Title: Perioperative concentrations of neurofilament light (NfL) in serum and cognitive trajectories 6 months after cardiac surgery: A secondary analysis of a prospective observational trial.
(Brief title: Perioperative serum NfL and long-term cognition after cardiac surgery)

Author(s): Conreur C, Momeni M, Khalifa C

Hospital/Institute: Department of Anesthesiology
Cliniques universitaires Saint-Luc
Avenue Hippocrate, 10
1200 Brussels (Belgium)

Objective: To study the cognitive trajectories of cardiac surgery patients 6 months postoperatively, and evaluate whether higher perioperative concentrations of serum NfL, a biomarker of axonal injury, are associated with a decline in cognition.

Background: Higher concentrations of serum NfL (at baseline and postoperatively) have been associated with an increased risk of postoperative delirium.[1] Recently, a study suggested that the perioperative course of serum NfL might also be a predictor of cognitive status up to 1 year after surgery.[2]

Methods: This is a secondary analysis of a prospective observational study (NCT03706989) including 220 adult patients undergoing elective cardiac surgery under cardiopulmonary bypass. Written informed consent was obtained. Patients completed a Mini-Mental State Evaluation (MMSE) the day before surgery. Serum NfL quantification was performed using Single Molecule Array technology. From the initial protocol, only baseline and postoperative day 1 measurements were considered for this analysis. A Telephone Interview for Cognitive Status-Modified version (TICS-M)[3] test was submitted to the patients 6 months postoperatively. MMSE and TICS-M scores were divided into quartiles allowing intra-individual comparisons between preoperative and postoperative results. NfL values were log-transformed to obtain normally distributed data. Linear regression analyses assessed the relationship between the change in cognition [6 months after surgery – baseline] and (1) logNfL at baseline, (2) logNfL at day 1, (3) absolute change [logNfL at day 1 – logNfL at baseline]. Wilcoxon rank sum test was used to compare postoperative to baseline cognitive tests. Continuous variables are expressed in means ± SD or medians (P_{25}, P_{75}). Categorical variables are expressed in numbers (%). A *P*-value <0.05 was considered statistically significant.

Results: 197 patients (89.5%) completed the TICS-M. Patients' characteristics are detailed in Table 1. The median concentration of serum NfL was 15.6 pg ml^{-1} (10.6, 22.6) at baseline and 20.9 pg ml^{-1} (14.6, 30.8) at day 1. At 6 months, 86/197 patients (43.7%) presented a stable cognitive status, 62 (31.5%) had a cognitive decline and 49 (24.8%) a cognitive improvement. There was no significant association between the change in cognition and logNfL at baseline (β [95% CI], -0.06 [-0.71 to 0.60]; *P*=0.865), logNfL at day 1 (β [95% CI], -0.06 [-0.75 to 0.63]; *P*=0.865), or the difference (day 1 – baseline) (β [95% CI], 0.007 [-0.96 to 0.97]; *P*=0.989).

Table 1

Age, years	69 (60, 76)
Low educational level (< 9 years)	59 (29.2) (n=202)
GFR, ml min^{-1}	76 (60, 88)
EuroSCORE II, %	1.69 (0.96, 2.76)
Surgical time, min	230 ± 58
Cardiopulmonary bypass time, min	103 ± 36
Length of hospital stay, days	8 (7, 10)

(number of patients with available data are mentioned between brackets)

Conclusions: A majority of our patients presented at least a stabilization of their cognitive status 6 months after surgery. Higher concentrations of serum NfL were not associated with a decline in cognition.

By submitting this abstract, the first author certifies that all authors agree on its content and on its submission.

References:
(1) Fong TG, Vasunilashorn SM, Ngo L, *et al*; SAGES Study Group. Association of plasma neurofilament light with postoperative delirium. *Ann Neurol* 2020;**88**(5):984-994.
(2) Brown CH, Lewis A, Probert J, *et al*. Perioperative neurofilament light plasma concentrations and cognition before and after cardiac surgery: A prospective nested cohort study. *Anesthesiology* 2022;**137**(3):303-314.
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