Comment on: a multicentre outcome analysis to define global benchmarks for donation after circulatory death liver transplantation

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Submitted Mar 06, 2022. Accepted for publication Mar 16, 2022.
doi: 10.21037/hbsn-22-84
View this article at: https://dx.doi.org/10.21037/hbsn-22-84

In this multicenter, international retrospective study, Schlegel et al. aimed at determining reference results of liver transplantation (LT) with Maastricht type 3 donation after cardiac death (DCD) grafts using the well-known benchmark methodology (1).

Seventeen European (n=11) and North American (n=6) centers enrolling more than 2,000 DCD LT over a period of 16 years were collected. Grafts harvested and preserved using “dynamic” (regional normothermic circulation and/or machine perfusion) techniques were not included. After exclusion of non-optimal cases (functional warm ischemia time >30 minutes; cardiac arrest >15 minutes, recipient MELD score >20), more than 1,000 ideal or so-called “benchmark” cases were retained and constituted the study group. Among these, benchmarks (corresponding to the 75th percentile of median values within each center) were established for: (I) intra and post-operative data including duration of transplantation (≤6.8 hours), blood loss and transfusion (≤3 packed red blood cell units), renal replacement therapy (≤9.6%), duration of ICU (≤3 days) and hospital (≤16 days) stays; (II) specific complications (primary non function (≤2.5%), anastomotic stricture (≤28.4%), ischemic cholangiopathy (≤16.8%), early artery thrombosis (≤4.5%); and (III) morbidity and mortality at 3, 6 and 12 months postoperatively (example at 12 months: severe complications ≤66%; CCI ≤38.9; graft loss ≤14.4%; retransplantation ≤6.9%; mortality ≤9.6%). In addition, sub-group analyses revealed that morbidity and mortality were higher in high-risk patients (retransplantation, prolonged functional warm ischemia time, recipient MELD score >20) and that dynamic harvesting and preservation techniques provided better outcomes than conventional harvesting methods and also than standard cold storage preservation, especially in the setting of prolonged warm ischemia time.

This is the first study providing benchmark values for LT using DCD grafts. The benchmark methodology is now widely recognized and its use in this study is appropriate (2). In addition, the high number of patients enrolled and the sole inclusion of grafts harvested using the standardized rapid procurement technique followed by static cold storage preservation (corresponding to the reference technique) provide strong reference values for further comparisons with strategies currently employed in other countries (regional normothermic circulation and/or machine perfusion) (3–6) and with forthcoming strategies.

The results of the present study should however be interpreted with caution. First, exclusion of optimal cases was only based on warm ischemia time and recipient MELD score. A more detailed description of the characteristics of the donors, especially concerning pre and intra procurement biological tests (transaminase levels) along with histologic characteristics of the grafts such as the degree of steatosis would have been relevant. As a matter
of fact, various protocols, such as the French protocol include those characteristics to validate the indication of LT and it is likely that some of the benchmark cases in the present study would not have been transplanted in some countries. In this setting, analysis of the factors associated with failure to reach benchmark values would have allowed identifying other characteristics and would have likely led to reclassifying benchmark cases into high-risk cases. Second, the relevance of some of the established benchmark criteria may be largely questioned. On one hand, duration of transplantation makes little sense as no correlation between operative time and postoperative outcomes has been shown in this study. On the other hand, various criteria such as duration of ICU and hospital stays may widely vary according to local and or national practices. As a matter of fact, some centers keep patients in ICU several days on a routine and protocol basis. Likewise, duration of hospital stay may widely vary according to national practices and some countries favor early hospital discharge even though it may increase readmission rates.

In this study, roughly half of the entire cohort was considered as ideal cases and this rate reached up to 75% in some centers. Furthermore, 71% of benchmark cases were included after 2011. This emphasizes that the place of DCD LT is continuously increasing and that DCD LT is frequently performed in favorable situations. For example, 40% of patients were transplanted for HCC and consequently low MELD scores, even in North American centers in which liver insufficiency still represents the main indication for LT. Also, in the setting of continuous innovation (7), establishing benchmark values may be questionable. Indeed, results of DCD LT are likely to rapidly improve in upcoming years and reference values may not be reached yet.

In this study, no case from France was included. The main reason is that the national protocol imposes use of regional normothermic circulation. Yet, DCD LT may only be performed in a context of “short” warm ischemia time (<30 minutes) and “low” recipient MELD score (<25), which corresponds to benchmark cases in the reported study. France is not an isolated case, and it should be emphasized that various countries use other strategies such as super-fast harvesting with or without regional normothermic circulation or machine perfusion.

Finally, on a purely methodological basis, we should keep in mind that the benchmarking method, even though largely employed, has never been adequately validated. Moreover, the authors did not clearly follow STROBE rules for good reporting in medical literature (8) and management of missing data has not been discussed.

In conclusion, the study is of great importance. It provides a reference level of performance regarding DCD LT using basic procurement and storage techniques. The continuous development of DCD LT involves various innovating strategies of selection, procurement, storage, assessment, and repair of DCD grafts. In a near future, these benchmark values are likely to be challenged by the results of more elaborated DCD LT protocols.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, Hepatobiliary Surgery and Nutrition. The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-22-84/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Hobeika C, Lesurtel M, Cauchy F. Comment on: a multicentre outcome analysis to define global benchmarks for donation after circulatory death liver transplantation. HepatoBiliary Surg Nutr 2022;11(2):270-272. doi: 10.21037/hbsn-22-84