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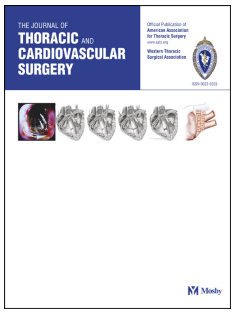

The Paradox between Randomized Controlled Trials and Propensity Score Matched Real World Data. Moving from Dissonance to Dialogue?

B. Zane Atkins, MD, Gabriel S. Aldea, MD

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The Paradox between Randomized Controlled Trials and Propensity Score Matched Real World Data.

Moving from Dissonance to Dialogue?

B. Zane Atkins, MD and Gabriel S. Aldea, MD

Division of Cardiothoracic Surgery

University of Washington, Seattle, WA

Heart teams are increasingly challenged to accurately inform individual patients with symptomatic aortic stenosis (AS) and high- or intermediate-risk features to help select an optimal individualized treatment strategy. There is an emerging controversy how to share and analyze available data most accurately. Is it best to report data from randomized control trials (RCTs) or is it more accurate to present data from larger meta-analyses, propensity scored matched controls (PSM) and real-world registry data (RWD) and registries? Surprisingly, conclusions from these sets of data appear to be discordant.

Several foundational prospective RCTs reported comparable outcomes for TAVR and SAVR. The PARTNER 1 study[1] screened 3105 patients, 77% of patients were screened out, 699 were randomized to either TAVR or SAVR and only 125 of 699 patients (17.5%) were alive and had full follow up to five years. The study reported equivalent five-year mortalities for TAVR and SAVR (67.8% vs. 62.4%). Stroke rates (10.4% vs. 11.3%), MI rates (2.9% vs. 5.9%) as well as mean valve area, mean gradient and LV mass index were also comparable for both therapies. The U.S. Core Valve study[2] screened 995 patients, randomized 759 and reported equivalent 3 year outcomes for TAVR and SAVR for mortality (32.9% vs. 39.1%), stroke rate (8.1% vs. 11.8%), re-intervention (2.4% vs. 0.4%) with better effective orifice area for TAVR (1.79 vs. 1.53 cm^2) but higher incidence of moderate to severe paravalvular regurgitation (5.9% vs. 0%). These studies as well as comparable RCT studies of intermediate risk patients led to modification of AHA/ACC and ESC guidelines that present TAVR and SAVR as equally effective alternative therapies. This article by Armoiry and colleagues assessed RWD by using the French Medical Information System (PSMI) to assess longer term (5 year) data in a larger patient cohort of propensity-score matched (PSM) high risk patients (n=1598) with complete follow up. Compared to SAVR, the study demonstrates a higher mortality for TAVR (51.5% vs. 36.2%, HR of 1.56, CI95% 1.33-1.84). The 5-year mortality for TAVR was somewhat lower than that of PARTNER 1 (51.5%), comparable at 3 years to U.S. Core Valve study (33.7%) but lower than both RCTs for SAVR at 3 and five years (23.1% and 36.1%, p<0.001). Compared to SAVR, TAVR also had higher hazard rations for stroke (1.64, CI95% 1.1-2.5), MI (2.3, CI95% 1.1-4.7) and permanent pacemaker (HR2.4 CI95%1.8-3.2). A trend toward re-operation was also noted (2.3% vs. 1.1%, p=0.09, HR 2 CI95% 0.9-4.5). Finally, hospital utilization (days) were comparable for both, but TAVR incurred a higher five-year cost of approximately 13,500 Euros presumably secondary to the differential costs of the valve. These dramatic results challenge many of the previously assumed iron clad assumptions of non-inferiority.

The discordance between RCTs, and PSM real world registry data and meta-analyses of observational trials of propensity matched cohorts is increasingly recognized[3].