

Surgical Treatment of Patients with Ischemic Cardiomyopathy: The Significance of Right Ventricular Function

(#1999-61391 ... July 19, 1999)

S. V. Gureev, MD, E.N. Kasakov, A.Y. Kormer, E.N. Ostroumov, V. I. Shumakov

Institute of Transplantology and Artificial Organs, Moscow, Russia
Department of Coronary Surgery and Heart Transplantation

ABSTRACT

Background: Patients with ischemic cardiomyopathy (ICMP) awaiting heart transplantation (HT) have a high mortality rate, in part because of the lack of donor organs. Given this limitation, we propose to broaden the indications for coronary artery bypass grafting (CABG) in this group and to more accurately select patients with ICMP requiring myocardial revascularization or HT. In this study, we assessed the short and long-term results of CABG in patients with ICMP. We also assessed the role of the right ventricle and the diastolic function of both ventricles in patients with ICMP. Using this information, we propose indications for CABG and/or HT in patients with ICMP.

Methods: We analyzed 49 patients with ICMP undergoing workup as potential heart transplant candidates. The patients were divided into two groups. Group A included 19 patients submitted to isolated CABG based on the preoperative assessment of myocardial viability. Group B consisted of 30 patients determined to be best suited for HT (with five patients actually receiving a donor heart). All patients were assessed by radionuclide ventriculography (RVG) and functional testing in order to assess their myocardial viability. RVGs were obtained prior to coronary bypass as well as at two and twelve months postoperatively.

Results: Preoperative data in group A were: left ventricular end-diastolic dimension (LVEDD) 7.0 ± 0.32 cm, left ventricular ejection fraction (LVEF) $24.2 \pm 2.6\%$, and right ventricular ejection fraction (RVEF) $32.4 \pm 2.6\%$. For Group B, LVEDD was 7.7 ± 0.29 cm, LVEF was $22 \pm 2.7\%$, and RVEF

$26 \pm 2.6\%$. The operative mortality in group A was 16.6%. Three patients died in the early postoperative period, two of them due to acute cardiac failure, and one due to cerebral complications. The number of grafted arteries was 3.6 ± 0.2 . One year after coronary artery bypass, the resting LVEF increased to 33.3% (a 36% improvement compared with preoperative, $p < 0.001$). Three-year survival was 77% in group A and 26.8% in group B. Examination of the myocardial functional state after CABG showed that the LV diastolic and RV systolic parameters statistically improved. The decrease of RVEF was revealed in the orthostatic test in patients (group A) who died after CABG in the early postoperative period, and in group B that correlated with their parameters of the myocardial viability.

Conclusions: TCABG in the patients with ICMP significantly increases the functional reserves of the myocardium of both ventricles, mostly because of the improvement in the diastolic function of the LV. In the RV, the systolic function could restore even in the early postoperative period.

Preoperative analysis of the parametric images made after orthostatic test and nitroglycerin intake allow prediction, with 85 % sensitivity and 95% specificity, of the areas of the myocardium which will restore their function immediately after CABG ("hibernated myocardium"). The recovery of regional wall motion amplitude and of the response of the myocardium to coronary revascularization could continue during the first year after revascularization ("stunned myocardium"), most often beginning in the LV.

The decrease of the EF of the RV as a response to the "unloading" tests could be a result of the disturbance of the ventricles' interaction as well as the spreading of the scarring of the RV myocardium. This decrease could be a predictor of the possible development of the low cardiac output syndrome after CABG.

INTRODUCTION

Advances in the surgical treatment of coronary artery disease (CAD) have substantially improved the prognosis

Submitted to the Resident's 1998 Writing Award Competition through the generous support of Genzyme Surgical, Inc.

Address correspondence and reprint requests to: Sergey Vasilievich Gureev, MD, Scientific - Research Institute of Transplantology and Artificial Organs, Department of Coronary Surgery and Heart Transplantation, 125239, 8 Novopodmoskovny pereulok 4-32, Moscow, Russia, Phone: +07 095 450 25 10, Fax: +07 095 456 9911, E-mail: gureevs@orc.ru

Table 1. Clinical Characteristics of Patients with ICMP

	CABG (n = 19)	Drug group (n = 25)	Heart Transplantation (n = 5)
Sex	Male	Male	Male
Age (years)	47±6.7	45.7±5.4	46.8±4.8
Angina pectoris:			
SMI	10.2	0.0	0.0
II	—	11	63.0
III	33.3	33	33.4
IV	55.6	46	4.0
NYHA heart failure:			
III	67	62	84
IV	33	38	16
Number of MI	1.74±0.28	2.0±0.1	1.9±0.4
Sinus rhythm	100	84	83.7
AF	0.0	16	16.3

Designations: SMI = silent myocardial ischemia; FC = functional class; MI = myocardial infarction; AF = atrial fibrillation.

in patients with reversible ischemia. However, prognosis and treatment options in patients with ischemic myocardial dysfunction and congestive heart failure (CHF) still constitutes a serious problem. Ischemic cardiomyopathy (ICMP) is term used to describe a variant of CAD typified by multiple stenoses which cause sustained imbalance between oxygen supply and demand leading to myocyte loss, diffuse myocardial fibrosis, cardiac dilatation, and clinical heart failure [Burch 1972, Foulkner 1977, Kron 1989, Anversa 1990, Sonnenblick 1990]. Optimum treatment for patients with ICMP continues to be an area of discussion and dispute [Burch 1970, Anversa 1992, Hurt 1993, Luciani 1993, Rahimoda 1995, Iskandrian 1996, Shumakov 1998].

The first attempts at surgical correction of ICMP by CABG in the 1960's met with high mortality rates and heart transplantation subsequently became the preferred surgical treatment.

In the past four decades the incidence of heart failure has risen from 1 to 5 cases per 1000 individuals of the US and European populations, with CAD being the cause of heart failure in 60% of these cases. Patients with ICMP account for 6–8% of all patients with CAD and 40–50% of all patients included in the list of transplant candidates [Iskandrian 1994]. However, as the need for HT rises, the procedure remains severely limited by lack of donor organs. Furthermore, the three-year survival rate of patients with ICMP treated with medical therapy alone is no more than 25–30%. The high mortality among patients with ICMP who are awaiting HT has prompted cardiac surgeons around the world to reconsider indications for CABG in this group of patients (see Figure 1 ●).

In this study, we attempt to define the clinical, functional, and morphological characteristics of ICMP. We studied the role of the right ventricle and the diastolic function of

both ventricles. We compared the early and late outcomes of surgical treatment in ICMP — in both CABG and HT. Finally, we defined the indications and selection policy for CABG versus HT in patients with ICMP.

MATERIALS AND METHODS

Patient characteristics

From 1993 to 1997 the Department of Coronary Surgery and Heart Transplantation followed 49 patients with ICMP. All the patients were considered to be potential recipients of a donor heart. Patients with left ventricular aneurysm, valvular disease, or ventricular septal defect were excluded from the study. Thus, the study included 49 patients with ICMP who were divided into three groups:

- Group 1 - undergoing CABG (n = 19)
- Group 2 - undergoing HT (n = 5)
- Group 3 - medical management only (n = 25).

Among the 49 patients, five (10.2%) had no anginal symptoms, 5 (10.2%) were found to have silent myocardial ischemia (SMI), 17 (34.6%) experienced functional class III angina pectoris, and 22 (44.8%) experienced functional class IV angina, the duration of angina being a mean of 4.57±1.46 years. According to the degree of heart failure, the patients were divided as follows: 23 (47%) patients had NYHA functional class III, 26 (53%) functional class IV. The mean duration of clinical heart failure was 0.52±0.08 years. No patient had historical or current signs of arterial hypertension. The patients' clinical data are presented in Table 1 (●).

Patient assessment followed a protocol for potential donor heart recipients, comprised of physical examination, xray of the chest in three projections, ECG, echocardiogram, right and left cardiac catheterization, left ventriculography, selective coronary angiography, and radioisotopic ventriculography.

Cardiac catheterization

Our protocol included retrograde catheterization of the right and left ventricular chambers with recording of intracavitary pressure curves, left ventriculography and selective multiprojectional coronary angiography. Calculations were made of the following hemodynamic parameters: right atrial pressure (RAp), pulmonary artery systolic pressure (PAs), mean pulmonary pressure (PAm), pulmonary capillary wedge pressure (PCWp), and transpulmonary gradient (TPG) (PAs-PCWp difference). Thermodilution was used to measure cardiac output (CO).

Contrast ventriculography was performed with Judkins catheters inserted via femoral artery puncture using the Seldinger technique with imaging obtained in the 30 degree right oblique projection and in some cases in the left oblique projection.

Coronary angiography was conducted in three projections: frontal, left oblique, and right oblique. To define the lesion site more exactly, the arteries were divided into three

segments: proximal, intermediate, and distal. The narrowing of arteries was expressed as a percentage. First degree stenoses corresponded to less than 50% reduction in the arterial lumen; second degree stenoses had 50 to 75% reduction, and third degree stenoses had over 75% reduction.

Radioisotopic ventriculography

To evaluate myocardial viability, radioisotopic ventriculography was performed using unloading functional tests at rest (in recumbency), after administration of nitroglycerin 10-20 mg, and in the sitting position (orthostatic test) (see Figures 2a and 2b ). Using a Basicam gamma-chamber (Siemens, Germany) and a Russian information collection system (Goldrada), assessments of the following parameters were recorded: ejection fraction (EF); end-diastolic volume (EDV); end-systolic volume (ESV); maximum ejection rate (MER) and maximum filling rate (MFR) of the left ventricle (LV) and right ventricle (RV). Local assessments of segmental ejection fraction, a-phase, and amplitude by parametric images in 12 segments of each ventricle were also made.

Systolic-diastolic relationships

A correlation analysis of intracardiac hemodynamic parameters, as well as the parameters of left and right ventricular systolic and diastolic functions was performed to study cardiac performance as a unified process of interdependent phases of contraction and relaxation of the myocardium of the left ventricle (LV) and the right ventricle (RV).

Upon completion of the workup, the leading specialists of the Research Institute of Transplantation and the Research Department, Ministry of Health of the Russian Federation, jointly decided whether CABG or HT should be performed, or drug therapy continued.

Medical management (n = 25)

Medical management of ICMP, aimed at compensating heart failure, involved cardiac glycosides, diuretics, peripheral vasodilators (nitrates and angiotensin-converting enzyme inhibitors), antiarrhythmics, and electrolyte balance modifiers.

Coronary artery bypass grafting (n = 19)

The indications for coronary artery bypass surgery in the setting of ICMP were:

- 1) The surgical feasibility of grafting the affected coronary arteries
- 2) No less than functional class II angina
- 3) LVEF no less than 15%
- 4) RVEF no less than 30% at rest
- 5) Evidence of myocardial viability in the area of a stenotic artery
- 6) Congestive heart failure responsive to intensive drug therapy.

Preoperative preparation: The duration of preoperative preparation was a mean of 14.2 ± 2.1 days. Preparation

involved the administration of: 1) digoxin, in a mean chosen dose of 0.36 mg/day, 2) nitrosorbide, up to 200 mg/day, 3) capoten 25 mg/day, and 4) diuretics. Two patients required intermittent intravenous dobutamine 5 mcg/kg/min for 7-14 days pre-operatively. An intraaortic balloon-pump was inserted in two patients the day before surgery. Isoket was intravenously administered in nine (50%) patients 2-4 days prior to surgery. To protect the myocardium and to prevent reperfusion complications, 5 ml of 33% vitamin E solution were intramuscularly administered on the morning of surgery.

Surgical technique: Cardiopulmonary bypass was made via the ascending aorta with separate caval cannulation. The mean aortic cross clamp time was 79.7 ± 12.5 min and mean extracorporeal circulation time was 127.5 ± 14.5 min. For cardioplegia, "Custodiol" was used in all cases. The mean number of grafts per patient was 3.7 ± 0.3 . For grafting the LAD, the left internal mammary artery (LIMA) was used in 5 of 19 cases while a saphenous vein was employed in the remaining cases. Right coronary endarterectomy was performed in six (31.5%) and LAD endarterectomy was performed in 2 cases (10.5%).

Cardiac transplantation (n = 5)

The decision to proceed with HT was based mainly on contraindications for CABG, such as: 1) diffuse coronary disease (11% of cases), or 2) drug-resistant circulatory insufficiency and the absence of myocardial viability in the area of the involved arteries (89% of cases).

Orthotopic cardiac transplantation was performed in all 5 patients according to the Shumway-Lower technique. The graft ischemic time averaged 122.1 ± 9.1 min. while the mean extracorporeal circulation time was 169.4 ± 5.4 min. In four of five cases the donor's heart was taken in a remote location (distant procurement). Inotropic agents were used in all recipients in the early postoperative period. Data were recorded for analysis from pathology studies of the explanted hearts.

RESULTS

Preoperative Evaluation

Non-invasive instrumental findings: Incomplete bundle-branch block was detected in 11.1% of the patients. Arrhythmias were found in 22.2%, all patients having single ventricular extrasystole. The duration of rhythm disturbances was 0.9 ± 0.36 years. The number of prior myocardial infarction (MI) was 1.74 ± 0.28 . Of these, transmural and nontransmural MIs were 1.14 ± 0.12 and 0.06 ± 0.1 , respectively. Five patients (10.2%) had no history of MI. One, 2, 3, and 4 MIs had been experienced by 15 (30.6%), 17 (34.6%), 11 (22.4%), 1 (2.02%) patient, respectively. Anterior transmural (Q-wave) MI was detected in 37 patients (75%), and posterior transmural MI in 12 (25%). Nontransmural (non Q-wave) anterior and posterior MIs were identified in 7 (14.2%) and 42 (85.7%) of the patients, respectively. A combination of anterior and pos-

Table 2. Findings at Coronary Angiography (n = 49 patients)

	Coronary Stenosis (% of Patients)	Grade 3 Lesion (> 75% Stenosis) (% of Patients)	Total Occlusion (% of Patients)
Left Main	11.1%		
LAD	100%	55.1%	44.5%
Diagonal	22.0%	22.0%	
Circumflex	77%	33.9%	57.1%
Obtuse marginal	55.5%	55.5%	
RCA	88.8%	55.5%	44.5%

Designations: LAD = left anterior descending; RCA = right coronary artery.

terior transmural infarcts were evidenced in 22.4% of the patients, and 17 patients (34.6%) had concurrent transmural and large MIs at different sites.

Invasive instrumental findings: Pulmonary hemodynamic studies found: 16 patients (32.6%) had transpulmonary gradient over 15 mm Hg, PAs of 61.5 ± 4.2 mm Hg, and pulmonary vascular resistance (PVR) of 3.6 ± 0.3 Wood units. Eleven patients (22.4%) had TPG between 10-15 mm Hg, PAs of 34.8 ± 8.6 mm Hg, and PVR of 2.8 ± 0.5 Wood units. Twenty-seven patients (55%) had TPG less than 10 mm Hg, PAs of 39.9 ± 2.6 mm Hg, and PVR of 1.2 ± 0.18 Wood units.

X-ray contrast ventriculography revealed diffuse LV hypokinesis in all patients. The imaging revealed concurrent dyskinesis of one LV segment in 17 patients (34.6%). First degree mitral regurgitation was detected in 27 patients (55%). Coronary angiographic findings are outlined in Table 2 (●). The data on central hemodynamics and myocardial contractile function are presented in Table 3 (●).

Systolic-diastolic relationships (Radioisotopic ventriculographic data): A clear correlation was noted only for the maximum filling rate (MFR) of LV and RV, $r = 0.49$ ($p = 0.015$), which is a measure of diastolic performance. As this takes place, EF was most closely correlated with MFR in the LV, $r = 0.7$ ($p < 0.001$) whereas it was with the maximum ejection rate in the RV, $r = 0.7$ ($p < 0.001$).

Analysis of explanted hearts: The characteristic morphological signs of ICMP were: 1) increased cardiac mass, 2) biventricular dilatation, 3) severe coronary atherosclerotic lesions, and, 4) disproportionately thinned LV wall. The hearts were removed along the atrioventricular sulcus so only the ventricular mass was measured. These ranged from 400 to 550 g (mean 475 g). All hearts had dilated right and left ventricles without formation of aneurysm. Despite the greater cardiac mass, the thickness of the LV wall was not increased. On measurement in the areas without necrosis and fibrosis, LV wall thickness was 1.2 ± 0.1 cm. Examination of coronary arteries in these hearts revealed significant atherosclerotic lesions with areas of stenosis and occlusion. One heart was found to have papillary muscular fibrosis; another had intertrabecular thrombi. Five hearts had extensive large fibrotic changes: those in the apical-septal portions with the involvement of the anterior and posterior LV walls in two

hearts; those in the anterior LV wall and ventricular septum in two hearts; and those in the posterior LV wall and apex in one heart.

A histological study showed myocardial scars formation in all hearts. Foci of myocyte hypertrophy and areas of interstitial and perivascular fibrosis were visible in the noninfarct zones.

Surgical Treatment

Coronary artery bypass surgery: Out of 19 patients, there were 3 deaths (perioperative mortality of 15.8%). Sixteen patients (84.2%) survived to hospital discharge. One perioperative death was due to right ventricular failure. The second perioperative death occurred in a patient who developed acute postoperative heart failure requiring a centrifugal left ventricular assist device for 23 days and intra-aortic balloon contrapulsation for six days. The patient died from bleeding into the right pleural cavity (infarct of the lower lobe of the right lung at autopsy). After an extensive stay in the intensive care unit due to biventricular heart failure, the third patient died from cerebral complications on postoperative day 28. Autopsy revealed cerebral thromboembolism.

Long term follow-up lasted from 1.5 to 5.5 years. A fourth patient died at home three months after surgery; the cause of death was unknown. At present 15 (78.9%) of the original 19 patients are still alive. No significant differences in hemodynamics, cardiac sizes, and resting EF of the left and right ventricles, the duration of extracorporeal circulation or aortic clamp time were found between the survivors and non-survivors.

In the early postoperative period all patients required inotropic support, which continued for an average of 4.0 ± 1.1 days. Three (15.7%), 7 (36.8%), and 5 (26.3%) patients developed acute myocardial insufficiency, atrial fibrillation, and respiratory failure, respectively.

When analyzing preoperative non-invasive data, the survivors demonstrated improved RV ejection fraction with nitrates as opposed to a decline in RVEF seen in the non-survivors ($p < 0.01$, Table 4 ●). No differences in resting or stimulated LVEF were found between CABG survivors and the non-survivors. Similar findings were revealed while examining the changes in the maximum ventricular ejection rate (see Table 5 ●).

Fifteen patients were examined before and within the first month after myocardial revascularization. The examinations were made on days 3-8 before and 7-14 days after surgery (see Tables 6 and 7 ●). Following CABG, LVEF varied only slightly ($29 \pm 4\%$ at rest and $29 \pm 5\%$ in the sitting position). However, LVEF significantly increased in response to NG ($34 \pm 5\%$) ($p < 0.05$). Resting RVEF did not improve significantly, but did increase from 28% to 38% in response to NG ($p < 0.05$). The greatest improvement in RVEF was noted in response to orthostatic (sitting) testing ($39 \pm 3\%$) ($p < 0.01$). A significant reduction in the resting LV volumes did not induce changes in cardiac output (CO). With decreased LV volumes in the early postoperative period, CO was maintained by increasing heart rate. During orthostatic test-

Table 3. Central hemodynamic and myocardial contractile parameters in patients with ICMP

Parameter	CABG (n = 19)	Drug Group (n = 25)	Heart Transplantation (n = 5)
EchoCG data			
EDV (ml)	287.7±32.2	297±31.5	289±15.7
EDD (cm)	7.0±0.26	7.7±1.3	7.7±0.9
LVEF %	26.0±3.6	23.±1.9	21±3.5
Swanz-Gans catheter cardiac cavitary probing data			
PSP (mm Hg)	29.5±2.5	44.5±4.2	42.8±0.4
EDP (mm Hg)	25.1±3.2	23±1.8	24±3.2
TPG (mm Hg)	8.1±1.6	14.9±2.7	7.2±2.2
HVR Wood units	2.0±0.1	2.6±0.2	2.0±0.4
CI l/min/m ²	2.2±0.3	2.0±0.14	2.0±0.1

Designations: EchoCG = echocardiography; EDV = end-diastolic volume; EDS = end-diastolic size; LV EF = ejection fraction of the left ventricle; PSP = systolic pressure in the pulmonary artery; TPG = transpulmonary gradient; PVR = pulmonary vascular resistance; CI = cardiac index.

ing, the postoperative reduced LV volume at rest (recumbency) returned to preoperative values.

All survivors demonstrated preoperative reductions in biventricular EDV and ESV in response to orthostatic testing, which suggested that the myocardium could actively reduce the cavity in diastole. In the non-survivors, there was no decrease in CO and ventricular volumes in response to orthostatic testing; but there was a paradoxical tendency for increased ventricular volume, mainly of the right ventricle. Autopsy data revealed transmural changes in the myocardium and in the wall

Table 4. Baseline values of ejection fractions of the left and right ventricles and cardiac output (before surgery) in survivors and non-survivors of CABG for ICMP (according to radioisotopic ventriculographic data)

Parameter	At Rest	Orthostatic	NG, 20 mg
CABG (n = 19)			
Survivors (n = 15)			
LVEF, %	27±0.4	27±0.5	30±0.3
RVEF, %	28±0.2	30±0.4	34±0.3*
HR	75±0.4	69±0.11	76±0.9
CO, l/min	4.3±0.3	3.7±0.6*	4.9±0.7
Deceased (n = 4)			
LVEF, %	28±0.3	30±0.4	30±0.3
RVEF, %	32±0.7	28±0.7	19±0.4*
HR	81±0.5	83±0.4	86±0.4
CO, l/min	5.0±0.2	4.3±0.2	4.1±1.1

Designations: * difference significance ($p < 0.01$) is indicated as compared to the baseline value (recumbency) of the respective parameter; LVEF = ejection fraction of the left ventricle; RVEF = ejection fraction of the right ventricle; HR = heart rate; CO = cardiac output; NG = nitroglycerin test (20 mg nitroglycerin sublingually).

Table 5. The maximum ventricular ejection and filling rates in survivors and non-survivors of CABG for ICMP (according to radioisotopic ventriculographic data)

Parameter	At Rest	Orthostatic	NG, 20 mg
CABG (n = 19)			
Survivors (n = 15)			
LV MER	147±0.16	165±0.30	166±0.22
RV MER	176±0.17	194±0.35	221±0.26*
LV MFR	108±0.9	133±0.20	130±0.21
RV MFR	132±0.17	148±0.27	139±0.14
Deceased (n=4)			
LV MER	209±0.25	199±0.39	183±0.11
RV MER	208±0.43	260±0.32	237±0.15
LV MFR	127±0.21	132±0.14	115±0.10
RV MFR	194±0.56	171±0.40	190±0.28

Designations: * difference significance ($p < 0.01$) is indicated as compared to the baseline value (recumbency) of the respective parameter; MER = maximum ejection rate; MFR = maximum filling rate; NG = nitroglycerin test.

of the RV in two of the four deceased. These data imply that foci of RV fibrosis play an important prognostic role. The relatively high resting RVEF may confuse investigators who do not perform functional testing. The responses of EF in both left and right ventricles to functional testing such as nitrates or orthostasis appear to be more accurate prognostic indicators than resting EF in patients with ICMP.

The assessment of LV function alone is rather difficult with the chamber dilatation that is associated with coronary disease and complicated by cardiac fibrosis. However, by concurrently evaluating RV function, we ascertained that a substantial reduction in RVEF in response to "unloading" functional tests is an important predictor of low cardiac output syndrome in the early post CABG period. At the same time increased RVEF in response to "unloading tests" suggests that the interventricular interac-

Table 6. Changes in ejection fraction (%) in patients with ICMP before and after CABG (according to radionuclide ventriculographic data)

Parameter	Before Revascularization	After Revascularization
CLV Ef, %		
At rest	27±4	29±4
Orthostatic	27±5	29±5
NG, 20 mg	30±3	34±5
RV Ef, %		
At rest	28±2	32±2
Orthostatic	30±4	39±3 ($p < 0.01$)
NG, 20 mg	4±3	38±5

Designations: At rest = lying; Orthostatic = sitting; EF = ejection fraction; LV = left ventricle; RV = right ventricle; NG = nitroglycerin test (20mg nitroglycerin sublingually).

Table 7. Changes in ventricular volumes in patients with ICMP before and after CABG (according to radioisotopic ventriculographic data)

Parameter	Before Revascularization	After Revascularization
LV EDV		
At rest	245±20	186±27 ($p < 0.01$)
Orthostatic	201±21 ($p < 0.05$)	195±22
NG, 20 mg	249±34	164±44 ($p < 0.05$)
RV EDV		
At rest	174±36	107±25 ($p < 0.05$)
Orthostatic	71±29	167±33
NG, 20 mg	172±33	113±17 ($p < 0.05$)
LV ESV		
At rest	186±18	128±19 ($p < 0.01$)
Orthostatic	131±27 ($p < 0.05$)	114±29
Ng, 20 mg	175±31	145±33
RV ESV		
At rest	125±33	73±15 ($p < 0.01$)
Orthostatic	131±29	103±29
NG, 20 mg	121±24	68±7 ($p < 0.01$)

Designations: EDV = end-diastolic volume; ESV = end-systolic volume; LV = left ventricle; RV = right ventricle; NG = nitroglycerin test.

tion is maintained (LV is capable of maintaining RV function or vice versa) and allows us to predict a positive benefit from myocardial revascularization.

Examination of Patients one Year After CABG

One year following CABG all patients were symptomatically improved with lower functional class. Radioisotopic ventriculography was performed in 10 of the 15 survivors at 12-44 months following revascularization. Resting LVEF increased from 26.8 to 35.3% (a 36% improvement) ($p < 0.001$). The reduction in LV volume immediately after surgery changed to an increase in the late postoperative period, with elevations in EF of both left and the right ventricles, and an increase in CO.

A tendency for increases in EDV and EDS in the late periods after CABG was found in most patients. Two groups of patients were identified: one group predominantly showed increases in EF of both the left and the right ventricles; the other exhibited larger right ventricular volumes. All the patients had increased CO. In this case, the smaller the LV volume and size increases, the more LVEF rises.

The results of our follow-up studies indicate that clinical improvement rises in the biventricular minute volume and EF in patients with ICMP within the first year after myocardial revascularization. This is accompanied by a reduction in the ventricular cavities in the early postoperative period. However, just three or six months later there was ventricular dilatation during adaptation to increasing exercise. At the same time the clinical signs of heart failure were virtually absent.

Before surgery, 7 ± 1 LV segments and 6 ± 2 RV segments were hypokinetic in recumbency, 3 ± 1 LV segments recovered their function in response to orthostatic testing, and the same number recovered function in response to NG in the other four patients. In the RV, 2 ± 1 segments recovered their function in response to orthostatic testing in four patients and the same number recovered function in response to NG in three patients.

Seven to 14 days after revascularization, 100% and 80% of the segments which had earlier recovered their function in response to orthostatic and NG, respectively, functioned at resting (see Figure 4a Ⓢ).

After 12 months, an examination of 12 patients revealed an additional recovery of RV function (at least three segments) in 8 of 10 examinees, and of the left ventricle in one patient (see Figure 4b Ⓢ).

These findings indicate: 1) the sublingual use of nitroglycerin may reveal the areas of the viable myocardium at 85% sensitivity and 95% sensitivity, 2) the regional function of the myocardium may continue to recover within a year after its revascularization, and 3) more commonly the LV recovers regional movement amplitude of its myocardium before the RV.

Cardiac Transplantation

One patient died in the early postoperative period. The cause of death was progressive global heart failure in the presence of sepsis with the development of the disseminated intravascular coagulation syndrome and shock lung syndrome. The specific features of the early postoperative period are presented in Table 8 (Ⓢ).

After surgery, all patients had triple immunosuppressive therapy. At year two following HT, one patient of the four survivors was diagnosed as having acute graft rejection successfully treated with steroid pulse therapy. After HT, no patient had clinical signs of circulatory insufficiency or angina pectoris.

DISCUSSION

The diagnosis of ICMP is made on the basis of clinical findings and investigations which reveal multiple coronary lesions, diffuse cardiac fibrosis, secondary cardiac dilatation, decreased myocardial contractility, hemodynamic impairment, and symptoms of congestive heart failure. The characteristic morphological findings of ICMP are biventricular dilatation, (unassociated with aneurysm), increased total cardiac mass associated with thinning of the left ventricular wall, and severe coronary atherosclerotic lesions.

The quality of life for medically treated patients with ICMP is poor and rapidly decreases over time with discouraging long term survival. In our study, we found significant improvement in symptoms and survival for appropriately selected patients who underwent CABG for ICMP. Late survival (at 3 years) following CABG was excellent, with 78% of patients still alive. In addition, most patients improved from NYHA Class III or IV heart failure up to functional classes I and II. Most patients were able to elim-

Table 8. The Specific Features of the Early Postoperative Period in ICMP Patients Undergoing Heart Transplantation

Patient	Complications	Outcome	Follow-up duration
1. Pt. S.	Respiratory failure. Persistent sinus nodal dysfunction. Permanent pacemaker was implanted for 28 days.	Discharged	> 4 years
2. Pt. K.	Transient sinus nodal dysfunction for 14 days.	Discharged	> 3 year
3. Pt. A.	Pericardial effusion. Single myocardial puncture.	Discharged	> 2 year
4. Pt. Kh.	Persistent sinus nodal dysfunction. Permanent pacemaker was implanted for 13 days.	Discharged	> 1 year
5. Pt. N	Sepsis	Died after 7 days	

inate or significantly reduce the need for antianginal and heart failure medications. The exception was one patient who continued to be dependent on maintenance therapy with diuretics despite a successful CABG. The medically treated cohort in our study continued to experience more congestive heart failure than those having undergone coronary artery bypass surgery.

Orthotopic transplantation results in steady-state normalization of all hemodynamic parameters and substantially enhances the quality of life. However, the limitation in number of donor hearts makes this therapy less available than conventional revascularization. Thus, our group studied a series of preoperative variables that could potentially assist in selecting ICMP patients for CABG rather than transplantation. Our aim was to identify patients who would benefit and who could undergo CABG at a reasonable perioperative risk.

Myocardial function in patients with ICMP is characterized by marked left ventricular systolic impairment and, as a result, a greater role of the right ventricle in maintaining cardiac pump function. In these patients, interventricular relationships (the capacity of the right ventricle to maintain the function of the left or vice versa) are predominantly affected in diastole, so that functional tests that reduce inflow to the heart (unloading tests) may assess the reserve capacities of the myocardium as a whole as well as each ventricle in particular. At the same time unloading tests are safer and simpler than loading (exercise) tests.

We evaluated numerous preoperative hemodynamic, angiographic, and ventricular functional parameters in an attempt to identify those patients with ICMP who would survive CABG for ICMP. We sought evidence of myocardial viability which could be used to predict functional improvement after revascularization. Our data concluded that indicators of right ventricular performance were the

most important predictors of perioperative mortality. Indicators of left ventricular viability or function did not appear to demonstrate statistically significant differences between survivors and non-survivors in this study. As for benefit, revascularization did improve resting end-systolic and end-diastolic volumes of both ventricles, with more pronounced improvement seen with unloading tests (see Table 9).

Our conclusions agree with several other authors [Polak 1997, Cherrier 1998] in regards to the importance of resting right ventricular ejection fraction as a prognostic indicator in patients with congestive heart failure and CAD. When there is profound LV systolic dysfunction, the parameters of RV function are more dynamic than those of the LV and they enable the degree of myocardial dysfunction to be more accurately evaluated. The function of the right ventricle should be studied in all patients with ICMP. We must also emphasize the need for assessing RV reserves using orthostatic and nitroglycerin testing in order to more accurately define surgical perioperative risk and thereby contribute to the appropriate decision for revascularization versus transplantation. Our data indicates that RV functional assessment with and without unloading is a predictor of survival after CABG for ICMP and assists in case selection.

In conclusion, the indications for CABG in patients with ICMP at our institution are: 1) suitable coronary target vessels, 2) congestive heart failure that is responsive to medical therapy, 3) severe angina pectoris, 4) LV end-diastolic size no more than 7.5 cm, 5) cardiac index no lower than 2 liter/min/m², and 6) satisfactory resting RV function and an adequate response to unloading functional tests.

The indications for heart transplantation in patients with ICMP at our institution are: 1) the technical impossibility of coronary grafting (inoperable lesions), 2) circulatory insufficiency refractory to drug therapy, 3) end-diastolic LV diameter over 7.5 cm, 4) cardiac index less than 2 liter/min/m², and 5) poor resting RV function and an inadequate ventricular response to unloading functional tests.

Table 9. Dimensions of Cardiac Cavities and Ejection Fraction in Patients with ICMP (according to EchoCG data)

LVEDD, cm	7.35 ± 0.4
LVEF, %	22.9 ± 2.2
LVEDV, ml	284.5 ± 27.5

Designations: EchoCG = echocardiography; LVEDD = end-diastolic size of the left ventricle; LVEF = ejection fraction of the left ventricle; LVEDV = end-diastolic volume of the left ventricle.

REFERENCES

1. Anversa P, Sonnenblick EH. Ischemic cardiomyopathy: pathophysiologic mechanisms. *J Prog Cardiovasc Dis* 23:49-70, 1990.
2. Anversa P, Kajstura J, Reiss K, et al. Ischemic cardiomyopa-

- thy: myocyte cell loss, myocyte cellular hypertrophy, and myocyte cellular hyperplasia. *J Ann NY Acad Sci* 752:47–64, 1995.
3. Beltrami CA, Finato N, Rocco M, et al. Structural basis of end-stage failure in ischemic cardiomyopathy in humans. *Circulation* 89:151–63, 1994.
4. Burch GE, Gills TD, Colcough HL. Ischemic cardiomyopathy. *Amer Heart J* 79: 291–3, 1994.
5. Burch GE, Giles TD. Ischemic cardiomyopathy: diagnostic, pathologic and theoretical consideration. *Cardiovascular clinics – Philadelphia: FA Davis Co.* 4:203–19, 1972.
6. Burch GE, Harb JM. Ischemic cardiomyopathy. *Amer Heart J* 83:340–50, 1972.
7. Di Donato M, Maoili M, Sabatier M. End-stage ischemic heart disease: effect of complete myocardial revascularization and left ventricular path repair following scar resection. *Mechanisms of heart failure.* Kluwer Academic Publisher: 369–75, 1995.
8. Hare JM, Walford GD, Hruban RH, et al. Ischemic cardiomyopathy: endomyocardial biopsy and ventriculographic evaluation of patients with congestive heart failure, dilated cardiomyopathy and coronary artery disease. *J Amer Coll Cardiol.* 20:1318–25, 1992.
9. Helfant RI, Pine R, Meister SG, et al. Nitroglycerin to unmask reversible asynergy: Correlation with postcoronary bypass ventriculography. *Circulation*: 50:108–13, 1974.
10. Iscandrian AS, Helfeld H, Lemlek J, et al. Differentiation between primary dilated cardiomyopathy and ischemic cardiomyopathy based on right ventricular performance. *Amer Heart J* 123: 768–73, 1972.
11. Polak JF, Holman BL, Wynne J, Colucci WS. Right ventricular ejection fraction: an indicator of increased mortality in patients with congestive heart failure associated with coronary artery disease. *JACC* 2:217–24, 1983.
12. Shumakov VI, Kazakov EN, Gureev SV, et al. Additional criteria for selection patients with ischemic cardiomyopathy for aortocoronary bypass grafting or heart transplantation. *J Heart Failure* 5:525–526, 1998.