Surgical Techniques

27

Michele Colledan and Stefania Camagni

Key Points

- Different types of technical variant grafts and full-size grafts have been used in paediatric LT. Nowadays, transplantation of LLSs from split liver and living donation appears the most effective strategy to transplant small children.
- Organ availability and donor-to-recipient size matching guide the choice of a specific graft type on a case-by-case basis.
- The best results overall may be achieved at high-volume centres with extensive experience with all graft types and age groups, which may allow transplantation according to each recipient's special needs. A liberal split policy and an active LDLT program should be complementary resources in Western countries for the purpose of eliminating paediatric wait-list mortality.
- For a safe and effective implantation of a LLS, it is important to keep in mind some recipient-related and graft-related peculiarities:
  - Small children easily tolerate cross-clamping of the infrahepatic and the suprahepatic vena cava, so total clamping is preferred to side clamping even in case of caval preservation since it allows a large opening over the orifices of the hepatic veins for outflow reconstruction.
  - A hypoplastic portal vein is a common feature in patients with biliary atresia, so the need for a specific technical solution is not that unusual.
  - The arterial anastomosis site depends on both the recipient's arterial axis and the graft arterial pedicle.
  - Biliary reconstruction consists of a single or double end-to-side hepaticojejunostomy, depending on the presence of the left bile duct or of two separate segmental ducts.
  - An optimal graft orientation is fundamental to avoid portal vein kinking and outflow obstruction.
- Further reduction of LLSs, the use of LLSs from small deceased paediatric donors and delayed abdominal closure may be useful strategies to transplant infants less than 5–6 kg in weight.
- In experienced hands, APOLT is being increasingly accepted as a valid alternative to standard LT in selected cases of ALF, allowing over two-thirds of these patients the chance of an immunosuppression-free life. Even though its acceptance is controversial, APOLT may be a safe alternative to standard LT also in the setting of NCMLD, preserving the option of later gene therapy without lifelong immunosuppression.

Research Needed in the Field

- **Size Matching**

  Size matching is crucial for the outcome of paediatric LT but any of the current approaches to this issue may be questionable since no evidence-based guidelines exist and the safe size matching range is unknown [1]. So, research on this issue may help improve both graft and patient survival.

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- **Graft Inflow Modulation**

When transplanting a cirrhotic child with portal hypertension, graft inflow modulation may allow optimal portal and arterial flow. The most appropriate haemodynamic parameters to guide the application of graft inflow modulation and the best graft inflow modulation strategies are still a topic of debate [2, 3]. So, prospective multicentre trials should be encouraged to further explore this issue.

- **Prevention of Biliary Complications**

Biliary complications are a major source of morbidity after paediatric SLT and LDLT. No gold standard for their prophylaxis has been established so far [4, 5]. Thus, the need for further investigation into this issue is undeniable. Provided a high index of clinical suspicion and an attitude to early aggressive diagnosis are shared, prospective multicentre trials would be advisable.

- **APOLT**

The best candidates to APOLT have not been clearly identified yet. Besides, in the setting of NCMLD, the required auxiliary graft volume to replace the deficient enzymatic activity is unknown and the ideal strategy to manage portal steal has not been defined yet [6, 7]. So, APOLT appears as another field needing further research.

27.1 Graft Types for Paediatric Liver Transplantation

27.1.1 From Full-Size to Reduced-Sized Grafts

Since 1967, when Starzl accomplished the first successful case [8], for almost two decades, all paediatric liver transplantations (LT) have been performed using size-matched whole organs from deceased donors. Unfortunately, such grafts were hardly available. In 1984, Bismuth firstly reported a paediatric LT with a segmental graft obtained by reducing the size of an adult liver [9]. Actually, a similar case had been previously performed by Starzl in 1975 but was reported only in 1990 [10]. The reduced-sized technique appeared to be the solution to the shortage of appropriate-sized donors for small children and soon became the procedure of choice for this population with good results [11–13]. Anyway, as the reduction of an adult liver generated only one transplantable graft, the problem of organ shortage was merely shifted from the paediatric to the adult population. So, two strategies were developed to supply the paediatric demand for small-sized grafts without detriment to the adult waiting list: split LT (SLT), resulting from the division of a deceased donor liver into two transplantable parts, and living donor LT (LDLT). The first ex situ split (see paragraph "Ex situ versus in situ split liver") was described by Pichlmayr in 1988 [14], while the first successful LDLT was reported by Strong in 1989 [15]. Initially, SLT had a limited diffusion because the outcomes reported by the early series were worse than those obtained by full-size LT and LDLT [16–18]. In 1995, a retrospective analysis of the European Split Registry showed improved survival for the first time, raising new interest in SLT [19]. In the same year, Rogiers described the first in situ split [20] (see paragraph "Ex situ versus in situ split liver"). The introduction of the in situ technique offered another big contribution to the progressively increasing diffusion of SLT [21–28].

Nowadays, transplantation of left lateral segment grafts (LLSs), from split liver or living donation, is the most common strategy to transplant small children, who represent the largest portion of paediatric candidates to LT.

Figures 27.1 and 27.2 present the evolution over time of graft types for paediatric LT in Europe according to ELRT/ELITA data [29].

This chapter will focus on deceased donor paediatric LT, particularly on SLT, LDLT being the object of another specific chapter of this textbook.

The use of a specific graft type from a deceased donor depends on donor-to-recipient size matching.

27.2 Split Liver

Split liver, namely the division of a deceased donor liver into two transplantable parts, is based on the fundamental principle that a partial liver graft with a suitable arterial and portal inflow together with the corresponding venous and biliary drainage and sufficient hepatocyte mass can fulfil the role of a whole organ [30, 31]. Along with LDLT, SLT evolved from the advancements of hepatobiliary surgery and an improved understanding of liver segmental anatomy (Fig. 27.3).

27.2.1 Ex Situ Versus In Situ Split Liver

Split liver can be performed ex situ or in situ. The former technique consists of dividing the whole liver on the back-table after standard procurement. The latter, derived from the experience of living donor liver procurement, consists of dividing the whole liver in the heart-beating deceased donor. The in situ technique offers the advantage of shortening the ischaemia time, which allows for long-distance sharing between transplant centres as well. Theoretically, it may also improve the control of bleeding from the cut parenchymal surface of the grafts [22]. On the other hand, it significantly increases the donor operation time and general complexity, which must be

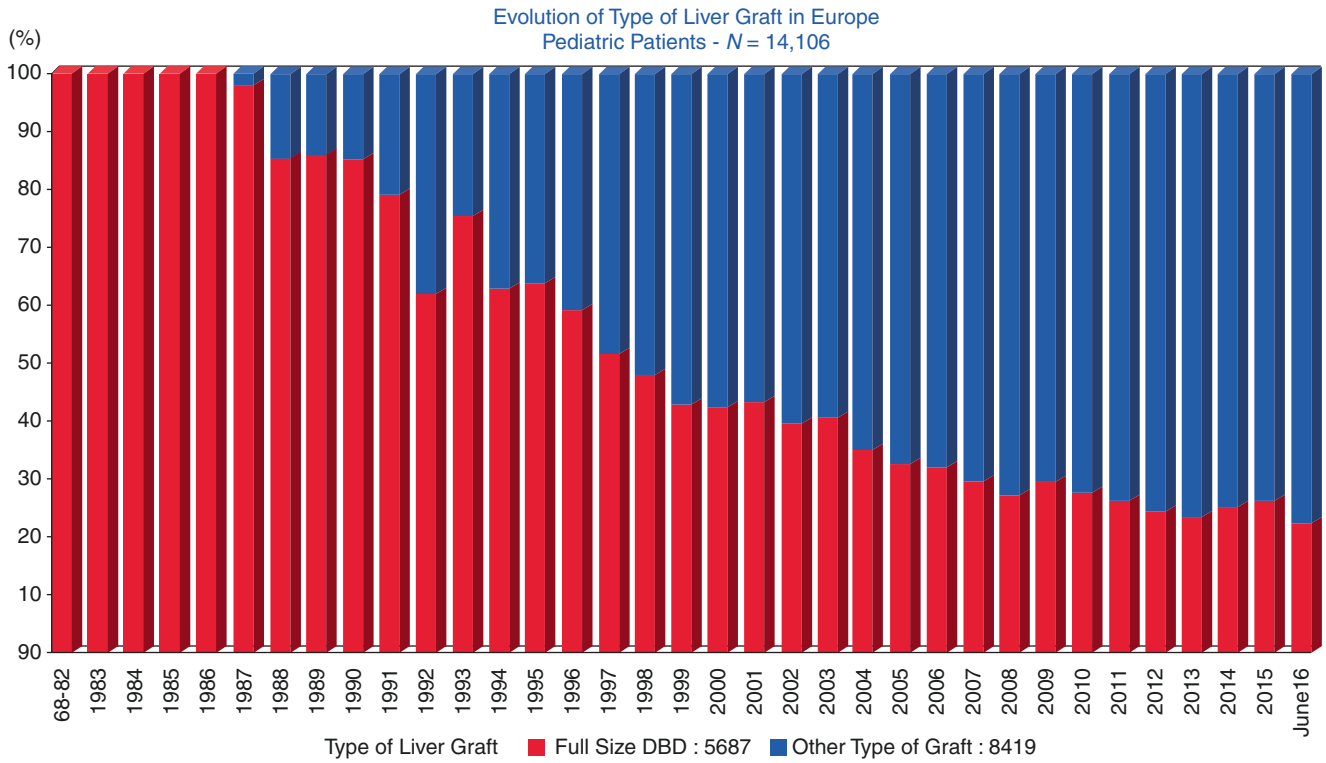

Fig. 27.1 Evolution over time of graft types for paediatric LT in Europe (ELTR/ELITA data, kindly provided by Dr. Vincent Karam)

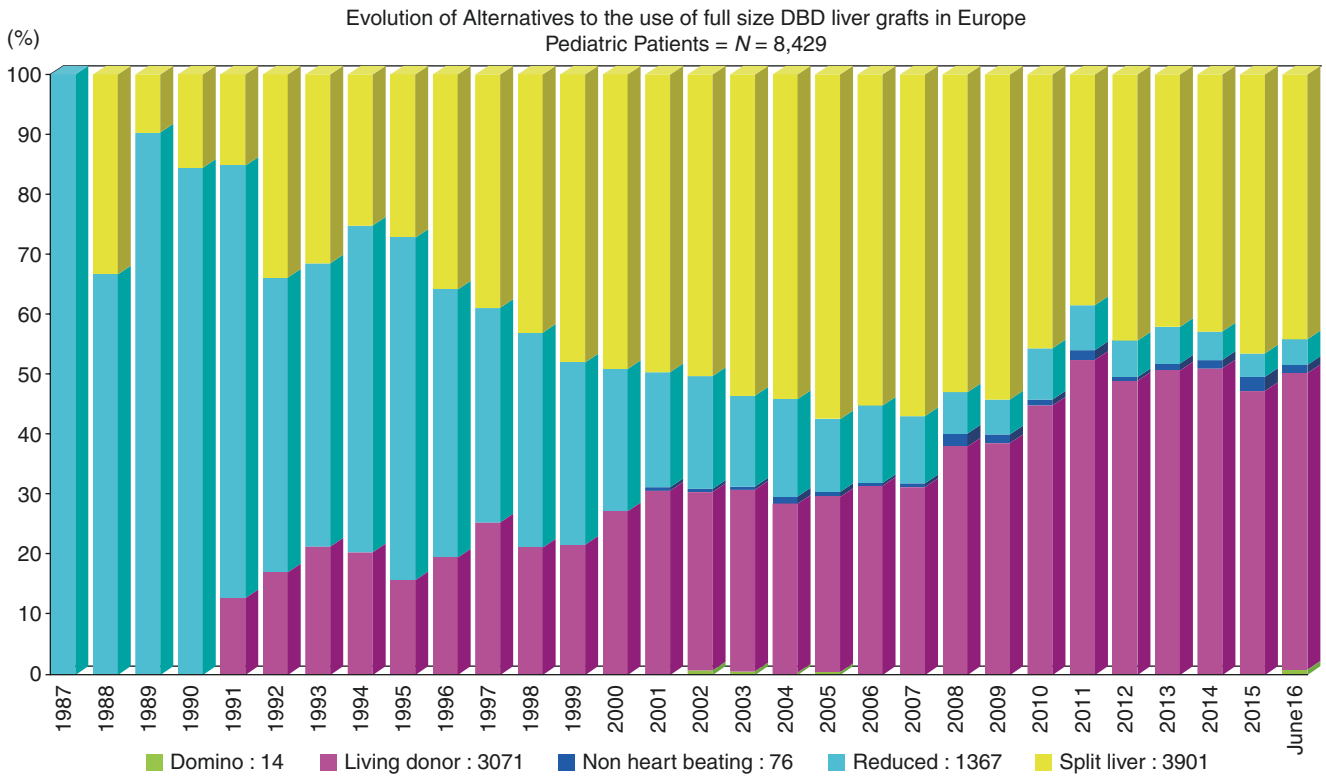

Fig. 27.2 Evolution over time of the alternatives to full-size grafts from donors after neurological determination of death (DBD) for paediatric LT in Europe (ELTR/ELITA data, kindly provided by Dr. Vincent Karam)

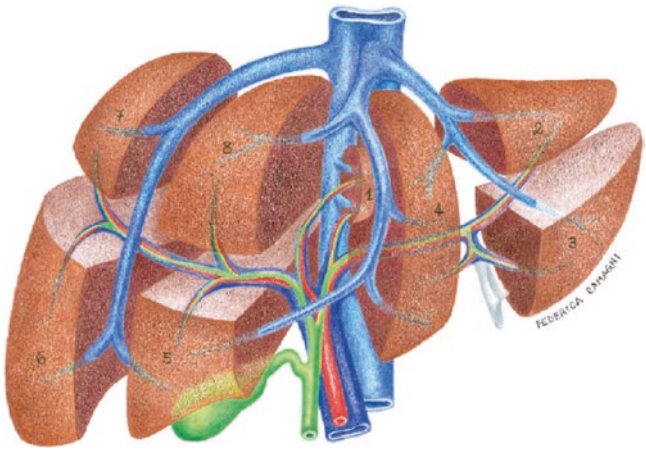

Fig. 27.3 Liver segmental anatomy

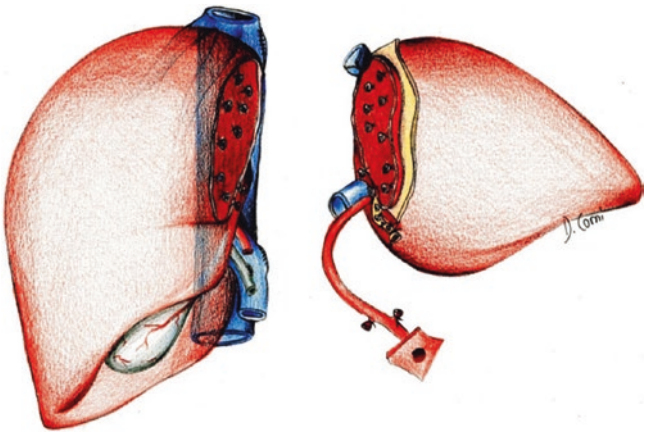

Fig. 27.4 ACSL (this figure, published in "Transplant Rev 2005;19:221–231", has been reproduced with permission from Elsevier)

considered for organisational aims. No prospective studies comparing the two techniques are available but the reported series of ex situ and in situ split liver show similar outcomes [32, 33]. The in situ technique is the preferred and substantially exclusive choice for split liver at our centre.

27.2.2 Types of Split Liver

The concept of split liver involves two different entities.

The adult/child split liver (ACSL) generates an extended right graft (ERG), including the Couinaud segments I and IV to VIII [34], and a LLS, including segments II and III (Fig. 27.4). The former is suitable for transplantation into an adult (or an adult-sized child), while the latter is appropriate for transplantation into a small child usually not exceeding 30 kg in weight [33]. Despite controversies on the quality of this kind of grafts still exist and the debate on the outcomes of SLT is still open [35], the ACSL represents a well-established procedure at the main paediatric transplant centres in Western countries.

The adult/adult split liver (AASL) generates two similar-sized grafts, usually a full-right one (FRG), including segments V to VIII, and a full-left one (FLG), including segments I to IV (Fig. 27.5). These grafts are suitable for transplantation into two small adults or large children exceeding 25–30 kg in weight [33]. The first attempt of dividing an adult whole liver into two grafts to be transplanted into two adult-sized recipients was made in 1989 by Bismuth, who used this strategy for emergency grafting of two patients with fulminant hepatic failure [36]. Unfortunately, both of them died of causes not specifically related to the surgical technique. In 1999, our group first reported the long-term successful application of an original technique of AASL, derived from the experience of living donor right lobe procurement [37]. Subsequently, case reports and larger series

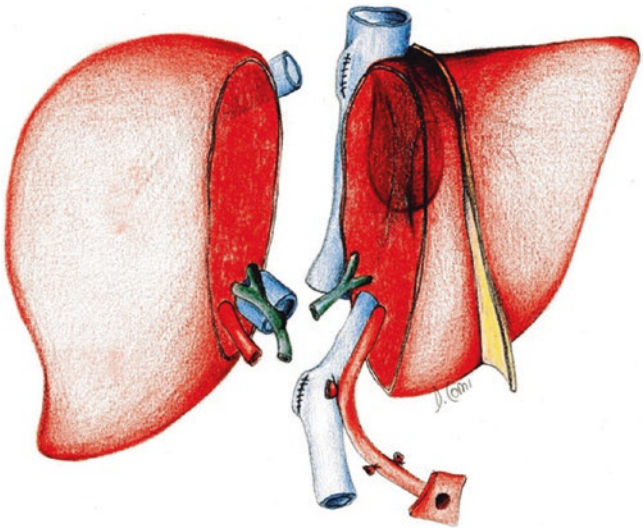

Fig. 27.5 AASL (this figure, published in "Transplant Rev 2005;19:221–231", has been reproduced with permission from Elsevier)

of AASL from Western transplant centres were published with encouraging results [38–45]. Anyway, this very complex procedure is still less standardized than ACSL and its diffusion remains limited.

27.3 Adult/Child Split Liver

27.3.1 Donor Selection

Although specific selection criteria vary among centres [30, 33, 46–49], it is agreed that the ideal donor for ACSL should be young and not obese, should not have a history of liver disease, should have a short intensive care unit stay, should

be haemodynamically stable and should have normal or near normal liver function tests [50]. The North Italian Transplant program, the referral organization to which our centre belongs, identified the following donor eligibility criteria: age <60 years, intensive care unit stay <5 days, low inotropic support and normal or near normal liver function tests [49]. At our centre, the split liver technique is used aggressively for size adapting in any donor whose liver is deemed suitable for transplanting a child on the waiting list, with no specific criteria for the split procedure itself [33, 51]. The only exception is haemodynamic instability, which represents a reasonable technical contraindication to the in situ technique [33].

27.3.2 Size Matching

Size matching is crucial for the outcome of paediatric LT. A too small graft may be unable to meet the functional demands of the recipient, leading to small-for-size syndrome. Conversely, a too large graft may be damaged by vascular thrombosis or necrosis due to inadequate perfusion and may result in the impossibility to close the abdomen, with increased mortality [33, 52–54]. Unlike LDLT, generally SLT cannot rely on a precise preoperative assessment of the volume of the donor LLS. In theory, the LLS accounts for the 25–30% of the total liver volume. Anyway, the LLS volume is highly variable and cannot be predicted by simple anthropometric variables [53]. No evidence-based guidelines concerning size matching are available, and the safe size matching range remains unknown [1]. At our centre, when the recipient is a small child, the rule about size matching provides for transplanting the liver as a whole (Fig. 27.6) or ERG for a donor-to-recipient weight ratio (DRWR) between 0.5 and 2 and for transplanting a LLS for a DRWR between 2 and 12 [33], which usually translates into a graft-to-recipient weight ratio (GRWR) between 1.5% and 6% or somewhat more. In case of ERGs, it has to be kept in mind that they are expected to represent about 70–75% of the total liver volume.

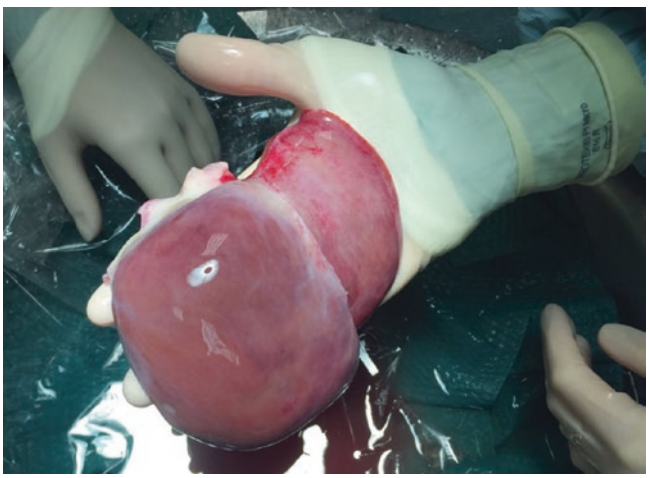

Fig. 27.6 Full-size liver graft from a paediatric donor

27.3.3 Attribution of the Vascular and Biliary Supply and Choice of the Transection Plane

No consensus exists on the allocation of the whole arterial axis, including the celiac, common and proper hepatic artery [33, 55]. One of the grafts has necessarily to rely only on its named branch. The policy of most paediatric transplant centres provides for retaining the celiac axis with the LLS [26, 27, 33, 56, 57]. In fact, the size of the right hepatic artery is usually larger than that of the left hepatic artery and appropriate for a safe anastomosis. Devascularisation of segment IV, which happens when its arterial supply arises from the proper of left hepatic artery, is generally only an occasional cause of minor morbidity in the recipient of the ERG. Anyway, the allocation of the whole arterial axis should be discussed time after time with the ERG team, taking into consideration the specific arterial anatomy and reciprocal needs. Figure 27.7 shows two different LLS, one retaining the whole arterial axis (a) while the other retaining only the left hepatic artery (b).

Conversely, the allocation of the portal, biliary and hepatocaval pedicles is unanimously agreed upon: the LLS retains the left branch of the portal vein, the left hepatic duct and the left hepatic vein, while the ERG retains the portal vein, the common bile duct and the inferior vena cava (Fig. 27.4).

Two techniques have been employed for ACLS, the trans-umbilical and the trans-hilar [14, 16, 17, 36, 58]. One of the distinctive characteristics of the two approaches is the line for liver division. The trans-umbilical technique sets the cut surface through the umbilical fissure, thus producing a pure LLS, including only segments II and III. Instead, the trans-hilar technique sets the transection line somewhat on the right of the umbilical fissure, thus including a variable portion of segment IV along with the LLS. Recently, de Ville de Goyet retrospectively compared the outcomes of the two approaches, which appeared to be equally safe and effective [55]. At our centre, almost all ACSL have been performed following the trans-umbilical technique, which will be described in the next paragraph.

27.3.4 Surgical Technique

This paragraph describes the technique for in situ ACLS adopted at our centre [33].

The donor operation begins with the evaluation of the LLS. The definitive judgement on size matching depends on the estimation of its volume. The feasibility of the splitting procedure is assessed by excluding technical contraindications such

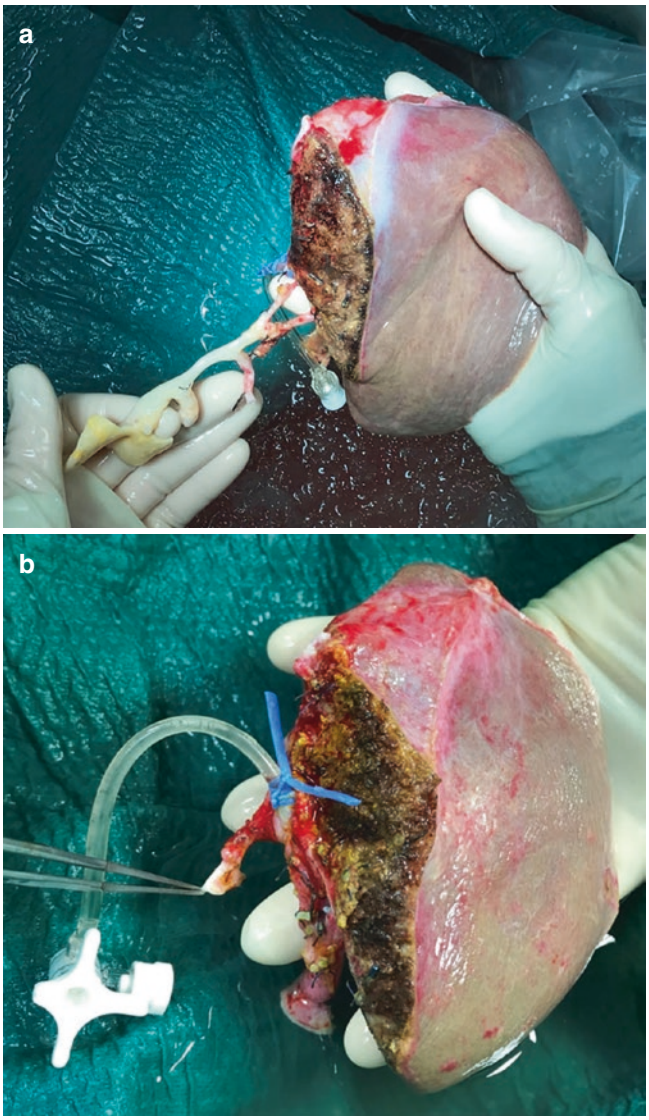

Fig. 27.7 (**a**) The LLS retains the whole arterial axis. (**b**) The LLS retains only its named branch (indicated by the forceps), which, anyway, appears to be large enough to allow for a safe anastomosis in a primary transplant recipient

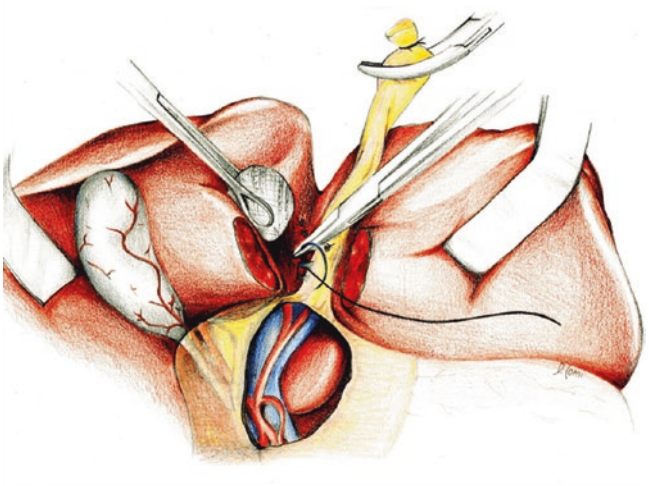

Fig. 27.8 ACSL: dissection of the umbilical fissure (this figure, published in "Transplant Rev 2005;19:221–231", has been reproduced with permission from Elsevier)

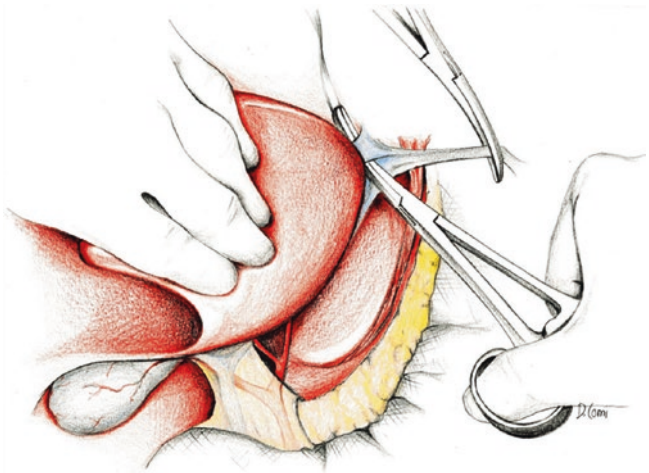

Fig. 27.9 ACLS: isolation of the left hepatic vein (this figure, published in "Transplant Rev 2005;19:221–231", has been reproduced with permission from Elsevier)

as an undivided portal vein at the hilum [59, 60] and a left-sided gallbladder, which may be associated with portal and biliary anomalies [61]. Finally, a biopsy may occasionally help assess the liver quality at the surgeon's discretion: at our centre, macrovescicular steatosis >10% is considered a relative contraindication to split liver, depending on the recipient's conditions.

After standard manoeuvres for aortic control, the division of the liver is started.

The origin of the right hepatic artery is identified and the left hepatic artery is isolated. Then, the umbilical fissure is dissected with suture ligation and section of the portal branches connecting the round ligament and the Rex recessus with segment IV (Fig. 27.8). The left branch of the portal vein is encircled. So, the left aspect of the hilar plate is exposed. After sectioning the hepatogastric, left triangular and coronary ligaments and dissecting the Arantius' ligament, the left hepatic vein is encircled at its confluence into the inferior vena cava (Fig. 27.9). Returning to the hepatic pedicle, the left portion of the hilar plate is encircled and sectioned sharply with the knife at the level of the planned parenchymal transection. Then, an umbilical tape is passed around the left hepatic vein, along the sulcus of Arantius and between the left hepatic pedicle and the parenchyma to emerge in the umbilical fissure. Traction on its edges helps the subsequent parenchymal transection [62], which is carried along the falciform ligament. After parenchymal transection, the liver is divided into two still perfused grafts, connected only by their vascular pedicles (Fig. 27.10).

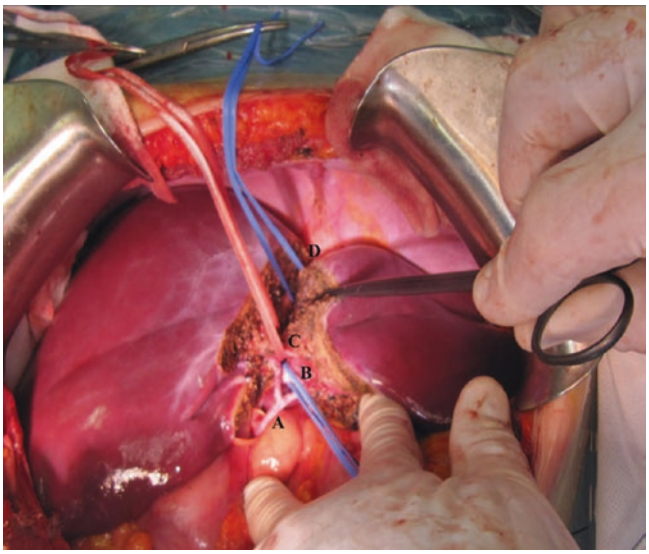

Fig. 27.10 LLS and ERG from in situ split connected only by their vascular pedicles and by the hilar plate. (A) Left hepatic artery. (B) Left branch of the portal vein. (C) Left portion of the hilar plate (the hilar plate can be sectioned either before or after aortic cross-clamping and cold flushing). (D) Left hepatic vein

The multiorgan procurement is then carried on in the standard fashion. After aortic cross-clamping and cold flushing, the two liver grafts are retrieved separately.

In the ex situ technique, the procedure for liver division on the back-table is the same as in the in situ technique.

27.4 Adult/Adult Split Liver

27.4.1 Donor Selection and Size Matching

Even if precise parameters have not been identified, consensus exists on limiting the AASL procedure to optimal donors; thus selection criteria are more restrictive than for ACSL [45, 50, 63–65].

Size matching is a delicate issue, too. As for ACSL, an accurate preoperative measurement of FLG and FRG volume is generally not feasible. So, size matching is based on the estimation of FLG and FRG volume as about the 40 and 60% of the donor total liver volume respectively, FLG volume being particularly unpredictable, and on a desired GRWR of at least 1% [33, 45, 65]. When the grafts from AASL are shared between a child and an adult, the FLG is usually assigned to the former.

27.4.2 Attribution of the Vascular and Biliary Supply

It is agreed that the whole arterial axis and the portal trunk should be left with the FLG to ensure optimal blood supply to segments I and IV, FRG blood supply relying on the right arterial and portal branches. The common bile duct is preferentially kept with the FRG, whereas the left hepatic duct, normally longer than the right, is left with the FLG [31]. The retrohepatic vena cava is generally attributed to the FLG, the FRG retaining the right hepatic vein [66, 67], or divided into two patches, one for each graft [68]. Optimal outflow may be obtained by dividing also the middle hepatic vein longitudinally into two halves to be shared between the two grafts [69].

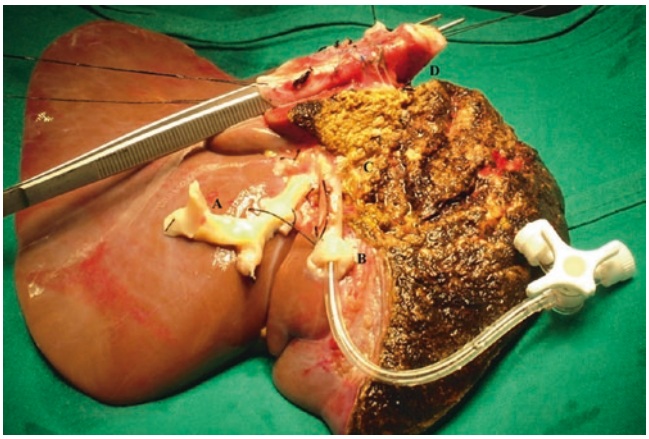

Fig. 27.11 FLG retaining the whole arterial axis (A), the portal trunk (B), the left hepatic duct (C) and the inferior vena cava (D)

Figure 27.5 illustrates the most common allocation of the vascular and biliary supply in AASL. Figure 27.11 shows a FLG retaining the whole arterial axis, the portal trunk, the left hepatic duct and the retrohepatic inferior vena cava, as more commonly performed at our centre.

27.5 Recipient Operation

The following paragraphs will describe the surgical techniques adopted at our centre [33].

27.5.1 Total Hepatectomy

A bilateral subcostal incision is performed (Fig. 27.12). The round ligament is ligated and divided and the falciform ligament is sectioned. Being biliary atresia the most common indication to paediatric LT, adhesions from a previous Kasai procedure are a frequent finding and have to be carefully dissected. In the presence of a Roux-en-Y loop from a previous Kasai procedure, it is divided at the porta hepatis and preserved for reuse. Otherwise, in the presence of the biliary tree, both the cystic duct and the common hepatic duct or the common bile duct are ligated and sectioned (Fig. 27.13). The left and right hepatic arteries are isolated, ligated and dissected as close to the liver as possible to keep any options for

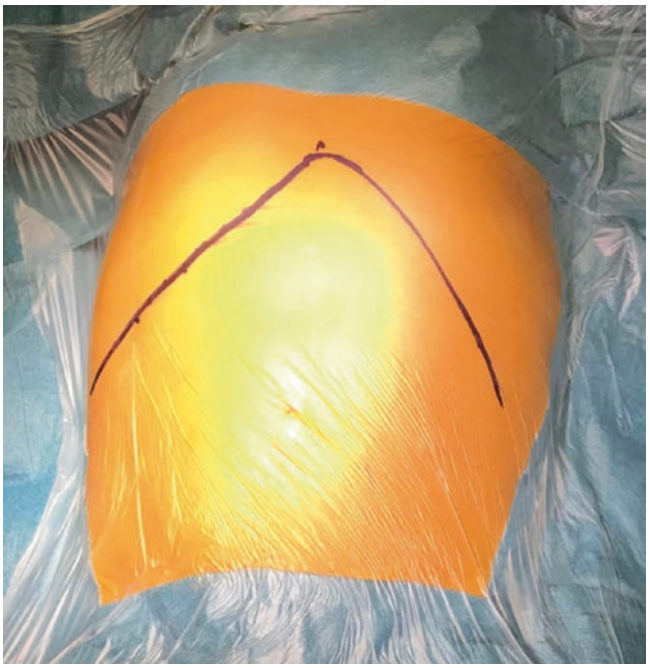

Fig. 27.12 Planned bilateral subcostal incision

Fig. 27.13 Suture ligation of the cystic duct (indicated by the arrow)

the subsequent graft implantation (Fig. 27.14). For the same purpose, it may be useful to mobilise the arterial axis from the proper hepatic artery to the gastroduodenal artery or even further. The portal vein is then skeletonized from its bifurcation to a level depending on its calibre (Fig. 27.15). After hilar dissection, the left and right liver lobes are mobilised. On the left, the hepatogastric, triangular and coronary ligaments are divided (Fig. 27.16). On the right, the triangular and coronary ligaments are sectioned, and the right lobe is

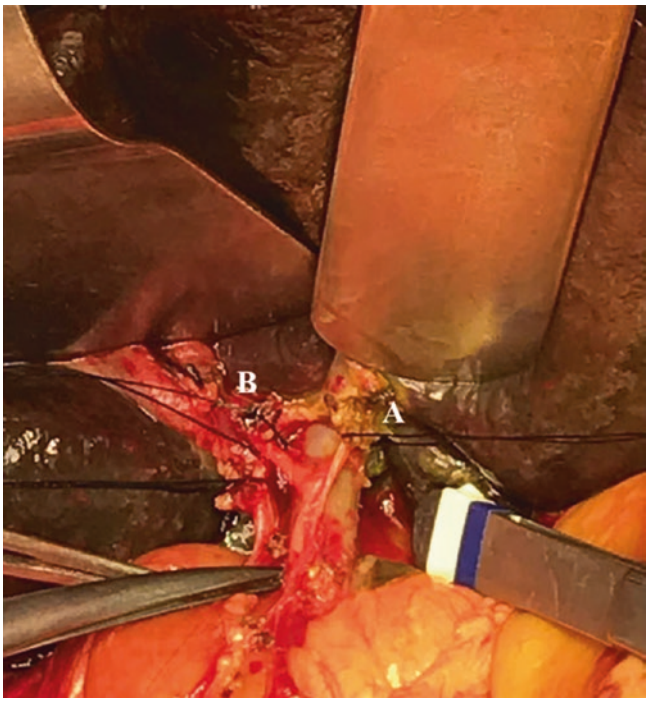

Fig. 27.14 Suture ligation and dissection of the left (A) and right (B) hepatic arteries as close to the liver as possible

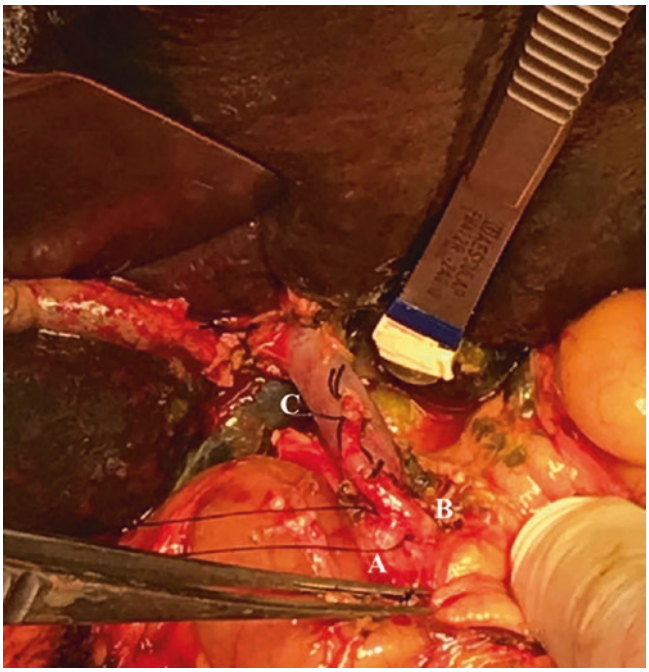

Fig. 27.15 Mobilisation of the arterial axis from the proper hepatic artery to the gastroduodenal artery (A) and the common hepatic artery (B). Isolation of the portal vein (C) from its bifurcation to the splenomesenteric confluence

freed from its retroperitoneal attachments (Fig. 27.17). Depending on the graft type or on the specific condition or on the preferred technique for hepatic venous outflow recon-

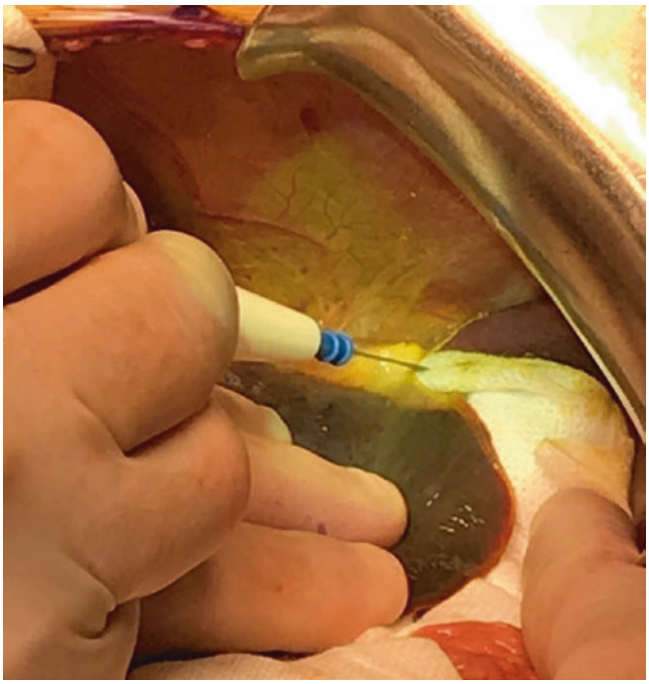

Fig. 27.16 Division of the left triangular and coronary ligament

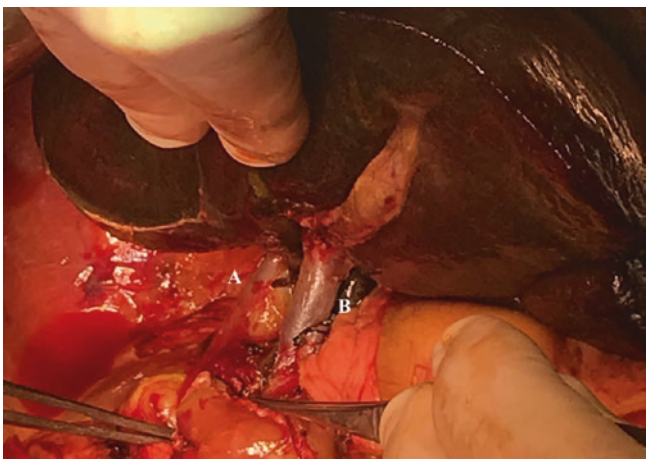

Fig. 27.17 Mobilisation of the right lobe (A, inferior vena cava; B, portal vein)

struction, the retrohepatic vena cava can be preserved or removed with the native liver. In small children, cross-clamping of the infrahepatic and the suprahepatic vena cava is easily tolerated, so it is preferred to side clamping even in case of caval preservation since it allows for a large opening over the orifices of the hepatic veins for outflow reconstruction (Fig. 27.18). After cross-clamping of the portal vein and of the infrahepatic and the suprahepatic vena cava, the native liver is excised.

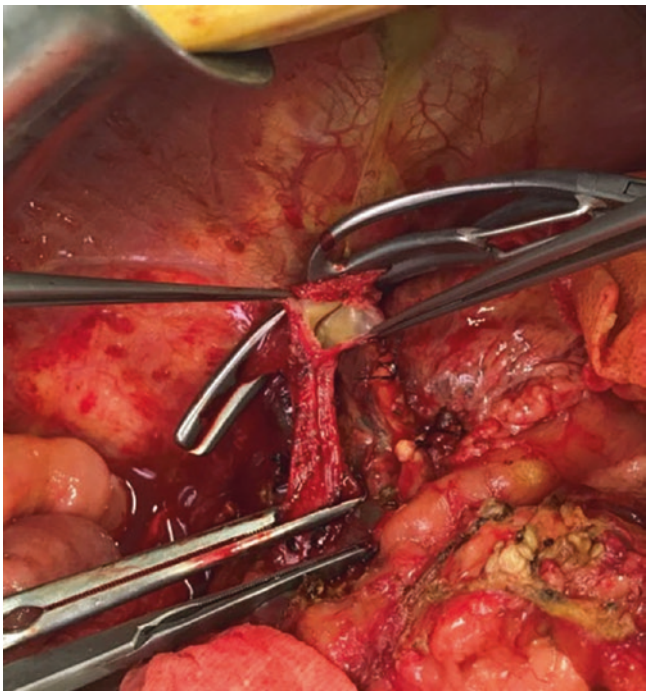

Fig. 27.18 Preserved native vena cava after total hepatectomy. Double cross-clamping of the infrahepatic and the suprahepatic vena cava allows a large opening over the orifices of the hepatic veins

27.5.2 Implantation of the Left Lateral Segment

Being transplantation of LLSs from split liver or living donors the most common strategy for LT in small children, the implantation of this kind of graft will be discussed extensively while the implantation of other types of graft will be just briefly mentioned.

Although relatively well tolerated in small children, it is important to limit the cross-clamp time in order to avoid prolonged stasis in both systemic and portal circulation. Moreover, once the graft is put into the operative field, any effort should be made to keep the implantation rewarming time as short as possible.

If the native vena cava has been preserved, as it usually happens, a triangular end-to-side anastomosis is performed between the graft hepatic vein and an opening including one, two or all the orifices of the native right, middle and left hepatic veins using non-absorbable polypropylene sutures (Fig. 27.19). This technique, first proposed by Broelsch and Emond [70, 71], enables a large anastomosis for outflow optimization. Other techniques have been described with a similar rate of outflow complications [72–76]. If the retrohepatic vena cava has been removed with

the native liver to achieve a radical resection in case of liver malignancies or for anatomical or technical reasons, it may be replaced by a donor venous graft. At our centre, first the venous graft is implanted on the LLS hepatic vein at the back-table, and then a double caval end-to-end anastomosis is performed (Fig. 27.20). The back-table preparation of the neo-cava allows to limit the cross-clamp time. Literature on caval replacement in paediatric LT with LLSs is scanty. We have recently presented the results of a monocentric retrospective cohort study comparing caval preservation and caval replacement in paediatric recipients of primary LT with deceased donor LLSs. Since no statistical difference in the incidence of hepatic venous outflow complications has been verified, we deem caval replacement safe and effective and consider it a useful option in case of liver malignancies, Budd-Chiari syndrome or severe hypoplasia of the retrohepatic vena cava [77]. Occasionally, in case of congenital interruption or absence of the inferior vena cava with azygous or hemiazygos continuation, a third approach is needed: an end-to-end anastomosis may be performed between the graft hepatic vein and the cloaca of the recipient's hepatic veins, directly draining into the right atrium [78]. Whatever the technique, during the outflow reconstruction the liver graft is flushed with Ringer's lactate solution.

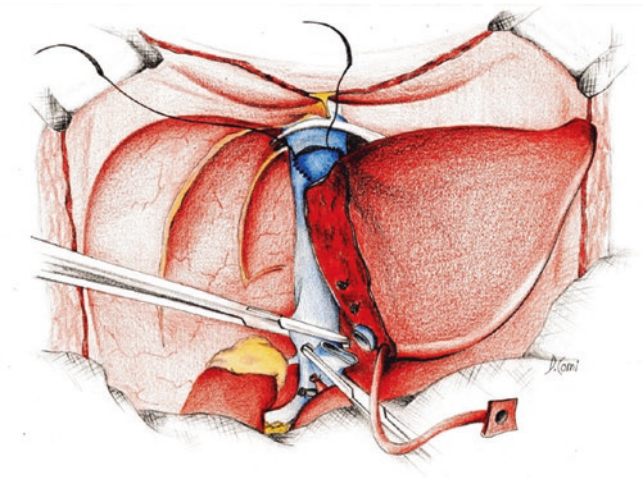

Fig. 27.19 Caval preservation: triangular end-to-side anastomosis between the graft hepatic vein and the orifices of the native hepatic veins (this figure, published in "Transplant Rev 2005;19:221–231", has been reproduced with permission from Elsevier)

Then comes the end-to-end anastomosis between the graft left portal branch and the recipient's portal vein. In the presence of a hypoplastic portal vein, which is a common feature in patients with biliary atresia, a donor venous graft may be interposed between the spleno-mesenteric confluence and the LLS portal branch [79]. Portoplasty may be an alternative option: after dissection of the portal vein down to the spleno-mesenteric confluence, a longitudinal venotomy is performed, and a donor patch venous graft is sutured to the recipient's portal vein; then, an end-to-end anastomosis between this reconstructed vessel and the graft portal stump is done [80, 81]. In the event of haemodynamically significant portosystemic shunts, their ligature should be attempted in order to avoid portal flow diversion from the liver and subsequent portal vein thrombosis. A singular condition is represented by Abernethy malformation type 1, which is characterized by the congenital absence of the portal vein and by an extrahepatic end-to-side portocaval shunt (Fig. 27.21) [82]. In this case, the portocaval shunt is discontinued, and a standard end-to-end portal anastomosis is performed with the interrupted vessel. Whatever the technique, the orientation of the liver graft is crucial to prevent portal vein kinking and subsequent thrombosis. We are used to place it in a rather central position, rotated about 30–45° to the right on an axial plane and clockwise on a coronal plane [33].

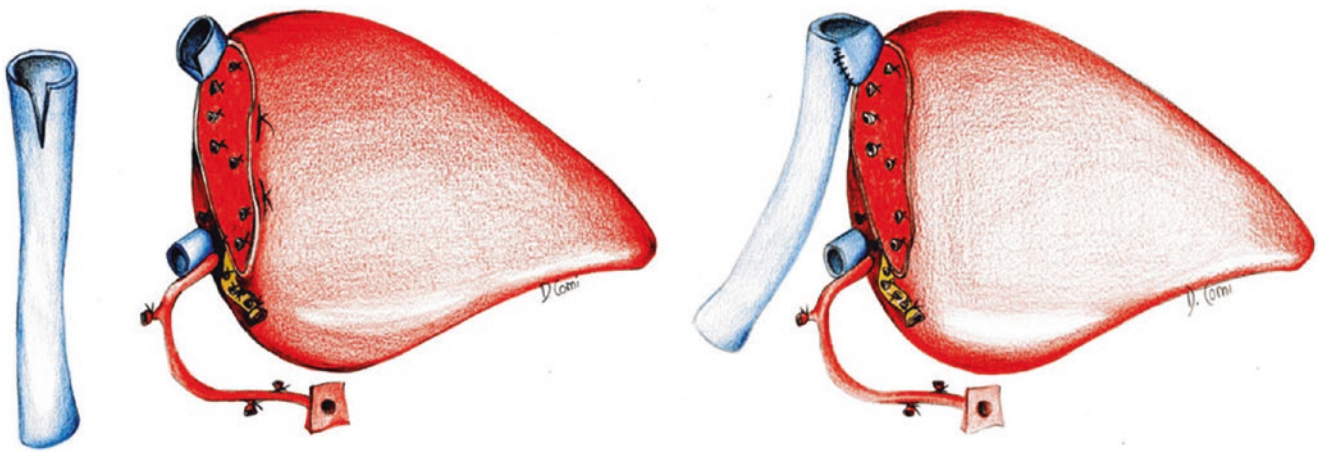

Fig. 27.20 Caval replacement by back-table implantation of a venous graft on the LLS hepatic vein

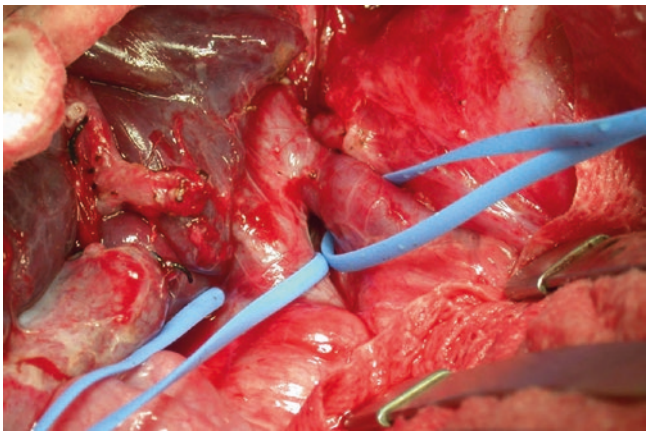

Fig. 27.21 Abernethy malformation type 1

Once the portal anastomosis has been completed, the removal of portal and caval clamps allows graft reperfusion by portal flow and ends the warm ischaemic time.

The next step consists of restoration of hepatic arterial flow. The choice of the arterial anastomosis site depends on the graft arterial pedicle and on the recipient's arterial axis. The graft and the recipient's arterial branches to be anastomosed should be congruent in calibre, and the resulting vessel should not kink or twist. Children affected by biliary atresia often have a large arterial axis, so the anastomosis can be safely performed on their common or proper hepatic artery most of the times. On the contrary, Alagille syndrome is characterized by a hypoplastic arterial axis, so the supraceliac or infrarenal aorta could be an option for the anastomosis, with or without an interposition graft. Microvascular techniques using both intraoperative microscopy and high-power loupe magnification have been described, with the most recent series showing similar results with any of these strategies [83–87].

At our centre, it is common practice to use absorbable polydioxanone sutures for portal anastomosis in order to prevent stricture formation by allowing these small calibre vascular anastomoses to grow over time.

Finally, biliary reconstruction is accomplished by end-to-side hepaticojejunostomy, using the same loop of the previous Kasai operation, if present, or preparing a new Roux-en-Y loop. Even in the presence of a normal native bile duct, a direct duct-to-duct anastomosis is generally avoided. A single or double anastomosis may be necessary, depending on the presence of the left bile duct or of two separate segmental ducts (Fig. 27.22). As few interrupted stitches as possible of absorbable polydioxanone suture are used for the hepaticojejunostomy, with careful mucosa-to-mucosa apposition. At our centre, a transanastomotic stent is usually placed with the purpose of preventing biliary complications.

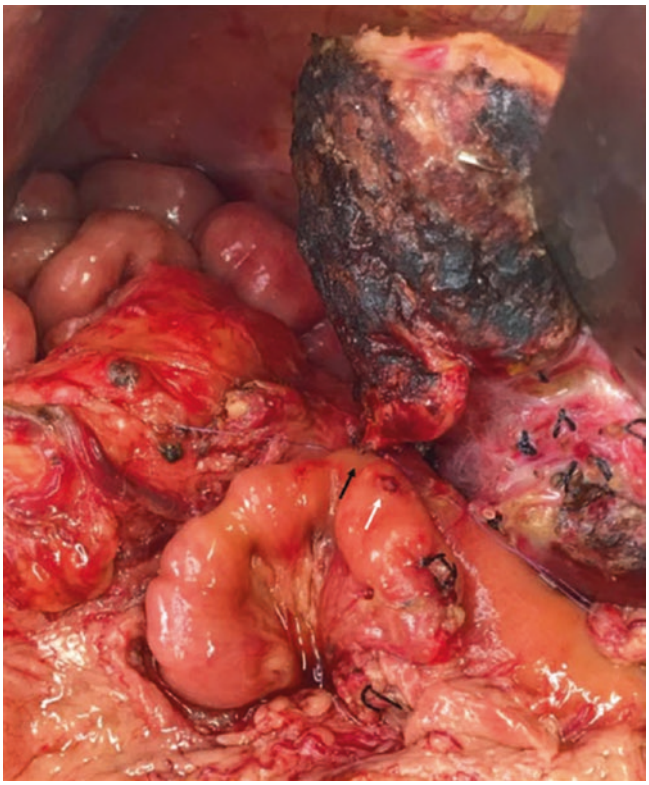

Fig. 27.22 Double hepaticojejunostomy: the black arrow indicates the first anastomosis, the white arrow indicates the enterotomy for the second one

27.5.3 Implantation of the Extended Right Graft and of the Full-Size Graft

Since the ERG retains the inferior vena cava, the portal vein and the common bile duct, its implantation and that of a full-size graft are almost identical.

If the native vena cava has been removed, a double caval anastomosis is performed. If, instead, the native vena cava has been preserved, the piggyback technique is adopted, so an end-to-side anastomosis is performed between the graft suprahepatic vena cava and a common cuff at the confluence of the native hepatic veins. In this case, side clamping may be an option in large children with a native vena cava of adequate calibre.

As described in the previous paragraph, the next steps are portal and arterial anastomosis and biliary reconstruction.

In the particular above-mentioned case of Abernethy malformation type 1, if a caval side clamping is feasible, arterial prior to portal reperfusion may be an option, leaving the congenital portocaval shunt intact until arterial reperfusion (Fig. 27.23).

For biliary reconstruction, the choice between an end-to-end duct-to-duct anastomosis and an end-to-side hepaticojejunostomy is guided by both anatomical and technical considerations.

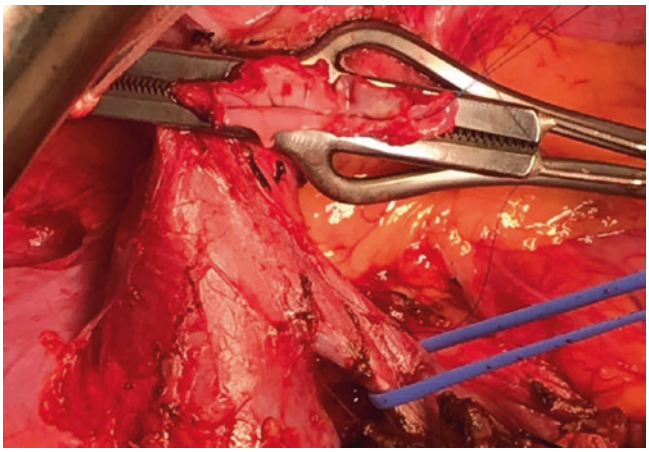

Fig. 27.23 Preservation of the congenital portocaval shunt during side clamping of the native vena cava

In the presence of an ERG, a careful check for biliary leaks from the sutured orifice of the left hepatic duct or from the small caudate lobe ducts is mandatory.

27.5.4 Implantation of the Full-Left Graft and of the Full-Right Graft

Size-matching is the main reason why the most commonly used graft from AASL for paediatric LT is the FLG, whose volume is smaller than that of the FRG.

Since the FLG retains the inferior vena cava, the portal vein and the whole arterial axis, its implantation is very similar to that of a full-size graft. The implantation of the FRG, instead, is very similar to that of a right lobe from a living donor.

In case of split cava technique, the caval patch of any graft is anastomosed to the recipient's side clamped inferior vena cava in a side-to-side fashion.

Whatever the biliary pedicle of any graft, biliary reconstruction may be performed by both an end-to-end duct-to-duct anastomosis and an end-to-side hepaticojejunostomy.

27.5.5 Retransplantation

Basically, surgical technique of paediatric liver retransplantation is the same as just described for primary LT. Anyway, enhanced complexity due to the previous transplant itself is almost the rule. Sometimes, retransplantation is really a surgical challenge. Explantation of the previous graft may be highly demanding due to adhesions, whose dissection may be particularly laborious, and to peculiar anatomical conditions. Available vascular pedicles for the new anastomoses are the result of both the ability of dissecting them free and the complications of the previous transplant. For instance, the isolation of the retrohepatic vena cava may occasionally be so troublesome that it may not be preserved. Chronic portal vein thrombosis not timely treated by Meso-Rex bypass [88] may entail the need for an alternative vessel for the new anastomosis: a jump graft between the recipient's splenomesenteric confluence and the graft portal stump may be an option; a varix or, in the presence of a splenorenal shunt, the left renal vein may be considered in adults but are hardly ever a viable option in children. It is worthwhile to underline that chronic portal vein thrombosis is an important risk factor for early mortality after retransplantation (personal unpublished data), hence the need for a timely and aggressive management of this complication [88]. Occasionally, neither the hepatic artery nor its branches are available for the arterial anastomosis, which therefore has to be performed with the supraceliac or the infrarenal aorta, with or without an interposition graft. Finally, if hepaticojejunostomy is the choice for biliary reconstruction, the same loop of the previous transplant is usually reused.

27.6 Results of Paediatric LT by Graft Type

The impact of graft type on the outcome of paediatric LT has been a matter of lively debate for more than two decades. Anyway, it still remains unclear. Several studies using data from different transplant systems, both registry and single centre data, have reported conflicting results. Actually, these studies are heterogeneous in that they analyse different geographical realities with different organ supply and allocation policy. Besides, they share limitations due to their common retrospective nature: on the one hand, centres with a wide range of experience contribute to registry data to different extents; on the other hand, even the biggest single centre series does not have the statistical power of registry-based studies. We are going to elucidate what just stated by describing some important studies published in the last 15 years.

First, we are going to focus on North America. In 2004, Roberts presented an analysis of the Scientific Registry of Transplant Recipients database. Among the 2277 children aged less than 2 years who had received their first transplant between 1989 and 2000, those transplanted with living donor grafts had a significantly lower risk of graft failure during the first post-transplant year than those transplanted with both full-size and split or reduced grafts from deceased donors. They had a significantly lower mortality risk than those transplanted with split or reduced grafts from deceased donors, too. The benefits of LDLT seemed to be lost for older children [89]. In 2007, two different studies using data from the Studies of Pediatric Liver Transplantation registry reported discrepant results. Soltys, who investigated late events among children who had received their first transplant between 1995 and 2004, demonstrated similar rates of graft

loss after the first post-transplant year for technical variant grafts from both deceased and living donors and full-size grafts [90]. Instead, Diamond showed increased morbidity and mortality for children who had received their first transplant between 1995 and 2006 with technical variant grafts from both deceased and living donors compared to those transplanted with full-size grafts. 30-day and 2-year morbidity was significantly increased for any type of technical variant compared to full-size grafts. Moreover, split and reduced grafts from deceased donors represented an independent predictor of retransplantation or death [91]. Moving to the United Network for Organ Sharing (UNOS) database, different studies reported conflicting results once again. In 2004, Abt presented the outcomes of 3125 children who had received their first transplant between 1991 and 2001. For those aged less than 3 years, 3-year graft survival was significantly higher after LDLT compared to transplantation with both full-size and split or reduced grafts from deceased donors. Conversely, for those aged between 3 and 12 years, it was transplantation with full-size grafts to offer a significant 3-year graft survival advantage over any type of technical variant grafts [92]. In 2008, Becker reported an analysis of 1260 LT performed between 2002 and 2004 in children aged less than 12 years. 30-day patient survival was significantly higher after transplantation with full-size compared to any type of technical variant grafts, including living donor ones. However, adjusted 1-year graft and patient survival was comparable among all graft types and age groups [93]. In 2013, Cauley published a study on 2683 children aged less than 2 years who had received their first transplant with both full-size and split or reduced grafts from deceased donors between 1995 and 2010. Graft and patient survival turned out to be similar among graft types for patients transplanted after 2000 [94]. In 2017, Alexopoulos showed that, among children who had received their first transplant for biliary atresia between 2002 and 2014, those less than 7 kg in body weight had significantly better graft survival after transplantation with technical variant grafts from both deceased and living donors compared to those transplanted with full-size grafts [95]. We are going to complete this picture of paediatric LT in North America with a monocentric study published by Hong in 2009. He focused on the Dumont UCLA Transplant Center experience. Among the 442 paediatric LT performed between 1993 and 2006, he found no significant difference in long-term graft and patient survival by graft type (full-size grafts and LLSs from both split liver and living donation). Anyway, LLSs from split liver showed a significantly higher rate of primary non-function, while LLSs from living donation had a significantly higher rate of portal vein thrombosis [96].

Now, let us move to Europe. In 2004, Broering presented the first ever reported series with more than 100 paediatric LT recipients with an actual 6-month patient survival of 100%. He analysed 132 consecutive LT performed at the University Hospital Hamburg-Eppendorf between 2001 and 2003. Actual graft survival and the rate of biliary complications appeared to be similar among LDLT and split and full-size LT [97]. In 2003, Gridelli described Bergamo experience with 124 paediatric patients transplanted for end-stage cholestatic liver disease between 1997 and 2002. He demonstrated comparable 4-year graft and patient survival after split and full-size LT [98]. In 2007, Bourdeaux reported on 235 consecutive paediatric primary LT performed at Saint-Luc University Clinics between 1993 and 2002. Of them, 100 were LDLT, while 135 were deceased donor LT with both full-size and split and reduced grafts. Actuarial 1- and 5-year graft survival was significantly higher after LDLT compared to deceased donor LT. Moreover, actuarial 1- and 5-year graft and patient survival was significantly higher after LDLT compared to deceased donor LT for children aged less than 2 years. At multivariate analysis, deceased donor grafts appeared to be significantly correlated with hepatic artery thrombosis, while living donor grafts turned out to be significantly correlated with acute rejection [99]. ELTR analysis revealed comparable early up to 10-year graft survival after SLT and whole LT for 14,022 children transplanted between 1988 and 2016; instead, longer-term graft survival resulted to be significantly better for children transplanted with full-size graft [29]. Finally, in 2017, Battula showed the very good results of the intention to split policy adopted at Birmingham transplant centre. Of the 724 paediatric LT performed between 1992 and 2014, 516 were split LT. 1-, 5- and 10-year graft and patient survival was excellent after split LT, and paediatric wait-list mortality was eliminated during the last 4 years of the study period [100].

In conclusion, as paediatric waiting lists everywhere include mostly small children but size-matched whole organs from deceased donors are a scarce resource, there is no alternative to the use of LLSs from split liver and living donors for this population. Actually, not being whole organs as timely disposable as LLSs, it might be worthless to compare the outcomes of LT by this kind of grafts. Technical variant grafts from both split liver and living donation have greatly contributed to virtually eliminate paediatric wait-list mortality in some European countries [98, 100, 101]. Technical variant grafts have become significantly safer over time. This is likely the effect of a learning curve regarding surgical experience, donor and recipient selection and matching and short- and long-term post-transplant patient management. The contradictory reported results of paediatric LT with LLSs from split liver and living donation should be interpreted critically in light of both data sources and centre-specific variables [32, 102]. LDLT with LLSs offers the indisputable advantage of scheduling transplantation at a recipient-controlled time, before the development of life-threatening complications or severe malnutrition, with very

low donor mortality and morbidity [32, 89, 99, 103]. Anyway, the adoption of a liberal split policy timely provides grafts of excellent quality to transplant most paediatric patients when they are still clinically stable [98].

We think that the best results overall may be achieved at high-volume centres with extensive experience with all graft types and age groups, which may allow transplantation according to each recipient's special needs. We agree with Mazariegos that the ability to use the appropriate graft type in a timely fashion implies a clear understanding of each recipient's specific condition, including the degree of portal hypertension, anatomical variations and risk factors [104]. We firmly believe that deceased donor SLT and LDLT should be complementary resources in Western countries, with regular access to both of them. If, on the one hand, LLSs from split liver and living donation represent an adequate pool to fulfil the needs of small children, on the other hand, the supply of size-matched grafts for large children is actually a problem. Whole organs or ERGs from paediatric donors and LLSs of sufficient volume are a scarce resource, so a possible solution lies in enhancing the program of AASL and providing size-matched FLGs.

27.7 Liver Transplantation in Very Small Infants

LT in newborns and infants weighting less than 5–6 kg has always represented a surgical challenge because of both the difficulty of a safe size matching and technical issues. The related literature reports conflicting results. Cauley's analysis of the UNOS database showed a significantly higher risk of graft failure and mortality for recipients weighting less than 6 kg [94]. In the few small series looking exclusively at children under 5 kg in weight, graft and patient survival ranges between 50% and 77% and between 55% and 86%, respectively [105–110]. Mekeel described comparable overall graft and patient survival for recipients weighting less than 5 kg and for those weighting more than 5 kg [110]. Broering observed no disadvantage concerning mortality in children under 5 kg in weight [97]. Our group reported satisfactory long-term graft and patient survival and a low rate of surgical complications after LT in children less than 6 kg [111]. For sure, the best results of LT in very small infants are the effect of a learning curve for both surgical aspects and perioperative care.

Whole organs from matched paediatric donors are rarely available. Besides, neonatal livers are mostly considered not suitable for transplantation due to their immature function [112–114]. The outcomes of full-size grafts from donors weighting less than 6 kg, regardless of donor age, are controversial. Concerns are about the functional maturity of newborn donor livers and the risk of vascular thrombosis. Mekeel reported comparable overall graft survival for children transplanted with full-size grafts from donors weighting less than 6 kg and for those transplanted with full-size grafts from donors weighting more than 6 kg [110]; others, instead, have described high rates of graft failure due to vascular complications and primary non-function with the same kind of grafts [95, 107, 112].

LLSs from adult or adult-sized donors are often too big for recipients less than 5–6 kg in weight. A GRWR more than 6% may occasionally result in insufficient blood supply to the graft, in the risk of compartment syndrome in case of abdominal closure and in a higher rate of early episodes of acute rejection [33, 52–54, 115, 116]. So, two approaches have been developed to transplant very small infants without the deleterious effects of large-for-size grafts: further reduction of LLSs from both deceased and living adult donors, in order to tailor them to the recipient size, and transplantation of LLSs from deceased paediatric donors less than 10 years old or 40 kg in weight. A third strategy to address this problem is represented by delayed abdominal closure, which will be discussed in a specific paragraph, since it may be useful not only in the presence of large-for-size grafts. However, it is worthwhile to underline that, even in case of GRWR more than 6%, LT has been safely performed without any need for neither further graft reduction nor delayed abdominal closure [98].

Further reduction of a LLS may be both anatomical, leading to a monosegment, and nonanatomical, providing a hyper-reduced graft that is larger than a monosegment but smaller than a LLS. Both these techniques were first adopted in deceased donor LT and subsequently borrowed by LDLT. Experience with transplantation of monosegments and hyper-reduced grafts is limited, and no data directly comparing the outcomes of these two techniques are available. They both seem to be satisfactory options for very small infants, but it is still unknown which of these grafts represents the best choice [117]. Regarding monosegmental LT, reduction of a LLS to segment II appears technically more demanding than creating a segment III graft, since it involves a hazardous dissection at the base of the umbilical fissure [118]. Besides, segment II is usually smaller than segment III. So, monosegmental LT seems safer and easier with segment III rather than with segment II [115]. Hyper-reduced grafts were proposed as a versatile alternative to monosegments. The supporters of this approach advocate that it allows to tailor the graft size to any specific needs on a case-by-case basis much more than monosegmental LT and that it oversteps some technical pitfalls of monosegmental LT. The basic principle is to reduce the size of a LLS without compromising its vascular inflow and outflow. So, parenchymal planes of resection are usually a sagittal plane resecting the graft left lateral edge and a transverse plane resecting the graft inferior edge. No dissection at the base of the umbilical

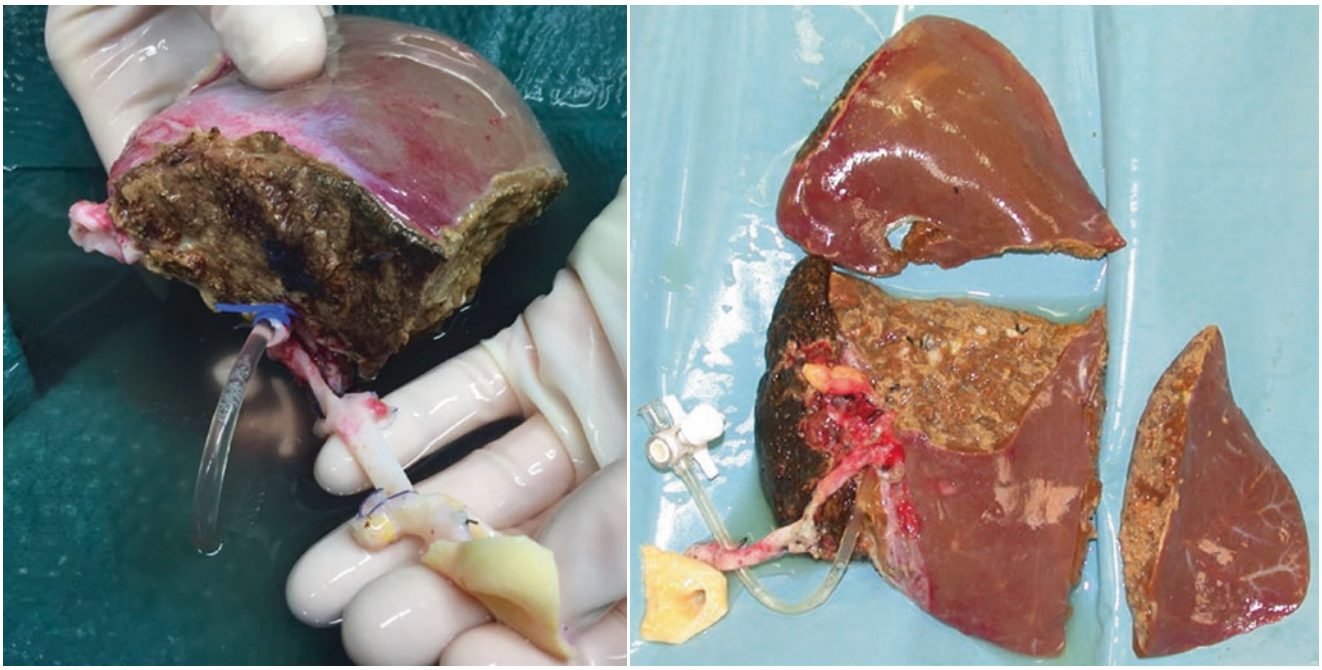

Fig. 27.24 Two different types of hyper-reduced LLSs. Both LLSs were derived from in situ split of a deceased donor liver and further reduced ex situ

fissure is needed. The implantation of a hyper-reduced graft is similar to that of a LLS, being their vascular pedicles exactly the same [119, 120] (Fig. 27.24).

Split LT from paediatric donors less than 10 years old or under 40 kg in weight was proved to be an effective strategy to increase organ availability by a prospective Italian multicentre study. Survival and complication rates were not significantly different between recipients of grafts from paediatric donors aged less than 10 years or weighting less than 40 kg and recipients of grafts from older or larger paediatric donors. Difficulties in vascular and biliary reconstructions appeared to be balanced by optimal graft quality [121, 122] (Fig. 27.25).

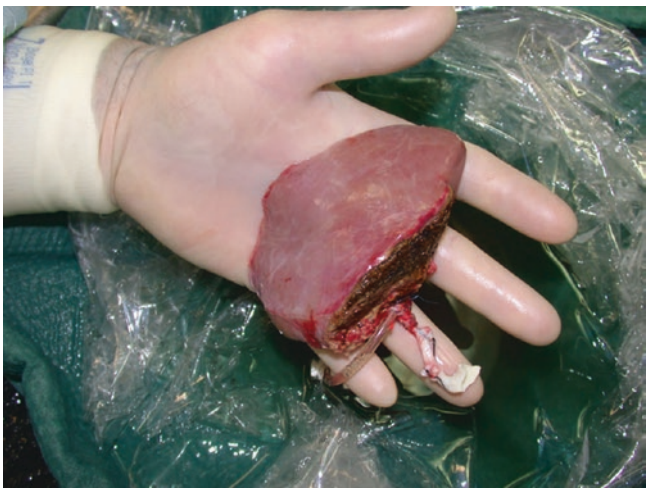

Fig. 27.25 LLS from in situ split of the liver of a paediatric deceased donor of 20 kg in weight

27.8 Delayed Abdominal Closure

Delayed abdominal closure after paediatric LT may be a useful option in some particular conditions. It may avoid abdominal compartment syndrome not only in the presence of a large-for-size graft, as previously mentioned, but also in case of massive intestinal oedema due to prolonged stasis in portal circulation [123]. Moreover, it may allow the ideal orientation of the graft, which is fundamental for an optimal inflow and outflow, in case of an unfavourable relationship between the graft anteroposterior diameter and anteroposterior abdominal depth [120, 123]. So, it gives time either for graft or abdominal wall remodelling or for resolution of portal hypertension.

Many strategies for delayed abdominal closure have been described, each with pros and contra, and different materials have been used as well.

Available meshes are both non-absorbable and absorbable synthetic ones, such as polypropylene, polytetrafluoroethylene, Gore-tex and polyglactin meshes and extracellular matrix-derived biological ones [123].

One approach consists of temporarily abdominal dressing with subsequent staged reduction in size until definitive closure with or without a prosthesis. Some

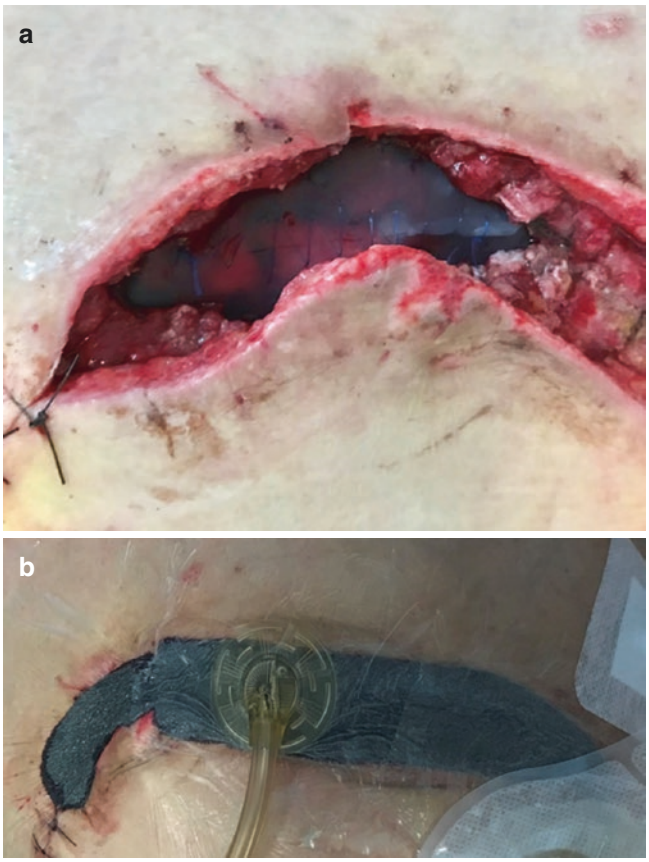

Fig. 27.26 (**a**) Downsized silastic mesh secured to the muscle fascia. (**b**) Sealed wound dressing connected to a vacuum pump over the silastic mesh

groups, including ours, have adopted the following two- or multistep technique: a silastic mesh, which is a reinforced silicone sheet, is secured to the muscle fascia and subsequently downsized until definitive mass muscle closure or definitive closure with interposition of an absorbable synthetic mesh to fill in the fascial defect; the skin may be closed over the silastic mesh; otherwise a sealed wound dressing connected to a vacuum pump may be employed [123, 124] (Fig. 27.26). Others have used a similar approach, with a synthetic mesh for temporarily abdominal dressing and a biological one for an early definitive closure [125].

Very early primary abdominal wall augmentation by means of a biological mesh represents an alternative strategy. The rationale for this technique is both to limit any possible risk of infection associated with an open abdomen and to avoid any possible complication associated with the use of synthetic meshes [126]. Biological meshes seem to integrate into the abdominal wall as a result of a process of incorporation [125, 126].

Finally, abdominal closure with a non-vascularized allotransplantation of the same donor abdominal rectus fascia has been reported [127].

Delayed abdominal closure and graft size reduction are not mutually exclusive; they may rather be complementary options in the presence of a large-for-size graft. They may be further combined with the use of prosthetic materials supporting the graft in order to avoid outflow obstruction due to caval compression [120, 128].

27.9 Auxiliary Partial Orthotopic Liver Transplantation

Auxiliary partial orthotopic liver transplantation (APOLT) is a special technique of LT where a portion of the native liver is resected and replaced by a size-matched partial graft, which is implanted in an orthotopic position. In small children, a LLS from split liver or living donation is generally an adequate auxiliary graft. Although technically easier, a left lobectomy of the native liver does not create enough space for an adult LLS to be implanted, so a left hepatectomy appears to be the best option.

The main indications for APOLT are ALF and NCMLD. APOLT has also been reported for Abernethy malformation type 1 complicated by hyperammonaemia and hepatopulmonary syndrome with complete resolution of symptoms [129].

27.9.1 Auxiliary Partial Orthotopic Liver Transplantation in Acute Liver Failure

In the setting of ALF, APOLT can act as a bridge to native liver regeneration, so that patients can be spared lifelong immunosuppression [103, 117, 130]. Children with a high potential for native liver regeneration and with a favourable clinical status are the best candidates for APOLT. Conditions with an excellent regenerative potential are represented by acetaminophen overdose, hepatitis A and E and mushroom poisoning. Patient's clinical status is fundamental since APOLT is more technically demanding and consequently more time consuming than standard LT, so patients with haemodynamic instability, severe systemic inflammatory response syndrome or intracranial hypertension may not tolerate this prolonged procedure [6]. In experienced hands and in carefully selected recipients, APOLT has provided excellent results in terms of both graft and patient survival and complication rate, allowing over two-thirds of these patients the chance of an immunosuppression-free life [131, 132]. Thus, it is being increasingly accepted as a valid treatment option for children with ALF [6].

27.9.2 Auxiliary Partial Orthotopic Liver Transplantation in Non-cirrhotic Metabolic Liver Diseases

The rationale for APOLT in the setting of NCMLD is to provide sufficient liver mass to produce the missing enzyme and correct the metabolic abnormality. It would be reasonable to think that APOLT may be limited to NCMLD with the liver as the main site of the defective gene expression [133]. As a matter of fact, among NCMLD, Crigler-Najjar syndrome type 1 (CNS1) and urea cycle disorders are the main indications to APOLT [7]. In particular, CNS1 represents the archetypal NCMLD suitable for it since it has been shown to be corrected by the replacement of less than 12% of total hepatocyte volume and less than 5% of hepatic enzymatic activity. Anyway, APOLT has been reported in case of propionic acidaemia, characterized by the liver as a part of a multisystem disorder, with adequate metabolic control and stabilization of the disease [7, 133]. APOLT has some advantages over standard LT: first, in case of failure of the auxiliary graft, the native remnant can support general liver function without any risks for the patient's life; second, if gene therapy becomes clinically available, the native remnant can be treated and lifelong immunosuppression can be avoided [103, 117, 130]. Anyway, there is some scepticism in accepting APOLT for NCMLD. In fact, concerns for technical difficulties and for the risk of long-term graft atrophy due to the functional competition with a structurally normal native remnant exist. Slow progress in gene therapy research does not help, too. However, most of the above-mentioned issues have been recently addressed, and APOLT for NCMLS has been proved to be feasible with good results in experienced hands [133].

In the setting of NCMLD, domino APOLT represents an original strategy aiming at expanding the organ pool. A donor partial graft is used for APOLT in a NCMLD recipient, whose resected partial graft is transplanted into a child affected by a different NCMLD as an auxiliary graft. A further evolution of domino APOLT for the purpose of "donorless" transplantation may be cross-domino APOLT, where LLSs may be swapped between children with different NCMLD with no need for a donor [7, 133].

27.9.3 Surgical Technique

In small children, the preferred practice is to perform a left hepatectomy of the native liver and to replace it with a LLS.

The implantation of this auxiliary graft is similar to that of a LLS in standard LT. Outflow reconstruction is accomplished by means of an end-to-side anastomosis between the graft left hepatic vein and the stump of the native left and middle hepatic veins. For portal anastomosis, either the orifice of the left portal branch or a fresh venotomy on the main portal trunk may be used. In case of NCMLD, portal vein modulation is necessary to avoid portal steal and achieve preferential portal flow to the graft. On the contrary, portal vein modulation is usually unneeded in the setting of ALF since portal flow is preferentially directed to the graft due to the stiffness of the collapsed native remnant. Arterial anastomosis often represents a technical challenge because discrepancy between the left hepatic artery of the graft, from an adult donor, and the left hepatic artery of the paediatric recipient is common. Finally, hepaticojejunostomy is performed for biliary reconstruction [6, 133].

27.10 Conclusions

A wide range of technical options, in terms of both graft type and surgical strategies, are available for paediatric LT. Extensive experience with any graft type and any age group may timely allow for the appropriate solution. A clear understanding of each recipient's specific condition and awareness of graft-related peculiarities are the keys for the success of paediatric LT.

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