European Heart Journal (2005) **26**, 2630–2636
doi:10.1093/eurheartj/ehi498

Clinical research

Percutaneous coronary intervention for chronic total occlusions: the Thoraxcenter experience 1992—2002

Angela Hoye, Ron T. van Domburg, Karel Sonnenschein, and Patrick W. Serruys*

Department of Interventional Cardiology, Erasmus MC, Thoraxcenter Bd 404, Dr Molewaterplein 40, 3015 GD Rotterdam, The Netherlands

Received 17 September 2004; revised 30 July 2005; accepted 25 August 2005; online publish-ahead-of-print 23 September 2005

KEYWORDS
Occlusion;
Prognosis;
Angioplasty

Aims Chronic total occlusions (CTOs) are commonly found on diagnostic angiography, and there is some evidence from one study that successful percutaneous revascularization leads to an improvement in long-term survival rates. However, this study included patients treated for unstable angina with short-duration occlusion, and stent implantation was utilized in only 7%. We re-evaluated the long-term outcomes of a large consecutive series of patients with a CTO of >1-month duration treated at our centre, with stent implantation utilized in the majority.

Methods and results All patients treated with percutaneous coronary intervention (PCI) between 1992 and 2002 were retrospectively identified from a dedicated database. A total of 874 consecutive patients were treated for 885 CTO lesions. Mean follow-up time was 4.47 $\pm$ 2.69 years (median 4.10 years). Patients were evaluated for the occurrence of major adverse cardiac events (MACE) comprising death, acute myocardial infarction, and need for repeat revascularization with either coronary artery bypass surgery or PCI. Successful revascularization was achieved in 576 lesions (65.1%), in which stent implantation was used in 81.0%. At 30 days, the overall MACE rate was significantly lower in those patients with a successful recanalization (5.5 vs. 14.8%, $P < 0.00001$). At 5 years, survival was significantly higher in those patients with a successful revascularization (93.5 vs. 88.0%, $P = 0.02$). In addition, there was a significantly higher survival free of MACE (63.7 vs. 41.7%, $P < 0.0001$), with the majority of events reflecting the need for repeat intervention. Independent predictors for survival were successful revascularization, lower age, and the absence of diabetes mellitus and multivessel disease.

Conclusion Successful percutaneous revascularization of a CTO leads to a significantly improved survival rate and a reduction in major adverse events at 5 years. Most events relate to the need for repeat reintervention, and the introduction of drug-eluting stents, with low-restenosis rates, encourages the development of technologies to improve recanalization success rates. However, failed recanalization may be associated acutely with an adverse event, and new technologies must focus on a safe approach to successful recanalization.

Introduction

Recent data suggest that approximately one-half of patients with significant coronary disease on angiography have at least one chronic total occlusion (CTO).[1] Yet, data suggest that percutaneous coronary intervention (PCI) for a CTO accounts for approximately only 10–15% of angioplasty procedures, with the majority of patients treated with either coronary artery bypass surgery (CABG) or medical therapy. When compared with non-occlusive lesions, PCI for a CTO is associated with lower procedural success rates predominantly related to the inability to cross the lesion. However, technical advances in the design of angioplasty equipment, particularly of specialized wires, have improved recanalization rates. The choice of therapy for patients with a CTO (PCI vs. CABG vs. medical therapy) is dependent on local policies, and outcomes of revascularization are dependent on operator experience. In the current study, we analysed the trends in revascularization and the treatment of CTOs at the Thoraxcenter, Rotterdam, between 1992 and 2002.

In addition, the long-term outcomes of patients with PCI for a CTO were analysed. Previously, a large single centre series of more than 2000 patients importantly demonstrated that successful percutaneous revascularization of a CTO confers a significant 10-year survival rate when compared with failed revascularization.[2] This study analysed patients treated between 1980 and December 1999 in the Mid-America Heart Institute and included all patients treated for an occluded vessel, provided they had not had a myocardial infarction within the preceding 7 days. Therefore, those with relatively recent thrombotic occlusions and unstable angina were included. Indeed, one of the multivariable

* Corresponding author. Tel: +31 10 4635260; fax: +31 10 4369154.
E-mail address: p.w.j.c.serruys@erasmusmc.nl

predictors for long-term mortality was percutaneous intervention undertaken in patients with unstable angina. In addition, only 7% of patients with successful revascularization were treated with stent implantation. Long-term outcomes of CTOs have been improved because the widespread introduction of stent utilization, which is associated with reduced rates of restenosis and re-occlusion when compared with balloon-only angioplasty.[3–6] In the current study, we analysed whether the benefits demonstrated in the MAHI study are applicable to PCI carried out in chronic occlusions in another tertiary centre. In our study, CTO was more strictly defined, those with occlusion related to unstable angina and recent (<1 month) occlusion were excluded, and in addition, stent implantation was used in the majority.

Methods

Demographic and procedural data regarding all patients undergoing PCI at our centre are prospectively entered into a dedicated database. All procedures undertaken for an occluded vessel between 1 January 1992 and 31 December 2002 were retrospectively identified ($n = 2131$). Those treated in the setting of acute myocardial infarction (AMI) and recent (<1 month) occlusion were excluded, leaving a total of 874 consecutive patients treated for CTO.

CTO was defined as a lesion exhibiting thrombolysis in myocardial infarction flow grade 0–1. All patients included had at least one occlusion within a native vessel; occlusions within saphenous vein grafts were excluded. Duration of occlusion was estimated to be at least 1 month on the basis of a history of sudden chest pain, a previous AMI in the same target vessel territory, or the time between the diagnosis made on coronary angiography and PCI. Procedures were undertaken using standard techniques of the time. All patients were treated with heparin to maintain an ACT >250 s and all were on long-term aspirin therapy. For those treated with stent implantation prior to 1996, additional anticoagulation was provided with the use of warfarin given for 1 month. Subsequent to that time, a thienopyridine was used (ticlopidine or clopidogrel). Procedural success was defined as successful recanalization and dilatation of the vessel with or without stent implantation, with a final residual diameter stenosis <50%.

Median follow-up time was 4.48 years (quartiles 2.72, 6.64 years). All patients were assessed for the occurrence of major adverse cardiac events (MACE) comprising death, non-fatal AMI, and repeat revascularization (PCI and/or CABG). Long-term survival status was assessed by written enquiries to the Municipal Civil Registries. Follow-up clinical data were determined from electronic hospital archives and by questionnaires sent to all living patients. The referring physician and institutions as well as the general practitioners were directly approached whenever necessary. Complete 30-day clinical follow-up was obtained in all patients, with complete long-term follow-up data obtained in 99% patients up to 1 April 2004. The diagnosis of AMI required an elevation of creatine kinase to twice the upper limit of normal, together with a rise in creatine kinase-MB fraction. If made following patient admission to another hospital, the diagnosis of AMI was confirmed through direct contact with the referring physician, using the same criteria.

Statistics

Discrete variables are presented as percentages and compared with Fisher's exact test. Continuous variables are expressed as mean $\pm$ SD and compared with Student's *t*-test. Cumulative survival free of major adverse events were calculated according to the Kaplan–Meier method. The log-rank test was used to compare event-free survival between the groups. Multivariable analyses were performed using backward and forward stepwise Cox regression. Baseline characteristics were included if they were (i) associated with high incidence of cardiac events ($P < 0.1$) or (ii) known risk factors from the literature. Pre-selected variables were age, gender, diabetes mellitus, hypertension, hypercholesterolaemia, presence of multivessel disease, impaired left ventricular function, prior AMI, prior PCI, prior CABG, use of a glycoprotein IIb/IIIa inhibitor, target vessel, successful procedure, and use of a stent. The proportional hazard assumptions were investigated by testing the constancy over time of the log-hazard ratio for each model. In addition, the proportional hazard assumption for all covariates was tested using Schoefeld residuals. According to these tests, the proportional hazard assumption was not validated. Linearity was checked graphically and by inclusion of continuous variables both according to quintiles. Absence effect of the grouped variable indicates that the effect is linear. Also assumptions of linearity were assessed and satisfied using a general linear model univariate method. No deviation from linearity was found in any continuous variable. To investigate interaction, an interaction model was performed using a likelihood ratio test in the multivariable Cox. Interaction was performed on all selected variables. However, no interaction was found. Odds ratio with corresponding 95% confidence intervals is reported. All tests were two-tailed; because of the large number of statistical tests, *P*-values should be interpreted with caution. Although no specific level of significance is defined, a *P*-value of 0.01 should be considered for strong evidence in support of a true effect.

Results

Between 1 January 1992 and 31 December 2002, a total of 874 patients underwent PCI for at least one CTO. Of these, 11 had attempted revascularization of two CTOs, making a total of 885 attempted lesions. Overall, successful revascularization was achieved in 576 lesions (65.1%), with failure in the remaining 309 (34.9%). Of the 11 patients with attempted therapy of two CTOs, PCI outcome was the same in both lesions in eight patients. The remaining three patients with both one success and one unsuccessful PCI have been excluded from further analysis. The baseline demographics for the remaining patients are presented in *Table 1*. There were no significant differences in characteristics, though a trend towards an increase in two- and three-vessel disease in those in whom PCI for occlusion was unsuccessful. Over time, the proportion of patients with coronary disease who underwent revascularization with PCI as opposed to CABG surgery increased with time (*Figure 1*). Similarly, there was a trend to an increased proportion of PCI for CTO (*Figure 2*). Percutaneous CTO therapy was undertaken utilizing the contemporary techniques of the time including specialized hydrophilic, tapered tip, and stiff wires when available, with the laser wire used in 72 (8.1%). However, despite the introduction of more specialized technologies, the success rate of recanalization did not improve (*Figure 2*). Following successful recanalization, the overall use of stent implantation was 81.0%, with stent utilization increasing with time (*Figure 3*).

The 30-day MACE rates are presented in *Table 2*. In addition, this table demonstrates the events directly related to the procedure and occurring within the first 48 h. A failed recanalization procedure was associated with a significantly higher rate of MACE in the immediate period following the procedure. In the long term, all outcomes were significantly worse following a failed attempt at revascularization. The 5-year survival was significantly lower when revascularization was successful (*Figure 4*)

Table 1 Baseline patient demographics and target vessel site respect to a successful against an unsuccessful CTO revascularization procedure

	CTO success ($n = 567$)	CTO failure ($n = 304$)	*P*-value
Age (years)	59.6 ± 10.8	60.5 ± 10.4	0.2
Male sex (%)	73.6	72.2	1.0
Diabetes mellitus (%)	12.0	9.1	0.2
Hypertension (%)	20.3	21.0	0.7
Hypercholesterolaemia (%)	48.6	43.3	0.2
Family history of coronary disease (%)	21.9	18.8	0.3
Impaired LV function (%)	32.5	38.1	0.5
Previous myocardial infarction (%)	55.7	49.2	0.2
Previous PCI (%)	24.3	23.0	0.9
Previous CABG (%)	8.7	10.4	0.4
Vessel disease			0.03
Single vessel (%)	46.0	32.6	
Two vessel (%)	36.2	40.5	
Three vessel (%)	17.8	27.0	
Number of lesions	573	306	
Target vessel of the lesion			0.8
RCA (%)	42.2	52.6	
LAD (%)	33.2	26.5	
LCX (%)	24.4	20.6	
LMS (%)	0.2	0.3	

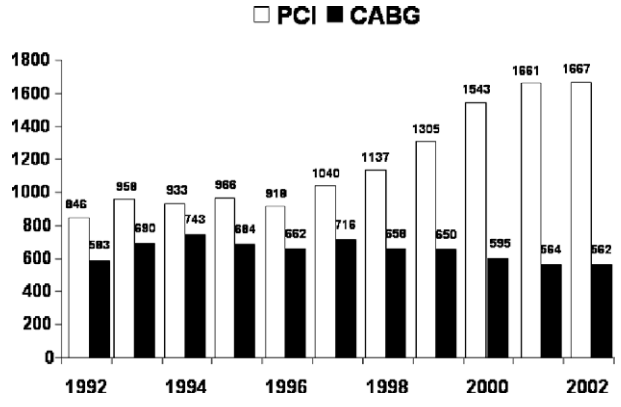

Figure 1 Trends in the number of revascularization procedures with PCI against CABG at the Thoraxcenter.

and the survival free of AMI, CABG, and MACE were also significantly lower (*Figures 5–7*). By multivariable analysis, the independent predictors for survival and MACE following PCI for CTO are presented in *Table 3*. The presence of multivessel disease was an independent predictor for both survival and MACE. The cumulative survival free of MACE with respect to the presence of single against multivessel coronary disease is shown in *Table 4*.

Overall, survival was significantly lower in those patients with diabetes mellitus (*Figure 8*). Within the diabetic population, 5-year survival was 84.9% in those with a successful recanalization against 79.1% following unsuccessful recanalization, $P = 0.4$, suggesting that most of the benefit in terms of survival following successful recanalization is in the non-diabetic group. However, the beneficial effect of successful recanalization of a CTO on survival free of MACE remains clearly apparent (*Figure 9*), irrespective of diabetic status. Successful recanalization led to a 5-year MACE-free survival of 63.7 and 62.3% in those with and without diabetes mellitus, respectively. Following unsuccessful recanalization, the 5-year MACE-free survival was 42.0 and 41.5% for those with and without diabetes mellitus, respectively, $P < 0.0001$.

Discussion

The present study evaluated only consecutive patients with CTO of at least 1-month duration and for the first time confirms a 5-year survival benefit in successful recanalization of these lesions. In addition, there was a significant reduction in MACE, particularly the need for revascularization with CABG. Independent predictors of survival were a successful recanalization, lower age, and the absence of diabetes mellitus and multivessel disease. Independent predictors of major adverse events were an unsuccessful recanalization, multivessel disease, and non-usage of stent implantation.

Although one large series of the long-term outcomes of patients following PCI for CTO has been published, the authors acknowledged that their study was limited as they did not always know the duration of occlusion.[2] Indeed, analysis of 100 consecutive patients who had been included in the study demonstrated that 42% were of <1-month duration. These patients are likely to have thrombotic occlusions rather than the fibrotic/calcific lesion of a CTO. This difference in lesion pathophysiology may affect the long-term outcome; indeed, one of the independent predictors for survival in the MAHI study was therapy for unstable angina. In the present study, we have confirmed that a successful outcome following PCI for a truly chronic occlusion does confer a significant benefit on survival and reduces the rate of MACE with a marked reduction in the need for CABG.

The difference in the rate of MACE between those with a successful and unsuccessful recanalization was apparent

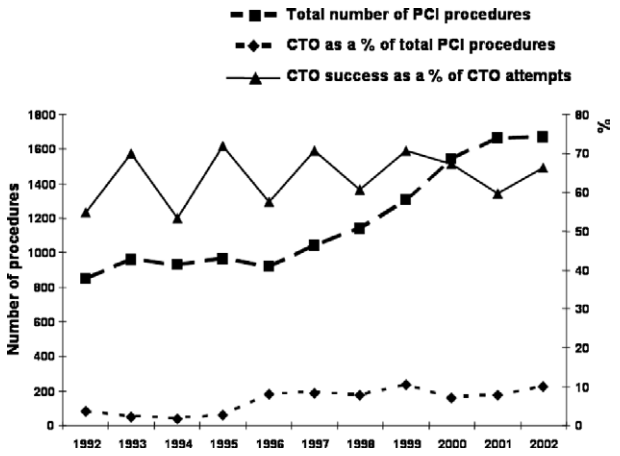

Figure 2 Trends in the increase in the proportion of PCI for a CTO and success rates of PCI for a CTO with respect to the year of intervention.

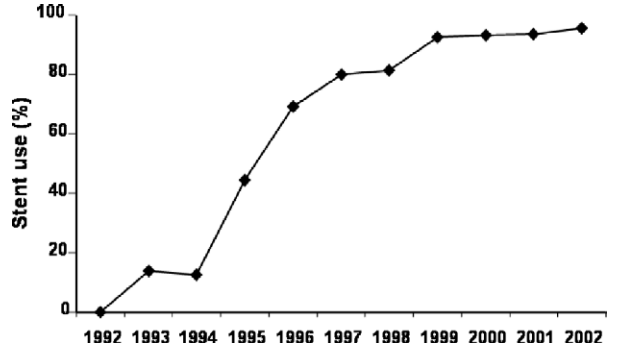

Figure 3 Utilization of stent implantation following successful recanalization of a CTO with respect to the year of intervention.

Table 2 Incidence of MACE at 2 and 30 days

	CTO success ($n = 567$)	CTO failure ($n = 304$)	*P*-value
Death, *n* (%)			
2 days	2 (0.4)	3 (1.0)	0.2
30 days	4 (0.7)	6 (2.0)	0.09
Death or AMI, *n* (%)			
2 days	3 (0.5)	5 (1.6)	0.1
30 days	7 (1.2)	7 (2.3)	0.2
Death or CABG, *n* (%)			
2 days	7 (1.2)	13 (4.3)	0.004
30 days	10 (1.8)	30 (9.9)	<0.00001
MACE, *n* (%)			
2 days	14 (2.5)	17 (5.6)	0.02
30 days	31 (5.5)	45 (14.8)	<0.00001

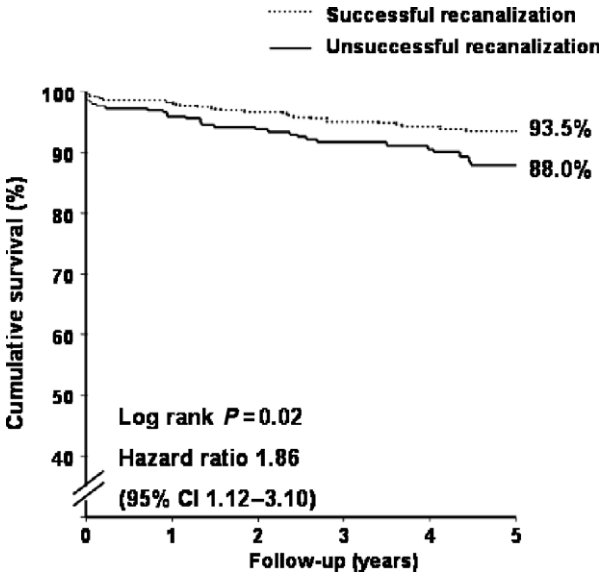

Figure 4 Cumulative survival at 5 years with respect to the outcome of attempted recanalization of a CTO.

immediately (at 48 h), which is predominantly related to the need for emergency CABG in the failed recanalization group. Therefore, an acute complication of CTO recanalization confers serious adverse consequences in the short term, which would have been potentially avoided if an alternative treatment option had been undertaken. It is particularly important to note that the mortality rate of those with a failed procedure was not insignificant at 1.9% at 30 days.

The present study demonstrated a 5-year survival benefit following successful CTO recanalization. The possible reasons for the improved survival are beyond the scope of the present study. There were differences in the medical therapy received by the two groups, which could potentially be a confounding factor. Unlike those with a failed recanalization, the group with a successful recanalization together with stent implantation was treated with additional medical therapy with warfarin, ticlopidine, or clopidogrel. However, this was given for only 1 month, and it is unlikely that such a short duration of therapy is the reason for the improved long-term outcomes. More likely, improved survival may relate to the greater proportion of viable but inadequately perfused myocardium. The improvement in prognosis following successful revascularization might relate to the associated improvement in left ventricular function[7,8] or a reduction in the risk of ischaemic-driven malignant arrhythmia. In addition, a successful procedure could potentially avoid the need for CABG with its associated mortality risk.

In the present study, the survival benefit of successful CTO recanalization was most apparent in those with multivessel rather than single-vessel disease. Indeed, the patients with single-vessel disease and failed recanalization had a very high rate of survival at 5 years of 98.9%. Approximately half of these patients underwent CABG or repeat reintervention with PCI, with a survival free of MACE at 5 years of 45.8%. The remaining patients were treated with medical therapy alone, and although this constitutes only a relatively small number of patients, the excellent survival rate suggests that from a prognostic point of view, medical therapy may not be unreasonable. Little data are currently available on the outcomes of patients with a CTO who are managed with optimal medical therapy (aspirin, beta-blocker, statin, ACE-inhibitor, etc.). In particular, those with an excellent collateral circulation may have a very good prognosis. Therefore, our study does not provide scientific proof to support a broad generalized recommendation

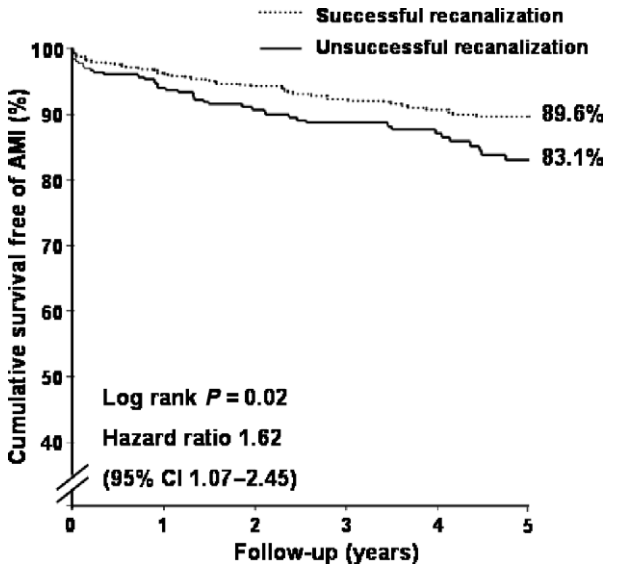

Figure 5 Cumulative survival free of AMI at 5 years with respect to the outcome of attempted recanalization of a CTO.

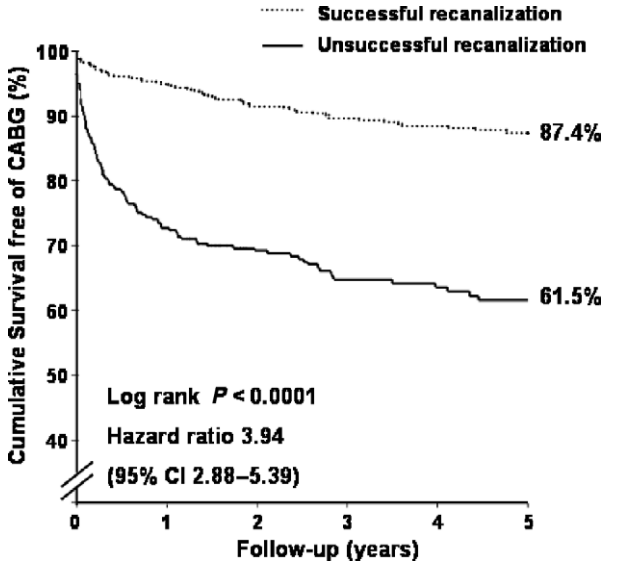

Figure 6 Cumulative survival free of CABG at 5 years with respect to the outcome of attempted recanalization of a CTO.

to try to open all CTOs; a randomized study comparing 'best' medical therapy with a more aggressive strategy of attempted recanalization would be required to assess this. Importantly, we need studies with more detailed assessment of left ventricular function, degree of viability, and ischaemic burden, both pre-procedure and at follow-up, to determine the relationship these factors have on long-term survival.

The Thoraxcenter in Rotterdam is a tertiary referral centre for PCI, taking referrals from 13 surrounding hospitals covering a large region. The majority of patients requiring repeat reintervention, whether it be percutaneous or surgical, come back to be retreated in our centre. As in other centres, the number of percutaneous revascularizations increased over time, whereas that of CABG gradually decreased. In addition, the relative number of PCI procedures carried out for a chronic occlusion also increased

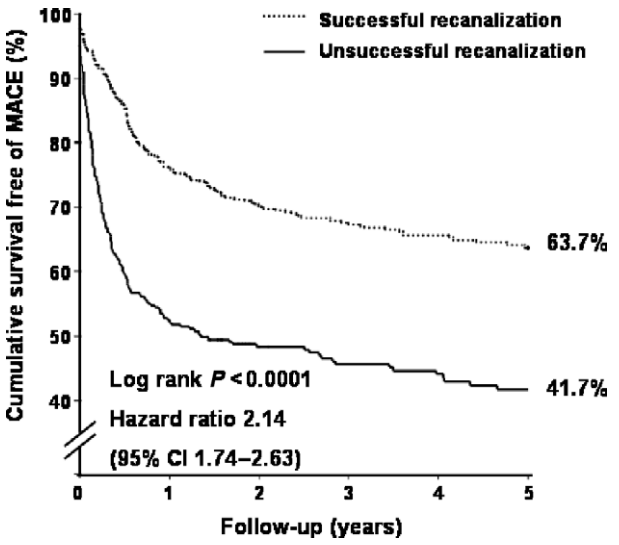

Figure 7 Cumulative survival free of MACE [death, AMI, or repeat reintervention (percutaneous or bypass surgery)] at 5 years with respect to the outcome of attempted recanalization of a CTO.

Table 3 Independent predictors of death and MACE after attempted PCI of a CTO

	Hazard ratio	95% CI	*P*-value
Death			
Successful revascularization	0.58	0.34–0.98	0.04
Age	1.04	1.02–1.07	0.002
Diabetes mellitus	2.49	1.33–4.66	0.005
Multivessel disease	4.29	1.93–9.55	<0.001
MACE			
Successful revascularization	0.55	0.44–0.70	<0.001
Multivessel disease	1.43	1.14–1.79	0.002
Use of a stent	0.69	0.54–0.88	0.002

with time. However, the overall success rate of recanalization remained stable despite the advances in the technology of specialized wires and other equipments. The chances of successful recanalization are known to be dependent on lesion morphology and it is possible that with time and the increase in PCI for CTO, relatively more complex lesions were attempted.

It is well recognized from large-scale studies that mortality is higher following PCI procedures in those with diabetes when compared with those without diabetes mellitus.[9,10] Our study concurs with these results, with a significantly lower 5-year survival in diabetics (83.6 vs. 92.7%, $P = 0.001$). However, the beneficial effect of successful recanalization of a CTO on overall survival free of major adverse events was clearly apparent to be irrespective of diabetic status (*Figure 9*).

Of those patients with a successful revascularization, the majority of subsequent adverse events relate to a need for repeat reintervention. Long-term results have been shown to improve with the advent of stent implantation, with reduced rates of restenosis and re-occlusion when compared

Table 4 Cumulative survival free of MACE at 5 years with respect to the presence of single vs. multivessel coronary disease

	Single vessel			Multivessel		
	CTO success ($n = 261$)	CTO failure ($n = 99$)	*P*-value	CTO success ($n = 306$)	CTO failure ($n = 205$)	*P*-value
Death (%)	97.3	99.0	0.3	92.5	86.3	0.02
Death or AMI (%)	94.6	96.0	0.6	88.6	82.0	0.03
Death or CABG (%)	91.6	70.7	<0.0001	86.9	61.5	<0.0001
MACE (%)	72.0	47.5	<0.0001	61.1	42.9	<0.0001

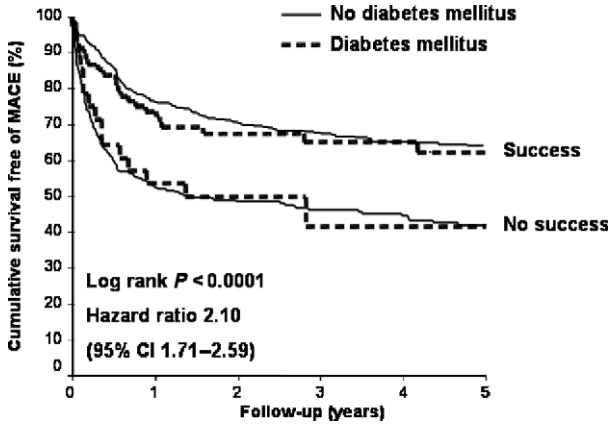

Figure 8 Cumulative survival at 5 years with respect to diabetic status.

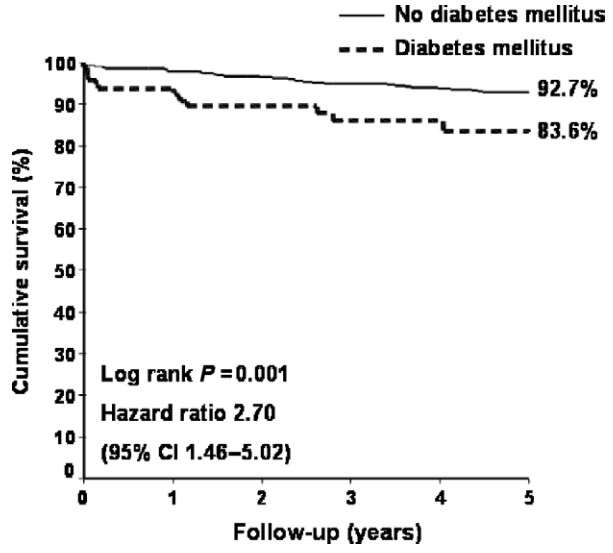

Figure 9 Cumulative survival free of MACE [death, AMI, or repeat reintervention (percutaneous or bypass surgery)] at 5 years with respect to the diabetic status and the outcome of attempted recanalization of a CTO.

with results of balloon-only angioplasty. However, the recent introduction of drug-eluting stents will further improve on these results. Data from our own centre have shown a significant higher cumulative survival free of MACE at 1 year with the sirolimus-eluting stent when compared with bare metal stent implantation (96.4 vs. 82.8%, $P < 0.05$).[11] Similar results have also been shown with the paclitaxel-eluting stent.[12] These results encourage the development of further technologies to facilitate safe and successful CTO recanalization.

Limitations

The present study is limited by being a retrospective observational analysis of outcomes. However, it comprises a large cohort of patients with complete clinical follow-up obtained in virtually all. The study is further limited by the lack of randomized comparison with a group of patients treated with medical therapy alone or those treated directly with CABG. In addition, the possible reasons for improved survival in the successful recanalization group have not been fully explored and require further study.

Conclusions

Successful percutaneous revascularization of a CTO leads to a significantly improved survival rate and a reduction in major adverse events at 5 years. Most events relate to the need for repeat reintervention, and the introduction of drug-eluting stents, with reduced restenosis rates, encourages the development of further technologies to improve recanalization success rates. However, failed recanalization may be associated acutely with a major adverse event, and new technologies must focus on a safe approach to successful recanalization. Additional studies are needed to evaluate the comparative prognostic value of CTO recanalization when compared with optimal medical therapy, particularly in patients with single-vessel disease.

Conflict of interest: we confirm that there are no conflicts of interest.

References

1. Christofferson RD, Lehmann KG, Martin GV, Every N, Caldwell JH, Kapadia SR. Effect of chronic total coronary occlusion on treatment strategy. *Am J Cardiol* 2005;**95**:1088–1091.
2. Suero JA, Marso SP, Jones PG, Laster SB, Huber KC, Giorgi LV, Johnson WL, Rutherford BD. 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. *J Am Coll Cardiol* 2001;**38**:409–414.
3. Lotan C, Rozenman Y, Hendler A, Turgeman Y, Ayzenberg O, Beyar R, Krakover R, Rosenfeld T, Gotsman MS. Stents in total occlusion for restenosis prevention. The multicentre randomized STOP study. The Israeli Working Group for Interventional Cardiology. *Eur Heart J* 2000;**21**:1960–1966.

4. Sirnes PA, Golf S, Myreng Y, Molstad P, Emanuelsson H, Albertsson P, Brekke M, Mangschau A, Endresen K, Kjekshus J. Stenting in Chronic Coronary Occlusion (SICCO): a randomized, controlled trial of adding stent implantation after successful angioplasty. *J Am Coll Cardiol* 1996;**28**:1444–1451.
5. Rubartelli P, Niccoli L, Verna E, Giachero C, Zimarino M, Fontanelli A, Vassanelli C, Campolo L, Martuscelli E, Tommasini G. Stent implantation versus balloon angioplasty in chronic coronary occlusions: results from the GISSOC trial. Gruppo Italiano di Studio sullo Stent nelle Occlusioni Coronariche. *J Am Coll Cardiol* 1998;**32**:90–96.
6. Buller CE, Dzavik V, Carere RG, Mancini GB, Barbeau G, Lazzam C, Anderson TJ, Knudtson ML, Marquis JF, Suzuki T, Cohen EA, Fox RS, Teo KK. Primary stenting versus balloon angioplasty in occluded coronary arteries: the Total Occlusion Study of Canada (TOSCA). *Circulation* 1999;**100**:236–242.
7. Rambaldi R, Hamburger JN, Geleijnse ML, Poldermans D, Kimman GJ, Aiazian AA, Fioretti PM, Ten Cate FJ, Roelandt JR, Serruys PW. Early recovery of wall motion abnormalities after recanalization of chronic totally occluded coronary arteries: a dobutamine echocardiographic, prospective, single-center experience. *Am Heart J* 1998;**136**: 831–836.
8. Ermis C, Boz A, Tholakanahalli V, Yalcinkaya S, Semiz E, Sancaktar O, Benditt DG, Deger N. Assessment of percutaneous coronary intervention on regional and global left ventricular function in patients with chronic total occlusions. *Can J Cardiol* 2005;**21**:275–280.
9. Pell JP, Pell AC, Jeffrey RR, Jennings K, Oldroyd K, Eteiba H, Hogg KJ, Murday A, Faichney A, Colquhoun I, Berg G, Starkey IR, Flapan A, Mankad P. Comparison of survival following coronary artery bypass grafting vs. percutaneous coronary intervention in diabetic and non-diabetic patients: retrospective cohort study of 6320 procedures. *Diabet Med* 2004;**21**:790–792.
10. Seven-year outcome in the bypass angioplasty revascularization investigation (BARI) by treatment and diabetic status. *J Am Coll Cardiol* 2000;**35**:1122–1129.
11. Hoye A, Tanabe K, Lemos PA, Aoki J, Saia F, Arampatzis C, Degertekin M, Hofma SH, Sianos G, McFadden E, Van Der Giessen WJ, Smits PC, De Feyter PJ, Van Domburg RT, Serruys PW. Significant reduction in restenosis after the use of sirolimus-eluting stents in the treatment of chronic total occlusions. *J Am Coll Cardiol* 2004;**43**:1954–1958.
12. Werner GS, Krack A, Schwarz G, Prochnau D, Betge S, Figulla HR. Prevention of lesion recurrence in chronic total coronary occlusions by paclitaxel-eluting stents. *J Am Coll Cardiol* 2004;**44**:2301–2306.