Future research appears warranted to focus on further reducing periprocedural TAVR complications, including strokes, vascular events, and short- and long-term risk and prevention of paravalvular AR.

The CABG Surgery Off-or On-Pump-Revascularization Study

Written by Maria Vinall

Results of a study that was designed to compare the benefits and risks of performing coronary artery bypass grafting surgery (CABG) off-pump (beating heart) versus on-pump showed no difference in major clinical events at 30 days, with off-pump procedures associated with reduced rates of transfusions, reoperations for bleeding, acute kidney injury, and respiratory infection/failure but an increased rate of early repeat revascularizations.

The Coronary Artery Bypass Grafting Surgery Off- or On-Pump Revascularization Study [CORONARY; NCT00463294] was designed to test the hypothesis that off-pump CABG would reduce short-term (30 days) major clinical events and that these benefits would be maintained over the long term (5 years). The short-term study results were presented by Andre Lamy, MD, Population Health Research Institute, McMaster University, Hamilton, Ontario, Canada.

CORONARY was a randomized, double-blind international trial (79 centers in 19 countries). Eligibility included patients who were undergoing planned isolated CABG with median sternotomy and at least 1 of the following risk factors: age ≥70 years, peripheral vascular disease, cerebrovascular disease, carotid stenosis >70%, and renal insufficiency. Patients were also eligible if they were aged 60 to 69 and years had at least 1 *additional* risk factor or were aged 55 to 59 years with at least 2 *additional* risk factors—diabetes, urgent revascularization, smoker, or left ventricular ejection fraction (LVEF) ≤ 35%. Each operation was performed by a surgeon with expertise (>2 years; >100 procedures) in the specific type of surgery that the patient was assigned to receive. The first coprimary outcome was a composite of mortality, nonfatal stroke, nonfatal myocardial infarction (MI), and new renal failure that required dialysis at 30 days. The 5-year results will be available in 2016 and comprise the first coprimary outcome plus repeat coronary revascularization at a mean of 5 years. Secondary efficacy outcomes included rates of blood transfusion, recurrent angina, cardiovascular death, and cost-effectiveness.

A total of 4572 subjects (mean age 68 years) participated in the study. Most (81%) were men, and one-third had a prior MI. Baseline preoperative angiograms indicated that the majority (off-pump 56.1%; on-pump 60.4%) had triple-vessel disease. At 30 days, 9.8% and 10.3% of patients who received off-pump versus on-pump procedures reached the primary composite outcome (HR, 0.95; 95% CI, 0.79 to 1.14; p=0.59). Off-pump CABG was associated with significantly fewer blood transfusions and reoperation for bleeding, less acute kidney injury, and fewer respiratory complications but more early repeat coronary revascularizations (Table 1). No difference in primary outcome was noted at hospital discharge, nor were there any differences by subgroup.

Table 1. Outcomes at 30 Days.

	Off-pump	On-pump	RR (95% CI)	p value
Blood transfusions	50.7%	63.3 %	0.80 (0.75–0.85)	<0.001
Reoperation for bleeding	1.4%	2.4%	0.61 (0.40–0.93)	0.02
Acute kidney injury	28.0%	32.1%	0.87 (0.80–0.96)	0.01
Respiratory complications	5.9%	7.9%	0.79 (0.63–0.98)	0.03
Early repeat coronary revascularizations	0.7%	0.2%	HR, 4.01 (1.34–12.0)	0.01

The investigators concluded that in experienced hands, both procedures are reasonable options, based on short-term results. The difference in morbidity that was observed in the 30-day results may or may not lead to clinically significant differences during the long-term follow-up that is being conducted. Whether the unblinded nature of the trial (both patients and investigators were aware of study group assignment, but the endpoint adjudication committee members were unaware) or this interim report will bias the long-term follow-up of trial patients is unclear [Lamy A et al. *N Engl J Med* 2012].

Moderate PE Treated with Thrombolysis (MOPETT Study)

Written by Maria Vinall

Pulmonary embolism (PE) is one of the most common preventable causes of death (responsible for >100,000 deaths annually) and the third leading cause of cardiovascular mortality. Thrombolysis with standard doses of 100 mg tissue plasminogen activator (t-PA) over 2 hours is recommended in appropriately selected severe PE patients (patients with hemodynamic instability

and shock), but these patients only represent 5% of all presentations with PE. Patients with moderate PE constitute a more prevalent population; however, there are often concerns about major bleeding (which occurs in 6% to 20% of cases) and intracranial hemorrhage (ICH; 2% to 6% of cases) in moderate PE patients when larger doses of t-PA are employed. In addition, practitioners are hesitant to use t-PA when patients are hemodynamically stable and/or receiving concomitant parenteral anticoagulation due to concern that the risks outweigh the benefits. PE is exquisitely sensitive to thrombolysis, as the lungs are the point of convergence of venous circulation; so, a majority of IV-delivered t-PA converges to the clot, making t-PA ideal for the treatment of this population of patients.

New data from the Moderate Pulmonary Embolism Treated with Thrombolysis (MOPETT) study, presented by Mohsen Sharifi, MD, A.T. Still University, Mesa, Arizona, USA, suggest that moderate PE patients may be managed with reduced-dose t-PA and modified anticoagulation.

MOPETT was a randomized trial of 121 patients (45% men; mean age 59 years). Sixty-one patients received t-PA that was dose-adjusted for weight (for those ≥50 kg, an initial dose of 10 mg t-PA over 1 minute, followed by a 40-mg infusion over 2 hours; for those <50 kg, a total t-PA dose of 0.5 mg/kg, delivered as an initial dose of 10 mg over 1 minute, followed by the remainder as an infusion over 2 hours) in addition to a 20% to 30% reduction in anticoagulant dose (either enoxaparin or heparin), and 60 subjects received anticoagulation alone (standard of care). The coprimary endpoints were pulmonary hypertension (PH) and a composite of PH plus recurrent PE after 28 months of follow-up. The determination of PH was by echocardiography, defined as an estimated pulmonary artery systolic pressure (PASP) >40 mm Hg. Secondary endpoints included in-hospital bleeding, duration of hospitalization, and mortality. Patients were included in this study if they had symptomatic PE plus 2 of the following risk factors for post-PE mortality: chest pain, tachypnea >22 respirations per minute, tachycardia resting heart rate >90 beats per minute, dyspnea, jugular venous pressure >12 cm H_20, cough, or oxygen desaturation <90%.

Serial changes in PASP from baseline to 28 months by treatment strategy are shown in Table 1. After 28 months, 16% of t-PA patients experienced PH (the first coprimary endpoint) compared with 57% of those who were assigned standard anticoagulation (p<0.001). Patients who were treated with t-PA also had significantly fewer incidences of the second coprimary endpoint, a composite of PH plus recurrent PE at 28 months (16% vs 63%; p<0.001). Secondary events occurred infrequently, in particular mortality, and are shown according to treatment assignment in Table 2. No significant in-hospital bleeding occurred with either strategy.

Table 1. Serial Changes in PASP from Baseline to 28 Months by Treatment Strategy.

	t-PA (n=58)	Standard of Care (n=56)	p value
Initial PASP (mm Hg)	50±6	51±7	0.40
PASP (mm Hg) change within 48 hours	-16±3	-5±2	<0.001
PASP at 6 months	31±6	49±8	<0.001
PASP at 28 months	28±5	43±6	<0.001
PAH at 28 months*	9	32	<0.001
PAH and recurrent PE at 28 months*	9	35	<0.001

*PAH=Pulmonary Arterial Hypertension; PASP=Pulmonary Artery Systolic Pressure >40 mm Hg; PE=pulmonary embolism.

Table 2. Secondary Events By Treatment Strategy.

	t-PA (n=61)	Standard of Care (n=60)	p value
Recurrent PE (%)	0	3 (5)	0.077
Mortality (%)	1 (1.6)	3 (5)	0.301
Recurrent PE + mortality (%)	1 (1.6)	6 (10)	0.0489
Hospital stay, days	2.2±0.5	4.9±0.8	<0.001

PE=pulmonary embolism.

The authors concluded that the use of low-dose thrombolysis appeared to be safe and effective in moderate PE to reduce PH, recurrent PE, and hospital stay without an increase in bleeding risk or ICH. However, hard clinical events, such as mortality, clinically evident right-heart failure, and major bleeding events, were infrequent. Larger and long-term studies that test this strategy in representative patients are necessary to ultimately determine whether modified aggressive reperfusion therapy provides more benefit than harm in PE.

Pacemaker Therapy In Patients With Neurally Mediated Syncope and Documented Asystole

Written by Maria Vinall

Michele Brignole, MD, Ospedali del Tigullio, Lavagna, Italy, presented evidence from the International Study on Syncope of Uncertain Etiology 3 Study [ISSUE3; NCT00359203], demonstrating that cardiac pacing therapy is effective for prevention of recurrent syncope in patients with neurally mediated syncope (NMS) and documented asystole. These data contradict previous data from two