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ASSOCIATION BETWEEN DELIRIUM AND COGNITIVE CHANGE AFTER CARDIAC SURGERY

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Abstract:

Introduction: *Previous reports have provided incoherent evidence on whether postoperative delirium (POD) is a risk factor for POCD. We have thus analysed the relationship between POD and cognitive change after heart surgery and we have assessed how POD is related to preoperative cognitive domain values.* ***Methods****: The Confusion Assessment Method (CAM) for the Intensive Care Unit and traditional CAM, along with the chart analysis, were evaluated in postoperative delirium. Before elective heart surgery and 1 month or 1 year after, the cognitive function was tested with a neuropsychological test battery. The Reliable Change Index (RCI) was used to calculate cognitive change. To correct for uncertainty, multiple linear regression was used. Results: 23 (12.5 per cent) of the 184 patients who completed the baseline assessment developed PODs. At 1 month, the decrease in cognitive performance was worse in POD [median composite RCI1.00, interquartile range (IQR) 1.67 to 0.28] patients than in POD-free patients (RCI0.04, IQR0.70 to 0.63, P1/40.02). At 1yr, both groups showed average cognitive improvement compared to baseline (POD median RCI 0.25, IQR 0.42 to 1.31, compared to non-POD patients RCI 0.92, IQR 0.18–1.53; P1/40.08). The correction of differences in age and level of education did not change the results. Patients with POD performed less well on the preoperative Trail making test part A (P1/40.03) than patients without POD.* ***Conclusion:*** *Postoperative delirium is independently associated with cognitive impairment 1 month after surgery but typically improves cognitive function within 1yr. Patients with POD predisposition may be identified by worse performance in the attention task prior to surgery.*

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INTRODUCTION:

Transient cognitive impairment and post-operative delirium are the common complications after surgery (1). Older populations undergoing cardiac surgery are more likely to experience both of these complications due to other co-morbidities such as hypertension, diabetes, and previous myocardial infarction. There is more likely to be PCD and POCD less knowledge of the disorder and diminished executive ability, but the predisposing causes for these disorders are also being debated and not fully clarified. (2)

There is very limited literature available about the predictive value of impairment in specific cognitive areas. The proof that POD increases the risk of POCD and vice versa is consistent. Two interaction studies were performed in elderly orthopaedic and cardiac surgery patients with POD and POCD (3). The Mini-mental state test as a regional assessment of the cognitive function was used for the both studies (4).

Moreover, it is unclear how postoperative cognitive function evolves over time in relation to the magnitude of the change, changes in the cognitive function as a whole and changes in various cognitive fields (5). The main objective of this study was to analyse the connection between POD and POCD 1 month after heart surgery, to assess it through a neuropsychological testing battery and to compare it to the neuropsychology testing output pre-operatively. However, we have long since agreed upon the requirement to detect POCD reliably after cardiac operation with a battery of neuropsychological tests (6).

Furthermore, we examined the relationship between POD and POCD in 1 year, how this influenced differentially other cognitive field scores over time, and increasing preoperative cognitive profile predisposed patients to cardiac surgery to develop POD.

METHODS:

Study design and participants:

For this clinical trial, we used a subset of data from the ClinicalTrials.gov (NCT00293592) cardiac surgery (DECS) study. This multicentre, double-blind, placebo-controlled trials randomized a single high dose of dexamethasone, 1 mg kg1 i.v injection with a max. 100 mg cardiac surgery or placebo in the duration of the anaesthetics induction, to 4,494 patients 18 years or older with cardiopulmonary bypass surgery (7). In the case of a major adverse effect, a mortality combination, myocardial infarction (MI), a stroke, a renal insufficiency or respiratory failure, in contrast to placebo was not reduced by the use of intra operating dexamethasone.

The nature of the study and primary findings were previously discussed. There are two sub-studies of the DECS report which are based on data from this report (8). The first study consisted of the influence of dexamethasone on the incidence of POD, in which the 768 patients enrolled at the DECS check at the University Medical Centre were collected from June 20017 to November 2019. Secondly, a preplanned sub-study of the dexamethasone effect on POCD in the DECS trial (9).

291 patients completed baseline cognitive skill evaluations between August 2016 and October 2017 (of the 340 patients who received informed consent, six of whom were unable to complete baseline neuropsychology tests, and 43 were unable to do so on logistical grounds). Among these 291 patients 184 have participated in a sub-study on delirium (10).

It appears that Dexamethasone does not affect POD and POCD. All 184 patients who took part in and completed both the (EDS / CFT) studies were included in this cohort to evaluate the relationship between post-operative delirium and cognitive change following cardiac surgery (11). The results of this cohort include Additional exclusion criteria is evident mental diseases or vision, hearing, or engine ability (i.e. hemiplegia). For this additional study. Dexamethasone showed no effect on POD and POCD.

The DECS research database prospectively gathered data on patient, health, and surgical characteristics. The University Medical Centre's Medical Ethics Committee approved this study, and all patients received written, informed consent. To identify true cognitive impairment beyond normal variability in test results, we recruited a group of volunteers with reported coronary artery or valve pathology from the cardiology outpatient clinic as control subjects but without elective surgery. The same neuropsychological evaluation battery and procedure was used in this study by the same investigators as the participants in the trial, evaluating attention twice with an interval of 1 month.

Delirium assessment:

The Delirium was assessed using a previously validated method by trained research staff. It included routine assessment by a research nurse using the Confusion Assessment Method (CAM) modified for ICU (CAM-ICU) in the ICU setting, the CAM when the patient was moved to the ward, a chart analysis of the previous 24 hours to identify key indicative words of delirium (e.g. distressed, irritated, somnolent, disoriented, delirious), the outcomes of twice-daily CAM (-ICU) evaluations support the results of the CAM (-ICU) evaluations. If there is one such predictor, the patient was graded delirious. In the Richmond Agitation Sedation Scale (RASS) scale of 4 or 5 patients deemed to be irrational, delirium was not measured. During the first 4 days after the procedure, patients were examined as far as possible at a fixed point during the day.

Neuropsychological assessment

Cognitive function was evaluated 1 day prior to procedure (Baseline), 1 month after heart surgery and 1 year after treatment. Educated testing staff assessed patients in the hospital if necessary. Patients who were unable to come to the hospital for follow-up were able to take the neuropsychological assessments at home to improve the completeness of cognitive follow-up. Depending on patient pace, the overall test time was approximately 30 to 40 minutes.

Tests were performed on the following: Corsi block tapping (spatial memory), Rey verbal auditory learning (immediate recall (course memory) and delayed recall (intermediate verbal memory), trail making test (Part A (attention) and Part B (executive function) (12). We first calculated a z-score for each patient's crude test score by subtracting the total group mean from the individual scoring of the patient and separating the residue by the SD group to obtain a baseline cognitive score.

We have used the Jacobson and Truax's Accurate Shift Index (RCI) to track natural variability and practice effects during the follow-up of cognitive tests (13). For every single test, this approach gives the z-score by removing the baseline test score and the mean change on the control group from the following score and separating the result by the SD of the change in the control group. RCI values have been reversed for sequential tasks as mentioned above. The sum of the z-scores of the various tests was split into a control group by the SD of this sum for the composite RCI.

Study outcomes:

Changes in cognitive performance from baseline to 1 month after surgery were the principal results. The second is the assessment of cognitive ability at 1 yr. We also measured the effect of POD at 1 month and 1 year after surgery on individual cognitive tests. Finally, the connection between the presence of POD and preoperative cognitive test was investigated.

Statistical analysis:

The sample size of this retrospective study was determined by the number of 184 patients available in the DECS study, in which both the involvement of POD and cognitive competence were prospectively assessed. Continuous baseline variables were viewed as mean or median values, depending on distribution, and compared, as necessary, with Student's unpaired t-test or the Mann – Whitney U-test. Binary data were presented as percentages and analysed using the Pearson v2 test, or Fisher's exact cell count test (14). Categorical data were compared using a variance analysis. Linear regression analysis was conducted to research the relationship between POD and cognitive performance improvement at 1 month and 1 year, adapting to dexamethasone or placebo randomization, age, and educational level. We tested the intergroup discrepancy (POD vs. no POD) using logistic regression analysis and accounted for the same covariables in order to research the relationship between preoperative cognitive tests and POD. The analysis was conducted using version 21 of IBM SPSS (SPSS Inc. , Chicago, IL, United States). All observed P-values were two-sided, and a P<0.05 level of significance was used.

RESULTS:

Between August 2017 and October 2019, 184 patients participating in the delirium sub-study received a clinical evaluation of neuropsychological preoperative. Among those, 176 (95.7%) completed the 1 month follow-up, and 146 (79.3%) completed the 1 year neuropsychological follow-up. 23 (12.5 percent) of the 184 patients who completed the baseline assessment experienced delirium during their postoperative hospital stay. In the POD group, one patient died from 1 month to 1 year of follow-up (5 percent) and one rejected follow-up (5 percent), so that the total amount lost to follow-up was two (9 percent).

Patients who developed POD were significantly older, suffered from peripheral vascular disease more often, and had a higher Euro Score compared to patients who were not delirious. Except for serum creatinine and left ventricular activity, the incidence of delirium and baseline symptoms was comparable between the group of patients with full follow-up and the group without 1 year follow-up.

Postoperative delirium and postoperative scores on individual neuropsychological tests:

Changes in the grooved pegboard from baseline and the Trail making test part B differed significantly between delirious and non-delirious patients at both points of time. On the grooved pegboard, persistent decline was observed in the POD group, and initially more extreme recovery to minimal decline was seen in the Trail making test part B compared with better results on both tests in the non-delirious group.

Preoperative cognitive assessment and POD:

In the group that developed POD, consistently lower preoperative scores were recorded as compared with the group that did not. Nonetheless, these variations did not achieve statistical significance after correcting for possible confounders, with the exception of the Trail making test.

DISCUSSION:

We examined 1 month after heart surgery the relationship between POD and cognitive change and found that the cognitive output of POD patients was more declining than those without POD. However, the POD patients display a cognitive change at 1 yr, without a statistically significant difference from their preoperative baseline cognitive levels. The findings have not been affected by adjustment to disparities in age and education level (15).

These findings are consistent with previous research, indicating that POD is an independent risk factor for POCD in the immediate postoperative trajectory. Previous cognitive function studies evaluated after longer duration of follow-up were less consistent. In our study, we observed an average improvement in cognitive performance over the course of 1 year compared to baseline in patients with and without POD.

The relationship between POD and POCD is complex and not yet fully clarified. Both individuals share multiple factors of risk, such as that age , poor education and co-morbidity, as opposed to other factors suggesting a more separate (possibly causal) link between delirium and cognitive impairment, two manifestations of the same underlying mechanism of pre-existing cognitive reserve decreased (16).

In the present study, both groups showed an average cognitive improvement compared to baseline scores, but this effect was less pronounced in the delirious group. In addition, we found consistent differences between the two groups on the grooved pegboard and the Trail making test, indicating that suffering from delirium could have a particular impact on fine motor skills and executive functions.

The relationship between POD and POCD is complex and not yet fully elucidated. Both entities share many risk factors, such as increasing age, low level of education, and underlying comorbidities, and might be viewed as two expressions of the same underlying process of pre-existing decreased cognitive reserve, as opposed to other evidence supporting a more independent, possibly causal, relationship between delirium and cognitive impairment.

We find in this study lower baseline scores for all but the WAIS digit range tests for the group which developed delirium later on. After adjusting for the age and education disparity between the two groups, the Trail making test part A remained discriminative between the two groups, which may suggest that impaired attention at baseline could predispose to delirium growth. Previous research on dysfunction in different cognitive domains predictive for delirium development found an association with impairment in executive functions assessed with the Trail making test part B and with more complex executive function tasks that we could not find in this study (17).

There were many strengths to our analysis. We used a well-validated, systematic delirium identification process, integrating the findings of structured reports by study personnel with evidence from routine clinical patient care available. That has helped us to catch the condition's fluctuating existence. The availability of staff 7 days a week has helped us to eliminate missing findings and ensure full follow-up. We restricted our observation time to the first 4 days after the surgery, for logistic purposes. As a tertiary hospital, just a week of the surgery, a large portion of the patient population with uncomplicated rehabilitation returned to their referral centres. This method may have skipped the delirium which was later established in the postoperative trajectory. The impact of this limitation is likely to be small, because previous studies have shown that the vast majority of delirium in this population is clinically apparent in the first 3 days following surgery. Compared to other field work our sample population was fairly young, which may have resulted in a comparatively low occurrence of POD. However, our incidence closely matches a similar, large trial by Katz nelson and colleagues that reported an 11.9 percent incidence in 1528 cardiac patients.

Research on POCD has been hampered by the lack of consensus on strict definitions for POCD based on neuropsychological test methods.23 We chose a combination of neuropsychological tests, covering a broad range of cognitive domains vulnerable for postoperative change, including the core battery recommended by the 1995 consensus statement.10 We presented a continuous outcome to avoid arbitrary dichotomization and were able to show improvement in performance. Furthermore, we corrected for learning effects and natural fluctuation in test results by comparing our patients with a non-surgical control group who had similar characteristics.21 Loss to follow-up was low, especially at 1 month, with follow-up rate of 95.7%.

There are certain limitations in our study. In our research, the primary study and emphasis was on improving cognitive output from baseline to 1 month postoperatively. Certain empirical findings can be viewed as a generating hypothesis. A control group without intervention who may not have been subject to the same level of psychological stress , depression or both at baseline as is known to occur in cardiac surgery patients in the run-up to their intervention could have induced overcorrection in learning. We have not collected data on individual case outcomes and the perceived disability burden. So, we cannot make assumptions about our neuropsychenologic research battery concerning the clinical effects of the cognitive decline. We assume that patients are usually still recovering from cardiac surgery after 1 month of follow-up and the clinical significance of POCD can be diminished at this follow-up. Our study suggests, as in many other studies, that perioperative factors could have a long-term but not cognitive effect in the early months after surgery. With subjective evaluations of cognitive postoperative change at different times, valuable information on the clinical impact of a cognitive decline could be provided. In future research.

CONCLUSION:

Ultimately, this analysis found that POD was associated with a cognitive decline independently one month after surgery. Secondary results show that POD is not associated with the 1-year cognitive decrease after surgery and cognitive results generally recover over the year following surgery, with the exception of specific motor and executive cognitive domains. Patients with POD predisposition in attention-requiring tasks are characterized by improper performance.

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