Angiographic coronary diffuseness and outcomes in dialysis patients undergoing coronary artery bypass grafting surgery

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Abstract

Objective: Pre-operative dialysis-dependent renal failure (DDRF) is a predictor of morbidity and mortality following coronary artery bypass grafting surgery (CABG). Whether this is due in part to a more diffuse coronary atherosclerotic burden in these patients is unknown. The purpose of this study was to compare coronary atherosclerotic disease burden in patients with and without pre-existing DDRF undergoing CABG. Methods: From a retrospective analysis of a single-centre cardiac surgical database, consecutive DDRF patients undergoing isolated CABG (n = 35) were matched to 70 non-dialysis-dependent (NDD) patients without renal failure by procedure, age, sex, functional status, ejection fraction, number of diseased vessels, and diabetes. Pre-operative angiograms were analyzed by a single, blinded adjudicator using a modification of a previously published coronary diffuseness score (range: 0–45). Angiographic scores and baseline and outcome characteristics were compared using $\chi^2$ tests, Fisher’s Exact tests, and $t$-tests as appropriate. Results: No statistical differences were found among pre-operative characteristics between the two groups. The mean angiographic coronary diffuseness scores for the dialysis and non-dialysis groups were 18.2 and 20.6, respectively ($p = 0.13$). Transfusion was more frequent (77 vs. 23%, $p < 0.0001$) and median length of stay longer (9 vs. 7 days, $p = 0.02$) in the DDRF group. There were no differences in the number of distal anastomoses performed in the two groups. Low rates of peri-operative myocardial infarction, stroke, re-operation, and in-hospital mortality were observed in both groups. Conclusions: Objective quantification revealed that patients with DDRF undergoing CABG did not have a greater coronary artery atherosclerosis disease burden than matched controls who did not have pre-operative DDRF. This may be due to pre-operative patient selection bias. The increased morbidity and mortality of CABG in patients with DDRF is more likely to be due to the multiple adverse systemic effects of renal failure and dialysis on the cardiovascular system as opposed to diffuseness of distal coronary disease.

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1. Introduction

A strong relationship exists between renal and cardiovascular disease. Despite significant therapeutic advances, cardiovascular disease remains the leading cause of mortality in North America, and of patients with dialysis-dependent renal failure (DDRF), cardiac disease accounts for a full 44% of deaths [1]. It has been demonstrated that patients with DDRF incur significant 5-year all-cause (89.9%) and cardiac mortality (70.2%) following myocardial infarction (MI) [2]. Reduced procedural success, higher in-hospital and late major cardiac events, and lower 1-year actuarial survival (75 vs. 97%) occur with percutaneous coronary interventions [3] in DDRF patients.

Similarly, many reports have cited DDRF as a predictor of adverse clinical outcomes among patients following coronary artery bypass grafting (CABG). Operative mortality remains between 0 and 36% with most reports falling in the 10–15% range [4–10]. Of patients who leave hospital, improvements in quality of life are limited with significant long-term mortality (32–71% at 5 years) [4,5,7,8,10].

In the largest reported cohort study to date, of 279 DDRF patients undergoing CABG in the Northern New England Cardiovascular Disease Study Group, DDRF emerged as an independent predictor of mortality with an adjusted odds ratio of 3.1 (95%, CI 2.1–4.7) [9]. DDRF also predicted increased post-operative morbidity in the form of
mediastinitis and stroke, more than doubling the odds of these adverse events. Other series corroborate these bleak findings [6,10].

Many theories abound as to why the morbidity and mortality of CABG is greater in DDRF patients [11–13]. Paramount among these is the assumption that such patients have more diffuse distal coronary artery disease [14,15]. It is generally accepted among cardiac surgeons that diffuse distal coronary disease and poor run-off in grafted coronary targets increase the morbidity and mortality of CABG. To our knowledge, no study has attempted to quantitate the severity of coronary artery diffuseness in patients with DDRF who undergo CABG.

The purpose of this study was to objectively quantitate and compare the burden of diffuse angiographic coronary atherosclerosis between DDRF patients and non-dialysis-dependent (NDD) patients without renal failure undergoing CABG. We hypothesized that there would be no difference in the degree of coronary artery disease diffuseness between the two groups of patients. Secondarily, we compared short-term post-operative outcomes between these groups.

2. Materials and methods

2.1. Patient assembly and clinical measures

Using a database from a single university-affiliated centre (Maritime Heart Center Cardiac Surgery Database), a retrospective case-matched comparison was undertaken. Between March 1995 and December 2000, 35 DDRF patients undergoing isolated CABG were identified and computer-matched 1:2 to 70 NDD patients without renal failure undergoing CABG. We hypothesized that there would be no difference in the degree of coronary artery disease diffuseness between the two groups of patients. Secondarily, we compared short-term post-operative outcomes between these groups.

2.2. Angiographic scoring

Pre-operative angiograms were reviewed by a single, blinded adjudicator using a modification of a previously described coronary diffuseness score [16]. In brief, we divided the left ventricle into nine segments similar to CASS criteria. Then, the coronary arterial branches supplying each segment were assigned a weight based on the estimated amount of left ventricular myocardium each supplied. For example, a large distal left anterior descending (LAD) coronary artery was assigned a greater weight than a small diagonal branch of the LAD. To account for patient-to-patient variations in size of individual coronary branches, weights assigned to each segment were adjusted in steps of 0.5, such that the summed weight for all coronary segments remained nine. Standard criteria were employed to determine the magnitude of a coronary arterial lesion and whether such a lesion was deemed severe enough to jeopardize adequate blood flow to the distal segment of myocardium. A lesion was defined as significant if it was visually estimated to result in at least a 50% reduction in luminal diameter for the left main coronary artery or at least 70% for all other branches. Segments perfused by coronary branches without a significant proximal stenosis were not considered at risk and thus assigned a grade of 0. In contrast, segments distal to a significant coronary lesion were considered at risk and assigned a grade of 1–5 based on the vessel caliber and extent of atherosclerosis. For example, a large diameter LAD (≥2 mm) distal to a significant single proximal lesion (>70% occlusion) would be assigned a grade of 1. In contrast, a severely diseased LAD (<1 mm) distal to that same proximal lesion would be assigned a grade of 4. The catheter diameter was used as a reference (8F = 2.63 mm, 6F = 2.00 mm). The grade assigned to each segment took into account all stenoses with the exception of the most proximal stenosis. Segments at risk and considered inaccessible to revascularization by CABG were assigned the worst grade (5), regardless of vessel caliber. However, a completely occluded artery (i.e. 100% proximal lesion) well visualized via collateral filling was graded in the same way as other segments. A completely occluded artery that was not visualized was also assigned a grade of 5 regardless of whether the other vessels were of good caliber. For convenience, contiguous segments not separated by a significant focal stenosis were weighted and graded as 1 unit.

Angiograms were then assigned a coronary diffuseness score calculated as the summed products of the weights and grades for each myocardial segment. Diffuseness scores ranged in values from 0 to 45, higher values indicating more severe diffuse coronary disease. Thus, this method allows for the quantification of distal coronary disease while at the same time retaining the capability of allowing for anatomic variations in the distribution and size of different coronary branches and the area of myocardium supplied by each. An angiogram with a score of 45 would indicate that all segments were at risk (triple vessel disease or left main plus right coronary artery disease) with all distal vessels graded as 5 (severely diseased averaging 0.5 mm or less in diameter). On the other hand, a patient with an equivalent amount of myocardium at risk with distal arterial segments graded as 1 (angiographically normal with a diameter of at least 2 mm) would have a distal coronary diffuseness score of 9.

2.3. Angiographic scoring reliability

Intra-observer reliability was previously evaluated by presenting the scorer with a different set of 30 angiograms on two separate occasions and comparing the results. To preserve blinding, identifying information from these
angiograms was removed prior to scoring. These re-readings were separated by at least 2 weeks. The reader had no knowledge of clinical outcomes at the time angiograms were scored. A Pearson correlation of 0.872 was obtained for the two sets of readings.

2.4. Statistical analysis

Statistical analysis was performed using Statistical Analysis Systems (SAS, Release 8.2, SAS Institute Inc., Cary, NC). Categorical variables were compared using χ² or Fisher’s Exact tests, and continuous variables were compared with two-tailed t-tests. No correction for multiple testing was applied.

3. Results

During the study period, 35 DDRF patients underwent isolated CABG. Patient characteristics for the DDRF and NDD groups are detailed in Table 1. No statistical differences were noted. In particular, the prevalence of risk factors known to possibly affect coronary disease diffuse-ness such as smoking, hypertension, and dyslipidemia were similar between the two groups (Table 1).

All procedures were done on cardiopulmonary bypass with moderate (32–34 °C) hypothermia and cold-blood cardioplegia. No statistical differences in numbers of internal mammary artery (84 vs. 80%, p = 0.58) and radial artery (11 vs. 3%, p = 0.27) conduits were found for NDD and DDRF patients, respectively. Equal numbers of distal anastomoses were constructed in the two groups (p = 0.86), as shown in Table 2.

All 105 angiograms were available for diffuseness scoring. Mean ± SD scores were 18.2 ± 7.6 and 20.6 ± 7.6 for DDRF and NDD patients, respectively. This result did not reach statistical significance (p = 0.13). The difference of the means of the scores (95% confidence interval) was 2.4 (−0.7, 5.6).

Short-term outcomes are displayed in Table 3. The DDRF group more frequently required transfusions of blood product (77 vs. 25%, p < 0.0001). They also remained in hospital for greater median LOS (9 vs. 7 days, p = 0.02). Low rates of major complications are noted, with no statistically significant differences between groups. Prolonged ventilation (>24 h) occurred more commonly in the DDRF group, although this result did not reach significance (p = 0.24).

Mortality was similar (9 vs. 6%) for DDRF and NDD patients, respectively. Among the DDRF patients there were two cardiac deaths at 2 days post-operatively with multi-system failure in both, and re-operation for tamponade and gastrointestinal complications in one; a third DDRF patient succumbed after 16 days with peritonitis. Four NDD patients suffered mortality: one had a stroke and developed renal failure (died on post-operative day 106 with prolonged mechanical ventilation and tracheostomy); one had an additional pneumothorax while in hospital (died on day 1); and two had gastrointestinal complications (bleeding and ischemic bowel, and died on days 22 and 23, respectively).

4. Discussion

Coronary artery disease remains problematic for patients requiring dialysis. Using a case-matched design, we retrospectively examined all DDRF patients undergoing isolated CABG in a single centre to determine if there is a difference in the severity of coronary angiographic diffuseness between DDRF patients and controls. Because our study sample size was small, we did not detect a statistically significant difference in the burden of coronary artery disease between these groups of patients, and no additional DDRF patients were available for study during this period of...
angiographic diffuseness between DDRF and NDD patients. The subset of DDRF patients undergoing CABG. Contrary to DDRF patients [6,14,15]. This is also assumed to be true in burden of diffuse coronary artery disease exists amongst survival is expected in the DDRF group. Apart from pre-operative dialysis dependence, these patients had poor cardiac function (94% in NYHA class III or IV) and low EF (86% less than 40% EF). Nevertheless, aggressive surgical intervention was achieved, with comparable numbers of distal grafts used as well as the equally high rates of arterial conduit use. With this approach, an acceptable mortality (9%) was observed that compares favourably with results from published studies. Higher rates of transfusion and longer LOS were noted in DDRF patients compared with NDD patients. The higher transfusion rates are most likely due to lower pre-operative red blood cell counts in dialysis patients, many of whom require erythropoietin for this very reason. A trend to prolonged ventilation (>24 h), a surrogate for poor outcome [17], was observed in DDRF patients. The 6% mortality in the NDD CABG group at first appears to be high. However, this may be attributable to the significant comorbidities of these patients, who were matched according to several important predictors of post-operative mortality to the generally high-risk DDRF group. Specifically, it should be noted that 94% of these patients were in NYHA class III or IV and that 86% had an EF <40%. In as much as NYHA classes III and IV and poor EF are strong independent predictors of outcome in cardiac surgery [18], the 6% mortality rate observed in the NDD group appears acceptable. No long-term follow-up data are available currently, although fairly low 5-year survival is expected in the DDRF group.

Numerous reports have suggested that an increased burden of diffuse coronary artery disease exists amongst DDRF patients [6,14,15]. This is also assumed to be true in the subset of DDRF patients undergoing CABG. Contrary to these findings, we did not observe a significant difference in angiographic diffuseness between DDRF and NDD patients. This is the first report that we are aware of that has attempted to compare coronary atherosclerotic disease burden objectively in patients with and without DDRF undergoing CABG. We suspect that our results reflect a high degree of selection within our surgical DDRF population. The DDRF CABG group likely represents a subset of patients on dialysis whose coronary anatomy is amenable to surgical revascularization, thus these patients may manifest similar coronary diffuseness scores as our control group. It would be important to apply our angiographic scoring technique to DDRF patients who were deferred CABG surgery to ascertain whether these patients have a significantly higher coronary artery diffuseness score than NDD patients.

There is agreement among cardiac surgeons that the degree of diffuse distal coronary artery disease is an important factor in predicting morbidity and mortality following CABG. However, it has been exceedingly difficult to quantify the degree of angiographic diffuseness objectively. A recent study has clearly demonstrated that impaired distal run-off of the LAD artery or the circumflex marginal branch is a strong independent predictor of operative mortality in patients undergoing CABG [19]. Our results suggest that the increased morbidity and mortality in DDRF patients undergoing CABG may be due to causes other than an increased coronary artery disease burden and poor distal run-off as is commonly assumed.

It is interesting to hypothesize therefore that DDRF portends a risk of higher morbidity and mortality following surgery, regardless of the diffuseness of coronary artery disease burden prior to CABG. In this regard, a host of abnormalities known to exist in end-stage DDRF patients may contribute to these poor outcomes. For example, the glycoxidation and lipoperoxidation products in the collagen of the myocardium in DDRF patients is significantly elevated compared with age-matched control subjects [20], and an increase in oxidative stress is well recognized in the uremic state [21]. Furthermore, DDRF patients are known to have higher plasma levels of inflammatory mediators such as soluble vascular cell adhesion molecule-1 and soluble E-selectin, indicating a state of endothelial activation and inflammation [22]. In addition, studies have shown that the low-density lipoprotein of DDRF patients is potentially more atherogenic as it induces a greater monocyte-endothelial cell adhesion [23]. That C-reactive protein (CRP) concentrations are significantly increased in DDRF patients may explain the all-cause and cardiovascular mortality seen in these patients [24]. Finally and perhaps most importantly, it is well established that in chronic renal failure there exists a marked impairment in endothelium-dependent relaxation (endothelial dysfunction), a factor known to be a precursor for the development and progression of coronary artery disease [25]. Thus, it is evident that a host of pathophysiologic abnormalities exist in DDRF patients which may contribute to their poorer outcomes.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Short-term outcomes</th>
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<tr>
<td></td>
<td>NDD</td>
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<tr>
<td>Transfusion (%)</td>
<td>23</td>
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<tr>
<td>Re-operation, n (%)</td>
<td>1 (1%)</td>
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<tr>
<td>Per-operative myocardial infarction</td>
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<tr>
<td>Stroke, n (%)</td>
<td>1 (1%)</td>
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<tr>
<td>Deep wound infection, n (%)</td>
<td>1 (1%)</td>
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<tr>
<td>Atrial fibrillation (%)</td>
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<tr>
<td>Prolonged ventilation (%)</td>
<td>11</td>
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<tr>
<td>Median length of stay (days), (quartiles)</td>
<td>7 (6.9)</td>
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<tr>
<td>Mortality, n (%)</td>
<td>4 (6%)</td>
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following CABG independently of the degree of distal coronary artery diffuseness.

This report is limited by a retrospective design, small sample size, and a single-centre experience. Larger-scale studies may be helpful to answer definitively whether increased coronary artery disease burden truly exists in DDRF patients and alters their outcome after CABG. However, the experience of CABG in DDRF patients is more likely to be due to their multiple systemic physiologic abnormalities and not a greater degree of diffuse coronary artery disease.

In summary, DDRF patients undergoing CABG do not have a greater degree of distal coronary artery disease burden (as assessed by angiography) relative to matched NDD CABG patients. The poorer short- and long-term outcomes after CABG in DDRF patients are likely to be due to factors other than severity of coronary artery disease.

References


