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CLINICAL RESEARCH **Clinical Trials**

Immediate Results and One-Year Clinical Outcome After Percutaneous Coronary Interventions in Chronic Total Occlusions

Data From a Multicenter, Prospective, Observational Study (TOAST-GISE)

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OBJECTIVES We sought to investigate the success rate and the acute and 12-month clinical outcome of percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) in the contemporary era.

BACKGROUND The technique of PCI involving CTO has improved over time. However, limited data on acute and follow-up results in patients treated with PCI on CTO in recent years are available.

METHODS Four hundred nineteen consecutive patients scheduled for PCI of CTO of ≥30 days of duration were enrolled in 29 centers; 390 CTOs were confirmed in 376 patients in an independent core laboratory. The end points were technical and procedural success, in-hospital and 12-month major adverse cardiac events (MACE) occurrence, and 12-month symptomatic status.

RESULTS Technical and procedural success was obtained in 77.2% and 73.3% of lesions, respectively. In-hospital major adverse cardiac events occurred in 5.1% of patients. Multivariate analysis identified CTO length >15 mm or not measurable, moderate to severe calcifications, duration ≥180 days, and multivessel disease as significant predictors of PCI failure. At 12 months, patients with a successful procedure experienced a lower incidence of cardiac deaths or myocardial infarction (1.05% vs. 7.23%, $p = 0.005$), a reduced need for coronary artery bypass surgery (2.45% vs. 15.7%, $p < 0.0001$), and were more frequently free of angina (88.7% vs. 75.0%, $p = 0.008$) compared with patients who had an unsuccessful procedure.

CONCLUSIONS Successful PCI was achieved in a high percentage of CTOs with a low incidence of complications. At one-year follow-up, patients with successful PCI of a CTO had a significantly better clinical outcome than those whose PCI was unsuccessful. (J Am Coll Cardiol 2003;41:1672–8) © 2003 by the American College of Cardiology Foundation

Percutaneous coronary intervention (PCI) of chronic total occlusion (CTO) is one of the major challenges in interventional cardiology. The primary success rate is relatively low, mainly due to inability to cross the occlusion with the guidewire (1–13), while the recurrence rate is higher than that of subtotal stenoses (14,15). Moreover, the overall procedure and fluoroscopy times are longer and equipment use higher than with PCI of nonoccluded vessels (16).

Several reports, usually based on single-center experience, have shown that the immediate success has improved over time, along with the increased experience and skill of the operators (3,7,12,13) and the availability of new specialized guidewires or more sophisticated technologies for crossing occluded arteries (17–22). In addition, randomized studies have demonstrated that stent implantation reduces restenosis and reocclusion rates (23–29). Furthermore, some retrospective studies suggest that successful PCI of a CTO confers a long-term survival advantage (6,11–13), but this issue has not been investigated with prospective studies.

Thus, we performed a prospective, multicenter, observational study—Total Occlusion Angioplasty STudy—supported by GISE (Società Italiana di Cardiologia Invasiva), or TOAST-GISE, on consecutive patients treated with PCI of a CTO in order to evaluate the success rate, the in-hospital and clinical outcome, and their correlation with predefined clinical and angiographic variables.

METHODS

Study design. From June 1999 to January 2000, a multicenter, prospective, observational clinical study was conducted in 29 Italian centers. All consecutive patients scheduled to undergo PCI on a CTO of a native coronary artery

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Abbreviations and Acronyms

CABG	= coronary artery bypass graft surgery
CTO	= chronic total occlusion
MACE	= major adverse cardiac events
MI	= myocardial infarction
PCI	= percutaneous coronary intervention
TIMI	= Thrombolysis In Myocardial Infarction
TLR	= target lesion revascularization
TOAST-GISE	= Total Occlusion Angioplasty Study-Società Italiana di Cardiologia Invasiva

were considered for enrollment. The exclusion criteria were the estimated duration of a CTO <30 days or an acute myocardial infarction (MI) within the previous 30 days. No other predefined clinical inclusion or exclusion criteria were considered, and the indication for PCI was decided by individual investigators at the participating centers. The study protocol was approved by the institutional review board at each participating center, and all patients provided written informed consent.

The angiograms of the target procedures were sent to an independent core angiographic laboratory at Milan Cardiovascular Research, that assessed all angiographic qualitative and quantitative variables. The automated edge-detection system CMS (Medis, Neunen, The Netherlands) was used for quantitative coronary angiography.

The aim of the study was to investigate the procedural success of PCI of CTO, in-hospital major adverse cardiac events (MACE), one- and five-year MACE occurrence, and anginal status in patients who underwent PCI of a CTO. To evaluate the effect of the vessel patency on clinical outcome avoiding the confounding effect of in-hospital events such as Q-wave MI or coronary artery bypass surgery (CABG), only patients discharged free of those events were included in the follow-up analysis.

Definitions. A CTO was defined as obstruction of a native coronary artery with no luminal continuity and with Thrombolysis In Myocardial Infarction (TIMI) flow grade 0 or 1 (30). The duration of the occlusion had to be more than 30 days, estimated from clinical events such as MI, sudden onset or worsening of the symptoms, or proven by previous angiography. If the duration of the occlusion was uncertain, but the investigators had no clear reason to date the CTO <30 days, the patient was enrolled.

Technical success was defined as restoration of TIMI flow grade 2 or 3 with a residual stenosis of <50% assessed by quantitative coronary angiography performed at the angiographic core laboratory. Procedural success was defined as technical success without in-hospital MACE. Major adverse cardiac events were defined as death, Q-wave and non–Q-wave MI, urgent CABG, or urgent repeat PCI. The diagnosis of Q-wave MI was documented by the presence of new pathologic Q waves on the electrocardiogram. Serum total creatine kinase was determined 8 and 24 h after the PCI, while creatine kinase-MB fraction was measured only if total creatine kinase was above the upper normal limit. Non–Q-wave MI was defined as any increase of total creatine kinase with increase of MB fraction, without new abnormal Q waves. At clinical follow-up, MACE-free survival was defined as freedom from cardiac death, Q-wave and non–Q-wave MI, or target lesion revascularization (TLR), either surgical or percutaneous. All deaths were considered cardiac unless otherwise documented. All MIs were counted as events, whether or not associated with new revascularization procedure.

Interventional technique. The operators performed the procedure according to their standard practices via the femoral or brachial approach. All procedural and technical details and the choice of devices were left to the operator's judgment. Ticlopidine (500 mg daily) or clopidogrel (75 mg daily) was prescribed to all patients for four weeks after stent implantations; aspirin was given indefinitely.

Follow-up. A follow-up visit or telephone interview was scheduled at 30 days, 6 months, 1 year, and then yearly for up to 5 years. An exercise tolerance test was recommended after six months in event-free patients. In this report, the data up to one year are presented.

Statistical analysis. Continuous data are presented as mean ± SD and differences are compared using Student *t* test. Discrete variables are expressed as counts and percentages. In two-by-two tables, differences were assessed by Fisher exact test. In two-by-three and two-by-four tables, differences were assessed by chi-square test. All statistical tests were two-tailed.

Logistic regression analysis was used to assess the relationship between baseline clinical and angiographic characteristics and technical success and to investigate the predictive value of CTO success, together with baseline variables, on MACE rate during follow-up. All analyses were performed using SPSS version 11 statistical software (SPSS Inc., Chicago, Illinois). A p value of <0.05 was considered significant.

RESULTS

Between June 1999 and January 2000, 29 Italian centers participated in the study for a median of 120 days (range 37 to 214 days). During the study period, a total of 6,322 PCIs were performed in the participating centers. In 419 PCIs, a total of 443 CTO were targeted. The enrollment per center was ≤10 patients in 9 centers, 11 to 20 patients in 14 centers, and >20 patients in 6 centers. The prevalence of patients with CTO on the overall PCI population in the different centers was 7.1 ± 2.9% (range 2.9% to 13.5%).

Subsequently, 19 CTOs were excluded because either the angiogram of the procedure was not available or the image quality did not allow an adequate analysis in the core laboratory. Of the remaining 424 CTOs, 34 (8%) were excluded because they were judged to be subtotal at core laboratory evaluation. Interestingly, in 32 (94.1%) of those

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Table 1. Patient Baseline Characteristics for CTO Success and Failure Groups

	All Patients (n = 376)	CTO Success (n = 289)	CTO Failure (n = 87)
Age (yrs, mean ± SD)	58.3 ± 10.2	58.0 ± 9.9	59.4 ± 10.9
Male	323 (85.9%)	249 (86.2%)	74 (85.1%)
Family history of CAD	158 (42.0%)	126 (43.6%)	32 (36.8%)
Diabetes	67 (17.8%)	50 (17.3%)	17 (19.5%)
Insulin treatment	7 (1.86%)	4 (1.38%)	3 (3.45%)
Hypertension	200 (53.2%)	153 (52.9%)	47 (54.0%)
Hyperlipidemia	218 (58.0%)	169 (58.5%)	48 (56.3%)
Smoking			
Active	134 (35.6%)	107 (37.0%)	27 (30.3%)
Previous	115 (30.6%)	83 (28.7%)	32 (36.8%)
Prior MI	258 (68.6%)	198 (68.5%)	60 (69.0%)
Prior CABG	19 (5.0%)	13 (4.5%)	6 (6.9%)
Prior PCI	48 (12.8%)	32 (11.1%)	16 (18.4%)
Angina			
Stable	264 (70.2%)	203 (70.2%)	61 (70.1%)
Unstable	66 (17.5%)	52 (18.0%)	14 (4.8%)
Silent ischemia	41 (10.9%)	29 (10.0%)	12 (13.8%)
NYHA class 3 to 4	15 (4.0%)	9 (3.1%)	7 (8.0%)
Multivessel disease	181 (48.1%)	129 (44.6%)	52 (59.8%)*
Ejection fraction (%, mean ± SD)	55.9 ± 9.7	55.7 ± 9.6	56.3 ± 10.1

*p = 0.014.

CABG = coronary artery bypass graft surgery; CAD = coronary artery disease; CTO = chronic total occlusion of coronary artery; CTO success = technical success on all CTOs targeted in a patient; LV = left ventricle; MI = myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention.

cases, the PCI was successful. Thus, the final study population consisted of 376 patients with 390 CTOs targeted.

Baseline clinical characteristics. The baseline clinical characteristics of the patients are shown in Table 1. The majority of patients had a history of a previous MI (61.7% in the region of myocardium supplied by the target vessel) and had symptoms of angina. About one-half of the patients presented with multivessel disease. The viability of the myocardium supplied by the target vessel was not investigated by protocol, but in 70% of patients the presence of normal or only reduced regional systolic wall motion of that area evaluated either by angiography or echocardiography, suggested the presence of viable myocardium.

Procedural outcome and in-hospital complications. Technical success was obtained in 77.2% and procedural success in 73.3% of the lesions (Table 2). Among the failed procedures, inability to cross the lesion with a guidewire, inability to cross with a balloon, and inability to dilate were the reason for failure in 81%, 11.4%, and 7.6% of cases, respectively. One patient died because of massive pulmonary embolism 48 h after successful PCI. Two patients underwent emergency CABG: one patient developed a retrograde dissection of the left main trunk during an attempt to recanalize the left anterior descending artery and the other patient presented subacute thrombosis of a stent implanted in a nonoccluded vessel after an unsuccessful procedure on the CTO. This patient was treated with repeat PCI and then CABG and eventually developed a Q-wave MI. Another patient presented subacute stent thrombosis and

Table 2. Technical and Procedural Success and In-Hospital Complications of 376 Patients

Technical success	301 (77.2%)*
Procedural success	286 (73.3%)*
Death	1 (0.26%)
Q-wave MI	1 (0.26%)
Non–Q-wave MI	16 (4.3%)
Urgent CABG	2 (0.53%)
Urgent repeat PCI	2 (0.53%)
Cerebrovascular accident	0
Vessel perforation	8 (2.1%)*
In-hospital MACE	19 (5.1%)

*Referring to 390 CTOs total.

MACE = major adverse cardiac event (death, MI, urgent repeat PCI, and urgent CABG). Other abbreviations as in Table 1.

was treated with repeat PCI and developed a non–Q-wave MI. In a further 15 patients, a postprocedural increase in both total creatine kinase and MB fraction was found, with a total of 16 non–Q-wave MIs (4.3%). Perforation of the vessel occurred in 8 patients (2.1%) without relevant clinical sequelae. Overall, in-hospital MACE occurred in 19 patients (5.1%).

CTO characteristics. All baseline characteristics of the target lesions and their relationship with technical success are shown in Table 3. Most CTOs presented TIMI flow grade 0. In 30% of the cases, the duration of the CTO could not be estimated, whereas in the remaining cases the median estimated duration was 70 days (interquartile range: 40, 120). In 50% of the cases, the length of the CTO could not be assessed; in the remaining cases the mean CTO length was 13.4 ± 9.13 mm (median 10.7 mm; range 1.5 to 63 mm).

Procedure-related characteristics. In 165 (43.9%) patients, the procedure was done at the end of diagnostic angiogram. A large variety of guidewires with different mechanical properties were used, and they were grouped into three categories, based on the producers' specifications: soft or floppy in 35.1% of lesions, intermediate in 34.4%, and stiff or dedicated to CTO treatment in 30.5%. At least one stent was implanted in 89.7% of successfully recanalized CTOs. Glycoprotein IIb/IIIa antagonists were used in 39 (10.4%) patients.

After successful procedure, the average proximal reference diameter was 3.13 ± 1.66 mm; the minimal luminal diameter was 2.27 ± 0.56 mm, and diameter stenosis was 22.53 ± 13.32% at quantitative coronary angiography. In 76 patients, PCI was performed on at least one additional vessel.

Determinants of procedural success. In univariate analysis, the characteristics that had a significant relationship with technical outcome were the vessel site of CTO, duration and length of CTO, stump morphology, and presence of multivessel disease. No other characteristic was found to be correlated with PCI outcome (Table 3). At multivariate analysis, CTO length ≥15 mm or not measurable, duration ≥180 days, presence of moderate to severe calcifications, presence of multivessel disease, and stump morphology not clearly identifiable were associated with the technical failure of the PCI (Table 4).

Table 3. Univariate Analysis of CTO Characteristics Relevant to Technical Success

CTO Baseline Characteristics	No. of CTOs (%)	Technical Success n (%)	p Value
Vessel			0.017
LMCA*	1	1 (100)	
LAD	156	131 (84.0)	
LCX	86	59 (68.6)	
RCA	147	110 (74.8)	
Duration (days)			<0.001
30–89	150	126 (84.0)	
90–179	72	62 (86.1)	
≥180	51	32 (62.7)	
Not determinable	117	81 (69.2)	
Length (mm)			0.016
<8	66	59 (89.4)	
8–14.9	65	54 (83.1)	
≥15	65	49 (75.4)	
Not determinable	194	139 (71.6)	
TIMI flow			0.074
Grade 0	322	242 (75.2)	
Grade 1	65	56 (86.2)	
Calcification			0.051
Absent to mild	305	239 (78.4)	
Moderate to severe	23	13 (56.5)	
Not determinable	62	49 (79.0)	
Stump morphology			0.001
Abrupt	157	117 (74.5)	
Tapered	167	142 (85.0)	
Not determinable	66	42 (63.6)	
Side branch from stump			0.457
Absent	235	178 (75.7)	
Present	149	118 (79.2)	
Bridging collaterals			0.349
Absent	270	213 (78.9)	
Present	113	84 (74.3)	
Vessel diameter (mm)			0.244
<2.4	81	65 (80.2)	
2.4–2.89	89	73 (80.0)	
≥2.9	87	68 (78.2)	
Not determinable	133	95 (71.4)	
LV wall motion			1.000
Normal or hypokinetic	264	206 (78.0)	
Akinetic or dyskinetic	97	76 (78.4)	
Number of CTO PCI/center			0.140
<20	211	173 (82.0)	
≥20	179	128 (71.5)	

In few cases, angiographic characteristics such as TIMI flow, side branch from stump, bridging collaterals, and LV wall motion were not determinable. These cases are not included in the Table. Number of CTO PCI/center indicates the number of CTOs included in the registry by the participating centers. *The single case of LMCA CTO was excluded from chi-square computation. Therefore, the p value refers only to the differences among LAD, LCX, and RCA.

LAD = left anterior descending artery; LCX = left circumflex artery; LMCA = left main coronary artery; LV = left ventricle; RCA = right coronary artery; TIMI = Thrombolysis In Myocardial Infarction. Other abbreviations as in Table 1.

One-year follow-up. The one-year clinical follow-up is complete for 369 of 373 (98.9%) patients who were discharged free of Q-wave MI or urgent CABG. During follow-up, patients with a successful procedure experienced a significantly lower incidence of overall MACE, cardiac deaths, and composite end point cardiac death or MI, as well as a reduced need for CABG (Table 5). Because the only significant difference in baseline characteristic between patients with CTO success and CTO failure was the prevalence of multivessel disease (Table 1), we analyzed separately patients with single-vessel and multivessel disease (Table 5). The excess of cardiac death or MI was evident only in patients with multivessel disease.

Table 4. Multivariable Predictors of Technically Unsuccessful Procedures

	Hazard Ratio	95% Confidence Limits	p Value
Length ≥15 vs. <8 mm	3.9	1.1–13.5	0.028
Length not measurable vs. <8 mm	3.8	1.2–10.8	0.019
Moderate to severe calcification	3.5	1.1–10.1	0.023
Duration ≥180 days	3.1	1.3–7.4	0.013
Multivessel disease	2.3	1.2–4.3	0.009
Stump morphology not discernable	2.2	1.0–4.8	0.048

Two noncardiac deaths, occurring one and nine months after enrollment, were caused, respectively, by esophageal cancer and stroke. The other four fatalities were considered cardiac deaths. Only one Q-wave MI was observed and was not related to the study CTO. During follow-up, seven patients with failed recanalization underwent a repeat PCI involving the target vessel (four cases of a second attempt at the CTO and three cases of transmyocardial laser revascularization that was counted, for the purpose of this study, as an equivalent of TLR).

In a multivariate analysis including all baseline characteristics listed in Table 1, the only variable associated with MACE-free survival was the initially successful PCI (odds ratio 0.24, 95% confidence interval 0.07 to 0.80, p = 0.018). No independent predictor of freedom from death or MI could be identified.

The clinical status and exercise tolerance at 12 months in 308 event-free patients are shown in Table 6. Patients with a successful CTO procedure presented significantly less anginal symptoms and could more frequently perform a negative exercise test than patients with a failed procedure.

DISCUSSION

Study design. The study was designed to look at the state of the art of PCI in CTO. The available data on this subject are derived from studies that present substantial limitations. Most studies reported early results from single centers, which tend to be particularly experienced in this subset of patients (1–11). In recent years, various guidewires and other more complex devices designed for CTO treatment have become available. Several studies described the results of such new devices in selected patients (17–23), but there are no data on their overall impact on the procedural outcomes in unselected patients. Therefore, limited information on the incidence and results of PCI of CTO in contemporary interventional practice is available.

Another important methodologic limitation of previous studies dealing with PCI of CTO is the absence of an independent assessment of qualitative and quantitative an-

Table 5. 12-Month Clinical Outcome of 369 Patients Discharged Free of Q-Wave MI and CABG

	All Patients			Single-Vessel Disease			Multivessel Disease		
	CTO Success n = 286 n (%)	CTO Failure n = 83 n (%)	p Value	CTO Success n = 160 n (%)	CTO Failure n = 35 n (%)	p Value	CTO Success n = 126 n (%)	CTO Failure n = 48 n (%)	p Value
All deaths	3 (1.05)	3 (3.61)	0.130	1 (0.63)	1 (2.86)	0.327	2 (1.59)	2 (4.17)	0.305
Cardiac death	1 (0.35)	3 (3.61)	0.037	0	1 (2.86)	0.179	1 (0.79)	2 (4.17)	0.185
Nonfatal Q-wave MI	1 (0.35)	0	1.000	0	0	—	1 (0.79)	0	1.000
Nonfatal non–Q-wave MI	1 (0.35)	3 (3.61)	0.037	1 (0.63)	0	1.000	0	3 (6.25)	0.020
Any nonfatal MI	2 (0.70)	3 (3.61)	0.077	1 (0.63)	0	1.000	1 (0.79)	3 (6.25)	0.064
Cardiac death or MI	3 (1.05)	6 (7.23)	0.005	1 (0.63)	1 (2.86)	0.327	2 (1.59)	5 (10.4)	0.018
CABG	7 (2.45)	13 (15.7)	<0.0001	2 (1.25)	4 (11.4)	0.010	5 (3.97)	9 (18.7)	0.003
PCI, TLR	27 (9.44)	7 (8.43)	0.834	12 (7.50)	4 (11.43)	0.495	15 (11.9)	3 (6.25)	0.405
Any TLR	33 (11.5)	19 (22.9)	0.012	14 (8.75)	7 (20.0)	0.069	19 (15.1)	12 (25.0)	0.182
Any PCI	38 (13.3)	9 (10.8)	0.584	18 (11.2)	4 (11.4)	0.976	20 (15.9)	5 (10.4)	0.471
Any MACE	35 (12.2)	21 (25.3)	0.005	15 (9.38)	7 (20.0)	0.082	20 (15.9)	14 (29.2)	0.056

TLR = target lesion revascularization. Other abbreviations as in Tables 1 and 2.

Table 6. Clinical Status After 12 Months of a PCI on a CTO in Patients Discharged Free of Q-Wave MI and CABG and MACE-Free During Follow-Up

	CTO Success (n = 248)	CTO Failure (n = 60)	p Value
No angina	220 (88.7%)	45 (75.0%)	0.008
ETT performed	210 (84.7%)	42 (70.0%)	0.010
Maximal ETT	155 (62.5%)	20 (33.3%)	<0.0001
Negative ETT	181 (73.0%)	28 (46.7%)	0.0001

ETT = exercise tolerance test. Other abbreviation as in Tables 1 and 2.

giographic parameters. Obviously, the angiographic assessment is critical in excluding subtotal lesions from the study group and in validating important end points such as procedural success. The possibility to predict which CTOs are more likely to be treated successfully is still of utmost importance for patient selection, but the criteria for such selection are derived from studies that are conditioned by the above-mentioned limitations.

In this study, the success of the PCI of CTO was defined as residual stenosis <50%. In most recent studies the threshold value for success is 30% residual stenosis. However, most of those studies regard selected patients with subtotal stenosis undergoing stent implantation, whereas our study included consecutive patients with CTO not necessarily treated with stenting. In addition, we favored the concept of "open vessel," that is the restoration of antegrade flow, that is not limited by a residual stenosis of <50%. Furthermore, we planned a clinical follow-up of five years because an increasing number of studies (6,11–13) suggest the unfavorable long-term outcome of patients with unsuccessful recanalization of CTO.

In-hospital results. Of the 424 lesions evaluated at the core laboratory, 34 (8%) were excluded, being judged subtotal stenoses. These cases were distributed among the participating centers and included those with extensive experience and high-volume activity. In these lesions, a successful dilation was obtained in 32 out of 34 (94.1%) lesions. In the absence of an independent angiographic assessment of baseline CTO characteristics, these lesions would have been included in the study and the success rate would have spuriously increased. This finding, previously not reported, underlines the importance of an accurate angiographic analysis to avoid the inclusion of subtotal stenoses in CTO series. The technical and procedural success rates (77.2% and 73.3%, respectively) observed in this study were relatively high and compare favorably with previously published single-center data (1–13) that varied between 51% and 73%. It cannot be argued from our data whether this high success rate was due to increased operator experience, better case selection, or availability of newer equipment, particularly guidewires dedicated to CTO treatment. Interestingly, the higher success rate was not associated with an increase in acute complication rate, potentially related to the use of more aggressive devices and techniques. Major adverse cardiac events occurred in 19 (5.1%) patients

with a prevalence of non–Q-wave MI (16 [4.25%] patients). Clearly, the incidence of such events depends on the definition criteria. It is likely that, using more stringent criteria, based on creatine kinase-MB fraction or troponin elevation, the observed rate of non–Q- wave MI would have been higher. Uneventful vessel perforation occurred in eight cases (2.1%). These complication rates are similar to those reported in most other studies (1,3–5,8,12,13,17).

Predictors of success. At univariate analysis, the presence of multivessel disease, vessel site of CTO, CTO duration, CTO length, and stump morphology were significantly associated with the procedural outcome (Table 3). At multivariate analysis, the presence of multivessel disease, CTO length ≥15 mm or not measurable, the presence of moderate to severe calcifications of CTO, duration ≥180 days, and not-determinable stump morphology were confirmed to be associated with a procedural failure (Table 4). Nonidentifiable angiographic characteristics, such as CTO length and stump morphology, could be related, at least in some cases, to inadequate procedural methodology, such as poor image quality.

With regard to CTO duration, an increase in PCI failures was observed only in CTOs lasting more than six months. Also, the reduced CTO success in patients with multivessel disease, already reported (6,12,13), may be related to a more extensive and chronic disease, although the influence of selection criteria cannot be ruled out.

Several angiographic variables identified as negative predictors of success in previous studies, such as the presence of side branch at CTO stump (8,9), bridging collaterals (3,8), abrupt stump morphology (3,6–9), and TIMI flow grade 0 (1,6) had no predictive value in our study.

Comparison of predictors of success between the different studies is unreliable for the following reasons. Most studies were relatively small (1,2,5, 9,11,12) and lacked the statistical power to identify such factors. In the larger studies, information about some important variables, such as CTO duration and/or angiographic morphology, was incomplete or absent (3,4,6,13). In addition, the definition of CTO varied greatly, with studies including (1,3,6–8,13,14,19,20) or excluding (2,5,10,17,21) TIMI flow grade 1 CTO, others including occlusions as recent as three days old (3,4), and others excluding CTO of less than three (12,19), two (10) or one (21) month(s) of duration.

One-year follow-up. During the 12 months following PCI of CTO, we found a significantly higher incidence of cardiac death, combined rate of cardiac death and MI, and CABG in patients with a failed procedure as compared with patients with a successful PCI. At multivariate analysis, the only factor associated with one-year MACE-free survival was the successful procedure; no independent predictor of death or MI was identified. This excess of cardiac death and MI in patients with failed CTO PCI has been reported in other studies (6,11–13), but it has never been observed as early as at 12 months. This finding, although statistically significant, is based on the occurrence of few events and needs to be confirmed during a longer follow-up. In patients with failed PCI, the higher need for CABG surgery is not unexpected and it has already been reported in several studies (4,6,11,12).

Analyzing patients with single-vessel and multivessel disease separately, we found that a higher rate of combined cardiac death and MI was evident only in patients with multivessel disease (Table 5). In both single-vessel and multivessel disease, the TLR rate after a successful procedure was remarkably low (8.7% and 15%, respectively). This finding can be related to the extensive use of stents and to the fact that no routine angiographic control was scheduled. On the other hand, in event-free patients after successful PCI, 88.7% of the patients had no angina symptoms and 73.8% of those performing an exercise test were able to reach the maximum heart rate for age, reflecting the good functional outcome of the procedure (Table 6). A better clinical outcome (angina status and exercise tolerance) after successful procedures was reported in other studies in the stent era (21).

Study limitations. The results of the study may have been influenced by selection criteria, operator experience, and technique varying among the participating centers. Therefore, they may not be fully reproducible under different conditions. We have no information about collateral flow to the CTO vessel because in most of the angiograms analyzed, the baseline diagnostic coronary angiography was not included. In our study, the clinical relevance of successful PCI of a CTO is based on the comparison with patients in whom the procedure was unsuccessful. The question as to whether recanalization of a CTO can lead to a better clinical outcome and in which patients should be evaluated with randomized studies.

Conclusions. These data represent the largest reported multicenter series of consecutive patients treated with PCI of CTO with independent core laboratory evaluation of all angiographic variables. A high success rate with a low incidence of complications was observed. Predictors of a failed procedure were multivessel disease and CTO characteristics such as length, duration, and presence of moderate to severe calcifications. Other angiographic characteristics, previously reported as associated with procedural outcome, did not confirm their predictive value. A successful PCI was associated with better clinical outcome at one year, with lower need of CABG, lower cumulative rate of cardiac death and MI, and better clinical status with less angina and better exercise tolerance. Percutaneous coronary intervention can be an effective therapeutic option in selected patients with CTO.

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APPENDIX

Sites and investigators participating in TOAST-GISE. The number of patients enrolled in each center is given in parenthesis. Genoa: P. Rubartelli, C. Giachero (37); Mercogliano: P. Rubino, L. Salemme (35); Ancona: R. Piva, G. Gabrielli (34); Milan: A. Colombo, C. Di Mario (34); Udine: G. Bernardi, L. Spedicato (25); Milan: F. Bedogni, M. Onofri (22); Legnano: S. De Servi, M. D'Urbano (18); Treviso: Z. Olivari, M. Spolverato (17); Pescara: L. Paloscia, G. Contegiacomo (13); Bologna: A. Marzocchi, C. Marozzini (13); Pedara: S. Tolaro, R. Raciti (13); Cagliari: A. Bande, B. Loi (13); Salerno: P. Giudice, C. Baldi (12); Brescia: L. Niccoli, F. Ettori (12); Napoli: F. Piscione, G. De Luca (12); Bari: A. Bortone, E. De Cillis (11); Pisa: A. S. Petronio, U. Limbruno (10); Cuneo: G. Steffenino, A. Della Valle (10); Rozzano: P. Presbitero, L. Maiello (10); Rome: R. Violini, A. Parma (10); Modena: A. Benassi, G. D'Annibale (9); Perugia: C. Giombolini, S. Santucci (8); Catania: C. Tamburino, B. Francaviglia (8); Rome: M. A. Mazzari, C. Trani (8); Novara: C. Cernigliaro, M. Sansa (7); Brescia: G. B. Danzi, C. Capuano (5); Rome: P. Gioffrè, F. Tomai (5); Bari: A. Gaglione, F. Tiecco (5); Palermo: G. Saccone, O. Manzi (3). **Steering Committee:** Z. Olivari, P. Rubartelli, F. Piscione, F. Ettori, A. Fontanelli. **Core Angiographic Laboratory:** MCR, Milan, Italy, M. A. Bonardi. **Data Coordinating Center:** Cardioricerche, Milan, Italy: G. Lanteri.