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High prevalence of lumbar spinal stenosis in cases of idiopathic normal-pressure hydrocephalus affects improvements in gait disturbance after shunt operation

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ABSTRACT

Objective: Idiopathic normal-pressure hydrocephalus (iNPH) is characterized by symptoms of dementia, urinary incontinence, and gait disturbance; however, gait disturbance tends to persist after shunt surgery. Gait disturbance and urinary dysfunction are also major symptoms of lumbar spinal stenosis (LSS). Currently, the epidemiology of the complications of LSS in iNPH is unclear. Here, we evaluated the coexistence rate of LSS in iNPH cases.
Methods: This was a retrospective case–control study. Between 2011 and 2017, 224 patients with a median age of 78 years, including 119 males, were diagnosed with iNPH and underwent lumboperitoneal shunts or ventriculoperitoneal shunts. LSS was diagnosed with magnetic resonance imaging by two spine surgeons. Age, sex, body mass index (BMI), Timed Up and Go (TUG) test, Mini Mental State Examination (MMSE) score, and urinary dysfunction were examined. We compared the changes in these variables in the group of patients with iNPH without LSS versus those with both iNPH and LSS.
Results: Seventy-three iNPH patients (32.6%) with LSS had significantly higher age and BMI. The existence of LSS did not alter the postoperative improvement rates of MMSE and urinary dysfunction; however, TUG improvement was significantly impaired in the LSS-positive group.
Conclusions: LSS affects improvements in gait disturbance of iNPH patients after shunt operation. Because our results revealed that one-third of iNPH patients were associated with LSS, gait disturbance observed in iNPH patients should be considered a potential complication of LSS.

1. Introduction

Idiopathic normal-pressure hydrocephalus (iNPH) is characterized by three clinical symptoms, gait disturbance, dementia, and urinary incontinence,[1–3] with ventricular dilation and normal cerebrospinal fluid pressure.[4] The disturbance of cerebral spinal fluid absorption often requires a ventriculoperitoneal or lumboperitoneal shunt operation.[5,6] However, some patients with iNPH show poor improvement in gait disturbance after a shunt operation.[7] Lumbar spinal stenosis (LSS) causes symptoms similar to those observed in iNPH, including intermittent claudication and bladder and/or rectal dysfunction.[8,9] Numbers of patients with iNPH or LSS are increasing in countries with an aging society, such as Japan.[5,10–14] Diabetes mellitus (DM) is associated with iNPH cases[15,16] and is also a risk factor for LSS.[17] Type 2 DM is the result of

Abbreviations: BMI, body mass index; DM, diabetes mellitus; DSCSA, dural sac cross-sectional area; iNPH, idiopathic normal-pressure hydrocephalus; LPS, lumboperitoneal shunts; LSS, lumbar spinal stenosis; MMSE, Mini Mental State Examination; MRI, magnetic resonance imaging; TUG, timed up and go test.

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interactions between environmental factors and a strong hereditary component.[18] Moreover, deleterious mutations in several genes contribute to LSS etiology.[19] This evidence suggests a common genetic background between iNPH and LSS, which causes a syndrome consisting of gait disturbance and urinary dysfunction. iNPH and LSS occur more frequently in the elderly,[5,11] so there may be a complication. Therefore, the cause of the gait disorders should be differentially diagnosed before shunt surgery. Because the coexistence rate of LSS in patients with iNPH is currently unclear, we investigated the prevalence of LSS in patients with iNPH, and hypothesized that postoperative outcomes for patients with iNPH with LSS would be inferior to those without LSS.

2. Material and methods

2.1. Ethical statement

The study was conducted according to the guidelines of the Declaration of Helsinki, was approved by the Ethics Committee on Clinical Research at the Japanese Red Cross Kagoshima Hospital (approval no. 2018-9-1), and followed the STROBE guidelines.

2.2. Participants

We retrospectively studied the records of patients who underwent magnetic resonance imaging (MRI) of the lumbar spine prior to surgery for iNPH. The following inclusion criteria were used: 1) patients over 60 years old; 2) patients with one or more of the three signs of gait disturbance, cognitive impairment, and dysuria[5,20]; 3) ventriculomegaly with an Evans' index >0.3 and high-convexity and medial subarachnoid space tightness on coronal MR images[21]; and 4) normal cerebrospinal fluid content and pressure. The following exclusion criteria were used: an absence of prior illness or injury (such as head injury, subarachnoid hemorrhage, or meningitis).[22]

2.3. Demographic data

Between 2011 and 2017, 224 consecutive patients aged over 60 years, including 119 males, were diagnosed with iNPH and underwent lumboperitoneal shunts (LPS) or ventriculoperitoneal shunts in the Japanese Red Cross Kagoshima Hospital. Patient demographic and clinical characteristics before and after surgery, including age, sex, body mass index (BMI), rates of patients with gait disturbance, dementia, urinary incontinence, and dural sac cross-sectional area (DSCSA) were collected from their medical records. Gait disturbance was evaluated by clinical examination by a neurosurgery specialist, history of walking difficulty, and the Timed Up and Go (TUG) test.[21,23] A neurosurgeon filmed the TUG test to check for improvements in leg opening, stride length, and forward leaning posture, as well as the number of steps and walking seconds 7 days before the tap. Surgery was performed on the improved group. Dementia was evaluated using the Mini Mental State Examination (MMSE); patients with an MMSE score lower than 24 were defined as having dementia.[24] Urinary dysfunction was defined as the presence of urinary incontinence or nocturia based on the iNPH grading scale.[25] Improvements in symptoms were evaluated at the first outpatient visit after discharge from the hospital (at 1 month postoperatively) and were defined as a faster time in the TUG test, higher MMSE score, and improvement in patient satisfaction with urination compared with preoperative values.

2.4. Definitions of iNPH and LSS

All patients with a clinical diagnosis of iNPH underwent a lumbar tap to obtain a definitive diagnosis. A neurosurgeon checked the improvement in gait disturbance after draining the cerebrospinal fluid. iNPH was diagnosed according to the diagnostic criteria of the iNPH guidelines.[5] Patients were diagnosed with LSS when the most narrowed part of the DSCSA was less than 75 mm^2 calculated on MRI,[20,26–29] which was analyzed using a Magnetom Avanto 1.5T instrument (Siemens Healthineers, Erlangen, Germany). The MRI assessments were performed by two spine specialists, including one spine surgeon who was an instructor accredited by the Japanese Society for Spine Surgery and Related Research.

2.5. Shunt operation

A neurosurgeon performed the shunt operations to treat iNPH. Although VPS is currently the major surgical procedure for iNPH, therapeutic interventions with LPS were also reported to be effective.[22] Furthermore, the efficacy and safety of adjustable LPS were comparable with VPS for the treatment of patients with iNPH. In this study, we mainly selected the LPS procedure for iNPH patients without LSS because it is less invasive and avoids damage to the brain, despite the relatively high shunt failure rate.[7,22] We mainly performed VPS in cases of spinal canal stenosis cephalad to L2/3 on MRI images or when a patient requested that particular procedure.

2.6. Statistics

The data were examined using Wilcoxon's test and Fisher's exact test. Pearson's correlation coefficient analysis was performed to assess correlations between variables. Multivariable stepwise binomial logistic regression analyses were performed to correlate demographic data. *p*-values less than 0.05 were considered statistically significant. Statistical analyses were performed using JMP software (version 15: SAS Institute, Cary, NC, USA).

3. Results

3.1. Patient characteristics and factors inversely correlated with the DSCSA and TUG values

Overall, 224 patients suffering from iNPH were included in this study (Fig. 1). The median height of the patients was 1.54 m. Overall, 13 of the 224 patients (5.8%) were current smokers and 59 of the 224 patients (26.3%) had a history of smoking.

Seventy-three patients (32.6%) had LSS (iNPH-LSS group) and the DSCSA of the remaining 151 cases (67.4%) was within the normal range (iNPH group). The demographic and preoperative clinical characteristics of the iNPH and iNPH-LSS groups are shown in Table 1. The iNPH-LSS group had significantly higher BMI scores than the iNPH group, whereas no difference was observed for age, sex, TUG scores, MMSE score, and the degree of urinary dysfunction. In the iNPH group, 140 of 151 patients (92.7%) had an LP shunt, and in the iNPH with LSS group, 45 of 73 (61.6%) patients had an LP shunt. Pearson's correlation coefficient analysis showed four inverse correlations: DSCSA vs age ($r = -0.18$), DSCSA vs BMI ($r = -0.18$), preoperative TUG time vs BMI ($r = -0.18$), and preoperative TUG time vs preoperative MMSE score ($r = -0.41$) (Table 2).

3.2. Improvements in gait disturbance, dementia, and urinary dysfunction after surgery for iNPH

The improvement rate in gait disturbance was significantly decreased by approximately 10% in the iNPH-LSS group compared with the iNPH group ($p < 0.01$), whereas there were no evident changes in the improvement rates of dementia and urinary dysfunction (Table 3). Table 4 shows the TUG and MMSE values in the iNPH and iNPH-LSS groups before and after the shunt operations. Both groups showed substantial improvements in the TUG time and MMSE score postoperatively. However, the value of TUG steps was significantly improved in the iNPH group, but not in the iNPH-LSS group. TUG improvement was inferior in the iNPH-LSS group compared with the iNPH group (Supplementary

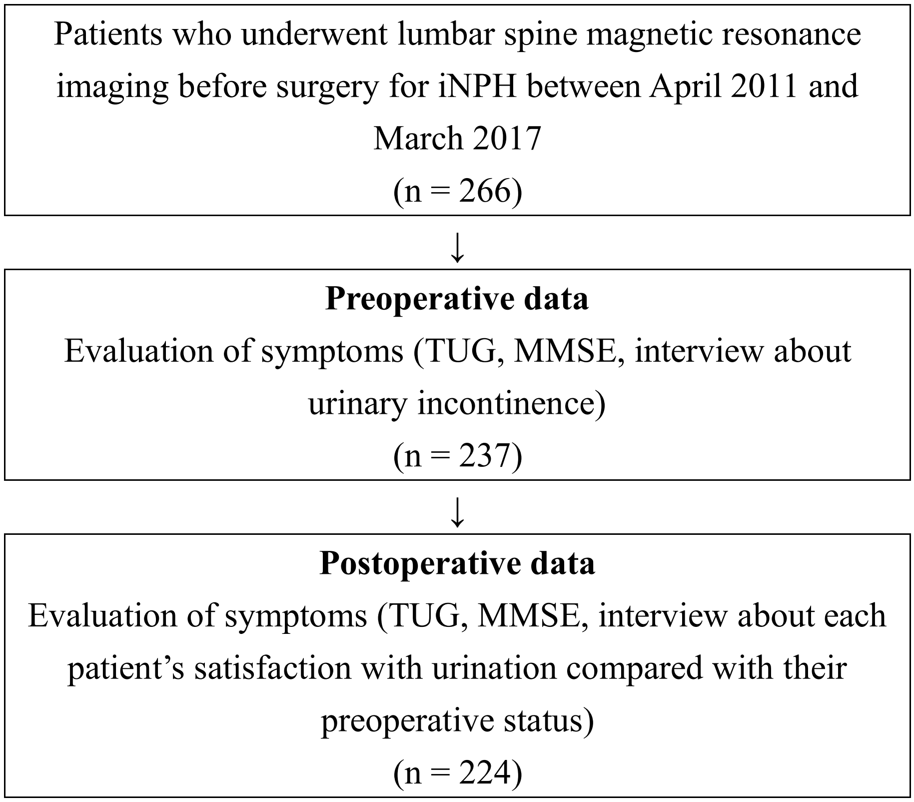

Fig. 1. Flowchart of the study. We examined the records of 266 patients who underwent lumbar spine magnetic resonance imaging before surgery for iNPH between April 2011 and March 2017. The TUG, MMSE, and presence of urinary incontinence were evaluated preoperatively in 237 patients and postoperatively in 224 patients. iNPH: idiopathic normal-pressure hydrocephalus; TUG: Timed Up and Go test; MMSE: Mini Mental State Examination.

Table 1
Preoperative patient characteristics in the iNPH and iNPH-LSS groups.

	Total (*n* = 224)	iNPH group (*n* = 151)	iNPH-LSS group (*n* = 73)	*p*
Age (years)	78.0 (74.0–82.8)	78.0 (73.0–82.0)	79.0 (75.5–83.5)	0.12
Sex (male) (n)	119	77	42	0.39
BMI (kg/m^2)	22.5 (20.1–25.4)	22.0 (19.9–24.6)	23.5 (20.4–26.1)	0.01
TUG (sec)	23.0 (17.0–38.0)	24.0 (18.0–44.0)	21.5 (16.0–32.3)	0.09
TUG (steps)	28.0 (21.3–38.0)	28.0 (22.0–39.0)	25.0 (20.0–36.0)	0.06
MMSE (points)	22.0 (17.0–25.0)	22.0 (17.0–25.0)	21.0 (16.0–24.0)	0.25
Urinary dysfunction (*n*)	201	133	68	0.35
Lumboperitoneal shunt (*n*)	185	140	45	<0.0001

Data are presented as the median (25% quartile–75% quartile) or the number of patients (*n*).
Data were analyzed using the Wilcoxon test and Fisher's exact test.
BMI: body mass index; iNPH group: patients with idiopathic normal-pressure hydrocephalus; iNPH-LSS group: patients with idiopathic normal-pressure hydrocephalus and concomitant lumbar spinal stenosis; MMSE: Mini Mental State Examination score; TUG: Timed Up and Go test.

Table 1). Multivariate logistic regression analysis indicated LSS was a factor that inhibited gait improvement after shunt surgery for iNPH (Table 5). Indeed, one patient in the iNPH-LSS group underwent lumbar decompression surgery following shunt surgery. Conversely, four patients in the iNPH group underwent shunt surgery following the initial lumbar decompression surgery. Therefore, 4 of 224 patients underwent spinal surgery before shunting, and 1 underwent spinal surgery after shunting.

Table 2
Analysis of the correlations between variables.

Variables	Correlation coefficient
	DSCSA
Age (years)	−0.18**
BMI (kg/m^2)	−0.18**
Preoperative TUG (sec)	0.10
Preoperative MMSE (points)	0.10
Variables	Correlation coefficient
	Preoperative TUG (sec)
Age (years)	0.21**
BMI (kg/m^2)	−0.18**
DSCSA (mm^2)	0.10
Preoperative MMSE (points)	−0.41**

**$p < 0.01$.
Data were analyzed using Pearson's correlation analysis.
BMI: body mass index; DSCSA: dural sac cross-sectional area; MMSE: Mini Mental State Examination score; TUG: Timed Up and Go test.

4. Discussion

4.1. Comorbidity of LSS in iNPH is relatively high

To the best of our knowledge, this is the first epidemiological investigation of complications of LSS in iNPH patients. Gait disturbance in iNPH is characterized by a wobbly gait, especially when changing direction.[2,5] However, gait disturbance in LSS is characterized by a gait with a forward-bent posture.[8] With regard to urinary dysfunction, iNPH

Table 3
Postoperative improvement rates in symptoms in the iNPH and iNPH-LSS groups.

	iNPH group (n = 151)	iNPH-LSS group (n = 73)	p
Improvement in gait disturbance (n)	90.1% (n = 136)	80.8% (n = 59)	0.01
Improvement in dementia (n)	58.9% (n = 89)	63.0% (n = 46)	0.66
Improvement in urinary dysfunction (n)	68.2% (n = 103)	69.9% (n = 51)	0.86

Data were analyzed using Fisher's exact test.
iNPH group: patients with idiopathic normal-pressure hydrocephalus; iNPH-LSS group: patients with idiopathic normal-pressure hydrocephalus and concomitant lumbar spinal stenosis.

is characterized by the urge for urinary incontinence associated with an overactive bladder,[30] whereas LSS is characterized by dysuria and urinary retention.[31] Although it is possible to distinguish between iNPH and LSS by a detailed diagnosis of the patient's condition when symptoms are present, patients with iNPH may show LSS on imaging without symptoms.

We found that the lumbar spinal canal was narrow in 32.6% of iNPH patients. This is striking because previous studies reported the prevalence of LSS was 6% in 850 lumbar myelograms[32] or 13.1% in 17,744 patients.[33] We speculate the reason for the increased prevalence of LSS in our iNPH patients was that the individual risks of LSS and iNPH were reported to be significantly higher in older adults compared with younger individuals.[34] Our participants with iNPH had a relatively advanced mean age. In addition, obesity affects pain related to spinal stenosis and is associated with abnormal mechanical forces, in addition to the presence of chronic circulating inflammatory chemicals from active adipose tissue.[35] Indeed, our iNPH patients with LSS had a high BMI. In addition, we found that smaller DSCSA correlated with older age and higher BMI. Therefore, our findings suggest that older age and higher BMI are useful predictors of LSS in patients with iNPH. Finally, iNPH and LSS might share a common genetic background. Importantly, a previous study showed that people with familial iNPH were more likely to have spinal stenosis than non-iNPH relatives, although this did not reach statistical significance.[15]

4.2. *Patients with iNPH with LSS on imaging have poorer gait improvement after shunt surgery than those without LSS*

In the present study, we used the TUG test as an index of gait ability and used the MMSE as an index of dementia. The TUG test and MMSE had a relatively strong negative correlation (Table 2). General cognitive function was reported to affect the physical performance of patients with mild cognitive impairment.[36] The TUG test is a sensitive and specific index of the risk of falling.[37] Previous studies reported that patients with LSS had a mean raw TUG test time of 10.2 s before surgery,[38] whereas patients with iNPH had a median TUG test time of 15.2 (11.7–21.0) seconds.[21] In our study, the median TUG test time was 23.0 (17.0–38.0) seconds and these were patients with relatively severe symptoms.

Table 5
Risk factors for gait improvement after shunt surgery for iNPH.

Variables	Odds ratio	p
Age	0.98 (0.91–1.06)	0.65
BMI (kg/m^2)	1.03 (0.91–1.16)	0.66
Male	1.15 (0.40–3.32)	0.63
Lumbar spinal stenosis	0.24 (0.09–0.65)	0.01
Smoking history	1.19 (0.32–4.41)	0.80

Patients were diagnosed with lumbar spinal stenosis when the most narrowed part of the DSCSA was less than 75 mm^2 calculated on MRI.
BMI: body mass index; DSCSA: dural sac cross-sectional area; iNPH: idiopathic normal-pressure hydrocephalus.

This study demonstrated that the rate of improvement in gait disturbance was significantly lower in the iNPH-LSS group compared with the iNPH group. This result suggested that the reason for some patients not showing an improvement in gait disturbance after shunt surgery for iNPH might be related to the complication of LSS, and vice versa.

It was previously reported that the DSCSA did not significantly correlate with the incidence of neurogenic bladder.[39] In our study, there was no statistically significant difference in the improvement rate of urinary dysfunction after shunt operation between the iNPH-LSS and iNPH groups. This may be because we diagnosed LSS by DSCSA.

4.3. *Limitations*

There were five limitations in our study. First, this was a retrospective single-center study; thus, selection bias may have occurred. Therefore, we should perform a multicenter study to confirm our findings. Second, patients were diagnosed with LSS alone by evaluating medical records, on the basis of the most narrowed part of the DSCSA being narrower than 75 mm^2 on MRI. We could not evaluate more detailed comprehensive physical examination findings of LSS, such as the presence of numbness and pain of the lower extremities. Third, there were differences in the shunt operation techniques. Therefore, we cannot exclude the possibility that differences in the two surgical techniques among iNPH patients with or without LSS were responsible for the different outcomes in improved gait disturbance. Fourth, we cannot exclude the influence of vascular claudication because we did not measure the ankle brachial index. Finally, although the involvement of cervical stenosis and disproportionately enlarged subarachnoid space hydrocephalus (DESH) have been reported,[40] we cannot exclude the influence of cervicothoracic stenosis in the present study.

5. Conclusions

Higher BMI was associated with LSS in patients with iNPH. Importantly, iNPH patients showed a significantly high prevalence (32.6%) of LSS compared with the reported general LSS prevalence and the rate of gait disturbance improvement was lower in iNPH patients with LSS. Therefore, when examining patients with iNPH, we should consider the concomitant presence of LSS.

Table 4
TUG and MMSE values in the iNPH and iNPH-LSS groups before and after shunt operations.

	iNPH group			iNPH-LSS group		
	Preoperative	Postoperative	p	Preoperative	Postoperative	p
TUG (steps)	28.0 (22.0–39.0)	22.0 (18.0–30.0)	<0.001	25.0 (20.0–36.0)	25.0 (20.0–38.5)	0.13
TUG (sec)	24.0 (18.0–44.0)	18.0 (14.0–26.5)	<0.001	21.5 (16.0–32.3)	18.0 (13.5–28.0)	0.047
MMSE	22.0 (17.0–25.0)	24.0 (20.0–28.0)	<0.001	21.0 (16.0–24.0)	24.0 (18.5–28.0)	<0.001

Data are presented as the median (25% quartile–75% quartile) and were analyzed using the paired t-test.
iNPH group: patients with idiopathic normal-pressure hydrocephalus; iNPH-LSS group: patients with idiopathic normal-pressure hydrocephalus and concomitant lumbar spinal stenosis; MMSE: Mini Mental State Examination score; TUG: Timed Up and Go test.

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Data statement

The datasets generated during the current study are available from the corresponding author upon reasonable request.

CRediT authorship contribution statement

Hiroyuki Tominaga: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Hiroto Tokumoto:** Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Shingo Maeda:** Writing – original draft. **Ichiro Kawamura:** Conceptualization, Supervision. **Masato Sanada:** Data curation. **Kazumasa Kawazoe:** Conceptualization, Data curation. **Eiji Taketomi:** Conceptualization, Supervision. **Noboru Taniguchi:** Conceptualization, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.wnsx.2023.100236.

References

1. Stolze H, Kuhtz-Buschbeck JP, Drucke H, et al. Gait analysis in idiopathic normal pressure hydrocephalus–which parameters respond to the CSF tap test? *Clin Neurophysiol*. 2000;111(9):1678–1686. https://doi.org/10.1016/s1388-2457(00)00362-x.
2. Stolze H, Kuhtz-Buschbeck JP, Drucke H, Johnk K, Illert M, Deuschl G. Comparative analysis of the gait disorder of normal pressure hydrocephalus and Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 2001;70(3):289–297. https://doi.org/10.1136/jnnp.70.3.289.
3. Williams MA, Thomas G, de Lateur B, et al. Objective assessment of gait in normal-pressure hydrocephalus. *Am J Phys Med Rehabil*. 2008;87(1):39–45. https://doi.org/10.1097/PHM.0b013e31815b6461.
4. Hakim S, Adams RD. The special clinical problem of symptomatic hydrocephalus with normal cerebrospinal fluid pressure. Observations on cerebrospinal fluid hydrodynamics. *J Neurol Sci*. 1965;2(4):307–327. https://doi.org/10.1016/0022-510x(65)90016-x.
5. Mori E, Ishikawa M, Kato T, et al. Guidelines for management of idiopathic normal pressure hydrocephalus: second edition. *Neurol Med -Chir*. 2012;52(11):775–809. https://doi.org/10.2176/nmc.52.775.
6. Wilson RK, Williams MA. Normal pressure hydrocephalus. *Clin Geriatr Med*. 2006;22(4):935–951. https://doi.org/10.1016/j.cger.2006.06.010. viii.
7. Kazui H, Miyajima M, Mori E, Ishikawa M, Investigators S-. Lumboperitoneal shunt surgery for idiopathic normal pressure hydrocephalus (SINPHONI-2): an open-label randomised trial. *Lancet Neurol*. 2015;14(6):585–594. https://doi.org/10.1016/S1474-4422(15)00046-0.
8. Takahashi K, Miyazaki T, Takino T, Matsui T, Tomita K. Epidural pressure measurements. Relationship between epidural pressure and posture in patients with lumbar spinal stenosis. *Spine*. 1995;20(6):650–653.
9. Thome C, Borm W, Meyer F. Degenerative lumbar spinal stenosis: current strategies in diagnosis and treatment. *Dtsch Arztebl Int*. 2008;105(20):373–379. https://doi.org/10.3238/arztebl.2008.0373.
10. Costandi S, Chopko B, Mekhail M, Dews T, Mekhail N. Lumbar spinal stenosis: therapeutic options review. *Pain Pract*. 2015;15(1):68–81. https://doi.org/10.1111/papr.12188.
11. Kalff R, Ewald C, Waschke A, Gobisch L, Hopf C. Degenerative lumbar spinal stenosis in older people: current treatment options. *Dtsch Arztebl Int*. 2013;110(37):613–623. https://doi.org/10.3238/arztebl.2013.0613. quiz 624.
12. Deer T, Sayed D, Michels J, Josephson Y, Li S, Calodney AK. A review of lumbar spinal stenosis with intermittent neurogenic claudication: disease and diagnosis. *Pain Med*. 2019;20(Suppl 2):S32–S44. https://doi.org/10.1093/pm/pnz161.
13. Kitab S, Lee BS, Benzel EC. Redefining lumbar spinal stenosis as a developmental syndrome: an MRI-based multivariate analysis of findings in 709 patients throughout the 16- to 82-year age spectrum. *J Neurosurg Spine*. 2018;29(6):654–660. https://doi.org/10.3171/2018.5.SPINE18100.
14. Fujita N. Lumbar spinal canal stenosis from the perspective of locomotive syndrome and metabolic syndrome: a narrative review. *Spine Surg Relat Res*. 2021;5(2):61–67. https://doi.org/10.22603/ssrr.2020-0112.
15. Rasanen J, Huovinen J, Korhonen VE, et al. Diabetes is associated with familial idiopathic normal pressure hydrocephalus: a case-control comparison with family members. *Fluids Barriers CNS*. 2020;17(1):57. https://doi.org/10.1186/s12987-020-00217-0.
16. Hudson M, Nowak C, Garling RJ, Harris C. Comorbidity of diabetes mellitus in idiopathic normal pressure hydrocephalus: a systematic literature review. *Fluids Barriers CNS*. 2019;16(1):5. https://doi.org/10.1186/s12987-019-0125-x.
17. Asadian L, Haddadi K, Aarabi M, Zare A. Diabetes mellitus, a new risk factor for lumbar spinal stenosis: a case-control study. *Clin Med Insights Endocrinol Diabetes*. 2016;9:1–5. https://doi.org/10.4137/CMED.S39035.
18. Ali O. Genetics of type 2 diabetes. *World J Diabetes*. 2013;4(4):114–123. https://doi.org/10.4239/wjd.v4.i4.114.
19. Jiang X, Chen D. The identification of novel gene mutations for degenerative lumbar spinal stenosis using whole-exome sequencing in a Chinese cohort. *BMC Med Genom*. 2021;14(1):134. https://doi.org/10.1186/s12920-021-00981-4.
20. Schizas C, Theumann N, Burn A, et al. Qualitative grading of severity of lumbar spinal stenosis based on the morphology of the dural sac on magnetic resonance images. *Spine*. 2010;35(21):1919–1924. https://doi.org/10.1097/BRS.0b013e3181d359bd.
21. 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. https://doi.org/10.1016/j.wneu.2017.05.137.
22. Miyajima M, Kazui H, Mori E, Ishikawa M, Sinphoni-Investigators obot. One-year outcome in patients with idiopathic normal-pressure hydrocephalus: comparison of lumboperitoneal shunt to ventriculoperitoneal shunt. *J Neurosurg*. 2016;125(6):1483–1492. https://doi.org/10.3171/2015.10.JNS151894.
23. Larsson A, Wikkelso C, Bilting M, Stephensen H. Clinical parameters in 74 consecutive patients shunt operated for normal pressure hydrocephalus. *Acta Neurol Scand*. 1991;84(6):475–482. https://doi.org/10.1111/j.1600-0404.1991.tb04998.x.
24. Braekhus A, Laake K, Engedal K. The mini-mental state examination: identifying the most efficient variables for detecting cognitive impairment in the elderly. *J Am Geriatr Soc*. 1992;40(11):1139–1145. https://doi.org/10.1111/j.1532-5415.1992.tb01804.x.
25. 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(1):37–45. https://doi.org/10.1159/000111149.
26. Schonstrom N, Bolender NF, Spengler DM, Hansson TH. Pressure changes within the cauda equina following constriction of the dural sac. An in vitro experimental study. *Spine*. 1984;9(6):604–607. https://doi.org/10.1097/00007632-198409000-00011.
27. Schonstrom N, Hansson T. Pressure changes following constriction of the cauda equina. An experimental study in situ. *Spine*. 1988;13(4):385–388. https://doi.org/10.1097/00007632-198804000-00001.
28. Schonstrom N, Lindahl S, Willen J, Hansson T. Dynamic changes in the dimensions of the lumbar spinal canal: an experimental study in vitro. *J Orthop Res*. 1989;7(1):115–121. https://doi.org/10.1002/jor.1100070116.
29. Ogikubo O, Forsberg L, Hansson T. The relationship between the cross-sectional area of the cauda equina and the preoperative symptoms in central lumbar spinal stenosis. *Spine*. 2007;32(13):1423–1428. https://doi.org/10.1097/BRS.0b013e318060a5f5. discussion 1429.
30. Krzastek SC, Bruch WM, Robinson SP, Young HF, Klausner AP. Characterization of lower urinary tract symptoms in patients with idiopathic normal pressure hydrocephalus. *Neurourol Urodyn*. 2017;36(4):1167–1173. https://doi.org/10.1002/nau.23084.
31. Sone A, Moda Y, Koyama K, Tanaka H. Voiding dysfunctions in patients with lumbar spinal canal stenosis. *Nihon Hinyokika Gakkai Zasshi*. 1994;85(4):611–615. https://doi.org/10.5980/jpnjurol1989.85.611.
32. De Villiers PD, Booysen EL. Fibrous spinal stenosis. A report on 850 myelograms with a water-soluble contrast medium. *Clin Orthop Relat Res*. 1976;115:140–144.
33. Fanuele JC, Birkmeyer NJ, Abdu WA, Tosteson TD, Weinstein JN. The impact of spinal problems on the health status of patients: have we underestimated the effect? *Spine*. 2000;25(12):1509–1514. https://doi.org/10.1097/00007632-200006150-00009.
34. Yabuki S, Fukumori N, Takegami M, et al. Prevalence of lumbar spinal stenosis, using the diagnostic support tool, and correlated factors in Japan: a population-based study. *J Orthop Sci*. 2013;18(6):893–900. https://doi.org/10.1007/s00776-013-0455-5.
35. Rubin DI. Epidemiology and risk factors for spine pain. *Neurol Clin*. 2007;25(2):353–371. https://doi.org/10.1016/j.ncl.2007.01.004.
36. Uemura K, Shimada H, Makizako H, et al. Cognitive function affects trainability for physical performance in exercise intervention among older adults with mild cognitive impairment. *Clin Interv Aging*. 2013;8:97–102. https://doi.org/10.2147/CIA.S39434.

37. Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the Timed up & Go Test. *Phys Ther*. 2000; 80(9):896–903.
38. Stienen MN, Maldaner N, Joswig H, et al. Objective functional assessment using the "Timed up and Go" test in patients with lumbar spinal stenosis. *Neurosurg Focus*. 2019;46(5):E4. https://doi.org/10.3171/2019.2.FOCUS18618.
39. Inui Y, Doita M, Ouchi K, Tsukuda M, Fujita N, Kurosaka M. Clinical and radiologic features of lumbar spinal stenosis and disc herniation with neuropathic bladder. *Spine*. 2004;29(8):869–873. https://doi.org/10.1097/00007632-200404150-00009.
40. Naylor RM, Lenartowicz KA, Graff-Radford J, et al. High prevalence of cervical myelopathy in patients with idiopathic normal pressure hydrocephalus. *Clin Neurol Neurosurg*. 2020;197, 106099. https://doi.org/10.1016/j.clineuro.2020.106099.