

Cognitive Outcomes Five Years After Not Undergoing Coronary Artery Bypass Graft Surgery

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Background. Patients with coronary artery disease who underwent coronary artery bypass graft surgery have a high risk of cognitive decline 5 years after the procedure. It is conceivable that this is not caused by the operation, but by natural aging.

Methods. Psychologists repeatedly administered a battery of seven neuropsychological tests with eight main variables to 112 subjects without known coronary artery disease, with a time interval of 5 years. Cognitive decline was defined as deterioration in performance beyond normal variation in at least two of the eight main variables. The incidence of cognitive decline in the control subjects was compared with the incidence of cognitive decline in the 281 participants of the Octopus Study, who underwent coronary artery bypass graft surgery 5 years earlier. Patients and control subjects were age-matched.

Results. After 5 years, cognitive outcome could be determined in 99 of 112 control subjects (88%) and 240 of 281 coronary artery bypass graft surgery patients (85%). Cognitive decline was present in 82 (34.2%) of 240 coronary artery bypass graft surgery patients and in 16 (16.2%) of 99 control subjects (crude odds ratio, 2.69; 95% confidence interval, 1.48 to 4.90). However, after correction for differences in age, sex, education, and baseline comorbidity between the patients and the control subjects, the odds ratio was 1.37 (95% confidence interval, 0.65 to 2.92).

Conclusions. We were unable to demonstrate that patients who underwent coronary artery bypass graft surgery have more cognitive decline after 5 years than control subjects without coronary artery disease.

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Coronary artery bypass grafting (CABG) effectively relieves angina, but can be complicated by short-term and long-term postoperative cognitive decline [1–3]. Two recent studies in 261 and 281 patients reported a 42% and 34% incidence of cognitive decline, respectively, 5 years after CABG [2, 3]. Cognitive decline after CABG has been attributed to the use of cardiopulmonary bypass [4, 5]. The Octopus Study, however, allocated patients to CABG with or without cardiopulmonary bypass and found no benefit of avoiding cardiopulmonary bypass. At 5 years the incidence of cognitive decline was 33% after off-pump CABG and 35% after on-pump CABG [3].

This result raised the hypothesis that the high incidence of long-term postoperative cognitive decline after CABG may be less related to the use of cardiopulmonary bypass or any other feature of the operation, but merely reflects normal aging [6]. This prompted us to appreciate the long-term cognitive status of CABG patients relative to the natural change in cognitive function with time. We therefore compared the 5-year neuropsychological per-

formance of the CABG patients who were included in the Octopus Study with the cognitive status of similarly aged control subjects who had not undergone CABG.

Patients and Methods

Patients

Between March 1998 and August 2000, 281 patients suffering from coronary artery disease underwent CABG with or without cardiopulmonary bypass in the Octopus Study. The main results have been reported elsewhere [3, 7]. Because no difference in the incidence of cognitive decline was found between patients operated on with or without cardiopulmonary bypass (35% and 33%, respectively, at 5-year follow-up), all 281 CABG patients were regarded as one group in the present study.

To measure the natural variation in performance and practice effects during repeated neuropsychological testing, we have also studied a group of 112 control subjects. They were recruited between April 2000 and March 2001 through an advertisement in a local newspaper, age-matched to the CABG patients included in the Octopus Study, but not suffering from coronary artery disease [8]. The natural variation in cognitive performance observed in these control subjects during a short period of 3 months has been reported elsewhere [8].

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*The members of the Octopus Study Group are listed in the Appendix.

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Table 1. Baseline Characteristics of the Patients and the Control Subjects^a

Characteristics	CABG Patients (n = 281)	Control Subjects (n = 112)	p Value
Age (y)	62.0 (54.3–68.2)	60.3 (55.4–65.1)	0.32
Education (y)	9 (8–10)	10 (10–15)	<0.01
Female sex (%)	32	49	<0.01
Diabetes (%)	13	5	0.04
Hypertension (%)	42	23	<0.01
Pulmonary disease (%)	9	3	0.07

^a Age and education are presented as medians, with 25th and 75th percentiles in parentheses.

CABG = coronary artery bypass graft.

To evaluate the difference in long-term cognitive decline between CABG patients and subjects who did not undergo CABG, we now compared neuropsychological test performance at 5-year follow-up between both cohorts. The study was approved by the medical ethics committees of the participating centers.

Design

The present study was a nonrandomized age-matched cohort study comparing long-term cognitive outcomes of CABG patients and control subjects without coronary artery disease.

Outcome Measure (Cognitive Decline)

The CABG patients and the control subjects underwent the same cognitive assessment at two points in time, with an interval of 5 years. For the CABG patients, the neuropsychological test battery was administered on the day before and 5 years after their surgery. Patients and control subjects underwent additional assessments 3 and 12 months after baseline assessment; the results of these latter two assessments have been reported elsewhere [7, 8].

The test battery comprised seven neuropsychological tests with eight main variables and was executed by trained psychologists. Testing procedures were similar for control subjects and patients [8]. In accordance with the Statement of Consensus on Assessment of Neurobehavioral Outcomes after Cardiac Surgery, the test battery included tests for motor skills, verbal memory capacity, and attention [9]. Each test yielded one or more variables, with different ranges per variable. Eight main variables were chosen a priori to be used in the analysis. The cognitive domains that were covered, the tests, and the eight main variables are listed in the Results section.

To determine the presence of cognitive decline, each individual's performance on the neuropsychological tests at 5-year follow-up was compared with his or her performance on the same tests 5 year earlier. Cognitive decline was defined as deterioration beyond the normal variation in cognitive performance. The normal variation in performance was measured in a short interval of 3 months in the control population (baseline assessment and 3-month

follow-up). To define cognitive decline at 5 years in both the patients and the control subjects, the scores of the eight main variables were first standardized using the formula of reliable change (RC) as proposed by Jacobson and Truax [10]:

$$RC = [(performance\ at\ 5\ years - performance\ at\ baseline) - practice\ effect] / SDdiff$$

The practice effect is the control subjects' mean improvement from baseline to 3 months after baseline. The SDdiff is the standard deviation of the control subjects' mean 3-month performance minus baseline performance. Patients and control subjects were considered as experiencing cognitive decline at 5-year follow-up if they had either an overall mean RC score equal to or less than -1.96 , or an RC score equal to or less than -1.96 in two or more main variables.

Patients and control subjects who had experienced a stroke and subjects unable to undergo testing because of Alzheimer's disease were also considered to have cognitive decline.

Data Analysis

Incidences of cognitive decline after 5 years in patients and control subjects were compared using the odds ratio and 95% confidence interval, with adjustment for possible remaining differences in age between the two groups. Multivariable logistic regression analysis was used to correct for other baseline differences between the patients and the control subjects, and thus for potential confounding. We considered the following potential confounders: female sex, years of education, diabetes, hyper-

Table 2. Reasons for Failure of Neuropsychological Assessment

Reason	CABG Patients (n = 281)	Control Subjects (n = 112)
Appeared unsuitable for neuropsychological testing at 1st assessment	1	3
Withdrawal immediately after recruitment	3	0
Withdrawal after baseline assessment	3	0
Failure to administer baseline tests (logistic)	3	0
Readmittance to hospital or too ill for follow-up assessment	1	2
(Noncerebral) mortality at time of 5-year cognitive follow-up	20	2
Not motivated for follow-up/withdrawal	10	3
Unable to contact subject (change of address and telephone number)	0	3
Total number of subjects with failed neuropsychological assessment	41	13
Total number of subjects with successful neuropsychological assessment	240	99

CABG = coronary artery bypass graft.

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