

Liver transplantation in China: Achievements over the past 30 years and prospects for the future

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SUMMARY Over the last three decades, liver transplantation (LT) in China has made breakthroughs from scratch. Now, new techniques are being continuously incorporated. However, LT in China differs from that in other countries due to cultural differences and the disease burden. The advances made in and the current issues with LT in China need to be summarized. Living donor LT (LDLT) has developed dramatically in China over the last 30 years, with the goal of increasing transplant opportunities and dealing with the shortage of donors. Western candidate selection criteria clearly are not appropriate for Chinese patients. Thus, the current authors reviewed the literature, and this review has focused on the topics of technological advancements in LDLT and Chinese candidate selection. The Milan criteria in wide use emphasize tumor morphology rather than pathology or biomarkers. α -fetoprotein (AFP) and pathology were incorporated as predictors for the first time in the Hangzhou criteria. Moreover, Xu *et al.* divided the Hangzhou criteria into type A (tumor size ≤ 8 cm or tumor size > 8 cm but AFP ≤ 100 ng/mL) and type B (tumor size > 8 cm but AFP between 100 and 400 ng/mL), with type B serving as a relative contraindication in the event of a liver donor shortage. In addition, surgeons in Chengdu and Shanghai have the ability to perform a laparoscopic hepatectomy for right and left lobe donors, respectively. China has established a complete LT system, including recipient criteria suitable for Chinese people, a fair donor allocation center, a transplant quality monitoring platform, and mature deceased donor or living donor LT techniques.

Keywords hepatocellular carcinoma; living donor liver transplantation; Hangzhou criteria; donation after cardiac death; donation after brain death

1. Introduction

Primary liver cancer is the seventh most common malignant tumor according to the World Health Organization and the fourth leading cause of cancer-related mortality. It has soared to the second leading cause of cancer-related mortality in China, after lung cancer. In 2020, the number of cases surpassed 410,000, with more than 390,000 deaths, placing a huge burden on China's health system (1). Hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (ICC), and other uncommon liver cancers are types of primary liver cancer. HCC accounts for a sizable chunk of the total therein. The main etiological factors for HCC are liver cirrhosis, hepatitis, and aflatoxins, while the high incidence of HCC in China is attributed to the high prevalence of the hepatitis B virus. HCC treatment options include hepatectomy, trans arterial chemoembolization (TACE), radiofrequency ablation (RFA), liver transplantation (LT), and conservative

therapy. However, only LT can eliminate the tumor and underlying liver disease at the same time. Accordingly, LT is the treatment of choice for end-stage liver disease and early-stage HCC (2).

China has seen remarkable progress in orthotopic LT since 1977, when it was first performed on the Chinese mainland. According to the China Liver Transplant Registry (CTLR), LT cases in China account for more than a third of all LT cases worldwide (3). As of June 2015, a total of 29,360 cases of LT were performed, about 50% of which were performed to treat HCC (2). With economic and technological advances, LT in China is no longer constrained by the procedure but rather by a scarcity of donors and a high rate of postoperative recurrence. Under such conditions, efforts are being made to address the issue of a donor shortage and to improve the prognosis for transplant patients. The legal framework for government oversight in 2007 was the initial step to regular organ transplantation. However, several ethical and legal issues remained. The pilot

program for organ donation after cardiac death (DCD) in 2012 represented a milestone in Chinese organ transplantation (4). At the same time, general surgery specialists have successfully devised Chinese transplant indications such as the Shanghai Fudan Criteria, the Hangzhou Criteria, and the West China Criteria with the goal of expanding the transplant indications of the Milan criteria without diminishing prognosis.

In 2002, surgeons at West China Hospital performed the first adult-to-adult LDLT in mainland China, further resolving the problem of the liver donor shortage at the surgical level (5). In 2013, physicians at West China Hospital studied 290 living donors from 2002 to 2012, focusing on reasons why donor hepatectomy was 'not feasible' (6). There were two main reasons for the failure of the operation in the 5 donors, namely poor liver quality and inappropriate biliary anatomy. All 5 donors recovered without complications and the long-term follow-up was good, indicating that China has achieved a low rate of 'no go' donor hepatectomy and that abandonment of surgery had no effect on short-term and long-term outcomes. Laparoscopic donor hepatectomy started late in mainland China, and until 2014 only a few transplant centers had performed this procedure. A prospective case-matched study confirmed the advantage of these minimally invasive approaches in reducing the duration of hospitalization and administration of analgesics, but the total cost of hospitalization was significantly higher (7). In fact, previous studies in mainland China tend to favor LDLT and laparoscopic donor harvesting. Therefore, the current review aims to describe the progress of LT in China over the past 30 years by describing the selection of Chinese recipients, with a special focus on the achievements of and issues with LDLT and laparoscopic donor hepatectomy in mainland China.

2. Advances in standardization of LT procedures

LT in China has gone through three stages over the past 30 years. The first stage is from the initial LT (1977) to 2005. During this period, various transplant centers came to the fore but there was no platform to assess and control the quality of LT. With the establishment of the CTRL in 2005 and the formulation of a legal framework for government oversight of LT in 2007, all transplant centers were instructed to upload data and accept inspections by the Ministry of Health of China in 2008. Afterwards, the number of transplant centers plummeted, but the quality of surgery was better. The increasing number of LT operations rely on a sufficient number of liver donors. Influenced by the traditional Confucianist view that a corpse should be intact, resistance to organ donation still exists. The Chinese Organ Transplant Response System (COTRS) was created in 2012 to change unethical practices, combat illicit organ trading, and to end transplantation

tourism in order to make the procedure more open and efficient (4). When voluntary organ donation became the main source of organ donation marks the beginning of the second phase. In 2015, the Chinese Government declared voluntary organ donation to be the sole legal type of organ donation, ushering in a new age of organ transplantation in the country. By December 2021, there were 37 842 organ donors and 113,294 donated organs (8).

3. Selection criteria for treatment of HCC

The first appearance of LT was in the context of treating unresectable HCC. Because of its high recurrence rate, HCC was later deemed a contraindication for LT. In 1996, Mazzaferro *et al.* presented the first liver transplant selection criteria on HCC, the Milan criteria (9). Later, sets of criteria were proposed by various experts in order to broaden the Milan criteria's strict requirements for the number and size of tumors, including the Pittsburgh criteria (10), the Navarro criteria (11), and the University of California San Francisco (UCSF) criteria (12). The Milan criteria and UCSF criteria are the criteria that are most widely used internationally. Chinese patients diagnosed with HCC often do not meet the Milan criteria due to the high incidence of HBV, and these guidelines are too strict for them, so many patients with HCC who might benefit from the procedure are excluded. Therefore, Chinese experts put forward criteria for choosing Chinese patients. The following is a summary of those criteria.

3.1. Chengdu (West China) criteria

Patients who meet the Milan criteria can also undergo liver resection in China, with the same prognosis as LT. Due to high costs and long waiting times, LT was only seen as an adjunct to liver resection for a period (13). Yan *et al.* (13) reported in 2005 that LT can provide a satisfactory prognosis for patients with large HCC outside the Milan criteria. Thus, they defined LT indications as follows: 1) Small liver cancer and resectable liver cancer with severe liver cirrhosis or hepatic insufficiency, 2) Unresectable large liver cancer without main portal vein tumor thrombus (PVTT) or distant metastasis, and 3) Main PVTT should be regarded as a contraindication. Yan *et al.* studied 112 patients from February 1999 to February 2005 and found that those with unresectable large liver cancer can still have a good survival rate after LT, with the exception of those with main PVTT. If a single tumor was larger than 10 cm or numerous cancers were still limited to the hemi-liver, the 3-year survival rate was as high as 77%. Patients with a tumor that has progressed to the entire liver without extrahepatic metastasis had a 2-year survival rate of 73.8%. Patients with main PVTT, in contrast, had a 1-year survival rate of only 20%. The

Chengdu criteria provide a new treatment option for unresectable liver cancer, but they do not specify the size and number of the tumors. The Chengdu criteria were preliminary criteria, and they are rarely mentioned in subsequent studies.

3.2. Shanghai Fudan criteria

In 2006, Fan *et al.* put forward new criteria for China based on the UCSF criteria (14). The Shanghai Fudan criteria are as follows: 1) The tumor has not invaded the blood vessels or lymph nodes, 2) The tumor size for patients with a single tumor must not surpass 9 cm in diameter, and 3) The number of tumors in a patient with numerous tumors should not exceed 3. Each one must be no larger than 5 cm in diameter. The tumor's overall diameter must not surpass 9 cm. Compared to patients who failed to meet the criteria, those who met the criteria had an advantage in terms of their overall survival rate (OS) and tumor-free survival rate (TFSR) (OS&TFSR: Log rank $p < 0.001$). There was no discernible difference between patients who met the Milan criteria and those who met the Shanghai Fudan criteria but exceeded the Milan criteria (OS: $p = 0.429$; TFSR: $p = 0.952$). Thus, the Shanghai Fudan criteria have further expanded the indications for LT without diminishing prognosis.

3.3. Hangzhou criteria and new techniques

In 2008, Zheng *et al.* proposed new criteria for LT, the Hangzhou criteria (15). The Hangzhou criteria are as follows: 1) The tumor has not invaded the blood vessels or lymph nodes and 2) The total diameter of the tumor cannot exceed 8 cm or more than 8 cm, AFP is less than 400 ng/mL, and the cancer is well- or moderately differentiated. Further research indicated that AFP ≤ 100 ng/mL and a tumor burden ≤ 8 cm were two independent prognostic factors, so the Hangzhou criteria were stratified into two types (16) (Table 1). Type A confers a better prognosis than type B and suggests that a patient may be an optimal candidate for LT while type B can be regarded as a relative contraindication due to the shortage of liver donors. The Hangzhou criteria included AFP and pathology as evaluation for the first time, leading to a new model for LT recipient selection. Later, in 2018, Fan *et al.* and Mazzaferro *et al.* established a competing risk model for analysis using the aforementioned factors such as AFP and tumor size and number (17). Nowadays, as an alternative to doctors' experience, artificial intelligence has been used to guide the selection of patients with HCC. When the patient's clinical test data and imaging data are entered into the gradient boosting decision tree (GBDT) algorithm, the system will output a series of results including diagnosis, treatment recommendations, and survival and relapse data. The system has been verified,

Table 1. Subgroups according to the Hangzhou criteria

Item	Type A		Type B
Tumor size (cm)	≤ 8	> 8	> 8
>AFP (ng/mL)	N.A.	≤ 100	100 ~ 400

indicating that recipient selection for LT will be fairer, more accurate, and more efficient in the future.

4. Living donor LT (LDLT)

From the early years to present, HCC remains the main indication for LT in China. The success of LT depends on whether there are sufficient donors, which is the most important issue in organ donation worldwide, and the same holds true in China. Back in 2004, professors cited LDLT as a critical way to deal with the donor shortage in China (18). In mainland China, LT gradually emerged in the 1990s and West China Hospital successfully performed the first adult-to-adult LDLT in mainland China only in 2002 (5). Deputy Minister of Health Huang Jiefu said, "Following the first LDLT at West China Hospital, Tianjin, Beijing, Shanghai, and many other places have also performed LDLT, and China's LT entered a period of rapid development especially after 2006".

Ensuring the donor's safety and postoperative quality of life is the doctor's first priority. As early as 2013, donor hepatectomy in China has been validated as low-risk and highly efficient, and even the abandonment of the procedure did not diminish the donor's prognosis (6). However, there are several issues to be mindful of. The biggest problem is the accuracy of preoperative liver quality assessment. As previously mentioned, donation was abandoned in 5 candidates of 290 donors; 2 were attributed to worsening liver condition (massive cirrhotic nodule and severe steatosis, respectively) and 1 was due to small residual liver volume (6). After the first 35 cases, Chinese experts replaced the risk of hemorrhage due to biopsy with a comprehensive evaluation of 3 aspects: body mass index (BMI), hepatitis virus infection, and a related history of drinking or smoking. How can serious steatosis be predicted without a biopsy? A simple formula containing the BMI and computed tomography (CT) data appears to solve the problem [$HMS = 47.7 + 1.48BMI - 1.14CT$] (19). A point worth noting is that the model appears to be unable to reliably predict hepatic macrovesicular steatosis $< 5\%$ in a candidate. When calculating the residual liver volume, Chinese experts referred to both CT data and the Chengdu formula [$SLV(mL) = 11.5 \times BW(kg) + 334$ (SLV: standard liver volume; BW: body weight)]. The Chengdu formula has proven to be reliable in LDLT (20). In 2015, a preoperative non-invasive model for evaluation of liver fibrosis in donor livers was proposed (21). The current manner of assessing remnant liver

volume is based on graft size, while the quality of the liver is another factor that affects 'functional size'. Both approaches were used in a candidate for whom donation was abandoned due to insufficient postoperative liver volume, but the 'margin of error' resulted in an eventual miscalculation. As the experts say: 'This is unpredictable and unexpected but it infrequently occurs in LDLT'.

Graft size is a crucial factor in ensuring the success of LDLT, but the importance of good venous drainage of the anterior sector of the right hemiliver has been recognized. If middle hepatic vein (MHV) tributaries from these segments are ligated and the MHV is not included in the liver graft, venous congestion of Couinaud's segments V and VIII of the right hemiliver graft is common (22). After portal vein reperfusion, the effects of a compromised venous outflow may be evident in some circumstances. Segments V and VIII can become swollen and turgid and have a dusky discoloration. Although a graft without the MHV is prone to a disorder in hepatic segment V & VIII blood return, extended donor hepatectomy potentially increases the risk for donors, and especially for those with hepatic steatosis, hepatitis, or of advanced age (23). Because hepatitis and cirrhosis are so common in China, 'borderline donors' who are positive for the hepatitis B core antibody (HBcAb) but negative for hepatitis B surface antigen (HBsAg) must be used (6). Back in 2005, Yan *et al.* reported the first 13 cases of LDLT without the MHV in grafts in mainland China (24). A 3D technique was used to preoperatively reconstruct the structure of the hepatic vein and to assess the remnant liver volume, and the branches of the right inferior hepatic vein and MHV > 5 mm are preserved. In the aforementioned study, the inferior right hepatic vein (IRHV) was reconstructed in 5 patients, and 1 or 2 thick branches of the MHV were reconstructed *via* an autologous saphenous vein bypass in 5 patients, ensuring that hepatic venous drainage was sufficient after reperfusion and ensuring the transplanted liver's survival and function. Moreover, Yan *et al.* enhanced the procedure in two ways. After excising the right hepatic vein (RHV) stump and expanding the right hepatic vein opening downward to the recipient's inferior vena cava (IVC), they directly anastomosed the RHV of the graft with the opening of the RHV of the recipient's IVC, without retaining the RHV remnant, preventing the compression and distortion caused by the existence of the remnant blood vessel between the right liver and the IVC and effectively ensuring RHV return. In the second enhancement, when the MHV branch is bypassed, the autologous saphenous vein is anastomosed with the branch opening of the MHV in the preservation container to reduce the anastomosis time on the operating table. Utilizing these surgical improvements, the same research group reported on 160 cases of consecutive living donor right hepatectomy between 2002 to 2008 (25). They used the Clavien grading system to define and grade the severity of donor complications; all donated livers were

right lobe grafts without the MHV and all IRHVs > 5 mm in diameter were preserved for subsequent anastomosis to the recipient IVC. The occurrence of complications was as follows: A Grade 1 complication involving any deviation from the normal postoperative course without the requirement for medication and intervention (whether local therapy or surgery) was noted in 18.1% (29/160). A Grade 2 or 3 complication requiring medication or intervention was noted in 14.4% (23/160). No life-threatening complications or deaths occurred, validating the ability of the Chinese surgical approach to ensure donor safety.

Small-for-size syndrome (SFSS) is another problem with LDLT due to insufficient donor liver volume. Thus, right-lobe hepatectomy is often required to obtain a graft with adequate liver volume. How is surgery performed when the only available donor has an insufficient right lobe? In 2006, a Chinese group successfully implemented an adult-to-adult (A-A) LDLT combined with a cadaveric split left lateral segment (26). The patient received a right lobe without the MHV from a living donor and a left lateral segment from a cadaveric donor. The right lobe with the MHV from the cadaveric donor was transplanted into another patient. The advantage of this approach is that it maximizes the use of a cadaveric donor and it reduces the requirement for the graft size harvested from a donor, therefore protecting the donor's safety. Moreover, this approach theoretically results in a satisfactory prognosis since the right lobe and the left lateral segment can be implanted orthotopically in their original position. However, experts have suggested that this technique should not be considered as a standard treatment and that it should only be performed in unusual circumstances. If a patient has SFSS, selective transplenic artery embolization may be a solution (27). A case report indicated that after receiving a small-for-size right lobe from a living donor, a liver graft recipient showed clinical signs of protracted cholestasis and intractable ascites. A computed tomography scan revealed congestion in liver segments V and VIII, and both Doppler ultrasonography and vena cava angiography revealed a lack of patency of the anastomosis between V5/V8 and the internal vena cava, indicating blocked outflow of the segment V and VIII anastomosis. The Chinese approach can rapidly reduce the portal venous flow rate, thereby decreasing serum total bilirubin and eliminating ascites. Accordingly, selective splenic artery embolization is a technically simple procedure for the treatment of portal overperfusion injury in SFSS.

5. Laparoscopic donor hepatectomy

LDLT, a procedure without any health benefits but a risk of death for living donors, poses potential ethical dilemmas. The close relationship between a donor and recipient motivates the donor to save the recipient's life regardless of the cost. The most serious concern

with LDLT is donor safety. A point worth noting is that donor complications can still occur (28) and even result in death (29). Even without serious complications, the large permanent abdominal scar following standard open surgery results in emotional and physical stress for some living donors, and particularly young women, possibly leading to hesitancy in undergoing donor hepatectomy. A recent meta-analysis reported that laparoscopic surgery was associated with a shorter duration of hospitalization, less blood loss, fewer postoperative complications, and a longer operating time than open surgery (30). Minimally invasive donor hepatectomy (MIDH) including laparoscopy-assisted hepatectomy, total laparoscopy hepatectomy, and indocyanine green fluorescence (ICG) image-guided total laparoscopic hepatectomy are becoming the main approaches of the future. A study reported that MIDH was superior to open donor hepatectomy (ODH) in terms of blood loss, the duration of hospitalization, and overall complications without compromising liver function (31). However, the study in question did not perform a subgroup analysis based on the type of MIDH (laparoscopy-assisted or total laparoscopy). A larger graft is known to be riskier for living donors than a smaller one. According to an analysis of donor hepatectomy in Japan, the morbidity risk generally increased as the hepatectomy mass increased from left lateral section donation (8.2%) to left lobe donation (12.0%) and then to right lobe donation (19.0%). Right lobe donors suffered a significantly higher rate of complications than lateral segment and left lobe donors. ($p < 0.0001$, and $p < 0.0001$, respectively) (32) In 2002, the world's first left hepatic lobectomy (resection of segments II and III) was performed laparoscopically to save a child 1 year of age who had biliary atresia (33). Studies in greater numbers of patients in several experienced hospitals have validated laparoscopic left lateral sectionectomy (L-LLS), which is now regarded as the standard treatment for adult-to-pediatric donation (33-35). However, there is no consensus on left lobe or right graft procurement in adult-to-adult LDLT (36). Laparoscopy-assisted donor hepatectomy (LADH) requires more from the surgical team, which must be familiar with both living donor hepatectomy and laparoscopic liver surgery. Surgeons were concerned that LADH would have to be converted to an open approach. A study of a large series of 66 cases reported that 2 eventually had to be converted to open donation in the interest of donor safety (37). Owing to these technical difficulties, LADH in China was initially performed as right lobe MIDH, in which the hands were introduced in the abdomen while still maintaining the pneumoperitoneum. A meta-analysis indicated that LADH is associated with less intraoperative blood loss, less analgesic use, and fewer postoperative complications but a similar duration of hospitalization and increased operating time (38). In 2016, the first purely laparoscopic right hemihepatectomy in a living donor was performed

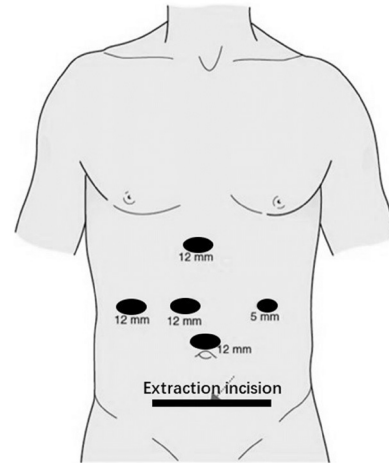


Figure 1. Trocar placement for total laparoscopic right hemihepatectomy in a living donor.

domestically, further reducing the length of the incision (39) (Figure 1).

5.1. L-LLS

Interestingly, a left lateral graft was the first living donor liver graft to be harvested conventionally (40) and laparoscopically (33). The left lateral section accounts for 15-30% of total liver volume, so postoperative liver failure is unlikely to occur. Hence, laparoscopic procedures for donor hepatectomy involving a left lateral section donation are the least contentious (41). At present, a consensus has been reached on the feasibility and safety of pure laparoscopic sectionectomy (42). A liver incision on the left side of the falciform ligament, which is a well-defined surface landmark where the vertical section of the left portal vein is located, is the standardized laparoscopic procedure. The arterial inflow, biliary drainage, and portal venous branches of each segment and subsegment of the left lateral section converge intra-parenchymally within the Glissonian sheath on the left side of the falciform ligament, so all pedicles to segments 2 and 3 will be divided by transecting along the left side of the falciform ligament (43). In 2020, Chinese surgeons reported the first case of single-port L-LLS, and they achieved satisfactory cosmetic results (44) (Figure 2). The bifurcation and dividing point of the bile duct were determined using intraoperative ICG fluorescence cholangiography. However, the feasibility of advanced manipulation is based on the simple anatomy in the patient. Thus, an experienced surgical team should carefully identify donors and recipients.

5.2. Laparoscopic right hepatectomy (LRH)

Right liver grafts have the ability to meet the metabolic demands of a larger recipient, so right lobe hepatectomy

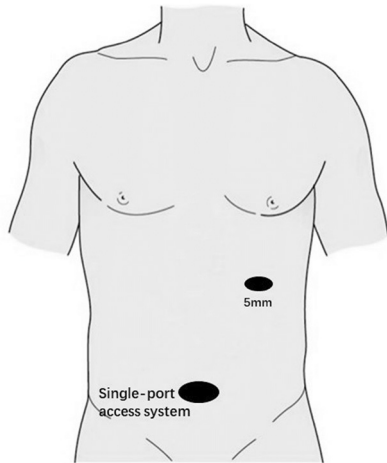


Figure 2. Trocar placement for single-port laparoscopic left lateral sectionectomy in a living donor.

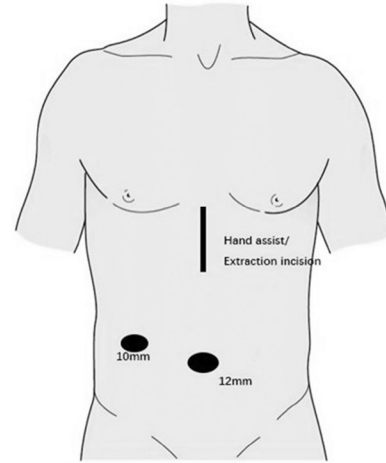


Figure 3. Trocar placement for hand-assisted laparoscopic right hemihepatectomy in a living donor.

is more common (45). Due to technical difficulties, LRH was initially performed as laparoscopy-assisted right hepatectomy (LARH) in which hands were introduced into the abdomen through an upper midline incision (Figure 3). The hilar dissection and parenchymal transection were done openly, while only the right lobe mobilization was done with hand-assisted laparoscopy. In 2014, a prospective study indicated that LARH was successfully performed in 25 Chinese patients; none had to be converted to conventional open surgery (7). Based on experience performing LARH on patients with a benign tumor, the amount of fat tissue in the abdomen rendered laparoscopic mobilization of the right liver lobe technically problematic in some overweight individuals due to an inadequate surgical field. Under such circumstances, a 5-cm midline epigastric extraction incision, a 12-mm umbilical port, and a 10-mm right lateral subcostal port appear to be insufficient to complete the procedure. Thus, several technical modifications were made. First, for some overweight donors ($BMI > 25 \text{ kg/m}^2$), the surgeon should install a laparoscopic retractor to clear the surgical field by adding an additional 12-mm right lateral subcostal port in the right midaxillary line. Second, if access to the retrohepatic IVC after dissection of the right hepatic ligaments is problematic, the remaining laparoscopic surgery, which includes dissection of the short hepatic veins and posterior vena cava ligament, is performed under direct view through the upper middle incision.

A preliminary comparative study in China reported that purely laparoscopic right hepatectomy (PLRH) was associated with less blood loss, fewer postoperative complications, and a shorter duration of postoperative hospitalization but also higher postoperative ALT and AST compared to LARH and open right hepatectomy (ORH) (46). That study confirmed the feasibility and safety of PLRH, but it also indicated that PLRH

must be performed in highly specialized centers with adequate postoperative monitoring and support. A point worth noting is that LRH results in a larger liver graft with multiple bile duct openings. This makes recipient intracorporeal suturing more challenging and results in more bile leakage. Despite quality preoperative magnetic resonance cholangiopancreatography (MRCP) and real-time ICG fluorescence cholangiography, surgeons may still be hesitant to determine the accurate bile duct dividing point and they may prefer to shift to the right side. When dividing the bile duct, experts replace the intracorporeal suturing with two clips at the remnant side. Two clips occupy space, so the dividing point of the bile duct may have been shifted more to the right than intended (47). To compensate for the constraints caused by the significantly shorter bile duct and portal vein resulting from the use of twin clips and a stapler, highly experienced and talented surgeons are required. In conclusion more time is needed to transition from a hybrid to a purely laparoscopic approach.

5.3. Laparoscopic left hepatectomy (LLH)

The harvesting of a left lobe graft is restricted due to its relatively small volume compared to the right lobe. In 2021, a study reported on 285 patients in a Shanghai cohort who underwent left lobe LDLT (48). Results confirmed that LLH could be performed as safely as open surgery. In an innovative approach, the surgical team combined ICG fluorescence imaging with laparoscopic donor liver harvesting because of the unique staining features of ICG. Laparoscopy with ICG fluorescence can theoretically reduce intraoperative blood loss and reduce the likelihood of post-operative biliary complications, as indicated by the aforementioned study. Hence, LLH with or without ICG should be considered as a valuable adjunct when

unsatisfactory donor conditions are encountered.

6. Prospects for the future

LT requires multidisciplinary cooperation, so the development of LT is a sign of the development of comprehensive medical prowess. Deceased donors account for a substantial portion of organ donations, but brain death was not been adopted as a standard until now. The Chinese Ministry of Health published criteria and operational requirements for brain death in 2003 (49,50), but they have not been promoted in a long time. There seems to be no end to the debate on ethical issues in this area. A point that should be stressed is that many countries have established a complete legal framework for brain death, so China should promptly catch up with the rest of the world. Donation after brain death (DBD) has irreplaceable advantages since DBD can maintain blood flow even after "death", thereby resulting in better liver function. In addition, the liver comes from a deceased donor and can be split in situ, which can reduce cold ischemia time compared to in vitro splitting. Hence, DBD should be legalized and implemented as soon as possible.

For numerous reasons, LDLT is being investigated as a possible replacement to DDLT. First, living donors represent a flexible source of donors and thereby minimize waiting time, the high rate of dropouts, and deaths during the waiting period. Second, better graft function will be achieved as a result of an optimized preoperative plan and shorter warm and cold ischemia times. Third, LDLT involving relatives results in immunological benefits and therefore reduces incidents of rejection because of the genetic compatibility between the donor and the recipient. LDLT is known to have a comparable survival rate to DDLT. However, the rate of recurrence for the two treatment modalities remains a subject of controversy. A study in Canada indicated that LDLT had a worse DFS according to a quantitative analysis of non-randomized studies (51). Several other studies have yielded similar results (52,53). This phenomenon was thought to be due to the transplantation of more advanced HCC or "fast-tracking" to transplant. Patients undergoing LDLT consistently tended to fall outside the Milan criteria. A study in Guangzhou indicated that LDLT does not compromise patient survival or promote the recurrence of HCC in comparison to DDLT, and especially for patients meeting Milan criteria (54). Intent-to-treat (ITT)-OS was measured from the time of registry for transplantation. According to one study, LDLT was linked to a superior 5-year ITT-OS (55). Notably, LDLT is sometimes utilized as a salvage procedure in individuals in whom all other treatments have failed. The aforementioned study was based on ITT principle to avoid this selection bias. Hence, LDLT should receive more emphasis and receive the same attention as DDLT.

Today, surgeons in China are capable of performing every type of LDLT and laparoscopic donor hepatectomy. Chinese doctors have improved the techniques to suit Chinese patients. Owing to the current donor shortage, LDLT should be actively promoted.

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