



## Review Article

## Review of anesthesia in liver transplantation



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## ABSTRACT

Liver transplantation (LT) is a well-accepted treatment modality of many end-stage liver diseases. The main issue in LT is the shortage of deceased donors to accommodate the needs of patients waiting for such transplants. Live donors have tremendously increased the pool of available liver grafts, especially in countries where deceased donors are not common. The main ethical concern of this procedure is the safety of healthy donors, who undergo a major abdominal surgery not for their own health, but to help cure others. The first part of the review concentrates on live donor selection, preanesthetic evaluation, and intraoperative anesthetic care for living liver donors. The second part reviews patient evaluation, intraoperative anesthesia monitoring, and fluid management of the recipient. This review provides up-to-date information to help improve the quality of anesthesia, and contribute to the success of LT and increase the long-term survival of the recipients.

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## 1. Introduction

The first liver transplantation (LT) was performed by Starzl et al.<sup>1,2</sup> in 1963. Since then, there has been a stream of continuous improvements in surgical techniques, anesthetic management, and postoperative immunosuppressive treatment in LT, which have improved the long-term survival rate of patients who undergo LT. LT is now an accepted treatment modality in many end-stage liver diseases.<sup>3–5</sup> The main problem in LT is the wide disparity between supply (available donors) and demand (patients needing liver grafts).<sup>3–5</sup> To increase the pool of donors from the conventional beating heart, brainstem-dead donors, various efforts—such as using marginal donor from controlled non-heart beating donor by perfusion of cold preservation solution in the femoral artery immediately after cardiac arrest,<sup>6</sup> or regional extracorporeal membrane oxygenation (ECMO) perfusion of the abdominal organs after cardiac arrest,<sup>7</sup> or systemic ECMO support after cardiac death—have been performed.<sup>8</sup> Improvement in the surgical technique via using reduced liver graft has shortened the waiting period of pediatric recipients and eliminated death in the waiting list.<sup>9</sup> The

technique of split liver graft<sup>10,11</sup> has doubled the pool of donor grafts.<sup>12</sup> However, the problem of organ shortage remains. Living donor liver transplantation (LDLT) is another option to address the shortage of deceased donors.<sup>13–18</sup> It has indeed increased the donor pool, especially in countries where deceased donors are not common.<sup>5</sup> If donor shortage continues owing to the growing need for liver grafts, LDLT will play an important role in the future of LT.<sup>19</sup> Because of the cultural, religious, and social differences between the West and the East, the strategy used to overcome the problem of organ shortage is also different. Western countries tend to perform more deceased donor LTs,<sup>20</sup> whereas in Asia LDLT is more common.<sup>5,14,21</sup> Interested readers can refer to Chen et al's<sup>5</sup> review on why LDLT flourishes in Asia. As anesthesiologists, we have to provide safe anesthesia to LT patients and resolve hemodynamic problems as they arise using the improvements in surgical techniques in LT. This review focuses more on anesthesia in living liver donors and the problems adherent to LDLT. The second part reviews the topics of patient evaluation, anesthesia monitoring, intraoperative blood loss, and blood transfusion for recipients.

## 2. Live liver donor

The liver is an organ that can—within a few weeks or months—regenerate to its original volume even after a large part of

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its tissue, up to 70%, has been surgically removed; the 30% remnant liver remains sufficiently functional to meet the metabolic needs of the donors.<sup>22,23</sup> Therefore, a healthy person can donate part of his/her liver for LT. The first successful Asian cadaveric LT was performed by Chen et al<sup>24</sup> in 1984. Since then, the number of cadaveric LTs in Asia has remained very low.<sup>5,21</sup> In 1990, the first Asian LDLT was performed in Japan,<sup>18,25</sup> and this was quickly followed in Taiwan, Hong Kong, South Korea, China, and other Asian countries.<sup>26</sup> Today, LDLT is a well-accepted treatment modality and has become a daily practice in treating patients with liver diseases requiring LT in Asia.<sup>5</sup>

### 2.1. Beneficial aspects of LDLT

There are many advantages in LDLT when compared with deceased donor LT. First, LDLT shortens the waiting period for recipients to receive the donor graft. Second, LDLT is an elective surgery, whereas in deceased donor LT, the procedure often takes place outside of routine hours. The team members may be tired from their daily work, and the staffing levels may be low and usually with less personnel as compared with those in routine practice. The surgeons and anesthesiologists, caring for the liver transplant recipients, must prepare themselves to perform and manage a complex and prolonged surgery in patients, who may have unstable hemodynamics owing to massive blood loss from profound coagulopathy, hypothermia, complex metabolic and electrolyte disturbances,<sup>27</sup> and nature of the surgical procedure, such as a sudden decrease in venous return and cardiac output by clamping of the inferior vena cava (IVC) with or without venovenous bypass.<sup>28,29</sup> It is a very challenging work both physically and mentally for all the participants. By contrast, LDLT usually starts in the normal office hours, and all members of the transplant team are in good condition with high staffing level to start their daily clinical tasks. Furthermore, the recipients are usually well prepared and are in good medical shape, in that they have been optimally improved preoperatively by surgeons, anesthesiologists, hepatologists, cardiologists, and other specialists of the LT team. LDLT is not linked with the national organ allocation program, and the rank priority of grafts does not follow the MELD (Model for End-Stage Liver Disease) score as it is stated in the principle of the United Network for Organ Sharing.<sup>30</sup> Once a suitable donor is available, LDLT can be performed, thus shortening the waiting period and eliminating potential death among the patients in the waiting list.<sup>31</sup> The quality of the liver graft is good as it is procured from a healthy donor with stable hemodynamics without needing inotropic drugs for support during the organ procurement, and it has very short cold ischemic time, thereby minimizing preservation injury.<sup>32</sup> Likewise, LDLT recipients are usually less sick and in better condition in comparison with deceased LT recipients; therefore, the outcome is similar to or even better than that of deceased LT recipients in terms of graft and patient survival.<sup>18,33,34</sup> Emond et al<sup>35</sup> reported that the 1-year survival rate of pediatric LDLT was 94% (compared to 88% in deceased LT). Meanwhile, Chen et al<sup>36</sup> reported a 5-year LDLT survival rate of 98% for biliary atresia patients, 94% for patients with hepatitis B virus cirrhosis, and 90% for patients with hepatocarcinoma. LDLT started with pediatric LT using the left lateral segment<sup>13,17</sup> and has gradually undergone an evolution to adult to adult right lobe LT.<sup>37–39</sup>

### 2.2. Donor selection

The biggest ethical concern arising from LDLT is the safety of the donors, who undergo major abdominal surgeries not for their health or benefit, but risk themselves with a variable rate of perioperative morbidity and even mortality.<sup>40</sup> The donor selection

criteria may vary in different centers,<sup>41,42</sup> but all have the same principle—to minimize the risk to the donor and maximize the benefit to the recipient.<sup>43</sup> The evaluation process is performed stepwise in three to four steps,<sup>41,44</sup> aiming to ensure that the potential donor is healthy enough for this procedure, and to identify and rule out the potential donor from any unsuitable condition—such as too complicated or abnormal liver vascular-, biliary anatomy and small liver volume—that may increase the risk of complications to the donor. Several formulas, such as the graft–recipient body weight ratio and graft–weight in percentage of standard liver mass, are used to ensure an adequate liver mass in the donor and the recipient.<sup>45</sup> Failure or delay in identification of unsuitable conditions, may lead to intraoperative abandonment of the procurement procedure. This kind of aborted hepatectomy is a near-miss event, and the reported rate is about 1.1–1.2%.<sup>46</sup>

The potential living liver donor is usually a close relative of the recipient, who must abide, if there is any, with local regulations on live organ donation.<sup>41</sup> The donor should be a healthy adult, younger than 60 years, who is competent, and willing to donate part of his or her liver without any coercion.<sup>41,47</sup> The complete preoperative evaluation includes medical, physical, laboratory, psychosocial, and imaging assessments by noninvasive computed tomography (CT), CT volumetry, multiple detector three-dimensional CT angiography,<sup>48</sup> three-dimensional magnetic resonance cholangiography,<sup>49</sup> and abdominal echo to identify and confirm that the liver is anatomically suitable to be donated and to ensure donor safety.<sup>41,50</sup> Informed consent for donation should be obtained from the donor after explanation of the donor risk without bias.<sup>41,50</sup> A potential donor should be excluded if the individual is a carrier of hepatitis B, or is infected with hepatitis C and human immunodeficiency virus; however, donors who are hepatitis B core antibody-positive are considered acceptable because of the high prevalence of hepatitis B infection in Asian countries.<sup>41</sup> Perioperative active immunization and prophylaxis lamivudine given to the recipient, who will receive the hepatitis B core antibody-positive graft, may prevent *de novo* hepatitis B virus infection after LDLT.<sup>51</sup> A blood group that was identical or compatible was required in the past,<sup>41</sup> but now a donor who is ABO incompatible (ABOi) is deemed acceptable when there is no other suitable potential donor available.<sup>52–55</sup> Operations in donors with abnormal liver function, moderate fatty liver, and infection with fever should be postponed until normalization of laboratory data and improvement of the degree of fatty liver have been attained.<sup>41,56</sup>

### 2.3. Donor anesthesia

Complete medical history, physical examination, preliminary laboratory, serologic tests and radiological examinations should be performed and carefully evaluated by the anesthesiologist prior to the operation. Diabetes mellitus or hypertension with regular control is accepted.<sup>41</sup>

General intubation anesthesia under standard monitors including invasive arterial blood pressure and central venous pressure (CVP) measurements is performed. It may be used with<sup>57</sup> or without epidural analgesia.<sup>56,58,59</sup> General anesthesia can be maintained with inhalational agents, balanced anesthesia, or total intravenous anesthesia.<sup>60</sup> Live donor hepatectomy is unlike ordinary deceased total hepatectomy, in that the IVC should be preserved for the live donor. It is also different from the ordinary liver resection—there, the live donor partial hepatectomy with preservation of graft viability and adequacy, in terms of liver volume and function for both the recipient and the donor, is of principal importance.<sup>56</sup> Live donor hepatectomy is, therefore, performed without control of the hepatic inflow,<sup>56,59</sup> such as the Pringle maneuver, to protect the graft and remnant liver from ischemic injury.

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