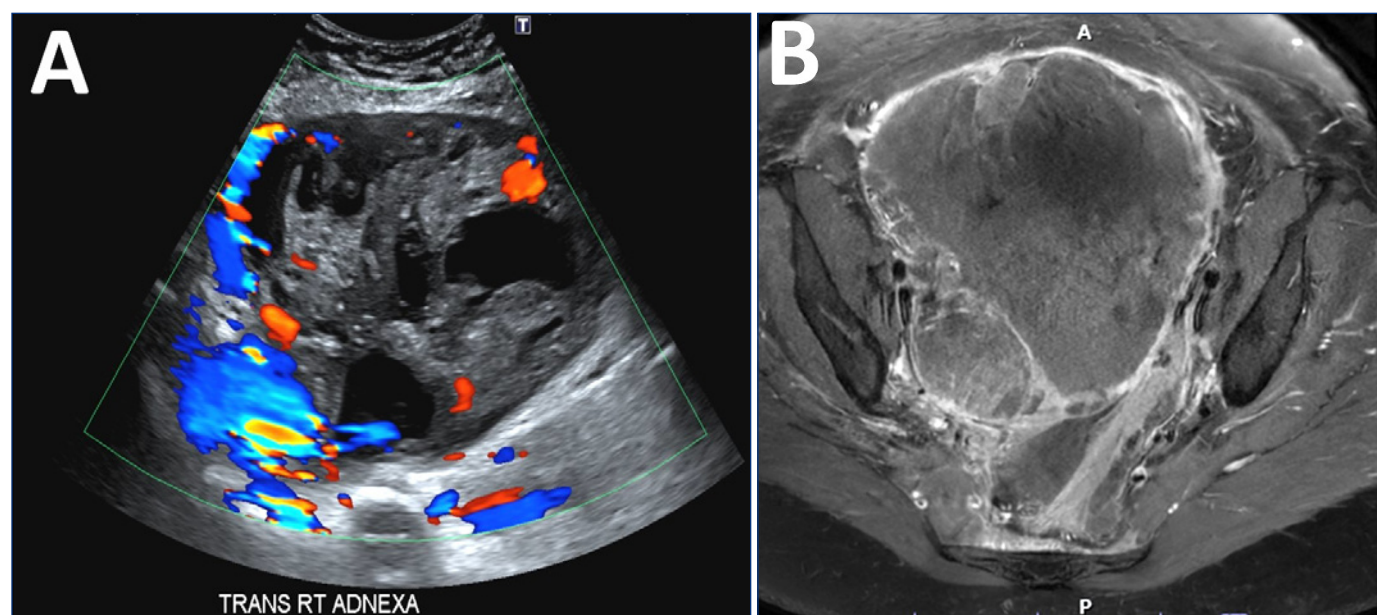
in MCTs are diagnostically challenging. Frozen section evaluation can be particularly limited due to extensive necrosis, mucinous debris, or low tumor cellularity, which may obscure malignant components. Most reported cases occur in postmenopausal women and often present as large adnexal masses, sometimes with signs of rupture or adhesions.^{5,6} However, these tumors can also occur in reproductive-age patients, emphasizing the importance of considering MT in younger individuals as well. A literature review of PubMed for the past 10 years from 2015–2025 has identified less than 10 reported cases of mature teratoma with malignant transformation of mucinous adenocarcinoma.

The diverse gross and microscopic appearance of MCTs is due to the presence of well-differentiated tissues derived from all three germ layers: ectoderm, mesoderm, and endoderm.⁶ Ectodermal derivatives, such as skin, hair, and neural tissue are the most encountered components, with MT typically arising from squamous epithelium, becoming squamous cell carcinoma. However, this process can also involve the endodermal layer, leading to rare cases of adenocarcinoma. Among these, mucinous adenocarcinoma is an exceptionally rare form of MT, often displaying intestinal-type features that can closely resemble metastatic GI tumors.⁶ We present another rare case of mucinous adenocarcinoma arising within a mature teratoma in a woman in her 30s. This case highlights the diagnostic challenges of distinguishing primary ovarian mucinous carcinoma from metastasis, especially when arising in a teratoma.

CASE REPORT

A multiparous woman in her 30s (gravida 2, para 2) presented to the hospital with pelvic pain, right lower back pain, and vaginal bleeding for 10 days. Her other symptoms included constipation, bloating, and early satiety. The initial physical examination revealed a distended and tender abdomen, dark brown blood in the vaginal vault, posteriorly oriented cervix and anteverted uterus. Pelvic ultrasound imaging revealed an ORADS-5 right adnexal cystic and solid lesion measuring about 19 cm [Figure 1A]. Further investigation with pelvic computed tomography (CT) and magnetic resonance imaging (MRI) revealed a large multicystic mass with calcifications measuring 18 × 17 × 13 cm [Figure 1B], arising from the right ovary, suggestive of a dermoid cyst. Preoperative CT

Figure 1. [A] Transvaginal ultrasound showing a 19 cm right adnexal mass with mixed solid and cystic components and both internal and peripheral Doppler flow. **[B]** MRI of pelvis showing a large multiloculated pelvis with thick enhancing septations, measuring up to 18 cm.



of the chest, abdomen, and pelvis demonstrated no definite evidence of metastatic disease. Tumor markers were notable for CA-125: 63.1 U/mL (normal: <35), CEA: 28.5 ng/mL (normal: <3), and CA 19-9: 81 U/mL (normal: <35). AFP was within normal limits at 4.4 ng/mL (normal: <10).

The patient underwent exploratory laparotomy with right salpingo-oophorectomy, bilateral pelvic and para-aortic lymphadenectomy, infracolic and infragastric omentectomy, and left ovarian cystectomy. Upon entering the peritoneal cavity, ascites was noted and sent for cytologic studies. Severe adhesions were found between the mass and small bowel, pelvic wall, left tube and ovary, cul de sac, and rectal mesentery. Lysis of these adhesions led to rupture of the mass extruding brown fluid and fibrinopurulent material. Frozen sections from the right ovary showed immature teratoma, and sections from the small bowel were negative for tumor.

Grossly, the right ovarian mass measured 19 x 17.5 x 13 cm and weighed 1,174 grams. Serial sectioning revealed hair with solid yellow and necrotic areas in the cyst. Microscopic analysis demonstrated components of both a mature teratoma and mucinous adenocarcinoma. This raised the differentials of (1) malignant transformation of a benign teratoma, or (2) a collision tumor comprising of a mature teratoma and mucinous carcinoma, either of primary ovarian origin or metastatic from the GI tract. The tumor cells were positive for CK20, CDX2, SATB2, and showed patchy positivity for CK7 [Figure 2A-C]. They were negative for PAX-8, GFAP, synaptophysin, and chromogranin. The proliferation index by Ki-67 was high at 80% [Figure 2D]. No tumor was found in the extra-ovarian tissue, and all lymph

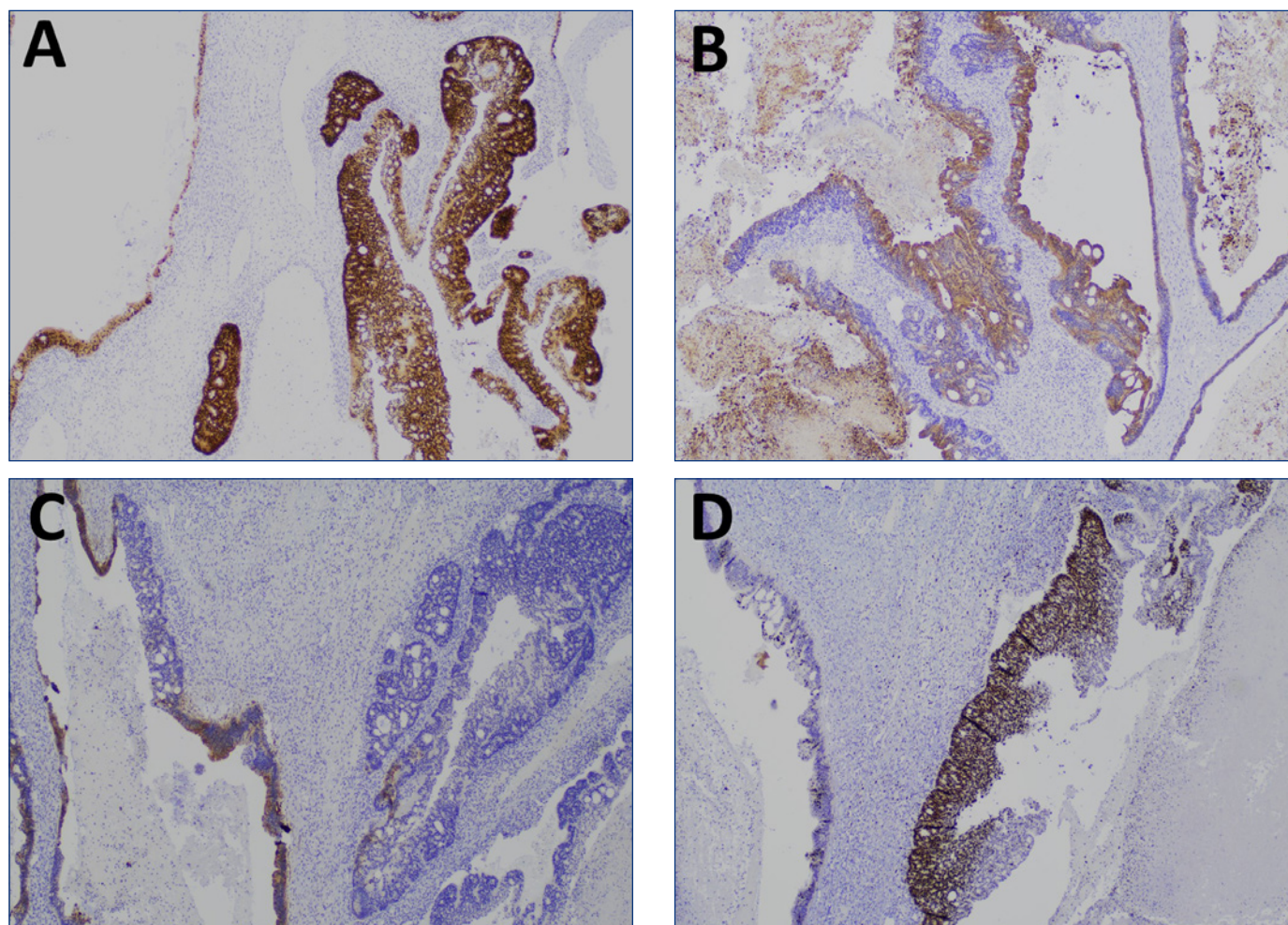
nodes and peritoneal biopsies were negative. The tumor was staged as FIGO IC1 due to surgical spill of cystic contents. Peritoneal fluid was negative for malignancy on cytology. The immunophenotype (CK20+, CDX2+, SATB2+, patchy CK7+, PAX8-) supports intestinal differentiation but does not distinguish between primary ovarian and metastatic GI origin. Grossly and morphologically, the mature teratoma is intermixed with the mucinous tumor, with no intervening normal ovarian stroma. Although metastatic GI carcinoma cannot be entirely ruled out, the pathologic findings and lack of extra-ovarian disease strongly favor a primary ovarian origin with the carcinoma arising from the endodermal component of the MCT.

Her post-operative course was uneventful. Genetic testing revealed no clinically significant mutations. A variant of unknown significance (VUS) was identified but did not influence clinical management. She began treatment with six cycles of chemotherapy, seven weeks after her operation, with CT imaging planned to follow the final cycle. Her CA-125 levels were 19 U/mL at two months postoperatively, 34.5 U/mL at three months, 18.6 U/mL at four months, and 16.7 U/mL at five months (normal: <35).

DISCUSSION

Malignant transformation of mature cystic teratomas (MCTs) is rare, occurring in only 1–3% of cases, and is most frequently observed in postmenopausal women, typically over the age of 50.⁵ The present case is notable given the patient's young age, highlighting that although uncommon, MT can occur in reproductive-age women and should

Figure 2. Immunohistochemistry showing tumor positivity for [A] CDX2, [B] CK20, and [C] CK7, and a [D] high Ki-67 proliferation index.



not be excluded based on age alone. Although malignant changes are rarely recognized preoperatively,¹ our case had early radiologic changes suspicious for malignancy.

The mechanisms underlying MT in MCTs are not fully understood but are thought to be associated with long-standing, untreated tumors that undergo genetic instability over time.^{6,7} Prior studies have shown that MT is more frequently observed in older patients (>45 years) and in large tumors (>10 cm) (8–10). Because any of the tridermal components can undergo transformation, various types of malignancies, including basal cell, sebaceous tumor, carcinoid, transitional cell carcinoma, adenosquamous, melanoma, and leiomyosarcoma have been found to arise from MCTs.^{1,6,11}

Accurate diagnosis is critical, as the immunohistochemical profile of mucinous adenocarcinoma arising in MCTs can mimic metastatic GI tumors. Most reported mucinous carcinomas arising from MCTs display a CK20+/CK7 profile,⁴ corresponding to a lower GI origin; however, one study describes a MCT-associated mucinous carcinoma with CK20+/CK7+ profile.² Our case showed a similar pattern

with strong positivity for CK20 and patchy positivity for CK7. One study analyzing 42 cases of mucinous neoplasms arising in MCTs found universal CDX2 positivity,¹² consistent with the findings in our case. Although SATB2 is a sensitive marker for lower GI tumors and is not typically expressed in the female reproductive tract,^{3,13} its positivity in our case was interpreted in the context of the mature elements of the tumor and clinical findings, supporting a primary ovarian origin rather than metastatic disease. PAX-8 is typically negative in GI tumors and is variable in ovarian primaries.³ A large retrospective study evaluating ovarian and GI tumors concluded that ovarian mucinous tumors associated with teratomas can show a similar immunoprofile to GI tumors, making the diagnosis reliant on the teratoma element.³ Absence of a GI primary on clinical and radiologic evaluation, lack of metastatic disease, and the presence of mature teratoma elements support a primary ovarian origin in this case.

Distinguishing primary ovarian carcinoma from metastatic disease is crucial for guiding treatment, determining

prognosis, and deciding whether ancillary studies or further extra-ovarian work-up are needed. For example, colon carcinoma in a young female patient would indicate genetic testing for Lynch syndrome. Our patient underwent Myriad genetic testing which found only a VUS, which was not believed to have contributed to the disease process.

The standard surgical approach for this type of tumor involves a total hysterectomy, bilateral salpingo-oophorectomy, and surgical staging with omentectomy, appendectomy, lymphadenectomy, peritoneal biopsies, and peritoneal washing.¹⁴ However, younger patients may desire fertility-preserving surgery, in which a unilateral salpingo-oophorectomy with complete surgical staging, as performed in our case, may be considered. According to the National Comprehensive Cancer Network (NCCN) guidelines, management of mucinous ovarian carcinoma is primarily stage dependent. Stage I disease may be managed with observation or adjuvant systemic therapy, depending on the risk factors. Although our patient had early-stage disease, the intraoperative spill and fertility-sparing surgery were contributing factors in the decision to proceed with six cycles of adjuvant chemotherapy. One of the preferred regimens for mucinous carcinoma stage IC is Carboplatin/Paclitaxel every three weeks,¹⁵ which is what our patient received. The prognosis for stage I adenocarcinoma arising from a MCT is relatively good compared to that of later-stage disease.¹⁶ Since adenocarcinomas arising from MT are quite rare, most studies assessing relapse risk are conducted on mucinous ovarian carcinomas without an associated-MCT component. Factors associated with lower recurrence risk include early FIGO stage, lower pathological grade, and no visible residual disease after debulking.¹⁷

CONCLUSION

Mucinous carcinoma arising from MCTs presents a diagnostic conundrum due to its rarity and variable immunohistochemical and imaging characteristics. Ovarian mucinous carcinomas arising in MCTs may demonstrate an immunoprofile that overlaps with GI tumors, including expression of CK20, CDX2, and SATB2, with variable CK7 and PAX-8 expression. Ovarian mucinous tumors associated with teratomas may not have an established dominant immunoprofile due to their rarity; therefore, diagnosis should rely on morphologic findings and identification of the teratomatous component rather than immunohistochemistry alone. Clinicians must integrate systemic imaging (MRI, PET/CT) with tumor marker trends (e.g., elevated CA19-9, CA125) and histopathology to determine tumor origin, tailoring surgical and chemotherapeutic strategies accordingly.

References

1. Park JH, Whang SO, Song ES, Choi SJ, Lee WY. An ovarian mucinous cystadenocarcinoma arising from mature cystic teratoma with para-aortic lymph node metastasis: a case report. *J Gynecol Oncol.* 2008;19(4):275. doi:10.3802/jgo.2008.19.4.275
2. Atsukawa N, Nakai G, Omura S, Yamamoto K, Yamada T, Ohmichi M, et al. Imaging features of mucinous carcinoma arising from mature teratoma showing cytokeratin 7+ and cytokeratin 20+ expression profile: A case report. *Radiol Case Rep.* 2024 Apr;19(4):1288–93. doi:10.1016/j.radcr.2024.01.001
3. Meagher NS, Wang L, Rambau PF, Intermaggio MP, Huntsman DG, Wilkens LR, et al. A combination of the immunohistochemical markers CK7 and SATB2 is highly sensitive and specific for distinguishing primary ovarian mucinous tumors from colorectal and appendiceal metastases. *Mod Pathol.* 2019 Dec;32(12):1834–46. doi:10.1038/s41379-019-0302-0
4. Clark ME, Will MD. Intestinal-Type Adenocarcinoma Arising in a Mature Cystic Teratoma of the Ovary. *Int J Gynecol Pathol.* 2016 Jul;35(4):352–6. doi:10.1097/PGP.0000000000000258
5. Kikkawa F, Ishikawa H, Tamakoshi K, Nawa A, Suganuma N, Tomoda Y. Squamous cell carcinoma arising from mature cystic teratoma of the ovary: A clinicopathologic analysis. *Obstet Gynecol.* 1997 Jun;89(6):1017–22. doi:10.1016/S0029-7844(97)00117-8
6. Abdoli Shadbad M, Derogar R, Shekarchi AA, Akbari F, Jafari Shobeiri M. Mature cystic ovarian teratoma with squamous cell carcinoma transformation: a case report and literature review. *Horm Mol Biol Clin Investig.* 2024 Apr 1;45(1):35–9. doi:10.1515/hmbci-2023-0001
7. Bouri S, Simon P, D'Haene N, Catteau X, Noël JC. P53 and PIK3CA Mutations in KRAS/HER2 Negative Ovarian Intestinal-Type Mucinous Carcinoma Associated with Mature Teratoma. Porpora MG, editor. *Case Rep Obstet Gynecol.* 2020 Jan;2020(1):8863610. doi:10.1155/2020/8863610
8. Hackethal A, Brueggmann D, Bohlmann MK, Franke FE, Tinneberg HR, Münstedt K. Squamous-cell carcinoma in mature cystic teratoma of the ovary: systematic review and analysis of published data. *Lancet Oncol.* 2008 Dec;9(12):1173–80. doi:10.1016/S1470-2045(08)70306-1
9. Rim SY, Kim SM, Choi HS. Malignant transformation of ovarian mature cystic teratoma. *Int J Gynecol Cancer.* 2006 Jan;16(1):140–4. doi:10.1136/ijgc-00009577-200601000-00023
10. Peterson WF. Malignant Degeneration of Benign Cystic Teratomas of the Ovary. A Collective Review of the Literature. *Obstet Gynecol Surv.* 1957 Dec;12(6):793–830. doi:10.1097/00006254-195712000-00001
11. Bacalbasa N, Cretoiu D, Halmaciu I, Diaconu C, Iliescu L, Dima S, et al. Squamous Cell Carcinoma from Abscessed, Mature Cystic Ovarian Teratoma – A Case Report and Literature Review. *In Vivo.* 2020;34(4):2141–6. doi:10.21873/in vivo.12020
12. Hershkovitz D, Vlodavsky E, Simon E, Ben-Izhak O. KRAS mutation positive mucinous adenocarcinoma originating in mature ovarian teratoma: Case report and review of literature. *Pathol Int.* 2013 Dec;63(12):611–4. doi:10.1111/pin.12123
13. Atwi D, Kamal M, Quinton M, Hassell LA. Malignant transformation of mature cystic teratoma of the ovary. *J Obstet Gynaecol Res.* 2022 Dec;48(12):3068–76. doi:10.1111/jog.15409
14. Gadducci A, Guerrieri ME, Cosio S. Squamous cell carcinoma arising from mature cystic teratoma of the ovary: A challenging question for gynecologic oncologists. *Crit Rev Oncol Hematol.* 2019 Jan;133:92–8. doi:10.1016/j.critrevonc.2018.10.005
15. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Ovarian Cancer [Clinical Practice Guideline] [Internet]. National Comprehensive Cancer Network; 2026 [cited 2026 Apr 8]. Available from: <https://www.nccn.org>
16. Miyasaka A, Nishikawa T, Kozawa E, Yasuda M, Fujiwara K, Hasegawa K. Advanced Mucinous Adenocarcinoma Arising from a Mature Cystic Teratoma: A Case Report and Literature Review. *Case Rep Oncol.* 2016 Jun 27;9(2):331–7. doi:10.1159/000447258
17. Hollis RL, Stillie LJ, Hopkins S, Bartos C, Churchman M, Rye T, et al. Clinicopathological Determinants of Recurrence Risk and Survival in Mucinous Ovarian Carcinoma. *Cancers.* 2021 Nov 21;13(22):5839. doi:10.3390/cancers13225839

Authors

Tanin Zadeh, DO, Department of Pathology, Harbor-UCLA Medical Center, Torrance, CA.
 Komeil Mirzaei Baboli, MD, Department of Pathology, Harbor-UCLA Medical Center, Torrance, CA.
 Sara Salehiazar, MD, Department of Pathology, Yale School of Medicine, New Haven, CT.
 Truc Tran, MD, Department of Pathology, Harbor-UCLA Medical Center, Torrance, CA.

Correspondence

Tanin Zadeh, DO
 Department of Pathology and Laboratory Medicine
 Harbor-UCLA Medical Center
 1000 W Carson St, Torrance, CA, 90502
 424-306-6400
TZadeh@dhs.lacounty.gov

Disclosures

Funding: Not applicable

Conflicts of interest/Competing interests: The authors declare that they have no conflicts of interest relevant to this study.

Ethics approval: Not applicable

Consent to participate: Consented

Written consent for publication: Consented

Factor V Deficiency and Mechanical Valve Replacement: Challenges in Perioperative Hemostasis and Anticoagulation

DANIEL IDOATE DOMENCH, MD; ROBIN REID, MD; DUA AZIM, MD; SYED EHSANULLAH, MD; ADITYA SANJEEVI, MD; ANIKET RAO, MD

ABSTRACT

Factor V deficiency is a rare autosomal recessive bleeding disorder marked by impaired thrombin generation and variable bleeding risk. Perioperative management becomes particularly challenging in high-risk surgeries, such as aortic valve replacement, due to the absence of targeted replacement therapies and the limited efficacy of fresh frozen plasma (FFP) in restoring factor V levels. We report the case of a 30-year-old woman with congenital factor V deficiency (baseline activity 18%) who underwent successful mechanical aortic valve replacement and mitral valve repair for infective endocarditis. She received preoperative FFP aiming for a factor V level >20%. Her perioperative management included careful monitoring with a total of 23 units of FFP administered. Despite persistently low postoperative F levels (<20%), she experienced minimal bleeding complications, limited to transient anemia and one episode of gross hematuria requiring platelet transfusion. Outpatient follow-up revealed heterozygosity for both factor V Leiden and a prekallikrein variant, potentially explaining her relatively mild bleeding phenotype. This case highlights the disconnect that may exist between laboratory values and clinical bleeding risk, emphasizing the need for individualized perioperative planning and cautious anticoagulation management.

KEYWORDS: Factor V deficiency; Factor V levels; Bleeding risk; fresh frozen plasma; aortic valve replacement; perioperative management

INTRODUCTION

Factor V is mainly produced by hepatocytes and stored in platelet alpha granules, where it plays an essential role in facilitating localized thrombin production during hemostasis. It plays a key role in hemostasis and coagulation by combining with activated factor X to form the prothrombinase complex, which converts prothrombin into thrombin.¹ Factor V deficiency is an exceptionally rare autosomal recessive bleeding disorder, affecting roughly one in a million individuals (homozygous form).² It results in prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT) on laboratory testing.³ Patients with activity levels

above 10% are often asymptomatic, levels between 1% and 10% may be associated with mild to moderate bleeding, and levels below 1% are classified as severe (or parahemophilia) with risk of spontaneous hemorrhage.¹ Interestingly, several reports have documented cases in which patients with even severe factor V deficiency did not exhibit significant bleeding.^{4,5} Laboratory values do not always reflect a patient's actual bleeding risk. In surgical contexts, especially those involving high-risk procedures like mechanical valve replacement, management becomes particularly challenging. Balancing the risk of bleeding against the need for effective anticoagulation demands meticulous perioperative planning, individualized treatment strategies, and close interdisciplinary coordination.

CASE PRESENTATION

We present the case of a 30-year-old woman with a self-reported remote history of congenital factor V deficiency and recent cesarean delivery four months ago, who developed worsening heart failure secondary to *Enterococcus faecalis* infective endocarditis (IE) involving the aortic valve (AV). A few months postpartum, she was hospitalized with sepsis and was found to have *Enterococcus* bacteremia. Transesophageal echocardiography (TEE) confirmed AV involvement. She was treated with intravenous (IV) vancomycin and cefepime. Despite appropriate therapy, she re-presented with acute decompensated heart failure and pulmonary edema, prompting further evaluation and management. Of note, the patient reported that her mother told her she was diagnosed with factor V deficiency in childhood, although no prior formal hematologic records are available to confirm this. Interestingly, despite this reported diagnosis, she has no clinically significant bleeding history, including menorrhagia, epistaxis, excessive bleeding with dental procedures, or postpartum hemorrhage.

Repeat imaging revealed severe aortic regurgitation (AR) and moderate mitral regurgitation (MR). Cardiothoracic surgery recommended mechanical AV replacement and mitral valve (MV) repair. Due to her history of factor V deficiency, her bleeding risk was assessed. Her International Society on Thrombosis and Hemostasis (ISTH)-Bleeding Assessment Tool (BAT) score was 0, which suggests no evidence of an increased bleeding tendency based on history. Laboratory

results showed: PT 15.9 seconds (ref 10.2–12.9), INR 1.4 (ref 0.9–1.1), aPTT 38.6 seconds (ref 25.1–36.5), mild anemia with Hb of 10g/dl along with normal fibrinogen and platelet count, and isolated factor V activity of 18.2% (ref 50–180); other coagulation factor levels were normal. Moreover, renal and liver function tests were within normal limits too. Despite abnormal labs, her unremarkable bleeding history suggested low perioperative hemorrhage risk. Accordingly, the patient and team proceeded with mechanical AV replacement for superior durability, accepting lifelong warfarin anticoagulation.

PERIOPERATIVE MANAGEMENT

Preoperative planning included transfusing fresh frozen plasma (FFP) at 15–20 mL/kg to target factor V activity of 20% [6]. For her 90 kg weight, this corresponded to ~1350 mL of FFP. Thus, she received a total of four units of FFP (1275 mL) before surgery. Platelet transfusion was considered due to the platelet-associated factor V pool, but was reserved for active bleeding. Postoperatively, the patient was immediately started on a heparin infusion along with warfarin in the setting of a mechanical AV; the initial INR goal was set at 2.5–3.5 due to prolonged INR at baseline, which was later reduced to 2.0–3.0 prior to discharge. Daily factor V trough levels were monitored; levels remained between 12–19%, with most values consistently above 15%, prompting FFP supplementation as needed. She ultimately received

a total of 23 units of FFP perioperatively, corresponding to a cumulative volume of 7,225 mL.

Despite no intraoperative bleeding, the patient developed postoperative anemia, with hemoglobin decreasing from ~8 g/dL immediately after surgery to a nadir of 6.8 g/dL by postoperative day 4, when she received her first unit of blood. She also had one episode of frank hematuria on post-operative day 7, for which she received one unit of platelets. There was no evidence of valve-induced hemolysis in her blood work or peripheral smear. **Figure 1** and **Table 1** elucidate detailed perioperative factor V activity levels and corresponding transfusion and laboratory data.

Figure 1. Factor V Activity Timeline

The vertical axis shows plasma factor V activity (%), while the horizontal axis denotes hospital day, including surgery and postoperative days (POD 1–11).

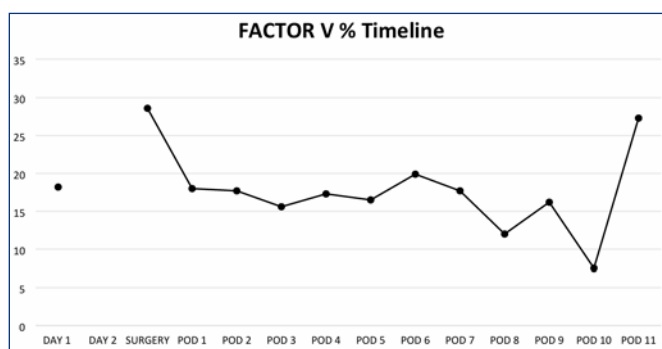


Table 1. Postoperative Hematologic Parameters, Transfusions, and Anticoagulation in a Patient With Factor V Deficiency Undergoing Mechanical Aortic Valve Replacement

	Day 1	Day 2	Surgery	Pod 1	Pod 2	Pod 3	Pod 4	Pod 5	Pod 6	Pod 7	Pod 8	Pod 9	Pod 10	Pod 11
Factor V (%)	18.2		28.6	18	17.7	15.6	17.3	16.5	19.9	17.7	12	16.2	7.5	27.3
FFP Transfused (units)		3	1	2	3	3	3	3	1		2	1	1	
PLT Transfusion (units)											1			
PRBC (units)									1	1	1			
Hb (g/dL)	10.3	10.1	8.3	7.9	8.2	7.2	6.8	6.3	6.2	6.8	6.7	7.3	7.7	8
HCT (%)	34	34	27	26	28	25	23	22	22	23	27	24	25	26
PLT ($\times 10^3/\mu\text{L}$)	416	406	267	241	278	244	237	240	277	257	256	276	302	329
INR	1.4		1.5	1.6	1.7	1.9	2.1	2.2	2.1	2.3	2.4	2.3	2.1	1.9
PT (sec)	15.9		17.5	18.1	20	21.7	24.2	24.9	24.4	26.4	27.5	26.4	24.8	21.8
aPTT (sec)	38.6		35.2	39.8	41.1	57.9	46.9	86.7	80.8	80.4	92.3	98.4	116.2	
Heparin Infusion			Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Enoxaparin (mg, subq)			40											
Warfarin (mg)			3	3	4	4	4	4	5	4	5	5	6	6
Aspirin (mg)			81	81	81	81	81	81	81	81	81	81	81	81

FFP: fresh frozen plasma; PLT: platelet; PRBC: packed red blood cell; Hb: hemoglobin; HTC: hematocrit; INR: international normalized ratio; PT: prothrombin time; PTT: partial thromboplastin time; POD: post-operative day; subq: subcutaneous

OUTPATIENT FOLLOW-UP

Following her hospitalization, the patient was seen in the hematology clinic for further evaluation of her factor V deficiency. Genetic testing confirmed two factor V mutations: one classified as likely pathogenic and the other as a variant of uncertain significance (VUS). Interestingly, she was also heterozygous for factor V Leiden and carried a heterozygous prekallikrein variant, both of which may confer a prothrombotic predisposition. No inhibitors were detected.

Moreover, coagulation studies were obtained to assess the effect of warfarin therapy in the context of underlying factor V deficiency. Vitamin K-dependent factors were variably suppressed: factor II at 48.2% (normal 60–180%), factor VII at 38.3% (65–170%), and factor X at 27.7% (75–150%), while factor IX remained relatively preserved at 73.1% (65–150%). Her INR was elevated at 2.0, consistent with therapeutic anticoagulation. Factor V activity remained low at 21.4%, similar to her prior levels.

These findings highlight the importance of measuring individual factor levels when interpreting INR in patients with baseline coagulation abnormalities, particularly rare bleeding disorders, to avoid misinterpretation of anticoagulation efficacy.

DISCUSSION

Factor V deficiency is a rare bleeding disorder characterized by low levels of factor V. Unlike other coagulation factor deficiencies, there are no concentrated factor V products available. Its rarity combined with the lack of targeted replacement therapies makes management particularly challenging, especially in high-risk surgical settings such as cardiothoracic procedures. Thus, clinicians rely on supportive transfusion strategies, primarily FFP, for management of factor V deficiency.² Additionally, platelets store factor V within their alpha granules, representing a potential supplemental source. However, the role of platelet-derived factor V in major surgeries, such as the one described in this case report, is not well established. Further research is needed to determine whether this could serve as a reliable alternative when plasma alone is inadequate or contraindicated. Recombinant activated factor VII (rFVIIa) has been reported as a bypassing agent in exceptional cases where standard therapy with FFP is contraindicated or has failed, promoting thrombin generation independently of factor V by directly activating factor X; however, its routine use is limited, and evidence is largely anecdotal.^{7,8}

A unique aspect of this case is the requirement for long-term anticoagulation following mechanical valve replacement. Patients with congenital bleeding problems are typically barred from having a mechanical prosthesis due to their increased bleeding risk. With meticulous perioperative management, including FFP supplementation to achieve a factor V activity level of 20%, she successfully tolerated

both major cardiac surgery and therapeutic anticoagulation with heparin and warfarin, experiencing only a single episode of frank hematuria. Daily postoperative monitoring showed factor V activity consistently above 15%, aligning with European Network on Rare Bleeding Disorders (EN-RBD) registry data suggesting patients with activity >10% are often asymptomatic and may not experience spontaneous bleeding.⁹ Thus, our case contributes to a growing body of evidence suggesting that with careful management, warfarin therapy is not contraindicated in patients with factor V deficiency.

Our case also underscores an essential principle that laboratory values alone do not always correlate with clinical bleeding risk. The discrepancy between factor activity and clinical phenotype has been documented previously and supports a patient-specific approach to perioperative planning and anticoagulation.¹⁰ It is unclear whether her relatively mild phenotype was due to her factor V level being slightly above the minimum hemostatic threshold (>15%) or by concurrent pro-thrombotic mutations, such as heterozygous factor V Leiden and prekallikrein variants, that mitigated her bleeding risk.

It is important to note that anticoagulation management in individuals with rare bleeding disorders is inherently complex. Warfarin inhibits vitamin K-dependent factors (II, VII, IX, X), though the degree of suppression is not always uniform. In this patient, all these factors, except IX, were reduced to ≤30% after she was started on warfarin, suggesting therapeutic anticoagulation despite an already prolonged baseline INR. These findings underscore the importance of monitoring individual factor levels, rather than relying solely on INR, to guide safe anticoagulation in patients with baseline coagulation abnormalities.

In conclusion, this case illustrates the complexities involved in managing rare bleeding disorders during high-risk cardiothoracic surgery. Despite persistently low postoperative factor V levels, the patient tolerated mechanical aortic valve replacement and long-term anticoagulation without significant bleeding events. Her clinical stability, even in the face of subtherapeutic factor V activity, emphasizes the importance of individualized management guided by bleeding history and clinical presentation rather than laboratory values alone. The case also reinforces the need for tailored transfusion and anticoagulation strategies and highlights the ongoing need for targeted factor V therapies to improve outcomes in this challenging patient population.

References

1. Stoj KM, Pierro J. Factor V Deficiency. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
2. Asselta R, Peyvandi F. Factor V deficiency. *Semin Thromb Hemost.* 2009;35(4):382-389. doi:10.1055/s-0029-1225760
3. Huang JN, Koerper MA. Factor V deficiency: a concise review. *Haemophilia.* 2008;14(6):1164-1169. doi:10.1111/j.1365-2516.2008.01785.x
4. Choi S, Song M. Successful coronary stenting in a patient with factor V deficiency in the absence of fresh frozen plasma transfusion: Case report. *Medicine (Baltimore).* 2017;96(50):e9274. doi:10.1097/MD.00000000000009274
5. Duckers C, Simioni P, Spiezia L, et al. Low plasma levels of tissue factor pathway inhibitor in patients with congenital factor V deficiency. *Blood.* 2008;112(9):3615-3623. doi:10.1182/blood-2008-06-162453
6. Meidert AS, Kinzinger J, Möhnl P, et al. Perioperative Management of a Patient with Severe Factor V Deficiency Presenting with Chronic Subdural Hematoma: A Clinical Report. *World Neurosurg.* 2019;127:409-413. doi:10.1016/j.wneu.2019.04.080
7. Ardillon L, Lefrançois A, Graveleau J, et al. Management of bleeding in severe factor V deficiency with a factor V inhibitor. *Vox Sang.* 2014;107(1):97-99. doi:10.1111/vox.12134
8. González-Boullosa R, Ocampo-Martínez R, Alarcón-Martín MJ, Suárez-Rodríguez M, Domínguez-Viguera L, González-Fajo G. The use of activated recombinant coagulation factor VII during haemarthroses and synovectomy in a patient with congenital severe factor V deficiency. *Haemophilia.* 2005;11(2):167-170. doi:10.1111/j.1365-2516.2005.00956.x
9. Peyvandi F, Palla R, Menegatti M, et al. Coagulation factor activity and clinical bleeding severity in rare bleeding disorders: results from the European Network of Rare Bleeding Disorders. *J Thromb Haemost.* 2012;10(4):615-621. doi:10.1111/j.1538-7836.2012.04653.x
10. Barg AA, Livnat T, Kenet G. Factor XI deficiency: phenotypic age-related considerations and clinical approach towards bleeding risk assessment. *Blood.* 2024;143(15):1455-1464. doi:10.1182/blood.2023020721

Authors

Daniel Idoate Domench, MD, Department of Internal Medicine, Rochester General Hospital, Rochester, NY.
 Robin Reid, MD, Department of Hematology and Oncology, Rochester General Hospital, Rochester, NY.
 Dua Azim, MD, Department of Internal Medicine, Rochester General Hospital, Rochester, NY.
 Syed Ehsanullah, MD, Department of Hematology and Oncology, Rochester General Hospital, Rochester, NY.
 Aditya Sanjeevi, MD, Department of Internal Medicine, Rochester General Hospital, Rochester, NY.
 Aniket Rao, MD, Department of Internal Medicine, Rochester General Hospital, Rochester, NY.

Disclosures

Conflict of Interest: The authors declare no conflicts of interest related to this manuscript.

Ethics Approval: This case report was prepared in accordance with institutional policies. Institutional review board approval was not required for single patient case reports.

Patient Consent: Informed consent was obtained from the patient for publication of this case report.

Acknowledgments: The authors acknowledge the use of AI-assisted language tools for grammar and style corrections in the preparation of this manuscript.

Data Availability: Data sharing is not applicable to this article as no new datasets were generated or analyzed during this study.

Funding: The authors received no specific funding for this work.

Correspondence

Dua Azim, MD
 120 Buell Dr. Apt B, Rochester NY, 14621
 duaazeem456@gmail.com

Atypical Bullous Sweet Syndrome

JONATHAN LONDON, MD; JOHN PATRESAN, MD; ALEXANDER BELKIN, MD; RADOWAN ELNAIR, MD

ABSTRACT

Sweet syndrome (acute febrile neutrophilic dermatosis) is characterized by fever, leukocytosis, and tender erythematous skin lesions with neutrophilic infiltrate. Although associated with granulocyte colony-stimulating factor (G-CSF) use, its occurrence with pegfilgrastim—the pegylated form—is rare, with fewer than five reported cases. Sweet syndrome has also been rarely linked to FLT3 inhibitors such as quizartinib. We report a 71-year-old male with acute myeloid leukemia who developed bullous Sweet syndrome following concurrent exposure to pegfilgrastim and quizartinib.

KEYWORDS: Atypical Sweet Syndrome; Pegfilgrastim; Quizartinib

INTRODUCTION

Sweet syndrome (SS) is a rare disorder characterized by tender erythematous nodules or plaques, fever, arthralgia, and systemic symptoms, diagnosed by clinical presentation and histological evidence of neutrophilic infiltrate on skin biopsy.¹ It is most commonly idiopathic, but is also associated with myeloproliferative disorders, autoimmune diseases, infections, and medications, including G-CSF, antihypertensives, antibiotics, antipsychotics, and NSAIDs.¹ Pegfilgrastim-associated SS has been reported in fewer than five cases,² and FLT3 inhibitors such as quizartinib have been implicated in rare cases as well.³ We report a 71-year-old male with acute myeloid leukemia (AML) who developed atypical bullous SS after receiving both pegfilgrastim and quizartinib.

CASE PRESENTATION

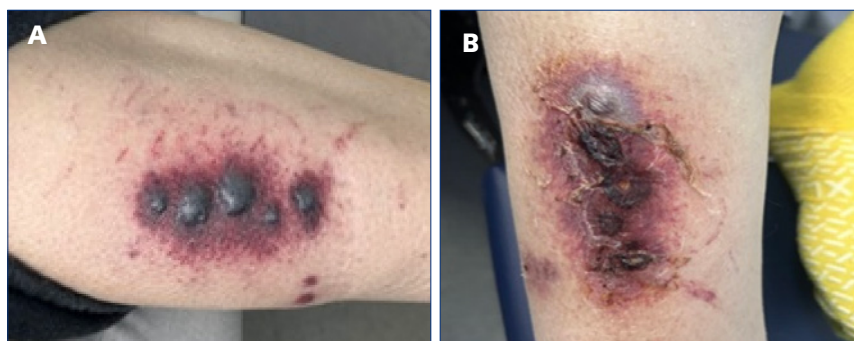
A 71-year-old male with a history of stage III sigmoid adenocarcinoma (treated with colectomy and 12 cycles of adjuvant chemotherapy) was diagnosed 13 months later with AML. Next-generation sequencing was positive for FLT3-ITD, IDH2, NPM1, and SRSF2. He received 7+3 induction with cytarabine and daunorubicin, followed by high-dose cytarabine consolidation with

intrathecal methotrexate and quizartinib 35.4 mg daily. On day 4 of consolidation, he received pegfilgrastim 6 mg subcutaneously without immediate adverse effects. Notably, he had previously tolerated 10 doses of pegfilgrastim during adjuvant chemotherapy for his colon cancer without incident. Six days after pegfilgrastim and four days after starting quizartinib, he presented following a fall and was found to have a blistering rash of several days' duration. He was otherwise asymptomatic. Vital signs showed a low-grade fever of 99.7°, blood pressure 137/98 mmHg, heart rate 110 bpm, and respiratory rate 16/min with normal oxygen saturation. Examination revealed purple-red erythematous necrotic lesions on the left ear, right shin, right dorsum of the hand, chest, and abdomen [Figure 1A]. Labs were notable for WBC $0.1 \times 10^3/\mu\text{L}$, Hgb 9.3 g/dL, and platelets $6 \times 10^3/\mu\text{L}$; the comprehensive metabolic panel was unremarkable. Skin biopsy from the right hand demonstrated papillary dermal edema with superficial lymphohistiocytic inflammation and scattered neutrophils, consistent with resolving SS. A prednisone taper was initiated at 50 mg daily, reduced by 10 mg every three days, with subsequent clinical improvement [Figure 1B].

DISCUSSION

Sweet syndrome, also known as acute febrile neutrophilic dermatosis, is a rare inflammatory disorder characterized by fever, neutrophilic leukocytosis, and painful erythematous plaques or nodules typically on the face, neck, and upper

Figure 1. [A] Initial examination revealed purple-red erythematous necrotic lesions on the left ear, right shin, right dorsum of the hand, chest, and abdomen. [B] Examination following the initiation of prednisone taper significantly improved the rash.



extremities.^{1,4} It is most commonly idiopathic, but may be secondary to infections, malignancies, autoimmune diseases, and drugs, including G-CSF, FLT3 inhibitors, antihypertensives, antibiotics, antipsychotics, and NSAIDs.^{1,5} Drug-induced SS typically presents abruptly within days to weeks of exposure. Sweet syndrome predominates in women (4:1), and most commonly occurs between ages 30 and 60.¹

The pathophysiology of SS remains incompletely understood; proposed mechanisms include hypersensitivity to infectious or tumor antigens leading to neutrophil activation, and cytokine dysregulation.^{1,5} Diagnosis requires histopathologic confirmation. Classic findings include dense neutrophilic infiltrate in the reticular dermis, with papillary dermal edema, leukocytoclastic nuclear debris, swollen endothelial cells, and dilated vessels also frequently present.^{1,5}

Clinically, SS presents with tender skin lesions—appearing red or purple-red as papules, nodules, or plaques—typically on the upper extremities, face, and neck, accompanied by fever (which may be absent), and constitutional symptoms, including myalgia, arthralgia, headache, and malaise.^{1,4,5} Recognized clinical variants include bullous, cellulitis-like, and necrotizing SS.⁶ Bullous SS, which may present with tense or flaccid blisters, is uncommon with unknown incidence⁶—the presentation seen in our patient.

Management of drug-induced SS involves discontinuation of the offending agent and systemic corticosteroids, the mainstay of treatment.¹ A 2-4 week prednisone taper starting at 40-60 mg daily is typically effective; dapsone, doxycycline, colchicine, methotrexate, and cyclosporine are alternatives for refractory or relapsing cases.¹

G-CSF agents are widely used to mitigate chemotherapy-induced neutropenia. Pegfilgrastim, the pegylated form of filgrastim, offers the convenience of a single dose per cycle due to its prolonged half-life. While filgrastim-associated SS is relatively well documented, pegfilgrastim-induced SS has been reported in fewer than five cases.^{2,7} Our patient was also initiated on quizartinib, a FLT3 inhibitor, four days prior to presentation. Fewer than 10 cases of FLT3 inhibitor-induced SS have been reported in the literature.³

The temporal proximity of both agents—pegfilgrastim administered six days before admission and quizartinib initiated four days prior—makes it difficult to attribute causality to either drug alone. A synergistic effect cannot be excluded. The bullous morphology further distinguished this from a typical SS presentation.

CONCLUSION

We report a rare case of bullous SS likely triggered by pegfilgrastim and/or quizartinib in a patient with AML, highlighting the importance of clinical vigilance for this adverse effect in patients receiving these agents. Further research is warranted to investigate whether concurrent use of multiple SS-triggering agents confers a synergistic risk.

References

1. Vashisht P, Goyal A, Hearth Holmes MP. Sweet Syndrome. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; September 12, 2022.
2. Clarey D, DiMaio D, Trowbridge R. Deep Sweet Syndrome Secondary to Pegfilgrastim. *J Drugs Dermatol*. 2022;21(4):422-424. doi:10.36849/JDD.4794
3. Yang L, Zhang R, Ma H. Sweet syndrome induced by FLT3 inhibitors: case report and literature review. *Hematology*. 2024;29(1):2337230. doi:10.1080/16078454.2024.2337230
4. Rochet NM, Chavan RN, Cappel MA, Wada DA, Gibson LE. Sweet syndrome: clinical presentation, associations, and response to treatment in 77 patients. *J Am Acad Dermatol*. 2013; 69(4):557-564. doi:10.1016/j.jaad.2013.06.023
5. Cohen PR. Sweet's syndrome—a comprehensive review of an acute febrile neutrophilic dermatosis. *Orphanet J Rare Dis*. 2007;2:34. Published 2007 Jul 26. doi:10.1186/1750-1172-2-34
6. Joshi TP, Friske SK, Hsiou DA, Duvic M. New Practical Aspects of Sweet Syndrome. *Am J Clin Dermatol*. 2022;23(3):301-318. doi:10.1007/s40257-022-00673-4
7. White JM, Mufti GJ, Salisbury JR, du Vivier AW. Cutaneous manifestations of granulocyte colony-stimulating factor. *Clin Exp Dermatol*. 2006;31(2):206-207. doi:10.1111/j.1365-2230.2005.01996.x

Authors

Jonathan London, MD, Department of Hematology/Oncology, Roger Williams Medical Center, Providence, Rhode Island.
 John Patresan, MD, Department of Hematology/Oncology, Roger Williams Medical Center, Providence, Rhode Island.
 Alexander Belkin, MD, Department of Hematology/Oncology, Roger Williams Medical Center, Providence, Rhode Island.
 Radowan Elnair, MD, Department of Bone Marrow Transplantation and Cellular Therapy, Roger Williams Medical Center, Providence, Rhode Island.

Disclosures

The authors have no disclosures.

Correspondence

Jonathan London, MD
 Roger Williams Medical Center
 825 Chalkstone Ave, Providence, RI 02908
 631-624-3438
Jonathan.London@chartercare.org

FREE TO FOCUS ON KARLY.



With healthcare's constant complexities and distractions, it can be difficult to focus on patients. We can help, with proven medical professional liability insurance and so much more. So you are free to focus on delivering superior patient care.

- Medical Professional Liability Insurance
- Claims Analytics
- Risk Mitigation
- Medicare Contractual Risk Protection
- And more

coverys.com 800.225.6168

COVERYS



FREE TO FOCUSSM

Decreasing Ghost Scanning in Point-of-Care Ultrasound: Impact of a Visual Prompt to Save Images

ROBERT BRADSHAW, MD; CURTIS XU, MD; DAVID CANNATA, MD; TRENT SHE, MD; ZACHARY BOIVIN, MD

ABSTRACT

BACKGROUND: Ghost scanning, performance of point-of-care ultrasound without image archival, can adversely affect patient care, billing, quality assurance, and result in medicolegal concerns. This study evaluated the Extended Focused Assessment with Sonography in Trauma (eFAST) ghost-scanning rate during trauma activations after placement of a low-cost visual reminder.

METHODS: This single-center study was conducted from December 1, 2022 to November 30, 2023. Patients were included if they were the highest level of emergency department trauma activation. A ghost scan was classified as a documented eFAST examination in the electronic medical record nursing documentation without archived eFAST images in the picture-archiving and communication system. Six months of EMR review established a baseline ghost-scanning rate. Subsequently, a large label reminding clinicians to save images was placed prominently on the ultrasound machines for a six-month period with prospective chart review. The primary outcome was the absolute and relative difference in ghost-scanning rates after the label intervention. Differences between periods were analyzed using a two-tailed Mann–Whitney U test.

RESULTS: A total of 325 trauma encounters were included. In the pre-intervention period, 66 eFAST examinations were identified among 143 encounters, of which 74.2% (49) were ghost scans. In the post-intervention period, 86 eFAST examinations were identified among 182 encounters, of which 54.7% (47) were ghost scans, representing a 19.5% absolute reduction ($p = 0.013$).

CONCLUSION: The low-cost visual reminder was associated with a meaningful reduction in ghost scanning during eFAST examinations. Further investigation into similar interventions and their generalizability to other institutions is warranted.

KEYWORDS: POCUS; phantom scanning; ghost scanning; ultrasound; trauma

BACKGROUND

Ghost scanning, when a point-of-care ultrasound (POCUS) is performed without images being archived, is a known problem in emergency medicine and has patient care, billing, quality improvement and quality assurance (QA/QI) and medicolegal implications.¹⁻⁵ Guidelines from the Centers for Medicare and Medicaid, the American Institute of Ultrasound in Medicine, as well as the American College of Emergency Physicians recommend that all POCUS examinations should include a representative image saved with clinically relevant anatomy and pathology.^{6,7}

The highest level of trauma activations at a hospital often includes unstable patients, and the POCUS operator may prioritize other tasks over image archival.⁸ POCUS workflow may also be a barrier to saving images, as patients may not be registered or be registered under a temporary identification in the electronic medical record (EMR). Physicians may use POCUS to make immediate clinical decisions in trauma resuscitations, such as a positive Extended Focused Assessment with Sonography in Trauma (eFAST), resulting in prompt transfer to the operating room, without recognizing the benefit of saving images. Institutional culture may also prevent images from being saved if there is a lack of understanding about the dangers of ghost scanning, if images are not archived, or if POCUS examinations are not billed, resulting in a high rate of ghost scanning.

Some strategies to reduce the incidence of ghost scanning include locked ultrasound machines, personalized email reminders, implementation of barcode scanners, and didactic teaching about the value of saving images. These strategies are often time-consuming for ultrasound faculty, increase costs, and fail to reach a broad audience. One strategy that the authors propose as an effective reminder is a non-obstructive visual cue to save an image while performing a POCUS, offering a low-cost investment with minimal time investment. However, the magnitude of the effect is unclear. Therefore, our study aim was to assess the change in ghost-scanning rates when a label was placed on the ultrasound machine reminding the operator to save images as part of an emergency department (ED) QA/QI project for eFAST examinations. Trauma activations were chosen due to the ease of which they can be tracked in the EMR, the nursing documentation that occurs, and the previously seen high rates of ghost scanning.^{3,4}

METHODS

Study Design

This was a single-center, prospective QA/QI project that took place between December 1, 2022 and November 30, 2023. Patients were included if they were at least 18 years of age, arrived as the highest level of trauma activation, and had a POCUS documented by a nurse in the resuscitation run sheet within the EMR. Patients were excluded if there was insufficient EMR data, if their trauma designation was downgraded, if the trauma was without injury to the chest or torso, or if the mechanism of trauma was a burn. Institutional Review Board approval was obtained at the study institution.

A trauma resuscitation was defined as a patient with a life-threatening traumatic injury or meeting specific trauma criteria defined by the institution.⁴ An ED nurse trained in critical care was responsible for real-time EMR documentation of trauma resuscitation events, including the performance of an eFAST examination. This run sheet documentation was found to be accurate in prior studies with a similar methodology and served as an indicator for eFAST performance during the trauma resuscitation.^{3,4}

The time from December 1, 2022 to May 31, 2023 served as a baseline for ghost scanning. A previous study at the institution showed a ghost-scanning rate of 86.5% for eFAST examinations from July 1, 2019 to July 1, 2021.⁴ Because this previous data was presented at the study institution, it was important to establish a new baseline to accurately assess the benefit of the visual reminder to save images. Starting June 1, 2023 through November 30, 2023, a label reading, "Please save all ultrasound clips even if not ordered," was placed prominently on the screen of the Sonosite LX (FUJIFILM Sonosite, Inc., Bothell, WA) ultrasound machine [Figure 1] that is dedicated to the department's critical care area where trauma resuscitations are managed. This visual

reminder was placed without informing the emergency medicine or trauma teams, and only the study team was aware ghost scanning was being evaluated for a QA/QI project.

Setting

The study was performed at a Level 1 trauma center with over 115,000 annual patient visits and an active ED POCUS program with approximately 7,500 POCUS examinations performed annually and global ultrasound privileging for attendings.⁹ The ED is staffed by approximately 60 emergency medicine attendings and has a three-year emergency medicine residency program with 54 residents. ED residents participate in 16 hours of dedicated ultrasound training during their first month, at least four weeks of dedicated POCUS training by the end of their second year, and are required to perform a minimum of 500 POCUS examinations, with 50 of them being eFAST examinations prior to graduation. The hospital uses an order-based POCUS workflow, with the intended workflow requiring an order to first be placed in the EMR prior to starting a POCUS examination, selection of the correct patient on the ultrasound machines, and for the images to be saved by the operator. Saved images upload to the picture archival and communication system (PACS) with interpretation occurring in the EMR; there is no POCUS manager or middleware system. There is an option to save images without a patient identification on the ultrasound machine where the images are uploaded to the PACS under a temporary identification, and remain searchable by both time and date. These anonymous images can later be linked with a patient's chart, but only remain available for viewing on PACS and not the EMR itself.

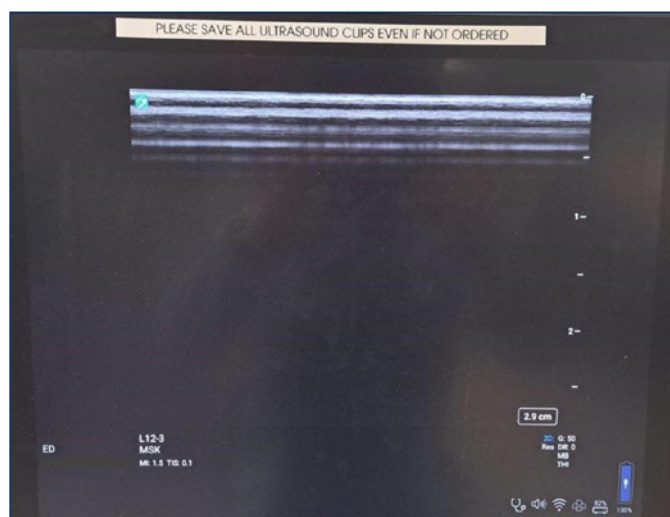
Trauma resuscitations at the study institution are managed in a six-bed critical care area staffed by a care team, including an attending emergency medicine physician and a resident, fellow, or both. For the highest level of trauma responses, the trauma surgery team and trauma surgery attending are present throughout the duration of the patient's initial care.

All ED attendings are globally credentialed to perform POCUS and receive training in POCUS as a condition for their board certification. Quality assurance of 10% of POCUS examinations was performed by clinical ultrasound fellowship trained faculty members. Although the ED nurse practitioners and physician assistants as well as the trauma service may also perform eFAST examinations, there was no formal credentialing guidelines in place for these personnel in our ED at the time of the study. The ED care team is primarily responsible for the eFAST performance and saving of images.

Chart Review

Trauma resuscitations were identified utilizing a pre-existing trauma registry in the EMR documenting all trauma team activations. Manual chart review and abstraction was

Figure 1. Visual prompt placed on an ultrasound machine



completed by three investigators (RB, CX, DC) unblinded to the research question, and a fourth investigator (TS) randomly selected 10% of cases to review for accuracy. A one-hour meeting was held for all investigators to develop a consistent review process for all EMR variables.

A ghost scan was defined as an eFAST examination, identified based on the EMR nursing run sheet, with no associated images saved to the PACS. If an eFAST was performed during the patient encounter, study investigators (RB, CX, DC) reviewed the PACS during the date and time of the patient visit to evaluate for any saved images attributable to the patient. If there were no images associated with the patient, investigators reviewed the PACS for eFAST studies that took place within 30 minutes of the eFAST time documented within the EMR. This iterative search was established so that any images obtained prior to patient registration were accounted for.

Outcomes

The primary study outcome was the absolute and relative difference in ghost-scanning rates from the initial six-month phase to the subsequent six-month phase, when a visual reminder was added to the ultrasound machine.

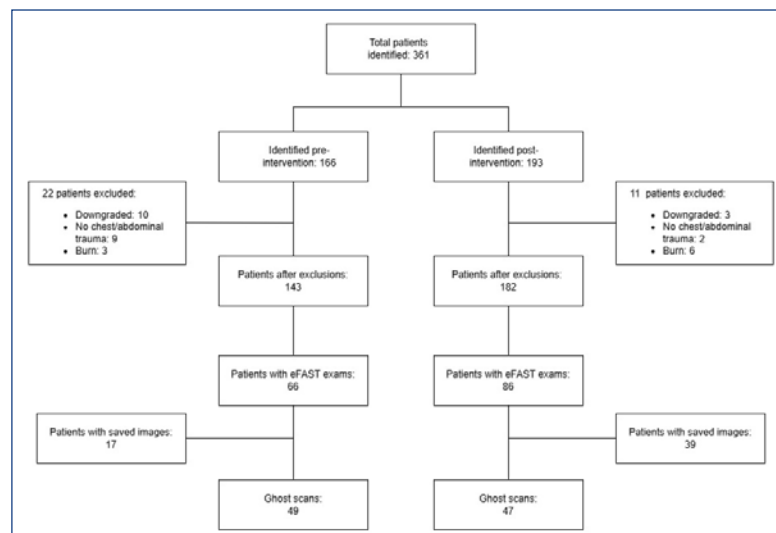
Data Analysis

The prevalence of ghost scanning was calculated in Microsoft Excel (Redmond, WA). Tests of normality on the data was performed using a Shapiro-Wilk test, and a two-tailed Mann-Whitney *U* test was performed to assess for differences in pre-intervention and post-intervention variables. Alpha <0.05 was used to determine statistical significance. This additional testing was conducted with IBM SPSS Version 27 (Armonk, NY).

RESULTS

There were 166 trauma activations in the pre-intervention period and 193 in the post-intervention period for a total of 359 patients reviewed. A total of 23 patients were excluded from the pre-intervention period, 10 due to being downgraded from a full trauma activation, 9 were determined to have an isolated head injury without associated thoracic or abdominal trauma, and 4 with a burn as their primary injury. During the post-intervention period, 11 patients were excluded, 3 due to downgrade, 2 with isolated head injuries without associated thoracic or abdominal trauma, and 6 with burns as their primary injury [Figure 2]. After exclusions, the pre- and post-intervention periods had 143 and 182 patients respectively, for a total of 325 patients. The total cohort included 229 (70.5%) male patients with an average age of 45.1 (SD 21.2). Demographically, the cohort was 52%

Figure 2. Flowchart of patients included for analysis



(172) Caucasian, 17.8% (58) African American, 19.7% (64) Hispanic, and 9.5% (31) other/unknown race.

Of the 143 patients in the pre-intervention period, 66 (46.2%) eFAST examinations were performed based on nursing run sheet review, with 49 (74.2%) identified as ghost scans due to lack of identified images within PACS. In the post-intervention period, a total of 86 (47.3%) documented eFAST examinations were identified from the 182 trauma activations, with 47 (54.7%) labeled as ghost scans. This represents an absolute reduction of 19.5%, and a relative reduction of 26.3%, of ghost eFAST examinations following the label intervention, which was statistically significant ($p = 0.013$). There was no statistically significant difference in the percentage of eFAST examinations performed post-intervention compared to pre-intervention ($p = 0.84$). There was also a similar number of positive eFAST examinations in the pre-intervention period ($n = 17$, 25.8%) compared to the post-intervention ($n = 22$, 25.6%) ($p = 0.98$).

DISCUSSION

Ghost scanning remains a significant barrier to patient care, medical billing, quality improvement and quality assurance, and poses a potential medicolegal risk.^{2,3} However, there is limited research on strategies to mitigate ghost scanning. The optimal strategy to reduce the prevalence of ghost scanning remains unclear and will likely require a broad, multi-step approach to address the numerous barriers to saving ultrasound examinations.^{10,11} The goal of this label intervention was to place a visual prompt within view of the POCUS operator, who may be more likely to archive images or prompt questioning about the image archival processes if they were unfamiliar. In this single-centered study, nearly 75% of eFAST examinations performed during the highest

level of trauma activations were ghost scans prior to the intervention, with the number dropping to approximately 55% following the intervention. The absolute reduction of approximately 20% is notable given that the intervention was low cost and easy to implement, resulting in continuation of the label intervention.

There have been limited studies evaluating strategies to reduce ghost scanning. A study by Kolbenson et al demonstrated a reduction in ghost scanning from 100% (no images archived) to 30% through implementation of a POCUS curriculum and resources for internal medicine residents.¹⁰ While our intervention saw less of an absolute reduction, it did not require ultrasound faculty oversight, email reminders, curriculum implementation, or other time intensive interventions. Additionally, given the high number of trauma activations per year, a 20% decrease in the ghost-scanning rate has the potential to impact many patients.

Our single-center study supports that simple, low-cost interventions may offer an affordable means of reducing the rate of ghost scans during high-acuity patient encounters. This intervention is likely to have variable results at different institutions; however, as the causes of ghost scanning are multifactorial and can result from differences in POCUS workflow, ED staffing, patient volumes, operator experience, and average patient acuity.^{3,11} Despite this, our intervention offers an essentially zero-cost investment with little to no perceivable risk to the patient, institution, or POCUS operator. This sticker intervention serves as a first step towards reducing ghost scanning, as part of a multi-step process, including improvements in overall infrastructure, POCUS machine technology, and programs designed to target POCUS operators who do not archive images. However, these strategies require a significant investment in faculty time and warrant further investigation to determine the extent of their impact and optimal implementation. Given the low cost and low-risk nature of our label intervention, and its substantial improvement in ghost-scanning rates, we suggest this be trialed at other institutions as a component of larger ghost-scanning interventions to assess its effectiveness to decrease ghost scanning across institutions.

One study drawback was that we cannot rule out the influence of the Hawthorne Effect on our study results, despite our efforts to reduce its effect. The previous study at our institution showing a high ghost-scanning rate was publicized to the hospital's ED and trauma team, which may have played a role in improving our ghost-scanning rate even after accounting for our study's washout period. If the emergency medicine or trauma teams were aware of our study taking place, it may have influenced their likelihood of saving images. There were no additional email reminders or educational sessions about eFAST image archival that took place during the study period. To our knowledge, the only individuals aware of this study taking place were the study team members; however, the study members were part of

the pool of potential providers that may have cared for these trauma patients.

There are several other limitations to this study that warrant mention. The retrospective EMR review is a proxy for eFAST performance, as direct video review was unavailable at our institution. There is a chance that eFAST images were saved and were not identified during review due either to incorrect archiving or POCUS machine upload failures, leading to an overestimation of ghost scanning. However, it would be expected that this effect would be equal before and after our intervention, as there were no major changes to the EMR review, image archival processes, or machine hardware. This study took place at a single institution with its own unique barriers to image acquisition and workflow practice patterns that may not be present at other institutions and limits the generalizability of this study. This study was not designed to evaluate the specific traumatic injuries suffered by patients and their clinical outcomes, which could have affected the prevalence of ghost scanning, as higher acuity patients may result in increased ghost scanning. We attempted to mitigate this limitation by selecting only patients with the highest level of trauma activation, and our results showed no difference in positive eFAST examinations between the pre- and post-intervention groups. Alternatively, there may have been a difference in ghost-scanning rates for positive and negative eFAST examinations, but the study was underpowered to detect any differences. The seasonality of trauma may have served as a confounder, as it is possible that certain injury or trauma patterns were more heavily represented in one of the intervention periods, influencing ghost-scan rates.

CONCLUSION

Prior to our intervention, ghost scans accounted for nearly three-quarters of eFAST exams taking place during the highest level of trauma activations at our institution. Our label-based intervention demonstrated a 19.5% absolute reduction and a 26.3% relative reduction in ghost scanning, showing promise as a low-cost intervention in reducing rates of ghost scanning. The post-intervention ghost-scanning rate of 54.7% suggests a need for further ghost scanning interventions. The label-based intervention is one part of a multi-step approach to decrease ghost scanning, and the generalizability of this intervention to other institutions and workflow structures warrants further investigation.

References

1. Hughes D, Corrado MM, Mynatt I, et al. Billing I-AIM: a novel framework for ultrasound billing. *The ultrasound journal*. 2020;12:8.
2. Lewiss R. "The Ultrasound Looked Fine": Point-of-Care Ultrasound and Patient Safety. *PSNet [internet]*. 2018.
3. Boivin Z, Dwyer KH, Pare JR, et al. Prevalence of ghost scans in point-of-care ultrasound for trauma patients: A multicenter study. *The American journal of emergency medicine*. 2025.
4. Boivin Z, Xu C, Doko D, Herbst MK, She T. Prevalence of Phantom Scanning in Cardiac Arrest and Trauma Resuscitations: The Scary Truth. *Pocus j*. 2023;8:217-222.
5. Ma IWY, Francavilla ML, Nomura JT, et al. Governance Considerations for Point-of-Care Ultrasound: a HIMSS-SIIM Enterprise Imaging Community Whitepaper in Collaboration with AIUM. *J Imaging Inform Med*. 2025.
6. McKenzie D. Ultrasound Reimbursement FAQ. ACEP 2022.
7. Ultrasound Guidelines: Emergency, Point-of-Care, and Clinical Ultrasound Guidelines in Medicine. *Ann. Emerg. Med*. 2023; 82:e115-e155.
8. Westein R, Nickel L, Phelan MB. Phantom Scanning in Point-of-Care Ultrasound after Out-of-Hospital Cardiac Arrest: Impact of Clinical Presentation in a Single-Center Analysis. *J Emerg Med*. 2025.
9. Boivin Z, Venkatesh AK, Moore CL. Variation in point-of-care ultrasound privileges in academic emergency departments. *Academic Emergency Medicine*. 2025.
10. Kolbenson L, Salman T, Oro A, Olszynski P. Seeing Ghosts: A Quality Improvement Intervention to Decrease Phantom Scanning Through Increased Image Archiving of POCUS by Internal Medicine Residents. *Pocus j*. 2025;10:11-18.
11. Piro KM, Carney PA, Smith CJ. Just In Time! Assessment of Internal Medicine Resident Point of Care Ultrasound (POCUS) Attitudes and Behaviors After Spaced Intervention at Two Residency Programs. *Pocus j*. 2024;9:93-101.

Authors

- Robert Bradshaw, MD, Advanced Emergency Ultrasound Fellow, Department of Emergency Medicine, Boston Medical Center, Boston, MA.
- Curtis Xu, MD, Instructor of Emergency Medicine, Department of Emergency Medicine, Yale School of Medicine, New Haven, CT.
- David Cannata, MD, Emergency Medicine Resident, Department of Emergency Medicine, University of Vermont, Burlington, VT.
- Trent She, MD, Assistant Professor of Emergency Medicine, Department of Emergency Medicine, Hartford Hospital, Hartford, CT.
- Zachary Boivin, MD, Assistant Professor of Emergency Medicine, Department of Emergency Medicine, Yale School of Medicine, New Haven, CT.

Disclosures

Statement of Funding: No funding was received for this study from any sources.

Conflicts of Interest: None of the authors have any conflict of interests to disclose.

Data-sharing Statement: Not applicable

Ethical Approval: Ethical approval to report this submission was obtained from the Hartford Hospital Institutional Review Board.

Correspondence

Zachary Boivin, MD
464 Congress Avenue #260
New Haven, CT, 06519
603-913-3558
Zboivin.md@gmail.com

Evaluating the Reliability, Accuracy, and Readability of ChatGPT-3.5 and GPT-4 in Providing Patient Education Related to Glenohumeral Joint Osteoarthritis

MOHAMAD Y. FARES, MD; TARISHI PARMAR, BSc; PETER BOUFADEL, MD; MOHAMMAD DAHER, MD; JONATHAN BERG, BSc; ADAM Z. KHAN, MD; BRIAN W. HILL, MD; JOHN G. HORNEFF, MD; JOSEPH A. ABBOD, MD

ABSTRACT

OBJECTIVES: Chatbots have been increasingly recognized as modern tools that provide patients with reliable health-related information. This study aimed to evaluate and compare ChatGPT-3.5 and GPT-4's ability to answer glenohumeral osteoarthritis-related questions.

METHODS: Fifteen questions were derived from the 2020 AAOS Clinical Practice Guidelines for the Surgical Management of Glenohumeral Joint Osteoarthritis. Questions were categorized into three groups: risk factors, implant/intraoperative considerations, and pain/functional outcomes. ChatGPT-3.5 and GPT-4 were prompted with these questions, and responses were evaluated by four fellowship-trained shoulder and elbow surgeons. Each response was rated on a scale (scores:1-5) based on relevance, accuracy, clarity, completeness, and evidence-based support. Data was analyzed descriptively and statistically to compare the scores between ChatGPT-3.5 and GPT-4.

RESULTS: Average score for ChatGPT-3.5 was 19.7/25, with "Risk Factor" prompts achieving the highest mean score. GPT-4 averaged 18.7/25, with "Functional Outcomes" prompts scoring highest. However, there were no statistically significant differences between different prompt themes for GPT-3.5 and GPT-4. "Clarity" category received the highest score for GPT-3.5, while "Relevance" was highest for GPT-4. Both models scored lowest on "Evidence-based" prompts. On the Flesch-Kincaid scale, GPT-3.5 responses had a significantly higher score of 18.3 compared to GPT-4's 15.4, indicating a more difficult reading level in GPT-3.5's responses.

CONCLUSION: Both ChatGPT-3.5 and GPT-4 performed adequately in providing well-informed medical responses to patient queries about glenohumeral osteoarthritis. Future chatbot versions should focus on providing evidence-based content through systematic and reliable reviews of literature, in an accessible readable manner.

KEYWORDS: artificial intelligence; chatbot; patients; health information; Flesch-Kincaid

INTRODUCTION

One of the oldest goals of computer science: "to create a machine that imitates intelligent human behavior" is the definition of modern-day artificial intelligence (AI).^{1,2} Among the spectrum of generative AI models, ChatGPT has emerged as a revelation, owing to its sophisticated capabilities in handling intricately demanding tasks. Developed by OpenAI (San Francisco, California), ChatGPT has a multitude of uses, including promoting teaching and learning.³ On March 14, 2023, OpenAI also launched GPT-4, the latest version of ChatGPT: a multimodal model that accepts both images and text as input, thus furthering its usage.⁴ As expected, the benefits of ChatGPT do not come without the shortcomings. The potential drawbacks of ChatGPT, such as fabricated references, biased training data, outdated knowledge, factual inaccuracies, and inconsistency in quality, raise crucial concerns about its effectiveness in answering questions.^{5,6}

From providing medical facts to patients,⁷ to providing answers and explanations for examination questions to medical students,⁸ to helping doctors make diagnoses,⁹ ChatGPT is being increasingly used in the field of medicine. However, considering the limitations of ChatGPT, its use in healthcare has been a topic of skepticism.⁷⁻⁹ Consequently, numerous research projects have been undertaken to assess ChatGPT's reliability, efficiency, and accuracy in medical contexts.¹⁰⁻¹⁵ Studies assessing ChatGPT's capacity to address medical school-level questions have found it capable of answering at a level comparable to a third-year medical student.¹¹ Further ChatGPT's expertise has been put to test by researchers around the world in a range of medical subspecialties like plastic surgery,¹² ophthalmology,^{16,17} obstetrics/gynecology,¹⁸ neurosurgery,^{19,20} orthopedic surgery and others.^{13-15,21,22} Studies have yielded mixed and variable results highlighting the need for niche, subspecialty and topic specific evaluation of ChatGPT's skills.

Although research has examined ChatGPT's efficacy in responding to orthopedic questions,^{14,15,23-26} there has been limited attention directed specifically towards questions related to shoulder and elbow orthopedics. Furthermore, a majority of these evaluations have focused on inquiries typical of medical students or healthcare professionals, overlooking questions from the patient's viewpoint. Despite an exhaustive literature review, no studies have been identified

that investigate ChatGPT's responses to inquiries patients might pose about glenohumeral osteoarthritis or total shoulder arthroplasty (TSA) procedure. With an anticipated surge in shoulder arthroplasty procedures to approximately 350,558 in 2025, and the growing reliance of patients on ChatGPT for medical advice,²⁷ it is crucial to assess ChatGPT's capability to accurately and consistently address patient queries concerning the TSA procedure. Therefore, the purpose of this study was to evaluate and compare ChatGPT-3.5 and GPT-4's ability to answer questions adopted from the 2020 American Academy of Orthopaedic Surgeons (AAOS) Clinical Practice Guidelines for the Surgical Management of Glenohumeral Joint Osteoarthritis.²⁸

METHODS

The methodology was adopted, in part, from a similar study assessing ChatGPT's ability to answer orthopedic-related questions.¹⁴ The questions were derived from the 2020 AAOS Clinical Practice guidelines for the Surgical Management of Glenohumeral Joint Osteoarthritis.²⁸ Fifteen of the 22 reviewed recommendations were reformulated by

MYF and TP into question formats reflecting a patient's viewpoint, i.e., framed as patient-posed inquiries while preserving the original clinical content. The seven excluded recommendations were primarily technical or intraoperative in nature and could not be meaningfully reformulated as patient-posed questions. Consequently, the questions were organized into three primary categories according to the theme of the prompt: 1) risk factors: assessing the impact of preoperative risk factors on postoperative results; 2) implant/intraoperative: considerations pertaining to implants and intraoperative choices; and 3) pain/functional outcome: interventions influencing postoperative pain levels and functional outcomes [Table 1]. Attention was given to ensure incorporation of questions encompassing diverse levels of AAOS recommendations: 5 strong, 4 moderate, 1 limited, and 5 consensus.

Each prompt was provided to both ChatGPT-3.5 and ChatGPT-4 and the responses were recorded using Microsoft Excel (state of Washington). Each prompt included an explicit requirement that the information provided be supported by cited sources. All queries were conducted between May 25 and May 30, 2024 using the ChatGPT-web-based

Table 1. Questions derived from the 2020 AAOS Clinical Practice guidelines for the surgical management of glenohumeral joint osteoarthritis

	QUESTION		AAOS RECOMMENDATION	STRENGTH OF AAOS RECOMMENDATION
RISK FACTORS	1	Do obese patients with glenohumeral osteoarthritis experience an increase in rate of post-operative complications?	No	Strong
	2	Is gender/sex associated with better or worse post-operative outcomes?	No	Strong
	3	Do patients with glenohumeral joint osteoarthritis who have more comorbidities experience higher rates of early post-arthroplasty complications?	Yes	Strong
	4	Is smoking associated with inferior post-operative outcomes?	Yes	Moderate
	5	Will patients with higher pre-operative function experience less functional improvement than patients with lower pre-operative outcomes?	Yes	Moderate
	6	Is depression associated with inferior post-operative outcomes in patients with glenohumeral joint osteoarthritis undergoing arthroplasty?	Yes	Moderate
INTRAOPERATIVE	7	Can surgeons utilize subscapularis peel, lesser tuberosity osteotomy, or tenotomy when performing shoulder arthroplasty?	Yes	Moderate
	8	Can surgeons utilize pegged or keeled glenoid components in patients with glenohumeral joint osteoarthritis and a well-functioning rotator cuff?	Yes	Strong
	9	Can clinicians utilize stemmed, stemless or resurfacing prosthesis for patients with glenohumeral joint osteoarthritis undergoing total or hemi-arthroplasty?	Yes	Limited
	10	Would use of tranexamic acid during shoulder arthroplasty result in reduced blood loss and reduced risk of blood transfusion?	N/A	Consensus
FUNCTIONAL OUTCOME	11	Is there a benefit associated to the use of hyaluronic acid in the treatment of glenohumeral joint osteoarthritis?	No	Strong
	12	Should post-operative physical therapy be recommended to patients following shoulder arthroplasty?	N/A	Consensus
	13	Should opioids be prescribed as routine and long-term pain management of glenohumeral osteoarthritis?	N/A	Consensus
	14	Should anatomic total shoulder arthroplasty be performed on patients with small, isolated, repairable supraspinatus tears?	N/A	Consensus
	15	Is same-day discharge an option after shoulder arthroplasty in select patients?	N/A	Consensus

interface. Each prompt was entered individually in a new chat session to prevent contextual carryover between queries. Chat history was cleared after each prompt to further ensure independence of responses. Outputs were generated once per prompt without repeated runs. In order to evaluate the chatbots' responses to each question, a rating scale based on five categories was used: relevance, accuracy, clarity, completeness and evidence-based. Relevance referred to the correlation of the answer to the posted inquiry; accuracy referred to the alignment of the answer to the AAOS guidelines; clarity referred to the ease of comprehension; completeness referred to the comprehensiveness of the provided response and evidence-based referred to the authentication of claims with relevant citations provided by the bots. Four shoulder and elbow fellowship-trained surgeons were asked to evaluate both ChatGPT-3.5 and ChatGPT-4's responses to every question, and the surgeons were blinded as to which chatbot provided which response. Possible scores for every attribute ranged between 1 and 5, and as such, the overall score of the responses ranged between 5 and 25. The description of each attribute was mentioned at the top of the forms for the surgeons to increase convenience and minimize personal bias in interpreting the attributes. Mean scores were derived by calculating the average scores from every surgeon for every chatbot response. In addition, the Flesch-Kincaid grade level was calculated to evaluate the readability of each chatbot's response to each prompt.

Derived scores from the shoulder and elbow surgeons were recorded and analyzed. Descriptive statistics were used to describe the scores of the chatbots' responses to the derived prompts. Analysis of variance (ANOVA) testing with a post-hoc Tukey's test was then conducted to compare the scores between different question categories and different scoring categories for both ChatGPT-3.5 and GPT-4. An independent t-test was used to compare the overall response scores between ChatGPT-3.5 and GPT-4, as well as the overall readability between the two chatbots. A P-value less than 0.05 was considered significant. All statistical analyses were conducted using the statistical package for the social sciences for Windows software version 25.0 (IBM SPSS, 2017).

RESULTS

ChatGPT-3.5

The average score of a prompt response by ChatGPT-3.5 was 19.7/25, with question 10 achieving the highest mean score at 22.3, and question 13 achieving the lowest mean score at 15.5/25 [Table 2].

Mean score was highest for "Risk Factor" prompts scoring at 4.15/5. This was followed by "Intraoperative" prompts with a score of 3.9/5, and "Functional Outcomes" prompts with a score of 3.9/5. We have provided

additional details about the average scores of ChatGPT-3.5 for the different prompt themes in our study [Table 3]. There was no statistical significance when exploring the differences of scores between different prompt themes in ChatGPT-3.5 ($p=0.887$).

Overall, the average ChatGPT-3.5 response in our study received a mean score of 4.7/5 on relevance, 4.2/5 on accuracy, 4.8/5 on clarity, 3.9/5 on completeness, and 2.5/5 on being evidence-based. Generally, the average ChatGPT-3.5's response scored lower on being evidence-based than on relevance ($p=0.001$), accuracy ($p=0.01$), clarity ($p<0.001$), and completeness ($p=0.027$).

On average, ChatGPT-3.5 response received a Flesch-Kincaid grade level of 18.3 (range: 15.4-20.4), indicating a reading level pertaining to a college graduate (very difficult to read).

Table 2. Average Prompt Score for both ChatGPT and GPT-4

Questions	ChatGPT-3.5	GPT-4
1	19.5	16.25
2	20.25	12.75
3	19.75	19
4	21.5	19.25
5	21	18.25
6	22.5	19.5
7	16.75	14.25
8	17.75	19.5
9	20.25	18
10	22.25	21
11	21.5	21.25
12	20.75	19.25
13	15.5	20.75
14	16.75	19.5
15	19	21.75
Total Average	19.7	18.7

Table 3. Performance of ChatGPT-3.5 when responding to AAOS prompts according to type of question and rating category

ChatGPT-3.5	Risk Factors		Intraoperative		Functional Outcomes	
	Average	Standard Deviation	Average	Standard Deviation	Average	Standard Deviation
Relevance	4.88	0.16	4.56	0.31	4.40	0.28
Accuracy	4.45	0.67	3.75	0.79	4.19	0.47
Clarity	4.78	0.18	4.88	0.14	4.68	0.28
Completeness	3.92	1.24	3.81	1.23	4.04	0.86
Evidence-based	2.71	0.72	2.38	0.92	2.35	0.93
Average	4.15		3.88		3.93	

GPT-4

The average score for a prompt response by GPT-4 was 18.7/25, with Question 15 achieving the highest mean score at 21.8/25 and Question 2 achieving the lowest mean score at 12.8/25 [Table 2]. While the average prompt response score for ChatGPT-3.5 was higher than that of GPT-4, this was not deemed significant on independent t-test analysis ($p=0.239$; MD: 1.0233).

Mean score was highest for “Functional Outcomes” prompts scoring at 4.1/5. This was followed by “Intraoperative” prompts with a score of 3.7/5, and “Risk Factors” prompts with a score of 3.5/5. We have provided additional details about the average scores of GPT-4 for the different prompt themes in our study [Table 4]. There was no statistical significance when exploring the differences of scores between different prompt themes in GPT-4 ($p=0.485$). There was also no statistically significant differences in mean scores between ChatGPT-3.5 and GPT-4 when responding to “Risk Factors” prompts ($p=0.285$), “Intraoperative” prompts ($p=0.751$), and “Functional Outcomes” prompts ($p=0.759$).

Overall, the average GPT-4 response in our study received a mean score of 4.3/5 on relevance, 4.0/5 on accuracy, 4.0/5 on clarity, 3.1/5 on completeness, and 2.1/5 on being evidence-based. Generally, the average GPT-4’s response scored lower on being evidence-based than on relevance ($p=0.003$), accuracy ($p=0.007$), and clarity ($p=0.008$). In addition, there was also no statistically significant differences in mean scores between ChatGPT-3.5 and GPT-4’s responses according to relevance ($p=0.097$), accuracy ($p=0.326$), clarity ($p=0.078$), completeness ($p=0.307$), and being evidence-based ($p=0.312$).

On average, GPT-4’s response received a Flesch-Kincaid grade level of 15.4 (range: 12.7–17.6), indicating a reading level pertaining to a college graduate (very difficult to read). That being said, the Flesch-Kincaid grade level of GPT-3.5’s responses was significantly higher than that of GPT-4’s responses ($p<0.001$), indicating a more difficult reading level in GPT-3.5’s responses.

Table 4. Performance of ChatGPT-3.5 when responding to AAOS prompts according to type of question and rating category

ChatGPT-4	Risk Factors		Intraoperative		Functional Outcomes	
	Average	Standard Deviation	Average	Standard Deviation	Average	Standard Deviation
Relevance	4.25	0.62	4.25	0.54	4.50	0.53
Accuracy	4.04	0.37	3.85	0.27	4.45	0.50
Clarity	4.00	0.71	4.23	0.49	4.60	0.43
Completeness	3.13	0.70	3.56	0.31	4.15	0.72
Evidence-based	2.08	0.88	2.63	0.78	2.80	1.05
Average	3.50		3.70		4.10	

DISCUSSION

With the increasing reliance on ChatGPT by patients for medical advice across various medical specialties, it becomes essential to assess its credibility and efficiency, particularly in niche subspecialties and specific topics.²⁹ Moreover, as new models of ChatGPT gain popularity, it is important to compare their performance in addressing these questions, in order to highlight areas of improvement and address noteworthy limitations. Our study evaluated and compared the performance of ChatGPT-3.5 and GPT-4 in answering questions related to the surgical management of glenohumeral joint osteoarthritis from a patient’s perspective. The findings indicate that both models provide moderate-quality responses, with average scores of 19.7/25 for ChatGPT-3.5 and 18.7/25 for GPT-4. These scores reflected interesting perceptions regarding the relevance, accuracy, clarity, completeness, and evidence-based support of ChatGPT responses.

Interestingly, ChatGPT-3.5 performed slightly better overall, with better readability scores than their more advanced counterpart.

Both ChatGPT-3.5 and GPT-4 performed similarly well in our study, with no significant differences overall ($p=0.239$). It was seen that responses related to “Risk factors” questions had highest scores for ChatGPT-3.5, while those relating to “Functional Outcomes” had highest scores for GPT-4. Moreover, it was noted that both chatbots had significantly lower scores on being “evidence-based” when compared to other scoring categories. This has multiple implications on performance. Chatbots derive responses to scientific inquiries based on the available scientific literature online.^{30,31} Hence, limitations in responses reflect either weaknesses in the available literature or shortcomings in the processing methods by which chatbots screen and gather information from scientific sources.^{30, 31} In this setting, a new more specialized chatbot powered by advanced AI technology, termed Consensus has emerged, focusing particularly on enhancing the academic research experience, using improved search capabilities, and employing a research-oriented interface.³² Perhaps future studies would prove the superior efficacy and accuracy of this chatbot when compared to its predecessors.

When assessing readability of responses based on the Flesch Kincaid grading level, both chatbots showcased reading levels that may not be accessible to patients with lower health literacy. That being said, ChatGPT-4 demonstrated a lower Flesch-Kincaid grading level than GPT-3.5, suggesting more readable content, which may provide more accessible information for a broader audience. This highlights important areas of improvement for future chatbots, while improving accuracy

and reliability of information is essential, doing so in an accessible and more readable manner is of major importance.

Our study showed that Chat GPT-3.5 performed better on average than GPT-4, though the difference was not significant overall. This finding is notable because GPT-4 is reportedly significantly more capable of solving difficult problems with better accuracy due to improved reasoning and a much larger base of learned information.³³ This result also falls in contrast with previous studies comparing the performance of both GPT-models in responding to medical questions. GPT-4 was found to answer more accurately on orthopaedic assessment examinations than ChatGPT-3.5.³⁴ GPT-4 was also found to answer Orthopedic In-Training Examination (OITE) questions with significantly better accuracy than ChatGPT-3.5.³⁵ For other medical specialties too, GPT-4 has performed significantly better than GPT-3.5.³⁶⁻³⁸

To our knowledge, this is the first study to assess ChatGPT-responses to patient-related queries targeting glenohumeral osteoarthritis. Nevertheless, several limitations exist. We asked shoulder surgery experts to rate ChatGPT's answers, introducing subjectivity as a potential limitation of our study. To address this, we provided detailed criteria for each characteristic and score to ensure a consistent evaluation. Additionally, we minimized bias between GPT-3.5 and GPT-4 by blinding the surgeons to which responses corresponded to which model. The experts were also provided with the AAOS recommendations and their strengths for each question to guide their assessments.

Beyond evaluator subjectivity, this study is subject to several limitations inherent to large language model-based analyses. Model outputs may vary over time due to temporal drift as underlying models are updated, which may limit reproducibility. Responses may also differ across repeated runs for the same prompt. Since our methods did not include repeated sampling, within-prompt variability could not be quantified. Additionally, LLM outputs are sensitive to prompt phrasing, and alternative wording may have yielded different responses despite similar intent. These factors should be considered when interpreting the findings and when comparing results across studies or time points.

CONCLUSION

While both ChatGPT-3.5 and GPT-4 demonstrate substantial potential in providing well-informed medical responses to patient queries about glenohumeral osteoarthritis, enhancements remain necessary and essential to ensure the reliability and accessibility of their answers. Future versions should focus on incorporating more evidence-based content and more accessible language to cater to diverse patient populations with varying levels of health literacy. Additionally, patients should be mindful of the limitations of current chatbots when considering the medical advice and information provided by it. Further research should explore future iterations of ChatGPT and assess their ability to respond to queries related to other niche medical subspecialties, in an aim to evaluate improvement and ensure continuous growth.

References

1. Rawassizadeh R, Sen T, Kim SJ, et al. Manifestation of virtual assistants and robots into daily life: vision and challenges. *CCF Transactions on Pervasive Computing and Interaction*. 2019;1:163-174. DOI: 10.1007/s42486-019-00014-1.
2. Feuerriegel S, Hartmann J, Janiesch C, Zschech P. Generative AI. *Business @amp; Information Systems Engineering*. 2023;66:111-126. DOI: 10.1007/s12599-023-00834-7.
3. BalDoo-Anu D, Owusu Ansah L. Education in the Era of Generative Artificial Intelligence (AI): Understanding the Potential Benefits of ChatGPT in Promoting Teaching and Learning. *Journal of AI*. 2023;7:52-62. DOI: 10.61969/jai.1337500.
4. Aydin Ö, Karaarslan E. Is ChatGPT Leading Generative AI? What is Beyond Expectations? *Academic Platform Journal of Engineering and Smart Systems*. 2023;11:118-134. DOI: 10.21541/apjess.1293702.
5. Ray PP. ChatGPT: A comprehensive review on background, applications, key challenges, bias, ethics, limitations and future scope. *Internet of Things and Cyber-Physical Systems*. 2023;3:121-154. DOI: 10.1016/j.iotcps.2023.04.003.
6. Tyson J. Shortcomings of ChatGPT. *Journal of Chemical Education*. 2023;100:3098-3101. DOI: 10.1021/acs.jchemed.3c00361.
7. Walker HL, Ghani S, Kuemmerli C, et al. Reliability of Medical Information Provided by ChatGPT: Assessment Against Clinical Guidelines and Patient Information Quality Instrument. *J Med Internet Res*. 2023;25: e47479-e47479. DOI: 10.2196/47479.
8. Jeyaraman M, K SP, Jeyaraman N, et al. ChatGPT-in Medical Education and Research: A Boon or a Bane? *Cureus*. 2023;15: e44316-e44316. DOI: 10.7759/cureus.44316.
9. Mehnen L, Gruarin S, Vasileva M, Knapp B. ChatGPT as a medical doctor? A diagnostic accuracy study on common and rare diseases. Cold Spring Harbor Laboratory, 2023.
10. IStrong E, DiGiammarino A, Weng Y, et al. Chatbot vs Medical Student Performance on Free-Response Clinical Reasoning Examinations. *JAMA Intern Med*. 2023;183:1028-1030. DOI: 10.1001/jamainternmed.2023.2909.
11. Gilson A, Safranek CW, Huang T, et al. How Does ChatGPT Perform on the United States Medical Licensing Examination (USMLE)? The Implications of Large Language Models for Medical Education and Knowledge Assessment. *JMIR Med Educ*. 2023;9:e45312-e45312. DOI: 10.2196/45312.
12. Gupta R, Herzog I, Park JB, et al. Performance of ChatGPT on the Plastic Surgery Inservice Training Examination. *Aesthetic Surgery Journal*. 2023;43:NP1078-NP1082. DOI: 10.1093/asj/sjad128.
13. Daher M, Koa J, Boufadel P, et al. Breaking barriers: can ChatGPT compete with a shoulder and elbow specialist in diagnosis and management? *JSES Int*. 2023;7:2534-2541. DOI: 10.1016/j.jseint.2023.07.018.
14. Magruder ML, Rodriguez AN, Wong JCJ, et al. Assessing Ability for ChatGPT to Answer Total Knee Arthroplasty-Related Questions. *The Journal of Arthroplasty*. 2024. DOI: 10.1016/j.arth.2024.02.023.
15. Lum ZC. Can Artificial Intelligence Pass the American Board of Orthopaedic Surgery Examination? Orthopaedic Residents Versus ChatGPT. *Clin Orthop Relat Res*. 2023;481:1623-1630. 2023/05/23. DOI: 10.1097/CORR.0000000000002704.
16. Antaki F, Touma S, Milad D, et al. Evaluating the Performance of ChatGPT in Ophthalmology: An Analysis of Its Successes and Shortcomings. *Ophthalmol Sci*. 2023;3: 100324-100324. DOI: 10.1016/j.xops.2023.100324.
17. Balas M, Ing EB. Conversational AI Models for ophthalmic diagnosis: Comparison of ChatGPT and the Isabel Pro Differential Diagnosis Generator. *JFO Open Ophthalmology*. 2023;1:100005. DOI: 10.1016/j.jfop.2023.100005.
18. Grünebaum A, Chervenak J, Pollet SL, et al. The exciting potential for ChatGPT in obstetrics and gynecology. *American Journal of Obstetrics and Gynecology*. 2023;228:696-705. DOI: 10.1016/j.ajog.2023.03.009.
19. Kuang Y-R, Zou M-X, Niu H-Q, et al. ChatGPT encounters multiple opportunities and challenges in neurosurgery. *Int J Surg*. 2023;109:2886-2891. DOI: 10.1097/JS9.0000000000000571.

20. Hopkins BS, Nguyen VN, Dallas J, et al. ChatGPT versus the neurosurgical written boards: a comparative analysis of artificial intelligence/machine learning performance on neurosurgical board-style questions. *Journal of Neurosurgery*. 2023;139:904-911. DOI: 10.3171/2023.2.jns23419.
21. Kasthuri VS, Glueck J, Pham H, et al. Assessing the Accuracy and Reliability of AI-Generated Responses to Patient Questions Regarding Spine Surgery. *JBJS*. 2021;10:2106.
22. Chalhoub R, Mouawad A, Aoun M, et al. Will ChatGPT be able to replace a spine surgeon in the clinical setting? *World Neurosurgery*. 2024;185:e648-e652.
23. Fayed AM, Mansur NSB, de Carvalho KA, et al. Artificial intelligence and ChatGPT in Orthopaedics and sports medicine. *J Exp Orthop*. 2023;10:74-74. DOI: 10.1186/s40634-023-00642-8.
24. Giorgino R, Alessandri-Bonetti M, Luca A, et al. ChatGPT in orthopedics: a narrative review exploring the potential of artificial intelligence in orthopedic practice. *Front Surg*. 2023; 10: 1284015-1284015. DOI: 10.3389/fsurg.2023.1284015.
25. Kaarre J, Feldt R, Keeling LE, et al. Exploring the potential of ChatGPT as a supplementary tool for providing orthopaedic information. *Knee Surg Sports Traumatol Arthrosc*. 2023;31:5190-5198. DOI: 10.1007/s00167-023-07529-2.
26. Kuroiwa T, Sarcon A, Ibara T, et al. The Potential of ChatGPT as a Self-Diagnostic Tool in Common Orthopedic Diseases: Exploratory Study. *J Med Internet Res*. 2023;25:e47621-e47621. DOI: 10.2196/47621.
27. Wagner ER, Farley KX, Higgins I, et al. The incidence of shoulder arthroplasty: rise and future projections compared with hip and knee arthroplasty. *Journal of Shoulder and Elbow Surgery*. 2020;29:2601-2609. DOI: 10.1016/j.jse.2020.03.049.
28. Khazzam M, Gee AO, Pearl M. Management of Glenohumeral Joint Osteoarthritis. *Journal of the American Academy of Orthopaedic Surgeons*. 2020;28:781-789. DOI: 10.5435/jaaos-d-20-00404.
29. Clark M, Bailey S. Chatbots in Health Care: Connecting Patients to Information. *Canadian Journal of Health Technologies*. 2024;4.
30. Aleedy M, Shaiba H, Bezbradica M. Generating and analyzing chatbot responses using natural language processing. *International Journal of Advanced Computer Science and Applications*. 2019;10.
31. Liu J, Wang C, Liu S. Utility of ChatGPT in Clinical Practice. *J Med Internet Res*. 2023; 25:e48568-e48568. DOI: 10.2196/48568.
32. Consensus. AI Search Engine for Research, <https://consensus.app/> (2024).
33. Koubaa A. GPT-4 vs. GPT-3.5: A concise showdown. 2023.
34. Massey PA, Montgomery C, Zhang AS. Comparison of Chat GPT-3.5, ChatGPT-4, and Orthopaedic Resident Performance on Orthopaedic Assessment Examinations. *The Journal of the American Academy of Orthopaedic Surgeons*. 2023;31:1173-1179. 2023/09/04. DOI: 10.5435/JAAOS-D-23-00396.
35. Rizzo MG, Cai N, Constantinescu D. The performance of ChatGPT on orthopaedic in-service training exams: A comparative study of the GPT-3.5 turbo and GPT-4 models in orthopaedic education. *J Orthop*. 2024;50:70-75.
36. Lewandowski M, Łukowicz P, Świetlik D, Barańska-Rybak W. ChatGPT-3.5 and ChatGPT-4 dermatological knowledge level based on the Specialty Certificate Examination in Dermatology. *Clinical and Experimental Dermatology*. 2023. DOI: 10.1093/ced/llad255.
37. Lee GU, Hong DY, Kim SY, et al. Comparison of the problem-solving performance of ChatGPT-3.5, ChatGPT-4, Bing Chat, and Bard for the Korean emergency medicine board examination question bank. *Medicine (Baltimore)*. 2024;103:e37325-e37325. DOI: 10.1097/MD.00000000000037325.
38. Lee TJ, Rao AK, Campbell DJ, et al. Evaluating ChatGPT-3.5 and ChatGPT-4.0 Responses on Hyperlipidemia for Patient Education. *Cureus*. 2024;16: e61067-e61067. DOI: 10.7759/cureus.61067.

Authors

Mohamad Y. Fares, MD, Division of Shoulder and Elbow Surgery, Rothman Orthopaedic Institute, Philadelphia, PA.
 Tarishi Parmar, BSc, Penn State College of Medicine, Centre County, PA.
 Peter Boufadel, MD, Division of Shoulder and Elbow Surgery, Rothman Orthopaedic Institute, Philadelphia, PA.
 Mohammad Daher, MD, Brown University, Providence, RI.
 Jonathan Berg, BSc, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA.
 Adam Z. Khan, MD, Southern Permanente Medical Group, CA.
 Brian W. Hill, MD, Palm Beach Orthopaedic Institute, West Palm Beach, FL.
 John G. Horneff, MD, Division of Shoulder and Elbow Surgery, Department of Orthopaedics, University of Pennsylvania, Philadelphia, PA.
 Joseph A. Abboud, MD, Division of Shoulder and Elbow Surgery, Rothman Orthopaedic Institute, Philadelphia, PA.

Disclosures

Study Location: Research was performed at the Rothman Orthopaedic Institute, Philadelphia, PA.

Declaration of Conflicts of Interests: JAA would like to disclose: Royalties from a company or supplier; Disclosures; Osteocentric Technologies, Enovis, Zimmer-Biomet, Stryker, Globus Medical, Inc. Stocks in: Shoulder Jam, Aevumed, Oberd, Ots Medical, Orthobullets, Atreon, Restore 3D. Research support from a company or supplier as a PI; Disclosures; Enovis, Arthrex. Royalties, financial or material support from publishers; Disclosures; Wolters Kluwer, Slack Orthopaedics, Elsevier. Board member/committee appointments for a society; Disclosures; American Shoulder And Elbow Society, Mid Atlantic Shoulder And Elbow Society, Shoulder 360, Pacira.

Declaration of Funding: None

Declaration of Ethical Approval: This study does not involve any patients or patient-related information and as such, does not require Institutional Board Review approval.

Declaration of Informed Consent: Not applicable.

Correspondence

Mohamad Y. Fares, MD
 Division of Shoulder and Elbow Surgery
 Rothman Orthopaedic Institute
 925 Chestnut St, Philadelphia, PA 19107
mohamadfaresmd@gmail.com

Transitioning Young Adult Patients from Pediatric to Adult Rheumatology Practices in Rhode Island

VICTORIA KOENIGSBERGER, BA; MEGHAN GEARY, MD; ALI YALCINDAG, MD; MADELEINE WARD, MD

ABSTRACT

BACKGROUND: Young adults with rheumatic conditions encounter challenges when transitioning to an adult rheumatologist. At the Hasbro Pediatric Rheumatology Clinic, patients aged 18 and older were historically provided a list of adult rheumatologists; however, no formal transition process existed. We assessed the feasibility and acceptability of a pilot model to systematically transition pediatric patients to an adult rheumatologist using aspects of the Six Core Elements of Health Care Transition (HCT) from Got Transition®.

METHODS: A multidisciplinary team facilitated the program. Eligibility included: 18 years of age with stable, confirmed (or suspected) rheumatic disease. Program structure was implemented across three pediatric and one adult visit. Patient-reported transition readiness was assessed at initial and final pediatric visits using the Transition Readiness Assessment (TRA) from Got Transition®.

RESULTS: Sixty-four patients aged 18 and older had appointments with the Hasbro Pediatric Rheumatology Clinic from May 1, 2024 to Jan. 31, 2025. Thirteen were eligible; eight entered the pilot (61.5%). The mean age at recruitment was 19.5 years (range: 18–23). The study achieved a 62.5% retention rate, with 80% completion of video visits with adult rheumatologists and zero no-shows. TRA scores were high at baseline, although of note patients initially scored their readiness lower in areas related to transition confidence and navigating health care. The greatest mean score increase was seen for navigating health care (+2.7).

CONCLUSION: This rheumatology transition pilot demonstrated preliminary feasibility. Systemic changes to reimbursement and clinician education are needed to support HCT sustainability.

KEYWORDS: transition to adult care; rheumatology; adolescent; young adult; chronic medical condition

an increasing number of them require continued care into adulthood.¹ It is estimated that nearly 20% of children and young adults in the United States live with a complex chronic condition.² Transition from pediatric to adult care is a complex process known as health care transition (HCT), which should include three aims: planning, transfer, and integration of the patient into adult care. Less than 20% of pediatric patients across all subspecialties receive appropriate HCT, which should include discussion regarding transition spanning multiple appointments, beginning as early as ages 12–14.³ Appropriate HCT per meta-analysis data has been shown to improve adherence to care, the patient's quality of life, and self-care skills.⁴

The transition from pediatric to adult healthcare systems is particularly important in rheumatology, as most childhood rheumatic conditions are chronic and patients require regular, ongoing care. Several professional organizations, such as the American Academy of Pediatrics (AAP) and the American College of Physicians (ACP), have developed consensus statements for appropriate HCT.⁵ While some medical centers have designed HCT programs using these guidelines, standardization varies widely. Got Transition® is one organization that has been an innovator in the creation of a standardized approach for HCT, known as the Six Core Elements of HCT. This approach includes: transition policy, transition tracking and monitoring, transition readiness, transition planning, transfer of care, and transfer completion.⁶ The American College of Rheumatology (ACR) has adopted Got Transition® practices and developed a transition toolkit.⁷

In Rhode Island, one pediatric rheumatologist at Hasbro Children's Hospital provides care for patients with childhood-onset rheumatic conditions. Rheumatology care for adult patients is split between academic and hospital-based group practices. Unlike academic medical centers where comprehensive pediatric and adult care is available within the same or adjacent facilities, pediatric and adult academic rheumatology practices in Rhode Island operate in different locations. Most adult rheumatology care in greater Providence spreads across three locations: Brown Medicine, an academic multispecialty practice in East Providence, Rhode Island; Brown University Health Rheumatology, a private multispecialty practice in Pawtucket, Rhode Island; and the Center for Primary Care in Providence, Rhode Island, staffed

INTRODUCTION

Children with complex chronic illnesses such as systemic lupus erythematosus (SLE), cystic fibrosis (CF), and inflammatory bowel disease (IBD) are living longer, and

by fellows from the Brown Rheumatology Fellowship Program. The fragmented nature of rheumatology care for adult patients in Rhode Island likely contributes to a challenging transition from one system to another.

Prior to this study, discussion regarding transition began at age 18 at the Hasbro Pediatric Rheumatology Clinic, which was significantly later than recommended. Furthermore, while these patients were told they should start to find an adult rheumatologist, no formal transition process existed. Recognizing the gaps in care that existed for transition-age rheumatology patients, we sought to develop and pilot a formal HCT pathway to prepare and facilitate the transition for these patients. Additionally, we aimed to reduce the geographic dispersion of pediatric and adult sites through a novel, video, warm hand-off between the pediatric and adult rheumatology teams during patients' final pediatric visits. The goal of this study was to assess the feasibility and acceptability of the pathway for transition-age patients and clinicians, and to investigate its preliminary role in shaping patient transition readiness.

METHODS

Study Setting and Team

This study employed a single-arm, prospective pilot and feasibility design. To facilitate the pilot, a team of pediatric and adult physicians and ancillary staff was established. This team included one research assistant, two primary care physicians with an interest in HCT, one pediatric rheumatologist, 10 adult rheumatologists (attendings and fellows), as well as practice managers. The pediatric rheumatology team determined appropriate patients for this pilot.

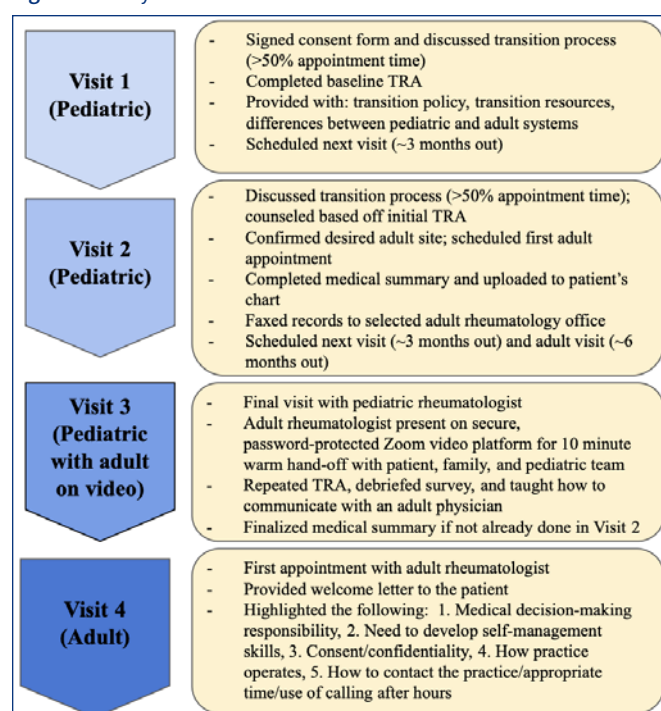
Patient Selection and Eligibility

The targeted sample size was 10–15 patients. Eligibility criteria included: age 18 and older, confirmed or suspected rheumatic disease, stable disease and/or in clinical remission, English-speaking, and seen by the pediatric rheumatology team within the last six months. These patients were approached by a member of the research team during their regular scheduled pediatric appointment. Patients who were seen by telehealth were not eligible for this study, to ensure consistent delivery of paper consent forms and transition materials, as well as in-person counseling. All study recruitment, transition-related education and counseling, and joint adult and pediatric provider video visits took place during patients' scheduled rheumatology appointments, and there was no separate billing for this work during either pediatric or adult visits. The research assistant led recruitment and counseling for the pilot; however, the program was designed such that a nurse or other allied health professional could replicate it in future iterations. This study was approved by the Brown University Health Institutional Review Board (IRB #2065997-5).

Study Protocol

For this study, patients engaged in a series of four visits: two with the pediatric rheumatologist; one with the pediatric rheumatologist and the adult rheumatologist, if possible, on video; and one visit with the adult rheumatologist. These visits were based upon various elements of Got Transition[®], with a particular focus on transfer of care and transfer completion. The complete protocol is detailed in **Figure 1**. Transition readiness was assessed at baseline and final pediatric appointments (Visits 1 and 3) using the Transition Readiness Assessment (TRA) from Got Transition[®] (**Appendix A [Email author for appendices]**). This was a validated survey that assessed patient transition readiness across four domains: self-perceived importance of transition to adult care; confidence in ability to transition from pediatric to adult care; managing individual health needs; and using health care.

Figure 1. Study Protocol



Data Analysis

The primary aim of this study was feasibility, as measured by recruitment rate (percentage of eligible patients enrolled), retention rate (percentage of patients completing all four appointments), and the percentage of patients receiving a joint video hand-off. Successful feasibility metrics were defined as: >50% recruitment rate, >50% retention, and >50% completion of video hand-offs. Patient demographics, including select social determinants of health (transportation access, insurance type), were abstracted from Epic and from patient interviews. The secondary aim included preliminary patient transition readiness, which was assessed by patient transition readiness assessment (TRA) scores

completed during the initial and final pediatric visits. Data were analyzed using descriptive statistics and individual-level changes due to the small sample size. Categorical variables (feasibility outcomes and demographics) are reported with frequencies. Continuous variables (TRA scores) are displayed with means and standard deviations to show the impact on the overall cohort and individual variability.

RESULTS

Sixty-four patients aged 18 and older had appointments scheduled during the recruitment period, from May 1, 2024 to Jan. 31, 2025 [Figure 2]. Of these, 13 patients (20.3%) were eligible and approached. The other 51 patients were excluded due to: virtual appointment, no suspected or confirmed rheumatic disease, no-show, or clinical instability. Ultimately, eight patients (61.5%) consented and enrolled in the study. Reasons for declining enrollment included: planning to transfer to a rheumatologist in another state, not interested and/or not ready to move to an adult rheumatologist yet. Five participants (62.5%) were retained throughout the study period. Of those retained, four (80%) completed their transition to an adult rheumatologist, with one (20%) still awaiting their first appointment. Of note, four (80%) of those retained had the opportunity to participate in a joint, video, hand-off meeting between the pediatric and adult rheumatologists during their final pediatric appointment. There were zero no-show appointments among participants after they entered the study.

Baseline demographic characteristics of the pilot cohort are shown in Table 1. This includes all participants who were enrolled in the study, including those who did not complete the pilot. The mean age at recruitment was 19.5 years (SD: 1.5). Most participants were female and Caucasian, and the most common diagnosis was systemic lupus erythematosus. The majority had access to a personal source of transportation and were commercially insured.

Changes in transition readiness were analyzed using data from participants who completed both initial and final TRAs (n = 4), shown in Table 2. For participants who completed both surveys, the overall scores for transition self-confidence as well as self-management skills (managing health and navigating health care) increased, even while the perceived importance of transition decreased slightly. The greatest improvement was observed for using/navigating health care, with a group mean increase from 8.8 to 11.5 points, and an average individual improvement of 2.8 points (SD: 3.8). Only one participant's score did not change, though notably this individual had a near-perfect score across all domains. The specific sub-domains that appeared to have the greatest mean score increases were making doctors' appointments and having a copy of my current plan of care (mean change +50.0%, n = 4). Two sub-domains—knowing what to do in a medical emergency and knowing how to fill out medical forms—were the only ones that showed a score decrease (mean change -25.0%, n = 4).

Figure 2. Study Inclusion

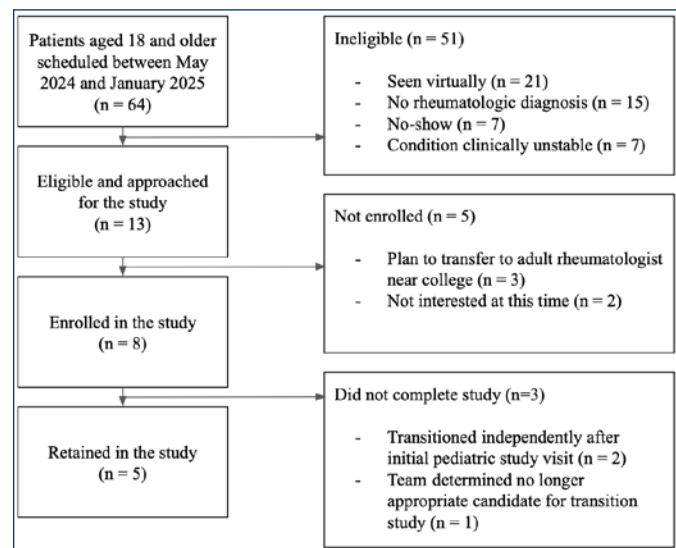


Table 1. Baseline Participant Demographics (n = 8)

Characteristic/Demographics	n or Mean (SD)
Gender	
Male	2
Female	6
Age	19.5 (1.5)
Race/ethnicity	
Native American/Alaska Native	0
Asian	1
Black/African American	0
Hispanic/Latino	2
Native Hawaiian or Pacific Islander	0
White/Caucasian	5
Primary Rheumatic Diagnosis	
Juvenile Idiopathic Arthritis	1
Systemic Lupus Erythematosus	2
Discoid Lupus	1
Gout	1
Mixed Connective Tissue Disease	1
Raynaud's Phenomenon	1
Immune Dysregulation	1
Insurance Type	
Public	3
Private/Commercial	5
Personal Source of Transportation	
Yes	7
No	1

Table 2. Initial and Final Transition Readiness Assessment Scores (n = 4)

	Visit or Score change	Importance (0-10)	Confidence (0-10)	Managing Health (0-9)*	Navigating Health Care (0-14)*
Overall Mean (SD)	Initial	7.0 (4.7)	5.5 (4.4)	7.3 (2.1)	8.8 (5.1)
	Final	6.8 (4.6)	6.0 (4.6)	8.3 (1.5)	11.5 (2.1)
Mean change	N/A	-0.2	+0.5	+1.0	+2.7
Mean individual change (SD)	N/A	-0.3 (0.5)	+0.5 (0.6)	+1.0 (2.0)	+2.8 (3.8)

* Complete survey questions/domains are shown in Appendix B. TRA response options were as follows: 1) I know this; 2) I need help with this; and 3) Someone needs to do this...(Who?). Each question that was answered using option one was given one point, while options two and three were given zero points.

DISCUSSION

This is the first study in Rhode Island that has been undertaken to improve the transition from pediatric to adult care in rheumatology. While systematized pediatric to adult HCT has started to be implemented in other settings in Rhode Island, such as primary care and pulmonology, to our knowledge, this study has been the first to incorporate a warm hand-off using video. Overall, while the transition pilot study did not meet our target sample size of 10–15 participants, it did meet all feasibility goals, evidenced by 61.5% recruitment rate, 62.5% retention rate, and 80% completion of joint video visits. Most notably, there were zero no-show appointments among participants after they entered the study. It is possible that discussion of the transition process allowed patients and their families to become more engaged in their care overall. Patients, their parents/guardians, and clinicians all verbalized appreciation for having a systematized process for moving patients from one system to another within Rhode Island's "really confusing" (Parent 1) healthcare landscape. At our institution, Got Transition[®] helped provide a foundational toolkit that was able to be adopted by our system. The bidirectional communication that resulted from adopting this framework, particularly our choice to implement a video hand-off call between the patient and the pediatric and adult rheumatologists, was especially well-received by all parties involved.

Baseline transition readiness scores in this pilot cohort were generally high. Other studies have noted that transition importance and confidence scores tend to increase as patients move from age 12 to 26,⁸ therefore the high overall scores might be attributable to the age group chosen for the pilot (at least 18 years of age). Given that two participants in our cohort dropped out after the first visit to manage their transition independently, the intervention may be too long for certain young adults. Thus, future iterations of similar programs should be tailored to patients' individual needs.

While most patients felt that moving to an adult rheumatologist before age 22 was important, they reported slightly less confidence in their ability to do so. We suspect this could be due to participants' concerns about "getting used to

a new doctor" (Participant 4), and perceptions that "pediatric doctors listen better and take their time" (Participant 2). Most participants reported knowing their health needs and being able to explain them to others. Initial knowledge regarding navigating healthcare, such as getting referrals to other providers, was more mixed. Specifically, "[having] trouble making appointments over the phone" (Participant 2) was cited as a barrier, which could be attributed to generation-based preferences for virtual over phone-based scheduling options.⁹ Nevertheless, this domain showed the greatest mean growth among participants retained in the study, with a 2.8-point average individual increase. Interestingly, while several participants' scores were stagnant for transition importance and confidence, two participants' (Participants 3 and 4) scores increased for navigating healthcare. This finding suggests that a structured HCT program such as this one could help develop patients' navigation skills, even if their confidence and self-perceived importance of transition do not change. Final TRA results from several participants across multiple visits, however, do not suggest a substantial change in transition readiness between appointments. It is possible that the limited time course of this study, one year, and the nature of the intervention, education provided within pre-existing appointment slots, as opposed to intensive educational sessions outside of regular appointments, were not sufficient to induce large changes in transition readiness.

As part of our program, adult rheumatologists were provided with detailed verbal and written patient summaries, as well as information regarding the nuances of conditions such as juvenile idiopathic arthritis and childhood-onset systemic lupus erythematosus. This information was finite in scope to accommodate the limited time in adult rheumatologists' schedules and the pilot nature of this study. However, in the future, more comprehensive education is needed for adult clinicians to welcome these patients into their practices. Increasingly, studies have called for integration of transition training within undergraduate and graduate medical education to best support the biomedical and psychosocial needs of young adults with medical complexity. Additionally, the next steps would be to reach out to/include federal agencies and philanthropic organizations to support formal transition-related training for adult physicians.¹⁰

Limitations

There were several limitations to this study, most notably the small sample size. Recruitment was challenging given the rarity of childhood rheumatic diseases and the transient nature of this population, adults aged 18 to 25, many of whom moved back and forth for college. Moreover, a significant number (n = 21) of patients 18 and older were only seen

virtually during the recruitment timeframe. Evidence from the literature suggests that young adults tend to prefer telehealth over in-person visits,¹¹ therefore, recruitment might be more successful in this population if incorporated using virtual modalities.

The multi-system nature of patients' rheumatologic conditions presented challenges as well. While transfer to additional specialties (i.e., nephrology, hematology) was out of scope for this project, patients and families mentioned that participation in the study helped demystify pediatric-to-adult transition. Additionally, it prompted them to consider discussing the move to an adult clinician with their non-rheumatology pediatric specialists. However, many families discussed the dearth of adult specialists, particularly primary care clinicians, as the primary barrier to transitioning to adult care in Rhode Island. Ultimately, larger systemic change is needed to bring more adult and pediatric physicians, as well as advanced practice practitioners, to Rhode Island.

Additionally, TRA survey data included three responses: 1) I know this; 2) I need help with this; and 3) Someone needs to do this...(Who?). Patients would sometimes choose "Someone needs to do this...(Who?)" while not choosing "I know this" or "I need help with this." This response did not necessarily provide a good assessment of where the patient was at or their readiness when our goal was to increase patient autonomy and self-assessment of their skills. This was a limitation of the survey, as it ultimately did not provide a clear understanding of their transition readiness. In future iterations, we would recommend delving further into discussion regarding these responses, and whether they should be included.

Lastly, time proved a significant barrier to the long-term success and sustainability of this process. The pediatric rheumatologist was allotted 15 minutes for follow-up appointments, which was an insufficient amount of time to discuss both the patient's medical needs and the transition. While the research team took additional time (if needed) immediately following the patient's appointment to discuss transition-related topics, it is unlikely that the pediatric rheumatologist will be able to cover this information without additional staff support and/or scheduled, billable appointment time with relevant current procedural terminology (CPT) codes (i.e., 96160, 99451, etc.)¹² in the future. Time for video exchanges with adult rheumatologists also proved challenging. The adult rheumatologists blocked off 10-15 minute time slots in their schedules to meet with the pediatric rheumatologist and patient via video; however, this did not count as a billable appointment in their schedules. Given the small number of study participants, clinicians expressed that the method was manageable. However, this model might be more difficult to implement in a larger cohort without structural policy changes, such as value-based payment models. Promisingly, Rhode Island has

recently begun to lead efforts in this area. For example, in early 2026, Rhode Island Medicaid intends to compensate for several transition-related services as part of Medicaid's Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) Benefit.¹³ Ultimately, continued investment in such work is needed to support transition sustainability.

CONCLUSION

In summary, this pilot rheumatology transition program using the core elements from Got Transition[®] demonstrated preliminary feasibility and high acceptability, with notable success incorporating warm hand-offs utilizing video. Our goal is that the program will be expanded to include a larger cohort of rheumatology patients in the coming years, in order to best assess the needs of this population. We also hope this model can be applied to other specialty clinics that treat patients with complex chronic illnesses, and do not currently have a systematized transition program.

References

1. Blackwell CK, Elliott AJ, Ganiban J, Herbstman J, Hunt K, Forrest CB, Camargo CA Jr; program collaborators for Environmental influences on Child Health Outcomes. General Health and Life Satisfaction in Children With Chronic Illness. *Pediatrics*. 2019 Jun;143(6):e20182988. doi: 10.1542/peds.2018-2988. Epub 2019 May 6. PMID: 31061222; PMCID: PMC6564050.
2. Children and Youth with Special Health Care Needs NSCH Data Brief | June 2022. Accessed March 02, 2025. <https://mchb.hrsa.gov/sites/default/files/mchb/programs-impact/nsch-data-brief-children-youth-special-health-care-needs.pdf>
3. Mubanga N, Baumgardner DJ, Kram JFF. Health Care Transitions for Adolescents and Young Adults With Special Health Care Needs: Where Are We Now? *J Patient Cent Res Rev*. 2017 Apr 25;4(2):90-95. doi: 10.17294/2330-0698.1406. PMID: 31413975; PMCID: PMC6664372.
4. Schmidt A, Ilango SM, McManus MA, Rogers KK, White PH. Outcomes of Pediatric to Adult Health Care Transition Interventions: An Updated Systematic Review. *J Pediatr Nurs*. 2020 Mar-Apr;51:92-107. doi: 10.1016/j.pedn.2020.01.002. Epub 2020 Jan 22. PMID: 31981969.
5. White PH, Cooley WC; Transitions Clinical Report Authoring Group; American Academy of Pediatrics; American Academy of Family Physicians; American College of Physicians. Supporting the Health Care Transition From Adolescence to Adulthood in the Medical Home. *Pediatrics*. 2018;142(5):e20182587. *Pediatrics*. 2019 Feb;143(2):e20183610. doi: 10.1542/peds.2018-3610. Erratum for: *Pediatrics*. 2018 Nov;142(5):e20182587. doi: 10.1542/peds.2018-2587. PMID: 30705144.
6. McManus M, White P, Pirtle R, Hancock C, Ablan M, Corona-Parra R. Incorporating the Six Core Elements of Health Care Transition Into a Medicaid Managed Care Plan: Lessons Learned From a Pilot Project. *J Pediatr Nurs*. 2015 Sep-Oct;30(5):700-13. doi: 10.1016/j.pedn.2015.05.029. Epub 2015 Aug 1. PMID: 2623 9121.
7. Pediatric to Adult Rheumatology Care Transition. American College of Rheumatology. Updated 2023. Accessed December 10, 2023. <https://rheumatology.org/pediatric-to-adult-rheumatology-care-transition>
8. Lestishock L, Cuomo C, Hickam T, Johnson-Hooper T, Maddux M, Muzzall E, McManus M, White P. Self-perceived im-

- portance and confidence of adolescents transitioning to adult care. *Health Care Transit*. 2024 Nov 28;3:100086. doi: 10.1016/j.hctj.2024.100086. PMID: 39712478; PMCID: PMC11657790.
9. *Gen Z Won't Pick Up the Phone: How Healthcare Providers Need to Shift Their Communications*. *Thejournalofmhealth.com*. 2024, October 16. <https://thejournalofmhealth.com/gen-z-wont-pick-up-the-phone-how-healthcare-providers-need-to-shift-their-communications/>
 10. *Strengthening the Adult Primary Care Workforce to Support Young Adults with Medical Complexity Transitioning to Adult Health Care*. 2023. https://www.gwhwi.org/uploads/4/3/3/5/43358451/yamc_workforce_final_report_may2023__05.02.23_.pdf
 11. There May Be a Generation Gap in Telehealth's Future. American Hospital Association. Accessed March 05, 2025. <https://www.aha.org/aha-center-health-innovation-market-scan/2021-06-29-there-may-be-generation-gap-telehealths-future>.
 12. Schmidt A, McManus M, White P, Muntean-Turner S, Lalor K. *2025 Coding and Payment Resource for Transition from Pediatric to Adult Health Care* [Review of 2025 Coding and Payment Resource for Transition from Pediatric to Adult Health Care]. Got Transition.org. <https://www.gottransition.org/resource/?2025-coding-tip-sheet>
 13. *Paying For Health Care Transition Services Under Medicaid's Early and Periodic, Screening, Diagnosis, and Treatment (EPS-DT) Benefit: Rhode Island State Example*. 2024. https://downloads.aap.org/AAP/PDF/RI_EPSDT_and_Transition_Payment_FINAL_v3_2025-03.pdf?gl=1

Authors

Victoria Koenigsberger, BA, The Warren Alpert Medical School of Brown University, Providence, Rhode Island.

Meghan Geary, MD, Assistant Professor of Medicine, Clinician Educator, Department of Medicine, The Warren Alpert Medical School of Brown University, Providence, Rhode Island.

Ali Yalcindag, MD, Professor of Pediatrics, Clinician Educator, Division of Rheumatology, Department of Pediatrics, The Warren Alpert Medical School of Brown University, Providence, Rhode Island.

Madeleine Ward, MD, Assistant Professor of Pediatrics, Clinician Educator, Department of Pediatrics, The Warren Alpert Medical School of Brown University, Providence, Rhode Island.

Disclosures

Acknowledgments: The research team would like to thank Maria Cortinez for her help in facilitating several video visits with the participants and their medical teams.

Conflict of Interest Statement: None of the authors discloses any conflicts of interest.

Statement of Funding: This project was made possible in part by a Ruth Sauber Fellowship from The Warren Alpert Medical School of Brown University, the Brown Primary Care-Population Medicine Program, and a Rheumatology Research Foundation Medical and Graduate Student Preceptorship Award.

Ethics Statement: Ethical approval to report this submission was obtained from the Brown University Health Institutional Review Board (IRB #2065997-5).

Prior Presentation: Presented at the 2025 Rhode Island American Academy of Pediatrics (AAP) Annual Meeting in Warwick, RI, 2025, 17th Annual International Health Care Transition Research Consortium at the 26th Annual Chronic Illness and Disability Conference: Transition from Pediatric to Adult-Based Care in Houston, TX, and the 2025 American College of Rheumatology (ACR) Convergence Annual Meeting in Chicago, IL.

Correspondence

Victoria Koenigsberger, BA
222 Richmond Street
Providence, RI 02903
victoria_koenigsberger@brown.edu

Screening for Celiac Disease in Children: Practical Guidance for Primary Care Providers

PRERANA BARANWAL, MD

ABSTRACT

Celiac disease is prevalent in the pediatric population. However, screening for celiac disease can be confusing given the variety of tests available and current guidelines are not always widely known in the medical community. As most children with celiac disease will initially present to their primary care providers (PCPs), PCPs play an integral role in identifying patients at risk for celiac disease. This review provides practical guidance for PCPs screening pediatric patients for celiac disease.

KEYWORDS: Celiac disease; pediatrics; gastroenterology; gluten; screening

INTRODUCTION

Celiac disease is an autoimmune systemic disorder with a genetic component in which gluten exposure/consumption can lead to an inflammatory enteropathy with gastrointestinal and/or extraintestinal signs/symptoms of varying severity.¹ Celiac disease is highly prevalent in the pediatric population, with 0.7–1.4% of children affected globally by the disease,² thus making it one of the most common autoimmune disorders in children.³ The presenting signs/symptoms of celiac disease can be variable. Commonly, children can present with abdominal pain, constipation, diarrhea, vomiting, slow weight gain/weight loss, poor linear growth, or rashes, and some children can have no signs/symptoms at all.¹ Given the variable presentation, children sometimes remain undiagnosed.⁴ Early identification of celiac disease is vital not only for symptomatic improvement, but also in order to address potential complications of the disease as soon as possible (such as weight/growth issues, micronutrient deficiencies, certain types of cancer, fertility issues, etc.).¹ According to current guidelines in North America, screening for celiac disease occurs via bloodwork, and confirmation of celiac disease is through an esophagogastroduodenoscopy, or an upper endoscopy with biopsies.^{1,5-7} As most children with celiac disease initially present to their primary care provider, pediatricians and other primary care providers caring for children play a key role in identifying patients who need to be screened for celiac disease. However, screening for celiac disease can often be confusing, as there are many different tests available and guidelines are not always

widely known in the medical community. This review provides practical guidance for primary care providers screening pediatric patients for celiac disease. This review is intended to be an overview; individual patients may need different approaches based on their specific signs/symptoms.

WHICH CHILDREN SHOULD BE SCREENED?

Symptomatic Children

Celiac disease can be highly variable in presentation and can present with signs/symptoms (gastrointestinal and/or extraintestinal) or can be asymptomatic. Common signs/symptoms at presentation for pediatric patients include but are not limited to abdominal pain, constipation, diarrhea, vomiting, slow weight gain/weight loss, poor linear growth, rash, fatigue, abdominal distention, bloating, iron deficiency anemia, dental enamel erosions, joint pain, osteopenia, short stature, delayed puberty, neurologic abnormalities (including but not limited to migraines, neuropathy, seizures, movement disorders, difficulty concentrating), and elevated liver enzymes.¹

Children at High-Risk for Celiac Disease

The following groups of children are at high-risk for celiac disease and should be screened for celiac disease, even if they are asymptomatic^{1,5,8}:

- Children who have a first-degree relative with celiac disease
- Children with selective IgA deficiency
- Children with Trisomy 21
- Children with type 1 diabetes
- Children with juvenile idiopathic arthritis
- Children with autoimmune thyroid disease
- Children with autoimmune liver disease
- Children with Williams Syndrome
- Children with Turner Syndrome

For asymptomatic children in these higher-risk populations, current guidelines in North America recommend that screening for celiac disease begin at around three years of age (on a gluten-containing diet for at least one year prior to testing),^{1,5} or when the related condition is initially diagnosed,^{1,5} and if the initial testing is negative, at intervals thereafter.^{1,5}

Of note, a gluten-containing diet of greater than or equal to 10g of gluten (two slices of whole wheat bread) per day for

greater than or equal to eight weeks¹ is generally considered adequate to allow for more reliable screening results.

INITIAL TESTING TO SCREEN FOR CELIAC DISEASE

There are a variety of tests associated with celiac disease, which can make it difficult to know which test to use and in what age group. Furthermore, hospitals/clinics often have non-specific names assigned to certain tests, such as “celiac panel,”¹ which may or may not include the testing a patient actually needs. **Table 1** includes a general guideline as to which test to use in various groups in the pediatric population.

Importantly, the child should be on an adequate gluten-containing diet at the time of performing the screening tests. Consuming a gluten-free or gluten-limited diet may lead to a false negative result.^{1,5}

Table 1. Summary of Initial Screening Tests for Celiac Disease for Pediatric Patients

Group	Initial Screening Test(s)
≥2 years old	Tissue transglutaminase IgA (TTG-IgA) and immunoglobulin A (IgA)
<2 years old	Tissue transglutaminase IgA (TTG-IgA) and deamidated gliadin peptide IgG (DGP-IgG)
Selective IgA Deficiency	Tissue transglutaminase (TTG-IgG) or deamidated gliadin peptide (DGP-IgG)

Children ≥2 Years Old

In children ≥2 years old, tissue transglutaminase IgA (TTG-IgA) and immunoglobulin A (IgA) are recommended as initial screening tests, as they are the most reliable and cost-effective.¹ The anti-endomysium antibody IgA (EMA-IgA) is more specific but less sensitive (99% specificity, 73% sensitivity) than the TTG-IgA test (97.9% specificity, 92.8% sensitivity) and is more expensive,^{1,9} and thus is not recommended as the initial screening test in this age group.

Children <2 Years Old

In children <2 years old, TTG-IgA and EMA-IgA tests are not as sensitive.¹ Thus, in this age group, tissue transglutaminase IgA (TTG-IgA) and deamidated gliadin peptide-IgG (DGP-IgG) are recommended as initial screening tests by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN),¹ though recent adult guidelines have suggested otherwise.¹⁰

In the Case of Selective IgA Deficiency

In children with selective IgA deficiency, which is seen more often in children with celiac disease,¹ the IgA-based screening tests are not reliable. As such, IgG-based tests should be used for screening, such as tissue transglutaminase IgG (TTG-IgG) or deamidated gliadin peptide-IgG (DGP-IgG).¹

The Role of Antigliadin Antibody Tests

Antigliadin antibody IgA (AGA-IgA), antigliadin antibody IgG (AGA-IgG) are not recommended for initial screening for celiac disease.¹

The Role of HLA-DQ2 and HLA-DQ8

HLA-DQ2 and HLA-DQ8 are genetic markers for celiac disease but they can also be present in up to 40% of the general population.^{1,11} A positive result for one or both of these markers is not diagnostic of celiac disease. However, a negative result for both makes celiac disease unlikely. These tests are expensive and are generally not used as an initial screening test for celiac disease.^{1,11} They can be used in equivocal or unclear cases for additional information, such as if there is a discrepancy between serological testing and endoscopic pathology, and the diagnosis of celiac disease is in question.^{1,11}

Other Situations

It is important to remember that in the setting of an acute infection, tissue transglutaminase (TTG) may be elevated, and will return to normal after the infection is resolved.¹ If the TTG is found to be elevated in this setting, it is recommended to repeat the testing once the infection has resolved.¹

Similarly, children with autoimmune conditions that are associated with celiac disease may have an elevated TTG-IgA that is unrelated to celiac disease.¹ In these cases, if the TTG-IgA is less than three times the upper limit of normal, EMA-IgA should be tested.¹ If the EMA-IgA is positive, then referral to a gastroenterologist is warranted, as endoscopy with biopsies is likely necessary to confirm the diagnosis of celiac disease.¹ If the EMA-IgA is negative and the patient does not exhibit other signs/symptoms that could suggest celiac disease, then repeating screening tests for celiac disease in 6–12 months and monitoring signs/symptoms is recommended.¹

WHAT TO DO IF SCREENING FOR CELIAC DISEASE IS POSITIVE

If a screening test for celiac disease is positive, the patient must be referred to a gastroenterologist for further evaluation and management. Typically, after discussion with the patient/family, the gastroenterologist will perform an upper endoscopy with biopsies to confirm the diagnosis of celiac disease.^{1,12} Importantly, once a screening test for celiac disease is positive, the patient should ideally stay on a gluten-containing diet until they are able to see the gastroenterologist and undergo upper endoscopy. If the child is already consuming a gluten-free diet or a gluten-limited diet when undergoing upper endoscopy with biopsies, this may lead to a false negative result.^{1,5}

PCPS' ROLE IN DIAGNOSIS AND MANAGEMENT OF CELIAC DISEASE

PCPs play an integral role in the diagnosis and management of celiac disease.¹³ As they are usually the first provider a patient will see, PCPs can facilitate the process of recognizing signs/symptoms of celiac disease, knowing who and when to screen for celiac disease, and coordinating referral to gastroenterology as appropriate. Furthermore, PCPs play an important role in long-term follow up as well, including but not limited to monitoring weight gain and linear growth, monitoring for nutritional deficiencies or other potential complications related to celiac disease, and emphasizing the importance of adherence to the gluten-free diet for management of celiac disease.

CONCLUSION

Celiac disease is an autoimmune disease that can have a highly variable presentation and which is highly prevalent in the pediatric population.¹ Early recognition and appropriate screening is important to not only treat the signs/symptoms of celiac disease, but also to address potential complications related to celiac disease. PCPs play a vital role in this process and are at the frontlines of initiating appropriate screening for patients.¹³

References

- Hill ID, Fasano A, Guandalini S, et al. NASPGHAN Clinical Report on the Diagnosis and Treatment of Gluten-related Disorders. *J Pediatr Gastroenterol Nutr.* 2016;63(1):156-165. doi:10.1097/MPG.0000000000001216
- Singh P, Arora A, Strand TA, et al. Global Prevalence of Celiac Disease: Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol.* 2018;16(6):823-836.e2. doi:10.1016/j.cgh.2017.06.037
- Roberts SE, Morrison-Rees S, Thapar N, et al. Systematic review and meta-analysis: the incidence and prevalence of paediatric coeliac disease across Europe. *Aliment Pharmacol Ther.* 2021;54(2):109-128. doi:10.1111/apt.16337
- Catassi C, Verdu EF, Bai JC, Lionetti E. Coeliac disease. *Lancet.* 2022;399(10344):2413-2426. doi:10.1016/S0140-6736(22)00794-2
- Hill ID, Dirks MH, Liptak GS, et al. Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr.* 2005;40(1):1-19. doi:10.1097/00005176-200501000-00001
- Husby S, Murray JA, Katzka DA. AGA Clinical Practice Update on Diagnosis and Monitoring of Celiac Disease-Changing Utility of Serology and Histologic Measures: Expert Review. *Gastroenterology.* 2019;156(4):885-889. doi:10.1053/j.gastro.2018.12.010
- Zingone F, Bai JC, Cellier C, Ludvigsson JF. Celiac Disease-Related Conditions: Who to Test? *Gastroenterology.* 2024;167(1):64-78. doi:10.1053/j.gastro.2024.02.044
- US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, et al. Screening for Celiac Disease: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2017;317(12):1252-1257. doi:10.1001/jama.2017.1462
- Chou R, Bougatsos C, Blazina I, Mackey K, Grusing S, Selph S. Screening for Celiac Disease: Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA.* 2017;317(12):1258-1268. doi:10.1001/jama.2016.10395
- Rubio-Tapia A, Hill ID, Semrad C, et al. American College of Gastroenterology Guidelines Update: Diagnosis and Management of Celiac Disease. *Am J Gastroenterol.* 2023;118(1):59-76. doi:10.14309/ajg.0000000000002075
- Brown NK, Guandalini S, Semrad C, Kupfer SS. A Clinician's Guide to Celiac Disease HLA Genetics. *Am J Gastroenterol.* 2019;114(10):1587-1592. doi:10.14309/ajg.0000000000000310
- Fasano A, Catassi C. Clinical practice. Celiac disease. *N Engl J Med.* 2012;367(25):2419-2426. doi:10.1056/NEJMcp1113994
- Tye-Din JA. Review article: Follow-up of coeliac disease. *Aliment Pharmacol Ther.* 2022;56 Suppl 1:S49-S63. doi:10.1111/apt.16847

Author

Prerana Baranwal, MD, Assistant Professor of Pediatrics, The Warren Alpert Medical School of Brown University; Pediatric Gastroenterologist, Hasbro Children's Hospital, Providence RI.

Disclosures

Ethical-approval Statement: Ethical approval is not applicable to this article.

Conflicts of Interest: None

Correspondence

Prerana Baranwal, MD
Division of Pediatric Gastroenterology, Nutrition, & Liver Diseases
Hasbro Children's Hospital
593 Eddy Street, Providence RI 02903
401-444-8306
prerana_baranwal@brown.edu

Metabolic Dysfunction-Associated Steatotic Liver Disease: A Review and Cases Regarding Liver Transplantation

KIMBERLY HO, MD; PAIGE MCLEAN DIAZ, MD

INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as nonalcoholic fatty liver disease (NAFLD), is a large global public health issue. MASLD encompasses a spectrum ranging from steatosis to metabolic dysfunction-associated steatohepatitis (MASH, formerly NASH), advanced fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). The nomenclature change reflects the recognition that metabolic dysfunction is the primary driver of this disease.¹ This review synthesizes current understanding of MASLD epidemiology, pathophysiology, screening strategies, and management approaches with particular emphasis on recently approved therapeutics and clinical scenarios including liver transplantation.

EPIDEMIOLOGY AND BURDEN OF DISEASE

The global prevalence of MASLD has increased dramatically over the last three decades, rising to more than 50% in some populations.² The current estimated global prevalence is 38.2%.² Per the Global Burden of Disease (GBD) 2021 data, there are increasing rates and trends of point prevalence, annual incidence, and disability-adjusted life-years (DALYs) across 204 countries with approximately 2.2 times as many DALYs in 2021 compared to three decades prior.³

The prevalence of MASLD is substantially higher among specific subgroups. A meta-analysis of 156 studies including 1.8 million people with type 2 diabetes (T2DM) found a global MASLD prevalence of 65% and MASH 32%.⁴ The bidirectional relationship is clinically significant as well. MASLD increases the risk of new-onset T2DM by a factor of 2.2 or 3.4 in the presence of advanced liver disease.⁵

MASLD increases the risk of cirrhosis and HCC. A meta-analysis of 64 studies showed a pooled incidence rate of HCC of 1.25 per 1000 person-years among persons with MASLD, but 20 per 1000 person-years among persons with MASLD-related cirrhosis.⁶ Beyond hepatic complications, MASLD increases the risk of fatal and nonfatal cardiovascular disease (CVD) by a factor of 1.5 independent of traditional risk factors and by 2.5 in the presence of severe liver disease.⁷ Additional extrahepatic manifestations include increase risk of new-onset heart failure,⁸ atrial fibrillation,⁹ CKD,¹⁰ and other extrahepatic cancers by a factor of 1.2–1.5.¹¹ The leading causes of death in MASLD are CVD, extrahepatic cancers, and cirrhosis-related complications, in that order.¹

NATURAL HISTORY

The highest number of coexisting metabolic disorders in MASLD patients includes T2DM, obesity, and hypertension.¹ In roughly 30% of MASLD patients, disease progression is driven by lipotoxic effects (i.e., adiposity, or accumulation of visceral fat, and insulin resistance) leading to hepatocellular damage and lobular inflammation, which are the hallmark features of MASH that progress to fibrosis and cirrhosis.¹²

Liver fibrosis is staged on a five-point scale from F0 to F4. Patients with F0 (no fibrosis) or F1 (perisinusoidal or portal fibrosis) have an estimated time to cirrhosis of 30 to 35 years. F2 (perisinusoidal and portal or periportal fibrosis) represents a critical threshold since it is a strong predictor of death from any cause and liver-related complications. Progression to cirrhosis from F2 is approximately 20 years. F3 (septal and bridging fibrosis) progresses to cirrhosis in about five years. Once cirrhosis (F4) develops, there is less than 10% chance per year of reversing to MASH with a 0.5–2.5% annual risk of HCC and 10% annual risk of hepatic decompensation.¹

Additional factors that hasten MASLD progression include alcohol, genetic variants (i.e., PNPLA3, TM6SF2, APOB), and hepatitis B and C infection.¹

PATHOPHYSIOLOGY

The pathophysiology of MASLD is multifactorial. Insulin resistance in adipose tissue increases intracellular lipid droplets and flux of free fatty acid into liver, thereby activating stress and inflammatory pathways. This promotes cell death, fibrinogenesis, and carcinogenesis.^{1,13}

De novo lipogenesis (DNL) is markedly elevated in patients with MASLD/MASH.¹⁴ Obesity and insulin resistance disrupt signals from the gastrointestinal tract and adipose tissue that normally regulate carbohydrate, lipid, and amino acid metabolism. In MASLD/MASH, increased glucose flux via DNL leads to higher conversion of glucose into blood lactate, which is released into portal circulation and taken up by hepatocytes and hepatic stellate cells, contributing to fibrosis. Fructose that is metabolized into acetyl-CoA also serves as a key substrate for DNL and induces gastrointestinal inflammation in gut macrophages.

On a cellular level, MASLD/MASH is associated with mitochondrial structural abnormalities, such as swollen mitochondria, fragmented cristae, and decreased mitochondrial

density.^{14,15} These mitochondrial damages reduce hepatic fatty acid oxidation. While this initially stimulates pathways for mitochondrial biogenesis, there is poor reserve to do this in MASH.¹⁵ Furthermore, in high concentrations of glucose substrates in MASLD/MASH, the flux of lactate is higher, which has important implications for the liver. Hepatic stellate cells utilize lactate, which is a key cellular contributor to liver fibrosis. As such, this may explain higher risk of MASH in patients with T2DM.^{14,15}

Genetic variants also contribute to MASLD/MASH pathophysiology. The PNPLA3 I148M variant, which encodes liver and adipose expressed membrane-bound lipid droplet-associated protein, results in increased lipid droplet stability and accumulation.¹⁶ This variant has been found associated with increased MASLD risk and higher rates of fibrosis, cirrhosis, and HCC.¹⁷

Insulin regulation, which physiologically insulin would inhibit adipose tissue lipolysis, is defective in MASLD/MASH. Insulin resistance increases more fatty acid delivery to the liver even in the postprandial state, driving both increased DNL flux, impaired adipose tissue lipolysis, and steatosis.¹⁷

Some basic science research has suggested leveraging other biochemical pathways in the liver and the futile lipid cycle to help systemic metabolic homeostasis. One of which is the glycerol/fatty acid cycle, which involves repetitive hydrolysis of glycerides and re-esterification of fatty acids into glycerides in the liver. This allows fatty acids to be sequestered as glycerol in the liver instead, reducing fatty acid stores in liver. Moreover, this cycle requires ATP consumption and may help reduce metabolic burden in MASLD/MASH.¹⁸

SCREENING AND DIAGNOSIS

Risk factors for MASLD include T2DM, multiple metabolic risk factors (i.e., atherogenic dyslipidemia [elevated triglycerides and apolipoprotein B, small LDL particles, and low HDL cholesterol concentrations], elevated blood pressure, elevated plasma glucose, a prothrombotic state, and a proinflammatory state), and elevated liver enzymes.¹⁹

Fibrosis-4 index (FIB-4) is a widely used screening methods for MASLD/MASH in primary care clinics and uses noninvasive blood-based fibrosis biomarkers calculated from age, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and platelet count.¹ FIB-4 stratifies patients into low, indeterminate, and high-risk for MASLD. Low-risk patients can be managed by primary care providers with re-evaluation every one to three years. Indeterminate-risk patients should be referred for additional testing based on liver-specific biomarkers, vibration-controlled transient elastography (VCTE), Enhanced Liver Fibrosis (ELF) test, or histology. High-risk patients should also have a VCTE and be referred to a hepatologist.¹

MANAGEMENT FOR MASLD, MASH, AND MASH CIRRHOSIS

Lifestyle Modifications

Lifestyle modification remains the cornerstone of MASLD management and is indicated for all patients at risk, including those with low-risk FIB-4.^{1,20} Weight loss targets are stratified by therapeutic goal: 1) at least 5% to reduce liver steatosis; 2) 7–10% to reduce liver inflammation; and 3) at least 10% to reduce liver fibrosis.²⁰ However, less than 20% of individuals achieve and maintain requisite levels of weight loss over sustained periods.¹ The Mediterranean diet, physical exercise (ideally >150 minutes per week of moderate or 75 min/week of vigorous intensity), and alcohol and smoking abstinence are recommended. Alcohol is the strongest modifiable risk factor with increased risk for liver-related mortality in overweight or obese males starting at 15 drinks per week. Overall, there is no quantifiable recommended safe level of alcohol consumption. Per the European Association for the Study of Liver (EASL) Practice Guidelines, avoidance of alcohol for individuals with or at risk for MASLD is generally recommended.²⁰ Vitamin E supplementation may also help reduce liver inflammation, specifically reduction in aminotransferases, steatosis, and cellular ballooning on biopsy.²¹ However, vitamin E has not been shown to have an antifibrotic benefit. As such, recent guidelines do not widely recommend vitamin E supplementation but can be considered in select individuals without diabetes to improve steatosis.²²

EXISTING FDA-APPROVED PHARMACEUTICAL THERAPY

Resmetirom

Resmetirom, a selective thyroid hormone receptor beta (THR-beta) agonist, was the first FDA-approved medication for treating noncirrhotic MASH with moderate to advanced fibrosis (F2-3) in March 2024.²³ The approval was based on the phase 3 MAESTRO-NASH trial, which randomized 966 patients with biopsy-proven MASH and F1-3 fibrosis to receive resmetirom 80 mg, 100 mg, or placebo daily for 52 weeks.²³ Both resmetirom doses achieved the primary endpoints (MASH resolution without worsening of fibrosis) in 25.9% (80 mg) and 29.9% (100 mg) versus 9.7% (placebo). There was fibrosis improvement by at least one stage without worsening of MASH in 24.2% (80 mg) and 25.9% (100 mg) versus 14.2% (placebo).

Resmetirom improves hepatocyte mitochondrial function, promotes mitochondrial biogenesis and mitophagy, increases hepatic fatty acid beta-oxidation, decreases lipotoxic burden, regulates bile acid synthesis, facilitates hepatic uptake of LDL, and thereby lowers triglyceride and cholesterol level. The most common adverse events are nausea and diarrhea.^{24,25}

Treatment initiation does not require liver biopsy. Per AASLD guidelines, noninvasive tests such as VCTE would

suffice to identify adults with MASH and F2-3 fibrosis. The recommended dosage is 100 mg daily for person over 100 kg or 80 mg for those less than 100 kg.²⁶ Main exclusion criteria include compensated or decompensated cirrhosis, active liver diseases, sub-optimally managed thyroid disease, or ongoing alcohol consumption (>20 g/day for women or >30 g/day for men).²⁷

Semaglutide

Semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, received accelerated FDA approval in August 2025 for treating MASH with moderate to advanced fibrosis (F2-F3) based on interim results from the phase 3 ESSENCE trial.^{1,28} At 72 weeks, subcutaneous semaglutide 2.4 mg weekly achieved both primary histologic endpoints, which was resolution of MASH without worsening of fibrosis (62.9% vs 34.3% placebo) and fibrosis stage reduction without worsening of MASH (36.8% vs 22.4% placebo).²⁸ Semaglutide also achieved combined resolution of MASH and reduction in liver fibrosis in 32.7% vs 16.1% with placebo with mean body weight reduction of 10.5% vs 2% with placebo.²⁸ The most common adverse events were diarrhea, nausea, constipation, and vomiting. Per the AASLD guidelines from November 2025, semaglutide is not approved as an indication for patients with MASH cirrhosis. Those with compensated cirrhosis on semaglutide for another FDA-approved indication should be monitored carefully.²⁹

Other Emerging Pharmaceutical Therapy

Multiple therapeutic classes are under active investigation for MASH, with incretin-based agents showing the most promising results to date. GLP-1 receptor agonists and dual/triple incretin agonists, including tirzepatide, survodutide, and retatrutide, have demonstrated substantial rates of MASH resolution and reductions in liver fat, with tirzepatide achieving up to 62% resolution without fibrosis worsening in phase 2b trials.^{1,30,31} PPAR agonists (i.e., lanifibranor) and FGF21 analogues have also shown meaningful improvements in steatohepatitis and fibrosis in mid- to late-phase trials.^{1,27,32-42} Additional approaches, including SGLT2 inhibitors, genetic therapies targeting variants such as PNPLA3 and HSD17B13, and metabolic pathway modulators (i.e., DGAT2 and fatty acid synthase inhibitors), demonstrate varying degrees of efficacy, though some programs have been discontinued due to limited benefit.⁴³⁻⁴⁶ Emerging agents targeting inflammation and fibrosis pathways, such as phosphodiesterase inhibitors, adenosine receptor agonists, and glucocorticoid receptor modulators, are in earlier stages of development.^{44,47-59} While several therapies show encouraging results, no single agent has demonstrated universal efficacy, and combination strategies are increasingly being explored to address the multifactorial pathogenesis of MASLD.

MANAGEMENT OF COMORBID CONDITIONS

Cardiovascular Risk Factors

Statins should be used when indicated for cardiovascular risk reduction. The side effect of elevated transaminases is not associated with clinically significant liver disease and typically resolves spontaneously without medication interruption.⁶⁰

Diabetes Management

GLP-1 receptor agonists are preferred for T2DM management in patients with MASLD given their dual benefits for glycemic control and liver histology.^{61,62} Pioglitazone is an alternative, but it causes dose-dependent weight gain that can be mitigated when combined with SGLT2 inhibitors or GLP-1 receptor agonists.⁶¹ Combination therapy with pioglitazone and GLP-1 receptor agonists has shown to reduce hepatic steatosis.²⁷

Bariatric Surgery

Bariatric surgery is indicated for treatment of obesity and T2DM when inadequately controlled by lifestyle modification, particularly in patients with BMI >35 and MASLD.⁶³ Sleeve gastrectomy is preferred over Roux-en-Y gastric bypass after liver transplantation due to fewer malabsorption issues.

LIVER TRANSPLANTATION

Per the United States Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR) (2022), MASLD was second most common indication for liver transplantation in non-HCC patients and is the most common in HCC pts.^{64,65} Similar trends are observed in Europe, Latin America, and the Middle East.⁶⁶⁻⁷³ Liver transplantation is indicated for patients with MASLD who develop decompensated cirrhosis or HCC.²⁰

Patients with MASLD awaiting transplantation are typically older, have higher BMI, and have greater prevalence of metabolic comorbidities including diabetes, hypertension, dyslipidemia, coronary artery disease, and chronic kidney disease.⁷⁴ Per AASLD guidelines, BMI >40 is a relative contraindication for liver transplantation.⁷⁵ The EASL guidelines recommend BMI <35 for optimal outcomes.²⁰ Pre-transplant optimization includes comprehensive cardiovascular risk assessment, diabetes optimization, weight reduction with consideration of bariatric surgery if BMI >35, nutritional assessment to minimize sarcopenia risk, and regular HCC surveillance.²⁰ Management of post-transplant MASLD continues to be a multidisciplinary, multifaceted approach including lifestyle modification, metabolic comorbidity management, regular surveillance for fibrosis progression, and immunosuppression.²⁰

MASLD liver transplant recipients demonstrate favorable outcomes comparable to non-MASLD patients. Per the

California Liver Network Study, MASLD patient post-transplant survival at five years was at least 83%.⁷⁴ Other studies found that five-year survival for patients with MASLD in addition to other liver diseases were comparable to patients without MASLD.^{76,77} However, recurrent MASLD occurs in almost all recipients by five years post-transplantation. Recurrent MASLD and MASH was found to occur in frequencies of 35–49% and 11–24%, respectively.⁷⁸ Fibrosis occurred in 4–25%.⁷⁸ This is likely driven multifactorially, including metabolic comorbidities, immunosuppressive medication and steroids, donor-related factors, and chronic inflammation. Adverse outcomes such as disease-related cirrhosis (0–2%), graft failure (3–9%), re-transplant (0–1%), HCC (0%), and mortality (0%) were fortunately infrequent five years post-transplant.⁷⁸

CLINICAL SCENARIOS

Case 1: When to consider liver transplant?

A 60-year-old female with T2DM, obesity (BMI 38), and MASH cirrhosis presents with new-onset ascites requiring large-volume paracentesis and a MELD-Na score of 18.

Liver transplantation should be considered when patients with MASLD develop decompensated cirrhosis (i.e., ascites, hepatic encephalopathy, variceal bleeding) or HCC.²⁰ When the MELD-Na score is greater than 10, referral to hepatology should be made. When the MELD-Na score is greater than 14, consideration for liver transplantation is recommended.⁷⁹ The median survival from first hepatic decompensation to death or transplantation in MASLD is approximately two years with ascites being the most common initial liver-related event (69.5%).⁸⁰ Pre-transplant evaluation should include comprehensive cardiovascular risk assessment given the high prevalence of coronary artery disease in MASLD patients, diabetes optimization preferably with GLP-1 receptor agonists, and weight reduction strategies. Per above, BMI >40 is a relative contraindication as stated in the AASLD guidelines, and EASL recommends BMI <35 for optimal outcomes.²⁰ Despite higher comorbidity burden, MASLD patients demonstrate favorable post-transplant outcomes comparable to non-MASLD recipients with five-year survival of 83–88%.

Case 2: How to assess for response to resmetirom or semaglutide?

A 60-year-old male with T2DM, BMI 35, MASH and F2 fibrosis has been on resmetirom 100 mg daily for 12 months. His liver stiffness by VCTE has decreased from 13 kPa to 9 kPa. He asks whether he should continue therapy or consider switching to semaglutide.

Overall, validated stopping rules for MASH pharmacotherapy have not been established. For resmetirom, treatment response is suggested by reductions from baseline in ALT (>17 U/L or $\geq 20\%$), liver stiffness by VCTE ($\geq 30\%$),

MRE ($\geq 20\%$), or ELF score (≥ 0.5) at 72 weeks. Patients are recommended to continue therapy if these endpoints are met. Resmetirom should be discontinued if hepatotoxicity develops (AST or ALT >5x ULN on two occasions, total bilirubin >2.5 mg/dL with elevated transaminases, or INR >1.5 with elevated liver enzymes).²⁶

For semaglutide, similar response criteria apply (reductions in ALT (>17 U/L or $\geq 20\%$), CAP ($\geq 30\%$), VCTE LSM ($\geq 30\%$), MRE ($\geq 20\%$), or ELF (≥ 0.5)). Non-response may be suspected if ALT or noninvasive tests worsen.²⁹ For patients with T2DM or obesity requiring cardiometabolic benefits, semaglutide may be preferred given its established cardiovascular and renal protective effects. Semaglutide should be avoided if there is a history of medullary thyroid carcinoma, pancreatitis, or severe gastroparesis.

This patient is responding appropriately to resmetirom given the decrease in liver stiffness over 30% and does not prompt an urgent switch. Semaglutide can be considered if he is no longer meeting those endpoints and may help T2DM management.

Case 3: When to screen for HCC when patient has fibrosis?

A 60-year-old man with T2DM and MASLD with F3 fibrosis and FIB-4 >2.3 inquires about need for HCC surveillance. Guidelines typically target patients with F3 (advanced) fibrosis, cirrhosis (F4), or chronic hepatitis B for HCC screening. It is generally not routinely recommended for patients with F2 (moderate) fibrosis.^{37,81} AASLD specifically recommends against routine use of HCC surveillance in patients with MASLD who have advanced fibrosis (F3) but without cirrhosis (Level 3, Weak Recommendation). They note that while nearly one-fourth of MASLD-related HCC occurs in the absence of cirrhosis, these patients have a very low annual HCC incidence of 0.008 per 100 person-years, making surveillance not cost-effective.³⁷ However, surveillance may be considered on a case-by-case basis in select patients with clinical suspicion for under-staging of fibrosis by noninvasive markers or biopsy, evidence of fibrosis progression, or additional high-risk features such as diabetes.³⁷

For this patient with F3 fibrosis and T2DM, and elevated FIB-4, close monitoring with repeat noninvasive testing every one to two years is warranted to detect progression to cirrhosis. We also recommend formal HCC surveillance with VCTE and AFP every six months given additional risk factors.

GAPS IN THE FIELD AND FUTURE DIRECTIONS

There remain critical gaps in MASLD management. Despite a few approved therapies and multiple emerging trials, optimal treatment selection for individual patients remains unclear. Head-to-head clinical trials comparing current medications are lacking.⁸² No reliable predictors identify

patients likely to respond to resmetirom or semaglutide, and guidelines are needed to determine best practices for stopping ineffective medications. Combination therapy (i.e. resmetirom and semaglutide together for example) have also not been studied. There are also geographic and ethnic differences in MASLD prevalence, progression, and treatment response, which require further investigation. For example, large scale clinical trials on GLPs have limited representation from minority groups, which the authors of this review are actively studying. Furthermore, no liver-directed pharmacotherapies are yet available for MASLD-related cirrhosis, which is a major unmet need.²⁰ More research and real-world prospective cohort studies are needed to improve risk stratification, better identify patients at risk for progressive MASH, and consider potential applications in the advent of artificial intelligence.

CONCLUSION

In summary, MASLD is a leading cause of chronic liver disease worldwide, driven by the global epidemics of obesity and T2DM. It has substantial morbidity and mortality from both hepatic and extrahepatic complications. Resmetirom and semaglutide are major therapeutic advances as the first FDA-approved medications for noncirrhotic MASH with F2-F3 fibrosis. Effective MASLD management requires a multidisciplinary approach incorporating lifestyle modifications, optimization of other metabolic comorbidities, judicious use of pharmacotherapy, and consideration of liver transplantation among individuals with decompensated cirrhosis or HCC. This review highlights the areas that require additional work to address the growing clinical burden of MASLD, including cost-effective diagnostic and treatment strategies and collaborative care coordination to provide holistic patient care.

References

[Editor's note: Email corresponding author for complete list of references]

1. Targher G, Valenti L, Byrne CD. Metabolic Dysfunction-Associated Steatotic Liver Disease. *N Engl J Med*. Aug 14 2025; 393(7):683-698. doi:10.1056/NEJMra2412865
2. Younossi ZM, Golabi P, de Avila L, et al. The global epidemiology of NAFLD and NASH in patients with type 2 diabetes: A systematic review and meta-analysis. *J Hepatol*. Oct 2019;71(4):793-801. doi:10.1016/j.jhep.2019.06.021
3. Zhang H, Zhou XD, Shapiro MD, et al. Global burden of metabolic diseases, 1990-2021. *Metabolism*. Nov 2024;160:155999. doi:10.1016/j.metabol.2024.155999
4. En Li Cho E, Ang CZ, Quek J, et al. Global prevalence of non-alcoholic fatty liver disease in type 2 diabetes mellitus: an updated systematic review and meta-analysis. *Gut*. Nov 2023; 72(11):2138-2148. doi:10.1136/gutjnl-2023-330110
5. Mantovani A, Petracca G, Beatrice G, Tilg H, Byrne CD, Targher G. Non-alcoholic fatty liver disease and risk of incident diabetes mellitus: an updated meta-analysis of 501 022 adult individuals. *Gut*. May 2021;70(5):962-969. doi:10.1136/gutjnl-2020-322572
6. Thomas JA, Kendall BJ, Dalais C, Macdonald GA, Thrift AP. Hepatocellular and extrahepatic cancers in non-alcoholic fatty liver disease: A systematic review and meta-analysis. *Eur J Cancer*. Sep 2022;173:250-262. doi:10.1016/j.ejca.2022.06.051
7. Mantovani A, Csermely A, Petracca G, et al. Non-alcoholic fatty liver disease and risk of fatal and non-fatal cardiovascular events: an updated systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. Nov 2021;6(11):903-913. doi:10.1016/s2468-1253(21)00308-3
8. Mantovani A, Petracca G, Csermely A, et al. Non-alcoholic fatty liver disease and risk of new-onset heart failure: an updated meta-analysis of about 11 million individuals. *Gut*. Jul 25 2022; doi:10.1136/gutjnl-2022-327672
9. Mantovani A, Morandin R, Sani E, et al. MASLD Is Associated With an Increased Long-Term Risk of Atrial Fibrillation: An Updated Systematic Review and Meta-Analysis. *Liver Int*. Jan 2025;45(1):e16128. doi:10.1111/liv.16218
10. Mantovani A, Petracca G, Beatrice G, et al. Non-alcoholic fatty liver disease and risk of incident chronic kidney disease: an updated meta-analysis. *Gut*. Jan 2022;71(1):156-162. doi:10.1136/gutjnl-2020-323082
11. Mantovani A, Petracca G, Beatrice G, et al. Non-alcoholic fatty liver disease and increased risk of incident extrahepatic cancers: a meta-analysis of observational cohort studies. *Gut*. Apr 2022; 71(4):778-788. doi:10.1136/gutjnl-2021-324191
12. Le P, Payne JY, Zhang L, et al. Disease State Transition Probabilities Across the Spectrum of NAFLD: A Systematic Review and Meta-Analysis of Paired Biopsy or Imaging Studies. *Clin Gastroenterol Hepatol*. May 2023;21(5):1154-1168. doi:10.1016/j.cgh.2022.07.033
13. Mashek DG, Khan SA, Sathyanarayan A, Ploeger JM, Franklin MP. Hepatic lipid droplet biology: Getting to the root of fatty liver. *Hepatology*. Sep 2015;62(3):964-7. doi:10.1002/hep.27839
14. Steinberg GR, Valvano CM, De Nardo W, Watt MJ. Integrative metabolism in MASLD and MASH: Pathophysiology and emerging mechanisms. *Journal of Hepatology*. 2025;83(2):584-595. doi:10.1016/j.jhep.2025.02.033
15. Fromenty B, Roden M. Mitochondrial alterations in fatty liver diseases. *J Hepatol*. Feb 2023;78(2):415-429. doi:10.1016/j.jhep.2022.09.020
16. Romeo S, Kozlitina J, Xing C, et al. Genetic variation in PNP-LA3 confers susceptibility to nonalcoholic fatty liver disease. *Nat Genet*. Dec 2008;40(12):1461-5. doi:10.1038/ng.257
17. Do A, Zahrawi F, Mehal WZ. Therapeutic landscape of metabolic dysfunction-associated steatohepatitis (MASH). *Nat Rev Drug Discov*. Mar 2025;24(3):171-189. doi:10.1038/s41573-024-01084-2
18. Sharma AK, Khandelwal R, Wolfrum C. Futile lipid cycling: from biochemistry to physiology. *Nat Metab*. May 2024;6(5):808-824. doi:10.1038/s42255-024-01003-0
19. Grundy SM, Cleeman JJ, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*. Oct 25 2005;112(17):2735-52. doi:10.1161/circulationaha.105.169404
20. European Association for the Study of the L, European Association for the Study of D, European Association for the Study of O. EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). *J Hepatol*. Sep 2024;81(3):492-542. doi:10.1016/j.jhep.2024.04.031
21. Sanyal AJ, Chalasani N, Kowdley KV, et al. Pioglitazone, Vitamin E, or Placebo for Nonalcoholic Steatohepatitis. *New England Journal of Medicine*. 2010;362(18):1675-1685. doi:10.1056/NEJMoa0907929
22. Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology*. May 1 2023;77(5):1797-1835. doi:10.1097/hep.0000000000000323

23. Harrison SA, Bedossa P, Guy CD, et al. A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis. *New England Journal of Medicine*. 2024;390(6):497-509. doi:10.1056/NEJMoa2309000
24. Kelly MJ, Pietranico-Cole S, Larigan JD, et al. Discovery of 2-[3,5-dichloro-4-(5-isopropyl-6-oxo-1,6-dihydropyridazin-3-yl)oxy]phenyl]-3,5-dioxo-2,3,4,5-tetrahydro[1,2,4]triazine-6-carbonitrile (MGL-3196), a Highly Selective Thyroid Hormone Receptor β agonist in clinical trials for the treatment of dyslipidemia. *J Med Chem*. May 22 2014;57(10):3912-23. doi:10.1021/jm4019299
25. Saponaro F, Sestito S, Runfola M, Rapposelli S, Chiellini G. Selective Thyroid Hormone Receptor-Beta (TR β) Agonists: New Perspectives for the Treatment of Metabolic and Neurodegenerative Disorders. *Front Med (Lausanne)*. 2020;7:331. doi:10.3389/fmed.2020.00331
26. Chen VL, Morgan TR, Rotman Y, et al. Resmetirom therapy for metabolic dysfunction-associated steatotic liver disease: October 2024 updates to AASLD Practice Guidance. *Hepatology*. Jan 1 2025;81(1):312-320. doi:10.1097/HEP.0000000000001112
27. Cusi K, Abdelmalek MF, Apovian CM, et al. Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) in People With Diabetes: The Need for Screening and Early Intervention. A Consensus Report of the American Diabetes Association. *Diabetes Care*. Jul 1 2025;48(7):1057-1082. doi:10.2337/dci24-0094
28. Sanyal AJ, Newsome PN, Kliers I, et al. Phase 3 Trial of Semaglutide in Metabolic Dysfunction-Associated Steatohepatitis. *N Engl J Med*. Jun 5 2025;392(21):2089-2099. doi:10.1056/NEJMoa2413258
29. Bansal MB, Patton H, Morgan TR, Carr RM, Dranoff JA, Allen AM. Semaglutide therapy for metabolic dysfunction-associated steatohepatitis: November 2025 updates to AASLD Practice Guidance. *Hepatology*. Nov 7 2025;doi:10.1097/HEP.0000000000001608
30. Loomba R, Hartman ML, Lawitz EJ, et al. Tirzepatide for Metabolic Dysfunction-Associated Steatohepatitis with Liver Fibrosis. *N Engl J Med*. Jul 25 2024;391(4):299-310. doi:10.1056/NEJMoa2401943
31. Nouredin M, Harrison SA, Loomba R, et al. Safety and efficacy of weekly pemvidutide versus placebo for metabolic dysfunction-associated steatohepatitis (IMPACT): 24-week results from a multicentre, randomised, double-blind, phase 2b study. *Lancet*. Dec 6 2025;406(10520):2644-2655. doi:10.1016/s0140-6736(25)02114-2
32. Harrison SA, Rolph T, Knott M, Dubourg J. FGF21 agonists: An emerging therapeutic for metabolic dysfunction-associated steatohepatitis and beyond. *J Hepatol*. Sep 2024;81(3):562-576. doi:10.1016/j.jhep.2024.04.034
33. Schlein C, Talukdar S, Heine M, et al. FGF21 Lowers Plasma Triglycerides by Accelerating Lipoprotein Catabolism in White and Brown Adipose Tissues. *Cell Metab*. Mar 8 2016;23(3):441-53. doi:10.1016/j.cmet.2016.01.006
34. Geng L, Lam KSL, Xu A. The therapeutic potential of FGF21 in metabolic diseases: from bench to clinic. *Nat Rev Endocrinol*. Nov 2020;16(11):654-667. doi:10.1038/s41574-020-0386-0
35. Zhang J, Li Y. Fibroblast Growth Factor 21 Analogs for Treating Metabolic Disorders. *Front Endocrinol (Lausanne)*. 2015;6:168. doi:10.3389/fendo.2015.00168
36. Caon E, Martins M, Hodgetts H, et al. Exploring the impact of the PNPLA3 I148M variant on primary human hepatic stellate cells using 3D extracellular matrix models. *J Hepatol*. Jun 2024;80(6):941-956. doi:10.1016/j.jhep.2024.01.032
37. Singal AG, Llovet JM, Yarchoan M, et al. AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. *Hepatology*. Dec 1 2023;78(6):1922-1965. doi:10.1097/HEP.0000000000000466
38. Valenti L, Dongiovanni P, Ginanni Corradini S, Burza MA, Romeo S. PNPLA3 I148M variant and hepatocellular carcinoma: a common genetic variant for a rare disease. *Dig Liver Dis*. Aug 2013;45(8):619-24. doi:10.1016/j.dld.2012.12.006
39. Abul-Husn NS, Cheng X, Li AH, et al. A Protein-Truncating HSD17B13 Variant and Protection from Chronic Liver Disease. *N Engl J Med*. Mar 22 2018;378(12):1096-1106. doi:10.1056/NEJMoa1712191
40. Mak LY, Gane E, Schwabe C, et al. A phase I/II study of ARO-HSD, an RNA interference therapeutic, for the treatment of non-alcoholic steatohepatitis. *J Hepatol*. Apr 2023;78(4):684-692. doi:10.1016/j.jhep.2022.11.025
41. Lin J, Huang Y, Xu B, et al. Effect of dapagliflozin on metabolic dysfunction-associated steatohepatitis: multicentre, double blind, randomised, placebo controlled trial. *Bmj*. Jun 4 2025;389:e083735. doi:10.1136/bmj-2024-083735
42. Stefan N, Yki-Järvinen H, Neuschwander-Tetri BA. Metabolic dysfunction-associated steatotic liver disease: heterogeneous pathomechanisms and effectiveness of metabolism-based treatment. *Lancet Diabetes Endocrinol*. Feb 2025;13(2):134-148. doi:10.1016/s2213-8587(24)00318-8
43. O'Farrell M, Duke G, Crowley R, et al. FASN inhibition targets multiple drivers of NASH by reducing steatosis, inflammation and fibrosis in preclinical models. *Sci Rep*. Sep 19 2022;12(1):15661. doi:10.1038/s41598-022-19459-z
44. Li W, Alazawi W, Loomba R. Current and emerging therapeutic landscape for metabolic dysfunction-associated steatohepatitis. *Lancet Gastroenterol Hepatol*. Feb 2026;11(2):150-162. doi:10.1016/S2468-1253(25)00260-2
45. Yen CL, Stone SJ, Koliwad S, Harris C, Farese RV, Jr. Thematic review series: glycerolipids. DGAT enzymes and triacylglycerol biosynthesis. *J Lipid Res*. Nov 2008;49(11):2283-301. doi:10.1194/jlr.R800018-JLR200

Authors

Kimberly Ho, MD, Department of Medicine, Alpert Medical School of Brown University, Providence, RI.

Paige McLean Diaz, MD, Department of Medicine, Division of Gastroenterology, Alpert Medical School of Brown University, Providence, RI.

Correspondence

Kimberly Ho, MD
kimberly_ho@brown.edu
khol@brownhealth.org

Intensity of Healthcare Utilization Among Pediatric Hospice Patients Receiving Concurrent Care

JACKIE LEE, MD; HAL EDMONSON, MD, MDiv; TESSA CENTRACCHIO, MSN; REBECCA E. MACDONELL-YILMAZ, MD, MPH

ABSTRACT

BACKGROUND: As children with life-threatening conditions near end-of-life, their disease burden and care requirements tend to increase, leading to high intensity of care in the hospital. Previous studies have examined patterns of healthcare usage among these children receiving hospice, but little is known about the impact of pediatric hospice involvement on healthcare utilization compared with usual care. We aimed to examine whether pediatric patients enrolled on concurrent hospice care utilize healthcare services at the same rate as prior to hospice enrollment.

METHODS: A retrospective chart review examined deceased pediatric patients enrolled on the HopeHealth pediatric hospice between January 1, 2022 to December 31, 2023 who had received hospice care for more than seven days and who spent at least one day on hospice out of the hospital. We compared the number of hospital admissions and ICU days during the period between hospice enrollment and death (post-hospice) to the equivalent duration of time prior to hospice enrollment (pre-hospice).

PRIMARY RESULTS: All patients had fewer hospital days and PICU days post-hospice compared to pre-hospice. Nine patients had no hospital days following hospice enrollment, of which four had had zero hospital days prior to hospice enrollment.

PRINCIPAL CONCLUSIONS: In this single-center study, patients receiving concurrent hospice care had fewer hospital days, ICU days, and invasive procedures compared to during the equivalent duration of time prior to hospice enrollment. Provision of hospice support alongside continued disease-directed care may lead to decreased inpatient admissions and interventions. More study is needed to better understand this potential correlation.

KEYWORDS: hospice; concurrent care; pediatric end-of-life

BACKGROUND

Children with life-limiting or terminal conditions often experience increased intensity of care as they near end-of-life (EOL).^{1,2} However, this level of care is not always consistent with the goals or wishes of the child and family. The goals of pediatric palliative and hospice care are to enhance the quality of life for a child and family living with life-threatening conditions, prevent and minimize suffering, and facilitate medical care that is concordant with their hopes and values.³ Further, Section 2302 of the Affordable Care Act removed prior barriers to hospice care for children insured by Medicaid or Children's Health Insurance Program (CHIP) by allowing for concurrent care, through which children with a terminal condition may continue receiving disease-directed treatment alongside the support and comfort-focused care of hospice.⁴ Many commercial insurance providers follow this model as well.⁵ There is an expanding body of data to support the need for psychosocial support in this population,⁶ and examining patterns of healthcare utilization among children receiving hospice.^{7,8} However, recent assessments reveal persistent misunderstandings and lack of clarity among clinicians, families, and hospice agencies regarding the concurrent care benefit.⁹

In order to better understand the impact of hospice support on intensity of care in our region, we examined patients who received hospice care through a dedicated pediatric hospice team, focusing on healthcare utilization as measured by number of hospitalizations, days spent in intensive care, and Emergency Department visits prior to and after hospice enrollment. Our hope is that understanding these patterns may facilitate evidence-based allocation of resources for pediatric hospice programs and improve overall care of children and their families at end-of-life.

OBJECTIVES

The objectives of this study were:

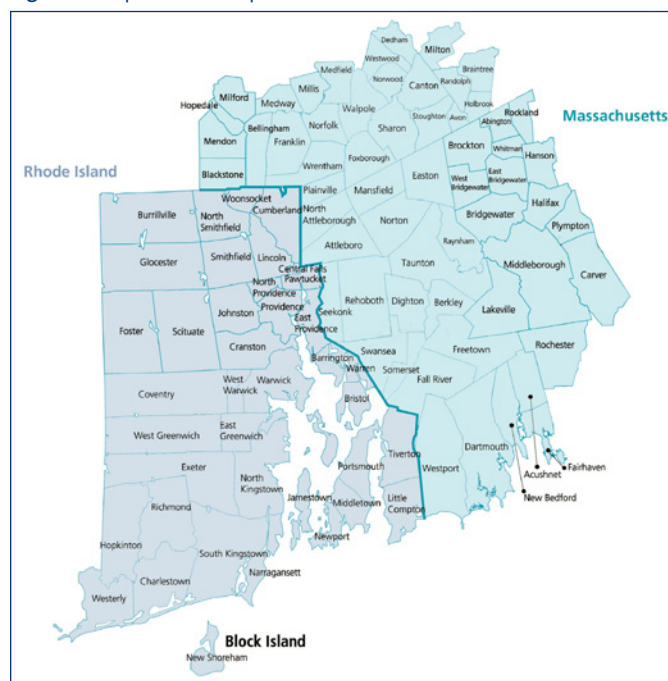
- To compare the rate of healthcare utilization among terminally ill children after enrollment on concurrent hospice care as compared to during the same length of time prior to hospice enrollment.
- To share the experience of one hospice organization providing hospice care concurrently alongside disease-directed interventions.

METHODS

We performed a retrospective analysis of pediatric patients enrolled on concurrent hospice care through a single institution between January 1, 2022 and December 31, 2023, who subsequently died. HopeHealth, the nation's second-oldest hospice organization, serves patients throughout Rhode Island and southeastern Massachusetts [Figure 1] and developed a dedicated pediatric team in 2022. Patients under age 21 years are eligible for concurrent care in Massachusetts; the age limit has been extended to 26 years in Rhode Island. Exclusion criteria for the study included hospice enrollment less than seven days prior to death, revocation of hospice services prior to death, and zero days spent at home while enrolled in hospice. Additionally, despite the provision of concurrent care, hospitalization at institutions outside of HopeHealth's service area [Figure 1] necessitates discharge from hospice; thus, patients who were hospitalized at institutions outside of Rhode Island and southeastern Massachusetts were not included, both due to this disruption in hospice service and unavailability of data from outside institutions [Figure 2].

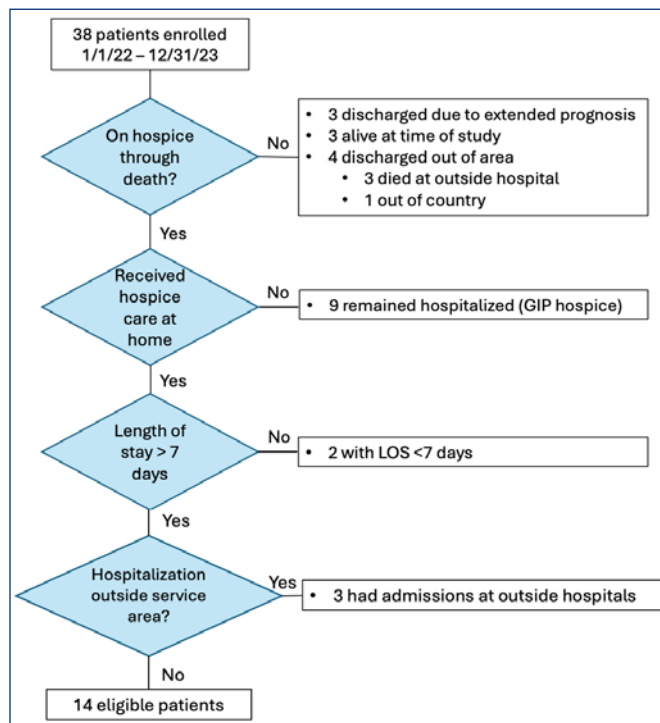
The post-hospice period was defined as the number of days between hospice enrollment and death. The pre-hospice period was the same duration of time prior to hospice enrollment, or between birth and hospice enrollment if shorter. We examined healthcare utilization within the post-hospice period and pre-hospice period, comparing the number of hospital admissions, Emergency Department visits at Women and Infants Hospital or Hasbro Children's (the

Figure 1. HopeHealth Hospice Service Area



<https://www.hopehealthco.org/where-we-help>

Figure 2. Identification of Eligible Patients



only hospitals within HopeHealth's service area at which the included patients received care) within each time period. This study was given non-research designation by the Brown University Health IRB.

Analysis

Data from pre- and post-hospice periods were manually extracted from the electronic medical records (EMR), including the number of hospital days, ICU days, and the number of Emergency Department visits.

RESULTS

Thirty-eight patients had enrolled on the pediatric hospice service during the study period. Fourteen fit the eligibility criteria [Figure 2]. Demographics and clinical characteristics are described in Table 1. Average patient age at time of enrollment was eight years and from three days to 22 years. Nine patients were male and five patients were female. The most common class of diagnosis was an oncologic disorder (57%).

Over the study period, all patients had equal or fewer total hospital days and fewer total ICU days during the post-hospice period compared to the pre-hospice period [Figure 3]. Nine patients had no hospital admissions following hospice enrollment. Of these, six had also zero hospital days prior to hospice enrollment. In these six cases, hospice enrollment was initiated in the outpatient setting and the duration of each patient's survival post-enrollment was shorter than

Table 1. Demographics and Clinical Characteristics of Eligible Patients

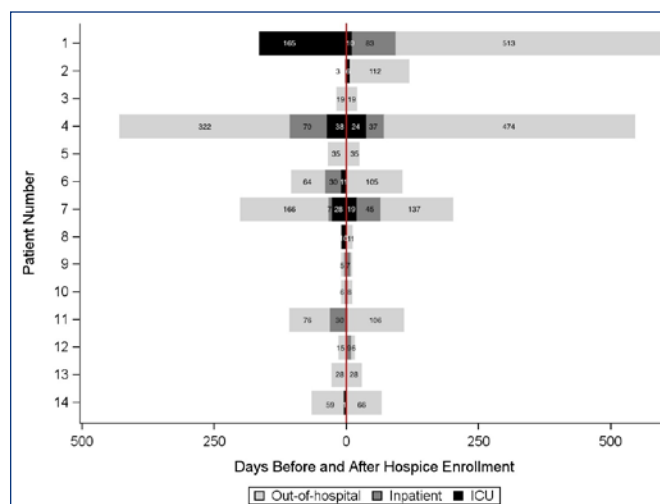
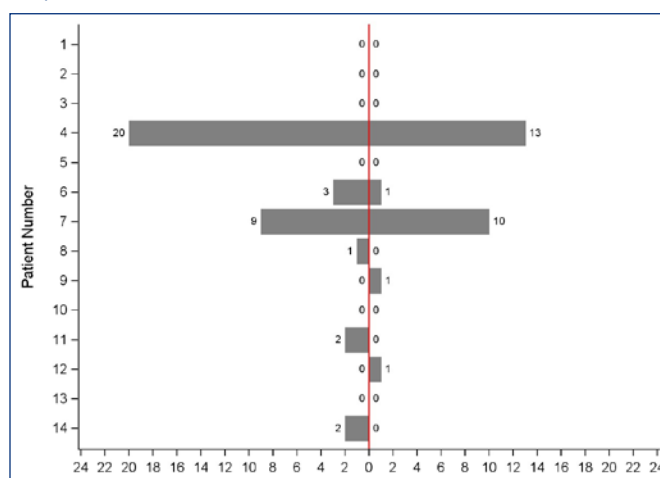
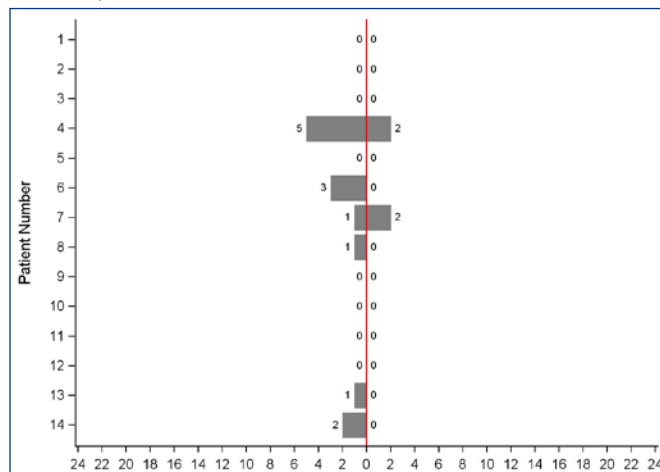
Patient #	Age at Hospice Enrollment	Sex	Diagnosis Type	Location of Death
1	5 Mo	M	Genetic Disorder	Hospital (Wards)
2	3 D	M	Genetic Disorder	Hospital (PICU)
3	2 Yr 10 Mo	M	Oncology	Inpatient Hospice
4	1 Yr 2 Mo	F	Neurological Disorder	Inpatient Hospice
5	7 Yr 3 Mo	M	Oncology	Home
6	12 Yr 4 Mo	F	Oncology	Home
7	12 Yr 3 Mo	M	Cardiomyopathy	Hospital (Wards)
8	4 Yr 4 Mo	M	Oncology	Home
9	15 Yr 10 Mo	M	Oncology	Hospital (Wards)
10	19 Yr 10 Mo	M	Oncology	Hospital (Wards)
11	22 Yr 7 Mo	F	Oncology	Inpatient Hospice
12	11 Yr 8 Mo	F	Genetic Disorder	Home
13	2 Yr 3 Mo	M	Oncology	Home
14	7 Yr 3 Mo	F	Neurological Disorder	Home

the length of time that elapsed between their last hospitalization and their hospice enrollment. Almost all patients had equal or fewer total hospital admissions [Figure 4] and Emergency Department visits [Figure 5] in the post-hospice period compared to the pre-hospice period.

DISCUSSION

Children with life-limiting or terminal conditions often experience increased intensity of care at EOL. Hospital admissions and Emergency Department visits are often psychosocially disruptive to patients and families and increasingly costly; as of 2019, the average cost of a pediatric hospitalization involving ICU care had nearly doubled since 2001.¹⁰ While the Affordable Care Act allows for ongoing disease-directed care and interventions alongside hospice support, it is not yet clear what impact concurrent care has on the frequency or intensity of disease-directed care.

The current study serves as a first step in exploring the impact of concurrent hospice care on the use of disease-directed interventions. The results demonstrated that pediatric patients receiving concurrent hospice care spent the same number or fewer days in the hospital and fewer days in the ICU after hospice enrollment compared to the equivalent duration of time prior to enrollment. Nearly all had fewer or no hospital admissions after enrolling in hospice and most had fewer Emergency Department visits. This suggests that patients and their families were able to spend more time at home and that the overall costs of care may have decreased compared to continuing care without hospice involvement.

Figure 3. Cumulative In-Hospital, ICU, and Out-of-Hospital Days Before and After Hospice Enrollment**Figure 4.** Total Numbers of Inpatient Admissions Before and After Hospice Enrollment**Figure 5.** Total Numbers of Emergency Department Visits Before and After Hospice Enrollment

This study was limited in that it examined patients within a single hospice agency and results may not be generalizable to other populations. Due to its small size, it was not adequately powered to assess the statistical significance of these results. Enrollment was also limited by the requirement that patients had spent time at home after hospice enrollment; this criterion was used deliberately to eliminate patients whose only time on hospice was while receiving general inpatient level of hospice care in the hospital, typically following an acute injury or illness.

We utilized patients' time prior to hospice enrollment as a control against which to compare their time receiving concurrent care, which poses several challenges. Patients who enrolled on hospice shortly after birth did not have an equivalent period of "pre-hospice" time to examine. Further, we speculate that healthcare utilization would have continued at the same intensity through EOL if patients had not enrolled on hospice, though it is possible that patients' and families' goals may have evolved in that time even without hospice involvement, still leading to decreased healthcare utilization. Still, literature over the past 20 years has consistently shown that children dying from a variety of conditions continue to suffer significant symptoms,^{11,12} and more recent studies illustrate a continued use of high-intensity care at the end of life in pediatric patients with terminal diagnoses,¹³ lending credence to the assumption that intensity of care would not have declined without hospice involvement.

CONCLUSIONS

In this single-center study, pediatric patients receiving concurrent hospice care had the same or fewer hospital days and Emergency Department visits and fewer total ICU days during their time on hospice compared to the equivalent duration of time prior to hospice enrollment. Provision of hospice support alongside continued disease-directed care may lead to decreased inpatient admissions and interventions and, as a result, fewer healthcare expenditures. More study is needed to better understand this correlation and the degree of potential impact.

References

1. Ananth P, Melvin P, Feudtner C, Wolfe J, Berry JG. Hospital Use in the Last Year of Life for Children With Life-Threatening Complex Chronic Conditions. *Pediatrics*. 2015;136(5):938-946. doi:10.1542/peds.2015-0260
2. Widger K, Brennenstuhl S, Nelson KE, et al. Intensity of end-of-life care among children with life-threatening conditions: a national population-based observational study. *BMC Pediatr*. 2023;23(1):375. doi:10.1186/s12887-023-04186-9
3. Pediatric Palliative and Hospice Care. NHPCO. Published April 1, 2019. <https://www.nhpco.org/pediatrics/>
4. Lindley LC, Keim-Malpess J, Svyarenko R, Cozad MJ, Mack JW, Hinds PS. Pediatric Concurrent Hospice Care: A Scoping Review and Directions for Future Nursing Research. *J Hosp Palliat Nurs*. 2020 Jun;22(3):238-245. doi: 10.1097/NJH.0000000000000648. PMID: 32282559; PMCID: PMC7716801.
5. Steinhorn D, Lindley L, Daley M. Cost Analysis of Pediatric Concurrent Care: Commercial vs Medicaid Payer (\$722). *Journal of Pain and Symptom Management*. 2020;59(2):540-541.
6. Stephenson J. Palliative and hospice care needed for children with life-threatening conditions. *JAMA*. 2000;284(19):2437-2438. doi:10.1001/jama.284.19.2437
7. Lindley LC, Svyarenko R, Mooney-Doyle K, Mendola A, Naumann WC, Keim-Malpess J. Patterns of Health Care Services During Pediatric Concurrent Hospice Care: A National Study. *Am J Hosp Palliat Care*. 2022;39(3):282-288. doi:10.1177/10499091211018661
8. Svyarenko R, Lindley LC, Mooney-Doyle K, Mendola A, Naumann WC, Mack JW. Patterns of Healthcare Services Among Children With Advanced Cancer in Concurrent Hospice Care. *Cancer Nurs*. 2022;45(6):E843-E848. doi:10.1097/NCC.0000000000001067
9. Weaver MS, Smith SM, Torkildson C, Fisher D, Hawley B, Ware A, Davis H, Williams CSP, Lindley LC. The State of Pediatric Concurrent Hospice Care in the United States. *Pediatrics*. 2025 Sep 1;156(3):e2025071610.
10. Killien EY, Keller MR, Watson RS, Hartman ME. Epidemiology of Intensive Care Admissions for Children in the US From 2001 to 2019. *JAMA Pediatr*. 2023;177(5):506-515
11. Wolfe J, Grier HE, Klar N, Levin SB, Ellenbogen JM, Salem-Schatz S, Emanuel EJ, Weeks JC. Symptoms and suffering at the end of life in children with cancer. *N Engl J Med*. 2000 Feb 3;342(5):326-33.
12. Marcus KL, Kao PC, Ma C, Wolfe J, DeCoursey DD. Symptoms and Suffering at End of Life for Children With Complex Chronic Conditions. *J Pain Symptom Manage*. 2022 Jan;63(1):88-97.
13. Widger K, Brennenstuhl S, Nelson KE, Seow H, Rapoport A, Siden H, Vadeboncoeur C, Gupta S, Tanuseputro P. Intensity of end-of-life care among children with life-threatening conditions: a national population-based observational study. *BMC Pediatr*. 2023 Jul 24;23(1):375.

Authors

Jackie Lee, MD, Department of Pediatric Palliative Care, Boston Children's Hospital, Boston, MA.
 Hal Edmonson, MD, MDiv, Department of Emergency Medicine, University of Wisconsin-Madison, Madison, WI.
 Tessa Centraccio, MSN, Division of Pediatric Palliative Care, Hasbro Children's and HopeHealth, Providence, RI.
 Rebecca E. MacDonell-Yilmaz, MD, MPH, Division of Pediatric Palliative Care, Hasbro Children's and HopeHealth, Providence, RI.

Disclosures

Funding: Not applicable

Conflicts of interest/Competing interests: The authors declare that they have no conflicts of interest relevant to this study.

Ethics approval: Not applicable

Consent to participate: Not applicable

Consent for publication: Not applicable

Correspondence

Rebecca E. MacDonell-Yilmaz, MD, MPH
 Division of Pediatric Palliative Care
 Hasbro Children's
 593 Eddy St., Providence, RI 02903
 401-473-9005
rmacdonellyilmaz@brownhealth.org



Rhode Island Monthly Vital Statistics Report

Provisional Occurrence Data from the Division of Vital Records

VITAL EVENTS	REPORTING PERIOD		
	FEBRUARY 2026	12 MONTHS ENDING WITH FEBRUARY 2026	
	Number	Number	Rates
Live Births	727	10,655	10.1*
Deaths	812	10,552	10.0*
Infant Deaths	1	37	3.5#
Neonatal Deaths	0	24	2.3#
Marriages	250	6,546	6.2*
Divorces	172	2,456	2.3*

* Rates per 1,000 estimated population

Rates per 1,000 live births

Underlying Cause of Death Category	REPORTING PERIOD			
	AUGUST 2025	12 MONTHS ENDING WITH AUGUST 2025		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	199	2,315	211.0	2,450.0
Malignant Neoplasms	180	2,163	197.1	4,325.0
Cerebrovascular Disease	43	436	42.2	517.5
Injuries (Accident/Suicide/Homicide)	58	789	71.9	9,046.5
COPD	45	484	44.1	509.5

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 estimated population of 1,097,379 for 2020 (www.census.gov)

(c) Years of Potential Life Lost (YPLL).

NOTE: Totals represent vital events, which occurred in Rhode Island for the reporting periods listed above.

Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.



Why join RIMS?

The Rhode Island Medical Society is your voice at the State House and in the community. In 2025, we secured wins on prior authorization, clinician wellness, and primary care funding—but this work depends on physician support. Without membership, RIMS cannot continue to advocate, educate, and protect the profession. Join or renew today—and consider getting involved in one of our committees. Together, we are stronger. The Rhode Island Medical Society is the only organization dedicated solely to advocating for physicians and their patients in our state.

In 2025, RIMS members helped

- Eliminate prior auth for PCP-ordered services (3-year Medicaid pilot)
- Secure fair Medicaid rates—up to 100% of Medicare starting Oct. 2025
- Protect physician wellness with the Clinician Wellness & Support Act

We're not stopping here

RIMS is fighting for the future of telemedicine, tackling workforce shortages, and reducing administrative burdens.

Click to join

<https://rhodeislandmedicalsociety.wildapricot.org/Join-us/>

Wins for providers

RIMS worked to secure and support key budget investments.

Medicaid primary care rate increase

Up to 100% of Medicare rates
Starting October 2025

Medicaid prior authorization pilot

Eliminates prior authorization for Medicaid for three years
Starting October 2025

Physician loan repayment funding

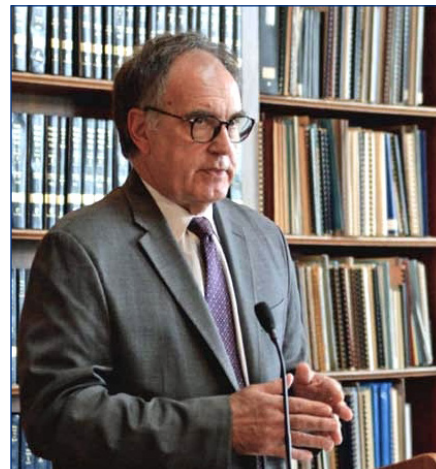
Includes \$200,000 in funding to recruit and retain clinicians

Health center funding

Sustained investments in FQHCs and community health

Health services funding assessment

\$30M annually for primary care and other critical programs



Our priorities

RIMS focused on strengthening Rhode Island's healthcare system, protecting physicians' well-being, reducing administrative burdens, and improving access to care. Together with members, specialty societies, and partner organizations, we made significant progress on our top priorities.

The Rhode Island Prior Authorization Reform Act (SB 168/HB 5120)

Eliminates prior authorization for admissions, services, and procedures ordered by in-network primary care physicians in a three-year pilot.

Effective: October 1, 2025.

Status: Passed and signed

Sponsored by: Rep. Brandon Potter;
Sen. Melissa Murray



The Rhode Island Clinician Wellness and Support Act (SB 695/HB 6036)

Recognizes RIMS' Physician Health Program in statute, strengthens confidentiality protections, and updates licensing language to encourage clinicians to seek care without fear.

Status: Passed and signed

Sponsored by: Rep. John "Jay" Edwards;
Sen. Bridget Valverde

"I'm Sorry" Bill (H6210/S66)

Although not yet enacted, RIMS made significant progress this session on legislation to allow physicians to express sympathy or apologize after an adverse outcome without it being used as evidence of liability. We met twice with the Rhode Island Association for Justice (trial lawyers) and reviewed their suggested language—which we ultimately could not support—laying important groundwork for next session.

Sponsored by: Rep. Teresa Tanzi;
Sen. Pamela Lauria

IT ALL STARTS HERE! JOIN OR RENEW IN 2026 **RHODE ISLAND MEDICAL SOCIETY**

The Rhode Island Medical Society is the statewide home for physician advocacy, education, wellness, and leadership. This past year, RIMS delivered meaningful wins for Rhode Island physicians, including:

- » **MAJOR PRIOR AUTHORIZATION REFORM**
- » **STRONGER CLINICIAN WELLNESS PROTECTIONS**
- » **MEDICAID RATES TO 100% OF MEDICARE**
- » **12 SPECIALTY SOCIETIES SUPPORTED AND 35+ EDUCATION PROGRAMS**
- » **CONFIDENTIAL SUPPORT THROUGH THE PHYSICIAN HEALTH PROGRAM**

Your membership strengthens our voice at the State House and supports the future of medicine in Rhode Island.

JOIN OR RENEW TODAY AT
rimericalsociety.org/membership

Questions about individual or group membership?
EMAIL **membership@rimered.org**



**YOUR VOICE.
YOUR PATIENTS.
YOUR PROFESSION.**





RIMS gratefully acknowledges the practices who participate in our discounted Group Membership Program



BROWNHealth
UNIVERSITY

Emergency Medicine
Medicine
Miriam Hospital Hospitalists
Primary Care
Surgery



CCAP

COMPREHENSIVE COMMUNITY ACTION PROGRAM
YOUR COMMUNITY'S HELPING HAND



east bay community action program
THE BRIDGE to SELF-RELIANCE

Thundermist!
HEALTH CENTER

**UNIVERSITY
ORTHOPEDICS**

Healers. Innovators. Teachers.



WellOne
Primary Medical and Dental Care



Wood River
Health Services
The Heart of South County since 1976

From Classroom to Community: Medical Students Address Women's Health Literacy Through Community Education

NADINE NAJAH, BA; FATINE OLIVEIRA, BSc; BRIAN VU, BA; MALIA PERALES, BA; SANJANA KONDA, BSc;
ODINAKA ANYANWU, MD; SRILAKSHMI MITTA, MD

INTRODUCTION

As many as 80 million American adults have limited health literacy, which can hinder their ability to understand, access, and communicate health information critical to their well-being.^{1,2}

Health literacy plays an essential role in patient, family, and community communication with providers.^{1,2} Yet, limited health literacy remains a growing public health challenge in the United States (US), with disproportionately higher rates among Black and Hispanic populations.³ Limited health literacy is associated with reduced access to healthcare, poorer self-reported health, and worse health outcomes.^{1,3,4} Locally, in the greater Providence County of Rhode Island, as many as one-quarter of adults are in the lowest literacy-proficiency level, exceeding state and national averages, with providers at federally qualified community health centers in the state reporting that many of their patients demonstrated limited health literacy.^{2,4,5} Among women, lower health literacy has been associated with a decreased understanding and utilization of preventive screening and a greater reliance on passive decision-making.¹ Barriers such as limited appointment times, patient hesitation, and medical jargon can hinder patient education in the clinical setting.⁶ Recognizing these disparities and needs, medical students at Brown University developed an annual Women's Community Health Fair (WCHF) to deliver accessible, community-centered, and culturally informed women's health education. This commentary describes the planning process, impact, medical students' organizer reflections, and potential for future expansion for the WCHF.

DESIGNING THE WOMEN'S COMMUNITY HEALTH FAIR

In early 2025, a collaborative effort was launched between a medical student team and faculty mentors from The Warren Alpert Medical School of Brown University to design the WCHF agenda. The leadership team connected with community-based organizations (CBOs) focused on supporting women and underrepresented populations, including the Women's Resource Center, Progreso Latino, and the Rhode Island Free Clinic. These CBOs served as support in generating interest, encouraging attendance, and providing



Figure 1. Keynote session by Wilthone A. Johnson-Goncalves, MSW, LICSW

language-based aid to promote participation with the WCHF.

A major objective for the 2025 forum was the expansion of content beyond reproductive health to topics such as nutrition, mental health, and healthy aging in recognition that women's health spans multiple medical domains [Figure 1]. Speakers represented a range of disciplines and medical specialties, as well as youth leaders in health from Youth Voices of RI. Speakers were advised to deliver their content using strategies that accommodate limited health literacy, such as using visual aids, conveying content in plain language, and providing materials in participants' native languages.²

The free, day-long program was hosted at the medical school building and featured keynote lectures, concurrent breakout sessions for attendees to choose from, and small Q&A sessions in different languages. We offered live, in-person Spanish translation for every session, reflecting both the prominence of Spanish speakers as the second-largest language group in Rhode Island and patterns in participant-registration data. We also provided additional free services to reduce barriers for participation, including meals, childcare, and an array of CBO booths that focus on improving women's health education and access to healthcare, namely the Urban Perinatal Education Center, the Brown Medical Library, the Community Libraries of Providence, and Clinica Esperanza [Figures 2A, B].



Figure 2 A. Booth by the Brown Medical Library and Community Libraries of Providence

RESPONSES

“I feel empowered”

To assess the impact of our community education program, we distributed a multilingual survey with Likert scales and open-ended responses to attendees. Survey findings suggest that the program improved attendees’ confidence in communicating health concerns across social and clinical contexts. For instance, one attendee, a mother of a teenage daughter, shared that attending the teen-led health session allowed her to better understand her daughter’s potential health concerns and how to talk to her and her daughter’s provider about them. Another attendee commented that she felt empowered throughout the event to engage in self-care and prioritize her own health. These findings reflect our mission to provide attendees with tools to improve their health literacy, enhance provider-patient communication, and shared decision-making.¹ Community education efforts can ultimately serve to build healthy habits, partake in preventative healthcare, and ultimately improve health outcomes.

Reflections as Medical Students

From our context as health trainees, organizing and hosting the education event was a rewarding learning and leadership experience. The event highlighted the reality that health-literacy levels vary and are a significant contributor to health prevention. One notable example was an attendee asking if their intrauterine device (IUD) protected them from sexually transmitted infections (STIs); while receiving barrier protection counseling for STI prevention at the same time as IUD placement is commonplace, there are gaps in patients’ understanding.

Listening to attendees’ questions, we realized that foundational knowledge of health varies widely. Even keeping



Figure 2B. Booth by the Urban Perinatal Education Center

patient conversation open-ended by asking, “What questions do you have?” while glancing at a clock to ensure we make it to the next station during our Objective Structured Clinical Examinations (OSCEs) does not always address health literacy. Data indicate that most patients leave a doctor’s office not understanding what their physician told them or knowing how they should take medication.⁷ Instead, gauging what patients already understand about a certain topic will allow a physician to fill in gaps in knowledge and confront misconceptions.^{1,7}

Additionally, evidence-based, community-engaged, experiential learning has been shown to improve students’ understanding of social determinants of health and increase confidence in working with underserved populations, reinforcing the value of hands-on community education in medical training.⁸ We strongly encourage medical students and more advanced trainee providers to engage in patient education efforts and to explore personal strategies for identifying and addressing limited health literacy within their patient populations. Early engagement during medical training, rather than deferring these skills to independent practice, is critical for building sustainable, patient-centered, communication habits.

WHERE DO WE GO FROM HERE?

Future iterations of the WCHF will continue to prioritize empowering women’s autonomy in their healthcare, increasing accessibility, and addressing low-health literacy across Rhode Island. Interdisciplinary collaboration among medical trainees, healthcare providers, and CBOs is key to ensuring programming reflects community needs. We aim to incorporate participant and speaker feedback and deepen

CBO partnerships by expanding the event into a lecture series hosted at community venues across RI that are already familiar and accessible to residents. Other updates include establishing an online presence, recruiting providers or community leaders whose identities reflect those of the population, and designing sessions that first elicit attendee knowledge before delivering content. The goal is to create a discussion-based environment rather than an academic-based environment. These changes aim to enhance the reach, inclusivity, and approachability of the event while reducing barriers to attendance.

Hosting the Women's Community Health Fair two years in a row as medical students with a growing and dedicated team has been an enriching experience and learning opportunity. Community education initiatives such as the WCHF allow organizers to reflect on their responsibilities as educators of a diverse patient population, recognize the contexts within which patients receive care, and develop the skills to address social determinants of health.

References

1. Corrarino JE. Health literacy and women's health: Challenges and opportunities. *Journal of Midwifery & Women's Health*. 2013;58(3):257–264. <https://doi-org.revproxy.brown.edu/10.1111/jmwh.12018>
2. Greaney ML, Wallington SF, Rampa S, Vigliotti VS, Cummings CA. Assessing health professionals' perception of health literacy in Rhode Island community health centers: A qualitative study. *BMC Public Health*. 2020;20(1):1289. <https://doi-org.revproxy.brown.edu/10.1186/s12889-020-09382-1>
3. U.S. Department of Education, National Center for Education Statistics (NCES). *Highlights of the 2023 U.S. PIAAC Results*. NCES.ed.gov. https://nces.ed.gov/surveys/piaac/2023/national_results.asp
4. Barbara Bush Foundation for Family Literacy. *Literacy Gap Map*. map.barbarabush.org. <https://map.barbarabush.org/>
5. U.S. Department of Education, National Center for Education Statistics (NCES). *U.S. PIAAC Skills Map: State and County Indicators of Adult Literacy and Numeracy*. NCES.ed.gov. <https://nces.ed.gov/surveys/piaac/skillsmap/>
6. Alicea-Planas J, Pose A, Smith L. Barriers to providing health education during primary care visits at community health centers: Clinical staff insights. *Journal of Community Health*. 2016;41(2):220–225. <https://doi-org.revproxy.brown.edu/10.1007/s10900-015-0085-2>
7. Graham S, Brooke J. Do patients understand? *The Permanente Journal*. 2008;12(3):67–69. <https://doi.org/10.7812/TPP/07-144>
8. Denizard-Thompson N, Palakshappa D, Vallevand A, et al. Association of a health equity curriculum with medical students' knowledge of social determinants of health and confidence in working with underserved populations. *JAMA Network Open*. 2021;4(3):e210297. <https://doi.org/10.1001/jamanetworkopen.2021.0297>

Authors

Nadine Najah, BA, The Warren Alpert Medical School of Brown University, Providence, RI.
 Fatine Oliveira, BSc, The Warren Alpert Medical School of Brown University, Providence, RI.
 Brian Vu, BA, The Warren Alpert Medical School of Brown University, Providence, RI.
 Malia Perales, BA, The Warren Alpert Medical School of Brown University, Providence, RI.
 Sanjana Konda, BSc, The Warren Alpert Medical School of Brown University, Providence, RI.
 Odinaka Anyanwu, MD, Department of Family Medicine, The Warren Alpert Medical School of Brown University, Providence, RI.
 Srilakshmi Mitta, MD, The Warren Alpert Medical School of Brown University, Women & Infants Hospital's Center for Obstetric and Consultative Medicine, Providence, RI.

Disclosures

Acknowledgments: Authors Nadine Najah and Fatine Oliveira are co-first authors. All authors contributed to the concept, preparation, and writing of the manuscript and approved the final version. We would like to thank Lauren Fletcher and Dr. Edward Feller for their insights and guidance.

Funding: The research findings described herein were made possible by the support of the Dr. Veronica Petersen '55 and Dr. Robert A. Petersen Educational Enhancement Fund at the Warren Alpert Medical School of Brown University. Dr. Odinaka Anyanwu was supported by the HIV and Other Infectious Consequences of Substance Abuse training program (T32DA013911), funded by the National Institutes of Health.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Correspondence

Fatine Oliveira
fatine_oliveira@brown.edu

Mary Edwards Walker, MD: Civil War Physician and Advocate for Women's Rights

MARY KORR
RIMJ MANAGING EDITOR

Fifty years ago, an article in the March 1976 issue of the *Rhode Island Medical Journal* unravels the story of a pioneering woman physician and suffragette, with family roots in Rhode Island, who volunteered and was taken prisoner during the Civil War.

Titled "Mary Edwards Walker, M.D., 1832–1919,"¹ it was written by the Journal's then editor-in-chief, the late **SEEBERT GOLDOWSKY, MD**. An avid historian, the article recounts that while he was combing through old newspaper files of the *Newport Mercury*, he came across an article from its Nov. 7, 1863 edition which intrigued him. It began:

"Dr. Mary E. Walker, a patriotic lady, who has conferred innumerable blessings on the sick and wounded in the army of the Potomac, was last week subjected to considerable annoyance in Pittsburgh, on account of the singularity of her dress. She wore pants, a military overcoat and cape, underneath which was a tunic reaching below the knees. She had on a white turndown collar, and a necktie neatly adjusted. In this eccentric garb, it is not strange that she became the object of much curiosity; and among the thousand and one surmises as to who she was, it was rumored that she was a rebel spy! But as soon as it became known as to who she was, and that she had adopted this style of dress because it

Figure 1. Photo of Mary E. Walker, MD, taken by Matthew Brady, circa 1865, resides in the National Archives, and appeared in the March 1976 article in the *Rhode Island Medical Journal*. She is wearing her Army uniform.

better suited the noble work in which she was engaged, she was treated with all the courtesy and respect which were due to a person of her character and mission." [Figures 1,2.]

Rhode Island Roots

Dr. Goldowsky's research found that Dr. Walker's roots stemmed from America's earliest days. She was born in Oswego, NY, on Nov. 26, 1832, the fifth daughter of Alvah and Vesta Whitcomb Walker, originally from Massachusetts. She and her siblings were eighth-generation direct descendants of the



Figure 2. Assistant Surgeon Mary E. Walker, MD, of Medical Staff U.S. Volunteers Infantry Regiment in skirt and trousers with Congressional Medal of Honor badge.

[LIBRARY OF CONGRESS/
M.B. BRADY & CO., 1865]

Dr. Mary E. Walker's Congressional Medal Commendation

Whereas it appears from official reports that Dr. Mary E. Walker, a graduate of medicine, "has rendered valuable service to the government, and her efforts have been earnest and untiring in a variety of ways," and that she was assigned to duty and served as an assistant surgeon in charge of female prisoners at Louisville, KY., under the recommendation of Major-Generals Sherman and Thomas, and faithfully served as contract surgeon in the service of the United States, and has devoted herself with much patriotic zeal to the sick and wounded soldiers, both in the field and hospitals, to the detriment of her own health, and has endured hardships as a prisoner of war four months in a southern prison while acting as contract surgeon; and

Whereas by reason of her not being a commissioned officer in the military service a brevet or honorary rank cannot, under existing laws, be conferred upon her; and

Whereas in the opinion of the President an honorable recognition of her services and suffers should be made;

It is Ordered: That a testimonial thereof shall be hereby made and given to the said Dr. Mary E. Walker, and that the usual medal of honor for meritorious services be given her.

Given under my hand in the city of Washington, D.C. this 11th day of November, A.D. 1865.

Andrew Johnson, President

By the President: Edwin M. Stanton, Secretary of War



Figure 3. One of the earlier images of the Walker Family Homestead, also referred to as the Philip Walker House, on Massasoit Avenue in East Providence. It is listed on the National Register of Historic Places.

[[HTTPS://WWW.PRESERVERI.ORG/WALKER-HOUSE](https://www.preserveri.org/walker-house)]

"Widow Walker," who came to Plymouth Colony before 1643 and settled in Rehoboth, MA. Widow Walker's son, Philip, built a home in 1676, and due to subsequent boundary relocations, is now the Rumford section of East Providence. Known as the Deacon Walker House, it is extant and on the National Register of Historic Places [Figure 3].

Mary's father spent most of his time running a "free open" school on the Oswego family farm. He is described as a "self-taught physician" in the Mary Walker collection of papers at Syracuse University. The collections states, "her parents were what was termed 'free thinkers.'" She and her siblings were "raised to question everything. Helping on the farm, Mary often wore trousers and shirts because they were more comfortable. She was a non-conformist throughout her life."² The farm was also a stop on the Underground Railway.

Her father, seeing Mary's interest in science and medicine, encouraged his daughter to study medicine. Dr. Goldowsky's article states that "she amused herself by reading coroners' reports and medical books borrowed from their family doctor."

Medical School

In 1853, she was admitted to the Syracuse Medical College (no relation to Syracuse University), described as an "Eclectic" school. It welcomed women and advocated for co-education. Chartered by the State of New York, it was one of several similar Eclectic medical schools in the nation.

The papers of Abraham Lincoln at the Abraham Lincoln Presidential Library and Museum, Springfield, Ill., state that, "At Syracuse Medical College, Mary E. Walker studied pathology, obstetrics, diseases of women and children, pharmacy, anatomy, physiology, principles of surgery, medical law, and more...She advocated against the practices of bleeding, blistering and giving patients heavy doses of mercury."³

Mary graduated, in 1855, at the age of 23. Shortly thereafter she married fellow graduate **ALBERT MILLER, MD**, and the couple opened a practice in Rome, NY, where she practiced pediatrics and saw mostly women patients. Their one child died in infancy. The marriage ended in divorce several years later.

Civil War

When the Civil War broke out, Dr. Walker volunteered her services in field hospitals near the Union front lines, including at the Battle of Fredericksburg and in Chattanooga after the Battle of Chickamauga. Various accounts of her life report that she requested to join the Union Army as a surgeon but was rejected because she was a woman. Officially allowed to serve only as a nurse, she worked as an unpaid field surgeon. But in September 1863 she was formally employed as a civilian surgeon by the Army of the Cumberland, becoming the first female surgeon employed by the US Army. She was later appointed assistant surgeon of the 52nd Ohio Infantry.

Prisoner of war

The collection of her papers at Syracuse University reported that, "On April 10, 1864, she was captured by Confederate troops, and arrested as a spy, just after she finished helping a Confederate doctor perform an amputation. She was sent to Castle Thunder in Richmond, Virginia, and remained there until August 12, 1864, when she was released as part of a prisoner exchange."²

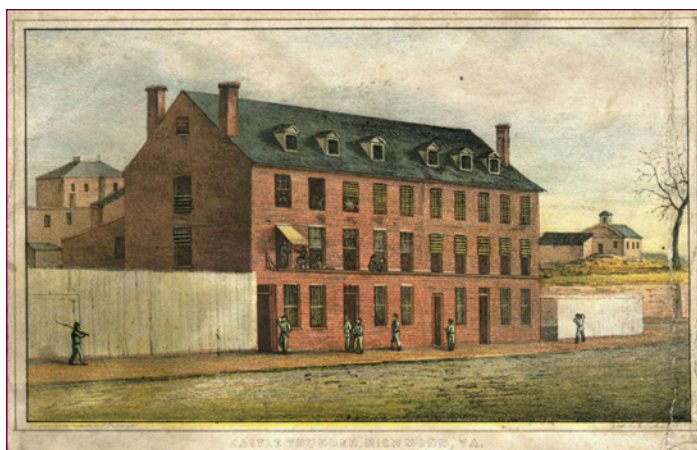


Figure 4. Castle Thunder, Richmond, VA, where Mary E. Walker, MD, was imprisoned by the Confederates during the Civil War.

[[HTTPS://ENCYCLOPEDIAVIRGINIA.ORG/ENTRIES/CASTLE-THUNDER-PRISON](https://encyclopediavirginia.org/entries/castle-thunder-prison)]

According to the Uncommon Wealth, Voices from the Library of Virginia, she wrote from Castle Thunder in a letter to her mother: "I hope you are not grieving about me...I am living in a three-story brick 'castle' [Figure 4] with plenty to eat and a clean bed to sleep in." The reality however, was quite different. Living in a rat-infested room and fed a diet of moldy bread and rice, she weighed only 60 pounds when she left the castle. She continued to serve as an Army doctor throughout the rest of the Civil War."⁴

Congressional Medal of Honor

She was presented with the Congressional Medal of Honor for Meritorious Service in 1865, signed by President Andrew Johnson. [See sidebar.] The award was rescinded in 1917, along with 900 others, due to reappraisals by a medals' committee which

stated a recipient had to be in active combat. She refused to surrender her bronze medal, and wore it for the rest of her life. At the request of a great-niece, it was reinstated in 1977 by President Jimmy Carter.

For most of her life she lived in Washington, D.C., where she had opened a medical practice. But while imprisoned at Castle Thunder, she suffered permanent partial vision loss, which ultimately led her to stop practicing medicine. She also spent much of her post-war years writing several books and on the lecture tour in this country and in Europe. Her most notable book, *Hit: Essays on Women's Rights*, was published in 1870.

According to her biography in the series "Changing the Face of Medicine" at the National Library of Medicine, "Despite the controversy surrounding her career and her politics, Dr. Mary Walker was proud of her accomplishments as a physician and an advocate for women's rights. As she concluded in 1897, 'I am the original new woman...Why before Lucy Stone, Mrs. Bloomer, Elizabeth Cady Stanton and Susan B. Anthony were—

before they were, I am. In the early '40's, when they began their work in dress reform, I was already wearing pants...I have made it possible for the bicycle girl to wear the abbreviated skirt, and I have prepared the way for the girl in knickerbockers.'"⁵

Dr. Walker took to dressing in a top hat and black suit in her middle and later years, always wearing her Medal of Honor pinned to the jacket [Figure 5]. In her 80s, she suffered a fall at the Capitol in Washington, D.C., and after recovering,

returned to the family homestead in Oswego, NY. She died at a neighbor's home there at the age of 87, on Feb. 21, 1919.

In March 1919, *Providence Magazine* published an article titled "Dr. Mary E. Walker of Rhode Island Family," and described her as a frequent visitor to the East Side of Providence in the prior six years, where she had numerous personal friends.



Figure 5. Mary Edwards Walker, MD, in 1911, head-and-shoulders portrait, facing left, wearing top hat and coat.

[LIBRARY OF CONGRESS, PHOTO BY BAIN NEWS SERVICE]

The article lauded her as a "valued Army doctor during the Civil War. After the war she was authorized by Congress to wear male apparel. She was of fine character and extremely modest."

As in life, her death made headlines nationally as well. The *New York Times* edition of Feb. 23, 1919 termed her a "Crusader" [Figure 6]. It stated her "livelihood was earned during all these years by her medical practice and by writing, which were supplemented by an Army pension."

By all accounts, Dr. Walker never walked the straight and narrow, but was a trailblazer. The symbol of what she considered the greatest recognition of her life's work as a physician is depicted on her tombstone: the Congressional Medal of Honor [Figure 7]. ❖

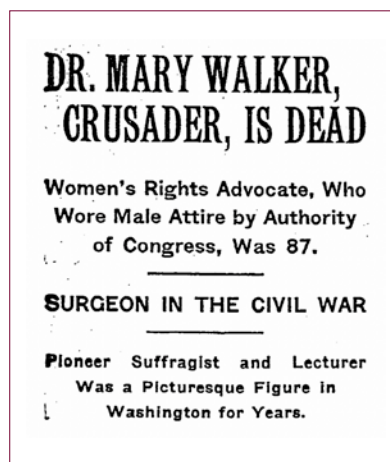


Figure 6. Headline in the *New York Times* on her death in 1919.



Figure 7. Gravestone in Rural Cemetery, Oswego, NY.

[<https://www.findagrave.com/memorial/23089/MARY-EDWARDS-WALKER>]

References

1. Goldowsky S. Mary Edwards Walker, M.D., 1832-1919. *Rhode Island Medical Journal*. 1976 March;59(3):118-140. <https://dn790000.ca.archive.org/0/items/rhodeislandmedic5919rhod/rhodeislandmedic5919rhod.pdf>
2. https://library.syracuse.edu/digital/guides/w/walker_me.htm
3. Walker, Mary E. Abraham Lincoln Presidential Library and Museum, Springfield, Ill. <https://papersofabrahamlincoln.org>
4. <https://uncommonwealth.lva.virginia.gov/blog/2024/12/11/war-comes-to-chatham-manor/>
5. https://www.nlm.nih.gov/exhibition/changing-the-face-of-medicine/physicians/biography_mary_walker.html?id=item-324

Correspondence

mkorr@rimed.org

Progress against lung cancer drives down cancer mortality

WASHINGTON, DC — Cancer death rates fell for both men and women from 2019 to 2023, continuing a downward trend that has lasted more than 20 years, according to the 2026 Annual Report to the Nation on the Status of Cancer published in the journal *Cancer*. The continued decline in cancer deaths is driven largely by accelerated progress against lung cancer.

The special topic of the report focuses on changes in lung cancer risk factors and related outcomes during the first quarter of the 21st century. Despite significant progress, lung cancer remains the second most common cancer in both men and women and the leading cause of cancer death in the U.S. Researchers noted that, beyond further reductions in cigarette smoking and supporting tobacco-free environments, sustaining progress against lung cancer may depend on access to early cancer detection, timely diagnosis, and state-of-the-art treatment.

The report also examines trends in new U.S. cancer cases from 2003 to 2022. Overall rates of new cancer cases rose slightly each year from 2018 to 2022, driven by increases in breast cancer among women and prostate cancer among men. Breast and prostate cancer remain the most common cancers among women and men, respectively. Despite the increase in prostate cancer, the overall rate of new cancer cases among men remained stable.

The *Annual Report to the Nation on the Status of Cancer* provides yearly updates on cancer rates and trends in the United States and each year includes a special topic of interest. The report is a collaborative effort among the Centers for Disease Control and Prevention (CDC); the National Cancer Institute (NCI), part of the National Institutes of Health; the American Cancer Society; and the North American Association of Central Cancer Registries (NAACCR). This year the report examines trends in new U.S. cancer cases from 2003 to 2022 and deaths from 2004 to 2023. The report uses cancer registry data supported by CDC and NCI and compiled by NAACCR, as well as cancer death data from CDC's National Center for Health Statistics.

For more information and to read the full report, go to [Annual Report to the Nation on the Status of Cancer, featuring 21st century progress against lung cancer-Henley-2026-Cancer-Wiley Online Library](#) ❖

CDC data show encouraging progress in youth health

WASHINGTON, DC — Recently the Centers for Disease Control and Prevention (CDC) released new data highlighting recent improvements in mental health and dietary behaviors among U.S. high school students. Youth Health in Focus, provides a snapshot of the health and well-being of high school students.

The report describes national Youth Risk Behavior Survey (YRBS) data from 2023 to 2025, as well as 10-year trends from 2015 to 2025. Data are presented across five focus areas: dietary behaviors, physical activity, sleep, digital behaviors, and mental health and suicide risk.

Key Improvements

- Many of the mental health and suicide risk indicators improved, including persistent feelings of sadness or hopelessness, which improved from 40% to 33%; poor mental health, which improved from 29% to 23%; and seriously considering suicide, which improved from 20% to 14%.
- Daily fruit consumption rose from 33% to 39%, daily vegetable consumption rose from 58% to 63%, and the share of students drinking plain water at least three times a day rose from 54% to 58%.
- Regarding improvements in youth physical activity, more students played on a sports team (52% to 58%).

"These are meaningful improvements, and they show that progress is possible when schools, families, and communities work together to support young people," said **JENNIFER SHUFORD, MD, MPH**, CDC's deputy director and chief medical officer. "At the same time, too many students are still struggling with daily health behaviors that can negatively affect their long-term health."

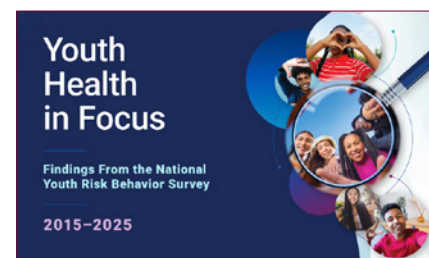
Barriers

Despite noted gains, the report highlights areas where youth continue to face barriers:

- Daily physical activity, muscle-strengthening activity, and meeting recommended activity guidelines remained unchanged, and fewer students attended physical education daily from 2023 to 2025.
- Only about 1 in 4 (24%) students got at least 8 hours of sleep on an average school night in 2025, similar to 23% in 2023. Insufficient sleep is linked to poor mental health, difficulty concentrating, and risky behaviors such as not wearing a seat belt or texting while driving.
- About 1 in 3 (36%) students reported social media use every hour or more in 2025, similar to 37% when measurement began in 2023. Nearly 1 in 2 (46%) students who drove in the past month texted or emailed while driving in 2025, similar to 42% reported in 2023. Digital behaviors can influence many aspects of health, including sleep, physical activity, nutrition, safety, and mental well-being.

For more than 35 years, the CDC's Youth Risk Behavior Survey has provided nationally representative data that help schools, families, communities, and public health leaders identify emerging challenges, monitor long-term trends, and guide evidence-based action. These critical data inform prevention strategies, shape school health programs and highlight where support is needed most.

The report highlights select statistically significant differences. The full 2025 YRBS dataset, the Youth Health in Focus report, and supporting materials are available on CDC's website at www.cdc.gov/yrbs. ❖



Starr Foundation \$37M investment will create alliance to advance breakthroughs in aging research, clinical care

PROVIDENCE [BROWN UNIVERSITY] — With a \$37 million investment from the Starr Foundation, Brown University and Brown University Health will launch a new partnership to accelerate breakthroughs in aging research, clinical trials and patient treatments.

By integrating University research with the health system's clinical trial network, the Starr Healthspan Innovation Alliance aims to bridge the gap between scientific discovery and life-changing treatments for major age-related diseases of the modern era.

The funding will enable Brown University to build on and expand the work of the Center on the Biology of Aging, support groundbreaking laboratory research, and recruit leading researchers in the burgeoning field of geroscience, which is the study of the genetic, molecular and cellular mechanisms of aging. It will also expand clinical trials across Brown University Health, strengthening the ecosystem in which faculty-led research flows from laboratories to hospitals to patients.

"This alliance, made possible by the transformative philanthropic gift from the Starr Foundation, deepens our shared commitment to clinical excellence and academic innovation," said **JOHN FERNANDEZ**, president and CEO of Brown University Health, Rhode Island's largest healthcare system. "By combining our extensive clinical trial infrastructure with Brown's cutting-edge research on aging biology, we will bring novel treatments to patients faster than ever before. At its heart, this partnership is about helping people stay active, vibrant and present as they age for the moments that matter most with their families."

"Brown University's innovative scientists and the exceptional clinicians at Brown University Health are uniquely positioned to translate groundbreaking research into effective treatments for patients," said Starr Foundation Chair **JEFFREY W. GREENBERG**. "The Starr Foundation is proud to support this transformative alliance, with combined expertise that will accelerate breakthroughs for aging-related diseases to improve the human health span."

The alliance creates pathways for discoveries made in Brown University laboratories to be assessed in clinical trials in the health system's network, enabling the rapid flow of innovation to identify new medicines, devices and diagnostic tests, **MUKESH K. JAIN, MD**, senior associate provost for life sciences, senior vice president for health affairs and dean of medicine and biological sciences at Brown University.

"Our overarching vision has always been to build an integrated, comprehensive biomedical ecosystem that allows innovations to move seamlessly from discovery to real-life impact," Dr. Jain said. "With the Starr Healthspan Innovation Alliance, we are connecting our outstanding researchers at Brown's world-class Center on the Biology of Aging with the clinical trials unit at Brown University Health, ensuring science and research can flourish from the bench to bedside."

The Starr Foundation's investment will establish two new endowed faculty positions in geroscience at Brown University and support research activities at the Center on the Biology of Aging, which has long been at the leading edge of research in this area.

The Starr Foundation was established in 1955 by Cornelius Vander Starr, a global entrepreneur and humanitarian, and has been stewarded forward across generations by longtime foundation chair Maurice R. ("Hank") Greenberg, and now by his son Jeffrey. In addition to his role as Starr Foundation chair, Jeffrey Greenberg is a dedicated Class of 1973 Brown University alumnus and a former trustee of the Corporation of Brown University. He is a current member of Brown University Health's Board of Directors.

"What makes this alliance so compelling is the extraordinary opportunity to bridge laboratory research directly with clinical trials and patient care," Greenberg said. "By uniting the visionary scientists at Brown University's Center on the Biology of Aging with the dedicated healthcare and research teams across Brown University Health, the alliance is poised to dramatically speed up the progress from scientific discovery to life-transforming clinical trials." ♦

RI gets \$1M federal grant to strengthen 988 Suicide and Crisis Lifeline

PROVIDENCE — U.S. Senators **JACK REED** and **SHELDON WHITEHOUSE** and U.S. Representatives **SETH MAGAZINER** and **GABE AMO** announced that Rhode Island is receiving \$1,057,919 in federal funds to help support the state's suicide prevention efforts, administer the 988 Suicide & Crisis Lifeline, and ensure they have the tools, training, and staffing levels needed to effectively respond to suicide

risks and help save people in crisis.

The 988 Suicide and Crisis Lifeline provides free, confidential support and crisis care referrals from trained counselors to anyone experiencing severe distress and/or suicidal thoughts. People can access the Lifeline by calling or texting 988.

Senator Reed co-authored the law creating the 988 Suicide & Crisis Lifeline—the National Suicide Hotline Designation

Act (Public Law No: 116-172)—which directed the Federal Communications Commission (FCC) to designate 988 as the universal telephone number for a national suicide prevention and mental health crisis hotline, similar to the way 911 is set up as a free, three-digit number available 24/7 for urgent help. Prior to that, the hotline used a 10-digit number that was harder for people to remember.

Struggling Rhode Islanders in need or those seeking help for a loved one in crisis have called or texted Rhode Island's 988 Call Center more than 40,000 times over the last several years.

In Rhode Island, Horizon Healthcare Partners (HHP), along with its member agencies, is among the hundreds of organizations nationwide raising awareness about the importance of seeking help and prioritizing mental health. HHP staffs 988's call center and BHLINK with Community Care Alliance. BH Link has been answering these calls since the summer

of 2019, when the Department of Behavioral Healthcare, Developmental Disabilities and Hospitals (BHDDH), which funds BH Link, chose to take advantage of the fact that the center was already answering calls 24/7.

The members of the Congressional delegation noted that 988's text feature—which connects users to a live counselor—is especially helpful to younger people who may be less comfortable or overwhelmed speaking to someone over the phone. The text feature is part of a

nationwide strategy to reduce the incidence of suicidal ideation, behavior, and deaths by young people.

According to the U.S. Centers for Disease Control and Prevention (CDC), suicide was responsible for nearly 49,000 deaths in 2024, and the rate among men was nearly four times higher than women. The CDC also reports that suicide is one of the highest leading causes of death in the United States, ranking second for Americans aged 10 to 14, 15 to 24, and 25 to 36. ❖

Providence College Athletics, University Orthopedics announce new partnership focused on student-athlete care

PROVIDENCE — Providence College Athletics and Learfield announced a new, multi-year partnership with University Orthopedics, naming the regional sports medicine leader the Official Orthopedic Provider for 19 of Providence College's 21 Division I varsity teams, including men's and women's basketball.

University Orthopedics is a regional leader in orthopedic care, with more than 70 board-certified, fellowship-trained physicians specializing in sports medicine and a wide range of orthopedic conditions. The partnership—which also includes PC cross country, field hockey, golf, lacrosse, soccer, softball, swimming and diving, tennis, track, and volleyball—will provide the school's student-athletes with specialized orthopedic and sports medicine care, with a focus on injury prevention, treatment, and recovery.

"University Orthopedics has a long history of caring for athletes at every level, and we're proud to bring that experience to Providence College," said **JULIA KATARINCIC, MD**, University Orthopedics president. "These student-athletes put an incredible amount of work into competing at the highest level, and our goal is to provide the specialized care they need to stay healthy, recover from injuries, and get back to the sports they love. We're excited to become part of the Friars' community and look forward to building a strong partnership both on and off the field."

"University Orthopedics has a world-class sports medicine team, and we are excited to partner with Providence College," said **BRETT OWENS, MD**, Chief of Sports Medicine.

University Orthopedics will also host community-focused events featuring Providence College student-athletes and coaches, creating opportunities to connect with Friars fans and the broader Rhode Island community.

"We are excited to be partnering with one of the premier orthopedic care teams in the nation," Providence College Athletic Director **STEVE NAPOLILLO** said. "The health and welfare of our student-athletes is always our top priority. We are grateful for the support and generosity of University Orthopedics, which allows our athletes to compete at the highest level."

The partnership will provide University Orthopedics with visibility across Providence College men's and women's basketball and Olympic sports through in-venue signage, game sponsorships, digital content, radio integrations, and other branded initiatives.

"We're excited to welcome University Orthopedics to the Friars' family through a partnership that puts the health and well-being of our student-athletes at the forefront," said **JEFF GUARINO**, Vice President & General Manager of Providence Friars Sports Properties. "Their expertise in orthopedic and sports medicine care will be a valuable resource for our athletics program, while the partnership creates meaningful opportunities to connect with our fans and the Rhode Island community."

Providence Athletics and University Orthopedics worked closely to develop the partnership with Friars Sports Properties, the locally based team of Learfield, the media and technology company powering college athletics. ❖

VA awards \$8,720,113 in grants to fight Veteran homelessness

PROVIDENCE — The Department of Veterans Affairs awarded \$8,720,113 in grants to five community organizations to help Veterans in FY 2027 who are homeless or at risk of becoming homeless, including in Rhode Island.

This funding is part of a record-high \$1.17 billion in grants awarded to 680 organizations across the country to fight Veteran homelessness. The grants follow VA's success in housing 51,936 homeless Veterans in Fiscal Year 2025, the highest number in seven years.

Resource and supportive services grants will be distributed through the agency's Supportive Services for Veteran Families (SSVF) program to:

- Prevent the imminent loss of a home.
- Identify new, more suitable housing situations for Veterans and families.
- Rapidly re-house Veterans and their families who are homeless and might remain homeless without assistance.

Funds for transitional housing and intensive supportive services will be distributed through the agency's Grant and Per Diem (GPD) program to:

- Fund transitional housing with supportive services or service centers.
- Support transition-in-place housing, where Veterans remain in their current housing unit while receiving services to help them move toward permanent, stable housing.
- Provide special housing designed to better serve women Veterans and those who are chronically mentally ill, frail, or elderly.

"VA medical centers across Rhode Island remain committed to ensuring Veterans have access to safe, stable housing and the supportive services they need to thrive," said **LAWRENCE CONNELL**, Director of VA Providence. "These grants strengthen our partnerships with community organizations and help us reach Veterans where they are, providing resources that make a meaningful difference in their lives." ❖

RIDOH launches new men's mental health campaign

PROVIDENCE — The Rhode Island Department of Health (RIDOH) is launching a new statewide campaign targeting working-age men to address the stigma surrounding mental health. Man Therapy, a research-based, nationally acclaimed campaign, takes a creative approach to reshaping the conversation about men's mental health in Rhode Island.

The campaign provides resources for men and the people in their lives on depression, divorce, and suicide, among other topics. The campaign resources are available at www.mantherapy.org. Rhode Island resources are available on the "Get Support Close to Home" tab on the main page.

This site and this new campaign are a way for people to learn more about men's mental health, examine their own challenges, and consider steps that can put them on the path to treatment and recovery, all within an easy-to-access online portal," said Director of Health **JERRY LARKIN, MD**. "With Man Therapy, people can learn about mental health and explore options to support their mental health wellness, ranging from personal approaches to professional therapy and other resources."

The campaign is running through April 2027 online, on social media, and through gas station ad platforms.

Upon visiting www.mantherapy.org, men and their loved ones will find they have a virtual appointment with Dr. Rich Mahogany—a character created to greet visitors, make them feel at ease, and provide an overview of what they will find and explore during their visit. Dr. Mahogany is dedicated to cutting through denial with a fresh approach, using a straightforward style and practical, useful advice for men. His tone debunks the age-old stigma that says mental health disorders are an unmanly sign of weakness.

The campaign is a part of broader work to prevent suicide and promote mental health among Rhode Island men. It builds on the success of the award-winning "You Good, Man?" campaign which provided an emotional appeal to encourage men to check in on the mental health of their friends and colleagues.

Comprehensive Suicide Prevention Grant team focuses on men ages 25–64, a population with a disproportionately high burden of suicide. From 2020 to 2024, the rate of suicide deaths among Rhode Island men was almost two times higher than the rate of suicide for the overall Rhode Island population. An average of 79 suicide fatalities was seen amongst Rhode Island men every year during this period. From 2020 to 2024, 61% of males ages 25–64 who died by suicide had a known circumstance of a current mental health problem at the time of death. Additionally, according to the 2024 Rhode Island Behavioral Risk Factor Surveillance System (BRFSS) survey, 10.9% of men reported that they usually or always feel lonely.

In addition to Man Therapy, RIDOH's suicide prevention efforts also extend to younger Rhode Islanders. The Department recently received the SAMHSA Garrett Lee Smith Youth Suicide Prevention grant, which empowers states and Tribes to implement youth suicide prevention and early intervention strategies for individuals up to age 24. Together, these initiatives support a comprehensive approach across the lifespan to suicide prevention while recognizing that different populations may benefit from different strategies and resources.

For more information and to explore the resources available through Man Therapy, visit www.mantherapy.org. Visit preventsuicideri.org for local resources, trainings, and data. ❖

Newport Hospital first in RI to implement da Vinci 5 Surgical System

NEWPORT — Newport Hospital is now first in Rhode Island to be using the da Vinci 5 surgical system, Intuitive's most advanced and integrated robotic-assisted surgical platform, to significantly enhance the hospital's minimally invasive surgical capabilities. The new equipment was fully funded by Newport Hospital's generous donor community following a year of fundraising and preparation by teams across the hospital.

The da Vinci 5 is an important advancement for Newport Hospital's surgical program, supporting the hospital's commitment to providing experienced specialists, advanced technology and compassionate care close to home. The system will be used for minimally invasive procedures in urology, gynecology, thoracic surgery and general surgery.

"This milestone for Newport Hospital would not have been possible without the extraordinary generosity of our donor community," said **TENNY THOMAS, MD**, President and Chief Medical Officer of Newport Hospital. "Their support allows us to continue investing in innovative technology that strengthens the care available to our patients and community. We are deeply grateful to every donor and member of our team who helped bring this advanced surgical system to Newport."

The surgeon-directed da Vinci 5 system translates a surgeon's hand movements into smaller, precise movements of instruments inside the patient's body. The surgeon remains fully in control throughout every procedure. The platform includes wristed instruments, enhanced 3D visualization, intuitive motion and an ergonomic design intended to support surgeons as they perform minimally invasive procedures.

The system is designed as a future-ready platform, with the capacity to incorporate continued technological advancements. Its addition further expands Newport Hospital's investments in contemporary, leading-edge surgical technology alongside the knowledge and skill of its experienced surgeons.

"Bringing the da Vinci 5 to Newport Hospital is an exciting step forward for surgical care in our community," said **JAMES D. VALENTE, MD**, Medical Director, Chair of Surgery. "This technology enhances the tools available to our surgeons and strengthens our ability to offer advanced minimally invasive surgical options in a convenient community hospital setting."

The addition of the da Vinci 5 complements Newport Hospital's growing surgical capabilities, which also include the Zimmer Biomet ROSA Knee System. The ROSA system provides real-time data and enhanced precision during total knee replacement procedures, supporting personalized orthopedic care. ❖

Saint Anne's Hospital receives state approval for EP lab

FALL RIVER — Saint Anne's Hospital has received approval from the Massachusetts Department of Public Health for a new electrophysiology (EP) laboratory, which will expand access to specialized heart care for residents across Greater Fall River. The approval, granted on September 9, 2026, marks an important step in the hospital's ongoing efforts to strengthen cardiovascular services and meet the growing needs of the region.

The new EP lab will be developed within existing space on the Saint Anne's Hospital campus and will provide advanced diagnostic and treatment services for patients with heart rhythm disorders. The project includes the build-out of approximately 6,200 square feet of previously approved shell space to accommodate the lab and supporting clinical areas.

Cardiovascular disease remains one of the region's most significant health challenges. Fall River has the highest incidence of cardiac disease in Massachusetts and a coronary heart disease rate that is 24 percent higher than the state average, according to the Centers for Disease Control and Prevention (CDC).

"This investment reflects Brown Health's commitment to building a comprehensive cardiovascular program that delivers exceptional care across our communities," said **ATHENA POPPAS, MD**, Chief of Cardiology and Director of the Brown Health Cardiovascular Institute. "Expanding electrophysiology services at Saint Anne's Hospital will enhance access to leading-edge treatments and strengthen the continuum of cardiovascular care available to patients throughout southeastern Massachusetts."

The hospital is currently targeting a Fall 2027 opening for the new EP lab, pending final planning and construction timelines. ❖

Appointments



Guy R. Nicastri, MD, FACS, appointed Chief Quality Officer at CharterCARE Health

PROVIDENCE — **GUY R. NICASTRI, MD, FACS**, has been appointed Chief Quality Officer at CharterCARE Health of Rhode Island. This new role is a condition of state approval for CharterCARE's

sale and divestiture from Prospect Medical Systems.

Dr. Nicastri will lead the Medical Staff Performance Improvement Plan, working with medical staff leaders and members of both Our Lady of Fatima Hospital and Roger Williams Medical Center. He will also oversee the quality, risk management, and infection control departments, while ensuring regulatory compliance and fostering a culture of continuous quality improvement.

Board-certified in general surgery, Dr. Nicastri has special expertise in advanced laparoscopy/robotics, advanced hernia repairs, foregut surgery for reflux/GERD, breast cancer, skin cancer, including melanoma, colorectal surgery, and treatment/surgery for gallbladder disease.

Throughout his professional career in Connecticut and here in Rhode Island, Dr. Nicastri served in numerous administrative and leadership roles including chief of surgery, OR committee chair, medical executive committees, performance improvement committees, and utilization review committees.

CharterCARE CEO **JEFFREY LIEBMAN** stated, "Dr. Nicastri's decades-long clinical experience and commitment to quality improvement make him ideally suited to lead our effort to facilitate alignment between quality initiatives and the hospital's strategic plan."

He has been recognized for excellence in medical education and is an Associate Professor of Surgery and Family Medicine at the Warren Alpert Medical School of Brown University. A graduate of Boston College, he received both his medical degree and his Master of Science in Physiology from Georgetown University School of Medicine. ❖

Recognition



Brandon del Pozo, PhD, receives 2026 Bruce M. Selya Award for Excellence in Research

PROVIDENCE — **BRANDON DEL POZO, PhD, MPA, MA**, has been named the recipient of the 2026 Bruce M. Selya Award for Excellence in Research, one of Brown University Health's highest hon-

ors recognizing emerging leaders whose research advances academic medicine and improves healthcare delivery.

Dr. Del Pozo is being recognized for his research at the intersection of public health, substance use, policing, and criminal justice, an area of growing importance as communities seek more effective responses to addiction, overdose, and behavioral health challenges. His work explores how law enforcement practices and public policy influence health outcomes and examines ways to better align public health and public safety systems.

"My research explores the emerging connection between public health and public safety, investigating how policing can shape individual and community health outcomes," said Dr. del Pozo. "While encounters with law enforcement can contribute to negative health effects, they also present opportunities to protect and improve health."

Since joining Brown University Health in 2020 as a post-doctoral fellow at The Miriam Hospital, Dr. del Pozo has built a research portfolio focused on opioid use disorder, overdose prevention, harm reduction, drug policy, and evidence-based approaches to addressing substance use. Today, he serves as an assistant professor of medicine at The Warren Alpert Medical School of Brown University, assistant professor of health services, policy and practice at the Brown University School of Public Health, and a research scientist at Rhode Island Hospital.

His research has been published in leading peer-reviewed journals, including *JAMA Network Open*, the *American Journal of Public Health*, and the *International Journal of Drug Policy*. The findings from his work have informed policy discussions and public health practices at the local, national, and international levels.

As the 2026 Selya Award recipient, Dr. del Pozo will deliver a featured presentation at Brown University Health's 33rd Annual Research Day on October 29, 2026, titled "Substance Use Research at the Crossroads of Health, Safety, and Justice." ❖

Recognition

Brown University Health's Cancer Institute Stem Cell Transplant Program earns national accreditation for quality and safety

PROVIDENCE — The stem cell transplant program at Brown University Health's Cancer Institute has earned accreditation from the Foundation for the Accreditation of Cellular Therapy (FACT), an internationally recognized organization that sets standards for quality and safety in cellular therapy and transplantation. Effective for three years, the accreditation gives patients and referring physicians added confidence that the program meets nationally recognized standards for safe, high-quality care.

The accreditation recognizes that the program meets rigorous standards across all aspects of care, from treatment planning and patient safety to quality monitoring and ongoing improvement. For patients facing blood cancers and other serious conditions that may require a stem cell transplant, FACT accreditation provides reassurance that they are receiving care from a program that has undergone a comprehensive review by experts in the field.

"Receiving FACT accreditation reflects the clinical rigor, expertise and sustained quality standards that guide every aspect of our stem cell transplant program," said **RABIN NIROULA, MD**, clinical program director, Brown University Health Cancer Institute. "This recognition underscores our commitment to delivering safe, compassionate and evidence-based care for patients throughout their treatment journey."

To earn accreditation, programs must demonstrate compliance with rigorous standards related to patient care, safety, quality management, staff training and clinical outcomes. Accredited programs are also required to undergo regular reviews and maintain ongoing compliance with established standards.

"This achievement represents years of collaboration, preparation and continuous improvement by a dedicated multidisciplinary team," said **KATIE CHERENZIA**, clinical manager, Brown University Health Cancer Institute. "Most importantly, it reflects our shared focus on supporting patients and families with the highest level of care at every step." ❖

Fatima Hospital, Roger Williams laboratories earn CAP accreditation

PROVIDENCE — CharterCARE announced that Our Lady of Fatima Hospital and Roger Williams Laboratories have earned accreditation from the College of American Pathologists (CAP) following recent on-site inspections.

Recognized for its rigorous standards, CAP accreditation reflects a laboratory's commitment to quality, safety and continuous improvement. The accreditation process evaluates laboratory operations against established standards designed to promote excellence in laboratory medicine and support high-quality patient care.

During the CAP accreditation process, inspectors review a laboratory's records and quality-control procedures as well as staff qualifications, equipment, facilities, safety programs and overall management. The inspection process is designed to verify that laboratory practices meet CAP requirements and reflect current best practices.

CAP accreditation places Our Lady of Fatima Hospital and Roger Williams Laboratories among more than 8,000 CAP-accredited facilities worldwide. ❖

Obituary



ORAZIO BASILE, MD, of Cumberland, passed away peacefully on September 12, 2026. Dr. Basile was born in Providence, graduating from Classical High School and Brown University.

He was a diplomate of the University of Bologna and received his Doctor of Medicine and Surgery degree.

He was the first foreign-trained physician ever selected by Rhode Island Hospital through the matching internship program. He completed his internship and residency in internal medicine at Rhode Island Hospital before continuing his training in dermatology at Massachusetts Memorial Hospital-Boston University Medical Center in Boston.

After completing his dermatology training, Dr. Basile maintained offices in Providence and Westerly before eventually limiting his practice to Woonsocket and northern Rhode Island. He received his certification in dermatology in 1970 and was soon thereafter awarded a fellowship in the American Academy of Dermatology.

Throughout his career, Dr. Basile was deeply committed to both patient care and the education of future physicians. He served as a consultant in Dermatology to many nursing homes throughout northern Rhode Island as well as Zambano Memorial Hospital. He was also Chief of Dermatology at Pawtucket Memorial, Woonsocket, and Fogarty Hospitals and held medical staff appointments at Rhode Island Hospital and Westerly Hospital.

His dedication to teaching was particularly meaningful to him. Dr. Basile held teaching appointments in dermatology at Brown University and Brown Medical School and served as an Assistant Professor of Clinical Dermatology. In 2004, he received a Distinguished Teaching Award in recognition of 25 years of teaching at the medical school.

Dr. Basile was an active member of numerous professional organizations, including the Rhode Island Medical Society, Providence Medical Association, Rhode Island Dermatology Society, New England Dermatology Society, International Pediatric Dermatology Society, and The Dermatology Foundation. Among his many leadership positions, he served as President of the Woonsocket District Medical Society and the Rhode Island Dermatology Society, Delegate to the Rhode Island Medical Society, and Staff Secretary-Treasurer of the Woonsocket Hospital medical staff.

While Dr. Basile accomplished much throughout his distinguished medical career, his greatest pride and joy was his family. He leaves behind his beloved wife, Shaindele (Stern) Basile, and his children, Elizabeth Basile, Paula Basile, and Michael Basile and his wife Tiffany, as well as his granddaughter, Talli Basile.

Dr. Basile will be remembered for his dedication to medicine, his commitment to teaching, his love of travel and learning, and, most importantly, for the love he shared with his family and those fortunate enough to know him. ❖