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Original Article

Patient-Reported Postoperative Neuropsychological Deterioration After Heart Valve Replacement and Coronary Artery Bypass Grafting

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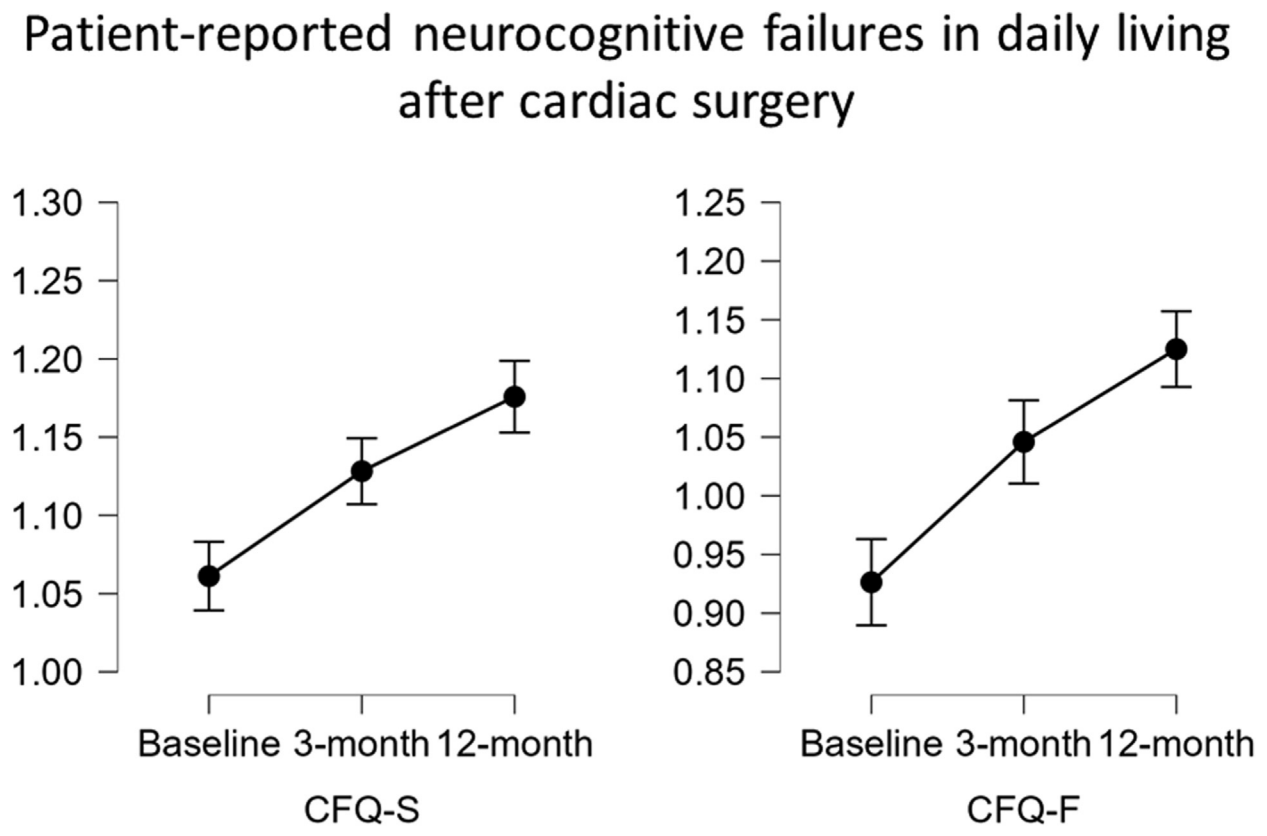

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ABSTRACT

Background: Postoperative cognitive decline (POCD) after cardiosurgical interventions are well described through objective psychometric tests. However, a patient's subjective perception is essential to clinical assessment and quality of life. This study systematically evaluated patient-reported POCD between subjects undergoing coronary artery bypass grafting and heart valve replacement.

Methods: This study was a multicentre, prospective questionnaire survey conducted at the cardiac surgery departments at the Kerckhoff Clinic in Bad Nauheim and the University Hospital in Giessen, Germany. We included patients undergoing elective coronary artery bypass grafting (CABG), aortic valve replacement (AVR), mitral valve replacement or reconstruction (MVR), and combined surgery (CABG + valve replacement [VR]) with extracorporeal circulation. The Hospital Anxiety and Depression Scale, the Cognitive Failures Questionnaire (CFQ) for Self-assessment (CFQ-S), and the external assessment (CFQ-foreign [F]) were completed preoperatively, as well as at 3 and 12 months postoperatively.

Results: A total of 491 patients were available for analyses (CABG = 182, AVR = 134, MVR = 93, CABG + VR = 82). POCD and postoperative depression increase (PODI) were observed for each surgical procedure. (At the 3-month follow-up: CFQ-S [CABG = 7.1%, AVR = 3.7%, MVR = 9.7%, CABG + VR = 9.8%]; CFQ-F [CABG = 9.9%, AVR = 9.7%, MVR = 9.7%, CABG + VR = 15.9%]; PODI [CABG = 7.7%, AVR = 9.7%, MVR = 6.5%, CABG + VR = 8.5%]. At the 12-month follow-up: CFQ-S [CABG = 6.6%, AVR = 7.5%, MVR = 15.1%, CABG + VR = 7.3%]; CFQ-F [CABG = 7.1%, AVR = 14.9%, MVR = 10.8%, CABG + VR = 9.8%]; PODI [CABG = 10.4%, AVR = 11.2%, MVR = 6.5%, CABG + VR = 4.9%]). No significant between-group effects were observed for the CFQ-S, CFQ-F, or the Hospital Anxiety and Depression Scale.

Conclusions: For clinicians, paying attention to patients' self-reported experiences of reduced cognitive function and symptoms of depression following cardiac surgery is important. Such reporting is an indication that interventions such as cognitive training or psychotherapy should be considered.

RÉSUMÉ

Contexte : Le déclin cognitif postopératoire (DCPO) à la suite d'interventions de chirurgie cardiaque est bien décrit par des évaluations psychométriques objectives. Cependant, la perception subjective du patient est essentielle à l'évaluation clinique et à la qualité de vie. Cette étude visait à évaluer de façon systématique le DCPO déclaré par le patient chez des sujets ayant subi un pontage aortocoronarien ou une chirurgie valvulaire.

Méthodologie : Cette étude prospective multicentrique par questionnaire a été menée aux services de chirurgie cardiaque de la clinique Kerckhoff de Bad Nauheim et de l'hôpital universitaire de Giessen, en Allemagne. Elle a porté sur des patients ayant subi un pontage aortocoronarien (PAC), un remplacement valvulaire aortique (RVA), un remplacement ou une reconstruction de la valvule mitrale (RVM) ou une chirurgie combinée (PAC et remplacement valvulaire [RV]) avec circulation extracorporelle, en situation non urgente. L'échelle d'évaluation de l'anxiété et de la dépression à l'hôpital (HADS), le questionnaire d'auto-évaluation des déficits cognitifs (CFQ-S) et le questionnaire d'évaluation externe des déficits cognitifs (CFQ-F) ont été remplis avant l'intervention chirurgicale, ainsi que 3 et 12 mois après la chirurgie.

Résultats : Au total, les résultats de 491 patients étaient disponibles aux fins d'analyses (PAC = 182, RVA = 134, RVM = 93, PAC et RV = 82). Des cas de DCPO et une augmentation postopératoire des symptômes de dépression (APOD) ont été observés après chacune des interventions chirurgicales. (Lors du suivi après 3 mois : DCPO selon le CFQ-S [PAC = 7,1 %, RVA = 3,7 %, RVM = 9,7 %, PAC + RV = 9,8 %]; DCPO selon le CFQ-F [PAC = 9,9 %, RVA = 9,7 %, RVM = 9,7 %, PAC + RV = 15,9 %]; APOD [PAC = 7,7 %, RVA = 9,7 %, RVM = 6,5 %, PAC + RV = 8,5 %]. Lors du suivi après 12 mois : DCPO selon le CFQ-S [PAC = 6,6 %, RVA = 7,5 %, RVM = 15,1 %, PAC + RV = 7,3 %]; DCPO selon le CFQ-F [PAC= 7,1 %, RVA = 14,9 %, RVM = 10,8 %, PAC+ RV = 9,8 %]; APOD [PAC = 10,4 %, RVA = 11,2 %, RVM = 6,5 %, PAC + RV = 4,9 %]). Aucun effet intergroupe significatif n'a été observé relativement aux questionnaires CFQ-S et CFQ-F ou à l'échelle HADS.

Conclusions : Il est important que les cliniciens portent attention aux déclarations des patients en ce qui concerne la diminution des fonctions cognitives et les symptômes de dépression à la suite d'une chirurgie cardiaque. De telles déclarations sont une indication que des interventions comme l'entraînement cognitif ou la psychothérapie doivent être envisagées.

Neurocognitive disorders such as delirium[1] and postoperative cognitive decline (POCD)[2] have been observed following cardiac surgery. In patients undergoing coronary artery bypass grafting (CABG), the prevalence of POCD ranges from 28% between the first and fourth postoperative month to 22% between the sixth and 12th postoperative month.[2] POCD is usually defined as a decline of one standard deviation in cognitive domains such as memory, attention, and speech, as shown by comparisons of preoperative and postoperative cognitive assessments.[2] POCD can be related to reduced quality of life,[3] increased economic costs,[4] and long-term cognitive decline.[5] Several risk factors have been identified in the development of POCD, including preoperative factors (eg, age, depression, cognitive impairment), intraoperative factors (eg, duration of surgery), and postoperative factors (eg, delirium).[6,7] POCD often appears at a subclinical level and thus remains unrecognized by physicians and family members. However, patients and their relatives report increased cognitive failures in daily life for at least 3 months following cardiac surgery.[8,9] Even 1 year after surgery, relatives indicate impaired cognitive abilities in patients' daily life.[8] Additionally, evidence has been found of increased depressive symptoms postoperatively.[10]

The purpose of this prospective study was to examine how patients and their relatives perceive patients' cognitive changes in the short- and long-term. The study focused on patients who underwent different cardiac surgical procedures, specifically CABG and valve replacement (VR).

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See page 623 for disclosure information.

Material and Methods

Trial design and enrollment

This study was a multicentre, prospective questionnaire survey conducted at the cardiac surgery departments of the Kerckhoff Heart and Thorax Centre in Bad Nauheim and the University Hospital in Giessen, Germany. The Ethics Committee of the Justus Liebig University Giessen (Reference: 242/14) approved the study protocol, and the patients' provision of informed consent. The study complies with the Declaration of Helsinki.

Inclusion criteria were patients of any age above 18 years scheduled for elective cardiac surgery with extracorporeal circulation, including CABG, aortic valve replacement (AVR), mitral valve replacement and/or reconstruction (MVR), and combination surgery (CABG + VR).

The study coordinator screened the patient information on elective cardiac surgery for eligibility criteria. Potential participants were provided with comprehensive information about the study and received an informed consent form by mail. Signed informed consent forms were returned by the participants and collected at the Kerckhoff Heart Centre.

At baseline, the following information was documented: age, sex, education level (years of schooling and university education), medical history, and nicotine abuse. Additionally, patients had to complete the Cognitive Failures Questionnaire (CFQ) for Self-assessment (CFQ-S),[11] the Memory Complaint Questionnaire (MCQ; K.J.H. Heß, unpublished data, 2005), and the German version of the Hospital Anxiety and Depression Scale (HADS).[12] The patients' relatives completed the foreign-assessment version of the CFQ (CFQ-F).[11] All questionnaires were sent to the patients by mail before surgery. During the perioperative period, the duration of surgery, the extracorporeal circulation (ECC) time, and the cross-clamp time were recorded. In the postoperative phase, the length of stay in the intensive care unit and the regular ward, surgery-related complications (particularly delirium) documented in the medical records, and patients' self-reported confusion were assessed. The psychological questionnaires (CFQ, MCQ, HADS) were completed at 3 and 12 months postoperatively and were returned by the patients via mail.

Outcome measures

The primary outcomes of this study are the reported cognitive changes by patients and their relatives for each surgical procedure group at 3 and 12 months, as compared to their preoperative baseline assessment. Secondary outcomes include the parametric differences in the reported cognitive changes between the surgical procedure groups. Additionally, the study examines the between-group effects of subjective POCD, postoperative depression increase (PODI), and delirium.

Questionnaires

A validated German 25-item version of the CFQ-S[13] was used. Close relatives of the patients completed an 8-item CFQ-F[14] to evaluate cognitive failures, as seen from their perspective. The CFQ assesses failures in daily living related to memory, attention, action, and perception. The validated German version of the MCQ; K.J.H. Heß, unpublished data) also was included to gain further insight into memory function. All questionnaires were completed on a 5-point scale ranging from "never = 0" to "very often = 4." Furthermore, the CFQ-S data were analyzed based on the 3-factor model (forgetfulness, distractibility, false triggering) developed by Rast et al.[15] Patients also were required to complete the validated German version of the HADS,[12] which is a standardized screening instrument consisting of 2 scales measuring anxiety (HADS-A) and depression (HADS-D) experienced during the previous week. Each scale comprises 7 items with 4 response options. Higher scores on all questionnaires (CFQ, MCQ, HADS) indicate a worse condition or more severe symptoms.

Statistical analyses

Sample size estimation. The sample size calculation for this study was based on the secondary outcome, which focused on the parametric between-group effects of postoperative cognitive decline. No published data were available to estimate the required sample size for this outcome. A conservative approach was taken to avoid underestimating the total sample size. A small effect size ($f = 0.1$) was used in the calculation. For a repeated-measures analysis of variance (RMANOVA) with interaction effects, a desired power of 0.85, an alpha level of 0.05, 4 groups, and 3 measurement time points (at baseline, 3-month, and 12-month follow-up), the calculated total sample size was 260 (65 patients per group). Considering a dropout rate of 20% between each time point (see flowchart), the estimated total sample size was adjusted to 635 patients. The patients returned the questionnaires at a higher rate than the expected dropout rate, so recruitment was halted upon receipt of 530 questionnaires from patients preoperatively.

Analysis of missing data. Missing data handling for all questionnaires was conducted as follows: If patients answered at least 50% of all items per questionnaire factor at each time point, the mean score of that factor was calculated to determine the final value. In cases with missing data for psychological parameters (CFQ, MCQ, HADS) at follow-up assessments, owing to patient dropout (as depicted in the flowchart), multiple imputation using the fully conditional specification method was performed in SPSS (version 22, IBM, Armonk, NY). The imputation process involved setting the number of iterations to 10, and the number of imputations to 23. A linear regression model was used with the following predictors: group, age, education (in years), and the questionnaire values from baseline, 3 months, and 12 months follow-up. If complete questionnaires were missing at baseline, but follow-up data from the same subject were available, the missing baseline data were imputed also. The average of the 23 imputations was calculated for each questionnaire parameter to replace the missing data.

Analysis of demographics and operative details. Between-group effects in parametric variables were calculated by analyses of variance. When the assumption of variance homogeneity (as determined by the Levene test) was not met, Welch correction and Brown-Forsythe correction by skewed distribution were used. Post hoc comparisons were conducted

using the Tukey correction to account for multiple tests. In cases in which unequal variances were observed, the Games-Howell procedure was used for post hoc comparisons. Normality of distribution was evaluated through a visual inspection of the distribution plot. Nominal variables were analyzed using Pearson's χ^2 test.

Analysis of outcomes. To assess the main effects on CFQ, MCQ, and HADS for all patients, as well as the between-group effects, we conducted RMANOVAs. Assumptions for an RMANOVA were tested using Levene's test for variance homogeneity and Mauchly's test for sphericity. If sphericity was violated, alpha levels were adjusted using the Greenhouse-Geisser correction. Post hoc explorative RMANOVAs for each single group were Bonferroni corrected by comparing a family of 3. The effect size was reported as η^2 and Cohen's d. To control for the possibility of confounder variables affecting the between-group effects, all pre-, peri- and postoperative variables that showed statistical differences between the groups (as shown in Table 1) were included as covariates in the RMANOVA.

Patient- and relative-reported POCD was defined as a decline of at least one standard deviation (SD)[8] from pre- to post-assessment in CFQ-S, CFQ-F, and MCQ. Frequencies of PODI were defined as an increase of at least 1 SD from pre- to post-assessment in the depression subscale of the HADS (HADS-D). To measure the difference of 1 SD between pre- and post-assessment, z scores were calculated by subtracting the individual raw values from the mean value of the total baseline data and dividing the result by the SD of the total baseline data. The frequencies of POCD and PODI were compared between the groups using Pearson's χ^2 tests. Multiple χ^2 post hoc comparisons were corrected using the false discovery rate method.[16]

Interrater reliability related to POCD between patient assessments (CFQ-S) and peer assessments (CFQ-F) was calculated using Cohen's kappa statistic, which takes into account the possibility of agreement by chance.[17]

The criterion for statistical significance was set at $P < 0.05$. All analyses were conducted using SPSS (version 22, IBM) and JASP (version 0.17.1, University of Amsterdam, The Netherlands) statistical software.

Results

A total of 530 questionnaires were returned to the Kerckhoff Clinic by the patients before surgery. After screening for valid inclusion criteria, a total of 491 patients were used for statistical analysis (CABG, n = 182; AVR, n = 134; MVR, n = 93; and CABG + VR, n = 82). See Figure 1 for the number of patients excluded from each group at the subsequent measurement time points. Results for baseline characteristics and pre-, peri-, and postoperative details are shown in Table 1. Results for POCD and PODI are shown in Table 2. The mean and SD of all parameters per surgery type and time points are shown in Supplemental Table S1.

In the analysis of all groups together, RMANOVA showed significant increases from baseline to both the 3-month and 12-month follow-up assessments for the following assessments: CFQ-S ($F = 26.496$, $P < 0.001$, $\eta^2 = 0.051$); MCQ ($F = 36.189$, $P < 0.001$, $\eta^2 = 0.069$); CFQ-F ($F = 31.785$, $P < 0.001$, $\eta^2 = 0.061$); forgetfulness ($F = 22.182$, $P < 0.001$, $\eta^2 = 0.043$); distractibility ($F = 13.830$, $P < 0.001$, $\eta^2 = 0.027$); and false triggering ($F = 18.240$, $P < 0.001$, $\eta^2 = 0.036$). Anxiety, as measured by the HADS, showed a decrease from the preoperative baseline assessment to the 3-month follow-up assessment (mean difference [MD] = 1.081, d = 0.3, $P < 0.001$), followed by an increase from the 3-month to the 12-month follow-up assessment (MD = −0.315, d = −0.09, $P = 0.019$). Depression, in contrast, appeared to remain stable from the preoperative assessment to the 3-month postoperative assessment (MD = 0.029, d = 0.01, $P = 0.828$) but increased from the 3-month to the 12-month follow-up assessment (MD = −0.326, d = −0.09, $P = 0.039$). See Figure 2 for a visual representation of the time course of the questionnaire parameters.

In terms of each surgical procedure, CABG showed increased scores for the following assessments: CFQ-S (baseline to 12-month: MD = −0.107, d = −0.24, $P < 0.001$); MCQ (baseline to 3-month: MD = −0.109, d = −0.18, $P = 0.021$; baseline to 12-month: MD = −0.180, d = −0.31, $P < 0.001$); CFQ-F (baseline to 12-month: MD = −0.212, d = −0.33, $P < 0.001$; 3-month to 12-month: MD = −0.145, d = −0.23, $P < 0.001$); forgetfulness (baseline to 12-month: MD = −0.132, d = −0.25, $P < 0.001$; 3-month to 12-month: MD = −0.089, d = −0.17, $P = 0.008$); distractibility (baseline to 12-month: MD = −0.081, d = −0.16, $P = 0.028$); and false triggering (baseline to 12-month: MD = −0.115, d = −0.25, $P < 0.001$). CABG showed decreased scores in HADS-A (baseline to 3-month: MD = 1.140, d = 0.31, $P < 0.001$; baseline to 12-month: MD = 0.723, d = 0.19, $P = 0.007$); and increased scores in HADS-D (3-month to 12-month: MD = −0.595, d = −0.16, $P = 0.029$).

AVR showed increased scores in the following assessments: CFQ-S (baseline to 12-month: MD = −0.102, d = −0.22, $P < 0.001$); MCQ (baseline to 12-month: MD = −0.200, d = −0.36, $P < 0.001$; 3-month to 12-month: MD = −0.112, d = −0.21, $P = 0.025$); CFQ-F (baseline to 3-month: MD = −0.176, d = −0.27, $P = 0.001$; baseline to 12-month: MD = −0.242, d = −0.37, $P < 0.001$); forgetfulness (baseline to 12-month: MD = −0.109, d = −0.20, $P = 0.014$); distractibility (baseline to 12-month: MD = −0.086, d = −0.17, $P = 0.041$); and false triggering (baseline to 12-month: MD = −0.079, d = −0.17, $P = 0.032$). AVR showed decreased scores in HADS-A (baseline to 3-month: MD = 0.959, d = 0.27, $P = 0.001$).

MVR demonstrated increased scores in the following assessments: CFQ-S (baseline to 3-month: MD = −0.097, d = −0.21, $P = 0.024$; baseline to 12-month: MD = −0.145, d = −0.32, $P < 0.001$); MCQ (baseline to 3-month: MD = −0.148, d = −0.27, $P = 0.009$; baseline to 12-month: MD = −0.188, d = −0.34, $P < 0.001$); CFQ-F (baseline to 3-month: MD = −0.194, d = −0.31, $P < 0.001$; baseline to 12-month: MD = −0.182, d = −0.29, $P = 0.001$); forgetfulness (baseline to 12-month: MD = −0.125, d = −0.25, $P = 0.017$); distractibility (baseline to 12-month: MD = −0.160, d = −0.32, $P = 0.001$); and false triggering (baseline to 12-month: MD = −0.109, d = −0.24, $P = 0.016$). MVR demonstrated decreased scores in HADS-A

Table 1. Demographics, and pre-, peri-, and postoperative characteristics

Characteristic	CABG (n = 182)	AVR (n = 134)	MVR (n = 93)	CABG + VR (n = 82)
Demographics				
Age, y				
mean (SD)[†,§,¶]	68.0 (8.5)	68.0 (9.9)	61.5 (11.1)	70.5 (9.1)
Sex[**,††,‡‡]				
Women	20 (11.0)	44 (32.8)	37 (39.8)	29 (34.4)
Men	162 (89.0)	90 (67.2)	56 (60.2)	53 (64.6)
Education, y, mean (SD)[‖‖,¶¶]	10.9 (3.2)	10.4 (2.8)	11.9 (3.7)	10.5 (2.6)
Medical history				
Body-mass index [kg/m^2], mean (SD)[††, §§,¶]	27.8 (3.9)	28.5 (5.3)	25.4 (3.7)	27.6 (4.7)
Coronary heart disease[**,††,§,‖‖,¶¶]	169 (92.9)	39 (29.3)	16 (17.6)	71 (86.6)
Heart attack[**,††,‡]	24 (13.2)	1 (0.8)	1 (1.1)	2 (2.4)
Atrial fibrillation (paroxysmal)	13 (7.1)	9 (6.8)	7 (7.7)	12 (14.8)
Atrial fibrillation (tachyarrhythmia absoluta)	1 (0.5)	1 (0.8)	3 (3.3)	0 (0.0)
Atrial fibrillation (persistent)	7 (3.8)	11 (8.3)	8 (8.8)	9 (11.0)
Pacer implantation	4 (2.2)	4 (3.0)	2 (2.2)	1 (1.2)
Arterial hypertension[*,††,§§,¶¶]	146 (80.2)	90 (67.7)	42 (46.2)	64 (78.0)
Peripheral artery disease[*,††,¶]	19 (10.4)	3 (2.3)	0 (0.0)	6 (7.3)
Stroke	10 (5.5)	4 (3.0)	1 (1.1)	6 (7.3)
Transient ischemic attack	3 (1.6)	3 (2.3)	4 (4.4)	2 (2.4)
Renal insufficiency (composed)[†,¶¶]	17 (9.3)	8 (6.0)	1 (1.1)	12 (14.8)
Diabetes[*,††,§,¶¶]	57 (31.3)	24 (18.0)	4 (4.4)	20 (24.4)
Obesity[†]	45 (24.7)	28 (21.1)	9 (9.9)	14 (17.1)
Hyperlipoproteinemia[**,††,‡,§§,¶]	113 (62.1)	51 (38.3)	13 (14.3)	38 (46.3)
COPD	16 (8.8)	13 (9.8)	6 (6.6)	9 (11.0)
Nicotine abuse				
None	63 (34.6)	68 (51.1)	48 (53.3)	30 (37.0)
Ex[*,†]	97 (53.3)	54 (40.6)	34 (37.8)	40 (49.4)
Acute	22 (12.1)	11 (8.3)	8 (8.9)	11 (13.6)
Perioperative details, mean (SD)				
Duration of surgery, min[**,††,§,‖‖,¶¶]	221.5 (49.9)	173.0 (52.4)	194.7 (36.9)	229.2 (54.0)
Duration of extracorporeal circulation, min[††,‡‡, §§,‖‖]	96.0 (33.5)	92.3 (35.5)	125.8 (32.2)	118.1 (37.9)
Cross-clamp time, min[††,‡‡,§§,‖‖]	61.6 (17.9)	62.6 (21.2)	75.0 (21.8)	83.4 (34.4)
Postoperative details				
Length of stay, h, (ICU), mean (SD)	38.9 (36.9)	38.4 (43.5)	41.2 (47.5)	49.3 (39.6)
Length of stay, d (post-ICU), mean (SD)[‡,¶]	12.0 (3.4)	12.7 (4.7)	12.0 (4.1)	14.2 (5.1)
Pacer implantation[‡]	5 (2.8)	9 (6.8)	3 (3.3)	10 (12.2)
Atrial fibrillation	34 (19.0)	30 (22.7)	27 (29.7)	17 (21.7)
AV block	2 (1)	6 (4.6)	3 (3.3)	4 (4.8)
Pericardial effusion	8 (4.4)	11 (8.3)	7 (7.7)	8 (10.9)
Delirium[‡,‖]	9 (4.9)	6 (4.5)	5 (5.5)	12 (14.6)
Confusion	19 (11.1)	12 (9.6)	13 (14.3)	9 (11.3)
Renal failure	9 (4.8)	6 (4.6)	2 (2.2)	6 (7.2)
Pneumothorax	6 (3.3)	3 (2.3)	5 (5.5)	4 (4.9)
Restricted oxygenation	5 (2.7)	0 (0)	2 (2.2)	3 (3.6)
Bleeding-associated rethoracotomy	2 (1)	3 (2.3)	3 (3.3)	4 (4.8)

Data are number of subjects (%), unless otherwise indicated. Ex- and acute nicotine abuse were related to no nicotine abuse. Coronary artery bypass grafting (CABG) + valve replacement (VR) = CABG + aortic valve replacement (AVR) or mitral valve replacement or reconstruction (MVR).

AV, atrioventricular; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; SD, standard deviation.

Between-group effects < 0.05 are indicated as follows:

Between-group effects < 0.001 are indicated as follows:

* CABG vs AVR.

† CABG vs MVR.

‡ CABG vs CABG + VR.

§ AVR vs MVR.

‖ AVR vs CABG + VR.

¶ MVR vs CABG + VR.

** CABG vs AVR.

†† CABG vs MVR.

‡‡ CABG vs CABG + VR.

§§ AVR vs MVR.

‖‖ AVR vs CABG + VR.

¶¶ MVR vs CABG + VR.

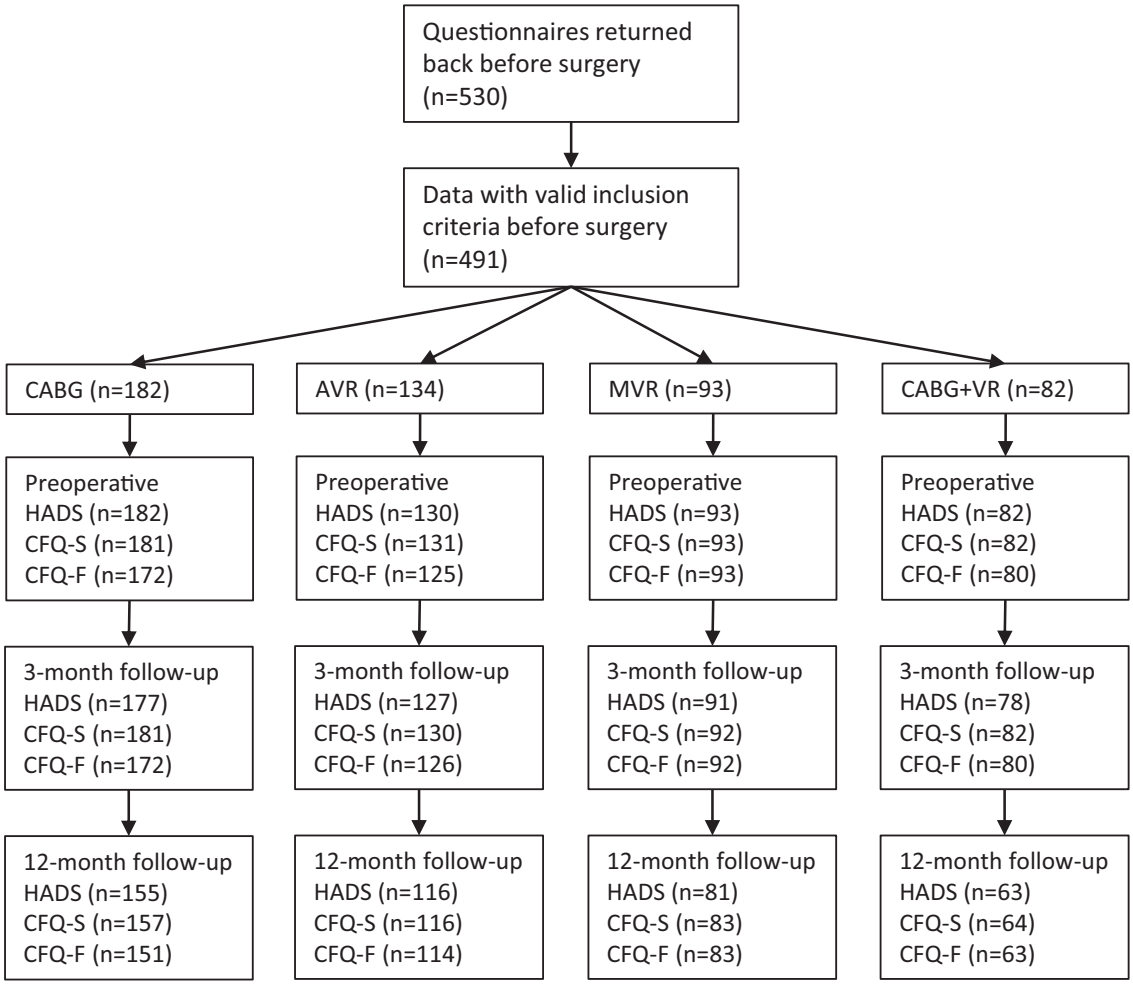

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flowchart illustrating all steps in the study from baseline to follow-up and analysis. Coronary artery bypass grafting (CABG) + valve replacement (VR) = CABG + aortic valve replacement (AVR) or mitral valve replacement or reconstruction (MVR). Cognitive Failures Questionnaire (CFQ)-Self-assessment (S)_includes the Memory Complaint Questionnaire (MCQ). CFQ-F, CFQ for Foreign-assessment; HADS, Hospital Anxiety and Depression Scale.

Table 2. Postoperative neuropsychological characteristics

Follow-up	CABG (n = 182)	AVR (n = 134)	MVR (n = 93)	CABG + VR (n = 82)
3 mo				
POCD (CFQ-S)	13 (7.1)	5 (3.7)	9 (9.7)	8 (9.8)
POCD (MCQ)	22 (12.1)	13 (9.7)	13 (13.9)	16 (19.5)
POCD (CFQ-F)	18 (9.9)	13 (9.7)	9 (9.7)	13 (15.9)
POCD (forgetfullness)	16 (8.8)	8 (5.9)	9 (9.7)	10 (12.2)
POCD (distractibility)	15 (8.2)	5 (3.7)	10 (10.8)	7 (8.5)
POCD (false triggering)	18 (9.9)	10 (7.5)	9 (9.7)	8 (9.8)
PODI	14 (7.7)	13 (9.7)	6 (6.5)	7 (8.5)
12 mo				
POCD (CFQ-S)	12 (6.6)	10 (7.5)	14 (15.1)	6 (7.3)
POCD (MCQ)	18 (9.9)	15 (11.2)	11 (11.9)	12 (14.6)
POCD (CFQ-F)	13 (7.1)	20 (14.9)	10 (10.8)	8 (9.8)
POCD (forgetfullness)	10 (5.5)	11 (8.2)	11 (11.8)	8 (9.8)
POCD (distractibility)	14 (7.7)	12 (8.9)	11 (11.8)	8 (9.8)
POCD (false triggering)	15 (8.2)	10 (7.5)	10 (10.8)	8 (9.8)
PODI	19 (10.4)	15 (11.2)	6 (6.5)	4 (4.9)

Data are number of subjects (%). Coronary artery bypass grafting (CABG) + valve replacement (VR) = CABG + aortic VR (AVR) or mitral valve replacement or resconstruction (MVR).

CFQ, Cognitive Failures Questionnaire; CFQ-F, CFQ-Foreign-assessment; CFQ-S, CFQ-Self-assessment; MCQ, Memory Complaint Questionnaire; POCD, postoperative cognitive decline; PODI, postoperative depression increase; VR, valve replacement.

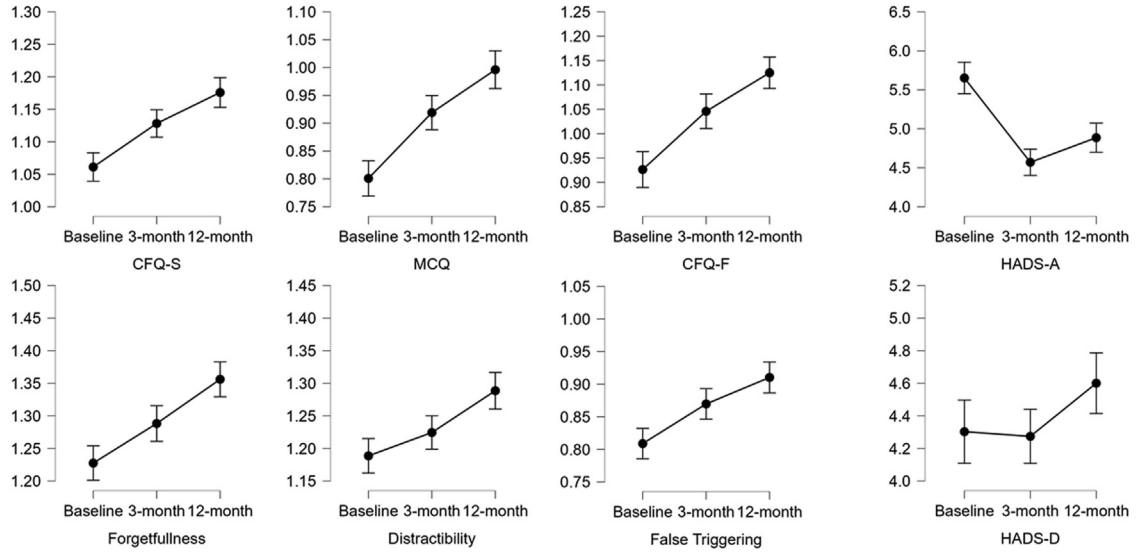

Figure 2. Main effects of all patients (n = 491) from baseline to 3-month and 12-month follow-up assessment. Shown are the mean values (higher scores indicating a worse condition), including 95% confidence intervals. Forgetfulness, distractibility, and false triggering relate to the factor-model by Rast et al.[15] CFQ, Cognitive Failures Questionnaire; CFQ-F, CFQ for Foreign-assessment; CFQ-S, CFQ for Self-assessment; HADS, Hospital Anxiety and Depression Scale; -A, anxiety subscale; -D, depression subscale; MCQ, Memory Complaint Questionnaire.

(baseline to 3-month: MD = 1.308, d = 0.39, $P < 0.001$; baseline to 12-month: MD = 1.204, d = 0.36, $P < 0.001$).

For the CABG + VR surgical procedure, scores were increased for the following assessments: CFQ-S (baseline to 12-month: MD = −0.119, d = 0.24, $P = 0.024$); MCQ (baseline to 3-month: MD = −0.154, d = −0.24, $P = 0.025$; baseline to 12-month: MD = −0.229, d = −0.36, $P < 0.001$); and forgetfulness (baseline to 3-month: MD = −0.129, d = −0.23, $P = 0.040$; baseline to 12-month: MD = −0.159, d = −0.28, $P = 0.008$). CABG + VR showed decreased scores for HADS-A (baseline to 3-month: MD = 0.893, d = 0.24, $P = 0.010$; baseline to 12-month: MD = 0.853, d = 0.23, $P = 0.015$).

No significant between-group effects related to CFQ, MCQ, or HADS were observed in the RMANOVA or in the analyses of POCD and PODI. In an adjusted RMANOVA considering pre-, peri-, and postoperative variables that showed significant differences between the surgical procedures as covariates, none of the covariates changed the between-group effects from a nonsignificant to a significant result.

Post hoc exploratory analyses showed that CABG with VR had a higher frequency of delirium compared to isolated CABG ($\chi^2[1] = 7.25$, $P = 0.007$; odds ratio [OR] = 1.92, 95% confidence interval [CI] 0.29-2.10) and AVR ($\chi^2[1] = 6.68$, $P = 0.01$; OR = 1.28, 95% CI 0.26-2.30).

At the 3-month follow-up, relatives of the patients identified a higher number of POCD cases (n = 53) using the CFQ-F, compared to the patients' self-assessments (n = 35) using the CFQ-S ($\chi^2[1] = 27.17$, $P < 0.001$; OR = 1.82, 95% CI 1.06-2.57). Similarly, at the 12-month follow-up, relatives of the patients identified a higher number of POCD cases (n = 51) using the CFQ-F, compared to the patients' self-assessments (n = 42) using the CFQ-S ($\chi^2[1] = 59.93$, $P < 0.001$; OR = 2.38, 95% CI 1.67-3.08). Interrater reliability between patients (CFQ-S) and relatives (CFQ-F) in assessing the occurrence of POCD showed weak agreement at the 3-month and 12-month follow-ups (respectively, Cohen's kappa = 0.229, and Cohen's kappa = 0.347).

Discussion

The overall patient population's cognitive failures in daily living increased from baseline to the 3-month and 12-month follow-up assessments. Our previous study focusing on patients with isolated AVR also revealed increased cognitive errors as measured by the CFQ-S from baseline to the 3-month follow-up.[8] In the current analysis, we further demonstrated a decline in memory, as measured by the MCQ, in patients with isolated AVR, even beyond 1 year. External assessments (CFQ-F) indicated persistent deterioration in patients' everyday cognition beyond 1 year. An important point to note is that although these findings are statistically significant, the increase in cognitive failures from the preoperative period to the 12-month follow-up time point is comparatively minimal. The CFQ and MCQ scale has 5 levels (never = 0, rarely = 1, sometimes = 2, often = 3, very often/always = 4). As shown in Figure 2, the baseline data start primarily within the "rarely" level and do not surpass the next level—"sometimes"—until the 12-month follow-up examination. However, these results represent the average of the entire study sample, which includes individual patients experiencing potentially clinically relevant cognitive deterioration.

Subjectively assessed POCD using the 1-SD method (pre- to post-test) was observed in each surgical procedure, with frequencies ranging from 3.7% to 15.9%, depending on the questionnaire model and time point. Specifically, CABG patients had a POCD frequency (defined by the CFQ-S model) of 7.1% at the 3-month follow-up, and 6.6% at the 12-month follow-up. To our knowledge, this study is the first to define POCD using a questionnaire-based patient-reported assessment. Previous studies that measured POCD frequencies using cognitive psychometric tests in CABG patients reported

a postoperative prevalence of about 28% (months 1-4) and 22% (months 6-12).[2] Taken together, POCD frequencies as measured with cognitive tests appear to be higher than those measured with questionnaires. This difference may be attributed to the greater sensitivity of cognitive tests in identifying postoperative decline, as patients often do not perceive their own deficits. In contrast, questionnaires might be more likely to reflect what limits patients in their daily lives. However, when the reliable change index is used to determine POCD, considering practice effects, the POCD rates appear to be lower.[2] Regarding AVRs, the POCD frequency at the 12-month follow-up (7.5%) in this study closely aligns with findings from other studies (7.5%) using the reliable change index method.[18]

When comparing VR surgeries, AVR, compared to MVR, shows a greater decline from baseline to the 1-month follow-up. However, the rate of decline converges in both groups by the 2-6-month follow-up.[19] These findings are consistent with our results, as we found no group differences between the VR methods at the 3-month vs 12-month follow-up.

Although we observed deterioration in cognitive outcomes across different surgical methods, we found no significant group differences, whether based on patients' self-reports or their relatives' assessments. This lack of difference suggests that CABG and VR may not have differential effects on patients' cognitive outcomes as measured by questionnaires.

We observed an increase in depressive symptoms from the 3-month to the 12-month follow-up assessment. The frequencies of PODI varied across the different surgical procedures, ranging from 4.9% to 11.2%. An important point to note is that we did not use commonly defined criteria for diagnosing depression disorders.[10] Therefore, the frequency of PODI observed in our study does not necessarily correlate with clinically relevant depression.

Furthermore, we have seen a higher frequency of delirium in patients who underwent combination surgery (CABG + VR), compared to the level in those with isolated CABG and AVR. We conducted a post hoc exploratory analysis to investigate potential factors contributing to this difference. Our analysis revealed a correlation between delirium and surgery time ($r = 0.097$, $P = 0.031$), circulation time ($r = 0.141$, $P = 0.002$), and cross-clamp time ($r = 0.132$, $P = 0.004$). These findings are consistent with previous studies that have reported a link between delirium and surgery, circulation, and cross-clamp time.[20,21]

Relatives of patients tend to evaluate POCD more critically than do the patients themselves, as suggested by our previous study.[8] This difference may be the result of patients not perceiving their cognitive changes with enough sensitivity or choosing not to report them due to shame. Conversely, relatives may overestimate the deterioration in patient-related cognitions, owing to their awareness of the potential neuropsychological complications associated with serious cardiac surgery or a sense of overprotection and a desire for prompt and appropriate treatment.

Limitations

Given that our study focused solely on patients undergoing cardiac surgery using ECC, we cannot directly compare our results with those of patients who did not undergo ECC or those from a healthy control group. We also did not evaluate the recommended research term "postoperative mild and major neurocognitive disorders," as defined by Evered et al.[22] We did not do such an evaluation because we did not include objective psychometric tests or specific questions about postoperative changes in instrumental activities of daily living or the patient's subjective perception of a decrease in postoperative cognition abilities with explicit reference to heart surgery, such as asking, "Do you think your heart surgery has impaired your memory/attention/speech, etc.?". These questions may have more clinical relevance, as they might detect deficits that are not captured by psychometric tests or questionnaires alone, as a decrease of 1 SD from pre- to postassessment is considered significant. However, objective psychometric evaluation of statistically confirmed cognitive changes still can be useful in predicting or identifying the onset of clinically relevant deterioration. Regarding assessment of postoperative delirium, we relied on information documented in the medical records. Given that we did not conduct a systematic assessment of postoperative delirium, the frequency of cases in our sample may be underreported.

Conclusions

Our study findings indicate that depression and cognitive failures in daily living tend to increase following cardiac surgery. We did not observe significant differences in these findings based on the type of surgical procedure performed. This result suggests that, regardless of the specific surgical approach, clinicians should be aware of the reported deterioration in patients' psychopathology after cardiac surgery. To address these issues, clinicians should consider implementing screening methods to promptly identify patients who are at risk for postoperative cognitive and affective impairment.[23,24] Early identification of these individuals allows for appropriate interventions to be initiated. Cognitive training programs[25,26] and psychotherapy[27] are examples of interventions that can be considered. These approaches aim to mitigate the negative effects of cognitive failures and depression, with potential to improve patients' overall well-being and quality of life.

Ethics Statement

The Ethics Committee of the Justus Liebig University Giessen (Reference: 242/14) approved the study protocol, and the provision of patients' informed consent. The study complies with the Declaration of Helsinki.

Patient Consent

The authors confirm that all participants provided written informed consent.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2023.11.007.