TO THE EDITOR: Although Leon et al. (Oct. 21 issue) report that transcatheter aortic-valve implantation (TAVI) is better than standard therapy, a look at the Placement of Aortic Transcatheter Valves (PARTNER) trial shows that this conclusion is unfounded. What the authors call “standard therapy” was — in 84% of the patients — a wholly discredited procedure that was largely discontinued years ago. This discredited procedure, aortic valvuloplasty, has been relegated to class III — that is, “not useful and may be harmful” — since 1998. Aortic valvuloplasty fell out of favor years ago because of “dismal” (40%) event-free 1-year survival.

The unexpectedly high rate of death in the control group was undoubtedly due to the use of this outdated, dangerous procedure. It is notable that the lowest 1-year rates of death (33%) in the PARTNER study were among the 12 patients in the standard-therapy group who underwent surgical aortic-valve replacement. The standard therapy in patients with aortic stenosis who are not surgical candidates is medical therapy alone. Unfortunately, the PARTNER study did not include a valid control group, and thus we do not know how TAVI compares with standard therapy.

Rita F. Redberg, M.D.
University of California at San Francisco Medical Center
San Francisco, CA
redberg@medicine.ucsf.edu

Dr. Redberg reports being a member of the Cardiovascular Device expert panel. No other potential conflict of interest relevant to this letter was reported.


TO THE EDITOR: In the study by Leon et al., despite randomization, the patients assigned to TAVI had a significantly better logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) than those receiving standard therapy (26.4±17.2 vs. 30.4±19.1, P=0.04). This difference raises the question of whether the better outcome (reduced rates of death from any cause) in the patients who underwent TAVI reflects the positive effect of the experimental treatment or the better baseline conditions of this patient group.

Sabrina Trippoli, Pharm.D.
Laboratory of Pharmacoeconomics
Florence, Italy

Andrea Messori, Pharm.D.
Società Italiana Farmacia Ospedaliera
Florence, Italy

No potential conflict of interest relevant to this letter was reported.

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**TO THE EDITOR:** The PARTNER trial investigators report on a tremendous advance in the care of patients with aortic stenosis who are at high surgical risk.

Major societies of cardiology have recognized the need for cost-effectiveness analyses of TAVI. Preliminary studies have suggested that TAVI may be cost-effective; however, large studies are lacking. Although the subgroup analysis in this study suggested that TAVI improved symptoms and functional capacity, the results of quality-of-life assessments were not reported. Given the demonstrated increase in periprocedural strokes and bleeding complications, future investigations should consider the cost-effectiveness of TAVI and the patient’s quality of life after this procedure, especially in patients at elevated, but not prohibitive, surgical risk. The decreases in mortality after TAVI reported by the authors are remarkable. However, in the targeted population of elderly persons with multiple coexisting conditions, limited life expectancy, and disproportionate health care expenditures, a careful consideration of the cost-effectiveness and quality-of-life benefits of TAVI is warranted, especially in the context of recent domestic health care reform initiatives.

Jonathan Newman, M.D., M.P.H.
Daichi Shimbo, M.D.
Columbia University
New York, NY
jn2169@columbia.edu

No potential conflict of interest relevant to this letter was reported.


**THE AUTHORS REPLY:** In response to Redberg: the 358 patients in the PARTNER trial had aortic stenosis, severe cardiac symptoms (93% of the patients had New York Heart Association class III or IV symptoms), and multiple coexisting conditions (mean Society of Thoracic Surgeons [STS] score, 11.6%). These conditions were considered “inoperable” by surgeons and cardiologists.

In these “sickest of the sick” patients with inoperable aortic stenosis, balloon aortic valvuloplasty is entirely appropriate as an important component of standard therapy. Balloon aortic valvuloplasty is a class IIb recommendation in the most recent guidelines of the American College of Cardiology and American Heart Association (AHA) and the European Society of Cardiology, and it is considered reasonable therapy in patients with aortic stenosis as a bridge to aortic-valve replacement or as palliation in patients who cannot undergo aortic-valve replacement because of coexisting conditions.

In the PARTNER study, balloon aortic valvuloplasty was safe (one death and two strokes occurred within 7 days after balloon aortic valvuloplasty in 150 patients). Balloon aortic valvuloplasty was a successful bridge to aortic-valve replacement in 11 of the 12 patients with initially inoperable aortic stenosis who subsequently underwent aortic-valve replacement. Among patients in the standard-therapy group in the PARTNER study, the rate of death from any cause at 3 months was 20 percentage points lower among patients who underwent balloon aortic valvuloplasty than among patients who did not undergo this procedure, and patients who underwent balloon aortic valvuloplasty had a significant mortality benefit over the course of the trial (P=0.04 by the log-rank test). Therefore, as compared with patients who underwent TAVI, the patients with inoperable aortic stenosis who underwent balloon aortic valvuloplasty and received optimal medical therapy composed an entirely valid control group in the randomized PARTNER trial.

In response to Trippoli and Messori: the baseline characteristics of the patients in the PARTNER trial were generally well balanced, but there were some differences, including a higher logistic EuroSCORE (but a similar STS score) and more frequent chronic obstructive pulmonary disease and atrial fibrillation in patients receiving standard therapy and more frequent calcified (porcelain) aorta in patients undergoing TAVI. In a small, randomized trial such as PARTNER (which involved 358 patients), such baseline disparities are commonly observed, and after adjustment for baseline risk imbalances, there were still marked
differences in the mortality end point between the test and control therapies.

In response to Newman and Shimbo: we agree that formal quality-of-life and cost-effectiveness studies are required to best determine the ultimate benefit of TAVI. These studies were embedded in the PARTNER trial design, and the quality-of-life assessment was reported on by Cohen at the recent AHA meeting. In summary, among survivors, significant differences in results of the Kansas City Cardiomyopathy questionnaire and other quality-of-life measures were observed; these results favored TAVI over standard therapy at 1, 6, and 12 months. Cost-effectiveness analyses from the PARTNER study are ongoing. These quality-of-life outcomes suggest that in the PARTNER patient cohort, TAVI not only adds years to life, but also adds life to years.

Martin B. Leon, M.D.
Craig R. Smith, M.D.
Columbia University Medical Center
New York, NY
ml2398@columbia.edu

Induced Pluripotent Stem Cells in Long-QT Syndrome

TO THE EDITOR: Moretti et al. (Oct. 7 issue) report that patient-derived pluripotent stem cells recapitulated features of a cardiac disorder through reprogramming. The authors clearly show the directed differentiation of such stem cells into functional cardiac myocytes. With regard to pluripotency, they tested for expression of pluripotency markers, but data on teratoma formation were missing. We would be grateful if the authors would provide information on any correlation between functional differentiation and teratoma formation (e.g., whether stem-cell clones with good differentiation potential have a tendency to fail to form teratomas). Although criteria for the authenticity of such cells may vary in the context of specific applications, there has been discussion of whether standards for characterization of these cell lines require teratoma assays.

In addition, the need for standards for teratoma assays, especially for human cells, has been proposed. Induced cardiomyocytes may replace induced pluripotent stem cells, but there may be an interesting (positive or negative) correlation between the functional differentiation ability and teratoma-forming ability of human induced pluripotent stem cells.

Shigeo Masuda, M.D., Ph.D.
Yutaka Hanazono, M.D., Ph.D.
Jichi Medical University
Tochigi, Japan
hanazono@jichi.ac.jp

No potential conflict of interest relevant to this letter was reported.


THE AUTHORS REPLY: An important issue regarding the derivation of human induced pluripotent

E. Murat Tuzcu, M.D.
Cleveland Clinic Foundation
Cleveland, OH

Since publication of their article, the authors report no further potential conflict of interest.

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