

Does apolipoprotein E (APOE) genotype influence the occurrence of postoperative delirium (POD) in cardiac surgical patients developing higher postoperative systemic inflammation?

A secondary analysis of a prospective observational study

Khalifa C.¹, Ivanoiu A.², Bonhomme V.³, Momeni M.¹

¹Department of Anaesthesiology, Cliniques universitaires Saint-Luc, Brussels, Belgium, ²Department of Neurology, Cliniques universitaires Saint-Luc, Brussels, Belgium, ³Department of Anaesthesiology, Centre Hospitalier Universitaire de Liège, Liège, Belgium

Background – Postoperative delirium (POD) is a common complication after cardiac surgery. However, predicting the occurrence of POD remains challenging, as its leading causes have not been completely elucidated yet.

Among predisposing factors, age and pre-existing cognitive impairment are the most important ones. It has been suggested that POD shares some epidemiologic characteristics with Alzheimer's disease (AD).¹ Although APOE ϵ 4 genotype is a well-known genetic risk factor of AD, current literature failed to demonstrate a direct association between APOE ϵ 4 carrying and a higher risk of experiencing POD.

Recently, a study pointed to a potential indirect influence of APOE genotype : the «gene-protein interaction» concept.² Indeed, the authors suggested that APOE ϵ 4 carriers might be at higher risk of POD under specific circumstances, such as whenever they develop an important postoperative systemic inflammation.

Objective – The aim of this study was to evaluate whether there was an indirect influence of APOE ϵ 4 genotype on the relationship between the occurrence of POD and higher postoperative levels of C-reactive protein (CRP) in the specific context of cardiac surgery.

Methods – This is a secondary analysis of a prospective observation study (NCT03706989) on predictive factors of POD in cardiac surgery. We included 220 adult patients who underwent a first elective cardiac surgery with cardiopulmonary bypass (CPB).

For each enrolled patient, a blood sample for APOE genotyping was collected during the hospital stay. Patients were classified as APOE ϵ 4 (+) when they presented at least one ϵ 4 allele. Postoperative CRP levels in serum were monitored according to local standard protocols and the peak of CRP was recorded for every patient. CRP levels were considered high when > P₇₅ of the entire cohort.

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 flowchart review, were used to screen any episode of POD until hospital discharge

Statistical analysis – Comparisons between groups were performed using a Chi-square test for dichotomous variables and a Mann-Whitney U test or a Student t-test for continuous variables, depending on normality assumption. A p-value < 0.05 was considered statistically significant.

Results – The incidence of POD was 29.5% (65/220 patients). Patients' characteristics and intraoperative data are detailed in Table 1. POD (+) patients were significantly older and had higher EuroSCORE II scores. There was no difference regarding the types of surgery between both groups (p = 0.180). However, POD (+) patients had higher CPB time than patients who did not develop POD.

	POD – (n = 155)	POD + (n = 65)	p
Age, y	67 (59-74)	74 (64-79)	<0.001
Sex, male	128 (82.6)	52 (80.0)	0.651
EuroSCORE II, %	1.50 (0.88-2.53)	2.43 (1.32-3.99)	<0.001
MMSE, /30	29 (27-29)	28 (26-29)	0.047
Surgical time, min	226 ± 57	238 ± 60	0.170
CPB time, min	99 ± 33	112 ± 40	0.015

Table 1 – Patients' characteristics and intraoperative data. Data are expressed as mean (± SD), medians (P₂₅-P₇₅) or numbers (%). MMSE = Mini Mental State Examination

The distribution of APOE genotypes throughout the cohort is shown in Figure 1. In total, 53 patients were APOE ϵ 4 (+) (24%). Among them, 14 developed POD. No direct association between APOE ϵ 4 genotype and the occurrence of POD was found (p = 0.56). Classification of APOE ϵ 4 (+) patients according to POD and the peak of postoperative CRP levels is shown in Table 2. Ten of the APOE ϵ 4 delirious patients (71.4%) reached the highest CRP level, but the correlation was not statistically significant (p = 0.104).

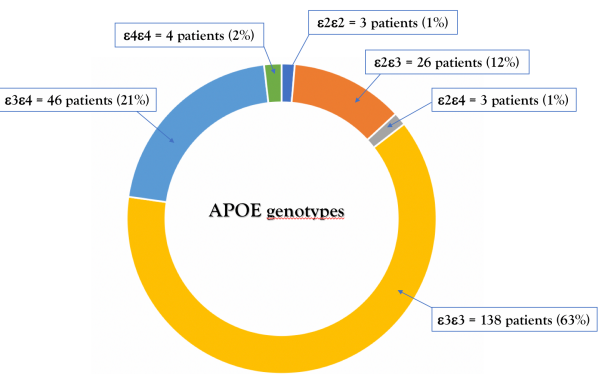


Figure 1 – Distribution of APOE genotypes in the population.

	APOE ϵ 4 (+) POD (-) (n = 39)	APOE ϵ 4 (+) POD (+) (n = 14)
CRP (mg/dl) < P ₇₅	21 (53.8)	4 (28.6)
CRP (mg/dl) > P ₇₅	18 (46.2)	10 (71.4)

Table 2 – Classification of APOE ϵ 4 patients according to POD and CRP. Data are expressed as numbers (%)

Conclusions – Results of this underpowered observational study suggest that APOE ϵ 4 might indirectly potentialise the risk of POD after cardiac surgery conferred by a higher postoperative systemic inflammation. Further studies are needed to investigate this «gene-protein interaction» concept.