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Mortality in trials on trans-catheter aortic valve implantation vs surgical aortic valve replacement: a pooled analysis of Kaplan-Meier derived individual patient data

Background / Study Objective

- All published trials on TAVI/SAVR are individually underpowered to evaluate all-cause mortality, being designed on composite outcomes. Moreover, existing meta-analyses give limited information as they are focused on fixed time-point, such as 30 days or 1 year, and cannot intercept the potential effect of the treatments on longer expectancy of life in intermediate or low risk profiles.
- We designed a pooled analysis of Kaplan-Meier-estimated individual patient data from trials comparing TAVI and SAVR to evaluate their effects on:
 - long-term all-cause mortality
 - to examine the potential time-varying effect
 - to model their Hazard Ratio over time

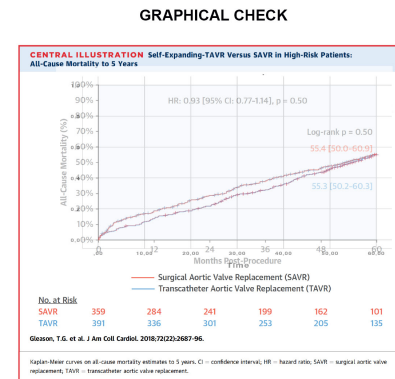
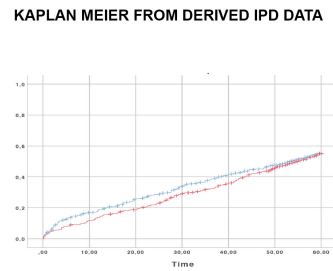
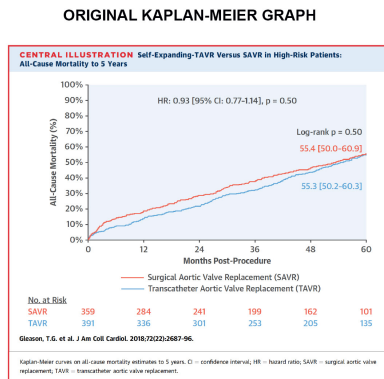
Patients

- We identified six eligible trials:
 - PARTNER 1 A trial
 - CoreValve US Pivotal High Risk trial
 - NOTION trial
 - PARTNER 2A
 - SURTAVI
 - PARTNER 3

Pooled dataset with 6367 participants randomly assigned

- TAVI (3252 patients)
- SAVR (3115 patients)

- Enhanced secondary analysis of survival curves was performed reconstructing the data from published Kaplan-Meier curves

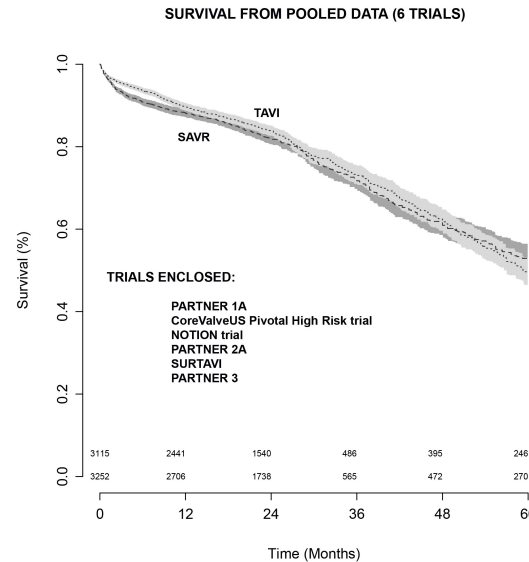


- Comparison between reconstructed individual patient time-to-event data was performed with Kaplan-Kaplan Meier estimates and random-effect Cox model
- Landmark analysis was employed in order to overcome the proportional hazards assumption failure.

Results 1

- Pooled survival at follow-up

- 1 year: 0.88 (0.87-0.89)
- 2 years: 0.82 (0.80-0.83)
- 5 years: 0.53 (0.49-0.57).



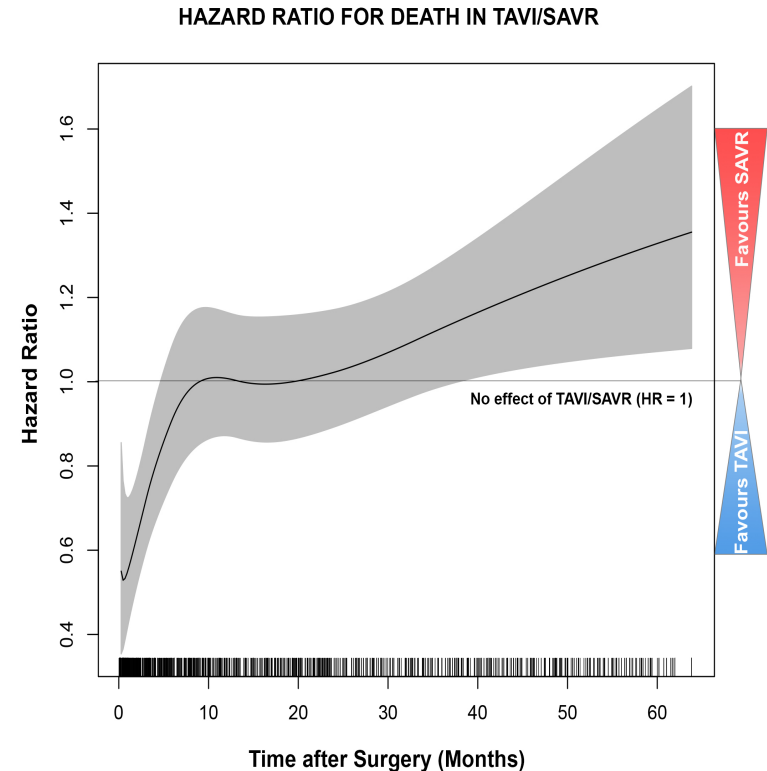
- The adjusted HR (TAVR vs SAVR) for all-cause mortality estimated with random-effect Cox model was 0.94 (95% CI 0.85 -1.06, p-value 0.27)
- the assumption of hazard-proportionality was not fulfilled and landmark analysis was performed

Results 2

0 - 12 months: incidence of mortality was significantly lower in TAVI group (Log-rank p-value <0.001) and the HR adjusted by risk profile was **0.85 (95%CI 0.73 – 0.99, p-value 0.003)**

12 - 40 months: No difference between TAVI and SAVR (adjusted HR 0.93, 95%CI 0.77 – 1.12; p-value 0.43)

40 - 60 months: reversal of HR (**HR 1.30; 95%CI 1.01-1.67; p-value 0.04**) favoring SAVR on TAVI.



Conclusion

- Mortality in trials on TAVI vs SAVR is affected by treatments with a time-varying effect.
- TAVI is related to **significantly better survival in the first months after implantation**, compared to SAVR
- TAVI is related to **significantly worst survival 40 months after implantation**, compared to SAVR