

Climbing PCI success rates in complex chronic total occlusions: joining “The Club”

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Coronary chronic total occlusions (CTO) have been termed the “last frontier” of percutaneous coronary intervention (PCI)¹, and remain one of the most technically challenging lesion subsets with lower rates of procedural success, higher complication rates, greater radiation exposure, and longer procedure times compared with interventions in non-CTO stenoses. For these reasons, CTO remains a common indication for referral for coronary artery bypass grafting (CABG)². However grafting of the CTO can also be challenging, as shown in the SYNTAX (SYNergy Between PCI With TAXUS and Cardiac Surgery) clinical trial CTO subset, in which successful bypass grafting of the CTO was achieved in only 69%³.

A large body of evidence suggests that successful CTO PCI results in improved clinical outcomes. Global improvements in left ventricular function have been reported by following successful CTO PCI^{4,6}, while un-revascularised CTO has been reported to increase mortality in the setting of incomplete revascularisation with multivessel coronary artery disease⁷. Numerous single-centre studies have reported reduced mortality for patients undergoing a successful CTO PCI compared with those who undergo an unsuccessful attempt^{8,9}. However, definitive data regarding a survival advantage are lacking due to the absence of a prospective randomised trial.

Despite the growing body of data suggesting improved outcomes with CTO PCI, attempt rates among patients identified with a CTO remain low (about 11%-13%) and seem unchanged over time during recent years¹⁰. Indeed, the contemporary Canadian Multicentre CTO Registry showed similar findings, with marked variation between PCI centres (Fefer P et al, personal communication).

A temporal analysis of CTO PCI trends from the Mayo clinic documented improved procedural success for attempted revascu-

larisation following the introduction of coronary stents, but no significant improvement above the 70% mark in the subsequent 15 years¹¹. Similar success rates are demonstrated in the Canadian Multicentre CTO Registry (Fefer P et al, personal communication). However, recently published registries from Japan¹²⁻¹⁴, Europe¹⁵ and the United States¹⁶ have reported success rates in the 85-90% range with low rates of periprocedural MACE.

The paper by Galassi et al¹⁷ in this issue of EuroIntervention describes the in-hospital PCI outcomes in a 16-centre registry of 1,983 consecutive CTO lesions. Overall procedural success was attained in 82.9% with a relatively low complication rate: periprocedural MI: 1.3%; coronary perforation: 2.6%; tamponade and pericardiocentesis: 0.5%; access site complications: 0.7%; and in-hospital death: 0.3%. Notably, the retrograde approach was undertaken in 11.8% of cases and, compared with the antegrade approach, was associated with lower technical success rate (64.5% vs. 83.2%, $p<0.001$), more frequent coronary perforation (4.7% vs. 2.1%, $p=0.04$), extended fluoroscopy time and greater contrast load. Similar to previous series, long (>20 mm) and heavily calcified lesions were associated with procedural failure which, in turn, was associated with increased 30-day mortality and non-fatal MI compared with patients successfully revascularised (1.9% vs. 0, $p<0.001$ and 3.6% vs. 0.8%, $p<0.001$, respectively).

The authors are to be commended for this important undertaking of recording and following all cases of CTO PCI. Indeed, the results of this registry demonstrate the successful adoption in Europe of specialised techniques learned from our Japanese colleagues with similar success and complication rates as those reported from Japan. A number of caveats apply beyond the non-randomised nature inherent to all registries. First, all procedures were carried out in centres with a specific program for CTO treatment accom-

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plished by skilled operators and staff. Thus, it is unlikely that these results will be reproducible in non-CTO specialised centres. Secondly, the current report only refers to patients referred for PCI and does not inform us how many CTO lesions were turned down for PCI or referred for CABG (also, 15% of PCI CTO patients in this registry were asymptomatic). Thus, the registry may be biased toward cases with a priori higher likelihood of success, again arguing against the generalisability of the results to all CTO lesions. Thirdly, angiographic data was not assessed independently by a core lab. This could result in inclusion of sub-total occlusions and overestimation of angiographic success. Indeed in the TOAST-GISE study⁷ in which an angiographic corelab was used, 8% of angiograms were excluded, being judged subtotal stenoses.

Notwithstanding these weaknesses, this is a very well conducted and important document which underscores the improved acute results of PCI CTO in recent years beginning in Japan and now iterated in widely disparate clinical and cultural environments.

Now that CTO PCI seems to be technically feasible, how should we proceed from here?

1. We should recognise that CTO PCI is a specialty procedure. Dedicated PCI operators working within centres of excellence should likely be the model of CTO delivery of care in the future. Quality assurance data from individual centres should be available to determine quality of care at each site.
2. Various technical issues regarding the treatment of CTOs remain unclear. A case in point is the retrograde technique. While it is clear that this continues to be a challenging yet enabling technique in certain cases, it is associated with significantly lower (though still reasonable) success rates (65%), higher complication rates and much longer procedure times and contrast exposure. These suggest that it should be limited to highly trained individuals who have high procedure volumes with this technique and that patient selection should be very stringent.
3. Are we currently under-treating CTO by PCI based on recent registries reporting success rates consistently >80% with low complication rates. Supporting this notion, data from the Canadian Multicentre CTO registry suggests that a large proportion of CTO patients with significant viability are not being revascularised by PCI or by CABG (Fefer et al, personal communication).
4. Despite the technical expertise and dedicated equipment used by the operators participating in this study, 17.1% of patients were not successfully revascularised. These patients demonstrated markedly worse 30-day outcomes. Novel devices (BridgePoint Medical System catheters/guidewires¹⁸) and intra-plaque manipulation with collagenase prior to PCI recently reported at Late Breaking Trials, 2011 EuroPCR, are both past the first-in-man phases of development with encouraging results that may further increase CTO PCI success rates in these challenging cases.
5. Lastly, but maybe most importantly, it is high time for a well planned randomised trial which will prospectively allocate patients with CTO to different treatment strategies. This should be an international

effort and should include detailed angiographic and functional data regarding left ventricular contractility and viability in the CTO territory as well as quality of life indicators. While we seem to be very close to conquering the “last frontier”, the onus is on us to prove that what we are doing indeed has clinical benefit and which subsets of patients are most likely to benefit from the procedure.

Conflict of interest statement

B. Strauss holds intellectual property on the use of collagenase in chronic total occlusions, and is founder of Matrizyme Pharma, a company that is commercialising collagenase for use in chronic total occlusions. P. Fefer has no conflict of interest to declare.

References

1. Stone GW, Kandzari DE, Mehran R, Colombo A, Schwartz RS, Bailey S, Moussa I, Teirstein PS, Dangas G, Baim DS, Selmon M, Strauss BH, Tamai H, Suzuki T, Mitsudo K, Katoh O, Cox DA, Hoye A, Mintz GS, Grube E, Cannon LA, Reifart NJ, Reisman M, Abizaid A, Moses JW, Leon MB, Serruys PW. Percutaneous recanalization of chronically occluded coronary arteries: a consensus document: part I. *Circulation* 2005;112:2364-72.
2. Christofferson RD, Lehmann KG, Martin GV, Every N, Caldwell JH, Kapadia SR. Effect of chronic total occlusion on treatment strategy. *Am J Cardiol* 2005;95:1088-91.
3. Serruys P. SYNTAX: Chronic total occlusion subsets. Paper presented at: Cardiovascular Research Technologies (CRT) 2009. March 4-6, 2009; Washington, DC.
4. Chung CM, Nakamura S, Tanaka K, Tanigawa J, Kitano K, Akiyama T, Matoba Y, Katoh O. Effect of recanalization of chronic total occlusions on global and regional left ventricular function in patients with or without previous myocardial infarction. *Catheter Cardiovasc Interv* 2003;60:368-74.
5. Cheng AS, Selvanayagam JB, Jerosch-Herold M, van Gaal WJ, Karamitsos TD, Neubauer S, Banning AP. Percutaneous treatment of chronic total coronary occlusions improves regional hyperemic myocardial blood flow and contractility: insights from quantitative cardiovascular magnetic resonance imaging. *JACC Cardiovasc Interv* 2008;1:44-53.
6. Kirschbaum SW, Baks T, van den Ent M, Sianos G, Krestin GP, Serruys PW, de Feyter PJ, van Geuns RJ. Evaluation of left ventricular function three years after percutaneous recanalization of chronic total coronary occlusions. *Am J Cardiol* 2008;101:179-85.
7. Olivari Z, Rubartelli P, Piscione F, Etori F, Fontanelli A, Salemme L, Giachero C, Di Mario C, Gabrielli G, Spedicato L, Bedogni F; TOAST-GISE Investigators. Immediate results and one-year clinical outcome after percutaneous coronary interventions in chronic total occlusions: data from a multicenter, prospective, observational study (TOAST-GISE). *J Am Coll Cardiol* 2003;41:1672-8.
8. 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;38:409-14.

9. Valenti R, Migliorini A, Signorini U, Vergara R, Parodi G, Carrabba N, Cerisano G, Antoniucci D. Impact of complete revascularization with percutaneous coronary intervention on survival in patients with at least one chronic total occlusion. *Eur Heart J* 2008; 29:2336-42.
10. Grantham JA, Marso SP, Spertus J, House J, Holmes DR Jr, Rutherford BD. Chronic total occlusion angioplasty in the United States. *JACC Cardiovasc Interv* 2009;2:479-86.
11. Prasad A, Rihal CS, Lennon RJ, Wiste HJ, Singh M, Holmes DR Jr. Trends in outcomes after percutaneous coronary intervention for chronic total occlusions: a 25-year experience from the Mayo Clinic. *J Am Coll Cardiol* 2007;49:1611-8.
12. Morino Y, Kimura T, Hayashi Y, Muramatsu T, Ochiai M, Noguchi Y, Kato K, Shibata Y, Hiasa Y, Doi O, Yamashita T, Morimoto T, Abe M, Hinohara T, Mitsudo K; J-CTO Registry Investigators. In-hospital outcomes of contemporary percutaneous coronary intervention in patients with chronic total occlusion insights from the J-CTO Registry (Multicenter CTO Registry in Japan). *JACC Cardiovasc Interv* 2010;3:143-51.
13. Mitsudo K, Yamashita T, Asakura Y, Muramatsu T, Doi O, Shibata Y, Morino Y. Recanalization strategy for chronic total occlusions with tapered and stiff-tip guidewire. The results of CTO new techniQUE for STandard procedure (CONQUEST) trial. *J Invasive Cardiol* 2008;20:571-7.
14. Rathore S, Katoh O, Matsuo H, Terashima M, Tanaka N, Kinoshita Y, Kimura M, Tsuchikane E, Nasu K, Ehara M, Asakura K, Asakura Y, Suzuki T. Retrograde percutaneous recanalization of chronic total occlusion of the coronary arteries: procedural outcomes and predictors of success in contemporary practice. *Circ Cardiovasc Interv* 2009;2:124-32.
15. Sianos G, Barlis P, Di Mario C, Papafaklis MI, Bfttner J, Galassi AR, Schofer J, Werner G, Lefevre T, Louvard Y, Serruys PW, Reifart N; EuroCTO Club. European experience with the retrograde approach for the recanalisation of coronary artery chronic total occlusions. A report on behalf of the euroCTO club. *EuroIntervention* 2008;4:84-92.
16. Thompson CA, Jayne JE, Robb JF, Friedman BJ, Kaplan AV, Hettleman BD, Niles NW, Lombardi WL. Retrograde techniques and the impact of operator volume on percutaneous intervention for coronary chronic total occlusions an early U.S. experience. *JACC Cardiovasc Interv* 2009;2:834-42.
17. Galassi AR, Tomasello SD, Reifart N, Werner GS, Sianos G, Bonnier H, Sievert H, Ehlradad S, Bufe A, Shofer J, Gershlick A, Hildick-Smith D, Escaned J, Ergilis A, Sheiban I, Thuesen K, Serra A, Christiansen E, Buettner A, Costanzo L, Barrano G, Di Mario C. In-hospital outcomes of percutaneous coronary interventions in patients with chronic total occlusion: insights from the ERCTO (European Registry of Chronic Total Occlusion) registry. *EuroIntervention* 2011;7:472-79.
18. Werner G, Schofer J, Sievert H, Kugler C, Reifart N. Multicentre experience with the BridgePoint devices to facilitate recanalisation of chronic total coronary occlusions through controlled subintimal re-entry. *EuroIntervention* 2011;7:192-200.