SPECIAL SECTION

OSTEOPOROSIS, METABOLIC BONE DISEASES, and FRAGILITY FRACTURES

GUEST EDITORS: JAKE LITTMAN, ScM, MPH; ROY K. AARON, MD
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Preface: The Fracture Liaison Service

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GUEST EDITORS

Enter Jane Doe: a 76-year-old woman with no known medical problems and no currently prescribed medications. She looks well for her age, is active in her community, and walks 3-5 miles per day. One day while out walking, she falls from standing height and suffers a displaced fracture of the femoral neck. Ms. Doe has just experienced one of the most common forms of low-energy fractures, also known as fragility fractures, in the elderly. She is taken by ambulance to her local emergency room where X-ray confirms her diagnosis, and she receives surgical treatment by way of total hip replacement. The surgery is performed without complication, and through subsequent physical therapy, she regains some of her mobility and independence. Within a year, however, she suffers a second fracture, leaving her permanently disabled and in need of home care.

Meanwhile, Ms. Doe’s grandson suffers a wrist fracture while playing basketball. At 12 years old, this is the third fracture of his life. He complains of intermittent blurry vision, but his clinical examinations are otherwise normal, and his parents and physicians conclude that he is an overactive child who is prone to injury. His fracture is treated without complications, but months later he suffers bilateral retinal detachments leaving his vision permanently impaired.

Now, let us envision the contribution of a Fracture Liaison Service (FLS) to the care of these two patients. After receiving surgical treatment for her hip fracture, Ms. Doe is referred to an FLS where a comprehensive history is obtained, a physical examination with emphasis on the skeleton is performed, bone density is determined via dual-energy absorptiometry (DEXA) scanning, and laboratory analysis including investigation of bone turnover marker (BTM) levels is conducted. She is determined to have hyperparathyroidism and undergoes treatment with eventual normalization of her bone density. She regains most of her prior function and avoids subsequent fracturing.

Her grandson is evaluated at the FLS and is found to have a spinal DEXA scan Z-score of -2.5, an age-comparative measure indicating severely low bone density. Clinical suspicion of genetic pathology is raised, and a consult is obtained. NextGen whole exome sequencing reveals heterozygous LRP5 mutations, and an ensuing ophthalmologic workup confirms a diagnosis of familial exudative vitreoretinopathy (FEVR), a genetic disorder that can lead to low bone density, multiple fractures, retinal detachments, and permanent vision loss if not properly treated. He receives appropriate treatment and eventually graduates from high school with no further fractures and preserved vision.

In both cases, the identification of their fractures as signal events led to the detailed evaluation and specific diagnosis and treatment of their underlying pathology. This illustrates the main thematic approach an FLS takes in treating the fracture patient. Put simply, the FLS is a centralized hub for the complete management of fracture patients, including the exploration, diagnosis, and treatment of underlying pathologies that predispose to subsequent fractures. The FLS alleviates the fragmentation of care often found among orthopedic, endocrine, and primary care services regarding which is primarily responsible for the longitudinal evaluation and management of fracture patients. This was once aptly termed the “Bermuda Triangle of osteoporosis care of fractures,” referring to the observed phenomenon of osteoporotic fracture patients disappearing from interdisciplinary care teams without proper management due to discordance on who is ultimately responsible for their long-term care.1

In “The Roles of a Fracture Liaison Service,” the framework for the evaluation and management of fragility fracture patients in the FLS is discussed in detail, including the history, physical examination, determination of bone density, and laboratory analysis. The clinical and economic benefits of FLS are explored, and a real-world application of the FLS paradigm, the Rhode Island Fracture Liaison Service, is detailed.

In “Osteoporosis and Fragility Fractures,” osteoporosis and fragility fractures are discussed as well as their relationship to each other and to the FLS. The epidemiology, pathophysiology, evaluation, and management of osteoporosis are explored, and the clinical importance, epidemiology, predisposing factors, outcomes, and preventative strategies for fragility fractures are elucidated.

In “Osteomalacia and Renal Osteodystrophy,” the clinical classifications, presentations, pathophysiologies, and treatment modalities for various osteomalacias are discussed as alternative bone diseases to osteoporosis producing low bone density. Renal osteodystrophy, a specific form of metabolic bone disease affecting chronic kidney disease and kidney transplant patients characterized by osteomalacia and hyperparathyroidism, is presented.
In “Monoclonal Gammopathies in a Fracture Liaison Service,” the spectrum of disorders characterized by the overproduction of plasma B-cells and immunoglobulin known as monoclonal gammopathies are discussed, with special emphasis on monoclonal gammopathy of uncertain significance (MGUS), a pre-malignant form of multiple myeloma. The clinical presentation of MGUS and its association with osteoporosis and fracture are explored and highlighted with data from the Rhode Island FLS, leading to the conclusion that the term “MGUS” be replaced with “MGSS,” or “monoclonal gammopathy of skeletal significance.”

In “Hyperparathyroidism in a Fracture Population,” the clinical presentation, diagnosis, and treatment of primary hyperparathyroidism (PHPT) are discussed, with special emphasis on its effects on the skeleton. Normocalcemic hyperparathyroidism (NPHPT), a variant of PHPT defined by normal serum calcium and persistently elevated parathyroid hormone levels, is also presented. Current evidence linking NPHPT to osteoporotic fractures, including observations from the Rhode Island FLS, is presented, raising the question if serum calcium measurements alone are sufficient to evaluate parathyroid function in the setting of osteoporotic fractures.

Finally, in “Vertebral Compression Fractures,” the epidemiology, clinical presentation, diagnosis, and treatment (including surgical and non-surgical management) of vertebral compression fractures (VCFs) are discussed. The susceptibility of VCF patients to subsequent fractures and their consequences is also described, as well as pharmacotherapy and the role an FLS can play in mitigating the sequelae of primary VCFs.

**FLS MODELS**

It is important to note that several types of bone health programs exist and an FLS is but one example. While the Rhode Island FLS specifically addresses patients who have already suffered a fracture, some alternative programs are designed to screen asymptomatic populations to find and treat low bone density in the hopes of decreasing fracture incidence. As might be expected, these programs are especially popular with closed panel models of health care delivery such as Accountable Care Organizations and Health Maintenance Organizations. Regardless of approach, the primary goal of all bone health programs should be the reduction of injury via multidisciplinary, comprehensive, high-quality, and cost-effective patient care. The recognition of the potential contributions of FLS programs is of importance to any medical groups serving elderly, osteoporotic, and fracture patients.

An FLS regards a fragility fracture as a signal symptom of metabolic bone loss, physical compromise, or environmental hazards, alerting clinicians to the presence of comorbidities and providing a framework for the identification of patients with a recent fracture, the diagnostic workup of the fragility fracture patient, the treatment of underlying contributors to the fracture, and follow-up to reduce sequelae. Because most patients in an FLS are defined as “symptomatic” by virtue of their fracture, the prevalence of intercurrent diseases and life circumstances in FLS patients is relatively greater than in the general population and offers the opportunity for study. Approaches and findings in our FLS are described in this volume. It is our hope that the findings of the FLS will find their way into screening programs and individual patient care.

**Reference**


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The editors acknowledge with gratitude the support of The Miriam Hospital and University Orthopedics, Inc.

The editors also owe a great debt of gratitude to the late Henry Mankin, MD, former chair of orthopedics at Harvard and the Massachusetts General Hospital, who taught metabolic bone diseases in an orthopedic context. Dr. Mankin sought to infuse orthopedic diagnoses and treatment with clinical medicine and its basic sciences for a fuller understanding of surgical pathology and treatment potential. He was a charismatic personality and brilliant teacher, and an anecdote serves as an illustration.

Using the biblical story of Lot’s wife being turned into a pillar of salt, Dr. Mankin described the fate of an individual who consumed a high phosphate hamburger and a high calcium milkshake and then received a blast of vitamin D by going out into the sun as being turned into stone for exceeding the calcium-phosphorous solubility product. While Lot’s wife’s crystallization was due to her disobedience, the crystallization of Dr. Mankin’s information was due to rapt attention.

Dr. Mankin could not know the long-term impact of his teaching in this community, and this could be a reminder to us all that we will most likely not realize the widespread effects of our teaching on our students and on the care of our patients.

**Guest Editors**

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ABSTRACT
The roles of a fracture liaison service (FLS) are extensive and include, but are not limited to: 1) providing a standardized framework for the evaluation and management of low-energy fractures, also known as fragility fractures; 2) improving patient outcomes through the recognition of fragility fractures as signal events requiring further diagnostic explanation; and 3) lowering direct and indirect healthcare expenditures. One of the central tenets of the FLS is its recognition of fragility fractures as warning signs of underlying pathology, often osteoporosis or other metabolic bone diseases. This understanding, combined with the application of a multidisciplinary management team specialized in diagnosing and treating such pathologies, allows for better short- and long-term management of patients and concordant improvement in outcomes. This article should be viewed as a thematic introduction to the FLS, with others in this volume each illustrating specific examples of how FLS paradigms facilitate the roles described herein.

KEYWORDS: Fracture Liaison Service (FLS); osteoporosis; fractures; falls

INTRODUCTION
Fracture Liaison Services (FLSs) have emerged from two clinical observations. First, low-energy fractures, particularly in individuals over age 60, often result in significant functional morbidity, pain, loss of independence, and death. Second, low-energy fractures can be prevented by medical, physical, and environmental interventions, all dependent upon a sensitive understanding of the physiology of the fractures and their consequences. Low-energy fractures, also known as fragility fractures, are signal events, often the presenting symptoms of an underlying pathology requiring further diagnostic exploration. Therefore, in a very real sense, patients with low-energy fractures are not “asymptomatic.” On the contrary, they are frequently found to have metabolic bone diseases such as osteomalacia, hyperparathyroidism, and especially osteoporosis that result in decreased bone density and disruption of bone micro-architecture leading to diminished ability to withstand applied stresses. Presentations in this volume will concentrate on metabolic contributions to fractures and on common fracture patterns that should be recognized for their association with functional impairment and secondary fractures. Thematically, the volume makes several points:

• The signal value of fragility fractures should not be ignored or minimized.
• Certain fractures, especially vertebral compression fractures, often signal an increased incidence of subsequent fractures.
• Screening bone density is only an initial step in the treatment of fractures. It does not yield a diagnosis, and, in itself, is not a basis for therapy. All patients with fragility fractures deserve a metabolic bone evaluation.
• The evaluation of bone density in the context of fractures frequently reveals medical conditions that contribute to decreased bone density and falls.
• Appropriate therapy depends upon accurate diagnosis of causal and contributory factors to the fracture history and bone density.
• Several medications are available for the treatment of decreased bone density depending upon the extent of bone loss, fracture history, and co-existing medical conditions.

CLINICAL FINDINGS IN THE RHODE ISLAND FRACTURE LIAISON SERVICE
By carrying out a metabolic bone investigatory program as described here, we have made some surprising findings that have enabled more targeted approaches to therapy. Reports of disease prevalence are particular to each FLS referral base. In our case, fractures are the triggering symptom. Renal and transplant patients are treated on those services, respectively, and are discussed in a later article in this volume. Nonetheless, some observations can reinforce the consensus on coordinated evaluation of fracture patients. Within the last 2 years, of 265 consecutive patients with osteoporosis and fractures on our service, we detected 28 patients with primary hyperparathyroidism and 27 patients with monoclonal gammopathy of uncertain significance [MGUS], both discussed in subsequent articles, as well as 10 patients with hematologic malignancies including multiple myeloma, Waldenström’s macroglobulinemia, chronic lymphocytic
leukemia, mast cell leukemia, and lymphomas. In addition, the FLS has evaluated and treated osteoporosis associated with several genetic diseases including osteogenesis imperfecta, Marfan’s syndrome, Ehlers-Danlos syndrome, and familial exudative vitreoretinopathy (FEVR), as well as neuromuscular conditions including muscular dystrophy and cerebral palsy. As discussed in an ensuing article, malabsorption-related osteomalacia has posed challenges to raising vitamin D levels depending upon the severity and cause of the malabsorption. Combined, 75/302 (25%) of patients referred for osteoporosis or osteoporotic fractures were diagnosed with another condition, usually serious, and therapy was targeted at those diseases. This reflects a major thematic approach of our FLS. Without a diagnostic approach such as that described below, these conditions could be missed and, therefore, mistreated.

**CLINICAL APPROACH**

A fragility fracture is often defined as one resulting from a fall from a standing height. However, there are other considerations such as the surface upon which one falls, the circumstances of the fall, etc. In general, the fractures of concern are low-energy fractures and ones with unusual injury mechanics. The clinical approach to the patient with a fragility fracture consists of a history focused on skeletal biology, a focused physical examination, occasional X-rays, determination of bone density, laboratory evaluation of skeletal biology, and a treatment plan that takes into account the patient’s medical and fracture history, severity of bone loss, chemistry, and clinical diagnoses.

1. **History** – A general medical history with an emphasis on the skeleton inquires about the patient’s fracture history, history of falls, acuity of vision and hearing, balance, loss of height, the home environment, diet (especially dairy intake or lactose intolerance), medications that may have an adverse effect on the skeleton, medical exposures such as corticosteroids, and general bone hygiene including caffeine intake, alcohol consumption, and smoking habits (Table 1). The physical and environmental contributions to fractures should be part of every screening conversation. Causes of secondary osteoporosis are described in the *Osteoporosis and Fragility Fractures* article in this volume.

2. **Physical Examination** – A focused skeletal examination includes gait and balance stability, core muscle strength, and spinal deformity (especially kyphosis) that might indicate previous fractures. Rapid, simple tests of lower extremity strength are available, such as “timed up and go” and rising from a chair, that suggest a need for physical therapy for muscle strengthening and gait stability to prevent falls. In the kyphotic patient, lateral thoracic spine X-rays may be indicated to detect previous vertebral compression fractures since these fractures can be almost asymptomatic yet result in deformity and indicate risk for subsequent fractures.

Sensitivity to loss of thoracic height can be important since vertebral compression fractures can result in the lower ribs abutting the pelvis, resulting in impaired sitting and loss of thoracic volume. Several studies have found that pulmonary function can be compromised in patients with osteoporotic vertebral compression fractures compared to patients with chronic low back pain without osteoporosis. Reductions in both vital capacity and forced expiratory volume (FEV1) have been correlated with spinal osteoporotic fractures and resulting spinal deformity and decreased thoracic volume, indicating that reductions in pulmonary function can be correlated with osteoporotic spinal deformities that can be detected and quantified by clinical and radiographic assessment.

3. **Determination of Bone Density** – Dual-energy absorptiometry (DEXA) scanning has several major advantages in the evaluation of the skeleton. It is rapid, noninvasive, and non-enclosed. The radiation exposure is trivial (Figure 1). It provides 2-dimensional measurements of bone density which are reported in g/cm² and compares them to age-related norms (Z-score) and values at age 20 (T-score). The

**Table 1. Static and Potentially Alterable Risk Factors for Osteoporotic Fractures**

<table>
<thead>
<tr>
<th>Static Factors</th>
<th>Potentially Alterable Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic factors: old age, female sex, Asian or White race</td>
<td>Low bone density</td>
</tr>
<tr>
<td>Personal and/or family history of adult fracture</td>
<td>Lifestyle factors: low BMI, sedentary lifestyle, smoking, excessive alcohol consumption, low dietary calcium intake</td>
</tr>
<tr>
<td>Menopause onset prior to age 45</td>
<td>Iatrogenic contributions: glucocorticoids, sedatives, anti-hypertensives, polypharmacy</td>
</tr>
<tr>
<td>Physical frailty</td>
<td>Environmental factors: obstructed walkways, poor lighting, unequal surfaces, etc.</td>
</tr>
<tr>
<td>Deterioration in mental status</td>
<td>Estrogen deficiency</td>
</tr>
</tbody>
</table>

**Figure 1. Patient undergoing DEXA scan and technician**

Bone mineral density or bone strength is measured with a type of low-energy X-ray called a DEXA scan. The scan is entirely noninvasive, non-enclosed, and takes approximately 15 minutes to complete. The measurement of an individual’s bone mineral density is compared to values of the normal population to determine the extent of bone loss. Patients under active treatment should have follow-up DEXA scans at 1-2 year intervals.
well-established, age-related normative values are based upon very large numbers of individuals. Graphic display of data is often helpful, particularly in serial studies following progression and treatment (Figure 2). It does have some limitations in that normative values are available for the spine, hips, and wrist/forearm only. While the output of DEXA appears simple, one has to interpret the data with sensitivity to the effects of deformity, arthritis, and previous fractures that can give spurious results, especially in the spine. Some vertebrae may need to be excluded from the analysis. Particular attention must be paid to the femoral neck density since this is a frequent site of hip fractures. Extrapolation of density from one anatomic site to another should be done in the total context of the patient's history. Additionally, not all DEXA machines are equally calibrated, and care has to be taken when comparing results between machines. Ideally, the patient would be serially scanned on the same well-calibrated machine. While DEXA is a safe and widely available clinical tool for monitoring bone density and can accurately determine areal [two-dimensional] bone mineral density, it cannot be extrapolated to a three-dimensional volumetric density. Additionally, it does not have the ability to accurately assess structural micro-architecture nor to differentiate between cortical and trabecular bone compartments. Collectively, these constraints limit the ability of DEXA to estimate bone strength and do not allow it to provide microstructural information which can be used to assess bone quality.4

It must be appreciated also that the DEXA scan measures only bone density and does not give a clinical diagnosis of osteoporosis. Other conditions can produce low bone density and are treated quite differently, so that a biochemical analysis of the patient with low bone density is important to make an accurate diagnosis and target therapy, with or without fractures.

4. Laboratory Analysis – In 1994, Henry Mankin, then chair of orthopedics at Harvard and Massachusetts General Hospital, wrote a seminal paper on metabolic bone diseases in the orthopedic setting and described the relevant comprehensive analysis of the skeleton. While clinicians often have their individual preferences as to what constitutes core and supplementary studies, one well-targeted initial approach was described by Mankin and reviewed several times (Table 2). The laboratory approach to the skeleton consists of 1) exploring conditions other than osteoporosis that can be associated with decreased bone density such as hyperparathyroidism or hematologic malignancies, most commonly multiple myeloma; 2) identifying modifiable conditions, commonly low serum 25-hydroxy vitamin D, chronic renal failure, and secondary hyperparathyroidism, and 3) informing the appropriate choice of pharmacotherapy once primary osteoporosis is identified as the cause of low bone density. In this last category, bisphosphonates require adequate renal function, denosumab requires adequate serum calcium and vitamin D, and osteoanabolics require a normal, or at least explainable, bone-specific alkaline phosphatase.

<table>
<thead>
<tr>
<th>Goals</th>
<th>Procedures</th>
</tr>
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<tbody>
<tr>
<td>Exclude non-osteoporotic causes of low bone mass and skeletal fragility</td>
<td>Laboratory tests: Serum calcium, creatinine, alkaline phosphatase, protein electrophoresis, 24-hour urine chemistry, serum parathyroid hormone, bone turnover markers</td>
</tr>
<tr>
<td>Identify modifiable conditions such as low serum 25-hydroxy vitamin D, chronic renal failure, secondary hyperparathyroidism</td>
<td>X-ray of thoracic and/or lumbar spine for patients with loss of height and/or deformity</td>
</tr>
</tbody>
</table>

Bone turnover markers (BTMs) are a series of protein biomarkers released by osteoblasts and osteoclasts, or from bone matrix during bone remodeling. They can reflect the degree of bone formation or resorption and can provide prognostic information on the risk of fracture, progression of disease, and response to therapy. Many BTMs are under study with several currently in clinical use. Two clinically used BTMs are the C- and N-terminal telopeptides of type I collagen, the most common protein in bone matrix. The two terminal telopeptides, noted as CTX and NTX, respectively, are released by osteoclastic resorption of bone and are useful in identifying the degree of bone resorption. CTX is generally assayed in serum; NTX is assayed in urine. They have broadly similar clinical utility. Two BTMs reflect bone formation in remodeling: bone-specific alkaline phosphatase and osteocalcin. There are several genetic isoforms of alkaline phosphatase produced by the liver, intestine, and
ROLE OF AN FLS IN OSTEOPOROTIC FRACTURE CARE

Care of patients with fragility fractures is often compromised by a lack of coordination and shared expertise. Active interventions in an FLS have been shown to result in a decreased incidence of second fractures. Anti-osteoporotic therapy after a fragility fracture results in a 40% decrease in the 3-year risk of a subsequent fracture. The advantages of a coordinated post-fracture program were demonstrated by an FLS that achieved accurate diagnosis and secondary fracture prevention in 414/430 (96%) of patients with an osteoporotic fracture. Many other studies have demonstrated that coordinated care of osteoporotic fractures in organized FLS programs improves evaluation, treatment, and outcomes, and reduces fracture-related morbidity and mortality. Coordinated care in an FLS program has also been shown to result in substantial reductions in secondary fractures. As a consequence of these demonstrations, a consensus has developed around the clinical benefits of an organized FLS program. Evidence-based clinical guidelines for the evaluation and treatment of low-energy, geriatric, and fragility fractures have been developed by the American Society of Bone and Mineral Research, 39 stakeholder societies, and the NIH. While these are subject to updating, the overarching recommendation is that the FLS care delivery model is the most effective means for treating patients with low-energy fractures (i.e., fragility fractures), and that FLS programs consistently initiate and comply with best practice diagnosis and treatment guidelines more often than do traditional models.

EPIDEMIOLOGY AND ECONOMICS OF LOW-ENERGY FRACTURES

The FLS takes the position that a fracture is a signal event indicating a propensity for functional decline and reflecting underlying reduced bone density, increased fall risk, and the presence of environmental hazards. Importantly, a previous low-energy fracture is among the strongest risk factors for subsequent fractures. More specifically, patients with a low-energy fracture of the wrist, hip, proximal humerus, or ankle have a 2- to 4-fold greater risk for subsequent fractures than do individuals who have never experienced a fracture. Up to 30%-40% of patients with a vertebral compression fracture will experience additional vertebral fractures within 3 years. Compared to individuals with no history of fracture, a patient with a vertebral fracture has nearly a 5-fold increased risk of a subsequent vertebral fracture and a 6-fold increased risk of non-vertebral fractures. Notably, fractures of the spine and wrist are associated with an increased incidence of secondary hip fractures. Hip fractures account for over 350,000 hospitalizations/year, or 30% of all fracture-related hospitalizations. Outcomes after hip fractures in the elderly are often complicated by morbidity, disability, and death. Overall, 24% of these patients die within a year after fracture. Half of hip fracture patients do not regain their pre-fracture function, and many lose their functional independence and require long-term care. Taken together, these data indicate that patients who have experienced a low-energy fracture of any type have a markedly greater risk of subsequent fractures with associated morbidity than do individuals who have not fractured.

The economics of low-energy fracture care are similarly compelling. It has been estimated that the annual medical cost of treating hip fracture patients in the US exceeds $10 billion. Hip fractures are related to age and the geriatric population, and therefore as the population ages, the incidence of hip fractures can be expected to increase concurrently. As a consequence of demographic changes, medical costs related to hip fractures have been predicted to rise to $25.3 billion by 2025, and costs associated with all osteoporotic fractures are predicted to rise to over $95 billion by 2040. Multiple cost-effectiveness analyses have demonstrated the potential for substantial savings resulting from increased use of FLSs within the US healthcare system, with one 2021 study concluding that per every 1 million patients with Medicare coverage receiving secondary fracture prevention after an osteoporotic fracture, $418 million dollars could be saved and 30,000 quality-adjusted life-years could be gained. These data are especially compelling when observed in concert with the estimation that the annual incidence of osteoporotic fractures in the US is expected to rise to 3.2 million by 2040, indicating a potential cost savings of $1 billion or more per year by that time through the widespread implementation of FLSs. Other studies have demonstrated that the potential for savings is not specific to the US. Lastly, it is important to note that the economic benefits of the FLS model extend not only to direct health care expenses, but to patients and their families as well due to lifestyle changes, institutionalization, and family care often associated with the longitudinal effects of recurrent fractures, with one study estimating the indirect cost of fractures in 2018 to be $8.2 billion. The extent to which social and economic factors burden patients and families can be minimized by the timely diagnosis and management of the underlying disease processes by an FLS.
CONCLUSIONS
An FLS provides a systematic approach to osteoporotic fracture care that 1) recognizes low-energy fractures as signal events requiring further inquiry, 2) provides a framework for the comprehensive evaluation of underlying and often unexpected pathology, 3) facilitates appropriate treatment, 4) reduces the risks of secondary fractures with their attendant morbidity and mortality, 5) lowers costs for patients and healthcare systems; and 6) improves patient outcomes. This article provides an entryway into the subsequent presentations in this volume that each highlight distinct yet interconnected roles an FLS plays in providing multidisciplinary, comprehensive, high-quality, and cost-effective patient care.

References


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Osteoporosis and Fragility Fractures

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Abstract

Osteoporosis and fragility fractures (FFs) are closely intertwined as the former is a common predisposing factor to the latter. This causal relationship is due to low bone density of osteoporosis and compromised bone microarchitecture, leading to structural failure, decreased ability to withstand applied stresses, and increased propensity to fracture. Osteoporosis can be idiopathic or due to a variety of secondary causes, and numerous treatment strategies are available. FFs are common injuries among the elderly and are caused by factors both intrinsic and extrinsic to the patient. The clinical and economic significances of osteoporosis and FFs are substantial, with considerable associated morbidity and mortality, and billions spent on healthcare expenditures in the US annually. Osteoporosis and FFs are two of the most important topics related to fracture liaison services (FLSs), and their understanding is integral to appreciating the benefits an FLS can provide for patients and providers.

Keywords: Osteoporosis; fragility fracture; pharmacotherapy; hip fracture; vertebral compression fracture

Introduction

Osteoporosis is the most common cause of low bone density. It derives its clinical significance from its predisposition to fractures, often caused by low energy injuries and termed “fragility fractures.” Fractures of the spine and hips in osteoporotic individuals often result in deformity, loss of function, a variety of morbidities, and premature death. Osteoporosis is quite prevalent in the US with estimates of 40,000,000 adults suffering from low bone density. Osteoporotic fractures, which are common, result in substantial morbidity and mortality, with a woman's lifetime risk of dying from a hip fracture roughly equivalent to her risk of dying from breast cancer.

Secondary forms of osteoporosis can result from endocrine disorders, genetic mutations, and hematologic malignancies [Table 1]. Other causes of secondary osteoporosis include physical immobilization, often from neuromuscular diseases, premature menopause, athletic amenorrhea, anorexia nervosa, and alcoholism. Common medications contributing to osteoporosis include glucocorticoids, oral hypoglycemics, anticonvulsants, proton pump inhibitors, and immune modulators. Adjuvant hormonal therapies for both breast and prostate cancer reduce bone density and increase the risk of fracture. Aromatase inhibitors deprive bone of estrogen. Gonadotropin-releasing hormone (GnRH) agonists produce androgen deprivation.

Other important causes of secondary osteoporosis are related to end-stage organ failure and organ transplantation. The most rapid bone loss is observed in the first 3–6 months post-transplant and is multifactorial, with contributions from pre-transplant bone loss. Immunosuppressive agents, prominently glucocorticoids but also the calcineurin inhibitors, contribute to transplant-related bone loss. Cyclosporine and tacrolimus inhibit the enzyme calcineurin, which plays an important role in bone remodeling and whose inhibition results in increased bone resorption. Other immunosuppressants such as rapamycin and mycophenolate mofetil (CellCept) do not contribute to post-transplant bone loss. Post-transplant bone loss and fracture risk have been reported to range from 6–53% after cardiac, pulmonary, or liver transplantation. Patients with chronic renal disease pre-transplant are especially prone to reduced bone density because of the decreased renal parenchyma and inability to convert cholecalciferol to the active form, 1,25 dihydroxy vitamin D. Bone density and fractures particular to specific organ transplantations have been described in detail.

Bone Structure and Osteoporosis

Bone is characterized, in part, by an ongoing remodeling process of resorption and formation of both osteoid, the organic...
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component of bone matrix, and mineral in the form of calcium hydroxyapatite. An imbalance in remodeling in favor of resorption results in the net reduction of bone tissue per unit volume. Osteoporosis is characterized histologically by low trabecular bone volume and number, cortical thinning due to endosteal reabsorption, increased bone porosity, and compromised bone microarchitecture. Notably observed are thin, discontinuous trabeculae that reduce the ability of bone to withstand applied stresses and predispose to structural failure or fracture (Figure 1). Structural compromises are due to bone resorption, reduced osteoid formation, and decreased mineralization.

The histopathologic characteristics of osteoporosis are reflected in conventional radiographic features that provide clues to reduced density of both cortical and trabecular bone and indicate the need for further investigation. Cortices normally occupy about 50% of the diameter of the diaphysis on the anteroposterior X-ray. Endosteal resorption, cortical thinning, and concomitant medullary canal widening reflect the presence of severe osteoporosis (Figure 2). Bone trabeculae normally align coincident with patterns of stress and loss of trabeculation can be an early indicator of decreased bone density. Tensile trabeculae are lost before compressive trabeculae. Loss of compressive trabeculae usually indicates severely reduced bone density (Figure 3).

CELL BIOLOGY

Osteoporosis results from an imbalance between osteoblastic bone formation and osteoclastic bone resorption in bone remodeling. Remodeling of bone consists of the coupled activity of osteoclasts and osteoblasts communicating by endocrine and paracrine signaling. In a remodeling cycle, osteoclasts first resorb bone matrix closely followed by osteoblastic new bone formation. Endocrine regulation by estrogen, thyroid and parathyroid hormones, glucocorticoids, and vitamin D acting through cell surface receptors is essential for maintenance of bone volume and structure. Receptors for bone morphogenetic proteins and low-density lipoprotein receptor-related protein 5 (LRP5) have been found on osteoblast precursors. LRP5 functions as a Wnt receptor and is important for bone formation since deletion of LRP5 results in profound osteoporosis. The Wnt pathway is a complex, highly conserved signaling pathway that regulates cell fate commitment and is crucial in determining polarity and axis patterning in embryogenesis. The family of Wnt proteins regulate bone formation through the LRP5 receptor. Wnt signaling is regulated in part by sclerostin, a protein synthesized by osteocytes, that binds to the LRP5 receptor on osteoblasts and inhibits canonical Wnt signaling.
resulting in a decrease in bone formation. Studies of the genetics of the osteoporosis pseudoglioma syndrome have shown mutations in the LRP5 gene. Recently, biopharmaceuticals have been developed which inhibit sclerostin expression allowing greater Wnt binding to LRP5, resulting in enhanced activation of canonical Wnt signaling and preserving bone mass in the remodeling process.

PATHOPHYSIOLOGY – BONE AS A CALCIUM DONOR

Maintenance of serum calcium concentration is a homeostatic priority because of the dependence upon it of cell membrane signal transmission including neuromuscular excitation-contraction coupling of skeletal and cardiac muscle. Responses to hormonal regulation, the conductivity of nerves, and the contractility of muscle are directly affected by cytosolic calcium concentration. To accomplish this homeostatic regulation, parathyroid hormone and 1,25, dihydroxy vitamin D interact with three organ systems, renal, gastrointestinal, and skeletal, to regulate serum calcium concentration within appropriate levels to ensure both normal membrane transmission and the calcium-phosphorus solubility product. Among the organs maintaining serum calcium concentration, bone is unique in that its role as a calcium donor can compromise its structure and lead to decreased bone density and fractures. In fact, the role of bone as a calcium donor takes precedence over its structural roles of support, leading to the perspective that the primary function of bone is to act as the reservoir for serum calcium. Chronic, low-grade demand for serum calcium exerts a downward physiologic pressure on bone calcium stores and can lead to resorption of calcium from bone and osteoporosis. In response to serum calcium requirements, parathyroid hormone and vitamin D increase intestinal absorption of calcium, enhance renal tubular reabsorption of calcium, induce a phosphate diuresis, and produce osteolytic via osteocytic bone resorption. It is only bone that suffers a loss of structural integrity in this complex interaction to maintain serum calcium concentration.

DEXA SCANNING IN OSTEOPOROSIS

Bone density determination by dual-energy X-ray absorptiometry (DEXA) scanning is described in The Roles of a Fracture Liaison Service in this volume. The T-score is utilized as the DEXA criterion for osteoporosis. The World Health Organization has defined osteoporosis as either a T-score below -2.5 in men and postmenopausal women over 50, or a low-energy hip or spine fragility fracture regardless of bone mineral density. DEXA scanning is very useful in osteoporosis but, as pointed out, it must be appreciated that it does not provide a pathological cause of reduced bone density and needs to be interpreted in the whole patient context.

PHARMACOLOGIC TREATMENT OF OSTEOPOROSIS

Two therapeutic strategies are applied to the medical treatment of osteoporosis. Because bone loss is often due to overactive resorption, anti-resorptive agents are the first-line therapy, especially if excessive resorption is shown by bone turnover markers. Repairing microstructural damage requires the use of osteoanabolics. Prior to instituting pharmacotherapy, adequate serum calcium and vitamin D need to be assured and deficiencies corrected. Combining dietary and supplemental sources, about 1000–1200 mg/day of calcium and 1000–2000 IU/day of vitamin D for individuals with osteoporosis are recommended.

Pharmacotherapy needs to be tailored to the specific patient’s medical condition, fracture history, DEXA scans, and laboratory evaluation. For example, oral agents may not be suitable for individuals with gastroesophageal reflux, Barrett’s esophagitis, or bariatric surgery. Additionally, most medications have time limitations and long-term therapies are often complicated by the need for sequential prescriptions.

Oral bisphosphonates such as alendronate (Fosamax), risendronate (Actonel), and others, may be the agents of choice in mild to moderate osteoporosis. They exhibit different efficacies and durations of action but all are anti-resorptive. They are analogues of pyrophosphate, bind to the surface of hydroxyapatite crystals, and inhibit osteoclastic bone resorption. Since they depend upon renal clearance, patients should have a creatinine clearance >30 ml/min. Bisphosphonates cannot be used for >5 years because of atypical femur fractures discussed in the section on fragility fractures below.

Denosumab (Prolia) is a human monoclonal antibody that acts as a decoy receptor for receptor activator of nuclear factor kappa-B ligand (RANKL) and inhibits the differentiation and activation of osteoclasts. It is an injectable anti-resorptive and may be a better choice for some patients who cannot take oral agents, assuming they can and will take adequate calcium supplements since it can lower serum calcium concentration. Denosumab increases the mineral density of the hip and spine and reduces resorptive bone markers to a greater degree than bisphosphonates. It has been shown to reduce hip and vertebral fractures by 40–60%. Denosumab is not dependent upon renal function and does not produce gastrointestinal symptoms. It has been associated with increased risks of a variety of infections, however, and should not be used in patients who are subject to recurrent infections, have impaired immune systems, or are on immunosuppressive agents.

Two parathyroid hormone-related agents are of interest for their anabolic effects on building bone density. Parathyroid hormone (PTH) 1–34, teriparatide (Forteo) and the PTH-rP analogue, abaloparatide (Tymlos) produce both cortical and trabecular bone formation and reconnect discontinuous trabeculae. The parathyroid analog osteoanabolics should not
be used in individuals with risks of sarcomas. Patients need to be screened for possible bone malignancies and recommended usage is limited to 2 years.

**FRAGILITY FRACTURES**

Fragility fractures, as defined by the International Osteoporosis Foundation, are fractures that result from low-energy trauma, such as a fall from standing height. Common fragility fracture patterns include fractures of the distal radius, vertebrae, proximal humerus, hip, and pelvis. Nine million fragility fractures occur annually worldwide, equating to one fracture every three seconds. Approximately 1 in every 3 women and 1 in every 5 men over the age of 50 will experience an osteoporosis-related fracture during the course of their lifetimes, with these proportions anticipated to rise. In 2010, there were an estimated 158 million individuals at high risk for fragility fracture and this figure is projected to double by 2040. Individuals who experience fragility fractures incur an 86% increased risk of a subsequent fracture. Among these individuals, between 5–10% of patients experience a subsequent hip fracture, with 23% occurring within a year of their first hip fracture and 70% within the first five years. Patients with a history of vertebral osteoporotic fracture have a 2.3-fold increased risk of future hip fracture and a 1.4-fold increased risk of distal forearm fracture. Given this data, it is important that primary care physicians and orthopedic surgeons collaborate to recognize, prevent, and treat osteoporosis.

**THE IMPORTANCE OF FALLS IN FRAGILITY FRACTURES**

Important associations with low-energy fractures are falls and poorly arranged living spaces contributing to falls. Falls are a major contributing cause of fractures and can be associated with muscle weakness, balance disturbances, and impaired vision and hearing that predispose to environmental distractions. One study identified bone-related and fall-related risk factors and, while these risk factors may overlap, the study points out the importance of falls in low-energy fractures. Related contributions to falls and fractures are unsafe environments which can result from cluttered or obstructed walkways, poor lighting, insecure floor mats, unstable area rugs, unsafe bathrooms with slippery surfaces, and the absence of grab bars in showers and bathtubs. Iatrogenic contributions to propensity to fall center on medications such as sedatives and anti-hypertensives, as well as polypharmacy that leads to unsafe medication interactions. The physical and environmental contributions to fractures are not to be neglected and should be part of every screening conversation.

**TREATMENT OF FRAGILITY FRACTURES**

Several general principles exist among patterns of osteoporotic fracture presentations. For example, distal radius fractures, which are among the most common fragility fractures, can often be managed with closed reduction and splinting/casting as the first line of treatment. Proximal humerus fractures can also often be managed nonoperatively when sufficiently well-aligned, with sling immobilization being a common first-line treatment modality. Conversely, hip fractures are typically managed surgically with fracture fixation or replacement arthroplasty procedures to prevent complications related to immobility, such as deep venous thrombosis, pneumonias, and decubitus ulcers. Specific patient characteristics, such as overall health, functional status, fracture morphology, and patient activity level, are essential to consider when deciding between operative or nonoperative management.

**Figure 4. Illustration demonstrating the interactions of falls and low bone density in the fracture diathesis**

Bone-related and fall-related risk factors interact with low bone density contributing to fractures.

**Table 2. Risk Factors for Fracture**

<table>
<thead>
<tr>
<th>Bone-Related Risk Factors</th>
<th>Fall-Related Risk Factors</th>
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<tbody>
<tr>
<td>Fracture history</td>
<td>&gt;1 fall last year</td>
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<tr>
<td>Mother with fracture history</td>
<td>Psychoactive drugs</td>
</tr>
<tr>
<td>Body mass index (BMI) &lt; 19</td>
<td>Low level of activities of daily living</td>
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<tr>
<td>Severe immobility</td>
<td>Articular symptoms</td>
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<tr>
<td>Glucocorticoids</td>
<td>Impaired vision</td>
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<td></td>
<td>Urinary incontinence</td>
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<td></td>
<td>Parkinson’s Disease</td>
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(Adapted from reference 19 with permission.)
Fractures in the setting of osteoporosis are particularly challenging to treat for multiple reasons and require special consideration by the treating clinician. Osteoporotic bones are less dense than healthy bone, often leading to more comminuted, complex periarticular fracture patterns. In addition to meticulous surgical technique, specialized implants [e.g., fixed angle or locking devices] and more robust implants may be required to obtain and maintain adequate fracture alignment in the operating room. Due to the mechanical properties of osteoporotic bone resulting from porous cancellous and thin cortical bone, rigid implants must be used for added support and longevity. As such, implant loosening, implant retention, and peri-implant fractures are more common complications of osteoporotic fracture treatment. Fragility fractures typically occur in elderly and metabolically depleted patients who have decreased capacity to manage their functional limitations and weight-bearing status, leading to increased falls and corresponding increased loading of the fixation constructs. Additionally, elderly individuals often have marginal nutritional and hydration status and other medical comorbidities making them more vulnerable to post-traumatic complications including infection, poor wound healing, and venous thrombosis. Brisk mobilization is desirable to counteract some of these morbidities adding to the challenges of stabilizing or replacing osteoporotic bone to facilitate early weight bearing.

CONSIDERATIONS WHEN USING BISPHOSPHONATES

Bisphosphonates are first-line medications in the treatment of osteoporosis, but like most medications are associated with particular risks. Although concerns have been raised about retardation of fracture healing, studies have failed to detect differences in time to fracture healing and other outcomes with bisphosphonate use in surgically repaired hip and distal radius fractures. Atypical femur fractures (AFFs) are an important clinical entity about which to be aware in patients treated with bisphosphonates, especially those patients treated for over 5 years. AFFs are defined by a characteristic type of subtrochanteric, short-oblique hip fracture originating in the lateral cortex of the proximal femur and occurring with no or minimal trauma. AFFs may occur without prodromal symptoms or may be preceded by a dull, aching pain in the proximal thigh. This type of pain should not be disregarded. A high index of suspicion should be maintained for this fracture type in patients on long-term bisphosphonates, especially with thigh pain, and should stimulate imaging. AFFs may appear as stress fractures on plain X-rays but they also may be invisible on X-rays and seen only on MRIs. Therefore, patients presenting with proximal thigh pain and normal X-rays on long-term bisphosphonates should be studied with an MRI.

Although the relative risks of AFFs are high in patients on bisphosphonates, their absolute risk is extremely low, ranging from 3.2 to 50 cases per 100,000 person-years. However, long-term use (>3 years) may be associated with higher risk (>100 per 100,000 person-years). The risk-benefit ratio of bisphosphonates is highly supportive of their use assuming that the duration of use is kept below 5 years. An investigation of the cost-benefit of the risk of AFFs versus fragility fracture prevention with bisphosphonates analyzed 196,000 women who were aged 50 or older receiving bisphosphonates and concluded that reductions in the risk of osteoporotic hip fractures during 1–10 years of bisphosphonate use far outweighed the increased risk of AFF among White patients, with a less quantifiable effect among Asian patients.
OUTCOMES OF FRAGILITY FRACTURES

Fragility fractures have a substantial impact on a patient’s personal, family, and financial life. The impact of fragility fractures, particularly those of the hip, can lead to early morbidity and mortality. Patients often experience some degree of loss of function, primarily independent gait, and loss of overall personal and functional independence. Mortality in the first year after hip fracture surgery ranges between 15% and 36%. Also, there are significant financial burdens placed on patients with fragility fractures, with those related to inpatient medical services, skilled nursing facilities, and homecare, comprising the highest expenses.

PREVENTION OF FRAGILITY FRACTURES

Fragility fractures are, to a degree, preventable through assessment of risk and multimodal therapy. A full evaluation of risk factors should be carried out as described above. Antiresorptive agents are first-line medications that should be considered in patients identified as at-risk for fragility fractures. Certain modifiable factors, such as tobacco use and excessive alcohol intake, are detrimental to bone health. Therefore, cessation of tobacco use and limiting alcohol consumption should be recommended. Adequate intake of calcium and vitamin D are important nutritional factors to consider. The National Osteoporosis Foundation recommends 1200 mg/day of calcium [from diet or supplement] as well as 800–1200 IU/day of Vitamin D for all adults over 50 years of age. Weight-bearing exercise is another important consideration for high-risk patients. A Cochrane review investigated the effect of exercise on prevention of bone loss and fractures in postmenopausal women and identified a statistically significant improvement of bone mineral density associated with exercise. Since these fractures are commonly a result of falls, patient safety at home must be considered. Related recommendations include balance training exercises, avoiding central nervous system depressants, careful monitoring of hypertension medication, and recommending visual corrective devices when needed. Finally, the U.S. Preventive Services Task Force recommends bone mineral density testing in all women aged 65 years and older and in postmenopausal women younger than 65 years with increased risk as determined by a formal clinical risk assessment. They currently do not recommend screening men due to insufficient evidence.

CONCLUSIONS

Osteoporosis is the most common cause of low bone density. It derives its clinical significance from its association with fragility fractures and their attendant morbidity and mortality. (1) Osteoporosis may be idiopathic, postmenopausal, or senile, and may result from multiple secondary causes as well; (2) cortical and trabecular resorption and porosity lead to structural weakness and predispose to fractures; (3) assuming appropriate causal diagnosis, pharmacologic treatments are available to increase bone density and decrease the risk of fractures; (4) falls are associated with osteoporotic fractures and can be due to both bone-related and fall-related factors as well as unsafe environments; (5) and despite state-of-the-art surgical therapy, fragility fractures often pose grave consequences in terms of morbidity and mortality, as well as economic, family, and personal costs.

References


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Osteomalacia and Renal Osteodystrophy

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ABSTRACT

Osteomalacia is defined by the undermineralization of newly formed bone due to a lack of available calcium, phosphorus, or vitamin D. Causative factors of osteomalacia include nutritional deficiency, diminished absorptive capabilities (often due to gastrointestinal disorders), and renal insufficiency. Renal osteodystrophy is a specific form of metabolic bone disease defined by the presence of osteomalacia and associated hyperparathyroidism secondary to a malfunction in, or absence of, renal parenchyma. This reduces the conversion of vitamin D to its active form, thus leading to a cascade of effects that negatively impact the stability of the skeleton. Osteomalacia occurs across a spectrum of severity and can produce severe consequences for specific populations, including patients with dietary, nutritional, and absorptive deficiencies. Renal osteodystrophy affects patients with chronic kidney disease, those undergoing dialysis, and renal transplant patients. Special considerations must be taken into account when assessing the bone health of patients fitting these criteria.

KEYWORDS: Osteomalacia, renal osteodystrophy, chronic kidney disease (CKD), reduced calcium absorption

INTRODUCTION

Osteomalacia is defined as “the lack of available calcium or phosphorus [or both] for mineralization of newly formed osteoid.” In classic papers, Henry Mankin, former chair of orthopedics at Harvard and Massachusetts General Hospital, reviewed the osteomalacias and the identification of vitamin D deficiency as the prototype of the disease. He provided an etiological classification of the osteomalacias as deficiency, absorptive, and renal. In addition to vitamin D deficiency, osteomalacia can be produced by a variety of other conditions that impair mineralization (Table 1). The most common causes of osteomalacia are gastrointestinal disorders causing malabsorption, including enteric, hepatobiliary, and pancreatic diseases, short bowel syndrome, and some bariatric procedures. Less commonly these days, but still to be considered, are medications including the anti-convulsants phenobarbital, phenytoin, and carbamazepine, which can alter hepatic vitamin D metabolism. Renal osteodystrophy is a special case in which osteomalacia coexists with hyperparathyroidism.

Table 1. Etiological Classification of Rickets and Osteomalacia

<table>
<thead>
<tr>
<th>I. Deficiency Rickets and Osteomalacia</th>
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<tbody>
<tr>
<td>A. Vitamin D deficiency</td>
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<tr>
<td>B. Calcium deficiency</td>
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<td>C. Phosphorus deficiency</td>
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<td>D. Chelators in diet</td>
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<tr>
<th>II. Absorptive Rickets and Osteomalacia</th>
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<tbody>
<tr>
<td>A. Gastric abnormalities</td>
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<tr>
<td>B. Biliary disease</td>
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<tr>
<td>C. Enteric absorptive defects</td>
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<tr>
<th>III. Renal Tubular Rickets and Osteomalacia</th>
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<tr>
<td>A. Proximal tubular lesions</td>
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<tr>
<td>B. Proximal and distal tubular lesions</td>
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<td>C. Distal tubular lesions (renal tubular acidosis)</td>
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| IV. Renal Osteodystrophy |

CLINICAL PRESENTATION

The clinical presentation of osteomalacia is often asymptomatic but, when severe, mainly reflects symptoms of hypocalcemia, including myalgias, muscle spasms, and bone pain. More severe symptoms related to hypocalcemia include tetany and seizures, chronic vitamin D deficiency can lead to long bone and limb angular deformities. Undermineralized newly formed bone is the hallmark of both osteomalacia and rickets, the juvenile form of osteomalacia. On radiographs, bones appear osteopenic often with a ground glass appearance and indistinct trabeculae. Stress fractures with radiodense lines adjacent to regions of radiolucency may be seen on the concave sides of bones. These are termed Looser lines, also called Milkman pseudofractures, after the aptly named radiologist, Louis Milkman, who described the radiological appearance of pseudofractures in osteomalacia (Figure 1). Characteristic osteomalacic
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hip fractures resemble slipped femoral capital epiphyses and may occur over time with minimal symptoms. Stress fractures are common and may be seen by MRI and technetium bone scans; they may not be apparent radiographically until a healing callus is present. Histologic characteristics of osteomalacia are trabeculae covered with long, wide osteoid seams due to the lack of mineralization, contributing to the ground glass radiologic appearance of trabeculae (Figure 2). On bone biopsy with tetracycline labeling, smudged, indistinct tetracycline labels occur from the impaired mineralization.

PHYSIOLOGY OF DEFICIENCY OSTEOMALACIA

Apart from its structural function, bone serves as a reservoir for calcium. Calcium plays a critical role in cell membrane signaling and neuromuscular signal transmission; there is a narrow range of safety for serum and cytosolic calcium concentrations. Hypercalcemia causes hypotonicity, hyporeflexia, obtundation, and coma, whereas hypocalcemia causes hypertonicity, hyperreflexia, and seizures. The homeostatic priority of maintaining soluble calcium concentration utilizes three organ systems to achieve rigorous control: the gastrointestinal, renal, and skeletal systems. The skeletal system is unique as a calcium donor because the downward pressure of transient calcium deficiency can lead to compromise of bone structure and increased fracture risk. In this context, bone resorption to maintain serum calcium homeostasis takes priority over the structural role of bone.6

Serum calcium exists in ionized and protein-bound forms, with the ionized form being metabolically active and critical for cell signaling. In states of decreased serum calcium, the body’s homeostatic response includes regulation via PTH and vitamin D. Vitamin D is a fat-soluble vitamin which has two main sources: ergocalciferol is a plant-derived dietary source, and cholecalciferol, which derives from 7-dehydrocholesterol. After irradiation in the skin which opens these molecules’ sterol rings, two hydroxylation steps take place.7 The first occurs in the liver to form 25(OH)D, the storage form of vitamin D, and the second in the kidney to form 1,25 di(OH)D, the metabolically active form, or 24,25 di(OH)D which is less active and less regulatory. Active vitamin D raises serum calcium concentration by increasing intestinal calcium absorption, promoting a renal phosphate diuresis, increasing renal tubular reabsorption of calcium, and increasing the transfer of calcium from bone to serum. Parathyroid hormone stimulates the production of 1,25 di(OH)D, and both hormones increase serum ionized calcium concentration.6 Vitamin D deficiency can be nutritional and has several other etiologies. Direct sunlight is required to irradiate dietary vitamin D and open its sterol rings. Individuals with reduced sunlight exposure, such as those who live in locations farther from the equator, can have lower serum vitamin D levels.8 Additionally, heavily pigmented skin with high levels of melanin can affect the irradiation of vitamin D. Obesity and increased age can also result in reduced production of vitamin D to its active form.

DEFICIENCY RICKETS

Rickets is the juvenile form of osteomalacia and occurs in skeletons with open growth plates.9 Because rickets and osteomalacia are failures of mineralization, it is not surprising that rickets is manifest largely in the physis (Figure 3). Deficiency in mineralization of the physis results in the growth of unmineralized cartilage reflected radiographically as cupping, widening, or flaring of the growth plate, with blurring of the mineralization front. Femoral neck fractures are characteristic of osteomalacia and resemble slipped capital femoral epiphyses. The prototype of the juvenile form is nutritional rickets, usually due to vitamin D or calcium.
deficiency. While rickets is less prevalent in the industrialized world, it is still present there in unusual situations. Rickets can be seen as a result of malnutrition in nutritionally deprived populations or as a result of individual dietary eccentricities and emotional eating disorders. Whether or not florid growth plate abnormalities are present, an index of suspicion should be maintained in children with the appropriate medical histories and atypical fractures. Bone density determination will assist in the diagnosis and detailed laboratory investigation is usually warranted.

**A ABSORPTIVE OSTEOMALACIA**

A range of gastrointestinal conditions can cause malabsorption of nutrients and absorptive osteomalacia, decreased bone density, and fractures. Malabsorption of nutrients from the gastrointestinal tract has profound effects on the skeleton by depriving osteocytes of hormonal control and osteoid of its constituent calcium. The subject of malabsorption is quite complex and, for our purposes, will be broadly considered in two forms.

1. Pancreatic insufficiency, pancreatitis, cystic fibrosis, and hepatobiliary diseases, including cirrhosis and alcoholism, reduce the secretion of bile and pancreatic enzymes and impair the ability to digest and absorb fats including the fat-soluble vitamins, A, D, E, and K, contributing to an absorptive vitamin D-deficient osteomalacia and low serum 25(OH)D.

2. Enteric malabsorption is due to the loss of absorptive surfaces of the duodenum and proximal jejunum. Loss of absorptive villi can be due to inflammatory diseases such as Crohn’s disease, celiac disease, and sprue, surgical short bowel syndrome, or small intestinal bacterial overgrowth syndrome.

Other forms of absorptive osteomalacia occur due to intestinal binding of calcium. Calcium absorption from the gastrointestinal tract is regulated by vitamin D and PTH. Vitamin D is fat-soluble and is dependent on bile salts for absorption, which primarily takes place in the proximal duodenum and proximal jejunum. Chelating agents such as oxalate (in spinach), phytate (in coarse cereals), or excessive concentrations of phosphate or free fatty acids make calcium more difficult to absorb as calcium can bind to these molecules creating materials that are insoluble in body fluids.

**MALABSORPTION AND FRACTURES AFTER BARIATRIC SURGERY**

Bariatric surgery has been very helpful to patients with morbid obesity. However, like many medical interventions, it has its risks and management challenges. Bariatric surgery can have negative consequences for the skeleton, including osteomalacia and increased risk of fractures. Current procedures involve (1) Restriction or reduction in stomach size such as gastric banding and gastric sleeve procedures, and (2) Malabsorption procedures that bypass segments of the proximal stomach and small intestine such as the Roux-en-Y gastric bypass. The influences upon the skeleton that occur after surgery are specific to the procedure type, with the most pronounced metabolic abnormalities and bone loss seen after procedures that result in the most malabsorption.

Bone disease among bariatric surgery patients is influenced by pre-operative abnormalities in bone and mineral metabolism related to morbid obesity. The effects of obesity on the skeleton can be profound and often center around vitamin D deficient osteomalacia secondary to sequestration of vitamin D in adipose tissue. Vitamin D deficiency is often the source of hyperparathyroidism in obese individuals.

The hip is the most consistent site for bone loss after bariatric procedures. Measurements of hip bone density show losses in the range of 6–10% 1 year after bariatric procedures, and these can be seen for 10 years after surgery. The bone loss that occurs after bariatric surgery is likely multifactorial. Proposed mechanisms include skeletal unloading, abnormalities in calciotropic hormones, and changes in gut hormones. Increased bone resorption can be assessed by elevated levels of the blood and urine bone resorption markers, NTX and CTX. Evaluation of bone biopsies up to 4 years after bariatric procedures have shown alterations in micro-architecture including decreased cortical thickness, declining mineralization, and increases in osteoid volume consistent with hypovitaminosis D and hyperparathyroidism.

The risk of fractures, including fragility fractures, in this clinical setting is increased at the hip, spine, and wrist. Management of nutritional deficiencies after bariatric procedures can often be done using high doses of ergocalciferol. After replacement, maintenance doses of calcium [1000-1200 mg/d] and vitamin D [2000 IU/d] can be used with monitoring of serum 25(OH)D, PTH, serum and urine calcium, and DEXA bone density with adjustment of supplements as necessary. Bone densities may decline but replacement therapy can often keep the densities out of the osteoporotic range.
RENALE OSTEODYSTROPHY

Patients with advanced kidney disease are at high risk of bone disorders that range from osteitis fibrosa to adynamic bone disease, also known as osteomalacia. Osteitis fibrosa is a result of overactivation of the parathyroid gland resulting in excess parathyroid hormone (PTH) release. This leads to increased bone turnover and, in advanced cases, brown tumor formation. Renal osteodystrophy denotes hyperparathyroidism, lack of osteoid mineralization (osteomalacia), and bone resorption, described previously as osteitis fibrosa cystica (Figure 5). Isolated osteomalacia is a result of over-suppression of the parathyroid gland decreasing PTH release. This results in decreased osteoclast and osteoblast activity and low bone turnover, leading to the formation of brittle bones that are prone to fractures. In addition to direct bone pathology, calcium, phosphorous, and PTH dysregulation leads to increased cardiovascular disease from vascular calcification. Hormones and minerals involved in the process include PTH, Fibroblast Growth Factor-23 (FGF-23), 1,25-dihydroxyvitamin D (calcitriol), calcium, and phosphorous (Table 2).

The nephron is the functional unit of the kidney, and each kidney is comprised of approximately one million nephrons. Nephrons are responsible for converting 25-hydroxy vitamin D, the inactive storage form, to 1,25-dihydroxyvitamin D (calcitriol), the metabolically active form of vitamin D. With a loss of renal parenchyma, the ability to produce active vitamin D decreases. Nephrons also regulate phosphorus homeostasis by excretion and reabsorption as needed. Nephrons are a target of FGF-23, PTH, and calcitriol. The exact mechanisms of interaction are not fully understood, but studies are ongoing. In chronic kidney disease (CKD), the number of functioning nephrons decreases over time. The physiology of CKD is summarized in Table 2. As the quantity of nephrons decreases in advanced CKD, phosphorous excretion diminishes, resulting in elevation of serum phosphorus concentration. Osteocytes sense this elevation in serum phosphorous and secrete FGF-23 which acts on the nephron and enhances phosphaturia. In addition to phosphaturia, FGF-23 also suppresses the synthesis of calcitriol. As the CKD progresses, phosphorous excretion...
phosphorous intake to less than 800 mg/day. At recommended dietary phosphate load and therefore are asked.

Patients on dialysis lose their ability to excrete the rec-

DIALYSIS

Serum concentration above 80 pg/ml of intact PTH is diagnostic of hyperparathyroidism. Secondary hyperparathyroidism can be diagnosed if the PTH level is elevated above 80 pg/ml, advanced CKD is present, and serum calcium level is normal. Aggressive suppression of PTH to below 80 pg/ml in CKD leads to adynamic bone diseases and other adverse effects. The target treatment range for elevated PTH is unclear, but expert guidelines suggest that PTH levels of 2–10 times the upper limit of normal are acceptable. Progressive increase in serum PTH level, even if within the therapeutic range mentioned above, warrants intervention to prevent tertiary hyperparathyroidism. Intervention can be in the form of reducing serum phosphorus levels through dietary modification, starting patients on a phosphate binder with meals, using vitamin D analogs like paricalcitol and hectorol, or adding a calcimimetic such as cinacalcet if the PTH continues to rise. Parathyroidectomy is reserved for patients with tertiary hyperparathyroidism. Conversely, over-suppression of PTH by administering a vitamin D analog or a calcimimetic will lead to adynamic bone disease resulting in brittle bone and increased risk of fracture.

DIALYSIS

Patients on dialysis lose their ability to excrete the recommended dietary phosphate load and therefore are asked to limit phosphorous intake to less than 800 mg/day. At times, this becomes challenging given the abundance of phosphorous in foods generally considered healthy, such as dairy products, beans, grains, and nuts. Phosphorous is cleared by dialysis mostly via diffusion. This clearance is limited to 800–1200 mg per dialysis session. In our current dialysis delivery structure, patients receive dialysis three times a week. Based on this, patients are in a net positive phosphorus balance for 4 out of 7 days per week. Even with dietary phosphorous binders, it becomes challenging to regulate serum phosphorus concentration as there is active calcium and phosphorus release from bones driven by PTH secretion. Therefore, an aggressive dietary phosphorous restriction is recommended to avoid hyperphosphatemia, elevated FGF-23, decreased serum calcium concentration, elevated PTH secretion, and increased bone resorption.

TRANSPLANTATION

Kidney transplant recipients may also experience calcium, phosphorous, and bone pathology due to adverse interactions among the parathyroid gland, kidney, and bone. Most transplant recipients with an adequately functioning transplanted kidney do not experience these pathologic interactions, but, depending on their transplanted kidney function, they may need to modify their dietary habits and regulate phosphorus intake. Studies have shown that hypophosphatemia leads to improved transplant graft survival and improved cardiovascular mortality. This is thought to be due to enhanced phosphorous from functioning transplanted graft, leading to a reduction in FGF-23 level, which is linked to cardiovascular mortality. Depending on the length of end-stage renal disease status, previous phosphorus control, and PTH levels, transplant patients are often at risk of tertiary hyperparathyroidism requiring parathyroidectomy. They are also at risk of severe hypocalcemia post parathyroidectomy due to hungry bone syndrome. In end-stage renal disease patients, persistently elevated PTH levels deplete bone of calcium and phosphorus stores. Once the parathyroid gland is removed, calcium and phosphorus are aggressively taken up by bone. This leads to a precipitous drop in serum calcium and phosphorus concentration risking acute arrhythmia and respiratory failure if unaddressed.

As kidney disease advances, either in the native or transplanted kidney, phosphorous excretion declines leading to hyperphosphatemia. This leads to elevation of FGF-23 and decreased calcitriol synthesis resulting in hypocalcemia. Hypocalcemia leads to increased elevation of PTH. Persistent, unregulated elevation of PTH can lead to tertiary hyperparathyroidism and osteitis fibrosa. Conversely, over-suppression of PTH via administration of calcitriol can also have negative consequences in the form of osteomalacia. Therefore, it is essential that patients regulate their phosphorus intake to prevent hyperparathyroidism and maintain good bone health.

Figure 6. Mechanisms of CKD progression leading to secondary hyperpara-thyroidism.
CONCLUSIONS

Pathologically low serum vitamin D has profound effects on the skeleton including hormonal dysregulation of osteocytes and mineralization deficiency. [1] Reduced gastrointestinal calcium absorption exerts a downward pressure on serum calcium concentration that can lead to secondary hyperparathyroidism to maintain serum calcium but at the expense of bone calcium and resulting decreased bone density. [2] In all forms of osteomalacia, the structural function of the skeleton is sacrificed to maintain serum calcium concentration, resulting in loss of skeletal mass, reduced bone density, and elevated fracture risk. [3] Renal osteodystrophy consists of osteomalacia, secondary hyperparathyroidism, and bone resorption. The lack of renal parenchyma in CKD results in an inability to convert 25(OH)D to its active form and diminished phosphate excretion leading to hyperphosphatemia and hypocalcemia.

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Monoclonal Gammopathies in a Fracture Liaison Service

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ABSTRACT
Monoclonal gammopathies are a spectrum of disorders characterized by the overproduction of plasma B-cells and immunoglobulin. Monoclonal gammopathy of uncertain significance (MGUS), a pre-malignant form of multiple myeloma, is defined by relatively low bone marrow concentration of clonal plasma cells and asymptomatic clinical presentation. New evidence, however, points to an association of MGUS with osteoporosis, microarchitectural bone deficiency, and fractures, and it has been suggested that it be renamed “Monoclonal Gammopathy of Skeletal Significance.” The prevalence of MGUS in the general geriatric population is estimated to be 3–8%, while the prevalence in geriatric vertebral fracture patients is 15%, and the prevalence in all fracture patients within the Rhode Island Fracture Liaison Service is 10%. Therefore, MGUS and other monoclonal gammopathies should be suspected in all patients diagnosed with osteoporosis or an osteoporotic fracture, and patients diagnosed with monoclonal gammopathies should be evaluated for osteoporosis and fracture risk and treated appropriately.

KEYWORDS: monoclonal gammopathy of undetermined significance; multiple myeloma; plasma cell neoplasms; fractures

INTRODUCTION
Monoclonal gammopathies represent a spectrum of bone marrow disorders caused by clonal expansion of plasma B-cells that overproduce an immunoglobulin, or monoclonal paraprotein, with consequences that are similarly variable. The most common resulting malignancy is multiple myeloma (MM), which is characterized by >10% of these plasma cells in the bone marrow with end-organ dysfunction such as hypercalcemia, renal dysfunction, anemia, and bone lesions, also known as “CRAB” signs. Multiple myeloma is the second most common hematologic malignancy, and will likely be diagnosed in over 30,000 Americans this year. At the other end of the monoclonal gammopathy continuum is monoclonal gammopathy of unknown significance (MGUS), a pre-malignant condition defined by low bone marrow concentrations of clonal plasma cells (<10%) and thus low circulating serum monoclonal protein. It is characterized by clinically asymptomatic disease without constitutional symptoms, anemia, lymphadenopathy or hepatosplenomegaly. It is becoming clearer that, despite its name, MGUS is rarely of no clinical significance, with subcategories including monoclonal gammopathy of renal significance (MGRS), monoclonal gammopathy of neurological significance, and the proposed monoclonal gammopathy of skeletal significance, indicating that low circulating monoclonal protein concentrations may still have limited but important end-organ effects. Blurring the line between the two extremes is smoldering multiple myeloma (SMM). Monoclonal gammopathies can also result in the development of solitary plasmacytoma of bone, solitary extramedullary plasmacytoma, light chain (AL) amyloidosis, or Waldenström Macroglobulinemia.

CLINICAL FEATURES OF MGUS
MGUS is the most common monoclonal gammopathy, found in approximately 3% of adults over age 50 and in 5% of adults older than the age of 70. Interestingly, one study found the risk of MGUS to be 3.6% in patients with osteoporosis and 2% in those patients without osteoporosis. Another study of patients with acute osteoporotic vertebral fractures found the risk of MGUS to be up to 15%. The rate of progression from MGUS to MM over a lifetime varies, based on the amount of monoclonal paraprotein, the involved to uninvolved free light chain ratio, and the immunoglobulin isotype. The average risk of progression is approximately 1% each year. This is a linear risk as long as significant growth of the plasma cell clone does not move patients from the diagnosis of MGUS to smoldering multiple myeloma. Lifetime risk depends upon age at diagnosis. For a 65-year-old individual with an estimated life expectancy of 20 years, the risk can be considerable and justifies close follow-up.

Screening laboratory studies for monoclonal gammopathies should include serum protein electrophoresis (SPEP) with immunofixation (IFE), kappa and lambda free light chains with ratio, and quantitative immunoglobulins (IgG, IgA, IgM). If a patient has a non-IgG paraprotein, an abnormal serum free light chain ratio, a serum monoclonal protein of 1.5 g/dL or more, or a symptom concerning for multiple
myeloma, bone marrow assessment is recommended. M protein spikes of over 3g/dL are more likely to be associated with malignancy while spikes under 3g/dL are usually not. However, a significant number of patients with myeloma may have a low M spike and, therefore, all patients with M spikes need oncologic evaluation. Most of the clinical interest is focused on the gamma region of the SPEP which contains primarily IgG immunoglobulins. Figure 1 displays an SPEP with a large M spike in the gamma region representing a monoclonal gammopathy. Approximately 70% of MGUS is comprised of IgG, 15% of IgM and 12% of IgA.

MGUS, OSTEOPOROSIS AND FRACTURE

A consensus panel identified MGUS as a “non-malignant B-cell disorder that is the most common plasma cell dyscrasia and is associated with an increased risk of developing serious B-cell disorders.” This group pointed out that, from the perspective of the skeleton, individuals with MGUS have an increased risk of osteoporosis and osteopenia and an increased likelihood of developing fractures, especially in the vertebrae. Because of the prevalence of vertebral compression fractures, MGUS patients with significant back pain should be evaluated by MRI to rule out both vertebral fractures and myeloma. Given that MGUS is associated with a higher risk of osteoporosis/osteopenia and associated skeletal complications, especially fractures, it was recommended in the consensus statement that anyone with age-inappropriate or atypical bone loss undergo screening for the presence of a monoclonal gammopathy. It was further recommended that MGUS patients who have evidence of vertebral compression fractures or who are osteoporotic be initiated on anti-resorptive therapy, and that MGUS patients with osteopenia be strongly considered for treatment as well. Bisphosphonates have been shown to improve bone density in the setting of monoclonal gammopathies. Other studies have confirmed that MGUS is a risk factor for fracture, particularly in the vertebrae, and have reported that vertebral compression fractures in patients with MGUS may be asymptomatic and may occur in patients without osteoporosis but still may be predictors of subsequent fractures. In one report, 18.4% of MGUS patients had at least one vertebral compression fracture and none were traumatic in nature. Concordant data from US and European studies in largely Caucasian populations have suggested that overall fracture rates are increased approximately 1.7-fold, and vertebral fractures are increased up to approximately 6.3-fold in MGUS subjects when compared to the general population. The observations that MGUS is associated with an increased risk of fractures has been supported by other studies showing that the risk of fracture at any anatomic site is 1.4–2.5 times greater in MGUS than in control populations. Because of the propensity to fracture, the International Myeloma Working Group has recommended bisphosphonates for all MGUS patients with either osteopenia or osteoporosis.

Having established the increased prevalence of fractures in MGUS patients, it is of substantial importance to examine the inverse: the prevalence of MGUS in the fracture population. Previously unrecognized MGUS is a relatively common finding in patients with fractures, as evidenced by a recent study which demonstrated that 6% of otherwise healthy subjects aged 50 years and older who sustained a hip fracture had MGUS.

Understanding the mechanisms of bone loss in MGUS is of importance since the majority of these patients do not receive any therapy to increase bone density despite a substantially higher tendency to fracture. Monoclonal gammopathies are associated with excess bone resorption as assessed by increased levels of N-telopeptide of type I collagen. In one study of bone biopsies in 87 patients evaluated for MGUS, 45% of MGUS patients had criteria for excess bone resorption compared to 79% patients with indolent multiple myeloma and 93% of patients with overt myeloma. Bone resorption was more frequent (52%) in MGUS patients that had progressive disease and subsequently developed myeloma. This study concluded that excessive bone resorption in MGUS is associated with progression and is an early sign of malignancy.

It has also been shown that MGUS patients have increased osteoclastogenesis and abnormally high bone resorption producing deterioration of skeletal microarchitecture and reduction in bone strength and ability to resist stress, leading to fracture. Two studies have shown that patients with MGUS exhibit decreased bone mineral density at the proximal femur. High-resolution QCT has demonstrated decreased cortical and trabecular thickness, widening of the endosteal canal, increased cortical porosity, and increased bone width,
all typical features of osteoporosis.\textsuperscript{16,19} [Figure 2] The trabecular number and separation did not differ between the different groups. Micro-finite element analysis revealed that these microarchitectural alterations contributed to decreased biomechanical strength with an 8.9% reduction in the apparent modulus of elasticity.\textsuperscript{3} Together, these observations characterize structural abnormalities in cortical and trabecular bone that result in decreased bone strength and contribute to the reduced ability of bone in MGUS to withstand applied stress and a heightened susceptibility to fracture.

Although over 20 cytokines that suppress osteoblast function or enhance osteoclast activity have been identified in multiple myeloma, few have been studied in MGUS. Two that are active in both myeloma and MGUS are macrophage inflammatory protein-1 alpha (CCL3/MIP-1\(\alpha\)), a macrophage chemokine that, among other things, activates osteoclasts and is seen in inflammatory conditions associated with bone resorption [i.e., rheumatoid arthritis], and dickkopf-related protein 1 (DKK1) that inhibits the Wnt/\(\beta\)-catenin signaling pathway by blocking LRP6 receptor interactions and is seen in both myeloma and osteolysis. Circulating levels of the osteoclast activating factor, CCL3/MIP-1\(\alpha\), have been shown to be increased nearly 6-fold and circulating levels of the osteoblast-suppressive factor DKK1 are increased approximately 2-fold in MGUS patients compared to age, sex, and body mass matched control subjects.\textsuperscript{18} These cytokines contribute to producing osteoporosis in monoclonal gammopathies. Since so few of the cytokines active in bone destruction in myeloma have been studied in MGUS, it may be that cytokines other than those described may also participate in reducing bone density and increasing fracture risk in MGUS.

**MGUS in the Rhode Island Fracture Liaison Service**

The National Osteoporosis Foundation has reported that over 60% of American adults over the age of 50 will sustain fragility fractures.\textsuperscript{20} Frequently, it is in the treatment of these fractures that monoclonal gammopathies are diagnosed.

Accordingly, laboratory evaluation of low bone mass in our FLS will occasionally detect conditions that require further evaluation. SPEP is a useful screening test for identifying monoclonal gammopathies and is performed on patients evaluated for decreased bone mass and osteoporotic fractures. In our FLS, of 265 consecutive patients with osteoporosis and fracture, we diagnosed 27/265 (10%) with MGUS. This is compared to a report of 6% of fracture patients with MGUS.\textsuperscript{19} Since about 1% /year of patients with MGUS develop multiple myeloma or other malignant monoclonal gammopathies, depending upon the patient’s age at diagnosis, the lifetime cumulative risk can be substantial. The finding of MGUS requires oncologic evaluation and lifelong follow-up. Since MGUS has a higher risk of fractures than do age- and gender-matched cohorts without gammopathies, it is not surprising to find a higher prevalence of MGUS in fracture patients and in an FLS than in the general population. In addition to MGUS, the FLS has found 10 patients with a variety of hematologic malignancies including multiple myeloma, Waldenström macroglobulinemia, chronic lymphocytic leukemia, mast cell leukemia, and lymphomas.

**Multiple Myeloma, Osteoporosis, and Fracture**

Multiple myeloma is one of several hematologic malignancies associated with decreased bone density, including lymphoproliferative diseases and Waldenström macroglobulinemia. Myeloma is a malignancy of plasma cells, which develop from B lymphocytes, and is characterized by IgG paraprotein. Decreased bone density can be diffuse in myelomatosis or localized in plasmacytomas. In a fracture liaison service, evaluation of decreased bone density by SPEP will usually detect abnormalities in the IgG region which can be explored in more detail with immunoelectrophoresis.

A typical antibody is characterized by 2 IgG heavy chains and 2 IgG light chains. Two types of light chains exist, kappa and lambda, each encoded by a separate gene. Monoclonal IgG light chains produced by malignant plasma cells are called Bence-Jones proteins and are associated with myeloma. Abnormal IgG proteins can be further characterized by immunoelectrophoresis and the concentration of kappa and lambda light chains can be quantified. The typical ratio of free kappa to lambda is 0.26:1.65. Alterations in this ratio are associated with malignancies.

Of the potential end malignancies associated with monoclonal gammopathies, the best studied for bone disease is MM. The complex pathophysiologic effects can be distilled into bone destruction and failure of bone formation.
Numerous factors have been described in this dynamic imbalance in bone homeostasis. The Notch signaling pathway influences the receptor activator of nuclear factor kappa-B ligand (RANKL) and the osteoprotegerin (OPG) system, activating osteoclasts and inhibiting osteoblasts. This signal is amplified by tumor necrosis factor (TNF) secreted by malignant plasma cells. CCL3 (MIP-1α) has also been implicated as a chemokine that influences osteoclast differentiation and inhibition of osteoblast activity. More recently, extracellular vesicles have been implicated in promoting this osteoblast/osteoclast imbalance, and represents a potential therapeutic target. The results may include osteopenia, osteoporosis, lytic bony lesions, and fractures [Figure 3]. These can be widespread but often have a predilection for the spine, skull, and long bones. Lytic lesions rarely appear in patients below the elbow or below the knee.

For adults in the United States over 50 years of age, the prevalence of osteoporosis and osteopenia is approximately 12% and 43%, respectively. By comparison, bone lesions and bone density changes occur in 80% of patients with MM. While there is a demonstrated increased fracture risk in MGUS, up to 74% in one study, the mechanism is not well understood, and recent studies have not found an associated decrease in bone mineral density or higher rate of progression to MM in patients with MGUS and fracture.

Skeletal events have an important effect on mortality for patients with MM. One study found that patients diagnosed with MM at the time of a fracture have a 28% higher risk of death than patients with new MM and no fractures. Another study found that patients requiring up-front radiation therapy for treatment of painful bony lesions have an increased risk of death compared to those patients who do not require radiation at diagnosis. Even after MM diagnosis, patients who develop a fracture have a 2-fold increased risk of death compared to those without fractures, highlighting the importance of bone health in patients with monoclonal gammopathies. The treatment of MM often involves bone strengthening measures including supplemental calcium and vitamin D. Aggressive use of bisphosphonates or RANKL inhibitors are recommended for patients with multiple myeloma to reduce risk of fracture. Currently, there are no guidelines advocating for bone-modifying agents in patients with MGUS without concurrent fracture or reduced bone density.

WALDENSTRÖM MACROGLOBULINEMIA

Waldenström macroglobulinemia is one of a closely related group of plasma cell malignancies that can present with osteoporosis and fractures. Plasma cells develop from B lymphocytes in bone marrow and lymph nodes and produce diverse groups of antibodies. Dysregulated plasma cell multiplication produces clonal expansion and the production of incomplete antibodies or, M-proteins (IgM), related to multiple myeloma and monoclonal gammapathies. Men are affected more than women and the average age of onset is 65 years. The etiology is unknown.

In addition to osteoporosis and fractures, patients with macroglobulinemia may have anemia, hyperviscosity syndrome, cryoglobulinemia, hepatosplenomegaly, lymphadenopathy, hemorrhage, and recurrent bacterial infections. In one study, 1/3 of patients’ DEXA scans had hip T-scores of <–2.0 and 15/45 (33%) of patients had a vertebral compression fracture. In a study of 45 bone biopsies in patients with elevated IgM (36 men and 9 women), 2/3 of the abnormal antibodies were composed of kappa chains. Structurally, the bone abnormalities were comprised of both reduced formation and excessive resorption. Bone formation rates and mineralization surfaces were decreased and microresorptive osteoclastic surfaces were increased, contributing to bone fragility and inability to repair microdamage.

The initial diagnosis of Waldenström macroglobulinemia is suggested by an abnormal SPEP. Immunofixation studies will characterize the abnormal immunoglobulin. Treatment of Waldenström macroglobulinemia is with one of several chemotherapeutic agents, such as ibrutinib and rituximab, often in combination with corticosteroids. While helpful in controlling the clonal expansion of plasma cells, the treatment may not help, or even worsen, the osteoporosis.
CONCLUSIONS

Despite the original characterization of MGUS as a condition of “undetermined significance,” there is now clear epidemiologic evidence that patients with MGUS have a significantly increased fracture risk and that the prevalence of MGUS is increased in patients with osteoporosis and fractures.4 Because MGUS is associated with a significant prevalence of microarchitectural bone deficiency and a greater risk of fracture than age and gender-matched cohorts without gammopathies, it has been proposed that the term “MGUS” be replaced by the term, “monoclonal gammopathy of skeletal significance.”[1] The prevalence of MGUS in the geriatric population has been reported to be 3–8%; 15% in vertebral fractures, 6% in hip fractures, and, in our FLS, 10% of all fractures. [2] The prevalence of fractures in MGUS is 18% in vertebral fractures. Concordant data suggest that overall fracture rates are increased approximately 1.7-fold, and vertebral fractures are increased to approximately 6-fold.[3] MGUS should be suspected in patients referred to an FLS, or those with osteoporosis on DEXA, and patients should not just be given treatment for osteoporosis without an evaluation including for MGUS. [4] Orthopedic surgeons, and FLS programs, are in unique positions to screen for and identify metabolic bone diseases that have substantial implications for appropriate skeletal therapy. Identification of MGUS is a contribution to bone health, and even longevity, that evaluation of osteoporosis and fractures should not ignore.

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ABSTRACT

Primary hyperparathyroidism (PHPT) is a common endocrine disorder that results in excess parathyroid hormone (PTH) secretion and hypercalcemia. PHPT is usually caused by an adenoma and its presentation is often asymptomatic, though it can negatively impact the skeleton via osteoporosis mostly affecting cortical bone and fracture. The diagnosis of PHPT is made by clinical presentation and biochemical and hormonal assessment. Surgical treatment guided by ultrasound sonography and/or 99mTc-sestamibi scintigraphy is generally curative.

Normocalcemic hyperparathyroidism (NPHPT) is a variant of hyperparathyroidism defined by normal serum calcium and persistently elevated serum PTH levels. Limited data exist on NPHPT’s effects on the skeleton, though current evidence suggests a positive correlation between the disorder and the presence of osteoporotic fractures. Taken together, patients affected by the various manifestations of hyperparathyroidism and their associated homeostatic disturbances represent a not insignificant portion of fracture patients seen in a fracture liaison service.

KEYWORDS: hyperparathyroidism; bone density; osteoporosis; fracture

INTRODUCTION

Primary hyperparathyroidism (PHPT) is an endocrine disorder that is associated with hypercalcemia as a result of overactive or unsuppressed parathyroid hormone (PTH) secretion. It is among the most common endocrine disorders and affects three times as many women than men with a peak incidence in the sixth decade. It has an estimated prevalence of 1 per 1000 males and 2–3 per 1000 females. PHPT classically affects the skeleton and the kidneys can also have nontraditional PTH-related disorders and complaints with an effect on the quality of life. It is readily diagnosed with biochemical and hormonal studies and when indicated can be cured with surgery. In more recent years, patients with normocalcemic PHPT have been described and reported.

CLINICAL PRESENTATION

With the introduction of widespread biochemical screening, the most common clinical presentation of PHPT is that of asymptomatic hypercalcemia found on routine laboratory testing. Patients may develop traditional target organ manifestations such as osteoporosis, skeletal fractures, nephrolithiasis, and nephrocalcinosis. Many other patients have non-traditional problems that may include peptic ulcer disease, pancreatitis, constipation, fatigue, lethargy, muscle aches, and brain fog, which are well described in the literature. Although renal disease occurs in less than 20% of patients, nephrocalcinosis and reduced renal function are easily appreciable both clinically and biochemically. Neurocognitive symptoms of anxiety, poor concentration, and cognitive decline are more subtle and not often attributable to the PHPT.

NORMOCALCEMIC HYPERPARATHYROIDISM

Normocalcemic hyperparathyroidism (NPHPT) is a variant in which total and ionized serum calcium levels are normal despite elevated serum PTH levels. This diagnosis can be made only when calcium and PTH levels have been confirmed on several occasions and causes of secondary hyperparathyroidism have been excluded such as medications, vitamin D insufficiency, chronic kidney disease, renal calcium loss, and gastrointestinal disorders which affect calcium absorption. Vitamin D deficiency or insufficiency is particularly common in northern latitudes including the New England area. Diminished vitamin D levels can cause an elevation in serum PTH levels. A serum 25-hydroxyvitamin D of ≥30 ng/ml is necessary for a diagnosis of NPHPT. If the 25-hydroxyvitamin D level is <30 ng/ml, patients should be supplemented with vitamin D and repeat measurements should be obtained at an appropriate time. A well-documented 7-year case study of an osteoporotic patient with NPHPT describes the pathophysiology in clinical detail. The study revealed a rising PTH with normal ionized calcium and a progressive decrease in cortical bone density manifested at the distal radius.
CLINICAL EFFECTS OF PTH ON THE SKELETON

The skeletal impact of PHPT differs from post-menopausal osteoporosis in that cortical bone is mostly affected while trabecular bone is relatively preserved. The pattern of bone loss is measured by dual-energy X-ray absorptiometry (DEXA). Because bone loss in PHPT is largely from cortical bone, bone mineral density (BMD) is most affected at the distal one-third of the radius, least at the lumbar spine with its high component of trabecular bone, and intermediately at the hip. This is inverse to what would be expected to be seen in idiopathic osteoporotic bone loss, which centers around loss of trabecular bone in the vertebrae and hip. As such, 3-site DEXA is advised in all patients with PHPT. More sophisticated bone imaging such as trabecular bone score (TBS) have also shown reduced trabecular bone in PHPT, likely due to deterioration of bone microarchitecture. Even in mild PHPT, catabolic skeletal effects of PTH can increase the risk of fragility fractures. There is clear evidence of increased fracture risk in a variety of locations including the forearm, rib, hip, and vertebrae. In addition, severe and longstanding disease can cause progression to osteitis fibrosa cystica, with subperiosteal resorption of distal phalanges, tapering of distal clavicles, salt-and-pepper degranulation of the skull, bone cysts, and brown tumors. There are limited data regarding bone disease associated with NPHPT, although there is evidence of its overall negative impact on the skeletal system. An undefined fraction of patients with NPHPT may exhibit cortical bone loss in the distal forearm, and patients need to be followed for some time to document the stability of cortical bone.

PRIMARY HYPERPARATHYROIDISM IN THE RHODE ISLAND FRACTURE LIAISON SERVICE

Of a consecutive series of 265 patients diagnosed in the Fracture Liaison Service (FLS) with a fracture and reduced bone density measurement, 28/265 (10.6%) patients had an elevated serum PTH level, in keeping with a substantially higher prevalence than in the general population. This is compared to a study of 444 patients with hip fractures and 444 non-fractured controls. In that study, 21/444 (4.7%) of the patients with fractures had elevated serum PTH and calcium levels compared to 5/444 (1.1%) of non-fracture controls fulfilling the criteria for PHPT suggesting that PHPT enhances fracture risk [p<0.01]. However, of the patients in the FLS, only one had an elevated serum calcium. The creatinine levels were normal in all patients. These data are in keeping with a report of 156 women screened for osteoporosis in whom 14/156 (9.0%) had NPHPT. Of patients with NPHPT, 21.4% experienced a fracture. These observations suggest a relatively high prevalence of PHPT and possibly NPHPT in an osteoporotic fracture population, and an association of NPHPT with structural bone loss and pathological fracture. While the prevalence of NPHPT in a fracture population is not definitively known, our observations would suggest a substantial prevalence. This observation suggests that serum calcium levels alone may not be an adequate screening marker of hyperparathyroidism in the fracture population, and that serum PTH levels should be assessed.

DIAGNOSIS

The diagnosis of PHPT is made biochemically, with workup including albumin-corrected serum calcium and ionized calcium, phosphorus, PTH, 25-hydroxyvitamin D, and creatinine levels. If albumin-corrected calcium, calculated as measured total serum calcium in mg/dL + 0.8 x [4.0 – serum albumin concentration in g/dL], and/or ionized calcium are found to be persistently elevated with serum PTH levels above the upper limit of normal of 65 pg/mL, the diagnosis of primary hyperparathyroidism can be established. The serum phosphorus concentration is typically in the lower limit of the normal range.

PTH plays a complex role in calcium and phosphate homeostasis, and as such, its levels can fluctuate across a wide range. In a patient with hypercalcemia, an elevated serum PTH level or an unsuppressed level would be in keeping with a diagnosis of PHPT. 24-hour urine calcium excretion greater than 300 mg in males and greater than 250 mg in females are consistent with hypercalcemia. Hypercalciuria in patients with PHPT may or may not be associated with calcium stone disease. Generally, normal calcium/creatinine ratios vary from 0.05 to 0.25 and ratios greater than 0.25 are in keeping with hypercalciuria. Urinary calcium measurements can also be used to distinguish PHPT from familial hypocalciuric hypercalcemia, which is characterized by urinary calcium excretion of less than 100 mg/24 hours, and a calcium to creatinine ratio less than 0.01.

Serum 25-hydroxyvitamin D levels should be checked in all patients as vitamin D deficiency or insufficiency is common in patients with PHPT and may be associated with more severe skeletal disease. There is also evidence that reductions in serum PTH levels can occur when insufficient or deficient vitamin D levels are repleted. There is a greater percentage of patients with serum PTH levels that fall within the normal reference range when serum 25-hydroxyvitamin D levels are normal. Vitamin D repletion is appropriate when serum levels are less than 30 ng/ml. There are currently no specific recommendations for therapeutic regimens to replete 25-hydroxyvitamin D nor specific goals for repletion established in PHPT. This is an area that was recommended for future research by the Fourth International Workshop on the Management of Asymptomatic Primary Hyperparathyroidism. A number of studies of vitamin D repletion in patients with PHPT have indicated no deleterious or negative effects.
PATHOPHYSIOLOGY
PTH is an essential polypeptide that maintains calcium and phosphate homeostasis. Its secretion is regulated by the serum ionized calcium concentration. Normally, elevated serum calcium levels would suppress PTH secretion while a lowered serum calcium would stimulate its secretion. In the kidneys, PTH acts on the proximal renal tubules to enhance calcium reabsorption and phosphate excretion. Assuming intact renal parenchyma, PTH also facilitates the second hydroxylation step of vitamin D and synthesizes the metabolically active form, 1,25-dihydroxy vitamin D, which in turn increases calcium absorption from the intestine. Together, PTH and 1,25-dihydroxy vitamin D raise serum calcium levels by increasing renal tubular reabsorption of calcium, increasing calcium absorption in the small intestine, and mobilizing calcium from bone. PTH also promotes an increase in phosphate excretion by decreasing renotubular reabsorption of phosphate. In bone, PTH acts on osteoblasts, osteoclasts, and osteocytes. The ultimate effect of calcium and phosphate in bone depends on PTH levels and whether secretion is chronic or intermittent, with chronic PTH secretion resulting in bone loss [Figure 1]. While the kidneys and small bowel suffer no structural damage from their participation in maintaining serum calcium concentration, bone experiences decreased calcium density and structural weakness predisposing to fracture.

Figure 1. Calcium-parathyroid hormone-vitamin D axis.

CELL BIOLOGY
PTH produces bone resorption and hypercalcemia by acting directly on osteoblast and mesenchymal stromal precursor cells, which secondarily increase the differentiation and function of osteoclasts. Osteoclasts themselves do not have receptors for PTH, but cells of the osteoblastic lineage, among others, express the receptor activator of NF-kB ligand (RANKL). RANKL attaches to RANK, a receptor on the cell surface of osteoclasts and osteoclast precursors, to stimulate cell differentiation to the osteoclast phenotype. This process can be modified by osteoprotegerin, a soluble decoy receptor produced by osteoblasts and marrow stromal cells which modifies the effects of RANKL by inhibiting the interaction of RANKL and RANK. The hallmark of an activated osteoclast is the ruffled border which represents invaginations of the cell membrane that increase the surface area of the osteoclasts and seals the cells to bone. The osteoclasts then acidify the bone under the seal and dissolve the mineral phase of the bone. Lysosomal cathepsins erode the organic phase of bone [Figure 2]. The combined process of dissolution of the inorganic and organic phases of bone, especially under the direction of PTH, produce erosions in bone known as Howship's lacunae and tunneling or, a “cutting cone” [Figure 3].

Figure 2. Osteoclast in Howship’s Lacunae (asterisk)
Hyperparathyroidism creates porosity in bone by indirectly stimulating osteoclastic resorption of both the organic and inorganic phases of bone.

Figure 3. Osteoclastic cutting cone
Activated osteoclasts create a tunneling effect, resorbing bone, increasing porosity, and leading to mechanical weakening of bone under stress.
HISTOPATHOLOGY
Normal parathyroid glands each weigh 30–40 mg and are grey-tan to grey-yellow in color. Each person typically has four glands, with the superior pair of parathyroid glands arising from the fourth brachial pouches in embryo while the inferior parathyroid glands develop from the third brachial pouch along with the thymus gland. Parathyroid glands are composed of three different cell types: chief cells, clear cells, and oxyphil cells. Chief cells [4–8 µm diameter] primarily produce PTH, which is synthesized within prominent endoplasmic reticula and dense Golgi regions. Clear cells are chief cells with increased glycogen content. Oxyphil cells are larger than chief cells [6–10 µm] and increase in number with age. Their role is currently unclear, but they may derive from chief cells and may secrete PTH. The proportion of fat to glandular mass increases with age and may reach up to 60–70% of total volume.19

PHPT can be caused by a single gland adenoma (approximately 80% of cases) or parathyroid hyperplasia (15–20%).2,20 Most adenomas are composed of chief cells, with a smaller portion comprised of oxyphilic cells, clear cells, and, least commonly, lipoaenomas. Typically, adenomas are separated from the adjacent rim of normocellular parathyroid gland by a fibrous capsule (Figure 4). The component cells may be arranged in cords, nests, sheets, and follicles, and center around blood vessels. Chief cells in adenomas have larger nuclei that stain hyperchromic and are pleomorphic. Parathyroid hyperplasia is due to an increase in parenchymal cell mass in all four glands. The enlargement of glands is relatively symmetric in most cases.20 The glandular fat content decreases significantly, and chief cell hyperplasia typically predominates with some foci of clear cells.21 At the cellular level, there is both an increase in cellularity as well as a change in secretion function. There is typically a reduced sensitivity to the calcium set-point which leads to over-secretion of PTH.

IMAGING
Ultrasound sonography and ⁹⁹mTc-sestamibi scintigraphy are the most common imaging techniques used to localize parathyroid adenomas. On ultrasound examination, parathyroid glands are homogeneously hypoechoic and anatomically separate from the thyroid gland. Internal vascularity as seen by Color Doppler is typically in a peripheral distribution (Figure 5).22 By scintigraphy, a radiotracer is preferentially absorbed by overactive parathyroid glands to assist surgeons with preoperative planning. The ⁹⁹mTc-sestamibi scintigraphy is typically combined with single photon emission computed tomography (SPECT) to provide additional detail and anatomical relationships (Figure 6). Sestamibi scans are typically positive with the presence of an adenoma and generally negative in patients with hyperplasia. In addition, 4-dimensional CT scan (4-D CT) can be a helpful adjunct in reoperative cases and is preferred by some surgeons for initial localization.23 It is important to note that imaging plays no role in making the diagnosis of PHPT. The diagnosis and indication for surgery are based on biochemical findings and the traditional or classical parathyroid clinical findings.

Figure 4. Parathyroid adenoma
Hematoxylin-Eosin stain of enlarged parathyroid gland. Many chief cells, without stromal fat, and a rim of normal parathyroid tissue can be seen.

Figure 5. Adenoma seen on sonogram
Color Doppler sonogram showing a typical hypoechoic adenoma deep in relation to the lower pole of the thyroid with ring-pattern vascularity.
Surgery is indicated for all patients with symptomatic PHPT including polydipsia, nephrolithiasis, diminished GFR, osteoporosis, or neurocognitive dysfunction. The Fourth International Workshop on the Management of Asymptomatic Primary Hyperparathyroidism guidelines also recommend surgery for asymptomatic patients with age less than 50, a substantially elevated calcium (more than a point above the upper limit of normal), underlying renal disease, or osteoporosis at any site. Parathyroidectomy is low-risk surgery performed by identifying and resecting the diseased parathyroid glands. Intraoperative serum PTH levels are routinely measured after resection of a lesion or lesions to confirm operative success. A calcimimetic is a compound that reduces serum PTH and calcium levels by an inhibitory effect on calcium sensing receptors. This therapy can be used in patients with symptomatic or severe hypercalcemia who are poor surgical candidates. Though not a treatment, vitamin D should be appropriately supplemented during observation or while awaiting surgery as insufficiency is associated with more severe and progressive disease. In a double-blinded randomized trial, hyperparathyroid patients who received daily vitamin D supplementation before parathyroidectomy had a 2.5% increase in lumbar spine BMD compared to the placebo. After parathyroidectomy, BMD increased significantly at the total hip and femoral neck within the vitamin D group. Several studies have shown significant increases in T-scores after parathyroidectomy in the lumbar spine, total hip, and femoral neck up to two years after parathyroidectomy as a result of normalized calcium and PTH levels. A study using the FRAX fracture risk assessment tool has shown an improvement in the 10-year risk for both hip and major osteoporotic fractures in patients who undergo parathyroidectomy compared to those who are managed with observation. Overall, improvements in BMD and reduced fracture risk demonstrate a clear benefit of parathyroidectomy in patients with PHPT or NPHPT. Given that surgery is the only curative treatment option for PHPT, both symptomatic and asymptomatic patients should be evaluated by an experienced endocrinologist and an experienced parathyroid surgeon once the diagnosis been made.

There are no formal recommendations for management of pre-existing osteoporosis after successful parathyroidectomy given the limited data. A study of 30 patients with moderate to severe PHPT found a change in mean lumbar spine T-scores from −3.4 before parathyroidectomy to −0.43 one year after surgery and a +1.2 two years after the surgery. The mean total hip T-scores improved from −3.19 preoperatively to −0.90 at one year, and −0.40 at two years, after parathyroidectomy. The total hip had significant improvements in T-score at consecutive time intervals of 6 months, 1 year, and 2 years after parathyroidectomy. These data suggest that surgery can lead to an eventual resolution of osteoporosis or at least an improvement without further medication over a period of time. A retrospective cohort study evaluated bisphosphonates for the treatment of osteoporotic patients after parathyroidectomy and found no reduction in fracture risk compared to patients who were managed with observation alone, while parathyroidectomy alone demonstrated improvements. It may be that pharmacological management of osteoporosis post-parathyroidectomy may not be necessary. However, close follow-up of bone density, biochemical markers, and vitamin D repletion is recommended. Data on best post parathyroidectomy osteoporotic treatments are not yet clear and should be determined on a case-by-case basis.

CONCLUSIONS

PHPT is a common endocrine disorder diagnosable by clinical features but more commonly by screening serum studies. PTH regulates, and is regulated by, serum calcium concentration. (1) Regulation of serum calcium concentration by PTH occurs by controlling renal calcium reabsorption, vitamin D hydroxylation, gastrointestinal calcium absorption, serum phosphate concentration, and bone calcium content. (2) Of these mechanisms, only bone suffers structural compromise in its role as a calcium donor. (3) PHPT has specific imaging characteristics that guide surgical approach. (4) Surgery is generally curative. (5) NPHPT is a distinct variant of PHPT that may be more prevalent in the fracture population.
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ABSTRACT
Fragility fractures, particularly in the hip and spine, are the most common complication of osteoporosis. In the US, approximately 1–1.5 million vertebral compression fractures (VCFs) occur annually. While patients may present with sudden onset of low back pain and limited mobility, more than two-thirds of VCFs are asymptomatic and are detected incidentally. X-rays are the standard imaging modality for diagnosis, with CT and MRI indicated if neurological deficits are present or a malignant cause is considered. Initial management is often non-surgical, with medications, physical therapy, and bracing. Surgical management in the form of cement augmentation (kyphoplasty or vertebroplasty) or instrumented fusion can be considered after failure of non-operative treatment, cases of deformity, or neurologic deficits. Subsequent VCFs occur frequently, and risk factors for refracture include advanced age, low bone mineral density, and low BMI. Treatment of primary VCFs with anti-resorptive medication is essential to reduce the risk of subsequent fractures.

KEYWORDS: vertebral compression fractures; osteoporosis; secondary fractures

INTRODUCTION
Osteoporosis is the most commonly encountered metabolic bone disease, which affects 200 million people worldwide.1 The disease is defined as a progressive loss of bone mineral density (BMD) as measured by dual-energy x-ray absorptiometry (DEXA). A score more than 2.5 standard deviations below the population average (T-score) indicates osteoporosis.2 Due to the drop in estrogen after menopause and the consequent imbalance between bone resorption and formation, postmenopausal women have the greatest risk of developing osteoporosis.3–5 Other risk factors include malignancy, low BMI, use of steroid medication, use of alcohol or tobacco, physical inactivity, and calcium deficiency.6–8

VCFs are the most reported fragility fracture in patients with osteoporosis. Approximately 1 to 1.5 million VCFs occur each year in the US, with an incidence rate of 40% in women over 80 years old.9,10 With an aging population, the incidence of VCF will continue to grow, and therefore clinicians should be mindful of the presentation and management of these patients. Furthermore, patients with VCFs are at high risk of subsequent fractures, and it is important to consider bone density optimization for these patients and reduction of the risk factors for the development of additional fragility fractures. Previous studies have demonstrated that one prior VCF increases the risk of subsequent VCFs by 5-fold, and 2 previous VCFs increases the risk of future VCFs by 12-fold.11 Analysis of data across 373 centers found that among 381 patients who had a VCF, the incidence of a new VCF in the following year was 19.2%.12 A systematic review investigated the risk factors of secondary fractures after vertebroplasty, which included history of prior fractures, advanced age, reduced bone marrow density, and bone cement leakage.13 Low BMI and the number of treated vertebrae were also established as moderate risk factors for refracture in another systematic review.14

CLINICAL FEATURES
The most common cause of a VCF is osteoporosis, although a diagnosis of malignancy should be considered in patients under 50 years old without history of trauma.15 Patients with osteoporosis may develop a VCF after minor events, including coughing, sneezing, and lifting. In patients with severe osteoporosis, an estimated 30% of fractures occur when the patient is in bed.11,16

Risk factors for VCF can be modifiable or non-modifiable, which can guide clinicians in lifestyle optimization and identifying higher-risk patient groups. Nonmodifiable factors include advanced age greater than 70 years, female sex, history of steroid use, and Caucasian race. Modifiable factors include alcohol and tobacco use, physical inactivity, low BMI, and dietary deficiency of calcium and vitamin D.11 The first step in preventing VCFs is the management of modifiable risk factors including treatment for osteoporosis.

The classically described symptom of a VCF is sharp or dull pain that is aggravated by movement or positional changes.11 In many patients, this pain can be mild and attributed to another cause. Furthermore, 66% of patients with osteoporotic VCFs are asymptomatic, and their VCFs are discovered incidentally when imaging studies are performed for other reasons.17 Red flags which may suggest a pathological
fracture (e.g., due to malignancy) include weight loss, other systemic symptoms, and persistent non-resolving pain. Other complications of vertebral compression fractures include chronic pain, constipation, increased risk of venous thrombosis, and prolonged immobility, which can result in reduced functional ability and psychological issues.

In addition to these complications, VCFs also have a detrimental burden on healthcare expenditure, with an annual medical cost of $746 million per year in the United States [Table 1].

### Table 1. Symptoms and complications of vertebral compression fractures

<table>
<thead>
<tr>
<th><strong>Symptoms</strong></th>
<th><strong>Complications</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Sudden onset low back pain, which can occur after a low energy event such as sneezing or turning in bed</td>
<td>• Chronic pain</td>
</tr>
<tr>
<td>• Increased pain while walking or standing</td>
<td>• Kyphosis, predominantly thoracic</td>
</tr>
<tr>
<td>• Limited spinal mobility</td>
<td>• Height loss</td>
</tr>
<tr>
<td></td>
<td>• Loss of mobility: Resulting in pressure sores, risk of deep venous thrombosis, pneumonia, and psychological distress</td>
</tr>
<tr>
<td></td>
<td>• Gastrointestinal complications: Including constipation which can cause subsequent decreased appetite, nausea, and poor nutrition</td>
</tr>
<tr>
<td></td>
<td>• Decreased pulmonary function: Leading to pneumonia and exacerbation of chronic airway disease</td>
</tr>
</tbody>
</table>

(Adapted from reference 28 with permission.)

### IMAGING

History and physical examinations, including a neurological assessment to evaluate arms, legs, and bladder function, are the initial steps in evaluation, followed by imaging. Compression fractures can often be diagnosed with plain radiography, including lateral and anteroposterior views. Clinicians should have a low threshold for imaging studies since inciting events are often low-energy and more than two-thirds of patients are asymptomatic. If not previously recorded, DEXA scans should be acquired soon after the diagnosis of a VCF to evaluate for underlying osteoporosis and determine disease severity.

A normal radiograph of the vertebral column should demonstrate a similar size and shape of the vertebrae across adjoining levels with horizontal endplates. A VCF is characterized by a reduction in vertebral height of 20%, or 4-mm loss from the baseline. The Genant classification is commonly utilized to grade vertebral fractures based upon their morphology and height loss. Loss of height is graded from 0 (normal) to 3 (severe fracture), and morphology is reported as wedge, biconcave, or crush [Figure 1].

Advanced imaging (CT or MRI) is rarely required but may be indicated to differentiate between benign versus malignant and acute versus chronic fractures. Patients with
new or progressing neurological deficits merit advanced imaging to identify a retropulsed fracture where a bony fragment extends to the spinal column causing compression. MRI is typically the imaging of choice, as the characteristic signal intensities and enhancement patterns are well described for malignancy and a more recent fracture will demonstrate edematous changes. Radiological guidance should be sought when there are diagnostic concerns. For example, the intra-trabecular hemorrhage in an acute fracture may mimic a malignant cause and require further interpretation.

MANAGEMENT

Treatment for a VCF can be non-surgical or surgical. The goals of management are to achieve adequate pain relief, restore mobility, and prevent future fractures through addressing the underlying cause. In most cases, this involves careful evaluation of bone health and optimization of osteoporosis. Clinicians should discuss the benefits and risks of non-surgical and surgical treatment with a consideration for patient preferences and co-morbidities.

Non-surgical

Pain is a common presenting symptom of VCFs, and patients can describe this as intense. Achieving adequate pain relief is important to prevent prolonged bed rest and encourage early mobility. Although many patients experience pain relief over the first 6–8 weeks as fracture healing occurs, some patients have chronic pain.

Subsequent to a VCF, a number of different medications can be used for pain relief including non-steroidal anti-inflammatory drugs (NSAIDs), opioids, calcitonin, and muscle relaxants. NSAIDs are a common first-line therapy due to their ease of accessibility and low cost. Despite their effectiveness and overall safety, patients should be aware of risks, including peptic ulceration, gastrointestinal bleeding, and kidney disease. This class of medication should also be used carefully in the elder population who generally have reduced creatinine clearance and are less tolerant of NSAIDs. Whenever possible, the patient’s primary physician should be involved in the decision to use this class of medication. When NSAIDs are insufficient or contraindicated, opioids and muscle relaxants can be beneficial, but their use in the geriatric population is also cautioned due to sedative effects, constipation, nausea, and potential for dependency. Calcitonin is a medication that has been used in the past for osteoporosis treatment, but also can provide acute relief of bone pain. A systematic review investigating its use in VCFs found strong efficacy for the management of acute back pain, but insufficient evidence for chronic pain due to older fractures. Calcitonin is available intranasally and adverse effects include dizziness, flushing, and gastrointestinal disturbance. Additionally, the use of calcitonin may be limited due to its relatively higher cost. A review of US, UK, and Canadian national guidelines found inconsistent guidance on the use of these medications, with several stating weak evidence.

For non-pharmacologic options, patients pursuing non-surgical management may consider the use of bracing, physical therapy, and nerve root blocks. Physical therapy can strengthen the axial musculature and improve posture, which will assist with early mobilization and reduce the long-term likelihood of falls. Rehabilitative exercise is also beneficial for all osteoporotic patients. Bracing can be used for a period of 4–12 weeks, although the evidence for its effectiveness is limited. Braces are also not without risks and can cause muscular atrophy and deconditioning when used for an extended period.

Patients may commence with a trial of non-surgical management, but careful follow-up should ensue to monitor for pain relief or progression of symptoms, as well as to observe for adverse effects.

Surgical

Although patients may commence with non-surgical treatment, clinicians must be aware of the indications for surgical management. An immediate referral to a surgeon is merited if a patient complains of leg weakness or pain, which indicates neurological deficit and demands further evaluation. Furthermore, if patients exhibit no improvement in their pain level and disability over 6 weeks of conservative therapy, then surgical management should be considered.

Kyphoplasty and vertebroplasty are percutaneous cement-augmentation techniques to manage symptomatic...
VCFs. These are both minimally invasive procedures where bone cement is injected into the fractured vertebral body. The procedure can be performed either inpatient or outpatient depending on individual patient characteristics. Several specialties can perform kyphoplasty and vertebroplasty, including surgical specialties (orthopedic surgery and neurosurgery) and non-surgical specialties (anesthesia, pain medicine, and radiology). Recent trends suggest that cement-augmentation procedures are being performed increasingly by non-surgeons. The indication for these procedures in osteoporotic VCF is intense and sustained pain adjacent to the fracture with failure of conservative management for a minimum of 3 weeks. These procedures can also be used for pain relief in patients with osteolytic bony metastases. Hirsch et al published a clinical care pathway using the RAND/UCLA Appropriateness Method. The multidisciplinary expert panel recommended that cement augmentation procedures be considered in patients with positive findings on advanced imaging (preferably MRI) and worsening symptoms, and in patients with 2–4 of the following unfavorable characteristics: progressive height loss, vertebral body height loss greater than 25%, kyphotic deformity, or severe impact on daily functioning. Contraindications for these procedures include coagulation disorders, infection, allergy to bone cement, tumor involving the spinal canal, and unstable fractures.

In a vertebroplasty, fluoroscopic guidance is used to inject cement into the fractured cancellous bone. This can alleviate pain and prevent further loss of height. A kyphoplasty is similar to a vertebroplasty but involves an inflated balloon tamponade to restore vertebral height and create a cavity which can be subsequently filled with cement. This has theoretical advantages over vertebroplasty since it minimizes cement extravasation, restores vertebral height, and reduces kyphosis. In practice, clinical studies have found both procedures to be effective with no differences between patient-reported outcome measures.

Complications of cement-augmentation procedures are low but include bleeding, infection, and neurological injury. Cement extravasation is a rare yet catastrophic complication which can lead to arterial embolization or compression of neural elements. This complication is more common in vertebroplasty where cement is injected at higher pressure. A systematic review and meta-analysis comparing cement-augmentation procedures to non-surgical management of osteoporotic VCF found superior pain outcomes in the surgically treated patients, demonstrating their efficacy.

SECONDARY FRACTURES

One of the challenges following cement augmentation procedures is the risk of a subsequent VCF, which often happens at the adjacent vertebral levels to cement injection. In a radiological study, new VCFs occurred in approximately one-third of patients, and in more than half of these the fracture occurred within 3 months of vertebroplasty at the adjacent vertebral level. Several studies have considered if novel VCFs are the result of osteoporotic progression or the consequence of vertebral stiffness by cement augmentation. Several biomechanical studies have reported minimal changes in stresses and strains at adjacent levels to the kyphoplasty and conclude that adjacent segment fractures are more likely due to progression of osteoporosis rather than the intervention.

Moon et al followed 111 female patients with osteoporotic VCFs who underwent kyphoplasty. The 1-year incidence rate of new compression fractures was 15.5% which is lower than the rate in natural osteoporotic progression. The authors conclude that the lower incidence rate observed in their study sample could be related to a higher percentage of patients who were receiving medication for osteoporosis and recommend that spine surgeons should consider postoperative utilization of anti-osteoporotic medication to prevent novel fractures. This is supported by a meta-analysis which found that low BMD is a high-risk factor for refracture. In fact, a 1% increase in BMD has been associated with a 3% reduction in risk of VCF. This evidence emphasizes the role of metabolic treatment for primary VCFs to optimize treatment outcomes and reduce the risk of subsequent fractures. Furthermore, Moon et al found that one third of patients with subsequent VCFs were clinically asymptomatic, which emphasizes the importance of careful monitoring.

Figure 2. A: Intraoperative image of a kyphoplasty demonstrating vertebral body access, B: balloon inflation, and C: cement injection.
follow-up. In patients with a primary VCF, follow-up imaging should be considered. This can include AP and lateral radiographs to detect progressive kyphosis or coronal plane deformity 2-4 weeks after diagnosis. A repeat MRI should be considered in the presence of new or progressing neurological symptoms, which may indicate an additional fracture, infection, or tumor.44,45

Due to the high likelihood of additional fragility fractures after a primary VCF is identified, such as distal radius fractures, geriatric hip fractures, or additional VCFs, many institutions have implemented the concept of a fracture liaison service to identify high-risk patients and pursue early diagnostics and potential intervention. These services have shown benefit in improving patient outcomes, and early referral should be considered if one of these services is available to patients with the new diagnosis of a VCF.45

**CONCLUSIONS**

VCFs are the most common fragility fracture affecting patients with osteoporosis. [1] Patients can present with acute pain although many are diagnosed asymptomatically after incidental imaging. [2] Plain radiographs are the modality of choice for diagnosis, while CT and MRI imaging may be required if a patient has neurological deficits, or a malignancy is a considered cause for the fracture. [3] Initial management is often non-surgical for at least 3 weeks before cement-augmentation procedures are considered. [4] A critical component in the management of VCF is the initiation of strategies for fracture prevention. If not performed recently, a DEXA scan should be ordered to monitor BMD. Patients should be educated on lifestyle changes such as smoking cessation and exercise, with referral to physiotherapy if assistance is needed to promote a regular program. [5] Pharmacologic treatment should be strongly considered for treatment of osteoporosis and fracture prevention. Medications to treat osteoporosis include bisphosphates (which are common first-line therapeutics), denosumab [a RANK ligand inhibitor], selective estrogen receptor modulators [raloxifene], and recombinant human parathyroid hormone [teriparatide]. To prevent the progression of osteoporosis, it is also crucial to normalize calcium and vitamin D levels and provide dietary supplementation. [6] Early referral to a fracture liaison service or other provider who manages osteoporosis may improve outcomes in these patients and reduce risk of future fragility fractures. [7] An individual who experiences a VCF has a 5-fold increased risk of having a subsequent one, thereby justifying treatment regardless of bone mineral density.

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Rothia Mucilaginosa Peritonitis Complicating Peritoneal Dialysis
CONNIE GE; JOEY GU; ANKUR D. SHAH, MD

ABSTRACT
For the 11% of dialysis patients worldwide who receive peritoneal dialysis (PD) to treat their end-stage kidney disease (ESKD), recent PD-associated peritonitis is estimated to contribute to 5-30% of reported mortality.1,2 These infections are most commonly caused by coagulase-negative Staphylococcus (32%), followed by culture-negative peritonitis (16%), and the timely identification and targeted treatment of peritonitis is critical to avoid complications such as PD catheter removal.3 Here, we present a case of atypical Rothia mucilaginosis peritonitis in a PD patient.

KEYWORDS: peritonitis, rothia mucilaginosa, peritoneal dialysis, PD-associated peritonitis

CLINICAL PRESENTATION
A 48-year-old woman with a history of ESKD secondary to infection-associated glomerulonephritis on continuous cycling peritoneal dialysis (CCPD) for three years, presented with a one-day history of abdominal pain. She had been in her usual state of health until the prior day, when she began experiencing suprapubic abdominal pain, accompanied by nausea, vomiting, fevers, chills, and foul-smelling urine. Her past medical history was significant for Type 2 diabetes mellitus, hypertension, secondary hyperparathyroidism, anemia, and obstructive sleep apnea. Medications included calcitriol 2mcg daily, metoprolol succinate 100mg daily, torsemide 100mg twice daily, darbepoetin alfa in polysorbate 140mcg injection weekly. Her only allergy was to oxycodone, which resulted in hives.

Previously, the patient had a history of Streptococcus mitis peritonitis [3.5 years prior] that required PD catheter replacement as well as a Pseudomonas exit site infection [six months prior] treated with two weeks of intraperitoneal vancomycin. One month prior to this admission, the patient had Staphylococcus epidermidis peritonitis and completed two weeks of intraperitoneal vancomycin.

On examination, the temperature was 98.0, the blood pressure 153/79 mm Hg, the heart rate 83 beats per minute, the respiratory rate 20 breaths per minute, and the oxygen saturation 97% while the patient was breathing ambient air. Cardiopulmonary exam was notable for clear lung fields and no adventitious cardiac sounds. The mucous membranes were moist. Abdominal exam was notable for mild, diffuse tenderness to palpation without rebound or guarding. The peritoneal catheter exit site did not show any drainage or erythema. Edema was absent. Presentation labs were notable for a BUN 41, creatinine 11.7, and WBC of 7.7.

A clear peritoneal effluent sample showed 257 cells/mm^3 with 79% neutrophils. Treatment for presumed peritonitis was started with intraperitoneal vancomycin and IV ceftriaxone, and subsequently narrowed as culture-specified vancomycin-sensitive S. mitis and R. mucilaginosa. The patient completed a two-week course of intraperitoneal vancomycin and, at her two-week post-discharge follow-up appointment, reported improvement of her general abdominal pain with persistence of pain at the drain during cycling.

DISCUSSION
This patient receiving peritoneal dialysis with a history of peritonitis and recent antibiotic use was found to have R. mucilaginosa infection, a rarely reported pathogen in the peritoneal dialysis patient. R. mucilaginosa is an encapsulated, biofilm forming, gram-positive and catalase-positive coccus, that is usually part of normal oropharyngeal and upper respiratory tract flora. R. mucilaginosa is commonly associated with dental plaque or other periodontal disease but has been reported to cause severe or systemic infection in some patients. In particular, patients with history of malignancy, neutropenia, or other immunosuppressing conditions or medications, are at increased risk of R. mucilaginosa bacteremia, and hardware-associated R. mucilaginosa infections have been reported for patients with central lines, prosthetic valves, subdural drains, and PD catheters.5,6 Treatment with ciprofloxacin, which R. mucilaginosa is often resistant to, is an established risk factor for both PD-associated peritonitis and non-peritonitic infections.5,6 Although our patient did not have a history of ciprofloxacin treatment, she did have a recent two-week course of intraperitoneal vancomycin within one month prior to her R. mucilaginosa peritonitis, which may have allowed the opportunistic growth of this usually commensal bacterium.

R. mucilaginosa has rarely been associated with peritonitis, and of the five cases of R. mucilaginosa peritonitis reported...
Staphylococcus epidermidis is the most frequently causing peritonitis, especially in patients undergoing peritoneal dialysis. The most common agent of PD-associated peritonitis is coagulase-negative Staphylococci, which were responsible for 80% of the infections reported in the English literature (Table 1). All patients under treatment with systemic antibiotics achieved full symptom resolution.

In conclusion, although *R. mucilaginosa* is a rare cause of PD-associated peritonitis, it is a potential threat to patients undergoing peritoneal dialysis. Early identification and broad antibiotic coverage are necessary for effective treatment.

**References**


**Table 1. Case reports of PD-associated peritonitis from *R. mucilaginosa***

<table>
<thead>
<tr>
<th>Ref</th>
<th>Age/Sex</th>
<th>Prior peritonitis</th>
<th>Relevant medical history</th>
<th>Modality*</th>
<th>Symptoms</th>
<th>Antibiotic regimen and duration**</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>57F</td>
<td>1x Culture negative</td>
<td>Kidney allo-transplant, removed secondary to glomerulo-nephritis</td>
<td>CAPD</td>
<td>Fever to 40°C, cloudy effluent</td>
<td>Cephalothin + aztreonam (intraperitoneal), duration not described</td>
<td>Full resolution without recurrence, though transitioned to hemodialysis</td>
</tr>
<tr>
<td>6</td>
<td>58M</td>
<td>2x streptococcus mitis</td>
<td>DM HTN</td>
<td>CAPD</td>
<td>Cloudy effluent, abdominal pain</td>
<td>Cefazolin and ceftazidime (intraperitoneal), 2 weeks</td>
<td>Full resolution without recurrence</td>
</tr>
<tr>
<td>10</td>
<td>49M</td>
<td>1x klebsiella oxytoca, 1x micrococcus sp, 1x Culture negative</td>
<td>Hypertensive nephrosclerosis</td>
<td>CAPD</td>
<td>Cloudy effluent, abdominal pain</td>
<td>Amoxicillin and rifampin, duration not described</td>
<td>Full resolution without recurrence</td>
</tr>
<tr>
<td>8</td>
<td>41F</td>
<td>none</td>
<td>2 failed kidney transplants, Poor dentition</td>
<td>CCPD</td>
<td>Cloudy effluent, diffuse abdominal pain</td>
<td>Vancomycin (intraperitoneal) and rifampin (oral), 3 weeks</td>
<td>Full resolution without recurrence</td>
</tr>
<tr>
<td>7</td>
<td>60M</td>
<td>3x Culture negative, 1x coagulase-negative staphylococcal</td>
<td>HIV nephropathy</td>
<td>CCPD</td>
<td>Cloudy effluent, diffuse abdominal pain</td>
<td>Vancomycin (intraperitoneal), 2 weeks</td>
<td>Full resolution without recurrence</td>
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</tbody>
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* CAPD: Continuous ambulatory peritoneal dialysis; CCPD: Continuous cyclic peritoneal dialysis.

**Describes the final antibiotic regimen used; in many cases, patients were started on different antibiotics empirically.

*CAP and CCPD: Continuous cyclic and ambulatory peritoneal dialysis.*


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Central Retinal Vein Occlusion Secondary to Necrotizing Pancreatitis

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KEYWORDS: central retinal vein occlusion, hypercoagulability, necrotizing pancreatitis

CASE PRESENTATION

A 22-year-old male with a significant past medical history for alcohol use disorder and recent prolonged hospitalization for acute necrotizing pancreatitis complicated by multiorgan failure presented to the ophthalmology clinic a few weeks after discharge with one-week blurry vision (20/200 OD). During his hospitalization, he was diagnosed with systemic inflammatory response syndrome, which required multiple courses of antibiotics, a decompressive laparotomy, and debridements for worsening sepsis. In addition, he was found to have persistent intra-abdominal collections, which was drained over several weeks after the surgeries. The patient reported no other ocular complaints of pain or visual disturbances.

Intraocular pressure was 11 mm/Hg OD and 14 mm/Hg OS, and confrontation visual fields were full OD but defective in the inferior temporal left visual field. Slit-lamp examination was unremarkable for both eyes. Dilated fundus examination revealed scattered flame shaped intraretinal hemorrhages on the macula and in the periphery, intraretinal exudates, attenuated arteries, and dilated, tortuous retinal veins (Figure 1). OCT revealed a blunted foveal contour with central intraretinal and subretinal fluid OD (Figure 2). Fluorescein angiography was consistent with ischemic central retinal vein occlusion (CRVO), complicated by cystoid macular edema (Figure 3). The patient was diagnosed with ischemic CRVO OD.

Figure 1. Fundus image OD. Fundus examination reveals scattered flame shaped intraretinal hemorrhages on the (a) macula and (b) in the periphery, (c) intraretinal exudates, (d) attenuated arteries, (e) and dilated, tortuous retinal veins.

Figure 2. OCT image reveals a blunted foveal contour with (a) central subretinal and (b) intraretinal cystic fluid change OD.

Figure 3. Fluorescein angiography findings are consistent with ischemic CRVO.
Hypercoagulable workup revealed mildly elevated serum homocysteine (17.4μMol/L, ref 5.0–13.9 μMol/L) and positive beta-2 glycoprotein antibody titer (36, ref <21 SAU [40 is the cutoff for antiphospholipid antibody syndrome]). Treatment included intravitreal anti-VEGF injections every four weeks and warfarin initiated by hematology. Three months later, repeat APAS testing resulted negative, with beta-2 glycoprotein 1 IgM 1.1 (0.0–20.0 U/ml) and IgG 6.8 (0.0–20.0 U/ml) and warfarin was discontinued. At evaluation two months after CRVO, visual acuity improved (20/125 OD) and cystoid macular edema resolved. Most recent clinic visit showed a VA of 20/60 OD.

**DISCUSSION**

A significant risk factor for CRVO in patients under 40 years includes hypercoagulability.1 Our patient suffered from a complicated course of acute necrotizing pancreatitis in the setting of severe alcohol use disorder. Shortly after, he developed a CRVO OD, and his hypercoagulable workup showed mildly elevated homocysteine levels and a positive titer for beta-2 glycoprotein antibody. He was initiated on warfarin treatment and monthly intravitreal anti-VEGF injections, and repeat blood work three months later showed normalization of homocysteine and beta-2 glycoprotein levels, confirming that the patient suffered from a transient hypercoagulable state induced by necrotizing pancreatitis and prolonged hospitalizations.

There were several concurrent mechanisms contributing to the pancreatitis-induced hypercoagulability. Our patient was diagnosed with pancreatitis-induced systemic inflammatory response syndrome, which has been postulated to damage endothelial cells.2 Damage to endothelial cells can disrupt acetylcholine-mediated venous relaxation and activate platelets, leading to hypercoagulability.2 Furthermore, infectious agents have been shown to induce the formation of antiphospholipid antibodies such as anti-β2-glycoprotein 1 antibodies, through molecular mimicry between structures of bacteria and β2-glycoprotein-1-derived amino acid sequences.3,4 Our patient was found to have temporarily elevated beta-2 glycoprotein antibody levels, secondary to acute pancreatitis-induced sepsis, subsequently contributing to a hypercoagulable state, and was also found to have mildly elevated homocysteine levels. Acute pancreatitis can lead to the nitration of cystathionine β-synthase in the pancreas, blocking the trans-sulphuration pathway and concomitantly leading to impaired homocysteine metabolism and homocysteine accumulation.5 Elevated homocysteine increases oxidative stress, impairs normal endothelial functioning, and can induce thrombosis.6 The majority of patients with antiphospholipid antibodies do not develop thrombosis, and thus it is theorized that a “second hit” must be present.7 The combination of elevated beta-2 glycoprotein antibody levels as well as homocysteine contributed to a significant hypercoagulable state that led to a CRVO.

Only 10–15% of CRVOs are seen in patients younger than 40 years old and indicate unusual underlying concurrent mechanisms.8 Thus, when encountered, extensive workup including imaging, hypercoagulable profile screening, and comprehensive blood work must be conducted to determine potential etiologies.

**References**


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**Disclosures**

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PATIENT 1
A 30s-year-old male with no past medical history presented to the emergency department (ED) with a painful penile and scrotal rash that began six days prior. [Figures 1,2] He endorsed a preceding week of fatigue, headache, malaise, myalgias, and low-grade fevers. In the ED he was found to be febrile to 102; he had bilateral inguinal lymphadenopathy, and the pictured rash. He reported a single unprotected sexual encounter with a male in Boston roughly two weeks prior. In both cases the pictured lesions were swabbed in the ED. For both patients, orthopox PCR testing was positive as performed by Rhode Island Department of Health, and monkeypox was confirmed positive by rt-PCR via the CDC. Both patients were admitted to the hospital and went on to develop additional lesions scattered throughout their bodies. Each patient received tecovirimat and subsequently recovered uneventfully as the lesions healed within 3–4 weeks.

PATIENT 2
A 40s-year-old male with a history of untreated HIV presented to the ED with one day of the pictured single painful lesion to his nose. [Figure 3] Associated symptoms included one day of fatigue, headache, myalgias, sore throat, nausea, subjective fevers, chills, non-productive cough, and mild shortness of breath. He had no other lesions at time of presentation. He reported one isolated unprotected sexual encounter with a male in New York about one week prior to symptoms onset.

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Visual Joint Angle Assessment: Does Accuracy Improve with a Higher Level of Orthopaedic Surgery Training?

EDWARD J. TESTA, MD; JOSEPH A. GIL, MD; NIKITA LAKOMKIN, MD; HEATHER HANSEN, MD; ARISTIDES I. CRUZ, JR., MD, MBA

ABSTRACT

INTRODUCTION: The purpose of this study was to evaluate the accuracy of visual joint angle assessments by orthopaedic surgery trainees amongst various levels of training.

METHODS: Sagittal plane photographs of several joints at various angles were distributed to trainees within an orthopaedic residency program. Joint angles were estimated and compared to those obtained with a goniometer. Inter- and intra-rater reliability and ANOVA were conducted to assess differences between groups.

RESULTS: Twenty trainees were studied. The percent error for knee measurements differed at 23.1%, 26.2% and 11.1% for the PGY 2–3, PGY 4–5 and PGY 6 groups, respectively (P=0.024). Percentage error for ankles showed the greatest variability at 69.7–96.3%. Intra-rater reliabilities for all visual joint angle assessment were similar amongst groups.

CONCLUSIONS: Visual joint angle assessments vary amongst trainees, with PGY 6s most accurately identifying knee joint angles. Visual assessment is inaccurate compared to goniometric measurements, thus limiting visual measurements during patient encounters.

KEYWORDS: goniometer, range of motion, residency training

INTRODUCTION

Joint range of motion (ROM) is an objective measure that is used by surgeons and therapists alike to assess severity of disease, guide clinical decisions, set benchmarks, and monitor the progress of rehabilitation. ROM measurements facilitate communication between physicians, physical therapists, and patients. Thus, this communication depends on the accuracy and reproducibility of joint angle measurements among providers. Ellis et al demonstrated that goniometer-based measurements are a reliable method for obtaining these measurements.\(^1\)\(^2\) However, more recent investigations have shown that variability in the technique used to measure the joint results in decreased accuracy of goniometric measurement of joint angles.\(^3\)\(^4\) Orthopaedic consultations are commonly provided by a range of clinicians, such as physician assistants, junior or senior residents, or attending surgeons. Experience with physical examination maneuvers and patient assessment logically improve as residents become more senior, yet junior residents are the more common orthopaedic consultation provider at academic institutions.\(^5\)\(^7\) Thus, there may be differences in the abilities of junior and senior residents in the assessment of joint ROM, which may alter patient diagnosis and management. However, to our knowledge, the effect of level of training on the accuracy and reproducibility of joint angle measurements has not been investigated.

The purposes of the current study are to assess the accuracy of visual joint ROM measurements in both the upper and lower extremity compared to the gold standard of goniometric measurement and to assess the relationship between level of orthopaedic training and accuracy of such joint angle measurements. Our hypotheses are that the accuracy of visual assessment of joint angles performed by orthopaedic surgery trainees improves with a higher level of training and that visual ROM measurements will be comparable to goniometric measurements.

METHODS

After obtaining approval from our institutional review board, a series of five sagittal plane photographs of the ankle, knee, elbow, and wrist positioned at various angles were electronically distributed to all residents and fellows affiliated with a single academic orthopaedic surgery training program. Participants were instructed to visually estimate the joint angle in each photograph. Participants remained anonymous except for year in training. Participants estimated the joint angle in the same 20 photographs one week after the initial assessment. Each participant’s visual assessment of joint angles was compared to the joint angle measurement obtained with a smartphone-based goniometer application [Angle Meter Pro, Nakhon Phagdeechar].

The photographs were distributed via the REDCap [Research Electronic Data Capture] program [Vanderbilt University, Nashville, TN]. Study data was also collected and managed using the REDCap program. REDCap is a secure, web-based application designed to support data capture for research studies. The REDCap program does not record internet protocol [IP] addresses.
STATISTICAL ANALYSIS

The mean percent error for participants’ assessment of joint angles was calculated. Percent error was calculated by taking the difference between each rater's measurement and the goniometric measurement and dividing this value by the goniometric measurement. Inter-rater and intra-rater reliability was calculated using the intraclass correlation coefficient (ICC). The qualitative agreement levels of the ICC were interpreted as follows: 0–0.2 indicate poor agreement, 0.2–0.4 indicate fair agreement, 0.4–0.6 indicate moderate agreement, 0.6–0.8 indicate good agreement, and 0.8–1.0 indicate excellent agreement. One-way analysis of variance was conducted to assess differences in the mean percent error between the three groups. A cutoff of $P<0.05$ was considered statistically significant.

RESULTS

Twenty residents and fellows completed the survey twice. There were 7 postgraduate year (PGY) 2–3, 7 PGY 4–5, and 6 PGY 6 trainees (Table 1). In the lower extremity, the mean percent error for the knee measurements was 23.1%, 26.2% and 11.06% for the PGY 2–3, PGY 4–5 and PGY 6 groups, respectively ($P=0.024$) (Table 2). The mean percent error for the ankle was 96.3%, 69.7% and 81.9% for the PGY 2–3, PGY 4–5 and PGY 6 groups, respectively ($P=0.30$) (Table 2). The inter-rater reliability for visual joint angle assessment was 0.987 [95% Confidence Interval (CI), 0.962–0.998] for knee and 0.719 [95% CI, 0.459–0.956] for the ankle. The difference between the PGY 2–3, PGY 4–5 and PGY 6 was not significantly different (Table 3). Similarly, the intra-rater reliability for visual joint angle assessment of the knee and ankle was not significantly different between the PGY 2–3, PGY 4–5 and PGY 6 groups (Table 4).

In the upper extremity, the mean percent error for the elbow measurements was 32.3%, 25.2% and 24.9% for the PGY 2–3, PGY 4–5 and PGY 6 groups, respectively ($P=0.25$) (Table 1). The mean percent error for the wrist was 22.9%, 27.7% and 30.1% for the PGY 2–3, PGY 4–5 and PGY 6 groups, respectively ($P=0.54$) (Table 1).

<table>
<thead>
<tr>
<th>Table 1. Characteristics of Raters and Presented Cases</th>
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<tbody>
<tr>
<td>Rater Characteristics</td>
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<tr>
<td>Training Level</td>
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<tr>
<td>PGY 2–3</td>
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<td>PGY 4–5</td>
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<td>PGY 6</td>
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<th>Table 2. Percent Error Among Different Trainee Levels</th>
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<td>Anatomic Region</td>
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<tr>
<td>Knee</td>
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Note: PGY, Post-graduate year; * denotes statistical significance at $P<0.05$

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<tr>
<th>Table 3. Inter-Rater Reliability for Angle Assessment</th>
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<tr>
<td>Raters Anatomic Regions ICC 95% Confidence Interval</td>
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<tr>
<td>All Raters Knee 0.987 0.962–0.998</td>
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<tr>
<td>Ankle 0.719 0.459–0.956</td>
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<tr>
<td>Elbow 0.951 0.870–0.994</td>
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<tr>
<td>Wrist 0.969 0.914–0.996</td>
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<tr>
<td>PGY 2–3 Knee 0.983 0.948–0.998</td>
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<tr>
<td>Ankle 0.863 0.652–0.982</td>
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<td>Elbow 0.971 0.911–0.996</td>
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<td>Wrist 0.977 0.928–0.997</td>
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<td>PGY 4–5 Knee 0.987 0.958–0.998</td>
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<tr>
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<td>Elbow 0.971 0.912–0.997</td>
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<td>Wrist 0.969 0.907–0.996</td>
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<tr>
<td>PGY 6 Knee 0.994 0.979–0.999</td>
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<tr>
<td>Ankle 0.566 0.222–0.924</td>
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<tr>
<td>Elbow 0.901 0.722–0.987</td>
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<td>Wrist 0.964 0.886–0.996</td>
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Note: ICC, intraclass correlation coefficient; PGY, Post-graduate year

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<td>Anatomic Regions Training Level Mean ICC</td>
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Note: ICC, intraclass correlation coefficient; PGY, Post-graduate year
and 21.1% for the PGY 2–3, PGY 4–5 and PGY 6 groups, respectively ($P=0.19$) [Table 2]. The mean percent error of the visual assessment was significantly higher compared with the mean percent error of the goniometer ($P<0.001$). The inter-rater reliability for visual joint angle assessment was 0.951 (95% CI, 0.870–0.994) for the elbow and 0.969 (95% CI, 0.914–0.996) for the wrist [Table 3]. Similarly, the intra-rater reliability for visual joint angle assessment of wrist and elbow was not significantly different between the PGY 2–3, PGY 4–5 and PGY 6 groups [Table 4].

**DISCUSSION**

Effective communication between physicians, therapists, and patients regarding many musculoskeletal conditions depends on accurate joint ROM measurements. Previous investigations have demonstrated that variability in goniometric techniques used to measure joint angles results in decreased accuracy. The current study reveals that, when compared to goniometric measurement, the mean percent error of sagittal plane visual joint angle assessments of the knee, wrist, and elbow range from approximately 11% to 32%, while the ankle ranged from 69% to 96% among trainees. The mean percent error of visual joint angle assessment of the knee was significantly lower in PGY 6 group compared to the PGY 2-3 and PGY 4-5 groups. However, the inter-observer and intra-observer reliability of visual joint angle assessment of the knee were not significantly different between different levels of orthopaedic training. The mean percent error, inter-observer, and intra-observer reliability of visual joint angle assessment of the ankle, wrist, and elbow were not significantly different between different levels of orthopaedic training. While visual assessment of sagittal plane joint angles of the aforementioned joints do not differ in inter- and intra-observer reliability between PGY training levels, these measurements, particularly in the ankle, are inaccurate compared to goniometric measurement.

Precise understanding of ROM measurements are essential in hand and upper extremity surgery as stiffness is a common complication after various injuries and surgeries. Moreover, therapy protocols and surgical treatments may vary depending upon ROM measurements, imploiring clinicians to obtain accurate measurements for ideal communication amongst providers. While goniometers are widely used for joint angle measurements, several investigations have shown that variability in the technique used to measure the joint ROM results in decreased accuracy of goniometric measurement of joint angles. McVeigh et al compared visual and goniometer measurements of wrist, index metacarpophalangeal (MCP) joint, and index proximal interphalangeal (PIP) joint angles by 20 hand surgeons and 20 hand therapists to radiographic measurements of these joint angles. Their findings demonstrated no difference in goniometric and visual measurement of the wrist and MCP, while the goniometric measurement was more accurate for the measurement of the PIP. In contrast to the findings of the aforementioned study, the difference between visual measurement of joint angles compared to smartphone application-based goniometric measurement was substantially higher in our study. A possible reason for this discrepancy is that orthopaedic trainees have less experience with visual joint angle measurements when compared to more experienced hand surgeons and hand therapists.

The ankle was found to have the highest variability with respect to percent error when comparing visual joint angle measurements to the goniometric measurements, with errors ranging from 69% to 96% among trainees. Previous research demonstrated that the inter-rater reliability of goniometric measurement of ankle joint ROM was low to moderate. While this differs from our plantar-dorsiflexion measurements in the sagittal plane, it highlights the important finding that goniometric ankle motion values may be difficult to reliably and consistently obtain. In contrast, Allington et al demonstrated that if a strict protocol is followed, including utilizing trained physical therapists to obtain measurements, visual and goniometric joint angle measurements of the ankle is reliable and reproducible. Konor et al found that even notice evaluators were able to produce good reliability and low measurement errors in ankle joint angles. Thus, physical therapists rather than orthopaedic trainees, and the utilization of techniques other than visual measurements, may be the most appropriate way to evaluate ankle joint angles.

In the current study, visual joint angle measurements were compared to joint angle measurements obtained with a smartphone-based goniometer application. Smartphone applications of joint angle measurements are at least equivalent if not superior in reliability when compared to traditional goniometric joint angle measurements. Milanese et al compared the intra- and inter-observer reliability of physical therapists measuring knee ROM using a smartphone application and a goniometer. Both methods were found to be reliable with no significant difference in novice or experienced examiners using either device. Werner et al found that joint angle measurements of the shoulder obtained with a smartphone based application had excellent agreement to those obtained with a traditional goniometer. When considering the aforementioned data in the context of the results of the current study, smartphone-based goniometers remain a useful and reliable tool for joint angle ROM measurements and may have value within the armamentarium of a joint angle evaluator.

There are several limitations of this study. First, the joint angle measurements were collected anonymously, which may have led participants to spend less time interpreting the joint angles, resulting in less accurate responses. However, the request for anonymous participation allowed us to collect de-identified data and may have encouraged participation from trainees who would be otherwise reluctant to participate if they felt that they would be evaluated relative to their peers based on the accuracy of their responses. Second, the sample size of each subgroup of respondents was
CONCLUSIONS

A precise understanding of ROM measurements are essential in musculoskeletal medicine as a means of effective communication amongst medical providers of various training levels and physical therapists alike. In comparison to goniometric measurement, the mean percent error of sagittal plane, visual joint angle assessments of the knee, ankle, wrist, and elbow joints among trainees ranges widely from 11.1–96.3%. The mean percent error of visual joint angle assessment of the knee was significantly lower in PGY 6 group compared to the PGY 2–3 and PGY 4–5 groups. On the contrary, the mean percent error, inter-observer and intra-observer reliability of visual joint angle assessment of the ankle, wrist, and elbow were not significantly different between different levels of orthopaedic training. While visual assessment of sagittal plane joint angles of the studied joints does not differ in inter- and intra-observer reliability between various levels of orthopaedic training, it is relatively inaccurate compared to goniometric measurement and must be used cautiously in ROM measurements during telehealth or in-person visits.

References


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Feasibility of a Self-Measured Blood Pressure Monitoring Program to Reduce Uncontrolled Hypertension

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ABSTRACT

BACKGROUND: Hypertension is a common, serious condition affecting about one-third of adults in the United States. Self-measured blood pressure (SMBP) monitoring, combined with clinical support, is recommended to improve hypertension control and patient outcomes.

METHODS: We conducted a retrospective analysis of a SMBP monitoring program that supported recruited patients in using wireless Bluetooth monitors to track their blood pressure at home and gave outpatient practices real-time access to patients’ measurements. We analyzed SMBP measurements, practice-user log data, and patient and practice experience evaluations.

RESULTS: Project staff recruited 17 outpatient practices and 187 patients. After four weeks, 64% of participants consistently monitored their blood pressure at least three times per week. A majority of patients (79%) reported an increased ability to manage their hypertension. In total, clinicians received 1,849 alerts and documented 409 actions.

CONCLUSIONS: This analysis demonstrates the feasibility of combining SMBP with real-time access to home measurements by outpatient practices.

KEYWORDS: hypertension, blood pressure, self-monitoring, ambulatory medicine remote patient monitoring

INTRODUCTION

Hypertension is a common, serious condition that affects about a third of U.S. adults. The risk of hypertension increases with age, for those with limited social and economic resources, and for those who are overweight or obese, and hypertension frequently coexists with other risk factors and chronic diseases. Furthermore, racial disparities exist: Black Americans have greater risk for hypertension and poor outcomes related to hypertension compared to White Americans. About half of people with hypertension do not have their blood pressure under control, which increases cardiovascular morbidity and mortality.

Adherence to hypertension treatment, which includes healthy lifestyle adoption, pharmacotherapy, or a combination, is essential for blood pressure control, but barriers may hinder patients from seeking treatment, adopting a healthier lifestyle, or taking their medication appropriately. For example, patients may face challenges accessing transportation to primary care practices, pharmacies, physical activity facilities, or grocery stores. Therefore, patient engagement, social support, and self-management strategies to improve adherence are critical.

Self-measured blood pressure (SMBP) monitoring, combined with additional clinical support, has been recommended to improve adherence to medications and behavioral modifications, particularly for the elderly. Therefore, Healthcentric Advisors, a nonprofit healthcare quality improvement organization, implemented an SMBP monitoring program in Rhode Island. The program supported participants in using home blood pressure monitors to regularly track their blood pressures and to wirelessly provide real-time data to the participants’ physicians. The objective of this study was to assess the feasibility of this SMBP monitoring program through an analysis of user-log data, as well as patient and practice evaluations. We hypothesized that implementing an SMBP monitoring program is feasible from the perspectives of both patients and physician practices.

METHODS

Participants and Setting

The SMBP intervention was intended to engage patients with uncontrolled hypertension in Rhode Island to measure and self-manage their blood pressure. Healthcentric Advisors partnered with 17 outpatient practices to identify and recruit eligible patients, with a focus on populations who are disproportionately impacted by hypertension. The program began in September 2019 and is ongoing. This study includes data from September 2019 through November 2020.

Intervention

Participating practices either recruited patients directly (assessing them for eligibility during a patient encounter using a screening tool) or referred patients to project staff to screen via telephone. Inclusion criteria included uncontrolled hypertension, defined as a blood pressure greater than 140/90 mm Hg, and access to a cell phone or tablet with wireless Internet and Bluetooth capability. Patients signed a participation agreement to acknowledge their commitment...
and understanding that project staff would share their data with their primary care practice and would use de-identified results to evaluate the success of the program.

Participants were trained in SMBP techniques by a member of the practice or by project staff. Patients were provided with an Omron Series 10 wireless Bluetooth-enabled blood pressure monitor at no cost. Each time that patients measured their blood pressure with the monitor, the results were transmitted directly into their Omron account. The results were then added to Healthcentric Advisors’ HIPAA-compliant database in real time through an Application Program Interface (API) created to connect patients’ secure Omron accounts with the database.

Clinicians and other staff (e.g., nurse care managers, care coordinators, practice-based pharmacists) at participating practices were able to view their patients’ results by logging into Healthcentric Advisors’ secure portal. The portal displayed several reports for practices, including trends of weekly averages by patient, alert reports, and action reports.

Automated email notifications alerted practice staff about high priority or outlier patient results. By default, outlier readings were defined as: low [below 100/60 mm Hg], high [between 160/100 mm Hg and 180/110 mm Hg], and critical high [above 180/110 mm Hg]. Clinicians could customize the parameters that defined outlier readings for specific patients. Based on feedback from participating practices, clinicians also had the option to receive consolidated alert emails during office hours. Clinicians were responsible for reviewing their patients’ blood pressure data and for making appropriate treatment changes.

The intervention included both clinician and patient education. Project staff prepared participating clinicians and their teams for successful implementation of SMBP monitoring through train-the-trainer sessions, in-person technical assistance, and webinars. Tools (e.g., blood pressure technique posters, hypertension control protocol) were distributed to support clinician knowledge of and adherence to best practices. All participating patients received education on SMBP and hypertension management during their onboarding session.

Outcomes
To measure the feasibility of the SMBP intervention, we analyzed the following: how frequently participants measured their blood pressure using the device, participant knowledge of proper blood pressure measurement technique, whether they found the blood pressure devices easy to use, whether they trusted the measurements, whether they felt their medications were changed as a result of the SMBP program, whether they felt their ability to manage their blood pressure had increased, and if they experienced any barriers to using the devices. We also assessed feasibility from the practice’s perspective by analyzing how many alerts clinicians received, whether clinicians acted on the SMBP values, if they felt the alerts were burdensome, if they trusted the blood pressure measurements, if they felt the SMBP program accelerated blood pressure control, and if they would recommend other practices use the SMBP devices with their patients. Since this is a feasibility study, the efficacy of the intervention at lowering blood pressure is not reported here.

Data Sources and Analytic Plan
The patient screening form collected key patient characteristics: gender, date of birth, height, weight, self-reported race and ethnicity, languages spoken at home, level of education attained, and type of health insurance. The portal database included blood pressure measurements for each recruited patient, alerts generated by outlier measurements, and actions taken by clinicians in response. Data on patients’ knowledge about taking blood pressure measurements came from a pre/post onboarding assessment administered by project staff. These onboarding assessments were administered during the first six months of the intervention, before onboarding responsibilities shifted from project staff to the practices themselves.

We also analyzed patients’ and practices’ responses to electronic evaluations about their experiences using the intervention. Practices completed this experience evaluation three and five months after implementing the intervention at their site; patients completed it after six months of participation in the SMBP program.

We calculated descriptive statistics using Microsoft Excel. The researchers had access to the dataset through their work at Healthcentric Advisors implementing the SMBP program. The intervention and analysis was funded by Healthcentric Advisors. This study was reviewed and approved by the Lifespan Institutional Review Board.

RESULTS
Project staff recruited 17 outpatient primary care sites, including community health centers, a solo practitioner, academic practices, and multispecialty private practices. Participating practices referred more than 500 patients with uncontrolled hypertension for the program. During the study period, 187 patients were fully on-boarded into the SMBP intervention (Table 1). Just over half the participants were male (56%), more than two-thirds were 50 years or older (71%), and most were White [83%]. Half had a college or professional degree [54%]. It took an average of seven calls and one in-person visit to fully onboard a patient.

Patient Feasibility
By their fourth week of participation, two-thirds of participants consistently monitored their blood pressure: 64% took at least 3 measurements per week, with an average of 7.6 measurements per patient during week 4 (Table 2). Among the 94 patients who took both the pre- and post-onboarding knowledge assessments, 88% either demonstrated improved knowledge or maintained a perfect score. Among the 63 patients who completed the experience evaluation, 92% agreed that it is easy to use the home blood pressure...
patients felt that their physician practice was making more frequent modifications to their regimen in response to their home blood pressure readings. Overall, 79% of patients reported an increased ability to manage their blood pressure (Table 2).

In the open-ended responses to the experience evaluation, patients expressed appreciation for the SMBP program and described positive impacts, such as increased motivation to control their blood pressure, more consistent adherence to their medications, and increased awareness of their diet and exercise routines. About half of respondents (48%) described barriers, most commonly challenges in finding time to take measurements or following their practice’s recommended schedule for measuring, and difficulty using the technology for the app or the monitor.

### Practice Feasibility
In total, 153 patients triggered 1,849 alerts, out of 29,361 total blood pressure measurements during the 15-month study period. Patients averaged 3.8 alerts overall during their first four weeks of participation. About half of the alerts were “high” (between 160/100 mm Hg and 180/110 mm Hg), 37% were “low” (below 100/60 mm Hg), and 11% were considered “critical high” (above 180/110 mm Hg) (Table 3). The number of alerts each week decreased over patients’ first four weeks of participation (Figure 1). During the entire study period, practice staff documented 409 actions in response to the alerts, with calls to patients as the most common action. On average, clinicians documented 1.4 actions per patient during the patient’s first four weeks of participation.

Among the seven clinicians and practice staff who completed the practice experience evaluation, all agreed that the SMBP program accelerated the process of blood pressure control for their patients, and that they would recommend this SMBP program to other practices. Most (six out of seven) clinicians and practice staff agreed that the alerts received through the SMBP program were more beneficial than burdensome, and that they felt comfortable making treatment changes based on home blood pressure readings received through the portal. Three comments noted that support staff sign into the portal, which makes it less burdensome to clinicians that the SMBP information is separate from their electronic health record (EHR).

### Table 1. Patient Characteristics (N=187)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>%  (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>44% (69)</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
</tr>
<tr>
<td>21-49</td>
<td>29% (49)</td>
</tr>
<tr>
<td>50-65</td>
<td>44% (75)</td>
</tr>
<tr>
<td>Over 65</td>
<td>27% (47)</td>
</tr>
<tr>
<td>BMI over 30</td>
<td>66% (110)</td>
</tr>
<tr>
<td>Race*</td>
<td></td>
</tr>
<tr>
<td>Black or African American</td>
<td>6% (9)</td>
</tr>
<tr>
<td>White</td>
<td>83% (123)</td>
</tr>
<tr>
<td>Multiple races</td>
<td>5% (8)</td>
</tr>
<tr>
<td>Other</td>
<td>6% (9)</td>
</tr>
<tr>
<td>Ethnicity*</td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino/a</td>
<td>4% (6)</td>
</tr>
<tr>
<td>Speak a language other than English at home</td>
<td>13% (21)</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
</tr>
<tr>
<td>Less than high school diploma</td>
<td>6% (7)</td>
</tr>
<tr>
<td>High school diploma</td>
<td>25% (32)</td>
</tr>
<tr>
<td>Some college</td>
<td>15% (19)</td>
</tr>
<tr>
<td>College degree</td>
<td>31% (39)</td>
</tr>
<tr>
<td>Graduate or professional degree</td>
<td>24% (30)</td>
</tr>
<tr>
<td>Type of health insurance</td>
<td></td>
</tr>
<tr>
<td>Medicare or Medicare Advantage</td>
<td>28% (45)</td>
</tr>
<tr>
<td>Medicaid</td>
<td>9% (15)</td>
</tr>
<tr>
<td>Dual coverage with Medicare/Medicaid</td>
<td>2% (3)</td>
</tr>
<tr>
<td>Commercial</td>
<td>60% (97)</td>
</tr>
<tr>
<td>No insurance</td>
<td>1% (2)</td>
</tr>
</tbody>
</table>

*Defined as at least 3 measurements per week.
**Includes patients with perfect scores both before and after onboarding.
Denominator for knowledge assessment = 94.
***Denominator for experience evaluation = 63.

SMBP = self-measured blood pressure

### Table 2. Patient Feasibility Outcomes (N=187)

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>%  (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients regularly self-monitoring their blood pressure after 4 weeks*</td>
<td>64% (120)</td>
</tr>
<tr>
<td>Mean number of SMBP measurements per patient during fourth week of participation</td>
<td>7.6 measurements</td>
</tr>
<tr>
<td>Patient knowledge related to SMBP and hypertension management improved after onboarding education**</td>
<td>88% (83)</td>
</tr>
<tr>
<td>Patients who agreed with the following statements:***</td>
<td></td>
</tr>
<tr>
<td>It is easy to use the blood pressure monitor.</td>
<td>92% (58)</td>
</tr>
<tr>
<td>I trust the blood pressure measurements that I take myself.</td>
<td>90% (57)</td>
</tr>
<tr>
<td>I feel that my physician practice is making more frequent modifications to my treatment in response to my home BP readings.</td>
<td>75% (47)</td>
</tr>
<tr>
<td>Since participating in the SMBP Pilot, I feel more able to manage my blood pressure.</td>
<td>79% (50)</td>
</tr>
</tbody>
</table>

* Defined as at least 3 measurements per week.
** Includes patients with perfect scores both before and after onboarding.
Denominator for knowledge assessment = 94.
*** Denominator for experience evaluation = 63.

SMBP = self-measured blood pressure

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**Note:** Totals for each variable may not sum to 187 due to missing data.
We found that engaging patients in an SMBP program that provides practices with real-time access to home blood pressure measurements was feasible for both patients and practices. Nearly two-thirds (64%) of patients regularly monitored their blood pressure four weeks into the program, with an average of 7.6 measurements per week. In terms of patient experience, 92% of patients felt the blood pressure monitor was easy to use, and 79% reported an increased ability to manage their blood pressure.

Clinical documentation showed that practice staff reviewed patients’ blood pressure data and made adjustments to medications between office visits. During patients’ first month of participation, clinicians received an average of 3.8 alerts per patient and documented an average of 1.4 actions per patient. The greatest number of alerts were generated in the first week of patient participation and then decreased substantially. Improvement in blood pressure over several weeks may have contributed to the decrease in alerts, as well as clinicians’ ability to adjust the values that triggered alerts for specific patients. The subset of clinicians who responded to the practice experience evaluation trusted the home blood pressure measurements, felt the SMBP program accelerated blood pressure control, felt the alerts were more beneficial than burdensome, and would recommend other practices use the SMBP devices with their patients.

An important element of the feasibility of this program from practices’ perspective was the involvement of both clinicians and other practice staff. Multiple practice staff members could be given access to the online SMBP portal, which facilitated timely response to patients’ blood pressure readings. Flexibility in who could monitor the portal made practices more amenable to implementing the program; they were usually able to identify a staff member in their practice who could devote a few hours per week to blood pressure management. In particular, a practice-based pharmacist is able to make suggestions regarding medication changes and to send a new prescription to the pharmacy.

Our results are consistent with literature on the importance of combining SMBP with additional support for patients with hypertension. A systematic review comparing SMBP to no self-monitoring found that self-monitoring was only effective when accompanied by additional clinical support, such as medication titration, education, or lifestyle counseling. We observed evidence of enhanced clinical support in our SMBP program (e.g., between visit communication among patients and practice staff, medication changes), as well as sustained patient engagement. In addition, the intervention included patient education, which may be responsible for patients’ self-reported increase in their ability to manage their blood pressure.

The recent growth of telemedicine underscores the importance of remote patient monitoring. Many factors support remote monitoring of blood pressure, including collection of data in the environment where patients spend most of their time, more frequent measurements which strengthens the accuracy of the blood pressure readings, greater patient engagement in their care; leading to better medication adherence, and reduction of clinical inertia on the part of primary care physicians. The COVID-19 pandemic has expanded the use of telemedicine to the care of chronic conditions, making remote patient monitoring an important tool in managing hypertension.

While our study has several strengths, the findings should be considered in the context of the following limitations. The patient participants in this SMBP program were mostly White, well-educated, and commercially insured, which may affect generalizability to other patient populations. The practices that opted to participate are likely different than practices that decline to participate in these types of pilot programs. For example, the participating practices may have

Table 3. Practice Feasibility Outcomes

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of blood pressure measurements</td>
<td>29,361</td>
</tr>
<tr>
<td>Total number of alerts during study period</td>
<td>1,849</td>
</tr>
<tr>
<td>Low blood pressure (&lt; 100/60)</td>
<td>688</td>
</tr>
<tr>
<td>High blood pressure (160/100 – 180/110)</td>
<td>962</td>
</tr>
<tr>
<td>Critical high blood pressure (&gt; 180/110)</td>
<td>199</td>
</tr>
<tr>
<td>Clinician actions**</td>
<td>409</td>
</tr>
<tr>
<td>Calls to patients</td>
<td>186</td>
</tr>
<tr>
<td>Medication changes</td>
<td>90</td>
</tr>
<tr>
<td>Messages to patients through medical record</td>
<td>63</td>
</tr>
<tr>
<td>Continued monitoring</td>
<td>51</td>
</tr>
<tr>
<td>Other***</td>
<td>50</td>
</tr>
</tbody>
</table>

* Blood pressure values included here for reference are the default alert settings. Clinicians could customize the parameters that defined outlier readings for specific patients. All blood pressures are given in mm Hg.

** Clinicians may document more than one category per action (e.g., medication change and call to patient).

*** Other actions included, for example, reporting of alerts to other practice staff and discussions with patients during previously scheduled visits.

Figure 1. Total Alerts by Patients’ Week of Participation

DISCUSSION

We found that engaging patients in an SMBP program that provides practices with real-time access to home blood pressure measurements was feasible for both patients and practices. Nearly two-thirds (64%) of patients regularly monitored their blood pressure four weeks into the program, with an average of 7.6 measurements per week. In terms of patient experience, 92% of patients felt the blood pressure monitor was easy to use, and 79% reported an increased ability to manage their blood pressure.

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While our study has several strengths, the findings should be considered in the context of the following limitations. The patient participants in this SMBP program were mostly White, well-educated, and commercially insured, which may affect generalizability to other patient populations. The practices that opted to participate are likely different than practices that decline to participate in these types of pilot programs. For example, the participating practices may have
more clinical staff to support physicians and better infrastructure. In addition, there was a small number of responses to the practice experience evaluation and a relatively small proportion of patient participants enrolled at the time of the patient experience evaluation.

Our results offer lessons for future SMBP and other remote monitoring programs. Extensive effort was required to recruit patients into the program, including referrals from practices, EHR messaging and letters via US mail to promote participation, and outreach calls. Patients who had discussed the SMBP program with their clinician prior to outreach calls were much easier to engage, illustrating the importance of clinician involvement in recruiting patients and conveying the value of home blood pressure measurements. Participating practices found that recruitment was less time-consuming when conducted in the context of an office visit, when introducing the program to the patient took just a few minutes. Strategies to promote recruitment of diverse participants are also needed, so as not to exacerbate the digital divide in health care. While project staff hoped to include a greater number of patients from populations disproportionately impacted by hypertension, only 17% of the participants in this pilot were non-White.

In conclusion, this study demonstrates the feasibility of a program combining SMBP with real-time access to home blood pressure measurements by outpatient patients. Practices regularly used the blood pressure monitors and found them easy to use, clinicians adjusted medications based on patients’ blood pressure data, and practices would recommend the SMBP program to others. Given the observed medication titration, we anticipate that participants would have improvements in their blood pressures; future studies should assess whether patients achieved better blood pressure control after participating in this type of SMBP program.

References


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Acknowledgment

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Disclaimer

N/A

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Patient Voices: Doctors and Diabetes Management
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ABSTRACT

OBJECTIVE: To assess the challenges of managing diabetes experienced by clients of a community-based social services organization via qualitative interviews; to develop recommendations for more effective diabetes education programming at the organization based on themes identified in the interviews.

METHODS: Staff at Progreso Latino in Central Falls recruited clients with diabetes and prediabetes to participate in interviews during the summer of 2019. Each interview used a structured question set and was conducted in the participant’s preferred language of Spanish or English. Investigators analyzed the interview transcripts and identified predominant themes.

RESULTS: Analysis of fourteen interviews yielded four predominant themes: uncertainty about diagnosis and treatment, fear as part of the discussion with providers, language barriers, and cultural barriers.

CONCLUSIONS: To strengthen diabetes education programming at a community-based organization, we recommend utilization of community health workers, development of culturally appropriate dietary recommendations, and creation of educational videos in clients’ preferred languages.

KEYWORDS: diabetes, community-based organization, Spanish, interview

INTRODUCTION

The American Diabetes Association (ADA) recommends that all people receiving a diagnosis of diabetes should be engaged in diabetes self-management education and support, either in healthcare or community-based settings, to gain the skills and understanding for living successfully with diabetes. However, not every program is well suited to every participant. Indeed, a 2018 review demonstrating the efficacy of diabetes self-management education programs notes the importance of tailoring a program to its target audience’s cultural needs. In its official statement, the ADA also makes mention of the importance of addressing cultural needs among other factors when designing diabetes programming.

While many agree on the importance of continuing diabetes education after an initial diagnosis is made, how this education can be optimized for Spanish-speaking and other non-English-speaking communities is uncertain. A study of health literacy found that self-efficacy, “the belief or confidence in one’s ability to have influence over events in one’s life,” may be even more critical than health literacy in determining health outcomes; as such, increasing diabetes self-efficacy in Spanish-speaking patients may decrease disparities in diabetes outcomes between Spanish-speaking and English-speaking patients. Self-efficacy is an essential objective of diabetes self-management education and support programs in general. Additionally, qualitative research offers an opportunity to amplify the voices of these patients, which might not otherwise be heard, and provide important insight into their experience with the disease.

The goal of this study was to develop recommendations for more effective diabetes programming at a community-based social service agency with predominantly Spanish-speaking clients. By relying on the voices of community members in creating recommendations, this study aimed to improve the organization’s diabetes education programming and strengthen the self-efficacy of its clients.

MATERIALS AND METHODS

Study Participants
This study was conducted in the summer of 2019 at Progreso Latino, a social services organization serving the Hispanic and Latino community in Providence County and throughout Rhode Island. Such a study is in line with Progreso Latino’s mission to promote personal growth and self-sufficiency among Rhode Island’s Latino and immigrant communities through a variety of programming. The state’s Hispanic- and Latino-identifying population rose almost 40% in the 2010s, comprising 16% of the state’s total population, or over 170,000 people, at the time of this study. Forty-three percent of the population of the state’s largest city, Providence, and 64% of the population of Central Falls, home to Progreso Latino, identify as Hispanic or Latino. For this study, Progreso Latino’s Wellness Center staff recruited participants from among their clients and regular visitors via flyers and face-to-face invitations. The Center regularly holds health screenings, organizes health fairs, and hosts...
workshops on various health and lifestyle topics. Progreso Latino’s clients with diabetes or prediabetes were considered eligible for the study.

**Interviews**

All interviews occurred in person at Progreso Latino. Each interview was conducted in the participant’s preferred language of either Spanish or English. A structured interview question set was developed in conjunction with Progreso Latino’s Wellness Center staff to direct the conversations. The interview guide included questions relating to participants’ experience of receiving the diagnosis of diabetes or prediabetes, the experience of managing the disease, experience with healthcare and healthcare providers in Rhode Island, and interest in additional diabetes education programming. The study was approved by the Brown University Institutional Review Board.

**Data Analysis**

Each interview was recorded and transcribed in its original language. Analysis of the interview transcripts followed the Immersion/Crystallization method. A group of five bilingual investigators, consisting of two internal medicine physicians, one geriatrician, one community health worker, and one medical student read and independently analyzed transcripts in their original form to identify salient themes. The transcripts were divided among readers such that at least three different investigators analyzed each interview. At an analysis meeting, all five of the investigators discussed and interpreted common themes, offering demonstrative quotations. The investigators then considered these results and agreed on four themes to be the most significant and predominant.

**RESULTS**

**Participant Characteristics**

Fourteen participants with a mean age of 70.3 years (range 40-87) represented three countries of origin: Colombia, Guatemala, and the Dominican Republic. Participants had lived in the US between 2 and 49 years. Twelve participants preferred to interview in Spanish, while two participants preferred English. Additional information about participants is provided in Table 1.

**Predominant Themes**

Four predominant themes emerged: uncertainty about diagnosis and treatment, fear as part of the discussion with providers, language barriers, and cultural barriers. Many participants described the uncertainty surrounding the original diagnosis of diabetes. Though many were aware of diabetes because of their family members’ experience with the disease, participants indicated that their understanding of the disease at the time of diagnosis was relatively limited. When asked what they were told by their doctor at the time of diagnosis, many participants recalled being prescribed medicine without understanding the disease process. As one participant put it, “The doctor simply told me that I had diabetes, that I could control it with medicine. And since then, I’ve been taking metformin, and it controls it for me.”

In response to the interview prompts about what was discussed with the medical provider when first diagnosed with diabetes, one participant, laughing, explained, “That I had diabetes. I hadn’t known it, but he told me, and he prescribed me medication.” In some cases, that uncertainty about the diagnosis and the management persisted to the time of the interview: “I think I’m prediabetic. I’m not sure what that means.”

Other recollections from participants’ early encounters with providers noted fear was used to motivate them: “The only thing he says to me is that I shouldn’t eat hardly anything, and that I should take my injections and take my pills because he knows diabetes progressively destroys every part of you.”

In those controlling their diabetes with lifestyle changes and pills alone, that fear often manifested in the threat of insulin. One participant commented on glucometers and insulin by noting: “I have that little machine, but I don’t use it because it scares me a lot. I put my hand out to the nurse like this, but dying of fear...The nurse said to me, because I felt so scared, she said, “What are you going to do when you have to use insulin?” I told her, “Well, I don’t know what is going to happen because you have to inject the insulin yourself.”

Participants often noted the difficulty created by language barriers between them and their providers especially when discussing diabetes and its management. Even with

---

**Table 1. Participant demographics.**

<table>
<thead>
<tr>
<th>Self-identified gender</th>
<th>Male</th>
<th>Female</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>14.3%</td>
<td>85.7%</td>
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<table>
<thead>
<tr>
<th>Interview language</th>
<th>Spanish</th>
<th>English</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>85.7%</td>
<td>14.3%</td>
</tr>
</tbody>
</table>

| Mean age (SD)          | 70.3 (14.9) |

<table>
<thead>
<tr>
<th>Country of origin</th>
<th>Colombia</th>
<th>Guatemala</th>
<th>Dominican Republic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>64.3%</td>
<td>21.4%</td>
<td>14.3%</td>
</tr>
</tbody>
</table>

| Years living in U.S. – Mean (SD) | 29.7 (13.7) |

<table>
<thead>
<tr>
<th>Level of education</th>
<th>&lt; High school</th>
<th>High school or GED</th>
<th>&gt; High school</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>69.2%</td>
<td>15.4%</td>
<td>15.4%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Years since diabetes diagnosis – Mean (SD)</th>
<th>11 (8.19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Range 0–31 with two participants unable to remember)</td>
<td></td>
</tr>
</tbody>
</table>
an interpreter present, a language barrier can affect the content and duration of the discussion. Regarding her doctor, one participant explained: “On the one hand [my PCP] pays attention to me, but on the other she doesn’t speak Spanish… I feel uncomfortable because I would like to just tell her how I feel…but [I have to tell] my daughter, ‘tell her this and that.’ She tells her what she wants to.… [Sometimes] I think it’s coming from her head because it’s not what I said.”

Several participants indicated that the challenges associated with the language barrier are commonly compounded by challenges associated with another barrier, that of cultural differences, when it comes to diabetes management. Various participants noted how their doctors’ unrealistic expectations for changes in their diets reflected a lack of understanding of the food they prefer and its greater significance: “It’s our culture, how we grew up since childhood, the food we ate… at this point in our life, radically changing that way of eating is very hard, it’s quite hard.”

Further, identifying a person’s preferred foods as problematic can come off as unnecessarily judgmental or condescending. As this same participant pointed out: “…but the same American doesn’t take care of himself…That very American suffers the same disease that we do because his food is also something that can’t be changed overnight. Like they are always telling us, junk food is what the American eats most, right!”

Conversely, Spanish-speaking participants who have found Spanish-speaking providers and providers with a more open approach to cultural differences note a high level of satisfaction. As one participant explained: “Well [my brothers] control their diabetes because they are in Santo Domingo, and there they take their medicine, but they also take many plants of the earth, natural, and then, well, their diabetes is good. When I’m in Santo Domingo, and I take lots of plants, I don’t have to take pills, I take many teas and such, and all is well… and I found a really good doctor… I say, ‘Oh, it’s great that I found you’ because he speaks Spanish; I don’t speak English. Then, well, you go to him, and you say to him, ‘I feel this,’ and he tries to do something to help you. Then, well, even if it’s not a prescription, let’s say teas or something, but he helps me more than most.”

### Table 2. Predominant themes identified by analysis and representative quotations in original language.

<table>
<thead>
<tr>
<th>Themes</th>
<th>Representative Quotations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Uncertainty</strong></td>
<td>El doctor… me dijo simplemente que tenía diabetes, que me la podía controlar con medicina. Y desde eso estoy tomando metformín, y me la controla. Que yo tenía diabetes. Yo no lo sabía, pero él me dijo y me recetó mis medicinas. I think I’m prediabetic. I’m not sure what that means.</td>
</tr>
<tr>
<td><strong>Fear</strong></td>
<td>Lo único que me dice [es] que no coma ni nada, y que me ponga la inyección y me tome las pastillas porque sabe que la diabetes le va destruyendo a un [a] todas las cosas. Pues [mis hermanos] controlan [la diabetes] porque están en Santo Domingo y allá ellos tomen su medicamento, pero toman muchas plantas de la tierra, natural, y entonces, pues ellos, su diabetes está bien. Yo cuando estoy en Santo Domingo, que tomo muchas plantas, no tengo que tomar pastillas, yo tomo muchos tés y esos, todo bien.… y yo lo consiguió muy bueno médico… yo digo “ay, que bueno que le encontré” porque él habla español, yo no hablo inglés. Entonces pues tú vas adonde él, y tú le dices “yo me siento esto,” y él trata de hacer lo que sea para ayudarte. Entonces, pues aunque no es receta, vamos a decir tés o cosa, pero [él me ayuda] más que mucho.</td>
</tr>
<tr>
<td><strong>Language barrier</strong></td>
<td>Por un lado [la doctora de medicina general] me atiende, pero por otro ella no habla español…me siento incómoda porque yo quisiera decir lo que yo siento…pero [tengo que decir] a mi hija, “dile a ella esto y esto.” Ella le dice lo que ella quiere…. [A veces] yo creo que es de la cabeza de ella porque no es lo que dije. On finding a language concordant physician: Pues [mis hermanos] controlan [la diabetes] porque están en Santo Domingo y allá ellos tomen su medicamento, pero toman muchas plantas de la tierra, natural, y entonces, pues ellos, su diabetes está bien. Yo cuando estoy en Santo Domingo, que tomo muchas plantas, no tengo que tomar pastillas, yo tomo muchos tés y esos, todo bien.… y yo lo consiguió muy buen médico… yo digo “ay, que bueno que le encontré” porque él habla español, yo no hablo inglés. Entonces pues tú vas adonde él, y tú le dices “yo me siento esto,” y él trata de hacer lo que sea para ayudarte. Entonces, pues aunque no es receta, vamos a decir tés o cosa, pero [él me ayuda] más que mucho.</td>
</tr>
<tr>
<td><strong>Cultural barrier</strong></td>
<td>On food: Es…la cultura de nosotros, cómo crecimos desde niño, la comida que consumíamos... a esta altura de la vida de nosotros, cambiar radicalmente esa forma de comer es muy difícil, es bien difícil. …pero el mismo americano no se cuida…. El mismo americano sufre la misma enfermedad que nosotros porque también su comida es algo que no está para cambiarse los de la noche a la mañana. Como siempre nos están diciendo la comida chatarra lo que más come el americano, ¿sí?</td>
</tr>
</tbody>
</table>
DISCUSSION

This is, to our knowledge, the first study designed specifically to understand the needs of Rhode Island’s Hispanic population with diabetes. In doing so, it follows in the footsteps of other community-based observational and interventional studies of groups with diabetes such as Benavides-Vaello, Brown, and Vandermause’s interview-based study of Mexican-American women in South Texas and Kim et al.’s self-management education intervention in the Korean American community in Maryland. The existence of such studies underscores the importance of understanding the challenges of living with diabetes experienced by specific communities in order to offer the best interventions to each community.

Our investigators identified four salient themes present in the interview transcripts: uncertainty about diagnosis and treatment, fear as motivation, language discordance with providers, and poor cultural understanding by providers. In their review, Cersosimo and Musi also identified poor understanding of diagnosis/treatment, language discordance, and cultural barriers as difficulties associated with diabetes management in Hispanic/Latino patients. Participants in this study and others eliciting patients’ experiences in healthcare have noted the multitude of difficulties of communicating via a personal interpreter. As our participants made clear, interactions with even the most patient and attentive physicians can be hindered significantly by a lack of language concordance. Further, language discordance has been shown to measurably impact diabetes management; data from the DISTANCE trial revealed participants with language-discordant physicians were more likely to have poor glycemic control than those with language-concordant physicians.

Cultural understanding may be just as crucial to successful diabetes interventions. Culturally tailored diabetes education programs serving a variety of groups have been well-received and successful in improving diabetes management among participants. One study examining a program designed for the Mexican American community of Dallas, Texas attributed its success to the program’s leader, a community health worker, and suggested that community health workers are crucial to reaching people in underserved areas.

Fear as motivation seems to be well known to patients and practitioners. In one study, physicians reported fear of insulin among their Hispanic patients. In their review, Fu, Qiu, and Radican found that fear of insulin or fear of injection has a negative impact on successful diabetes control. Indeed, though fear is not a positive motivator, it appears that physicians have not removed it from their practice.

This study is limited in its scope by the relatively small number of interviews collected and the small number of countries of origin represented among participants. Progreso Latino serves members of Rhode Island’s Latino and immigrant communities, who number in the hundreds of thousands; tens of thousands of these Rhode Islanders live with diabetes, and the 14 participants in this study are certainly not representative of the full diversity of experience among this large population. However, the sample size does accomplish this study’s qualitative goal of amplifying multiple voices that reveal common experiences among the population of interest.

Notably, our study did not directly reveal additional challenges associated with the control of diabetes that others have seen in Hispanic/Latino communities, such as lack of access to healthy food or health insurance. However, the participant population was very representative of Progreso Latino’s regular visitors with diabetes. As such, the results of this study are well suited to this organization’s needs. Similar recruitment and interview methods could be employed at other organizations to yield similarly well-suited results.

With these principles and the patients’ voices in mind, our investigators make the following recommendations for diabetes education programming at Progreso Latino. To address the issues of uncertainty, language barriers, cultural barriers, and fear as motivation we recommend increasing the number of liaisons between community and health organizations. Spanish-speaking community health workers that can interpret both language and culture are ideally suited to meet people with new diabetes diagnoses at Progreso Latino and educate them about making practical adjustments to habits and lifestyle. To complement this, we recommend culturally appropriate methods of education about dietary changes. This could include distributing a cookbook with healthy recipes and holding cooking demonstrations with clients and their families. Lastly, we recommend providing clients with educational videos in their preferred language to allow for continued learning at home, this can further address the uncertainties of diagnosis and management of the disease. Changing habits in the face of a new diagnosis is difficult for every patient, but the results of these interviews suggest that these measures could potentially ease those difficulties for Progreso Latino’s clients.

These recommendations will form the basis for adaptations that Progreso Latino makes to its existing programming. The organization’s Wellness Center has already begun to publish supporting materials on its website, including informative bilingual videos. It has also distributed a cookbook with accompanying nutritional labels entitled Savoring Health: A Healthy Latinx Cookbook, available in print and online.

In order to gauge the effectiveness of these adjustments to programming, another study should be conducted that examines satisfaction, enhanced self-efficacy, and improved health outcomes of Progreso Latino’s clients with diabetes.

This study provides a model in Rhode Island for involving community members in the design of community resources for their benefit by eliciting their experiences via interviews. Doctors must interview their patients daily, provide
individualized counsel, and engage in shared decision making to produce the best outcomes; it is in these interviews that the truth of experience is revealed. Community-based organizations can reach these same people outside the constraints of the doctor’s office and are able to continue this conversation, reinforce the teaching about a new diagnosis, and empower their clients to take charge of their care. Other studies have shown that listening carefully to their voices and adjusting resources available to them accordingly is both feasible and essential; with that in mind, it is our duty to do so for our local communities.

References

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Disclosures
None

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Use of Telemedicine by Rhode Island Physicians

EMILY COOPER, MPH; JACQUELINE HASKELL, MS; SAMARA VINER-BROWN, MS; REBEKAH L. GARDNER, MD

BACKGROUND
Prior to the COVID-19 pandemic, physicians were as likely to make a video call to their patients as they were to make a house call. A 2016 American Medical Association survey found that just 15% of physicians worked in practices using telemedicine. A 2017 review of telemedicine policy trends noted Medicare’s restrictive telemedicine reimbursement policies and cited a contemporaneous prediction by the National Business Group on Health that “virtually all large employers will cover telehealth services for their employees by 2020.” Their prediction was only wrong by about three months. Insurers and regulators swiftly made changes to reimbursement policies in response to the COVID-19 pandemic. The Centers for Medicare & Medicaid Services (CMS) approved temporary changes to the rules for telemedicine visits on March 17, 2020, and Rhode Island issued an executive order to expand telemedicine services and to ensure parity in reimbursement the following day. Additional executive orders renewed this expansion, and legislation mandating permanent support for telemedicine reimbursement in Rhode Island was signed into law on September 24, 2021.

What has been the impact of these pandemic-related reimbursement changes? Over the past 12 years, the Rhode Island Department of Health (RIDOH) has surveyed physicians and other clinicians about their use of health information technology (HIT), including telemedicine. Prior surveys focused on the uptake and use of electronic health records (EHRs) and electronic prescribing, as well as the influence of technological advancements and legislation on HIT adoption and clinician workflow. The 2021 survey provided an opportunity to explore the effect of the COVID-19 pandemic on the adoption of telemedicine and physicians’ experience using it.

METHODS
RIDOH’s public reporting program, the Healthcare Quality Reporting Program, administers the Rhode Island HIT Survey to all licensed physicians, physician assistants, and nurse practitioners. This program is legislatively mandated to publish reports intended to help consumers compare healthcare practitioners in Rhode Island. The survey, first piloted in 2008, was administered annually from 2009-2015 and biennially starting in 2017. HIT Survey data are used to report process measures relating to HIT adoption and use.

The 2021 Physician HIT Survey was administered to 4,466 physicians licensed in Rhode Island, in active practice, and located in Rhode Island, Connecticut, or Massachusetts. New questions were added to the 2021 survey to address the expanded use of telemedicine services in Rhode Island as a result of the COVID-19 pandemic. Telemedicine was defined for survey purposes as “remote, real-time communication between a patient and clinician, in lieu of a face-to-face visit.” The questions focused on physicians’ experience with telemedicine in the year prior to survey administration [June 2020–May 2021], including which telemedicine platform or technology they used, the amount of time spent on various telemedicine-related tasks, and barriers to offering telemedicine. Physicians were also asked whether they had used telemedicine prior to the COVID-19 pandemic. We piloted all new questions in the 2021 survey, including this set of questions, with a subset of physicians using cognitive debriefing to test question comprehension and the response process, as well as the face validity of the included constructs.

RESULTS
The survey received a total of 1,772 responses, for a response rate of 40%. Among the respondents, 1,556 reported providing direct patient care and completed the full survey. Overall, 80% of physician respondents reported using telemedicine to care for patients in the prior year [June 2020–May 2021]. Higher proportions of office-based physicians reported using telemedicine [91%], compared to hospital-based physicians [55%]. Among all respondents, only 11% had used telemedicine before the pandemic [12% of office-based physicians and 10% of hospital-based physicians].

Among physicians who had used telemedicine in the prior year, 39% used mostly audio-only technology (e.g., a telephone call). Almost a quarter [23%] used mostly audio/video platforms (e.g., Zoom), and 38% used a combination of audio-only and audio/visual technology. The most common platforms and technologies used by physicians to provide telemedicine were regular phone calls [65% of office-based physicians and 53% of hospital-based], followed by Doximity [32%] and Doxy.me [28%] among office-based physicians, and by Zoom [35%] among hospital-based physicians.
When asked about time spent on common tasks related to telemedicine, almost a third of office- and hospital-based physicians reported spending a “moderately high” or “excessive” amount of time assisting patients with technology during an encounter (Figure 1). More than one in five spent a “moderately high” or “excessive” amount of time on telemedicine-specific documentation. Across all tasks, higher proportions of hospital-based physicians, compared to office-based physicians, reported spending a “moderately high” or “excessive” amount of time on every task type (Figure 1).

All respondents were asked about barriers to providing telemedicine. The highest proportion (41%) reported that their specialty often requires a procedure or examination that must be done in-person (Figure 2). The next most commonly cited barrier was that patients struggled to use technology during encounters (36%), followed by patients not having needed technology (33%). Among the subset of physicians who had not used telemedicine during the past year, the most frequently cited barrier to caring for patients using telemedicine was that their specialty often requires a procedure or examination that must be done in-person (60%).

In free-text responses, physicians provided more details about technology issues, reimbursement, and the need or preference for in-person visits. Additional barriers included challenges in specific populations (e.g., older adults, children, behavioral health patients), patients’ expectations for the timing or level of care during telemedicine visits, and patients multi-tasking (e.g., multiple respondents described patients driving or shopping during visits).

**DISCUSSION**

The COVID-19 pandemic dramatically accelerated the uptake of telemedicine in Rhode Island, initiating a demonstration project of its feasibility and merits on a scale not previously seen. Prior to the pandemic, only 12% of outpatient physicians in the state had used telemedicine; within a year, that number increased to 91%. The 2021 HIT Survey examined Rhode Island physicians’ early experiences using telemedicine, and the results align with a recent national study, which documents a surge in use of telemedicine for outpatient care in the first few months of the pandemic. In that analysis, the authors found that telemedicine claims were 78 times higher in April 2020 than in February 2020.

As in Rhode Island, broader insurance coverage for telemedicine across the US likely contributed to the increase in use. Almost half of states amended laws or policies to require more robust reimbursement during the pandemic.

Alongside the staggering increase in telemedicine adoption, we identified challenges related to physicians’ and patients’ access to and use of technology. These barriers have been noted by others, prior to the pandemic, but may have been exacerbated, in part, by the rushed nature of the implementation. They should be addressed as Rhode Island moves forward with incorporating telemedicine into routine practice. On the physician side, we recommend prioritizing efficient clinical workflows, access to integrated technology, and staff support of telemedicine visits. On the patient side, we advocate for increased access to and proficiency with technology, as well as consistent broadband internet availability.

There are various limitations to this data. First, all clinician data are self-reported. Second, recent survey years have had a lower response rate than previous survey years. Survey response rates between 2013 and 2015 were above 60%, whereas the 2017, 2019, and 2021 rates were all between...
40–43%. We suspect this dip in response rate is tied to the transition to biennial survey administration in 2015. Third, the fact that RIDOH distributes the survey may influence how clinicians respond to more personal questions about challenges implementing care. Finally, distributing the survey electronically may bias the sample by not including clinicians without computer access.

Based on our findings, we recommend that future surveys extend the inquiry into use of telemedicine in several ways. Surveys could be designed to 1) employ mixed methods to more fully investigate the physician perspective, 2) capture the patient and family experience using telemedicine, and 3) explore the quality of care delivered using telemedicine technologies. These additions would broaden our understanding of the impact of telemedicine implementation over the past few years. While our study primarily examined barriers to using telemedicine, future surveys should include questions asking for physicians’ perspectives on the benefits of telemedicine, as well. Additionally, physicians’ use of telemedicine overall has evolved since the first year of the pandemic. It is likely that some of the challenges identified in this study have been resolved. Certain telemedicine tasks may now take less time, as practices have deployed EHR templates and patients have become more accustomed to these types of visits. The next administration cycle of the Rhode Island HIT Survey in 2023 will be able to assess how use of telemedicine is changing, building on the baseline set of data from the 2021 survey.

The uptake and use of telemedicine during the COVID-19 pandemic demonstrates that given the right conditions – high need and reimbursement parity – large-scale implementation of telemedicine is feasible and acceptable to physicians and patients. Future research should focus on whether physicians and patients are willing to use telemedicine when not in the midst of a pandemic, the quality of care provided via telemedicine, the cost-effectiveness compared to in-person visits, and how to improve the experience for all.

The results shared above represent a fraction of the findings from the 2021 HIT survey. The full report can be accessed at https://health.ri.gov/publications/annualreports/HealthInformationTechnologyPhysicianSurveySummary.pdf. The HIT Survey data are also publicly available as a de-identified research data file. Please contact Emily Cooper, MPH, (ecooper@healthcentricadvisors.org) for more information.

References


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Disclosures

None

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Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

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<tr>
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<td>Divorces</td>
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* Rates per 1,000 estimated population
# Rates per 1,000 live births

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<td>2,179</td>
</tr>
<tr>
<td>Cerebrovascular Disease</td>
<td>55</td>
<td>435</td>
</tr>
<tr>
<td>Injuries (Accident/Suicide/Homicide)</td>
<td>107</td>
<td>1008</td>
</tr>
<tr>
<td>COPD</td>
<td>40</td>
<td>368</td>
</tr>
</tbody>
</table>

(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.
Adventures

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Institutional Review Board (IRB) Overreach

JOSEPH H. FRIEDMAN, MD

Institutional Review Boards (IRBs) are committees at institutions where clinical research is performed or where members of the institution perform clinical research related to their institutional jobs. Each institution has an Institutional Officer, registered with the federal government, who appoints a minimum of five people. One must be a scientist, one a non-scientist and one should represent patients. Consultants are added on an ad hoc basis as needed for expertise. The committees are overseen by the federal government and their decisions cannot be overturned by the institution they work for.

There is no question they are crucial for overseeing clinical research. Medical research has a horrific history with regard to its concerns for patients. Many patients were used as subjects for a variety of research endeavors without their consent, or even knowledge. While almost everyone is aware of Nazi experiments on humans, not all Americans are aware of the Tuskegee experiments on unwitting African Americans, prostate cancer experiments on “Bowerie bums,” radiation and LSD experiments on American soldiers, and a host of other less infamous cases. Publicity describing these cases caused an outcry that culminated in the formal development of principles and structures for protecting patient safety, and the freedom to choose whether or not to participate in any research endeavor. I have had many protocols reviewed by IRBs and thus have some experience. My projects have always been mundane, carrying little more risk than routine clinical care.

Chart review studies
My concern about the overreach of IRBs began when they started to require approval for my chart review studies. These are studies in which I review my own charts to determine how useful some intervention I used in the routine treatment of patients has been, if I want to report the effect of a particular medication or other intervention for my patients. Instead of trying to recall the last few patients I saw, I might want to review all the patients I’ve seen with a particular condition, determine how many got a particular treatment, and see how that affected outcome in some way. The purpose of the intervention was to treat the patient, not to do research on them, but once I had some experience, I felt it incumbent to determine how useful the treatments had been. One might think that NOT reviewing the experience is tantamount to uninformed care. We all recall our last few cases, but are not so good at recalling the last 100. There is an old joke about what a doctor means when he discusses his clinical outcomes at a conference. “In my experience,” means one case. “In my series,” means two cases. “In case after case after case,” means three cases. Yet to do a chart review with the intent of publishing the results, even though there would be no means of identifying the participants, requires IRB approval. This is not hard to get if you know how to navigate the web-based process, which requires choosing among tens of possible forms to complete, but it is time consuming, and often requires revisions when statements do not fit the required boilerplate templates.

The IRB is often overwhelmed with large numbers of complex protocols and delays are common, although less so with chart review projects that have no risk and are often expedited. The fault lies not with the IRBs, but the federal rules by which they operate. Recently I proposed a research project in which an anonymous Monkey survey (email) would be sent to about 100 medical prescribers asking them to rank 5 choices in renaming a particular drug-induced movement disorder. I asked the IRB if this would require approval. The surprising answer was that it would, but only if I wanted to publish it. I was surprised that publication had anything
to do with it, since the role of IRBs is to protect patients. I was unsure if the fact that patients were not involved, and that all data would be from people unknown to me, hence to any reader, would allow me to bypass approval, but I hadn’t thought publication would have anything to do with it. But publication, for reasons unclear to me, is central to the IRB interpretation of what research is.

One problem associated with requiring IRB approval is that it takes weeks to months to get. As a result, students, house staff and fellows who are rotating through a clinic are unable to do this sort of research, or almost any at all, other than for joining ongoing projects. In the not-too-distant past, a student/resident/fellow could come across an interesting case and decide to evaluate other patients seen in the clinic with the same problem, and start work on it as soon as other cases could be found. Now this is reserved for students or residents who return the next year and start the wheels rolling for IRB approval in the interim. It also might mean, and I’m unsure if the IRB even knows, that I might need to have approval to review charts to present my findings at a conference, even if I choose to not publish the results, if the conference publishes abstracts of the presentations. This might even be interpreted to mean that it might make it a violation for me to present my results to anyone who might choose to use these results in a publication, citing a “personal communication.” Yet, it would be clearly immoral for me to refuse agreement to publish the results of a study that might have clinical importance for some patients. Would it be more ethical to be quoted as saying that I reviewed the results and know whether an intervention was useful and what its safety issues are, but am not allowed to state the results until the project is reviewed and approved?

Yet we can’t fault the IRB for doing its job. Several years ago, all research was halted at a prominent institution after a federal government review deemed its oversight insufficient.

One prominent IRB critic has published articles estimating the number of deaths caused by IRB-induced delays or interference with proposed studies that ultimately led to better care, but not in time for some patients to benefit from it. This physician and ethicist, like all physicians who have used IRBs, is a strong supporter of them. They serve an important function. Physicians and medical professionals have patient care as their mission. These are ethically driven professions, but the unethical among us are as unethical, or worse, than any others. Past behavior has taught us that we need oversight.

The problem now is the transformation that has taken place from its true mission of IRB as protector of patients to protectors of hospitals and government institutions. It is not too late, and probably not too difficult, to change.

Author
Joseph H. Friedman, MD, is Editor-in-Chief Emeritus of the Rhode Island Medical Journal, Professor and the former Chief of the Division of Movement Disorders, Department of Neurology at the Alpert Medical School of Brown University, Chief of Butler Hospital’s Movement Disorders Program and first recipient of the Stanley Aronson Chair in Neurodegenerative Disorders. He is the 2022 recipient of the Dr. Stanley M. Aronson Award of the Rhode Island Medical Society, given for Humanitarianism in Medicine.

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Women’s Orthopedic Leadership Forum: Combined Educational and Mentorship Program to Increase Gender Diversity

KELSEY E. BROWN, BA; AHSIA M. CLAYTON, BS; VANESSA LUND, MD; PATRICIA SOLGA, MD

The field of orthopedics lags in gender diversity when compared to other surgical subspecialties.¹-⁴ According to the 2019 annual Association of American Medical Colleges (AAMC) report of medical school enrollment, about 50.5% of medical students in the United States are women.⁵ The 2020 AAMC Physician Specialty Data Report showed that of the 19,064 total active orthopedic surgeons, only 1,099 (5.8%) self-identified as female.⁶ Several studies in the literature have noted reasons why women may not choose orthopedic surgery, including perceived physical requirements, difficulty with work/life balance, male physician predominance, and lack of mentorship and exposure.⁷,⁸

In the past few years, several programs have taken steps to correct the lack of mentorship opportunities for gender, racial, and ethnic minorities in orthopedics. Mentorship is reported as being important in students’ decision on what field to pursue.⁹ “Pipeline” programs such as the Ruth Jackson Orthopedic Society (RJOS), Nth Dimensions, and the Perry Initiative target students as early as high school and continue mentoring them through undergraduate education and medical school for the purpose of increasing students’ exposure to and interest in orthopedics.¹⁰ Other organizations, such as Black Women Orthopedic Surgeons, offer mentorship and supportive spaces for practicing Black female orthopedic surgeons. These existing programs have laid the groundwork for establishing pipeline and mentorship programs aimed at increasing diversity in orthopedic surgery. Inspired by these programs, the Women’s Orthopedic Leadership Forum (WOLF) aims to provide a combined educational and mentorship program aimed at encouraging more women from the greater Providence community and the Warren Alpert Medical School of Brown University to pursue careers as orthopedic surgeons.

WOLF PROGRAM DESCRIPTION

WOLF was founded in 2018 by Dr. Patricia Solga, a pediatric orthopedic surgeon and Clinical Assistant Professor and Senior Advisor to the Chairman for Diversity in the Department of Orthopedics at Brown University. WOLF is primarily led by female medical students who are interested in orthopedics. Each year, four to six members are added to WOLF’s general body. Our mission is to increase the number of women interested in orthopedic surgery through early exposure to the field, mentorship, networking, and community engagement.

EARLY EXPOSURE

High School Students

One of the strategic goals of WOLF is to expose young women to orthopedics as early as high school, which has been shown through early outreach programs such as the Perry Initiative to increase interest in the field and, in the long term, increase the number of women who match in orthopedic surgery residency.⁵ Each year WOLF hosts 10-15 young women from Juanita Sanchez Educational Complex Cooley High School, a local school in Providence, which is categorized as “underperforming” by the Providence Public School District.¹¹ The students travel to the Alpert Medical School (AMS) campus for lectures on basic musculoskeletal anatomy using orthopedic models and X-rays, musculoskeletal injuries and their treatment. Students are provided hands-on anatomy lessons in the cadaver lab at AMS, and casting/splinting workshops led by medical students, residents, and attendings. Students also receive certificates of completion as an incentive to continue participating. To further increase interest, the group is working on expanding instruction outside of the classroom and into settings that provide a more creative approach to learning.

Medical School Students

WOLF at AMS is open to women in the first year of medical school, primarily recruited through an activities fair at the start of the academic year. The group also created an Instagram account to increase social media presence and outreach efforts. While any female-identifying medical students are invited to join, the group primarily attracts women who are interested in either orthopedics or surgery in general. By joining, members are invited to attend panel discussions, social events, teaching sessions and networking opportunities. The panels have covered a variety of topics including careers in orthopedics and preparing for residency applications.
Networking & Mentorship
During AMS pre-clinical years, students are assigned a community mentor – a practicing physician who teaches them basic clinical skills, i.e., taking a history, doing a physical exam, and giving oral presentations. In order to ensure that WOLF members have access to mentorship, Dr. Solga works closely with AMS to pair WOLF students with orthopedic surgery physicians in the community. WOLF advisors also help female medical students establish connections with orthopedic surgery attendings and residents, both at Brown and other institutions. This network opens doors for female medical students to engage in shadowing as well as clinical research. Although mentorship for medical students starts in preclinical years, special attention is paid to third-year members, to help them be competitive when applying for orthopedic residency programs.

Community Engagement
Though the group’s primary mission is closing the gender diversity gap in orthopedics through early exposure, mentorship, and networking, it has recently implemented a community service component. During the COVID-19 pandemic, when US schools transitioned to virtual instruction, it created barriers to learning, especially in low-income areas, such as lack of access to technology, inability to afford personal tutors, and parents choosing between remaining employed or staying home to assist with navigating online instruction.12 These barriers have contributed to some students falling behind academically. Given this, WOLF has implemented a tutoring program for students at Juanita-Sanchez Educational Complex Cooley High School.

As academic scholars themselves and near-peers, WOLF members have a unique opportunity to inspire students to excel both academically and socially. By providing tutoring in a multitude of different subjects tailored to each student’s learning style, WOLF members can help close academic gaps for high school students in need. While this is the first of WOLF’s community engagement efforts, the group is planning to assist with helping the students prepare college applications and find internship opportunities.

WOLF’S SUCCESS
Since WOLF was started in 2018, the total number of AMS medical students matching into orthopedics has doubled (2018: four students; 2021: eight students). Between 2018–2021, the percentage of female AMS medical students matching into orthopedics has increased by 25%. There have been 20 female medical students involved in leadership roles in WOLF since its inception and eight have graduated from AMS. Two prior WOLF leaders (25%) matched into orthopedics and four (50%) matched into other surgical specialties including general surgery, obstetrics and gynecology, and urology. Of the current rising fourth-year class of WOLF leaders, three (60%) are planning to apply into orthopedics. While matching into orthopedics is not the only measure of WOLF’s effectiveness, further studies are needed to assess other measures including, but not limited to, number of publications completed by WOLF’s medical students, graduation rates of WOLF’s high school students and overall desire to pursue careers within the field of orthopedics.

DISCUSSION
While many of WOLF’s efforts have been successful, the group must reflect on its work over the past years and redesign activities moving forward to reflect post-pandemic society. We aim to think critically about how to recruit more female students into orthopedics, evaluate the success of the group’s community efforts, and showcase our efforts to act as a model for other medical schools interested in increasing underrepresented groups’ entry into orthopedics.

The group’s next steps and future programming will be guided by a series of needs-assessment surveys of various groups involved with WOLF, the first of which would be an evaluation of the mentorship needs and preferences for female medical students pursuing orthopedics in New England. The second needs assessment will be geared towards leadership at local high school administrators to better understand what forms of support the high school students need on the path to college and ultimately medical school.

With better-informed programming, WOLF will ideally be able to engage more students and faculty. In order to reach more members, WOLF will continue to grow its social media presence to advertise ongoing events, promote networking, and engage other students both inside and outside of Rhode Island, as well as engage with more students all along the pipeline to orthopedics. In addition, social media allows WOLF to engage with other institutions to share best practices and ideas for growth.

CONCLUSION
Through all of these initiatives, AMS’ WOLF program is taking critical steps to decrease significant gender gaps in orthopedics. Using an innovative model that includes early exposure, mentorship, and community engagement, WOLF is engaging young women at critical touch-points to patch the leaky pipeline into orthopedic surgery. Future studies should assess the efficacy of WOLF’s efforts by tracking how many of its students continue on to orthopedic surgery residency, fellowship, and ultimately jobs as orthopedic surgeons, including faculty appointments and orthopedic leadership positions.
References


5. AAMC Medical School Enrollment Survey: 2019 Results:24.


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Disclosures

The authors have no disclosures.

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- 2. Canada
- 3. UK
- 4. Australia
- 5. India
- 6. China
- 7. Germany
- 8. Italy
- 9. Brazil
- 10. Netherlands

Looking up from 10th Avenue, The Edge juts out 80 feet and is 1,100 feet overhead.
Looking down at 10th Avenue far below while standing on the platform’s triangular glass floor.

**NEW YORK CITY, NEW YORK**

Mike E, Migliori, MD, Ophthalmologist-in-Chief at Rhode Island Hospital, and Chair of RIMS Public Laws Committee, views the September journal from The Edge, a cantilevered sky deck on the 100th floor at 30 Hudson Yards in Manhattan. The Edge is the highest outdoor platform in the western hemisphere, and features a glass floor and frameless glass panels that slant outward, enabling breathtaking views of the streets below and the nearly 360° views of the skyline and beyond. Lower Manhattan and the Freedom Tower can be seen in the distance, and the Hudson River is on the right.

Wherever you may be, or wherever your travels may take you, check the Journal on your mobile device, and send us a photo: mkorr@rimed.org.
Working for You: RIMS advocacy activities

September 1, Thursday
American Medical Association (AMA) Federation Health Equity Exchange

September 6, Tuesday
RIMS Physician Health Committee (PHC): Herbert Rakatansky, MD, Chair

September 7, Wednesday
Council of New England State Medical Societies (CNESMS) and New England Delegation (NED) Leadership meeting: Peter Hollman, MD, AMA Delegate; Alyn Adrain, MD, CNESMS President

September 12, Monday
Office of the Health Insurance Commissioner (OHIC) Measure Alignment meeting: Peter Hollmann, MD, Past President
RIMS Board of Directors meeting: Elizabeth Lange, MD, Immediate Past President; Thomas Bledsoe, MD, President
RIMS Advocacy Presentation to Alpert Medical School Students

September 13, Tuesday
Rhode Island Foundation Long Term Health Planning Committee: Stacy Paterno, staff
OHIC Administrative Simplification Task Force meeting: Peter Hollman, MD, Past President; Elizabeth Lange, MD, Immediate Past President
RIMS Retired Doctors Eat Out (RODEO) Luncheon: Fredrick Christian, MD, Past President; Candice Dyer, MD, Past President, Co-Chairs
Department of Labor and Training (DLT) Fee Schedule Task Force meeting

September 15, Thursday
Federation of State Physician Health Programs – Peer Enhancement & Effectiveness Review [PEER™] Committee (PEERC): Kathleen Boyd, MSW, Director, RIMS Physician Health Program
Executive Office of Health and Human Services [EOHHS] Health Information Technology (HIT) Steering Committee meeting: Stacy Paterno, staff
AMA Advocacy Update

September 20, Tuesday
National Government Services Key Stakeholder meeting

September 21, Wednesday
RIDOH Primary Care Physicians Advisory Committee [PCPAC]: Elizabeth Lange, MD, Immediate Past President
RIMS Retired Doctors Eat Out (RODEO) Luncheon: Fredrick Christian, MD, Past President; Candice Dyer, MD, Past President, Co-Chairs
Department of Labor and Training (DLT) Fee Schedule Task Force meeting

September 22, Thursday
RIMS Climate Change and Health Committee

September 23, Friday
Rhode Island Health Workforce Planning: Health Workforce Data Collection & Analytics Workgroup

September 26, Monday
Reproductive Rights Roundtable with Senator Whitehouse: Thomas Bledsoe, MD, President; Heather A. Smith, MD, MPH, President-Elect; Kara Stavros, MD, Vice President
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For more information about group rates, please contact Ali Walz, RIMS Director of Member Services
Bradley Hospital awarded five-year, $8.6M federal grant

Funds aimed at mental and behavioral health services in schools

EAST PROVIDENCE — Emma Pendleton Bradley Hospital has been awarded a five-year, $8.6 million federal grant to help provide mental and behavioral health services in schools across the state, Gov. DANIEL J. MCKEE, Lt. Gov. SABINA MATOS, R.I. Education Commissioner ANGELICA INFANTE-GREEN and R.I. Department of Children, Youth and Families Acting Director KEVIN AUCOIN announced recently.

The funding, from the U.S. Department of Health & Human Services’ Substance Abuse and Mental Health Services Administration, will support Bradley Hospital in participating in the Project Advancing Wellness and Resiliency in Education – or Project AWARE – partnership with DCYF and the R.I. Department of Education. State officials say the project’s purpose is to increase awareness of mental health issues among school-aged youths and to provide training for school personnel to detect mental health issues, respond to them, and connect the affected students’ families to needed services.

The funding will help continue running Project AWARE programs in schools in Pawtucket, Providence and Woonsocket for four more years, state officials said. The program in these districts, state officials say, will annually impact more than 35,000 students and 3,000 school personnel as the partners implement professional and paraprofessional training, mental health-related promotions, awareness, prevention, intervention and resilience activities to ensure that students have access and are connected to appropriate and effective behavioral health services.

In a statement, Bradley Hospital President Dr. HENRY SACHS said too many children and young adults are dealing with varying mental health issues, such as depression, addiction and substance uses, that is impacting their well-being. He said it is “imperative” that schools are supported in having “culturally-competent and developmentally appropriate mental wellness programs that can connect students in need to effective behavioral health services and interventions.”

NIH grant to examine universal postpartum depression for moms

PROVIDENCE — Maternal mental health is a critical public health component of perinatal care and maternal safety. Postpartum depression can have lasting consequences for the mother, child, and family. After each birth, 1 in 7 women will experience postpartum depression.

A team of researchers from Michigan State University, Care New England Health System, and Henry Ford Health is collaborating on a $6.2 million National Institutes of Health (NIH) mental health research grant, “The ROSE Scale-Up Study: Informing a decision about ROSE as universal postpartum depression prevention.”

The Reach Out, Stand Strong, Essentials for New Mothers [ROSE] program, funded by NIH through the end of 2022, has served low-income women at 98 prenatal clinics. Study findings show that ROSE prevents half of the cases of postpartum depression. Additionally, health care and community agencies find it is more feasible to provide ROSE as universal prevention for all women.

“The newly funded program will be the first study to look at the effectiveness of postpartum depression among a general population of women and women screening negative for postpartum depression risk,” said CARON ZLOTNICK, PhD, one of two PIs on the grant and Professor of Psychiatry, OB/GYN and Internal Medicine at the Warren Alpert Medical School of Brown University and Director of Research for the Department of Medicine at Women and Infants Hospital. “If we find the intervention is effective, we can work to scale up the program, strengthen families while supporting moms, and reduce costs within the healthcare system.”

VA report shows drop in Veteran suicides; awards suicide-prevention grants

WASHINGTON — On Sept. 19th, the Department of Veterans Affairs released the 2022 National Veteran Suicide Prevention Annual Report, which shows that Veteran suicides decreased in 2020 for the second year in a row, and that fewer Veterans died by suicide in 2020 than in any year since 2006.

As a part of VA’s comprehensive efforts to end Veteran suicide, VA also announced the grantees for the Staff Sergeant Parker Gordon Fox Suicide Prevention Grant Program, a first-of-its-kind program that provides VA funding for local suicide prevention programs, and the finalists for Mission Daybreak, a suicide prevention grand challenge. The SSG Fox award provides $750,000 to the Rhode Island Department of Health, applicable to the Veteran’s Integrated Service Network (VISN) 1, New England Healthcare System. These efforts are key aspects of VA’s 10-year National Strategy for Preventing Veteran Suicide and the Biden-Harris administration’s plan for Reducing Military and Veteran Suicide.

Key findings from the 2022 National Veteran Suicide Prevention Annual Report include:

• In 2019 and 2020, Veteran suicides decreased in consecutive years by 307 and 343 deaths – the biggest decrease in the suicide count and rate since 2001.
• From 2018 to 2020, the age- and sex-adjusted suicide rate among Veterans fell by 9.7%
• Among women Veterans, the age-adjusted suicide rate fell by 14.1%, compared to 8.4% among non-Veteran women. The age-adjusted suicide rate for women Veterans in 2020 was the lowest since 2013, and the age-adjusted suicide rate for Veteran men was the lowest since 2016.
• From 2019 to 2020, Veteran suicide rates fell across all racial groups.
• Comparisons of trends in Veteran suicide and COVID-19 mortality over the course of 2020 and across Veteran demographic and clinical subgroups did not indicate an impact of the COVID-19 pandemic on Veteran suicide mortality.
CDC opening applications for monkeypox vaccine equity pilot program

WASHINGTON, D.C. – Local, state, and territorial health departments, as well as tribal governments and local non-governmental organizations, can partner together and begin submitting requests to access monkeypox vaccine through the recently announced Monkeypox Vaccine Equity Pilot Program. This new pilot program is intended to reach populations that may face barriers to monkeypox vaccination, which may include differences in language, location of vaccination sites, vaccine hesitancy, mistrust of government, lack of access to on-line scheduling technology, accessibility/disability issues, immigration status, and stigma.

“We have a responsibility to address inequities that have been highlighted by this outbreak, and this program will help make a difference,” said CDC Director Rochelle Walensky, MD, MPH. “This outbreak is affecting members of the gay, bisexual, and other men who have sex with men community at an unequal rate, and it has disproportionately affected the Black and Hispanic communities. Distributing monkeypox vaccines in a way that addresses and reduces these disparities is the goal of this program and is a high priority for CDC and our public health partners.”

Up to 50,000 doses of JYNNEOS vaccine have been allocated for the Monkeypox Vaccine Equity Pilot program. Successful proposals will demonstrate new, innovative ways to reach populations that are most affected by monkeypox based on local or national data. Projects should prioritize groups:

- with risk factors that increase their chances of getting or spreading monkeypox,
- who are over-represented among monkeypox cases and less likely to be vaccinated, and
- whose barriers to vaccination may be addressed by the activities proposed.

Special consideration will be given to projects addressing disparities among Black/African American and Hispanic/Latino gay, bisexual, and other men who have sex with men (MSM) and transgender people who face barriers in accessing vaccines. Examples include pop-ups and other events associated with community-based organizations (CBOs) or clinics that work with MSM and transgender people, especially those who are Black/African American and Hispanic/Latino, who are not reached by current allocations or vaccine administration channels.

Local health departments and organizations interested in applying should contact their state or territorial health departments or tribal governments. More information, including details on the application, can be found here. 

Providence College establishes School of Nursing and Health Sciences

PROVIDENCE – For the first time in its 105-year-history, Providence College will offer academic programs in nursing and health sciences through a newly established School of Nursing and Health Sciences.

The Rhode Island Board of Nurse Registration and Nursing Education granted formal approval to the college on Monday, September 12, for a new bachelor of science in nursing degree program. It is the first bachelor’s in nursing program approved by the state in a decade.

In addition to the nursing major, the new school – which was formally established in the spring of 2022 – will offer a bachelor’s degree in health sciences, along with the existing health policy and management major.

The college will begin enrolling students for the new programs in the fall of 2023. The nursing major is expected to be added soon to the Common Application for students applying to the Class of 2027. Applicants already are able to select the health sciences major.

The inaugural dean of the School of Nursing and Health Sciences is Kyle J. McInnis, ScD. McInnis previously was provost at Johnson & Wales University and led the establishment of a new School of Health Sciences, with a nursing program, at Merrimack University. McInnis was recruited in November 2021 to spearhead the new school with the charge of developing health programs that are “uniquely PC.”

“A PC nursing degree will be distinctive because of a mission-focused approach that is aligned with our Catholic and Dominican identity,” McInnis said. “We will offer transformative learning experiences aimed at caring for the whole human being, to ensure that students gain competencies that address physical, mental, and spiritual health for all people entrusted to their care.”

Integrated within the college’s liberal arts curriculum, the school will provide students options to explore areas of study such as medical humanities and dual language courses complemented by immersive community and global health experiences gained locally and abroad.
BCBSRI certifies 21 new LGBTQ safe zones

PROVIDENCE – Blue Cross & Blue Shield of Rhode Island (BCBSRI) has newly designated 21 healthcare sites as LGBTQ Safe Zones, certifying that the providers have demonstrated care designed to meet the specific needs of LGBTQ patients.

More than 70 practices have achieved BCBSRI Safe Zone designation since the program began in 2016 and this unusually large class of certified providers was bolstered by the commitment of Coastal Medical. All but two of the new Safe Zones are affiliated with Coastal Medical, a primary care driven practice of more than 125 providers serving 120,000 patients.

“We applaud Coastal Medical for taking the initiative to join our Safe Zone program and for demonstrating to their patients that providing quality care to LGBTQ patients is a priority. Coastal’s participation greatly expands the program’s reach to LGBTQ patients across Rhode Island,” said Matt Collins, MD, MBA, executive vice president and chief medical officer for BCBSRI. “Safe Zones facilitate access to affirming care for this under-served community with specific healthcare needs, one that has historically struggled with healthcare interactions, and has often foregone necessary regular care due to feelings of alienation, stress, frustration and fear.”

A member of the Lifespan health system, Coastal Medical has more than 20 medical offices across Rhode Island, two of which had previously been designated Safe Zones.

The following are the latest Coastal offices designated as Safe Zones: Bald Hill Pediatrics, Cardiology Specialists, Coastal365, Coastal Family Medicine, Coastal’s West Exchange Street Lab, East Greenwich Primary Care, East Providence Internal Medicine, Garden City Primary Care, Greenville Internal Medicine, Hillside Family Medicine, Lincoln Primary Care, Musculoskeletal Health Program, Narragansett Family Medicine, Newport Primary Care, Providence/Edgewood Primary Care, Pulmonary & Internal Specialists, Pulmonary & Sleep Medicine Specialists, Toll Gate Pediatrics, Wakefield Primary Care, and Warren Avenue Primary Care. Coastal’s Narragansett Bay Pediatrics and Waterman Pediatrics practices were also designated as Safe Zones previously.

The two other new LGBTQ Safe Zones are:

- Fig Tree Acupuncture + Wellness: Based in Warwick, Fig Tree is committed to helping patients achieve optimal health through holistic education and empowerment. Fig Tree Acupuncture specializes in gut health, anxiety, insomnia and overall well-being.
- The Memory and Aging Program at Butler Hospital: Established in 1997, the program is affiliated with The Warren Alpert Medical School of Brown University and has played a major role in advancing the study and treatment of Alzheimer’s Disease and dementia.

The designation of these two sites, along with the Coastal locations, further diversifies the breadth of Safe Zones, which include primary care, behavioral health, oral health, child and family services, and organizations serving individuals who have experienced sexual assault, domestic abuse and substance abuse.

Certification requirements for BCBSRI LGBTQ Safe Zones include staff training specific to the care of LGBTQ patients, protection for patients and staff from discrimination based on gender identity or expression, gender neutral bathrooms, inclusive forms and procedures, and a public commitment to connecting with and serving the LGBTQ community.

BCBSRI solicits applications and designates new LGBTQ Safe Zones twice a year. To learn more about the program, or if you are a provider or practice looking to become certified as a BCBSRI LGBTQ Safe Zone, visit: bcbsri.com/providers/safezone-program.
AMA: Physician burnout rate spikes to new height

New study concludes COVID-19 pandemic exacerbated long-standing system issues that drive burnout

CHICAGO – The burnout rate among physicians in the United States spiked dramatically during the first two years of the COVID-19 pandemic, according to a newly published study in Mayo Clinic Proceedings. Researchers found that 2020 marked the end of a six-year period of decline in the overall rate of work-induced burnout among physicians. By the end of 2021, after 21-months of the COVID-19 pandemic, the physician burnout rate spiked to a new height that was greater than previously monitored by researchers.

"While the worst days of COVID-19 pandemic are hopefully behind us, there is an urgent need to attend to physicians who put everything into our nation’s response to COVID-19, too often at the expense of their own well-being," said AMA President JACK RESNECK Jr., MD. "The sober findings from the new research demand urgent action as outlined in the AMA’s Recovery Plan for America’s Physicians, which focuses on supporting physicians, removing obstacles and burdens that interfere with patient care, and prioritizing physician well-being as essential requirements to achieving national health goals."

The new physician burnout research builds on landmark studies conducted at regular intervals between 2011 and 2021 by researchers from the AMA, Mayo Clinic, and Stanford Medicine. Together, these studies found the overall prevalence of burnout among U.S. physicians was 62.8% in 2021 compared with 38.2% in 2020, 43.9% in 2017, 54.4% in 2014, and 45.5% in 2011. Each study consistently demonstrated that the overall prevalence of occupational burnout among physicians were higher relative to the U.S. workforce.

Since 2012, the AMA has led the national conversation on solving the physician burnout crisis and advocated for new thinking and solutions that acknowledge physicians need support, system reforms, and burden reduction. The COVID-19 pandemic exacerbated many of the drivers of physician burnout. Research has shown that due to COVID-related stress, 1 in 5 physicians intend to leave their current practice within 2 years.

The AMA’s ongoing work to mitigate physician burnout, as exemplified by the Recovery Plan for America’s Physicians, strives to attack the dysfunction in health care by removing the obstacles and burdens that interfere with patient care. The AMA website offers physicians and health systems a choice of cutting-edge tools, information and resources to help rekindle a joy in medicine.

Butler opens infusion suite for memory and aging program

PROVIDENCE – On Sept. 20th, Butler Hospital’s leadership team and staff held a ribbon-cutting ceremony to unveil its newly constructed infusion suite for the hospital’s Memory and Aging Program.

The new suite, located in the Weld Building on the Butler Hospital campus, was designed with vital input from clinical staff and others who will use the space. The bright, spacious and modern facility includes a refurbished reception area configured for improved patient comfort and customer service, a more spacious and efficient nurse’s station within sightline to patients for improved safety, and a lab processing room conveniently located adjacent to the nurse’s station. The new space also includes a large treatment room, a new added feature that provides an improved experience for both staff and patients while conducting blood draws, EKG testing and vital sign screening.

“Our new state-of-the-art infusion suite offers patients a relaxing environment while receiving the compassionate care they’ve come to expect from Butler Hospital,” said MARY MARRAN, president and COO, Butler Hospital.

She added, “I really hope that this new facility will make living with Alzheimer’s disease a little easier for patients who deserve a treatment experience that decreases their stress levels, and puts them more at ease.”

At the ribbon-cutting ceremony, STEPHEN SALLOWAY, MD, MS, founder of the program, said, “This new space is critical for growth, providing the expanded modern facility necessary for carrying out cutting-edge research. We are so grateful to our donors and supporters for helping to make this a reality. Together with our many study volunteers we are opening the modern era for the treatment of Alzheimer’s.”
CODAC, first responders included in prevention grants

PROVIDENCE – As drug overdose rates spike and a growing number of people seek treatment services for substance use disorder, CODAC Behavioral Healthcare, the largest non-profit, outpatient provider for opioid treatment in Rhode Island, is expanding its operations with the help of federal funds secured by U.S. Senators JACK REED and SHELDON WHITEHOUSE.

They joined LINDA HURLEY, President and CEO of CODAC Behavioral Healthcare, to discuss a new $750,000 earmark for CODAC to support the renovation and modernization of a new flagship facility at 45 Royal Little Drive in Providence. CODAC’s new headquarters will offer medical and administration services at this new, consolidated site which will allow for medical expansion due to necessity and patient need. CODAC, which serves about 5,000 people, has outgrown its current 14,000-square foot site on Huntington Avenue forcing some staff having to create work spaces out of closets.

Reed and Whitehouse also announced a new $800,000 First Responders-Comprehensive Addiction and Recovery Support Services Act Grant. This federal funding, which will be administered by the Rhode Island Department of Health (RIDOH), trains and equips first responders – such as police, firefighters, paramedics and other volunteer organizations – on how to respond to overdose-related incidents, including how to administer overdose reversal medication naloxone. Between February 2020 and November 2021, RIDOH and its community partners distributed 10,000 doses of naloxone. Getting additional naloxone kits into the hands of first responders and community members will prevent fatal overdoses and save more lives.

RI delegation announces $11.3M to combat opioid epidemic, improve mental health

WASHINGTON, DC – In an effort to connect Rhode Islanders struggling with mental health issues, opioid use disorder, and other behavioral health issues to treatment, recovery and prevention services, U.S. Senators JACK REED and SHELDON WHITEHOUSE and Congressmen JIM LANGEVIN and DAVID CICILLINE announced on Sept. 26th $11,371,485 in new federal grants for Rhode Island. Over $7.4 million in federal State Opioid Response Grant funding will enhance statewide opioid addiction prevention, treatment, and recovery support services. Federal grants will also invest in local Certified Community Behavioral Health Clinics (CCBHCs), which provide access to quality mental health care to residents across the state.

The Rhode Island Department of Behavioral Healthcare, Developmental Disabilities, and Hospitals (BHDDH) will receive $7,443,492 to help prevent opioid addiction statewide, reduce the number of prescription drug/opioid overdoses, increase access to treatment and reduce unmet needs through prevention, treatment, and gather data on addiction treatment and recovery resources.

Newport County Community Mental Health, Gateway Healthcare, Inc., and Thrive Behavioral Health, Inc. will each receive $1 million federal grants to improve community behavioral health services.

Comprehensive Community Action Program (CCAP) will receive $928,000 to treat adults with opioid use disorder and provide behavioral health counseling services.
**Appointments**

**Jordan Hebert, DO, named Kent’s new medical director of robotic surgery**

WARWICK – **JORDAN HEBERT, DO**, joined Care New England’s leadership team as the medical director of robotic surgery at Kent Hospital. He is a board-certified, fellowship-trained minimally invasive surgeon with specialized clinical expertise in bariatric surgery, hernia repair, abdominal wall reconstruction, colon surgery, and antireflux procedures.

Dr. Jordan Hebert was born at Kent Hospital, attended the Chariho school system in Richmond, Rhode Island, prior to graduating with highest honors from the Rochester Institute of Technology in Rochester, New York. Dr. Hebert then earned his doctorate degree at the University of New England COM in Biddeford, Maine. He subsequently completed internship through the Jefferson Health System in Stratford, New Jersey, followed by general surgery residency training with Hackensack Meridian Health PMC in North Bergen, New Jersey. Dr. Hebert next further advanced his surgical expertise via fellowship at Anne Arundel Medical Center in Annapolis, Maryland, earning certifications from both the Fellowship Council, as well as the American Society for Metabolic and Bariatric Surgery.

He is one of the few surgeons in the region trained to perform robotic abdominal wall reconstruction for patients with large complex hernias. Dr. Hebert was also the first surgeon in the state of Rhode Island to perform magnetic sphincter augmentation surgery, utilizing the LINX reflux management system to treat gastroesophageal reflux disease.

**Katherine P. MacCallum, MD, joins Brown Surgical Associates’ Division of Vascular and Endovascular Surgery**

PROVIDENCE – Brown Surgical Associates welcomed **KATHERINE P. MCCALLUM, MD**, to the practice’s Division of Vascular and Endovascular Surgery.

Dr. MacCallum’s professional interests focus on critical limb ischemia and limb salvage, surgical education, and vascular sequelae in diabetes.

Dr. MacCallum earned her medical degree from St. George’s University in Grenada, WI. She went on to complete her residency at Montefiore Medical Center and the Albert Einstein College of Medicine, and her fellowship in vascular surgery at Medstar Washington Hospital Center and Georgetown University.

**Amer Malik, MD, joins University Gastroenterology**

PROVIDENCE – University Gastroenterology recently announced **AMER MALIK, MD**, has joined the practice.

Dr. Malik is a board-certified and fellowship-trained gastroenterologist specializing in general gastroenterology, colorectal cancer, gastroesophageal reflux, and pancreatobiliary disorders.

Dr. Malik earned his medical degree at Imperial College of Science, Technology, and Medicine in London; completed his internship at New York University; and his residency at the Warren Alpert Medical School of Brown University. He later completed a fellowship in gastroenterology and interventional endoscopy at Stanford University in California.

**Gracie G. Luetters, MD, joins South County Health**

WAKEFIELD – **GRACIE G. LUETTERS, MD**, recently joined the general surgery team at South County Health. A da Vinci-certified surgeon, she has expertise in the surgical treatment of hernias, gallstones and cholecystitis, offering laparoscopic and robotic-assisted techniques as well as breast surgery and all other general surgery conditions.

Dr. Luetters began practicing medicine in 2019, after earning a medical degree from St. George’s University in Grenada. She then completed general surgery internship and residency at Albany Medical Center in New York.

Prior to joining South County Health, Dr. Luetters practiced acute care surgery and general surgery at Wentworth Douglass Hospital in Dover, New Hampshire, and Troy Surgical Associates, Samaritan Hospital Trinity Health in Troy, New York.
Obituaries

VINCENT A. ARMENIO, MD, 61, of Francis Street, Rehoboth, MA, died peacefully on September 24, 2022, at home surrounded by his loving family. He was the beloved husband of Dr. Jennifer Jeremiah Armenio.

Everyone who knew him felt his big heart and giving nature. Physician, philanthropist, entrepreneur, author, collector of Christmas nutcrackers and cuckoo clocks, and farmer, Dr. Armenio embraced all aspects of life. Whether spending time with family or friends or caring for the animals on his farm, his humanitarian spirit resounded in all his activities. His kindness and generosity reflected a deep spirituality which he demonstrated every day of his life. The times he spent with his wife and children at home and traveling created precious memories.

Dr. Armenio was board-certified in internal medicine and medical oncology. He received his fellowship training in hematology/medical oncology at Brown University School of Medicine. After receiving a B.A. from Lehigh University in three years, he graduated from Ross University School of Medicine, and then completed a residency in internal medicine created at Mount Sinai School of Medicine at Englewood Hospital in New Jersey. His research interests include medical oncology and clinical trials. He was a multiple Rhode Island Monthly Top Doc recipient.

A widely respected and recognized hematologist/oncologist, he held numerous leadership roles at Roger Williams Medical Center, including Chairman of the Department of Medicine and Associate Director of the Cancer Center, where he provided oversight of clinical affairs, quality care, program development, and outreach to community physicians and other providers. He most loved serving as the Internal Medicine Residency Program Director giving him the opportunity to guide many future physicians. Dr. Armenio has served on numerous committees at Roger Williams related to cancer care and quality and served as a Chairman of the Quality Oncology Practice Initiative (QOPI) committee at the Cancer Center.

Besides his wife of 23 years, he is survived by a son, Vincent J. Armenio of Rehoboth, MA; a daughter, Penelope A. Armenio of Rehoboth, MA; a brother, Father Peter Armenio of Chicago, IL and two sisters, Roseann Kiley and her husband John of Bethel, CT and Marion Sciancalepore and her husband Joseph of West Milford, NJ along with many adored nieces, nephews, cousins, patients and friends who will all deeply miss his extraordinary kindness and generosity.

Memorial donations may be made in Dr. Armenio’s name to the Dana Farber Cancer Institute or CharterCARE Foundation to support cancer research and patient care. For online condolences please visit wrwatsonfuneralhome.com.

PAUL W. BERNSTEIN, MD, age 99, of Barrington and West Island, MA, passed away August 24, 2022 surrounded by his loving family. He was the loving husband of Marian J. (Silverman) Bernstein, with whom he shared 69 years of marriage.

Born in Fall River, MA, he was the son of the late Max and Sophie (Lichterman) Bernstein.

A veteran of the U.S. Army, he served in the European Theatre during WWII. He earned a bachelor’s degree from the University of Massachusetts, Amherst, a master’s degree from Washington University, a PhD from New York University, and an MD from New York University College of Medicine.

Dr. Bernstein was a neurosurgeon for many years. He served as a former chairman of the Department of Neurosurgery at Memorial Hospital of Rhode Island, president of Pawtucket Memorial Association, and president of Rhode Island Neurosurgical Society.

In addition to his wife, survivors include: three children, Sandra A. Bernstein of North Falmouth, MA; Linda S. B. Farwell and her husband Jay of Milton, MA; and Michael C. Bernstein of Barrington, two grandchildren, Caleb and Korina Farwell and one nephew, Jerry Silverman. He was the brother of the late Lawrence M. Bernstein.

Memorial contributions in his honor may be made to Rhode Island Community Food Bank, 200 Niantic Ave., Providence, RI 02907.

Arrangements are in the care of Sugarman-Sinai Memorial Chapel, Providence.

RICHARD W. PERRY, MD, of North Kingstown passed away on September 11, 2022, in the embrace of his family at home on Narragansett Bay.

He was born on April 5, 1930, to Pete and Ruth Crane Perry on his grandfather’s farm in White Lake Township, Michigan, the middle child of five. His family left Michigan for Lusk, Wyoming, when Dick was 5 years old. The family returned to Michigan when Dick was 11.

He attended Pontiac High School, where he met Norma Jean Hoyt, and they married while undergraduates at Eastern Michigan University. Dick was admitted to the University of Michigan Medical School at the end of his third year and the young family moved to Ann Arbor. Dick decided to pursue cardiovascular surgery and returned to Michigan for six years of residency in adult and pediatric cardiovascular surgery. He described his career in surgery as the best job in the world.

The family moved to Rhode Island in 1965 where he entered private practice until 1987. In his new home state, he built his dream house on Narragansett Bay that has seen five decades
of family holidays, reunions and weddings and will remain a lodestar in all their lives.

Ever restless, in 1987 Dick and Norma decided to give up private practice. They moved to Germany where Dick became a Colonel in the US Army Medical Corps at Landstuhl Regional Medical Center in the Rhineland Pfalz. In 1990, Dick was sent to Saudi Arabia as the senior surgeon of the U.S. Army’s VII Corps 12th Evacuation Hospital. He retired from full-time duty at the VA in 2000.

Dick is survived by his wife, Norma, and his five children: Richard of Berkeley California (Letitia Volpp), Gail McConaghy of Atlanta, Georgia (Eric), Leslie Ahlborg of East Greenwich, Rhode Island (Lindsay), Steven of Arlington, Virginia (Audrey Sullivan) and Ann Becker of Amherst, Massachusetts (Klaus), as well as his nine grandchildren and four great-grandchildren. He is also survived by his younger siblings Walter and Violet. His older siblings Peter and Lillian predeceased him.

Donations in his memory may be made to Hope Health, 1085 North Main Street, Providence R.I. 02904 or online at https://www.hopehealthco.org/ways-to-give/memorial-giving/