

Survival of patients with well-developed collaterals undergoing CABG or medical treatment: An observational case-controlled study

İyi gelişmiş kolaterali olan KABG ya da tıbbi tedavi alan hastalarda sağkalım: Gözlemsel vaka-kontrollü çalışma

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ABSTRACT

Objective: The effects of coronary artery bypass grafting (CABG) on mortality have not been evaluated in patients with well-developed coronary collaterals. We investigated functional capacity, presence of angina, the occurrence of acute myocardial infarction, survival and mortality in patients with well-developed coronary collaterals both undergoing and refusing CABG.

Methods: The study was designed as a retrospective observational case-controlled study. Seventy-eight patients undergoing coronary angiography were included in this study. They had critical occlusion in the proximal left anterior descending artery (LAD) with Rentrop-3 collateral circulation towards LAD, and to proceed with CABG has been suggested. The patients were divided in two groups; first group proceeding with CABG (n=40) and the second, rejecting the surgery (medical treatment group; n=38). The rates of survival, the incidence of angina pectoris and acute myocardial infarction as well as the functional capacities were evaluated in all patients. Survival rates were evaluated using Kaplan-Meier survival analysis.

Results: No statistically significant difference was observed between the two groups regarding the baseline characteristics of patients, the presence of angina pectoris, the severity of angina pectoris according to CCS, the occurrence of acute myocardial infarction or stroke, and the functional capacity according to NYHA (p>0.05). Death due to cardiovascular reasons was observed in eight patients of CABG group and in five patients of medical treatment group (p=0.710). The 5-year survival rate was observed to be 80% in CABG group while it was observed to be 84% in the medical treatment group (p=0.730).

Conclusion: There was no significant difference regarding the survival rates in patients with well-developed coronary collaterals proceeding with CABG or medical treatment. (*Anadolu Kardiyol Derg 2012; 12: 97-101*)

Key words: Coronary collateral circulation, coronary bypass surgery, survival analysis, prognosis

ÖZET

Amaç: Bugüne kadar, iyi gelişmiş koroner kolaterali olan hastalarda baypas cerrahisinin mortalite üzerine etkisi değerlendirilmedi. Biz iyi gelişmiş kolaterali olan, baypas olmuş ve baypas'ı reddeden hastalar arasında sağkalım, mortalite, fonksiyonel kapasite, angina varlığı ve akut miyokart enfarktüs gelişimini araştırdık.

Yöntemler: Çalışma retrospektif, vaka-kontrollü gözlemsel bir çalışma olarak dizayn edildi. Koroner anjiyografi uygulanan, sol ön inen arter proksimalinden tam tıkalı olup, Rentrop-3 kolaterali olan ve baypas ameliyatı önerilen 78 hasta retrospektif olarak çalışmaya alındı. Hastalar baypas'ı kabul eden (Grup1, n=40) ve reddeden (Grup 2, n=38) hastalar olmak üzere iki gruba bölündü. Tüm hastalarda sağkalım, fonksiyonel kapasite, angina varlığı ve akut miyokart enfarktüs gelişimi araştırıldı. Sağkalım oranları Kaplan-Meier sağkalım analizi ile değerlendirildi.

Bulgular: İki grup arasında hastaların temel özellikleri, angina varlığı ve şiddeti, fonksiyonel kapasite, akut miyokart enfarktüsü veya inme gelişimi açısından istatistiksel olarak anlamlı farklılık yoktu. Kardiyovasküler sebeplere bağlı olarak ölüm Grup 1'de 8 hastada, Grup 2'de 5 hastada görüldü (p=0.710). Beş yıllık takip sonunda sağkalım oranı Grup 1'de %80 iken Grup 2'de %84 olarak izlendi (p=0.730).

Sonuç: İyi gelişmiş kolaterali olan baypas'a giden ve baypas'ı reddeden hastalar arasında sağkalım açısından farklılık görülmedi. (*Anadolu Kardiyol Derg 2012; 12: 97-101*)

Anahtar kelimeler: Koroner kolateral dolaşım, koroner baypas cerrahisi, sağkalım analizi, prognoz

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Introduction

Coronary collaterals do not have intervening capillary bed however they are anastomotic connections between different coronary arteries and as well as between portions of the same coronary artery (1). Coronary collaterals can be visualized on angiography and these coronary collaterals potentially suggest an important alternative source of blood supply especially after failing of the original vessels to provide sufficient blood (2).

During the period of acute coronary occlusion viability preservation of cardiac tissue, prevention of the aneurysm formation and limitation of the infarction size may be all supplied by coronary collaterals. They can regress with sufficient coronary perfusion during a relatively short period of time after successful revascularization. The importance of presence of coronary collaterals are defined especially in patients with stable coronary artery disease by presenting of patient better prognosis and statement of a decrease in ischemic events related to coronary circulation (3).

Collaterals effects on prognosis and survival in patients with and without coronary collateral undergoing coronary artery bypass surgery (CABG) had been investigated in the literature so far (4, 5). However, survival and mortality in patients having well-developed coronary collaterals undergoing CABG or medical treatment have not been investigated.

We investigated a possible difference of mortality rates in patients with well-developed coronary collaterals undergoing CABG or medical treatment.

Methods

Study design

The study was designed as a retrospective observational case-controlled study.

Study populations

Between January of 2004 and 2006, ninety-four of 1042 patients who underwent coronary angiography were enrolled in this study. They all had critical occlusion in the proximal left anterior descending artery (LAD) with Rentrop-3 collateral circulation towards LAD (Fig. 1, 2) and to proceed with CABG had been suggested to all patients. However, we could contact with only 78 of the patients.

The study population was then divided in two groups, as first group with CABG (n=40) and second group rejecting CABG (n=38, group proceeding with medical treatment).

Baseline variables

Data about patients' body mass index (BMI), age, sex, coexistent hypertension (HT) and diabetes mellitus (DM), smoking status, presence of angina pectoris and severity of angina pectoris according to Canadian Cardiovascular Society (CCS), functional capacity according to New York Heart Association (NYHA), the serum levels of total cholesterol, high-density lipoprotein

(HDL), low-density lipoprotein (LDL) and triglyceride, previous medications, and previous myocardial infarction (MI) history were recorded.

Follow-up and outcome definitions

The patients were followed-up once in six months by doing clinical visit, if they did not attend clinical visit at the Ada Tip Hospital to, we got information about them by telephone.

In the last examination of the patients, presence of angina pectoris, severity of angina pectoris according to CCS, functional capacity according to NYHA, the occurrence of MI during the follow-up were recorded. A diagnosis of acute MI was made by ST segment elevation, defined subsequently, in more than two leads, and associated with typical chest pain and corroborated by elevation of serum creatine kinase MB isoenzyme greater than two times the normal upper limit during the patients' clinical course. Death was considered as due to cardiac reasons unless it could be documented to be due to non-cardiac reasons. Stroke was defined as focal brain injury persisting over 24 hours.

Coronary angiography and grading of coronary collateral filling

Coronary angiography was performed by using Philips Multidiagnosis C2 (Philips, Eindhoven, Netherlands). Pressures were measured before and after injection of contrast material during the left ventriculography. Collateral flow was graded according to the Rentrop classification: 0=no filling of any collateral circulation, 1=filling of side branches of the artery to be perfused by collateral circulation, 2=partial filling of the epicardial artery by collateral circulation, and 3=complete filling of the epicardial artery by collateral circulation (6). Left ventricular ejection fraction was calculated in the right anterior oblique position of left ventriculography. Rentrop grade 3 was classified as well developed coronary collaterals. All angiographies were evaluated by two cardiologists who were ignorant of this study. The CABG decision was made according to the guideline of CABG (7). The complete revascularization was achieved in all patients who underwent CABG. All patients, undergoing or rejecting the surgery received the medical treatment.

Critical occlusions in right coronary (RCA) or circumflex (Cx) arteries along with LAD have been accepted as two-vessel disease while the presence of critical occlusion in three of the vessels were accepted as three-vessel disease.

Statistical analysis

Number Cruncher Statistical System (NCSS) 2007&PASS, 2008 statistical software (Utah, USA) statistical was used for statistical analyses.

The numeric results were expressed as mean \pm SD and categorical results were expressed as a number (percentage). Normality distribution of the variables was tested using one sample Kolmogorov Smirnov test. Differences between groups were

assessed using the Students' t- test for normal distributed data and Mann-Whitney U test for non-normal distributed data. The Chi-square test was used to compare the differences of categorical variables between the groups. The survival rate was determined using the Kaplan-Meier survival analysis, while Log- rank test was used for the comparison of survival rates between the groups. A p value <0.05 was considered statistically significant.

Results

Basal characteristics

The mean age was 56.3±9.4 years in the medical treatment group, and 57.9±6.2 years in the surgical treatment group (p=0.650). There were no statistically significant differences between the two groups regarding the variables of gender, BMI, coexistent HT and DM, hyperlipidemia, previous MI, the number of occluded coronary arteries, or the used medications (Table 1). During follow-up, all patients had been taking the medications prescribed at the initiation of the study. The mean number of surgical grafts was 3±2. Left internal mammary artery was used for LAD in all patients in surgical treatment group. Left ventricular ejection fraction was 54.2±5.2% in the medical treatment group, while it was equal to 50.2±3.0% in the CABG group (p=0.300).

Outcomes

Stroke was observed in one patient in the CABG group (p=1.00). The occurrence of acute MI during the follow-up was recorded in eight patients (21%) in the medical treatment group, and in six patients (15%) in CABG group (p=0.620). There were no statistically significant differences between the two groups in terms of the presence and the severity of angina pectoris according to CCS, and the functional capacity according to NYHA class (p>0.05) (Table 2).

Survival

The median follow-up time was 5.8 years (range 4 to 7). Death was not observed in both groups during the first two years. Cardiac death was seen in eight patients of CABG group (20%): three of them died because of cardiac death on the 3rd year of follow-up, five patients died because of acute MI on the 4th year of follow up. Also, cardiac death was seen in five patients of the medical treatment group (13%): among them 4 patients died because of acute MI on the 3rd year of follow-up, one patient died because of cardiac death on the 4th year follow-up (p=0.710).

Kaplan Meier analysis of survival demonstrated that the 5-year survival rate was 80% in CABG group, and 84% in the medical treatment group (Log rank Chi-square =3.112, p= 0.730, df=1) (Fig. 3).

Discussion

Results of this study have demonstrated that revascularization did not affect mortality and survival in patients with well-developed coronary collaterals in five years.

Table 1. Comparison of baseline clinical variables for matched patients

Clinical variables	Medical treatment (n=38)	CABG (n=40)	*p
Age, years	56.3±9.4	57.9±6.2	0.650
Male/ female	26/12	27/13	0.500
Body mass index, kg/m ²	27.4±4.9	28.0±5.1	0.710
Smoking, n (%)	10 (26)	18 (45)	0.230
Hypertension, n (%)	15 (39)	21 (52)	0.280
Total cholesterol, mg/ dl	182.5±60.6	190.0±30.0	0.680
LDL - C, mg/dl	121.7±45.3	118.2±26.0	0.350
HDL - C, mg/dl	39.5±6.2	40.0±8.1	0.220
Triglyceride, mg/dl	124.7±45.2	129.8±36.6	0.200
Diabetes mellitus, n (%)	12 (31)	16(40)	0.170
Previous MI, n (%)	20 (52)	25(62)	0.200
Number of critical CAD, n	2.2±0.7	2.3±0.7	0.700
LVEF, (%)	54.2±5.2	50.2±3.0	0.300
Medications			
Beta-blockers, n (%)	32 (84)	30 (75)	0.510
Nitrates, n (%)	21 (55)	12 (30)	0.600
Antiaggregants, n (%)	38 (100)	30 (75)	0.420
ACEI, n (%)	38 (100)	34 (85)	0.520
Statins, n (%)	38 (100)	30 (75)	0.300
Data are expressed as mean±sSD, and number (percentage) *unpaired Students' t- test, Chi-square test ACEI - angiotensin-converting enzyme inhibitor, CABG-coronary artery bypass grafting, CAD - coronary artery disease, HDL-C - high-density lipoprotein cholesterol, LDL - low-density lipoprotein cholesterol, LVEF- left ventricular ejection fraction, MI - myocardial infarction			

Table 2. Survival and quality of life in studied groups

Variables	Medical treatment (n=38)	CABG (n=40)	*p
Angina pectoris, n (%)	20 (53)	17 (42)	0.330
Classification of angina (CCS)	1.5±0.5	1.4±0.5	0.750
Functional capacity (NYHA)	1.4±0.6	0.9±0.9	0.210
AMI, n (%)	8 (21)	6 (15)	0.620
Stroke, n (%)	0 (0%)	1 (0.03)	1.000
Mortality, n (%)	5 (13)	8 (20)	0.710
5-year survival, %	84	80	0.730
Data are expressed as mean±sSD, and number (percentage) *unpaired Students' t- test, Chi-square test, Kaplan-Meier survival analysis AMI - acute myocardial infarction, CCS - Canadian Cardiovascular Society, NYHA - New York Heart Association			

Coronary collaterals may help protect the myocardium in patients with coronary artery disease. Timely enlargement of collaterals may even avoid transmural MI and death in symptomatic patients. During coronary occlusion, coronary collaterals limit myocardial ischemia (8). According to the study by Fukui et al. (9) well-developed coronary collaterals may predict pres-

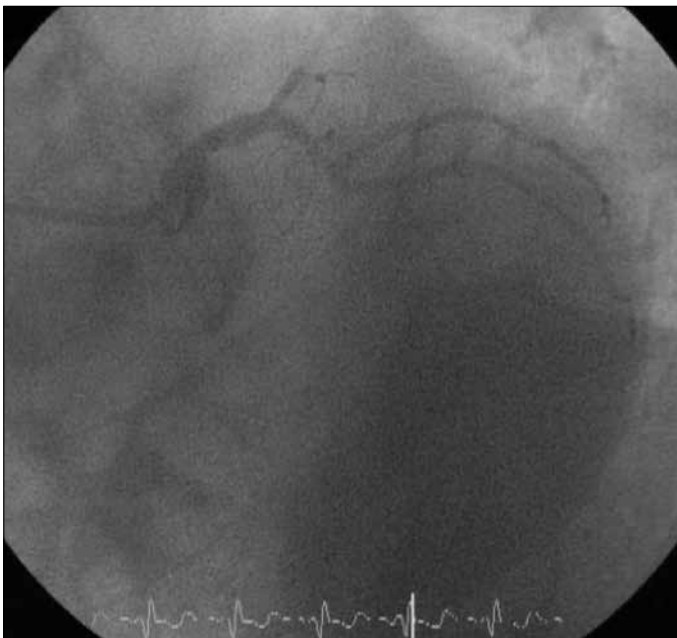


Figure 1. Coronary angiography view of total occlusion of proximal segment of the left descending coronary artery



Figure 2. Coronary angiography view of a large right-dominant coronary artery filling the entire left coronary circulation via collaterals and critical occlusion of the right coronary artery

ence of viable myocardium in patients having anteroseptal MI and also the infarction area may become minimized due to well-developed coronary collaterals. Besides, in a study by Sabia et al. (10) it is declared that in patients with a recent acute MI, the viability of myocardium may remain for a prolonged time and also as stated in this study, even in the presence of collaterals an occluded infarct-related coronary artery may be encountered. However, the relation between well-developed coronary collaterals and prognosis had not been fully assessed. In a

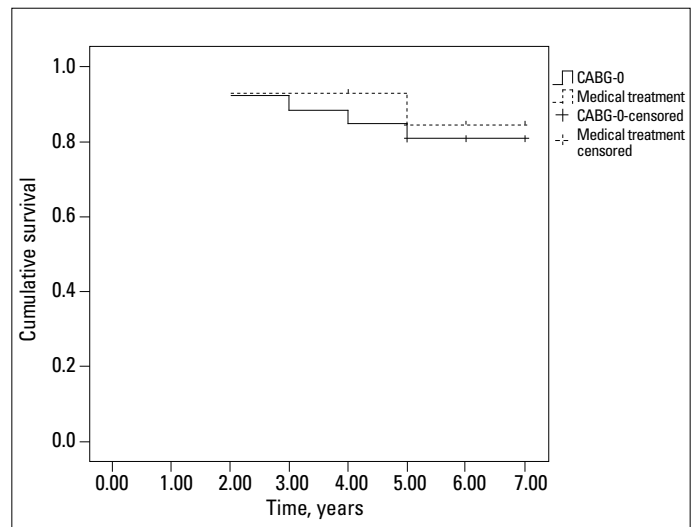


Figure 3. Rates of survival in studied groups

Kaplan-Meier survival analysis: Log rank $\chi^2=3.112$, $df=1$, $p=0.730$

CABG - coronary bypass surgery

published study by Antoniucci et al. (11) findings in patients with acute MI, having symptoms onset within 6 hours and underwent primary angioplasty or stenting revealed the importance of pre-intervention angiographic evidence of coronary collateral circulation. According to results of this study in respect of mortality rates, patients with coronary collateral circulation have lower levels of mortality compared with patients without coronary collaterals but in respect of clinical outcomes the effect of coronary collaterals is unclear. However, this study only considers the presence of coronary collaterals in patients with acute MI and the follow-up period is rather short. Nathoe et al. (12) interpreted the relationship between presence of collaterals in cardiac death and MI at first year after revascularization of coronaries such as implantation of stent and bypass grafting to infarction area. They have concluded at the end that the presence of coronary collaterals effect as lowering risks of cardiac death and myocardial infarction. They protect especially the patient with low-risk profile against unwanted cardiac events after coronary revascularization. The patients with low risk profile were defined as patients who did not have impaired left ventricular function and previously without myocardial infarction and have stable angina.

These studies have compared mortality between the patients who underwent coronary revascularization. We hypothesized that could there be any difference regarding mortality in patients with well-developed coronary collaterals who underwent coronary revascularization or just medically treated? This question has not been answered in literature yet (13, 14). Therefore, we investigated mortality, presence of angina, the occurrence of acute myocardial infarction and functional capacity in patients with well developed coronary collaterals undergoing CABG and rejecting CABG. In our study, there were no statistically significant differences between two groups in terms of presence of angina pectoris, the severity of angina pectoris according to

CCS, the occurrence of acute myocardial infarction and stroke, and the functional capacity according to NYHA. Death did not occur in both groups during the first two years.

In recently published The Occluded Artery Trial, Hochman et al. (15) compared percutaneous coronary intervention-stent placement and optimal medical therapy with optimal medical therapy alone in patients who had persistent coronary occlusion after MI. They reported that there was no significant difference in mortality between the percutaneous coronary intervention group and the medical-therapy group. However, in this trial the majority of patients in both groups (>87%) had collateral vessels in the beginning. Having collateral vessels from the outset could be accepted as the ground underlying the similarity between the groups regarding mortality.

Results of this study have demonstrated that revascularization did not affect mortality in patients with coronary collaterals. The rates of survival in the end of five years were similar in both groups in our study.

Study limitations

The major limitation of this study is the particularly small number of patients and retrospective design. Our study's results are preliminary. The results must be confirmed with findings that will be occurred from large populations in the future.

Conclusion

No significant difference regarding survival was observed in patients with well-developed coronary collaterals, receiving medical treatment alone and undergoing CABG. However, larger, prospective and multicenter studies are needed to clarify whether CABG is the essential treatment modality for these patients.

Conflict of interest: None declared.

Authorship contributions: Concept - E.T.; Design - M.Ak.; Supervision - M.A.Ç.; Resources - M.Al.; Material - E.D.; Data collection&/or Processing M.Al.; Analysis &/or Interpretation - M.Ak., Literature Search - M.A.Ç.; Writing - E.T.; Critical review - B.Ö.; Other - B.Ö.

References

1. Berry C, Balachandran KP, L'Allier PL, Lespérance J, Bonan R, Oldroyd KG. Importance of collateral circulation in coronary heart disease. *Eur Heart J* 2007; 28: 278-91. [\[CrossRef\]](#)
2. Sasayama S, Fujita M. Recent insights into coronary collateral circulation. *Circulation* 1992; 85: 1197-204.
3. Regieli JJ, Jukema JW, Nathoe HM, Zwinderman AH, Ng S, Grobbee DE, et al. Coronary collaterals improve prognosis in patients with ischemic heart disease. *Int J Cardiol* 2009; 132: 257-62. [\[CrossRef\]](#)
4. McMurtry MS, Lewin AM, Knudtson ML, Ghali WA, Galbraith PD, Schulte F, et al. The clinical profile and outcomes associated with coronary collaterals in patients with coronary artery disease. *Can J Cardiol* 2011; 27: 581-8. [\[CrossRef\]](#)
5. Caputo M, Anis RR, Rogers CA, Ahmad N, Rizvi SI, Baumbach A, et al. Coronary collateral circulation: effect on early and midterm outcomes after off-pump coronary artery bypass surgery. *Ann Thorac Surg* 2008; 85: 71-9. [\[CrossRef\]](#)
6. Rentrop KP, Cohen M, Blanke H, Phillips RA. Changes in collateral channel filling immediately after controlled coronary artery occlusion by an angioplasty balloon in human subjects. *J Am Coll Cardiol* 1985; 5: 587-92. [\[CrossRef\]](#)
7. Eagle KA, Guyton RA, Davidoff R, Edwards FH, Ewy GA, Gardner TJ, et al. American College of Cardiology; American Heart Association. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). *Circulation* 2004; 110: 340-437. [\[CrossRef\]](#)
8. Cohen M, Rentrop KP. Limitation of myocardial ischemia by collateral circulation during sudden controlled coronary artery occlusion in human subjects: a prospective study. *Circulation* 1986; 74: 469-76. [\[CrossRef\]](#)
9. Fukai M, Ii M, Nakakoji T, Kawakatsu M, Nariyama J, Yokota N, et al. Angiographically demonstrated coronary collaterals predict residual viable myocardium in patients with chronic myocardial infarction: a regional metabolic study. *J Cardiol* 2000; 35: 103-11.
10. Sabia PJ, Powers ER, Ragosta M, Sarembock IJ, Burwell LR, Kaul S. An association between collateral blood flow and myocardial viability in patients with recent myocardial infarction. *N Engl J Med* 1992; 327: 1825-31. [\[CrossRef\]](#)
11. Antonucci D, Valenti R, Migliorini A, Moschi G, Trapani M, Buonamici P, et al. Relation between preintervention angiographic evidence of coronary collateral circulation and clinical and angiographic outcomes after primary angioplasty or stenting for acute myocardial infarction. *Am J Cardiol* 2002; 89: 121-5. [\[CrossRef\]](#)
12. Nathoe HM, Koerselman J, Buskens E, van Dijk D, Stella PR, Plokker TH, et al. Determinants and prognostic significance of collaterals in patients undergoing coronary revascularization. *Am J Cardiol* 2006; 98: 31-5. [\[CrossRef\]](#)
13. Tatlı E, Büyüklü M. Is coronary revascularization necessary for patients with well-developed coronary collaterals and coronary artery disease? *Int J Cardiol* 2008; 28: 125: 103.
14. Tatlı E, Aktoz M, Aydın G, Yilmaztepe M, Altun A. Dilemma in the strategy of treatment: revascularization or medical treatment? *Anadolu Kardiyol Derg* 2008; 8: 397-8.
15. Hochman JS, Lamas GA, Buller CE, Dzavik V, Reynolds HR, Abramsky SJ, et al. Coronary intervention for persistent occlusion after myocardial infarction. *N Engl J Med* 2006; 355: 2395-407. [\[CrossRef\]](#)