

Myocardial injury in off-pump coronary surgery: a comparative study of off-pump versus coronary intervention

Off-pump koroner cerrahide miyokard hasarı: Off-pump cerrahi ile girişimsel yöntemi karşılaştırma

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Background: In this prospective study, we compared the degree of myocardial injury in patients undergoing elective coronary interventions (CI) for revascularization or off-pump coronary artery bypass surgery (OPCAB).

Methods: The study included 100 consecutive patients (83 males, 17 females; mean age 53 years; range 34 to 78 years) who underwent intracoronary stent implantation (n=50) or OPCAB (n=50) for coronary artery disease. To evaluate the degree of myocardial injury, blood samples were taken preoperatively and at postoperative 12 hours to measure cardiac troponin (cTn), creatine kinase MB (CK-MB), high sensitive CRP (hsCRP), and lactate levels. A 12-lead electrocardiogram was obtained before and following the procedure.

Results: There were significant differences between the two groups with regard to smoking, acetyl salicylic acid use, previous history of myocardial infarction, and left ventricular ejection fraction, whereas the mean number of affected vessels was similar. Compared to the basal values, cTn levels increased by 7.1% and 2.0%, CK-MB activity increased by 2.0% and 1.2% following OPCAB and CI, respectively (p<0.001). The increases were two-fold or more for cTn in 46% and 14% (p=0.001), CK-MB in 38% and 4% (p=0.001), hsCRP in 94% and 0% (p<0.001), and lactate in 38% and 0% (p=0.001) of OPCAB and CI patients respectively.

Conclusion: The extent of myocardial injury is significantly greater in the off-pump surgery group, as reflected by higher releases of biochemical cardiac markers.

Key words: Cardiac surgical procedures; cardiopulmonary bypass; creatine kinase isoenzymes/blood; coronary artery bypass; troponin/analysis; myocardial ischemia.

Amaç: Bu prospektif çalışmada, off-pump koroner arter bypass cerrahisi ile koroner girişim yapılarak elektif koroner revaskülarizasyon uygulanan hastalarda miyokardiyal hasar düzeyleri karşılaştırıldı.

Çalışma planı: Çalışmaya, koroner arter hastalığı nedeniyle off-pump koroner cerrahisi (n=50) veya koroner girişimle stent implantasyonu (n=50) uygulanan ardışık 100 hasta (83 erkek, 17 kadın; ort. yaş 53; dağılım 34-78) alındı. Miyokard hasarı derecesini belirlemek için, girişim öncesi ve girişimden 12 saat sonra kan örnekleri alınarak, kardiyak troponin (cTn), kreatin kinaz MB (CK-MB), high sensitive CRP (hsCRP) ve laktat düzeyleri ölçüldü ve elektrokardiyografik değerlendirme yapıldı.

Bulgular: İki grup arasında sigara içme, aspirin kullanımı, geçirilmiş miyokard infarktüsü ve sol ventrikül ejeksiyon fraksiyonu açısından anlamlı farklılık vardı. Tutulan damar sayısı ise benzer bulundu. Başlangıç değerleriyle kıyaslandığında, off-pump cerrahi ve koroner girişim uygulamalarında cTn'de artış sırasıyla %7.1 ve %2.0, CK-MB'deki artış %2.0 ve %1.2 (p<0.001) bulundu. Off-pump cerrahi ve koroner girişim sonrasında, incelenen parametrelerde iki kat veya üzerinde artış görülen olguların oranı cTn için sırasıyla %46 ve %14 (p=0.001), CK-MB için %38 ve %4 (p=0.001), hsCRP için %94 ve %0 (p<0.001), laktat için %38 ve %0 (p=0.001) idi.

Sonuç: Biyokimyasal göstergelerdeki yükselmeler, invaziv girişimle karşılaştırıldığında off-pump cerrahi grubunda miyokard hasarının daha fazla olduğunu göstermektedir.

Anahtar sözcükler: Kardiyak cerrahi işlemler; kardiyopulmoner bypass; kreatin kinaz izoenzimi/kan; koroner arter bypass; troponin/analiz; miyokard iskemisi.

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The benefits and satisfactory results gained by avoiding cardiopulmonary bypass and cross-clamping have led to a renewed interest in off-pump coronary artery bypass surgery (OPCAB).^[1-3] Recently, the off-pump technique has been compared with the conventional coronary bypass using biochemical parameters to evaluate the degree of cardiac injury during both procedures, and cardiac enzymes and various biochemical markers have been studied.^[4-10] The aim of this prospective study was to assess the degree of myocardial injury in OPCAB and coronary intervention (CI) in patients undergoing their first elective coronary revascularization procedure by comparing cardiac troponin (cTn), creatine kinase MB (CK-MB), high sensitive C reactive protein (hsCRP) and lactate concentrations.

PATIENTS AND METHODS

This prospective study included 100 consecutive patients who underwent intracoronary stent implantation or OPCAB for coronary artery disease between September 2003 and February 2004. The study protocol was approved by the Ethics Committee and an informed consent was obtained from each patient. Exclusion criteria were as follows: emergent cases, urgent cardiac surgery, new (<1 month) onset of myocardial infarction (MI), concomitant heart valve disease, unstable angina pectoris, left main coronary lesion, triple vessel disease, total coronary occlusion, evident intracoronary thrombus and previous coronary intervention (<1 month), renal and respiratory impairment, and reoperation.

Each group (OPCAB and CI) consisted of 50 patients. Demographic, clinical and preoperative data of the groups are shown in Table 1. Primary target vessels were the left anterior descending artery (LAD), obtuse marginal branches of the circumflex artery and/or the right coronary artery. Coronary artery stenosis involving 70% or more of the cross-sectional area was considered to be significant. The safe procedure was select-

ed according to the lesion anatomy (AHA/ACA classification) and TIMI classification.

Off-pump coronary artery bypass surgery. All procedures in the surgical group were performed through a median sternotomy. In accordance with our protocol, all patients routinely received 5000 IU heparin after harvesting the left internal mammary artery (LIMA), to obtain a target activated clotting time of ≥ 200 seconds. The pericardium was retracted with 0-silk sutures. Gauze swabs were inserted under the heart to achieve better visualization of the target vessel. Intravenous beta-blockers were used to maintain pharmacological bradycardia, the heart rate was kept at less than 70 beats/min. After arteriotomy, a mechanical coronary stabilizing device (Genzyme stabilizer, Genzyme Surgical Products, Cambridge, MA, USA) was used in all cases. The LAD was revascularized first. An apical suction device (Starfish positioner, Medtronic, USA) was used in nine patients in whom circumflex or right coronary artery anastomosis was required. All anastomoses were performed with 7/0 or 8/0 polypropylene sutures, using continuous suture technique. We used an oxygen blowing system of our own design to obtain blood-free area. Intracoronary shunt was not used. If a saphenous vein graft bypass was required, proximal anastomosis was performed under side clamping before distal anastomosis. The heparin effect was not reversed at the completion of the surgical procedure.

Percutaneous coronary intervention. The standard femoral arterial approach and a 7 F guide catheter was used in all the procedures. All patients received 15,000 IU heparin before the procedure. A provisional or direct stent was applied according to the coronary anatomy. Stent implantation was performed under a pressure of 10-18 atm aiming to obtain an optimal angiographic result. Total coronary balloon occlusion time was less than 60 seconds in all patients. All patients received 300

Table 1. Preprocedural patient profile of the treatment groups

Variable	Off-pump bypass (n=50)		Coronary intervention (n=50)		p
	No	Mean±SD	No	Mean±SD	
Mean age (years)		57.2		61.2	NS
Male/female	40/10		43/7		NS
Diabetes mellitus	12		11		NS
Hypertension	21		18		NS
Smoking	36		21		<0.001
Family history	17		24		NS
Acetyl salicylic acid use	13		44		<0.001
Beta-blocker use	30		31		NS
Preoperative myocardial infarction	32		12		<0.001
Number of diseased vessels		1.2±0.4		1.2±0.3	NS
Ejection fraction (%)		50.2±7.7		62.7±8.8	<0.001

NS: Not significant.

Table 2. Diseased coronary vessels and procedure-related results

	Off-pump bypass	Coronary intervention	<i>p</i>
Single vessel	41	42	>0.05
Left anterior descending artery (LAD)	41	23	
Circumflex artery (Cx)	–	6	
Right coronary artery (RCA)	–	13	
Two-vessel	9	8	>0.05
LAD + RCA	5	4	
LAD + Cx	4	3	
RCA + Cx	–	1	
Mortality	–	–	
Morbidity			
Myocardial infarction	1	–	
Intraaortic balloon pump support	–	–	
Inotropic support	3	–	
Malignant arrhythmia	–	–	
Atrial fibrillation	4	–	

mg acetyl salicylic acid and 300 mg clopidogrel loading just before the procedure.

Biochemical analyses. Blood samples for cTn, CK-MB, hsCRP, and lactate analyses were taken from the venous line preoperatively in the anesthetic room or catheterization laboratory and at postoperative 12 hours. The analyses were carried out using the Access Immunassay System (Beckman Coulter, Inc, Fullerton, CA, USA) for cTn; IMMAGE Immunochemistry System (Beckman Coulter, Inc.) for hsCRP, and Konelab 60i for CK-MB. The laboratory parameters were compared with regard to alterations between the baseline and postprocedure levels. Increases in the activities of the enzymes were expressed as folds of the basal levels (<1.5-, 1.5 to 2-, ≥2 -fold).

Electrocardiogram. A 12-lead electrocardiogram (ECG) was recorded before and following the procedure. Electrocardiographic diagnosis criteria for MI following the procedures were new Q-waves of more than 0.04 ms and a reduction in R-waves of more than 25% in at least two leads.

Statistical analysis. Statistical analysis was performed using SPSS 11.0 statistical software. Laboratory parameters obtained by pre- and postprocedural blood sampling were compared between the two groups and in the same group. Continuous parameters were expressed as mean±standard deviation (SD). Data were analyzed using the Mann-Whitney U-test and chi-square test. Statistically significant level was selected as *p*<0.05 with 95% confidence interval (CI).

RESULTS

There were significant differences between the two treatment groups with regard to smoking, acetyl salicylic acid

use, previous history of MI, and left ventricular ejection fraction (*p*<0.001; Table 1). The mean number of affected vessels was similar in two groups (Table 2).

Procedural data. The mean arterial occlusion time was 6.7±0.8 min (range 4.2 to 12.5 min) with OPCAB and 0.9±0.2 min with CI, respectively (*p*<0.001). In the off-pump group, the mean postoperative drainage was 680±350 ml, whereas there was no bleeding with CI. Inotropic support was started in the operating room and continued for 48 hours in three patients undergoing OPCAB. None of the patients required intraaortic balloon pump support. The mean extubation time was 5.5±3.6 hours. The mean duration of stay in the intensive care unit was 28±17.1 hours. The mean hospital stay was 5.1±1.4 days following OPCAB and 1.1±0.8 days following CI (*p*<0.001).

Complications. In the OPCAB group, one patient exhibited electrocardiographic change (anteroseptal MI) without any hemodynamic instability. Rehospitalization was required due to atrial fibrillation in four patients (8%), and to recurrent angina in one patient (2%) (Table 2).

In the CI group, rehospitalization was required in two (4%) patients due to recurrent angina. One patient (2%) underwent a subsequent intervention (PTCA) for early stent restenosis. Coronary bypass operation was not required.

Markers of myocardial injury. Compared to basal values, levels of cTn, CK-MB, and hsCRP increased in both groups. Lactate concentrations decreased after CI.

Changes in cTn, CK-MB, hsCRP, and lactate following OPCAB were significantly greater than those observed after CI (*p*<0.001; Table 3).

Table 3. Pre- and postprocedural enzyme levels

	Off-pump bypass			Coronary intervention			U	p
	Mean	±SD	Median	Mean	±SD	Median		
Cardiac troponin								
Basal value	0.096	0.10	0.05	0.05	0	0.05	615.5	<0.001
After the procedure	0.415	0.50	0.19	0.099	0.27	0.05		
% change	7.05	9.79	2.40	1.98	5.51	1		
CK-MB								
Basal value	15.54	5.65	14.50	17.02	5.14	16	355	<0.001
After the procedure	29.16	12.40	25.50	19.16	13.70	17		
% change	2.02	0.92	1.81	1.17	0.81	1		
C-reactive protein								
Basal value	1.18	2.01	0.49	0.89	2.34	0.41	118	<0.001
After the procedure	10.80	4.87	10.25	1.08	1.75	0.68		
% change	34.11	37.16	15.67	1.82	1.01	1.53		
Lactate								
Basal value	10.45	4.90	10	13.88	5.19	13	309	<0.001
After the procedure	17.75	7.35	16.30	10.91	5.32	9.45		
% change	1.97	1.09	1.68	0.85	0.37	0.75		

Activities of hsCRP, cTn, CK-MB and lactate showed a two-fold or more increase from basal levels in 94%, 46%, 38%, and 38% of patients following OPCAB, respectively.

In the CI group, cTn increased two-fold in 14% of the cases, and CK-MB in 4% of the cases. A two-fold increase in lactate or hsCRP levels was not observed in any of the cases. On the contrary, postprocedure lactate levels decreased in this group. All comparisons between the two groups showed significant differences in the degree of increases (p<0.001; Table 4).

DISCUSSION

Recently, less invasive surgical techniques and improved invasive revascularization techniques are comparable not only for patients' safety and their feasibility, but also for their late clinical and patency results. Regardless of the invasiveness of the procedure, distal myocardial microvessels and cells are affected from iatrogenic ischemic period and distal aggregates caused by revascularization procedures. In this study, we aimed to evaluate myocardial injury in off-pump surgery and percutaneous invasive procedures.

Table 4. Number of cases showing increased activity of markers

	Off-pump bypass		Coronary intervention		χ ²	p
	n	%	n	%		
Cardiac troponin						
I	16	32	43	86	31.88	<0.001
II	11	22	-	-		
III	23	46	7	14		
CK-MB						
I	8	16	44	88	52.05	<0.001
II	23	46	4	8		
III	19	38	2	4		
C-reactive protein						
I	-	-	33	66	89.80	<0.001
II	3	6	17	34		
III	47	94	-	-		
Lactate						
I	8	16	47	94	62.03	<0.001
II	23	46	3	6		
III	19	38	-	-		

I-III: These indicate groups of patients in whom the corresponding levels were (I) unchanged or elevation was smaller than 1.5 times, (II) 1.5 to 2 times, and (III) 2 times or more after the procedure, compared to baseline levels.

Recent studies suggest that off-pump coronary bypass is a safe and effective strategy for myocardial revascularization, and myocardial injury assessed by cardiac troponin release is reduced when compared with the conventional coronary bypass surgery via cardiopulmonary bypass and cardioplegic arrest.^[11,12] A period of coronary arterial occlusion is thought to cause myocardial damage with local ischemia. Only a short period of local ischemia occurs in off-pump surgery due to proximal clamping of native arteries by loops or bulldog clamps during stabilization. This period is not well studied and compared with less invasive techniques. We selected a prospective group of patients in whom percutaneous intervention was performed. In the same manner as coronary stenting, the same local ischemia is seen during the time between starting inflation of balloon in the coronary lumen and reforming the lesion. The difference between the occlusion times of the two groups could be another effect in the pathogenesis of the injury. Target lesions may also be affected by complications of coronary stenting such as atheromatous plaque rupture or distal embolization. These distal occlusions cause release of troponins and other cardiac enzymes as markers of myocardial injury.

We used a local pressure stabilizer to avoid epicardial edema and capillary rupture instead of vacuum devices causing undesirable side effects by epicardial suctioning. Compression of the native arteries by loops using a stabilization device such as Genzyme may not be suitable in diffuse atherosclerotic vascularity, as it may cause permanent narrowing of the lumen or atheroma dislocation and rupture. Arteriotomies and suture materials may also result in enzyme release.

In our study, we observed alterations in lactate and hsCRP concentrations, and significant differences between the two groups. Sternotomy, pericardiotomy, local trauma, and inflammation may account for these differences.

A new Q-wave and high levels of biomarkers showing myocardial necrosis are suggested to be strongly related to cardiac events, but the isolated appearance of a new Q-wave has no impact on the postoperative cardiac outcome.^[13,14] In our study, myocardial infarction was observed in only one patient by the detection of a new Q-wave in ECG recordings. The difference in cardiac enzymes between the two groups was not thought to be related to myocardial infarction. Higher elevations in cardiac troponin activity in the surgery group probably resulted from procedural differences or myocardial damage with non-Q myocardial infarction.

Our study groups were selected from consecutive patients and the percentage of preoperative MI was sig-

nificantly higher and ejection fraction was significantly lower in the off-pump surgery group. Although this suggested the presence of a decreased amount of viable myocardium, higher alterations in enzyme levels were observed in this group. The presence of decreased myocardial viability and, postoperatively, more affected myocardium in the off-pump group may reflect the extent of procedure-related damage to the myocardium.

We did not classify patients according to lesion anatomy. In general, a patient without a suitable coronary anatomy for stent implantation was suggested for surgery. Therefore, the more type C lesions in the bypass group, the more profound enzymatic changes and influence on observed cardiac events.

At present, off-pump bypass is a more serious alternative to conventional surgery for coronary interventions. Higher release of biochemical cardiac markers seen in the off-pump group shows that off-pump surgery causes more myocardial injury than coronary interventions. However, this may not be apparent in the early clinical course and late clinical results must be investigated in larger study groups.

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