Advanced clinical approaches in complex cardiovascular disease
Tan, Eng Shiong

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Chapter 8

Differences between Early, Intermediate and Late Angioplasty following Coronary Artery Bypass Grafting

Eng-Shiong Tan, Gillian Jessurun, Wouter Deurholt, Pieter van der Vleuten, Ad van den Heuvel, Tjark Ebels, Felix Zijlstra, and Rene Tio

*Critical Pathways in Cardiology, in press*
Abstract

The aim of the present study was to identify patients with recurrent ischemia after coronary artery bypass surgery (CABG) treated by percutaneous coronary intervention (PCI). Graft failure after CABG may be managed conservatively or treated by surgery or PCI. We sought to investigate clinical, angiographic and procedural characteristics in relation to clinical outcome. This was a retrospective single-centre study. Patients who underwent revascularization by PCI with a previous CABG were analyzed. Patients were divided in 3 groups, depending on interval between CABG and index-PCI; Group 1: Interval <72 hours. Group 2: Interval between 72 hours and 1 year. Group 3: Interval >1 year. 221 patients were studied. Clinical characteristics and survival curves were comparable in groups 2 and 3. Post-operative CK-MB and troponin values were significantly higher in group 1 (P=0.000). From group 1, significantly more patients (10.5%) required emergency-CABG after the index-PCI than compared to group 2 (2.1%) and group 3 (0%), (P=0.003). There were more off-pump CABG’s in group 1 than in the other two groups. Group 1 received less PCI’s in native ungrafted vessels compared to the other two groups. Mortality in group 1 (18.4 %) was higher than in the other 2 groups (7.4 and 4.5% respectively; P<0.05). Mortality in group 1 was higher in the acute phase of follow-up. PCI performed less than 72 hours after CABG is feasible but accompanied by a higher mortality and redo CABG. This outcome is probably related to the high-risk patient category.
Introduction

CABG has proven to be an excellent treatment for coronary artery stenosis\textsuperscript{1-3}. Since its introduction in 1962 until the first PCI in 1977, this modality was the single non-pharmacologic treatment for coronary artery stenosis. Despite the introduction of PCI, CABG remained for many years the main interventional treatment for coronary artery stenosis and was further improved by using arterial grafts instead of venous grafts\textsuperscript{4-7}. Over the past 2 decades, however, there have been important changes in PCI techniques, pharmacological adjuvant treatment and device technologies. This includes the adoption of coronary stents (1994), glycoprotein IIb/IIIa agents\textsuperscript{8-14} (1998) and upfront loading clopidogrel (2001). As a result, the risks for patients undergoing PCI have been reduced and outcome has improved. PCI has become the standard revascularization procedure in the setting of acute MI and is now being implemented in high-risk patients with comorbidity, high age and high-risk multi-vessel coronary anatomy\textsuperscript{3,15-17}. Moreover, the beneficial role of re-revascularisation by emergency PCI has been shown\textsuperscript{18}. Nevertheless, CABG continues to be a very important primary treatment in patients where PCI is not possible or unsuccessful. However, CABG still has its caveats. Graft- failure within six months of surgery has an incidence of 4% up to as high as 15% five years after surgery\textsuperscript{19-22}. In addition an incidence of myocardial ischemia early after CABG of 4%-7% has been reported within 72 hours of surgery\textsuperscript{22-26}. These data suggest that CABG may create a separate post-revascularisation patient category beside subjects after angioplasty. In patients who undergo PCI, restenosis remains a major clinical issue after drug eluting (7,4%) or bare metal stenting (10,7%)\textsuperscript{27}. Revascularisation for graft failure is caused by different mechanisms and subsequently warrants a variable and tailored clinical approach. We may divide graft failure in 1. anatomical and functional etiologies related to the technical aspects of the surgical intervention such as graft kinking, overstretch, anastomosis malfunction, distal microembolisation and traumatic spasm, 2. pharmacological effects of drug therapy such as spasm induced by high dose vasoactive agents especially following arterial bypass grafting, 3. unknown preexistent and natural progression of cardiovascular disease respectively such as a subclavian artery stenosis and obliterating coronary sclerosis, 4. late mechanical sequelae of surgery such as local obstructive scar tissue. The several causes may occur early or late following CABG. As reCABG was the treatment of choice in the earlier days, PCI has proven to be a valuable alternative. The aim of the present study was to investigate clinical, angiographic and procedural characteristics in relation to clinical outcome of patients with recurrent ischemia after CABG treated by PCI. Furthermore, we contemplate the clinical perception that PCI of bypass grafts and anastomoses immediately after surgery is hazardous.

Methods

Patient population

This was a retrospective single-centre study. All patients who underwent revascularization
by PCI between January 1999 and June 2005 after previous CABG were analyzed. MACE were recorded for all patients in this investigation. Patients who underwent recurrent revascularization after CABG by CABG (Re-CABG) were excluded.

Baseline, clinical and demographic characteristics as well as detailed information on the CABG procedures were retrospectively obtained from the medical records of these patients and from the institutional PCI-database. The patients were divided into three subgroups based on the interval between previous CABG and index-PCI: In the first group (group 1) the interval between CABG and index-PCI was <72 hours (early). In the second group (group 2) the interval between CABG and index-PCI was between 72 hours and 1 year (intermediate). In the third group (group 3) the interval between CABG and index-PCI was >1 year (late).

**Procedural features**
Primary angiographic features were location or sites of post CABG-PCI in arterial grafts and/or anastomosis, vein grafts and/or anastomosis and native vessels.

**Definitions**
Baseline clinical characteristics included history of coronary risk factors (Hyper-cholesterolemia, family history of coronary artery disease, hypertension, smoking status and diabetes) and history of previous coronary events (myocardial infarction, PCI and CABG). Emergency CABG was defined as an unscheduled CABG due to ongoing myocardial ischemia. The decision for percutaneous reintervention in group 1 was based on electrocardiographic and laboratory criteria suggesting ongoing ischemia. In group 2 and 3 invasive reintervention was justified following anginal complaints with objective signs of myocardial ischemia, silent ischemia or the clinical presentation of an acute coronary syndrome.

**Perioperative management**
All patients underwent coronary bypass surgery under midline sternotomy. Both, on pump coronary surgery and off-pump coronary surgery were performed.

Cardiopulmonary bypass was performed under mild hypothermia and cardioplegic arrest was achieved either with St.Thomas single dose cold cristalloid cardioplegia or with cold blood cardioplegia (according to Buckberg protocol). The choice between the two methods of cardioplegia was based upon surgeon’s preference, complexity of the surgical procedure and left ventricular function of the operated patient.

Off-pump coronary surgery was performed by using suction stabilizers and pericardial stitches. Hemodynamic monitoring was made by means of a Swan-ganz catheter and a transesophageal echocardiographic probe. Intracoronary shunts were used occasionally, in case of transient ischemia or hemodynamic deterioration.

**Cross-overs**
Patients who were scheduled for off-pump coronary surgery were converted to on-pump
coronary surgery, whenever hemodynamic deterioration occurred or the results of the
anastomoses were considered unsatisfactory.

Percutaneous coronary intervention

PCI was performed by a standard percutaneous technique through the femoral artery or
other access site as a secondary alternative. A 6 or 8 French guiding catheter was introduced.
Independent of the degree of urgency a prior hemodynamic assessment, which included the
pre-existent left ventricular function, was made to consider whether the insertion of an
intra-aortic balloon pump was mandatory. The primary objective of this mechanical pre-
treatment was to improve diastolic coronary perfusion and reduce the afterload for a
compromised left ventricular function. A secondary objective was to improve collateral
recruitment to counterbalance the overall ischemic insult. In addition, the preparation
phase included upstream pharmacological pre-treatment by the administration of various
drugs such as glycoprotein IIb/IIIa inhibitors for example in the presence of a large
thrombotic burden or vasoactive drugs for eminent circulatory failure.

In each procedure the operator followed the most simple and effective method, in a
procedural time as short as reasonable achievable. A direct stenting technique was attempted
whenever possible. The stent was delivered at inflation pressures $\geq 14$ atm. Delivery was
optimised by kissing balloon inflation in bifurcation lesions. In all cases clopidogrel was
given in a loading dose of 300 mg, followed by a daily dose of 75 mg during one year.
Patients received a standard treatment of 5000 units intravenous heparin before the
intervention, which was adjusted to the optimal level based on the activated clotting time
(200 combined with abciximab and 300 without abciximab). Abciximab was administered
in a weight-adjusted loading dose of 2 mg/ml followed by a 24 hour continuous intravenous
infusion of 0.15 mg/ml. When patients were on acenocoumarol or fenprocoumon in elective
procedures, this was withheld respectively 2 and 4 days prior to PCI.

Statistical analyses

Groups were compared with one-way ANOVA-tests. Log-rank tests were used to compare
the survival curves.

Results

Between January 1999 and June 2005, 4301 patients underwent CABG, 248 of them
(5.7%) needed additional revascularization therapy after the procedure. Twenty-seven patients
(10.9%) underwent re-revascularization by CABG: 22 in an acute setting within 72 hours
and 5 after 72 hours. A total of 221 patients (89.1%) underwent revascularization by PCI.
The latter were subject of this investigation. Baseline clinical characteristics are shown in
Patients were divided in 3 subgroups based on the interval between CABG and index-PCI: Group 1: Interval between CABG and index-PCI <72 hours. Group 2: Interval between CABG and index-PCI between 72 hours and 1 year. Group 3: Interval between CABG and index-PCI >1 year. No differences between the groups with respect to baseline clinical and angiographic characteristics were found. Post-operative troponin and CK-MB values were significantly higher in group 1 compared to the two other groups: Max. Troponin 117.0 µg/l in group 1 compared to 18.6 and 15.9 µg/l in groups 2 and 3 respectively: P=0.000. Max. And CK-MB 39.5 U/l in group 1 compared to 10.0 and 17.0 U/l in groups 2 and 3 respectively: P=0.000. There were more off-pump CABG’s in group 1 than in the other two groups: Twenty-two (57.9%) off-Pump CABG’s in group 1 compared to 32 (33.7%) and 29 (33.0%) off-pump CABG’s in groups 2 and 3 respectively: P=0.017.

Table 1. Baseline clinical and angiographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (N=38)</th>
<th>Group 2 (N=95)</th>
<th>Group 3 (N=88)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval CABG and PCI, days</td>
<td>1 (0-2)</td>
<td>124 (5-364)</td>
<td>872 (369-2092)</td>
<td>0.000</td>
</tr>
<tr>
<td>Age, Yrs</td>
<td>66.5 ± 10.0</td>
<td>64.0 ± 10.0</td>
<td>64.5 ± 10.1</td>
<td>0.432</td>
</tr>
<tr>
<td>Men</td>
<td>29 (76.3)</td>
<td>66 (69.5)</td>
<td>67 (76.1)</td>
<td>0.539</td>
</tr>
<tr>
<td>Body-mass index, kg/m²</td>
<td>26.0 ± 3.5</td>
<td>27.2 ± 3.5</td>
<td>26.3 ± 3.1</td>
<td>0.094</td>
</tr>
<tr>
<td>Body-mass index ≥ 25 kg/m²</td>
<td>23 (60.5)</td>
<td>66 (69.5)</td>
<td>54 (62.4)</td>
<td>0.328</td>
</tr>
<tr>
<td>Smoking</td>
<td>16 (42.1)</td>
<td>24 (25.3)</td>
<td>33 (37.5)</td>
<td>0.051</td>
</tr>
<tr>
<td>Hypertension</td>
<td>28 (73.7)</td>
<td>65 (68.4)</td>
<td>58 (65.9)</td>
<td>0.693</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>27 (71.1)</td>
<td>67 (70.5)</td>
<td>62 (70.5)</td>
<td>0.998</td>
</tr>
<tr>
<td>Positive family history</td>
<td>18 (47.4)</td>
<td>48 (50.5)</td>
<td>37 (42.0)</td>
<td>0.552</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5 (13.2)</td>
<td>24 (25.3)</td>
<td>21 (23.9)</td>
<td>0.304</td>
</tr>
<tr>
<td>Previous MI</td>
<td>13 (34.2)</td>
<td>31 (32.6)</td>
<td>28 (33)</td>
<td>0.985</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>4 (10.5)</td>
<td>5 (5.3)</td>
<td>4 (4.5)</td>
<td>0.404</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>12 (31.6)</td>
<td>17 (17.9)</td>
<td>23 (26.1)</td>
<td>0.187</td>
</tr>
<tr>
<td>Previous PCI + stenting</td>
<td>6 (15.9)</td>
<td>11 (11.6)</td>
<td>10 (11.4)</td>
<td>0.426</td>
</tr>
<tr>
<td>Max. troponin after CABG</td>
<td>117.0 (0.5-837.6)</td>
<td>18.6 (0.0-472.4)</td>
<td>15.9 (0.2-330.8)</td>
<td>0.000</td>
</tr>
<tr>
<td>Max. CK-MB after CABG</td>
<td>39.5 (3-172)</td>
<td>10.0 (1-146)</td>
<td>7.0 (1-104)</td>
<td>0.000</td>
</tr>
<tr>
<td>Off-Pump</td>
<td>22 (57.9)</td>
<td>32 (33.7)</td>
<td>29 (33.0)</td>
<td>0.017</td>
</tr>
<tr>
<td>Number of anastomoses</td>
<td>2.66 ± 1.15</td>
<td>2.53 ± 1.05</td>
<td>2.52 ± 1.04</td>
<td>0.781</td>
</tr>
<tr>
<td>Only arteries used</td>
<td>20 (52.6)</td>
<td>49 (51.6)</td>
<td>50 (56.8)</td>
<td>0.769</td>
</tr>
<tr>
<td>Only veins used</td>
<td>1 (2.6)</td>
<td>5 (5.3)</td>
<td>7 (8.0)</td>
<td>0.482</td>
</tr>
<tr>
<td>Arteries and venas used</td>
<td>17 (44.7)</td>
<td>41 (43.2)</td>
<td>31 (35.2)</td>
<td>0.459</td>
</tr>
<tr>
<td>Y-graft used</td>
<td>4 (10.5)</td>
<td>6 (6.3)</td>
<td>11 (12.5)</td>
<td>0.355</td>
</tr>
<tr>
<td>Single Vessel Disease</td>
<td>9 (23.7)</td>
<td>24 (25.3)</td>
<td>23 (26.1)</td>
<td>0.959</td>
</tr>
<tr>
<td>Two Vessel Disease</td>
<td>19 (50.0)</td>
<td>47 (49.5)</td>
<td>42 (47.7)</td>
<td>0.962</td>
</tr>
<tr>
<td>Three Vessel Disease</td>
<td>10 (26.3)</td>
<td>24 (25.3)</td>
<td>23 (26.1)</td>
<td>0.988</td>
</tr>
</tbody>
</table>

Groups compared with ANOVA-tests. Data are number (%) unless otherwise indicated. CABG=Coronary Artery Bypass Grafting, PCI=Percutaneous Coronary Intervention. MI=Myocardial Infarction. Follow-up time is the follow-up time after the index-PCI

Data on the PCI’s are shown in table 2 and figure 1. The total number of revascularizations on grafted native vessels and anastomoses (venous or arterial) is significantly higher (P=0.000) in group 1 (78.9%) compared to the other two groups (44% and 29% respectively). Although the success-rate of the index-PCI in all three groups did not differ,
there were significant (P=0.003) more additional emergency CABG-procedures after the index-PCI in group 1 (10.5%) compared to the other two groups (2.1% and 0.0% respectively).

### Table 2. Index-PCI data

<table>
<thead>
<tr>
<th>Group 1 (N=38)</th>
<th>Group 2 (N=95)</th>
<th>Group 3 (N=88)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success rate</td>
<td>32 (84.2)</td>
<td>80 (84.2)</td>
<td>81 (92.0)</td>
</tr>
<tr>
<td>Emergency CABG after index-PCI</td>
<td>4 (10.5)</td>
<td>2 (2.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Died during index-PCI</td>
<td>1 (2.6)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Revascularization on grafted native vessels and anastomoses (venous or arterial)</td>
<td>30 (78.9)</td>
<td>44 (46.3)</td>
<td>29 (33.0)</td>
</tr>
</tbody>
</table>

Groups compared with ANOVA-tests. Data are number (%) unless otherwise indicated. CABG=Coronary Artery Bypass Grafting, PCI=Percutaneous Coronary Intervention.

![Figure 1. PCI sites](image)

**Sites of the index-PCI after CABG are shown. At the left-hand side: PCI in grafts or native vessels receiving a graft. At the right-hand side: Un-grafted native vessels. CABG = Coronary Artery Bypass Grafting; PCI = Percutaneous Coronary Intervention; Group1: Interval between CABG and index-PCI <72 hours; Group 2: Interval between CABG and index-PCI >72 hours and <1 year; Group 3: Interval between CABG and index-PCI >1 year.**

All MACE were scored during a mean follow-up-period of 854 days - 2 years and 4 months - (SD 612 days - 1 year and 8 months) as seen in table 3 and figure 2A. There was a significant difference (P=0.000) in mortality in the acute phase after the index-PCI. The curves of group 2 and 3 run parallel while the curve of group 1 begins with a much higher mortality-rate in the acute phase (13.2%) and then stabilizes and run along with group 2 and 3 (1.1% and 0.0% mortality respectively in the acute phase).
Table 3. Major Adverse Cardiac Events (MACE) after index-PCI

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (N=38)</th>
<th>Group 2 (N=95)</th>
<th>Group 3 (N=88)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>8 (21.1)</td>
<td>7 (7.4)</td>
<td>4 (4.5)</td>
<td>0.008</td>
</tr>
<tr>
<td>Death in acute phase</td>
<td>5 (13.2)</td>
<td>1 (1.1)</td>
<td>0 (0.0)</td>
<td>0.000</td>
</tr>
<tr>
<td>(first 10 days after PCI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death in first 4 years after PCI</td>
<td>7 (18.4)</td>
<td>7 (7.4)</td>
<td>4 (4.5)</td>
<td>0.030</td>
</tr>
<tr>
<td>MI</td>
<td>3 (7.9)</td>
<td>2 (2.1)</td>
<td>0 (0.0)</td>
<td>0.546</td>
</tr>
<tr>
<td>PCI</td>
<td>3 (7.9)</td>
<td>17 (17.9)</td>
<td>24 (27.3)</td>
<td>0.821</td>
</tr>
<tr>
<td>CABG</td>
<td>4 (10.5)</td>
<td>2 (2.1)</td>
<td>0 (0.0)</td>
<td>0.384</td>
</tr>
</tbody>
</table>

Groups compared with ANOVA-tests. Data are number (%) unless otherwise indicated. CABG=Coronary Artery Bypass Grafting, PCI=Percutaneous Coronary Intervention. MI=Myocardial Infarction

Based on the survival curves as well as the clinical characteristics it can be concluded that patients in groups 2 and 3 have a comparable clinical course. Figure 2B depicts the survival curves of the patients with a PCI within 72 hours after CABG versus >72 hours. To determine the correlation between the risk factors for coronary artery disease (smoking, hypertension, hypercholesterolemia and diabetes) and survival time, a multivariate logistic regression analysis was used. In this analysis only smoking was significant (P=0.019).

Discussion

This study assessed the clinical course of subjects that had undergone PCI after CABG. The evaluation was made by dividing the study population in three groups defined by the period between the index-PCI and CABG and underlying related mechanisms of graft failure.

The data show that mortality in group 1 is higher during the acute phase of the index-PCI. On the long term this difference disappeared. This can be explained by the fact that group 1 is a high-risk group characterised by periprocedural myocardial infarction, worse Left ventricular function and hemodynamic status. Therefore, these patients are at higher risk at the beginning of the index-PCI. This is respectively illustrated and additionally made clear by two other findings: First, there were significantly higher post-operative troponin and CK-MB values found in group 1 compared to the other groups, which is directly linked to perioperative myocardial ischemia^{28-33}. Second, despite the fact that the success-rate of the index-PCI in all three groups did not differ, there were significantly more emergency CABG-procedures after the index-PCI in group 1 compared to the other two groups.

The high-risk character of group 1 is surgery-related. This is illustrated by the fact that there were significantly more PCI’s performed on grafted native vessels and anastomoses in this group than in the other two groups.
In addition a higher percentage off-pump CABG-procedures were present in group 1. This may have complicated the process where the anastomoses is made and partly explains the higher percentage graft or anastomosis failure.
The higher mortality in the first four years in group 1 is a problem of the acute phase. Later on, the mortality-rate is similar to that of the other two groups. This is illustrated by the initial steep drop in the survival curve. When we consider the first four years after the index-PCI we see a total mortality of 18 (8.1%) with a significant share of 7 (3.6%) for group 1.

Recent data on the occurrence of restenosis after coronary artery surgery shows that 4% has been reported after 6 months, but without clear clinical differences\textsuperscript{20,21}. 5% and 15% are reported respectively after 1 and after 5 years of surgery\textsuperscript{19}. It should be mentioned that the aforementioned postCABG restenotic lesion may have other tissue characteristics than the restenotic lesion following PCI. Other studies report an incidence of early myocardial ischemia (within 72 hours) after CABG of 1-10% of which an 4-7% corresponds to graft-failure\textsuperscript{18,23-26}. These numbers support the clinical conception that physicians should remain aware of potential graft failure after CABG. The mechanism of obstructive graft failure after CABG depends on the duration of the postintervention period. Early graft failure is most likely a surgical related mechanical cause with or without secondary thrombosis. Late graft failure is frequently the result of progressive atherosclerotic or vein graft disease and may also be combined with superimposed thrombosis. We found 5.7% graft-failure in our population which is similar to the prior reported figures.

**Clinical implications**
The shown feasibility and safety of PCI following CABG either at an early or late stage should encourage cardiologists and cardiac surgeons to implement collaborative efforts when signs of graft failure occur. An invasive approach facilitating routine cardiac catheterization and subsequent PCI should always be considered by the treating physicians. Periprocedural antitrombotic drug administration must be tailored to the clinical course of each individual patient.

**Study limitations**
This is a retrospective study. The implementation of new developments both for cardiac surgery and PCI should be considered when interpreting our data. Moreover, a possible learning effect for both treatment strategies may have influenced the results. A selection bias of patients should be included as part of the subjects with an indication for re-revascularisation may have been treated conservatively or by reCABG.

**Conclusions**
Clinical characteristics of patients undergoing PCI at varying time periods after CABG provide the opportunity to draw conclusions about the underlying disease process for recurrent ischemia. Emergency-PCI in the acute phase (<72 hours) after CABG is mostly performed on grafted native vessels and anastomoses and appears to be feasible. It is however accompanied with a higher mortality due to the high-risk qualification of this patient group.
Reference List


