

Original Article

The Eastern Quebec Study on Idiopathic Normal Pressure Hydrocephalus: Patient Characteristics and Demographic Insights

Florence Belzile-Marsolais^{1,2} , Sophie Chantal³, Adéline Nolin^{1,2} , Yannick Nadeau², Louis Verret^{2,4} and Carol Hudon^{1,5}

¹École de psychologie, Faculté des sciences sociales, Université Laval, Québec (QC), Canada, ²Clinique Interdisciplinaire de Mémoire, CHU de Québec-Université Laval, Québec (QC), Canada, ³Département de réadaptation, Hôpital de l'Enfant-Jésus, CHU de Québec-Université Laval, Québec (QC), Canada, ⁴Département de médecine, Faculté de Médecine, Université Laval, Québec (QC), Canada and ⁵Centre de recherche VITAM, Centre Intégré Universitaire de Santé et de Services Sociaux de la Capitale-Nationale, Québec (QC), Canada

ABSTRACT: Background: Idiopathic normal pressure hydrocephalus (iNPH) is characterized by gait disturbances, cognitive impairment and urinary dysfunction. Early diagnosis is essential to ensure timely shunt treatment. However, patient identification remains challenging due to limited studies, mostly from Asia and Europe, which restrict generalizability to other geographic areas. Moreover, demographic factors (age, sex, education) influence cognitive and gait performance in other neurological conditions, but their impact on iNPH remains unclear. This study aimed to characterize the demographic, vascular, cognitive and gait profiles of iNPH patients in Eastern Quebec (Canada) and determine how demographic factors influence performance outcomes. Methods: A retrospective chart review was conducted on 175 patients diagnosed with probable iNPH at a specialized neurology center in Eastern Quebec. Demographic data, vascular risk factors and cognitive and gait outcomes were extracted from medical records. Descriptive statistics were used to characterize the sample, and multiple linear regressions assessed the effect of demographic factors on performance outcomes. Results: The cohort had a mean age of 73.9 years and a mean education level of 11.9 years. Age and education significantly predicted over half of the cognitive test results, while age was the only significant predictor of gait. Hypertension (58%) and hyperlipidemia (47%) were more prevalent than diabetes (26%), differing from previous studies where diabetes was the second most reported vascular risk factor after hypertension. Conclusions: Clinical heterogeneity characterizes iNPH patients in Eastern Quebec. Differences in the prevalence of vascular risk factors compared to previous studies may reflect geographic variability in the clinical presentation of this condition.

RÉSUMÉ: Étude de l'Est du Québec portant sur l'hydrocéphalie à pression normale idiopathique: caractéristiques des patients et aperçu démographique. Contexte : L'hydrocéphalie à pression normale idiopathique (HPNI) se caractérise par des troubles de la démarche (gait), des troubles cognitifs et un dysfonctionnement urinaire. Un diagnostic précoce est essentiel pour assurer un traitement par dérivation dans un délai convenable. Cependant, l'identification des patients reste difficile en raison du nombre limité d'études, principalement en Asie et en Europe, ce qui limite les possibilités de généralisation à d'autres zones géographiques. De plus, les facteurs démographiques (âge, sexe, éducation) influencent également les performances liées à la cognition et à la démarche dans le cas d'autres pathologies neurologiques, mais leur impact sur l'HPNI n'est pas clair. Cette étude visait donc à caractériser les profils démographiques, vasculaires, mais aussi ceux liés à la cognition et à la démarche, dans le cas de patients de l'Est du Québec (Canada) atteints d'HPNI et à déterminer comment les facteurs démographiques influencent les résultats à des tests. Méthodes: Une étude rétrospective des dossiers a été menée sur 175 patients diagnostiqués avec une HPNI probable dans un centre de neurologie spécialisé de l'Est du Québec. Les données démographiques, les facteurs de risque vasculaire et les résultats en matière de cognition et de démarche ont été extraits des dossiers médicaux. Des statistiques descriptives ont été utilisées pour caractériser l'échantillon, tandis que des régressions linéaires multiples ont évalué l'effet des facteurs démographiques sur les résultats en matière de performance. Résultats: Notre cohorte avait un âge moyen de 73,9 ans et un niveau moyen d'éducation de 11,9 ans. L'âge et le niveau d'éducation ont permis de prédire de manière significative plus de la moitié des résultats à des tests cognitifs, alors que l'âge était le seul facteur prédictif significatif de la démarche. L'hypertension (58 %) et l'hyperlipidémie (47 %) étaient plus fréquentes que le diabète (26 %), ce qui diffère des études précédentes dans lesquelles le diabète était le deuxième facteur de risque vasculaire le plus signalé après l'hypertension. Conclusion: L'hétérogénéité clinique caractérise les patients de l'Est du Québec atteints d'HPNI. Les différences dans la prévalence des facteurs de risque vasculaire par rapport aux études antérieures peuvent refléter la variabilité géographique de la présentation clinique de cette maladie.

Keywords: aged; cognition; dementia; gait; normal pressure hydrocephalus

(Received 25 March 2025; final revisions submitted 3 July 2025; date of acceptance 6 July 2025)

Corresponding author: Florence Belzile-Marsolais; Email: florence.belzile-marsolais.1@ulaval.ca

Cite this article: Belzile-Marsolais F, Chantal S, Nolin A, Nadeau Y, Verret L, and Hudon C. The Eastern Quebec Study on Idiopathic Normal Pressure Hydrocephalus: Patient Characteristics and Demographic Insights. The Canadian Journal of Neurological Sciences, https://doi.org/10.1017/cjn.2025.10363

© The Author(s), 2025. Published by Cambridge University Press on behalf of Canadian Neurological Sciences Federation. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted re-use, distribution and reproduction, provided the original article is properly cited.

Highlights

- Clinical presentation of idiopathic normal pressure hydrocephalus may vary across geographic areas.
- Hypertension and hyperlipidemia were the most prevalent vascular risk factors, differing from previous studies where diabetes was the second most common.
- Age and education significantly predicted cognitive outcomes, while age was the only predictor of gait performance.

Introduction

Idiopathic normal pressure hydrocephalus (iNPH) is a condition that typically occurs in later life without an identifiable cause. It is characterized by a triad of progressive symptoms: gait disturbances, urinary dysfunction and cognitive impairment. These manifestations are associated with ventriculomegaly and normal cerebrospinal fluid (CSF) pressure. Due to its nonspecific symptoms, iNPH is often misdiagnosed. Early detection is critical, as timely intervention can lead to clinical improvement in up to 80% of patients, whereas failure to treat leads to progressive symptom exacerbation and irreversible loss of autonomy. Therefore, improving diagnostic accuracy is essential to optimize patient outcomes.

Vascular mechanisms are considered a key factor in the development of iNPH, with hypertension (65%) and diabetes (25%) being the most prevalent and well-studied risk factors.⁷ Other vascular risk factors, such as hyperlipidemia, overweight, smoking and coronary heart disease, have been investigated but remain less well documented, which may explain inconsistencies in their reported association with iNPH.7-11 Differences in clinical versus standardized diagnostic guidelines (e.g., American-European² or Japanese¹) further complicate study comparisons. In addition, most studies have focused on populations in Asia and Europe, raising concerns about the geographic generalizability of the findings. Notably, a study conducted in Hawaii found no significant association between vascular risk factors and iNPH in that region, suggesting that regional differences may influence the relationship. 12 These observations underscore the need for further research in other geographic areas to determine the generalizability of current findings. To date, no studies have investigated iNPH in the province of Quebec, Canada.

Moreover, a comprehensive evaluation of cognitive and gait impairments is essential for accurate iNPH identification. Cognitive assessments are often limited to a single screening tool such as the Montreal Cognitive Assessment (MoCA)¹³ or the Mini-Mental State Examination, 14 even though detailed neuropsychological testing is increasingly advocated. 1,15,16 Priority needs to be given to fronto-subcortical deficits, including executive function, psychomotor speed, attention and working memory. 1,16-20 Tests such as Coding and Symbol Search subtests from the WAIS-III,²¹ Grooved Pegboard,^{22,23} Stroop²³ and verbal fluency^{16,20,24} tasks are recommended.¹ Similarly, while gait and balance disturbances are traditionally assessed using grading scales based on clinician observations, 25 objective measures such as the Timed Up and Go test (TUG), 26-28 10-meter walk test (10MWT)^{28,29} and Berg Balance Scale (BBS) ^{30,31} are strongly recommended. Although test batteries have been proposed for iNPH, 16,20,24,32 their sensitivity remains limited by reliance on raw scores that do not account for individual demographic factors.

Demographic factors such as age, sex, and education significantly influence neuropsychological, ^{33–35} and physiotherapy^{36,37} outcomes.

Higher education and younger age are associated with better initial performance and more pronounced practice effects in cognitive testing, ^{38,39} particularly in cognitively intact individuals. ^{40–43} In Alzheimer's patients, for example, the impact of demographic factors seems to disappear. ^{44–46} Moreover, a study on the TUG test indicates that age, sex and cognitive status significantly affect gait performance in older adults. Among individuals with mild cognitive impairment, women and older participants exhibit longer TUG completion times compared to men across the majority of age groups. ⁴⁷ Although these demographic influences are established in other conditions, their impact on cognitive and gait performance in iNPH remains underexplored. This gap is particularly critical given the need to repeat tests, such as the CSF tap test, to predict treatment response.

Given the geographic variability observed in some aspects of iNPH risk factors, it is essential to document the demographic, vascular, cognitive and gait/balance profiles of iNPH patients across diverse geographic areas. The documentation of such profiles would enhance screening accuracy and facilitate the development of more tailored protocols to predict treatment response, especially in geographic areas such as Quebec, where iNPH remains under-investigated. Hence, a retrospective chart review study was conducted at the Centre Hospitalier Universitaire de Québec - Hôpital de l'Enfant-Jésus (CHU-HEJ). The specialized Department of Neurological Sciences at CHU-HEJ is recognized as a large neurological center in Canada and serves as the reference clinic of neurology in Eastern Quebec. Since 2010, a standardized assessment battery has been implemented at CHU-HEJ for iNPH patients, targeting fronto-subcortical deficit and gait and balance tests. The primary objective is to provide a comprehensive description of the demographic, vascular, cognitive and gait/ balance profiles of patients diagnosed with probable iNPH in Eastern Quebec, in accordance with the most recent guidelines established by the Japanese NPH Society.1 Additionally, a secondary exploratory objective is to determine how demographic factors (age, sex, education) influence cognitive and gait performance in iNPH patients.

Methods

Study design

A retrospective medical chart review was conducted on data from 175 patients with probable iNPH between January 2010 and May 2022 at CHU-HEJ. The 2021 Japanese NPH Society diagnostic criteria were applied retrospectively to the entire cohort.¹ All patients underwent both MRI and a standardized CSF tap test. The presence of radiological signs consistent with probable iNPH was demonstrated in all 175 patients, including ventriculomegaly (Evans' index ≥ 0.30) and disproportionately enlarged subarachnoid-space hydrocephalus. Following the CSF tap test, 119 patients were referred for shunt surgery based on clinically significant improvement, while 56 were not referred due to insufficient response. Of the patients referred, 114 patients underwent shunt surgery (5 patients declined surgery). Postoperative follow-up data were available for 94 of these patients, of whom 85 (90.4 %) met the criteria for definite iNPH based on clinical improvement. In the present study, the analysis was limited to baseline data from the 175 patients with probable iNPH. The post-shunt outcomes are reported exclusively for the purpose of documenting the final diagnostic classification.

Inclusion criteria included a diagnosis of probable iNPH, native French-speaking (since French is the most widely spoken language and the official language of Quebec) and completion of the

protocol at CHU-HEJ. Patients with known risk factors for the development of secondary hydrocephalus (subarachnoid hemorrhage or meningitis) or congenital NPH were excluded. The information collected was double-entered, and the two entries were compared for quality assurance purposes. The extracted data were anonymized for analysis. The study was conducted with the ethical approval of the *Comité d'éthique de la recherche du Centre Hospitalier Universitaire de Québec - Université Laval* (Project #2021-5509).

Patients' demographic and vascular risk factors

Age, biological sex and number of years of formal education were obtained from the patients' medical records on their first day of admission. To assess vascular risk factors, history of hypertension, diabetes mellitus, hyperlipidemia, stroke or transient ischemic attack, coronary artery disease, smoking and alcohol high-risk consumption were noted. A history of hypertension or hyperlipidemia was defined as a previous (or concomitant) diagnosis (or use of antihypertensive medication or statins); diabetes mellitus as a concomitant diagnosis; stroke or transient ischemic attack as a previous diagnosis of ischemic or hemorrhagic stroke or transient ischemic attack; and coronary artery disease as a concomitant diagnosis of myocardial infarction or angina pectoris. Smoking and alcohol consumption were assessed using data from interviews and clinical examinations. Smoking was defined as past or current cigarette smoking. Alcohol consumption was defined as current high-risk consumption, based on the Canadian Low-Risk Alcohol Drinking Guidelines.⁴⁸

Neuropsychological assessment

Neuropsychological assessment focused on cognitive domains corresponding to evidence-based deficits in patients with iNPH. 16,20,49-51 The assessment included a detailed evaluation of psychomotor speed, information processing speed, attention, short-term and working memory and executive functions. The administered tests were as follows: MoCA, 13 Grooved Pegboard test, 35,52 Delis-Kaplan Executive Function System (Trail Making Test conditions 1 to 5, Color-Word Interference [color naming, word reading and inhibition]),53 alphabetic verbal fluency (F-A-S or T-N-P) and categorical verbal fluency (animals), 34,53 Weschler Adult Intelligence Scale IV (Symbol Search, Coding, Digit Span forward and backward)²¹ and Neuropsychological Assessment Battery (Number and Letters subtests Part A).⁵⁴ Eighteen neuropsychological variables (scores) were selected for analysis. The tests were administered by qualified neuropsychologists according to standardized instructions for each test, except where noted. The 18 variables retained and the modifications made to the administration are presented in Table 1.

Gait/balance assessment

Gait and balance tests were selected to assess evidence-based gait (10MWT – Normal Pace, ⁵⁵ 10MWT – Dual-Task⁵⁶) and balance (TUG, ⁵⁷ BBS⁵⁸) disturbances in patients with iNPH. ^{4,29,31,56} Four gait/balance variables (scores) were selected for analysis. The tests were performed by qualified physiotherapists according to standardized instructions for each test, except where noted. The four variables retained and the modifications made to the administration are presented in Table 1.

Statistical analyses

To characterize the demographic, vascular, cognitive, and gait/balance profiles of probable iNPH patients who underwent the protocol, descriptive statistics were performed using IBM SPSS Statistics 29.0 software. Certain data were unavailable due to inherent constraints of the clinical setting, where some assessments were not systematically conducted due to factors such as limited time. Therefore, the number of data collected for each variable is indicated in each table.

To assess whether each demographic factor had an independent effect on cognitive and gait/balance test results, multiple linear regressions (standard) were performed for each cognitive and physical outcome. Analyses were performed using SAS 9.4 software, with an alpha threshold of 5 %. For each model, assumptions of normality and homogeneity of residual variance were tested.

Results

Demographics and frequency of vascular risk factors

Table 2 presents the patients' demographics and the frequency of vascular risk factors in the sample. The cohort had a slight male predominance (53 %). The age of patients ranged between 60 and 90 years, and the range of years of formal education varied between 3 and 23 years. Hypertension and hyperlipidemia were the most prevalent vascular risk factors.

Cognitive and gait/balance results

Table 3 presents the patients' cognitive profile, and Table 4 shows their gait/balance characteristics. The patients' results across all measures of cognition and gait/balance showed substantial variability, as indicated by the large standard deviations and ranges. A total of 132 patients out of 152 scored less than the MoCA cut-off of 26/30 (scores of 25 or below indicate cognitive impairment¹³).

Demographic factors predicting cognitive and gait/balance results

Table 5 and Table 6 present the demographic factors that predicted cognitive and gait/balance results, respectively. Age and education (alone or together) predicted two-thirds of the cognitive test results, while biological sex did not predict any. Regarding gait/balance tests, only age was found to be a significant predictor of performance.

Discussion

The objective of this study was to provide a description of the demographic, vascular, cognitive and gait/balance profiles of patients diagnosed with probable iNPH in Eastern Quebec. The sample consisted of 53% men, with a mean age of 73.9 years and mean education level of 11.9 years. Hypertension was the most common vascular risk factor, followed by hyperlipidemia. The cognitive and gait/balance assessments exhibited substantial heterogeneity, as evidenced by large standard deviations and wide score ranges, reflecting marked inter-individual variability in the severity of impairment among iNPH patients. A secondary objective was to examine demographic predictors of cognitive and gait/balance outcomes. Biological sex had no significant impact, while age predicted most outcomes. Education influenced cognitive performance but not gait/balance measures.

Table 1. Neuropsychological and gait/balance assessments: tests, modifications to instructions and variables retained for analysis

| Tests | Modifications to the original instruction | Variables |
|---|--|---|
| Neuropsychological assessment | | |
| Montreal Cognitive Assessment | - | Score out of 30. |
| Grooved Pegboard | Two trials administered for each hand (dominant and nondominant). | Fastest completion time in seconds for each hand. |
| Trail Making Test, conditions 1 to 5 | - | Time in seconds (for each condition). |
| Color-Word Interference test, conditions 1 to 3 | - | Time in seconds (for each condition). |
| Alphabetic verbal fluency | Letters F-A-S or T-N-P used. | Total number of correct responses for the three alphabetical letters. |
| Categorical verbal fluency | - | Total number of correct responses. |
| Symbol Search | - | Number of correctly completed lines minus the number of incorrectly completed lines. |
| Coding | - | Number of correct symbols that were copied. |
| Digit span forward | - | Sum of the points obtained for each correctly repeated series. |
| Digit span backward | | Sum of the points obtained for each correctly repeated series. |
| Number and letters – Part A | - | Result of the efficiency formula that includes the ratio of error count to completion time. |
| Gait/balance assessment | | |
| Timed Up and Go | - | Completion time in seconds. |
| 10MWT - Normal Pace | Patients were required to complete a practice trial, followed by two attempts. | Average walking speed of the two attempts in meters per second. |
| 10MWT – Dual-Task | Patients were required to complete a practice trial, followed by two attempts. | Average walking speed of the two attempts in meters per second. |
| Berg Balance Scale | - | Score out of 56. |

Note: 10MWT = 10-meter walk test.

Table 2. Demographics and frequency of comorbid vascular risk factors of probable iNPH patients

| probable INFT patients | |
|-------------------------------|----------------------|
| Clinical variables | Mean ± SD or n/N (%) |
| Age (years) | 73.9 ± 6.5 |
| Education (years) | 11.9 ± 3.9 |
| Biological sex (female) | 82/175 (47%) |
| Hypertension | 101/175 (58%) |
| Hyperlipidemia | 83/175 (47%) |
| Smoking (current/former) | 50/142 (35%) |
| Coronary artery disease | 55/175 (31%) |
| Diabetes mellitus | 46/175 (26%) |
| Alcohol high-risk consumption | 28/146 (19%) |
| Stroke/TIA | 14/175 (8%) |

Note: Data are presented as n/N (%); n= number of persons with corresponding risk factor; N= number of persons from the total sample who were examined for the corresponding risk factors. iNPH = idiopathic normal pressure hydrocephalus; SD = standard deviation; TIA = transient ischemic attack.

The demographic, vascular, cognitive and gait/balance profiles of the patients with probable iNPH in this study were generally in line with those reported in the literature, with a few exceptions. In the sample, males constituted 53% of the patients compared to 47%

 Table 3. Cognitive results of patients with probable iNPH

| Cognitive tests | n | M(SD) | Med | Range [min; max] |
|---------------------------------------|-----|---------------|--------|---------------------|
| MoCA (out of 30) | 152 | 21.07(3.89) | 22.00 | [9; 29] |
| Grooved Pegboard Test | | | | |
| Dominant hand, s | 170 | 130.64(53.36) | 112.00 | [66.00; 384.00] |
| Non-dominant hand, s | 162 | 153.84(69.09) | 133.00 | [75.00; 437.00] |
| D-KEFS TMT | | | | |
| Condition 1, s | 175 | 38.16(14.52) | 34.00 | [14.00; 95.00] |
| Condition 2, s | 173 | 79.19(33.28) | 69.00 | [21.00; 150.00] |
| Condition 3, s | 167 | 92.29(38.70) | 79.00 | [17.00; 150.00] |
| Condition 4, s | 148 | 194.98(52.37) | 232.50 | [62.00; 240.00] |
| Condition 5, s | 172 | 54.88(27.25) | 47.00 | [18.00; 150.00] |
| D-KEFS Color-Word Interference | | | | |
| Color, s | 138 | 43.06(11.40) | 41.00 | [25.00; 90.00] |
| Word, s | 141 | 30.52(10.28) | 28.00 | [18.00; 87.00] |
| Inhibition, s | 128 | 112.59(36.09) | 108.00 | [54.00; 180.00] |
| Verbal Fluency Test | | | | |
| Alphabetic (F-A-S or T-N-P), <i>n</i> | 159 | 21.11(8.97) | 21.00 | [4; 66] |
| | | | | (Continued) |

(Continued)

Table 3. Cognitive results of patients with probable iNPH (Continued)

| Cognitive tests | n | M(SD) | Med | Range [min; max] |
|----------------------------------|-----|--------------|-------|---------------------|
| Semantic (animals), n | 124 | 10.86(4.23) | 11.00 | [1; 21] |
| WAIS-IV | | | | |
| Symbol search, n | 149 | 14.75(6.64) | 14.00 | [0; 31] |
| Coding, n | 171 | 29.37(12.08) | 29.00 | [5; 66] |
| Forward digit span, n | 168 | 7.63(1.83) | 8.00 | [3; 12] |
| Backward digit span, n | 168 | 5.56(2.08) | 6.00 | [0; 10] |
| NAB Numbers and letters – Part A | | | | |
| Efficiency* | 174 | 57.85(16.23) | 54.95 | [11.02; 116.92] |

Note: iNPH = idiopathic normal pressure hydrocephalus; M = mean; SD = standard deviation; Med = median; MoCA = Montreal Cognitive Assessment; D-KEFS = Delis-Kaplan Executive Function System; TMT = Trail Making Test; WAIS-IV = Wechsler Adult Intelligence Scale-Fourth Edition; NAB = Neuropsychological Assessment Battery. *Efficiency is calculated with the formula ((236 - Numbers and letters Part A speed raw score). Numbers and letters Part A speed raw score).

Table 4. Gait/balance results of probable iNPH patients

| Gait or balance tests | n | M(SD) | Med | Range [min; max] |
|-----------------------|-----|--------------|-------|---------------------|
| 10MWT | | | | |
| Normal Pace (m/s) | 174 | 0.72(0.30) | 0.73 | [0.04; 1.78] |
| Dual-Task* (m/s) | 155 | 0.57(0.28) | 0.56 | [0.06; 1.34] |
| TUG, s | 173 | 23.18(15.17) | 19.39 | [9.77; 115.47] |
| BBS (out of 56) | 166 | 38.93(9.39) | 40.00 | [4; 56] |

Note: iNPH = idiopathic normal pressure hydrocephalus; M = mean; SD = standard deviation; Med = median; 10MWT = 10-meter walk test; TUG = Timed Up and Go test; BBS = Berg Balance Scale. * The occurrence of errors in the cognitive task (counting down in leaps of 3 from 100) was not considered.

females, representing only a modest male predominance. This contrasts with other studies that have reported a more pronounced overrepresentation of males. For instance, a recent Swedish prevalence study found that 2.1% of men had iNPH, compared to 0.96% of women, ⁵⁹ and a study in Hawaii reported that men are 1.96 times more likely to develop iNPH than women. ¹² Regardless of geographic location, these findings consistently indicate a higher risk for iNPH in men, suggesting that sex-related differences, such as the higher aqueductal CSF stroke volumes and average flow rates observed in men, ^{60,61} may provide valuable insights into the underlying pathophysiology. Although the degree of male predominance observed in our study was less marked, the overall trend remains present.

This study evidenced that hypertension was the most common vascular risk factor in patients with iNPH in Quebec, as observed in previous studies.^{7,8,62,63} Hypertension has been widely studied for its potential involvement in the pathogenesis of iNPH, with proposed mechanisms including arterial stiffening and increased pulse pressure, which may exert greater mechanical force on brain tissue and contribute to ventricular dilation, a phenomenon known as the Windkessel effect.^{10,64–69} In the literature, diabetes is the second most commonly reported vascular risk factor, with a prevalence of 25% in a recent meta-analysis.⁷ In this study, 26% of iNPH patients had diabetes. However, diabetes was not the second

most common vascular comorbidity in the current sample. Hyperlipidemia, smoking and coronary artery disease were more common than diabetes. These findings suggest that the prevalence of vascular risk factors differs accross geographic areas, which may influence their association with iNPH. It is also possible that risk factors beyond hypertension and diabetes have been less frequently studied, leading to an underestimation of their relevance in iNPH. Notably, previous studies have reported inconsistencies across different populations. For instance, while European and Asian cohorts typically show an association between vascular comorbidities and iNPH,^{7,64,70} a study conducted in Hawaii found no significant association.¹² Such discrepancies may reflect differences in genetic susceptibility, lifestyle or environmental exposures. Similarly, the higher prevalence of certain vascular risk factors in the present cohort may be influenced by populationspecific characteristics, such as socioeconomic status, gender and educational levels. 71,72 The role of these factors in iNPH remains underexplored. To clarify their contribution, future studies should compare vascular risk profiles in iNPH patients and matched controls within Quebec, where demographic and lifestyle factors may differ from those studied in European and Asian cohorts.

The significant heterogeneity observed in cognitive and gait/ balance profiles suggests substantial inter-individual variability in iNPH, which may reflect differences in disease stage. While the presence of the full triad (gait, cognitive, and urinary symptoms) is associated with more advanced stages of the disease, 1,5 there is currently no standardized framework for staging iNPH from early symptoms to severe impairment. Patients may be at different points along this continuum, ranging from subtle cognitive or gait/balance impairments to more pronounced dysfunction, contributing to the heterogeneity observed. This variability not only makes it challenging to identify iNPH patients based solely on baseline assessments but also likely reflects the complex clinical profiles and presence of comorbidities commonly seen in hospital-based cohorts referred to specialized neurological settings, as opposed to more narrowly selected research cohorts. This clinical complexity underscores the ecological validity of studying patients in real-world contexts and highlights the inherent challenges in diagnosing iNPH in such heterogeneous populations. Additionally, prior studies have reported similar variability in iNPH cohorts. 16,20,73 Future research should aim to stratify patients based on symptom severity and identify clinical or biomarker-based predictors of disease progression. Given the diagnostic challenges posed by this heterogeneity, post-CSF tap test improvement remains an important element to support the diagnosis and predict surgical outcomes.

The findings of this study indicate that demographic factors significantly influence cognitive and gait/balance performance in iNPH patients, particularly age and education level. In a cognitively healthy population, it is well established in both neuropsychology and physiotherapy that individual performance declines with advancing age.74-77 However, in the context of cognitive pathology, the influence of age appears to differ. For instance, one study found that while advancing age was associated with decreased performance on a balance test and the MoCA in cognitively healthy individuals, these associations were not observed in patients with Parkinson's disease.⁷⁸ Similar findings have been reported in individuals with advanced-stage Alzheimer's disease. 46 However, the present results support the hypothesis that age exerts an influence on performance in iNPH patients, particularly in attentional, processing speed, executive functioning, gait and balance tasks.

Table 5. Parameters estimate for variables predicting cognitive performances

| | | Female sex | | Age | | | Education | | |
|---|-------|------------|-------|-------|------|---------|-----------|------|---------|
| Effect | В | SE | p* | В | SE | p* | В | SE | p* |
| MoCA | -0.20 | 0.62 | 0.743 | -0.11 | 0.05 | 0.030 | 0.23 | 0.08 | 0.004 |
| Grooved Pegboard Test | | | | | | | | | |
| Dominant hand | 7.32 | 8.12 | 0.369 | 2.40 | 0.63 | < 0.001 | -0.48 | 1.05 | 0.644 |
| Non-dominant hand | -1.72 | 11.01 | 0.876 | 2.16 | 0.88 | 0.015 | -1.38 | 1.41 | 0.329 |
| D-KEFS TMT | | | | | | | | | |
| Condition 1 | -4.25 | 2.17 | 0.052 | 0.30 | 0.16 | 0.075 | -0.94 | 0.28 | 0.001 |
| Condition 2 | -2.04 | 4.97 | 0.681 | 1.19 | 0.38 | 0.002 | -1.78 | 0.64 | 0.006 |
| Condition 3 | -3.29 | 5.91 | 0.578 | 1.18 | 0.45 | 0.010 | -2.42 | 0.78 | 0.002 |
| Condition 4 | -0.64 | 8.75 | 0.942 | 1.58 | 0.67 | 0.019 | -3.15 | 1.17 | 0.008 |
| Condition 5 | 2.26 | 4.20 | 0.591 | 0.50 | 0.32 | 0.118 | -1.13 | 0.55 | 0.040 |
| D-KEFS Color-Word Interference | | | | | | | | | |
| Color | -2.54 | 1.95 | 0.196 | 0.39 | 0.16 | 0.017 | -0.15 | 0.25 | 0.559 |
| Word | -1.51 | 1.71 | 0.378 | 0.36 | 0.14 | 0.010 | -0.44 | 0.22 | 0.048 |
| Inhibition | 5.82 | 6.37 | 0.363 | 1.47 | 0.52 | 0.005 | -0.75 | 0.84 | 0.372 |
| Verbal Fluency Test | | | | | | | | | |
| Alphabetic (F-A-S or T-N-P) | 0.49 | 1.38 | 0.724 | -0.11 | 0.11 | 0.284 | 0.77 | 0.18 | < 0.001 |
| Semantic (animals) | -0.46 | 0.79 | 0.557 | -0.08 | 0.06 | 0.187 | 0.08 | 0.10 | 0.461 |
| WAIS-IV | | | | | | | | | |
| Symbol search | -0.01 | 1.07 | 0.989 | -0.22 | 0.09 | 0.012 | 0.38 | 0.14 | 0.007 |
| Coding | 0.40 | 1.77 | 0.821 | -0.44 | 0.13 | 0.001 | 0.87 | 0.23 | < 0.001 |
| Forward digit span | -0.09 | 0.28 | 0.749 | 0.00 | 0.02 | 0.922 | 0.12 | 0.04 | 0.001 |
| Backward digit span | -0.08 | 0.32 | 0.809 | -0.02 | 0.02 | 0.364 | 0.15 | 0.04 | < 0.001 |
| NAB Numbers and letters – Part A efficiency | 0.09 | 2.26 | 0.969 | -0.80 | 0.17 | < 0.001 | 1.29 | 0.29 | < 0.001 |

Note: B = parameter estimate; SE = standard error of the parameter estimate; MoCA = Montreal Cognitive Assessment; D-KEFS = Delis-Kaplan Executive Function System; TMT = Trail Making Test; WAIS-IV = Wechsler Adult Intelligence Scale-Fourth Edition; NAB = Neuropsychological Assessment Battery. * p < 0.05 are in bold.

Table 6. Parameters estimate for variables predicting gait/balance performances

| | Female sex | | | | Age | | | Education | | |
|-------------|------------|------|-------|-------|------|-------|-------|-----------|-------|--|
| Effect | В | SE | p* | В | SE | p* | В | SE | p* | |
| 10MWT | | | | | | | | | | |
| Normal Pace | -0.06 | 0.05 | 0.224 | -0.01 | 0.00 | 0.094 | 0.01 | 0.01 | 0.262 | |
| Dual-Task | -0.05 | 0.04 | 0.259 | -0.01 | 0.00 | 0.008 | 0.01 | 0.01 | 0.163 | |
| TUG | 4.02 | 2.31 | 0.084 | 0.47 | 0.18 | 0.008 | -0.35 | 0.30 | 0.237 | |
| BBS | -1.58 | 1.45 | 0.277 | -0.36 | 0.11 | 0.002 | 0.26 | 0.19 | 0.163 | |

Note: B = parameter estimate; SE = standard error of the parameter estimate; 10MWT = 10-meter walk test; TUG = Timed Up and Go test; BBS = Berg Balance Scale. * p < 0.05 are in bold.

Furthermore, education level was found to be associated with certain aspects of cognitive performance in iNPH patients. Higher education levels are known to enhance cognitive reserve and may delay the onset of cognitive decline.^{79–82} However, this protective effect appears to diminish as cognitive impairment progresses.⁸³ In the context of iNPH, cognitive deficits are rarely the first presenting symptoms of the triad.^{1,84} Thus, it is plausible that some iNPH patients, particularly those in the early stages of

cognitive decline, may continue to benefit from the protective effects of education. Additionally, higher education levels have been linked to a slower decline in executive functions.⁸⁵ Given that several studies have established a connection between executive function and gait and balance performance^{86–88} one might expect education to similarly influence motor abilities. The present study found an association between education level and executive functioning in iNPH, specifically on TMT condition 4 and

alphabetic verbal fluency tasks. However, no significant association was found between education level and gait or balance in iNPH patients. This contrasts with findings in other clinical populations, such as patients with Parkinson's disease, where lower education levels have been associated with both poorer executive functioning (as measured by the Trail Making Test Part B, p=0.018) and reduced balance (as measured by the BBS, p<0.001).⁸⁹ In summary, while education may modulate cognitive and motor interactions in some neurological conditions, its influence on gait and balance in iNPH remains ambiguous and warrants further investigation.

Interestingly, sex was not a significant predictor of cognitive or gait/balance outcomes, which contrasts with findings in non-iNPH older adults. For example, in cognitive testing, females have been reported to perform better than males on tasks assessing information processing speed, 90 such as Coding and Symbol Search subtests of the WAIS, 91 and psychomotor speed, such as the Grooved Pegboard test. 92 In the context of physiotherapy, the evidence is mixed. One study found no significant differences between males and females on the BBS, 93 whereas another reported that females had lower scores than males. 94 The absence of sexrelated differences in cognitive and gait/balance performance in iNPH patients observed in the present study may reflect the overriding impact of the disorder itself, which could mask the typical sex-based differences seen in healthy aging populations.

Overall, these findings support the notion that the impact of demographic factors differs in the iNPH population compared to other clinical populations and cognitively healthy individuals. Currently, the CSF tap test method is used to predict surgical response, with raw scores typically employed in the interpretation of outcomes. The results highlight the importance of thoroughly documenting demographic influences at baseline, as this foundational knowledge is essential for future research to evaluate their role in repeated assessments such as the CSF tap test. Understanding how demographic factors affect pre- and post-test performance could ultimately inform the integration of these factors into diagnostic and prognostic models, thereby refining assessment accuracy and supporting more individualized patient management.

Limitations

This study has limitations. The use of a hospital-based sample may have introduced a selection bias toward more severe cases, limiting the generalizability of the findings to the broader iNPH population. The retrospective design resulted in missing data, which may have affected the validity of some conclusions. Self-reported data on alcohol consumption and smoking may have been subject to recall bias. The neuropsychological protocol did not cover all cognitive domains, such as language (e.g., naming tasks), which could have supported differential diagnosis with other conditions, such as Alzheimer's disease. Additionally, the extraction of data from medical records may have been influenced by variability in clinical documentation practices, despite quality control procedures. Finally, while this study focused on the impact of demographic factors, other potential factors such as medication use, comorbidities and disease duration were not assessed and may have influenced performance outcomes. Future research with prospective designs and larger, more diverse cohorts is needed to address these limitations.

Conclusion

This study is the first to characterize the demographic, vascular, cognitive and gait/balance profiles of iNPH patients in Eastern Quebec. The findings demonstrate that age and education level significantly influence cognitive performance, while age is the sole significant predictor of gait and balance outcomes. In contrast, sex was not associated with any cognitive or gait outcomes, suggesting that the underlying pathology may override typical sex-related differences observed in the aging population. Documenting these demographic influences is necessary to better interpret pre- and post-CSF tap test changes and to improve the accuracy of treatment response assessments.

The substantial heterogeneity in cognitive and gait/balance profiles underscores notable inter-individual variability, likely reflecting differences in disease stage, and highlights the need to broaden assessment protocols. Incorporating additional cognitive tests, such as measures targeting functions not classically impaired in iNPH, could improve differential diagnosis or help identify comorbidities. Furthermore, the high prevalence of vascular risk factors, particularly hypertension and hyperlipidemia, underscores the need for closer monitoring and targeted management of these comorbidities in iNPH patients. Although the effect of vascular comorbidity on long-term outcomes after shunt surgery remains unclear, 11,95,96 it may be associated with more severe symptoms and a negative influence on prognosis. 18,97-99 Further studies with extended follow-up are needed to clarify the relationship between iNPH and vascular comorbidities. Finally, differences between this cohort and those reported in other geographic areas suggest that factors such as genetics or environment may contribute to the variability in iNPH clinical profiles. Larger prospective studies are needed to clarify these geographical variations and refine diagnostic and management strategies for diverse populations.

Acknowledgments. F.B-M. was supported by scholarships from the Canadian Institutes of Health Research (187549) and Fonds de Recherche du Québec (https://doi.org/10.69777/313551). This study was funded by the Normal Pressure Hydrocephalus Research Fund of the Clinique Interdisciplinaire de Mémoire at CHU-HEJ.

Author contribution. FBM, SC, LV and CH were involved in the conceptualization of the study. The methodology was developed by FBM, SC, YN, LV and CH. FBM and AN were responsible for project administration, as well as data collection. The formal analysis was conducted by FBM. SC, LV and CH provided supervision throughout the study. FBM wrote the original draft of the manuscript, and all authors contributed to the review and editing of the manuscript.

Funding statement. No targeted funding reported.

Competing interests. The authors have no potential conflicts of interest to disclose.

References

- 1. Nakajima M, Yamada S, Miyajima M, et al. Guidelines for management of idiopathic normal pressure hydrocephalus (Third edition): endorsed by the Japanese society of normal pressure hydrocephalus. *Neurol Med Chir* (*Tokyo*). 2021;61:63–97. doi: 10.2176/nmc.st.2020-0292.
- Relkin N, Marmarou A, Klinge P, Bergsneider M, Black PM. Diagnosing idiopathic normal-pressure hydrocephalus. *Neurosurgery*. 2005;57:S4–16. doi: 10.1227/01.neu.0000168185.29659.c5. discussion ii-v.

- Graff-Radford NR, Jones DT. Normal pressure hydrocephalus. Continuum (Minneap Minn). 2019;25:165–186. doi: 10.1212/con.0000000000000089.
- Wikkelsø C, Hellström P, Klinge PM, Tans JT. The European iNPH multicentre study on the predictive values of resistance to CSF outflow and the CSF tap test in patients with idiopathic normal pressure hydrocephalus. J Neurol Neurosurg Psychiatry. 2013;84:562–568. doi: 10.1136/jnnp-2012-303314
- Kiefer M, Unterberg A. The differential diagnosis and treatment of normalpressure hydrocephalus. *Dtsch Arztebl Int*. 2012;109:15–25. doi: 10.3238/ arztebl.2012.0015.
- Toma AK, Stapleton S, Papadopoulos MC, Kitchen ND, Watkins LD. Natural history of idiopathic normal-pressure hydrocephalus. *Neurosurg Rev.* 2011;34:433–439. doi: 10.1007/s10143-011-0316-7.
- Cai H, Yang F, Gao H, et al. Vascular risk factors for idiopathic normal pressure hydrocephalus: a systematic review and meta-analysis. Front Neurol. 2023;14:1220473. doi: 10.3389/fneur.2023.1220473.
- 8. Israelsson H, Carlberg B, Wikkelsö C, et al. Vascular risk factors in INPH: a prospective case-control study (the INPH-CRasH study). *Neurology*. 2017;88:577–585. doi: 10.1212/wnl.000000000003583.
- Krauss JK, Regel JP, Vach W, Droste DW, Borremans JJ, Mergner T. Vascular risk factors and arteriosclerotic disease in idiopathic normalpressure hydrocephalus of the elderly. Stroke. 1996;27:24–29. doi: 10.1161/ 01.STR.27.1.24.
- Jaraj D, Agerskov S, Rabiei K, et al. Vascular factors in suspected normal pressure hydrocephalus: a population-based study. *Neurology*. 2016;86:592– 599. doi: 10.1212/wnl.000000000002369.
- 11. Eklund SA, Israelsson H, Brunström M, Forsberg K, Malm J. 10-year mortality, causes of death and cardiovascular comorbidities in idiopathic normal pressure hydrocephalus. *J Neurol.* 2024;271:1311–1319. doi: 10. 1007/s00415-023-12067-5.
- Ghaffari-Rafi A, Gorenflo R, Hu H, Viereck J, Liow K. Role of psychiatric, cardiovascular, socioeconomic, and demographic risk factors on idiopathic normal pressure hydrocephalus: a retrospective case-control study. Clin Neurol Neurosurg. 2020;193:105836. doi: 10.1016/j.clineuro.2020.105836.
- Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc.* 2005;53:695–699. doi: 10.1111/j.1532-5415.2005.53221.x.
- 14. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12:189–198. doi: 10.1016/0022-3956(75)90026-6.
- 15. Saito M, Nishio Y, Kanno S, et al. Cognitive profile of idiopathic normal pressure hydrocephalus. *Dement Geriatr Cogn Dis Extra*. 2011;1:202–211. doi: 10.1159/000328924.
- Nimni M, Weiss P, Cohen C, Laviv Y. Neuropsychological assessments and cognitive profile mostly associated with shunt surgery in idiopathic normal pressure hydrocephalus patients: diagnostic and predictive parameters and practical implications. *Acta Neurochir (Wien)*. 2021;163:3373–3386. doi: 10. 1007/s00701-021-04976-z.
- Thomas G, McGirt MJ, Woodworth G, et al. Baseline neuropsychological profile and cognitive response to cerebrospinal fluid shunting for idiopathic normal pressure hydrocephalus. *Dement Geriatr Cogn Disord*. 2005;20:163– 168. doi: 10.1159/000087092.
- 18. Hellström P, Edsbagge M, Archer T, Tisell M, Tullberg M, Wikkelsø C. The neuropsychology of patients with clinically diagnosed idiopathic normal pressure hydrocephalus. *Neurosurgery*. 2007;61:1219–1226. doi: 10.1227/01.neu.0000306100.83882.81. discussion 1227–1218.
- Picascia M, Zangaglia R, Bernini S, Minafra B, Sinforiani E, Pacchetti C. A review of cognitive impairment and differential diagnosis in idiopathic normal pressure hydrocephalus. *Funct Neurol.* 2015;30:217–228. doi: 10. 11138/fneur/2015.30.4.217.
- Laidet M, Herrmann FR, Momjian S, Assal F, Allali G. Improvement in executive subfunctions following cerebrospinal fluid tap test identifies idiopathic normal pressure hydrocephalus from its mimics. *Eur J Neurol*. 2015;22:1533–1539. doi: 10.1111/ene.12779.
- Wechsler D. WAIS-IV: Wechsler Adult Intelligence Scale Fourth Edition (WAIS-IV). San Antonio (TX): Pearson; 2008.
- Klove DP. Grooved pegboard test. Lafayette, Indiana: Lafayette Instrument Company; 1963.

- Kamohara C, Nakajima M, Kawamura K, et al. Neuropsychological tests are useful for predicting comorbidities of idiopathic normal pressure hydrocephalus. *Acta Neurol Scand*. 2020;142:623–631. doi: 10.1111/ane.13306.
- 24. Allali G, Laidet M, Armand S, et al. A combined cognitive and gait quantification to identify normal pressure hydrocephalus from its mimics: the geneva's protocol. *Clin Neurol Neurosurg*. 2017;160:5–11. doi: 10.1016/j. clineuro.2017.06.001.
- Kubo Y, Kazui H, Yoshida T, et al. Validation of grading scale for evaluating symptoms of idiopathic normal-pressure hydrocephalus. *Dement Geriatr Cogn Disord*. 2008;25:37–45. doi: 10.1159/000111149.
- Mendes GAS, de Oliveira MF, Pinto FCG. The timed up and go test as a diagnostic criterion in normal pressure hydrocephalus. World Neurosurg. 2017;105:456–461. doi: 10.1016/j.wneu.2017.05.137.
- 27. Yamada S, Ishikawa M, Miyajima M, et al. Timed up and go test at tap test and shunt surgery in idiopathic normal pressure hydrocephalus. *Neurol Clin Pract*. 2017;7:98–108. doi: 10.1212/cpj.00000000000334.
- 28. Sundström N, Rydja J, Virhammar J, Kollén L, Lundin F, Tullberg M. The timed up and go test in idiopathic normal pressure hydrocephalus: a nationwide study of 1300 patients. *Fluids Barriers CNS*. 2022;19:4. doi: 10. 1186/s12987-021-00298-5.
- Chunyan L, Rongrong H, Youping W, et al. Gait characteristics and effects
 of the cerebrospinal fluid tap test in probable idiopathic normal pressure
 hydrocephalus. Clin Neurol Neurosurg. 2021;210:106952. doi: 10.1016/j.
 clineuro.2021.106952.
- Mori L, Collino F, Marzi A, et al. Useful outcome measures in INPH patients evaluation. Front Neurol. 2023;14:1201932. doi: 10.3389/fneur.2023.1201932.
- Gallagher R, Marquez J, Osmotherly P. Gait and balance measures can identify change from a cerebrospinal fluid tap test in idiopathic normal pressure hydrocephalus. *Arch Phys Med Rehabil*. 2018;99:2244–2250. doi: 10.1016/j.apmr.2018.03.018.
- 32. Roman A, Takkar P, Maiti T. Ten steps for NPH management: advancements in diagnosis and treatment of adult hydrocephalus. *Arq Bras Neurocir*. 2023;42:e200–e209. doi: 10.1055/s-0043-1774741.
- Larouche E, Tremblay MP, Potvin O, et al. Normative data for the Montreal Cognitive Assessment in middle-aged and elderly Quebec-French people. Arch Clin Neuropsychol. 2016;31:819–826. doi: 10.1093/arclin/acw076.
- 34. St-Hilaire A, Hudon C, Vallet GT, et al. Normative data for phonemic and semantic verbal fluency test in the adult French-quebec population and validation study in Alzheimers disease and depression. *Clin Neuropsychol.* 2016;30:1126–1150. doi: 10.1080/13854046.2016.1195014.
- Skogan AH, Oerbeck B, Christiansen C, Lande HL, Egeland J. Updated developmental norms for fine motor functions as measured by finger tapping speed and the grooved pegboard test. *Dev Neuropsychol*. 2018;43:551–565. doi: 10.1080/87565641.2018.1495724.
- 36. Pondal M, del Ser T. Normative data and determinants for the timed "up and go" test in a population-based sample of elderly individuals without gait disturbances. *J Geriatr Phys Ther*. 2008;31:57–63. doi: 10.1519/00139143-200831020-00004.
- 37. Steffen TM, Hacker TA, Mollinger L. Age- and gender-related test performance in community-dwelling elderly people: six-minute walk test, Berg Balance Scale, timed up & go test, and gait speeds. *Phys Ther*. 2002;82:128–137. doi: 10.1093/ptj/82.2.128.
- 38. Kiselica AM, Kaser AN, Webber TA, Small BJ, Benge JF. Development and preliminary validation of standardized regression-based change scores as measures of transitional cognitive decline. Arch Clin Neuropsychol. 2020;35:1168–1181. doi: 10.1093/arclin/acaa042.
- Mitrushina M, Boone KB, Razani J, D'Elia LF. Handbook of normative data for neuropsychological assessment. 2nd ed. New York, NY, US: Oxford University Press; 2005. p. 18–22, 64–65.
- Calamia M, Markon K, Tranel D. Scoring higher the second time around: meta-analyses of practice effects in neuropsychological assessment. *Clin Neuropsychol.* 2012;26:543–570. doi: 10.1080/13854046.2012.680913.
- 41. Mitrushina M, Satz P. Effect of repeated administration of a neuropsychological battery in the elderly. *J Clin Psychol*. 1991;47:790–801. doi: 10.1002/1097-4679(199111)47:63.0.co;2-c.
- 42. Duff K, Callister C, Dennett K, Tometich D. Practice effects: a unique cognitive variable. *Clin Neuropsychol.* 2012;26:1117–1127. doi: 10.1080/13854046.2012.722685.

- Jutten RJ, Grandoit E, Foldi NS, et al. Lower practice effects as a marker of cognitive performance and dementia risk: a literature review. *Alzheimers Dement (Amst)*. 2020;12:e12055. doi: 10.1002/dad2.12055.
- 44. Lubrini G, Gozalbo AS, Vincent C, Acedo C, López-Arrieta J, Garcia AF. P2-285: are the effects of age and education on neuropsychological performance the same in healthy individuals, individuals with mild cognitive impairment and those with Alzheimer's disease? *Alzheimers Dement.* 2013;9:P462–P462. doi: 10.1016/j.jalz.2013.05.932.
- LawsKR, IrvineK, GaleTM, et al. Sex differences in cognitive impairment in Alzheimers disease. World J Psychiatry. 2016;6:54–65. doi: 10.5498/wjp.v6. i1.54.
- 46. Rubin EH, Storandt M, Miller JP, et al. Influence of age on clinical and psychometric assessment of subjects with very mild or mild dementia of the Alzheimer type. *Arch Neurol.* 1993;50:380–383. doi: 10.1001/archneur.1993. 00540040042011.
- 47. Ibrahim A, Singh DKA, Shahar S. 'Timed up and go' test: age, gender and cognitive impairment stratified normative values of older adults. *PLoS One*. 2017;12:e0185641. doi: 10.1371/journal.pone.0185641.
- 48. Butt P, Beirness D, Gliksman L, Paradis C, Stockwell T. Alcohol and health in Canada: a summary of evidence and guidelines for low-risk drinking. Ottawa, ON: Canadian Centre on Substance Abuse; 2011. https://www.ccsa.ca/ alcohol-and-health-canada-summary-evidence-and-guidelines-low-riskdrinking.
- Devito EE, Pickard JD, Salmond CH, Iddon JL, Loveday C, Sahakian BJ. The neuropsychology of normal pressure hydrocephalus (NPH). *Br J Neurosurg*. 2005;19:217–224. doi: 10.1080/02688690500201838.
- Iddon J, Pickard J, Cross J, Griffiths P, Czosnyka M, Sahakian B. Specific patterns of cognitive impairment in patients with idiopathic normal pressure hydrocephalus and Alzheimers disease: a pilot study. *J Neurol Neurosurg Psychiatry*. 1999;67:723–732. doi: 10.1136/jnnp.67.6.723.
- 51. Peterson KA, Savulich G, Jackson D, Killikelly C, Pickard JD, Sahakian BJ. The effect of shunt surgery on neuropsychological performance in normal pressure hydrocephalus: a systematic review and meta-analysis. *J Neurol*. 2016;263:1669–1677. doi: 10.1007/s00415-016-8097-0.
- Strauss E, Sherman EMS, Spreen O. A compendium of neuropsychological tests: administration, norms, and commentary. 3rd edn. New York, NY, US: Oxford University Press; 2006. p. 1061–1066.
- 53. Delis DC, Kaplan E, Kramer JH. *Delis-Kaplan Executive Function System* (*D-KEFS*). San Antonio (TX): Psychological Corporation; 2001.
- 54. Stern RA, White T. Nab, Neuropsychological Assessment Battery: Administration, Scoring, and Interpretation Manual. Lutz (FL): Psychological Assessment Resources; 2003.
- 55. Kim HJ, Park I, Lee HJ, Lee O. The reliability and validity of gait speed with different walking pace and distances against general health, physical function, and chronic disease in aged adults. *J Exerc Nutrition Biochem*. 2016;20:46–50. doi: 10.20463/jenb.2016.09.20.3.7.
- Lilja-Lund O, Nyberg L, Maripuu M, Laurell K. Dual-task performance in older adults with and without idiopathic normal pressure hydrocephalus. Front Aging Neurosci. 2022;14:904194. doi: 10.3389/fnagi.2022.904194.
- 57. Podsiadlo D, Richardson S. The timed "Up & go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc.* 1991;39:142–148. doi: 10. 1111/j.1532-5415.1991.tb01616.x.
- 58. Berg KO, Wood-Dauphinee SL, Williams JI, Maki B. Measuring balance in the elderly: validation of an instrument. *Can J Public Health*. 1992;83:S7–11.
- Constantinescu C, Wikkelsø C, Westman E, et al. Prevalence of possible idiopathic normal pressure hydrocephalus in Sweden: a population-based MRI study in 791 70-year-old participants. *Neurology*. 2024;102:e208037. doi: 10.1212/wnl.0000000000208037.
- Schmid Daners M, Knobloch V, Soellinger M, et al. Age-specific characteristics and coupling of cerebral arterial inflow and cerebrospinal fluid dynamics. *PLoS One*. 2012;7:e37502. doi: 10.1371/journal.pone.0037502.
- Sartoretti T, Wyss M, Sartoretti E, et al. Sex and age dependencies of aqueductal cerebrospinal fluid dynamics parameters in healthy subjects. Front Aging Neurosci. 2019;11:199. doi: 10.3389/fnagi.2019.00199.
- 62. Eide PK, Pripp AH. Increased prevalence of cardiovascular disease in idiopathic normal pressure hydrocephalus patients compared to a population-based cohort from the HUNT3 survey. *Fluids Barriers CNS*. 2014;11:19. doi: 10.1186/2045-8118-11-19.

- Graff-Radford NR, Godersky JC. Idiopathic normal pressure hydrocephalus and systemic hypertension. *Neurology*. 1987;37:868–871. doi: 10.1212/wnl. 37.5.868.
- Deng Z, Wang H, Huang K, et al. Association between vascular risk factors and idiopathic normal pressure hydrocephalus: a Mendelian randomization study. *J Neurol.* 2023;270:2724–2733. doi: 10.1007/s00415-023-11604-6.
- Bonney PA, Briggs RG, Wu K, et al. Pathophysiological mechanisms underlying idiopathic normal pressure hydrocephalus: a review of recent insights. Front Aging Neurosci. 2022;14:866313. doi: 10.3389/fnagi.2022. 866313.
- 66. Egnor M, Yang L, Mani RM, Fiore SM, Djurić PM. A quantitative model of the cerebral windkessel and its relevance to disorders of intracranial dynamics. *J Neurosurg Pediatr*. 2023;32:302–311. doi: 10.3171/2023.1. Peds22372.
- Belz GG. Elastic properties and Windkessel function of the human aorta. Cardiovasc Drugs Ther. 1995;9:73–83. doi: 10.1007/bf00877747.
- Graff-Radford NR, Knopman DS, Penman AD, Coker LH, Mosley TH. Do systolic BP and pulse pressure relate to ventricular enlargement? *Eur J Neurol*. 2013;20:720–724. doi: 10.1111/ene.12067.
- 69. Greitz D. The hydrodynamic hypothesis versus the bulk flow hypothesis. *Neurosurg Rev.* 2004;27:299–300. doi: 10.1007/s10143-004-0349-2.
- Kuriyama N, Miyajima M, Nakajima M, et al. Nationwide hospital-based survey of idiopathic normal pressure hydrocephalus in Japan: epidemiological and clinical characteristics. *Brain Behav.* 2017;7:e00635. doi: 10. 1002/brb3.635.
- Adhikary D, Barman S, Ranjan R, Stone H. A systematic review of major cardiovascular risk factors: a growing global health concern. *Cureus*. 2022;14:e30119. doi: 10.7759/cureus.30119.
- 72. Di Cesare M, Perel P, Taylor S, et al. The heart of the world. *Glob Heart*. 2024;19:11. doi: 10.5334/gh.1288.
- Bluett B, Ash E, Farheen A, et al. Clinical features of idiopathic normal pressure hydrocephalus: critical review of objective findings. *Mov Disord Clin Pract*. 2023;10:9–16. doi: 10.1002/mdc3.13608.
- 74. Murman DL. The impact of age on cognition. Semin Hear. 2015;36:111–121. doi: 10.1055/s-0035-1555115.
- Noce Kirkwood R, de Souza Moreira B, Mingoti SA, Faria BF, Sampaio RF, Alves Resende R. The slowing down phenomenon: what is the age of major gait velocity decline? *Maturitas*. 2018;115:31–36. doi: 10.1016/j.maturitas. 2018.06.005.
- Cohen RA, Marsiske MM, Smith GE. Neuropsychology of aging. Handb Clin Neurol. 2019;167:149–180. doi: 10.1016/b978-0-12-804766-8.00010-8.
- Salthouse T. Consequences of age-related cognitive declines. Annu Rev Psychol. 2012;63:201–226. doi: 10.1146/annurev-psych-120710-100328.
- Gallagher R, Farella-Accurso M, Johnson D, et al. Do age and disease stage impact cognition and balance in older adults and persons with Parkinson disease? *Top Geriatr Rehabil*. 2019;35:224–230. doi: 10.1097/TGR. 00000000000000238.
- Clouston SAP, Smith DM, Mukherjee S, et al. Education and cognitive decline: an integrative analysis of global longitudinal studies of cognitive aging. J Gerontol B Psychol Sci Soc Sci. 2020;75:e151–e160. doi: 10.1093/ geronb/gbz053.
- Hall CB, Derby C, LeValley A, Katz MJ, Verghese J, Lipton RB. Education delays accelerated decline on a memory test in persons who develop dementia. *Neurology*. 2007;69:1657–1664. doi: 10.1212/01.wnl.0000278163.82636.30.
- Stern Y, Gurland B, Tatemichi TK, Tang MX, Wilder D, Mayeux R. Influence of education and occupation on the incidence of Alzheimers disease. *Jama*. 1994;271:1004–1010. doi: 10.1001/jama.1994.03510370 056032.
- Valenzuela MJ, Sachdev P. Brain reserve and cognitive decline: a nonparametric systematic review. *Psychol Med.* 2006;36:1065–1073. doi: 10. 1017/S0033291706007744.
- 83. Amieva H, Mokri H, Le Goff M, et al. Compensatory mechanisms in higher-educated subjects with Alzheimers disease: a study of 20 years of cognitive decline. *Brain*. 2014;137:1167–1175. doi: 10.1093/brain/awu035.
- 84. Isaacs AM, Williams MA, Hamilton MG. Current update on treatment strategies for idiopathic normal pressure hydrocephalus. Curr Treat Options Neurol. 2019;21:65. doi: 10.1007/s11940-019-0604-z.

- Hindle JV, Martyr A, Clare L. Cognitive reserve in Parkinson's disease: a systematic review and meta-analysis. *Parkinsonism Relat Disord*. 2014;20:1–7. doi: 10.1016/j.parkreldis.2013.08.010.
- 86. Iersel MBv, Kessels RPC, Bloem BR, Verbeek ALM, Olde Rikkert MGM. Executive functions are associated with gait and balance in communityliving elderly people. *J Gerontol A Biol Sci Med Sci.* 2008;63:1344–1349. doi: 10.1093/gerona/63.12.1344.
- 87. Kearney FC, Harwood RH, Gladman JRF, Lincoln N, Masud T. The Relationship between Executive Function and Falls and Gait Abnormalities in Older Adults: A Systematic Review. *Dement Geriatr Cogn Disord*. 2013;36:20-35. doi: 10.1159/000350031.
- 88. Hirota C, Watanabe M, Tanimoto Y, Kono R, Higuchi Y, Kono K. [A cross-sectional study on the relationship between the trail making test and mobility-related functions in community-dwelling elderly]. *Nihon Ronen Igakkai Zasshi*. 2008;45:647–654. doi: 10.3143/geriatrics.45.647.
- 89. Souza CdO, Voos MC, Francato DV, Chien HF, Barbosa ER. Influence of educational status on executive function and functional balance in individuals with Parkinson disease. *Cogn Behav Neurol.* 2013;26:6–13. doi: 10.1097/WNN.0b013e31828c5956.
- 90. Munro CA, Winicki JM, Schretlen DJ, et al. Sex differences in cognition in healthy elderly individuals. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn*. 2012; 19:759–768. doi: 10.1080/13825585.2012.690366,
- Roivainen E, Suokas F, Saari A. An examination of factors that may contribute to gender differences in psychomotor processing speed. BMC Psychol. 2021;9:190. doi: 10.1186/s40359-021-00698-0.
- 92. Ruff RM, Parker SB. Gender- and age-specific changes in motor speed and eye-hand coordination in adults: normative values for the finger tapping

- and grooved pegboard tests. *Percept Mot Skills*. 1993;76:1219–1230. doi: 10. 2466/pms.1993.76.3c.1219.
- Nakagawa HB, Ferraresi JR, Prata MG, Scheicher ME. Postural balance and functional independence of elderly people according to gender and age: cross-sectional study. Sao Paulo Med J. 2017;135:260–265. doi: 10.1590/ 1516-3180.2016.0325280217.
- 94. Avdić D, Skrbo A. Co-relation between risk factors of falls down and the Berg balance scale in elderly people (third age). *Bosn J Basic Med Sci.* 2003;3:49–55. doi: 10.17305/bjbms.2003.3571.
- Andrén K, Wikkelsö C, Sundström N, et al. Long-term effects of complications and vascular comorbidity in idiopathic normal pressure hydrocephalus: a quality registry study. *J Neurol*. 2018;265:178–186. doi: 10. 1007/s00415-017-8680-z.
- 96. Spagnoli D, Innocenti L, Bello L, et al. Impact of cerebrovascular disease on the surgical treatment of idiopathic normal pressure hydrocephalus. *Neurosurgery*. 2006;59:545–552. doi: 10.1227/01.Neu.0000230259.49167. 95. discussion 545–552.
- 97. Bådagård H, Braun M, Nilsson D, Stridh L, Virhammar J. Negative predictors of shunt surgery outcome in normal pressure hydrocephalus. *Acta Neurol Scand.* 2020;141:219–225. doi: 10.1111/ane.13200.
- 98. Uchigami H, Sato K, Samejima N, et al. Preoperative factors associated with shunt responsiveness in patients with idiopathic normal-pressure hydrocephalus. *Clin Neurol Neurosurg.* 2022;222:107425. doi: 10.1016/j.clineuro. 2022.107425.
- Kobayashi E, Kanno S, Kawakami N, et al. Risk factors for unfavourable outcomes after shunt surgery in patients with idiopathic normal-pressure hydrocephalus. Sci Rep. 2022;12:13921. doi: 10.1038/s41598-022-18209-5.