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Challenges in diagnosing normal pressure hydrocephalus: Evaluation of the diagnostic guidelines

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ABSTRACT

Purpose: To evaluate the present diagnostic guidelines of idiopathic normal pressure hydrocephalus (iNPH) in a sample from the general population.

Methods: A total of 168 individuals (93 females, 75 males), mean age 75 years (range 66–92) with and without symptoms of iNPH underwent a CT-scan of the brain, a neurological examination with assessment of the triad symptoms, i.e. gait disturbances, memory impairment and urgency incontinence. The participants were then diagnosed as "unlikely", "possible" and "probable" iNPH according to the American-European and the Japanese guidelines, respectively. Separately, a senior consultant in neurology diagnosed each patient based on the overall clinical picture.

Results: Obtaining a diagnosis of "probable iNPH" was three times more likely according to the American-European guidelines (n = 35) compared to the Japanese guidelines (n = 11) or the neurologist (n = 11). The concordance was highest (Kappa = 0.69) between the Japanese guidelines and the neurologist.

Conclusions: Considerable discrepancies were found when diagnosing iNPH according to two international guidelines and a neurologist, respectively. The Japanese guidelines, which include a minimum of two triad symptoms, were most concordant with the neurologist. As a step towards widely accepted, standardized diagnostic criteria, we suggest a revision of the current guidelines, preferably into one common diagnostic system.

1. Background

Idiopathic normal pressure hydrocephalus (iNPH) is a syndrome with gait disturbance, cognitive impairment and urinary symptoms that may resemble other disorders among elderly such as Parkinson's and Alzheimer's disease but have a characteristic neuroradiological picture [1,2]. The reported prevalence of iNPH varies from 0.5% to 2.9% in the elderly population [3] It is essential to identify patients with iNPH as 70–80% improve by ventricular shunting [4]. A recent study shows improvements in quality-adjusted life years and general cost effectiveness [5].

INPH still lacks widely accepted, standardized diagnostic criteria. Two independent committees of experts have come up with separate diagnostic guidelines with the aim to attain a more accurate and coherent way of diagnosing the disease [1,6].

A recent review article highlighted the design heterogeneity and use of separate diagnostic criteria among published epidemiological studies on iNPH [3]. Furthermore different scales have been used for measuring the severity of symptoms, ranging from visual inspection of gait patterns to more objective measurements of gait speed and number of steps [7,8]. Current guidelines are based upon assessments of clinical symptoms, however which tests that should be used as well as the cut-off limits between normal and impaired function have not yet been specified. Investigations of Cerebrospinal fluid dynamics are often performed as supplemental tests in diagnosing iNPH, however the value has been questioned [9,10].

The lack of a golden standard for the diagnosis of iNPH is problematic both in clinical practice and epidemiological research, therefore this study aimed to evaluate the diagnostic guidelines for iNPH in a sample from the general population. Specific aims were to find out the concordance between iNPH diagnoses according to the two diagnostic guidelines [1,6] and a neurologist, and explore the relation between the diagnoses and the degree of disability.

2. Material and method

2.1. Study population

This study is part of an ongoing population-based prospective study

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Table 1
Diagnostic criteria according to two separate international guidelines.

A. American-European guidelines [1]

	Probable[a]	Possible	Unlikely
Clinical features:	Gait/balance disturbance and at least one of the following: a) Cognitive impairment b) Urinary incontinence/urgency	Symptoms of either: a) Incontinence and/or cognitive impairment in the absence of gait/balance disturbance b) Gait disturbance alone	No component in the clinical triad or symptoms explained by other causes
Brain imaging	Ventriculomegaly (EI > 0.3) and at least one of the following: a) Narrow callosal angle b) Enlargement of the temporal horns c) Periventricular signal changes not attributable to ischemic changes or demyelination	Ventriculomegaly (EI > 0.3)	No evidence of ventriculomegaly

B. Japanese guidelines [6]

	Possible with MRI support	Possible	Unlikely
Clinical features	At least two of the clinical triad: Gait disturbance, cognitive impairment and urinary incontinence	At least two of the clinical triad: Gait disturbance, cognitive impairment and urinary incontinence	None of this
Brain imaging	Ventriculomegaly (EI > 0.3) and the following: a) Narrowing of the sulci over the high convexity/DESH [21]	Ventriculomegaly (EI > 0.3)	No evidence of ventriculomegaly

EI = Evans Index, DESH = Disproportionately enlarged subarachnoid space hydrocephalus.
[a] Not including the criteria ICP ≤ 20.

aimed to establish the prevalence of iNPH among the elderly. Using the Swedish population register to obtain participants, 1000 randomized individuals over the age of 65 living in the region of Jämtland Härjedalen (total of 28.000) were asked to participate in the study and answer a simple symptom questionnaire. A total of 673 individuals completed the questionnaire. Based on the questionnaire replies, a subgroup was selected for further examination at the neurological department at Östersund's Hospital between August 2014 and October 2015. The inclusion criteria for further clinical evaluation were a mandatory gait or balance impairment in addition to at least one more symptom. A total of 166 individuals met the inclusion criteria, 117 of these completed the study. Of the remaining 49, 27 withdrew or had incomplete testing, 20 were excluded because of severe neurological disorders such as hemiparesis after stroke, severe MS, brain tumor or Parkinson disease, diagnosed by neurologist and without ventriculomegaly. Two deceased before further investigations. A randomly selected group consisting of 51 people who reported less than two symptoms on the questionnaire, including 5 with an invalid combination of two symptoms, underwent the same tests giving a final study population of 168 individuals.

The ethical committee at Umeå University approved the study in 2014 (Dnr 2014/180-31).

2.2. Clinical and radiological examination

All study participants underwent computed tomography (CT) of the brain, neuropsychological and neurological examination. The neuropsychological assessment included Ray auditory verbal learning test (RAVLT), Grooved pegboard test, Swedish Stroop test and the Mini Mental state examination (MMSE) [11–14]. The clinical examination comprised Romberg's test, 10-metre walking test and evaluation of balance and gate with ordinal scales [12,15,16]. Urinary symptoms were rated by self-report with the Continence Scale [12]. The radiological features assessed were Evans index, callosal angle, size of temporal horns, periventricular hypodensites and DESH (Disproportionately enlarged subarachnoid space hydrocephalus) [17–21] Cerebrospinal fluid measurements were not performed.

The radiological and clinical evaluations were blinded i.e. those performing the clinical evaluations did not have access to the results of the CT scans and vice versa. The results from the clinical tests were graded according to a syndrome specific iNPH scale which consists of four independent domains; gait, balance, continence and neuropsychology with scores ranging from 0 to 100. A lower score corresponds to more symptoms [12].

A senior consultant in neurology (KL) with many years of experience of iNPH made a clinical diagnosis based on an overall assessment of radiology and symptoms, independent of any guidelines. In contrast, to avoid subjective use of the international guidelines (Table 1), fulfilments of each criterion were based strictly on the results of the clinical measurements with predefined cut-off limits between normal and impaired function. The cut-off levels for the radiological markers callosal angle (< 90°) and Evans index (> 0.30) were based on the literature [17,22] Cut-off levels for clinical symptoms were determined by optimizing sensitivity and specificity with the neurologist's diagnosis serving as the gold standard. For example, a MMSE value of < 28 was defined as pathological (Fig. 1). The corresponding cut-off level for the median size of the temporal horns was ≥ 4 mm and the cut-off scores

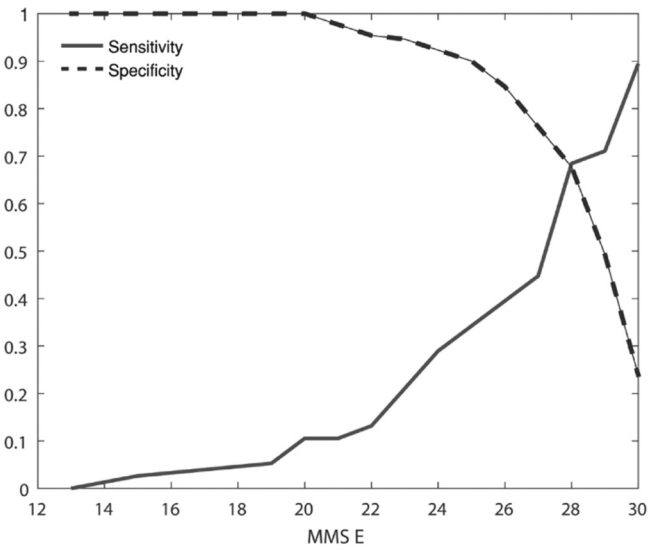

Fig. 1. Sensitivity and specificity for different MMSE values.