The PARTNER Trial: A New Paradigm for Treating Valvular Heart Disease

Written by Maria Vinall

The Placement of AoRTic TraNscathetER Valve (PARTNER) Trial showed for the first time that transcatheter aortic valve implantation (TAVI), when used in inoperable patients with severe symptomatic aortic stenosis (AS), is life-saving and the best therapeutic option compared with standard medical therapy. In high-risk (but operable) patients, no outcome differences were noted between TAVI and surgical replacement of the aortic valve (SAVR). Of concern were the higher rates of stroke and complications with TAVI. Martin Leon, MD, Columbia University, New York, New York, USA, discussed the results and impact of the PARTNER trial [NCT00530894].

In the PARTNER trial, patients who were considered not suitable for SAVR (inoperable patients; n=358) were randomized (1:1) to either transfemoral TAVI (Edwards SAPIEN Transcatheter Heart Valve) or standard therapy. The primary study endpoint was all-cause mortality at 1 year. The coprimary endpoint was a composite of all-cause mortality and repeat hospitalization.

All-cause mortality at 1 year was 50.7% and 30.7% (HR, 0.51; 95% CI, 0.38 to 0.68; p<0.001) and 68.0% and 43.3% (HR, 0.56; 95% CI, 0.43 to 0.73; p<0.001) at 2 years for standard therapy and TAVI, respectively. The rate of the composite endpoint of death from any cause or repeat hospitalization was significantly (p<0.001) reduced with TAVI. Repeat hospitalizations were cut in half by TAVI (35%) versus standard care (72.5%). TAVI patients had significantly (p<0.001) improved NYHA class, which was sustained out to 2 years. Quality of life, as assessed with the Kansas City Cardiomyopathy Questionnaire (KCCQ), was also significantly improved [Reynolds MR. *Circulation* 2011]. TAVI was cost-effective (1.59-year improvement in life expectancy at an incremental cost of $50,000/life-year gained). At 30 days, TAVI was associated with a higher incidence of major strokes (5.0% vs 1.1% for standard therapy; p=0.06) and major vascular complications (16.2% vs 1.1%; p<0.001) [Leon MB et al. *N Engl J Med* 2010].

High-risk patients (n=699) were randomized to receive either transfemoral or transapical TAVI or SAVR. The primary study endpoint was all-cause mortality at 1 year. The rates of death from any cause were 24.2% and 26.8% at 1 year (TAVI and SAVR, respectively; p=0.62). Despite minimal differences in NYHA functional class, TAVI patients had an earlier recovery that was also evident on the 30-day 6-minute walk test and KCCQ scores, which also showed that transfemorally treated patients did much better at 1 month, while the transapically treated patients did worse. Transfemoral procedures were less expensive and improved quality of life, while the opposite was true of the transapical approach. Stroke rates were higher and vascular complications were significantly (p<0.001) more frequent with TAVI [Smith CR et al. *N Engl J Med* 2011].

The PARTNER trial showed that TAVI should be the standard of care for patients with AS who are not candidates for surgery, provided that comorbidities do not overwhelm the benefits of TAVI, thus preventing a meaningful improvement in quality of life. For high-risk patients, transcatheter and surgical procedures for aortic valve replacement were associated with similar rates of survival at 1 year. An increased risk of stroke, vascular complications, and major bleeding that was associated with transcatheter replacement is a concern in both patient populations.

Despite the great success of the PARTNER trial, the discussants expressed concern over "indication creep" (the use of TAVI to treat very or less sick patients), the use of this

procedure in low-volume centers with poorer outcomes, and the evolution of technology that outpaces the ability of studies to evaluate safety and effectiveness. In general, the discussants recommend that careful attention be focused on patient selection with respect to life expectancy and noncardiac comorbidities that are unrelated to AS. Multidisciplinary heart teams should direct all aspects of the AS patient care. Increased experience of operators, improved devices (valves and delivery systems that are currently used in Europe), and new technologies for prevention of complications might reinforce the role of TAVI in the future.

Prevention Guidelines in Women Broaden the Definition of CV Risk

Written by Anne Jacobson

In 2011, the American Heart Association (AHA) published updated guidelines for the prevention of cardiovascular disease (CVD) in women [Mosca L et al. *Circulation* 2011]. Lori Mosca, MD, Columbia University Medical Center, New York, New York, USA, reviewed the major updates in the new guidelines.

One key change compared with earlier guidelines is the approach to risk stratification. Historically, the term "high risk" has been defined as patients whose 10-year risk of coronary heart disease (CHD) was >20%. However, this definition underestimates the true risk of CVD in women. The 2011 AHA guideline shifts the focus from coronary risk alone to incorporate broader risk factors for CVD. In the new CVD prevention guideline for women, "high risk" now describes patients with any of the following features:

- Established atherosclerotic disease, including:
  - Clinically manifest CHD, peripheral arterial disease, or cerebrovascular disease
  - Abdominal aortic aneurysm
- Estimated 10-year cardiovascular disease risk >10%, based on traditional CV risk factors
- Diabetes mellitus
- End-stage renal disease (ESRD) or chronic kidney disease (CKD)

In previous prevention guidelines, the term "at risk" was used to describe patients with one or more traditional risk factors for CVD, such as cigarette smoking, hypertension, dyslipidemia, obesity, physical activity, poor diet, and physical inactivity. The 2011 AHA guideline for the prevention of CVD in women adds two more risk factors to this list:

- Systemic autoimmune collagen vascular disease (eg, lupus and rheumatoid arthritis), and
- Pregnancy-related risk factors, including a history of pregnancy-induced hypertension, gestational diabetes, preeclampsia, or polycystic ovary syndrome.

These risk factors were added to reflect the unique underlying pathophysiology of CVD in women as compared with men. Notably, these are risk factors that tend to present more frequently in younger women. Although it is an intense focus of current research, it remains to be demonstrated that initiating lifestyle or pharmacological interventions in these patients changes the natural history of their progression to incident CVD.

Lifestyle Interventions

Lifestyle modifications are essential to cardiovascular risk reduction for all at-risk patients. Earlier guidelines used abstract concepts (eg, "moderate exercise") that were difficult for patients to follow. To help physicians educate patients about lifestyle interventions, the 2011 guidelines include specific and relevant examples. For instance, moderate exercise can include dancing fast for 30 minutes, raking leaves for 30 minutes, gardening for 30–45 minutes, or pushing a stroller 1 mile in 30 minutes.

Pharmacological Interventions

Aspirin is the only drug intervention with gender-specific recommendations. Among high-risk women (see above), aspirin (75 to 325 mg/day) is recommended unless it is contraindicated for those with established CHD (Class I recommendation) and is reasonable for those with diabetes, ESRD/CKD, or >10% estimated 10 year CVD risk (Class IIa recommendation). Clopidogrel should be substituted when aspirin is indicated but not tolerated (Class I recommendation).

Aspirin recommendations for other at-risk and healthy low-risk women without established CVD require weighing the benefits of preventive antiplatelet therapy against the risks. For women aged ≥65 years, aspirin (81 mg/day or 100 mg every other day) is considered useful (if blood pressure is controlled) for prevention of incident ischemic stroke and myocardial infarction when the risks of gastrointestinal bleeding and hemorrhagic stroke are considered low (Class IIa recommendation). For women aged <65 years, there