Pre-existing cognitive impairment as a factor influencing outcome after cardiac surgery

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Conventional methodology to investigate cognitive impairment after coronary artery bypass graft (CABG) surgery leaves unclear the potential for pre-existing cognitive deficits to influence outcome. Individuals with pre-existing deficits may be more vulnerable to the effects of CABG, hence biasing the results of a typical prospective trial if account is not taken of their state. The present study examined the effect of pre-existing cognitive impairment upon cognitive outcome in 81 patients undergoing CABG. Patients performed the Stroop Neuropsychological Screening Test and other psychometric assessments prior to and at 6 days and 6 months after CABG. Those with pre-existing cognitive deficits were significantly more likely to display impairment at 6-day and 6-month follow-ups than were those without pre-existing deficits. Greater age and lower pre-morbid intelligence were also significant predictors of post-CABG deficit, confirming earlier findings. The results imply both that pre-existing cognitive impairments may render patients more vulnerable to post-operative deficits and that, in the absence of such pre-existing impairments, CABG surgery does not inevitably lead to later deficits. The study also replicated previous findings showing a similar influence of pre-existing depression upon emotional state after CABG. Overall, the results confirm the importance both of a patient’s pre-existing cognitive and emotional states, and the methodology to assess them, in influencing outcome after cardiac surgery and the conclusions to be drawn as to the supposed adverse effects of the procedure.

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pre-existing deficits. The present study makes such an assessment by using the Stroop Neuropsychological Screening Test\(^5\) which has age-related impairment norms to define absolute impairment. The Stroop assesses attention and the ability to resist distraction, and is sensitive to impairment as a result of mild brain damage and to the subtle changes seen in mild to moderate dementia.\(^6\) Performance on the Stroop prior to CABG has already been shown to be predictive of post-operative outcome.\(^7\) However, critically, the investigators did not take account of whether the pre-operative performance was indicative of absolute impairment. Other studies which have employed the Stroop to investigate both CABG-related impairment\(^8\)\(^-\)\(^10\) and post-anaesthetic recovery\(^11\) have confirmed the sensitivity of the task to change from pre- to post-operative state but, again, without accounting for pre-operative impairment.

The potential importance of accounting for the patient’s pre-existing cognitive state in interpreting post-CABG deficits is not speculative but is confirmed by parallel research concerning the effects of CABG upon emotional state. Whilst the reported significant increases in depression after CABG have commonly been assumed to be a direct consequence of the procedure, research has shown that the presence of pre-existing depression is a significant determinant of the post-CABG state: patients who are not depressed beforehand are at substantially lower risk.\(^12\)\(^-\)\(^15\)

The methodology of the present study involves assessment of both absolute cognitive impairment and presence of depression prior to CABG, hence clarifying whether pre-existing impairments predict post-operative outcome, and replicating the existing results concerning depression and CABG outcome.

**Methods**

**Patients and procedure**

Following approval of the study by the Ethics Committee of the Western Infirmary, Glasgow, 120 patients (92 men, 28 women; 77.23%) undergoing coronary artery bypass graft (CABG) surgery gave informed consent to participate. The standard anaesthetic regimen was adapted as necessary according to the patient’s physical state and cardiac drug therapy. Patients were premedicated with temazepam or lorazepam orally the night before, and on the morning of surgery. After pre-oxygenation and establishing venous and arterial access, anaesthesia was induced with propofol and fentanyl. Tracheal intubation was facilitated, and neuromuscular blockade maintained by bolus doses of pancuronium. The lungs were inflated with at least 30% oxygen in nitrous oxide with varying doses of isoflurane. During cardiopulmonary bypass, additional fentanyl was given and a propofol infusion used. The bypass system, using a membrane oxygenator, was regularly adjusted according to measurements of pH and \(P_{\text{CO}}\). The patients were cooled to core temperatures between 28 and 32°C, and the heart arrested using St Thomas’s cardioplegia solution. Infusions of nitroglycerine and dopamine were used to support the heart and circulation as required. The patients were transferred to a cardiac intensive care unit for recovery, the majority being returned to the ward the next day.

**Psychometric assessment**

Patients were assessed 3 days before, and 6 days and 6 months after CABG. The Stroop Neuropsychological Screening Test\(^5\) consists of a sheet presenting a list of 112 colour names printed in incongruous colours (e.g. the word ‘blue’ printed in green ink). The subject was required to read through the list as quickly as possible, reading out the name of the colour in which the word is printed. The interference effect produced by the incongruity of the word name and the colour of its presentation renders the task very demanding of attention and concentration. The score is the number of words read correctly in 2 min. The task norms allow an individual’s score to be categorized as indicative of likely brain damage as a function of their age. Depression was assessed with the self-report Beck Depression Inventory\(^16\) using the conventional criterion of a score \(\geq 9\) as indicative of depression. Years of education are known to have a protective function from the adverse effects of CABG,\(^17\) hence pre-morbid intellectual status was assessed prior to CABG with the National Adult Reading Test (NART).\(^18\)

Personality characteristics of extroversion and neuroticism can predict post-surgical outcome\(^19\) and were assessed prior to CABG by the Eysenck Personality Questionnaire.\(^20\)

Statistical analysis was conducted with Minitab version 12 via Windows 95 on a Viglen Contender PC.

**Results**

Eighty-one of the 120 patients completed the assessments at all three periods (64 men, 17 women; 79.21%, the proportions being almost identical to the original full sample hence indicating equivalent attrition as a function of gender). The mean ages for men and women (SD; range) were 59.4 (8.7; 38–76) and 62.4 (10.0; 37–73) yr respectively. Because of the very small proportion of women participating in the study, the factor of gender is not considered further in the analysis. The mean NART error score of 15.2 (SD 6.85) corresponded to an average IQ of 111.\(^5\)

Table 1 shows the number and percentage of patients suffering cognitive impairment at 6 days or 6 months follow-up, or at both follow-ups, as a function of their pre-CABG state. Prior to CABG, 13 (16%) patients had pre-existing impairment. Postoperatively, 11 (85%) of the latter patients were impaired at 6 days, a total comprising six (46%) who were impaired only at 6 days and five (39%) who were impaired at 6 days and remained so at 6 months. In contrast, of the 68 (84%) who were not impaired prior to the
procedure, a total of nine (14%) became impaired at 6 days, these being eight (12%) who were impaired only at 6 days and one (2%) who was impaired at both follow-ups. By contrasting the proportion of patients who were impaired with those unimpaired before CABG and at follow-up, the presence of pre-CABG impairment was found to be a significant predictor of the post-procedure state (Fisher’s exact test, both $P<0.001$). There was no evidence of late-onset impairment: no patient was impaired at 6 months without having previously been impaired.

Table 1 also shows that depression as a function of the pre-CABG state follows an identical pattern to that for impairment. Of the 23 (28%) patients who reported pre-operative depression, a total of 18 (78%) continued to be depressed at 6 days follow-up, nine (39%) of these being depressed only at 6 days and nine (39%) being depressed at both follow-up periods. Of the 58 (72%) who were not depressed prior to CABG, a total of eight (14%) reported depression at 6 days follow-up, six (10%) of these being depressed only at 6 days and two (4%) being depressed at both follow-ups. By contrasting the proportions of patients who were depressed with those who were not depressed before CABG and at the subsequent two follow-ups, the presence of pre-CABG depression was found to be a significant predictor of the post-procedure state (chi-squared, both $P<0.001$). There was no evidence of late-onset impairment: no patient was impaired at 6 months without having previously been impaired.

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The prediction of post-CABG impairment on the Stroop task was assessed further by multiple linear regression with the independent continuous variables of age, NART error score, and scores of extroversion and neuroticism. The regression showed the variables of age and NART to be significant predictors, together accounting for 34% of variance in Stroop performance at 6 days ($P<0.001$) and 24% at 6 months ($P<0.01$). Thus, patients who were older, and those of lower pre-morbid intellectual capacity, were more likely to suffer post-CABG deficit. The personality factors were not predictive.

Table 1 also shows mean Stroop performance at each time point as in a conventional analysis to describe impairment as a change from baseline. The performance profile shows an immediate post-operative deterioration in performance, which is then followed by a marked recovery at 6 months to a level substantially above that of the pre-operative baseline. The significant main effect of time (ANOVA: $F_{2,240}=8.70$, $P<0.001$) is located in significant differences between performance at 6 months and that at 6 days and baseline (Tukey post-hoc comparisons). The outcome of this mean-based analysis suggests an overall recovery of function at 6 months and is in contrast to the preceding analysis, based on assessment of absolute impairment, which shows some 40% of patients to be impaired at the second follow-up.

### Discussion

The results confirm that pre-existing cognitive impairment is a significant determinant of whether deficits are observed after anaesthesia and surgery associated with CABG. Patients with a pre-existing attentional deficit as assessed by the Stroop task were significantly more likely to show post-CABG attentional impairment than those without such a deficit. MRI studies indicate that CNS abnormalities resulting from the patients’ chronic cardiac disease may underlie such pre-existing intellectual impairments.

The results also fully replicate earlier findings showing that post-CABG depression, too, is significantly determined by the patient’s state prior to the procedure. More generally, the results support previous findings that CABG outcome is predicted by age and pre-morbid intellectual status. Older patients, and those with

### Table 1

The number and percentage of patients suffering cognitive impairment and depression as assessed by Stroop Neuropsychological Screening Test and Beck Depression Inventory before and after coronary artery bypass graft surgery. Mean Stroop performance before and after surgery is shown in the lower panel of the table (SD in parentheses).

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Pre-operative status</th>
<th>Post-operative status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired</td>
<td>13 (16%)</td>
<td>6 (46%)</td>
</tr>
<tr>
<td>Unimpaired</td>
<td>68 (84%)</td>
<td>8 (12%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Depression</th>
<th>Pre-operative status</th>
<th>Post-operative status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressed</td>
<td>23 (28%)</td>
<td>9 (39%)</td>
</tr>
<tr>
<td>Not Depressed</td>
<td>58 (72%)</td>
<td>6 (10%)</td>
</tr>
</tbody>
</table>

Mean Stroop performance

<table>
<thead>
<tr>
<th>Pre-operative</th>
<th>6 days</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>85.5 (19.6)</td>
<td>80.4 (22.0)</td>
<td>93.3 (17.8)</td>
</tr>
</tbody>
</table>
lower pre-morbid intellectual function, were more likely to suffer post-CABG impairment.

Caution is required in extrapolating from the present study where only one cognitive assessment has been employed. Nonetheless, the obvious corollary of the results is that, unless allowance is made for pre-existing impairments, there is the risk of erroneously ascribing some adverse outcomes to a procedure and hence over-estimating its potential risks. Furthermore, where a procedure does exacerbate a pre-existing deficit, the full impact may be missed when using purely relative measures. For example, even a slight decline in the performance of an individual with a pre-existing impairment may be of considerable clinical consequence when compared with that of an individual without such impairment.

The latter issue of individual variation is also critical to full understanding of CABG-related impairment. It has been widely observed, both in the case of CABG and recovery from general anaesthesia, that individual variation is often masked when results are expressed in terms of group means and that this may lead to failure to detect both decline and improvement in a subgroup of patients.\(^2\)\(^22\)\(^25\)\(^\text{-}^27\) The present analysis demonstrates that simply comparing average pre- and post-CABG performance does not accurately describe the adverse impact of CABG upon Stroop performance and the recovery of function. The mean-based analysis gives the impression of overall recovery of function at 6 months whereas the assessment of absolute impairment shows a substantial proportion of the patients still to be impaired.

Whilst the detection of impairment is a principal concern in studying outcome after CABG, it is important also to be aware of potential improvements in function because of the procedure. Eight of the present patients who were impaired prior to CABG improved significantly to unimpaired status 6 months after surgery. Their mean change in Stroop score of 18.5 (SD 9.47) corresponds to a 28% improvement from their baseline (\(t_r=4.55, P=0.003\)) and contrasts markedly with the 5% improvement due to practice typically seen in ‘normal’ subjects.\(^5\) Whilst speculative given the present small sample, it has been proposed that such improvement reflects both practice and the beneficial effects of improved perfusion upon cognition.\(^23\)

The present attrition rate of 32% is virtually identical to that of a very recent study of pre-existing depression and CABG\(^14\) but it is higher than that of others.\(^12\)\(^13\)\(^15\) Attrition commonly affects studies involving long-term follow-up and may result in fundamental differences between those who continue with a study and those who ‘drop out’. Benedict\(^22\) has observed that when a group of particularly impaired individuals drop out of a CABG data set there is then the potential for the procedure to appear to exert a less adverse effect. Further analysis of the present data confirms that, pre-operatively, the proportions of those impaired and depressed were considerably higher amongst the drop-outs than those who continued with the study (36 vs 16%, and 44 vs 28%, for impairment and depression, respectively).

Whilst the differences are not statistically reliable because of the small numbers involved, they show that attrition has the potential to distort the results of such a study (\(P=0.21\) and \(P=0.10\), for impairment and depression, respectively).

A similar effect of attrition is seen in the results of Vingerhoets and colleagues.\(^8\) Some 48% of one of their CABG study groups dropped out between baseline and follow-up, the consequence being that the baseline Stroop performance of those who continued with the study (and against which long-term follow-up was evaluated) was some 23% better than that of the original sample.

Extensive studies of CABG-related cognitive deficits have led to detailed ‘Consensus Statements’ by Murkin and his colleagues regarding the tasks and methodology for such research.\(^2\)\(^2\)\(^2\)\(^8\)\(^2\)\(^2\)\(^9\) The present results confirm the specific consensus regarding pre-operative assessment: ‘A number of patients presenting [for CABG] may have pre-existing CNS abnormalities. [The] neuropsychologic state needs to be assessed[…] prior to operation to provide accurate baseline information.’ (p. 1289).\(^2\)\(^5\) The present results suggest that baseline information would be obtained more accurately with tasks that provide evidence of absolute functional status than the commonly used relative measures. They have the further virtue of being predictive of outcome.

The present results do not call into question the general principles outlined in the Consensus Statement for research into CABG impairment.\(^2\)\(^5\) There would seem merit, however, in a series of studies to contrast absolute and relative measures of cognition in their ability both to detect pre-existing deficits and to predict subsequent CABG-related impairment. Indeed, retrospective analysis of some published data sets might be capable of addressing this question where those studies have involved tasks with absolute performance norms which were not employed in the original analysis.

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Cognitive impairment after cardiac surgery

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