P43

CSF tau levels predict long-term outcome of patients with idiopathic normal pressure hydrocephalus: a longitudinal retrospective study

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Introduction: Idiopathic normal pressure hydrocephalus (iNPH) is a neurodegenerative condition burdened by diagnostic uncertainty and challenging therapeutic options, including the shunt surgery [1]. Cerebrospinal fluid (CSF) biomarkers reflect brain neuropathology, facilitating the diagnosis and the prognostic predictions. iNPH is lacking a disease-specific CSF biomarker [2]; however, a panel of neurodegeneration-related CSF biomarkers might support patients stratification and the subsequent therapeutic strategies.

Objectives: To predict long-term clinical outcome of iNPH patients through a panel of neurodegeneration-related CSF biomarkers.

Methods: We conducted a single-centre retrospective study over an 8 year-long period, identifying 32 iNPH patients with CSF biomarkers (amyloid-β-42, phosphorylated-181-tau, total-tau). Nineteen patients had a long-term follow-up (5 years at least). The clinical assessment was conducted at baseline through the iNPH grading scale (INPHGS) [3] and the modified Ranking Scale (mRS) [4]. At follow-up patients were staged with the mRS and grouped in "poor outcome" (mRS≥5) and "positive outcome" (mRS<5).

Results: "Poor outcome" iNPH patients presented CSF total-tau levels higher than "positive outcome" group (mean±st.dev.:300.58±114.10pg/ml vs.175.69±94.57pg/ml, p=0.041), also in a model adjusted for age (p=0.037). There were no significant differences in the amyloid-β-42 (mean±st.dev.: 719.86 ± 354.16pg/ml vs. 618.64 ± 240.51pg/ml, p=0.717), and phosphorylated-181-tau (mean±st.dev.:42,48 ± 20,63pg/ml vs. 33,52 ± 26,73pg/ml, p=0.237) levels. Receiver operating characteristic analysis provided for CSF total-tau an area under the curve of 0.778 with the cut-off value of 202.5 pg/mL allowing distinguishing the clinical outcome with a sensitivity of 75% and a specificity of 72.7%. At baseline CSF t-tau levels directly correlated with iNPHGS cognitive subscore (Spearman Rho 0.508, p=0.026).

Conclusions: CSF levels of total-tau mirror brain neuronal loss [5]. Although nonspecific for iNPH pathology, CSF total-tau seems to support the identification of frailer iNPH patients. Higher total-tau levels could predict a long-term poor clinical outcome (severe disability or death) independently from the surgery, helping physicians in therapeutic management of iNPH patients.

References:

[1] Giordan E, Palandri G, Lanzino G, Murad MH, Elder BD. Outcomes and complications of different surgical treatments for idiopathic normal pressure hydrocephalus: A systematic review and meta-analysis. J Neurosurg. 2019;131(4):1024-1036. doi:10.3171/2018.5.JNS1875.

[2] Blennow K. Cerebrospinal Fluid Protein Biomarkers for Alzheimer's Disease. NeuroRx. 2004;1(2). doi:10.1602/neurorx.1.2.213.

[3] Kubo Y, Kazui H, Yoshida T, et al. Validation of grading scale for evaluating symptoms of idiopathic normal-pressure hydrocephalus. Dement Geriatr Cogn Disord. 2007;25(1). doi:10.1159/000111149.

[4] Banks JL, Marotta CA. Outcomes validity and reliability of the modified rankin scale: Implications for stroke clinical trials - A literature review and synthesis. Stroke. 2007;38(3). doi:10.1161/01.STR.0000258355.23810.c6.

[5] Migliorati K, Panciani PP, Pertichetti M, et al. P-Tau as prognostic marker in long term follow up for patients with shunted iNPH. Neurol Res. 2021;43(1):78-85. doi:10.1080/01616412.2020.1831300.