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**Assessment of advanced age candidates for liver transplantation warrants more caution**

Parente A *et al*. Elderly and LT warrants caution

Alessandro Parente, Vincenzo Ronca

**Alessandro Parente, Vincenzo Ronca,** Liver Unit, Queen Elizabeth Hospital University Hospital Birmingham NHS Foundation Trust, Birmingham B15 2TH, United Kingdom

**Vincenzo Ronca,** Centre for Liver and Gastrointestinal Research, Institute of Immunology and Immunotherapy University of Birmingham, Birmingham B15 2TT, United Kingdom

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**Corresponding author: Alessandro Parente, FEBS, MD, Surgeon,** Liver Unit, Queen Elizabeth Hospital University Hospital Birmingham NHS Foundation Trust, Mindelsohn Way, Birmingham B15 2TH, United Kingdom. aleparen@gmail.com

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**Abstract**

For patients with fulminant liver failure and end-stage liver disease, liver transplantation remains the only effective treatment. Over the years, as a result of the ageing population, the average age of liver transplant donors and recipients has increased and currently about one quarter of patients receiving transplantation in the United States are above the age of 65. Recently, a study reported that patients aged 65 years or older had lower one-year survival compared to a younger cohort. Herein, we express our opinion about this interesting publication.

**Key Words:** Liver transplantation; Elderly patients; Age in liver transplantation; Frailty; Transplant assessment; Liver transplant outcomes

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**Core Tip:** As a result of the ageing population, the average age of liver transplant candidates has increased over the years and about one quarter of recipients receiving transplantation in the United States are over 65 years of age. The study reported that patients aged 65 years or older had lower survival at one year compared to a younger cohort. In addition, they have identified congestive heart failure to be strongly associated with poor outcomes in elderly. In this letter to the editor, we express our opinion about these interesting findings.

**TO THE EDITOR**

We read with great interest the study from Kleb *et al*[1]. The authors analysed the outcome of 260 elderly patients (65 years old) undergoing liver transplantation (LT) with the aim of identifying features associated with futility, defined as death within 90 d post transplantation. In this retrospective study, Kleb *et al*[1] demonstrated that congestive heart failure (CHF) is strongly associated with futility of LT in elderly patients. Furthermore, patients aged 65 years or older had even when adjusting for severity of liver disease and comorbidities.

LT is a life-saving procedure and it is the only efficient treatment for chronic liver diseases and acute liver failure. However, organ shortage is one of the main challenges that the transplant community continues to face. Indeed, donor availability is becoming an increasing problem globally, limiting the wider spread of LT. As a result of the ageing population, average age of donors and recipients has increased throughout the decades and about one quarter of LT recipients in the United States are over the age of 65[2]. In addition to the standard transplant assessment, when considering patients in this age group, close attention should be paid to cardiovascular diseases, frailty and performance status. Commonly, elderly recipients have more medical conditions, higher waitlist and post-transplant mortality as opposed to a younger cohort.

In a large study it has been demonstrated that, in recipients without hepatocellular carcinoma, advanced age at registration has been shown to be a considerable risk factor behind patients being too unwell to undergo transplantation and it has been linked with higher waitlist mortality[3]. With a competing risk analysis, Su *et al*[3] have shown interesting results with regards to age and transplantation. In fact, patients aged 64 to 69 years displayed higher waiting list mortality with an adjusted hazard ratio of 1.73 as opposed to 2.04 for those aged ≥ 70. In addition, age was linked to less likelihood of LT, with an adjusted hazard ratio of 0.89 and 0.86 in patients aged 64 to 69 years and ≥ 70 years, respectively.

This is one of several studies which highlight the relation between advanced age and LT outcomes. Interestingly, the authors identified CHF to be strongly associated with poor outcomes. Although the results by Kleb *et al*[1] are compelling, they need to be interpreted with caution. The data presented have been retrospectively reviewed, but some important indexes to estimate frailty and comorbidities, such as the Charlston Comorbidity Index[4] and Liver Frailty Index[5] have not been calculated. This would add a more precise evaluation of the pre-transplant status and comorbidities of the recipients that can influence outcomes. Secondly, the causes of death within 90 d from LT have not been reported. Therefore, it is difficult to estimate the clear relation between advanced age alone and futility, as death could be related to post-operative complications such as graft dysfunction, infection, or immunosuppression rather than recipient age itself. Thirdly, the cohort for this study is from a single-centre, hence as yet we cannot translate this to a broader population.

By way of conclusion, the authors have to be congratulated for their work. They have demonstrated with a well-conducted analysis that recipients aged 65 years and older had increased mortality at one year compared to patients below the age of 65. This finding is of great interest and warrants a thorough assessment of potential recipients with advanced age. In particular, as underlined also by other authors[6], a meticulous pre-transplant cardiological evaluation appears to be of high importance in elderly. Identifying additional pre-operative factors that can guide the decision-making to select low-risk patients in a wider population would be of great interest.

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**REFERENCES**

1 **Kleb C**, Faisal MS, Quintini C, Miller CM, Menon KVN, Modaresi Esfeh J. Factors predicting futility of liver transplant in elderly recipients: A single-center experience. *World J Transplant* 2021; **11**: 421-431 [PMID: 34722171 DOI: 10.5500/wjt.v11.i10.421]

2 **Flemming JA**, Kim WR, Brosgart CL, Terrault NA. Reduction in liver transplant wait-listing in the era of direct-acting antiviral therapy. *Hepatology* 2017; **65**: 804-812 [PMID: 28012259 DOI: 10.1002/hep.28923]

3 **Su F**, Yu L, Berry K, Liou IW, Landis CS, Rayhill SC, Reyes JD, Ioannou GN. Aging of Liver Transplant Registrants and Recipients: Trends and Impact on Waitlist Outcomes, Post-Transplantation Outcomes, and Transplant-Related Survival Benefit. *Gastroenterology* 2016; **150**: 441-53.e6; quiz e16 [PMID: 26522262 DOI: 10.1053/j.gastro.2015.10.043]

4 **Charlson ME**, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373-383 [PMID: 3558716 DOI: 10.1016/0021-9681(87)90171-8]

5 **Lai JC**, Covinsky KE, Dodge JL, Boscardin WJ, Segev DL, Roberts JP, Feng S. Development of a novel frailty index to predict mortality in patients with end-stage liver disease. *Hepatology* 2017; **66**: 564-574 [PMID: 28422306 DOI: 10.1002/hep.29219]

6 **VanWagner LB**, Harinstein ME, Runo JR, Darling C, Serper M, Hall S, Kobashigawa JA, Hammel LL. Multidisciplinary approach to cardiac and pulmonary vascular disease risk assessment in liver transplantation: An evaluation of the evidence and consensus recommendations. *Am J Transplant* 2018; **18**: 30-42 [PMID: 28985025 DOI: 10.1111/ajt.14531]

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