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EDITORIAL COMMENT

# Carotid Artery Stenting Before Cardiac Surgery

## A Promising Path Down a Muddy Road?*

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*Things alter for the worse spontaneously,*
*if they be not altered for the better designedly*
—Francis Bacon (1)

The management of synchronous carotid disease and coronary or valvular disease requiring surgical repair has been a constant challenge to clinicians for decades and for a variety of reasons. First, although it is a vexing problem, it is relatively infrequent, such that any single institution/operator experience in management will always be clouded by "the last case I did" syndrome, more reflective than definitive. Second, even in patients without carotid stenosis, the risk of stroke inherent in cardiac surgery from other sources (atheroembolic from aortic manipulation, air emboli, and so on) clouds the assessment of the neurological "natural" history of the unoperated carotid stenosis in this setting. However, it seems clear enough that the patient with symptomatic carotid disease is at most risk and requires further management consideration, but that most asymptomatic patients with unilateral disease can withstand a cardiac operation with little increase in overall stroke risk and, therefore, should not be subjected to carotid revascularization risks (2). Next, the published database that generally helps guide such decisions in practice comprises largely single-center reports, and usually retrospectively analyzed. A recent Cochrane attempt to review all the published randomized data on the subject could not be completed, because there were no such studies in existence (3). Further complicating matters, the therapeutic approaches are multiple—carotid endarterectomy (CEA) can be done either before, after, or combined with cardiac surgery, which might be on- or off-pump—and this further dilutes an already shallow pool of data. And lastly, the data that are available are of mixed quality with regard to ascertainment of important clinical events (always an issue in retrospective assessments), selection of patients for any given approach (such bias is inherent in the practice of medicine absent the "guidance" of an investigational protocol), and almost uniformly lack a control group (even nonrandomized).

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Into this tar pit wades the relative newcomer on the block, carotid artery stenting (CAS). The appeal of CAS as an alternative to CEA is obvious in patients with cardiac disease: the lack of anesthesia and physiological surgical "stress" in an obviously vulnerable population, often with multiple comorbidities and organ involvement. In support of this speculative advantage, periprocedural outcomes from the randomized SAPPHIRE (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy) trial in symptomatic high surgical risk patients trended better in CAS compared with CEA, 2.1% versus 9.3% ($p = 0.18$) (4). In addition, the recent National Institutes of Health CREST (Carotid Revascularization Endarterectomy versus Stenting Trial) randomized trial results, representing standard surgical risk patients enrolled from 2000 to 2008, demonstrated no differences between CEA and CAS in 1,321 symptomatic patients for the primary endpoint of death, stroke, and myocardial infarction (MI), 5.4 ± 0.9% versus 6.7 ± 1.0% ($p = 0.57$), respectively (5).

On this encouraging background, in this issue of *JACC: Cardiovascular Interventions,* Van der Heyden et al. (6) report the outcomes of patients with strictly symptomatic carotid stenosis requiring cardiac surgery, the first prospective study to singularly address the critical group in question. We must be mindful that, although it spanned 10 years, it is nevertheless a small study and therefore subject to the statistical vagaries that can confound results, so conclusions drawn should be appropriately circumspect. Consecutive patient outcomes were prospectively gathered from 1998 to 2008 in this single-arm study at an expert high-volume center, and both MIs and strokes appear to be appropriately ascertained. An embolic protection device (EPD) was used when available after 2002, but representative of only one-half of the treated population—important because meta-analyses have suggested that stroke outcomes are likely better with EPD use in CAS, although no large-scale randomized data exist (7). Specific to this analysis was the helpful reporting of events temporally and specifically related either to the CAS or to the cardiac surgery, most of which was done on-pump. Employing CAS, the authors demonstrated a remarkably low rate (1.5%) of MI in this group of patients with high-risk coronary anatomy and an acceptable rate of stroke (7.0%), all of which were minor

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(and 1 of which was contralateral, presumably due to aortic arch source during access attempts). There were only 2 additional events occurring after surgery—a death and a major stroke—for a combined rate of death, stroke, and myocardial infarction of 12.3%. Not surprisingly, the 5-year morbidity and mortality in this group was substantial, most of it vascular, and worse in elderly patients.

Do these results reflect the current outcomes expected from high-surgical-risk populations undergoing CAS? A fair question, because results in the United States for CAS have shown a dramatic improvement over the past decade, and complications have more than halved since the initial SAPPHIRE (4) and ARCHeR (ACCULINK for Revascularization of Carotids in High Risk Patients) studies (8). The death and stroke rate of 7.0% reported here is higher than the 2 most recent and largest prospective multicenter experiences with CAS in symptomatic patients: the combined CAPTURE 2 (Carotid ACCULINK/ACCUNET Post-approval Trial to Uncover Rare Events)/EXACT (Emboshield and Xact Post Approval Carotid Stent Trial) single-arm study outcomes in high surgical risk patients, and the CREST study in standard surgical risk patients, which were 5.7% and 6.0%, respectively. This might be related to the lack of EPD in the first one-half of the patients, an evolving technique over 10 years in a novel therapy, and the small numbers of subjects (i.e., 1 less stroke event and the rate becomes more contemporary). To the positive, all CAS-related strokes were minor, and it has been observed that most of these will resolve significantly and leave little if any residual neurological deficit (9,10).

That proviso aside, some answers to important questions might be forthcoming after considering this well-collected and clinically relevant data in the clinical management of the patient with symptomatic carotid disease requiring cardiac surgery. Is CAS better than no carotid intervention at all (i.e., have we satisfied Bacon's imperative to have "altered for the better designedly?"). What is the relative value of CAS versus CEA in the management of these patients?

Before making any comparison of these data with historical unoperated or CEA outcomes, 2 important caveats must be considered. First, there are very limited data with regard to prophylactic CEA in a purely symptomatic population, and to compare mixed populations that include significant numbers of asymptomatic patients is not a sound approach, because results would be expected to differ between these populations. Second, most prior studies have not been as vigilant about ascertaining related events as Van der Heyden et al. (6), specifically assessing with neurological evaluation before and after the procedures or documenting MI by prospectively checking enzyme and electrocardiograms. It has been amply demonstrated that the prospective evaluation of stroke in patients undergoing isolated CEA results in the trebling of strokes reported, mostly by picking up the minor strokes that otherwise go unnoticed by operators (11,12). Furthermore, the distinction between major and minor stroke has not typically been made in prior published reports on the subject. It is noteworthy that in the present study there was only 1 major stroke (after cardiac surgery), making the combined major stroke rate and death approximately 1.8% and comparing exceptionally well to the rate of 14.2% in historical/retrospective data, which presumably reported primarily major strokes (13). It has also been recently shown that CEA and CAS perioperative MI is a predictor of long-term mortality, regardless of size of the event (10), so that this is an important but generally undercounted/reported outcome. With regard to the outcomes with staged CAS and cardiac surgery seen here, they do in fact seem to be at least comparable to the stroke rate of 8.5% in unoperated symptomatic carotid disease undergoing cardiac surgery and to the rate of death and stroke in staged CEA and cardiac surgery, both of which might be underestimated for the reasons given previously (14,15).

It is tempting to suggest that CAS might be the preferred treatment in these cases, given the previously enumerated problems in comparisons with historical CEA outcomes, with the observed improvements in CAS outcomes over time and with routine EPD availability, and with the lack of associated major stroke in CAS. However, lacking a direct randomized comparison and given the difficult-to-compare historical data, it is not possible to make any definitive statements about the relative merits of 1 approach over the other. On the basis of the results reported by Van der Heyden et al. (6), we can conclude that a well-performed CAS by experienced operators is likely to be at least on par with CEA as a staged pre-treatment strategy and likely better than nothing at all, for managing symptomatic patients with carotid disease undergoing cardiac surgery. Perhaps even Bacon would be satisfied.

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