TOTAL: No Benefit to Routine Thrombectomy in STEMI

Written by Francesca Coltrera

The routine use of thrombectomy with manual aspiration in patients undergoing primary percutaneous coronary intervention (PCI) did not improve outcomes in the TOTAL trial, according to Sanjit S. Jolly, MD, MSc, McMaster University and Hamilton Health Sciences, Hamilton, Ontario, Canada [Jolly SS et al. *N Engl J Med*. 2015].

The data supporting the routine use of thrombectomy in patients undergoing PCI for STEMI have differed in prior studies. The single-center TAPAS trial, conducted in The Netherlands, showed that thrombectomy plus PCI reduced cardiac death at 12 months when compared with PCI only for STEMI [Viaar PJ et al. *Lancet*. 2008]. However, the TASTE trial—a large multicenter randomized trial conducted in Sweden—did not find any benefit with thrombectomy [Fröbert O et al. *N Engl J Med*. 2013]. The TOTAL trial is the largest primary PCI trial to date evaluating the benefit of routine thrombectomy in patients with STEMI undergoing PCI.

In the international multicenter TOTAL trial, 10 732 patients were randomized within 12 hours after onset of STEMI symptoms to receive thrombectomy with manual aspiration followed by PCI (n = 5033) or PCI alone (n = 5030). In patients randomized to PCI only, thrombectomy was allowed when PCI alone failed to clear occluded vessels (7% of cases). The baseline characteristics of the patients and the procedural characteristics were similar between the 2 groups.

The primary outcome was the composite of cardiovascular (CV) death, recurrent myocardial infarction (MI), cardiogenic shock, and NYHA class IV heart failure within 180 days. The primary safety outcome was stroke within 30 days.

There were no significant differences between the thrombectomy and PCI-only groups for the primary composite outcome (6.9% vs 7.0%; HR, 0.99; 95% CI, 0.85 to 1.15; *P* = .86) or its individual components (CV death, 3.1% vs 3.5%, *P* = .34; recurrent MI, 2.0% vs 1.8%, *P* = .62; cardiogenic shock, 1.8% vs 2.0%, *P* = .56; class IV heart failure, 1.9% vs 1.8%, *P* = .57). In addition, there were no significant differences in stent thrombosis (HR, 0.85; 95% CI, 0.60 to 1.21; *P* = .370) or target vessel revascularization (HR, 0.95; 95% CI, 0.75 to 1.22; *P* = .692) at 30 days. There were no difference in outcomes for any of the prespecified subgroups (ie, timing of symptom onset, TIMI grade, initial TIMI flow, MI type, or age), said Dr Jolly.

However, patients randomized to routine thrombectomy did have an increased risk of stroke (Table 1).

Table 1. Safety Outcomes in TOTAL Trial

	Thrombectomy (n = 5033)	PCI Alone (n = 5030)	HR (95% CI)	*P* Value
Stroke within 30 d	33 (0.7)	16 (0.3)	2.06 (1.13 to 3.75)	.015
Stroke or TIA within 30 d	42 (0.8)	19 (0.4)	2.21 (1.29 to 3.80)	.003
Stroke within 180 d	52 (1.0)	25 (0.5)	2.08 (1.29 to 3.35)	.002

Data presented in n (%).

PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

Source: Jolly SS et al. *N Engl J Med*. 2015.

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Further study is needed of the higher risk of stroke, and a detailed case review is underway to better understand how this might be related to the procedure, said Dr Jolly.

NOTION Trial: TAVR Not Superior to SAVR in Low-Risk Aortic Stenosis

Written by Eleanor Mayfield

In the first "all-comers" trial to randomize low-risk patients with aortic valve stenosis to transcatheter aortic valve replacement (TAVR) or surgical aortic valve replacement (SAVR), TAVR was safe and effective but not superior to SAVR on the primary outcome, the composite rate of death from any cause, stroke, or myocardial infarction (MI) at 1 year. Hans Gustav Hørsted Thyregod, MD, Copenhagen University Hospital, Copenhagen, Denmark, presented results from the prospective, randomized, multicenter, nonblinded NOTION trial [Thyregod HGH et al. *J Am Coll Cardiol*. 2015].

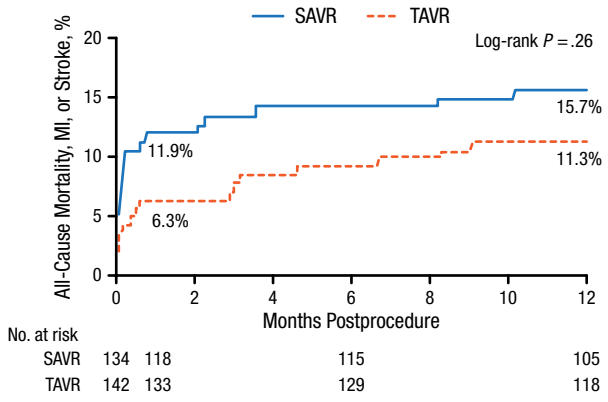
In previous studies of patients with extreme-risk aortic stenosis (AS) (Society of Thoracic Surgeons [STS] score > 15%) not considered as candidates for SAVR, the rate of the composite end point of death from any cause was 50.7% for standard therapy vs 30.7% for TAVR at 1 year [Leon MB et al. *N Engl J Med*. 2010]. The rate of all-cause mortality or major stroke at 1 year was 26% for TAVR-treated patients vs a prespecified objective performance goal of 43% [Popma JJ et al. *J Am Coll Cardiol*. 2014]. In high-risk patients (STS score 10% to 15%) randomly assigned to TAVR or SAVR, rates of death from any cause at 1 year were 24.2% for TAVR vs 26.8% for SAVR [Smith CR et al. *N Engl J Med*. 2011] and 14.2% for TAVR vs 19.1% for SAVR [Adams DH et al. *N Engl J Med*. 2014].

The objective of the NOTION trial was to compare TAVR with SAVR in an all-comers population of surgery-eligible patients aged ≥ 70 years. Investigators randomized

280 patients (mean age 79 years; 53% men) with low-risk severe aortic valve stenosis (mean STS score 3%) who were expected to live >1 year to TAVR (n=145) or SAVR (n=135). The primary outcome was a composite of death from any cause, stroke, or MI at 1 year. Secondary outcomes included safety and efficacy and echocardiographic outcomes. Baseline characteristics and comorbidities were not significantly different in the 2 groups.

In intention-to-treat analysis, the composite rate of death from any cause, stroke, or MI at 1 year was 13.1% for TAVR vs 16.3% for SAVR (P=.43). In as-treated analysis, rates for the primary end point also failed to reach statistical significance (Figure 1).

Figure 1. Death From Any Cause, Stroke, or Myocardial Infarction at 1 Year in As-Treated Population



MI, myocardial infarction; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

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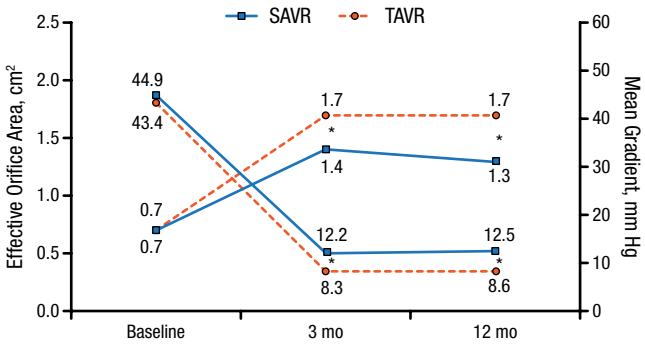
Figure 2. Aortic Valve Performance



SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

*P<.001.

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The only secondary outcomes to achieve statistical significance at 1 year were rates of atrial fibrillation (TAVR, 21.2% [n=142]; SAVR, 59.4% [n=134]; P<.001) and pacemaker implantation (TAVR, 38%; SAVR, 2.4%; P<.001). Among surviving patients at 1 year, 67.4% in the TAVR group (n=132) were NYHA class I compared with 81.7% in the SAVR group (n=120). A statistically significant difference (P<.001) favoring TAVR was seen for aortic valve performance (Figure 2). Rates of moderate-to-severe aortic valve regurgitation were 15.7% for TAVR vs 0.9% for SAVR at 1 year.

In summary, the NOTION trial failed to demonstrate that TAVR was superior to SAVR for the primary outcome of the composite rate of death from any cause, stroke, or MI after 1 year in patients with low-risk severe AS. Dr Thyregod concluded that long-term durability and morbidity data were required in lower-risk patients.

Ezetimibe Plus Simvastatin More Beneficial Than Simvastatin Alone in Reducing Recurrent Cardiovascular Events: A Secondary Analysis From IMPROVE-IT

Written by Maria Vinall

According to results of a secondary analysis of the IMPROVE-IT study presented by Sabina A. Murphy, MPH, Brigham and Women's Hospital, Boston, Massachusetts, USA, adding ezetimibe to simvastatin therapy significantly improved clinical outcomes beyond a first event compared with simvastatin alone. This analysis also confirmed the importance of continuing intensive combination lipid-lowering therapy after a first cardiovascular (CV) event.

Ezetimibe is a nonstatin lipid-lowering therapy that reduces cholesterol absorption in the intestine. When added to a statin, achievement of low-density lipoprotein cholesterol (LDL-C) levels <70 mg/dL or <100 mg/dL was approximately 20% higher compared with a statin alone [Morrone D et al. *Atherosclerosis.* 2012]. IMPROVE-IT [NCT00202878] was a phase 3, multicenter, randomized, double-blind, active-control trial that evaluated whether ezetimibe added to simvastatin improved CV outcomes compared with simvastatin therapy alone.

IMPROVE-IT included 18 144 moderate- to high-risk patients stabilized after acute coronary syndromes (≤10 days) receiving standard medical and interventional therapy. Patients with a LDL-C level between 50 and 125 mg/dL (or 50 to 100 mg/dL if they had been taking prior lipid-lowering therapy) were randomized in