

# The Evidence Base Dictating Practice in Patients With Concomitant Significant Coronary Artery and Carotid Artery Disease

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There is a degree of controversy regarding the optimal management of patients undergoing coronary artery bypass grafting (CABG) who are also found to have concomitant severe carotid artery disease.

The evidence base is less well understood for patients requiring surgical valve repair and carotid revascularization. Therapeutic strategies have previously included CABG alone, staged carotid endarterectomy (CEA) plus CABG, reverse-staged CABG plus CEA, synchronous CEA plus CABG on-pump (cardiopulmonary bypass), synchronous CEA plus off-pump CABG, staged transfemoral carotid artery stenting (TF-CAS) plus CABG, and more recently, staged transcatheter artery revascularization (TCAR) plus CABG.

The management controversy for patients with unilateral asymptomatic carotid disease is highlighted by conflicting reports. An updated systematic review and meta-analysis of stroke after cardiac surgery and its association with asymptomatic carotid disease demonstrated an uncertain evidence base supporting a strategy of prophylactic TCAR/TF-CAS/CEA in cardiac surgery patients with unilateral asymptomatic carotid disease.<sup>1</sup> However, cardiac patients with significant carotid disease were shown to be safely treated with concomitant CABG and CEA in a publication detailing the late results of combined carotid and coronary surgery using actual versus actuarial methodology in a 500-patient cohort.<sup>2</sup> Two randomized trials in this clinical setting came to different conclusions, thus adding to the management quandary.<sup>3,4</sup>

There is minimal controversy, however, regarding the benefits of carotid revascularization prior to cardiac surgery in patients with significant bilateral carotid disease (to include unilateral occlusion). The other notable cohort in this clinical setting is the patient with a symptomatic carotid stenosis requiring cardiac surgery; these patients are at significant stroke risk during cardiac surgery without prior carotid revascularization.

## PATHO-ETIOLOGIES OF INTRAPROCEDURAL STROKE DURING CABG

The underlying etiologies of the intraprocedural stroke hazard during CABG must be understood before addressing the role of carotid revascularization prior to CABG. These etiologies include aortic cross-clamping; the use of aortic cannulas; and, when on-pump (cardiac bypass), the fact that the normal peak and trough of the systolic and diastolic cardiac waveforms are averaged out to a lower-than-peak mean. Thus, strokes may arise from embolization of aortic atheroma (not avoided by prior carotid revascularization) or cerebral hypoperfusion (possibly avoided), the latter mostly occurring when there are significant bilateral carotid stenoses of hemodynamic relevance (hemodynamic relevance starts at a 75% stenosis of the carotid artery). Against these presumptions is a risk stratification publication from the Buffalo Cardiac-Cerebral Study Group, which revealed that 66% of periprocedural strokes in patients with a > 50% carotid stenosis undergoing carotid surgery occurred in the postoperative rather than intraprocedural setting, implying carotid lesion destabilization in the hypercoagulable milieu after cardiac surgery.<sup>5</sup>

## THE REASONABLE APPROACH TO TCAR WITH COMBINED CAROTID AND CARDIAC DISEASE

If within the current limitations of the knowledge base we are faced with an undeniable management challenge, we should consider a safe algorithm for sequential treatment of combined carotid and cardiac disease as described.

A fundamental premise for the safe performance of any vascular procedure is to understand the indications, contraindications, and technique described during the research of the medical device and follow the instructions for use. TCAR was developed as a surgically inspired procedure with control of the treated vessel with proximal occlusion and robust flow reversal while intervening. The

indication for TCAR, targeted carotid lesion, access, and overall anatomy of the carotid bifurcation need to be assessed. Just as important, all cases need to be performed with medical therapy compliance of dual antiplatelet therapy (DAPT) and statin therapy, while still being able to maintain heart rate and blood pressure for the flow reversal. Several of these fundamentals can be challenged when trying to treat a patient with both significant carotid and cardiac disease with multiple procedures. For the purposes of this article, *cardiac* means any acute/subacute CABG or surgical structural valve procedure. The carotid revascularization paradigms prior to percutaneous coronary intervention and transcatheter aortic valve replacement are different and will require further elucidation.

A simple way to look at these combinations is to consider how a patient presents for evaluation. This can evolve in presentation as carotid then coronary, coronary then carotid, or simultaneous symptomatic carotid and coronary. The management then requires a true team effort of the carotid team, cardiac team, and anesthesia services.

The team members all need to understand both the indications and procedural requirements for TCAR before their recommendation is made. The Society for Vascular Surgery (SVS) Vascular Quality Initiative database is now getting quite large with well over 2,000 patients and continued rapid growth. Based on the experience of the operator, access anatomy, and patient preference, TCAR can be performed under local or general anesthesia. Typically, the TCAR procedure time is in the range of just over 1 hour, which compares very favorably to CEA (ROADSTER 1, 74 min<sup>6</sup> vs CREST, 121 min<sup>7</sup>;  $P < .001$ ). This is likely one of the reasons that the myocardial infarction rate is significantly less for TCAR compared to CEA (0.9% vs 2.3%).<sup>8</sup> Further, the time required for flow reversal is typically under 10 minutes for most operators and cases. The reversal time is important from the standpoint of need for elevated rate-pressure product and the added associated cardiac risk for that brief period. These facts are all very important in considering the cardiac risk of the TCAR procedure itself.

### Carotid Then Coronary Presentation

An asymptomatic > 80% or symptomatic > 50% carotid lesion that is considered for intervention will also have some form of cardiac risk assessment. First, assume that the patient is a good candidate for TCAR from a carotid perspective. Then, a cardiac risk assessment needs to consider whether the patient can safely tolerate the desired rate-pressure product (rate > 70 bpm, BP 140–160 mm Hg systolic) for flow reversal in the TCAR procedure. If the patient is a good candidate from a cardiac perspective, then proceed with TCAR. However, if the patient's cardiac risk is too high for hemodynamics to maintain flow reversal, options

could include TF-CAS under local anesthesia or carotid endarterectomy under either local or general anesthesia, while accepting more stringent control of the hemodynamics (eg, tighter rate and pressure control). Again, this should be decided with the thoughtful input of all services involved.

### Coronary Then Carotid Presentation

Most patients who present with cardiac disease requiring treatment are in some way symptomatic, with either myocardial infarction, angina, exercise intolerance, or shortness of breath. The Society of Thoracic Surgeons (STS) now recommends all cardiac cases to have a carotid duplex prior to the cardiac procedure to help assess carotid disease and decrease the risk of stroke. As a result, carotid surgeons are called more often to provide input for the care algorithm. In most symptomatic cardiac cases, the cardiac disease should be treated first. The question is whether this should be done with coronary stenting under DAPT, CABG with just aspirin, or structural heart intervention (either an open or endovascular procedure) with associated anticoagulation indications. Most cardiac surgeons are reluctant to perform CABG or valve surgery under DAPT. If the team and patient elect to treat a severe carotid lesion first with either TCAR or TF-CAS, the patient should go through at least 30 days of DAPT before stopping the clopidogrel. This period allows stabilization and partial reendothelialization of the stented site, which is necessary for the patient to safely go on a heart-lung machine with low-pressure flow for the cardiac surgery. The team should not try to cut the DAPT interval shorter before surgery.

### SIMULTANEOUS PRESENTATION OF SYMPTOMATIC CAROTID AND CORONARY DISEASE

This scenario is rare in clinical practice. Again, input from the cardiac team will help guide decision making. If both vascular beds are truly acutely symptomatic, then these cases should often be managed with combined carotid endarterectomy and coronary/cardiac surgery, as the likely early cessation of DAPT after TCAR and before urgent cardiac surgery will render the patient at increased risk of stroke arising from platelet aggregation on the carotid stent and/or acute stent occlusion. CEA does not require DAPT (most importantly, the P2Y12 inhibitor component—clopidogrel [Plavix, Bristol-Myers Squibb Company and Sanofi]). However, decision-making will depend on both the severity of the lesions and symptoms caused by these lesions in both of these anatomic areas.

### TCAR AND CARDIAC SURGERY; TO REITERATE

Given the stringent requirements for the DAPT necessary for TCAR (and TF-CAS), synchronous rather than staged

TF-CAS/CABG and TCAR/CABG are fraught with risk and require pharmacological gymnastics; this practice cannot be supported. Many (but not all) cardiac surgeons will not perform CABG in patients on aspirin plus a P2Y12 inhibitor such as clopidogrel (Plavix) because of the excess bleeding risk. DAPT in advance of ENROUTE® Transcarotid Stent (Silk Road Medical) placement prior to TCAR and for 1 month following is strongly recommended, if not mandatory. These recommendations are listed in the SVS guidelines for the management of extracranial carotid disease under the section related to carotid stenting.<sup>9</sup> Omitting the DAPT regimen in the setting of TCAR is contrary to the FDA-approved labelling pertaining to implantation of the ENROUTE® Stent (and in fact, any FDA approved carotid stent).<sup>10</sup> Discontinuation of clopidogrel after TCAR prior to 30 days in order to perform an urgent CABG would be against SVS guidelines for TF-CAS/TCAR and would constitute off-label use for the ENROUTE® Stent. The performance of CABG and TCAR in the same operating room time frame (which has once been reported) requires that the CABG is performed first, without the required DAPT regimen, followed immediately by TCAR, wherein the patient is subsequently administered loading doses of clopidogrel (Plavix) or other P2Y12 inhibitor in recovery. This is an extremely high-risk strategy regarding the fate of the newly implanted carotid stent and defies both the SVS carotid stent guidelines for the pharmacologic regimen and the FDA labelling of the carotid stent. Clopidogrel (Plavix) is a pro-drug that requires hepatic enzyme metabolization into its active metabolite. This explains resistance through genetic polymorphisms, but also highlights that even loading doses require sufficient processing time until the full antiplatelet effect is achieved, meaning that post-loading is ineffective and fraught with unnecessary risk.

Staged TCAR and cardiac surgery, preferably 30 days apart, is very achievable.

## SUMMARY

The primary consideration can be summarized as “the separation of procedural risk” of the cardiac and carotid procedures. The requirement for synchronous coronary/valve and carotid procedures for urgent symptoms from both territories is relatively rare. The options for treatment of the carotid bifurcation have been safely expanded with the TCAR procedure, but TCAR cannot be recommended in those rare circumstances wherein both urgent carotid and coronary revascularization is required on account of the requirements for DAPT. When performed following the accepted instructions for use, excellent results have been achieved. The scenarios described in this article are a reasonable algorithm for consideration. Essential to success are an approved indication for the procedure, medication

compliance (DAPT and statin therapy preoperatively and for 30 days postoperatively), adequate anatomy (both cervical and cerebral), ability to reach the hemodynamics recommended for flow reversal (heart rate > 70 bpm and BP 140–160 mm Hg), and continuous hemodynamic monitoring postop (BP > 110 mm Hg). These factors must be considered reasonably attainable prior to consenting for TCAR in the patient who also has cardiac disease. ■

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