



Domino Liver Transplantation

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17.1 Introduction

Orthotopic liver transplantation is an established treatment for end-stage liver diseases and for some severe metabolic disorders and hepatic cancers, but an organ shortage is the limiting factor in meeting the need for the procedure. Explanted livers from patients with metabolic liver diseases who are undergoing liver transplantation, so-called domino livers, can be one of the solutions to diminish the organ shortage. Familial amyloidotic polyneuropathy (FAP) is an autosomal dominant disease associated with a mutation of the *TTR* gene. The liver produces variant transthyretin (TTR) amyloid fibrils, which accumulate in body connective tissues and various organs such as the heart, kidney, and small intestine. The result is dysfunction of these organs, leading to severe disability. The patients die 9–15 years after the onset of symptoms, due to malnutrition or heart complications. Until recently, the only potentially curative treatment has been liver transplantation. Because the FAP liver is entirely normal, apart from producing the mutated variant TTR, these explanted livers are well suited to be used for transplantation in selected patients. Obviously, there is a risk of transmitting the FAP disease by the explanted liver, but given the slow progression of FAP and the desperate situation of the potential domino liver recipient, we believe that the benefits outweigh the risks for selected recipients [1]. The first domino liver transplantation (DLT) using the explanted liver from an FAP patient was performed in Portugal in 1995. With time, the procedure has evolved strongly, and the technique is today used worldwide with good outcome [2, 3].

Because of the good results with domino FAP livers, other patients with isolated hepatic metabolic diseases were considered as potential domino liver donors. Examples of such metabolic disorders are primary hyperoxaluria, protein C deficiency,

certain urea cycle disorders (e.g., citrullinemia), and hypercholesterolemia. Considering the use of livers from donors with hepatic metabolic diseases other than FAP requires strict assessment of the benefit-risk ratio in the DLT recipient because the onset of manifest symptoms of the transmitted donor disease, at least for some disorders, appears to occur much more quickly than in recipients of domino FAP livers [2].

The DLT procedure includes two important factors that need careful consideration: (1) the risk of transmitting FAP or other metabolic disease by the transplanted liver and (2) the risk of surgical complications inherent in the demanding technique involving both the domino donor and recipient. Given that FAP has a low penetration rate even when there is a positive genetic diagnosis and that FAP patients do not show symptoms before the age of 15, one would expect manifest FAP disease in a DLT recipient to occur not earlier than 10–15 years after transplantation [2]. Some reports indicate, however, that the disease may manifest itself earlier than expected [2, 4–6], possibly as a consequence of the inevitable lifelong immunosuppressive medication after transplantation and that the mutated protein is introduced to the recipient at an adult age. Also, the safety of the domino donor must be carefully taken into account and given precedence.

These are crucial ethical issues to be considered, and the pros must be thoroughly balanced against the cons for both the donor and the recipient. Because FAP donor livers are normally functioning livers apart from producing the TTR variant, we believe that it is justified to use such livers for transplantation of patients with terminal liver diseases, whose life expectancy is shorter than the risk of acquiring the disease by graft transmission [7]. The DLT technique is well documented, and the procedure has been shown to be safe for both the domino liver donor and the domino liver recipient, yielding good results [8, 9]. It must be emphasized, however, that the surgery is demanding and should be carried out only by experienced surgeons trained in the technical procedure. From a technical point of view, it is essential to remember that the domino donor is also going to receive a transplant. Thus, when explanting the domino liver, the surgeon must leave enough long veins in the domino donor so that a subsequent vascular

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anastomosis is possible. Consequently, the explanted domino liver sometimes has very short hepatic and suprahepatic veins, requiring extensive back-table work in order to reconstruct and elongate the vessels for successful transplantation.

Criteria for acceptance as a domino liver graft recipient vary between centers. In our center, a DLT candidate must previously have been accepted for conventional liver transplantation. Examples are patients for whom palliative treatment rather than long-term cure remains the only option, as well as some elderly patients. Both the FAP donor and the domino recipient must be thoroughly informed about the procedure and the associated potential risks, which means

not only the operative risk but also the possible future risk of transmitting the metabolic disease with the graft. The recipient must be informed that the inevitable lifelong immunosuppressive treatment after the DLT may alter the natural course of the underlying disorder and may provoke transmitted disease symptoms earlier than expected [2].

To be accepted as a domino liver recipient at our institution, at least one of these three criteria should be fulfilled:

1. Hepatocellular carcinoma
2. Patient >60 years of age
3. Late retransplantation

Figure 17.1

(a) In a domino donor hepatectomy, the bile duct should be transected at a level that permits a single lumen on the graft side, enabling a secure duct-to-duct reconstruction, and the extrahepatic portal vein is cut approximately 2 cm from the junction of the splenic and superior mesenteric veins, leaving enough vessel length in the donor for a safe end-to-end portal reconstruction. (b) The domino donor liver is shown with the orifice of the transected subdiaphragmatic caval vein on the liver's dorsal side and the right hepatic vein and the common trunk of the middle and left hepatic veins on the ventral side

17.2 Domino Donor Hepatectomy: Technical Aspects

17.2.1 Approach to the Liver Hilum

The hepatectomy from domino donors must be performed in such a way that the liver may be safely used for transplantation in a domino recipient, but without jeopardizing the safety of the donor. The standard method of domino donor hepatectomy is outlined briefly as follows. After full mobilization of the liver from its attachments and after isolation of the hilar structures, the bile duct should be transected at a level that permits a single lumen on the graft side, enabling a secure duct-to-duct recon-

struction of the FAP domino, as shown in Fig. 17.1a. The extrahepatic portal vein is cut approximately 2 cm above the junction of the splenic and superior mesenteric veins, leaving enough vessel length in the FAP donor to enable a bypass plug in and a subsequent safe end-to-end portal reconstruction (Fig. 17.1a). Immediately after the transection of the portal vein, one large-bore catheter is inserted to the portal vein of the FAP patient for the bypass. Only then is the hepatic artery clamped and cut at the level of the gastroduodenal artery (GDA), thereby minimizing warm ischemia time. The hepatectomy usually includes the retrohepatic caval vein and the use of an external veno-venous bypass, because FAP patients lack portal collateral circulation and are hemodynamically fragile.

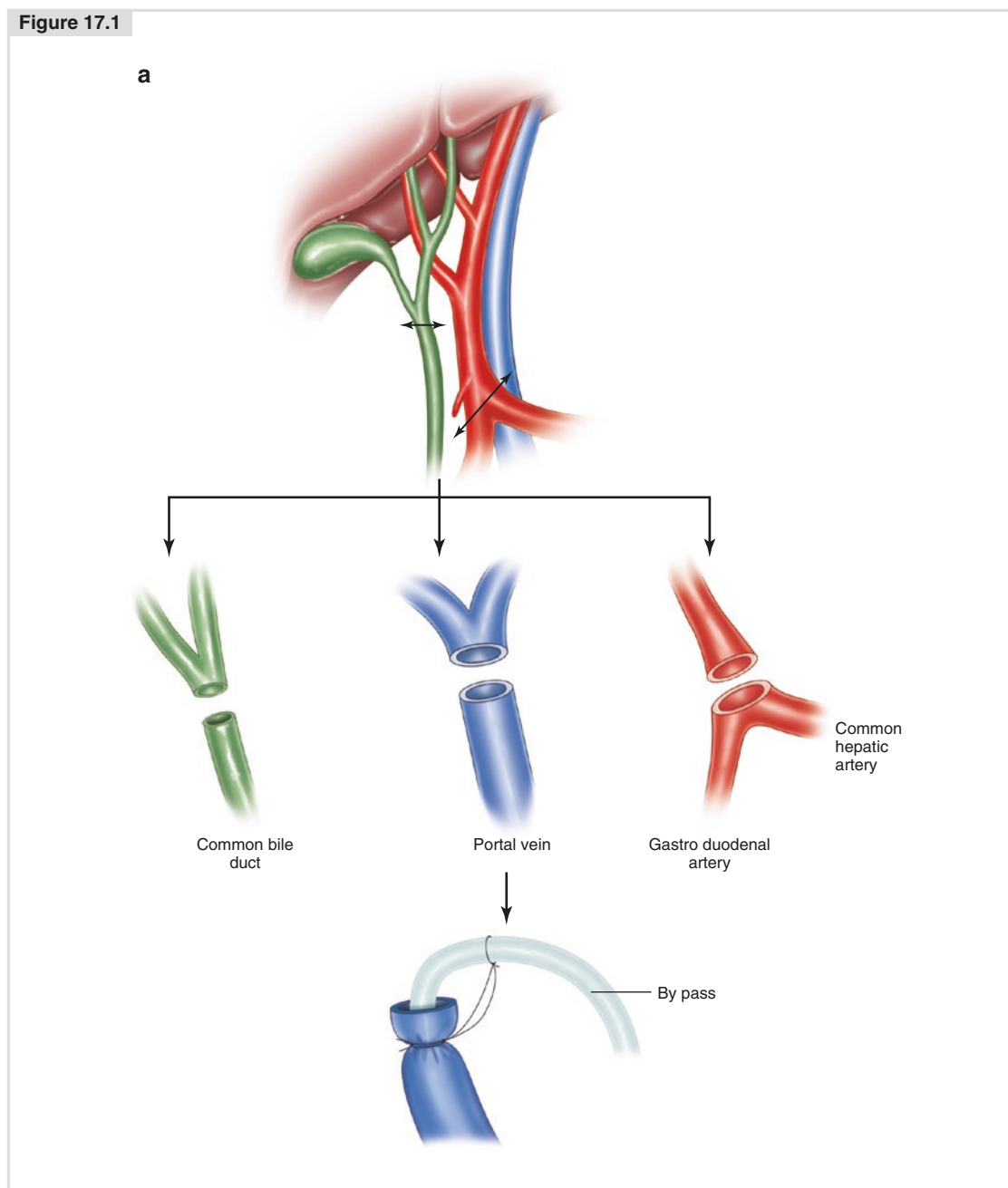
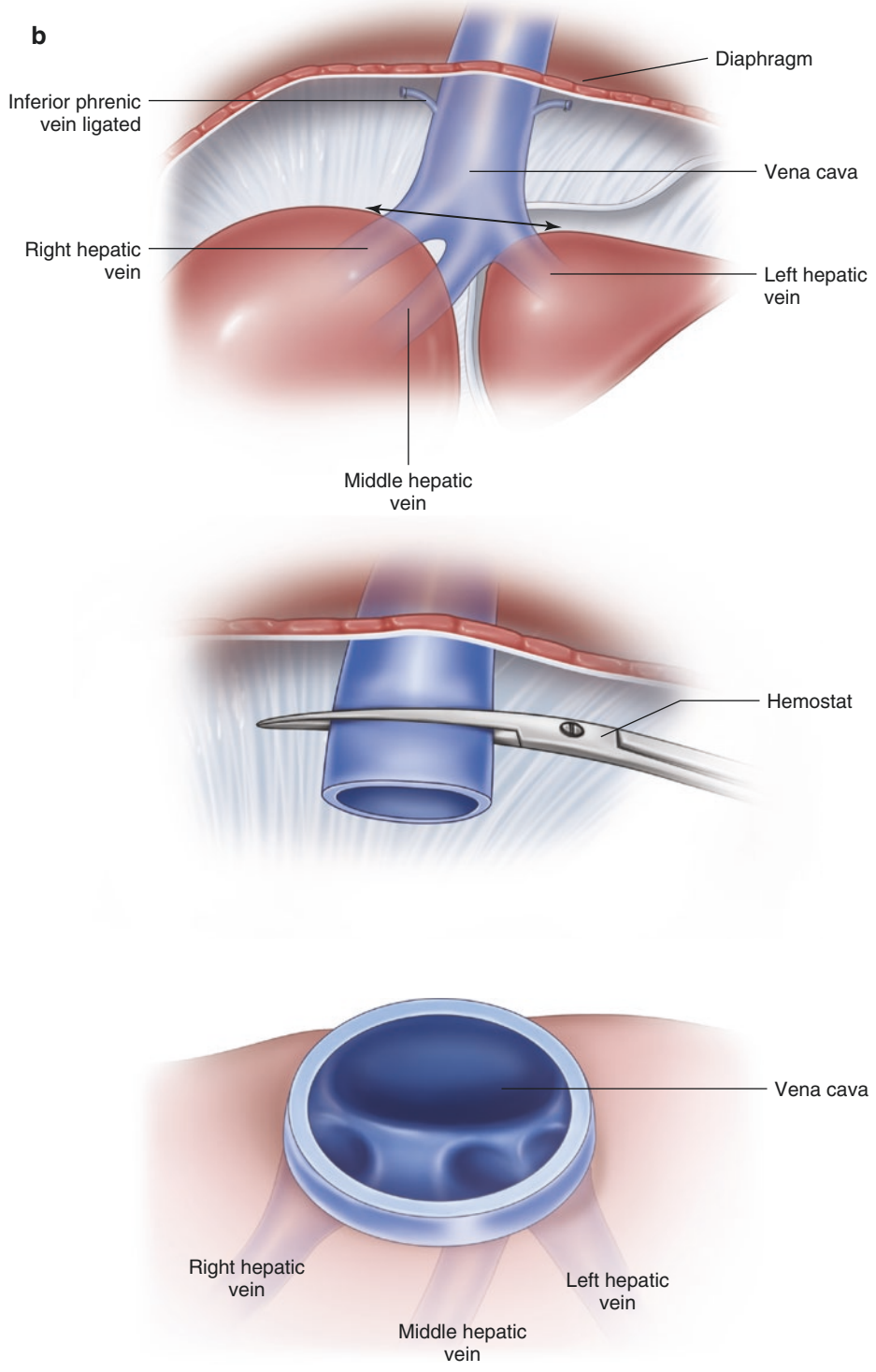


Figure 17.1

(continued)

Figure 17.1



17.2.2 Mobilization and Transection of the Caval Vein

We advise leaving a longer vena cava segment in the domino donor to facilitate a safe caval vein reconstruction (Fig. 17.1b). Thus, we accept a somewhat short and sometimes “defective” vena cava in the explanted domino liver. To maximize the length of the suprahepatic caval segment, the right and left phrenic veins are usually ligated and tran-

sected (Fig. 17.1b). The caval vein is to some extent dissected free from the diaphragm, and a Klintmalm vascular clamp is used to clamp the cava below the diaphragm. Figure 17.1b shows the domino donor liver with the orifice of the transected subdiaphragmatic caval vein on the liver’s dorsal side, the right hepatic vein and the common trunk of the middle and left hepatic veins on the ventral side. The septa of the hepatic veins are very close to the orifice of the caval vein.

Figure 17.2

Venoplasty reconstruction: **(A)** If the infrahepatic caval vein is long enough, a segment from its distal end can be used to create a patch for venous grafting **(a)**. The infrahepatic vena cava may be too short for the creation of a patch **(b)**, requiring a vein graft from the deceased donor who is giving the liver to the FAP patient. **(B)** If the suprahepatic vena cava is too short or deformed, the caval vein can be somewhat elongated by dissecting part of it from the liver parenchyma; to facilitate the anastomosis to the recipient’s vena cava, a septoplasty joins the right hepatic vein and the common trunk of the left and middle hepatic vein. **(C)** A venous patch from the domino liver’s infrahepatic vena cava, or a vein graft from a deceased donor, can be connected to the orifice of the vena cava in the liver graft using 5-0 or 6-0 polypropylene continuous or interrupted stitches. If the liver has a very short dorsal caval wall, the vein patch should be connected to the dorsal wall of the liver’s vena cava

17.2.3 Back-Table Work: Evaluation of the Explanted Liver and Its Vessels

When the liver is free, it is placed in a basin filled with ice-cold preservation solution (temperature about 4 °C). To remove any remaining blood, the explanted liver is perfused via the portal vein with an organ-preserving solution such as UW® Cold Storage Solution (Wisconsin Alumni Research Foundation [WARF], Bridge to Life Ltd., USA) or Custodiol® HTK solution (Dr. Franz Köhler, Chemie GmbH, Germany). It is not necessary to perfuse through the artery. The perfusion stops when the effluent is clear. The liver is carefully inspected in the cold

basin, and any parenchymal tears should be repaired. During the perfusion, the vessels should be inspected, and any holes or small leaking patent vessels should be ligated or sutured. The graft should be thoroughly inspected, and the length of the vessels should be evaluated for reanastomosis in the recipient. If needed, venoplastic reconstruction should be undertaken (Fig. 17.2A). The suprahepatic vena cava of domino grafts tends to be slightly to extensively short (especially its ventral wall). Sometimes the three hepatic veins remain as separate openings and must be reconstructed to make safe reanastomosis possible. There are several options for the reconstruction of the liver's vena cava. If the liver's infrahepatic caval vein is long enough, a

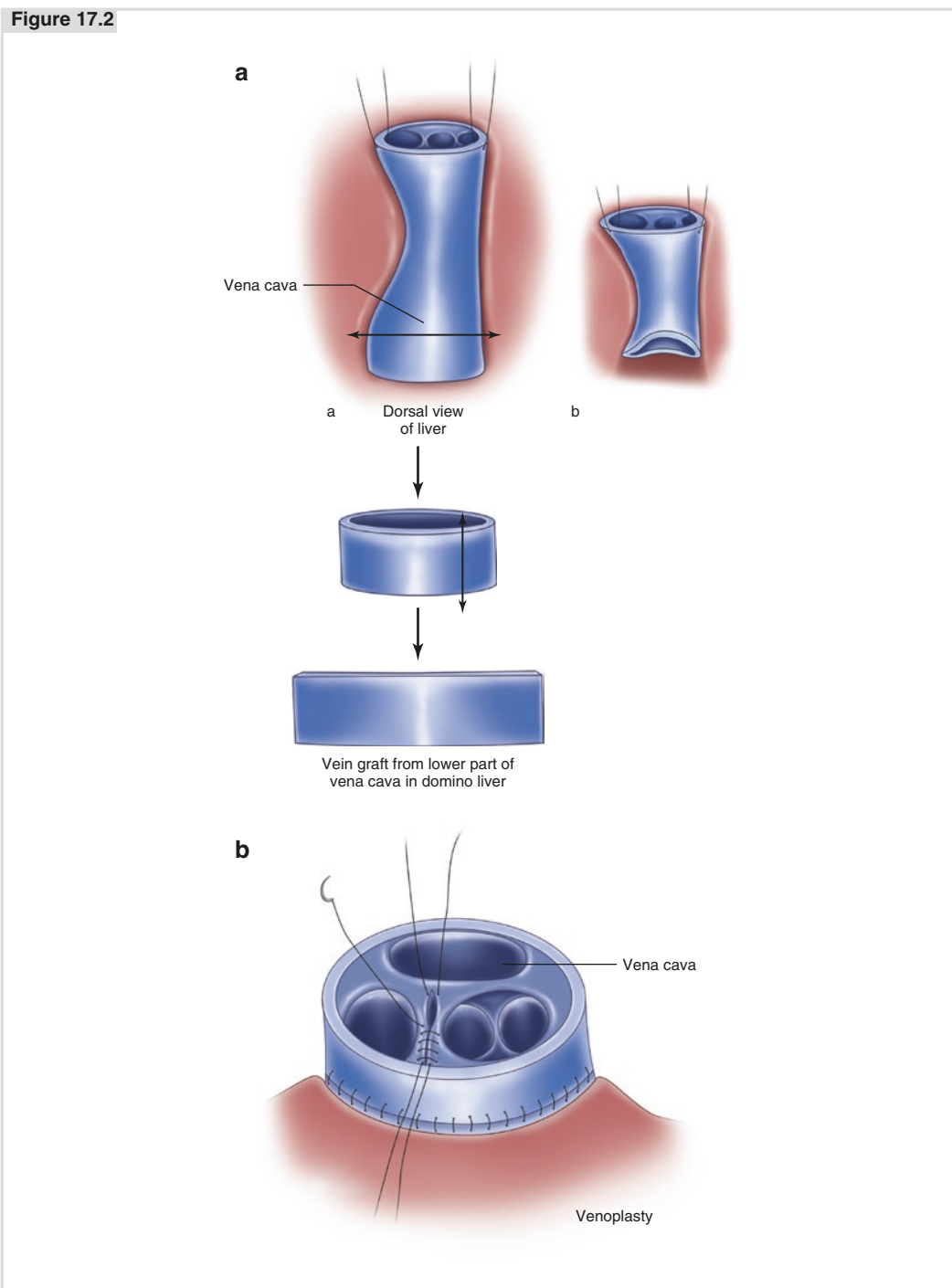
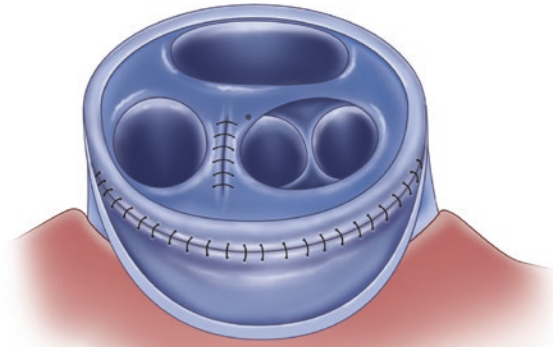


Figure 17.2

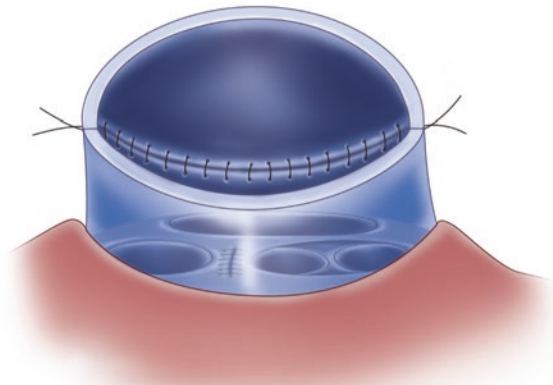
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Figure 17.2

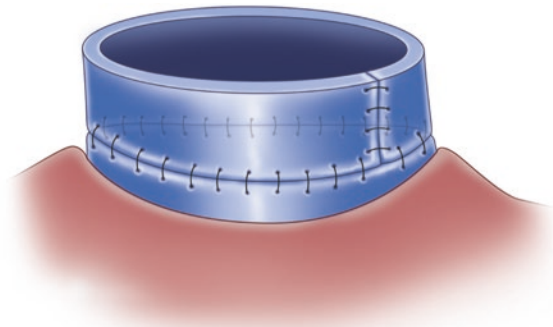
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**Venoplasty plus vein patch to ventral wall
(frequently needed)**



**Venoplasty plus vein patch to dorsal wall
(seldomly needed)**



Vein patch to whole wall

segment from its distal end can be used for venous grafting (Fig. 17.2A(a)). A useful venous patch can be obtained by cutting the circumference to create a rectangular patch, which can be used to elongate the anterior wall of the suprahepatic vena cava. If the liver's infrahepatic vena cava is too short, precluding the use of part of it as a venous patch (Fig. 17.2A(b)), a vein graft from the deceased donor who is giving the liver to the FAP patient should be used instead.

17.2.4 Venoplasty Reconstruction of the Suprahepatic Vena Cava

If the suprahepatic vena cava is very short or deformed, an anastomosis would be very risky or impossible, and therefore a venoplasty reconstruction should be undertaken (Fig. 17.2B). The caval vein can be somewhat elongated by meticulously dissecting part of it from the liver parenchyma, taking care not to damage the vessel wall. The inside of the orifice should be carefully inspected to understand the anatomy of the hepatic veins. To facilitate the anastomosis to the recipient's vena cava, a septoplasty is done by joining the right hepatic vein and the common trunk of the left and middle hepatic vein using 5-0 or 6-0 polypropylene continuous sutures, if they were separated during the donor procedure.

If a direct anastomotic suture between the domino liver's vena cava and the recipient's caval vein seems too difficult or risky because of vessel abnormalities, one should aim to correct the abnormalities as much as possible. A venous patch from the domino liver's infrahepatic vena cava, or a vein graft from the deceased donor, should be connected to the orifice of the vena cava in the liver graft using 5-0 or 6-0 polypropylene

continuous or interrupted stitches (Fig. 17.2C). The size and form of the patch will depend on the size and form of the tissue defect affecting the caval orifice. Reconstruction on the back table should be performed foreseeing the subsequent anastomosis between the reconstructed vein and the recipient's vena cava. Most often, the ventral wall needs to be lengthened because of the short distance to the liver parenchyma. Sometimes the transection of the donor's caval vein is done so that a long dorsal wall of the vena cava remains in the domino donor, leaving the liver with a very short dorsal caval wall. In such cases, the vein patch should be connected to the dorsal wall of the liver's vena cava (Fig. 17.2C).

One way of preserving the inferior vena cava during liver transplantation is by using the so-called piggyback technique. The idea of this procedure is to avoid retrocaval dissection, to reduce the risk of bleeding and facilitate caval anastomosis in patients receiving large-for-size grafts. The technique avoids the need for venous bypass, but the piggyback technique can be associated with some disadvantages and complications, including hepatic venous outflow obstruction and thrombosis in up to 10% of patients, in whom the inappropriate size of the hepatic vein outlet results in venous congestion of the liver allograft. If the piggyback procedure is considered, the tobacco-pouch suture will be placed at the edge of the infrahepatic vena cava using 3-0 polypropylene. If an infrahepatic cavo-cavostomy is planned, the suprahepatic vena cava is closed using a vein patch.

After completing the preparation of the vena cava, the portal vein is dissected free from surrounding tissues, extending the dissection as far as to the bifurcation of the right and left portal veins. The portal vein should be tested for leakage and any holes are repaired. Then the hepatic artery is

Figure 17.3

A conventional vena cava replacement with two caval end-to-end anastomoses. The suprahepatic vena cava has been lengthened by attaching a venous patch to facilitate the anastomosis

inspected and trimmed in preparation for the anastomosis. Any patent small vessel branches are ligated, and leaking holes in the wall are repaired by suture. When handling the artery, care must be taken not to injure the arterial intima.

Finally, the gall bladder is cut open and flushed empty of bile. A small catheter is carefully inserted into the bile duct and the duct is flushed. To preserve and secure the vascular supply to the common bile duct, the tissues and vessels surrounding the bile duct should not be dissected.

17.3 Transplantation in the Domino Liver Recipient

17.3.1 Venous Reconstruction with Cava Replacement

If possible, the hepatectomy of the domino liver recipient is performed in parallel to the donor operation. However, crucial vessels such as the hepatic artery and the portal vein should not be dissected free until it has been confirmed that the donor graft is usable. The hepatectomy is performed with or without vena cava, depending on the patient's underlying disease and the prevalent vascular status. Even in the case of a planned vena cava replacement procedure, the infrahepatic vena cava in the domino recipient should be kept as long as possible, given that the vena cava on the domino graft may be very short.

After the hepatectomy is completed and abdominal hemostasis has been secured, the liver is moved from the ice-fluid to the recipient operating table and placed in the operative field. The first step of the procedure is to reanastomose the caval veins of the recipient and the liver graft. First, the suprahepatic caval

veins are sutured, and then the infrahepatic caval vein anastomosis is completed. Figure 17.3 illustrates a conventional vena cava replacement with two caval end-to-end anastomoses. In such a case, an external veno-venous bypass should also be used in the domino recipient. The figure shows that the suprahepatic vena cava has been lengthened by attaching a venous patch to facilitate the anastomosis. When a patch is used, sometimes the vein needs to be trimmed to ensure a straight anastomosis. Continuous sutures with 3-0 and 4-0 polypropylene are used for the anastomosis. Without the use of an elongation patch, the orifices of the hepatic veins come very close to the anastomotic suture line, which could result in deformity with leakage and outflow problems. To minimize such risks, it is essential to use adequate, but not large, suture bites.

17.3.2 Venous Reconstruction Without Cava Replacement

The piggyback technique can be used for the venous reconstruction without the need of a veno-venous bypass. The suprahepatic vena cava of the graft is connected to the common trunk of the hepatic veins of the domino recipient (Fig. 17.4). The suture of the ventral wall must be done very carefully in order to avoid hepatic venous outflow obstruction. The recipient common trunk of the hepatic veins has to be prepared so that there is enough length for the anastomosis.

Alternatively, the infrahepatic vena cava of the domino graft can be connected to the preserved recipient vena cava by an end-to-side anastomosis. In such a case, the suprahepatic cava should be closed using a vein patch in order to prevent outflow obstruction of the hepatic veins (Fig. 17.4) [10]. This

Figure 17.3

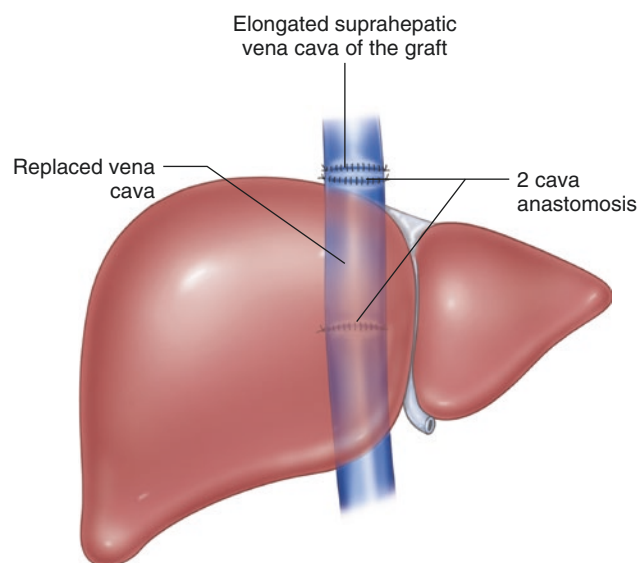
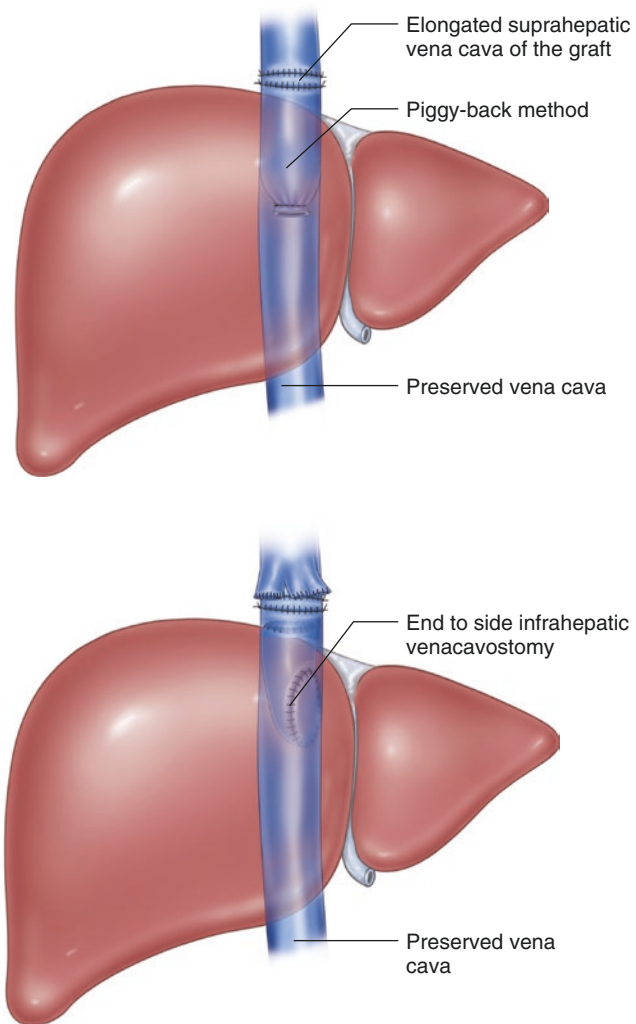


Figure 17.4

Piggyback technique to preserve the inferior vena cava: The suprahepatic vena cava of the graft is connected to the common trunk of the hepatic veins of the domino recipient. The tobacco-pouch suture is placed at the edge of the infrahepatic vena cava. If an infrahepatic cavo-cavostomy is planned, the suprahepatic vena cava is closed using a vein patch

Figure 17.4



method can be useful as a rescue anastomosis technique in the event of outflow obstruction in domino liver recipients in whom the piggyback procedure was previously used. In theory, a side-to-side anastomosis of the vena cava is also possible, but it is usually difficult to expose the vena cava of both the liver graft and the recipient and to have enough length.

17.3.3 Back-Table Work in Domino Livers Without Vena Cava

Some centers prefer to dissect the vena cava free from the liver when performing the domino donor hepatectomy,

thereby preserving and leaving the vena cava in the domino donor and avoiding the need for a veno-venous bypass. In such cases, there is no vena cava with the graft, and the hepatic veins are usually transected separately, as shown in Fig. 17.5. The middle and left hepatic veins can be joined by performing a septoplasty. If the distance between the common trunk and the right hepatic vein is long and there are short vein cuffs, a conduit graft of the inferior vena cava with the common iliac veins from the deceased donor or a venous patch should be used (Fig. 17.5) [11, 12]. The connected venous sheet-patch is transformed to a conduit shape for anastomosis suturing by the piggyback method (Fig. 17.5). The vascular connections between the

Figure 17.5

If the vena cava is left in the domino donor, the hepatic veins are usually transected separately. The middle and left hepatic veins can be joined by performing a septoplasty. If the distance between the common trunk and the right hepatic vein is long, a conduit graft of the inferior vena cava with the common iliac veins from a deceased donor or a venous patch should be used

domino recipient and a graft missing the vena cava is rebuilt only by using the piggyback method. The Y-graft or reconstructed patch graft is anastomosed to the common trunk of the recipient's hepatic veins (Fig. 17.6).

17.3.4 Portal Vein and Arterial Restoration in the Recipient

After the caval venous reconstruction, the portal vein is anastomosed by an end-to-end continuous suture with 5-0 poly-

propylene. Before finishing the suture, the surgeon must remember to leave a "growth factor" to allow expansion of the suture line and avoid stricture of the anastomosis when the vascular clamps are released and blood flow is restored to the portal vein.

The arterial anastomosis is usually undertaken by suturing the hepatic artery of the liver graft to the bifurcation of the recipient's gastroduodenal artery, using 6-0 polypropylene with continuous or interrupted stitches.

Figure 17.5

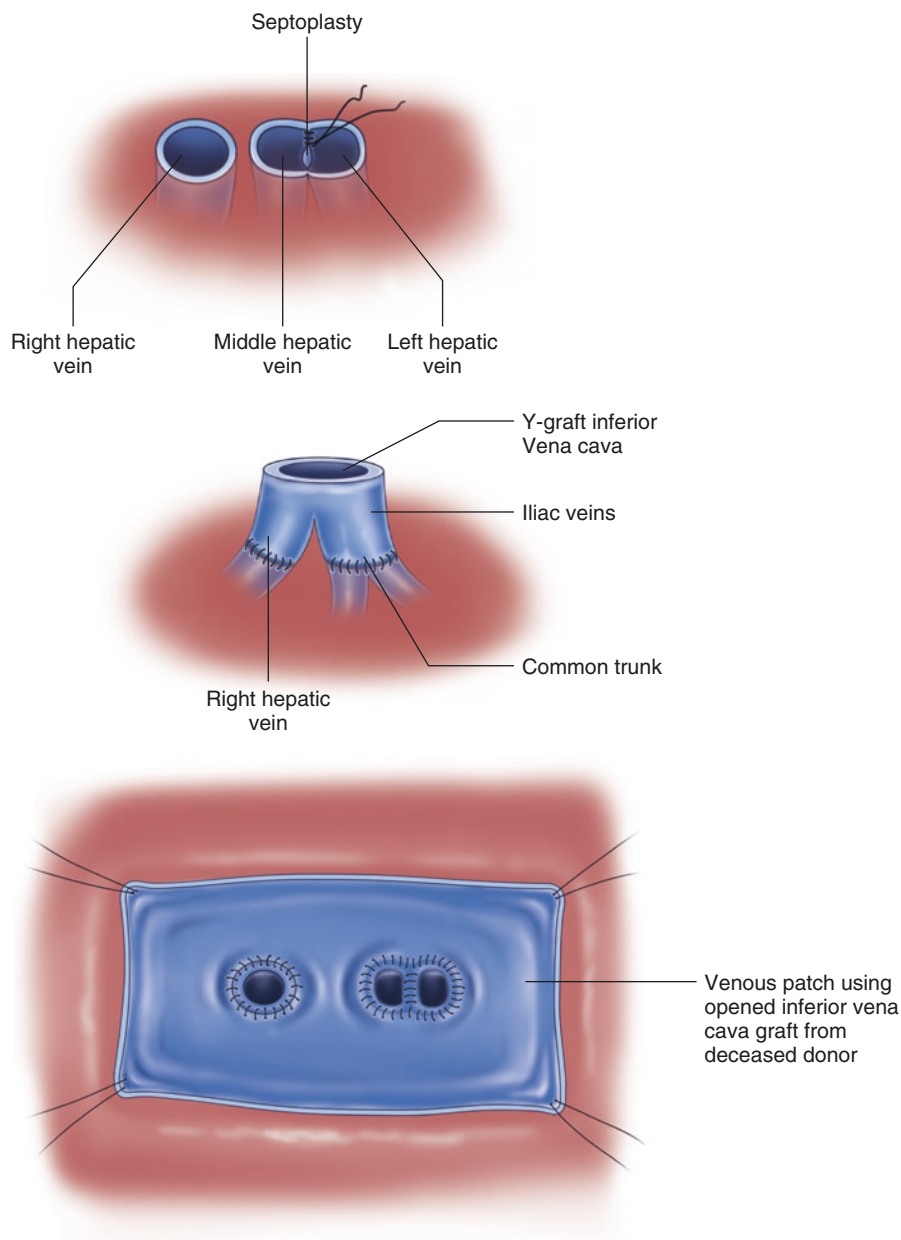
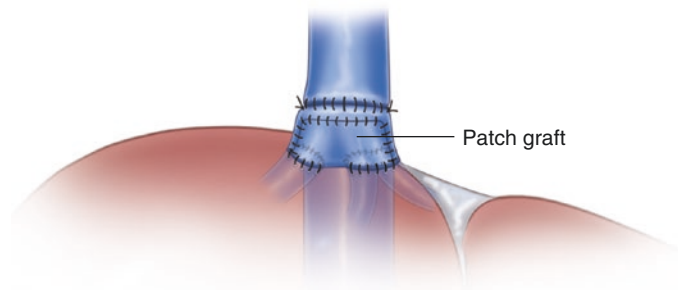
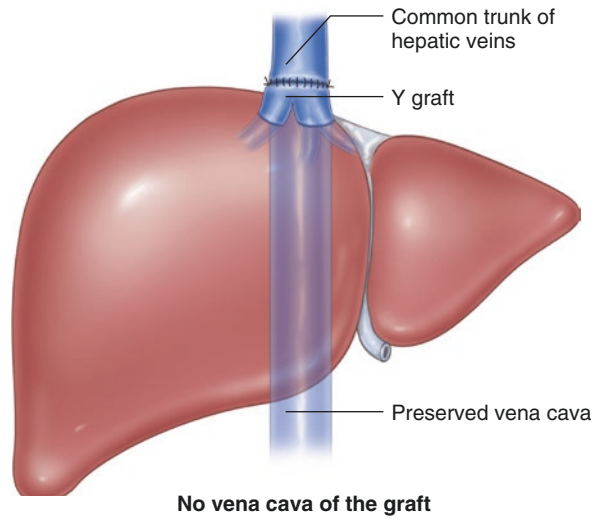


Figure 17.6

The Y-graft or reconstructed patch graft is anastomosed to the common trunk of the recipient's hepatic veins

Figure 17.6



17.3.5 Bile Duct Restoration in the Domino Liver Recipient

When all vascular connections have been accomplished, transplantation is completed by restoring the bile flow. Bile duct reconstruction can be undertaken by an end-to-end choledochocholedochostomy using continuous or interrupted 6-0 PDS sutures or by a Roux-en-Y choledochojejunostomy. The method will depend on the recipient's underlying disease and bile duct status. These procedures do not differ from bile duct restoration techniques in other liver transplant recipients.

17.4 Results

Studies have shown that FAP patients who underwent liver transplantation and agreed to simultaneously donate their native liver for domino transplantation had vascular and biliary complication rates and survival rates similar to those of FAP patients who did not donate their livers [1, 8]. Moreover, recipients of domino liver grafts had similar technical complication rates and similar morbidity and mortality rates as a control group [8]. Thus, it can be concluded that the domino procedure does not increase the operative risk to either the domino donor or the domino recipient. Nor does the long-term survival of these patients after transplantation seem to be inferior [7, 8].

With regard to the recipient of the domino liver, one must bear in mind the risk of transmitting the donor's underlying disease to the recipient. Transmission of the underlying donor metabolic disorder has been reported by some centers, and in these cases symptoms became manifest 7–10 years after DLT [2]. That being said, it should be emphasized that in most domino recipients, transmission has not become a clinical problem within 10 years.

17.5 Conclusion

DLT using an FAP liver has evolved to become an established procedure that should be undertaken by transplant surgeons who are experienced in managing FAP patients and performing such transplants. The DLT procedure has some important aspects that must be considered. First, the safety of the domino donor must not in any way be compromised. The hepatectomy in the FAP patient who donates the domino liver must be performed so that the liver may be safely used for transplantation in another patient, without increased risk to the donor.

In the recipient, the standard DLT technique is in many ways similar to conventional orthotopic liver transplanta-

tion. The technical difficulty is mainly in managing the reconstruction of the hepatic veins to avoid outflow obstruction. Reconstruction may be feasible without the use of a venous patch. In some cases, it may be necessary to perform a septoplasty between the common trunk of the middle and left hepatic vein and the right hepatic vein. If primary suture is not possible, a venous patch obtained from the infrahepatic vena cava of the domino graft or from the deceased donor should be used. The anastomosis may be performed by conventional cava replacement with venovenous bypass or by a piggyback technique to the preserved vena cava in the domino recipient. Explanting the donor FAP liver while preserving the vena cava is also compatible with domino donation. Moreover, the site of the anastomosis can be changed to the infrahepatic vena cava without any increased technical difficulty. Side-to-side caval anastomosis has not been reported in DLT, because the domino graft usually has a very short retrohepatic vena cava. The technical considerations and reconstructive aspects of the portal vein, hepatic artery, and bile duct are not particularly different from those of any orthotopic whole-graft liver transplantation.

The postoperative management is also similar to that of any non-domino liver transplantation patient. If postoperative clinical symptoms and laboratory tests indicate vascular outflow problems, one should investigate them radiologically, as for any liver transplant patient, and take appropriate measures.

In summary, from a technical point of view, DLT demands extra care with regard to the reconstruction of the hepatic veins and the vena cava cuff. Furthermore, it is extremely important that all FAP patients and all potential recipients of a domino graft are properly informed on the nature of the FAP disease, as well as of the potential risks related to the domino liver transplantation and the transmission of the donor's metabolic disorder. Because of the risk of disease transmission, we advocate that recipients of domino livers should be regularly monitored by extensive neurological protocols (including electroneurography) and should undergo cardiac evaluation at regular intervals. Any finding that raises suspicion of a de novo metabolic disorder should be assessed in combination with clinical symptoms, electroneurography findings, and tissue biopsy for the evidence of TTR amyloid deposits in order to confirm such a diagnosis.

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