

Postoperative delirium (POD) in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) is associated with higher perioperative serum levels of neurofilament light (NfL)

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Background – Postoperative delirium (POD) significantly increases perioperative morbidity and mortality. The underlying pathophysiological mechanisms of POD have not been fully elucidated so far.

In addition to perioperative episodes of cerebral hypoxia and/or hypoperfusion, neuroinflammation and a direct insult to the brain, induced by both anaesthesia and surgery may play a role.

In current clinical practice, the ideal biomarker, highly sensitive for brain injury, as well as highly specific for neuronal tissue, has not been determined yet.

Recently, much focus has been given to perioperative serum levels of neurofilament light (NfL), a subunit of the neurofilaments^{1,2}, as they are part of the scaffolding of axons and so, exclusively expressed by neuronal tissues.

Objectives – The specific objective of this preliminary analysis is to seek whether perioperative serum levels of NfL were higher in patients presenting POD, compared to those who did not experience it.

Materials & Methods – This preliminary overview is part of an ongoing research project (NCT03706989). So far, we have analysed the first 130 included adult patients who underwent an elective cardiac surgery with CPB under sevoflurane anaesthesia. In total, 220 patients are going to be included.

For every patient, 5 iterative blood samples were collected (before anaesthesia, 2 hours after admission in ICU, postoperative day 1, day 2 and day 5).

References - ¹Evered L. JAMA Neurol 2018;75:542-547, ²Casey CP. Brain 2020;143(1):47-54

Quantitative determination of NfL in serum was performed using a single-molecule array method (SiMoA®). Results with a coefficient of variance > 20% were repeated.

POD was assessed in ICU using the CAM-ICU, after an evaluation of the level of consciousness by the RASS (Richmond Agitation and Sedation Scale). At the ward, the CAM, in combination with a flow chart review, were used to screen any episode of POD until hospital discharge.

	POD – (n = 93)	POD + (n = 37)	p
Age, y	68 (58-76)	74 (65-79)	0.007
Male sex, %	82.8	73	0.206
Euroscore II, %	1.5 (0.9-2.42)	2.35 (1.28-3.7)	0.009
Open heart surgery, %	52.7	62.2	0.327
CPB time, min	94 (72-112)	107 (81-133)	0.044

Table 1 – Characteristics of the population

Statistical analysis – Continuous variables are expressed as median (P₂₅-P₇₅). A Mann-Whitney U test and a Chi square test were used to compare data between patients with and without POD. NfL results were log-transformed to obtain normally distributed data and a Student t-test was used for comparison between both groups.

A linear mixed model was performed to evaluate the impact of age and time on NfL levels. A repeated General Linear Model (GLM) was used to evaluate NfL levels over time. A binary regression analysis was used to predict POD including age and each NfL value that showed a significant difference in univariate analysis.

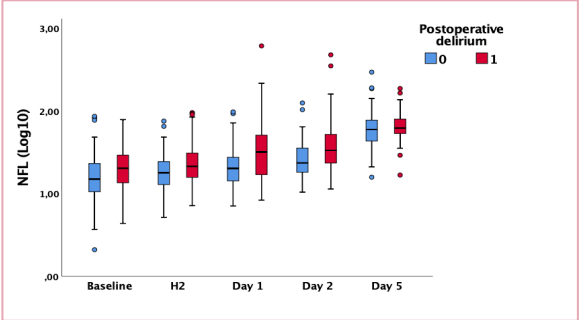


Figure 1 – Perioperative NfL values in serum (log-transformed results)

Results – 37 patients (28%) developed POD. They were significantly older and had a higher EuroSCORE II (Table 1). Age had a significantly effect on NfL values (p < 0.001). For all patients, perioperative NfL levels increased significantly over time after surgery (p < 0.001) (Figure 1).

Figure 2 (repeated GLM) shows that, over time, NfL levels were significantly higher in patients with POD, except at day 5 (p = 0.33; Student t-test).

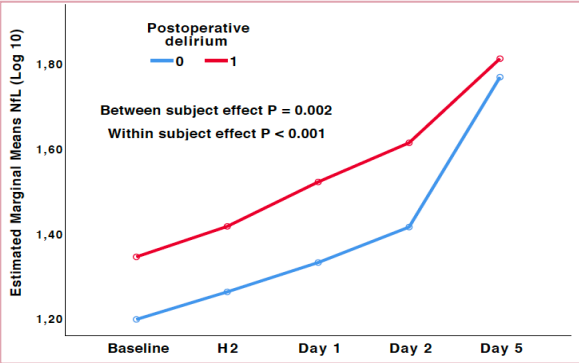


Figure 2 – Repeated GLM for NfL values (log-transformed results)



In univariate analysis, all perioperative NfL levels, except those at day 5, were significantly associated with POD.

When taking account for age > 74 years old (median age of patients presenting POD), we found that NfL values at 2 hours after admission in ICU, at day 1 and day 2 were significantly associated with the occurrence of POD, as detailed in Table 2.

	OR (95% CI)	p
NfL H2 (log ¹⁰)	6.92 (1.34-35.81)	0.02
Age > 74y	1.81 (0.8-4.06)	0.15
NfL day 1 (log ¹⁰)	7.56 (1.7-33.6)	0.008
Age > 74y	1.76 (0.77-4)	0.18
NfL day 2 (log ¹⁰)	10.08 (2.01-50.63)	0.005
Age > 74y	1.75 (0.77-3.99)	0.18

Table 2 – Binary regression analysis predicting POD

Conclusions – Our preliminary results indicate that NfL concentrations in serum significantly increase after cardiac surgery and are, in general, higher in patients with POD. These results also demonstrate that, independently from age, early postoperative NfL levels in serum are associated with higher odds of developing POD.

