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Background and aims: Autoimmune hepatitis (AIH) frequently recurs after liver transplantation (LT). We evaluated risk factors associated with the recurrence of AIH and its effects on patient and graft survival in a multicentre, international cohort from the International AIH study group.

Method: We included 736 patients (77% female, mean age, 42 ± 1 years) with AIH who underwent LT from January 1987 through June 2020, among 33 centers in North America, South America, Europe and Asia. Patients with overlap syndrome were excluded. Clinical data before and after LT, biochemical data within the first 12 months after LT, and immunosuppression after LT were analyzed to identify patients with a higher risk of recurrence of AIH based on a histological diagnosis. Cumulative probabilities of graft and overall survival after LT were calculated using semi-Markov models.

Results: AIH recurred in 20% of patients after 5 years and 31% after 10 years. Age at LT ≤42 years (HR, 3.01; 95% CI, 1.15–7.89; p = 0.03), use of mycophenolate mofetil post-LT (HR, 3.22; 95% CI, 1.40–7.41; p = 0.006), donor and recipient gender mismatch (HR, 2.68; 95% CI, 1.42–5.06; p = 0.002) and higher IgG pre-LT (HR, 1.03; 95% CI, 1.01–1.06; p = 0.008) were associated with a higher risk of AIH recurrence after adjusting for age at diagnosis, concomitant autoimmune disease, use of tacrolimus, cyclosporine, azathioprine, rejection episodes, living related-LT, Roux-en-Y bile duct anastomosis, bilirubin at 6-month, ALT at 6- and 12- month. In multivariate Cox regression with time-dependent covariate, recurrent AIH significantly associated with graft loss (HR, 9.63, 95% CI 4.73–19.61, p < 0.001) and death (HR, 2.09, 95% CI 1.09–3.99, p = 0.03) after adjusting for confounders. The 5-, 10-, 15- and 20-year probability of graft survival was 78%, 65%, 53% and 53% in patients with recurrent AIH and 96%, 93%, 93%, and 87% in patients without recurrence (Log rank, p < 0.001, Figure 1a). For the overall survival, probability was 81%, 73%, 55%, and 44% in patients with recurrence and 93%, 81%, 75%, and 61% in patients without recurrence (p < 0.001, Figure 1b).

Conclusion: In the largest global cohort study to date we demonstrate that recurrent AIH following liver transplantation is clinically meaningful and associates with younger age at LT, use of mycophenolate mofetil post-LT, gender mismatch and higher IgG pre-LT. Recurrent disease impacts graft and overall survival, highlighting the need for improved management strategies.