

The Mid-Term Results of Isolated Coronary Artery Bypass Graft Operation

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According to the obtained data, on the basis of preventive strategy and treatment, CABG has shown to have the excellent mid-term results. It is associated with marked improvement in major clinical outcomes, survival, quality of life, depressive symptomatology, myocardial contractility and functional classes of heart failure. The present study is the first experience in our country. It proves the necessity of existence of the secondary coronary preventive system in hospitals performing CABG operations. Further follow-up is ongoing.

Key words: coronary artery, stenosis, occlusion, operation, revascularization, reintervention, mortality.

Introduction. Coronary artery bypass grafting (CABG) is the gold-standard surgical treatment for coronary artery disease. Nevertheless patients undergoing bypass revascularization are at high risk for development of further coronary events. Ongoing atherosclerotic process results in stenosis and occlusion of bypass grafts as well as native coronary arteries. Therefore such a category of patients should be considered as the top priority for preventive cardiology.

537 outpatients (480 men and 57 women, mean age 58.2 ± 7.4 years) following primary isolated CABG operation were enrolled in the study. Mean duration of the follow-up was 932 ± 87 days. The primary end points were cardiac-related mortality rate, recurrent coronary events, rehospitalization and repeat revascularization; The secondary end points were heart failure functional classes, left ventricular ejection fraction (LVEF), health-related quality of life (HRQoL), depressive symptomatology, traditional and nontraditional risk factors and medication therapy. Cardiac-related mortality rate after over two years of the follow-up was only 0.55%. There were 5.40% of recurrent coronary events during the study period. Coronary reintervention and cardiac-related rehospitalization occurred rare enough – in 0.55% and 1.86%, respectively. There were statistically significant improvements in functional classes of heart failure and LVEF. The increase of LVEF was observed in patients with preoperatively poor LVEF. 14.2 \pm 5.3 months after CABG operation improvements in HRQoL and depressive symptomatology were observed. The target level of low-density lipoprotein cholesterol was achieved in 71% of patients. Nontraditional risk factors for coronary atherosclerosis — elevated levels of C-reactive protein, hyperfibrinogenemia, endothelial dysfunction and hyperlipoperoxidemia were prevalent. The first line agents after bypass revascularization were aspirin and statins.

According to the obtained data, on the basis of preventive strategy and treatment, the mid-term prognosis of CABG operation was excellent. The present study proves the

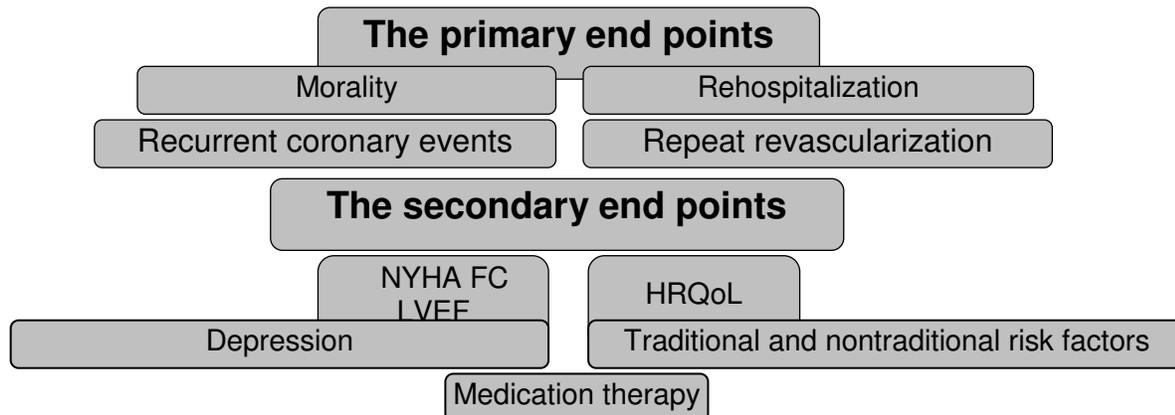
necessity of existence of the secondary coronary preventive system in hospitals performing CABG operations.

Coronary artery bypass grafting (CABG) is the most commonly performed “Open heart” operation in the world. CABG is the gold-standard surgical treatment for coronary artery disease. The improvement in patients’ clinical status and prognosis achieved by this method of myocardial revascularization is unequivocally proved. Nevertheless, it is noteworthy that even successful and complete revascularization is not able to protect the heart from complications of ongoing atherosclerosis and consequently, recurrent coronary events occur. To say more, bypass surgery may cause systemic inflammation, endothelial dysfunction, oxidative stress and other disorders resulting in the progression of atherosclerotic process in bypass grafts as well as in native coronary arteries (6, 20, 25, 30, 31). Hence patients following CABG are at high risk for development of further major coronary events. Therefore such a category of patients should be considered as the top priority for preventive cardiology.

The study was carried out in the system of Secondary Prevention of Coronary Heart Disease of Emergency Cardiology Center, where for today more than 1000 CABG operations are performed. The goal of the present research was to describe mid-term outcomes of the patients undergoing primary isolated bypass revascularization.

Material and methods. The study population consisted of 537 outpatients (480 men and 57 women) who had undergone bypass revascularization in our hospital between June 2001 and August 2007. The mean age of the patients was 58.2 ± 7.4 years (range 36-74 years). An exclusion criterion was CABG in conjunction with concomitant valve replacement or repair. Preoperative coronary angiography revealed three-vessel coronary artery disease in 72% (n=387) of the patients, 26% (n=140) had two-vessel coronary disease and only 2% (n=10) of the patients had one-vessel disease. A left main stem coronary artery stenosis greater than 50% was present in 5% (n=25) of cases. 38% arterial and 62% vein grafts were used. On-pump revascularization was performed in 95% (n=508), off-pump revascularization - in only 5% (n=29). In most of the patients (84%) complete revascularization was carried out, hence index of completeness of revascularization was > 1 . Mean duration of the follow-up was 932 ± 87 days. The mid-term prognosis of CABG operation was estimated by the primary and secondary end points of the study, which are displayed in figure 1. With regard to the cause of death a distinction was made between cardiac-related death (sudden death < 1 h of complaints, fatal acute myocardial infarction and congestive heart failure) and non-cardiac death (all other causes). The study design was prospective.

Figure 1. The primary and secondary end points of the study



Functional status of heart failure was evaluated by the New York Heart Association functional class (NYHA FC). Left ventricular ejection fraction (LVEF) was measured by echocardiography. Health-related quality of life (HRQoL) was estimated by the short form-36 questionnaires (32). To detect depressive disorders the Beck Depression Inventory (BDI) questionnaires (22) were used. Blood lipid profile parameters – low- and high-density lipoprotein cholesterol (LDL-C, HDL-C), triglycerides (TG) as well as nitric oxide (NO), C-reactive protein (CRP), fibrinogen and lipoperoxide levels were measured by the methods described previously in our works (7,8,9). Body composition was assessed according to the body mass index (BMI).

Continuous data were expressed as mean value \pm standard deviation and were compared using Student's t-test. A p value < 0.05 was considered statistically significant.

Results and discussion.

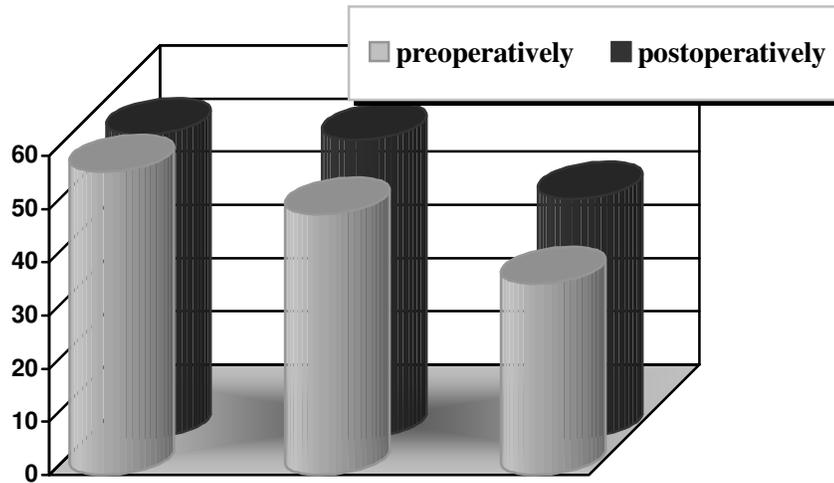
The primary end points. All patients were followed up clinically. Renewal of anginal symptoms and other cardiac events were carefully registered. The follow-up included clinical visits and telephone interviews.

During the follow-up all cause mortality rate was 1.48% (n=8). The cause of death was cardiac-related in 0.55% (n=3) of cases 20.7 \pm 6.5 months (range 10-31 months) after CABG and non-cardiac-related in 0.93% (n=5) of the patients. There were three coronary deaths — two patients died due to myocardial infarction, one patient died of sudden cardiac death. In other five cases the causes of fatal outcomes were unrelated to the coronary artery disease. The non-cardiac-related death were caused by cancer in two patients, stroke in one patient, aorta aneurysm in one patient and in one case the cause of death is unknown. During the follow-up period there was 5.40% of cases (n=29) of recurrent coronary events (21.3 \pm 2.4 months postoperatively, range 5-32 months). Recurrent coronary incidents were revealed by myocardial infarction in 13.8% (n=4) of cases, 6.9% (n=2) of the patients had unstable angina and the remaining 79.3% (n=23) had stable angina.

All cause rehospitalization rate was 2.97% (n=16). Among them in ten cases (62.5%) repeat hospitalization was cardiac-related - myocardial infarction, stable and unstable angina, congestive heart failure (19.3 ± 10.4 months postoperatively, range 5-31 months). Repeat revascularization (percutaneous coronary intervention) was performed in 0.55% (n=3) patients on average 17 ± 16.6 months after CABG (range 5-36 months). On the basis of angiography, vein grafts' occlusion and stenosis were observed. There were new lesions in native coronary arteries as well. There was also a case of subclavian artery occlusion. It is noteworthy that in all cases internal thoracic artery grafts were patent. Unfortunately, one patient undergoing repeat myocardial revascularization died of myocardial infarction five months after the procedure.

The secondary end points. Preoperatively 148 patients (27.5%) had heart failure. Of these, 75 had I-II NYHA FC and 73 - III-IV FC. The mean preoperative NYHA FC was 2.2 ± 0.21 (range I-IV). At the end of the follow-up the number of patients with heart failure was diminished. It was diagnosed in 102 (19%) cases. III-IV NYHA FC were observed in 32 patients. Among them three patients died. The causes of fatal outcomes in these cases were acute myocardial infarction, sudden death and stroke. The mean NYHA FC decreased by 0.5 and was 1.7 ± 0.12 (range I-IV). The improvement in NYHA FC was statistically significant ($p < 0.05$). Prior to CABG operation the mean LVEF was $53.3 \pm 7.2\%$ (range 37-72%). At the end of the follow-up the mean value of this parameter increased by 2.4 and became $55.7 \pm 6.3\%$ (range 41-73%). There was no significant change between LVEF before and after bypass revascularization, just a tendency of increasing. It should be noted that more than half of the patients - 59% had increased their preoperative LVEF by 0.05 or more. Fewer patients had LVEF less than 45 % approximately three years after CABG compared with preoperatively. It should be also emphasized that the increase of LVEF was more observed in those patients who preoperatively had low LVEF. By magnitude of this parameter the patients were divided into three groups. Prior to CABG the mean value of LVEF in the I group was $57.8 \pm 5.2\%$ (range 55-72%), in the II group — $45.2 \pm 3.3\%$ (range 40-54%) and in the III group — $37.8 \pm 3.4\%$ (range 37-39%). At the end of the follow-up there was only a tendency of increasing in LVEF in the I group, it became $58.1 \pm 4.6\%$. There was significant increase in LVEF in the II and III groups of the patients. In the II group it increased by 10.2 and became $55.4 \pm 3.9\%$ ($p < 0.05$). The III group of the patients with very low LVEF had statistically significant change of this parameter. It increased by 10.3 and was $48.1 \pm 3.7\%$ at the end of the follow-up ($p < 0.05$) (Figure 2).

Figure 2. LVEF dynamics prior to and after bypass operation



HRQoL was assessed in 313 patients. 224 patients were excluded because of several reasons: 8 patients died, 108 patients refused to complete questionnaires prior to surgery, 65 patients did not complete questionnaires after operation and in the remaining 43 cases questionnaires were not correctly completed. Baseline questionnaires were obtained a day before CABG at the time of admission and final questionnaires - as minimum a year after operation. The mean interval between completions of questionnaires was 14.2 ± 5.3 months. The Short-Form-36 was used to measure perceptions of health outcomes. The physical component summary (PCS) and the mental component summary (MCS) scores reflect a patient's overall physical and mental health status. The PCS and MCS scores have a possible range of 0 to 100, where higher scores indicate better health status. Very high PSC scores indicate no physical limitations, disabilities or decrements in well-being as well as a high energy level. Very low PCS scores indicate substantial limitations in self-care, physical, social and role activities, severe bodily pain or frequent tiredness. Very high MCS scores indicate frequent positive affect, absence of both psychological distress and limitations in usual social role activities due to emotional problems, while very low MCS scores indicate frequent psychological distress and substantial social and role disability due to emotional problems. Pre- and postoperative PCS and MCS scores are shown in table 1. There were statistically significant improvements in both — physical and mental components of HRQoL 14.2 ± 5.3 months after CABG operation.

Table 1. Physical and mental component summary scores before and after bypass operation (n=313)

Components of HRQoL	Scores		p
	Before CABG	After CABG	
Physical component	824±160	1137±183	<0.05
Mental component	683±53	844±61	<0.05

The patients were divided into 2 groups. Individuals in group 1, representing 63% (n=198) of patients, had improvement in their PCS score. In contrast, group 2 had no improvement in physical component of HRQoL. Almost the same data were found in connection with mental component. Group 1, which represented 60% (n=188) of participants, had improvement in their MCS score after CABG operation. The patients in group 2 showed no significant change. On the basis of obtained data the reasons of non-improvement in physical and mental components of HRQoL were: arterial hypertension, diabetes mellitus, obesity, metabolic syndrome, previous myocardial infarction, low LVEF, higher NYHA functional status, co-morbidities, especially hypothyroidism and chronic obstructive pulmonary disease and recurrent coronary incidents as well. For the socio-demographic variables non-improver status was associated with being female, old age and not being in the workforce.

To investigate the presence of depression prior to and after CABG operation we used BDI one day before and at average 14.2±5.3 months after bypass revascularization. The survey was conducted among 235 patients who completed BDI questionnaires. Depression was defined as a score of > or = 10 on the BDI. Of the 235 patients studied, a total of 137 (58%) were clinically depressed preoperatively. 14.2±5.3 months after operation depressive disorders occurred in 52 (22%) of participants. The proportion of females was higher in depression group pre- and postoperatively. The mean preoperative BDI score was 17.3±4.2 (range 1-29), whereas after surgical revascularization the same parameter lowered by 9.7 and became 7.6±2.1 (range 0-17). The difference between initial and final BDI scores was statistically significant (p< 0.05).

Comprehensive risk factor interventions are the cornerstone of preventive cardiology, particularly in patients undergoing myocardial revascularization. Preventive efforts should target each risk factor. It is known that any major risk factor, if left untreated for some years, has the potential to produce recurrent clinical events. Table 2 presents the prevalence of modifiable traditional risk factors 932±87 days after CABG operation. Among the listed three lipid risk factors we were especially focused on LDL-C. Our preventive strategy was addressed to achieve the target level of LDL-C. Most of the patients — 71% had LDL-C concentration ≤ 100mg/dl as it is strongly accepted in secondary coronary prevention (28).

Table 2. The prevalence of modifiable classical risk factors in patients following CABG operation (n=537)

Dyslipidemia: LDL-C > 100mg/dl HDL-C < 40mg/dl TG > 150mg/dl	29% 48% 45%
Hypertension	39%
Current smokers	3%
Body composition: Overweight (BMI 25-30kg/m ²) Obese (BMI > 30kg/m ²)	39% 6%
Physical inactivity	27%

Importance of the above listed traditional risk factors is well established, but they account for not more than half of cardiovascular risk (17). Consequently, they can not explain the high frequency of complications of atherosclerosis and generally the process of atherogenesis. This fact has led to considerable interest in novel risk factors in the modern world. Taking into consideration multifactorial nature of atherosclerosis, in parallel with classical risk factors, the assessment of novel - so-called nontraditional risk factors may provide clinically useful information for the evaluation of attributable risk in order to prevent of recurrent coronary events. Hence, one of the goals of the present study was to determine the prevalence of some nontraditional risk factors for coronary atherosclerosis, such as: elevated levels of CRP, hyperfibrinogenemia, endothelial dysfunction and hyperlipoperoxidemia. The listed nontraditional risk factors were examined in 232 patients 89.4±26.7 days after CABG operation. As it is shown in table 3 the prevalence of elevated levels of inflammatory markers — CRP and fibrinogen were 48% and 44%, respectively. Their mean plasma concentrations were 5.3±2.04mg/dl and 4.2±0.85 g/L. Endothelial function estimated by plasma NO level was impaired in 63% of cases. In these patients mean value of nitric oxide was 10.8±3.7 mkmol/L. Hyperlipoperoxidemia - marker of oxidative stress was the most prevalent. It was observed in 83% of patients. Mean plasma lipoperoxide level was upper limit of normal — 2.1±0.37 mkmol/L. The minority of patients (12%) lacked any of the investigated nontraditional risk factors. So, among patients following bypass revascularization the listed nontraditional risk factors were prevalent. The obtained data suggest that high frequency of these novel risk factors has prognostic value to identify patients at risk and to control the efficacy of pharmacologic interventions in clinical practice. This is especially important in patients undergoing CABG operation.

Table 3. Nontraditional risk factors in patients undergoing CABG operation (n=232)

Risk factors	Prevalence	Mean value
Elevated CRP	48%	5.3±2.04mg/dl
Hyperfibrinogenemia	44%	4.2±0.85g/L
Endothelial dysfunction (abnormal NO levels)	63%	10.8±3.7mkmol/L
Hyperlipoperoxidemia	83%	2.1±0.37mkmol/L

The establishment of systematic treatment plans for the management of risk factors after bypass revascularization is essential if optimal outcomes are to be achieved. Complete therapy for atherosclerosis in CABG patients involves secondary preventive drugs in postoperative period, regardless of its duration. It is known that medical treatment substantially reduces the likelihood of the recurrent major coronary events after CABG (12, 15). The status of prescribed medications 932±87 days after bypass revascularization is presented in figure 3. The first line agents were aspirin and statins. Aspirin use was almost universal, 97% of the patients were taking it. In the remaining 3% cases the drug was withdrawn due to ulcerogenic effect and aspirin resistance assessed by platelet aggregation test. In these cases aspirin was substituted by other antiaggregants. At the end of the study the mean dose of aspirin was 89.5±18.6 mg/day (range 75-150mg/day). The proportion of patients taking statins also was high enough - 92%. It should be underlined that among statin-treated patients 89% were taking these agents without interruption – from the time of discharge till the end of the study. In the remaining 8% of patients the reasons of not being on statin therapy were patients' refusal or adverse effects of these preparations. At the end of the follow-up the mean dose of statins was 20.1±9.4mg/day (range 10-80 mg/day). It is noteworthy that at this time point on the background of statin treatment the mean level of LDL-C was 97.8±7.2 mg/dl. More than half of the patients — 63% were taking ACE inhibitors. Other preparations were used less frequently. Generally the mean number of prescribed drugs was 2.13±0.27 at the end of the follow-up.

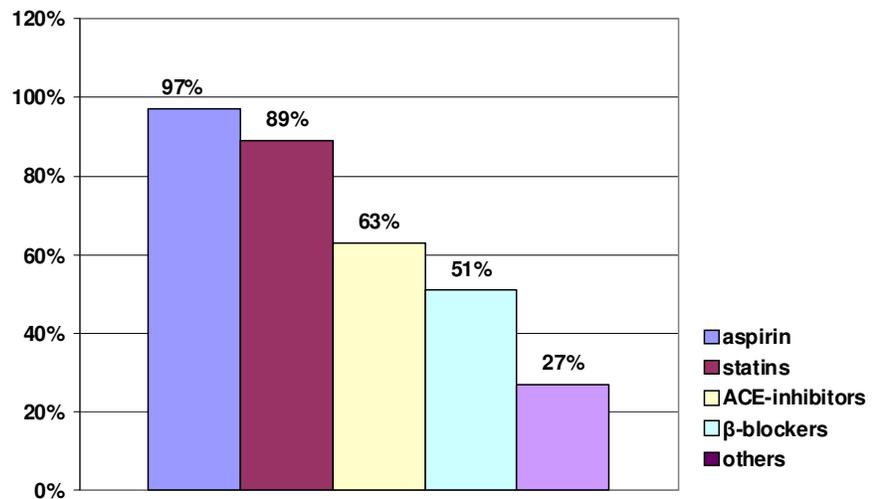


Figure 3. Percentage of the used medications after CABG operation

CABG has become a mainstay in the treatment of patients with coronary artery disease. Myocardial revascularization after CABG is a logical goal and improves outcome and survival. It is noteworthy that despite ongoing technologic advances obstructive changes often occurring in aortocoronary saphenous-vein bypass grafts remain the Achilles heel of this operation. Consequently, after CABG in some cases undesirable clinical outcomes - deaths and recurrent events take place. Inasmuch as the maintenance of results of myocardial revascularization is extremely important, in our center the system of secondary coronary prevention has been functioning. The present prospective study has described the results of preventive strategies and treatment in 537 patients undergoing isolated CABG operation in our hospital 932±87 days after revascularization. The obtained results showed that mid-term prognosis was excellent. The first and most important end point of the study — cardiac-related mortality rate after over two years follow-up was only 0.55% — much less than it is shown in other publications (2, 13, 23). There were 5.40% of recurrent coronary events during the follow-up. A bit different data were observed in other surveys (1, 13, 26). According to our data in comparison with other studies (14, 18) coronary reintervention (percutaneous coronary intervention) and cardiac-related rehospitalization occurred rare enough - in 0.55% and 1.86%, respectively. It is natural that congestive heart failure is undesirable clinical outcome of bypass revascularization and results in deteriorating in patients' clinical status. The presence and severity of ischemic left ventricular systolic dysfunction is an important predictor of prognosis after CABG operation. In concordance with some previous surveys (5, 10, 16) we found statistically significant improvements in two secondary end points of our investigation — NYHA FC and LVEF. At the same time it should be emphasized that the increase in LVEF was observed in patients with preoperatively poor LVEF (45.2±3.3%, 37.8±3.4%). CABG is aimed at alleviating patients' morbidity and prolonging their lives. Give the high success rate of such surgery in achieving these aims, it is clear why the assessment of HRQoL is of such importance. Longitudinal studies (24, 29) have confirmed that most patients report improved HRQoL following bypass revascularization through reduced symptoms, improved functioning and increased participation in activities. However, for a significant minority of patients, this improvement does not occur or the patient reports deterioration in HRQoL (19). Thus, potentially there are a number of trajectories a patient may follow after surgery — improve, maintain the same level, deteriorate, or a combination of these. One of the purposes of the present study was to examine HRQoL dynamics in CABG patients. Our finding is consistent with previous surveys (19, 21) that physical and mental components of HRQoL improve over time following bypass revascularization but there was the minority of patients (12%) who had no improvement. Some characteristics which were associated with poorer HRQoL outcomes after CABG were found.

On the basis of data of some trials preoperatively existing depression is an independent risk factor for complications and recurrent cases in postoperative period (3, 4, 29). Moreover, studies have concluded that depression is an independent predictor of mortality in CABG patients (27, 33). Hence, one of the secondary end points of the present study was to investigate the presence of depression prior to and after revascularization. According to our finding after over two years follow-up BDI scores were significantly improved. Postoperatively depressive symptomatology occurred in only 22% of the patients.

იზოლირებული კორონარული შუნტირების ოპერაციის შედეგები

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ე. შენგელია

(აკად. გ.ჩაფიძის სახ. „გადაუდებელი კარდიოლოგიის
ცენტრი,, თბილისი. საქართველო)

რეზიუმე:

კორონარული შუნტირების ოპერაცია გულის კორონარული დაავადების ქირურგიული მკურნალობის ოქროს სტანდარტს წარმოადგენს. მიუხედავად ამისა,

პაციენტები, რომელთაც გადატანილი აქვთ მიოკარდიუმის ქირურგიული რევასკულარიზაცია, რეკურენტული კორონარული ინციდენტების განვითარებისათვის მაღალი რისკის პაციენტებია. მიმდინარე ათეროსკლეროზული პროცესი იწვევს კორონარული ტორანსპლანტანტებისა და ნატიური კორონარული არტერიების სტენოზირებასა და ოკლუზიებს. გამომდინარე აქედან აღნიშნული კატეგორიის პაციენტები პრევენციული კარდიოლოგიის პრიორიტეტს წარმოადგენენ.

კვლევაში შეტანილი იქნა 537 ამბულატორიული პაციენტი (480 მამაკაცი და 57 ქალი, საშუალო ასაკი 58,2+/- 7,4 წელი.) რომელთაც ჩვენს კლინიკაში ჩატარებული ჰქონდათ იზოლირებული კორონარული შუნტირების ოპერაცია. დაკვირვების პერიოდის საშუალო ხანგრძლივობამ 932+/- 87 დღე შეადგინა. კვლევის პირველადი საბოლოო წერტილები იყო: ლეტალობა, რეკურენტული კორონარული შემთხვევები, რეჰოსპიტალიზაცია და განმეორებით რევასკულარიზაცია. მეორადი საბოლოო წერტილები იყო: გულის უკმარისობის ფუნქციური კლასი, მარცხენა პარკუჭის განდევნის ფრაქცია (მპ გფ), ცხოვრების ხარისხი, დეპრესიული სიმპტომატოლოგია, ტრადიციული და არატრადიციული რისკის ფაქტორები და დანიშნული პრეპარატები.

კვლევის განმავლობაში კარდიულმა ლეტალობამ 0,55%, ხოლო რეკურენტული კორონარული ინციდენტების სიხშირემ 5,40% შეადგინა. კორონარული რეინტერვენციისა და კარდიული მიზეზებით გამოწვეული რეჰოსპიტალიზაციის პროცენტული მაჩვენებელი შესაბამისად 0,55% და 1,86 აღმოჩნდა. აღინიშნა გულის უკმარისობის ფუნქციური კლასისა და მპ გფ-ის სტატისტიკურად სარწმუნო გაუმჯობესება. ამავდროულად მპ გფ-ის მომატება დაფიქსირდა პაციენტთა იმ კონტიგენტში, რომელთაც პრეოპერაციულად აღნიშნული მაჩვენებელი დაბალი ჰქონდათ. ოპერაციიდან 14,2+/- 5,3 თვის შედეგი აღმოჩნდა ასევე ავადმყოფთა ცხოვრების ხარისხისა და დეპრესიული სიმპტომატოლოგიის

გაუმჯობესება. დაბალი სიმკვრივის ლიპოპროტეინების ქოლესტერინის სამიზნე დონე სისხლში მიღწეული იქნა პაციენტთა 71% შემთხვევაში. კორონარული ათეროსკლეროზის არატრადიციული რისკის ფაქტორები – C-რეაქტიული ჰიპერპროტეინემია, ჰიპერფიბრინოგენემია, ენდოთელიუმის დისფუნქცია და ჰიპერლიპოპროქსიდემია საკმაოდ ხშირ შემთხვევაში დაფიქსირდა. მიოკარდიუმის ქირურგიული რევასკულარიზაციის შემდეგ ასპირინი და სტატინები პირველი რიგის პრეპარატები აღმოჩნდნენ.

ასე, რომ ჩატარებული კვლევის მონაცემების მიხედვით, პრევენციული ღონისძიებებისა და მკურნალობის ფონზე, კორონარული შუნტირების ოპერაციის შედეგები შესანიშნავია. წარმოდგენილი კვლევა ადასტურებს მეორადი კორონარული პრევენციის სისტემის არსებობის აუცილებლობას იმ კლინიკებში, სადაც ტარდება კორონარული შუნტირების ოპერაციები,

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