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Self-Reported Memory Symptoms with Coronary Artery Disease: A Prospective of CABG Patients and Nonsurgical Controls

Ola A. Selnes
Department of Neurology, The Johns Hopkins Hospital, oselnes@jhmi.edu

Maura A. Grega
Division of Cardiac Surgery, Johns Hopkins School of Medicine, mgrega@csurg.jhmi.jhu.edu

Louis M. Borowicz, Jr.
Zanvyl Krieger Mind/Brain Institute, lborowi1@jhmi.edu

Sarah Barry
Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, sbarry@jhsph.edu

Scott L. Zeger
Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, szeger@jhsph.edu

See next page for additional authors

Authors
Ola A. Selnes; Maura A. Grega; Louis M. Borowicz, Jr.; Sarah Barry; Scott L. Zeger; and Guy M. McKhann

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Ola A. Selnes, Ph.D.[1], Maura A. Grega, MSN[2]; Louis M. Borowicz, Jr., M.S.[5], Sarah Barry, M.S.[4], Scott Zeger, Ph.D.[4], Guy M. McKhann, M.D.[1,3,5]

Departments of Neurology[1], Surgery, Division of Cardiac Surgery[2], and Neuroscience[3], Johns Hopkins University School of Medicine;
Biostatistics[4], The Johns Hopkins Bloomberg School of Public Health;
and Zanvyl Krieger Mind/Brain Institute[5]

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Corresponding author:
Ola A. Selnes, Ph.D.
Department of Neurology
Meyer 100, The Johns Hopkins Hospital
600 North Wolfe St.
Baltimore, MD 21287
Phone: 410-955-3268
Fax: 410-955-0504
e-mail: oselnes@jhmi.edu

ABSTRACT

Background. Subjective memory complaints are common after coronary artery bypass grafting (CABG), but previous studies have concluded that such symptoms are more closely associated with depressed mood than objective cognitive dysfunction. We compared the incidence of self-reported memory symptoms at 3 and 12 months after CABG with that of a control group of patients with comparable risk factors for coronary artery disease but without surgery.

Methods. Patients undergoing CABG (n = 140) and a demographically similar nonsurgical control group with coronary artery disease (n = 92) were followed prospectively at 3 and 12 months. At each follow-up time, participants were asked about changes since the previous evaluation in areas of memory, calculations, reading, and personality. A Functional Status Questionnaire (FSQ) and self-report measure of symptoms of depression (CES-D) were also completed.

*Results***.** The frequency of self-reported changes in memory, personality, and reading at 3 months was significantly higher among CABG patients than among nonsurgical controls. By contrast, there were no differences in the frequency of self-reported symptoms relating to calculations or overall rating of functional status. After adjusting for a measure of depression (CES-D rating score), the risk for self-reported memory changes remained nearly 5 times higher among the CABG patients than control subjects. The relative risk of developing new self-reported memory symptoms between 3 and 12 months was 2.5 times higher among CABG patients than among nonsurgical controls (CI 1.24 – 5.02), and the overall prevalence of memory symptoms at 12 months was also higher among CABG patients (39%) than controls (14%).

Conclusions. The frequency of self-reported memory symptoms 3 and 12 months after baseline is significantly higher among CABG patients than control patients with comparable risk factors for coronary and cerebrovascular disease. These differences could not be accounted for by symptoms of depression. The self-reported cognitive symptoms appear to be relatively specific for memory, and may reflect aspects of memory functioning that are not captured by traditional measures of new verbal learning and memory. The etiology of these self-reported memory symptoms remains unclear, but our findings as well as those of others, may implicate factors other than cardiopulmonary bypass itself.

INTRODUCTION

Over 400,000 persons undergo coronary artery bypass grafting (CABG) each year in the United States. Although effective for the relief of angina, the most prominent symptom of coronary artery disease, both short- and long-term neurological complications are associated with this procedure. Postoperatively, the phenomena of stroke and encephalopathy are well recognized. Similarly, transient problems with memory are well recognized. Less well characterized are the longer term problems with cognition, reflected in the complaints of many patients that "I can't remember things the way I used to;" or "I'm just not quite the same" as before surgery. [1]

The most common approach to evaluate both short- and longer term postoperative cognitive changes has been to administer standardized neuropsychological tests before and after the surgery. An alternative approach has been to ask patients about self-perceived changes in memory and other cognitive functions. [2] Some studies that have compared these two approaches have concluded that subjective memory complaints do not necessarily correlate with objective measures of memory performance. Rather, subjective cognitive complaints tend to be more strongly associated with measures of mood, and many investigators have therefore concluded that subjective symptoms reflect an underlying depression rather than actual cognitive impairment. [3,4] These studies have typically relied on cross-sectional measurements of cognitive performance, however; consequently it is not known whether a similar relationship would be seen if subjective cognitive changes were compared with prospective longitudinal change in cognitive test performance. Although some studies have included surgical control groups, [5,6] few contemporary studies have included a nonsurgical control group with comparable risk factors for cerebrovascular disease.[7] A critical question is whether the self-reported changes are more common in CABG patients than in control patients with a comparable degree of cardiovascular disease.[8]

To further evaluate subjective cognitive changes after CABG, we elicited self-reports of change in personality, overall functional status, memory, and other cognitive functions at 3 and 12 months after surgery. We included a group of patients with coronary artery disease diagnosed by cardiac catheterization as our nonsurgical control group. The control patients were similar to the CABG patients in terms of risk factors for both coronary artery disease and cerebrovascular disease. In this report, we describe the incidence and prevalence of self-reported cognitive changes from baseline to 3 months and 12 months.

MATERIALS AND METHODS

Patients

Eligible CABG patients from all cardiac surgeons at our institution participated in the study, which was approved by the Johns Hopkins Institutional Review Board on 07/14/1997. Patients were approached who were native English speaking, not intubated, able to sit upright, and able to give informed consent. Enrollment was completed from September 1997 through March 1999. One-hundred and forty patients (approximately 12% of the 1129 patients who underwent CABG during that time period) agreed to participate in the study and completed written informed consent and baseline cognitive testing. For the nonsurgical controls, we asked three Johns Hopkins cardiologists to identify potential patients who were diagnosed with coronary artery disease (by cardiac catheterization). These patients were offered a study pamphlet at their office visit and were then contacted by study coordinators to determine if they were interested in participating. Patients were enrolled with the same inclusion criteria listed above for CABG patients except exclusion for previous cardiac surgery. Ninety-two patients provided written informed consent and completed baseline testing. The results of cognitive testing for this group of CABG and nonsurgical control patients have been reported separately. [9] Demographic characteristics, including age, gender, and race, and medical measurements were recorded at baseline. At 3 and 12 months after the baseline interview the patients had follow-up interviews during which they were questioned on a number of medically related factors.

Self-reported symptom assessment.

Using a semi-structured interview, we evaluated five subjective outcomes: memory, calculations (mental arithmetic, balancing checkbook or making change), personality, reading the newspaper, and reading books. These questions were designed to assess subjective complaints anecdotally expressed by our patients in a previous study. [10] Memory and calculations were binary outcomes assigned a value of 1 if a subject reported decline in his or her memory or ability to do calculations since the previous interview. They were thus measured only at the follow-up time-points. The question regarding change in personality was also asked only at the follow-up points. Patients were asked whether they considered that their personality had improved, changed for the worse, or stayed the same since the previous interview. Reading, defined similarly as to whether or not a patient typically read either newspapers or books, was assessed at each visit. Overall functional status was measured by the Functional Status Questionnaire (FSQ), which has nine questions in which a subject's score could range from 0 (lowest functional status) to a maximum of 36 points.[11] The Center for Epidemiological Studies Depression scale (CES-D) [12] was administered at baseline and at 3 and 12 months.

Operative technique

All patients underwent median sternotomy and received at least one arterial graft. Anesthetic technique was standardized and consisted of low-intermediate dose narcotics, inhalation agents, and paralytics. Cardiopulmonary bypass was carried out using a Sarns roller head pump, nonpulsatile flow, membrane oxygenator, alpha-stat pH blood gas management, antegrade crystalloid cardioplegia and topical hypothermia, moderate systemic hypothermia (28-32 °C), and pump flow rates to achieve a mean arterial pressure of 60-80 mmHg. Intraoperative ultrasound aortic scanning was not used routinely. Cardiotomy suction was returned to the CPB circuit for all patients. All surgeons but one used double clamp technique. The aortic cross clamp was applied and distal anastomoses were made. The aortic cross clamp was then released and a sidebiting clamp was applied once or twice, after which the proximal anastomoses were made.

Statistical Methods

We used logistic regression models to compare incidence and prevalence rates of each outcome between the CABG patients and controls. For newspaper and books, which were not measured as change from a previous interview, we defined the outcome as change from baseline to the follow-up point either for the worse (1), or otherwise (0). For personality, the improvement and no change categories were combined so that this was a binary variable in the same form as memory and calculations. We defined FSQ in the same way so that patients either had a decrease in FSQ from baseline or not.

We calculated crude relative risks and confidence intervals of self-reported symptoms comparing the CABG group and the NSC group by using 2x2 tables. Because the CABG intervention could not be randomly assigned to patients, the groups may differ in baseline characteristics. We used logistic regression models to estimate CABG relative risks while controlling for age, gender, and number of years of education, the demographic variables that were thought to be potential confounders. We calculated adjusted relative risks of each outcome at both 3 and 12 months. To determine whether the relative risks associated with having surgery were substantially reduced after controlling for depressed mood, we also fitted the logistic models adjusting for CES-D score measured at the same visit. Note that logistic regression gives coefficients that are log odds ratios, not log relative risks. We calculated estimated relative risks based on the mean value of all of the covariates for males, the more prevalent gender. By adjusting for potential confounders by logistic regression, the comparison of symptoms is effectively between CABG and NSC patients who are similar with respect to the measured variables. Because CABG was not randomized to patients, there may be unmeasured differences that cause residual confounding.

To study incidence and maintenance of subjective complaints, we fitted models to the outcome measurement at 12 months, stratifying on the 3-month outcome. The maintenance model was a logistic regression fitted to the patients who were complaining at 3 months, thus calculating the risk of deterioration between 3 and 12 months as compared to not getting worse, given that there had been an initial report of decline between baseline and 3 months. Hence we are calculating the risk of maintaining the reported decline. The incidence model is a logistic regression fitted to those people who reported no change at 3 months, so that a decline from 3 to 12 months is the first such event. We approximated the relative risks by odds ratios since very few patients or controls reported change for any of the outcomes. Confidence intervals could therefore be calculated directly by using the standard errors of the regression coefficients.

RESULTS

Demographic and medical characteristics

Of the 140 CABG patients seen before surgery, 116 completed 3-month follow-up testing; 17 refused; 1 died; and 6 were lost to follow-up. There were 120 who completed 12-month follow-up testing; 16 participants refused; 2 died; and 2 were lost to follow-up. Eighty-four of the 92 nonsurgical controls completed 3-month testing; 4 refused further testing; 1 died; and 3 were lost to follow-up. There were 83 participants who completed 1-year follow-up testing; 3 died; 3 were lost to follow-up; and 3 patients required CABG in the year after study enrollment. There were no differences in baseline demographics between participants who completed the study and those who did not.

Demographic characteristics for the CABG patients and the nonsurgical controls are shown in Table 1. The mean age was 2.4 years higher in the nonsurgical controls, but there were no other important differences in demographic characteristics between the two study groups. The CABG group did differ from the nonsurgical controls in several medical history variables, including a higher prevalence of peripheral vascular disease, history of recent myocardial infarction, and number of diseased vessels. In contrast, the frequency of previous percutaneous transluminal coronary angioplasty (PTCA) was statistically significantly higher among the nonsurgical controls. There was no meaningful difference in the prevalence of history of diabetes, hypertension, family history of Alzheimer's disease, or Apo-E distribution in the two groups. The baseline Functional Status Questionnaire score (FSQ) was lower in the CABG group, and the mean CES-D score was higher, suggesting a higher frequency of self-reported symptoms of depression among the CABG patients at baseline.

Frequency of subjective complaints at 3- and 12-month follow-up

The proportion of CABG patients and controls reporting changes in personality, functional status, memory, and other cognitive functions at 3 and 12 months after baseline is summarized in Table 2. The relative risks for having cognitive or personality changes is shown after adjustment for age, education, and gender, with and without adjustment for CES-D score. At 3 months, the CABG patients were more likely to report changes for the worse in memory, personality, and intellectual activities such as reading books than the nonsurgical controls. The risk of memory complaints among the CABG group was nearly 5 times higher than among the nonsurgical controls (95% CI 1.8 – 11.4) By contrast, there were no group differences in overall functional status (FSQ score) or the ability to perform calculations or read newspapers at 3 months. All of the participants reporting difficulties with calculations at 3 months also had self-reported memory complaints, but there was little overlap between memory complaints and self-reported symptoms for other domains.

The prevalence of self-reported changes for the worse in memory and personality at 12 months was also statistically significantly higher among CABG patients than among controls. After adjustment for CES-D score, the risk of having subjective memory complaints at 12 months was nearly 3 times higher among CABG patients than among controls (CI 1.8 – 6.3). The number of individuals reporting subjective symptoms in other cognitive domains was low, and there were no statistically significant group differences.

Incidence of subjective complaints at 12 months

We also stratified the subjects who reported subjective symptoms at 12 months by whether or not they had reported symptoms at 3 months (Figure 1). Of the 47 CABG patients reporting memory changes at 12 months, only 18 were persistent memory complainers, that is they had reported memory complaints at 3 months (56% of those complaining at 3 months.) The remaining 29 patients had new memory complaints at 12 months. The risk of reporting new memory complaints at 12 months was 2.5 times as great (95% CI 1.2 – 5.0) for CABG than for the nonsurgical controls (Table 3). There were no group differences in the incidence of self-reported changes for the worse in calculations, reading, personality, or functional status. Having subjective memory complaints at 12 months did not predict having complaints in other cognitive functions or personality.

Relationship of subjective symptoms to depression

To examine the role of depression, we estimated the relative risks of having memory complaints at 3 and 12 months after adjusting for scores on the CES-D (Figure 2) as well as demographic variables. The risk of reporting memory complaints, difficulties reading books, and personality change at 3 months remained statistically significantly higher among the CABG patients than controls even after adjusting for these variables (Table 2). For example, the relative risk of memory complaints at 12 months was 4.7 before and 4.9 after controlling for the CES-D score. Results were similar when we simultaneously controlled for levels of depressive symptoms at previous visits.

Relationship of subjective memory complaints to FSQ

There were no group differences in the self-reported overall functional status at 3 months or 12 months. At either time point, change in functional status was not associated with having subjective symptoms in memory or other cognitive complaints. Of those whose FSQ scores remained unchanged or improved from baseline to 3 months, a higher proportion of subjects among the nonsurgical controls then had a subsequent decline in FSQ score at 12 months. Of those whose FSQ scores declined between baseline and 3 months, there were no group differences in the proportion of subjects who worsened between 3 and 12 months.

Relationship of subjective memory complaints to neuropsychological test performance

Details of the neuropsychological test performance of these two groups have been previously published. [9] In contrast to the higher frequency of self-reported memory symptoms among the CABG patients, we did not find any differences between the two groups on summary measures of new learning and memory. Although the CABG patients had somewhat lower baseline performance on an overall (composite) measure of memory, there were no statistically significant differences between the nonsurgical controls and CABG patients in their overall trend of change from baseline to 3 or 12 months. (Figure 3) We considered whether the CABG group might differ from the nonsurgical controls in more detailed aspects of memory. Our study did not include specific measures of working memory, but the two groups had comparable performance on measures of attention (Rey Auditory Verbal Learning test Trial 1) and executive performance (Trail Making Test B). (Figures 4 and 5) We also compared the performance of CABG subjects with and without memory complaints, and there were no statistically significant differences in their Rey Auditory Verbal Learning Test Trial 1 or Trail Making test B performance.

COMMENT

Our findings show a higher frequency of self-reported changes in memory at 3 and 12 months among patients who have had CABG than among nonsurgical patients with comparable risk factors for coronary artery and cerebrovascular disease. Changes in personality were also more common among CABG patients than nonsurgical controls at 3 and 12 months, but when we stratified by the 3-month response, there was no statistically significant difference between CABG patients and controls in personality at 12 months. Somewhat surprisingly, the incidence of memory complaints continued to increase between 3 and 12 months for both the CABG and nonsurgical control patients. The self-reported cognitive changes after CABG appear to be relatively specific to memory, in that we found no difference in the incidence of subjective changes in calculations, reading, or overall functional status. The differences in self-reported memory and personality changes could not be accounted for by differences in levels of post-operative depression or demographic variables.

The reason why memory complaints are more prevalent in the CABG group remains unclear. Several previous studies have concluded that subjective symptoms after CABG are due to depressed mood.[3,4,13] This has become such established dogma that many patients who complain about changes in their memory after surgery are often told that they are "just depressed." Although depression may increase the likelihood of reporting subjective symptoms, it does not appear to be the entire explanation for the high frequency of subjective symptoms in our CABG group. Patients with subjective symptoms were more likely to be depressed, but having had surgery remained an important and statistically significant risk factor even after adjusting for the score on the CES-D. On the assumption that depression may lead to more nonspecific or global cognitive complaints, one would not expect the self-reported symptoms to be limited to memory if depression were the main source of these complaints. Additionally, we have observed that rates of depression after CABG decrease over time, whereas rates of self-reported memory symptoms increase over time.

We have considered other possible explanations for why self-reported memory symptoms are more common among CABG than nonsurgical controls, despite the lack of difference in objective cognitive performance. One such possibility is that the use of CPB is associated with some cognitive changes during the immediate postoperative period, but these changes are reversible as measured by objective neuropsychological measures. Because recovery of cognitive functions after surgery is a slow, gradual process, patients who experience transient decline in their memory may not be aware that they are more or less back to their pre-surgical level by 3 months and thus continue to perceive their memory as being worse than before surgery.

Estimates of the prevalence of subjective memory complaints in the general population suggest that up to one-third of older individuals may report subjective memory complaints. Age appears to be a strong predictor of having subjective memory complaints, as does having a close relative with history of dementia. [14] Since the mean age of the CABG patients was slightly lower than for the nonsurgical controls, however, we do not think that age can explain the difference in frequency of self-reported symptoms.

It is possible that having major surgery with general anesthesia could account for the difference in subjective complaints. The frequency of self-reported memory symptoms in our CABG group is similar to that which has been reported for noncardiac surgery. Johnson et al. found that 29% of their patients reported subjective symptoms of cognitive change at 3 months after undergoing major abdominal or orthopedic surgery.[15] A similar percentage of patients with subjective memory complaints at 6 months after noncardiac surgery was reported by Dijkstra and colleagues.[16] These, as well as several other studies that have investigated the relationship between subjective cognitive symptoms and objective test findings, have generally found a higher frequency of subjective symptoms than actual cognitive impairment as measured by neuropsychological tests.

Both the CABG and nonsurgical patients have risk factors not only for cardiovascular but also for cerebrovascular disease. There are several reasons to believe that the subjective symptoms may be related to progression of underlying cerebrovascular disease. First, the frequency of the subjective memory symptoms appears to be increasing over time for both the CABG and the nonsurgical controls. Some studies that have investigated subjective symptoms beyond 12 months report an even higher frequency of subjective memory complaints than we observed in our study. For example, Bergh and colleagues found that 60% of their CABG patients reported subjective memory symptoms up to 2 years after surgery. [2] This increase in subjective memory complaints over time would be more consistent with progression of underlying cerebrovascular small vessel ischemic disease than with a single exposure to cardiopulmonary bypass.

Second, studies that have compared the frequency of subjective memory complaints in CABG with either PTCA or off-pump surgery patients have found no group differences. In the study by Bergh and colleagues, the proportion of subjects reporting memory symptoms was similar among the patients with PTCA (63%) and those with CABG (60%). A more recent report from the Octopus trial found no significant differences between CABG and off-pump patients in the frequency of subjective cognitive symptoms at baseline, or change in symptoms from baseline to 12-month follow-up. [17]

Third, in a study examining the relationship between subjective cognitive symptoms and cerebral white matter lesions, more severe white matter lesions were found among those subjects with subjective complaints, even in the absence of abnormalities on neuropsychological testing. [18] These findings suggest that subjective cognitive symptoms may reflect subtle effects of mild underlying vascular disease that may not necessarily be detectable by objective neuropsychological testing.

We have also considered whether subjective symptoms may be a marker of future cognitive decline. There are several studies that have reported decline in cognitive performance between 1 and 5 years after CABG. A study from Duke University found that 42% of their patients had decline relative to their baseline performance when tested 5 years after surgery. One of the predictors of late decline was having cognitive decline during the immediate postoperative period. We and others have also found that a proportion of CABG patients decline in certain areas of cognitive test performance 5 years after surgery.[10,19,20] Because none of the long-term follow-up studies have included a control group, it is still unclear whether these late cognitive changes are specific to the use of cardiopulmonary bypass.

Subjective memory symptoms may represent a precursor of these late cognitive changes. A review of recent clinical and population-based studies concluded that subjective memory complaints might have different implications, depending on the age of the cohort studied. In middle-aged individuals, memory complaints may reflect depression, anxiety, or personality factors. By contrast, in older individuals, subjective memory complaints may be more likely to reflect actual change in cognitive functions. [21]

We have previously reported that the CABG group and nonsurgical controls in this study do not differ in terms of their performance on objective neuropsychological tests at 3 and 12 months[9]. A similar discrepancy between objective cognitive measures and self-reported symptoms has been reported for other studies that have examined postoperative cognitive outcomes after both cardiac [4] and noncardiac surgery. [8] These findings might suggest that subjective memory complaints do not reflect an underlying change in actual cognitive abilities. Alternatively, the relationship between subjective complaints and objective test performance may be complicated by subgroups of patients. For example, some patients with true memory impairment may not report any subjective changes because of lack of insight (anosognosia), whereas some patients with depression may report subjective symptoms despite normal memory. Another possibility is that when patients report changes in their memory, this might include a variety of perceived problems, ranging from difficulties with word-retrieval to inattention or absent-mindedness.

Some findings from recent studies comparing subjective memory symptoms and objective neuropsychological test performance suggest that subjective symptoms may reflect aspects of memory other than those captured by traditional measures of new learning and delayed recall. Working memory refers to an aspect of memory that is closely related to mechanisms of divided attention. It is a type of "memory" that permits manipulation of information while it is being maintained in a short-term, temporary store. The ability to repeat numbers in the reverse order of that being presented (Digit Span Backwards) is an example of a test that evaluates working memory. In samples of patients with HIV-related cognitive impairment, performance on measures of working memory was found to have the most robust association with subjective complaints, whereas traditional measures of new learning and delayed recall had a more modest association. [22] A similar relationship between performance on measures of working memory and subjective cognitive symptoms has also been found in other clinical samples, such as multiple sclerosis [23] and closed head injury. [24] We did not include specific measures of working memory in this study, but we did not find any differences between the CABG and nonsurgical groups on subtests closely related to working memory tests, such as measures of attention and executive functions.

Our study has several possible limitations. We did not assess self-reported cognitive symptoms at baseline (before surgery for the CABG group), and therefore, we cannot determine what proportion of the CABG patients may have had subjective memory complaints even before surgery. In studies that have included baseline assessment, one reported a similar preoperative level of subjective complaints among CABG and vascular surgery patients. [25] Our quantification of subjective complaints relied on a set of focused questions asking about perceived changes in memory and other cognitive functions. There is no current agreement on the best external criteria for validation of subjective memory complaint questionnaires. We chose these questions because they correspond to questions asked during a clinical interview or assessment.

In summary, our observations indicate that patients who have undergone CABG are more likely to report subjective memory symptoms than nonsurgical controls with coronary artery disease both at 3 months and 12 months after baseline assessment. These differences remain even after adjusting for demographic variables and depression scores. The explanation for the higher frequency of subjective complaints among CABG patients is not clear, but may reflect the combined effects of having had major surgery with general anesthesia and progression of underlying cerebrovascular disease. Continued follow-up of our cohort will help determine if the differences in subjective memory complaints between the CABG and nonsurgical controls will persist, and whether the presence of subjective memory complaints at 3 or 12 months will predict cognitive decline beyond the current 1-year follow-up.[26] If subjective symptoms are predictive of late cognitive changes, this may allow for new approaches to strategies for preventing such late decline. [27]

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Table 1:Baseline Demographic and Medical Characteristics

	CABG (N= 140)	NSC (N= 92)	*p*-value
Demographic data			
Mean age (years)	63.4 (9.6)	65.8 (9.2)	0.05
Gender (female)	25%	23%	
Ethnicity (white)	90%	94%	
Retired	43%	59%	
Married	77%	71%	
Mean education level (yrs)	14.1 (3.9)	14.4 (3.4)	
Medical History Info			
COPD	9%	5%	
Past CVA	6%	4%	
Carotid bruit	15%	8%	
Hypertension	62%	50%	
Diabetes	30%	23%	
PVD	16%	7%	0.02
TIA	6%	3%	
MI	46%	49%	
MI past month	18%	1%	0.0001
Chest pain	79%	61%	0.003
Pre-op a-fib	13%	17%	
FH Alzheimer's	14%	10%	
H/O smoking	68%	57%	
Current smoker	12%	3%	0.01
Mean # vessels diseased	2.75 (0.54)	1.95 (0.77)	0.0001
# vessels diseased 1	5%	32%	
2	15%	41%	0.0001
3	80%	27%	

Past PTCA	20%	53%	0.0001
Past CABG	9%	-	-
Past GA (5 years)	26%	25%	
Mean FSQ score (0-36)	31 (5)	33 (4)	0.0001
Mini-Mental Status Exam score (0-30)	27.5 (2.5)	27.9 (2.1)	
Mean CES-D score (0-60)	12.9 (9.6)	9.0 (7.6)	0.0001

Table 2 Relative risks (with confidence intervals) of self-reported symptoms for CABG patients as compared to nonsurgical control patients for various subjective outcomes

		Proportion with outcome		**Crude**		**Adjusted (no CESD)**		**Adjusted (with CESD)**	
Time	**Outcome**	**NSC(%)**	**CABG(%)**	**RR**	**CI**	**RR**	**CI**	**RR**	**CI**
3 months	Memory	5/84 (6%)	32/116 (28%)	4.63	(1.88,11.4)	4.72	(2.45,21.8)	4.96	(2.41,15.9)
	Calculations[1]	2/84 (2%)	5/116 (4%)	1.85	(0.35,9.76)	1.71	(0.32,9.23)	1.42	(0.25,8.18)
	Personality	5/84 (6%)	26/114 (23%)	3.83	(1.54,9.56)	3.58	(1.66,9.97)	3.63	(1.83,17.9)
	Paper[1]	2/84 (2%)	7/116 (6%)	2.63	(0.53,13.01)	2.88	(0.56,14.9)	2.93	(0.56,15.2)
	Books	4/84 (5%)	16/116 (14%)	2.90	(1.00,8.35)	3.32	(1.31,29.5)	3.03	(1.14,21.96)
	FSQ	27/84 (32%)	32/113 (28%)	0.88	(0.57,1.35)	0.94	(0.55,1.41)	0.88	(0.57,1.67)
12 months	Memory	12/83 (14%)	47/120 (39%)	2.71	(1.53,4.78)	2.52	(1.23,5.76)	2.83	(1.76,6.28)
	Calculations	4/83 (5%)	8/120 (7%)	1.41	(0.41,4.85)	1.57	(0.43,5.77)	1.46	(0.33,6.49)
	Personality	5/83 (6%)	22/120 (18%)	3.04	(1.20,7.71)	2.40	(1.06,7.74)	3.35	(1.17,17.4)
	Paper	4/83 (5%)	6/119 (5%)	1.05	(0.29,3.84)	1.20	(0.31,4.63)	1.24	(0.32,4.78)
	Books	5/83 (6%)	14/119 (12%)	1.95	(0.73,5.21)	1.80	(0.75,5.69)	1.85	(0.77,16.0)
	FSQ	32/82 (39%)	28/117 (24%)	0.61	(0.40,0.93)	0.56	(0.28,1.07)	0.57	(0.34,0.91)

[1] For Calculations and Paper the relative risk is approximated by the odds ratio under the rare disease assumption

Table 3 Incidence and maintenance models for self-reported symptoms at 12 months conditional on the 3-month responses

		Proportion with complaints at 12 months		Crude		Adjusted (no CESD)		Adjusted (with CESD)	
	Outcome	**NSC (%)**	**CABG (%)**	**RR**	**CI**	**OR[2]**	**CI**	**OR[2]**	**CI**
Incidence model No complaints at 3 months	Memory	9/74 (12%)	24/79 (30%)	2.50	(1.24,5.02)	3.04	(1.29,7.20)	2.96	(1.21,7.26)
	Calculations	3/77 (4%)	6/106 (6%)	1.45	(0.37,5.63)	1.84	(0.41,8.30)	1.40	(0.22,8.98)
	Personality	4/75 (5%)	8/83 (10%)	1.81	(0.56,5.76)	1.87	(0.53,6.58)	3.18	(0.71,14.1)
	Paper	2/77 (3%)	2/104 (2%)	0.74	(0.11,5.14)	1.00	(0.12,8.49)	1.01	(0.11,9.13)
	Books	4/75 (5%)	9/98 (9%)	1.72	(0.55,5.38)	1.88	(0.53,6.58)	1.66	(0.45,6.09)
	FSQ	14/53 (26%)	9/78 (12%)	0.44	(0.20,0.94)	0.30	(0.11,0.83)	0.30	(0.11,0.84)
Maintenance model Complaints at 3 months	Memory	3/5 (60%)	18/32 (56%)	0.94	(0.43,2.04)	0.64	(0.07,5.80)	1.80	(0.12,27.4)
	Calculations[1]	1/2 (50%)	1/5 (20%)	0.40	(0.04,3.74)	-	-	-	-
	Personality	1/4 (25%)	10/26 (38%)	1.54	(0.26,8.99)	2.53	(0.19,34.0)	1.72	(0.12,24.2)
	Paper[1]	2/2 (100%)	4/7 (57%)	0.57	(0.30,1.09)	-	-	-	-
	Books[1]	1/4 (25%)	3/13 (23%)	0.92	(0.13,6.60)	-	-	-	-
	FSQ	17/25 (68%)	17/31 (55%)	0.81	(0.53,1.22)	0.51	(0.15,1.77)	0.40	(0.10,1.62)

[1] Odds ratios are calculated instead of relative risks because of small group sizes.

Figure 1

Frequency of self-reported memory changes for CABG patients and nonsurgical controls at 3 and 12 months. At 12 months, the cross-hatched sections indicate the percent who had also reported subjective symptoms at 3 months.

Figure 2

Frequency of depression, as defined by a CES-D score of 16 or above, at baseline, 3 and 12 months for the CABG and nonsurgical control patients.

Figure 3

Longitudinal performance of the two study groups on a summary measure of memory. There is no difference between the two groups in their overall trends of performance over time ($p = 0.24$).

Figure 4

Longitudinal performance of the two study groups on a measure of attention (Rey Auditory Verbal Learning, Trial 1). There is no difference between the two groups in their overall trends of performance over time ($p = 0.16$).

Figure 5

Longitudinal performance of the two study groups on a measure of executive function (Trail Making test B). There is no difference between the two groups in their overall trends of performance over time ($p = 0.42$).

Figure 1

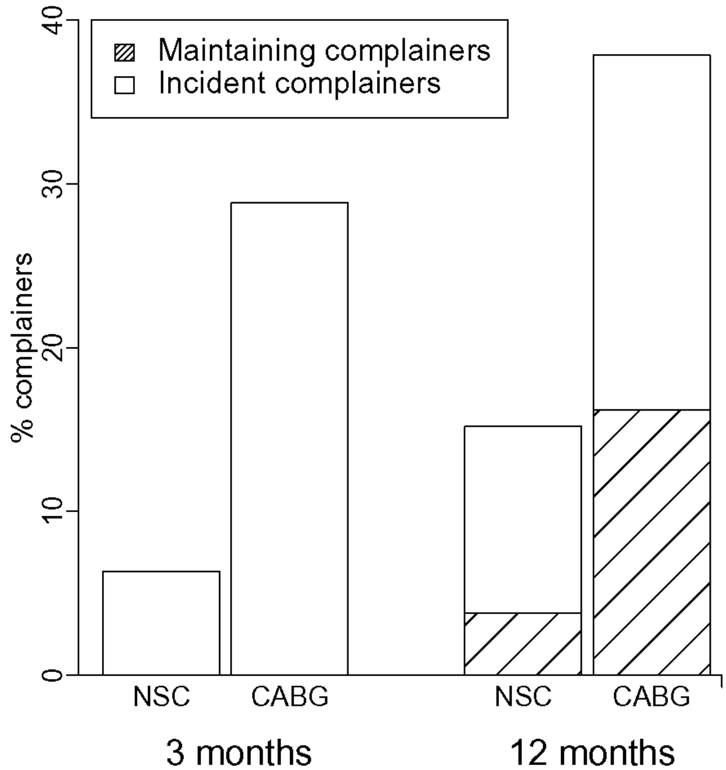

Maintaining complainers
Incident complainers
% complainers
0
10
20
30
40
NSC
CABG
NSC
CABG
3 months
12 months

Figure 2

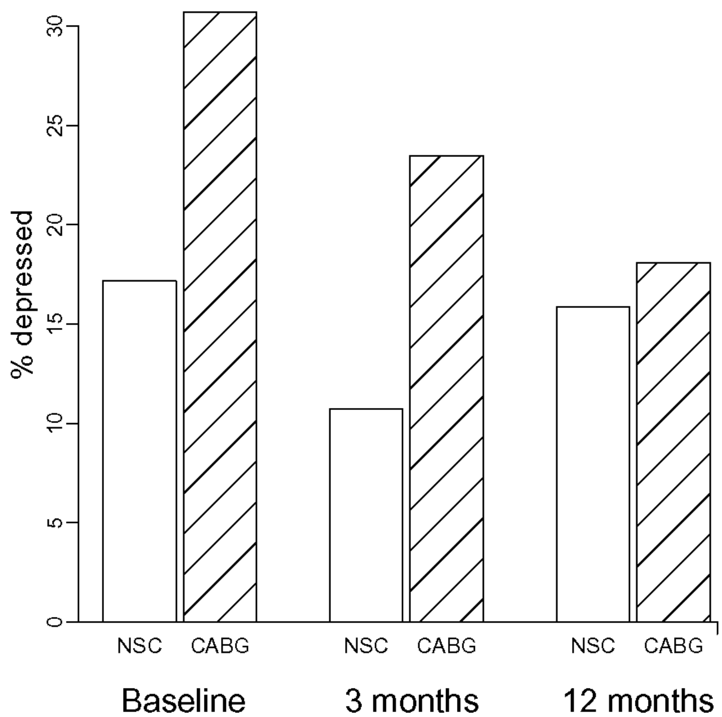

% depressed
0
5
10
15
20
25
30
NSC
CABG
NSC
CABG
NSC
CABG
Baseline
3 months
12 months

Figure 3

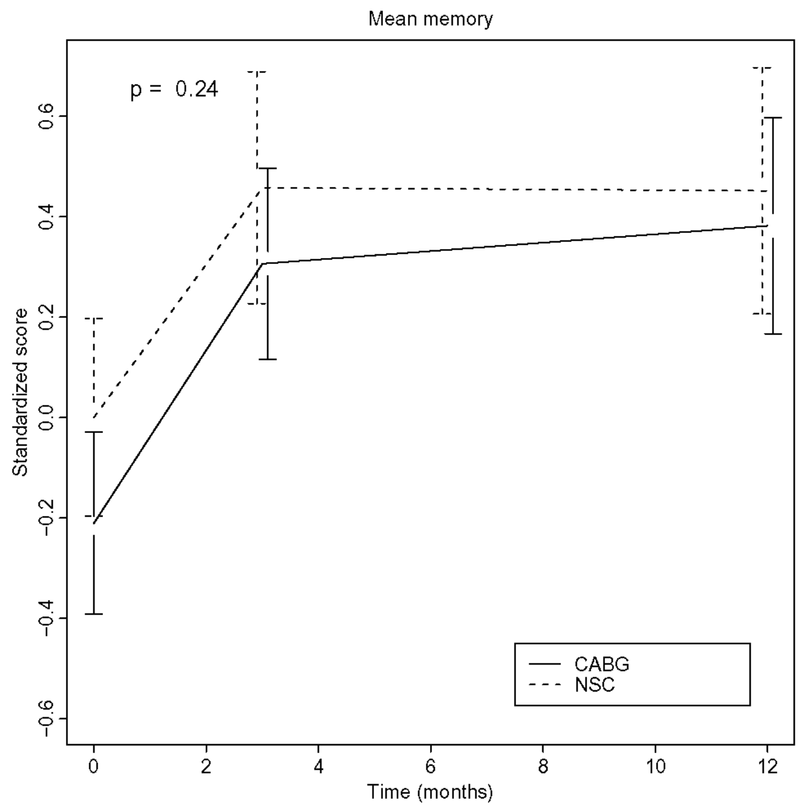

Mean memory
p = 0.24
Standardized score
0.6
0.4
0.2
0.0
−0.2
−0.4
−0.6
0
2
4
6
8
10
12
Time (months)
CABG
NSC

Figure 4

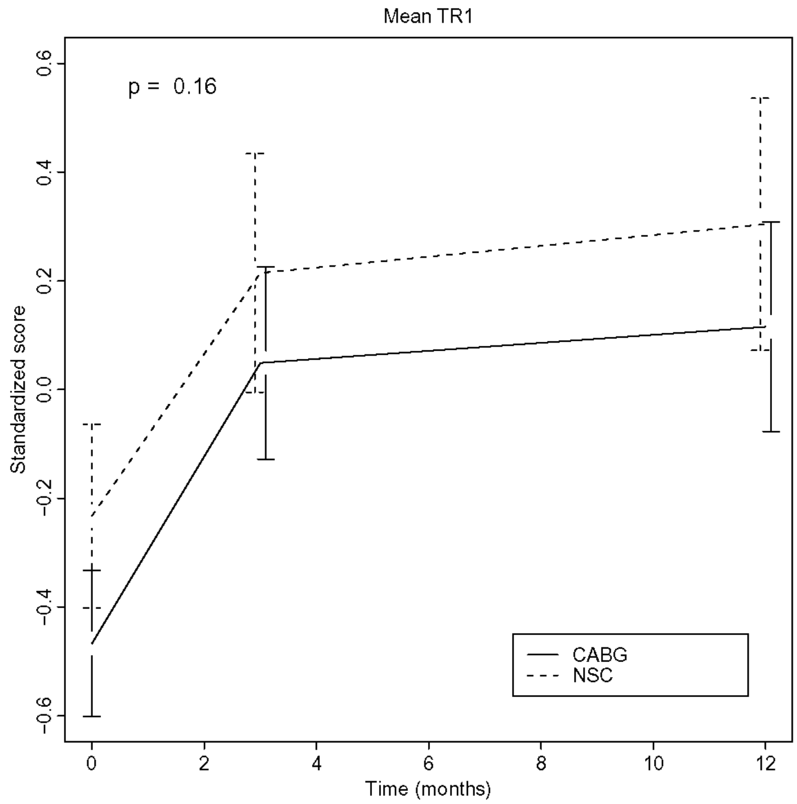
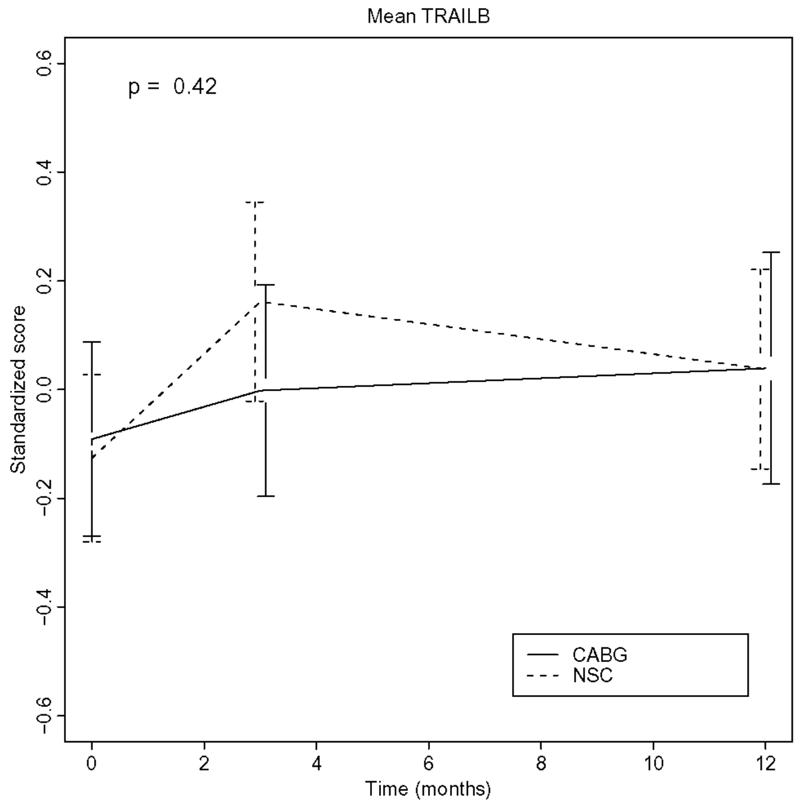

Mean TR1
p = 0.16
Standardized score
Time (months)
CABG
NSC
0.6
0.4
0.2
0.0
−0.2
−0.4
−0.6
0
2
4
6
8
10
12

Figure 5


Mean TRAILB
p = 0.42
Standardized score
0.6
0.4
0.2
0.0
−0.2
−0.4
−0.6
0
2
4
6
8
10
12
Time (months)
CABG
NSC