Table 1. Clinical End Point Events

	CTA (n = 4996)	Functional (n = 5007)	Adjusted HR (95% CI)	*P* Value
Primary end point composite	164	151	1.04 (0.83 to 1.29)	.750
All-cause death	74	75		
Nonfatal MI	30	40		
Unstable angina hospitalization	61	41		
Major procedural complications	4	5		
Primary end point plus catheterization without obstructive CAD	332	353	0.91 (0.78 to 1.06)	.217
Death or nonfatal MI	104	112	0.88 (0.67 to 1.15)	.348
Death, nonfatal MI, or unstable angina hospitalization	162	148	1.04 (0.84 to 1.31)	.703

CAD, coronary artery disease; CTA, computed tomographic angiography; MI, myocardial infarction.

Reproduced with permission from PS Douglas, MD.

Source: Douglas PS et al. *N Engl J Med*. 2015.

testing group ($P = .022$). The difference in the cumulative radiation exposure at ≤ 90 days was driven by the type of functional test ordered. A comparison of CTA vs stress testing with nuclear imaging revealed lower radiation in the CTA group (10.1 vs 12.0 mSv); however, in comparison to those patients undergoing a stress electrocardiogram or stress echocardiography, radiation in the CTA group was higher. No ionizing radiation exposure was received by 4% of patients in the CTA group vs 33% in the functional group ($P < .001$).

Dr Mark reported results of the economic substudy, whose primary objective was to measure and compare cumulative total costs of each strategy and to estimate the cost-effectiveness of anatomic strategy if it was shown to be superior. Medical costs considered in the calculation included initial diagnostic test technical fees, hospital-based facility costs, and physicians' fees for testing and hospital services. A total of 96% of patients were included in economic substudy across both testing groups. The results demonstrated that despite somewhat lower testing fees for CTA compared with functional testing, the net cost for CTA was higher, although the increase was not statistically significant (no *P* value reported). However, Dr Mark cautioned that outpatient medication costs were not included in the cost calculation, and the analysis of data on quality of life and the employment status was not yet completed.

Dr Douglas concluded that an initial strategy of CTA was not associated with better clinical outcomes than functional testing over a median follow-up of 25 months in this large, community-based population of symptomatic patients with suspected CAD who required noninvasive testing.

Percutaneous Treatment of Valvular Heart Disease, Atrial Fibrillation Examined in Various Studies

Written by Alla Zarifyan

The results of trials of the percutaneous treatment of aortic stenosis (AS) and mitral regurgitation (MR), including PARTNER 1 and CoreValve US Pivotal, showed a reduction in mortality, and registry data supported the safety of the MitraClip System. The AATAC-AF study showed that catheter ablation was superior to amiodarone for the treatment of persistent atrial fibrillation (AF).

PERCUTANEOUS TREATMENT OF VALVULAR DISEASE

Michael Mack, MD, The Heart Hospital Baylor Plano, Plano, Texas, USA, reported the results from long-term follow-up of the PARTNER 1 trial [Mack MJ et al. *Lancet*. 2015]. At 5 years, high-surgical-risk patients with severe AS who underwent transcatheter aortic valve replacement (TAVR) had similar mortality and other major clinical outcomes to those who were treated with surgical aortic valve replacement (SAVR).

The PARTNER 1 trial was an international, multicenter, randomized controlled trial that randomized patients who were at high surgical risk to either TAVR with the Edwards Sapien valve or SAVR. The primary end point of the trial was mortality at 1 year. Other key end points included valve performance and stroke rate.

A total of 699 patients were randomized to either TAVR (n = 348) or SAVR (n = 351). The median survival was 44.5 months in the TAVR group vs 40.6 months in the SAVR

group. All-cause mortality at 5 years was not significantly different between the groups, with a rate of 68% in the TAVR group vs 62% in the SAVR group (HR, 1.04; 95% CI, 0.86 to 1.24; $P = .76$).

There was also no significant difference between the groups in the rate of CV mortality, stroke, or rehospitalization. NYHA class, valve hemodynamics, and improvements in valve function were maintained in both groups at 5 years.

Dr Mack concluded that the results with TAVR are similar to those seen with SAVR at 5 years. Thus, TAVR is a viable alternative to surgery in high-surgical-risk patients, as patients treated with TAVR had similar mortality and other major clinical outcomes, including stroke, to those treated with SAVR.

Michael J. Reardon, MD, Houston Methodist Hospital, Houston, Texas, USA, presented the 2-year follow-up results of the CoreValve US Pivotal Trial [NCT01240902] that demonstrated TAVR using the Medtronic CoreValve reduced mortality when compared with SAVR in patients with severe AS.

The CoreValve US Pivotal Trial [Adams DH et al. *N Engl J Med*. 2014] was a multicenter, randomized, noninferiority comparison study of the self-expanding transcatheter CoreValve with SAVR in patients with severe AS deemed at increased risk for surgery. The primary end point analysis, all-cause mortality at 1 year, was 14.2% in the TAVR group and 19.1% in the SAVR group ($P_{\text{Superiority}} = .04$).

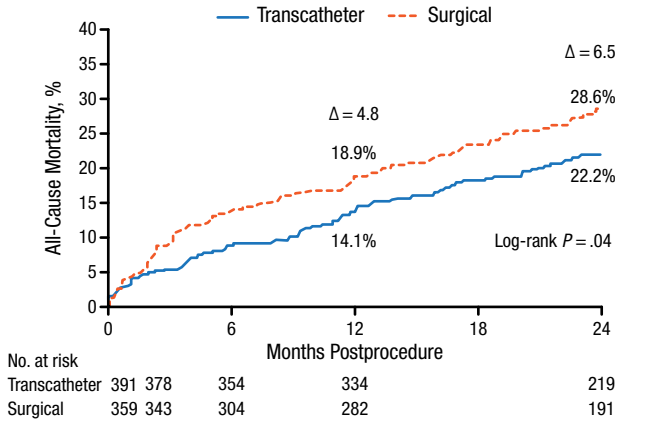
The as-treated population for 2-year results included 750 patients: 391 underwent attempted TAVR, and 359 underwent attempted SAVR. The median follow-up was 24 months. Key end points included 2-year mortality, neurological events, major adverse cardiac and cerebrovascular events, and echocardiographic outcomes.

At 2 years, all-cause mortality was 22.2% in the TAVR group and 28.6% in the SAVR group (log-rank $P = .04$; Figure 1). TAVR was also favored in all prespecified subgroup analyses.

The rate of stroke at 2 years was 10.9% in the TAVR group and 16.6% in the SAVR group (log-rank $P = .05$), while the difference in the rate of major stroke was not significant (log-rank $P = .25$). The rate of major adverse cardiac and cerebrovascular events was 29.7% in the TAVR group and 38.6% in the SAVR group (log-rank $P = .01$). Echocardiographic findings revealed that patients who underwent TAVR had significantly better valve performance over those who underwent SAVR at all follow-up visits ($P < .001$).

Dr Reardon concluded that the improvements in survival seen at 1 year for patients treated with TAVR over SAVR were maintained at 2-year follow-up. He also noted that he believes TAVR with the self-expanding valve should be considered as the preferred treatment in patients with symptomatic severe AS who are at increased risk for surgery.

Figure 1. All-Cause Mortality at 2 Years in CoreValve US Pivotal Trial



Reproduced with permission from MJ Reardon, MD.

Paul Sorajja, MD, Minneapolis Heart Institute at Abbott Northwestern Hospital, Minneapolis, Minnesota, USA, reported data from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy (TVT) registry, revealing the outcomes of transcatheter mitral valve repair (TMVR) with the MitraClip system when used for the treatment of patients with symptomatic MR.

The number of US patients affected by moderate or severe MR is expected to reach 5 million by 2030 [Enriquez-Sarano M, Sundt TM. *Circulation.* 2010]. Surgery is the standard of care; however, the risk of surgery is prohibitive for some patients. TMVR with MitraClip received FDA approval in 2013 and is indicated for symptomatic patients with grade ≥ 3 MR who are at prohibitive surgical risk.

All commercial cases with MitraClip enrolled in the TVT registry were identified and examined for in-hospital and 30-day outcomes for procedural success (postimplant MR grade ≤ 2 without CV surgery and in-hospital mortality), complications (cardiac perforation, major bleeding, stroke, myocardial infarction, mitral injury, or death), and device-related adverse events (AEs).

A total of 564 patients (median age 83 years; 56% men) were identified at 61 hospitals. Severe comorbidities were common; 57.2% of patients were classified as frail, and 94% had MR grade 3 or 4.

Procedural success was achieved in 91.8% of patients, with a complication rate of 7.8% and device-related AE rate of 2.7%. In-hospital mortality was 2.3%, and mortality at 30 days was 5.8%. Mean hospital stay was 3 days, with 81.9% of patients discharged directly to home. After implantation, 93% of patients had MR grade ≤ 2 and 63.7% had MR grade ≤ 1.

Dr Sorajja noted that the population in the TVT registry was older and had a higher prevalence of degenerative MR compared with other registries. He concluded that this first report of initial commercial experience with TMVR in the United States demonstrated that TMVR with MitraClip was safe and effective for patients with symptomatic MR and prohibitive surgical risk.

TREATMENT OF PERSISTENT AF

Luigi Di Biase, MD, PhD, Texas Cardiac Arrhythmia Institute at St David's Medical Center, Austin, Texas, USA, and Montefiore Medical Center, Bronx, New York, USA, presented the results of the AATAC-AF [NCT00729911] study, demonstrating that catheter ablation is superior to amiodarone in treating persistent AF and reduces hospitalizations and mortality in patients with heart failure.

AATAC-AF was a phase 4, multicenter, randomized, parallel-group study with the primary end point of long-term procedural success defined as freedom from AF, atrial flutter, or atrial tachycardia > 30 seconds while off antiarrhythmic drugs.

Patients (n = 203) were randomized either to catheter ablation (n = 102) or to amiodarone (n = 101). The baseline characteristics were similar between the groups, and all patients had ≥ 6-month follow-up. After the mean follow-up of 26 months, 70% of patients in the ablation group and 34% in the amiodarone group were free from AF recurrence (log-rank $P < .0001$). In the amiodarone group, 10.4% of participants had to discontinue due to AEs.

Among the 102 patients in the ablation group, 80 patients underwent pulmonary vein isolation (PVI) plus posterior wall and nonpulmonary vein trigger ablation, while 22 patients underwent PVI ablation alone. The success rate was higher in patients undergoing PVI plus ablation (78.8%) compared with PVI alone (36.4%; $P < .001$).

Predictors for AF recurrence were identified as amiodarone therapy (HR, 2.5; 95% CI, 1.5 to 4.3; $P < .001$) and diabetes mellitus (HR, 1.1; 95% CI, 1.07 to 1.26; $P = .01$).

The rate of hospitalization was significantly lower in the ablation group than in the amiodarone group (31% vs 57%, respectively; $P < .001$). All-cause mortality was also lower in the ablation group than in the amiodarone group (8% versus 18%, respectively; $P = .037$).

Dr Di Biase concluded that treatment of persistent AF with catheter ablation in patients with heart failure increased freedom from AF while reducing hospitalization and mortality. He cautioned that the potential socioeconomic implications of these results require further investigation.

Continued Dual Antiplatelet Therapy Beneficial in PEGASUS-TIMI 54 and DAPT Trials

Written by Alla Zarifyan

The use of dual antiplatelet therapy (DAPT) in which a P2Y12 receptor antagonist is combined with aspirin is recommended to reduce the risk of ischemic events or thrombosis in some at-risk patient populations. However, whether prolonged therapy may be beneficial for some patients has not been fully elucidated. Marc S. Sabatine, MD, Brigham and Women's Hospital, Boston, Massachusetts, USA, presented results of the PEGASUS-TIMI 54 trial [Bonaca MP et al. *N Engl J Med*. 2015], demonstrating that the addition of ticagrelor to low-dose aspirin reduced the risk of cardiovascular (CV) death, myocardial infarction (MI), or stroke, and increased the risk of TIMI major bleeding among patients with a history of MI. Robert W. Yeh, MD, Massachusetts General Hospital, Boston, Massachusetts, USA, presented results of a post hoc subgroup analysis [Yeh RW et al. *J Am Coll Cardiol*. 2015] of the DAPT Study showing that continuation of a thienopyridine plus aspirin vs aspirin alone beyond 1 year reduced the risk of ischemic events in patients with and without acute coronary syndromes (ACSs) receiving coronary stents.

PEGASUS-TIMI 54 was a multicenter, international, randomized, double-blind, placebo-controlled clinical trial that investigated whether long-term therapy with ticagrelor would reduce the risk of major adverse CV events in stable patients with a history of MI receiving low-dose aspirin. The primary efficacy end point was the composite of CV death, MI, or stroke. Secondary end points were CV death and all-cause death. The primary safety end point was TIMI major bleeding. Other safety end points included intracranial hemorrhage and fatal bleeding.

A total of 21,162 patients were randomized: 7050 received ticagrelor 90 mg BID, 7045 received ticagrelor 60 mg BID, and 7067 received placebo. The median follow-up was 33 months.

At 36 months, ticagrelor significantly reduced the rate of the primary composite end point at both doses, with 9.0% of patients in the placebo group experiencing