Acta Neurochirurgica (2021) 163:767–769
https://doi.org/10.1007/s00701-020-04700-3

EDITORIAL (BY INVITATION)

Predicting the outcome of normal pressure hydrocephalus therapy—where do we stand?

Joachim M. K. Oertel[1] · Matthias J. M. Huelser[1]

Received: 23 December 2020 / Accepted: 28 December 2020 / Published online: 20 January 2021

Normal-pressure hydrocephalus (NPH) is a treatable disease. It is the only form of dementia for which we do have effective treatment modalities. Permanent cerebrospinal fluid diversion via shunt insertion is the gold standard. The objective response to the shunt treatment is about 85% [6], at least for a certain time. The majority of patients (85 %) respond to this treatment, but what about the other 15%? How can we predict which patient will respond to treatment and who will not?

Well, the first step consists of being certain about the correct diagnosis, which can be tricky since the pathophysiology of NPH remains not entirely understood. Then, the most challenging aspect is to decide which patient will respond and who will not.

There are plenty of studies investigating the predictors of shunt response.

First of all, what about acquired risk factors? The existence of more than one cardiovascular risk factor seems to be a reliable clinical predictor for a negative outcome in normal pressure hydrocephalus [9]. Solely, age does not account as a risk factor [9, 11].

Commonly, the most important positive predictors for treatment response are considered to be the spinal tab test or continuous lumbar drainage. Even though, the only blinded prospective study on this subject demonstrated a positive predictive value of 88%, but also a negative predictive value of 18% [23]. This results only in an overall accuracy of 53% [6, 23]. Furthermore, continuous lumbar drainage over a few days shows very high positive predictive values, but it has also low negative predictive values [14], so in conclusion, a response to a lumbar drainage test correlates well with a positive response to shunt treatment [8], but a non-response should not exclude the patient from treatment [23], so this nonresponsive patient cohort should be subject to further investigations.

What about radiological findings predicting a treatment response? One study investigated 168 patients with normal pressure hydrocephalus for an association of certain radiological signs, such as disproportionately enlarged subarachnoid space hydrocephalus (DESH) sign, Evans-index, and callosal angle (CA), with the patient outcome after shunt treatment. In this study, no correlation between MRI findings and outcome could be demonstrated [1]. Additionally, the absence or presence of periventricular hyperintensities did not seem to correlate [10].

Although some evidence exists that the DESH sign correlates with a positive response to shunt therapy [7, 22], augmented postischaemic lacunes may imply a rather worse patient outcome [7].

In addition, in a study from 2014, the authors could show that a preoperative steeper CA correlated with a better response to surgery [21].

Similarly, the findings of Mantovani et al. that will be presented in the following demonstrated in their recent study with a statistically significant correlation of the so-called anterior callosal angle (ACA) with an improvement of gait and balance.

Furthermore, three studies with a fair amount of scientific evidence were able to relate a higher aqueduct velocity with positive responsiveness, especially in cases where a cerebrospinal infusion test had been pathological [2, 5, 16].

Furthermore, the reactivity of cerebral blood flow to acetazolamide (measured in prospective study via SPECT) seems to correlate significantly with a response to shunt treatment [3].

Measurement of ICP dynamics is an invasive but useful modality to clarify the question of responsiveness to treatment. Increased outflow resistance during a CSF infusion test seems to be a predictor [13, 19, 23]. Furthermore, pulsatile ICP like pulse pressure amplitudes and vasogenic slow waves can be used for forecasting treatment success [18, 20].

Lastly, there remains the question of whether or not patients with Alzheimer's disease as comorbidity (up to 19% of cases [17]) to NPH are eligible for shunt treatment? This

✉ Joachim M. K. Oertel
Joachim.oertel@uks.eu

[1] Department of Neurosurgery, Saarland University Medical Center and Saarland University Faculty of Medicine, Homburg, Saar, Germany

cannot be answered at this point sufficiently [12, 15]. There is some evidence that phospho-tau as a CSF biomarker seems to have a predictive value for higher postoperative morbidity but on the contrary, there is also data suggesting that patients with comorbid neurodegenerative diseases responded well to shunt treatment [4], but how does this scientific data translate into clinical practice?

In our opinion, the first step is performing a spinal tab test on patients with typical clinical signs and imaging findings for NPH. A special focus should be on the CA, in particular the ACA, when evaluating such as patient imaging. In cases of clinical improvement after spinal tab testing, shunt replacement therapy can be recommended, regardless of supposedly negative predictors. In cases of nonresponsiveness or contraindications for spinal tab testing, further diagnostic investigations such as SPECT imaging, measurement of aqueduct velocity or CSF infusion test, depending on the individual center expertise, may be helpful. In our center, ICP dynamics via telemetric measurement has proven to be a very valuable tool in such cases. In conclusion, despite there being negative predictors for shunt therapy, it is important that one weighs the positive against the negative predictors in individual decision-making for shunt surgery, and that the value of negative predictors should not be overestimated and therefore result in a patient not receiving adequate therapy.

Funding Open Access funding enabled and organized by Projekt DEAL.

References

1. Agerskov S, Wallin M, Hellstrom P, Ziegelitz D, Wikkelso C, Tullberg M (2019) Absence of disproportionately enlarged subarachnoid space hydrocephalus, a sharp callosal angle, or other morphologic mri markers should not be used to exclude patients with idiopathic normal pressure hydrocephalus from shunt surgery. AJNR Am J Neuroradiol 40:74–79. https://doi.org/10.3174/ajnr.A5910
2. Al-Zain FT, Rademacher G, Meier U, Mutze S, Lemcke J (2008) The role of cerebrospinal fluid flow study using phase contrast MR imaging in diagnosing idiopathic normal pressure hydrocephalus. Acta Neurochir Suppl 102:119–123. https://doi.org/10.1007/978-3-211-85578-2_24
3. Chang CC, Asada H, Mimura T, Suzuki S (2009) A prospective study of cerebral blood flow and cerebrovascular reactivity to acetazolamide in 162 patients with idiopathic normal-pressure hydrocephalus. J Neurosurg 111:610–617. https://doi.org/10.3171/2008.10.17676
4. Craven CL, Baudracco I, Zetterberg H, Lunn MPT, Chapman MD, Lakdawala N, Watkins LD, Toma AK (2017) The predictive value of T-tau and AB1–42 levels in idiopathic normal pressure hydrocephalus. Acta Neurochir 159:2293–2300. https://doi.org/10.1007/s00701-017-3314-x
5. Dixon GR, Friedman JA, Luetmer PH, Quast LM, McClelland RL, Petersen RC, Maher CO, Ebersold MJ (2002) Use of cerebrospinal fluid flow rates measured by phase-contrast MR to predict outcome of ventriculoperitoneal shunting for idiopathic normal-pressure hydrocephalus. Mayo Clin Proc 77:509–514. https://doi.org/10.4065/77.6.509
6. Halperin JJ, Kurlan R, Schwalb JM, Cusimano MD, Gronseth G, Gloss D (2015) Practice guideline: idiopathic normal pressure hydrocephalus: Response to shunting and predictors of response: report of the guideline development, dissemination, and implementation subcommittee of the American Academy of Neurology. Neurology 85:2063–2071. https://doi.org/10.1212/WNL.0000000000002193
7. Hong YJ, Kim MJ, Jeong E, Kim JE, Hwang J, Lee JI, Lee JH, Na DL (2018) Preoperative biomarkers in patients with idiopathic normal pressure hydrocephalus showing a favorable shunt surgery outcome. J Neurol Sci 387:21–26. https://doi.org/10.1016/j.jns.2018.01.017
8. Ishikawa M, Yamada S, Yamamoto K (2016) Early and delayed assessments of quantitative gait measures to improve the tap test as a predictor of shunt effectiveness in idiopathic normal pressure hydrocephalus. Fluids Barriers CNS 13:20. https://doi.org/10.1186/s12987-016-0044-z
9. Kiefer M, Eymann R, Steudel WI (2006) Outcome predictors for normal-pressure hydrocephalus. Acta Neurochir Suppl 96:364–367. https://doi.org/10.1007/3-211-30714-1_75
10. Kilic K, Czorny A, Auque J, Berkman Z (2007) Predicting the outcome of shunt surgery in normal pressure hydrocephalus. J Clin Neurosci 14:729–736. https://doi.org/10.1016/j.jocn.2006.03.028
11. Marmarou A, Young HF, Aygok GA, Sawauchi S, Tsuji O, Yamamoto T, Dunbar J (2005) Diagnosis and management of idiopathic normal-pressure hydrocephalus: a prospective study in 151 patients. J Neurosurg 102:987–997. https://doi.org/10.3171/jns.2005.102.6.0987
12. McGovern RA, Nelp TB, Kelly KM, Chan AK, Mazzoni P, Sheth SA, Honig LS, Teich AF, McKhann GM (2019) Predicting cognitive improvement in normal pressure hydrocephalus patients using preoperative neuropsychological testing and cerebrospinal fluid biomarkers. Neurosurgery 85:E662–E669. https://doi.org/10.1093/neuros/nyz102
13. Nabbanja E, Czosnyka M, Keong NC, Garnett M, Pickard JD, Lalou DA, Czosnyka Z (2018) Is there a link between ICP-derived infusion test parameters and outcome after shunting in normal pressure hydrocephalus? Acta Neurochir Suppl 126:229–232. https://doi.org/10.1007/978-3-319-65798-1_46
14. Panagiotopoulos V, Konstantinou D, Kalogeropoulos A, Maraziotis T (2005) The predictive value of external continuous lumbar drainage, with cerebrospinal fluid outflow controlled by medium pressure valve, in normal pressure hydrocephalus. Acta Neurochir (Wien) 147:953–958; discussion 958. https://doi.org/10.1007/s00701-005-0580-9
15. Pfanner T, Henri-Bhargava A, Borchert S (2018) Cerebrospinal fluid biomarkers as predictors of shunt response in idiopathic normal pressure hydrocephalus: a systematic review. Can J Neurol Sci 45:3–10. https://doi.org/10.1017/cjn.2017.251

16. Poca MA, Sahuquillo J, Busto M, Rovira A, Capellades J, Mataro M, Rubio E (2002) Agreement between CSF flow dynamics in MRI and ICP monitoring in the diagnosis of normal pressure hydrocephalus. Sensitivity and specificity of CSF dynamics to predict outcome. Acta Neurochir Suppl 81:7–10. https://doi.org/10.1007/978-3-7091-6738-0_2
17. Pomeraniec IJ, Bond AE, Lopes MB, Jane JA Sr (2016) Concurrent Alzheimer's pathology in patients with clinical normal pressure hydrocephalus: correlation of high-volume lumbar puncture results, cortical brain biopsies, and outcomes. J Neurosurg 124:382–388. https://doi.org/10.3171/2015.2.JNS142318
18. Santamarta D, Gonzalez-Martinez E, Fernandez J, Mostaza A (2016) The prediction of shunt response in idiopathic normal-pressure hydrocephalus based on intracranial pressure monitoring and lumbar infusion. Acta Neurochir Suppl 122:267–274. https://doi.org/10.1007/978-3-319-22533-3_53
19. Sorteberg A, Eide PK, Fremming AD (2004) A prospective study on the clinical effect of surgical treatment of normal pressure hydrocephalus: the value of hydrodynamic evaluation. Br J Neurosurg 18:149–157. https://doi.org/10.1080/02688690410001681000
20. Stephensen H, Andersson N, Eklund A, Malm J, Tisell M, Wikkelso C (2005) Objective B wave analysis in 55 patients with non-communicating and communicating hydrocephalus. J Neurol Neurosurg Psychiatry 76:965–970. https://doi.org/10.1136/jnnp.2004.039834
21. Virhammar J, Laurell K, Cesarini KG, Larsson EM (2014) The callosal angle measured on MRI as a predictor of outcome in idiopathic normal-pressure hydrocephalus. J Neurosurg 120:178–184. https://doi.org/10.3171/2013.8.JNS13575
22. Virhammar J, Laurell K, Cesarini KG, Larsson EM (2014) Preoperative prognostic value of MRI findings in 108 patients with idiopathic normal pressure hydrocephalus. AJNR Am J Neuroradiol 35:2311–2318. https://doi.org/10.3174/ajnr.A4046
23. Wikkelso C, Hellstrom P, Klinge PM, Tans JT, European i NPHMSG (2013) 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 84:562–568. https://doi.org/10.1136/jnnp-2012-303314