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EDITORIAL COMMENT

Minimizing Stroke and Mortality Risks in Coronary Revascularization*

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Whether undergoing cardiac surgery or interventional cardiology procedures, patients and physicians often consider stroke as the most devastating potential complication—for some, even more so than death. In the case of coronary revascularization, coronary artery bypass grafting (CABG) may result in cerebral infarction as a result of atheroembolism due to aortic cross-clamping, insertion of (and perfusion through) arterial cannulae, aortic manipulation for proximal anatamoses, and "watershed" infarcts due to hypoperfusion. Similarly, stroke during percutaneous coronary intervention (PCI) is precipitated by the manipulation of wires and catheters through the aorta via either the iliofemoral or subclavian systems or sometimes due to elaboration of coronary or graft atheroma into the central circulation. Both procedures may cause hemorrhagic stroke due to the high-dose antithrombotic and antiplatelet therapies (in the setting of PCI) that are required (1).

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The paper by Head et al. (2), in this issue of the *Journal*, provides a detailed, patient-level data meta-analysis of randomized trials comparing CABG to PCI specifically to understand the short- and long-term risks of stroke and its implications on survival (2). Among 11,518 patients with a mean follow-up of 3.8 years, 293 strokes occurred with greater frequency in the CABG group than in the PCI group at both 30 days (1.1% vs. 0.4%; $p < 0.001$) and 5 years (3.2% vs. 2.6%; $p = 0.027$). In a similar vein, it is interesting to note that all major commercial cardiac procedural registries (Society of Thoracic Surgeons, Transcatheter Valve Therapies, National Catheterization Data Registry) demonstrate a consistent trend toward reduced strokes in percutaneous versus surgical therapies (**Figure 1**). As such, the findings of the current clinical trials meta-analysis are consistent with "real-world" patient treatment. Whereas the registry data provided by us do not of course account for patient matching and inherent biases, it is fair to mention that those patients treated with percutaneous valve therapy in **Figure 1** were considered high surgical risk or inoperable based on commercial coverage guidelines. Therefore, we are likely to see these treatment risks decline with decreasing patient risk, device improvements, and dedicated cerebral embolic protection.

The stroke risk in the current analysis was driven by the initial period, as the stroke risk beyond 31 days was similar between the 2 groups (2.1% vs. 2.2%; $p = 0.72$). This is also an important finding, as there is often the concern raised that there could be a "catch-up" phenomenon for stroke among PCI patients due to the generally higher need for repeat revascularization compared with CABG. The findings of the current study are also consistent with a prior analysis of patients undergoing PCI or CABG for either left main or multivessel coronary artery disease (CAD) by Athappan et al. (3). Among 57 studies involving 80,314 patients, there was a significantly lower cumulative stroke risk at all time points between 1 and 5 years (odds ratio: at 1 year: 0.55, at 5 years: 0.79), again demonstrating the lack of a worse late-stroke hazard in the percutaneously treated group.

The detrimental effect of stroke is also well demonstrated in this analysis. Importantly, patients with early stroke experienced a substantially higher 5-year mortality than those without stroke, both after

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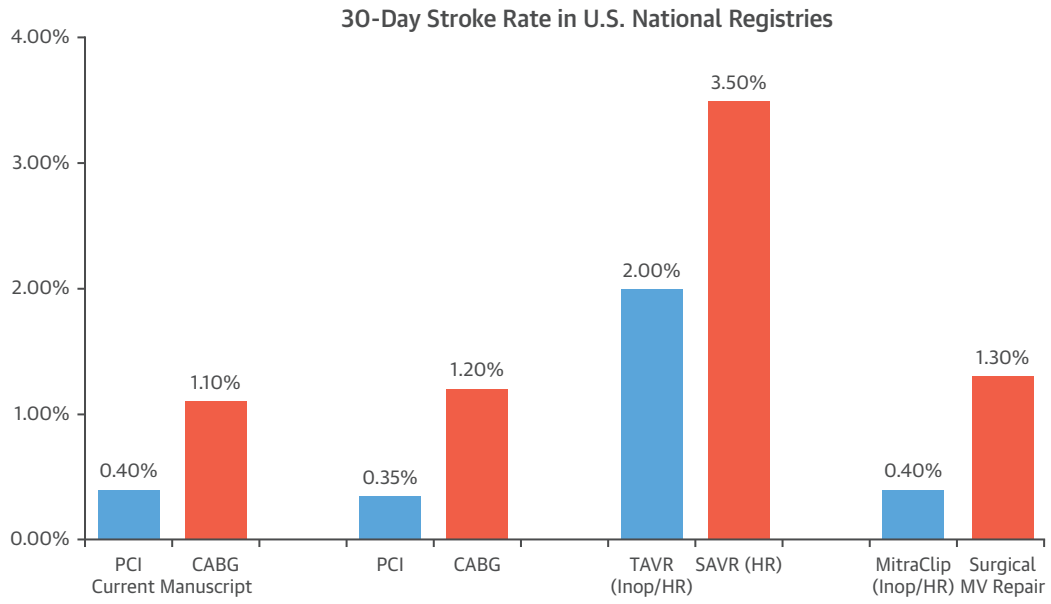
FIGURE 1 30-Day Stroke Rate in Surgical and Percutaneous Cardiac Procedure Registries (NCDR, STS, TVT)



Thirty-day stroke rate in surgical and percutaneous cardiac procedure registries (National Catheterization Data Registry [NCDR], Society of Thoracic Surgeons [STS], Transcatheter Valve Therapies [TVT]) (2,6–11). CABG = coronary artery bypass grafting; HR = high surgical risk; Inop = inoperable; MV = mitral valve; PCI = percutaneous coronary intervention; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

CABG (41.5% vs. 8.9%; $p < 0.001$) and PCI (45.7% vs. 11.1%; $p < 0.001$). A question that could not be addressed with the data available, however, was regarding the effect of stroke on patient morbidity. In this vein, Mack et al. (4) have previously provided a subgroup analysis of the SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) trial. They found that 68% of patients (21 of 31) with CABG-related stroke had residual deficits at hospital discharge compared with 47% of PCI patients (9 of 19). It is important, therefore, to be cognizant of how the relative risks of stroke and death are perceived by patients when discussing revascularization options.

Whereas the composite of stroke and death at 30 days favored PCI (1.6% vs. 2.4%; $p = 0.003$), at 5 years, it was equivalent (13.0% vs. 11.4%; $p = 0.69$). However, subgroup analysis showed that CABG was favored in the diabetic patients at 5 years (13.9% vs. 17.2%; $p = 0.031$) and those with high SYNTAX scores (although not those with left main disease), despite the fact that stroke alone at 5 years was higher with CABG in the diabetic group (4.9% vs. 2.6%; $p < 0.001$) (but not different in the nondiabetic group [2.6% vs. 2.4%; $p = 0.78$]). In routine clinical practice, diabetic patients with multivessel CAD are usually referred for CABG rather than PCI given the more favorable long-term survival of the former. Therefore, the current data should raise the following considerations: 1) conversation regarding the risks/benefits of each revascularization strategy should involve an express mention of both survival and stroke; 2) close follow-up to optimize stroke prevention therapies including lipid management and anticoagulation for atrial fibrillation given the continued stroke risk especially among diabetic patients undergoing CABG; 3) consideration of long-term dual antiplatelet therapy for diabetic patients after revascularization given the reduced stroke risk noted in subgroup analyses of clopidogrel and ticagrelor trials (albeit with higher risk of bleeding); and 4) attempt to further minimize CABG-related stroke risk by using bilateral internal mammary grafts to minimize proximal aortic anastomoses (safe even in diabetic patients). Another consideration is performance of off-pump CABG, which has demonstrated lower risk of stroke although with concerns for less-thorough revascularization and lower graft patency. Nevertheless, use of this technique along with the aortic "no touch" (or anaortic) approach with internal mammary artery grafting or