Trajectories of Cardiac Allograft Vasculopathy After Heart Transplantation and association with mortality: a population-based study

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Background: Cardiac allograft vasculopathy (CAV) is a major contributor of heart transplant recipient's mortality. However, the associations between CAV trajectories and mortality remains poorly described.

Purpose: We aimed to identify the different evolutive profiles of CAV and to determine the respective association with all-cause mortality.

Methods: Heart transplant recipients receiving care at 4 academic centers were included. Patients underwent prospective, protocol-based monitoring consisting of repeated coronary angiographies together with systematic assessment of clinical, functional, histological and immunological parameters. The mainoutcome was a prediction for CAV trajectories using unsupervised latent class mixed models. We then identified their association with all-cause mortality (NCT04117152).

Results: Overall, 1,301 patients were included (815 and 486 in the development and validation cohorts, respectively). The median follow-up post-transplant was 6.6 years (IQR=4.7) with 4,710 coronary angiographies analyzed (3.6±1.6 CAV assessments per patient). We identified 4 distinct profiles of CAV trajectories over 10 years that were characterized by i)Patients without CAV at baseline and non-progression (n=823, 63.3%), ii) patients without CAV at baseline and late onset CAV progression (n=79, 6.1%), iii) patients with mild baseline CAV and mild progression (n=261, 20.1), iv) patients with mild baseline CAV and accelerated CAV progression (n=138, 10.6%, discrimination 0.95). The 4 CAV trajectories showed gradient for all-cause mortality ($p<0.001$). Trajectories #3 and #4 were associated with higher mortality rates (10-year patient survival of 73.43% [95% CI 65.18–80.02] and 51.89% [95% CI 38.76–63.51], respectively) as compared with trajectories #1, and #2 that were characterized by 10-year patient survival of 80.01 [95% CI 76.38–84.82] and 83.49% [95% CI 71.34–90.80], respectively ($p<0.001$).

Conclusion: In a large multicentric and highly phenotyped prospective cohort of heart transplant recipients, we identified 4 robust CAV trajectories. These different profiles were associated with distinct prognosis. Our results provide the basis for a trajectory-based assessment of heart transplant patients for early patient risk stratification and patient monitoring.

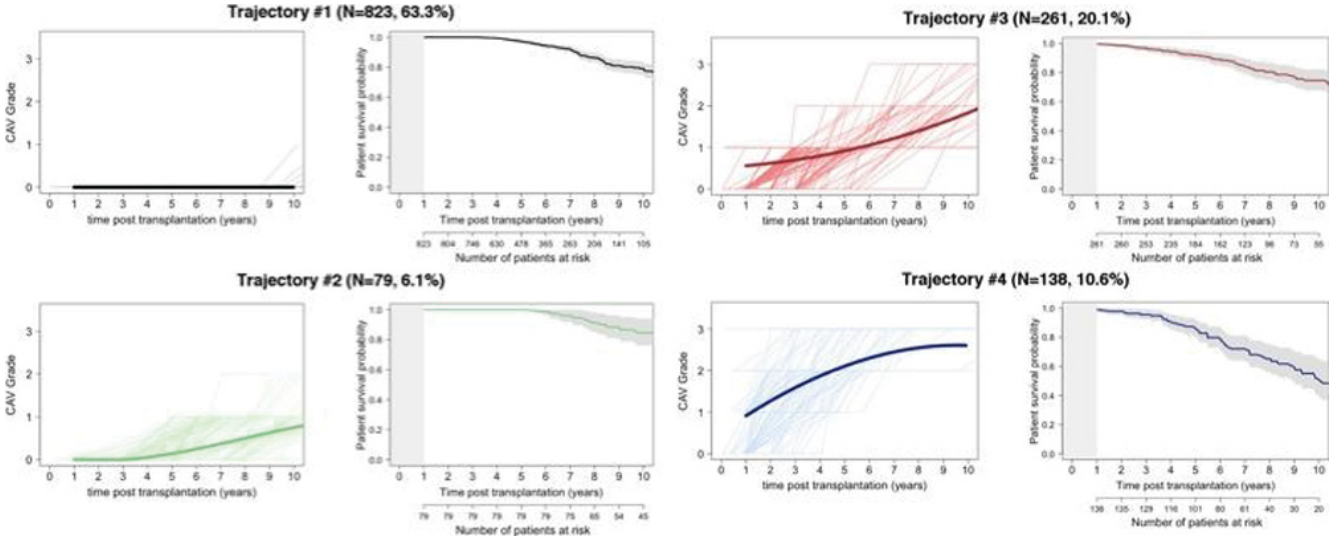

Figure 1. Overall 10-year survival probability according to the CAV trajectory in the overall cohort (n=1,301). The left part represents the main profiles CAV grades identified with latent class mixed models. Thick lines represent latent class trajectory; thin lines represent CAV individual patient trajectory. The right part represent the Kaplan Meier curves of the different trajectories.