Transplant International

LETTER TO THE EDITORS

Liver-first versus lung-first: a new dilemma in combined organ transplantation

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Dear Editors,

One-staged combined liver–lung transplantation (cLiLuTx) is a life-saving procedure for patients with dual organ failure [1]. The classic sequence dictates LuTx priority over LiTx, due to the tolerable cold ischemic time, which is considered shorter for the lungs (6–8 h) than for the liver (8–10 h). However, recent reports describe successful LuTx following longer ischemic time (10–12 h) [2,3], and safe extension of the lung out-of-body time by *ex vivo* lung perfusion (EVLP) [4]. Therefore, it may be that an inversed sequence—*liver-first*—could have several benefits.

The aim of this letter was to provide the pros and cons for each sequence, offering an instrument for multidisciplinary case-by-case evaluation. In general, for every cLiLuTx, the organ-specific disease severity should be evaluated. Additional considerations for the *liver-first* are as follows:

Firstly, in highly sensitized patients, transplanting the liver first might provide immunological benefit for the second organ preventing it from humoral rejection by donor-specific antibodies absorption [5]. Cross-match may turn negative after LiTx, and the second organ can safely be transplanted, as shown for combined liver–kidney/liver–heart transplantation [6].

Secondly, LiTx can provoke hemodynamic instability and need for massive transfusion. This process could harm the newly transplanted lungs, which are very sensitive to volume shifts, resulting in primary lung graft dysfunction (PGD). In case the native lungs are thought to withstand the surgical trauma of LiTx, the *liver-first* sequence should be considered.

Thirdly, in case of impaired coagulation, transplanting the lungs first would be too risky. Replacing the liver first, thereby restoring adequate coagulation and avoiding massive transfusion during LuTx, renders this procedure safer and attenuates the risk of pulmonary edema. Our first report of a *liver-first* sequence was in a patient with acute liver failure. EVLP was used to anticipate longer lung preservation time (OCS™Lung; Transmedics Inc, Andover, MA, USA) [7].

Fourthly, it has been demonstrated that LiTx-induced ischemia-reperfusion injury (IRI) is captured by the lungs [8]. Hypothetically, if the lungs would be transplanted first, this second hit of liver IRI could cause lung edema and provoke PGD.

Fifthly, a prolonged liver ischemic time may result in more biliary strictures and retransplantation [9].

However, the *liver-first* principle is not generally applicable:

Firstly, in severely injured lungs (e.g., purulent cystic fibrosis), a prolonged ventilation of the diseased lungs during a *liver-first* sequence could provoke remote organ injury and/or sepsis. Transplanting the lungs (sickest organ) first would limit this risk.

Secondly, during a *liver-first* procedure, oxygen delivery and carbon dioxide removal of the native lungs could be further impaired, resulting in need for intraoperative extracorporeal life support.

Thirdly, an extended lung ischemic time potentially increases the risk for pulmonary PGD [2].

Therefore if the LiTx is anticipated to be complicated, prolonging lung ischemic time to more than an acceptable 10–12 h, a *lung-first* sequence should be considered.

doi:10.1111/tri.13099

The Hannover group reported on eight *liver-first* sequences versus 15 *lung-first* procedures. The *liver-first* group had improved 5-year survival and shorter intensive care/hospital stay. In addition, the incidence of grade 2/3 PGD at 72 h post-transplant was much lower in the *liver-first* than in the *lung-first* group [10]. To fully elucidate the potential of an inversed—*liver-first*—sequence, further research and multicenter collaboration is needed, as more patients are being referred, following the increasing success of this complex transplant procedure [1].

Funding

The authors have declared no funding.

Conflict of interest

The authors have no conflict of interests to describe as reported by *Transplant International*. Following unrelated funding sources are mentioned: RV is a senior clinical research fellow of the Research Foundation Flanders (FWO), Belgium, and is supported by a research grant of UZ Leuven, Belgium (STG15/023). JP is holder of a chair in Abdominal Transplant Surgery from the Centrale Afdeling voor Fractionering (CAF), Vilvoorde, Belgium. GW and DVR were principal investigators for the INSPIRE trial comparing cold storage versus OCS Lung™ for preservation (Clinical Trials.gov number NCT 01630434) sponsored by for *Transmedics* (Andover, MA, USA).

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