

# Coronary artery bypass grafting using both internal mammary arteries in patients with diabetes mellitus

*Revascularização do miocárdio com emprego de ambas artérias mamárias internas em pacientes com diabetes mellitus*

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## Abstract

**Objective:** We sought to describe the use of both internal thoracic arteries (ITA) in patients with diabetes mellitus (DM) submitted to a coronary artery bypass grafting (CABG).

**Method:** Between January 1995 to August 2005, 4,569 patients received isolated CABG in our institution. Of the initial population, 1,298 had DM. The median age of the patients was 62 years and total mortality rate was 2.18% (100 patients). Both internal thoracic arteries were used in 700 patients. Patients were divided into two groups: with DM (group I, 148 patients), and without DM (group II, 552 patients). Patient selection for double ITA grafting was based on coronary artery anatomy and on the quality of sternum. The later was evaluated during the sternal transection. When these two factors were considered favorable, we have both ITAs dissected, regardless whether the patient had DM. During the dissection of both internal thoracic arteries, one must take care not to open the pleural spaces.

**Results:** There was a small difference between the two groups in terms of morbidity and mortality.

**Conclusion:** Our data suggests that patients with DM can benefit with the efficient use of both internal thoracic arteries with a small increase in the risk of complications, if its application is carefully indicated.

**Descriptors:** Myocardial revascularization. Mammary arteries. Internal mammary-coronary artery anastomosis. Diabetes mellitus

## Resumo

**Objetivo:** Descrever a utilização de ambas artérias mamárias internas (MIs) em pacientes submetidos à operação de revascularização do miocárdio (RM), que sejam portadores de diabetes mellitus (DM).

**Método:** No período compreendido entre janeiro de 1995 e agosto de 2005, 4.569 pacientes foram submetidos a RM

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em nossa instituição, sendo que 1.298 eram portadores de DM. A média de idade era de 62 anos, e a mortalidade global foi de 2,18% (100 pacientes). Ambas MIs foram empregadas em 700 pacientes, que foram divididos em dois grupos, portadores de DM (grupo I, com 148 pacientes) e não portadores de DM (grupo II, 552 pacientes). A seleção de pacientes para utilizar estes enxertos foi baseada nas características angiográficas das artérias coronárias e qualidade do esterno quando de sua transsecção. Quando ambos fatores eram considerados favoráveis, foram dissecadas ambas MIs, independente de o paciente ser portador ou não de DM. Durante a dissecação dos enxertos

arteriais, tomava-se o cuidado de procurar manter as cavidades pleurais fechadas.

**Resultados:** Houve pouca variação entre os grupos de pacientes no tocante a morbidade e mortalidade.

**Conclusão:** Nossos dados sugerem que pacientes portadores de DM podem se beneficiar do uso de ambas artérias MIs, com pouco acréscimo de risco quando sua aplicação for adequadamente indicada.

**Descritores:** Revascularização miocárdica. Artéria torácica interna. Anastomose de artéria torácica interna-coronária. Diabetes mellitus.

## INTRODUCTION

Diabetes Mellitus (DM) affects roughly 100 million people worldwide, and it is an important factor of mortality. DM increases by 2–4 fold the risk of coronary artery disease. The prevalence among patients submitted to myocardial revascularization ranges from 12–30%. DM is a predictor of poor prognosis after myocardial infarction, congestive heart failure, and in all modes of myocardial revascularization, whether percutaneous or surgical [1]. In spite of having had improvements in the primary and secondary prevention that led to decreased cardiovascular mortality rate in the general population, there is lower influence in diabetics who present higher cardiovascular mortality rate [2,3]. The use of the left internal thoracic artery (LITA) as graft in the myocardial revascularization surgery is a very well-known procedure, once the long-term patency with the following associated clinical benefits is well-documented. The left internal thoracic artery is considered the gold standard to be implanted in noble areas, especially into the anteroseptal wall of heart, frequently anastomosed to anterior interventricular branch [4]. Its use in diabetic patients is a predictor factor independently of the increase in patients' survival [5].

There are records in the current literature that suggest the two internal thoracic arteries graft are yet more beneficial than just one, in a 10-year-follow-up [6, 7], what seems to be particularly important in diabetic patients. Greater benefits have been shown with the myocardial infarction surgery, not only in terms of survival but also symptomatic relief and event-free reintervention [8]. It is believed that myocardial revascularization with the use of exclusive arterial graft is a valuable resource in order to extend this benefit.

In spite of the use of the right internal thoracic artery have been an object of debate by presenting historically contradicting outcomes regarding the left internal thoracic artery and of its routine application (lower than 4% of the myocardial revascularization cases), recently studies have shown higher rates of late permeability of right internal

thoracic artery grafts with lower incidence of long-term reinterventions in comparison with venous grafts suggesting an advantage of survival. Such a benefit seems more evident in young patients, but it cannot be ruled out that those other groups of less favorable prognostic can get advantages of this surgical strategy [9]. DM is long recognized as an important risk factor for infection and dehiscence of surgical wound [10]; therefore, there is a special concern with diabetic patients.

Based on previous publications, there is an inference that bilateral internal thoracic artery grafting may be contraindicated in diabetic patients. The reasons include the belief that this strategy is associated with high rates of deep sternal wound infection with consequent mediastinitis, sepsis, and death [11], besides the consumed additional operative time required for the second internal thoracic artery dissection, all make many surgeons believe that it is an unnecessary risk to dissect both internal thoracic arteries in these patients.

Lev-Ran et al. [12] have shown that bilateral internal thoracic artery grafts to branches of left coronary artery confers improved long-term survival and event-free survival in oral-treated diabetics. However, they also have suggested that the use of bilateral internal thoracic artery grafts in patients with type 2 DM, who require the use of insulin, can result in surgical wound major complications. These data are not support by the literature [13].

Although doubts persist, improvement techniques have been incorporated such as skeletonization of internal thoracic artery [14, 15], reinforced sternal synthesis methods, and continuous intravenous insulin infusion [16, 18] may have a positive impact in reducing the incidence of deep sternal wound infection complications. The use of artificial composite Y-graft or T-graft can increase the number of coronary arteries treated with arteries would tend to maximize the long-term benefits. Diabetic patients have a better evolution after myocardial revascularization than after angioplasty. This benefit is largely secondary to the use of internal thoracic artery grafts [8, 18]. The use of

multiple arterial grafts seems to be favorable in these patients [19]. There is recent evidence showing that bilateral internal thoracic artery grafts provide benefits to the long-term survival, although there are no randomized studies to support such findings [20].

**METHODS**

A retrospective analysis of the patients underwent isolated myocardial revascularization surgery in our service was performed from January 1995 to August 2005. Of the 4,569 procedures performed, 700 patients who have bilateral internal thoracic arteries dissected were enrolled in the study. This sample was divided into two groups: group I consisted of DM patients (n = 148); group II, gathered the non-DM patients (n = 552). An analysis of both groups was performed in terms of characteristics, occurrence of postoperative complications, and in-hospital mortality (Figure 1).

The selection of the patients was carried out in the intraoperative by combining two factors: coronary anatomy and quality of the sternum. The coronary anatomy was considered favorable in the presence of there an artery with an adequate caliber in the lateral wall of the left ventricle with a significant lesion (e" 70%). Such a vessel was chosen to receive the right internal thoracic artery. Once dissected, the artery was taken to the selected coronary artery by retroaortic route through the transverse sinus; the second factor, the quality of the sternum, evaluated during its transection. The use of the right internal thoracic artery was ruled out in the presence of significant osteoporosis. During the grafting dissections all the precautions were taken in order to preserve the pleural cavities.

All surgeries were performed using extracorporeal circulation, under moderate hypothermia (32°C), using an intermittent aortic clamping as a method of myocardial protection. The aorta remained clamped as far as it was necessary to perform each anastomosis being followed by a reperfusion period of nearly 2 minutes after each period of ischemia. Once the anastomoses have been completed, rewarm, stabilization of the hemodynamic conditions, removal of extracorporeal circulation (CPB), and heparin reversal with adequate doses of protamine were performed. The sternum was closed with the supply of steel staples (Sternum-Band® – Ethicon) in the presence of osteoporosis or if the patient was significantly obese (Body Mass Index > 32); otherwise 8 stainless steel wires for sternal symphysis were used. The closure of the subcutaneous tissue and the skin were performed in the normal manner.

**RESULTS**

The initial sample was composed of 4,569 patients whose demographic characteristics are shown in Table 1.

Table 1. Demographic characteristics of the baseline sample.

Variable	N = 4,569
Mean age (variance, SD)	62 a (20-94 ±10.22)
Male	959 (21%)
SHA	2,970 (65%)
Preoperative MI	1,599 (35%)
Smoking	1,828 (40%)
Mean number of grafts	3.3
Previous MR	548 (12%)
Mortality	100 (2.2%)

SAH - Systemic arterial Hypertension, MI – acute myocardial infarction, MR – myocardial revascularization

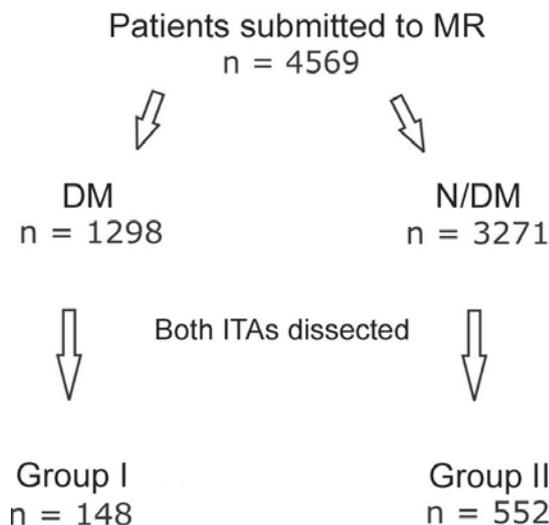


Fig. 1. Sample details. MR – myocardial revascularization, DM – diabetic, N/DM – non-diabetic, ITAs – internal thoracic arteries

**Morbidity and Mortality**

Regarding the diabetic and non-diabetic patients without distinction of bilateral versus single internal thoracic artery grafting, there was a slightly advantage to the non-diabetic patient with respect to mortality; however, there was no statistical significance; the number of vessels treated was similar in both groups (Table 2).

The sample of 700 patients with bilateral internal thoracic artery grafting is detailed in Table 3. One can note that the diabetic patients had a higher incidence of congestive heart failure (CHF) with a significant difference regarding the functional class and the left ventricle contractility dysfunction.

The non-diabetic group had a higher number of smoking patients and the diabetic group has a greater proportion of obese patients.

Table 2. Mean number of grafts and mortality of the baseline sample regarding the presence of diabetes mellitus DM. \*  $\chi^2 = 3,129$ ;  $p = 0.077$

DM	n	Mean n° of grafts	Mortality (%)
No	3,271	3.4	63 (1.92) *
Yes	1,298	3.2	37 (2.85) *
Total	4,569	3.3	100 (2.2)

Table 3. Sample of 700 patients with the use of both internal thoracic arteries

Variable	Group I n = 148	Group II n = 552	p
Mean age (variance, SD)	57.3 anos (20-83±9.49)	53.9 anos (31-79±8.43)	NS
Male	113	508	NS
Emergency surgery	2	13	NS
SAH	88	330	NS
CCS 3-4	35	158	NS
NHYA 3-4	21	26	0.000 *
Preoperative MI	47	201	NS
LVEF ~30%	3	12	NS
LVEF30%-50%	34	73	0.020 **
Creatinine ≥ 1.5 mg/dl	4	7	NS
Smoking	40	277	0.002 +
IMC > 32	22	47	0.058 +
Previous MR	3	12	NS
Mean number of grafts	3.4	3.5	NS

SAH – systemic arterial hypertension, CCS - Canadian Cardiology Society, NYHA - New York Heart Association, MI – acute myocardial infarction, LVEF – left ventricular ejection fraction, BIM – body mass index, MR – myocardial revascularization, NS – there was no statistical significance.

\*  $\chi^2 = 12.627$ ; \*\*  $\chi^2 = 5.414$ ; +  $\chi^2 = 9.964$ ; +  $\chi^2 = 3.608$ .

Table 4 lists the complications which have required surgical reintervention. There was no significant difference between both groups. In spite of the higher complication rates of the surgical wound in the diabetic group, there was no statistical significance regarding the non-diabetic group.

Table 4. Groups I and II reinterventions. There was no statistical significance in the data analyzed. NS – there was no statistical significance.

Reinterventions	Group I	Group II
Hemostasis review	3 (2.02%)	9 (1.63%) *
Resuture of surgical wound	2 (1.35%)	5 (0.9%) *
Pericardial drainage	1 (0.67%)	0 *
Others	0	3 (0.54%) *
Total	6 (4.04%)	17 (3.07%) *
		* NS

There was no significant difference regarding the mortality rate in both groups (Table 5).

Tabela 5. Mortalidade comparada nos grupos I e II não evidenciou significância estatística.

	Mortality
Group I	3 (2.02%)
Group II	4 (0.72%)

$p = 0.343$   $\chi^2 = 0.9$

## DISCUSSION

An increasing DM prevalence is being expected worldwide in the next few years. In 2030, it is estimated that 11 million people in Brazil will have diabetes mellitus [21]. Compared to the general population, the risk of death in these patients is 3 times higher, especially for those under the age of 69 and at the expenses of cardiovascular events, which can reach as high as 80% of all causes of death [22]. Such clinical picture justifies the efforts to define and implement the adequate management to be offered to this specific population.

The long-term success of myocardial revascularization surgeries is directly related to the patency of the grafts. In spite of the controversial data found in the literature, there are convincing reasons in order to justify the risk of dissecting two internal thoracic arteries in diabetic patients with the purpose of increasing the number of vessels with arterial bypass grafts. The utmost objective, if possible, is to perform a totally arterial myocardial revascularization. In addition, technical modifications were incorporated in order to achieve the objective.

### Skeletonization

Recently, it has been suggested that the skeletonization technique of internal thoracic artery reduces the risk of deep sternal wound complications [15, 22]. Some evidences have suggested that the sternal vascularization is less compromised when this technique is used compared to pedicled harvesting; the advantage of this technique is that a skeletonized artery is distinctly longer, expanding the graft as far as 3 cm [22]. This would facilitate the use of composite T-graft or Y-graft [4] increasing the diameter of the vessel. Convincing data are missing regarding the chance to damage the arterial grafting during its harvesting, what could compromise its feasibility and change the survival curves adversely [14]. There is no doubt that this technique is more complex, involves a learning curve and is time-consuming.

### Using composite grafts

The use of artificial T-graft or Y-graft, as well as sequential anastomoses, can maximize the usage of arteries, theoretically expanding the long-term benefit [23, 24]. In spite of encouraging evidences there is still a lack of evidences to support the routine use of these techniques.

### Reinforced Sternal Synthesis

Recognizing the high risk of de dehiscence and/or surgical wound infection, it seems logical to deduce that the application of methods to reinforce the sternum would be useful to avoid such events; however, earlier recognition of sternal wound complications and aggressive treatment seems to be the better procedure to deal with the clinical pictures of surgical wound infectious complications [10, 25].

### Use of continuous intravenous insulin

Compared with fractional subcutaneous insulin injections, continuous intravenous insulin infusion induced a significant reduction in serum glucose levels, in a prospective study of 2,467 consecutive patients, which led to a significant reduction in deep sternal wound infection rates [16]. In addition, there may have a beneficial effect regarding the cardiac contractility in postischemic periods. Because it is a reliable and simple method, it can be recommended more often, once it is usually reserved for patients with difficult control of blood glucose levels using subcutaneous infusions only.

### CONCLUSION

Our study showed a similar incidence of morbidity and mortality between diabetic and non-diabetic patients undergoing myocardial revascularization using bilateral internal thoracic artery (BITA) grafting.

A cautious selection of the patients and the accurate operative technique can benefit diabetic patients using bilateral internal thoracic artery (BITA) grafting.

### REFERENCES

1. Boccara F, Cohen A. Interplay of diabetes and coronary heart disease on cardiovascular mortality. *Heart*. 2004;90(12):1371-3.

2. Salles GF, Bloch KV, Cardoso CR. Mortality and predictors of mortality in a cohort of Brazilian type 2 diabetic patients. *Diabetes Care*. 2004;27(6):1299-305.
3. Toumpoulis IK, Anagnostopoulos CE, Balaram S, Swistel DG, Ashton RC Jr, DeRose JJ Jr. Does bilateral internal thoracic artery grafting increase long-term survival of diabetic patients? *Ann Thorac Surg*. 2006;81(2):599-607.
4. Loop FD, Lytle BW, Cosgrove DM, Stewart RW, Goormastic M, Williams GW, et al. Influence of the internal mammary artery graft on 10-year survival and other cardiac events. *N Engl J Med*. 1986;314(1):1-6.
5. Bypass Angioplasty Revascularization Investigation Investigators. Seven-year outcome in the Bypass Angioplasty Revascularization Investigation (BARI) by treatment and diabetic status. *J Am Coll Cardiol*. 2000;35(5):1122-9.
6. Lytle BW, Blackstone EH, Loop FD, Houghtaling PL, Arnold JH, Akhrass R, et al. Two internal thoracic artery grafts are better than one. *J Thorac Cardiovasc Surg*. 1999;117(5):855-72.
7. Taggart DP, D'Amico R, Altman DG. Effect of arterial revascularisation on survival: a systematic review of studies comparing bilateral and single internal mammary arteries. *Lancet*. 2001;358(9285):870-5.
8. Devey L, Nyawo B, Newby D, Campanella C. The SoS trial. *Lancet*. 2003;361(9357):615-6.
9. Burfeind Jr WR, Glower DD, Wechsler AS, Tuttle RH, Shaw LK, Harrell FE, et al. Single versus multiple internal mammary artery grafting for coronary artery bypass: 15-year follow-up of a clinical practice trial. *Circulation*. 2004;110[11 suppl 1]:II27-35.
10. Guaragna JC, Facchi LM, Baião CG, Cruz IBM, Bodanese LC, Albuquerque L, et al. Preditores de mediastinite em cirurgia cardíaca. *Rev Bras Cir Cardiovasc*. 2004;19(2):165-70.
11. Borger MA, Rao V, Weisel RD, Ivanov J, Cohen G, Scully HE, et al. Deep sternal wound infection: risk factors and outcomes. *Ann Thorac Surg*. 1998;65(4):1050-6.
12. Lev-Ran O, Braunstein R, Neshet N, Ben-Gal Y, Bolotin G, Uretzky G. Bilateral versus single internal thoracic artery grafting in oral-treated diabetic subsets: comparative seven-year outcome analysis. *Ann Thorac Surg*. 2004;77(6):2039-45.
13. Momin AU, Deshpande R, Potts J, El-Gamel A, Marrinan MT, Omigie J, et al. Incidence of sternal infection in diabetic patients undergoing bilateral internal thoracic artery grafting. *Ann Thorac Surg*. 2005;80(5):1765-72.
14. Bical OM, Khoury W, Fromes Y, Fischer M, Sousa Uva M, Boccara G, et al. Routine use of bilateral skeletonized internal thoracic artery grafts in middle-aged diabetic patients. *Ann Thorac Surg*. 2004;78(6):2050-3.

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15. Peterson MD, Borger MA, Rao V, Peniston CM, Feindel CM. Skeletonization of bilateral internal thoracic artery grafts lowers the risk of sternal infection in patients with diabetes. *J Thorac Cardiovasc Surg.* 2003;126(5):1314-9.
  16. Furnary AP, Zerr KJ, Grunkemeier GL, Starr A. Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients after cardiac surgical procedures. *Ann Thorac Surg.* 1999;67(2):352-62.
  17. Doenst T, Bothe W, Beyersdorf F. Therapy with insulin in cardiac surgery: controversies and possible solutions. *Ann Thorac Surg.* 2003;75(2):S721-8.
  18. Detre KM, Guo P, Holubkov R, Califf RM, Sopko G, Bach 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(5):633-40.
  19. Endo M, Tomizawa Y, Nishida H. Bilateral versus unilateral internal mammary revascularization in patients with diabetes. *Circulation.* 2003;108(11):1343-9.
  20. Rizzoli G, Schiavon L, Bellini P. Does the use of bilateral internal mammary artery (IMA) grafts provide incremental benefit relative to the use of a single IMA graft? A meta-analysis approach. *Eur J Cardiothorac Surg.* 2002;22(5):781-6.
  21. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care.* 2004;27(5):1047-53.
  22. Pevni D, Mohr R, Lev-Run O, Locer C, Paz Y, Kramer A, et al. Influence of bilateral skeletonized harvesting on occurrence of deep sternal wound infection in 1,000 consecutive patients undergoing bilateral internal thoracic artery grafting. *Ann Surg.* 2003;237(2):277-80.
  23. Dion R, Glineur D, Derouck D, Verhelst R, Noirhomme P, El Khoury G, et al. Long-term clinical and angiographic follow-up of sequential internal thoracic artery grafting. *Eur J Cardiothorac Surg.* 2000;17(4):407-14.
  24. Lemma M, Mangini A, Gelpi G, Innorta A, Spina A, Antona C. Is it better to use the radial artery as a composite graft? Clinical and angiographic results of aorto-coronary versus Y-graft. *Eur J Cardiothorac Surg.* 2004;26(1):110-7.
  25. Ridderstolpe L, Gill H, Granfeldt H, Ahlfeldt H, Rutberg H. Superficial and deep sternal wound complications: incidence, risk factors and mortality. *Eur J Cardiothorac Surg.* 2001;20(6):1168-75.