JACC: CARDIOVASCULAR INTERVENTIONS VOL. 7, NO. 7, 2014

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jcin.2014.01.164

Native Coronary Artery Patency After Coronary Artery Bypass Surgery

David Pereg, MD,* Paul Fefer, MD,*† Michelle Samuel, BA, MPH,* Rafael Wolff, MD,* Andrew Czarnecki, MD,* Saswata Deb, MD,‡ John D. Sparkes, MSc,* Stephan E. Fremes, MD,‡§ Bradley H. Strauss, MD, PhD*‖

Toronto, Ontario, Canada; and Tel Aviv, Israel

Objectives The aim of the study was to determine native coronary artery patency 1 year after coronary artery bypass grafting and to identify clinical and angiographic predictors for the development of a chronic total occlusion (CTO).

Background In contrast to the large body of information regarding graft patency, data regarding atherosclerosis progression and vessel patency in surgically bypassed native coronary arteries are less clear.

Methods Of the 440 patients who underwent 1-year follow-up angiography as part of the multicenter RAPS (Radial Artery Patency Study), included in our study were 388 patients (88%) for whom angiograms were available for review. Angiograms were reviewed for native coronary artery patency in an independent blinded manner.

Results On the pre-operative angiogram, CTO of at least 1 native coronary vessel was demonstrated in 240 patients (61.9%) having 305 occluded vessels. At 1 year after coronary artery bypass grafting, at least 1 new native coronary artery CTO occurred in 169 patients (43.6%). In 7.5% of patients, the native artery and the graft supplying that territory were both occluded. A new CTO was almost 5 times more likely to occur in coronary vessels with a pre-operative proximal stenosis >90% compared with vessels with proximal stenosis <90% (45.5% vs. 9.5%, respectively, $p < 0.001$). Patients with a new CTO had significantly more baseline Canadian Cardiovascular Society class 4 angina compared with patients without a new CTO. A new CTO was less likely to occur in the left anterior descending artery (18.4%), supplied by the left internal thoracic artery. When comparing radial artery and saphenous vein grafts, neither the type of graft nor graft patency had any association with native coronary artery occlusion.

Conclusions CTO of surgically bypassed coronary arteries 1 year after coronary artery bypass grafting is extremely common. (J Am Coll Cardiol Intv 2014;7:761–7) © 2014 by the American College of Cardiology Foundation

From the *Division of Cardiology, Schulich Heart Program, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; †Leviev Heart Center, Sheba Medical Center, Tel Aviv University, Tel Hashomer, Israel; ‡Division of Cardiovascular Surgery, Schulich Heart Program, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada; §Bernard S. Goldman Chair in Cardiovascular Surgery, Sunnybrook Health Sciences Center, University of Toronto, Toronto, Ontario, Canada; and ‖Reichmann Chair in Cardiovascular Sciences, Sunnybrook Health Sciences Center, University of Toronto, Toronto, Ontario, Canada. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received October 23, 2013; revised manuscript received December 18, 2013, accepted January 4, 2014.

Coronary artery bypass grafting (CABG) remains the most common revascularization mode for patients with multivessel coronary artery disease. Several studies have demonstrated better long-term patency and improved survival after CABG with internal thoracic artery (ITA) grafts (1–4). Therefore, the left ITA has traditionally been used to bypass the anterior coronary circulation. Furthermore, the multicenter RAPS (Radial Artery Patency Study) demonstrated that radial artery grafts are associated with a lower rate of graft occlusion at 1 year than are saphenous vein grafts (SVGs) (5). These findings have been supported by several smaller studies (6–8). Unlike the large body of information regarding graft patency, data regarding atherosclerosis progression in surgically bypassed native coronary arteries are less clear and derived mainly from studies conducted >3 decades ago, before the use of the left ITA and radial grafts and widespread statin use. The available studies have demonstrated accelerated atherosclerosis progression that was as much as 10 times as frequent in bypassed arteries as in comparable arteries that were not bypassed (9–13). Nevertheless, in most of those studies, follow-up angiograms were obtained several years after CABG using saphenous vein bypass grafts, and data regarding native coronary artery disease progression and especially the rate of postoperative complete occlusion are not clear. The status of the native coronary circulation and especially the prevalence of chronic total occlusion (CTO) in patients post-CABG are clinically important when considering revascularization after graft failure. A recent multicenter registry of CTO percutaneous coronary intervention (PCI) demonstrated lower technical success rates in patients with previous CABG compared with patients without previous CABG (14). The purposes of the current study were to determine native coronary artery patency 1 year after CABG and to identify clinical and angiographic risk factors for native coronary vessel occlusion using data from the RAPS database.

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CCS = Canadian Cardiovascular Society
CTO = chronic total occlusion
ITA = internal thoracic artery
LAD = left anterior descending artery
LCX = left circumflex artery
PCI = percutaneous coronary intervention
RCA = right coronary artery
SVG = saphenous vein graft

Methods

Study population. The study population consisted of patients enrolled in the multicenter RAPS between November 1996 and January 2001, which mandated 1-year follow-up angiography. The primary objective of the RAPS was to compare the longitudinal patency of the radial artery and saphenous vein. Details of the study protocol were previously published (5). Briefly, patients enrolled were younger than 80 years of age undergoing nonemergent primary isolated CABG for triple-vessel disease with an estimated left ventricular ejection fraction of >35%. The left ITA was used to bypass the left anterior descending artery (LAD) circulation, and patients were randomly assigned to 1 of 2 graft strategies: (1) the radial artery was used to graft the left circumflex artery (LCX) territory and an SVG was used for the right coronary artery (RCA) or (2) the radial artery was directed to the RCA territory and an SVG was used for the LCX system. The target vessels for the radial artery and study saphenous vein were deemed to be at least 1.5 mm in diameter with a proximal stenosis of at least 70% by visual inspection. The primary study endpoint was the proportion of radial arteries and study saphenous veins that were completely occluded at 1 year after surgery. Complete occlusion was defined as the absence of opacification of the target coronary artery (i.e., Thrombolysis In Myocardial Infarction flow grade 0). Of the 440 participants who underwent 1-year follow-up angiography, included in our study were only 388 patients for whom coronary angiograms were still available for review at the time of our study.

Study endpoints. The primary endpoint of our study was the occurrence of a new complete native coronary artery occlusion at 1 year post-surgery. In the present study, we focused only on the 3 main coronary vessels (i.e., LAD, LCX, and RCA). Therefore, diagonal branches, even if grafted, were excluded.

Perioperative management. The surgical technique used in this study was previously described (5). Patients were given 325 mg of aspirin daily within 6 h postoperatively and continued indefinitely. Oral nifedipine was initiated on the first postoperative day and continued to 6 months for prophylaxis against radial artery spasm.

Follow-up angiography. Patients underwent follow-up coronary angiography 8 to 12 months after surgery. The protocol required injection of each study graft with at least 2 orthogonal views. Analysis of baseline angiograms were conducted at enrollment to the RAPS by the local study investigators. The 1-year angiograms were reviewed by 2 interventional cardiologists who were blinded to the baseline interpretation. Coronary arteries were determined to be occluded if no contrast dye injected into it opacified the distal vessel (i.e., Thrombolysis In Myocardial Infarction flow grade 0).

Ethical considerations. Institutional research ethics board approval was obtained for this study. All patients provided informed consent.

Statistical analysis. The primary objective was to determine the patency of native coronary arteries at 8 to 12 months after CABG and to identify clinical and angiographic predictors of CTO. Student's *t* test was used to compare continuous variables with creatinine normalized by a log transformation. A chi-square, Fisher exact, or a Mann-Whitney *U* test was used where appropriate to compare categorical variables between patients with and without new

coronary CTOs. Statistical significance was assumed for $p < 0.05$.

Results

Patient characteristics. The 388 patients for whom 1-year post-operative coronary angiograms were available had a mean age of 60.3 ± 8.5 years and included 338 males (87.1%) (Table 1). This study was representative of the overall RAPS population, without any significant differences in baseline characteristics (5). CTO of at least 1 native coronary artery on the preoperative coronary angiogram was relatively common, with 240 (61.9%) of patients having 305 occluded vessels (Table 2, Fig. 1). The RCA was by far the most commonly occluded vessel on the preoperative angiogram (40%), followed by the LCX (19.5%) and LAD (18.8.%). The primary endpoint of at least 1 new complete native coronary artery occlusion at 1 year post-surgery occurred in 169 patients(43.6%) who had 212 new occluded coronary vessels, with the RCA still being the most commonly newly occluded vessel (38.6%, 34%, and 27.4% for the RCA, LCX, and LAD, respectively).

Table 1. Baseline Characteristics of Patients With or Without a New CTO at 1 Year Post-CABG

Characteristic	All (N = 388)	New CTO (n = 169)	No New CTO (n = 219)	p Value
Age, yrs	60.3 ± 8.5	60.8 ± 8.3	60 ± 8.6	0.94
Age >70 yrs	60 (15.5)	27 (16)	33 (15)	
Male sex	338 (87.1)	145 (85.8)	193 (88.1)	0.5
Preoperative MI	177 (45.6)	78 (46.2)	99 (40.2)	0.85
Nonelective surgery	125 (32.2)	63 (37.3)	62 (28.3)	0.06
Current smoker	68 (17.5)	29 (17.2)	39 (17.8)	0.87
Hypertension	180 (46.4)	81 (47.9)	99 (45.2)	0.59
Hypercholesterolemia	268 (69.0)	117 (69.2)	151 (68.9)	0.95
PVD history	27 (7.0)	13 (7.7)	14 (6.4)	0.62
Diabetes mellitus	106 (27.3)	45 (26.6)	61 (27.9)	0.79
Insulin treatment	20 (5.2)	6 (3.6)	14 (6.4)	0.21
CCS class of angina				0.0009
1	5 (1.3)	2 (1.2)	3 (1.4)	
2	95 (24.5)	33 (19.5)	62 (28.3)	
3	191 (49.2)	77 (45.6)	114 (52.0)	
4	97 (25.0)	57 (33.7)	40 (18.3)	
Left ventricular grade				0.92
1	191 (49.2)	91 (53.8)	100 (45.7)	
2	192 (49.5)	77 (45.6)	115 (52.5)	
3	4 (1.0)	1 (0.6)	3 (1.4)	
4	1 (0.3)	0	1 (0.4)	
Creatinine, μmol/l	89.7 ± 19.3	93.1 ± 21.5	92 ± 17.3	0.08

Values are mean ± SD or n (%).
CABG = coronary artery bypass grafting; CCS = Canadian Cardiovascular Society; CTO = chronic total occlusion; MI = myocardial infarction; PVD = peripheral vascular disease.

Table 2. Native Coronary Artery CTO Prevalence and Distribution on the Preoperative Angiogram and at 1 Year

Pre-operative angiogram	
Total no. of patients with ≥1 CTO	240 (61.9)
Total of CTO vessels	305
LAD	73 (18.8)
LCX	76 (19.5)
RCA	156 (40)
1-year angiogram	
Patients with ≥1 new CTO	169 (43.6)
Patients with 1 new CTO	133 (34.3)
Patients with 2 new CTOs	29 (7.5)
Patients with 3 new CTOs	7 (1.8)
New CTO in native coronary vessels	212
LAD	58 (27.4)
LCX	72 (34.0)
RCA	82 (38.6)
Total CTO in native coronary vessels	
LAD	131 (33.8)
LCX	148 (38.1)
RCA	238 (61.35)

Values are n (%).
CTO = chronic total occlusion; LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery.

Clinical predictors for native coronary artery occlusion. Although most baseline characteristics, including all the traditional cardiovascular risk factors, were comparable between the 2 groups, patients with a new native coronary vessel occlusion more frequently had Canadian Cardiovascular Society (CCS) class 4 angina pectoris (Table 1). There was also a trend toward a higher rate of nonelective surgery and higher serum creatinine levels among patients with a new native coronary artery occlusion. Sixty-eight percent of patients were treated with a statin at 1 year post-surgery. There was no significant difference in statin therapy rate between patients with or without a new native coronary vessel occlusion (66.9% and 68.9%, respectively, $p = 0.66$).

Angiographic predictors of native coronary artery occlusion. A new native coronary artery occlusion was almost 5 times more likely to occur in vessels with a proximal stenosis >90% by visual inspection on the pre-operative angiogram compared with vessels with a proximal stenosis <90% (Fig. 2). Furthermore, complete occlusions were more common in vessels bypassed by either an SVG or radial artery grafts (29.2% and 27.4%, respectively) compared with the LAD (18.4%) that was grafted by the left ITA (Fig. 3). In a comparison of vessels grafted by an SVG or radial artery, there was no association between graft type and native coronary artery patency.

Similar to the original RAPS results, radial artery grafts were associated with a lower rate of graft occlusion at 1 year. In our cohort, complete graft occlusion occurred in 12.9%

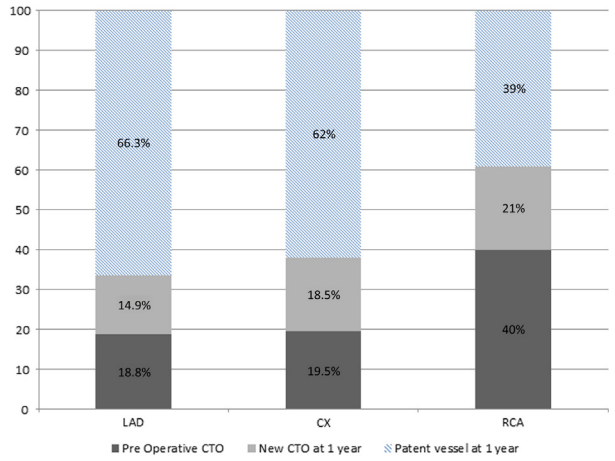

Figure 1. Native Coronary Artery Patency Pre-CABG and at 1-Year Follow-up

CTOs were most common in the RCA pre-CABG and lowest in the LAD. New CTOs also were more frequent in the RCA during the first year. LAD and CX occlusions were similar pre-CABG and at 1 year. CABG = coronary artery bypass grafting; CTO = chronic total occlusion; CX = left circumflex artery; LAD = left anterior descending artery; RCA = right coronary artery.

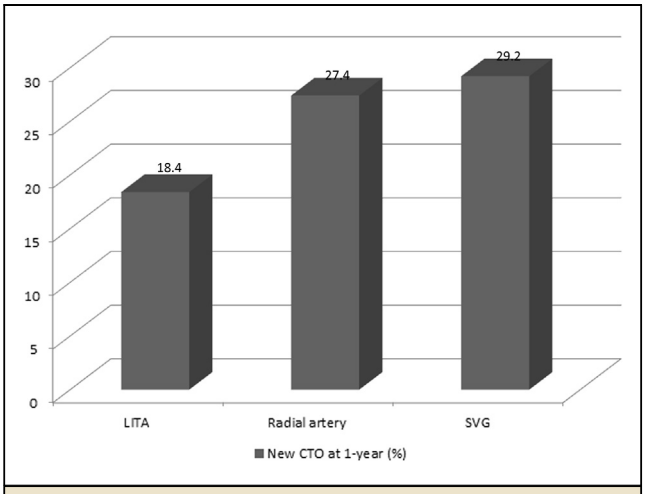

Figure 3. New Native Coronary Artery Occlusion at 1 Year After CABG According to the Graft Type

The risk of the development of a new CTO at 1 year was significantly lower in the LAD grafted by the left internal thoracic artery (LITA) compared with the CX and RCA that were grafted by either a radial artery graft or saphenous vein graft (SVG) ($p = 0.01$ for a comparison of radial artery and LITA graft; $p = 0.0025$ for a comparison of an SVG and LITA graft). There were no differences in native artery patency in arteries grafted with an SVG compared with the radial artery ($p = 0.7$). Other abbreviations as in Figure 1.

of SVGs and 8% of radial artery grafts (50 of 388 vs. 31 of 388). To assess a possible association between graft and new native vessel occlusion, grafts initially used to bypass a completely occluded coronary artery were excluded. Although patent grafts appeared to be associated with an increased risk of native coronary artery occlusion at 1 year, this association was not found to be statistically significant ($p = 0.26$) (Fig. 4). In 29 (7.5%) patients, a complete occlusion of both the bypassed native coronary artery and its graft was demonstrated on the 1-year coronary angiogram, causing the absence of antegrade distal blood flow to this territory.

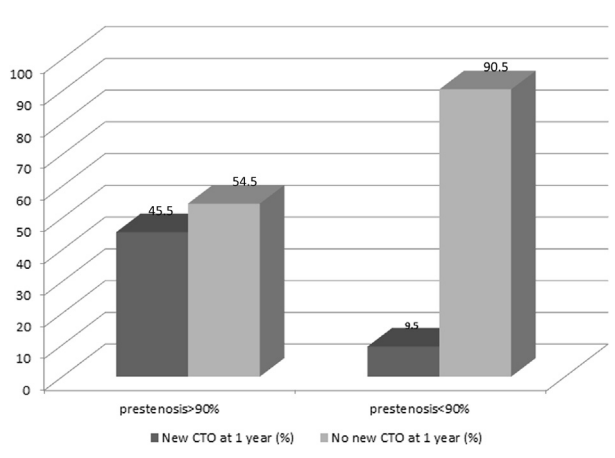

Figure 2. New Native Coronary Artery CTO at 1 Year According to Pre-Operative Stenosis Severity

A preoperative stenosis of >90% at baseline was associated with a significantly increased risk of progression to CTO at 1 year compared with preoperative stenosis <90% ($p < 0.0001$). CTO = chronic total occlusion.

Discussion

This clinical study included 388 patients who underwent bypass surgery using the same surgical technique and who underwent coronary angiography at 1 year as part of the study protocol. It was designed to assess native coronary artery patency at 1 year post-CABG, based on the multicenter RAPS database. We demonstrated that a complete occlusion of a native coronary vessel is common among the surgical population on both the pre- and postoperative angiograms with a new CTO of a native coronary artery developing in >40% of post-CABG patients at 1 year. Predictors of a new coronary artery occlusion included CCS class 4 angina and a proximal stenosis of >90% on the preoperative angiogram.

Disease progression in surgically bypassed coronary arteries has been the subject of several studies. A study of 85 men who had undergone CABG identified bypass grafts placed in 37 native arteries with mild atherosclerosis and 93 coronary vessels with mild atherosclerosis for which a bypass graft had not been placed (10). Progression of atherosclerosis, defined as further loss of at least 25% of the

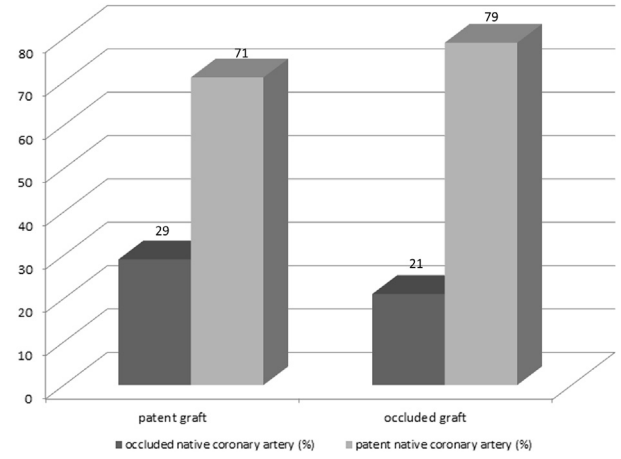

Figure 4. Relationship Between New Native Coronary Artery Occlusion and Graft Patency at 1 Year

Grafts used to bypass a coronary artery with CTO pre-CABG were excluded from this analysis. Patent grafts were associated with a modest but nonsignificant increase in native coronary artery CTO at 1 year ($p = 0.26$). Abbreviations as in Figure 1.

lumen, during an average follow-up period of 3 years was >10 times as frequent in bypassed arteries with minimal atherosclerosis as in comparable arteries that were not bypassed (38% vs. 3%). Another study of 109 patients evaluated 5 years after surgery demonstrated that the risk of disease progression was 3 to 6 times higher in grafted compared with ungrafted arteries (11). For grafted arteries, the risk of progression was twice as high in arteries with patent grafts compared with those with closed grafts. The majority (78%) of grafted arteries with progression were completely occluded. These findings were supported by another study of 82 patients examined 10 years after SVG bypass surgery (9). However, although these studies consistently demonstrated enhanced atherosclerosis in the bypassed coronary vessels, their results are limited by the relatively small population, repeat angiography was not mandated by protocol, angiographic follow-up was 3 to 10 years post-surgery, and all studies were performed 3 decades ago. Since that time, several aspects of CABG have changed dramatically, including surgical techniques such as the routine use of the left ITA to bypass the anterior coronary circulation and the introduction of radial artery grafts as well as adjuvant medical therapy such as potent statins and antiplatelet agents. Accelerated disease progression was demonstrated in 2 more recent studies (12,13). However, in these particular studies, follow-up coronary angiograms were not obtained routinely but only when symptoms developed in patients. Therefore, there may have been a selection bias in which only the patients with more severe coronary disease were evaluated.

The accelerated atherosclerosis and the relatively high rate of native coronary occlusion during the first operative year are clinically important when considering revascularization in post-CABG patients after graft failure. We demonstrated an occlusion of both the bypassed native coronary artery and its graft in 7.5% of patients. However, this rate is expected to increase later in the postoperative period due to further progression of atherosclerosis in the native coronary vessels and anticipated graft failure. Re-achieving coronary revascularization in post-CABG patients with CTO is challenging and associated with lower success rates. In a recent multicenter registry of CTO PCI, previous CABG was independently associated with lower technical success rate (odds ratio: 0.49; 95% confidence interval: 0.35 to 0.70; $p < 0.001$) (14). These findings highlight the fact that although coronary revascularization with CABG provides significant prognostic and symptomatic benefit, it is also associated with increased coronary disease atherosclerosis burden and limited future PCI options.

The mechanisms leading to disease progression and CTO formation in surgically bypassed native coronary arteries are not fully explained. Similar to previous reports, we demonstrated that the prevalence of all traditional cardiovascular risk factors, including diabetes mellitus, was similar among patients with and without new coronary artery occlusion at 1 year, suggesting that this process differs in some respects from the atherosclerosis in nonbypassed vessels. One plausible explanation is flow competition between the native vessel and the graft (9–13). High competitive flow has been demonstrated to result in low and oscillatory wall shear stress (15,16). These alterations in wall shear stress have been linked to enhanced coronary artery disease progression through marked impairment of endothelial function (15–17). Low wall shear stress up-regulates endothelin-1 (15,18) and thrombomodulin (19), while down-regulating nitric oxide and prostacyclin production (15,18) by endothelial cells. These alterations in endothelium-derived vasoactive agents alter vascular tone and influence atherogenic processes by promoting smooth muscle migration and proliferation (20), enhanced matrix breakdown (21), increased endothelial permeability to lipoproteins and collagen depositions (22), as well as leukocyte (23) and platelet (24) adhesion. These processes result in excessive remodeling, increased wall thickening, and enhanced atherosclerosis (25,26). These vascular changes further contribute to the underlying flow stasis and procoagulant state caused by the oscillatory wall shear stress (27,28), the nonlaminar flow, and the endothelial dysfunction, which can ultimately lead to atherothrombosis and coronary artery occlusion at the lesion site.

In the current study, the strongest predictor of a new native coronary vessel occlusion was the presence of CCS class 4 angina pectoris before surgery. Furthermore, a new

native coronary artery occlusion was almost 5 times more likely to occur in vessels with a proximal stenosis >90% on the pre-operative angiogram compared with vessels with proximal stenosis <90%. These findings suggest a positive correlation between baseline coronary artery disease severity and enhanced atherosclerosis, an association reported in previous studies (11,12).

Several studies, including the RAPS, have demonstrated that for all graft types, graft patency was lower in the absence of severe native vessel stenosis (5,29,30). This inverse association remained when native vessel patency was examined, with significantly more severe disease progression in a vessel bypassed by a patent compared with an occluded graft (11,13). In our study, patent radial artery or vein grafts appeared to be associated with an increased risk of native coronary artery occlusion at 1 year. However, this association was not statistically significant. This may be explained by the relatively low incidence of graft occlusion within the first year among patients included in the RAPS (8.2% for radial artery grafts and 13.6% for SVGs). Native coronary occlusion was significantly less frequent in the LAD that was bypassed by the left ITA compared with the LCX and RCA that were bypassed by either a radial artery or an SVG. This may be attributed to the larger vessel size of the LAD, which may decrease the risk of complete occlusion. Another potential explanation is the flow rate in the left ITA that may be associated with less stasis of blood through the native coronary artery.

Study limitations. Although our study is the first to evaluate native coronary artery patency at 1 year post-CABG, it has several limitations that require consideration. First, the study was based on the multicenter RAPS database. However, of the 440 RAPS patients who underwent 1-year follow-up angiography, our study included 388 patients (88%) for whom coronary angiograms were still available for review. Similar clinical and angiographic parameters in the 2 cohorts suggest that our cohort was very representative of the original RAPS. Although our study represents the largest patient cohort to date evaluated for native vessel patency after bypass surgery, our findings may still be limited by the relatively small sample size. Third, the primary endpoint was the occurrence of a new complete native coronary artery occlusion at 1 year post-CABG, and it did not include other measurements of coronary disease progression or clinical outcomes. The development of a CTO from a previously patent coronary artery is a critical step in coronary artery disease progression because revascularization by PCI of a CTO is much more challenging and associated with significantly lower success rates and a higher risk of periprocedural complications (14). Fourth, our study did not perform angiographic quantitative analysis of native coronary vessel size or various lesion characteristics such as length and distance of the lesion relative to the graft site, parameters that may affect the risk of vessel occlusion.

Conclusions

Even in contemporary cardiovascular surgical practice, the development of a new CTO of bypassed native coronary artery is common in post-CABG patients even within the first postoperative year. This process, which is secondary to enhanced coronary atherosclerosis, may result in the recurrence of symptoms that are particularly challenging for revascularization.

Reprint requests and correspondence: Dr. Bradley H. Strauss, Schulich Heart Program, Sunnybrook Health Sciences Centre, Room D-408, 2075 Bayview Avenue, Toronto, Ontario M4N 3M5, Canada. E-mail: Bradley.strauss@sunnybrook.ca.

REFERENCES

1. Goldman S, Zadina K, Moritz T, et al. Long-term patency of saphenous vein and left internal mammary artery grafts after coronary artery bypass surgery: results from a Department of Veterans Affairs Cooperative Study. J Am Coll Cardiol 2004;44:2149–56.
2. Cho KR, Kim JS, Choi JS, Kim KB. Serial angiographic follow-up of grafts one year and five years after coronary artery bypass surgery. Eur J Cardiothorac Surg 2006;29:511–6.
3. Gansera B, Schmidtler F, Angelis I, Kiask T, Kemkes BM, Botzenhardt F. Patency of internal thoracic artery compared to vein grafts—postoperative angiographic findings in 1189 symptomatic patients in 12 years. Thorac Cardiovasc Surg 2007;55:412–7.
4. Schmidt SE, Jones JW, Thornby JI, Miller CC, Beall AC. Improved survival with multiple left-sided bilateral internal thoracic artery grafts. Ann Thorac Surg 1997;64:9–14.
5. Desai ND, Cohen EA, Naylor CD, Fremes SE. A randomized comparison of radial-artery and saphenous-vein coronary bypass grafts. N Engl J Med 2004;351:2302–9.
6. Collins P, Webb CM, Chong CF, Moat NE. Radial artery versus saphenous vein patency randomized trial: five-year angiographic follow-up. Circulation 2008;117:2859–64.
7. Gaudino M, Cellini C, Pragliola C, Trani C, et al. Arterial versus venous bypass grafts in patients with in-stent restenosis. Circulation 2005;112:I265–9.
8. Zacharias A, Schwann TA, Riordan CJ, et al. Late outcomes after radial artery versus saphenous vein grafting during reoperative coronary artery bypass surgery. J Thorac Cardiovasc Surg 2010;139:1511–8.
9. Campeau L, Enjalbert M, Lespérance J, et al. The relation of risk factors to the development of atherosclerosis in saphenous-vein bypass grafts and the progression of disease in the native circulation. A study 10 years after aortocoronary bypass surgery. N Engl J Med 1984;311:1329–32.
10. Cashin WL, Sanmarco ME, Nessim SA, Blankenhorn DH. Accelerated progression of atherosclerosis in coronary vessels with minimal lesions that are bypassed. N Engl J Med 1984;311:824–8.
11. Kroncke GM, Kosolcharoen P, Clayman JA, Peduzzi PN, Detre K, Takaro T. Five-year changes in coronary arteries of medical and surgical patients of the Veterans Administration Randomized Study of Bypass Surgery. Circulation 1988;78:I144–50.
12. Hayward PA, Zhu YY, Nguyen TT, Hare DL, Buxton BF. Should all moderate coronary lesions be grafted during primary coronary bypass surgery? An analysis of progression of native vessel disease during a randomized trial of conduits. J Thorac Cardiovasc Surg 2013;145:140–8.
13. Hamada Y, Kawachi K, Yamamoto T, et al. Effect of coronary artery bypass grafting on native coronary artery stenosis. Comparison of internal thoracic artery and saphenous vein grafts. Cardiovasc Surg (Torino) 2001;42:159–64.
14. Michael TT, Karmpaliotis D, Brilakis ES, et al. Impact of prior coronary artery bypass graft surgery on chronic total occlusion revascularisation: insights from a multicentre US registry. Heart 2013;99:1515–8.

15. Meng X, Fu Q, Sun W, Yu J, Yue W, Bi Y. Competitive flow arising from varying degrees of coronary artery stenosis affects the blood flow and the production of nitric oxide and endothelin in the internal mammary artery graft. Eur J Cardiothorac Surg 2013;43:1022–7.
16. Nordgaard H, Swillens A, Nordhaug D, et al. Impact of competitive flow on wall shear stress in coronary surgery: computational fluid dynamics of a LIMA-LAD model. Cardiovasc Res 2010;88:512–9.
17. Malek AM, Alper SL, Izumo S. Hemodynamic shear stress and its role in atherosclerosis. JAMA 1999;282:2035–42.
18. Dancu MB, Berardi DE, Vanden Heuvel JP, Tarbell JM. Asynchronous shear stress and circumferential strain reduces endothelial NO synthase and cyclooxygenase-2 but induces endothelin-1 gene expression in endothelial cells. Arterioscler Thromb Vasc Biol 2004;24:2088–94.
19. Malek AM, Izumo S. Molecular aspects of signal transduction of shear stress in the endothelial cell. J Hypertens 1994;12:989–99.
20. Qi YX, Qu MJ, Long DK, et al. Rho-GDP dissociation inhibitor alpha downregulated by low shear stress promotes vascular smooth muscle cell migration and apoptosis: a proteomic analysis. Cardiovasc Res 2008;80:114–22.
21. Magid R, Murphy TJ, Galis ZS. Expression of matrix metalloproteinase-9 in endothelial cells is differentially regulated by shear stress. Role of c-Myc. J Biol Chem 2003;278:32994–9.
22. Niwa K, Kado T, Sakai J, Karino T. The effects of a shear flow on the uptake of LDL and acetylated LDL by an EC monoculture and an EC-SMC coculture. Ann Biomed Eng 2004;32:537–43.
23. Hsiai TK, Cho SK, Wong PK, et al. Monocyte recruitment to endothelial cells in response to oscillatory shear stress. FASEB J 2003;17:1648–57.
24. Nguyen KT, Eskin SG, Patterson C, Runge MS, McIntire LV. Shear stress reduces protease activated receptor-1 expression in human endothelial cells. Ann Biomed Eng 2001;29:145–52.
25. Stone PH, Coskun AU, Kinlay S, et al. Effect of endothelial shear stress on the progression of coronary artery disease, vascular remodeling, and in-stent restenosis in humans: in vivo 6-month follow-up study. Circulation 2003;108:438–44.
26. Chatzizisis YS, Coskun AU, Jonas M, Edelman ER, Feldman CL, Stone PH. Role of endothelial shear stress in the natural history of coronary atherosclerosis and vascular remodeling: molecular, cellular, and vascular behavior. J Am Coll Cardiol 2007;49:2379–93.
27. Koskinas KC, Chatzizisis YS, Antoniadis AP, Giannoglou GD. Role of endothelial shear stress in stent restenosis and thrombosis: pathophysiologic mechanisms and implications for clinical translation. J Am Coll Cardiol 2012;59:1337–49.
28. Wu MH, Kouchi Y, Onuki Y, et al. Effect of differential shear stress on platelet aggregation, surface thrombosis, and endothelialization of bilateral carotid-femoral grafts in the dog. J Vasc Surg 1995;22:382–90.
29. Yie K, Na CY, Oh SS, Kim JH, Shinn SH, Seo HJ. Angiographic results of the radial artery graft patency according to the degree of native coronary stenosis. Eur J Cardiothorac Surg 2008;33:341–8.
30. Moran SV, Baeza R, Guarda E, et al. Predictors of radial artery patency for coronary bypass operations. Ann Thorac Surg 2001;72:1552–6.

Key Words: coronary artery bypass grafting ■ coronary artery disease.