# Technical Aspects of Composite Arterial Grafting With Double Skeletonized Internal Thoracic Arteries\*

Dmitry Pevni, MD; Rephael Mohr, MD; Oren Lev-Ran, MD; Yosef Paz, MD; Amir Kramer, MD; Inna Frolkis, MD, PhD; and Itzhak Shapira, MD

*Background:* Complete myocardial revascularization with internal thoracic arteries (ITAs) improves long-term survival and decreases the rate of repeat operations, compared to vein grafts. Adequate length of the graft in coronary artery bypass graft (CABG) surgery is essential for providing complete arterial revascularization. Extra length can be obtained by skeletonization of both ITAs. In cases where the right ITA (RITA) is too short to bridge the distance to the target anastomotic site, it is used as a free graft in "composite" arterial grafting, a surgical technique in which free arterial conduits are proximally anastomosed end-to-side to an intact ITA.

*Objectives:* To describe alternative surgical procedures adapted to accommodate special anatomic requirements.

Design: Retrospective study from April 1996 to April 1999.

*Patients:* One thousand fifty patients underwent CABG surgery using bilateral skeletonized ITAs: 650 patients (482 men and 168 women; mean  $\pm$  SD age, 69  $\pm$  7 years) underwent composite arterial grafting. Two hundred sixteen patients (33.2%) were diabetics, 87 patients (13.4%) had severe left ventricular dysfunction (ejection fraction < 35%), and 27 patients (4.2%) underwent emergency operations.

*Interventions:* The RITA was used as a free graft connected to the *in situ* left ITA (LITA) in 618 patients. A free LITA was attached to *in situ* RITA in 32 patients, and minicomposite grafts (free distal LITA on the LITA or free distal RITA on the RITA) were constructed in 38 patients. The average number of grafts was 3.2 per patient (range, 2 to 6 grafts per patient).

Measurements and results: Operative mortality was 2.9% (n = 19), and there were 11 sternal wound infections (1.7%). Early recatheterization was performed in 41 symptomatic patients. The patency rate was 95%. The mean follow-up was 25 months (range, 14 to 36 months), and the 3-year survival was 92.5%, with 97% of the surviving patients being angina free.

Conclusions: Planning CABG surgery using bilateral skeletonized ITAs as arterial conduits affords greater choice in grafting approaches, especially when a composite technique is feasible. (CHEST 2003; 123:1348-1354)

Key words: composite graft; internal thoracic artery; revascularization; skeletonized

**Abbreviations:** BITA = bilateral internal thoracic artery; CABG = coronary artery bypass graft; CI = confidence interval; CPB = cardiopulmonary bypass; IABP = intra-aortic balloon pump; ITA = internal thoracic artery; LAD = left anterior descending artery; LITA = left internal thoracic artery; MI = myocardial infarction; OR = odds ratio; PDA = posterior descending artery; PTCA = percutaneous transluminal coronary angioplasty; RCA = right coronary artery; RGEA = right gastroepiploic artery; RITA = right internal thoracic artery; SVG = saphenous vein graft

**C** oronary artery bypass graft (CABG) surgery was traditionally carried out using an *in situ* internal thoracic artery (ITA) in combination with a saphenous vein graft (SVG). The patency of the SVG at 10 years postoperatively was only 50%, while that of an ITA was 93%.<sup>1–3</sup> This finding motivated using bilateral ITA (BITA) grafting in place of the combined single ITA with SVG approach. Several studies have reported potential survival benefit with bilateral ITA (BITA) grafting.<sup>1–3</sup> In addition, the use of BITA was associated with greater freedom from reinterven-

<sup>\*</sup>From the Department of Cardiac and Thoracic Surgery, Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.

Manuscript received February 21, 2002; revision accepted September 9, 2002.

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

Correspondence to: Dmitry Pevni, MD, Department of Cardiac and Thoracic Surgery, Tel Aviv Sourasky Medical Center, 6 Weizman St, Tel Aviv 64239, Israel; e-mail: pevni@tasmc. health.gov.il

tions and repeat operations.<sup>1</sup> Despite excellent results and low mortality and morbidity, until recently, application of the BITA approach was infrequent.<sup>4–7</sup>

The pedicled right ITA (RITA) was less useful than the left ITA (LITA) because it was not always long enough to reach the branches of the left or right coronary artery (RCA) without tension; this led to its use predominantly as a free graft, but with a lower patency rate when it is attached to the ascending aorta.<sup>8</sup> Another reason for cautious use of BITAs is related to the increased risk of sternal wound infection.<sup>6,7</sup> A surgical technique was developed in which the ITA is dissected as a skeletonized vessel.<sup>9,10</sup> This harvesting technique bestowed the advantages of greater length and greater spontaneous blood flow of a skeletonized vessel compared to pedicled ITA.11 The use of skeletonized ITAs allows the use of both ITAs as grafts to practically all coronary vessels requiring surgical revascularization, thus obtaining complete arterial revascularization. Another advantage of using the skeletonized ITA is the preservation of collateral blood supply to the sternum and decreased risk of infection.<sup>12,13</sup>

The bilateral skeletonized ITA technique is the preferred method for myocardial revascularization in our service. The routine use of the SVG was halted in 1996, and vein grafts are currently used as a fourth optional graft, after the radial artery and right gastroepiploic artery (RGEA), or in emergency CABG surgery.<sup>14</sup> For those cases in which an *in situ* RITA cannot loosely reach the left anterior descending artery (LAD), we use a composite arterial grafting technique whereby a free artery (usually the RITA)

is connected end-to-side to an *in situ* LITA. The patency rate of the free graft in this arterial arrangement is similar to that of the *in situ* ITA, and complete arterial revascularization can be achieved.<sup>15</sup>

Between April 1996 and April 1999, 1,050 consecutive patients underwent CABG surgery in our department with the use of skeletonized BITAs; 650 of these patients underwent this procedure using the composite arterial grafting technique, and 400 patients underwent *in situ* BITA. In this report, we describe how different anatomic variations were accommodated by altering the surgical technique for achieving complete arterial revascularization, and we report our results in this group of patients.

## MATERIALS AND METHODS

Four hundred eighty-two men and 168 women underwent CABG surgery using the composite arterial grafting technique by means of bilateral skeletonized ITAs. They comprised 62% of the 1,050 consecutive patients who underwent CABG surgery with bilateral skeletonized ITAs during this period in the Tel Aviv Sourasky Medical Center. The other 38% of patients underwent *in situ* BITA grafting. The preoperative and operative characteristics of patients receiving composite grafts are listed in Table 1.

The ITAs were dissected as skeletonized arteries<sup>9,10</sup> before heparin administration to decrease the risk of damage and hematoma formation in the region of the side branches during dissection. We favor elective opening of the pleura before ITA dissection in order to facilitate exposure. To avoid thermal injury to the ITA, it is extremely important to keep the cautery setting on "low" throughout the dissection. Using scissors or the tip of the cold cautery as a dissector, the artery can be gently separated from the chest wall, leaving the accompanying veins, fascia, and

Factors	Prevalence	Mortality With Factor	Mortality Without Factor	p Value
Female gender	168 (25.8)	10 (6.0)	9 (1.9)	0.01
Left main stenosis	176 (27.1)	10 (5.6)	9 (2.0)	0.029
Acute $MI < 1 \text{ wk}$	162 (24.9)	6 (3.7)	13 (2.7)	NS
Old MI	200 (30.8)	9 (4.5)	10 (2.2)	NS
Complicated PTCA	64 (9.8)	8 (12.5)	11 (1.9)	> 0.001
Ejection fraction $\leq 35\%$	87 (13.4)	4(4.6)	15 (2.7)	NS
Congestive heart failure	92 (14.2)	4 (4.3)	15 (2.7)	NS
Preoperative IABP	12 (1.8)	3 (25)	16 (2.5)	> 0.001
Diabetes	216 (33.2)	6 (2.8)	13 (3)	NS
Hypertension	287 (44.2)	6 (2.1)	13 (3.6)	NS
PVD	97 (14.9)	3 (3.1)	16 (2.9)	NS
Chronic renal failure	59(9.1)	2 (3.3)	17 (2.9)	NS
Severe COPD	62 (9.5)	2 (3.2)	17 (2.9)	NS
Emergency surgery	27 (4.2)	3 (11.1)	16 (2.6)	0.005
Repeat CABG surgery	14 (2.2)	2 (14.3)	17 (2.7)	0.006
Sequential grafts	502 (77.2)	15 (3.0)	4 (2.7)	NS
Use of GEA	119 (18.3)	3 (2.5)	16 (3.0)	NS
Use of SVG	50 (7.7)	2(4.0)	17 (2.8)	NS

Table 1—Study Patient Characteristics (n = 650) and Operative Mortality (n = 17)\*

\*Data are presented as No. of patients (%). PVD = peripheral vascular disease; GEA = gastroepiploic artery; NS = not significant.

adipose tissue in place. Forceps should never be used to grasp the artery itself, but they may hold the small remnants of soft tissue that cling to the adventitia of the ITA. Branches of the artery are divided between two silver clips using scissors. Once the branches are separated, scissors or low cautery are used to divide the remaining medial and lateral soft-tissue attachments.

The skeletonized artery is then put into a small syringe filled with 1:30 papaverine saline solution. This bath of warm papaverine suffices to relax any spasm produced during dissection without the risk of endothelial damage caused by other antispastic maneuvers, such as intraluminary papaverine injection or mechanical dilatation.

#### Surgical Technique

We prefer using BITAs as *in situ* grafts for left-side myocardial revascularization. We believe that more blood sources are associated with improved long-term outcome. The cross arrangement (the RITA to the LAD and the LITA to the marginal branches of the circumflex artery) is based on the assumption that patency rates of the RITA to the LAD are similar to those of the LITA.<sup>15</sup> When *in situ* RITA cannot loosely reach the LAD (*eg*, in cases of a very long ascending aorta, an enlarged right ventricle, a too distal or an unpredictable LAD anastomotic site), we use a composite arterial grafting technique, whereby a free artery (usually the RITA) is connected end-to-side to an *in situ* LITA.

We do not use the cross technique in cases with a short RITA, a very long ascending aorta, an enlarged right ventricle, or a too distal or unpredictable LAD anastomotic site. When the distal RITA cannot reach the LAD without undue tension, we use the RITA as a free graft, and a T-shaped anastomosis<sup>16</sup> to the LITA is prepared at the level of the main pulmonary artery before the patient is connected to cardiopulmonary bypass (CPB).

The proximal composite anastomosis of a free RITA on the LITA might sometimes be performed when the patient is receiving CPB, after constructing all distal anastomoses. This is the safest way to precisely determine the location of the composite anastomosis without compromising the LITA flow to the LAD.

Sequential grafting is essential for complete arterial revascularization with composite grafts. Our preferred approach is a diamond-shaped side-to-side anastomosis for branches of the circumflex artery. This approach carries the advantage of using the shortest possible ITA segments between anastomoses (Fig 1), thus improving the likelihood that the arterial length will be adequate. To prevent tension between anastomoses after filling the ventricle with blood, the length of the ITA segment between anastomoses should be 5- to 10-mm longer than the actual distance between coronary arteriotomies. For the intramyocardial coronary artery or for vessels buried inside a deep layer of epicardial fat, we use a parallel side-to-side anastomosis (Fig 1, *right*, *B*); constructing a diamond-shaped anastomosis in these cases exposes the ITA to the risk of seagull-wing kinking.<sup>17</sup>

Despite the extra length obtained with skeletonized ITA harvesting, the LITA may still sometimes not reach the distally located anastomotic site on the LAD. For such cases, a composite graft may be constructed where the *in situ* LITA is connected to a marginal branch of the circumflex and a free RITA is anastomosed end-to-side to the LITA with its distal end being connected to the LAD (Fig 2). Another variation of composite grafting is the small Y-graft, wherein a small distal section of an ITA is anastomosed end-to-side to a more proximal part of the same artery (Fig 3, *left*, A).

In cases which require revascularization of both the diagonal and circumflex system, the LITA is anastomosed to the LAD, and the diagonal artery is one of those supplied by the free RITA (sequential grafting; Fig 3, *right*, *B*). The proximal composite anastomosis of a free RITA on the LITA in this case has to be performed when the patient is receiving CPB, after constructing all distal anastomoses. When the diagonal artery is intramyocardial or buried deep in fat tissue, it is necessary to use either a parallel anastomosis or a small Y-graft to prevent seagull kinking (Fig 3, *left*, *A*).

## Revascularization of the Right Coronary System

An ITA grafted to the RCA has a low patency rate.<sup>2,5</sup> Since an arterial anastomosis on this calcified or fibrotic vessel tends to close, we prefer using the more distally located posterior descending artery (PDA). It is possible to reach the PDA with a free RITA attached end-to-side to an *in situ* LITA as a composite graft. When no graft to the posterior wall of the heart (the circumflex region) is necessary, the RITA may also encircle the apex of the right ventricle on its course to the PDA anastomotic site (Fig 4).

When the RITA is not long enough to reach the PDA, we use the RGEA as our graft of choice for the PDA. When the PDA is unsuitable for RGEA grafting, such as in cases with a potential for high competitive flow in the RCA, we select the SVG for



FIGURE 1. *Left*, A: Composite graft with an RITA on the LITA, sequential grafting with diamondshaped anastomosis and terminal T-shaped anastomosis. *Right*, B: Composite graft with an RITA on the LITA, sequential grafting with parallel side-to-side anastomosis. D = diagonal artery; M = marginal artery.



FIGURE 2. A free RITA is used for left descending artery and diagonal artery grafting, and an *in situ* LITA is used for the marginal artery. See Figure 1 legend for definition of abbreviation.

revascularization of the RCA system. To decrease the risk of spasm of the arterial grafts, all of the patients were treated with high-dose IV infusion of isosorbide dinitrate (4 to 20 mg/h) during the first 24 to 48 h after operation.<sup>14</sup>

#### Statistical Analysis

Data are expressed as mean  $\pm$  SD or proportions. The  $\chi^2$  test and two-sample t tests were used to compare discrete and continuous variables, respectively. Multivariate logistic regression analysis was used to predict unfavorable outcome events by various risk factors. The odds ratios (ORs) and 95% confidence intervals (CIs) are given. Postoperative survival is expressed by the Kaplan-Meier method. All analyses were performed by SPSS software (Version 9.0; SPSS; Chicago, IL).

## Results

The 650 study patients received from one to six grafts each (mean, 3.2 grafts). The average CPB time was  $75 \pm 27$  min, and the aortic cross-clamping time was  $65 \pm 20$  min. The RITA was used as a free graft connected to the *in situ* LITA in 618 patients (95%),

www.chestjournal.org

the free LITA was attached to the *in situ* RITA in 32 patients (4.9%), the small Y-graft was constructed in 38 patients (5.8%), the RGEA was used in 119 patients (18.3%), and SVGs were used in 50 patients (7.7%).

Operative mortality was 2.9% (n = 19). Increased mortality was noted in repeat operations (14.3%), failed transluminal coronary angioplasty percutaneous (PTCA) [8%], female patients (6%), and patients with left main disease (5.6%). However, preoperative use of an intra-aortic balloon pump (IABP) [OR, 20.5; 95% CI, 3.82 to 31.5] and failed PTCA [OR, 3.65; 95% CI, 0.96 to 13.87] emerged as the only independent predictors of early mortality (30 days). There were eight perioperative myocardial infarctions (MIs) [1.2%], and 12 patients (1.8%) sustained strokes. Sternal wound infection occurred in 11 patients (1.7%). Neither diabetes nor advanced age (> 70 years) were independent predictors of untoward events. COPD (OR, 8.8; 95% CI, 2.3 to 32.8) and failed PTCA (OR, 4.5; 95% CI, 1.07 to 18.6) were independent predictors of sternal infection.



FIGURE 3. *Left*, A: Minicomposite (small Y) graft; a small distal part of the LITA on an *in situ* proximal ITA. *Right*, B: The graft to the diagonal artery is the sequential anastomosis on the RITA. See Figure 1 legend for expansion of abbreviation.

Postoperative follow-up (mean,  $23 \pm 6$  months; range, 14 to 36 months) was available in 631 patients (97.6%). One-year and 3-year survival rates (Kaplan Meier) were 94.8% and 92.5%, respectively, and only 15 of the surviving patients (2.4%) reported return of angina. Forty-one patients underwent postoperative cardiac catheterization during the follow-up period: 15 patients had procedures because of chest pain, 6 patients underwent positive thallium single-photon emission CT, and the remaining 21 patients consented to elective catheterization within the framework of our learning to use the composite technique. One hundred three of the anastomoses (95.4%) were patent, and 5 were occluded (4.6%). In two of these five anastomoses, technical problems were noted in the site of the composite (free RITA on an in situ LITA) anastomosis.

# DISCUSSION

This report focused on the technical aspect of BITA grafting using free ITA attached to the in situ ITA (composite graft). The ITA is currently the conduit of choice in CABG surgery because of superior graft patency.<sup>18,19</sup> While the RITA and the LITA are comparable in size, flow capacity, and patency,<sup>20</sup> the pedicled RITA is less useful since its length is not always sufficient to reach the target anastomotic sites on the right or left coronary vessels. Instead, the RITA is used primarily as a free graft attached to the aorta, with a lower patency rate.<sup>8,15</sup> Several studies have been reported over the past few years showing survival benefit,<sup>1,3,5</sup> lower reintervention rate,<sup>1</sup> and better angina-free survival<sup>1,2</sup> after BITA grafting when compared with the use of a single ITA.

The T-graft was first utilized by Mills<sup>21</sup> and Sauvage et al.<sup>22</sup> Complete arterial revascularization was achieved in these series with two conduits in which the RITA is usually attached to the in situ LITA and directed to the lateral and posterior aspects of the left ventricle, while the LITA is directed to the anterior surface of the heart. Studies have shown that the skeletonized BITA composite graft has excellent blood flow reserve.23,24 Calafiore et al20 demonstrated a better patency rate for free RITAs as part of composite grafts from the *in situ* LITAs when compared to those attached to the aorta. They postulated that the lower patency rates of free arterial grafts arising from the aorta are related to exposure of these grafts to turbulence and its associated risk of intimal damage.<sup>20</sup>

A recent study has shown that using LITA with a composite free radial artery is associated with good early patency rate and clinical results<sup>25</sup>; however, survival benefit for this technique was demonstrated, so that it can be considered as an alternative approach in patients when the use of BITA unsuitable.

This study included 650 consecutive patients in whom a skeletonized BITA composite grafting was used. This technique preserved sternal collateral blood supply and resulted in a relatively low rate of sternal infection even in patients with increased risk for this complication: elderly and diabetic patients.<sup>6</sup> Diabetes mellitus is generally considered to be a major risk factor for sternal infections, especially when pedicled BITA is used. The risk in these circumstances was estimated to be five times higher than in patients with single ITAs used.<sup>26</sup> We found no evidence of this relationship in those receiving skeletonized BITAs. The only significant predictors



FIGURE 4. The free RITA encircles the apex of the right ventricle on its course to the PDA. See Figure 1 legend for expansion of abbreviation.

of sternal infection in this study were COPD and emergency cases with failed PTCA. Increased risk of sternal infection in patients operated on after failed PTCA is probably associated with low cardiac output. In addition, we noted that emergent surgery for failed PTCA and preoperative insertion of IABP were predictors for early mortality, and we now recommend avoiding the use of BITA grafting in these subgroups of patients in unstable clinical condition. For them, a more simplified approach, such as pedicled ITA and vein grafts, would be more suitable. In patients who are stabilized after IABP has been inserted for unstable angina pectoris, however, we still recommend BITA as first choice. In conclusion, we routinely perform and recommend complete arterial revascularization with bilateral skeletonized ITAs in most of the patients referred for CABG surgery as the most appropriate arterial conduits for the composite technique.

ACKNOWLEDGMENT: The authors thank Esther Eshkol for editorial assistance.

## References

- 1 Lytle BW, Blackstone EH, Loop FD, et al. Two internal thoracic artery grafts are better than one. Thorac Cardiovasc Surg 1999; 117:855–872
- 2 Pick AW, Orszulak TA, Anderson BJ, et al. Single vs bilateral internal mammary artery grafts: 10-year outcome analysis. Ann Thorac Surg 1997; 64:599-605
- 3 Buxton BF, Komeda M, Fuller JA, et al. Bilateral internal thoracic artery grafting may improve outcome of coronary artery surgery: risk-adjusted survival. Circulation 1998; 98: II1–II6
- 4 Loop FD. Coronary artery surgery: the end of the beginning. Eur J Cardiothorac Surg 1998; 14:554–571
- 5 Schmidt SE, Jones JW, Thornby JI, et al. Improved survival with multiple left-sided bilateral internal thoracic artery grafts. Ann Thorac Surg 1997; 64:9–14
- 6 Borger M, Rao V, Weisel R, et al. Deep sternal wound infection: risk factors and outcomes. Ann Thorac Surg 1998; 65:1050–1056

- 7 Fiore A, Naunheim K, McBride L, et al. Fifteen-year follow-up for double internal thoracic artery grafts. Eur J Cardiothoracic Surg 1991; 5:248–252
- 8 Tatoulis J, Buxton B, Fuller J. Results of 1,454 free right internal thoracic artery-to-coronary artery grafts. Ann Thorac Surg 1997; 64:1263–1268
- 9 Sauvage LR. Extensive myocardial revascularization using only internal thoracic arteries for grafting the anterior descending circumflex and right systems. In: Cardiac surgery: state of the art reviews (vol 6). Philadelphia, PA: Hanley & Belfus, 1992; 397
- 10 Cunningham JM, Gharavi MA, Fardin R, et al. Considerations in the skeletonization technique of internal mammary artery dissection. Ann Thorac Surg 1992; 54:947–950
- 11 Choi JB, Lee SY. Skeletonized and pedicled internal thoracic artery grafts: effects of free flow during bypass. Ann Thorac Surg 1996; 61:909–913
- 12 Parish MA, Asai T, Grossi EA, et al. The effects of different techniques of internal mammary artery harvesting on sternal blood flow. Thorac Cardiovasc Surg 1992; 104:1301–1307
- 13 Carrier M, Gregoire J, Tronc F, et al. Effect of internal mammary artery dissection on sternal vascularization. Ann Thorac Surg 1992; 53:115–119
- 14 Sofer D, Gurevitch J, Shapira I, et al. Sternal wound infection in patients after coronary artery bypass grafting using bilateral skeletonized internal mammary arteries. Ann Surg 1999; 229:585–590
- 15 Dion R, Etienne PY, Verhelst GK, et al. Bilateral mammary grafting. Eur J Cardiothorac Surg 1993; 7:287–294
- 16 Tector AJ, Amundsen S, Schmal TM, et al. Total revascularization with T-grafts. Ann Thorac Surg 1994; 57:33–39
- 17 Grondin CM, Limer R. Sequential anastomoses in coronary artery grafting: technical aspects and early and late angio-

graphic results. Ann Thorac Surg 1976; 23:1-8

- 18 Barner H, Barnett M. Fifteen to 21-year angiographic assessment of internal thoracic artery as a bypass conduit. Ann Thorac Surg 1994; 57:1526–1528
- 19 Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal mammary artery graft on 10-year survival and other cardiac events. N Engl J Med 1986; 314:1–6
- 20 Calafiore A, Di Giammarco G, Luciani N, et al. Composite arterial conduits for a wider arterial myocardial revascularization. Ann Thorac Surg 1994; 58:185–190
- 21 Mills NL. Physiologic and technical aspects of internal mammary artery coronary artery bypass grafts. In: Cohn LH, ed. Modern techniques in surgery. Mount Kisco, NY: Futura, 1982; 1–19
- 22 Sauvage MR, Wu H-D, Kowalsky PE, et al. Healing basis and surgical techniques for complete revascularization of the left ventricle using only the internal mammary arteries. Ann Thorac Surg 1986; 42:448–465
- 23 Wendler O, Hennen B, Markwirth T, et al. T grafts with the right internal thoracic artery to left internal thoracic artery vs the left internal thoracic artery and radial artery: flow dynamics in the internal thoracic artery main stem. Thorac Cardiovasc Surg 1999; 118:841–848
- 24 Royse AG, Royse CF, Gorves KL, et al. Blood flow in composite arterial grafts and effect of native coronary flow. Ann Thorac Surg 1999; 68:1619–1622
- 25 Tatoulis J, Royse AG, Buxton BF, et al. The radial artery in coronary surgery: a 5-year experience; clinical and angiographic results. Ann Thorac Surg 2002; 73:143–147
- 26 Lytle BW, Cosgrove DM, Loop FD, et al. Perioperative risk of bilateral internal mammary grafting: analysis of 500 cases from 1971 to 1984. Circulation 1986; 74(suppl):11137–11141