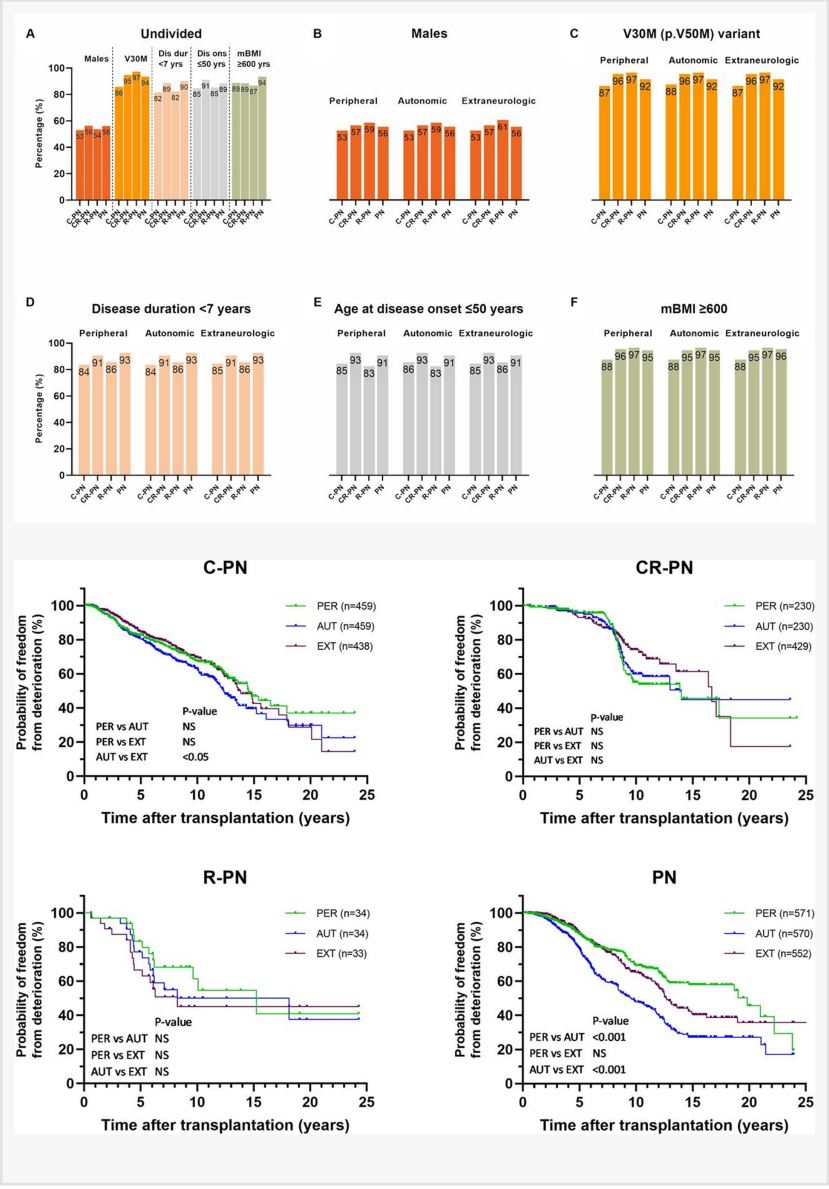
Cardio-Renal-Neural Phenotype Shapes Survival After Liver Transplant in ATTR Amyloidosis

An eGastroenterology study led by Dr. Henryk Wilczek found cardiac involvement predicts poorer long-term survival after liver transplant in ATTR amyloidosis



CHINA, June 11, 2026 /EINPresswire.com/ -- Background: from surgical standard to selective therapy

Hereditary transthyretin amyloidosis (ATTRv) is a multisystem disorder driven by misfolded transthyretin protein, leading to progressive neuropathy, cardiomyopathy, and organ dysfunction. Liver transplantation (LTx), which removes the primary source of mutant transthyretin, was historically the standard of care. However, the emergence of TTR-stabilizing and gene-silencing therapies has shifted treatment paradigms, leaving LTx reserved for selected patients. In this context, understanding which patients benefit the most from transplantation remains clinically important.

Study design: 30 years of global registry data

This retrospective study, published in the journal eGastroenterology, analyzed data from the Familial Amyloidotic Polyneuropathy World Transplant Registry (FAPWTR), including 1,762 patients who underwent isolated LTx between 1990 and 2012 across 82 centers in 21 countries. Patients were stratified into four phenotypes based on organ involvement prior to

transplantation: (1) polyneuropathy only (PN); (2) cardiac + polyneuropathy (C-PN); (3) renal + polyneuropathy (R-PN); (4) cardiorenal + polyneuropathy (CR-PN).
The study evaluated long-term survival and post-transplant disease progression across these groups.

Key finding 1: phenotype is a major determinant of survival
Overall survival after LTx was substantial, with:
- Median survival: 20.4 years
- 25-year survival rate: 32.4%

However, outcomes differed markedly by phenotype:
- Cardiac phenotype (C-PN): 15.2 years
- Cardiorenal phenotype (CR-PN): 20.8 years
- PN: 22.7 years

Cardiac involvement emerged as the strongest adverse prognostic factor, doubling mortality risk in univariable analysis and remaining significant after adjustment.

Key finding 2: clinical and nutritional factors influence outcomes
Several additional predictors of survival were identified:
- Older age at transplantation increased mortality risk
- Longer disease duration worsened outcomes
- Adverse nutritional status (modified body mass index) predicted poorer survival
- Non-V30M variants were associated with worse prognosis

Notably, each year increase in age at transplantation raised mortality risk by ~6%, while better nutritional status independently improved survival. These findings reinforce the importance of early referral and optimization before transplantation.

Key finding 3: autonomic neuropathy signals early disease progression
Post-transplant disease evolution revealed a distinct pattern:
- Autonomic neuropathy deteriorated earlier than peripheral neuropathy or organ involvement
- This effect was particularly pronounced in patients with PN phenotype

This suggests that worsening autonomic symptoms may serve as an early clinical marker of disease progression, potentially guiding the introduction of adjunct pharmacotherapy after transplantation.

Clinical implications: refining patient selection in the modern era
Although LTx is no longer the first-line therapy, the study provides several clinically relevant insights: (1) cardiac involvement should weigh heavily in decision-making, given its strong association with poorer survival; (2) renal involvement alone is not a contraindication to transplantation; (3) early intervention and good nutritional status remain critical for optimal outcomes; (4) post-transplant monitoring should prioritize autonomic symptoms as early warning signs. Importantly, these long-term data offer a benchmark for comparing emerging

therapies, including RNA-silencing drugs and gene-editing approaches.

Looking ahead: role of transplantation in the era of gene therapy
With the advent of therapies targeting TTR production—including RNA interference and CRISPR-based gene editing—LTx is now reserved for highly selected cases. Nevertheless, this study highlights that transplantation can still deliver decades-long survival benefit, particularly in carefully chosen patients without significant cardiac involvement.

Reference
Title of original paper: Amyloidogenic phenotypical variation affects post-transplant outcome of hereditary transthyretin amyloidosis: a retrospective study
Journal: eGastroenterology
DOI: http://doi.org/10.1136/egastro-2025-100243

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Funding information
This study was supported, in part, by an unrestricted grant to the FAPWTR from Alnylam, USA. The FAPWTR is supported by Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden. Astellas Pharma, Great Britain and Novartis, Sweden are previous sponsors of FAPWTR. The funding sources had no involvement in the collection, analysis and interpretation of data.

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