

Early angiographic control of perioperative ischemia after coronary artery bypass grafting[☆]

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Abstract

Objective: To assess the impact of immediate angiography in patients with defined clinical and laboratory criteria of perioperative myocardial infarction after coronary artery bypass operation. **Patients and methods:** Between January 1999 and December 1999 2052 patients underwent coronary artery bypass grafting in our institution. Out of this cohort 131 (6.4%) patients met the criteria of perioperative myocardial ischemia, which was defined as: (a) increase in the isoenzyme ratio of creatinine phosphokinase (CK/CK-MB) above 10%; (b) ischemic electrocardiographic episodes (defined as a new onset of elevated ST-segment change lasting at least 1 min and involving a shift from baseline of greater than or equal to 0.1 mV of ST-depression and a new association of a postoperative Q; (c) recurrent episodes of, or sustained ventricular tachyarrhythmia as well as ventricular fibrillation; (d) hemodynamic deterioration despite adequate inotropic support. **Results:** Angiography was performed in 108 patients (5.3%, group A) whereas 23 patients (1.1%, group B) were immediately re-operated due to severely compromised hemodynamics. Angiographic results in group A showed regular grafts in 45 patients (2.2%); 63 patients (3.1%) had either an occlusion ($n = 41$), incorrect anastomosis ($n = 29$), graft stenosis ($n = 14$), graft spasm ($n = 6$), displaced graft ($n = 6$), poor distal run-off ($n = 5$) or incomplete revascularization ($n = 2$). In group A 43 patients underwent a re-operation (34 patients) or an early angioplasty (nine patients). Due to poor coronary artery status no intervention was performed in the remaining 20 patients with angiographic findings. Operative findings in group B showed graft occlusion in ten patients (43.5%), incorrect anastomosis in five patients (21.7%), bleeding, stretched graft, venous graft spasm and displaced graft in one patient (4.3%) each, and no patho-morphological finding in 4 patients (17.4%). Thirty-day mortality rate was ten patients in group A (9.3%), all of them with angiographic findings, as opposed to nine patients (39.1%) in group B. **Conclusion:** ST-change and elevated CK/CK-MB enzyme ratio is highly indicative for possible graft failure and should be followed early angiographic control to assess the need for reintervention. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Coronary artery bypass grafting; Perioperative ischemia

1. Introduction

Perioperative myocardial infarction occurs with an incidence of 3.5–10% [1–3] and is a significant factor of morbidity and mortality of coronary artery bypass grafting (CABG), but its association with the aorto-coronary bypass in general as opposed to morphologic causes such as early graft occlusion, anastomotic stenosis, graft spasm, poor run-off, incomplete revascularisation, or displaced graft is difficult to determine, because of disagreement in appreciating the criteria for its detection. Localized ST changes indicate a high probability of graft failure and especially in combina-

tion with high levels of creatinine phosphokinase (CK-MB) isoenzyme [3]. Elevated enzyme levels due to minor myocardial cellular damage are frequently observed. In addition high enzyme levels, the presence of a variety of pathological patterns in the electrocardiogram (ECG) and appreciation of hemodynamic data is necessary to make the definite diagnosis of perioperative infarction. In our institution, we pursue a policy of early postoperative angiography, followed by re-operation if necessary, in patients showing criteria of myocardial infarction after coronary bypass operation. It has been shown that early re-operation in case of graft failure and/or incomplete revascularization is beneficial for the patient's myocardium [4]. This retrospective study sums up our experiences with this approach.

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2. Patients and methods

Between January 1999 and December 1999, 2052 patients underwent coronary artery bypass grafting at our institution. Operative procedures included CABG with cold crystalloid (Bretschneider) cardioplegic arrest as well as off-pump surgery via minimally invasive approach or thoracotomy. Upon arrival on the intensive care unit all patients were monitored continuously for arterial pressure, central venous pressure and 12-lead electrocardiogram (ECG). CK and CK-MB values and an additional 12-lead ECG were obtained at least four times within the first 48 h and once ever 24 h hereafter. Aspirin or Ticlopedin medication was started after extubation.

Myocardial ischemia was defined as follows: (a) increase in the isoenzyme ratio of CK/CK-MB above 10%; (b) ischemic electrocardio-graphic episodes (new onset of elevated ST-segment change lasting at least 1 min and involving a shift from baseline (adjusted for positional changes) of greater than or equal to 0.1 mV of ST depression (with slope less than or equal to 0) at J + 60 ms or 0.2 mV of ST elevation at the J-point) and a new association of a post-operative Q; baseline was adjusted for positional changes and temporal drift; (c) recurrent episodes of, or sustained ventricular tachyarrhythmia as well as ventricular fibrillation; (d) hemodynamic deterioration and left ventricular failure despite adequate inotropic support. All electrocardiographic episodes were verified with the use of the ECG monitor printout (ECG complexes) and a 12 lead electrocardiogram.

2.1. Statistics

The design of this study was retrospective. Continuous variables are presented as median range and categorical data are presented as actual number and percentages.

3. Results

Out of 131 patients (6.4%), who presented with lasting criteria of myocardial ischemia two groups were identified: 108 patients (5.3%, group A) were immediately evaluated by angiography, whereas 23 patients (1.1%, group B) were too unstable for angiography and went directly back into the operating room. Sixteen of one-hundred and eight patients (14.8%) in group A and 5 of 24 patients (20.8%) in group B were operated on in off-pump technique. There were no re-CABG or emergency CABG patients in this cohort of patients. None of the criteria were noted pre-operatively.

Definite myocardial infarction confirmed by elevated CK/CK-MB values above 10%, significant ST changes and/or new Q-waves were seen in 72 patients (57.4%) of group A (47 with angiographic findings and 15 with no angiographic findings) and 21 patients (91.3%) of group B (Table 1). In group A a total of 53 patients of 63 patients (84.1%) with angiographic findings showed to have more than a CK-MB

Table 1

Groups identified and mortality rate (patients at baseline $n = 2052$)

Signs of perioperative ischemia	$n = 131$	(6.4%)
Confirmed myocardial infarction	$n = 93$	(4.5%)
Mortality of all interventions	$n = 19$	(0.9%)
Group A		
Stable patients with angiography	$n = 108$	(5.3%)
On pump	$n = 92$	
Off-pump	$n = 16$	
Mortality	$n = 10$	
Pathological angiographic findings in bypasses	$n = 63$	(3.1%)
On pump (confirmed MI) $n = 55$ (42)		
Off-pump (confirmed MI) $n = 8$ (5)		
Mortality	$n = 10$	
No pathological angiographic findings in bypasses	$n = 45$	(2.2%)
On pump (confirmed MI)	$n = 37$ (15)	
Off-pump (confirmed MI)	$n = 8$ (0)	
Mortality	$n = 0$	
Group B		
Unstable patients without angiography	$n = 23$	(1.1%)
On pump (confirmed MI)	$n = 18$ (19)	
Off-pump (confirmed MI)	$n = 5$ (2)	
Mortality	$n = 9$	

value threshold level of 50 U/l, whereas only 15 out of 45 patients (33.3%) with no angiographic findings were above that level.

3.1. Group A

There were 74 males and 34 females with an over all median age of 64 years (range 36–79 years). Preoperative baseline characters are noted in Table 2. There was no endarterectomy performed in any of these patients.

Table 2

Clinical characteristics of group A ($n = 108$, 5.3%)

	n	%	Median
Age (male/female)	74/34		64
Diabetes mellitus	26	24.1	
Hyperlipidemia	53	49.1	
Hypertension	50	46.2	
EF < 30%	9	8.3	
30–50%	25	23.1	
> 50%	74	68.5	
Emergency	0		
Prior CABG	0		
Extent of CAD			
Single vessel	9	8.3	
Double vessel	33	30.5	
Triple vessel	66	61.1	
Number of grafts	269		3
Number of anastomoses	283		3
Cross clamp time (min)			43
Operation time (min)			155
Occurrence of symptoms (h)			12

Table 3

Number and type of grafts in group A and number and anatomical site of anastomoses in group A

	<i>n</i>	%
Total number of grafts	270	
Art. grafts	142	52.6
LIMA	102	37.7
RIMA	16	5.9
A. radialis	23	8.5
A. gastroepiploica	1	0.3
Ven. grafts	128	47.4
Number and anatomical site of anastomoses in group A		
	Ant.	Lat.
	126 (44.5%)	84 (29.7%)
	Post.	
	73 (25.8%)	
Arterial graft used	125	22
Venous graft used	1	63

Two-hundred and seventy grafts were used for 283 anastomoses. The median number of grafts per patient was three (range 1–5 grafts) that were used for a median of three distal anastomoses (range 1–5 anastomoses). Number and type of grafts used besides number and anatomical site of anastomoses are noted in Table 3. Median cross clamp time for patients on-pump was 43 min (range 12–112 min) with a median operation time of 155 min (range 70–353 min). Symptoms were noted at a median of 12 h post-operatively (range 0.5–96 h).

3.2. Clinical criteria leading to angiography

The majority of patients showed either new ST changes ($n = 72$, 66.6%) or an elevated CK/CK-MB ratio of $> 10\%$ ($n = 71$, 65.7%) besides sustained ventricular arrhythmia or fibrillation ($n = 31$, 28.7%), hemodynamic deterioration ($n = 20$, 18.5%), new branch block ($n = 9$, 8.3%), post-operative onset of Q wave ($n = 7$, 6.5%) and angina ($n = 6$, 5.5%). There were no adverse events noted following angiography. Data are summarized in Table 4.

3.3. Angiographic results in group A

Angiographic results showed patent grafts in 45 patients (41.7%) whereas pathologic findings were found in 63

Table 4

Indications for angiography in group A

	<i>n</i>	%
New ST change	72	66.6
CK/CKMB $> 10\%$	71	65.7
CKMB > 50 U/l	68	63.0
Sustained arrhythmia	31	28.7
Hemodynamic deterioration	20	18.5
Branch block	9	8.3
New postoperative Q	7	6.5
Angina	6	5.5

patients (58.3%). The commonest cause of graft failure was either an occlusion ($n = 41$, 65.1%), or an incorrect anastomosis ($n = 29$, 46.0%). An incorrect anastomosis led to a narrowing of the grafted artery of less than 50% in 12 patients, in the other patients with an incorrect anastomosis no abnormality of the native coronary was noticed. More venous grafts showed an occlusion than arterial grafts (20 as opposed to 14) but more arterial grafts showed an incorrect anastomosis than venous grafts (21 as opposed to eight). Further results were graft stenosis ($n = 14$, 22.2%) graft spasm ($n = 6$, 9.5%), displaced grafts ($n = 6$, 9.5%), poor distal run off ($n = 5$, 7.9%) or incomplete revascularization ($n = 2$, 3.1%). There was about an even percentage of grafts affected in relation to their anatomical site of anastomoses (anterior wall: 31.7%; lateral wall: 32.1%, posterior wall: 30.1%). All data are summarized in Table 5.

Comparing the main criteria leading to angiography (ST change in a ST-segment and an elevated CK/CK-MB ratio of $> 10\%$) revealed that a combination of both was found in 54 of the 63 patients (85.7%) with pathologic findings in bypasses as opposed to only 12 of 43 patients (27.9%) with no pathologic findings. Two of the patients with angiographic findings showed CK-MB values below 50 U/l, but eight patients with no findings showed CK-MB values below that threshold.

3.4. Consequences of angiographic findings

Out of 63 patients showing pathological angiographic findings, 47 patients (74.6%) showed myocardial infarction with elevated CK/CK-MB values above 10%, significant ST changes and/or new Q-waves. Thirty-four patients (53.9%) underwent immediate re-operation and nine patients (14.3%) received immediate angioplasty. After the redo procedure four patients (6.3%) required an intra aortic balloon pump (IABP), which was explanted after 3 days in three of them, one patient (0.9%) additionally required extracorporeal membrane oxygenation (ECMO) for temp-

Table 5

Angiographic results of grafts (63 patients) and angiographic findings by site

Occlusion (a/v)	41 (14/20) grafts	(65.1%)
Incorrect anastomosis (a/v)	29 (21/8) grafts	(46.0%)
(narrowing of the native bed $< 50\%$ in 12 patients)		
Graft stenosis (a/v)	14 (9/5)	(22.2%)
Graft spasm (a/v)	6 (4/2) grafts	(9.5%)
Displaced graft	6 grafts	(9.5%)
Poor distal run off	5 coron. arteries	(7.9%)
Incomplete revascularization	2 patients	(3.1%)
Angiographic findings by site (total number anastomoses $n = 283$)		
	<i>n</i>	%
Anterior wall	40	31.7
Lateral wall	27	32.1
Posterior wall	22	30.1

ary cardiopulmonary assistance. Due to poor coronary status 20 patients (31.7%) were treated conservatively without additional intervention. In all of the latter patients myocardial infarction was confirmed with elevated CK/CK-MB values above 10%, significant ST changes and/or new Q-waves.

3.5. Group B

There were 15 males and eight females with an over all median age of 65 years (range 43–84 years). All 23 patients in this group were in too unstable hemodynamic condition to be transported to the cath-lab. Twenty-two patients had circulatory collapse despite ongoing resuscitation on the intensive care unit and were rushed to the operating room whereas one patient developed circulatory collapse when leaving the operating room.

During re-operation graft occlusions due to acute thrombosis were found in ten patients (43.5%) as well as incorrect anastomosis in five patients (21.7%); additional findings were bleeding, stretched graft, venous spasm, and displaced graft in one patient each (4.3%). In the other four patients (17.4%) no evident morphological cause for their severely impaired hemodynamic status was found. In 22 patients an IABP was implanted during re-operation, six patients additionally required a temporary extracorporeal membrane oxygenation. Twenty-one of these patients (91.3%) had confirmed infarction with elevated CK/CK-MB values above 10% (with CK-MB values above 50 U/l) and significant ST changes. Data are summarized in Table 6.

3.6. Mortality rate

Mortality rate was 10 out of 108 patients (9.3%) in group A, with two patients operated on in off-pump technique. In all patients graft related pathological angiographic findings were noted: four patients died after re-vascularization, one patient additionally required an IABP implantation and ECMO-assist as well as six patients who were not re-operated due to poor coronary status - four of these additionally required an ECMO assist. All of the ten patients that died had confirmed myocardial infarction with elevated CK/CK-MB values above 10%, significant ST changes and/or new Q-waves.

Nine out of 23 patients died in group B (39.1%), two of

them had been operated on in off-pump technique. During re-operation all of these patients presented with graft occlusion and in all of them myocardial infarction was confirmed with elevated CK/CK-MB values above 10%, significant ST changes and/or new Q-waves.

4. Discussion

The detection and interpretation of perioperative myocardial ischemia following coronary bypass grafting still remains a challenging problem for the clinician. Perioperative pathologic patterns such as ST-changes and an elevation of the CK/CK-MB ratio besides ventricular arrhythmias, fibrillation and low cardiac output may be caused by definite morphologic factors. Among those are technical inadequacy with or without impact on the native coronary artery, early graft occlusion, or temporary changes such as graft spasm [5], overstretching, low arterial pressure. An imbalance between graft flow and myocardial demand as in the internal mammary artery malperfusion syndrome [6] or very seldom a steal phenomenon caused by a parallel branch of the internal mammary artery [7] may also be the cause. Procedure related factors affecting myocardial protection such as hypothermia [8–10], type and application of cardioplegia [11,12] in patients operated on pump and the trauma and manipulation in on- and off-pump CABG may all lead to reperfusion injury [13] and significant rise of CK-MB values [14–16].

With this study we intended to assess criteria for early identification and adequate management of perioperative ischemia. Localized ST-changes followed by an elevation of the CK/CK-MB ratio above 10% were the main criteria that led to an angiographic control on which an angiography was based on in hemodynamic stable patients after CABG. A combination of a new ST change in a ST-segment and an elevated CK/CK-MB ratio of >10% was found in the majority of patients (85.7%) with pathologic angiographic findings; only 27.9% of patients with no pathologic findings showed CK-MB values below 50 U/l, eight of them showing CK-MB levels below 50 U/l, thus assuming poor myocardial protection or other temporary disorders as mentioned above. Clinically we rely on CK/CK-MB ratio >10% rather than on a certain threshold level for the CK-MB value, although an elevation of CK-MB activity peaks of more than 50 U/l has been shown to support the diagnosis of myocardial infarction [17] which is also supported by our results since most of the patients (84.1%) with pathologic angiographic findings showed an elevation above that threshold. Only for the purpose of this study we retrospectively categorized CK-MB values above or below 50 U/l.

We have demonstrated that the majority (63 of 108 patients, 58.3%) of perioperative ischemias was explained by patho-morphological findings; however, there were only 12 of 29 patients (41.4%) in whom a technical incorrect anastomosis led to a narrowing of the native coronary bed

Table 6
Intraoperative findings of group B (n = 23)

		%
Occlusion (a/v)	10 (7/3) grafts	43.5
Incorrect anastomosis (a/v)	5 (3/2) grafts	21.7
Stretched graft	1 graft	4.3
Venous graft spasm	1 graft	4.3
Displaced graft	1 graft	4.3
Bleeding	1 patient	4.3
No finding	4 patients	17.4

which could possibly explain an infarction. In the other patients with a technical incorrect anastomosis and no change of the coronary bed there was no obvious reason other than the stenosis at the anastomotic site which, one might assume, should not necessarily lead to an infarction theoretically.

Angiography led to an exact diagnosis and identification of the cause which helped further decision making as most of the findings were graft related. Poor coronary status with no option for further re-revascularization led to a non-interventional course; all other patients showed a low risk for angioplasty or re-operation, underlining that re-intervention should be opted for if possible.

Mortality in all patients (groups A and B) with definite myocardial infarction was 22.9% (19 out of 83 patients) and 14.5% in patients with perioperative myocardial ischemia (19 out of 131 patients) and of was associated with poor coronary status and no option for re-revascularization as well as early hemodynamic deterioration. Nevertheless, the fatal infarction rate was less than 1% of all interventions (19 of 2052 patients).

Not much is known on the influence of perioperative myocardial ischemia and infarction on late survival. We will investigate that outcome in a follow-up.

In conclusion, we found that the combination of ST-segment change and CK/CK-MB ratio is highly effective in detecting graft failure. Early angiography should be performed in the stable patient in the event of perioperative ischemia after CABG since it allows for safe and precise diagnosis thus enabling early re-intervention and salvage of myocardium. Whenever repeat intervention in the stable patient can be performed after graft failure, the outcome is favorable whereas poor coronary artery status and hemodynamic instability were major causes of mortality.

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Appendix A. Conference discussion

Dr B. Messmer (Aachen, Germany): I may have missed it, but can you tell again, what was the time elapsed between surgery and your angiographic study in those patients?

Dr Fabricius: No, I didn't mention it. The time span of all patients was like an hour at least and 48 h at the most, and the median was 14, the median, and the median statistically was 19.8.

Dr Messmer: The fact is that I was a little bit surprised about the new Q-wave you postulated. It takes some time until you have a new Q-wave after perioperative ischemia.

Dr M Dullum (Washington, DC, USA): Was there any correlation between the size of the coronary vessels that you grafted and those that were occluded, that is, were they small vessels occluded when you looked at them, or not?

Dr Fabricius: No, we didn't work that up statistically.

Dr B. Walpoth (Bern, Switzerland): I think that in your Institute you do measure intraoperative flow routinely: therefore, I would be interested to know whether in any of the presented cases you measured abnormally low flow rates or grafts with failure. Is it a problem which occurred after the moment you measured your flow and you closed the patient? When did you do your angiographic follow-up studies?

Dr Fabricius: It is standard for all patients in the OR that the grafts are

being verified by flow measurement, and if flow measurements are fine, then the patient will proceed on to intensive care. So if afterwards problems arose, then it's an indication not to go to the OR but to go to the cath lab if the patient is stable seen by hemodynamic terms. So flow measurement was all right.

Dr M. Turina (Zurich, Switzerland): I am surprised with the last statement that this operation can be performed with a low risk. First, you had a 9.3% mortality, which is not so low, and, second, you excluded a substantial proportion of patients. You stated that only those who were stable enough were taken to the angiography. Can you tell us what happened to the patients who crashed and were not taken to the angiography but directly to the operating room?

Dr Fabricius: To your first question, those patients who had a higher mortality of 8.9% were actually the patients who were not operated on. That was exactly the patients who the policy was gone for noninterventional course due to poor coronary status.

And the second question?

Dr Turina: 9.3% mortality rate includes all patients who crashed, not only the group which was angiographed?

Dr Fabricius: No, no: 9.3% were all patients with an angiogram, and out of these, the majority accounted for the patients who were not operated on, 8.3%. So there was just one death related to a patient who was reoperated, actually.

Dr V. Subramanian (New York, NY, USA): Can you tell us if there is a difference in the OPCAB and beating heart, because you have a very high rate of angiographic occlusion, 65%, and there is no distribution changes in the anterior versus the lateral posterior? I presume that is all LIMA in the

anterior graft. If that is so, you have a very high rate of occlusion. Can you tell me if it is all LIMA where you had a problem?

Dr Fabricius: Out of these 108 patients, there were 12 patients either operated by MIDCAB or OPCAB, and five of those MIDCAB patients had problems with the left anterior LIMA, actually.

Dr P. Gerometta (Bergamo, Italy): Do you have any late follow-up data of those 41% of patients that had normal grafts at the perioperative angiography?

Dr Fabricius: The 30-day mortality of those normal patients was zero, they all went out of hospital, and that is all I know of them.

Dr Gerometta: Can you give us some details on the angiographic aspect of the grafts and coronary arteries of patients that underwent an early angiographic control? In my experience they often look very small as if they had spasm. How do you classify them?

Dr Fabricius: The contracted ones were accounted for into the group of the stenosed ones, because sometimes it is difficult for the doctor in the cath lab to say if it's either a stenosis or if it's a spasm. They would just rather guess. So for this study retrospectively we just included them all in this stenosis group.

Dr I. Munoz (Cordoba, Spain): In case of a stenosed anastomotic graft failure, what is your selection criteria for a PTCA or redo operation?

Dr Fabricius: Actually we ask the doctor from the cath lab, and if it is going to be an easy angioplasty being performed, then it's done right away or it's done later on, and if the problem is multifocal, let's put it that way, then we proceed to go to surgical reintervention again.