Study endpoint was all-cause mortality after LT. The disability score (PND) calculation. The primary autonomic dysfunction score, and polyneuropathy The pre-operative evaluation included physical examination, electrocardiography, echocardiography, autonomic dysfunction score, and polyneuropathy disability score (PND) calculation. The primary study endpoint was all-cause mortality after LT. The prognostic model predicting the individual probability of death within the first 5 years after LT was developed from the Cox proportional hazards model and was internally validated using bootstrapping.

At the time of LT, patients’ median age was 43 years, 61% were men, and 69% carried the Val50Met mutation. There were 81% patients in New York Heart Association (NYHA) functional class I, 40% had conduction disorders, 36% had a ≥12-mm interventricular septum on the echocardiograms, and the median left ventricular ejection fraction was 65%. All patients presented with neurological manifestations of ATTR: isolated sensory disturbances (PND I: 61%), difficulties with walking (PND II: 22%), and the need for cane(s) to walk (PND III: 17%). The vegetative score was abnormal in 82%, and 59% had orthostatic hypotension.

Over a median follow-up of 5.9 years after LT, 84 patients died, and cardiac events were the leading cause of death (38% of all deaths). The significant pejorative factors were PND score ≥III (hazard ratio [HR]: 1.75; 95% confidence interval [CI]: 1.04 to 2.96; p = 0.036), orthostatic hypotension (HR: 2.26; 95% CI: 1.39 to 4.22; p = 0.001), NYHA functional class ≥I (HR: 2.25; 95% CI: 1.18 to 4.27; p = 0.014), QRS duration ≥120 ms (HR: 1.90; 95% CI: 1.05 to 3.43; p = 0.035), thickened interventricular septum (for each millimeter: HR: 1.12; 95% CI: 1.04 to 1.20; p = 0.002).

The individual probability of death at 5 years was calculated as P_death = 1 - 0.735^coeff_sum - 1.27810), where coeff_sum = (0.57423 × PND score ≥III) + (0.77339 × orthostatic hypotension) + (0.9192 × NYHA functional class ≥I) + (0.60378 × QRS ≥120 ms) + (0.14589 × [interventricular septum thickness ≥6]). Risk can be computed using the online calculator. The calibration slope was 0.89 (95% CI: 0.64 to 1.15), the C-index of Harrell was 0.68 (95% CI: 0.45 to 0.88), and the concordance probability estimate was 0.71 (95% CI: 0.67 to 0.75). The area under the receiver-operating characteristic curve for the 5-year survival was 0.80, and significant differences of survival were found according to the 5-year death risk (Figure 1). Pre-operative identification of a high-risk profile (risk >50%) was retrospectively documented in 40 of 215 patients (19%).

The risk score was built from variables that measured the cardiac and neurological status regardless of mutation type. Therefore, our proposed score should be useful to gauge the risk of patients with rare variants of TTR and to take into account the phenotypic variability encountered among patients with a similar mutation. The study population was representative of a region where ATTR is not endemic and the 74% 5-year survival of our patients in line with the 77% previously reported (3). Previous reports

REFERENCES


Prediction of Long-Term Survival After Liver Transplantation for Familial Transthyretin Amyloidosis

Familial transthyretin amyloidosis (ATTR) is a rare, life-threatening, autosomal dominant disease involving mainly the heart and the peripheral nervous system due to a point mutation of the transthyretin (TTR) gene. By removing the main source of the mutated TTR, liver transplantation (LT) has become the standard treatment for ATTR (1). Because the demand for liver grafts exceeds the number of available organs and because new treatments have recently emerged, screening patients at high risk of death after LT is critical (2).

We identified 215 consecutive patients who underwent LT between 1993 and 2011. The diagnosis was made by the observation of both amyloid deposits in biopsy specimens and a TTR mutation. The pre-operative evaluation included physical examination, electrocardiography, echocardiography, autonomic dysfunction score, and polyneuropathy disability score (PND) calculation. The primary study endpoint was all-cause mortality after LT. The
suggested that septum thickness could be associated with a worse prognosis in ATTR patients with a liver transplant (4). Wide QRS complexes on electrocardiography were associated with an independent increased risk of death in our study, and this was consistent with the high frequency of conduction disorders in transthyretin cardiac amyloidosis.

The predictive model was internally validated by the bootstrap method, but further prospective studies will be required to confirm its external validity. Application of new imaging techniques and biomarkers may improve the risk stratification of patients with ATTR in further studies.

The risk prediction model proposed in this study accurately estimated the individual risk of death after liver transplantation for patients with familial transthyretin amyloidosis. The identification of high-risk patients should prompt the choice of liver transplantation with extreme caution, and alternate therapeutic strategies (e.g., combined heart and liver transplantations, new antiamyloid treatments) should be considered.

*Vincent Algalarrondo, MD, PhD
Marie Théaudin, MD, PhD
Béatrice Ducot, PhD
Pierre Lozero, MD, PhD
Denis Chemla, MD, PhD
Anouar Benmalek, PhD
Catherine Lacroix, MD
Daniel Azoulay, MD, PhD
Denis Castaing, MD
Cécile Cauquil, MD
François Rouzet, MD, PhD
Sylvie Dinanian, MD
Ludivine Elahou, MD
Dominique Le Guludec, MD
Didier Samuel, MD, PhD
Michel S. Slama, MD
David Adams, MD, PhD

*French Reference Center for FAP and Other Rare Peripheral Neuropathies (NNERF)
Service de Cardiologie
Hôpital Antoine Béclère
157 Rue de la Porte de Trivaux
Clamart 92140
France

E-mail: vincent.algalarrondo@u-psud.fr
http://dx.doi.org/10.1016/j.jacc.2015.08.870

FIGURE 1 Survival of ATTR Patients After Liver Transplantation According to the Risk Score

Survival of ATTR patients after liver transplantation differs significantly according to the score (log-rank test: p < 0.0001). For high-risk patients (score <50%), the 1-year survival rate was 70% and the 5-year survival rate was 31%. ATTR = transthyretin amyloidosis.
Letters

Neglecting Enterococci May Lead to a Misinterpretation of the Consequences of Last Changes in Endocarditis Prophylaxis American Heart Association Guidelines

We read with interest the paper by Pant et al. (1) in a recent issue of the Journal about the 2000 to 2011 trends of infective endocarditis (IE) in the United States. A main conclusion is that the incidence of streptococcal IE significantly rose since 2007, following the restriction of antibiotic prophylaxis of IE in the American Heart Association (AHA) guidelines. Streptococcal IE increased from 24.8% in 2000 to 27% in 2011, with higher incidence in the 2007 to 2011 period (2.22 cases per million population [1.64 to 2.80] vs. 0.85 cases per million population [0.50 to 1.20] in the 2000 to 2007 period) (1). The authors stated that their results contrast with data from Duval et al. (2), who did not report such an increase of streptococcal IE since the guidelines were modified, because short follow-up may preclude detection of this switch in the pattern of streptococcal IE. They also claim that a steady increase in streptococcal IE has also been reported in the United Kingdom since the National Institute for Health and Care Excellence guidelines were changed (3). However, U.K. guidelines not only limited indications for IE prophylaxis, but also completely stopped them in 2008. Hence, comparisons between AHA and National Institute for Health and Care Excellence guidelines should be carefully made.

The major caveat of the contribution by Pant et al. (1), however, is their neglect of enterococcal. The authors did not differentiate between enterococcal and other streptococcal IE, pooling all together. Enterococcal IE is a growing entity worldwide, especially in the United States, due to an aging population with numerous comorbidities acquiring the infection in the health care setting (4). Consequently, we suspect that the increase of overall streptococcal IE is not related to rising viridans group IE cases due to failing AHA guidelines, but rather to an increase of enterococcal IE hidden in the work of Pant et al. (1). All physicians must be aware of the “enterococcal menace” and not get distracted with crying wolves.

Juan M. Pericas, MD
Carlos Falces, MD, PhD
Asuncion Moreno, MD, PhD
Francesc Marco, MD, PhD
Carlos A. Mestres, MD, PhD, FECTS
*Jose M. Miro, MD, PhD
on behalf of the Hospital Clinic Endocarditis Study Group
*Infectious Diseases Service
Hospital Clinic
Villarroel, 170
Barcelona 08036
Spain

E-mail: jmmiro@ub.edu OR miro97@fundсорiano.es

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