Cognitive function in patients undergoing coronary angiography

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ABSTRACT

Objective To measure cognition in patients before and after coronary angiography.

Design Prospective observational cohort study.

Setting University teaching hospital.

Patients 56 patients presenting for elective coronary angiography.

Main outcome measures Computerised cognitive test battery administered before coronary angiography, before discharge from hospital and 7 days after discharge. A matched healthy control group was used as a comparator.

Results When analysed by group, coronary angiography patients performed worse than matched controls at each time point. When the cognitive change was examined for each individual, of the 48 patients tested at discharge, 19 (39.6%) were classified as having a new cognitive dysfunction, and of 49 patients tested at day 7, six (12.2%) were classified as having a new cognitive dysfunction.

Conclusions The results confirm that cognitive function is decreased in patients who have cardiovascular disease. Furthermore, coronary angiography may exacerbate this impaired cognition in some patients.

We recently observed substantial preoperative cognitive impairment (PreCI) in 35% of patients awaiting elective CABG surgery.⁹ Importantly, these impairments were relatively large in magnitude ($>2SD$ below healthy controls) and occurred across domains of memory, executive function and attention. We noted that they were quantitatively and qualitatively similar to those that have been reported in the prodromal stages of Alzheimer's disease (eg, Mild Cognitive Impairment, MCI). The presence of significant cognitive impairment prior to elective CABG surgery indicates that individuals with cardiovascular risk factors also carry some cerebrovascular risk, an observation which has been reported in population studies.^{10 11} This concept is supported by Ernest *et al* who showed that patients scheduled for CABG surgery had poorer cognitive function than healthy controls.¹²

Another possible explanation for at least some of the pre-CABG surgery cognitive impairment may be coronary angiography. Coronary angiography is the gold standard for the detection and delineation of coronary artery disease. It is an essential but invasive prerequisite for CABG surgery. Coronary angiography requires the passage of catheters from a peripheral arterial access point through the aorta, past the great vessels providing the cerebral circulation, to selectively cannulate the left and right coronary arteries. Multiple injections of 5–10 ml of radiological contrast are made while cineangiography is obtained. This is frequently accompanied by placement of a catheter into the left ventricle to allow a high-pressure injection of a contrast bolus to assess left ventricular contraction. Passage of the cardiac catheters can potentially dislodge atheroma from the aortic wall, which may embolise to the cerebral circulation leading to stroke or cognitive decline.¹³ Air emboli may also enter the circulation through the coronary catheters. Consequently, the angiogram itself may have contributed to the cognitive impairment that has been reported previously in people awaiting CABG surgery.

We hypothesised that these microemboli, although not leading to clinical neurological signs, may manifest as cognitive dysfunction after the coronary angiography procedure. This post-procedural cognitive dysfunction (PPCD) would subsequently be measured as the baseline cognition in patients before CABG surgery and may contribute to the high incidence of PreCI. Since all determinations of POCD derive from the baseline cognition measurement, any such effect of coronary angiography on cognition would have far-reaching implications on the determination of subsequent POCD. In order to identify PPCD after

Postoperative cognitive dysfunction (POCD) after coronary artery bypass (CABG) surgery has been the subject of many investigations since it was first described in 1987.¹ Although the exact cause remains unknown, many studies have confirmed that cognitive function declines after CABG surgery in a substantial number of patients^{2 3} and may persist for up to 5 years postoperatively.⁴ The methodology used to document these cognitive changes has invariably utilised a battery of neuropsychological tests administered to patients before surgery and then at variable time intervals after surgery. Any decrease in test scores from the presurgical assessment has been interpreted as an indication that cognitive function has declined. This approach has been explicit in all studies, regardless of whether analysis of the test results has been as continuous variables of the group⁵ or dichotomous variables of individual test scores.⁶

Although many of the issues relating to testing and analysis of POCD have been addressed extensively,^{7 8} the issue of preoperative cognition is an important subject because it is used as a baseline from which all cognitive changes are derived. It has recently become evident that many of the patients tested before surgery already have cognitive decline relative to control groups who do not have coronary artery disease.

coronary angiography, we measured cognition before and after angiography using a computerised neuropsychological test battery that has been validated for the assessment of changes in cognitive function.

METHODS

An observational prospective study was approved by the Institutional Human Research Ethics Committee, and written informed consent was obtained from all patients. We planned a pilot study of 60 patients in order to acquire preliminary data.

Eligible patients were aged 55 years or older scheduled to undergo elective coronary angiography. They had no past history of stroke, epilepsy or other neurological deficits and lived within a reasonable distance of the hospital to facilitate follow-up testing. Those who had difficulties with English, psychiatric illness, vision impairment or any other condition that would impede neuropsychological testing were excluded. A Mini Mental State Examination (MMSE) of 24 or greater was used to identify and exclude those patients with possible dementia.

Fifty-six control participants were drawn from the healthy ageing study conducted by CogState (Melbourne, Australia) and were age- and gender-matched. The control group underwent testing at similar times to the patient group: twice on the first day of assessment, 3 h apart and repeated 7 days later.

All patients were premedicated with temazepam 10 mg and phenergan 25 mg orally before coronary angiography. The coronary arteries were accessed via the right femoral approach using routine catheter techniques. A total of 90–130 ml of Ultravist (Bayer, Pymble, Australia) contrast medium and saline were administered during the procedure.

Patients completed a computerised neuropsychological test battery prior to coronary angiography and premedication, and the same battery 3–4 h after the angiography just before discharge. Tests were administered in a quiet room without distractions within the angiography suite by a trained investigator under the supervision of a neuropsychologist (PM). The tests were administered again 7 days after coronary angiography at each subject's house, and again every effort was made to do this in a quiet room without distractions.

The computerised test battery was supplied by CogState and consisted of five tests requiring approximately 10 min for completion. The tests measured psychomotor function (Detection task), attention (Identification task), visual memory (One Card Learning task) and executive function (Groton Maze Learning and Groton Maze Learning Recall) tasks. These tasks have been described in detail previously^{14–18} and were administered according to standard instructions. They are summarised in table 1. These computerised tasks have been shown to be at least as effective as conventional pen-and-paper tests in detecting cognitive decline after cardiac surgery.¹⁹ Importantly, the computerised tasks have been designed specifically for repeated use and subsequently have a higher test–retest reliability and fewer practice effects than conventional tasks.

Cognitive test data were analysed at both the group and individual level. For the group, means and standard deviations were

Table 2 Demographics, cardiovascular risk factors baseline characteristics

Patients undergoing coronary angiography (n = 56)	
Age	66.8 ± 7.5
Gender, M/F	39/17
Diabetes	15 (26.8)
Hypertension	33 (58.9)
Hypercholesterolaemia	35 (62.5)
Peripheral vascular disease	5 (8.9)
Diagnosed coronary artery disease	47 (83.9)
History of smoking	38 (67.9)
History of myocardial infarction	23 (41.1)
History of coronary artery disease	25 (44.6)
History of closed head injury with loss of consciousness	12 (21.4)
Family history of Alzheimer's disease or dementia	7 (12.5)
Family history of cardiovascular disease	34 (60.7)

Continuous variables are given as mean ± SD and categorical variables as frequency (percentage).

computed for each performance measure for controls and for the patients. These data were compared using a series of independent group t tests and effect size calculated using Cohen's d.²⁰

Cognitive change was also computed for individual patients using the reliable change index (RCI).^{6, 21} To compute an RCI the preoperative score (X_1) was subtracted from the postoperative score (X_2), giving ΔX for each individual participant for a given task. The mean expected change for the controls ΔX_c , was calculated in the same way and was then subtracted from this. This score was then divided by the SD for the change in test results of the control group SD (ΔX_c) (controlling for learning effects and normal variation across time). A $Z_{\text{composite}}$ was calculated by summing the RCI scores (which are similar to Z-scores). Cognitive dysfunction was then defined as a combined score Z score < -2, and/or two or more Z - scores for single tests < -2.⁶

Statistical analysis

Cognitive test scores were compared as a continuous variable and as a dichotomous variable after patients were classified as having PPCD. Univariable analysis was undertaken using unpaired t tests for continuous variables or Fisher exact test (one-tailed) for dichotomous parameters. Changes in group mean test scores over time were assessed using ANOVA. Tests were performed using STATA (Version 8.0 Stata Corporation, College Station, Texas). A p value of <0.05 was taken to indicate statistical significance.

RESULTS

From October 2005 to March 2007, informed consent was obtained from 56 patients presenting for elective coronary angiography. The patients' characteristics are shown in table 2. The mean age was 66.0 ± 7.5 years, and 69.6% were male. For the control group, the mean age was 66.1 ± 6.0, and 65.2% were males.

No patient suffered a stroke. The coronary angiogram showed that nine patients (16.1%) had no angiographically apparent

Table 1 Cognitive tasks

Task	Outcome measure	Description of task	Units	Psychological domain
Groton Maze Learning	Accuracy of performance	Navigate maze without errors	No of errors	Executive function
Detection (simple reaction)	Speed of performance	Respond to playing card turning over	log ₁₀ ms	Psychomotor
Identification (choice reaction)	Speed of performance	Respond to colour of playing card	log ₁₀ ms	Attention
One-card Learning	Accuracy of performance	Remembering previous playing cards	Arcsine accuracy	Visual memory
Groton Maze Learning Recall	Accuracy of performance	Navigate maze without errors	No of errors	Executive function

coronary artery disease. However, all nine patients presented with symptoms of coronary artery disease, and all had at least one clinical risk factor for vascular disease. Since cognitive measures in these patients differed significantly from those with positive angiograms in only one test (One Back task at discharge and day 7), all cognitive results of all patients who underwent coronary angiography were analysed together as the one group.

Follow-up assessments at discharge were not performed in eight (14%) patients because they were either admitted to hospital or feeling unwell. Seven patients (12%) were not tested at 1 week because they refused or could not be contacted. The 1-week follow-up was performed at 7.0 ± 1.7 days after the procedure.

The mean test results for coronary angiogram and control patients for each cognitive measure at each time interval are shown in table 3 and represented graphically in figure 1. Patients for coronary angiography performed worse than the healthy controls for each cognitive measure at each time point. This was statistically significant except for the Groton Maze Learning task and Groton Maze Learning Recall task at day 7. With these exceptions, Cohen's *d* showed that the effect size ranged from 0.5 to 1.5, indicating that the difference between the two groups was large for all other measures of cognition and time points. A two-way ANOVA showed an interaction between time and Groton Maze Learning and Groton Maze Learning Recall tasks.

When the cognitive change was examined for each individual, of the 48 patients tested at discharge, 19 (39.6%) were classified as having PPCD at discharge, and six (12.2%) of 49 were classified as having PPCD at day 7.

DISCUSSION

Patients scheduled for coronary angiography performed worse than age- and gender-matched healthy control patients on all

tests of cognitive function when tested prior to their procedure. The effect sizes ranged from 0.5 to 1.5, signifying that the magnitude of impairment in cognitive function in people before and after angiogram was moderate to large. The largest impairments observed in the angiogram group (ie, $>1SD$) was for measures of psychomotor function and attention. Memory and executive function were less impaired. These results confirm the presence of impaired cognitive function in patients with cardiovascular disease and are in agreement with mounting reports of decreased cognition in patients with cardiovascular disease described in patients before both percutaneous cardiac intervention²² and cardiac surgery.^{9, 23} In contrast to prior studies, the cognitive tests in the current study were performed prior to coronary angiography and thus further implicate cardiovascular disease as an association of cognitive decline independent of any effect of coronary angiography.

The results are also consistent with population studies which show a definite association of cognitive impairment with cardiovascular disease.²⁴ This is in keeping with the repeated observation that subjects with risk factors for coronary artery disease are known to suffer from cognitive decline.²⁵

Importantly, in the control group, performance on each of the cognitive tests remained relatively stable over the study period. The absence of any practice related improvement in performance on these tests is consistent with the aims of the test battery and also with data published showing that in the absence of true central nervous system (CNS) change, performance remains stable on the CogState battery of tests.²⁶

The performance on most of the cognitive tests also remained stable in the angiogram group, albeit at a lower level than that observed in controls. The stability of performance in the angiogram patients underscores the reliability of the cardiovascular cognitive impairment. In the angiogram group, the only aspect of cognition to change over the study period was executive function as measured by the GMLT. Here, performance improved from the baseline at the Day 7 assessment. The magnitude of this improvement was such that at Day 7, the difference in performance on the GMLT between control and angiogram group was no longer statistically significant. The absence of any practice effects in the controls or for the baseline and 3 h postprocedural assessment in the angiogram groups makes it unlikely that the improvement observed at Day 7 in the angiogram group was the result of a practice effect. We also think it unlikely that the improvement in executive function at Day 7 reflected a direct benefit of angiogram; if this were the case, improvement would have been observed for some or all of the other cognitive tests. It is possible that the improvement on Day 7 reflects a random fluctuation in performance on the GMLT. Therefore, at this stage, we cannot interpret the result for the GMLT.

When PPCD was defined as a dichotomous variable, PPCD was present in 19 (39.6%) patients at discharge and six (12.2%) patients after 1 week. Individual analysis, rather than group analysis, may be considered to give a more accurate indication of cognitive dysfunction, because increases in function for some patients do not cancel out decreases in function in other patients.²⁷ Moreover, the criteria by which PPCD was defined are considered conservative.²¹ Using the same criteria for defining cognitive dysfunction, Moller *et al*²⁸ reported an incidence of 25% of POCD 1 week after non-cardiac surgery. The incidence of 39.6% at discharge may be due to the residual effects of drugs given for sedation during angiography. However, the incidence of 12.2% PPCD after 1 week, although less than that reported after invasive surgery, is concerning. It signifies

Table 3 Results of cognitive tests

Baseline				
Test	Coronary angiogram (n = 56)	Controls (n = 56)	p Value	Cohen's d
SRT	2.64 ± 0.20	2.47 ± 0.11	0.000	1.1
ChRT	2.81 ± 0.15	2.70 ± 0.06	0.000	1.0
LnT	0.68 ± 0.18	0.76 ± 0.15	0.012	0.5
GMLT	77.86 ± 29.15	54.66 ± 19.72	0.000	0.9
GMLTR	11.34 ± 6.10	7.93 ± 3.78	0.000	0.7
Discharge				
Test	Coronary angiogram (n = 48)	Controls (n = 56)	p Value	Cohen's d
SRT	2.64 ± 0.16	2.45 ± 0.08	0.000	1.5
ChRT	2.81 ± 0.11	2.71 ± 0.06	0.000	1.1
LnT	0.65 ± 0.14	0.79 ± 0.14	0.000	0.9
GMLT	78.58 ± 31.58	54.79 ± 18.11	0.000	0.9
GMLTR	11.79 ± 6.53	8.66 ± 4.30	0.004	0.6
Day 7				
Test	Coronary angiogram (n = 49)	Controls (n = 56)	p Value	Cohen's d
SRT	2.63 ± 0.17	2.46 ± 0.12	0.000	1.2
ChRT	2.79 ± 0.12	2.70 ± 0.06	0.000	1.0
LnT	0.66 ± 0.15	0.77 ± 0.16	0.000	0.7
GMLT	63.02 ± 22.93	57.96 ± 17.62	0.205	0.2
GMLTR	10.14 ± 5.58	9.39 ± 3.65	0.412	0.2

All variables given as mean ± SD

SRT = simple reaction time (log₁₀ms); ChRT = choice reaction time (log₁₀ms);

LnT = one card learning task (arcsine Hit Rate);

GMLT = Groton maze learning task (number of errors);

GMLTR = Groton maze learning task recall (number of errors).

Figure 1 Results of cognitive tests. CA, coronary angiogram.

that some patients with coronary artery disease not only start from a lower cognitive baseline but are vulnerable to further decline following coronary angiography.

The aetiology of cognitive dysfunction after coronary angiography is open to conjecture. Cardiac catheterisation and coronary angioplasty have been shown to be associated with gaseous and solid cerebral microemboli. Studies using Trans-Cranial Doppler have demonstrated microemboli in almost 100% of patients.^{13 29 30} Despite the frequent occurrence, no clinical neurological deficits have been linked to these emboli.

Nevertheless the presence of cerebral emboli, which may not be severe enough to cause overt stroke, may manifest as a cognitive decline.

CONCLUSIONS

The findings confirm the presence of poor baseline cognitive function in patients with coronary artery disease and the presence of further decline in some patients after coronary angiography. Further studies are indicated to confirm these results and elucidate details of the part coronary angiography may play in

exacerbating cognitive decline in an already impaired group of patients. Additionally, the role of cerebral emboli in cognitive change requires further attention.

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Competing interests PTM is a principal at Cogstate, Melbourne, Australia.

Patient consent Obtained.

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