

## TEMPORAL TRENDS IN TRANSTHYRETIN FAMILIAL AMYLOID POLYNEUROPATHY SURVIVAL OVER A CENTURY

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**BACKGROUND:** Comprehensive long-term data on transthyretin familial amyloid polyneuropathy (TTR-FAP) survival are scarce. We estimated disease natural long-term survival using data from the largest and oldest patient's cluster in the world.

**METHODS:** Registry data from the Portuguese referral centres were merged until Dec2015 encompassing 1,675 Val30Met untreated patients. Kaplan-Meier survival estimates were obtained and Cox proportional hazards model used to estimate hazard ratios (HR) and 95% confidence intervals (CI). We analysed survival trends using five cohorts: born before 1934, 1934–43, 1944–53, 1954–63 and after 1963, adjusted by gender and late-onset.

**RESULTS:** Natural long-term median survival since disease onset is 11.55 years (95%CI: 11.01-11.99) and has increased from 10.01 years (born before 1934, 95%CI: 9.38-11.01) to 11.92 years (born after 1963, 95%CI: 9.44-12.34). Being male (HR 1.29, 95%CI: 1.15–1.43) and late-onset (HR 1.38, 95%CI: 1.18–1.61) were found to be important risk factors associated with increased mortality. The 1934–43, 1944–53, 1954–63 cohorts are associated with increased survival ( $p < 0.01$ ) as compared with those born before 1934. The cohort born after 1963 also has a positive trend ( $p = 0.059$ ) however without statistical significance, possibly due to higher selection into disease modifying interventions that impacted negatively the number and characteristics of untreated patients.

**CONCLUSIONS:** If untreated, long-term survival since TTR-FAP disease onset is very poor, particularly in males and late-onset patients. Surveillance enhancement and multidisciplinary care provided by FAP referral centres can explain part of the observed increase in survival. Improvement in early referral to specialized centres is warranted. This may be achieved through better disease awareness and definition of a well identified network of referral centres.