Does the hybrid algorithm has real impact on long-term outcomes or should only be used as a valuable approach for CTO crossing?

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The hybrid algorithm to chronic total occlusion (CTO) percutaneous coronary intervention (PCI) (*Figure 1*) was published in 2012 and provided a systematic, angiographybased, approach to crossing coronary CTOs in 4 steps: (I) dual coronary angiography, which is essential to determine the characteristics of the lesion, especially occlusion length and the presence of collaterals appropriate for the retrograde approach; (II) systematic review of 4 lesions characteristics (proximal cap, lesion length, quality of distal vessel, and presence of interventional collaterals); (III) initial crossing strategy selection based on the aforementioned 4 parameters; and (IV) early change if the initially selected crossing strategy fails to achieve crossing within a reasonable period of time (1).

The hybrid algorithm provided a structured approach to CTO crossing and has been adopted by several operators in several countries with encouraging results (*Table 1*) (2-10). The Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (Progress CTO) (7), the UK Hybrid CTO registry (8), and the Registry of Crossboss and Hybrid procedures in France, the Netherlands, Belgium and United Kingdom (RECHARGE) (9) registries have shown that application of the hybrid algorithm in CTO PCI can result in high procedural success (86–91%) and acceptable major adverse complication rates (1.6–2.6%). The OPEN-CTO Registry reported 86% procedural success rate in 1,000 consecutive CTO PCIs performed at 12 high volume US centers with an in-hospital major

complication rate of 7.0% driven by clinical perforation (4.9%) (10). OPEN CTO demonstrated that successful CTO PCI was associated with significant improvement in angina, dyspnea and depression at 1 month follow-up, but longer-term outcomes after hybrid CTO PCI have received limited study.

One of the criticisms of the hybrid approach has been the recommendation for using antegrade dissection reentry (ADR) for lesions ≥ 20 mm in length. ADR is best achieved using dedicated equipment (the CrossBoss catheter and the Stingray balloon and guidewire), which are not universally available and can be costly. Moreover, ADR could potentially increase the extent of dissection and stent length and predispose to complications, such as perforation. Alternative algorithms, such as the Asia Pacific CTO PCI algorithm (11), have been proposed, favoring antegrade wire escalation (AWE) instead of ADR. We recently presented and published the CrossBoss First randomized clinical trial that compared AWE with ADR in CTO PCI. CrossBoss First randomized 246 patients to CrossBoss (n=122) or wire escalation (n=124) at 11 US centers (12). Technical and procedural success were 87.8% and 84.1%, respectively and were similar in the two groups. Crossing time was similar: 56 (interquartile ranges, 33–93) min in the CrossBoss vs. 66 [36-105] min in the wire escalation group (P=0.323), as was as the incidence of procedural major adverse cardiovascular events (3.28% vs. 4.03%, P=1.000). However, on post hoc subgroup analyses, upfront use of the CrossBoss

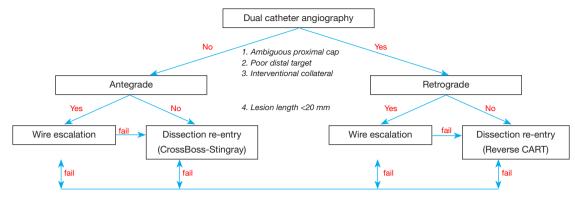


Figure 1 The hybrid algorithm.

catheter was associated with shorter crossing time than wire escalation in CTOs due to in-stent restenosis {median 41 [23–58] vs. 66 [32–111] min, P=0.047}. Moreover, ADR was the final successful strategy in 22% of the AWE group patients, demonstrating the importance of ADR in achieving procedural success in CTO PCI. This is especially true for more complex occlusions, which are less likely to be crossed using AWE and more often require use of ADR or retrograde techniques (13,14).

Another criticism of the hybrid approach has been a potential association of dissection/re-entry techniques with worse long-term outcomes, specifically higher rates of restenosis and reocclusion. This has been a concern for both ADR and retrograde dissection and re-entry (RDR) (*Table 2*) (15-20). Several studies have shown favorable long-term outcomes with use of ADR, but have been limited by small size and relatively short duration of follow-up.

Wilson et al. reported 1-year outcomes of 805 patients who underwent successful CTO revascularization using dissection and re-entry techniques (DART, both antegrade and retrograde) versus procedures that did not use dissection/re-entry (no DART group) at 7 UK centers between 2012 and 2014 as part of the UK hybrid registry. As has been previously reported (21), DART was used more frequently in more complex CTOs and was associated with longer stent length and larger contrast volume and radiation dose. The primary endpoint of the study was a composite of cardiac and non-cardiac death, myocardial infarction, unscheduled target vessel revascularization and target lesion revascularization and the mean follow-up time was 11.5±3.8 months. Follow-up angiography was scheduled in approximately one fourth of the patients (24%), mainly for distal vessel reassessment and was more frequently performed in the DART group (32% vs. 17%, P<0.001), which could potentially bias the results in favor of the no DART group. Overall, use of DART as the final CTO recanalization technique was not associated with higher rate of adverse event as compared with the no-DART group (10.3% vs. 7.0%, P=0.1). On multivariable analysis only lesions length (>25 mm) was independently associated with the incidence of adverse events at 12 months follow, suggesting that use of DART is safe.

Does this data mean that antegrade and retrograde crossing techniques should be frontline CTO crossing strategy? This may not necessarily be true. In the UK hybrid registry, 30-day major complication rates were numerally higher with more complex crossing techniques: AWE, 1.8%; retrograde wire escalation (RWE, 2.3%); ADR, 0.6%; and RDR, 2.9%. Moreover, retrograde strategies were associated with numerically higher rates of Ellis grade 3 perforation (AWE 1.0%, ADR 1.2%, RWE 2.3%, RDR 2.9%). Using retrograde techniques carries increased risk as compared with antegrade techniques (22) and should, therefore, be used with caution and when truly necessary to achieve recanalization.

Moreover, despite the reassurance provided by the UK hybrid registry long-term outcomes, when (antegrade or retrograde) dissection/re-entry is used, every attempt should be made to minimize the extent of dissection. In a recent meta-analysis extensive dissection and re-entry was associated with higher risk for subsequent adverse events (23). Extensive dissection re-entry, such as the subintimal tracking and re-entry (STAR) should only be used as bailout, because of significant side branch loss potentially leading to periprocedural myocardial infarction and/or high restenosis and reocclusion rates due to poor outflow. Similarly, new techniques are emerging for minimizing the extent of dissection in the reverse controlled antegrade and

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Table 1 Summary of published	registries using the h	hybrid algorithm for chronic total	occlusion percutaneous coronar	v intervention

Authors	Study period	Centers (n)	Case number (n)	Technical success (%)	Procedural success (%)	Overall MACE (%)	Death (%)	Acute MI (%)	Stroke (%)	TVR (%)	Pericardial tamponade (%)
Smaller (n<1,000) hybrid CTO registries											
Vo et al. (2)	2012–2013	1	50	92	92	0.0	0.0	0.0	0.0	0.0	0.0
Pershad et al. (3)	2011–2013	2	198	95	88	-	-	-	-	-	_
Daniels et al. (4)	2011–2013	-	194	93	-	-	0.0	-	-	-	2.0
Basir <i>et al</i> . (5)	2011–2015	1	297	93	91	4.4	1.5	0.7	1.1	0.7	1.9
Shammas et al. (6)	2012–2013	1	67	95.5	-	4.5	-	-	-	-	-
Large (n≥1,000) hybrid CTO registries											
Christopoulos et al. (7)	2012–2015	11	1,036	91	90	1.7	0.3	0.7	0.1	0.2	0.5
Wilson <i>et al</i> . (8)	2012–2014	7	1,156	90	-	1.6	0	0.8	0.4	0.0	0.7
Maeremans et al. (9)	2014–2015	17	1,253	89	86	2.6	0.2	0.2	2.2	0.1	1.3
Sapontis <i>et al</i> . (10)	2013–2017	12	1,000	86	85	7.0	0.9	2.6	0.0	0.1	4.8

CTO, chronic total occlusion; MACE, major adverse cardiac event; MI, myocardial infarction; PCI, percutaneous coronary intervention; TVR, target vessel revascularization.

Authors	Centers (n)	Patient number (n)	Follow-up duration	Crossing strategy	Overall MACE (%)	Mortality (%)	Acute MI (%)	TVR (%)
Mogabgab et al. (15)	1	170	Median 1.81 years	ADR	35.2	5.5	3.7	30.0†
Hasegawa et al. (16)	30	323	Median 12 months	DART*	11.3	1.9	0.0	9.4
Amsavelu et al. (17)	1	173	Median 11 months	DART*	N/A	2.4	4.9	24.41
Maeremans et al. (18)	17	1,165	Mean 363±1 days	DART*	9.3	2.7	1.7	5.5
Azzalini <i>et al</i> . (19)	1	223	Median 24 months	ADR	4.3	-	-	3.1
Galassi <i>et al</i> . (20)	1	1,395	Mean 24.7 months	Retrograde	13.6	3.9	3.4	13.0

*, DART includes ADR and RDR; †, composite of re-PCI in target and non-target vessels, re-CABG in target and non-target vessels; I, composite of ACS, TLR and TVR. ADR, antegrade dissection and re-entry; DART, dissection and re-entry technique; MACE, major adverse cardiac event; MI, myocardial infarction; RDR, retrograde dissection and re-entry; TVR, target vessel revascularization; CTO, chronic total occlusion; PCI, percutaneous coronary intervention.

retrograde subintimal tracking (reverse CART) technique. For example the "directed" reverse CART (also called "contemporary reverse CART") technique involves use of small antegrade balloon size and more active, intentional vessel tracking and penetration with a controllable retrograde wire within the CTO segment (24). In cases of extensive dissection it may be preferable to not implant stents, and just perform balloon angioplasty with stenting deferred until a later time, once the dissections have healed (investment procedure). In summary, the results of the study by Wilson *et al.* provide reassurance that using (limited) DART techniques is unlikely to significantly impair the long-term outcomes after CTO PCI. Without DART techniques the success rate of CTO PCI would likely be significantly lower, especially in more complex CTOs. Mastering DART techniques remains important for CTO PCI operators and should be done progressively, starting with ADR, advancing to retrograde via septal collaterals or bypass grafts and finally to retrograde via epicardial collaterals.

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Footnote

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