

Surgical issues in retrieval and implantation

ABSTRACT

With increasing demand for organ transplantation and patients deteriorating or dying on the waiting list, organs are now being increasingly used from donors previously considered too marginal. This requires improvements to donor management during the retrieval process, and of the organ during transport and subsequent implantation, in order to maintain outcomes.

Surgical practices for the retrieval, preservation and implantation of donor livers remain unstandardized with different centres and surgeons using a variety of techniques. However, with increasing demand for transplantation, organs are now being increasingly used from donors previously considered unsuitable (or marginal), reinforcing the concept of optimal donor management during the retrieval, transfer and implantation processes.

This article reviews surgical considerations regarding the optimal retrieval, preservation and subsequent implantation of donated livers.

UK organ donation

The Human Tissue Act 2004 allows the cadaveric donation of organs in England, Wales and Northern Ireland with donations most commonly occurring after brainstem death, a diagnosis of which can only be reached once a number of preset criteria are excluded (*Table 1*). Brainstem death can be defined as the irreversible loss of the capacity for consciousness combined with the irreversible loss of the capacity to breathe and is defined by the absence of reflexes with pathways through the brainstem. Such findings in a comatose and ventilator-dependant patient

(with a known aetiology) are sufficient for the diagnosis of death within the UK (in the USA and elsewhere, whole brain death is required before donation and requires an alternate set of clinical criteria to be met). Following the diagnosis of brainstem death, management aims change from preservation of cerebral function to optimization of organ function for transplantation (*Table 2*) and the management of the plethora of complications that occur in the brainstem dead (including hypotension (80%), diabetes insipidus (65%), disseminated intravascular coagulation (30%), arrhythmias (30%), pulmonary oedema (20%), metabolic acidosis (10%), hypothermia and seizures).

A lesser number of organs is retrieved after cardiac death (donation after cardiac death), which can be diagnosed in the absence of circulation combined with the presence of simultaneous and irreversible apnoea and unconsciousness. A third group comprise live donors of part of the liver, which represent a small minority of donated organs within the UK.

In 2015–16 1047 livers were donated for transplant in the UK (715 after brain death, 296 after circulatory death and 36 living lobe donors; www.odt.nhs.uk/pdf/activity-report/liver_activity.pdf). This donation occurs under the auspices of the National Organ Retrieval Service, which was established by NHS Blood and Transplant in 2010 and is a crucial component of the transplantation pathway, coordinating a continuous and ongoing nationwide service for organ retrieval in the UK. There are currently eight teams regularly retrieving intra-abdominal organs within the UK (based in Birmingham, Cambridge, Cardiff, Kings College Hospital, Leeds Manchester, Newcastle, Oxford and Royal Free Hospital).

Liver retrieval operation

The logistics of the liver retrieval procedure vary depending upon donor type (usually cadaveric donation after brainstem death or donation after cardiac death) and the necessity for retrieval of other abdominal or thoracic organs. Thus, careful preoperative planning and communication must take place between anaesthetic, theatre, coordinating, abdominal surgery and thoracic surgery teams. The anaesthetic and intensive care teams are crucial in the maintenance of haemodynamic parameters – the presence of hypotension in particular is a significant factor affecting future organ quality and in patients donating after brainstem death organ function should be supplemented with fluids and inotropes as necessary to maintain a systolic blood pressure >50 mmHg and oxygen saturations >70%; in patients donating after cardiac death, where such systemic support has (by definition) been

Mr James RA Skipworth*, Specialist Registrar, Hepatopancreaticobiliary and Liver Transplant Surgery, Department of Hepatopancreaticobiliary and Liver Transplant Surgery, Royal Free Hospital NHS Trust, London

Mr Gabriele Spoletini*, Senior Clinical Fellow, Hepatopancreaticobiliary and Liver Transplant Surgery, Department of Hepatopancreaticobiliary and Liver Transplant Surgery, Royal Free Hospital NHS Trust, London

Mr Charles Imber, Consultant Hepatopancreaticobiliary and Liver Transplant Surgeon, Lead for Liver Transplant/ National Organ Retrieval Service, Department of Hepatopancreaticobiliary and Liver Transplant Surgery, Royal Free Hospital NHS Trust, London NW3 2QG

Correspondence to: Mr C Imber (charles.imber@nhs.net)

* These authors contributed equally to the manuscript

withdrawn, the organ may be declined (for prolonged functional warm ischaemia) if such parameters persist for longer than 30 minutes.

In patients donating after brainstem death dissection can be performed before (warm phase) or after (cold phase) perfusion of the organ with preservation solution, whereas in patients donating after cardiac death the goal should be to begin organ perfusion as soon as possible, with virtually all dissection taking place in the cold phase.

Identification of anatomical structures is often technically easier before perfusion, allowing more limited dissection in the cold phase and thus rapid organ extraction. However, injuries during warm phase dissection carry a more significant risk of organ loss and a balance must therefore be achieved between dissection in the two phases, guided by the stability of the patient and the retrieving surgeon's experience.

The retrieval procedure itself is started by performing a full laparotomy from xiphisternum to suprapubic and a careful inspection of all four quadrants to assess for pathology that may contraindicate proceeding with donation. The distal infrarenal aorta is then isolated (taking care to preserve aberrant renal vessels if renal retrieval is also to take place) and a perfusion catheter inserted and secured (in patients donating after cardiac death, perfusion would now be commenced). A Cattell–Braasch manoeuvre subsequently medializes the right colon, duodenum and small bowel to expose the inferior vena cava, left renal vein, aorta and right perinephric fat via division of the white line of Toldt. A median sternotomy (taking care to protect the liver with large packs), performed with the use of a Gigli saw, then allows entry into the anterior mediastinum and the pericardium is opened longitudinally (this manoeuvre should be coordinated with the thoracic team if present).

The liver can subsequently be mobilized by careful division of the right and left triangular ligaments and inferior peritoneal attachments, taking care to avoid traction injuries to the liver, and the lesser omentum examined for the presence of an aberrant left hepatic artery. It is also critical to palpate posterolaterally to the common bile duct for an aberrant right hepatic artery arising from the superior mesenteric artery – if identified its relationship to the head of pancreas needs to be assessed and carefully dissected. The gallbladder is subsequently opened and washed out with normal saline, and the gastroduodenal, splenic and hepatic arteries exposed and assessed for the presence of aberrant courses or branches.

In donation after brainstem death patients, perfusion can now be performed (with University of Wisconsin solution), either via an aortic catheter alone or with dual portal venous perfusion (particularly if the liver graft is marginal or to be split, or pancreatic retrieval is to take place) via cannulation of the portal vein, following delivery of 20 000 U heparin. Aortic cross clamp subsequently takes place (following discussion with cardiac and anaesthetic teams) and the suprahepatic inferior vena cava divided in the chest to allow venting of the circulating volume.

The cold phase then commences via dissection of the porta hepatis along the superior border of the pancreas and duodenum, and the common bile duct, common hepatic artery and portal vein divided proximally leaving

Table 1. Exclusion criteria for the diagnosis of brainstem death

Exclude potentially reversible circulatory, metabolic and endocrine disturbances	Normothermia	Temperature >34°C
	Normal cardiovascular system, respiratory and blood gases	Mean arterial pressure >60 mmHg
		Partial pressure of oxygen >10 kPa and partial pressure of carbon dioxide <6.0 kPa
		Absence of acidaemia or alkalaemia (pH 7.35–7.45)
Normal electrolytes	K ⁺ >2 mmol/litre	
	Na ⁺ 115–160 mmol/litre	
	Mg ²⁺ or phosphate 0.5–3.0 mmol/litre	
	Glucose >3.0 mmol/litre	
Exclude potentially reversible causes of apnoea	Drugs	Muscle relaxant
		Neuromuscular
		Depressants
	Cervical cord injury	
If doubt or inability to complete tests	Imaging	Direct, computed tomography or magnetic resonance angiography
		Positron emission tomography
	Neurophysiology	Brainstem evoked potentials
		Electroencephalogram
		Specialist input

Table 2. Criteria for organ preservation following diagnosis of brainstem death and during multi-organ retrieval

Parameter	Criteria
Cardiovascular system	Mean arterial pressure >60–70 mmHg
	Central venous pressure 8–10 mmHg
	Inotrope dose <10 µg/kg/min Dobutamine or dopamine Avoid noradrenaline
Respiratory system	Oxygen saturations >95%
	Partial pressure of oxygen >10.5 kPa
	Inspired oxygen content <40%
Other parameters	pH 7.35–7.45
	Temp 35–37°C
	Urine output >1 ml/kg/hr
	Na ⁺ <155 mEq/dl
	Haemoglobin >10 g/dl and haematocrit >0.3

long lengths of each structure to facilitate subsequent implantation (taking care if the pancreas is also to be

retrieved; if not, the neck of the pancreas can be transected to expose the confluence of portal vein, superior mesenteric vein and splenic vein).

The inferior vena cava is transected above the renal veins and the aorta divided below the level of the coeliac axis and all crural and connective tissue divided to free the liver. The diaphragmatic domes are split to facilitate extraction and the liver carefully lifted out and into a bucket of slushed ice. The liver is subsequently vacuum-packed on ice using a triple steri-bag technique, after being completely immersed in University of Wisconsin solution, before urgent courier to the implanting centre. Iliac arteries and veins are also retrieved to facilitate vascular reconstruction as necessary, and skin closure performed with a whip-stitch.

Table 3. Contraindications to organ donation to be reviewed on an individual, case by case basis

Absolute contraindications to organ donation	85 years or above
	Primary intracerebral lymphoma
	Metastatic intracerebral tumours
	Any active malignancy with evidence of metastases (including lymph nodes) within 3 years of donation
	Active invasive cancer in last 3 years excluding non-melanoma skin cancer and primary brain tumour
	Melanoma (except completely excised stage 1 cancers)
	Active haematological malignancy
	Definite, probable or possible human transmissible spongiform encephalopathy (e.g. Creutzfeldt–Jakob disease and variant Creutzfeldt–Jakob disease)
	Active or untreated tuberculosis
	West Nile virus infection
	Human immunodeficiency virus (HIV) disease (but not infection)
	Long warm ischaemic time
	Combination of age and multiple comorbidities
	Liver-specific contraindications to organ donation
Cirrhosis	
Portal vein thrombosis	
Severe hepatic steatosis (visual inspection at retrieval)	

Table 4. Parameters comprising the donor risk index

Parameter	Relative risk
Age <40 years	1.00
40–49 years	1.17
50–59 years	1.32
60–69 years	1.53
>70 years	1.65
Donor height (per 10 cm decrease)	1.07
Cause of death cerebrovascular accident	1.16
Cause of death other	1.20
Race (African American vs Caucasian)	1.19
Donation after cardiac death (vs donation after brainstem death)	1.51
Partial/split (vs whole) liver	1.52

From Feng et al (2006)

Donor factors crucial to outcome

Certain absolute contraindications to organ donation exist (Table 3); however, if these are not met, objective assessment of individual retrieved organs remains problematic. Certain donor- or graft-related factors have been associated with poor outcome (e.g. prolonged hypotensive episodes, donor age >55 years, high inotrope requirement, hypernatraemia, cold ischaemia >12 hours, warm ischaemia time >40 minutes and moderate–severe macrosteatosis >30%) and the presence of these characteristics has led such liver grafts to be termed marginal. The effects of such risk factors are exacerbated in organs donated after cardiac death, and careful consideration needs to be given to the use of marginal livers in this sub-group.

A donor risk index using a combination of donor factors predicts liver graft failure and can provide an individualized and integrated risk estimate for an individual organ (Feng et al, 2006) (Table 4). As the donor risk index increases, the survival benefit of liver transplantation at any given MELD (model for end stage liver disease) score decreases. The mean donor risk index in Europe is 1.71 (573 patients with 2.5 years follow-up), whereas the donor risk index in the USA is 1.41 (Ozhathil et al, 2011).

There is no evidence that performing multi-organ retrieval (as opposed to single organ) compromises individual graft function (there is some evidence that the opposite is true) although most studies to this effect have assessed renal rather than hepatic function. However, organ damage at multi-organ retrieval is probably under-reported and is minimized in those teams retrieving over 50 organs per year (Wigmore et al, 1999). Similarly, performing concurrent liver and pancreas retrieval has no deleterious effect upon the function of either organ (Sterioff et al, 1989; Schlumpf et al, 1990; Dunn et al, 1991) and en bloc resection of the liver and pancreas with subsequent separation on the back-table has been associated with functional improvements in both liver and pancreas in some studies (improved early liver function, reduced mean dissection time, reduced primary non-function and reduced in-hospital length of stay; Imagawa et al, 1996).

Certain studies have reported that warm dissection compromises liver condition (Klar et al, 1995), probably

via activation of Kupffer cells leading to increased oxygen consumption (Schemmer et al, 1998, 2001), suggesting that it would be preferable to perform more cold phase dissection where possible. However, cold perfusion is a non-physiological process and it remains unclear how the perfusate should be administered. Evidence remains conflicting, but most studies suggest that high-pressure aortic perfusion is associated with improved liver graft function and survival (Iaria et al, 2001) (potentially via a reduction in the incidence of biliary tract ischaemia during perfusion; Moench et al, 2003), whereas high pressure portal perfusion is deleterious and should therefore be avoided (Tokunaga et al, 1988). Despite its widespread use, there is limited or no evidence that dual perfusion improves liver graft function.

Methods of organ preservation

Preservation is aimed at maintaining organ viability during transport from the donor hospital to the transplant centre and during organ preparation on the back-table. The main strategy for preservation is cold storage, which is based upon the principle of minimizing metabolic cellular activity during a period of deprivation of blood flow and, consequently, of oxygen and nutrients (Clavien et al, 1992). Several new technologies are currently in development and appraisal, which include normothermic or hypothermic machine perfusion (Figure 1), and normothermic regional perfusion, which essentially converts a donation after cardiac death into a donation after brainstem death, thus improving the quality of organ retrieved. Phase I studies have proven the feasibility and safety of such hypothermic (Guarrera et al, 2010) and normothermic (Ravikumar et al, 2016) (Figure 1) perfusion, while randomized studies are still in progress.

Refinement of preservation solutions has allowed increases in the amount of cold-storage time that livers can withstand. The most commonly used preservation solutions are University of Wisconsin, histidine-tryptophan-ketoglutarate and Celsior, which vary in the composition of electrolytes, impermeants, buffers, antioxidants and energy precursors they contain, but share similar goals of reducing graft oedema, intracellular acidosis and production of reactive oxygen species, and providing energy substrates for metabolism (Adam et al, 2015; Latchana et al, 2015).

The avoidance of hepatic ischaemia via the provision of oxygen and metabolic substrates remains the rationale behind the development of machine perfusion, which, because of the need to expand the donor pool via the use of marginal quality organs, has gained popularity over the last decade (Ravikumar et al, 2015). Marginal livers (e.g. steatotic, old, donation after cardiac death) are more susceptible to the detrimental effects of ischaemia (Seehofer et al, 2013) but promising results from initial human machine-perfusion studies have led to wider utilization of such organs which might otherwise be declined by those using conventional cold storage preservation.

Back-table surgery

Back-table surgery is usually performed at the recipient hospital during, or just before, laparotomy and hepatectomy in the recipient. The main steps include:

1. Assessment of the integrity of the organ, the presence of aberrant vascular anatomy and potential injuries
2. The removal of tissue attachments such as diaphragm, right adrenal gland and peri-adventitial connective and ganglionic tissue
3. Preparation of cuffs of the suprahepatic and infrahepatic vena cava, cleaning of the portal vein and hepatic artery, and inspection of the bile duct
4. Repair, as necessary, of damaged vascular structures or reconstruction of aberrant vessels to minimize the number of anastomoses to be performed.

A right replaced hepatic artery arising from the superior mesenteric artery is often of large calibre and is the most common aberrant vessel requiring reconstruction, whereas small accessory arteries may be sacrificed as reconstruction often only adds procedure complexity, prolongs cold ischaemic time and increases the risk of postoperative thrombosis. The graft may be flushed at the end of this phase or just before revascularization during implantation, using Ringer's or albumin solutions to wash out potassium-rich preservation solutions and prevent potential post-reperfusion cardiac arrhythmias or arrest.

Liver implantation procedure

The recipient operation is performed through an upper midline laparotomy extended to the right flank, with or without a left-sided extension. The classic hepatectomy procedure involves excising the recipient inferior vena cava en bloc with the liver and directly replacing it with the donor's graft and inferior vena cava, thus necessitating two end-to-end anastomoses at the supra- and infra-hepatic inferior vena cava and requiring complete portal and vena caval clamping for a variable time from completion of

Figure 1. Example of machine preservation circuit. From Ravikumar et al (2016).

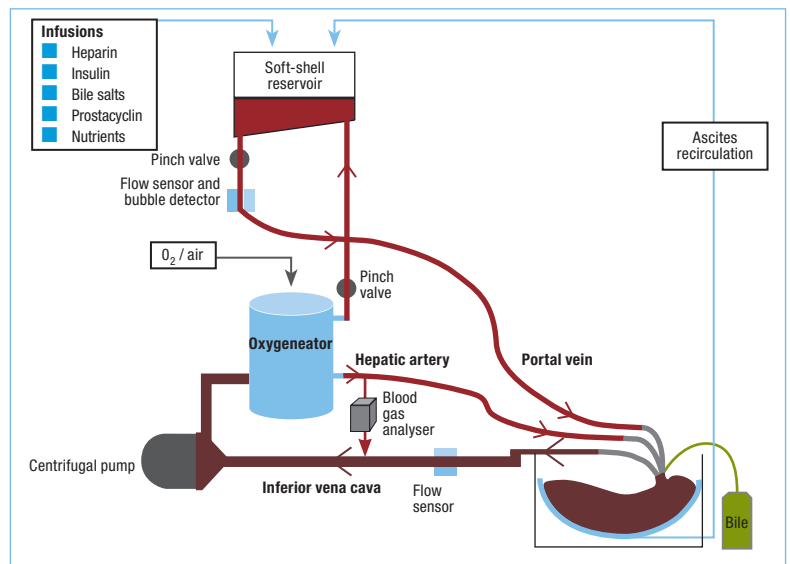
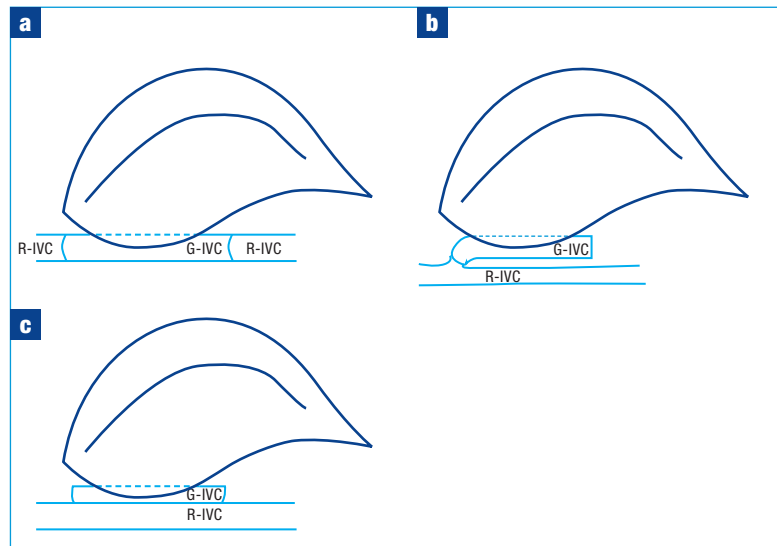


Figure 2. Techniques of caval anastomosis. a. Hepatectomy with inferior vena cava replacement. b. Classic piggy-back. c. Side-to-side piggy-back. G-IVC = graft inferior vena cava, R-inferior vena cava = recipient's inferior vena cava.



the hepatectomy to revascularization of the new organ (originally performed with the aid of veno-venous bypass to avoid venous congestion (Starzl et al, 1963) (*Figure 2a*)).

However, in 1989, Tzakis et al described the 'piggy-back' technique, which preserves the recipient inferior vena cava and involves anastomosis of the supra-hepatic donor inferior vena cava to the anterior inferior vena cava of the recipient in an end-to-side fashion (Tzakis et al, 1989) (*Figure 2b*). This allows a shorter anhepatic phase, lower blood losses and preserved outflow to the kidneys (via avoidance of complete caval occlusion). A 'side-to-side piggy-back' was subsequently proposed by Belghiti et al in 1992 and has gained widespread acceptance because it reduces the incidence of caval anastomotic stenosis (at the cuff of the suprahepatic veins) reported with Tzakis' technique (Belghiti et al, 1992) (*Figure 2c*).

The recipient portal vein is subsequently anastomosed in an end-to-end fashion to the donor portal vein. In the presence of recipient portal vein thrombosis, thrombectomy, use of collateral vessels and porto-caval hemitransposition have all been used with varying success (Lai et al, 2014).

Arterial anastomosis is also usually performed end-to-end with the aim of juxtaposing nearly equal calibres of recipient and donor hepatic arteries; however, depending upon arterial quality, diameter and length, the level of the anastomosis may vary greatly.

The most common biliary anastomosis performed is an end-to-end choledocho-choledochostomy, thus maintaining endoscopic access to the biliary tree. In the event of bile duct size discrepancy or damage (e.g. children, atresia, primary sclerosing cholangitis) a choledocho-jejunosotomy is preferred. The use of T-tubes has been the source of debate but these are generally reserved for selected cases where concern exists regarding stricture formation or early leakage, or for the monitoring of bile output (Sun et al, 2015).

Other surgical procedures: liver splitting and live donation

Various strategies have been used to address the shortage of available organs.

Split liver transplantation

The conventional split liver procedure divides the liver to provide a right extended graft (segments I and IV–VIII) for one adult recipient and a left lateral graft (segments II–III) for a paediatric recipient. Such procedures have been applied variably across centres and countries with successful outcomes for both recipients when performed in experienced hands (Wilms et al, 2006).

Performing split liver transplantation for two adult recipients is a more challenging procedure, which divides the liver into right (segments V–VIII) and left (segments I–IV) hemi-grafts. A higher morbidity is generally reported with this technique, albeit with similar mortality to whole liver transplantation (Hashimoto et al, 2014). Biliary complications remain the most frequently encountered problem because of the variability of ductal anatomy and the need to use small calibre bile ducts during biliary anastomosis.

Live donor liver transplantation

Live donor liver transplantation was pioneered in the 1980s in the USA (Broelsch et al, 1991) and has become the main source of donation in Eastern countries, where brain dead donation is generally poorly accepted. Left lateral hepatic sectionectomy is now offered laparoscopically for paediatric live donor liver transplantation (Cherqui et al, 2002), whereas in adult live donor liver transplantation, right or left hemilivers are used. Many technical variations have been proposed to avoid small-for-size syndrome in the recipient and to maintain donor safety. This remains paramount, and with careful donor selection and perioperative care a donor mortality of 0% was reported in >3000 live donor liver transplantations performed in South Korea (Lee, 2015).

Postoperative outcomes and complications

Arterial complications include hepatic artery thrombosis, which has a reported incidence of approximately 5%, and less commonly stenosis and aneurysm formation. Interventional radiology techniques allow intra-arterial thrombolysis or stenting for the management of such sequelae. Arterial revascularization carries the highest success rates in the early stages of hepatic artery thrombosis, whereas late hepatic artery thrombosis usually necessitates retransplantation (as initial biliary tree necrosis is followed by parenchymal necrosis) (Mourad et al, 2014). Aggressive anticoagulation protocols have been implemented in attempts to prevent hepatic artery thrombosis in high-risk patients (e.g. complex vascular reconstructions, primary sclerosing cholangitis, thrombophilic disorders) with varying success (*Table 5*).

Continued on p. 271

Continued from p. 270

Portal vein and inferior vena cava complications (stenosis and thrombosis) are more rare with a reported incidence of 2.7% and 1.8% respectively (Settmacher et al, 2000).

Biliary complications consist of bile leaks (usually within the first few postoperative days) and strictures, which can occur either at the anastomosis (as a result of technical failure or ischaemia) or at non-anastomotic sites (ischaemia). Patients with hepatic artery thrombosis and live donor or donation after cardiac death liver grafts are at higher risk for biliary complications, which are usually managed via a non-operative, endoscopy-based strategy. Surgical intervention is usually reserved for biliary lesions which remain resistant or unsuitable for such techniques (Pascher and Neuhaus, 2005).

Other surgical complications include haemoperitoneum, wound infection and dehiscence, incisional hernia, pleural effusion and rarely intestinal perforation or obstruction. Overall, perioperative outcomes in the modern era of liver transplantation have improved significantly and

despite a variety of potential complications, the complex multidisciplinary management of such patients has led to 1-year survival rates >90%.

Conclusions

Standardization of retrieval and implantation strategies to reduce warm ischaemia time and organ injury may help improve donor outcomes but require further study. Methods of improving donor selection and optimizing donors during retrieval and subsequent preservation, particularly in the presence of organ shortages resulting in increasing numbers of donation after cardiac death and marginal donors, may also lead to improved outcomes. Current strategies for expansion of the donor pool include the use of living donors and split cadaveric liver grafts. [BJHM](#)

Conflict of interest: none.

Adam R, Delvart V, Karam V et al, the ELTR contributing centres, the European Liver, Intestine Transplant Association (ELITA) (2015) Compared efficacy of preservation solutions in liver transplantation: a long-term graft outcome study from the

Table 5. Example protocol for post-transplantation anticoagulation

	Low risk group	Intermediate risk group	High risk group	Very high risk group
Criteria for risk assessment	Normal liver graft, normal vascular reconstruction, uneventful operation	Donor age >60 years, donor cerebrovascular accident, donation after cardiac death donor, >mild steatosis, small hepatic artery or with right accessory artery but artery reconstruction with conduit of large calibre, complete portal vein thrombectomy, primary sclerosing cholangitis, (cytomegalovirus infection), hypertension, hypercholesterolaemia, diabetes mellitus, hypercoagulable thromboelastogram	Complicated small arterial reconstruction (very small artery, previous hepatic artery thrombosis), venous: Budd–Chiari syndrome, inherited thrombophilias, recurrent deep vein thrombosis or pulmonary embolus, mechanical heart valves	Intraoperative with re-do arterial anastomosis as a result of thrombosis formation, ?low flow state (consider aortic conduit also, in which case they may fall in different risk group), specified situation
When to start	6 hours postoperative, international normalized ratio <2, platelets >50 000 x10 ⁹ /litre (omit if criteria not met, do not correct)	6 hours postoperative, international normalized ratio <2, platelets >50 000 x10 ⁹ /litre (omit if criteria not met, do not correct)	6 hours postoperative, international normalized ratio <2, fibrinogen >1.5 g/litre, platelets >50 000 x10 ⁹ /litre (omit if criteria not met, do not correct)	Intraoperative international normalized ratio <2.5, fibrinogen >1.5 g/litre, platelets >50 000 x10 ⁹ /litre. Consider supporting platelets to maintain heparin administration
Intensive therapy unit	Heparin 5000 U subcutaneous three times per day	Heparin 5000 U subcutaneous three times per day	Unfractionated heparin intravenous, starting at 18 U/kg/hr (no bolus dose), and infusion rate adjusted aiming for APTTR 1.8–2.5	Unfractionated heparin intravenous, starting at 10 U/kg/hr (in theatre; consider 18 U/kg/hr in intensive therapy unit), and infusion rate adjusted aiming for APTTR 1.8–2.5
Ward	Tinzaparin 4500 U subcutaneous once per day	Tinzaparin 4500 U subcutaneous once per day, aspirin 75 mg orally once per day from day 7 (in addition to tinzaparin)	Continue unfractionated heparin intravenous with therapeutic APTTR. Change to tinzaparin 175 U/kg once per day early, add aspirin 75 mg orally once per day from day 7 (arterial) or change to warfarin (venous) from day 7	Continue unfractionated heparin intravenous with therapeutic APTTR, change to tinzaparin 175 u/kg once per day early, start warfarin on day 7 with target international normalized ratio 2–3, stop tinzaparin when international normalized ratio therapeutic
Discharge	Nil	Aspirin 75 mg orally once per day lifelong	Aspirin 75mg orally once per day, replace with warfarin if venous indication	Warfarin with target international normalized ratio 2–3

APTTR = activated partial thromboplastin time ratio

KEY POINTS

- Surgical techniques for the retrieval and implantation of donor livers remain unstandardized with various centres and surgeons using different strategies.
- A donor risk index, using a combination of donor factors, correlates closely with liver graft failure, thus providing an individualized and integrated risk estimate for an individual organ. The combination of marginal donors with high model for end-stage liver disease score recipients can lead to poor outcomes.
- Modalities of organ preservation are evolving with a growing interest in new technologies including machine preservation and normothermic regional perfusion, while cold storage remains the mainstay in clinical practice. Further clinical data are required to formally assess these strategies.
- The donor pool can be safely expanded via the inclusion of marginal quality organs and with the use of living donors and split cadaveric liver grafts.
- Despite a high morbidity risk, the multidisciplinary management of medical and surgical complications makes liver transplantation an extremely successful procedure with >90% 1-year survival rates.

- European Liver Transplant Registry. *Am J Transplant* **15**(2): 395–406. <https://doi.org/10.1111/ajt.13060>
- Belghiti J, Panis Y, Sauvanet A, Gayet B, Fékété F (1992) A new technique of side to side caval anastomosis during orthotopic hepatic transplantation without inferior vena caval occlusion. *Surg Gynecol Obstet* **175**(3): 270–272.
- Broelsch C, Whittington PF, Emond JC et al (1991) Liver transplantation in children from living related donors. Surgical techniques and results. *Ann Surg* **214**(4): 428–439, discussion 437–439. <https://doi.org/10.1097/00000658-199110000-00007>
- Cherqui D, Soubrane O, Husson E et al (2002) Laparoscopic living donor hepatectomy for liver transplantation in children. *Lancet* **359**(9304): 392–396. [https://doi.org/10.1016/S0140-6736\(02\)07598-0](https://doi.org/10.1016/S0140-6736(02)07598-0)
- Clavien PA, Harvey PR, Strasberg SM (1992) Preservation and reperfusion injuries in liver allografts. An overview and synthesis of current studies. *Transplantation* **53**(5): 957–978. <https://doi.org/10.1097/00007890-199205000-00001>
- Dunn DL, Morel P, Schlumpf R et al (1991) Evidence that combined procurement of pancreas and liver grafts does not affect transplant outcome. *Transplantation* **51**(1): 150–156. <https://doi.org/10.1097/00007890-199101000-00023>
- Feng S, Goodrich NR, Bragg-Gresham JL et al (2006) Characteristics associated with liver graft failure: the concept of a donor risk index. *Am J Transplant* **6**(4): 783–790. <https://doi.org/10.1111/j.1600-6143.2006.01242.x>
- Guarrera JV, Henry SD, Samstein B et al (2010) Hypothermic machine preservation in human liver transplantation: the first clinical series. *Am J Transplant* **10**(2): 372–381. <https://doi.org/10.1111/j.1600-6143.2009.02932.x>
- Hashimoto K, Quintini C, Aucejo FN et al (2014) Split liver transplantation using Hemiliver graft in the MELD era: a single center experience in the United States. *Am J Transplant* **14**(9): 2072–2080. <https://doi.org/10.1111/ajt.12791>
- Iaria G, Tisone G, Pisani F et al (2001) High-pressure perfusion versus gravity perfusion in liver harvesting: results from a prospective randomized study. *Transplant Proc* **33**(1-2): 957–958. [https://doi.org/10.1016/S0041-1345\(00\)02284-3](https://doi.org/10.1016/S0041-1345(00)02284-3)
- Imagawa DK, Olthoff KM, Yersiz H, Shackleton CR, Colquhoun SD, Shaked A, Busuttil RW (1996) Rapid en bloc technique for pancreas-liver procurement. Improved early liver function. *Transplantation* **61**(11): 1605–1609. <https://doi.org/10.1097/00007890-199606150-00010>
- Klar E, Kraus T, Osswald BR et al (1995) [Induction of impaired hepatic microcirculation by in situ hilus preparation in liver explantation]. *Zentralbl Chir* **120**(6): 482–485.
- Lai Q, Spoletini G, Pinheiro RS, Melandro F, Guglielmo N, Lerut J (2014) From portal to splanchnic venous thrombosis: What surgeons should bear in mind. *World J Hepatol* **6**(8): 549–558. <https://doi.org/10.4254/wjh.v6.i8.549>
- Latchana N, Peck JR, Whitson BA, Henry ML, Elkhammas EA, Black SM (2015) Preservation solutions used during abdominal transplantation: Current status and outcomes. *World J Transplant* **5**(4): 154–164. <https://doi.org/10.5500/wjt.v5.i4.154>
- Lee SG (2015) A complete treatment of adult living donor liver transplantation: a review of surgical technique and current challenges to expand indication of patients. *Am J Transplant* **15**(1): 17–38. <https://doi.org/10.1111/ajt.12907>
- Moench C, Moench K, Lohse AW, Thies J, Otto G (2003) Prevention of ischemic-type biliary lesions by arterial back-table pressure perfusion. *Liver Transpl* **9**(3): 285–289. <https://doi.org/10.1053/jlts.2003.50015>
- Mourad MM, Liouis C, Gunson BK et al (2014) Etiology and management of hepatic artery thrombosis after adult liver transplantation. *Liver Transpl* **20**(6): 713–723. <https://doi.org/10.1002/lt.23874>
- Ozhathil DK, Li YF, Smith JK, Tseng JF, Saidi RF, Bozorgzadeh A, Shah SA (2011) Impact of center volume on outcomes of increased-risk liver transplants. *Liver Transpl* **17**(10): 1191–1199. <https://doi.org/10.1002/lt.22343>
- Pascher A, Neuhaus P (2005) Bile duct complications after liver transplantation. *Transplant Int* **18**(6): 627–642. <https://doi.org/10.1111/j.1432-2277.2005.00123.x>
- Ravikumar R, Leuvenink H, Friend PJ (2015) Normothermic liver preservation: a new paradigm? *Transplant Int* **28**(6): 690–699. <https://doi.org/10.1111/tri.12576>
- Ravikumar R, Jassem W, Mergental H et al (2016) Liver transplantation after ex vivo normothermic machine preservation: a Phase I (first-in-man) clinical trial. *Am J Transplant* **16**(6): 1779–1787. <https://doi.org/10.1111/ajt.13708>
- Schemmer P, Schoonhoven R, Swenberg JA, Bunzendahl H, Thurman RG (1998) Gentle in situ liver manipulation during organ harvest decreases survival after rat liver transplantation: role of Kupffer cells. *Transplantation* **65**(8): 1015–1020. <https://doi.org/10.1097/00007890-199804270-00001>
- Schemmer P, Enomoto N, Bradford BU, Bunzendahl H, Raleigh JA, Lemasters JJ, Thurman RG (2001) Activated Kupffer cells cause a hypermetabolic state after gentle in situ manipulation of liver in rats. *Am J Physiol Gastrointest Liver Physiol* **280**(6): G1076–G1082.
- Schlumpf R, Morel P, Sutherland D, Moudry-Munns K, Gruessner R, Payne W, Dunn D (1990) Combined procurement of pancreas and liver grafts does not affect transplant outcome. *Transplant Proc* **22**(4): 2074–2075.
- Seehofer D, Eurich D, Veltzke-Schlieker W, Neuhaus P (2013) Biliary complications after liver transplantation: old problems and new challenges. *Am J Transplant* **13**(2): 253–265. <https://doi.org/10.1111/ajt.12034>
- Settmacher U, Nüssler N, Glanemann M, Haase R, Heise M, Bechstein W, Neuhaus P (2000) Venous complications after orthotopic liver transplantation. *Clin Transplant* **14**(3): 235–241. <https://doi.org/10.1034/j.1399-0012.2000.140309.x>
- Starzl TE, Marchioro TL, Vonkaulla KN, Hermann G, Brittain RS, Waddell WR (1963) Homotransplantation of the liver in humans. *Surg Gynecol Obstet* **117**: 659–676.
- Sterioff S, Marsh CL, Munn SR, Hayes DH, Perkins JD (1989) Pancreaticoduodenal allograft procurement in combination with liver allograft procurement. *Transplant Proc* **21**(1 Pt 3): 2767–2768.
- Sun N, Zhang J, Li X, Zhang C, Zhou X, Zhang C (2015) Biliary tract reconstruction with or without T-tube in orthotopic liver transplantation: a systematic review and meta-analysis. *Expert Rev Gastroenterol Hepatol* **9**(4): 529–538. <https://doi.org/10.1586/1747-4124.2015.1002084>
- Tokunaga Y, Ozaki N, Wakashiro S et al (1988) Effects of perfusion pressure during flushing on the viability of the procured liver using noninvasive fluorometry. *Transplantation* **45**(6): 1031–1035. <https://doi.org/10.1097/00007890-198806000-00007>
- Tzakis A, Todo S, Starzl T (1989) Orthotopic liver transplantation with preservation of the inferior vena cava. *Ann Surg* **210**(5): 649–652. <https://doi.org/10.1097/00000658-198911000-00013>
- Wigmore SJ, Seeny FM, Pleass HCC, Praseedom RK, Forsythe JLR, the Kidney Advisory Group (1999) Kidney damage during organ retrieval: data from UK National Transplant Database. *Lancet* **354**(9185): 1143–1146. [https://doi.org/10.1016/S0140-6736\(98\)09409-4](https://doi.org/10.1016/S0140-6736(98)09409-4)
- Wilms C, Walter J, Kaptein M et al (2006) Long-term outcome of split liver transplantation using right extended grafts in adulthood: A matched pair analysis. *Ann Surg* **244**(6): 865–873, discussion 872–873. <https://doi.org/10.1097/01.sla.00000247254.76747.f3>