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Coronary Artery Bypass Graft Surgery in Patients with Ischemic Cardiomyopathy and Severe Left Ventricular Dysfunction: Short and Long-Term Results

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ABSTRACT

Background: We evaluated the prognostic value of preoperative parameters, surgical risk, functional benefits and long-term survival after myocardial revascularization in patients with established ischemic cardiomyopathy.

Methods: Seventy-one patients with ischemic cardiomyopathy, severe left ventricular dysfunction (left ventricular ejection fraction < 30%), and myocardial perfusion evaluated by Thallium-201 scintigraphy, were studied before and after myocardial revascularization, during hospitalization and throughout 48 months (average) of late follow-up.

Results: The early postoperative mortality was 2.8% and the five-year survival rate was 62.8%. When the survival rate was studied, there was no correlation with 1) the presence of Q-waves on preoperative cardiogram, 2) the presence of ischemia on Tl-201 scintigraphy, 3) the degree of left ventricular ejection fraction, or 4) the presence of angina. There was a statistically significant difference for survivors and non-survivors in the following parameters: 1) functional class IV of CHF, and 2) the presence of left bundle-branch block (LBBB).

Conclusions: Our surgical results confirm that myocardial revascularization is a safe procedure, and that it increases late survival and improves the quality of life in patients with ischemic cardiomyopathy and severe left ventricular dysfunction. We also observed that due to heterogeneous coronary and myocardial patterns of ischemic cardiomyopathy, preoperative prognostic parameters are difficult to establish. Preoperative functional class IV congestive heart failure, and LBBB were the main predictors of poor outcome following surgical revascularization for ischemic cardiomyopathy.

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INTRODUCTION

Ischemic cardiomyopathy was reported by Burch et al in 1970 after observing the presence of coronary artery disease in the anatomicopathological findings of patients with dilated cardiomyopathy [Burch 1970]. Studies on the etiology of congestive heart failure (CHF) show a significant presence of coronary artery disease [McKee 1971, Cohn 1991, Yusuf 1992]. The clinical course of ischemic cardiomyopathy has been shown to be unfavorable with a lower survival rate when compared to other types of cardiomyopathies [Franciosa 1983].

A number of studies have shown favorable results from surgical revasularzation when compared to continual medical therapy [Yatteau 1974, Manley 1976, Faulkner 1977, Hellman 1980, Alderman 1983, Hochberg 1983, Mochtar 1985, Passamani 1985, Pigott 1985, Fox 1986, Bonous 1988, Kron 1989, Wechsler 1989, Louie 1991, Christakis 1992, Elefteriades 1993, Luciani 1993, Oliveira 1993, Mickleborough 1995, Kaul 1996]. Encouraging results following coronary artery bypass grafting (CABG) reported by these authors emphasize the need for early diagnosis. Hibernating or stunned myocardium may be responsible in part for the contractile dysfunction which recovers after myocardial reperfusion [Braunwald 1986, Kloner 1989, Rahimtoola 1989, Bolli 1992].

However, the criteria for surgical indication, surgical risk, functional benefits and late follow-up of these patients remain uncertain. This study is aimed at assessing these parameters in patients undergoing coronary artery bypass surgery for coronary artery disease associated with severe left ventricular dysfunction.

MATERIALS

Inclusion and Exclusion criteria

The intent of this study was to document the early and late outcome of surgically revascularized ischemic cardiomyopathy. Patients were identified as having ischemic cardiomyopathy and included in the study if they demonstrated the following criteria during preoperative evaluation:

1) Chronic coronary artery disease with CHF and/or angina

2) Left ventricular (LV) ejection fraction (EF) less than 30% by contrast ventriculography

3) Coronary artery stenosis of at least 70% or greater in one or more major coronary vessels

4) Heterogeneous distribution on myocardial perfusion scintigraphy with Thallium-201 following dipyridamole infusion.

The following additional criteria were outside the scope of this study and were used to exclude patients from analysis, including co-morbid conditions, which would limit the ability to determine the long-term outcome of revascularization:

1) Previous coronary artery bypass grafting i.e. "redo"
2) Left ventricular aneurysm
3) Moderate to severe mitral insufficiency
4) No major coronary stenosis greater than 70%
5) Chronic renal failure
6) Hepatic insufficiency
7) Neoplastic diseases
8) Severe obstructive pulmonary disease

Seventy-one consecutive patients with a diagnosis of ischemic cardiomyopathy were prospectively studied. Sixty-two of them were male with a mean age of 58 years (ranging from 48 to 70 years). All patients were classified according to the NYHA and the Canadian Heart Association functional classes for CHF and angina, respectively.

Electrocardiographic Evaluation

The electrocardiographic pattern was evaluated in 12 leads, recorded at 25 mm/sec. The presence of Q-wave interval > 0.04 sec, Q-wave amplitude of 20% of the following R wave, the presence of right or left bundle-branch block, atrioventricular conduction disorders, presence of atrial fibrillation, and alterations of ST-T ventricular repolarization were assessed and categorized.

Coronary Cineangiography and Hemodynamic Evaluation

Sones' method for coronary cineangiography was used and performed by Phillips angiography equipment with injection of contrast media in multiple projections. Ventriculography was captured in 30° right anterior oblique (RAO) projections beginning preoperatively and repeated again between postoperative days 10 and 14. Left ventricular end-diastolic blood pressure values, aortic pressure tracings, and heart rate were obtained before ventriculography. The method of area length was used to evaluate global EF and Chatterjee's method was used to determine the regional EF [Chatterjee 1973]. Ventricular volume was calculated by Dodge's method using the theory of error dissemination [Dodge 1960].

Scintigraphic Evaluation

Thallium-201 scintigraphy was carried out immediately after and four hours after the infusion of intravenous dipyridamole at 0.5 mg/kg followed by an injection of Tl-201 74 Mbq. This was accomplished both preoperatively and between postoperative days 10 and 14 for most of the patients. The images were obtained from left anterior oblique (LAO) 40°, LAO 60° planar visualization, and anterior visualization in gamma-chamber model Ohio Nuclear provided with DataSystem 150. Perfusion images were divided into septal, anterior, apical, inferior, lateral, and dorsal segments and were analyzed quantitatively.

Surgical Treatment

Coronary artery bypass grafting was carried out using cardiopulmonary bypass and myocardial protection with Saint-Thomas's cardioplegic solution or intermittent aorta clamping and hypothermia at 28°C. Intra- and postoperative hemodynamic monitoring was carried out with the aid of a Swan-Ganz catheter.

Evaluation and Follow-up

Immediate and late follow-up was carried out by the same observer through inpatient hospital visits, information from other medical centers, letters, or telephone calls to patients living in other cities or states. Mean follow-up time was 48 months up to a limit of 60 months. The patients were evaluated in the following areas: functional class for CHF or angina, EKG, chest x-ray, echocardiogram, and the mode of death (pump failure or sudden death).

Statistical Analysis

Diagnostic parameters were analyzed in regard to the actuarial survival rate by Kaplan-Meier's test (non-parametric test). The survival rates of patients were compared using log-rank statistics in the following areas: different CHF and angina functional classes, presence of Q waves in the EKG, presence of ischemia in Tl-201 scintigraphy, and EF. Fisher's exact test, Chi-squared test and Student's T-test were used for the comparative analysis of the preoperative prognostic parameters between surviving and non-surviving patients.

RESULTS

The clinical data shown in Table 1 (◎) demonstrate a predominance of male patients, a high incidence of tobacco addiction (76%), and a high incidence of previous

Table 1. Clinical Data

	N	%
Gender		
Male	62	87.3%
Female	9	12.6%
Age (years)	58	(48-70)
Risk Factors		
Diabetes	20	29%
Hypertension	23	33%
Tobacco	54	76%
Previous Infarct	45	64%
ECG		
Q-waves	53	75.7%
T-wave inversion	11	17%
Left bundle branch block	8	11.2%

myocardial infarction (64%). The electrocardiographic analysis revealed the frequent presence of Q waves (76%) along with left bundle-branch block (LBBB) with intraventricular conduction disorder in 11.2%. Right bundle-branch block, AV conduction disorders and atrial fibrillation were not observed in this series.

Dipyridamole thallium scintigraphy demonstrated three patterns of perfusion defects (see Table 2): 1) permanent low uptake (without redistribution) corresponding in most of the cases to the area of myocardial fibrosis, 2) significant transient low uptake (with redistribution) in the area with myocardial ischemia, and 3) permanent low uptake related to transient low uptake in segments with residual ischemic areas after a previous infarction. Our results showed transient low uptake alone or combined with permanent low uptake in 65.1% of myocardial perfusion in the evaluated patients. In 33.7% of the patients there was no redistribution, suggesting the presence of fibrosis. Due to marked pulmonary uptake in one patient, the redistribution images were considered to be inconclusive.

An improvement was seen in Tl-201 perfusion response following revascularization in 35% of the wall segments, and 61% maintained the initial pattern. Worsening of perfusion was observed in only 4%. An improvement in wall motion was observed in 61% of the segments, whereas motion was maintained in 18% and decreased in 21% of the segments (see Table 3).

A postoperative inversion was observed in New York Heart Association Functional Class for CHF (see Table 4).

Table 2. Perfusion Defects with Thallium-201 after Preoperative Dipyridamole Infusion in 71 Patients.

Thallium Defect	N	%
Permanent	24	33.7%
Transient	10	14.4%
Permanent and Transient	36	50.7%
Inconclusive	1	1.4%

Table 3. Regional Wall Motion and Perfusion Following CABG*

	Myocardial Perfusion** N (%)	Wall Motion Analysis*** N (%)
Improved	23 (35%)	40 (61%)
Unchanged	40 (61%)	14 (18%)
Worsened	3 (4%)	12 (21%)

*A total of 66 segments sampled in 22 Patients after Coronary Artery Bypass Grafting (3 Segments per Patient)
** Dipyridamole Thallium 201 Scintigraphhy
***Wall motion reported by Chatterjee's method

Of the 76.7% in preoperative NYHA Classes III and IV, only 17.5% continued in these classes postoperatively, and only three patients (4.5%) remained in Class IV. Of the 61.7% in NYHA Anginal Classes III and IV preoperatively, none continued in these classes postoperatively (see Table 4). Angina recurred in only seven patients (5%) during more intensive exercise. There was a statistically significant improvement in EF following revascularization from a mean of 19.2%, preoperatively, to a mean of 27.1%, postoperatively ($p<0.05$) (see Table 4). The hemodynamic response also showed a statistically significant improvement in left ventricular function with a reduction in LV end-diastolic pressure from a mean of 26.7 mmHg, preoperatively, to a mean of 18.5 mmHg, postoperatively ($p<0.01$). End-diastolic volume measurements remained unchanged.

Two deaths compromised a postoperative mortality of 2.8% (see Table 5). One patient died on postoperative day 7 due to atrial fibrillation with increased ventricular response (possibly due to left-chamber hypertension, which developed into ventricular fibrillation). Thallium

Table4. Alterations in the Clinical Classification of Congestive Heart Failure (CHF), Presence of Angina and Hemodynamic Data after Coronary Artery Bypass Grafting for Ischemic Cardiomyopathy

Parameter	Preoperative	Postoperative	P value
CHF (NYHA)			
I	4 (5.6%)	43 (62.3%)	
II	4 (5.6%)	14 (20.2%)	
III	26 (36.7%)	9 (13%)	
IV	37 (52.1%)	3 (4.6%)	
Angina			
I	28 (39.4%)	62 (95%)	
II	4 (5.6%)	7 (5%)	
III	8 (11.2%)	0 (0%)	
IV	31 (43.6%)	0 (0%)	
LV EDP (mmHg)	26.71±9.3	18.5±7.9	< 0.01
LV Ejection Fraction (%)	19.21±7.93	27.1±10.3	< 0.05
LV EDV (ml/m2)	59.1±25.7	65.1±20.9	NS
LV ESV (ml/m2)	39.4±19.1	38.1±12.5	NS

LV= left ventricle; EDP= end-diastolic pressure; EF = ejection fraction; EDV and ESV = end-diastolic and end-systolic volume.

Table 5. Early and Late Operative Mortality

Death	N	%
Early (< 30 days)	2	2.8%
Late	16	22.5%
Sudden Death	6	37.5%
CHF	8	50%
CVA*	2	12.5%

*CVA = Cerebrovascular accident (stroke)

scanning in this patient was inconclusive due to increased pulmonary uptake. The second death occurred on postoperative day 2 from low cardiac output. Late mortality was 7% per year. Of the 16 patients who died late, 37.5% had sudden death, 50% had low output, and 12.5% died from cerebrovascular accidents.

The comparison between survivors and non-survivors shows a greater number of cases in CHF Class IV (p= 0.004), and greater incidence of LBBB (p=0.015) among non-survivors (see Table 6).

When the survival rate of the patients undergoing CABG was analyzed with regards to preoperative prognostic factors, there was no correlation with:

1) the presence of Q waves on the preoperative EKG (even though the curve shows a trend towards greater survival in the group with no Q waves (see Figure 1),

2) the presence of ischemia in Tl-201 scintigraphy, even though the curve shows a trend towards greater survival in the group with objective ischemia (see Figure 2),

3) the severity of CHF (even though the curve shows a trend towards greater survival in Functional Classes I and II (see Figure 3),

4) the severity of angina (see Figure 4), or

5) the severity of LV ejection fraction (see Figure 5).

Table 6. Preoperative Comparative Parameters Between Survivors and Non-Survivors

	Survivors	Non-Survivors	P
Gender			
Male	50	13	
Female	5	3	
Age	60	59.4	
Number Vessels			
Single Vessel	1 (1.8%)	0	
Double Vessel	6 (10.9%)	3 (5.4%)	.0572*
Triple Vessel	48 (87.2%)	14 (87%)	
Thallium Scan			
Permanent Defect	8 (15.2%)	6 (33.4%)	
Transient	16 (30.1%)	4 (22.2%)	
Permanent + Transient 29	(54.7%)	7 (38.8%)	0.941**
Inconclusive	0 (0%)	1(5.6%)	
Anginal Class			
I	25 (45.4%)	5 (31.2%)	
II	3 (5.4%)	1 (6.2%)	0.454*
III	4 (7.2%)	3 (18.7%)	
IV	23 (41.8%)	7 (43.7%)	
CHF Class			
I	17 (30.9%)	0 (0%)	
II	4 (7.2%)	0 (0%)	
III	16 (29%)	4 (25%)	0.004*
IV	18 (32.7%)	13 (81.2%)	
LV Ejection Fraction (%)	19.91±7.19	17.12±9.76	0.227***
LV EDP (mmHg)	27±9.05	26.06±10.1	0.735***
LV EDV (ml)	303±133.31	313±55.09	0.870***
ECG criteria			
Q-waves	42 (76.3%)	11 (68.8%)	0.359*
Left bundle branch block 3	(5.4%)	5 (31.2%)	0.015*

* Fisher's exact test

** Chi-squared test

*** Student's t-test

DISCUSSION

The Framingham study [McKee 1971] showed that 46% of men and 27% of women with congestive heart failure had evidence of coronary artery disease, suggesting a greater role of hypertension in the etiology of myocardial dysfunction. The SOLVD [Yusuf 1992] and VHeFT-II studies [Cohn 1991] showed this association in 71% and 53% of their studied patients, respectively, suggesting a more important role of coronary artery disease in cardiomyopathy.

Franciosa et al. compared the survival rates of patients with ischemic cardiomyopathy and those with dilated cardiomyopathy, and observed a lower survival rate in the group with ischemic etiology (54% vs. 77% at one year, and 31% vs. 52% at two years) [Franciosa 1983].

Louie et al found a three-year survival rate of less than 25% in patients with a mean EF of 22% [Louie 1991]. Luciani et al showed a five-year survival rate of 28% in patients with a mean EF of 21% [Luciani 1993]. These studies show a worsening of the prognosis in patients with very low ventricular function.

Signs and symptoms of isolated congestive heart failure differed in several studies [Yatteau 1974, Manley 1976, Faulkner 1977, Hellman 1980, Alderman 1983, Hochberg 1983, Mochtar 1985, Passamani 1985, Pigott 1985, Fox 1986, Bonous 1988, Kron 1989, Wechsler 1989, Louie 1991, Christakis 1992, Elefteriades 1993, Luciani 1993, Oliveira 1993, Mickleborough 1995, Kaul 1996], ranging from 6% to 52%. When combined with angina they ranged from 24% to 41%, and to isolated angina from 49% to 100%. In our study, the incidence of Functional Class III and IV CHF was 61.6% and the incidence of angina was 54.4%, which is similar to reports in literature.

Tl-201 myocardial perfusion imaging may indicate the presence of a viable myocardium, since it depends on adequate perfusion, cellular integrity and metabolic function [Rozansky 1981, Iskandrian 1983]. It was observed that scintigraphy carried out after dipyridamole infusion shows similar results to that obtained after exercise, and may be used in patients who cannot undergo physical stress [Eichorn 1988].

A Tl-201 perfusion pattern associated with isolated ischemia or ischemia combined with necrosis was present

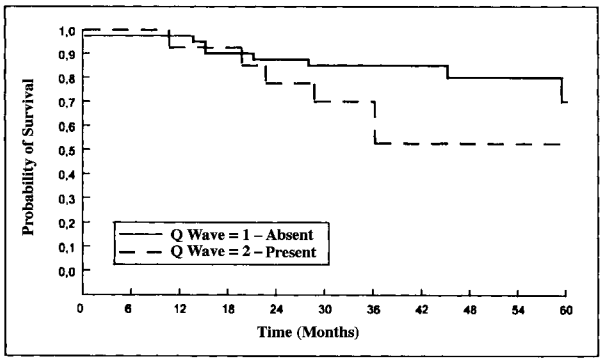


Figure 1. Survival Rate in Relation to Q Wave in EKG

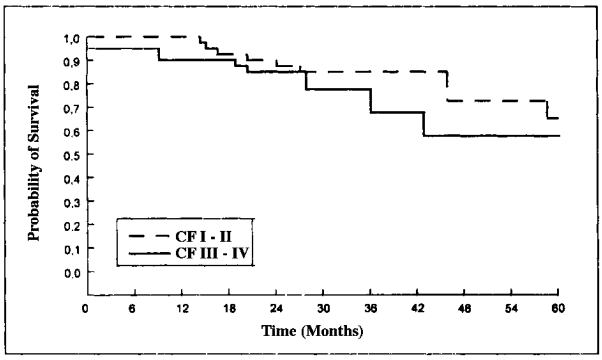


Figure 3. Survival in Late Follow-up of Coronary Artery Bypass Grafting According to CHF Functional Class

in 65.1% of the patients, whereas no redistribution was present in 33.7%. These results are similar to those in the literature and indicate the test's ability to detect ischemia of approximately 70%. In the presence of heart failure, there may be coronary flow redistribution with a decrease in endocardial perfusion due to greater tension of the ventricular wall. This may damage the redistribution of the Tl-201 marker and attenuate the action of dipyridamole. Tl-201 imaging does not distinguish the perfusion phases and the marker uptake by the cells and may not identify those with deficient perfusion, which are still metabolically active and are only evidenced by positron emission tomography (PET) [Dilsizian 1993, Di Carli 1994]. The heterogeneous pattern of myocardial perfusion found in our patients suggests the coexistence of normal, ischemic (stunned or hibernating), and fibrotic (necrosis or myofibrillar degeneration) myocardial areas [Flameng 1981].

Left ventricular ejection fraction can be influenced by the methodology used, the patient's hemodynamic status (increased left ventricular end-diastolic pressure (LVEDP)) and adrenergic condition. We observed mean values of 20.3 ±9.2, measured by planar contrast angiography in the right anterior oblique projection. The non-visualization of the lateral wall and increased LVEDP values (26.2±8.1) might, in some cases, hinder the evaluation of the cardiac function. Optimal ventriculography in severe myocardial dysfunction should be carried out with end-diastolic pressure in the optimal point of Starling's curve, approximately 18 mmHg.

Improvement in wall motion was observed in 61% of the cases after myocardial revascularization. Myocardial perfusion was improved in 35% of cases. This difference might result from several factors, such as the adrenergic influence that may stimulate the stunned myocardium which does not uptake Tl-201 (61%), or the technical difficulties in evaluating the perfusion of segments studied in left anterior oblique, anteroposterior, and lateral visualizations. It is likely that the early contractile response to myocardial reperfusion results from the presence of hibernating myocardium and the late response is related to stunned myocardium after extracorporeal circulation.

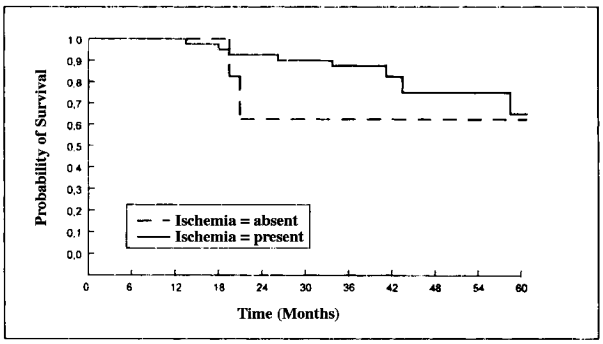
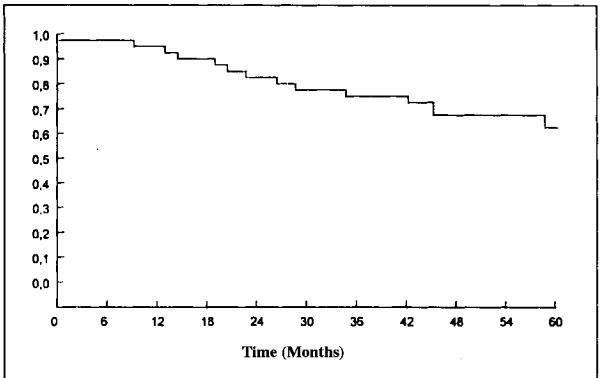


Figure 2. Survival Rate of Ischemia Recorded by Tl-201 Perfusion



Time (Months)	Survival	Deaths	Survival Standard Error
45	0.6981	0.3019	±0.0771
59	0.6283	0.3717	±0.0959

Total of Late Follow-up Cases = 69 (2 Deaths During the Hospital Phase)

Figure 4.Survival Rate (Kaplan-Meier's Method) of 71 Patients with Ischemic Cardiomyopathy Undergoing Coronary Artery Bypass Graft Surgery

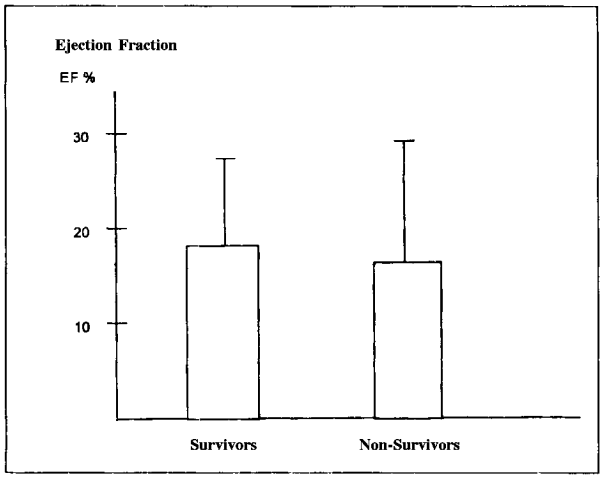


Figure 5.Standard Mean Deviation of Preoperative LV Ejection Fraction in Groups of Survivors and Non-Survivors

The significant improvement in global ejection fraction, the decrease in LV end-diastolic pressure, and the trend towards increased end-diastolic volume suggest improvement of LV compliance. This hemodynamic response is translated in clinical improvement as regression of signs and symptoms of CHF and angina (see Table 4). Of the 52.1% of patients in functional class IV preoperatively, only 4.5% remained in this class after myocardial revascularization. Of the patients in anginal class II, III and IV preoperatively (60.4%), only 5% remained in anginal class II, showing treatment efficacy of surgical revascularization in controlling symptoms and improving the quality of life in ischemic cardiomyopathy.

The reported immediate surgical risk of 2.8% is in agreement with a recently studied series ranging from 1.3% to 8.4%, corroborating the safety of the procedure in patients with stable clinical conditions despite severe ventricular dysfunction [Manley 1976, Mochtar 1985, Kron 1989, Louie 1991, Elefteriades 1993, Luciani 1993, Mickleborough 1995, Kaul 1996].

We observed a five-year survival rate of 62% which is similar to that observed in other studies: a three-year survival rate of 67% [Mochtar 1985], three-year survival rate of 73% [Kron 1989], three-year survival rate of 80% [Elefteriades 1993] and a five-year survival rate of 68% [Mickleborough 1995]. These data suggest a trend towards decreased survival after the third postoperative year. Sudden death was reported in 37.5% of the cases, probably due to the presence of arrhythmias and death due to pump failure in 50%.

When preoperative characteristics of the non-survivors were analyzed, there was a statistically significant difference in the presence of functional class IV CHF and left bundle-branch block. These findings proved to be predictive of a worsened late prognosis. Our findings regarding the prognostic value of functional class IV CHF is similar to those previously published. However, there are no reports in previous series on the prognostic values of LBBB.

We also found a slight trend toward greater survival in the following groups (although not statistically significant): 1) those without Q waves in the preoperative EKG; 2) those with ischemia on Thallium scanning, 3) those with a less compromised LV ejection fraction; and, 4) those in CHF functional classes I-II. If the hemodynamic and methodologic influences are minimized it is likely that LV ejection fraction measurement becomes more important in establishing late prognosis.

In conclusion, the presence of functional class IV congestive heart failure and left bundle-branch block were related to a worsened prognosis and late survival in patients undergoing coronary artery bypass graft surgery for established ischemic cardiomyopathy. Since the cause of death is multifactorial and ischemic cardiomyopathy has heterogeneous myocardial and arterial patterns, the prognostic influence of coronary artery bypass surgery are difficult to establish. However, the importance of the surgery in the treatment of ischemic cardiomyopathy is undeniable as it improves survival rates and quality of life in the group as a whole.

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