LONG-TERM SURVIVAL OF 3000 TRANSTHYRETIN FAMILIAL AMYLOID POLYNEUROPATHY PATIENTS OVER A CENTURY

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BACKGROUND: Comprehensive long-term survival data on transthyretin familial amyloid polyneuropathy (TTR-FAP) are scarce. We aimed to estimate long-term survival in this rare disease using data from the largest and oldest cluster of patients in the world.

METHODS: Registry data from the Portuguese referral centres were merged encompassing 3,026 Val30Met patients until Dec2015. Patient groups analysed comprised natural disease (n=1,675), treatment with liver transplant (LTx) (n=978) and disease modifying oral treatment with tafamidis (n=373). Kaplan-Meier survival estimates and Cox proportional hazards model were used to adjusted by gender, late-onset, treatment and time until treatment.

RESULTS: Overall, long-term median survival since disease onset was 13.29 years (95%CI: 13.01-13.94): 11.55 years (95%CI: 11.01-11.99) in the natural disease and 25.07 years (95%CI: 23.23-27.25) in the LTx group. Median survival was not reached in the tafamidis group, with 5 and 10 years' survival rate of 99.70% (95%CI: 97.91%-99.96%) and 94.55% (95%CI: 85.73%-97.98%). LTx (HR 0.15, 95%CI: 0.12-0.19) and tafamidis (HR 0.04; 95%CI: 0.02-0.12) are associated with increased survival, compared with natural disease progression. Being male (HR 1.19, 95%CI: 1.08–1.31), late-onset (HR 1.46, 95%CI: 1.27–1.68) and time until treatment (HR 1.07, 95%CI: 1.03–1.10) were found to be important risk factors associated with increased mortality.

CONCLUSIONS: Long-term survival of TTR-FAP Val30Met patients is poor. Although with higher short-term mortality, LTx significantly improved long-term survival. Tafamidis is associated with higher survival though longer follow-up data is needed. Shorter time between disease onset and treatment is associated with increased survival. In case of clinical progression under drug treatment it's important to further study how and when to cross over to other options in order to maximize long-term survival from sequential treatments.