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Editorial

Medical therapy or revascularization for patients with chronic total occlusion? A dilemma almost solved

Chronic total occlusion (CTO) of the coronary arteries are relatively common, observed in approximatively 15-25% of patients with coronary artery disease undergoing coronary angiography.[1-3] The right coronary artery represents the most common CTO vessel, which represents about half of the CTO cases.[4] The CTO prevalence is much higher (90%) among patients with prior coronary artery bypass graft (CABG),[4] while a CTO is found in only one tenth of patients referred for ST-elevation myocardial infarction (STEMI).[5]

Current guidelines recommend (class IIa B) that percutaneous revascularization of CTO of the coronary arteries should be considered in patients with angina resistant to medical therapy or with a large area of documented ischemia in the territory of the occluded vessel.[6] Indeed, advances in the procedures, experience, techniques, devices, and wires used to recanalize CTO lesions have significantly improve success rate during the recent years up to 85%.[7] Although, the procedure can be associated with complications, as success rates increased during the past years, the rate of major complications decreased to less than 2% and appears close to PCI of non-occluded coronary arteries.[7-10] Therefore, it remains of critical importance to answer in which populations recanalization of CTO lesions can either improve patient symptoms and quality of life, or prognosis.

The generally accepted principle is that registries or observational studies in a propensity matched analysis complement the information provided by randomization trials, but only the rigor of the randomization process could eliminate confounding factors and ensures that true difference are present between conventional and novel therapies. Up to date symptoms improvement and quality of life is the primary indication for CTO revascularization. Indeed, two published randomized-controlled clinical trials, i.e. the Euro CTO trial[11] and the IMPACTOR-CTO trial[12] reported symptom improvement after successful CTO-PCI. The Euro CTO trial randomized 407 patients to CTO PCI vs optimal medial therapy alone. At 12 months, compared with patients randomized to medical therapy only, patients randomised to CTO PCI had greater improvement in angina frequency [subscale change difference: 5.23, 95% confidence interval (CI) 1.75-8.71; $p = 0.003$], and quality of life [subscale change difference: 6.62, 95% confidence interval (CI) 1.78-11.46; $p = 0.007$], as assessed by the Seattle Angina Questionnaire.[11] The IMPACTOR-CTO trial randomized 94 patients with isolated right coronary artery CTO to CTO PCI vs optimal medical therapy alone.[12] At 12 months, compared with optimal medical therapy, CTO PCI patients had significant reduction in ischemic burden and improvement in six–minute walk distance and quality of life as assessed by the short Form-36 Health Survey.[12] Similar improvements have been observed in multiple observational studies and meta-analyses.[13-16]

Regarding the second point that is prognosis it remains still undetermined whether CTO PCI improves endpoint of death and traditional composite endpoints of death, myocardial infarction, or revascularisation altogether indicated as MACE. In this issue of Hellenic Journal of Cardiology Guo et al[17] from China add another important piece of information with an observational study where propensity score matching was performed to adjust for baseline characteristics analysis, and showed that CTO patients who underwent revascularization were not associated with a reduced risk of cardiac death alone but lower prevalence of target vessel revascularization and MACEs when compared to medical therapy. This is similar to what has been shown by other observational studies in a propensity matched analysis who demonstrated lower incidence of major adverse events with CTO PCI[2] as compared to medical therapy alone, even among patients with well developed collateral circulations.[18] Conversely, a randomized study[19] did not demonstrate any additional benefit of CTO PCI to medical therapy alone; however, this trial carried many caveats such as nearly 20% of patients in the no-CTO PCI group crossed over to CTO PCI within 3 days after randomization, and also the study was stopped early due to slow enrolment. Indeed, excessive scrutiny means heavy selection bias that may jeopardize the applicability of results to the general population with a majority of patients relatively asymptomatic, and vessels and lesions treated unlikely to be of prognostic relevance. Indeed, interpretation of randomized CTO PCI trials should also take into consideration that most of the time most symptomatic patients are excluded from trials, as nowdays revascularization “tout cour” is generally indicated by physicians and preferred by patients.

This summary highlight once again the complexity of this issue when considering prognosis especially in relatively healthy population with heart disease and CTO of relatively low complexity as the one of Guo and colleagues, and that one size approach does not fit for all. It is also important to be added that in case of significant wall motion abnormalities of the myocardium subtended by the CTO artery the diagnostic work-up should be primarily focused on the detection of myocardial viability. Without signs of myocardial viability, no recovery of left ventricular function can be anticipated and CTO revascularization should considered inappropriate.[20,21] Conversely, the presence of substantially myocardial viability prior to revascularization is a predictor for improvement of regional and

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global left ventricular function.[22] Myocardial ischemia and viability can be assessed using an array of non-invasive imaging tests[23,24] and the choice of non-invasive imaging for CTO patients should be based on local availability and expertise. Indeed, it is reasonable to identify a cohort of CTO patients that stand to benefit from CTO PCI, both in symptoms and clinical endpoint especially those with a depressed left ventricular ejection fraction below 35%. As such, we have provided a strong rationale[25] for the next era of randomized trials evaluating the potential benefits of CTO PCI. As with all interventional therapies, the onus is on the physicians, companies involved with CTO products, and patients who will need to partner and advocate for the right trials with right endpoints.

Finally we concur with Tousoulis[26] view that in the presence of a CTO lesion, the decision-making process leading to revascularization passes through 3 steps: symptoms which are not only angina but also dyspnea, assessment of ischemic burden such as for any other significant lesion whether or not the CTO is collateralized, and demonstration of viability by any means especially for those left ventricular wall severely impaired seen in those patients with low ejection fraction who might benefit most from revascularization.

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