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EDITORIAL COMMENT

TAVR in Nonagenarians

Pushing the Boundaries*

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The introduction of transcatheter aortic valve replacement (TAVR) has revolutionized the treatment of aortic stenosis, especially in high-risk patients and in the elderly. These patients would be considered either high risk or not eligible for surgical aortic valve replacement. The pivotal PARTNER-B (Placement of Aortic Transcatheter Valves) trial, which evaluated TAVR in high-risk U.S. patients, enrolled 358 patients (mean age 83 years) with aortic stenosis not considered to be suitable candidates for surgery and randomized them to TAVR versus continuing medical therapy (1). At 1 year, the death rate was 31% with TAVR versus 51% with medical therapy ($p < 0.001$). At 1 year, New York Heart Association functional class III or IV symptoms occurred in 25% of TAVR patients versus 58% of medical therapy patients ($p < 0.001$). However, at 30 days, major strokes occurred in 5.0% of TAVR patients versus 1.1% with medical therapy ($p = 0.06$). Thus, from the beginning, TAVR has been applied in an elderly population with good, although not perfect, results.

To further investigate the use of TAVR in the United States, in 2011, the STS/ACC (Society of Thoracic Surgeons/American College of Cardiology) established the TVT (Transcatheter Valve Therapy) Registry (2). This registry permitted investigation of much larger populations, with results representing virtually all U.S. TAVR procedures. In an initial report from the registry, there were 7,710 TAVR procedures at 224 hospitals, with a median age of 84 years. In-hospital mortality was 5.5%, and stroke incidence was 2.0%. Among 3,133 patients who were followed-up at 30 days, mortality was 7.6% and stroke incidence was 2.8%. Once again, we see that the broad initial experience in the United States was in the elderly.

It has been recognized from the beginning that TAVR would be applied in patients over the age of 90 years (3-10). The largest previous experience in nonagenarians was the observational PARTNER-I trial, comprised of 531 patients with a mean age of 93 ± 2.1 years, with 329 transfemoral (TF) and 202 transapical TAVR access procedures (3). For TF-TAVR, 30-day stroke risk was 3.6%, 30-day mortality was 4.0%, and 3-year mortality was 48%. For transapical TAVR (selected for patients whose vascular anatomy precluded TF-TAVR), 30-day stroke risk was 2.0%, 30-day mortality was 12%, and 3-year mortality was 54%. Health status, measured with the Kansas City Cardiomyopathy Questionnaire (KCCQ), showed improvement from baseline. Thus, it was established that TAVR in nonagenarians could be performed. This has now been investigated in the larger population in the STS/ACC TVT Registry.

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In this issue of the *Journal*, Arsalan et al. (11) evaluated outcome of TAVR at 30 days and 1 year, comparing clinical outcomes of patients ≥90 years versus <90 years of age. Health status was assessed with the 12-item version of the KCCQ. Between November 2011 and September 2014, 24,025 patients underwent TAVR in 329 hospitals, with 3,773 (15.7%) age ≥90 years. To establish long-term outcomes, the TVT Registry clinical records were linked to Medicare administrative claims using direct patient identifiers. The median age was 92 years in nonagenarians and 82 years in the younger group. The nonagenarian group included 24 centenarians. The 30-day and 1-year mortality rates were higher in nonagenarians

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(age ≥90 years vs. <90 years: 30-day: 8.8% vs. 5.9%; $p < 0.001$; 1-year: 24.8% vs. 22.0%; $p < 0.001$). There was not a statistically significant difference in stroke incidence at 30 days or 1 year (age ≥90 years vs. <90 years: 30-day: 2.9% vs. 2.4%; $p = 0.087$; 1-year: 4.4% vs. 3.9%; $p = 0.18$). Although nonagenarians had lower (worse) median KCCQ-12 scores at 30 days, there was no significant difference between the groups at 1 year. Baseline KCCQ scores were not presented. There are significant limitations to this study. In particular, 35% of patients could not be linked between the TVT Registry and the Medicare database, and thus could not be included in the 1-year follow-up. There were significant differences between those with and without Medicare linkage, and thus the missing data cannot be assumed to be missing at random. In addition, there was a high rate of missing KCCQ data (50% at 30-day and 62% at 1-year follow-up), severely limiting the ability to assess health status. Nonetheless, this is by far the largest published series of patients age >90 years undergoing TAVR.

The published data has now clearly established that TAVR can be done in nonagenarians with high but likely acceptable risk, but should it be done? One place to look for guidance is to the published cost-effectiveness data. The cost-effectiveness of TAVR was investigated in the PARTNER-B trial by Reynolds et al. (12). Data from the trial concerning survival, quality of life, medical resource use, and hospital costs were used to project life expectancy, quality-adjusted life expectancy, and lifetime medical care cost, permitting evaluation of cost-effectiveness. For TAVR patients, mean procedure and hospitalization costs were $42,806 and $78,542, respectively. Follow-up costs at 12 months were lower with TAVR ($29,289 vs. $53,621), but 1-year total costs remained higher ($106,076 vs. $53,621). TAVR was projected to increase life expectancy by 1.6 years (1.3 quality-adjusted life-years [QALY]) at an incremental cost of $79,837. This yielded an incremental cost-effectiveness ratio (ICER) for TAVR per life-year or QALY gained of $50,200 and $61,889, respectively. Thus, the initial costs were high and the difference in cost large, but the gain in life expectancy was quite large, yielding an ICER that is probably within a socially acceptable willingness-to-pay range. Although the authors conducted extensive sensitivity analyses, the results are still dependent on the assumptions that the investigators made. In particular, the estimation of life expectancy in the 2 arms is uncertain. A smaller gain in life expectancy could cause a dramatic increase in the ICER. The findings from PARTNER-B, with a mean age in the early 80s, cannot be directly generalized to patients >90 years. Although the 1-year mortality rate with TAVR was actually higher in PARTNER-B than in the TVT registry nonagenarians, the gain in life expectancy could still be smaller. Thus, there is reason to be concerned that TAVR in nonagenarians may exceed a societal willingness-to-pay threshold of perhaps $100,000 or even $150,000 per QALY gained. It must be borne in mind that the purpose of cost-effectiveness analysis, at least in the United States, is not to set policy, but to make explicit the assumptions that we make in choosing therapy and to help make more informed choices (13).

Whether to proceed with TAVR in a patient >90 years of age can be informed by the published data, but in the end this is a clinical decision. Although imperfect, the published data shows that the procedure can be done, albeit with upfront mortality and stroke risk, and for many patients will provide improvement in length and quality of life. Despite the size of the current study group, we still do not have sufficient experience to reliably identify those patients most likely to benefit, so firm standards for withholding TAVR from nonagenarians are not, at this time, appropriate. Results may be expected to improve with new prostheses, and costs may decrease at least somewhat as well. The patient's overall health status, as well as the desires of the patient and family, should be paramount in the decision as to whether to proceed. The procedure will be expensive. Although there may be a societal decision to withhold such care for patients over a certain age, the caregivers' responsibility in making the decision as to whether to proceed is to the patient and the patient's family (14,15).

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