

Idiopathic Normal Pressure Hydrocephalus – Neurosurgical Management of Dementia!

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IDIOPATHIC NORMAL PRESSURE HYDROCEPHALUS (iNPH) is a condition of disturbed cerebrospinal fluid (CSF) dynamics, of unknown cause, giving rise to ventricular enlargement with a normal intracranial pressure.¹ The phenomenology of iNPH is characterised by a slowly progressive impairment of gait and balance, cognitive deterioration, and urinary incontinence.² Treatment of iNPH is surgical, most often ventriculo-peritoneal shunts.³ Selection of patients for surgery is generally based on symptoms and signs, CT or MRI verified ventriculomegaly and most often the results of different CSF dynamic supplementary tests.

Patients at risk for developing iNPH is the aging population.⁴ As the population is aging due to a higher longevity in most of the developed but also developing countries, the prevalence of iNPH is very likely to increase. Also, elderly patients are looking for an improved quality of life, and are no longer willing to accept disabilities of ageing. iNPH is associated with many co-morbidities as a result of age-related conditions and other at-risk diseases, such as cerebrovascular disease and Alzheimer's disease.

A high rate of Alzheimer's disease (AD) pathology on cortical biopsy⁵ as well as subcortical white matter disease (SAE) on magnetic resonance imaging⁶ in patients with shunt-responsive iNPH suggests that iNPH, AD and SAE are interrelated and may share common pathophysiological mechanisms, e.g. an age-related stagnation of cerebrospinal fluid circulation.⁷

This was the background for a prospective clinical study carried out in Europe from 2004 to 2009, involving 12 study centers. In the European idiopathic NPH trial both "typical" and "questionable" NPH (the latter presenting with co-morbidity) candidates were included and shunted solely based on clinical and radiological grounds. CSF dynamics (TAP-TEST, Rout and compliance measurements) were performed in every patient, however, patients were shunted

irrespective of the CSF dynamic test results, and three and 12 months outcome of shunting was measured using pre- and postoperative measurement of motor and cognitive test batteries.

Among the study aims, one important question was whether the outcome of shunted patients with NPH is affected by the presence of dementia. The important cut-off separating "typical" from "questionable" iNPH patients was the MMSE score. Patients classified as "typical" had to show a mild to moderate cognitive impairment (MMSE scores greater than or equal to 21) with onset together with or after the gait disturbance, and including impaired wakefulness, slowness, and memory deficits, whereas patients presenting other (aphasia, apraxia or agnosia) or more severe cognitive deficits (MMSE scores less than 21) including an onset prior to the gait disturbance were classified as "questionable". Single cortical infarcts, moderate cortical atrophy and moderate to severe subcortical white matter disease were the radiological (MRI) criteria for "questionable" iNPH.

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142 patients were included in the final analysis, and one year outcome post shunting was assessed with the **modified Rankin Scale (mRs)** and a comprehensive iNPH scale based on motor and cognitive test batteries. Fifty-five patients were classified as Questionable; 28 had MMSE scores below 21 and 27 patients had either

a non-typical gait or MR changes with atrophy, cortical infarcts or moderate to severe white matter changes.

84% of iNPH patients diagnosed and referred for shunt surgery, based on clinical and MRI findings, were improved 12 months after surgery; measured by the iNPH scale. Of note is that, at one year, there was a two-fold increase of patients performing normally in the various cognitive domains tested, e.g., Stroop Test and **Rey Auditory Verbal Learning Test (RAVLT)**. The corresponding improvement rate measured by the mRs was 69%. 37% were improved by one step, 25% by two steps and 7% by three steps. The proportion of patients able to live independently (scores zero to two on the mRs) increased from 53% before surgery to 82% 12 months after shunt treatment.

The most important finding was that patients with "questionable" iNPH did not differ from patients with "typical" iNPH in regard to improvement in iNPH scale total score or the one year outcome in the modified Rankin Scale.

The European iNPH study results indicate that co-morbidity of dementia is not a factor influencing the outcome of shunting. Shunt operation should be recommended to patients presenting with iNPH symptoms and signs and compatible MRI/CT changes, and evidence of co-morbidity of dementia should not be an exclusion criterion for shunt treatment.

Whether shunt treatment is beneficial in iNPH patients presenting with co-existing AD or cerebrovascular disease, as suggested by the results of the European trial, needs to be further confirmed in the framework of a controlled prospective trial randomising possible iNPH with co-morbidity to shunt vs. no shunt treatment, and comparison of functional outcomes within a one year period.

This requires both infra-structure provided by focussed centres allowing an inter- and cross-disciplinary disease approaches and management. In the multi-

disciplinary NPH Center associated with the Memory Disorder Program at Butler Hospital, Providence, RI (Stephen Sallo-way, MD and Paul Malloy, PhD) iNPH patients with and without co-morbidity of dementia are currently included in a research protocol. The aim is to identify markers and clinical diagnostic criteria relevant and important to the co-morbidity in iNPH. This should allow better characterization of iNPH with co-morbidities, to establish and provide standardized criteria for the identification of this vulnerable patient population to prepare for a randomised controlled trial.

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Disclosure of Financial Interests

Petra M. Klinge, MD, PhD, is a Consultant for Codman and Johnson & Johnson.

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