



Comment on the article “Age and liver transplantation”

To the Editor:

We read with interest the paper from Durand *et al.* “Age and liver transplantation”.¹ The authors show that the percentage of elderly recipients (aged 65 years or more) has increased over time in Europe as well as in the USA. According to Durand, the reasons for this trend may be the more liberal policies regarding recipient age limits and the increased proportion of patients transplanted for hepatocellular carcinoma (HCC) or non-alcoholic steatohepatitis (NASH), which are diseases more typical of an advanced age.²

We would like to focus on this trend and point out a few differences that seem to be present between USA and Europe. Over the period 2002–2016 the percentage of elderly liver recipients (patients aged 65 years or more) passed from 6.3% to 15.7% in Europe¹ and from 6.8% to 18.6% in the USA.³ The percentage growth was in both country linear (Fig. 1). Interestingly, the analysis of covariance shows that the American slope is steeper than the European one ($p < 0.001$); in other words, the percentage of elderly recipients is growing faster in the USA.

Furthermore in Europe, over the period 2000–2016, the population median age rose from 37.7 years to 41.8,⁴ while in the USA it passed from 35.2 to 37.8 years:⁵ we find it curious that in a younger population the percentage of elderly patients transplanted is higher. The prevalence of HCC is similar in USA and Europe.⁶

A recent meta-analysis from Younossi *et al.* suggests that the prevalence of non-alcoholic fatty liver disease (NAFLD), which is the precursor of NASH is similar in the USA (24.13%; 95% CI 19.73–29.15) and in Europe (23.71%; 95% CI 16.12–33.45).⁷ It may seem strange that 2 countries with different prevalence in obesity (39.8% in the USA⁸ and between 19%–30% in Europe)⁹ have a similar prevalence of NAFLD; however, considering the 95% CI, we can assume the ratio of prevalence between the USA:Europe is between 0.5 and 1.8.

Data from United Network for Organ Sharing (UNOS) (96,446 liver transplants)³ and ELTR (91,183 liver transplants)¹⁰ show that while the percentages of patients transplanted for HCC in Europe and in the USA were similar in the period 2002–2016 (17.62% vs. 17.42%), the percentage of patients transplanted for NASH is 7 times higher in the USA over the same period (5.76% vs. 0.82%). The ratio 7:1 is more than 3 times the maximum expected of 1.8.

In other words, in the USA a patient affected by NASH has a chance at least 3 times higher of undergoing liver transplant than a patient with NASH in Europe. This setting may partially justify the observed higher percentage of over recipients over 65 years old in America.

It is not clear why USA physicians are more prone than European to transplant patients with NASH (that may depend on under-referral of patients with NASH to transplant centers in Europe, or it may be due to more restrictive criteria European physicians adopt in proposing liver transplant to older, often more obese, patients) and it is not the goal of the present letter to further investigate the phenomena, but we are willing to encourage research in this field.

Identifying and sharing selection criteria of elderly liver transplant candidates and liver transplant candidates with

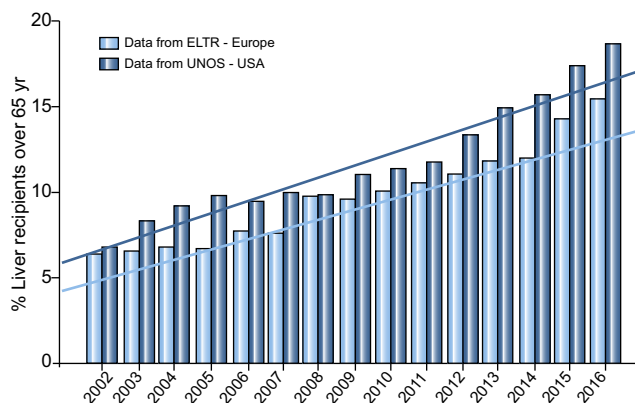


Fig 1. Percentage of liver transplants performed in recipients over 65 years old in Europe and USA between 2002 and 2016. Light blue line: regression line for ELTR data ($r^2 = 0.94$; slope = 0.616 [95% CI 0.523–0.710]; intercept = $-1,228.741$ [95% CI $-1,416.321$ to $-1,041.161$]). Blue line: regression line for UNOS data ($r^2 = 0.92$; slope = 0.741 [95% CI 0.610 to 0.873]; intercept = $-1,477.119$ [95% CI $-1,741.511$ to $-1,212.726$]). ELTR, European Liver Transplant Register; UNOS, United Network for Organ Sharing.

NASH is a priority, as transplantation will increasingly move to this demographic in the future.

Financial support

The authors received no financial support to produce this manuscript.

Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

Please refer to the accompanying ICMJE disclosure forms for further details.

Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhep.2019.02.007>.

References

- [1] Durand F, Levitsky J, Cauchy F, Gilgenkrantz H, Soubrane O, Francoz C. Age and Liver Transplantation. *J Hepatol* 2018, pii: S0168-8278(18)32626-6.
- [2] Su F, Yu L, Berry K, Liou IW, Landis CS, Rayhill SC, et al. 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.
- [3] UNOS. Accessed at: <https://unos.org/>. 2019.
- [4] WorldMeters. Accessed at <http://www.worldometers.info/world-population/europe-population/>. 2019
- [5] WorldMeters. Accessed at <http://www.worldometers.info/world-population/us-population/>. 2019
- [6] Mittal S, El-Serag HB. Epidemiology of hepatocellular carcinoma: consider the population. *J Clin Gastroenterol* 2013;47:S2–S6.
- [7] Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease—meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology* 2016;64:73–84.

Letters to the Editor

- [8] Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity among adults and youth: United States, 2015–2016. *NCHS Data Brief* 2017;288:1–8.
- [9] Blundell JE, Baker JL, Boyland E, Blaak E, Charzewska J, de Henauw S, et al. Variations in the prevalence of obesity among european countries, and a consideration of possible causes. *Obes Facts* 2017;10:25–37.
- [10] Adam R, Karam V, Cailliez V, O Grady JG, Mirza D, Cherqui D, et al. 2018 Annual Report of the European Liver Transplant Registry (ELTR) – 50-year evolution of liver transplantation. *Transpl Int* 2018;2018 (31):1293–1317.

Fabio Ferla^{1,*}
Andrea Lauterio¹
Riccardo De Carlis¹
Stefano Di Sandro¹

Niccolò Petrucciani²
Laura Benuzzi¹
Luciano De Carlis¹

¹ASST Grande Ospedale Metropolitano Niguarda, Chirurgia Generale e dei trapianti, Piazza dell'Ospedale Maggiore 3, 20162 Milano, MI, Italy

²Hôpital Henri-Mondor Ap-Hp, Chirurgie digestive hepato-biliaire, 51 Avenue du Maréchal de Lattre de Tassigny, 94010 Créteil, France

*Corresponding author. Address: ASST Grande Ospedale Metropolitano Niguarda, Chirurgia Generale e dei trapianti, Piazza dell'Ospedale Maggiore 3, 20162 Milano, MI, Italy.

Tel.: +39 3336706671.

E-mail address: fabio.ferla@ospedaleniguarda.it