Journal of the American College of Cardiology
© 2000 by the American College of Cardiology
Published by Elsevier Science Inc.

Vol. 35, No. 4, 2000
ISSN 0735-1097/00/$20.00
PII S0735-1097(99)00652-X

Percutaneous Revascularization of the Internal Mammary Artery Graft: Short- and Long-term Outcomes

Luis Gruberg, MD, George Dangas, MD, PHD, FACC, FESC, Roxana Mehran, MD, FACC, FESC, Mun K. Hong, MD, FACC, Ron Waksman, MD, FACC, Gary S. Mintz, MD, FACC, Kenneth M. Kent, MD, PHD, FACC, Augusto D. Pichard, MD, FACC, Lowell F. Satler, MD, FACC, Alexandra J. Lansky, MD, Gregg W. Stone, MD, FACC, Martin B. Leon, MD, FACC

New York, New York; and Washington, D.C.

OBJECTIVES We evaluated the short- and long-term clinical outcomes after percutaneous revascularization of the internal mammary artery (IMA) graft.

BACKGROUND Previous reports in a relatively small number of patients have indicated the safety of balloon angioplasty for the treatment of stenoses in the IMA graft. However, the use of alternative interventional techniques and their long-term results have not yet been evaluated.

METHODS We analyzed the in-hospital and one-year clinical outcomes of 174 consecutive patients who underwent percutaneous revascularization of 202 lesions located in the IMA graft, by either balloon angioplasty or stenting.

RESULTS Anastomotic lesions were evident in 128 cases (63%), and they were more commonly treated with balloon angioplasty (116/128, 91%), whereas lesions located at the ostium (n = 16, 8%) were more frequently treated with stents (11/16, 69%). Procedural success was 97% with excellent in-hospital outcome: 0.6% mortality rate, no Q-wave myocardial infarction (MI) and 0.6% rate of urgent bypass surgery. Cumulative one-year rates were: mortality 4.4%, MI 2.9% and target lesion revascularization (TLR) 7.4%.

CONCLUSIONS Revascularization of the IMA graft can be performed safely, with high procedural success and a low rate of in-hospital complications. Long-term follow-up showed very low TLR rate. (J Am Coll Cardiol 2000;35:944–8) © 2000 by the American College of Cardiology

The internal mammary artery (IMA) is currently considered the vascular conduit of choice for patients who undergo elective surgical coronary revascularization with a bypass to the left anterior descending coronary artery. When compared to saphenous vein grafts, IMA grafts have shown superior long-term patency rates, lower frequency of reoperation and lower long-term myocardial infarction and mortality rates (1–5). However, there is still a need for IMA graft revascularization owing to intrinsic atherosclerotic disease, distal anastomosis obstruction or damage to the vessel during the harvest procedure. With the increasing use of the IMA in coronary artery bypass graft (CABG), there is a growing need for percutaneous revascularization procedures of lesions located in the IMA grafts (6).

Previous early reports have shown that balloon angioplasty (percutaneous transluminal angioplasty; PTA) of the IMA can be performed safely with high procedural success and a relatively low incidence of clinical restenosis (6–13). However, information on the use of stents in the IMA has been limited to isolated case reports (14–16). The purpose of this study was to investigate the short- and long-term outcomes in a large cohort of patients who underwent percutaneous revascularization of the IMA graft in our institution.

METHODS

Patient population. Between January 1994 and April 1998, a total of 174 consecutive patients underwent 184 percutaneous revascularization procedures in 202 lesions of the IMA graft at the Washington Hospital Center. A total of 144 patients underwent PTA in 163 lesions (81%), and 30 patients underwent tubular slotted-stent implantation in 39 lesions (19%). Procedures performed via the IMA graft in the native coronary vessel were excluded from this analysis.

The purpose of the study was not to compare PTA versus stent outcomes, as they had different indications according to lesion location and angiographic characteristics; rather, we aimed to report on the overall results of a large consecutive series of unselected IMA graft interventions. The decision regarding whether patients should undergo

From the Cardiovascular Research Foundation, New York; and the Cardiac Catheterization Laboratory, Washington Hospital Center, Washington, D.C. Supported in part by an educational grant from the Cardiovascular Research Foundation, Washington, D.C.

Manuscript received August 5, 1999; revised manuscript received October 27, 1999, accepted December 7, 1999.

Abbreviations and Acronyms

CABG = coronary artery bypass graft
CCS = Canadian Cardiovascular Society
CK = creatine kinase
IMA = internal mammary artery
MI = myocardial infarction
MLD = minimal lumen diameter
PTA = percutaneous transluminal angioplasty
TIMI = Thrombolysis in Myocardial Infarction
TLR = target lesion revascularization

stenting or PTA was made by the operator at the time of the procedure based on vessel size, anatomy and lesion morphology. Ostial lesions, due to their accessibility and larger vessel diameter, were usually opted for stenting. Lesions located at the anastomotic site were treated more often by PTA due to proximal vessel tortuosity, smaller vessel diameter (natural vessel tapering), and because of prior reports of lower restenosis rates at this site and also to avoid the possibility of "jailing" the retrograde portion of the vessel with a stent (9).

Revascularization procedure. All patients underwent either PTA or stenting of the IMA graft with the transfemoral approach according to current guidelines with conventional catheter-based systems (17,18). Patients received aspirin 325 mg at least 24 h before the procedure and continued indefinitely afterwards, and patients who underwent stenting were treated concomitantly with either ticlopidine 250 mg bid for four weeks or clopidogrel 75 mg qd for four weeks per the routine protocol. Weight-adjusted heparin dosage was administered during the procedure to maintain an activated clotting time of 250 to 300 s. Heparin was routinely discontinued at the end of the procedure. Platelet glycoprotein IIb/IIIa inhibitors were administered in <2% of cases.

Angiographic analysis. Quantitative angiographic analysis was performed at the Angiographic Core Laboratory by an independent observer who was unaware of the purpose or outcome of the study. Analysis was done on cine frames demonstrating the stenosis in its more severe and nonforeshortening projection, using a computer-assisted, automated edge detection algorithm (ARTREK, Quantitative Cardiac Systems, Ann Arbor, Michigan) and standard morphological criteria (19). The contrast-filled catheter was used as the calibration standard. Arterial flow was graded using the Thrombolysis in Myocardial Infarction (TIMI) classification (20). Minimal lumen diameter (MLD) was defined as the point of maximal luminal narrowing in the analyzed segment. Ostial lesions began within 3 mm of the subclavian artery. Lesion length was measured as the distance from proximal to distal shoulder of the lesion in millimeters. Tortuosity was defined as the presence of two or more bends >45° proximal to the lesion.

Table 1. Patient Characteristics (n = 174)

Variables	
Male/Female	65/35%
Age (yrs)	63 ± 10
CCS angina class III–IV	60.8%
Prior myocardial infarction	57.1%
Prior coronary angioplasty	45.4%
Graft age (months)	43 ± 22
Hypertension	58.2%
Diabetes mellitus	36.4%
Hyperlipidemia	74.5%
Chronic renal insufficiency	8.7%
Left ventricular ejection fraction	0.43 ± 0.13

CCS = Canadian Cardiovascular Society.

Clinical demographics and follow-up. Baseline clinical demographics and laboratory results were obtained from hospital charts that were reviewed by an independent registered nurse who was unaware of the objectives and/or outcomes of the study. Data were entered prospectively in the database by our dedicated Data Coordinating Center. Non-Q-wave myocardial infarction (MI) was defined as a creatine kinase (CK)-MB enzyme elevation ≥5× normal without new Q waves. Clinical follow-up was performed by either telephone contact or office visit at three, 6 and 12 months. The occurrence of major late clinical events was recorded, including death, Q-wave MI and target lesion revascularization (TLR) (whether surgical or percutaneous). These events were adjudicated by supporting documents.

RESULTS

Baseline characteristics of 174 consecutive patients are summarized in Table 1. Mean age was 63 ± 9 years (range 36 to 87 years), with 35% women (n = 61). A previous MI had occurred in 99 patients (57%), while the left ventricular ejection fraction was 0.43 ± 0.13. One hundred and three patients (61%) had class III or IV angina according to the Canadian Cardiovascular Society (CCS) on admission, and 68 patients (39%) had angina at rest.

Angiographic characteristics. The left IMA was treated in 85% (n = 148) of the patients and the right IMA in 15% (n = 26). The bypassed vessel was the left anterior descending coronary artery in 86% of cases, the right coronary artery in 8% and the left circumflex in 6%. The anastomotic site of the IMA graft was the most frequently treated site (n = 128, 63%) of lesions, mainly with PTA alone (n = 116, 71%) (Table 2). Restenotic lesions accounted for 17% (n = 36) of all lesions. Ostial lesions (n = 16) represented only 8% of all lesions and were more frequently treated with stents (n = 11, 66%).

Mean lesion length was 10 ± 9 mm, with 25% (n = 51) of the lesions being longer than 10 mm and 6% (n = 12) longer than 20 mm. Proximal vessel tortuosity was found in 24% of the grafts, all of them treated with PTA alone.

JACC Vol. 35, No. 4, 2000
March 15, 2000:944–8

Table 2. Treatment Modality and Lesion Location

	Total (n = 202)	Ostial (n = 16)	Shaft (n = 58)	Anastomosis (n = 128)
Stent	39 (19%)	11 (29%)	16 (40%)	12 (31%)
PTA	163 (81%)	5 (3%)	42 (26%)	116 (71%)

PTA = percutaneous transluminal angioplasty.

Twenty-six (14.8%) of the grafts were totally occluded at the beginning of the procedure, whereas an additional 40 (22.8%) had impaired flow, either TIMI flow grade 1 (n = 28, 16%) or flow grade 2 (n = 12, 6.8%). At the end of the procedure, TIMI flow grade 3 was restored in 164 (94%) of the IMA grafts. The final flow was TIMI flow grade 1 in three patients (2%) and TIMI flow grade 2 in four patients (2%). Quantitative angiographic results are shown in Table 3.

In-hospital outcome. The in-hospital outcome is detailed in Table 4. There was one case of abrupt closure and one case of perforation resulting in two major complications: one death (0.6%) and one emergency coronary bypass surgery (0.6%). There were no cases of Q-wave MI, and there was an 8.5% incidence of non-Q-wave MI (n = 15). CK-MB fraction elevation >3× normal occurred in 12.5% of patients. Urgent repeat catheterization and repeat target lesion PTA was performed in six patients (3.3%).

Late clinical follow-up. Cumulative one-year follow-up results are detailed in Table 5. During this period six patients died (4.4%), and one experienced a Q-wave MI (0.7%). Two patients died of complications during revascularization procedures, two of unknown causes, one of complete atrioventricular (AV) block that developed after a hip fracture (three months after the procedure) and one of complications of an autoimmune syndrome. Overall TLR rate was 7.4% (n = 15). Patients who underwent stenting had a TLR rate of 15.4% (n = 6), and those who underwent PTA had a TLR rate of 5.4% (n = 9).

For the ostial site of the IMA graft, overall TLR was 25% (n = 4); 40% (2 of 5) for patients treated with PTA and 18% (2 of 11) for patients treated with stents.

For the anastomotic site, overall TLR was 7% (n = 9); 4.3% (5 of 116) for patients treated with PTA and 33% (4 of 12) for patients treated with stents.

For the shaft of the IMA graft, overall TLR was 13% (n = 2); 4.8% (2 of 42) for patients treated with PTA and 0% (0 of 16) for patients treated with stents.

DISCUSSION

This study evaluated the short-term and one-year clinical outcomes of a cohort of consecutive patients who underwent percutaneous revascularization of the IMA graft. This series represents the largest published experience with PTA and the first series of stenting of the IMA graft (14–16).

Although patients who underwent stenting and those who underwent PTA had comparable demographic and clinical characteristics, it would be misleading to compare the two groups in view of their completely different angiographic characteristics. Specifically, lesions treated with stents were located at the ostial site where the vessel was larger and easily accessible, whereas the majority of the lesions treated with PTA were located at the distal anastomosis site where the vessel is smaller owing to the natural tapering (see Methods section and Table 2).

Nevertheless, in-hospital procedural success and outcome were excellent for all patients despite the technical challenges imposed by graft tortuosity and the natural tapering of the vessel, which may limit the technical options available during the procedure (9,13). The tendency to deploy stents in the ostial portion of the graft and to treat the distal anastomosis site by PTA alone appeared to have produced excellent overall clinical results (Tables 4 and 5).

During hospitalization, major complications were scarce (Table 4) and the CK-MB elevation rates were rather low in

Table 3. Quantitative Angiographic Results

	Total (n = 174)	Stent (n = 39)	PTA (n = 163)
Preprocedural			
Reference diameter (mm)	2.08 ± 0.53	2.57 ± 0.41	2.01 ± 0.50
Minimal lumen diameter (mm)	0.66 ± 0.53	0.99 ± 0.62	0.61 ± 0.50
Diameter stenosis (%)	64.0 ± 21.1	59.6 ± 19.6	64.7 ± 21.3
Postprocedural			
Reference diameter (mm)	2.17 ± 0.46	2.64 ± 0.43	2.10 ± 0.42
Minimal lumen diameter (mm)	1.63 ± 0.62	2.49 ± 0.81	1.50 ± 0.47
Diameter stenosis (%)	24.7 ± 16.8	6.15 ± 22.7	27.6 ± 13.5

Values are mean ± SD.
PTA = percutaneous transluminal angioplasty.

Table 4. In-Hospital Outcomes

	Total (%)	Stent (%)	PTA (%)
Procedural success	96.7	96.8	96.7
Death	0.6	0	0.7
Q-wave MI	0	0	0
Non–Q-wave MI	8.5	6.3	9.0
CABG	0.6	0.0	0.7
Target lesion PTA	3.3	6.3	5.3
MACE	1.7	0	1.3

CABG = coronary artery bypass graft surgery; MI = myocardial infarction; PTA = percutaneous transluminal angioplasty; MACE = major adverse cardiac events (death, MI or emergency CABG).

comparison to reported rates for native coronary and for saphenous vein graft intervention. These facts may allude to a favorable future prognosis for the present cohort (21).

At one-year follow-up, TLR rates were low (7.4%) and comparable with those of previous reports (7,10). Although the true incidence of angiographic restenosis is unknown in the absence of angiographic follow-up, the reported one-year clinical restenosis rate appears lower than the rates reported for vein graft intervention: 17% after stenting and 26% after PTA (22). Previous reports have shown that IMA grafts have low restenosis rates after PTA, especially at the distal anastomosis site, but higher rates at the body of the graft (7,11–13). Although TLR rate was higher for ostial lesions in the present study, it is inappropriate to make a definitive comparison to the TLR rate of distal IMA graft lesions because of the small number of events. However, it is important to clarify that the TLR rate at the anastomostic site, where 63% (n = 128) of the treated lesions was 7% and the revascularization rate for PTA-treated lesions at this site was only 4.3%.

The higher long-term patency and low restenosis rate of the IMA graft when compared to saphenous vein grafts can be attributed to an apparent resistance of this vessel to accelerated atherosclerosis (23). The production of endothelial vasodilators (i.e., nitrous oxide and prostacyclin) by IMA grafts, platelet-to-vessel wall interaction, as well as different contractile and proliferative characteristics of their smooth muscle cells, may play an important role in proliferative graft disease, and therefore in graft patency rates (24–26). A recent study showed that smooth muscle cells from IMA have less pronounced growth activity in response to serum or platelet-derived growth factor-BB (PDGF-BB) than vein grafts, despite a normal PDGF receptor expression and function (27).

Furthermore, cyclin-dependent kinase inhibitors ($p27^{Kip1}$ and $p21^{Cip1}$), which cause cell cycle arrest in cultured cells in G1, are less downregulated in IMA grafts when compared to vein grafts, therefore diminishing smooth muscle cell proliferative response in IMA grafts (27). Differential growth properties of smooth muscle cells in vessels with different biological and molecular mechanisms—as well as the fact that IMA anastomotic lesions most likely represent scar tissue, compared to vein graft or native coronary lesions that are predominantly atherosclerotic plaque—may account for the difference in proliferative vascular response between IMA grafts and vein grafts, and possibly on the restenosis process after PTA in these vessels (28).

Table 5. One-Year Follow-up Results

	Total (%)	Stent (%)	PTCA (%)
Death	4.4	10.0	3.5
MI	2.9	5.0	2.5
Q-wave MI	0.7	0	0.8
Non–Q-wave MI	2.2	5.0	1.7
TLR	7.4	15.4	5.5
Percutaneous	6.4	12.8	4.9
Surgical	1.0	2.6	0.5

MI = myocardial infarction; TLR = target lesion revascularization.

Study limitations. The present study was a retrospective analysis; therefore, the results and the conclusions are subject to the limitations inherent in all such reports. Operator evaluation of each individual case and the selection of stenting versus PTA based on vessel size and lesion location were subjective, predicated on the general guidelines outlined in the Methods section. Patients did not undergo routine follow-up angiography to assess accurately the restenosis/reocclusion rates, which may be silent, particularly in patients who had initially presented with a totally occluded graft. Finally, the relatively small number of patients who underwent stenting did not allow for a formal comparison between the two treatment strategies, especially for patients who underwent treatment at the ostial site, where there seems to be arithmetically lower restenosis with stenting.

Conclusions. Percutaneous revascularization of the IMA graft can be performed with high procedural success and low rate of in-hospital complications and is associated with excellent long-term outcome. The TLR rate appears to be lower than in either native coronary arteries or saphenous vein grafts.

Acknowledgment
Dr. Luis Gruberg is the recipient of a fellowship from the Physicians Fellowship for Medicine in Israel.

Reprint requests and correspondence: Dr. George Dangas, Cardiovascular Research Foundation, 6th floor, 55 East 59th Street, New York, NY 10022. E-mail: gdangas@compuserve.com

REFERENCES

1. 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.
2. Lytle BW, Loop FD, Thurer RL, Groves LK, Taylor PC, Cosgrove DM. Isolated left anterior descending coronary artery atherosclerosis:

long-term comparison of internal mammary artery and venous autografts. Circulation 1980;61:869–76.
3. Acinapura AJ, Rose DM, Jacobowitz IJ, et al. Internal mammary artery bypass grafting: influence on recurrent angina and survival in 2100 patients. Ann Thorac Surg 1989;48:186–91.
4. Barbour DJ, Roberts WC. Additional evidence for relative resistance to atherosclerosis of the internal mammary artery compared to saphenous vein when used to increase myocardial blood supply. Am J Cardiol 1985;56:488.
5. Kay HR, Korns ME, Flemma RJ, Tector AJ, Lepley D. Atherosclerosis of the internal mammary artery. Ann Thorac Surg 1976;21: 504–8.
6. Ishizaka N, Ishizaka Y, Ikari Y, et al. Percutaneous transluminal angioplasty performed on internal mammary artery grafts. Br Heart J 1995;74:615–9.
7. Hearne SE, Davidson CJ, Zidar JP, Phillips HR, Stack RS, Sketch MH Jr. Internal mammary artery graft angioplasty: acute and long-term outcome. Cathet Cardiovasc Diagn 1998;44:153–6.
8. Khurana S, O'Neill WW, Sakwa M, Safian RD. Acute occlusion of a left internal mammary artery graft immediately after redo coronary artery bypass surgery: successful rescue PTCA. Cathet Cardiovasc Diagn 1997;41:166–9.
9. Crowley ST, Bies RD, Morrison DA, Barbiere CC. Percutaneous transluminal angioplasty of internal mammary arteries in patients with rest angina. Cathet Cardiovasc Diagn 1996;38:256–62.
10. Popma JJ, Cooke RH, Leon MB, et al. Immediate procedural and long-term results of internal mammary artery angioplasty. Am J Cardiol 1992;69:1237–9.
11. Dimas AP, Arora RR, Whitlow PL, et al. Percutaneous transluminal angioplasty involving internal mammary artery grafts. Am Heart J 1991;122:423–9.
12. Bell MR, Holmes DR, Vlietstra RE, Bresnahan DR. Percutaneous transluminal angioplasty of left internal mammary artery grafts: two years' experience with a femoral approach. Br Heart J 1989;61:417–20.
13. Shimshak TM, Giorgi LV, Johnson WL, et al. Application of percutaneous transluminal coronary angioplasty to the internal mammary artery graft. J Am Coll Cardiol 1988;12:1205–14.
14. Hadjimiltiades S, Gourassas J, Louridas G, Tsifodimos D. Stenting the distal anastomotic site of the left internal mammary artery graft: a case report. Cathet Cardiovasc Diagn 1994;32:157–61.
15. Almagor Y, Thomas J, Colombo A. Balloon expandable stent implantation of a stenosis at the origin of the left internal mammary artery graft: a case report. Cathet Cardiovasc Diagn 1991;24:256–8.
16. Bajaj RK, Roubin GS. Intravascular stenting of the right internal mammary artery. Cathet Cardiovasc Diagn 1991;24:252–5.
17. AHA/ACC Task Force report: Guidelines for percutaneous transluminal coronary angioplasty. A report of the American College of Cardiology/American Heart Association Task Force on assessment of diagnostic and therapeutic procedures. J Am Coll Cardiol 1993;22: 2033–54.
18. Pepine CJ, Holmes DR, Block PC, et al., for the Cardiac Catheterization Committee. ACC Expert Consensus Group. Coronary artery stents. J Am Coll Cardiol 1996;28:782–94.
19. Lansky AJ, Popma JJ. Quantitative angiography. In: Topol EJ, editor. Textbook of Interventional Cardiology. Philadelphia: Saunders, 1999: 725–47.
20. The Thrombolysis in Myocardial Infarction (TIMI) Study Group. The Thrombolysis in Myocardial Infarction (TIMI) Trial. N Engl J Med 1985;312:932–6.
21. Califf RM, Abdelmeguid AE, Kuntz RE, et al. Myonecrosis after revascularization procedures. J Am Coll Cardiol 1998;31:241–51.
22. Savage MP, Douglas JS, Sischman DL, et al., for the Saphenous Vein De Novo Trial Investigators. Stent placement compared with balloon angioplasty for obstructed coronary bypass grafts. N Engl J Med 1997;337:740–7.
23. Klein LW. Balloon angioplasty of internal mammary artery bypass grafts: bailing out the surgeons. Cathet Cardiovasc Diagn 1998;44: 157–8.
24. Yang Z, Ruschitzka F, Rabelink TJ, et al. Different effects of thrombin receptor activation on endothelium and smooth muscle cells of human coronary bypass vessels. Implications for venous bypass graft failure. Circulation 1997;95:1870–6.
25. Luscher TF, Diederich D, Siebenmann R, et al. Difference between endothelium-dependent relaxations in arterial and in venous coronary bypass grafts. N Engl J Med 1988;319:462–7.
26. Yang ZH, Stultz P, Von Segesser L, Bauer E, Turina M, Luscher TF. Different interactions of platelets with arterial and venous coronary bypass vessels. Lancet 1991;337:939–43.
27. Yang Z, Oemar BS, Carrel T, Kipfer B, Julmy F, Luscher TF. Different proliferative properties of smooth muscle cells of human arterial and venous bypass vessels. Role of PDGF receptors, mitogen-activated protein kinase and cyclin-dependent kinase inhibitors. Circulation 1998;97:181–7.
28. Dangas G, Fuster V. Management of restenosis after coronary intervention. Am Heart J 1996;132:428–36.