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

randomized trials [Connolly SJ et al. *JAMA* 2003; Raviele A et al. *Eur Heart J* 2004] that failed to prove the superiority of cardiac pacing over placebo for the prevention of syncopal recurrences in unselected patients who were affected by NMS. Prof. Brignole believes that the discrepancy between these findings may be explained by the current study's use of implantable loop recorders (ILRs) to document asystole in patients with NMS before beginning therapy.

This was a randomized, controlled, double-blind trial of cardiac pacing in 77 patients with NMS who had asystolic syncope ≥3 seconds or nonsyncopal asystole ≥6 seconds, as established with the use of an ILR. The primary endpoint was time to first syncope recurrence. Subjects with qualifying asystolic events had pacemakers implanted and were randomized 1:1 to either pacemaker on (PM on) or pacemaker off (PM off) groups. The study was stopped when a total of 27 primary endpoint events, irrespective of study arm, were reached. There were a total of 158 documented endpoints during the ILR screening phase; 56% patients had asystole, 23% had normal sinus rhythm, 10% had tachycardia, and 10% had bradycardia.

Baseline characteristics included a mean participant age of 63 years in each group, of which approximately half in each group was female (47% PM on, 59% PM off), and >60% had a prior hospitalization for syncope. Over 80% in the cohort had tilt table testing, with fewer patients in the PM on group having positive results than in the PM off group (42% vs 72%). Diabetes was present in 29% of patients, while 23% had structural heart disease. Overall, patients were characterized by recurrent syncope that began in middle or older age with severe presentations; mean pause, captured by an ILR of 11 seconds; and frequent injuries that were related to absence of warning symptoms.

After 24 months, 75% of PM on patients were free from recurrent syncopal episodes compared with 43% of patients who were randomized to PM off (log rank RRR, 57%; p=0.039). Complications were restricted to lead dislodgements (n=5) and 1 incidence of subclavian vein thrombosis.

The authors concluded that dual-chamber permanent pacing is effective in reducing recurrence of syncope in patients aged ≥40 years with severe asystolic NMS and suggest that the use of this invasive treatment may be effective for relatively benign NMS. The overall strategy of using an ILR in order to determine suitable patients for pacing likely contributed to the positive findings and explains the discrepancy with the negative results of previous randomized controlled trials.

In selected patients, syncope is recurrent, unpredictable, and associated with a high risk of trauma and poor quality of life. It often occurs while engaged in high-risk activity (eg, driving, machine operation, flying, competitive athletics). Prof. Brignole believes that the ILR screening phase is important in determining which patients should receive a pacemaker. Based on prior observations, 18% percent of patients who receive an ILR will be candidates for pacemaker therapy within 1 year, and approximately 40% will be candidates within 4 years.

BRIDGE-ACS: Multifaceted Quality Improvement Program Ups the Use of Evidence-Based Care in Brazil

Written by Rita Buckley

Outcomes from the Brazilian Intervention to Increase Evidence Usage in Acute Coronary Syndromes Trial [BRIDGE-ACS; NCT00958958] show that a simple, multifaceted, educational intervention can lead to significant improvements in the use of evidence-based medications in patients with acute coronary syndromes (ACS). Otavio Berwanger, MD, PhD, Research Institute Hcor-Hospital do Coração, São Paulo, Brazil, presented results from the study.

BRIDGE-ACS was a cluster-randomized (concealed allocation) trial that was conducted among 34 clusters (public hospitals) in Brazil. It enrolled a total of 1150 patients with ACS from March through November 2011, with follow-up through January 2012. The primary endpoint was the percentage of eligible patients who received all evidence-based therapies (aspirin, clopidogrel, anticoagulants, and statins) during the first 24 hours [Berwanger O et al. *JAMA* 2012; Berwanger O et al. *Am Heart J* 2012]. Secondary endpoints included adherence to all eligible evidence-based therapies during the first 24 hours and the use of aspirin, beta-blockers, statins, and ACE inhibitors at discharge; a composite evidence-based medicine score; and major cardiovascular (CV) events. CV endpoints, including mortality, CV death, recurrent ischemic events, and bleeding, were also measured as secondary endpoints. Outcomes were reviewed by blinded outcome assessors. The analyses were performed using an intention-to-treat principle.

The trial included general public hospitals from major urban areas with an emergency department that treated patients with ACS. Eligible subjects were consecutive patients who met standardized definitions of ACS (STEMI, NSTEMI, and unstable angina) as soon as