ANNALS OF SURGERY OPEN
OPEN

Comment on "Right Ex Situ Split Grafts for Adult Liver Transplantation A Multicenter Benchmarking Analysis"

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We read with interest the article by Boulanger et al[1] on their French multicenter benchmarking analysis using right ex situ split grafts for adult liver transplantation (LT).

The authors' benchmarking analysis compares the outcomes of 224 right ex situ split liver transplantations (SLTs) (169 G45678 and 55 G5678), performed in 4 high-volume transplant centers over the last 10 years, against the recently established outcomes benchmark in whole LT.[2]

France's split liver graft allocation policy prioritizes pediatric recipients and follows strict rules governing adult recipient selection for the contralateral graft (close proximity to the pediatric center, low-risk recipient selection based on local center priority), aimed to achieve the best possible donor-to-recipient (D/R) matching and shorten cold ischemia time (CIT).[1]

This practice led to overall 1- and 3-year recipient and graft survival rates (96%, 92.9%; and 91.5%, 88%) coming within the published benchmark cutoffs for low-risk whole LT.[1,2]

Italy's national policy of allocating the extended-right graft (G45678) to an adult on the basis of a standard allocation policy would appear a successful model.[3,4]

Indeed, the adoption of less stringent donor (median age: 34 years; interquartile range: 20–45) and recipient selection [median Model for End-stage Liver Disease (MELD) score 15; interquartile range: 9–21; 21.8% MELD score 20–30], together with our mandatory split liver policy (introduced in 2015) produced overall 1- and 3-year recipient and graft survival rates of 95.9%, 95.1%; and 91.4%, 90.6% for 193 G45678 SLTs performed in the period 2015–2019.[3,4]

We know one of the variables reported as strongly associated with SLT outcomes is donor age, with 40 years still a United Network for Organ Sharing (UNOS) cutoff criterion for splitting a liver graft.[1,5] In our experience, the overall 1- and 3-year recipient and graft survival rates were respectively, 95.9%, 95.1% for donor age ≤40 years; 91.4%, 90.6% for donor age >40 and ≤50 years; and 91.4%, 90.6% for donor age >50 years (Fig. 1). We observed that although donor criteria expansion significantly increased our median donor age, our outcomes remained within the published benchmark cutoffs for low-risk whole LT.[1,4]

Of course, in our experience, the improved results over time were seen to be largely due to a better recipient selection policy [reduction of recipient MELD score >30; fewer retransplant candidates; fewer retransplantations using split grafts (1.6% in the period 2015–2019)], but also to greater center experience, shorter CIT, and refinements and standardization of surgical technique.

From a technical point of view, the study by Boulanger and colleagues offers 2 main findings.

First, the Authors could not identify any significant donor, recipient, anatomical, or technical-related risk factors for early hepatic artery thrombosis (HAT) in their cohort.

In our mandatory split liver allocation policy, hepatic artery division is decided jointly by pediatric and adult surgeons intraoperatively, and the celiac trunk is retained with either the pediatric or adult graft according to D/R size and anatomical matching, as well as the recipient's clinical status (high urgency, retransplantation, or previous HAT).[3] These findings support the claim that a more liberal arterial division policy during the splitting procedure (both in situ and ex situ) is safe and feasible.

Second, in an SLT setting for 2 adult recipients, the Authors note that optimal graft venous outflow is paramount to assure early graft function and reduce the rate of early HAT.

Machine perfusion is a useful tool in the case of risky donors and to reduce CIT. Several centers have described a few SLTs after hypothermic oxygenated machine perfusion (HOPE), concluding that splitting during continuous HOPE is feasible and has the potential to shorten CIT, optimize logistics, and mitigate ischemia–reperfusion injury.[6,7]

We recently described a novel technique for full-left/full-right liver splitting, with concurrent splitting and reconstruction of the vena cava and middle hepatic vein, during dual HOPE.[8] We believe this emerging option could increase the number of SLTs for 2 adults with improved D/R matching, and consequently, better outcomes.

The manuscript by Boulanger and colleagues highlights some of the advantages of the ex situ splitting procedure, namely eliminating the need for highly skilled surgeons in the donor hospital, thereby simplifying logistics.

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Disclosure: The authors declare that they have nothing to disclose.

A.L. wrote the manuscript. A.L., U.C., R.D.C., D.B., E.G., D.P., M.C., E.A., and L.D.C. revised the manuscript. All authors contributed to and approved the manuscript.

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Annals of Surgery Open (2024) 4:e526

Received: 22 October 2024; Accepted 23 October 2024

Published online 21 November 2024

10.1097/AS9.0000000000000526

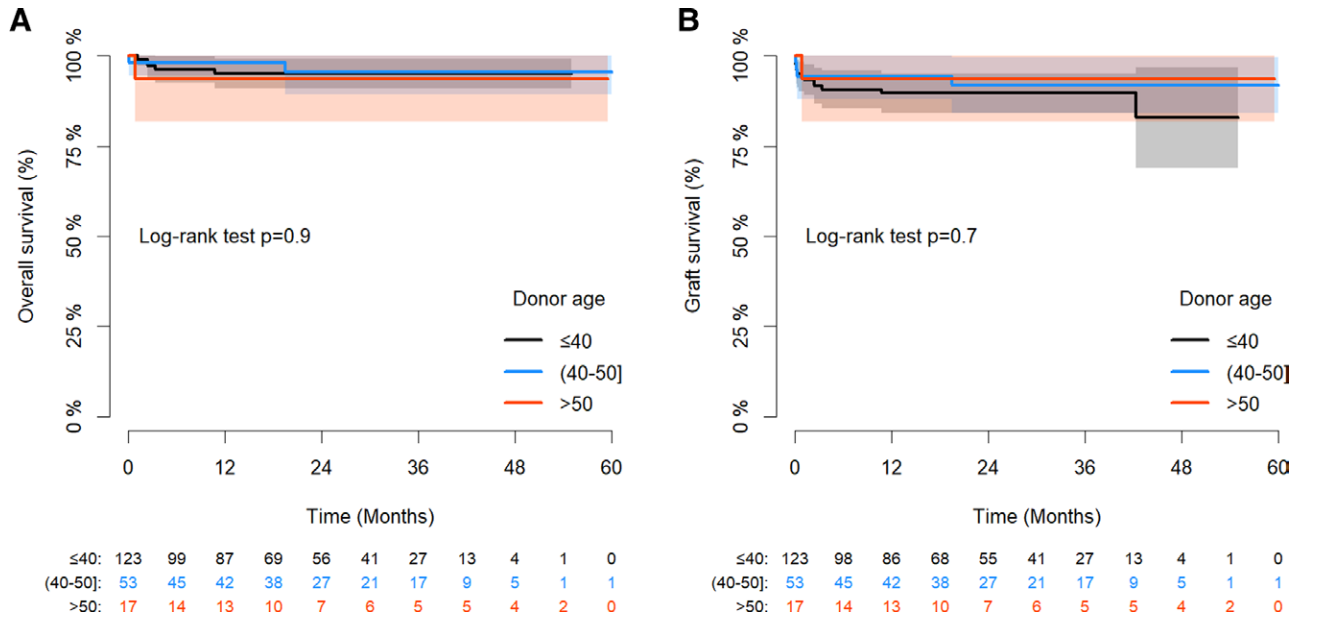

FIGURE 1. Kaplan–Meier curves by donor age for extended-right graft transplants in period 2015–2019. A, Overall survival. B, Graft survival.

The article also implicitly signals another pressing issue within the LT community: the transplant surgeon's core skill set. Many training environments still have no specific formal training requirements. The full technical spectrum of the transplant surgeon should include split-liver procedures, living donor liver hepatectomies, and partial graft implantation, including clinical fluency and confidence with the use of machine perfusion applications. In situ split-liver procedures should be a consistent component of the specific training requirements for LT surgeons.

Comparing the ex situ and in situ techniques is a long-standing debate.[9] In our opinion, the question should no longer be "ex situ or in situ split liver transplantation?"

We agree with Boulanger and colleagues that both in situ and ex situ techniques are interchangeable and should be applied where most appropriate and not according to preference as both can give equally good results. Transplant centers should master both techniques and propose a tailored approach based on D/R matching and CIT duration. Splitting the liver during machine perfusion could potentially combine the advantages of both the in situ and ex vivo technique, especially when prolonged CIT or graft complexity are likely, and would open the door to substantive improvements in the logistics of splitting.

We believe the improved adult SLT outcomes witnessed over time are probably due to better recipient selection, refinements in surgical technique, and conservative D/R matching. However, continuous, carefully managed expansion of donor selection criteria should also be pursued to increase the number of livers utilized as split grafts also in light of pediatric waiting-list mortality and living donor LT rates.

To sum up, the study by Boulager and colleagues is a laudable work focusing on how to improve outcomes of adult SLT, and their achievements will help dispel reservations that have contributed to delaying wider acceptance of SLT and its benefits.

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