LETTER TO THE EDITOR

A novel technique in mouse liver transplantation

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Dear Editors,

Rat liver transplantation (LT) model was established by Sun Lee in 1973 [1] and was modified with "Cuff" technique by Kamada and Calne in 1983 [2]. Since then, this small animal LT model has served as standard for LT basic research. With the increasing application of mouse-specific antibodies and the development of genetically modified mouse strains, organ transplantation in the mouse has become a powerful tool offering new insight into the mechanisms of transplantation biology. Mouse LT model was established by Qian *et al.* in 1991 [3]. Subsequently, this model has been modified [4,5] and widely used in research [6–10]. Mouse LT is one of the most challenging model among all organ transplantation models because of both the intricate anastomoses and the strict limitation of the anhepatic phase to enable survival conditions. The chief obstacle for success is not anastomosing tiny vessels, but the bile duct reconstruction with the need to insert a plastic stent in its lumen. The bile duct is only 0.1–0.2 mm in diameter, which makes placement of a stent difficult. While microsurgeons usually omit mentioning this issue in publications, the challenge of performing this anastomosis reduces the success rate of mouse LT, particularly for the beginners who are learning the procedure.

We herein report a novel method of main bile duct reconstruction in mouse LT using cholecystojejunostomy (CJ) anastomosis. The CJ drains bile from the liver through gallbladder to the jejunum. The new method is easier due to the proper diameter of the gallbladder (2–3 mm). It can be performed by microsurgeons, who master micro-vessel anastomosis.

Surgical procedure (see Video S1): The mouse LT is performed under a surgical microscope in mice anesthetized with isoflurane plus oxygen inhalation. After anastomosing supra- and infra-hepatic vena cava, portal vein (and hepatic artery, if performing arterialized mouse LT), both common bile ducts of the graft and the recipient should be ligated with 8-0 sutures. After all abdominal organs are placed back to the anatomical position, the gallbladder is exposed by dissecting back-side ligaments. The proximal jejunum is moved to the top of the gallbladder (Fig. 1a). Size-matched incisions are performed in the jejunum and at the top of the gallbladder with scissors (Fig. 1b). A 9-0 running suture anastomosis is performed between the gallbladder and

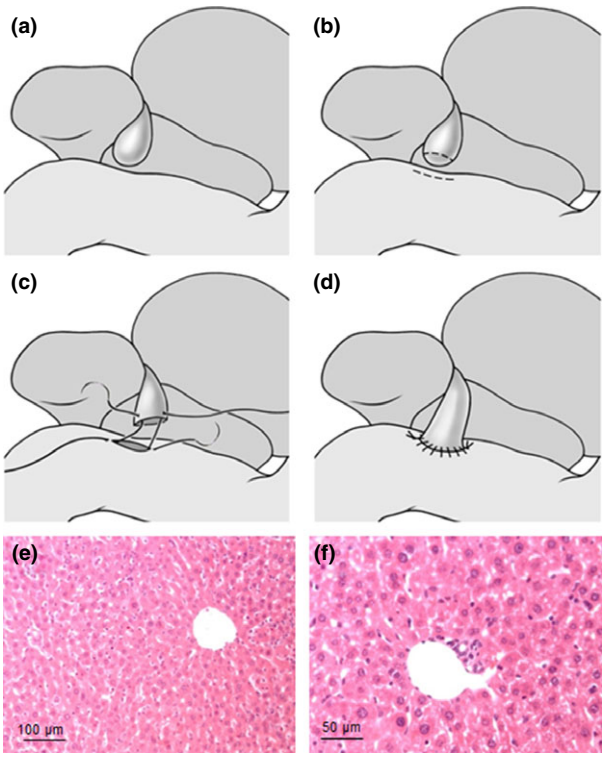

Figure 1 Bile duct drainage by cholecystojejunostomy in mouse liver transplantation. Common bile ducts of both graft and recipient are ligated before CJ. (a) The jejunum is placed orthotopically to facilitate the anastomosis. (b) Size- and orientation-matched incisions are made in the jejunum and at the top of the gallbladder with scissors. (c, d) A running suture technique is applied to complete the anastomosis. (e, f) H&E stainings of the liver graft showing normal liver 4 weeks after MLT using CJ method.

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the jejunum (Fig. 1c, d). Attention must be paid to the back side of the anastomosis, as the wall thickness between the gallbladder and jejunum is quite different. The suture must include whole layers of both jejunum and gallbladder.

We have performed 36 mice LT using the CJ method. In 8 cases, the indication was rescue of failed bile duct stent insertion. Six recipients developed a postoperative bile leak, 4 of those survived and 2 died following re-operation. Liver graft histology of surviving recipient mice showed normal liver tissue and normal bile duct 4 weeks after mouse LT with CJ (Fig. 1e, f).

As CJ is an easy alternative to the challenging end-to-end bile duct anastomosis in mouse LT and can be used in some experiments that stent method is not feasible, it may represent an alternative method in mouse LT.

Conflict of interest

The authors have no conflicts of interest to disclose.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article:

Video S1. Mouse LT using cholecystojejunostomy anastomosis.

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