Early Postoperative Cognitive Dysfunction and Blood Pressure During Coronary Artery Bypass Graft Operation

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Objective: To determine the relationship between change in blood pressure during coronary artery bypass graft operations and early cognitive dysfunction.

Design: Cohort study.

Setting: Quaternary care facility.

Patients: Fifteen patients undergoing coronary artery bypass graft operations who were at high risk for postoperative stroke. Preoperative and intraoperative mean arterial pressures (MAPs) were measured in all patients.

Intervention: A subset of patients underwent preoperative and postoperative magnetic resonance imaging.

Main Outcome Measure: Change in cognitive performance, using the Mini-Mental State Examination and other simple cognitive tests.

Results: A drop in MAP (preoperatively to intraoperatively) predicted a decrease in Mini-Mental State Examination score. When change in MAP was dichotomized (after excluding an outlier), subjects with a small decrease improved on the Mini-Mental State Examination by 1 point, whereas those with a large drop in MAP worsened by 1.4 points ($P = .04$).

Conclusion: A drop in MAP from a preoperative baseline may put patients at risk for early cognitive dysfunction after a coronary artery bypass graft operation.

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Many patients who undergo a coronary artery bypass graft (CABG) operation have preexisting vascular disease, and a subset have preexisting cognitive dysfunction. Although recent prospective controlled trials have suggested that CABG may not cause long-term cognitive dysfunction, there may be a subset of patients who experience short-term cognitive problems. Although patient characteristics like preoperative cognitive dysfunction and premorbid cerebrovascular disease are known risk factors for short-term cognitive dysfunction or encephalopathy, other factors that might contribute to this short-term cognitive dysfunction have not been well defined.

We have previously reported that, among patients with stroke after cardiac operations, a drop in mean arterial pressure (MAP) from baseline during cardiopulmonary bypass is associated with increased risk of bilateral watershed strokes. The purpose of this retrospective analysis was to determine if a decrease in MAP during a CABG operation was also a risk factor for cognitive dysfunction in the immediate postsurgical period.

METHODS

We enrolled 15 patients undergoing an on-pump CABG operation at the Johns Hopkins Hospital in Baltimore, Maryland, who were believed to be at high risk for postoperative stroke (as defined by our previously described risk stratification). Patients were tested 1 to 2 days preoperatively using the Mini-Mental State Examination (MMSE), Trail Making Tests A and B, and the modified Rankin scale. These tests were repeated 3 to 5 days postoperatively and, in a subset of subjects, repeated at 1 month postoperatively.

Change in MMSE was defined as preoperative MMSE score minus postoperative MMSE score (with a positive score representing performance decrement). Change in Trail Making Test performance was preoperative time minus postoperative time. Because a longer time represents worse performance, a negative value represents worsening performance.
Change in modified Rankin score was defined as a shift in category. A Rankin score of 0 or 1 was defined as a good outcome, with a score of 2 or higher consistent with a poor outcome. Patients were dichotomized as having shifted from a good to poor outcome or as having stayed in the same category (or improving).

Preoperative MAPs were recorded in all patients. Intraoperative MAP was defined as the mean value of all of the patient’s MAPs while the cardiopulmonary bypass pump was being used. Change in MAP was defined as preoperative MAP minus the mean intraoperative MAP.

All but 2 patients underwent postoperative magnetic resonance imaging with diffusion-weighted imaging (DWI). Diffusion-weighted imaging results were divided into 2 groups: having any acute restricted diffusion on DWI (consistent with acute stroke) or having no restricted diffusion.

Statistical analysis was performed using Stata, version 8.0 (Stata Corp, College Station, Texas), for Macintosh. t Tests and multiple linear regressions were performed to determine the relationships between dichotomized MAP difference and continuous change in cognitive performance, and between linear MAP difference and continuous change in cognitive performance. For the multivariate regressions, the models were adjusted for stroke probability, which is a composite risk score for postoperative stroke, including the following vascular risk factors: age; history of hypertension, diabetes, and stroke; and presence of carotid bruit. The model has been previously published. The analyses were repeated for (1) subjects, with exclusion of an outlier, as detected by visual inspection (by scatterplot) of the data, (2) all subjects, and (3) subjects without acute stroke on postoperative magnetic resonance imaging DWI. In addition, analyses of the association between any DWI lesion and change in MMSE score as well as the association between change in MAP and DWI lesion were each examined using t tests and logistic regression, respectively.

The age range for the 15 subjects was 57 to 81 years (median age, 71 years). The median preoperative MMSE score was 28. After visual inspection of all test results with scatterplots, 1 subject was found to be an outlier on all cognitive tests. This patient had a new acute stroke during the operation and had major worsening in performance across multiple tests. Results are reported first without inclusion of this patient and subsequently with inclusion of this patient.

EXCLUDING OUTLIER

All subjects had a decrease in MAP during surgery compared with their baseline blood pressures. Subjects who had a drop in MAP of 27 mm Hg or greater had a mean decrease in MMSE score of 1.4 points. In contrast, after exclusion of the outlier, subjects with a decrease in MAP of less than the median improved by a mean of 1 point (P = .04). In an unadjusted analysis of continuous change in MAP, each additional point decrease in MAP (from baseline) led to a 0.09-point greater decrement in MMSE score (P = .08). In an unadjusted analysis of continuous change in MAP (from baseline) to a 0.09-point greater decrement in MMSE score (P = .02, unadjusted) (Figure 1). When probability of stroke (calculated by our previously published risk model, which takes into account age; history of hypertension, diabetes, and stroke; and presence of carotid bruit) was adjusted for in a multivariate regression, the effect size and level of significance were essentially unchanged (β = .08; P = .02).

The Table and Figure 2 detail MMSE performance and blood pressure change. Preoperative MAP was also independently associated with a change in MMSE score. Subjects with higher preoperative MAPs were more likely to have a decrease in their MMSE score (P = .006, without outlier; P = .12, with outlier).

Although findings did not reach statistical significance for change in other cognitive tests, the pattern was similar. For Trail Making Test A (only with exclusion of the outlier), subjects with a greater drop in MAP had a mean increase of 25 seconds in completion time, whereas subjects with a smaller drop in MAP had a mean increase in completion time of 12.6 seconds (P = .70). For Trail Making Test B, these values were 73

Table. Preoperative and Postoperative MMSE Scores and Change in MAP

<table>
<thead>
<tr>
<th>Patient</th>
<th>Preoperative MMSE Score</th>
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<th>Change in MAP, mm Hg*</th>
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Abbreviations: MAP, mean arterial pressure; MMSE, Mini-Mental State Examination.

*Preoperative minus intraoperative MAP. In all cases, preoperative MAP was higher than intraoperative MAP.

b This patient was categorized as an outlier across multiple cognitive measures. Results are reported with and without inclusion of these data.
seconds longer in those with a greater drop in MAP and 52 seconds longer in subjects without a large drop in MAP ($P = .77$).

Preoperative and postoperative modified Rankin scale assessments were also used to quantify postoperative functional worsening. Among subjects who shifted in Rankin category from a good outcome preoperatively (score of 0 or 1) to a poor outcome postoperatively (score $\geq 2$), the mean drop in MAP was 39.7 mm Hg when the outlier was excluded (32 mm Hg when included). In subjects who did not have worsening of their general Rankin category, the mean decrease in MAP was 19.9 mm Hg ($P = .04$, without the outlier; $P = .19$, with the outlier).

**INCLUDING OUTLIER**

In general, the same analyses yielded similar results when the outlier (and thus all subjects) was included, but these results did not reach significance. Subjects with a smaller drop in MAP worsened, on average, by 0.1 point ($P = .40$), compared with a mean worsening of 1.4 points for subjects with a drop in MAP of more than the median. There was a mean decrease in the MMSE score of 0.05 point per additional point decrease in MAP ($P = .35$). When this analysis was repeated after adjusting for stroke probability group (a composite of vascular risk factors), the regression coefficient was 0.04 ($P = .36$).

For the analysis of preoperative MAP as a potential predictor of change in the MMSE score, subjects with a higher preoperative MAP were still more likely to have a decrease in their MMSE score, though this result was not statistically significant ($P = .12$). When change in Rankin category was analyzed, as described previously, subjects who shifted from good to poor Rankin category had a mean drop in MAP of 32 mm Hg, compared with 19.9 mm Hg for those who did not shift a major category ($P = .19$).

**NEUROIMAGING**

Diffusion-weighted imaging was completed in 13 of these subjects, 6 of whom had at least 1 acute DWI lesion, 1 of whom was the outlier. Owing to these small numbers, it was unclear what the effect of having had a new DWI lesion was. Nonetheless, there was a trend toward increased risk of having a DWI lesion in subjects with a larger decrease in MAP (patients with a drop in MAP that was greater than the median were 2.7 times as likely to have a DWI lesion ($P = .39$)). In addition, subjects with DWI lesions worsened by a mean of 1.9 points on the MMSE, and those without DWI lesions improved by a mean of 0.14 point ($P = .16$).

**EXCLUDING SUBJECTS WITH ACUTE INFARCT BY DWI**

Because of the apparent association of a DWI lesion with cognitive performance and change in MAP, the analysis was also repeated only among those subjects without radiographic infarction. Seven subjects had DWI performed and had no acute infarct. For these 7 subjects, those with a decrease in MAP of 27 mm Hg or higher had a mean decrease in MMSE score of 0.3 point, and those with a decrease in MAP of less than the median improved by 0.5 point on average ($P = .54$). In the linear regression analysis, the mean drop in MMSE score per additional point dropped in MAP was 0.02 ($P = .6$).

**LONG-TERM RESULTS**

Eleven of the subjects were followed up at 1 month for cognitive testing. The potential power of the study is clearly reduced further by this smaller sample size. For all 11 subjects, those with a preoperative to intraoperative drop in MAP of less than 27 mm Hg had no change, on average, in their MMSE score at 1 month compared with their preoperative performance. Those who had a drop of at least 27 mm Hg averaged a 0.2-point worsening in their MMSE score at 1 month postoperatively ($P = .53$).

When change in Rankin category was also reassessed at 1 month, only 1 subject who started in a good outcome category (Rankin score $= 1$) remained in a poor outcome category (Rankin score $= 3$). This subject had a drop in MAP of 38 mm Hg during the time of the operation.

**COMMENT**

Our data suggest that a change in MAP from a subject’s preoperative baseline may be associated with decrement in cognitive performance. Despite small patient numbers, the direction of performance is uniformly the same across multiple cognitive tests (either with or without exclusion of an apparent outlier), further supporting an association between change in blood pressure and change in cognitive performance. These data are also supported by the direction of effect in the small subsample of subjects who had no acute stroke by magnetic resonance imaging, though it is difficult to make any conclusions in this population, as it only includes 7 subjects. The short-term Rankin results should also be interpreted cautiously because this functional measure may be difficult to assess in the short-term period immediately after the operation.

Our data also reemphasize the importance of baseline testing in these patients, as has been pointed out else-
where. Clearly, many subjects had baseline MMSE scores in the impaired range (Table), and any apparent worsening in performance cannot be assessed without knowledge of baseline function.

The relationship between acute stroke on DWI and early cognitive dysfunction in our study is unclear. There have been conflicting reports in the literature on the association between magnetic resonance imaging findings and postoperative cognitive dysfunction. Some articles have suggested an association between new magnetic resonance imaging lesions and cognitive decline, with more recent studies failing to show such an association.

Our study is primarily limited by the small sample size. However, given the effect size, we found a significant effect of change in MAP, even with a small number of patients. Additionally, these patients were selected because of their increased risk status. It is unclear whether a drop in MAP is also potentially detrimental in subjects at lower risk. However, more patients who currently undergo a CABG operation, given the higher frequency of stenting and angioplasty, are of relatively high risk.

Other study limitations include the short-term follow-up and the limited set of cognitive tests performed on these patients. Additionally, there was an apparent relationship between preoperative MAP and change in performance on the MMSE. It may be that preoperative blood pressure is the most important factor in predicting outcome and that change in MAP is merely a surrogate for this preoperative value. The subset of subjects who had follow-up at 1 month were probably the healthier of the general group, as they were able to complete follow-up.

Another limitation is our choice to exclude the outlier in many analyses and their interpretation. Although inclusion of the outlier still led to the same direction of effect in almost all cases, it is possible that this outlier actually represents a larger proportion of the population and therefore needs to be included in any conclusions regarding these data. These data do not provide any definitive information on the potential relationship between change in blood pressure and short-term cognitive performance, but they emphasize the need for further studies to understand the precise nature of this relationship as well as how this relationship is affected by perioperative acute infarction.

Our preliminary data from a small group of subjects suggest that a substantial decrease in MAP from a patient’s baseline may be a risk factor for short-term cognitive dysfunction. This may be in part because of an increased risk for radiographic stroke. Future prospective studies are needed to further define the relationship between change in blood pressure and postoperative stroke as well as change in blood pressure and postoperative cognitive performance.

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