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

Vol. 38, No. 2, 2001
ISSN 0735-1097/01/$20.00
PII S0735-1097(01)01349-3

Procedural Outcomes and Long-Term Survival Among Patients Undergoing Percutaneous Coronary Intervention of a Chronic Total Occlusion in Native Coronary Arteries: A 20-Year Experience

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OBJECTIVES The study compared procedural outcomes and long-term survival for patients undergoing percutaneous coronary intervention (PCI) of a chronic total coronary artery occlusion (CTO) with a matched non-CTO cohort to determine whether successful PCI of a CTO is associated with improved survival.

BACKGROUND Percutaneous coronary intervention of a CTO is a common occurrence, and the long-term survival for patients with successful PCI of a CTO has not been clearly defined.

METHODS Between June 1980 and December 1999, a total of 2,007 consecutive patients underwent PCI for a CTO. Utilizing propensity scoring methods, a matched non-CTO cohort of 2,007 patients was identified and compared to the CTO group. The cohorts were stratified into successful and failed procedures.

RESULTS The in-hospital major adverse cardiac event (MACE) rate was 3.8% in the CTO cohort. Technical success has improved over the last 10 years (overall 74.4%, slope 1.0%/yr, $p = 0.02$, $R^2 = 49.9\%$) as did procedural success (overall 69.9%, slope 1.2%/yr, $p = 0.02$, $R^2 = 51.5\%$) without a concomitant increase in in-hospital MACE rates (slope 0.1%/yr, $p = 0.7$). There was a distinct 10-year survival advantage for successful CTO treatment compared with failed CTO treatment (73.5% vs. 65.1%, $p = 0.001$). The CTO versus non-CTO 10-year survival was the same (71.2% vs. 71.4%, $p = 0.9$). Diabetics in the CTO cohort had a lower 10-year survival compared with nondiabetics (58.3% vs. 74.3%, $p < 0.0001$).

CONCLUSIONS These data represent follow-up of the largest reported series of patients undergoing PCI for a CTO. The 10-year survival rates for matched non-CTO and the CTO cohorts were similar. Success rates have continued to improve without an accompanying increase in MACE rates. A successfully revascularized CTO confers a significant 10-year survival advantage compared with failed revascularization. (J Am Coll Cardiol 2001;38:409–14) © 2001 by the American College of Cardiology

Percutaneous coronary intervention (PCI) of a chronic total coronary artery occlusion (CTO) is now a well-accepted revascularization procedure accounting for approximately 10% of patients undergoing PCI (1–3). Few large series have been published on the long-term outcome (4,5). However, it is unclear whether successfully opening a CTO is associated with an improved outcome. A previous report of 354 patients demonstrated only a trend toward improved survival among those with successful angioplasty of a CTO (5). Another report (4) demonstrated significantly improved cardiac survival in a similar cohort of 480 patients. Utilizing the 20-year experience from the Mid-America Heart Institute (MAHI), we identified patients who underwent PCI of a CTO. We present here the in-hospital complication rates, success rates and long-term clinical outcomes in 2,007 consecutive patients with chronic total occlusions.

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Manuscript received June 12, 2000; revised manuscript received April 5, 2001, accepted April 11, 2001.

METHODS

Study design. Consecutive patients who underwent PCI of a chronically occluded native coronary vessel between June 1980 to December 1999 were included in this analysis. Patients were identified as undergoing single versus multivessel PCI. Multivessel PCI included elective interventions of additional vessels within 30 days of the initial procedure. Patients with acute occlusions and those with chronic total occlusion of a saphenous venous graft were not included in this analysis. Patients were identified using the MAHI Interventional Registry. Dedicated personnel have prospectively entered patients into the MAHI Registry. The registry contains baseline demographics, clinical and procedural characteristics and in-hospital outcomes.

To compare our total CTO cohort with patients who underwent PCI of nonoccluded stenoses, we applied propensity-scoring methods to the MAHI Interventional Registry, of 25,620 patients, so as to identify a matched non-CTO cohort. Predicted probabilities of CTO were

Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery
CPK = creatine phosphokinase
CTO = chronic total coronary artery occlusion
MACE = major adverse cardiac event
MAHI = Mid-America Heart Institute
MI = myocardial infarction
MVP = multivessel procedure
PCI = percutaneous coronary intervention
PTCA = percutaneous transluminal coronary angioplasty
SVP = single-vessel procedure

estimated using logistic regression on major clinical variables including diseased vessels, age, unstable angina, prior revascularization, prior myocardial infarction (MI), date of procedure and ejection fraction. Both CTO and non-CTO patients were matched by predictor values described by D'Agostino (6).

The CTO cohort and non-CTO cohorts were further stratified into single-vessel (SVP) and multivessel (MVP) procedures, and subsequently grouped on the basis of a technically successful procedure. Follow-up information was obtained through the Social Security Death Index. Long-term follow-up was available for 93.6% of the CTO cohort, with a mean follow-up time of 91.4 ± 55.4 months.

DEFINITIONS

A CTO was defined as a lesion exhibiting Thrombolysis In Myocardial Infarction flow grade 0–1 of a native coronary artery. Patients were excluded if they had sustained an acute MI within seven days prior to the procedure. Patients were identified as individuals admitted for PCI. Individuals, therefore, may be present more than once. Technical success was defined as the ability to cross the occluded segment with both a wire and balloon and successfully open the artery with a <40% residual stenosis in all views. Procedural success was defined as a technical success with no in-hospital major adverse cardiac event (MACE). A CTO success was defined as a technical success. A MACE was defined as the occurrence of death, Q-wave MI or urgent revascularization. Urgent revascularization was classified by operators caring for patients and required repeat PCI of target vessel during the same admission or coronary artery bypass graft surgery (CABG) including bypass of the target vessel. Routine creatine kinase or creatine kinase-MB fraction data were not routinely collected post-PCI. The MI component of MACE includes only the Q-wave MI rate. The non–Q-wave MI rate is presented separately. We identified both new Q-wave and non–Q-wave MIs. An SVP was defined as either PCI of the CTO segment only, or of the CTO segment plus additional lesions of the same occluded vessel. An MVP encompassed dilation in the occluded vessel plus dilation of vessels other than the CTO vessel within 30 days. Repeat percutaneous transluminal coronary angioplasty (PTCA) was defined as a subsequent procedure in the occluded vessel.

INTERVENTIONAL TECHNIQUE

Angioplasty was performed using standard over-the-wire techniques, as previously described (7). The technique has been modified over time by utilization of second-generation guide wires, including the Choice PT (Boston Scientific, Watertown, Massachusetts), Shinobi (Cordis, Miami, Florida) and Cross-It (Guidant, Santa Clara, California) wires. Stents were used after PTCA in 7.0% of the cohort. Stented patients were treated with coumadin for one month until post-stenting therapy was changed to a thienopyridine (ticlopidine or clopidogrel) in 1996 (8). All patients were treated with aspirin indefinitely, and all patients received heparin at the time of the procedure to achieve an activated clotting time of 250 to 350 s.

END POINTS AND STATISTICS

The primary end points for this analysis were in-hospital complications, procedural success rates and 10-year cumulative survival.

A propensity scoring method was used to identify a non-CTO cohort, matched on the basis of age, ejection fraction, diseased vessels treated, prior revascularization, prior MI, unstable angina status and chronological date treated (9). The propensity score is the estimated probability of group selection (in this case, of having a CTO). These scores were obtained using logistic regression, with CTO as the dependent variable on the selection covariates. By matching CTO and non-CTO patients with similar propensity scores, comparable cohorts were obtained having similar distributions of risk factors.

Data are listed as mean ± SD. Kaplan-Meier estimates were used to depict survival and events, and log-rank analysis was used to compare survival curves (in one case where survival curves crossed, the Wilcoxon rank-sum test was used). Continuous variables were analyzed for significance by the unpaired Student *t* test. Discrete variables were analyzed by chi-square or the Fisher exact test. All statistical calculations were performed with SAS version 6.12 statistical software. A p value of <0.05 was considered statistically significant. Time to all-cause mortality was compared between CTO success and failure groups using proportional hazards regression, controlling for major risk factors, including ejection fraction, age, diabetes, number of diseased vessels, creatinine and unstable angina. Adjusted hazard ratios, 95% confidence intervals and p values are reported.

RESULTS

Baseline demographics. We identified a total of 2,007 patients who underwent PCI of a CTO during the period of June 1980 to December 1999. The baseline demographics for this cohort and the matched non-CTO cohort are

Table 1. Baseline Demographics

	CTO (n = 2,007)	Non-CTO (n = 2,007)	p Value
Age (yrs)	60.6 ± 11.4	60.5 ± 11.4	0.7
Women	437 (21.8)	443 (22.1)	0.8
Age >70 yrs	473 (23.6)	475 (23.7)	0.9
Age >80 yrs	72 (3.6)	84 (4.2)	0.3
Diabetes	416 (20.7)	390 (19.4)	0.3
Insulin treatment	156 (7.8)	167 (8.3)	0.5
Hypertension	932 (46.4)	975 (48.6)	0.2
Hyperlipidemia	1158 (58.7)	1140 (58.3)	0.8
Morbid obesity	104 (5.9)	108 (6.2)	0.7
Creatinine >1.5 mg/dl	151 (7.9)	153 (8.1)	0.9
CCS angina class 4	740 (37.0)	768 (38.4)	0.8
Prior AMI	1101 (54.9)	1097 (54.7)	0.9
Prior PCI	721 (35.9)	738 (36.8)	0.6
Prior CABG	357 (17.8)	341 (17.0)	0.5
No. diseased vessels			0.1
1	501 (25.0)	502 (25.0)	
2	745 (37.1)	690 (34.4)	
3	761 (37.9)	815 (40.6)	
EF (%)	51.3 ± 13.8	51.7 ± 14.6	0.5
LVEF <40%	312 (22.6)	318 (22.7)	1.0
LVEF <30%	121 (8.8)	131 (9.3)	0.6
Total no. vessels stented			0.02
0	1787 (89.0)	1720 (85.7)	
1	174 (8.7)	229 (11.4)	
2	42 (2.1)	53 (2.6)	
3	4 (0.2)	5 (0.2)	

Data listed as number (percent of group), mean ± SD.

AMI = acute myocardial infarction; CABG = coronary artery bypass grafting; CCS = Canadian Cardiovascular Society; CTO = chronic total coronary artery occlusion; EF = ejection fraction; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty.

shown in Table 1. A significant number of patients had multivessel disease in both groups. The baseline demographics for patients with CTO success and failure are depicted in Table 2. The CTO failure group had a higher incidence of multivessel disease and prior CABG. There

Table 2. Baseline Characteristics for the CTO Success and Failure Groups

	CTO Success (n = 1,491)	CTO Failure (n = 514)	p Value
Age	60.4 ± 11.4	61.1 ± 11.5	0.3
Women	335 (22.5)	102 (19.8)	0.2
Diabetes mellitus	316 (21.2)	100 (19.5)	0.4
Insulin treatment	120 (8.0)	36 (7.0)	0.4
Hypertension	678 (45.5)	253 (49.2)	0.1
Hyperlipidemia	856 (58.3)	302 (60.2)	0.5
Creatinine >1.5 mg/dl	117 (8.2)	34 (7.1)	0.5
CCS angina class 4	561 (37.8)	178 (34.7)	0.2
Prior MI	834 (55.9)	266 (51.8)	0.1
Prior PCI	543 (36.4)	177 (34.4)	0.4
Prior CABG	246 (16.5)	111 (21.6)	0.009
No. diseased vessels			<0.001
1	407 (27.3)	93 (18.1)	
2	550 (36.9)	195 (37.9)	
3	534 (35.8)	226 (44.0)	
Ejection fraction (%)	51.1 ± 13.8	52.0 ± 13.7	0.3

CCS = Canadian Cardiovascular Society; CTO = chronic total coronary artery occlusion.

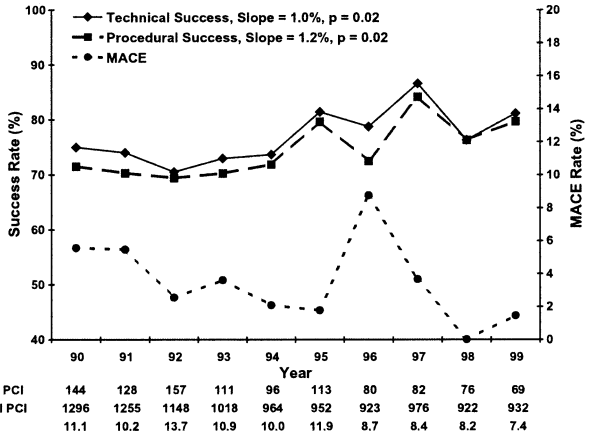

Figure 1. Technical success, procedural success and major adverse cardiac event (MACE) rates since 1990. CTO = chronic total coronary artery occlusion; PCI = percutaneous coronary intervention.

were 140 patients in this series who underwent an attempted PCI of a CTO more than one time.

Baseline anatomical characteristics. The CTO vessel was the right coronary artery in 729 (36.3%), the left anterior descending coronary artery in 752 (37.5%), the left circumflex coronary artery in 583 (29.0%) and the left main coronary artery in 10 (0.5%) patients. The majority of patients had only one CTO vessel treated (96.3%). One hundred forty-one patients (7.0%) had coronary stenting of the CTO segment following PTCA.

Technical and procedural success. The overall technical and procedural success rates were 72.3% (1,448 of 2,007 patients) and 69.9% (1,403 of 2,007 patients) for the total CTO cohort. The success rates are improving over time without an increase in MACE. Linear regression analyses of success rates over the last 10 years (Fig. 1) demonstrate improvements in both technical success (slope 1.0%/yr, $p = 0.02$, $R^2 = 49.9\%$) and procedural success (slope 1.2%/yr, $p = 0.02$, $R^2 = 51.5\%$). We found no change in MACE rates for the same period (slope −0.1%/yr, $p = 0.7$).

In-hospital complications. The in-hospital complications for the CTO and non-CTO cohorts are shown in Table 3. Total in-hospital MACE rates were similar among the two

Table 3. In-Hospital Complications for CTO and Non-CTO Cohorts

	CTO (n = 2,007)	Non-CTO (n = 2,007)	p Value
Death	27 (1.3)	17 (0.8)	0.13
Q-wave MI	10 (0.5)	12 (0.6)	0.67
Non–Q-wave MI	38 (1.9)	48 (2.4)	0.27
Urgent CABG	15 (0.7)	22 (1.1)	0.25
Urgent Re-PCI	30 (1.5)	40 (2.0)	0.23
Any dissection	357 (17.8)	267 (13.3)	<0.001
CVA	1 (0.01)	3 (0.1)	0.63
Vascular	34 (1.7)	50 (2.5)	0.08
MACE	76 (3.8)	75 (3.7)	0.9

Data listed as number of patients (percent of group).

CABG = coronary artery bypass grafting; CTO = chronic total coronary artery occlusion; CVA = cerebrovascular accident; MACE = major adverse coronary event; MI = myocardial infarction; Re-PCI = repeat percutaneous coronary intervention.

Table 4. In-Hospital Complications for CTO-Success and CTO-Failure Cohorts

	CTO Success (n = 1,491)	CTO Failure (n = 514)	p Value
Death	15 (1.0)	12 (2.3)	0.024
Q-wave MI	6 (0.4)	4 (0.8)	0.3
Non–Q-wave MI	22 (1.5)	16 (3.1)	0.02
Urgent Re-PCI	29 (1.9)	1 (0.2)	0.005
Any dissection	255 (17.1)	102 (19.8)	0.16
CVA	0 (0.0)	1 (0.2)	0.3
Vascular complications	29 (1.9)	5 (1.0)	0.1
MACE	48 (3.2)	28 (5.4)	0.023

Data listed as number of patients (percent of group).
CTO = chronic total coronary artery occlusion; CVA = cerebrovascular accident; MACE = major adverse coronary events; MI = myocardial infarction; Re-PCI = repeat percutaneous coronary intervention.

groups (CTO 76 [3.8%], non-CTO 75 [3.7%]). The Q-wave MI rate was 0.5% compared with 0.6% for the CTO and non-CTO groups, respectively, p = 0.6. The non–Q-wave MI rate was 1.9% compared with 2.4% for the CTO and non-CTO groups, respectively, p = 0.2. In-hospital complications for the CTO success and CTO-failure groups are shown in Table 4. The in-hospital MACE for CTO success was 3.2% versus 5.4% for CTO failure, p = 0.023. The Q-wave MI rate was 0.4% compared with 0.8% for the CTO success and CTO failed groups, respectively, p = 0.3. The non–Q-wave MI rate was 1.5% compared with 3.1% for the CTO success and CTO failure groups, respectively, p = 0.019. To determine the frequency of wire perforation with new-generation wires, 420 consecutive patients were identified who underwent a procedure between 1995 and 1999. We identified four wire perforations, or an incidence of 1.05%. Two patients had limited perforation requiring no additional therapy, and two had cardiac tamponade requiring urgent pericardiocentesis (0.5%). Both patients survived.

LONG-TERM RESULTS

Survival. Cumulative 10-year survival curves demonstrate a total CTO cohort survival of 71.2% compared with 71.4% for the matched non-CTO cohort (p = 0.9, Fig. 2A). Patients who had a successful revascularization of the occluded segment had a significantly higher survival at 10 years compared to the failure group (Fig. 2B, 73.5% vs. 65%, p = 0.001). There was no significant difference in 10-year survival between the CTO success group and the matched non-CTO success group (Fig. 2B, 73.5% vs. 71.9%, p = 0.33).

The SVP group of the CTO cohort experienced a superior 10-year survival when compared with the MVP group (Fig. 2C, 76.4% vs. 67.8%, p < 0.001). Similar to the total CTO cohort, the SVP success group had a significant

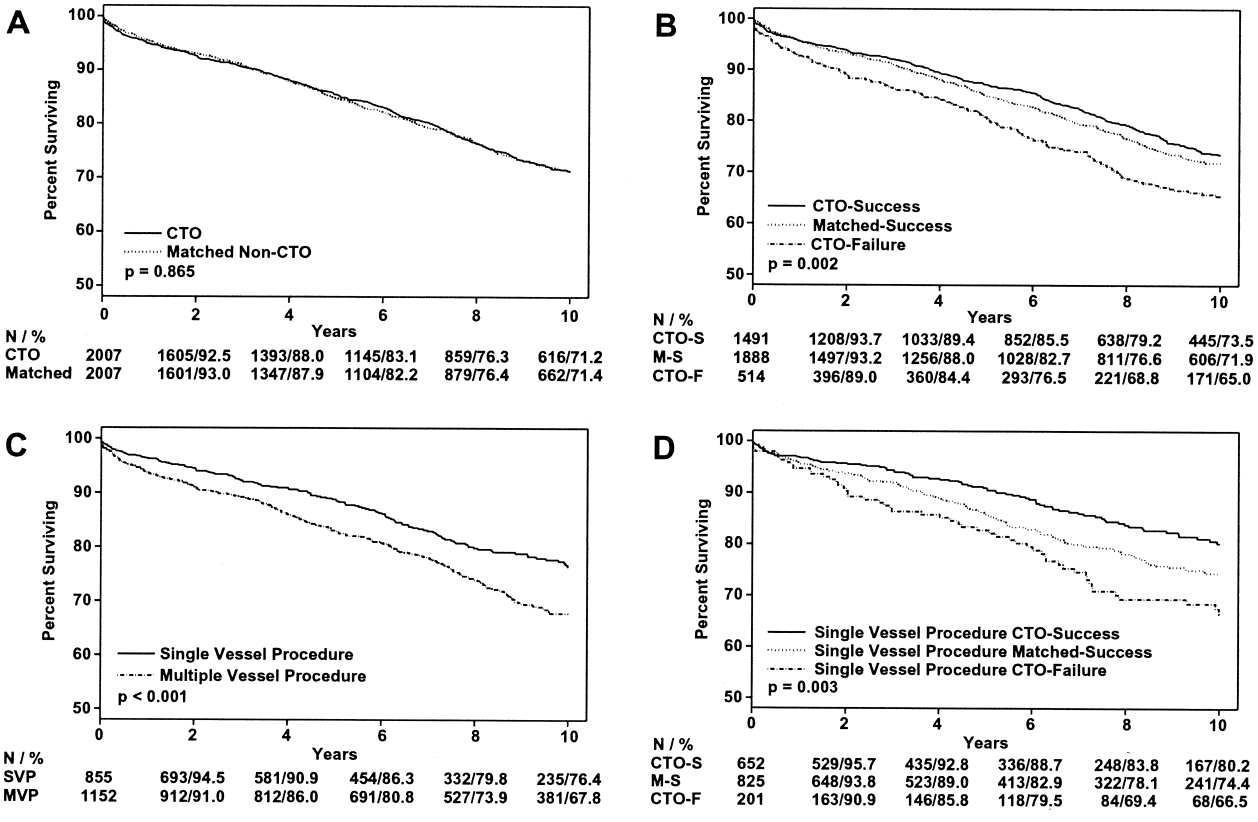

Figure 2. Cumulative 10-year survival. **(A)** Chronic total coronary artery occlusion (CTO) versus matched non-CTO cohorts. **(B)** CTO-success (CTO-S) versus matched non-CTO success (M-S) versus CTO-failure (CTO-F) groups. **(C)** Single (SVP) versus multivessel procedures (MVP). **(D)** Single-vessel procedure CTO-success (CTO-S) versus SVP matched non-CTO-success (M-S) versus SVP CTO-failure (CTO-F).

Table 5. Multivariable Predictors of Survival After PCI of CTO

	Hazard Ratio	95% Confidence Limits	p Value
CTO success	0.7	0.5–0.8	<0.0003
Age >70 yrs	1.9	1.5–2.4	<0.001
EF < 40%	2.1	1.7–2.7	<0.001
Diabetes mellitus	1.4	1.1–1.8	0.004
2-vessel disease	1.5	1.1–2.2	0.02
3-vessel disease	1.9	1.4–2.7	<0.001
Creatinine >2.0 mg/dl	2.2	1.3–3.9	0.005
Unstable angina	1.3	1.0–1.6	0.03

CTO = chronic total coronary artery occlusion; EF = ejection fraction; PCI = percutaneous coronary intervention.

Table 6. Multivariable Predictors of Survival for Patients Undergoing CABG After Failed Attempt of CTO

	Hazard Ratio	95% Confidence Limits	p Value
CABG ≤30 days	0.43	0.2–0.8	0.009
Age ≥70 yrs	1.9	1.3–2.8	0.0010
EF <40%	2.2	1.5–3.3	<0.001
Diabetes	1.3	0.9–2.0	0.17
2-vessel disease	1.4	0.2–2.9	0.3
3-vessel disease	1.8	0.9–3.5	0.11
Unstable angina	1.6	1.1–2.3	0.014

CABG = coronary artery bypass graft surgery; CTO = chronic total coronary artery occlusion; EF = ejection fraction.

survival benefit compared with the SVP failure group (Fig. 2D, 80.2% vs. 66.5%, p = 0.0008). Additionally, the SVP success group had a slightly better 10-year survival than the SVP matched non-CTO success group (80.2% vs. 74.4%, p = 0.02).

Table 5 depicts the significant multivariable predictors of long-term survival after an attempted PCI of a CTO. After an adjustment for differences in baseline characteristics for the CTO success and failure groups, a CTO success remained a significant independent predictor of long-term survival.

There were 514 CTO failures. Of these, 64 underwent CABG within 30 days. The 10-year survival was 71.2% (CABG) versus 63.9% (no CABG), p = 0.054 (Fig. 3). The benefit of CABG for patients in the failed PCI cohort remained significant following multivariable adjustment (Table 6).

DISCUSSION

Summary of findings. These data provide long-term follow-up on the largest series of patients undergoing PCI for a CTO reported to date. The CTO and matched non-CTO cohorts had a similar in-hospital MACE and 10-year survival, suggesting that long-term outcome is not significantly different for patients with a totally occluded versus a nonoccluded vessel. Of importance, successfully opening a CTO was associated with an improved 10-year survival. Successful revascularization of a CTO remained associated with improved long-term survival even following multivariable adjustment in this analysis. Further supporting this concept is the finding that patients undergoing CABG after a failed PCI have improved survival compared with those who did not undergo coronary surgery. In addition, we discovered that the SVP CTO success group had a better 10-year survival than the SVP matched non-CTO success group. These findings justify an aggressive attempt at PCI of a CTO in eligible patients.

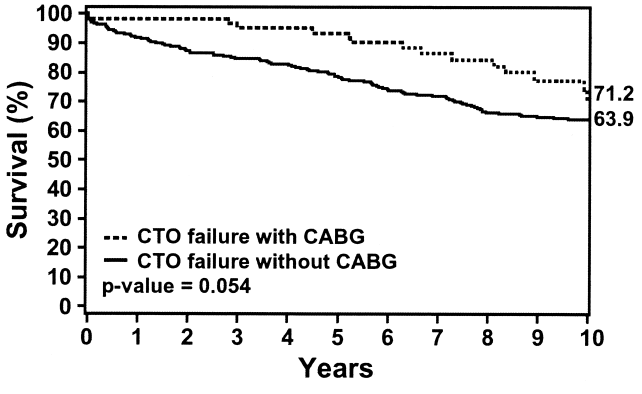

Figure 3. Kaplan-Meier event-free survival for patients with a failed chronic total coronary artery occlusion (CTO) procedure undergoing coronary artery bypass graft surgery (CABG) within 30 days and those with failed CTO procedure not undergoing CABG within 30 days.

There was a modest but statistically significant increase in technical and procedural success rates over the last 10 years. Importantly, this has not been associated with a concomitant increase in MACE rates. This is probably related to improved equipment, operator experience and improved case selection.

Prior studies. There have been few previous reports of long-term follow-up in large series of CTO patients undergoing PCI. Bell et al. (5) previously reported a trend for an increase in seven-year survival among 354 patients undergoing a successful angioplasty (82%) compared with a failed angioplasty (75%). In our larger experience, there was an 82.3% survival with CTO success versus 74.1% with CTO failure at seven years and 73.5% versus 65% at 10 years (log-rank p = 0.001). The survival data of Ivanhoe et al. (4) in 480 patients parallel that of ours. Cardiac survival at four years was significantly higher in successfully treated patients (99%) versus unsuccessfully treated patients (96%).

It was previously suggested (5) that a ceiling of approximately 70% in procedural success rates had been achieved. Stone et al. (6) previously reported a procedural success rate of 72%. These extended data, however, show improvement over time in both technical and procedural success rates. Over the last five years, the technical success rates have averaged 81.9%, and procedural success rates have averaged 78.6%. Furthermore, the MACE rates have not significantly changed over the years.

Study limitations. Our analysis is a retrospective study of prospectively collected data. We are unable to report the duration of occlusion for the entire CTO cohort. However, our group previously noted that in 100 consecutive patients, the mean duration of occlusion was 12 ± 20 months, with

58% of these occlusions being ≥1 month old (6). Approximately 10% of patients in this cohort received a stent; however, 32% of patients received stents since 1995. Thus, with the low percentage of patients receiving a stent, these findings cannot be completely extended to current practice patterns. We did not routinely collect creatine phosphokinase (CPK) data after interventions during the previous 20 years. All electrocardiograms were routinely assessed for new Q-waves, and CPK levels were obtained when there was clinical evidence for myocardial necrosis after PCI.

Conclusions. These data highlight a striking survival advantage among patients with a successfully opened occluded artery versus those whose procedure was unsuccessful. This work supports the concept of a time-independent benefit of reperfusion. These results elucidate the importance of revascularization of a CTO, and they represent long-term follow-up on the largest reported series of treated chronic coronary occlusions. Although success rates have continued to improve over time, attempted revascularization does not come without complications. The MACE rates, although constant, were found to be 3.8% overall. With proper training and by carefully selecting the lesions attempted, aggressive intervention of a CTO is justified.

Acknowledgments

The authors gratefully acknowledge the work of Jose A. Aceituno and Deborah J. Spiers for their expertise in the preparation of the manuscript.

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