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Darwin O, Butterfield ER



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Off-pump versus On-pump Coronary Artery Bypass Grafting: A Comparison of Long-term Graft Patency in Returning Patients

Darwin O, Butterfield ER

Institution

University of Nottingham
University Park Campus,
Nottingham NG7 2RD, UK

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Abstract

Objective: Since its inception, coronary artery bypass grafting (CABG) has conventionally been carried out using cardiopulmonary bypass (on-pump CABG, ONCAB). While off-pump CABG (OPCAB) has been increasingly used recently, and several reports have indicated short-term success rates comparable with ONCAB, very few studies have investigated these over the longer-term. This study aims to compare the long-term graft patency of OPCAB compared with ONCAB in a population of returning patients.

Methods: Data for patients who presented for coronary angiogram investigation at our tertiary cardiac surgery centre between October 1st 2000 and July 31st 2019 were retrospectively analysed, and those patients who had also undergone CABG more than 24 months prior were identified. Only patients who received left internal mammary artery (LIMA) to left anterior descending artery (LAD) graft in addition to non-sequential saphenous vein grafts (SVGs) were included for comparability. Any patients who were found to have graft failure due to distal native disease progression were excluded from the study. A total of 235 patients were included for statistical analysis and were divided into two groups: coronary angiogram performed between 2-7 years post-CABG, and greater than 7 years post-CABG.

Results: There were 142 patients in the 2-7 years post-CABG group (30 OPCAB, 112 ONCAB). After adjusting for confounding variables, there was a statistically significant difference in SVG failure rates between OPCAB and ONCAB (49.4% and 34.5% respectively; $p=0.050$).

There were 93 patients in the >7 years post-CABG group (66 OPCAB, 27 ONCAB). After adjusting for confounding variables, there was a statistically significant difference in SVG failure rates between OPCAB and ONCAB (42.7% and 19.1% respectively; $p=0.034$).

Overall, with all patients included and after adjusting for confounding variables, there was a statistically significant difference in SVG failure rates between OPCAB and ONCAB (44.8% and 31.9% respectively; $p=0.008$). The mean number of SVGs per patient was 1.69 in the OPCAB, and 1.87 in the ONCAB group. The overall SVG failure rate was 37.7%.

There was no statistically significant difference in LIMA graft failure rates in either the 2-7 years post-CABG group ($p=0.340$), >7 years post-CABG group ($p=0.140$), or overall ($p=0.336$).

Conclusions: In patients who receive diagnostic or interventional coronary angiogram more than 2 years after CABG, patients who underwent off-pump CABG had poorer saphenous vein graft patency than patients in the on-pump CABG group. No difference between the techniques was found in left internal mammary artery graft patency. While this study is limited in only analysing data from patients who are indicated for repeat coronary angiogram in the long-term, these are an important group of patients and the results from this study have relevance when considering CABG technique.

Key Words

Cardiopulmonary Bypass; Cardiac Surgical Procedures; Coronary Angiography

Corresponding Author:

Mr Oliver Darwin; E-mail: mzyod2@nottingham.ac.uk

Introduction

Coronary artery bypass grafting (CABG) has been shown to be an effective treatment for patients with extensive coronary artery disease^{1,2}. Over the past 30 years, many prominent and well-documented trials have shown that CABG was associated with greater incidence of long-term survival than medical

therapy alone in patients with extensive coronary artery disease^{3,4}. More recently, great interest has been given to the practice of off-pump CABG (OPCAB)⁵; that is, CABG without the use of cardiopulmonary bypass (CPB) with cardioplegic arrest, i.e. on-pump CABG (ONCAB). OPCAB has been shown to reduce postoperative complications

associated with CPB⁶⁻⁹, including haemodynamic instability⁸ and systemic inflammatory response^{10,11}. Thus, OPCAB has become a promising option in patients who require CABG, but may not be physiologically suitable for the stresses of CPB.

However, as the use of OPCAB has increased, concerns have been raised regarding the longer-term outcomes. Several studies have implicated OPCAB in incomplete vascularisation and lower rates of graft patency when compared to ONCAB¹²⁻¹⁵. While these works have identified a statistically significant difference in the outcomes between OPCAB and ONCAB, they typically involve patient follow-up over a relatively short term, with many of them completing follow-up for primary outcome before 2 years. As such, there is a sparsity of data from random controlled trials (RCTs) regarding the long-term outcomes of OPCAB versus ONCAB. Therefore, this study aims to focus on outcomes greater than 2 years following CABG.

Methods

Data for this report were retrieved retrospectively from the institutional database, the retrieval of which was approved by the hospital ethics review board. As such, International Review Board approval, patient consent statements, and clinical trial registration are not applicable for this study.

Data for patients who presented for coronary angiogram investigation at our tertiary cardiac surgery centre between October 1st 2000 and July 31st 2019 were retrospectively analysed, and those patients who had also undergone CABG more than 24 months prior were identified. A lower limit of 24 months was chosen, as the short-term comparison for graft patency between OPCAB and ONCAB has been thoroughly investigated previously; this study aims to investigate the long-term differences between the two techniques.

Only patients who received left internal mammary artery (LIMA) to left anterior descending artery (LAD) graft in addition to non-sequential saphenous vein grafts (SVGs) were included for comparability.

Any patients who were found to have graft failure due to distal native vessel disease progression were excluded from the study. Operations performed using minimally invasive surgical techniques, and those that included jump-grafting of vessels, were not included, to ensure an appropriate comparison. Patients without available operation notes or coronary angiogram reports were also excluded.

A total of 235 patients were included for statistical analysis. 'Graft failure' was defined as a non-patent graft at the time of coronary angiography without

distal native vessel disease progression. As previous studies have shown, the average time to failure of SVGs is approximately 7 years^{16,17}. As such, the patients were divided into two groups: coronary angiogram performed between 2-7 years post-CABG, and greater than 7 years post-CABG. Additional data points including age at time of CABG, time between CABG and coronary angiogram, indication for coronary angiogram, and sex were also collected for analysis.

All surgeries were performed via a standard median sternotomy approach. During the OPCAB surgeries, stabilisation devices were used to provide a stable surgical field; in all cases, either an Octopus IV or Octopus Evolution tissue stabiliser (Medtronic, Inc.) was used.

In all surgeries, the LIMA was anastomosed to the LAD. SVGs were harvested, grafted to the target vessels, and anastomosed to the ascending aorta in a non-sequential manner.

All analyses were performed using SPSS Statistics software v23.0 (IBM Corp., Armonk, NY). Statistical tests were performed using an alpha level of 0.05, with 95% confidence intervals (CI). Single-variable analysis was conducted using analysis of variance (ANOVA) to investigate the effect of individual variables on graft patency.

As this was a retrospective cohort study, there was no experimental control over variables, and no randomisation of patients. To reduce the potential for confounding variables to affect the result, logistic regression analysis was performed using analysis of covariance (ANCOVA) to adjust the outcomes for sex, age at time of CABG (in years), and time between CABG and coronary angiogram (in months). This allowed for the evaluation of the independent effect of OPCAB vs ONCAB on graft patency.

A pairwise comparison of estimated marginal means was conducted, allowing an estimate of the mean difference between the two groups.

Levene's test of equality of error variances was conducted to ensure homogeneity, with $p > 0.05$ deemed acceptable, meaning the homoscedasticity assumptions of the ANCOVA could be considered valid.

Using this method, the observed statistical power of the data was 0.797; this is only fractionally below the standard accepted power of 0.8, and thus this study design and sample size can be considered relatively robust, and its results considered in context.

Results

Overall, 235 patients were included in the analysis (96 OPCAB, 139 ONCAB). The mean age at the time of CABG was 61.77 years for the OPCAB group (range 38-81; S.D. 9.69) and 61.59 years for the ONCAB group (range 39-83; S.D. 10.59). The mean time between CABG and coronary angiogram was 110.83 months for the OPCAB group (range 26-225; S.D. 50.66) and 58.41 months for the ONCAB group (range 24-169; S.D. 33.38). The OPCAB group consisted of 20 females and 76 males; the ONCAB group consisted of 24 females and 115 males.

Of the 235 coronary angiograms performed, 151 were diagnostic, 73 were indicated for percutaneous coronary intervention, 8 were indicated for transcatheter aortic valve implantation, 1 was indicated for intra-aortic balloon pump, and 2 were indicated for rotablation.

A total of 422 SVGs were carried out (1.80 SV grafts/patient). The mean number of SVGs per patient was 1.69 in the OPCAB group (range 1-4; S.D. 0.62), and 1.87 in the ONCAB group (range 1-4; S.D. 0.71).

The most commonly grafted vessel was the posterior descending artery (n=159; 37.7%), followed by the first obtuse marginal artery (n=149; 35.3%), the first diagonal artery (n=41; 9.7%), the second obtuse marginal artery (n=34; 8.1%), the intermediate artery (n=17; 4.0%), the circumflex artery (n=16; 3.8%), and the third obtuse marginal and right coronary artery stem (n=3 for each; 0.7% for each).

One-way analysis of variable effects of all patients found a significant difference between the on-pump and off-pump groups ($p=0.019$) and between male and female ($p=0.041$). No significant effect was found with time between CABG and coronary angiogram ($p=0.386$), or age at time of CABG ($p=0.625$).

When performing ANCOVA analysis, all groups had a Levene's test of equality of error variances p -value >0.05 . Thus, there is no significant difference between the variances of the groups, indicating homogeneity of variances, and all ANCOVA results can be considered valid.

With all patients included and after adjusting for confounding variables, there was a statistically significant different in SVG failure rates between OPCAB and ONCAB (44.8% and 31.9% respectively; $p=0.008$). The estimated marginal mean difference between OPCAB and ONCAB SVG failure rates was 17.36% (95% CI: 4.67-30.05).

The overall SVG failure rate for all patients was 37.2%.

There were 142 patients in the 2-7 years post-CABG group (30 OPCAB, 112 ONCAB). The mean age at the time of CABG was 67.73 years for the OPCAB group (range 48-81; S.D. 9.12) and 61.62 years for the ONCAB group (range 39-81; S.D. 11.06). The mean time between CABG and coronary angiogram was 54.30 months for the OPCAB group (range 26-83; S.D. 19.04) and 44.55 months for the ONCAB group (range 22-81; S.D. 16.02). The overall SVG failure rate in the 2-7 years post-CABG group was 37.7%.

One-way analysis of variable effects in the 2-7 years post-CABG group found no significant difference between ONCAB and OPCAB ($p=0.082$), male and female ($p=0.115$), age at CABG ($p=0.694$), or time between CABG and coronary angiogram ($p=0.234$). After adjusting for confounding variables, there was a statistically significant difference in SVG failure rates between OPCAB and ONCAB (49.4% and 34.5% respectively; $p=0.050$). The estimated marginal mean difference between OPCAB and ONCAB SVG failure rates was 17.75% (95% CI: 0.01-35.50).

There were 93 patients in the >7 years post-CABG group (66 OPCAB, 27 ONCAB). The mean age at the time of CABG was 59.06 years for the OPCAB group (range 38-80; S.D. 8.74) and 61.44 years for the ONCAB group (range 46-77; S.D. 8.56). The mean time between CABG and coronary angiogram was 136.53 months for the OPCAB group (range 84-225; S.D. 37.99) and 115.44 months for the ONCAB group (range 84-169; S.D. 25.37). The overall SVG failure rate in the >7 years post-CABG group was 35.8%.

One-way analysis of variable effects in the >7 years post-CABG group found a significant difference between the ONCAB and OPCAB groups ($p=0.011$). No significant effect was found with sex ($p=0.177$), age at time of CABG ($p=0.499$), or time between CABG and coronary angiogram ($p=0.518$). After adjusting for confounding variables, there was a statistically significant difference in SVG failure rates between OPCAB and ONCAB (42.7% and 19.1% respectively; $p=0.034$). The estimated marginal mean difference between OPCAB and ONCAB SVG failure rates was 20.91% (95% CI: 1.58-40.24).

After adjusting for sex, age at time of CABG, and time between CABG and coronary angiogram, there was no statistically significant difference in LIMA graft failure rates in either the 2-7 years post-CABG group (OPCAB 10.0%, ONCAB 17.0%; $p=0.340$),

>7 years post-CABG group (OPCAB 12.1%, ONCAB 11.1%; $p=0.140$), or overall (OPCAB 13.5%, ONCAB 10.1%; $p=0.336$).

The overall LIMA-LAD failure rate for all patients was 11.5%.

Discussion

In this contemporary cohort of previous CABG patients who had undergone coronary angiography, the failure rates of saphenous venous grafts were greater in the off-pump CABG group than in the on-pump CABG group. This relationship held true for those patients who had angiography 2-7 years post-CABG, those who had angiography greater than 7 years post-CABG, and for all patients included in the study.

These results should be taken in context with other studies that have been performed comparing the two techniques. Several other large-scale observational studies, as well as several meta-analyses, have found that patients who underwent OPCAB have worse outcomes for short- and long-term survival than those who underwent ONCAB^{14,18-21}. This advantage that ONCAB has consistently been seen to have over OPCAB has been attributed to lower rates of incomplete revascularisation, and greater rates of graft patency²². There have been several explanations for this discrepancy, including the greater technical difficulty of completing anastomoses of coronary vessels in a heart that has not undergone cardioplegia. It has also been proffered that as ONCAB was the earlier developed technique, there have been more advances in technology and surgical practice that have addressed shortcomings in ONCAB as opposed to OPCAB²². We believe that our results, in conjunction with other studies done on the topic, suggest that on-pump CABG is the optimal choice for coronary artery bypass grafting in patients who are not contraindicated for cardiopulmonary bypass.

While the statistical power of this study design provided useable results with regards to the comparison in this patient population, this study was only carried out on patients who had previously undergone CABG and were also requested to have coronary angiography for clinical reasons. As such, there will be a number of patients who have undergone CABG, whether on-pump or off-pump, who did not require further angiography, and therefore the patency of their grafts could not be assessed.

While this is a limitation of the study design, it is an unavoidable consequence of conducting a retrospective analysis of patient data. However,

there has been considerable work done to indicate that a large proportion of patients who undergo CABG for revascularisation will require future investigation or intervention. One study found that 16.7% of patients who underwent CABG will require clinical angiography within 10 years²¹, while others found that 19% require re-bypass after 20 years²², and 36% require coronary reintervention after 30 years²³. As such, while this study is limited in its selection of patient population, the results can be presumed to represent a significant proportion of patients who have undergone CABG during the time period.

Conclusions

Of those previous CABG patients who underwent coronary angiography in our tertiary cardiac centre during the study period, those who underwent off-pump CABG had a significantly worse saphenous venous graft patency rate than those who underwent on-pump CABG. There was no difference in the LIMA-LAD graft patency rates. While this study is limited in covering only those CABG patients who underwent repeat angiography, it provides ample basis to conduct a more thorough long-term study inviting all patients to return for coronary angiography, to ascertain whether the results found here and elsewhere remain true.

Authors' contributions: ³/₄ Oliver Darwin and Ezmee R Butterfield have given substantial contributions to the conception or the design of the manuscript, Oliver Darwin to acquisition, analysis and interpretation of the data. All authors have participated to drafting the manuscript, Oliver Darwin revised it critically. All authors read and approved the final version of the manuscript.

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