



Long-Term Results of Coronary Artery Bypass Grafting with Extracorporeal Circulation and on Beating Heart in CHD Patients with Diabetes

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ABSTRACT

We compared long-term results for coronary artery bypass grafting in 195 patients with associated diabetes, 108 (55%) patients underwent coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB) and 87 (45%) patients underwent off – pump coronary artery bypass grafting (off – pump CABG). Mean follow-up was 56 ± 11 months. (≈ 4.6 years). Five-year survival and the "freedom" of recurrent angina pectoris in patients with diabetes who underwent CABG with CPB and off – pump CABG comparable. We have not received significant differences when compared to the five-year incidence of the myocardial infarction and re-revascularization between the groups. The benefits observed in patients after off – pump CABG, when comparing the frequency of "large" cardiovascular complications between the two groups.

Keywords: diabetes mellitus, coronary artery bypass grafting, cardiopulmonary bypass, coronary artery disease.

INTRODUCTION

In our days the prevalence of diabetes among patients undergoing myocardial revascularization is quite high and the various data confirm that it reaches 35% [1]. It is known that the presence of diabetes is associated with lower long-term survival after CABG. This tendency has been demonstrated by large-scale studies [2, 7]. In turn, it is known that the CPB is an independent risk factor for the development of some postoperative complications. Patel N.C. et al. concluded that the CPB is an independent risk factor for postoperative neurological complications. [8]. A lot of researches have indicated that the increased the frequency of neurological complications, the development of the syndrome of "small" cardiac output and renal failure in the immediate postoperative period during CABG with CPB compared with off – pump CABG. [3, 8, 9, 10]. The benefit of off – pump CABG in the immediate postoperative period recognizes a number of investigators. It is not a lot of studies with evaluating long-term complications in diabetic patients undergoing CABG by CPB and off – pump CABG and their results are contradictory. The aim of our study was a comparative evaluation of long-term complications in diabetic patients undergoing CABG with CPB and off – pump CABG.

MATERIALS AND METHODS



As a comparison of the two groups of patients shows - 108 (55%) diabetic patients underwent CABG with CPB and 87 (45%) diabetic patients underwent off – pump CABG. All patients were operated in the Bakoulev Scientific Center for Cardiovascular Surgery in the period from 2006 to 2008. Mean follow-up was 56 ± 11 months. (≈ 4.6 years). The duration of the maximum period of observation was 70.6 ± 8 months. (≈ 6 years), the minimum period of observation - 13 ± 2 months. (≈ 1 year). First planned postoperative examination was performed one year after surgery. Later, watching the patients included in the study. The course of the disease was evaluated based on interviews and examinations, as well as on the results of telephone interviews with the patients in conjunction with their official receive extracts and advice of the doctors are treating patients in their place of residence. We evaluated the patient's complaints, physical examination results, reflecting the dynamics of the postoperative course, and the frequency held during the observation period of cardiovascular events. We compared the five-year mortality, the offensive "big" cardiovascular events (death, nonfatal myocardial infarction (MI), nonfatal stroke, repeat revascularization) and the incidence of recurrent angina. Baselines clinical characteristics of 2 groups compared patients were comparable (Table. 1). The patients did not differ significantly by gender, age, risk factors and associated health conditions. However, diabetic patients after CABG with CPB, compared with diabetic patients after off – pump CABG, more often had a history of myocardial infarction and percutaneous coronary intervention, and often suffered from atrial fibrillation and cerebrovascular atherosclerosis.

Statistical evaluation of the results was performed using the software package Statistica 6.0. For characteristics with a normal distribution when comparing between groups used the t-student test. If not normal distribution characteristics for comparison of two groups used non-parametric U criterion of Mann-Whitney. Differences were considered statistically significant at $p < 0.05$. When processing survey data we used survival analysis using the Kaplan-Meier methods and the survival tables, when comparing actuarial curves used tests GEHA-Wilcoxon test and the F-Cox.

RESULTS AND DISCUSSION

Over the five-year period of observation in the total group of patients with diabetes ($n = 195$) due to various reasons 25 patients died (13%). In the group after CABG with CPB cumulative five-year survival rate at 1 year was 98.2% (Std. Error - 0.000), after 2 years - 95.5% (Std. Error - 0.002), after 3 years - 93.5% (Std. Error. - 0.007) after 4 years - 89.8% (Std. Error - 0.01) after 5 years - 88% (Std. Error. - 0.035) after 6 years - 87% (Std. Error - 0.047). Among patients after off-pump CABG cumulative five-year survival rate at 1 year was 98.8% (Std. Error - 0.000), after 2 years - 96.5% (Std. Error - 0.005), after 3 years - 93.1% (Std. Error. - 0.015), after 4 years - 88.5% (Std. Error - 0.041), after 5 years - 87.4% (Std. Error. - 0.035) after 6 years



- 87% (Std. Error - 0.051). Construction of the survival curves between treatment groups showed no statistically significant differences ($p = 0.5$) (Fig. 1).

Next, we had a five-year evaluated cumulative survival after CABG without the development of the "big" post-operative complications (death, myocardial infarction, stroke, and myocardial re-revascularization). All among diabetic patients was - 94 (48.2%) events. In the group CABG with CPB - 55 events, and the group off-pump CABG - 39 events. We received no significant differences in the incidence of myocardial infarction and need for repeat revascularization. However, the incidence of stroke over the observation period was significantly higher in the group CABG with CPB (Table. 2). Among diabetic patients after CABG with CPB cumulative survival without the development of the "big" cardiovascular events at 1 year amounted to 93.52% (Std. Error - 0.000), after 2 years - 83.3% (Std. Error - 0.004) 3 years - 69.4% (Std. Error - 0.016), after 4 years - 59.3% (Std. Error - 0.028), after 5 years - 53.7% (Std. Error - 0.037) 6 years - 49.1% (Std. Error - 0.046). Among patients after off-pump CABG cumulative survival without the development of the "big" cardiovascular events at 1 year amounted to 94.2% (Std. Error - 0.000), after 2 years - 87.4% (Std. Error - 0.011) through 3 years - 74.7% (Std. Error - 0.015), after 4 years - 64.4% (Std. Error - 0.026), after 5 years - 57.3% (Std. Error - 0.035) through 6 years - 55.2% (Std. Error - 0.044). Comparison of actuarial curves showed a statistically significant difference between groups ($p = 0.04$) (Fig. 2). There is the least amount of cardiovascular events during 5 years of observation among diabetic patients in the group with off-pump CABG. This difference is mainly ensured by the greater frequency of stroke in the group CABG with CPB, compared with the group off-pump CABG ($p = 0.035$). The other cardiovascular events, despite some quantitative predominance in the group CABG with CPB, significant differences between the groups did not reach. Over the five-year period of observation of patients studied was registered 45 (23%) cases of proven recurrent angina pectoris: one in the group with diabetes - 24 (22%) patients, in the control group without diabetes - 21 (24%). Among diabetic patients undergoing CABG with CPB, the five-year survival rate without recurrent angina pectoris was over 1 year - 96.3% (Std. Error - 0.001), after 2 years - 90.7% (Std. Error - 0.020) 3 years - 85.2% (Std. Error - 0.027), after 4 years - 79.6% (Std. Error - 0.034), after 5 years - 78.7% (Std. Error - 0.039), after 6 years - 77.8% (Std. Error - 0.046). Among diabetic patients undergoing off-pump CABG, the five-year survival rate without recurrent angina at 1 year was 97.7% (Std. Error - 0.005), after 2 years - 90.8% (Std. Error - 0.015), after 3 years - 86.2% (Std. Error - 0.022), after 4 years - 80.5% (Std. Error - 0.036), after 5 years - 77% (Std. Error - 0.036) after 6 years - 75.9% (Std. Error - 0.040). We found no significant differences between the groups (Fig. 3). Thus, we have not received any evidence of



the benefits of CABG procedures (with CPB or off-pump) in reducing the frequency of five recurrent angina pectoris.

The study Marcheix B. and Eynden FV (2008) evaluated the effect of diabetes on long-term survival in patients after off – pump CABG were obtained with comparable results in terms of the frequency of myocardial infarction and mortality among patients with diabetes and without. Itself diabetes was a potential risk factor for long-term myocardial infarction and congestive heart failure [5].

In the study Fukui T. et al. included 602 patients with coronary heart disease after off-pump CABG, of which 50% had diabetes; the freedom from cardiac death was 97.7% at 5 years follow-up. Freedom from the onset of the combined endpoint (death, myocardial infarction and re-revascularization) was 83.8%. This made it possible to conclude on acceptable results of off – pump CABG on the incidence of death and cardiovascular events. [4].

The study Matsuura K. et al. (2009) showed that holding off-pump CABG is recommended for most patients with poorly controlled diabetes (for glycosylated hemoglobin level greater than 6.5%) [6].

The results of our study are consistent with the opinion of most researchers indicating the comparable or even superior long-term results after the off-pump CABG. We found no significant differences in the five-year survival and freedom from recurrent angina in the two groups. The survival without the development of "large" cardiovascular events (death, stroke, repeat revascularization) after 5 years of observations was higher in the group off - pump CABG ($p=0.04$). The accuracy of the differences was due to a higher incidence of strokes occurred during the specified period of time in the group CABG with CPB. In turn, the reason for the increased incidence of stroke in the group CABG with CPB may be related to the initial clinical characteristics, patients in this group more often suffered cerebrovascular atherosclerosis and chronic atrial fibrillation, which could play a role in the development of stroke.

CONCLUSION

The five-year survival and freedom from recurrent angina pectoris in diabetic patients underwent CABG with CPB and off-pump are comparable. Significant benefits have been observed in patients after off-pump CABG, when we compared the "big" cardiovascular events between groups. However, in fairness, it should be noted that the decrease in the incidence of the "big" events observed in the group CABG with CPB compared to the group off-pump CABG, was due to significant increase in the incidence of stroke in this group that influenced the final result. We found no significant differences when compared to the five-year incidence of myocardial infarction and re- revascularization.



REFERENCES

1. Bockeria L.A., Golukhova E.Z., Sigayev I.Y. et al. Sovremennye podhody k hirurgicheskomu lecheniju IBS u bolnyh s saharnym diabetom. [Modern approaches to the surgical treatment of coronary artery disease in patients with diabetes mellitus]. Vestnik RAMN [Bulletin of RAMN]. 2012; 1: 20-26.
2. Detre K.M., Guo P., Holubkov R., et al. Coronary revascularization in diabetic patients. A comparison of the randomized and observational components of the Bypass Angioplasty Revascularization Investigation (BARI). Circulation 1999; 99:633–40.
3. Emmert M.Y., Salzberg S.P., Seifert B., et al. Is off-pump superior to conventional coronary artery bypass grafting in diabetic patients with multivessel disease? Eur J Cardiothorac Surg 2011;40:233–9
4. Fukui T., Takanashi S., Hosoda Y. et al. Early and Midterm Results of Off-Pump Coronary Artery Bypass Grafting. Ann Thorac Surg 2007; 83:115–9.
5. Marcheix B., Eynden F.V. Influence of Diabetes Mellitus on Long-Term Survival in Systematic Off-Pump Coronary Artery Bypass Surgery. Ann Thorac Surg 2008;86:1181–8.
6. Matsuura K., Imamaki M., Ishida A., et al. Off-pump coronary artery bypass grafting for poorly controlled diabetic patients. Ann Thorac Cardiovasc Surg. Vol. 15. №1, 2009. p-18-22.
7. Myers W.O., Blackstone E.H., Davis K. et al. CASS registry long term surgical survival. Coronary Artery Surgery Study. J Am Coll Cardiol 1999;33:488-98
8. Patel N.C., Deodhar A.P., Grayson A.D., et al. Neurological outcomes in coronary surgery: independent effect of avoiding cardiopulmonary bypass. Ann Thorac Surg 2002;74:400–5.
9. Srinivasan A.K., Grayson A.D., Fabri B.M. On-pump versus off-pump coronary artery bypass grafting in diabetic patients: a propensity score analysis. Ann Thorac Surg 2004;78:1604–9.
10. Stamou S.C., Jablonski K.A., Hill P.C. Coronary revascularization without cardiopulmonary bypass versus the conventional approach in high-risk patients. Ann Thorac Surg 2005;79:552–7.

Table 1

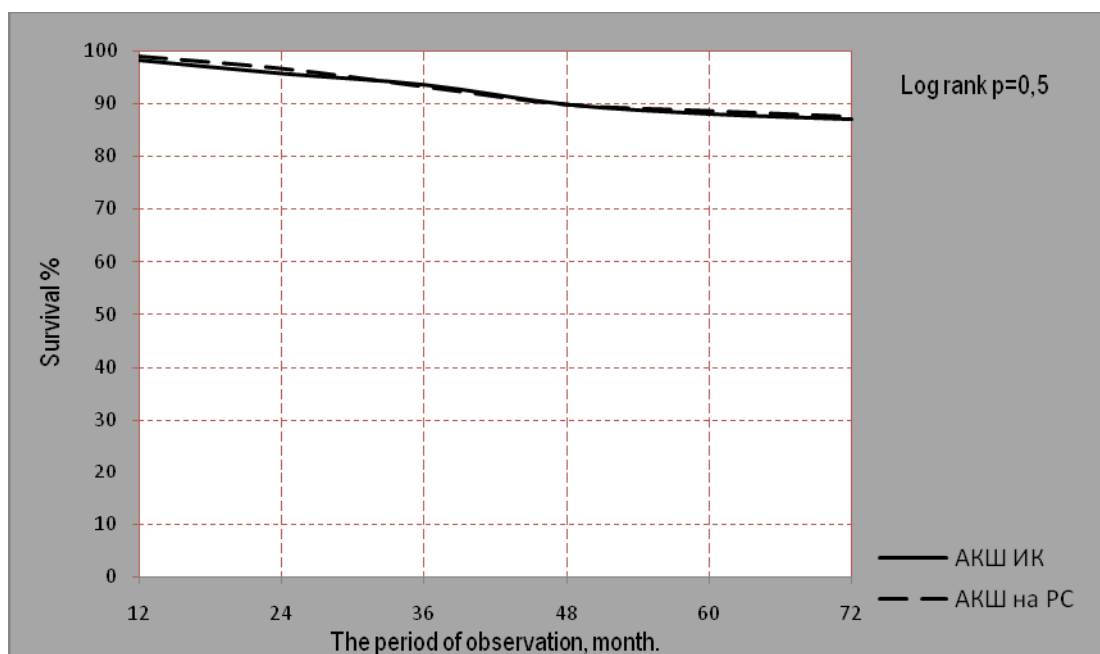
Baseline clinical characteristics of patients with diabetes

	CABG with CPB	Off-pump CABG	p
Age of	53+_5,9	57+5.1	-
Women, %	10 (9%)	12 (14%)	-
Myocardial infarction %	78 (72 %)	43 (49%)	0.01
percutaneous coronary intervention %	13 (12 %)	5 (6 %)	0.01
Chronic atrial fibrillation %	8 (7 %)	2 (2%)	0.001
Smoking %	27 (25 %)	36 (41 %)	-
cerebrovascular atherosclerosis %	20 (18,5%)	9 (10%)	0.02
A history of stroke %	4 (4%)	8 (9%)	-
Atherosclerosis of the lower extremities %	8 (7%)	7(8%)	-
Chronic lung disease %	21 (19%)	11 (13 %)	-
Chronic renal failure %	2 (1,8 %)	2 (2,3 %)	-
Left ventricular ejection fraction	52+_4,9	51+_8,9	-
Insulin-dependent diabetes mellitus type 2 %	16 (15%)	11 (13%)	-
BMI, kg / m2	29+-6,5	29+-5,3	-
Dyslipidemia %	50 (46%)	42 (48%)	-
arterial hypertension %	81 (75%)	76 (87%)	-
Revascularization`s index	2,9	3,0	-
Use of the left internal thoracic artery %	99%	100%	-

**Table 2**

The development of the "big" of cardiovascular events in diabetic patients after CABG with CPB and off-pump CABG over a five year period of observation

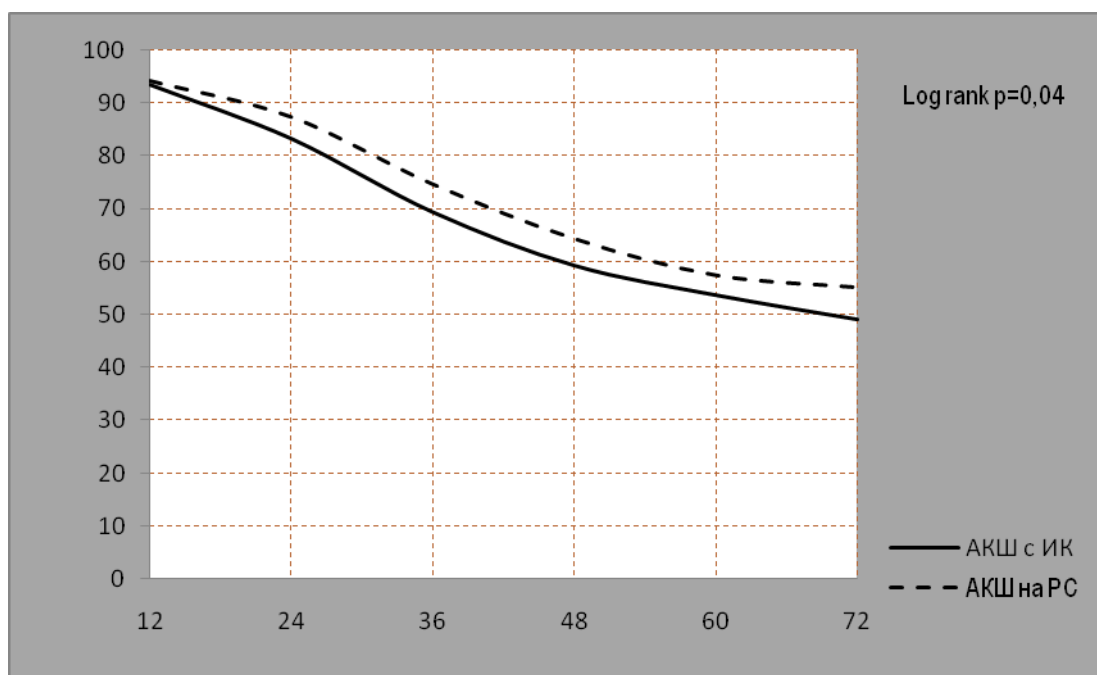
	Total: (n=195)	CABG with CPB (n=108)	Off-pump CABG (n=87)
Mortality	25 (12,8%)	14 (13%)	11 (12,6%)
Myocardial infarction	14 (7,18%)	8 (7,41%)	6 (6,9%)
Stroke	28 (14,4%)	18 (16,7%)	10 (11,5%)*
Re - revascularization	7 (13,8%)	15 (13,9%)	12 (13,8%)
Total:	94 (48,2%)	55 (50,9%)	39 (44,8%)



————— CABG with CPB

----- Off-pump CABG

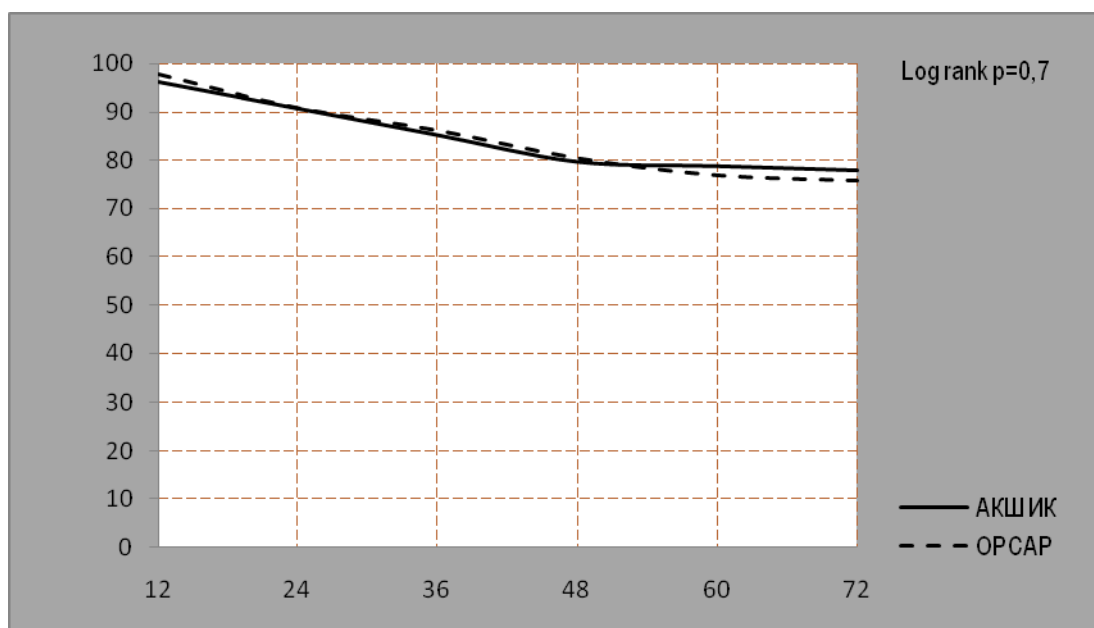
Figure 1. The five-year survival rate of diabetic patients after CABG with CPB and off-pump CABG.



———— CABG with CPB

----- Off-pump CABG

Figure 2. Survival without the development of "large" cardiovascular events after CABG in diabetic patients after CABG with CPB and off-pump CABG.



————— CABG with CPB

----- Off-pump CABG

Figure 3. Freedom from the recurrent angina pectoris in diabetic patients after CABG with CPB and off-pump CABG.

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