

## CTO PCI at the crossroads

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Chronic total occlusions (CTOs) lesions represent the last hurdle for modern day interventional cardiology. They are present in up to 30% of patients with significant coronary artery disease on angiography<sup>1</sup> and are seriously under-treated (<10%) by percutaneous techniques<sup>2</sup>.

There are three main reasons for this:

1. The low success rates, (averaging 65–70% in experienced hands), well below the standard for non-occlusive coronary lesions which remained unchanged over time<sup>3</sup> until recently.
2. The lack of strong evidence based medicine, namely prospective randomised trials, comparing percutaneous techniques with contemporary medical treatment, demonstrating superiority when successfully recanalising a CTO on hard clinical endpoints, such as long-term mortality, while keeping very low procedural complication rates.
3. The average results of balloon angioplasty and bare metal stents in this anatomical setting, with high rates of restenosis and reocclusion. The first generation of drug-eluting stents definitely improved clinical and angiographic endpoints, but there are still concerns about long-term outcomes related to increased stent thrombosis rates compared to BMS<sup>4</sup> and mechanical issues such as stent fractures<sup>5</sup>.

The two reports by Werner<sup>6</sup> and Reifart<sup>7</sup> address these issues in an effort to alert the interventional community and promote CTO PCI.

The ALKK registry reconfirms the lack of enthusiasm for treating CTOs in one of the largest PCI practices in Europe. The 7.6% success rate matches reports coming from overseas<sup>2</sup>. Considering the lack of duration of the occlusion in combination with characteristics such as high use of IIb/IIIa inhibitors and *ad hoc* procedures, as well as the younger age of the CTO patients, the

actual percentage, according to the contemporary definition, should be much lower. Moreover, the extremely low fluoroscopy times (only 13 min) are indicative that the majority of the CTOs were simple, or that the recanalisation procedure was incomplete when measured against current standards. On the other hand, they represent “real world” routine data and are indicative of the large space for improvement that remains before us, as well as the enormous efforts needed to move forward.

After a long time of stagnation and low success rates, retrograde techniques were developed and introduced into clinical practice in 2005<sup>8</sup>. The consequence of this was 3-fold: the revival of enthusiasm for CTO recanalisation, the development and refinement of dedicated materials and a training program on a global scale led by Japanese physicians. With contemporary retrograde techniques and materials success, rates entered the range of 90-95%. Even more important, while driven by the retrograde experience, there were serious developments in antegrade techniques, with reported success rates for the first time in the range of 80%<sup>9</sup>. The field was dominated by the use of soft polymer jacket hydrophilic wires, dedicated microcatheters and the establishment of the bilateral contrast injection. It is not only in the success rates, but also in the complexity of the CTOs that were now attempted that we reached a level never realised before.

The year 2006 was a transitional one for CTO practice in Europe. It was the year of the adoption and adaptation of all these new technologies and techniques coming from Japan. At the end of 2006, recognising the challenges and importance of these new developments, the EuroCTO club was established by a few dedicated physicians, and in 2007 published its position paper<sup>10</sup>.

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Soon after, the first European experience with retrograde techniques were reported where we were able to match the Japanese results both from the standpoint of efficacy and safety<sup>11</sup>. In 2009 the first meeting of the Club was held in Taormina, Sicily<sup>12</sup> and was established as an annual event (this year the meeting will be held in Greece, [www.eurocto2010.gr](http://www.eurocto2010.gr)). With respect to all these meetings, Werner's report might not represent contemporary CTO practices in Germany. An annual registration over a period of five years or longer would be very important to evaluate the effect of all of these efforts. The success rates of around 60% is well beyond the success rates reported in the dedicated group of experienced CTO operators. Unfortunately, modern antegrade and retrograde techniques still remain in the hands of few experts. Training interventional cardiologists in contemporary CTO techniques, including the retrograde approach, in numbers adequate to serve the purpose of treating a significant proportion of patients with CTOs successfully and without safety issues, should be the target. Currently, training in Europe is based on CTO dedicated meetings and proctoring sessions, the majority organised by members of the EuroCTO club. One direction for improvement would be the integration and expansion of all these activities into a united annual training program coordinated by the EuroCTO club and supported by all European experts. This will allow training sessions tailored to the needs of the audience at any given time, from the simplest basic antegrade to the most complex retrograde techniques.

The other obstacle for expanding CTO PCI treatment is persuading the cardiology community that its benefits outweigh its risks. There is considerable evidence for improvement in angina status<sup>13</sup> and left ventricular function<sup>14</sup>, even survival benefits<sup>3</sup>. The majority of these reports are retrospective and non-randomised and can be easily challenged, revealing a paucity of data in this direction. To fill in the gap, the European study on the Utilisation of Revascularisation versus Optimal medical therapy for the treatment of Chronic Total coronary Occlusions (EUROCTO study), focusing on hard clinical endpoints, has been designed and planned to start soon as a priority mission of the EuroCTO club. Research in that direction, if it finally confirms the positive reports available in the literature, will be a major step forward, persuading the cardiology community to refer these patients for percutaneous treatment.

First generation drug-eluting stents have been a major step forward in the treatment of CTOs by improving both immediate angiographic results and long-term clinical outcomes compared to bare metal stents, but has also raised concerns about long-term efficacy and safety<sup>4</sup>. Reifart et al report on the angiographic and clinical outcomes of a novel sirolimus-eluting stent with biodegradable polymer that was already developed in 2002! It is surprising that such a technology was tested in the hardest anatomical scenario, but the results, although referring to a small number of patients, look promising. Longer term follow-up, close to six years, should now be available, and would be very interesting to report, as would more extensive validation of this technology. Currently there are also other drug-eluting stents with similar characteristics already approved for routine use, their efficacy needs to be explored in a CTO setting. With the development of techniques and dedicated CTO materials, the complexity of CTOs

treated has dramatically increased over the last five years. Especially with the STAR technique and its variations, as well as the most complex retrograde techniques, we see longer and longer arterial segments stented subintimally, and therefore more efficacious and safer stents are necessary.

Management of patients with CTO remains challenging. Many have multivessel coronary artery disease with complex target lesions previously considered unsuitable for percutaneous intervention. Intense interest now focuses on exploration of novel materials and techniques to improve the success rate of CTO PCI, but soon we have to prove, based on long-term clinical outcomes, that its worth the effort, the cost and the risks involved, establishing it as a real therapeutic alternative to medical therapy and surgery.

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