The impact of sequential grafting on clinical outcomes following coronary artery bypass grafting


The Division of Cardiac Surgery, Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada

Received 12 December 2009; received in revised form 23 February 2010; accepted 3 March 2010; Available online 25 June 2010

Abstract

Objectives: Sequential anastomoses in coronary artery bypass grafting (CABG) offer theoretical advantages including increased graft flow and more complete revascularisation. However, published studies concerning the safety and efficacy of this technique are not definitive. The objective of this study was to assess the effect of sequential anastomoses on outcomes following CABG. Methods: Perioperative data were prospectively collected on all patients with triple-vessel disease who underwent first-time, isolated, on-pump CABG between 1995 and 2005 at a single centre. Patients with a left internal mammary artery graft to the anterior wall and saphenous vein grafts to the lateral and posterior walls were included. Results: Compared to patients without sequential anastomoses (n = 1108), patients with sequential anastomoses (n = 1246) were more likely to have an ejection fraction (EF) < 40% (14.9% vs 10.8%, p = 0.004), a recent myocardial infarction (19.3% vs 14.3%, p = 0.001) and an urgent/emergent operative status (19.6% vs 14.4%, p = 0.0008). Median follow-up was 78 months. After adjusting for clinical covariates, sequential grafting was not an independent predictor of in-hospital adverse events (odds ratio (OR) 1.15, 95% confidence interval (CI) 0.88—1.50, p = 0.31) or long-term mortality and/or readmission to hospital (hazard ratio (HR) 0.98, 95% CI 0.86—1.12, p = 0.74). Sequential grafting was an independent predictor of receiving greater than three distal anastomoses (OR 9.26, 95% CI; 6.27—13.67, p < 0.0001). Conclusions: Patients undergoing sequential grafting presented with greater acuity and worse systolic function. After adjusting for baseline differences, sequential grafting was not found to be an independent predictor of adverse events. These results support the safety of sequential anastomoses in patients undergoing CABG.

© 2010 European Association for Cardio-Thoracic Surgery. Published by Elsevier B.V. All rights reserved.

Keywords: Coronary disease; Revascularisation

1. Introduction

Coronary artery bypass grafting (CABG) is performed in patients with ischaemic heart disease with the aim of improving long-term clinical outcomes, including freedom from symptom recurrence, hospitalisation, repeat coronary intervention and death [1,2]. These benefits have consistently been linked to graft patency [3] and completeness of revascularisation [4—6]. Since its inception, several modifications to CABG surgery have been proposed to improve graft patency including the choice of conduit [7,8], distal target selection [9,10] and a sequential anastomotic technique [11,12]. Sequential grafting is a technique whereby more than one distal anastomosis is constructed per segment of conduit used, thus resulting in two or more distal anastomoses per single proximal anastomosis. The advocates of this technique describe the haemodynamic advantage of increased total graft flow through improved distal runoff and, by extension, increased graft patency rates [13,14]. In addition, they describe greater conservation of conduit and reduced aortic manipulation. Finally, sequential grafting is thought to facilitate more complete revascularisation by allowing anastomoses to smaller coronary arteries, which theoretically should translate into improved clinical outcomes [4—6]. Despite these purported benefits, the uptake of sequential grafting among surgeons has been variable. The criticism of this technique centres on the dependence of multiple grafts on a common inflow with the possibility of catastrophic consequences in the event of a proximal occlusion. The large myocardium at risk has been the principal deterrent against widespread adoption of sequential grafting. In addition,
surgeons opposing this technique have cited the disadvantages of increased conduit manipulation, suboptimal conduit lie and the complexity of certain side-to-side anastomoses [15].

In many centres, increasing numbers of patients are being referred for surgical revascularisation with diffuse coronary disease or for repeat CABG with limited available conduit. In this setting, the use of sequential grafting is likely to increase. However, to date, published reports concerning the safety and efficacy of sequential grafting have been conflicting in their results. Furthermore, most existing studies are no longer contemporary [16,17] or do not report clinical outcomes [18,19]. Hence, it was the objective of this study to provide a present-day assessment of the effect of sequential grafting on short- and long-term clinical outcomes following CABG.

2. Materials and methods

2.1. Study sample

All patients with triple-vessel disease (defined as significant (>50%) stenosis in each of the three (anterior, lateral and posterior) myocardial territories) who underwent first-time, on-pump, isolated CABG at the Queen Elizabeth II (QEII) Health Sciences Centre in Halifax, Nova Scotia, between 1 March 1995 and 31 March 2005 were identified through the Maritime Heart Center Cardiac Surgery Registry (MHCCSR). Only patients who received a single, in situ left internal mammary artery (LIMA) graft to the anterior wall and saphenous vein grafts (SVGs) to the lateral and posterior walls were included. Cases done off-pump or with multiple arterial grafts were excluded to minimise surgical variability. Approval from the institutional research ethics board was obtained prior to the study.

2.2. Sequential versus single grafting

Patients in whom the number of distal anastomoses performed with a saphenous vein graft exceeded the number of proximal anastomoses were determined to have received sequential grafts, whereas patients in whom the number of distal anastomoses performed with a saphenous vein graft equalled the number of proximal anastomoses were determined to have received single grafts. Surgeons were at liberty to choose their grafting strategy for each case. Factors influencing surgeons’ preference for sequential or single grafting may have included length of available conduit; desire to limit manipulation of the proximal aorta; and preconceptions regarding the safety and efficacy of sequential grafting.

2.3. Data collection and variable definitions

The MHCCSR is a detailed clinical registry that has prospectively collected pre-, intra- and postoperative information on all patients undergoing cardiac surgery at the QEII Health Sciences Centre from 1 March 1995 until the present. Clinical data from the MHCCSR are linked to government administrative data from Vital Statistics and the Canadian Institute for Health Information (CIHI) discharge abstract databases for the purposes of tracking long-term survival and readmission to hospital. These administrative databases were made available by the Population Health Research Unit at Dalhousie University. Although this research study includes data obtained from the Population Health Research Unit, the observations and opinions expressed are those of the authors and do not represent those of the Population Health Research Unit.

The following baseline demographic and clinical variables were considered: age, sex, diabetes, smoking history, renal insufficiency (preoperative serum creatinine >176 μmol l⁻¹ (1.99 mg dl⁻¹)), hyperlipidaemia, hypertension, ejection fraction (EF) less than or greater than 40%, recent myocardial infarction (within 21 days preceding surgery), history of cerebrovascular disease, history of peripheral vascular disease and operative urgency (emergent or urgent vs elective). Intra-operative variables of interest included the number of bypasses, cross-clamp and bypass times, and whether or not the patient left the operating room on intravenous inotropic therapy. The surgeon performing the operation was treated as a variable in the analysis.

The short-term outcomes of interest included in-hospital mortality and a composite outcome of in-hospital mortality, perioperative myocardial infarction, prolonged ventilation (>24 h), re-operation prior to discharge from hospital, permanent or disabling stroke and/or deep sternal wound infection. The long-term outcomes among those patients discharged alive from hospital were all-cause mortality and a composite outcome consisting of all-cause mortality and/or readmission to hospital for coronary ischaemia (angina and acute coronary syndromes), heart failure or repeat revascularisation.

2.4. Cardioangiographic data

To quantify the coronary artery disease burden between the two groups, perioperative data were linked to cardioangiographic data in the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) database, which captures all patients undergoing coronary angiography at the QEII Health Sciences Centre. Cardioangiographic data were available for a smaller group of patients operated on between July 2002 and June 2007, with similar inclusion and exclusion criteria as the overall cohort.

Three previously validated measures of coronary disease severity were assessed. In the Duke Jeopardy Score [20], the coronary tree is divided into six segments, and all segments distal to ≥70% stenosis are considered to be at risk. The Myocardial Jeopardy Index described in the Bypass Angioplasty Revascularization Investigation (BARI) calculates the total number of units jeopardised by ≥50% stenosis divided by the total left ventricular territory units [21]. The APPROACH Lesion Score is calculated by the sum of all jeopardised territories (those supplied by vessels with ≥70% stenoses) [22].

2.5. Statistical analysis

Patients, who underwent CABG surgery with a sequential grafting strategy, were compared to those who did not, using t-tests and Kruskal–Wallis tests for continuous variables and
χ² tests for categorical variables. Logistic regression was used to examine the association of sequential grafting with in-hospital adverse events after adjusting for differences between patients on the basis of each of the above-mentioned preoperative variables. The association between sequential grafting and the long-term outcome of interest was analysed using adjusted survival curves and Cox proportional hazards modelling techniques. All baseline characteristics were included in the fully adjusted multivariate Cox models. Participants were monitored at the time of death, readmission to hospital for any cardiac cause or at the date of last known follow-up.

The role of surgeon sequential volume in determining the impact of sequential grafting on long-term clinical outcomes was examined. Surgeon sequential volume was defined as the percentage of all isolated CABG cases performed by an individual surgeon using sequential grafts. A stratified analysis of high (≥70%), medium (30–70%) and low (<30%) sequential volume surgeons was carried out. For each sequential volume stratum, fully adjusted HRs were calculated using the long-term composite outcome as the outcome of interest and then compared across strata.

Differences in the severity of coronary disease were examined by comparing the Duke Jeopardy Score, the BARI index and the APPROACH lesion score between the sequential and non-sequential groups. The association between sequential grafting and the number of distals received at the time of CABG was examined using a logistic regression model that considered the coronary disease burden as measured by the Duke Jeopardy Score.

Statistical significance was indicated by a two-tailed p value <0.05. All analyses were performed using SAS version 8.2 (SAS Institute Inc., Cary, NC, USA).

### 3. Results

A total of 2354 patients formed the final study population. Of these, 1246 (52.9%) underwent CABG with a sequential grafting strategy. The average age of patients in this study was 66.6 ± 9.7 years and 26.1% were female. Median follow-up time for patients discharged from hospital alive was 78 months, and a total of 14 612 person-years of follow-up were available for analysis.

#### 3.1. Clinical characteristics

The baseline characteristics of patients who underwent CABG with a sequential or non-sequential grafting strategy are shown in Table 1. Compared to patients receiving non-sequential grafts, those receiving sequential grafts had higher rates of systolic dysfunction (14.9% vs 10.8%, p = 0.004) and recent myocardial infarction (19.3% vs 14.3%, p = 0.001) and presented with greater urgency (19.6% vs 14.4%, p = 0.0008). Intra-operatively, patients undergoing sequential grafting received a greater number of distal anastomoses (4.0 vs 3.0, p < 0.0001), had longer cross-clamp (80.7 vs 62.7 min, p < 0.0001) and total bypass times (119.5 vs 105.3 min, p < 0.0001) and had higher rates of inotropic support upon leaving the operating room (21.8% vs 15.3%, p < 0.0001) (see Table 2).

#### 3.2. Clinical outcomes

Patients receiving sequential grafts had higher rates of in-hospital mortality (2.6% vs 1.4%, p = 0.04) as well as the in-hospital composite outcome (14.5% vs 11.2%, p = 0.02). While rates of long-term mortality following discharge were similar between the groups (16.5% vs 18.3%, p = 0.25), rates of the composite long-term outcome including death and readmission for a cardiac cause were lower among patients receiving sequential grafts (37.0% vs 41.7%, p = 0.02). Crude rates of in-hospital and long-term adverse events are shown in Table 3.

After adjusting for baseline clinical covariates, sequential grafting did not emerge as an independent predictor of either in-hospital mortality (OR 1.68, 95% CI; 0.89–3.20), in-hospital mortality and/or morbidity (OR 1.15, 95% CI; 0.88–1.50), long-term survival (HR 1.04, 95% CI; 0.85–1.26) or long-term freedom from all-cause mortality and/or cardiac readmission (HR 0.98, 95% CI; 0.86–1.12) (see Fig. 1). Adjusted survival curves comparing the long-term composite outcome between patients undergoing sequential grafts and those undergoing single grafts are shown in Fig. 2. Although there were more crude events in the non-sequential group,
after adjusting for relevant co-morbidities there is no difference in long-term freedom from all-cause mortality and/or cardiac readmission between the two groups over time.

In the stratified analysis accounting for surgeon sequential volume, sequential grafting was not associated with long-term adverse events in the high- (HR 0.95, 95% CI; 0.64—1.43), medium- (HR 1.08, 95% CI; 0.91—1.28) or low- (HR 0.97, 95% CI; 0.62—1.52) volume sequential groups (see Fig. 3).

### 3.3. Cardioangiographic sub-analysis

Cardioangiographic data were available for 872 patients with triple-vessel disease undergoing first-time, isolated, on-pump CABG. The extent of coronary disease, as measured by the Duke Jeopardy Score (10 (interquartile range (IQR) 8—12) vs 10 (IQR 6—12); p = 0.72), the BARI index (94 (IQR 83—100) vs 94 (IQR 81—100); p = 0.75), or the APPROACH lesion Score (87 (IQR 75—100) vs 87 (IQR 74—100); p = 0.32), was similar between the sequential and non-sequential groups. After adjusting for baseline clinical variables and the Duke Jeopardy Score, sequential grafting was an independent predictor of receiving greater than three distal anastomoses (OR 9.26, 95% CI; 6.27—13.67, p < 0.0001).

### 4. Discussion

In this article, we used information from a large, prospectively collected surgical database to examine the association between sequential grafting and fatal and non-fatal outcomes in patients with triple-vessel disease undergoing first-time, isolated, on-pump CABG. We determined that sequential grafting was not independently associated with either in-hospital or long-term adverse events following CABG surgery.

Since its original description in 1971 by Flemana et al., the sequential bypass technique for myocardial revascularisation has been widely applied to CABG surgery. Following the adoption of this technique using venous conduit, McBride and Barner advocated its use in the construction of sequential arterial grafts [23]. The advantages of this grafting method include conservation of conduit and reduction in the number of aortic anastomoses [11,12]. In addition, by having greater than one target, sequential grafts may have better vascular runoff and thus improved flow and patency [11]. However, published reports concerning the safety and efficacy of sequential grafting have been conflicting in their results. Furthermore, existing studies no longer reflect contemporary surgical management [14,16,17], or are small series with selective angiographic follow-up on a subgroup of patients [18,19,24], or describe the purportedly superior results of sequential grafting with no direct comparator group. This is the first study to examine the effect of sequential grafting on clinical outcomes in a large, well-defined contemporary CABG population.

At the crux of the controversy surrounding sequential grafting is the size of the myocardial region at jeopardy in the...
event of a proximal occlusion. It has been suggested that a larger region is at risk than with the occlusion of a single graft, potentially leading to catastrophic consequences. Christenson and Schmuziger, however, observed that a proximal occlusion of a sequential bypass usually resulted in the recurrence of angina without infarction or sudden death [25]. Kieser et al. noted that non-sequential grafts may have a better 5-year patency rate than the distal anastomoses of sequential grafts [15]. The translation of these concerns into altered clinical outcomes was not established in this study.

Proponents of sequential grafting have further suggested a possibility of more complete revascularization by fashioning side-to-side anastomoses onto smaller coronary arteries that would previously not have been bypassed with single bypass grafts. Long-term survival following CABG surgery or percutaneous coronary intervention has been consistently associated with completeness of revascularization [4—6]. In this report, despite all patients having triple-vessel disease, patients undergoing CABG surgery with sequential grafting received a greater number of distal anastomoses compared with those receiving single grafts (4.0 vs 3.0). When the extent of coronary disease was considered within the sub-analysis cohort for whom cardioangiographic data were available, sequential grafting was the only independent predictor of receiving greater than three distal anastomoses at the time of CABG surgery. The lack of clinical benefit despite more extensive revascularisation may be due to a plateau effect seen with greater than three bypass grafts [6]. In other words, there may be no further benefit beyond one graft to the territory of each major epicardial artery.

The results of this study support the use of either grafting technique for venous conduits by surgeons at their discretion. Surgeons may prefer to employ sequential techniques in certain situations, including for patients with athero-occlusive disease, limited length of conduit and small target vessels. Sequential grafts may also be useful in the context of composite arterial grafting; however, further study is required before extrapolating our results with venous grafts to sequential arterial grafting strategies.

This study has other limitations that require comment. Although a wide range of clinical predictors of sequential grafting was considered in our analyses, our study was observational in nature and relied on retrospective data, thus allowing for bias from unmeasured confounders. Finally, angiographic data were limited and we could not ascertain vessel diameter, target coronary arteries for each grafting strategy or postoperative graft patency. Despite these limitations, to our knowledge, this report is the first to examine the effect of sequential grafting on clinical outcomes in a large, well-defined contemporary CABG population.

In conclusion, patients undergoing CABG surgery with sequential grafting techniques presented with greater acuity and worse systolic function. After adjusting for baseline differences, no independent association between sequential grafting and short- or long-term outcomes was found. The results of this report indicate the safety of this strategy and should reassure clinicians facing greater numbers of patients with advanced coronary artery disease or prior surgical revascularisation with limited available conduit who are likely to require sequential grafting.

References


