Multiorgan Procurement for Transplantation

A Guide to Surgical Technique and Management

Paolo Aseni
Antonino M. Grande
Luciano De Carlis
Editors

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In memory of Professor Vittorio Staudacher (1913–2005) and Professor Lino Belli (1924–1996) pioneers of transplant surgery, to honor their exceptional dedication and enthusiasm to transplant research.

Foreword

For this book edited by Paolo Aseni, Antonino M. Grande, and Luciano De Carlis, contributing authors were requested to discuss the latest advances in donor management and surgical techniques for multiorgan procurement. Today, modern transplant medicine can guarantee excellent short- and long-term results for all types of transplants, with survival rates of up to 80 % after 5 years and about 60–70 % after 10 years. In no other field of surgery, with the exception of benign or functional disorders, can such excellent results be achieved following complete failure of an organ. Currently two factors limit broader use of organ transplantation: on the one hand, the shortage of organ donors and, on the other hand, the increase in donors who are not ideal because their organ function is impaired. These two limitations prevail despite the fact that donor willingness in the general public is satisfactory to high throughout. Several other factors contribute here to play an equally important role like the lack of established ubiquitous facilities for donor recognition and the lack of logistics in donor management in several Central European countries or regions. New discussions on the definition of brain death in Germany and the increasing financial pressure on all hospitals are further aspects.

The first two parts provide a comprehensive look at problems ranging from donor recognition, general ethical aspects, but also the principles underlying the concept of brain death, the diagnosis and management of persons dying from intracranial pressure to organ harvesting with all its metabolic and hemodynamic alterations. No less important with a view to increasing transplants is the non-heart-beating concept that for health caregivers, but also for society and particularly the next of kin, can present emotionally exceptional circumstances and presumably only marginally improve the shortage of organs.

Part 3 and 4 deal with the role of surgery in organ harvesting, which in the case of multiorgan donors is usually conducted in brain dead patients. In addition to abundantly illustrated tips and tricks, these chapters demonstrate the enormous importance of this act in the transplant setting. Organ quality is not only influenced by donor factors. Indeed, damage and complications that can occur in the course of organ procurement can be deleterious for the recipient. The consequences can be impaired organ function, higher re-transplant frequency, and poorer survival. While countless discussions and the literature evidence this fact, it is given too little attention in daily routine. Principles such as “the best or the most experienced transplant surgeon” should harvest the organs are only rarely implemented, with as much to be said for the level

of anesthesiological management requiring the same standard of care when transferring the patient from the ICU to the operating room. This book also takes a look at special techniques such as liver splitting or bench surgery, namely, the preparation of donor organs for implantation. The interested reader will find answers and information on most questions related to organ donation that can influence work with other medical professionals on a daily basis.

The last section of this book, part 5, concerns live donation of liver and kidney. Much more important than the technical aspects and challenges of the donor operation, which today can be minimally invasive and still provide excellent results for donor and recipient, is the fact that a healthy person undergoes surgery for the removal of a kidney or part of his liver. This act of solidarity is unique among medical procedures. Here, donor safety must take priority over all other aspects and calls for a multistep workup algorithm that is not invasive whenever possible. In addition to psychological exploration and counseling, determination of the voluntary nature of the organ donation takes priority. By the same token, any financial motive should be ruled out as completely as possible. For living organ donation the highest surgical and anesthesiological expertise is required, because an avoidable complication is deemed bodily harm. A flat learning curve, which is a fact for many surgical innovations but also for inexperienced surgeons, is not justifiable here.

Finally, I would like to again emphasize the importance of this book and congratulate the editors as well as all the contributing authors on having brought together the important aspects of organ donation in such an excellent manner. This work should be considered a mandatory reading for all colleagues involved in the organ donation process and above all be a tribute to the donors, who through their solidarity help lessen suffering and sustain life.

Tuebingen, Germany Alfred Königsrainer

About the Editors

Paolo Aseni, after his degree in Medicine at the University of Milan in 1975, trained abroad in different centers in Germany and France: at the Medizinische Hochshule in Hannover and in Zentrum für Experimentelle Medizin in München in 1978, then in the next years, at the Hôpital Beaujon in Paris and in Hôpital Paul Brousse in Villejuif. Since 1980, he has been working at the Department of Surgery and Transplant Center in Niguarda Hospital in Milan, Italy. He is currently Associate Surgeon and responsible for the surgical training in Medicina d'Urgenza – Emergency Department in the same hospital. Since 1989, he has been also Assistant Professor for Anatomy and Human Macroscopic Morphology, University of Medicine, Milan.

Antonino M. Grande earned his degree in Medicine at the University of Pavia (Italy) in 1980. He trained abroad at the Department of Cardiovascular Surgery, Texas Heart Institute, Houston, Texas, USA, from 1982 to 1984 and then in Marseille (France). Since 1986, he has been working as attending surgeon at the IRCCS Fondazione Policlinico San Matteo in Pavia, Italy, in the Cardiac Surgery – Heart and Lung Transplant Department. Dr. Grande has also over 25 years of experience in cardiovascular postoperative intensive care; his main clinical interests include heart failure, heart/lung transplantations, and mechanical circulatory support. Between 2000 and 2010, he has been Assistant Professor for Surgical Anatomy at the University of Pavia.

Luciano De Carlis got his degree in Milan in 1979 and trained as visiting fellow at the Transplant Surgery Center in Pittsburgh (USA) in 1984, in 1987, and again in 1988, studying particular aspects in the field of liver, kidney, pancreas, heart, and heart-lung transplantation. Another important experience abroad, this time as visiting professor, was at the University of Tokyo in 2001. Prof. De Carlis has been working since 1985 at the Niguarda Hospital in Milan, Italy, specializing in particular in the field of renal, hepatic, and pancreatic transplantation. He is currently Professor of Surgery at the University of Milano-Bicocca School of Medicine, and Director of the Department of Surgery and Transplant Center at the Niguarda Hospital in Milan, where he introduced the first adult living donor liver transplantation program in Italy and, recently, the first Italian liver transplant program from "donation after cardiac death".

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Part I

Expanding the Donor Pool and Evaluation of the Possible Organ Donor

Ethics of Organ Donation

1

Antonino M. Grande and Paolo Aseni

Key Points

- The first basic principle is that all individuals can donate as well as receive an organ.
- A balance of all possible ethical considerations should be discussed, including transplant benefit and clinical utilitarian demand, with respect for an individual's choice whether to donate an organ in life or after death.
- The increasing success of living donor transplants (above all renal transplants) is the primary justification for using living donors, which can be considered a "regrettable necessity" due to the continuing shortage of deceased donors.
- A full informed consent is the minimum prerequisite for an altruistic living donor, and this consent can only be obtained if the donor has a proper understanding and correct information about the risk for the donation procedure and the donor mortality rate which is up to approximately 12–13 per 6,000 cases (0.2 %, including donors of left or right liver lobes and donors to both adult and child recipients) [1].
- It is inappropriate to discuss brain death and the consequences with the patient's family without also respecting donors and families in terms of the dignity, honesty, and authenticity of each person involved in the donation path.
- Criteria for the acceptance of living unrelated donors should be fully discussed by the local ethical committee and, as usually required by the majority of countries, by permission of the special legal courts.
- Living donor transplantation for commercial motivations must be strongly discouraged and is considered unacceptable by the majority of International Societies of Transplantation.

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1.1 Basic Principles in the Ethics of Organ Donation

The first ethical issue in organ transplantation involves organ shortage. Although researchers apply all their efforts to increase the donor pool,

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there are more people in need of a transplant than there are organs available.

Decision to Donate The choice to donate involves two different points of view:
(a) One's own organ donation after death
(b) Organ donation of a next of kin

Whether to donate an organ for transplantation is a personal decision that should be well informed and freely chosen. Information should be disseminated by establishing and implementing educational programs that address the key aspects of organ donation and transplantation. Organ donation is a "gift of life" with the aim of saving human lives. Furthermore, the establishment of potential donor registration consent in driver's licenses or other documents, including Internet sites, has been employed. However, these attempts have scarcely increased organ donation from deceased donors [1–7].

The majority of religions, including Christianity, Judaism, and Islam, do not object to this fundamental principle. For Catholics, transplants are morally and ethically acceptable, and organ donation is encouraged as an act of charity; Pope Pius XII [8] in 1956 declared that "A person may will to dispose of his body and to destine it to ends that are useful, morally irreproachable and even noble, among them the desire to aid the sick and suffering… This decision should not be condemned but positively justified." In August 2000, Pope John Paul II at the International Congress on Transplants in Rome [9] said "There is a need to instil in people's hearts, especially in the hearts of the young, a genuine and deep appreciation of the need for brotherly love, a love that can find expression in the decision to become an organ donor." The Conservative Movement's Committee on Jewish Laws and Standards has stated that organ donations after death represent not only an act of kindness but are also a "commanded obligation" that saves human lives. Leviticus 19:16 orders, "Do not stand by while your neighbor's blood is shed," which suggests that one should apply any resource to save a life. Islam allows and encourages donations by living and deceased donors. The first precept of Buddhism is to relieve suffering, and organ donation is considered as an act of generosity. Hinduism does not prohibit organ donations. Jehovah's Witnesses are often considered to be against organ donation because they oppose blood transfusion. However, a decision for or against transplantation is as an individual choice, because organ donation and transplantation can be accepted under the assumption that no blood is transfused during the transplant procedure [10].

A real increase in organ donation has been obtained in some countries in which the concept of "presumed consent" has been approved. This model implies that every adult individual who dies is a potential donor unless he has indicated his objection while alive and regardless of the wishes of his family. This mechanism is also called "silent consent"—the silence equals consent, in effect, and explicit opposition to donation should be expressed during life. Several countries in Europe and Asia, such as Spain and Singapore, have accepted this principle on moral and legal grounds and have increased organ donation from the average 20/million people seen in the United States, United Kingdom, and Canada to almost 40/million people in silent consent countries [2, 11].

The principle of presumed consent has created a real increase in donation, but is this strategy ethically acceptable? First, all the citizens should be correctly informed about presumed consent. Others can assert that people are neither the administrators nor the owners of their bodies. The respect for the dead person does not equate to the body's inviolability; organ use may be justified by the purpose of this practice—solidarity with those who suffer from highly disabling and debilitating diseases for which the only therapy is organ replacement. Therefore, behind the principle of presumed consent is the hope of creating greater awareness that individuals can donate body parts after death. The presumed consent to donate organs is justified by the fact that throughout the course of their life, individuals have never given explicit consent to join the society where they live. Consequently, there are no reasons to justify a different treatment when individuals die, as though they depart from the society where they lived; it is better to give priority to the relationship toward other members of the society of

which we have been a part during the course of life rather than a narrow and limited concept to maintain body integrity. However, while educational programs are essential, it is equally important to avoid creating clamor in the press surrounding particular medical situations for comatose patients. It is easy to find newspaper articles in which the donor is described as a man waiting to be executed. Readers would certainly be shocked to learn that just before the "execution," the donor suddenly and miraculously recovered. Therefore, for those that work every day in transplant surgery, it is not rare to read sensational headlines such as "The boy who came back from the dead: experts said car crash teen was beyond hope. His parents disagreed… His devastated parents were even asked to consider donating his organs," which goes on to read, "Convinced they saw a 'flicker' of life as Steven lay in a coma, John and Janet T. rejected advice to switch off his life support machine. They begged for another opinion – and it was a decision that saved him. A neurosurgeon found faint signs of brain activity, and two weeks later, Steven woke from his coma. Within seven weeks, he had left hospital. And four years on, the trainee accounts clerk says he owes everything to the persistence of his parents" [12].

Organs are priceless and donated on altruistic grounds, and all people can be regarded as potential organ donors after death has been declared. Even carriers of hepatitis B or C may donate organs. Special consideration needs to be given to the potential role of prisoners and people sentenced to death. On the one hand, death row inmates have asked for the right to donate their organs after execution [13]. Other attempts have been made to acquire organs from executed prisoners [14, 15].

In 2007, US senator Anderson proposed one bill that would release prisoners 60 days early for donating bone marrow and another that would give good behavior credit of up to 180 days to "any inmate who performs a particularly meritorious or humanitarian act," which would include living kidney donation [16]. Nevertheless, capital punishment remains ethically controversial and is unacceptable in a democratic state according to Beccaria [17], speaking in the eighteenth century. Ethical and moral antagonism to capital punishment are gaining ground and will undoubtedly compromise proposals to use organs from executed prisoners. Allegations have been made of prisoner executions and immediate organ harvesting in China [18].

1.2 Distribution of Available Organs

Organ allocation may be accomplished according to several criteria:

1. *Age*. To reduce patient waiting times for transplantation, a "preferred status" concept has been introduced. Consequently, several models of priority considering age have been proposed. Veatch [19] proposed a model known as "over-a-lifetime perspective."
2. *Maximum benefit*. A second model of allocation criteria is to obtain the maximum benefit, i.e., to increase the number of successful transplants. Examples of these criteria include the following:
   - Grade of urgency. The sickest patients have a preferred status; criticism to this criterion is that patient evaluation will not be objective if the physician is involved in the care, and there may be discrimination against patients who are healthier.
   - Probability that transplantation is successful, allocating organs to the patients who will presumably survive the longest.
   - Selection of organ recipients on the basis of their behavior. Sometimes this choice can be incredibly challenging. Consider the case reported by Dr. Cooley, pioneer in heart transplantation. A 17-year-old boy, living with a girlfriend who was 2 months pregnant by him and already had a 2-year-old child, was hospitalized for a cardiomyopathy related to cocaine and alcohol abuse. He underwent a heart transplant at the Texas Heart Institute (THI) in Houston, Texas, and he initially received regular immunosuppressive therapy. Then, the boy

went to Indiana, sporadically took his medication, and was incarcerated for assault and battery on his girlfriend. He started to have heart failure and returned to THI where he underwent an emergency implantation of a percutaneous ventricular assist device. His heart began to recover, and the device was removed after 72 h. At this point, he needed another transplant. The medical review board considered his eligibility and turned him down, considering that others on the waiting list were more deserving of a transplant and that retransplantation has a poorer success rate than initial transplantation [20].

3. *Length of wait*. A third model is the duration of waiting—the oldest patients on the list should have priority over those who come later. This model can be punitive for patients enrolled in several transplant centers.
4. *Culpability*. A recipient can be judged for their style of life, e.g., drug abuse, alcoholism, and smoking. Is it ethical to prioritize patients for organ allocation according to their contribution to society? Does this value discriminate against other individuals on the list?
5. *Recipient organ donor*. This means that to increase organ donation, transplant preference is given to people who previously registered as organ donors (or possibly registered in the same or nearest geographical areas).

1.3 Living Organ Donors

Taking organs from living donors represents a medical intervention that is totally different from ordinary surgical procedures. Individuals take risks or undergo harm for the sake of others, rather than for themselves, which is in sharp contrast to the ancient Latin ethical principle, "primum nihil nocere (first, do no harm)." Most organ donations occur after the donor has died, but some organs and tissues can be donated from living donors, and donor shortage is strongly supported by living donation. Living donation has increased as an alternative to deceased donation, and in the United States in 2013, 5,733 kidney grafts came from living donors [21]. Family members, friends, and even anonymous individuals can become living donors if they meet the requirements to donate.

Moreover, organ donation from living donors—of kidneys, bone marrow, and more recently, liver lobes and lungs—presents risks that vary from very low to high according to each of these procedures and that depend on several factors that do not always show predictable patterns. Therefore, living donation implies that the recipient knows and accepts that someone else will jeopardize his or her health for their survival. These grounds are clearly understandable and readily reconcilable in the case of donation to a next of kin. It is completely different in places that allow commercial organ gifting in exchange for monetary reward. There are several ways to bypass national laws against all forms of trading in organs; one of the most common is "transplant tourism." "Transplant tourists" are patients who travel to established destinations to find readily accessible organs for transplantation; these organs are available from the poor of that destination country who sell mostly kidneys but in some instances, a lobe of the liver or a cornea [22]. These practices have been well known for more than a decade. In 2004, the World Health Assembly (WHA) issued a resolution urging member states "to take measures to protect the poorest and vulnerable groups from transplant tourism and the sale of tissues and organs, including attention to the wider problem of international trafficking in human tissues and organs."

Antagonists of a market trade in human organs may affirm that an organ market exploits the helplessness of the poor, who would be attracted to the ability to alleviate his indigence at great risk to his health. Trade supporters may reply that any individual, even the most deprived, has the right to choose to self-harm, assuming "it is better to be without a kidney than without money." At the same time, the surgeon has a great moral responsibility: he will not be responsible for an individual being poor, but he will be responsible for his lack of an organ [23]. Greene makes this point in *The Tenth Man: Chavel a wealthy lawyer, is imprisoned in France during the German occupation.*

One night a resistence team shot up a nazi and the reprisal is immediate. A german guard comes to inform that three of 30 prisoners will be executed in the morning. The Third Reich does not care which three and the decision is up to the prisoners. They draw lots and Chavel is among the damned. But rather than accept his fate, Chavel will trade his position to a man named Janvier for his opulent wealth in favour of his mother and sister. What torments the protagonist is not Janvier's death before a Nazi firing squad, but the fact that he is at least partly morally responsible for his death. The novel shows Chavel's efforts to purge himself of the guilt that he feels about bartering for his life [24].

Despite the legislature governing the donation of human tissue (Human Tissue Act) [25] or its equivalent stating "It is an offense to charge a fee in relation to the donation of human organs," the buying and selling of organs for transplantation is rapidly increasing worldwide. The use of terms such as "rewarded gifting" or the idea of donors being transformed into vendors recalls symbolic fears of a Pandora's box [23]. Cameron and Hoffenberg [26] feel strongly that arguments in favor of the sale of organs were sufficiently persuasive and compelling to warrant further discussion. However, some interesting opposing positions (pros and cons) have been discussed by these authors about the ethics of living organ donation.

Pros: the supply of blood is only maintained by offering money; altruism will fail to supply all organs to meet demand:

- Payment to a live donor is compensation for pain, discomfort, inconvenience, and risk of operation.

Cons: organs should be considered priceless and donated for altruistic reasons, observed as a gift, freely given, and never bought or sold:

- Paid organ donation can inhibit cadaver donation with the risk that payment be demanded by relatives of deceased donors.
- Paid living transplantation is performed in poor circumstances and increases risks to the donor (these conditions are medically far from ideal, and success rates are low).
- A commercial objective encourages poor preoperative care for donors with inadequate screening for associated diseases, thus increasing the risk to the donor and the recipient beyond the actual risk of loss of life during kidney donation, which is estimated to be 0.03 %. The marginalization of paid living donation leads to its performance in less than ideal circumstances.
- The purchase of organs allows rich individuals to "jump the queue," thereby denying equity (access is denied to poor recipients because of lack of money, thus denying the basic ethical principle of justice). All organs would be sold to a central public agency that should be properly controlled to minimize exploitation, thereby ensuring informed consent from the donor; adequate pre-donor screening would be easily performed; the public agency would ensure that the organs are properly stored and matched to the best recipients and not to the highest bidder.

Some other ethical issues are particularly relevant for living donor liver transplantation (LDLT), a well-established strategy to decrease mortality for patients with end-stage liver disease on a waiting list and particularly for those affected by hepatocellular carcinoma (HCC), who are at high risk of dropping out from the waiting list. The scarcity of livers from deceased donors is one of the main obstacles of transplantation, and the waiting list mortality is approximately 20 % in Europe and 14 % in the United States. Living donor liver transplantation (LDLT) seems to offer some advantages over deceased donor transplantation. Advantages include the controlled timing of the procedure, the detailed collection of anatomical and biological information in the donor and recipient, and the control of immunological factors that may affect graft outcomes. However, a decline in the number of these procedures performed during the last decade in Western countries is evident, and LDLT remains highly scrutinized because donor deaths have been reported as have consistent morbidities, espe-

cially biliary tract complications, in the recipient. As a matter of fact, the Organ Procurement and Transplantation Network (OPTN) requires all living donor deaths to be reported within 72 h of the transplant center obtaining knowledge of said death. However, transplant centers have not always abided by the requirement, and the incidence of death among right-lobe donors is thought to be 1 % or greater [27]. Living donor liver transplantation (LDLT) is associated with a low but finite and well-documented risk of donor morbidity and mortality; therefore organizations and individuals involved in this activity must accept that donor death is a question of "when, not if" [28]. Candidate selection for particular patients, especially those waiting for liver transplantation for HCC, presents different challenging issues when we try to find thresholds for defining transplant benefit, justice, utility, and urgency. To limit futile organ transplantations, each one of these issues (benefit, justice, utility, and urgency) requires a perfect balance among different principles and criteria. Many scoring systems and other methodologies of transplant benefit evaluation are utilized in clinical practice. These scoring systems have advantages and disadvantages in clinical practice, especially when used for small subgroups of patients waiting for liver transplantation who are the sickest ones in the waiting list or have a growing HCC and are at risk to drop out. These issues are currently debated and offer some of the most challenging ethical dilemmas about living donor liver transplantation for transplant surgeons and hepatologists. Due to these considerations, the number of living donor liver transplants in adults peaked from 2001 to 2002 in Europe and the United States; then the procedure started to be used less in the United States, and there was no further increase in Europe. Split-liver transplantation, a procedure where one donor liver is divided into two hemilivers for two recipients, was considered an important method to overcome the organ shortage. To date, the principal beneficiaries have been adult/pediatric pairs with excellent outcomes for the adult and pediatric recipients. However, partial-liver grafts are predisposed to a higher rate of complications, resulting from anatomic variation, smaller graft size, and difficulty in vascular and biliary reconstruction, especially when the splitting procedure is performed for two adult recipients [29]. Despite some encouraging results in terms of survival, the ethical dilemma is that at present, the splitting procedure for two adults has not been fully validated in terms of real transplant benefit for two adult recipients receiving the left or the right hemiliver when compared to the single recipient receiving the whole liver [30]. Improving allocation policies for exchanging liver grafts among centers and close cooperation among centers with adequate experience in particular challenging surgical procedures should be encouraged; this interaction represents another important issue in the complex ethical debate.

References

1. Middleton PF, Duffield M, Lynch SV, Padbury RTA, House T, Stanto P, Verran D, Maddern G (2006) Liver donor liver transplantation-adult donor outcomes: a systematic review. Liver Transpl 12:24–30
2. Abouna GM (2001) The humanitarian aspects of organ transplantation. Transpl Int 14:117–123
3. United Network for Organ Sharing (UNOS) (1999). Annual report. https://www.unos.org/donation/
4. United Network for Organ Sharing (UNOS) (2002). 'Update', special edition, Winter. https://www.unos.org/donation/
5. Keown P (2001) Improving the quality of life: the new target for transplantation. Transplantation 7:S67–S74
6. Eggers PW (1998) Effect of transplantation on the medicare end stage renal disease program. N Engl J Med 38:223–229
7. Hunsicker LG (1999) Survival advantage for renal transplantation. N Engl J Med 341:1762–1763
8. Document 3 / Organ Donation and Transplantation. Source: Pope Pius XII (1956) "Tissue transplantation" (14 May 1956). The human body: papal teachings. In: O'Rourke KD, Boyle P (1999) Medical Ethics: Source of Catholics Teachings, Third Edition, Georgetown University Press, Washington, DC, pp 286–290
9. Address of the Holy Father John Paul II to the 18th international congress of the transplantation society. 29 Aug 2000. http://w2.vatican.va/content/john-paul-ii/en/speeches/2000/jul-sep/documents/hf_jp-ii_spe_20000829_transplants.html
10. Theological perspectives on organ and tissue donation. http://www.unos.org/donation/index.php?topic=fact_sheet_9

11. Jarvis R (1995) Join the club: a modest proposal to increase availability of donor organs. J Med Ethics 21:199–204
12. Eccles L (2012) The boy who came back from the dead: experts said car crash teen was beyond hope. His parents disagreed. Daily Mail online 25 Apr 2012
13. Longo C (2011) Giving life after death row. The New York Times. 5 Mar 2011
14. Patton L (1995) A call for common sense: organ donation and the executed prisoner. VA J Soc Policy Law 3:387–434
15. Bartz C (2005) Prisoners and organ donation. Available at: http://findarticles.com/p/ articles/miqa4100/is 200512/ ai n15957681
16. O'Reilly K (2007) Prisoner organ donation proposal worrisome. AMA News. Available at: http://www.amaassn.org/amednews/2007/04/09/prsb0409.htm
17. Beccaria C (1764) Dei delitti e delle pene E-text Editoria, Web Design, Multimedia. http://www.e-text.it/
18. Matas D, Kilgour D (2010) Bloody harvest: the killing of Falun Gong for their organs. Seraphim, Woodstock
19. Veatch RM (2000) Transplantation ethics. Georgetown UP, Washington, DC, pp 277–413
20. Cooley DA, Fung JJ, Young JB, Starzl TE, Siegler M, Chen PW (2008) Transplant innovation and ethical challenges. What have we learned? A collection of perspectives and panel discussion. We have come far, but selecting organ recipients remains an ethical minefield. Cleveland Clin J Med 75(Suppl 6):24–32
21. National Kidney Foundation. www.kidney.org/news/newsroom/factsheets/Organ-Donation-and-Transplantation-Stats
22. Delmonico FL (2009) The hazards of transplant tourism. Clin J Am Soc Nephrol 4:249–250
23. Elliott C (1995) Doing harm: living organ donors, clinical research and The Tenth Man. J Med Ethics 21:91–96
24. Greene G (1985) The tenth man. Penguin, London
25. South Africa: Government Gazzette, 9 Nov 2001; No. 22824
26. Cameron JS, Hoffenberg R (1999) The ethics of organ transplantation reconsidered: paid organ donation and the use of executed prisoners as donors. Kidney Int 55:724–732
27. Nelson EW, Childress JE, Peryman J, Robards V, Rowan A, Seely MS, Sterioff S, Swanson MR (1993). Financial incentives for organ donation: a report payment subcommittee OPTN/UNOS Ethics Committee. http://optn.transplant.hrsa.gov/resources/ethics/financial-incentives-for-organ-donation/
28. Surman O (2002) The ethics of partial liver donation. N Engl J Med 346:1038
29. Miller C, Smith M, Fujiki M, Uso T, Quintini C (2013) Preparing for the inevitable: the death of a living liver donor. Liver Transpl 19:656–660
30. Aseni P, De Feo TM, De Carlis L et al (2014) A prospective policy development to increase split-liver transplantation for 2 adult recipients: results of a 12-year multicenter collaborative study. Ann Surg 259:157–165

2 Policies for Boosting Donor Enlistment in the North Italy Transplant Program Macro-area

Tullia Maria De Feo, Massimo Cardillo, Nicola De Fazio, and Giuseppe Piccolo

Key Steps to Expand the Potential Donor Pool

1. Identify a key donation person in each procuring hospital
2. Optimize the management of each step of the donation-transplantation process
3. Improve the organizational models through the integrated work of procurement-donation professionals
4. Expand the donor selection criteria and optimize the use and suitability of organs

The growing imbalance between patients on waiting lists and organ availability for transplantation is the core problem for the transplantation community. This has been the case since the mid-1980s when the Spanish model stated, "*Sin donante no hay transplante*" (no donor, no transplant) and thus identified the crucial step of the donation-transplantation process. The search for strategies to increase the number of donors is still the priority of all transplant organizations, and all have learned from the Spanish ONT, which was by far the most effective organization, thanks to the establishment of the Hospital Transplant Coordinator, established in Catalonia in 1984.

The Spanish model predicts that transplantation is a health procedure that becomes possible if it is included in a circle where "the community gives and the community receives." The role of the transplant professional is as the tool that society uses to make this circle real; for this reason, health organizations should be organized to harmonize the different steps of the donation-transplantation process and leave nothing to improvisation. One of the attributes of the Spanish model was the separation of organ procurement from transplantation and the identification of a key donation person inside the procuring hospital, an experienced and trained health professional who is responsible for organ and tissue donor procurement. At the same time, organ allocation and exchange should be optimized but managed by professionals with special and different organizational skills.

The donation-transplantation process is a path defined by a series of different steps that are closely connected in a continuum from donor identification all the way through to organ transplantation. The process requires several hours to be completed, and a very large number of professionals participate, each having precise knowledge of the procedure and full awareness of their role.

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In Italy, Law 91, dated 1 April 1999, has acknowledged the system complexity and the need to define rules and precise procedures to make the process effective. In recent years, the organ procurement and transplantation system has grown as a network and is currently organized on three levels:

Local: the key figure is the Hospital Transplant Coordinator, an expert in the identification and management of the potential organ and tissue donor. The coordinator is entrusted with numerous tasks (e.g., monitoring the registry of patients who die in the hospital, identifying all potential donors, interviewing the donor family for death communication and consent to donate, assessing donor safety and suitability, etc.)

Regional: in each region, a Regional Transplant Center (CRT) is identified. The CRT has organizational functions concerning the procurement, allocation, and transplantation of organs and tissues, the application of the National Guidelines, the management of waiting lists, and monitoring the posttransplant patient.

National: this includes the CNT and the Technical Advisory Board, which is responsible for the strategic and technical-operational planning. Recently, the CNT has also acquired operational functions in organ allocation for the national programs (urgent, pediatric, or highly sensitized patients) in collaboration with CRTs.

We have depicted the recent scenario, as it has evolved since the end of the 1990s, but it would be useful to recall how transplant organizations were created in Europe and Italy at the dawn of the transplantation era.

2.1 Brief History of North Italy Transplant Program (NITp)

In the late 1960s, renal transplantation activity was beginning in many European Countries, and it soon became clear that organ allocation should be separated from transplantation. At that time, several transplant organizations were founded in Europe with the aim to coordinate the procurement-transplant process and allocate organs. In Italy, the first Regional References Centre (CRR) was founded in 1974, established by the Lombardy Region at the Immunology Service of the Maggiore Policlinico Hospital of Milano. Subsequently, in 1976, a collaborative agreement between the CRR and the Veneto Region produced the first Interregional References Centre (CIR) in Italy. At the same time, professors Piero Confortini, Edmondo Malan, and Girolamo Sirchia founded the North Italy Transplant program (NITp), the first transplant organization in Italy. The NITp References Centre was located in Milano and had the primary tasks of donor safety and suitability assessment, patient and donor immunological evaluation, and organ allocation. In the course of time, thanks also to the great dedication of Claudia Pizzi, Mario Scalamogna, and Francesca Poli, the NITp included other regions, such as Liguria, Marche, Friuli Venezia Giulia, and the Autonomous Province of Trento and included eighteen million inhabitants, corresponding to about one third of the Italian population. Some of the CIR tasks have been delegated to the respective CRT of the region that participates in the program.

The intuition that a large procurement area and a common pool of patients on the waiting list might improve the transplant chances of the most critical patients (urgent, long waiting, highly sensitized) has been the basis of the CIR success. Furthermore, the operation of a complex system such as the donation-transplantation process in a multiregional area can be a critical element. To add efficiency to the whole process, a model of "central" coordination was chosen. NITp CRR is entrusted with the tasks of receiving the referral of potential donors, allocating organs, managing patients on the waiting list for transplants, performing pre-transplant histocompatibility testing, surveying adverse events, and performing post-transplantation follow-up. NITp CRR therefore has an onerous task but also a great opportunity to be the connection between organ procurement and transplantation units. For this reason, the NITp working groups were born (e.g., kidney

transplant, liver transplant, organ and tissue procurement, pediatric transplant, etc.). Each group consists of the specific professionals, who, together with the NITp CRR coordinators, discuss the problems of the program, develop operational protocols, report critical cases, and propose strategies for improvement. The meetings, structured and constant over time, strengthen relations between operators, facilitating collaboration not only on the technical operations but also on the scientific side. The annual technical-scientific meeting is the opportunity to report to the NITp transplant community the work of all groups.

At the beginning of the 1990s, the NITp followed the Spanish model by also identifying the need of a continuous education program not only on the procurement side but also dedicated to all professionals involved in the donation-transplantation process. Thanks also to the continuous exchange with the associations of patients, the NITp has contributed to the development of the culture of donation in our country, and the collaborative structure of our program helped the procurement and transplantation units to share their experience. We have learned the lesson that donor procurement starts at the moment of donor identification, and the path proceeds through different phases; every pause along the path means "non-use" of the donor and "no transplant" for the patients. It is essential that the key donation person make every effort to remove all the obstacles that may interrupt the path in his hospital. The NITp has helped transplant coordinators to be recognized in their role and handle the crucial steps, identifying the best organizational model through the integrated work of all those who are involved in the path.

2.2 Donation-Transplantation Process

Identification and referral of the donor: the presence or absence of a neurosurgery department, the hospital organizational arrangement, and the type of intensive care are important factors that influence the organ donation rate, but the Transplant Donor Coordinator, a specifically trained professional, is the key figure in each hospital who can operate on all the factors to improve organ procurement.

Consent to donate: the identification of potential donors is essential to the process, but without the family consent to donate, there is no progression. The cultural aspects of society are certainly relevant, but a well-trained coordinator is essential for the approach to the donor's family.

Evaluation of the donor: great attention should be paid in donor selection, aimed at minimizing the risk of disease (infections, tumors) transmission with organ transplantation. The NITp References Center has an important role in this activity, and it is managed in collaboration with the other network professionals (intensive care unit staff, transplanting experts, counselors, and clinicians). This is a critical activity that requires great experience and clinical expertise.

Maintenance of the donor: a specific knowledge and expertise is required to contrast the effects of the catecholamine storm at the time of brain death, with the aim of maintaining an optimal oxygenation and perfusion of organs.

Suitability of organs: once donor safety is assessed, with the identification of a risk level in accordance with the national guidelines, it is necessary to define the functional quality of the individual organs through laboratory tests and radiological and/or histological evaluations. It is essential that the donor-procuring hospital set up a dedicated organization procedure to make all investigation facilities available in the short period of time for donor selection.

Organ allocation: regional reference centers are in charge of this step of the process. Criteria should be shaped on the principles of the organs' best use, transparency, and equity. It is essential that allocation centers operate on an adequate pool of recipients in a way that facilitates organ allocation to "difficult" patients (highly sensitized, urgent, pediatrics).

Activation of the transplant team: this is the task of the CRT and requires a high organizational capacity. All retrieval equipment should be

moved to the operation theater with the proper transportation mode with consideration for organizational criticalities and organ ischemia times.

Organ retrieval is a delicate moment that requires careful organization and good interaction among different surgical teams. It is also an important moment for completing the evaluation of the donor and/or organs.

Monitoring transplant and posttransplant: data collection and analysis are intended to monitor the program and verify the impact of the variables on transplant results, in terms of transplant complications and patient and graft survival.

A more careful monitoring and implementation of all these phases has allowed, over the years, not only an increase in the number of reported donors but also a minimization of the gap between donors referred and used.

In 1999, the Council of Europe acknowledged the importance of the process and established a working group to prepare guidance on the standards required and the quality assurance that should be achieved in services for organ and tissue transplantation. The first edition of the guide was published in 2002, and the document provides guidance for all the professionals involved in the donation-transplantation path to maximize organ and tissue safety and quality and to minimize the risks of the procedure. A member of NITp participated in the working group.

2.3 Increasing the Number of Donors

In the last few years, the population of cadaver donors changed significantly in terms of age and comorbidities, and the new challenge was to identify strategies to expand the criteria for donor selection. In the NITp since the early 1990s, donor age >60 years was not considered an exclusion criterion, and this policy allowed a total 10-year increase of 347 donors (approximately 10 % of the total) and 778 transplanted organs, with posttransplant survival results similar to those using organs from donors younger than 60. Since 2010, more than 50 % of the donors used were 60 years or older [1]. Figure 2.1 shows the procurement-transplantation activity since the beginning.

Expanding donor selection criteria may increase the risk of disease transmission with transplantation. Since the late 1990s, in the NITp area, the principle has been adopted that every donor carries a standard unavoidable risk and that the greatest risk for a patient on the waiting list is to not receive the transplant. Consequently, the approach to the assessment of donor safety has changed dramatically. Instead of absolute donation exclusion criteria, each donor can be associated with a degree of relative risk, which should be balanced with the potential benefit of the recipient. This policy was strongly supported in 2003 with the implementation of the first edition of the national guidelines on donor safety

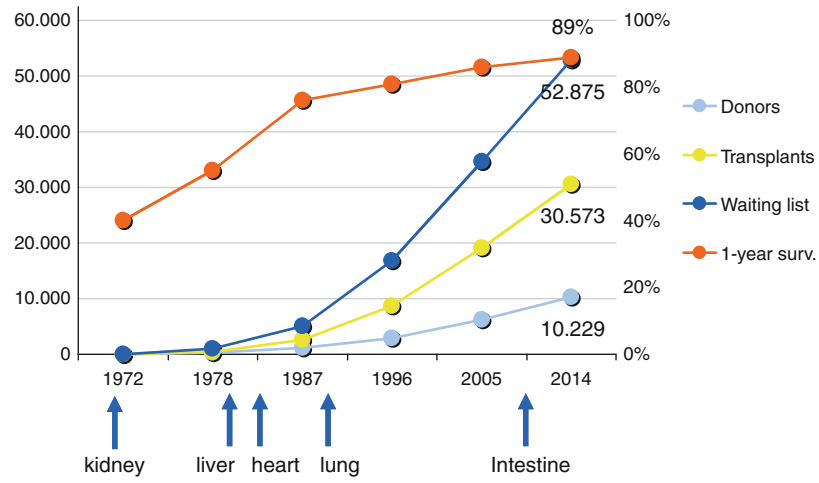

Fig. 2.1 Procurement and transplantation activity in North Italy Transplant program since 1972

and with the formal identification of second opinion figures, experts in the field of infectivology and pathology who can be contacted 24 h/day to receive advice on peculiar donor-transmittable diseases. Following the adoption of the national guidelines and the support of the second opinion, several donors previously considered unsuitable (e.g., HCV- or HBsAg-positive donors) have been used for proper recipients with good results (Fig. 2.2). Since 2003, the use of extended criteria for donor has been increasing (Fig. 2.3), but the total number of used donors remained steady in the last few years because the number of younger donors is continuously decreasing.

The transplantation community has recently doubled efforts to identify new sources of organs. Some countries have developed protocols to utilize organs from non-heart-beating donors (NHBDs); in Italy, this program is poorly implemented, due to the organizational difficulties caused by the different legislations on cardiac death certification, which impose a longer "no touch" period before organ harvesting and cause uncontrolled ischemic damage to organs. The program started in the Pavia hospital, where ten kidneys from NHBDs were transplanted, after the evaluation of their vascular resistance by a specific perfusion machine [2]. The extension of the use of these perfusion machines seems to open a horizon even for the harvesting of livers from this type of donor. Just as important and potentially promising, a recent double-lung transplant from a NHBD was performed in Milan. In this case also, a specific perfusion machine (EVLP) was used for "reconditioning" and using the lungs; the same protocol has also been adopted in the case of "marginal" lungs harvested from heart-beating donors and previously considered unsuitable for transplant [3].

Living donors represent another important source of organs. In Italy, kidney transplants from living donors represent only approximately 7 % of the total number of transplants compared with much higher percentages in other developed countries. In the last few years, new efforts have been promoted, also by the Centro Nazionale Trapianti, to improve the number of kidney transplants from living donors. This increase could be achieved through an improved awareness by doctors in the dialysis centers of the potential benefit of this therapy for the patient and the safety for the donor. Thus, information about this opportunity should be given to the patient at the time of enrollment on the waiting list. In recent years, the donation of a kidney by a living donor has become even safer, thanks in part to the development of techniques for mini-invasive surgical harvesting. Figure 2.4 shows the living donor kidney transplantation activity since 2003.

Some countries have developed special programs to overcome the immunological incompatibility of the donor-recipient pair in kidney living

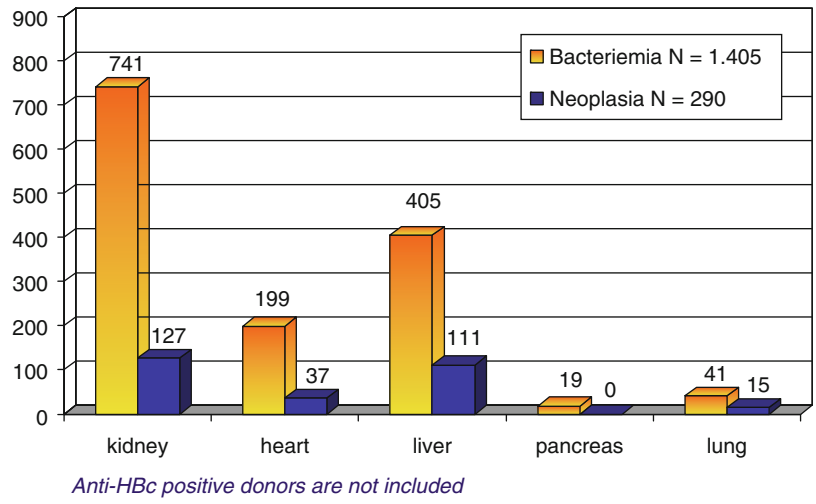

Fig. 2.2 Patients transplanted with organs from extended criteria donors (ECD) (2003–2013)

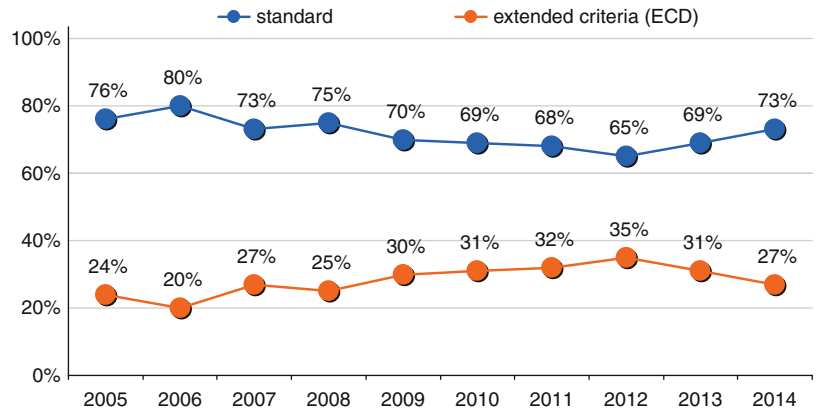

Fig. 2.3 Standard and extended criteria donors (*ECD*) used in North Italy Transplant program (*NITp*) area (2005–2014)

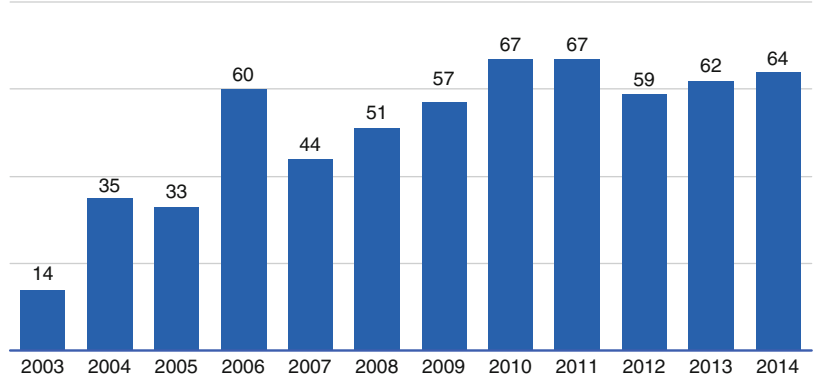

Fig. 2.4 Dual kidney transplantation 2003–2014

transplantation. The program, named crossover, consists of substituting familial with immunologically compatible pairs; the transplantation chain results from the donor of an incompatible pair becoming the donor of a compatible one, with a different recipient. The complexity of the program is created by the organizational difficulty of performing the transplants of all the pairs in the chain in a short period of time to avoid the risk that a donor whose recipient has already been transplanted will refuse donation for the subsequent pair. In this program, the transplantation chains may also be triggered by a "Samaritan" donor who liberally donates his/her kidney for the benefit of patients on the waiting list. Recently, the first case of a kidney transplant from a Samaritan donor was successfully performed in Italy, and the resulting chain allowed five other patients on the waiting list to be transplanted.

In 2001 in the NITp area, the first living donor liver transplant between two adults and one between an adult and a pediatric patient have introduced a new potential donation method. The delicate and challenging process of assessing donor suitability and the surgical complexity of intervention have reduced the initial expectations.

2.4 Increasing the Number of Organs

Alongside the identification of strategies for increasing the number of donors, the principle of a good use of the organs has been consolidated. In the 1990s, the technique for dividing the donor liver into two parts (split liver) optimized the use of a "scarce resource," allowing the transplantation of an adult and a pediatric recipient with a

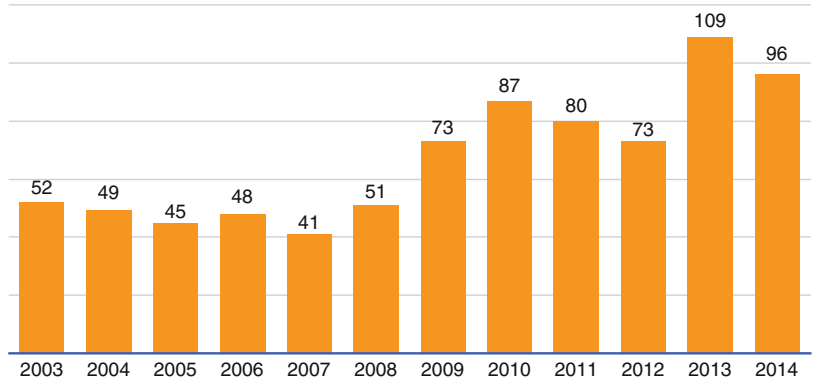

Fig. 2.5 Living donor kidney transplantation 2003–2014

single organ. Following the implementation of this strategy, the prognosis of children on the waiting list in the NITp area changed radically: the higher mortality rate in the pediatric list at 5 years was soon reduced to 3 % compared with 16 % in the pre-split liver era and has dropped to zero since 2005 [4]. Moreover, an improvement has also been highlighted on the adult waiting list, as adults no longer suffer from the competition with the pediatric list for the use of the whole liver [5]. After improving mortality in the pediatric list, efforts were concentrated on the adult list. In the late 1990s, the split technique was evolved for transplanting two adults [6]. The procedure, however, is more complex than the standard adult/pediatric one, especially with relation to donor selection and dimensional donor/recipient matching. For this reason, it remains an option in selected cases, despite the experience gained [7]. Another significant procedure experienced in the late 1990s was the simultaneous transplant of two kidneys in a single recipient, in the case of older donors and/or donors with a nonoptimal kidney function. Kidneys are deemed suitable for a single/double graft transplantation on the basis of a histological score; the rationale of this program is to measure and allocate the adequate "nephron mass" to the recipient, using donors who were previously discarded [8]. To date, approximately 700 dual kidney transplants (DKTs) were performed in the NITp area (Fig. 2.5), and the annual number is steadily increasing in association with a constant increase in the mean age of donors with very satisfactory results.

Last, considering all the effort produced by the transplant community to use all possible donors and organs, much more consideration should be given on the side of recipient information. All patients should be informed at the time of waiting list enrollment about the possibility to receive organs from standard or marginal donors, and their consent should be acquired to ease their decision whether to accept the organ at the time of donor availability.

References

1. North Italy Transplant program Annual Report. www.policlinico.mi.it/nitp
2. Rampino T, Abelli M, Ticozzelli E, Gregorini M, Bosio F, Piotti G, Bedino G, esposito P, Balenzano C, Geraci P, Dal Canton A (2010) Non-heart_beating-donor transplant: the first experience in Italy. G Ital Nefrol 27(1):56–68
3. Valenza F, Rosso L, Coppola S, Froio S, Palleschi A, Tosi D, Mendogni P, Salice V, Ruggeri GM, Fumagalli J, Villa A, Nosotti M, Santambrogio L, Gattinoni L (2014) Ex vivo lung perfusion to improve donor lung function and increase the number of organs available for transplantation. Transpl Int 27(6):553–561
4. Cardillo M, De Fazio N, Pedotti P, De Feo T, Fassati LR, Mazzaferro V, Colledan M, Gridelli B, Caccamo L, De Carlis L, valente U, Andorno E, Cossolini M, Martini C, Antonucci A, Cillo U, Zanus G, Baccarani U, Scalamogna M, NITp Liver Transplantation Working Group (2006) Split and whole liver transplantation outcomes: a comparative cohort study. Liver Transpl 12:402–410
5. Maggi U, De Feo TM, Andorno E, Cillo U, De Carlis L, Colledan M, Burra P, De Fazio N, Rossi G, Liver Transplantation and Intestine North Italy Transplant Study Group (2015) Fifteen years and 382 extended

right grafts from in situ split livers in a multicenter study: are these still extended criteria liver grafts? Liver Transpl 21(4):500–511
6. Colledan M, Andorno E, Valente U, Gridelli B (1999) A new splitting technique for liver grafts. Lancet (Letter) 353(9166):1763
7. Aseni P, De Feo TM, De Carlis L, Valente U, Colledan M, Cillo U, Rossi G, Mazzaferro V, Donataccio M, De Fazio N, Andorno E, Burra P, Split-Liver Study Group (2014) A prospective policy development to increase split-liver transplantation for 2 adult recipients: results of a 12-year multicenter collaborative study. Ann Surg 259:157–165
8. Ruggenenti P, Perico N, Remuzzi G (2006) Ways to boost kidney transplant viability: a real need for the best use of older donors. Am J Transplant 6:2543–2547

3 Preoperative Evaluation and Arrangements for Multiorgan Donation: General Principles and Contraindications

Antonino M. Grande and Paolo Aseni

Key Points of Coordinator Roles

- Promote and facilitate the entire donation process.
- Provide support to families regarding organ and tissue donation respecting individual and cultural differences.
- Be involved in the process of consent for donation.
- Ensure that donation proceeds in line with national legislation, policies, and procedures.
- Obtain all information to allow transplant centers to assess the suitability of potential donors.
- Assist in the optimization of organs for transplant through appropriate donor management.
- Maximize the placement of organs for transplant.
- Train donation services' team members.
- Collect data for organ donation-related audits.
- Facilitate and support the education of healthcare professionals and the general public.

Modified from Akyol M. and Tswen Wen VL. [1]

3.1 Organizational Problems: Donor Coordinators

In Italy, the United States, and the majority of Europe, the management of the patient after brain death, but before organ donation, has traditionally become a task under the responsibility of transplant coordinators.

Donor coordinators often have many years' experience in nursing or other similar health disciplines, but they are usually not physicians. Intensivists in the intensive care unit tend to decrease the time caring for patients after brainstem death to provide more support to those who are still living [1].

Intensivists use their resuscitative skills to continue to provide care to a patient who they cared for before the declaration of brain death, and each donor can be a potential source of organs for a number of patients on transplant waiting lists. When managing donors, evidence-based care

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should be applied to allow the best care for donor stabilization to optimize organ condition.

The lack of standardization of donor management is one of the reasons for failure to retrieve as many organs as possible [2]. For this reason, protocols for the organization and management of patients after brain death should be developed and implemented by all organ procurement organizations [3].

Donor coordinators have become an important role during the last 15 years, and they have contributed to the successful maximization of the number of potential donors in Spain and worldwide [4].

Coordinators may be affiliated with transplant centers or be part of an independent organization. Transplant coordinators who remain affiliated with transplant units and serve a dual role as donor and recipient coordinators may fulfill each role equally effectively, and this model may have important benefits. However, in terms of one of the most important outcome measures—maximizing the potential from deceased donation—international experience and the balance of evidence suggest that a superior framework involves dedicated donor coordinators based in potential donor hospitals. In some of the countries with the highest deceased donation rates, such as Spain, Portugal, and Italy, there are donor coordinators based in every hospital in the country [5]. They play an important role in increasing and maintaining donation awareness and provide education and support to the staff of potential donor hospitals. Donor coordinators will often help approach the donor family, participate in acquiring consent or authorization for donation, provide help with donor management in the critical care unit, and support the donor family during the process of donation. Donor coordinators will also liaise with legal authorities to facilitate donation and ensure that surmountable legal obstacles do not prevent organ donation. Donor coordinators will then inform organ retrieval teams and coordinate the retrieval process. The responsibility for transporting retrieval teams to donor hospitals and organs to their destinations may rest with the donor coordinator, with the transplant units, or be shared between them. The regionalization of donation services, together with a uniform approach to the travel arrangements, is probably going to improve the quality and safety of the travel services for the donor team [1].

Donor coordinators also share the responsibility for the appropriate documentation of donor details and the submission of information to the National Transplant Database as well as individual transplant units.

The coordinator should check the blood group and examine all the potential donor parameters—blood pressure, heart rate, temperature, urine output, central venous pressure, wedge pressure if a Swan-Ganz catheter is present, diuresis, and mechanical ventilator parameters—and provide warming to maintain a body temperature above 36.5 °C.

3.2 Exclusion Criteria for Infection Transmission from Organ Donors

Brain death predisposes a patient to infections as a result of severe injury to the cellular immune system [6] and hemodynamic instability with consequent bacterial translocation from the bowel [7]. Nevertheless, there is a strong trend toward expanded donation criteria or, as it is commonly stated, using borderline donors. Therefore, positive cultures or a clinical diagnosis of infection is not currently an absolute contraindication for organ donation.

The transmission of infections from the donor to the recipient constitutes a rare complication of transplantation that is frequently associated with significant morbidity and mortality because immunosuppressant drugs decrease resistance to infection [8, 9].

Most donor infection transmissions are expected, because laboratory screening allows the knowledge of donor infective status before transplantation. Infections, including cytomegalovirus (CMV) and hepatitis B virus (HBV), may occur and are monitored and treated with preemptive therapy and universal prophylaxis [10]. In other cases, the accepting center should match the risk of disease transmission with the risk tolerance and medical status of the recipient.

In addition to laboratory screening, it is mandatory to stratify risk from the donor medical and social history and a careful physical assessment [10]. In the United States, risk stratification considers donors either at increased risk or without identified risk for the transmission of infectious diseases; in Europe, a classification system was initially developed in 2002 by the Italian National Center for Transplantation (CNT) [11] and the CNT/European risk system [12] defined the risk for the transmission of infectiuos disease. According to this classification, donors are defined as follows:

1. *Unacceptable risk* includes absolute contraindication, with the exception of some life-saving transplantation procedures in the absence of other therapeutic options on a case-by-case basis.
2. *Increased but acceptable risk* includes cases where transmissible organisms or diseases are identified during the evaluation of the donor, but organ utilization is justified by the specific health situation of the recipient or the severity of their clinical condition.
3. *Calculated risk* (criteria referring to protocols for elective transplants) includes all cases where, even in the presence of transmissible diseases, transplantation is allowed for recipients with the same disease or with a protective serological status; this risk also applies to donors with documented bacteremia and/or bacterial meningitis provided that the donor was on targeted antimicrobial treatment for a minimum duration of 24–48 h.
4. *Not assessable risk* includes cases where the evaluation process does not allow an appropriate risk assessment for transmissible diseases.
5. *Standard risk* includes cases where the evaluation process did not identify a transmissible disease.

The following laboratory tests must be performed prior to organ evaluation [13] (Table 3.1):

Positive culture results or a clinical infection diagnosis should not lead to an absolute contraindication of organ donation. Many reports show that even Gram-negative bacteremia donors can provide favorable outcomes in kidney, liver, and heart transplantations [14, 15]. Decisions regarding organ retrieval from donors with active or suspected infections are affected by the recipient status/urgency and by the availability of other organ donors. The recipient, furthermore, should be adequately informed for consent.

Table 3.1 Obligatory laboratory screening tests for the donors

Test	Interpretation of a positive reaction
HBsAg	Organs are usually not accepted
Anti-Hbc	All organs can be used for recipients who are HBsAg, Anti-Hbc or Anti-Hbs positive
	Livers can be used for recipients without HBV markers, but lifelong antiviral treatment and surveillance is required
	Non-liver organs can be used for recipients without HBV markers; a single dose of Hepatitis B Immuno Globuline (HBIG) prior to revascularization should be given, and short-term antiviral treatment should be considered. If the donor is also anti-HBs positive, HBIG is not required
Anti-HBs	In combination with anti-HBc reactivity, see above
	If anti-HBc test is negative, all organs can be used (no risk, anti-HBs reactivity most likely due to previous immunization of donor)
Anti-HCV	Organs are usually not accepted but may be accepted if donor is HCV-positive
Anti-CMV IgG	Organs are accepted
Anti-HIV	Organs are not accepted

The evaluation of a large series of donors [16, 17] showed the presence of bacteremia in approximately 5 % at the time of organ retrieval, but no case of transmission of the isolated microorganism from donor to recipient was documented; bacteremia in the donor did not worsen the clinical outcome of solid organ transplant recipients. Cerutti et al. studied 610 consecutive liver transplants in a 5-year period at the Liver Transplant Center in Torino (Italy) [18]. In the study, one or more cultures were positive in 293 of 610 donors (48 %). Samples collected before harvesting were positive in 82 of 610 donors (13 %), and samples collected at harvesting and from preservation

fluid were positive in 256 of 610 donors (42 %). Culture-positive donors were significantly older and presented longer lengths of ICU stay than culture-negative donors.

Donors with hepatitis B or C, previously considered as absolute contraindications, can now have their livers harvested and implanted in recipients infected by the same viruses provided only minimal histologic changes (Ishak fibrosis and portal inflammation) are present in the graft [19].

Cytomegalovirus (CMV) carried within organs can determine CMV infection in recipients, especially in those who are CMV negative at the time of transplantation. Routine prophylaxis against CMV in these cases is mandatory and has markedly reduced CMV mortality and morbidity [20].

3.3 Donor Heart Exclusion Criteria

Improvement in the medical and surgical treatment of cardiac diseases has enhanced the longevity of the population and led to a constant increase in heart failure cases; after the clinical introduction of cyclosporine in the early 1980s, heart transplantation has represented the treatment of choice for end-stage heart failure. Through June 30, 2013, 116,104 cardiac transplants have been performed in more than 416 hospitals worldwide [21]. The notable increase of patients listed for heart transplantation has demanded a consequent modification of standard and traditional donor criteria [22] that were introduced in the early years of the cardiac transplant programs. Moreover, the increase in organ demand caused a shortage of available hearts, producing, in turn, the adoption of more severe recipient criteria that limit the number of patients in transplant lists [23, 24]. For this reason, certain donor criteria have been expanded to raise the available donor pool, considering and accepting the so-called marginal donors. In this case, we emphasize that attention should be oriented toward an individual evaluation of the recipient/donor, recognizing the patient hemodynamic status/urgency and not only the expanded criteria. Each potential recipient should be accurately evaluated, avoiding transplantation in patients with serious generalized disease, e.g., a septic status. Clinical judgment is needed to decide which marginal donor is adequate for our patient transplantation.

When wall motion abnormalities are found at echocardiography and the left ventricular ejection fraction is <0.45, even though the donor is stable with inotropic support, before the organ is refused, hemodynamic and metabolic management should be performed [25, 26]; stress echocardiography can be helpful in recognizing hearts eligible for donation.

Stress Echocardiography Dipyridamole stress echocardiography, performed in brain-dead potential donors with left ventricular resting global or discrete wall motion abnormalities, identifies hearts with severe morphologic abnormalities that were not considered for donation from eligible donors who showed an improvement in regional wall motion during stress (viability response) and normal function and coronary anatomy following transplantation [27].

Age and Ischemic Time In the early phases of transplant programs, donors older than 40 were excluded from the donor pool. However, donor shortage promoted the acceptance of donors up to 50 or 60 [28–31]. Using hearts from older donors, the outcome depends on other factors, chiefly ischemic time, which, when longer than 3–4 h, is associated with increased early mortality [32–37]. Lamour et al. [38] found that a 40-year-old recipient with congenital heart disease who received a 50-year-old donor heart with 3-h ischemic time had a 15 % probability of death within 1 year, compared with a 40 % probability of death within 1 year if that donor's ischemic time was 5 h. As indicated by the International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients [37], donors younger than 45 may be acceptable even with undesirable characteristics such as prolonged ischemic time, recipient comorbidities, and previous recipient operations with hemodynamically

destabilizing bleeding. Hearts from donors between the ages of 45–55 should safely implant when the projected ischemic time is ≤4 h and the potential recipient does not have comorbidities or surgical issues; donor hearts >55 years should be accepted carefully and balance the pros and cons for the recipient (Table 3.2).

Advanced age is a risk factor for death from any cause [39] and from early graft failure [40]. It is well known that at the beginning of the heart transplantation program, the donor upper age limit was 35 years, but after almost 50 years, this limit has progressively increased such that 50–55-year-old donors are now routinely considered. Nonetheless, serious well-known concerns about older donors are related to the transmission of coronary artery disease (CAD), hypertensive heart disease, or valvular degeneration from the donor heart. Many single-center analyses report that older donor hearts have not affected post-transplant survival [41–46].

Conversely, large multi-institutional studies [32, 33] and the International Heart and Lung Transplantation Registry [47] reported increased mortality in heart transplant recipients receiving older donor hearts. These differences are probably due to the smaller number of patients and short follow-up time in individual studies. Lietz et al. [48] found a direct correlation between increasing donor age and the risk of transplant-related coronary artery disease. At the first annual coronarography, they found that when compared with donors younger than 20, the third, fourth, and fifth decades of donor life increase the risk of CAD by 2.2-, 2.4-, and 2.6-fold, respectively.

Furthermore, the International Society for Heart and Lung Transplantation (ISHLT) registry data and other independent investigators [14–16] have suggested that an ischemic time >4 h may increase the risk for death in recipients receiving hearts from donors older than 50 years. Lietz [48] revealed that ischemic time >4 h and donor death resulting from cerebrovascular accident significantly contributed to poor early posttransplant outcomes. At the same time, it is important to consider that end-stage heart failure presents a significant risk of death while awaiting heart transplantation. The UNOS registry data (in the period 1991–1996) reveal that patients with blood group O have a median waiting time of 332 days; the median waiting time for patients >18 years old was 230 days [49]. Bennett et al. [50] outlined that despite the high risk resulting from the heart transplant, there was a clear long-term survival benefit for status I recipients who received older donor hearts. The data described by Lietz [48] are significant: in patients in status 1 (see Table 3.3), 6-month mortality of 70 % was observed when on a waiting list, and the risk of death was 8.5 times higher than that of status 1 patients who received an allograft from donors >40 years old, with a resulting 14 % 6-month mortality; when an older donor heart was implanted, mortality increased 1.6 times but was not statistically significantly different from recipients who received hearts from younger donors.

Table 3.2 Old donor heart criteria and extended criteria to increase donor pool

Donor heart allocation standard vs. extended criteria	
Standard criteria	Extended criteria
Age <55 years	Age >55 up to 70 years
No known cardiac disease. Ischemic time <120 min (Donor in the same center)	Ischemic time > 360 minutes
No high doses inotropes: Dopamine at a dose of 20 μg/kg/min or similar doses of other adrenergic agents (norepinephrine ≤ 0.2μg/kg/min) despite aggressive optimization of preload and afterload	High-dose inotropes >0.2 μg/kg/min
	Donor comorbidities

Table 3.3 There are four United Network of Organ Sharing (UNOS) status classifications based on condition

Status 1A or urgent need: requires intensive care hospitalization, life-support measures, certain cardiac supporting intravenous medications with a Swan-Ganz catheter, or mechanical-assist device(s)
Status 1B: dependent on intravenous medications or a mechanical-assist device—in the hospital or at home
Status 2: stable on oral medications and able to wait at home
Status 3 or inactive list: inactive due to a change in condition—patients do not lose time they have already accrued

Heart donors older than 70 should not be accepted; in our experience, two transplants utilizing 70-year-old donors were followed by early graft failure despite a short ischemic time.

In conclusion, if an older donor heart is transplanted, it is mandatory to avoid other known risk factors, e.g., a prolonged ischemic time.

Infections According to the guidelines of the ISHLT, hearts from donors with severe infections can be accepted if (1) the donor infection is community acquired and donor death occurs rapidly (within 96 h); (2) repeat blood cultures before organ procurement are negative; (3) pathogen-specific antimicrobial therapy is administered to the donor; (4) donor myocardial function is normal, and at the surgical inspection, endocarditis is absent [37] (Aug. 4, 2010).

Drug Intoxications Cocaine abuse increases the risk of acute myocardial infarction by increasing blood epinephrine and norepinephrine levels that in turn increase systemic blood pressure, heart rate, and myocardial oxygen demand. In the vessels, these effects create a deficiency of endothelium-derived relaxation factor with increased risk for intravascular thrombosis and decline of cardiac contractility [51, 52]. Direct toxic effects on the myocardium have been described, such as scattered foci of myocyte necrosis, and in some studies, contraction band necrosis, myocarditis, and foci of myocyte fibrosis [53]. These abnormalities may lead to cases of cardiomyopathy. Because intravenous (IV) cocaine is more toxic to the heart compared to non-IV cocaine, ISHLT recommends not accepting hearts from IV cocaine abusers [37, 54]. However, hearts from donors with a history of non-IV cocaine abuse appear to be safe in terms of the early postoperative period [37].

Alcohol Abuse Alcohol alters energy stores in the heart, reducing the effectiveness of calcium uptake by the sarcoplasmic reticulum [55] and reducing sodium-potassium adenosine triphosphatase (ATPase) activity, and it interferes with calcium-troponin binding, thus collectively reducing myosin-actin interaction. Early survival and graft function are inferior in the recipients of hearts from donors with a history of alcohol abuse [56, 57]. Nevertheless, there are reports where grafts from alcohol abusers did not show a survival disadvantage [58] or even had a protective effect [59]. In our personal experience at Divisione Cardiochirurgia Policlinico San Matteo Pavia, at least two hearts from alcohol abusers had early graft failure.

Carbon Monoxide Poisoning Carbon monoxide competes with oxygen to form carboxyhemoglobin (HbCO) instead of oxyhemoglobin; it has 210 times the affinity of oxygen for hemoglobin. Therefore, in an atmosphere of 21 % oxygen and 0.1 % carbon monoxide, the blood leaving the lungs will be approximately 50 % saturated with oxyhemoglobin and 50 % saturated with carboxyhemoglobin. At the cellular level, there is a leftward shift of the oxyhemoglobin dissociation curve with reduced oxygen delivery to the tissues and an impairment of mitochondrial cellular respiration due to the competition of carbon monoxide with oxygen for cytochrome a3 [60]. Because the myocardium is vulnerable when deprived of its oxygen, the consequent myocardial injury may determine a primary graft failure in the immediate postoperative period.

Reports on the outcomes of hearts from donors with carbon monoxide intoxication have yielded conflicting results [37, 61, 62]. As recommended by ISHLT [37], before accepting a graft from a donor who died from carbon monoxide poisoning, the graft should be carefully evaluated by ECG and echocardiogram with a minimal elevation of cardiac markers and minimal inotropic requirements; furthermore, the ischemic time should be short with a favorable donor to recipient weight ratio and low pulmonary vascular resistance.

Other Poisonings Grafts from donors with other types of poisonings, including cyanide [63–65], methanol, and ecstasy [66], have been transplanted with satisfactory outcome. In these cases also, cardiac clinical tests should be carefully evaluated.

Cardiac factors:

- Intractable ventricular arrhythmias represent a definitive contraindication.
- Valvular heart disease. A bicuspid aortic valve is not contraindicated if the valve function is maintained [37]. A moderate aortic insufficiency, not diagnosed prior to organ retrieval, may cause improper myocardial protection during cardioplegic infusion. Most valvular pathologies in the donor graft are considered a contraindication to heart transplantation; however, there are reports indicating successful bench repair or posttransplant repair/replacement for aortic and mitral valves [67–70].
- Coronary artery disease. Coronary artery disease in the transplanted heart represents a major concern for physicians involved in heart transplant programs. Coronary disease can be unrecognized, due to the lack of coronary angiography in the donor, or known. In both cases, there is a subsequent risk of early graft failure. Considering patients with early graft failure, the prevalence of coronary disease was 22.8 % [71]; moreover, some reports indicate that a transmitted coronary disease may accelerate graft vasculopathy [72, 73]. Grauhan [74] showed that when donor grafts with more than single-vessel disease are used, the risk of early graft failure is elevated; the risk is 6.3 % in donors without coronary disease, 7.5 % in donors with single-vessel disease, and 42.3 % in grafts with double- and triple-vessel disease. In contrast, Marelli et al. [75] reported the transplant of donor grafts with coronary disease in patients who were urgent cases or who would otherwise not have been offered heart transplants due to associated medical risk (alternate recipients, see below); 59 % of the patients received a concomitant coronary bypass procedure. The study reported that in the patients listed in status I, actuarial survival at 2 years was 50 vs. 81.3 % in the "alternate" recipients.
- Donor left ventricular hypertrophy. This is an important risk factor determining early graft failure, particularly when left ventricular donor wall thickness is >14 mm [76].
- Cardiac tumors. At echocardiography, a myxoma can be diagnosed. A right atrium myxoma can be bench removed, and there is only an embolic risk in the pulmonary circulation (lungs should not be evaluated in this case). When a myxoma is situated in the left atrium, there is a high risk of coronary embolism at the moment of cardiac harvesting when the aorta is clamped [77].
- Hemodynamic instability. It is well known that donor hemodynamic instability represents an important contraindication to heart retrieval. Hemodynamic instability appears primarily after the "catecholamine storm" when vasoplegia and hypotension may irreversibly compromise donation. For this reason, there is increasing evidence that the moderation of pathophysiological changes by active management in an intensive care unit can increase available grafts for transplantation, also recruiting donors considered marginal [78–80]. This active management is realized through the following approaches:
  - Swan-Ganz catheter insertion for cardiac index and wedge pressure measurements; central venous pressure alone is not a sufficient diagnostic tool for fluid administration monitoring.
  - If vasopressor drugs are needed, vasopressin at 2.4 units h^{-1} may reduce catecholamine administration; high doses of norepinephrine, > 0.2 μg/kg/min should be avoided. Canadian guidelines recommend vasopressin as a first-choice drug [81].
  - The management of electrolyte disturbances in the Eurotransplant region from 1997 to 2005 increased recipient mortality when donor sodium concentrations were <130 or >170 mmol/L^{-1} (BJA).
- Alternate recipient list. An alternate recipient list was proposed by Lacks [82] to transplant heart recipients at high risk and without standard criteria. These patients are coupled to marginal donor organs refused by other centers. The most frequent donor risks for the alternate recipient list were high inotropic doses, left ventricular hypertrophy, and hepatitis C seropositivity. A significant mortality was reported in the alternate recipient list [83–85],

although other reports show a survival similar to patients in the standard list [86].

3.4 Donor Lung Exclusion Criteria

Lung transplantation is hindered by donor shortage: less than 25 % of all brain-dead donors are deemed suitable for lung transplantation. Therefore, a very significant number of donor lungs are never used, despite consent. Aspiration, contusion, and infections are important events that occur as a consequence of brain death. The following two important factors play a key role in irreversibly (permanently) deteriorating lung function.

Hemodynamic Instability The mechanism causing the "catecholamine storm" (described above) is responsible for increased minute ventilation, hypertension, tachycardia, and cardiac arrhythmias. There is a net shift of blood volume from systemic circulation to the low-resistance pulmonary circulation, resulting in increased pulmonary venous pressure, which, in turn, causes transudative pulmonary edema. The acute increase in capillary pressure induces barotrauma capable of damaging the capillary-alveolar membrane. The structural damage to the pulmonary endothelium ultimately leads to vascular leakage and persistent protein-rich pulmonary edema [87, 88]. The end result is a neurogenic pulmonary edema.

Activation of Inflammatory and Immunological Pathways After brain death, there is an increase in inflammatory molecules that may threaten the lung function in the pre-donation period. When lung transplantation has been performed, ischemia can trigger the activation of macrophages, which release proinflammatory cytokines and result in an ischemia-reperfusion injury [89].

According to the ISHLT data, the criteria for the "ideal" donor are shown in Table 3.4 [90, 91]. In older donors, early and late survival was decreased, and if older donor age is matched with graft ischemic times longer than 6 h, this effect was pronounced. Moreover, De Perrot (Toronto Lung Transplant Program) [92] did not find a significant difference in 30-day mortality related to donor age, although mortality was significantly higher in recipients with pulmonary fibrosis and pulmonary hypertension compared to those with cystic fibrosis or emphysema. In the study, recipients from donors aged 60 or older had decreased 5- and 10-year survival compared with recipients from younger donors; the cause of death was predominantly bronchiolitis obliterans syndrome (BOS) in the older donor group, whereas it was predominantly sepsis in the younger group.

Table 3.4 The "ideal" lung donor criteria

Age <55 years
PaO_2 >300 mmHg on FIO_2 1.0, PEEP 5 cm H_2O
Clear chest X-ray
No chest trauma
No evidence of aspiration or sepsis
Tobacco history <20 pack-years
AB0 compatibility
Absence of organism on sputum stain
Absence of purulent secretions at bronchoscopy
No prior cardiopulmonary surgery

Most transplant centers prefer an ischemic time between 4 and 6 h. Lung preservation with an extracellular solution allows good results with ischemic times greater than 10 h [93, 94].

Gas exchange is considered the most important parameter for assessing lung function. The PaO_2/FIO_2 ratio should be >300 mmHg (obtain PaO_2 value, convert FIO_2 % in decimal value). However, the ratio can be easily modified by secretions, pulmonary edema, atelectasis, and aggressive donor management (recruitment maneuvers, low tidal volume, PEEP of 15 H_2O cm, bronchial aspiration, and bronchoscopy). Direct left and right pulmonary vein blood gas sampling is sometimes very important in reassessing the lungs individually, and partial pulmonary vein oxygen pressure was reported to correlate much more reliably than PaO_2 with the outcome in the recipient. By separate sampling of pulmonary vein PaO_2, it is possible to harvest at least one lung if the PaO_2/FIO_2 ratio is much better than in the sample obtained from the arterial peripheral catheter. Sometimes in young donors gas exchanges may be satisfactory also in case of severe chest trauma, but chest CT can show important massive, bilateral pulmonary

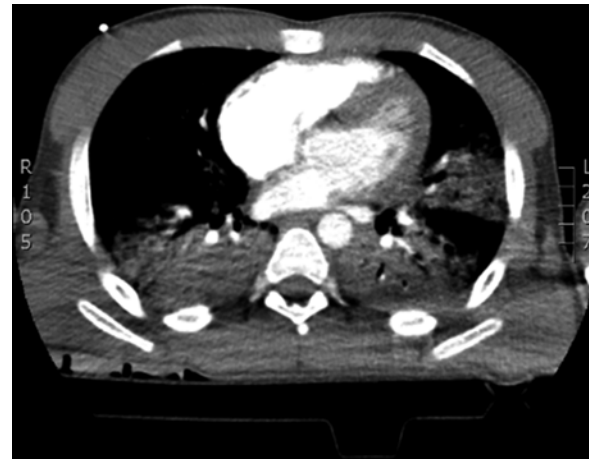

Fig. 3.1 Contrast-enhanced axial computed tomography scan through the thorax of a 19-year-old man after a motor vehicle accident shows massive, bilateral pulmonary contusions and hemothorax. At FIO_2 of 0.40 and 1, the PaO_2 was respectively 131 mmHg and 441 mmHg

contusions, pneumopericardium and hemopneumothorax (Fig. 3.1).

During the harvesting procedure, significant fluid losses are found. Additionally, 8 L of infused fluid are required, and most of this volume is blood, crystalloid, and colloid. If lungs are evaluated for transplantation, it is preferable to administer crystalloid to restrict hypovolemia. It is thought that large amounts of colloid can pass into the extracellular space due to endothelial permeability modification by the inflammatory molecules and can worsen lung function after transplantation by increasing the oncotic pressure. A large quantity of crystalloids may also produce a considerable increase of the central venous pressure and, if prolonged over time, may produce edema of the liver parenchyma and hamper liver graft function after transplantation. Liver edema may also have an adverse effect on bleeding during the splitting procedures of the liver.

At surgery, lungs are directly inspected to check zones of atelectasis, hemorrhagic contusion, edema, nodules that must undergo intraoperative wedge biopsy, and pneumonic infiltration. Then, lung compliance should be evaluated under direct vision by performing the "collapse test": an endotracheal tube is disconnected from the ventilator, and if the lungs remain inflated or slowly collapse (more than 10 s), this is a sign of interstitial space edema, infection, or emphysema (small airway obstructive disease).

A positive gram stain of tracheal aspirate should not preclude lung donation. The amount of secretions is much more significantly associated with a negative outcome. The University of Alabama at Birmingham showed that a positive donor gram stain is not necessarily associated with pneumonia development [95].

Alcohol Abuse Donor chronic alcohol abuse has been correlated with an increased risk of primary graft dysfunction. Pelaez et al. showed that donor alcohol abuse may have a great impact on the risk of primary graft dysfunction and that there is a clearly established link between alcohol abuse and ARDS (acute respiratory distress syndrome) [96].

Donor History of Asthma Asthma in the donor has been often considered a contraindication to lung transplantation primarily for the preoperative airway inflammation status that can affect transplantation outcome. Fatal asthma donors predispose the recipient to early and late graft dysfunction, especially refractory acute rejection [97]. However, the use of grafts from carefully selected donors with a history of asthma increases the donor pool and has satisfactory long-term results [97].

Ex Vivo Lung Perfusion Ex vivo lung perfusion (EVLP) was developed in the late 1990s by researchers at Lund University, in Lund, Sweden, who studied non-heart-beating donor lungs with the objective of increasing the number of organs suitable for transplantation [98]. Through experimental studies on pigs, a perfusion solution was developed to prevent edema formation and the

loss of lung function. The solution was designated Steen Solution® (Vitrolife; Gothenburg, Sweden). Steen Solution is an extracellular solution for lung preservation composed of electrolytes, dextran, and albumin. A noteworthy feature of the solution is its high oncotic pressure [99]. The first clinical use of EVLP [100] was described in 2001: the donor was a 54-year-old man who had suffered cardiac arrest due to acute myocardial infarction. The transplantation to a recipient patient with pulmonary emphysema was successful. ELVP has been performed by several lung transplant centers worldwide with good results. At the Toronto Lung Transplant Program, from September 2008 to December 2011, 253 lung transplants were performed with conventional preservation lungs. Primary graft dysfunction grade three at 72 h was recorded in 2 % EVLP vs. 8.5 % control ($P=0.14$), and time on mechanical ventilation, extracorporeal life support, ICU stay, hospital stay, and 30-day mortality were not different. Furthermore, similar 1-year survival rates were observed: 87 % for the EVLP group vs. 86 % for the standard group [101].

3.5 Liver Donor Exclusion Criteria

For heart and lung donation, the only absolute exclusion criteria are human immunodeficiency virus infection (HIV), uncontrolled tumor disease, and bacterial or viral infections, as previously discussed. All general clinical conditions, including biochemical, morphological, and functional conditions, must be considered for the donors and their organs to balance the decision regarding whether a liver graft can be used.

The classical clinical and morphological exclusion criteria of the hepatic donor, which years ago would have absolutely contraindicated donation, have now become relative contraindications. These criteria must only be considered if several contraindications occur simultaneously. Based on different studies, the principal liver viability marker is its gross and microscopic inspection. Less than 40 % steatosis evaluated on liver biopsy is fundamental to assure the normal function of the implanted graft, but in the absence of other contraindications, a steatosis of 50 % can be considered for the transplantation of the whole liver for special recipients at risk of dropout from the waiting list (HCC patients). Split-liver transplantation, a procedure where one donor liver is divided into two hemilivers for two recipients, is an important tactic for overcoming organ shortage. To date, the principal beneficiaries have been adult/pediatric pairs, and excellent outcomes have been described. However, the criteria for the liver-splitting technique require much more restrictive criteria than for conventional whole livers. Donor eligibility criteria for the split-liver procedure were as follows: age 55 or younger, no cardiac arrest episodes, less than 5 days in intensive care, low inotropic support (dopamine $\leq$5 mg/kg/min, dobutamine $\leq$10 mg/kg/min, and no epinephrine or norepinephrine requirement), Na+ $\leq$155 mg/L, liver enzymes no more than double the normal, and no macroscopic evidence of hepatic steatosis, or less than 20 % hepatic steatosis if a biopsy was taken, because liver biopsy was not routinely performed. Liver-splitting techniques for two adults are still experimental surgical procedures, and they have interesting results when these restrictive criteria are employed for donors and for particular pairs of recipients in which one is of small size [102].

Livers from elderly donors undoubtedly represent a diffuse problem: age limit criteria have become more flexible in recent years due to the worldwide decrease of young donors. The transplant teams have perceived that the most effective method to increase the number of donors is to increase their age acceptance; octogenarian donors can be considered, provided liver biopsy results in the absence of fibrotic changes [103]. Livers from positive HCV donors represent a small percentage of other possible sources. Hepatic donors' acceptance criteria that permit the use of HCV-positive donors without liver disease for HCV-positive recipients are increasing. The short-term results of these transplants do not differ from those obtained in HCV-positive recipients from HCV-negative donors. Recent reviews report studies in liver transplants with HCV-positive donor livers in HCV-positive recipients and showed similar graft

survival, patient survival, and hepatitis C recurrence in the recipient and in an HCV-positive hepatic recipient group in whom livers from HCV-negative donors were transplanted [104]. Although there are fewer data than for kidney transplants, somewhat encouraging results are seen with hepatic grafts from non-heart-beating donors; 5-year survival is slightly greater than 50 % [105].

Several additional contraindications pertaining to the living donor are the same as those stated below for living donor liver transplantation (LDLT). In addition to the contraindications previously mentioned, there are some particular absolute contraindications for a living donor. Donors having macrosteatosis (>20 %) on liver biopsy are rejected. Remnant liver volume cannot be less than 25 %. This is an issue especially when the right lobe graft is large. It is never an issue when the left lateral segment is the proposed graft and is rarely an issue if the left lobe graft is taken. The Human Organ Transplantation Act, in some countries, does not allow unrelated donation; this is to prevent donation under any type of coercion and to avoid any organ trade. The living donor should be between 18 and 55 years of age. A body mass index >30 for the donor is generally associated with a consistent degree of macrosteatosis; donors should be encouraged to reduce weight, and a liver biopsy should rule out liver steatosis >20 %. A liver attenuation index <5 on a plain CT scan is suggestive of steatosis. Such donors are either rejected or, in the absence of other donors, need to reduce weight, and a biopsy should be performed to rule out macrosteatosis >20 % [3]. Donors are also rarely rejected for anatomical reasons. Double artery, double portal vein, or multiple hepatic veins such as a V8 or a V6 can be anastomosed using specific surgical techniques, and these presentations should no longer preclude donation. However, multiple anatomical anomalies, e.g., a portal vein trifurcation with a right bile duct draining the segment IV, double right hepatic arteries in the donor, or multiple right-sided segmental portal vein tributaries draining into the left portal vein, are considered contraindications for LDLT. The majority of biliary anatomy in the donor is acceptable [106].

3.6 Kidney Donor Exclusion Criteria

The successful retrieval and transplantation of kidneys, pancreas, and other organs is dependent on the optimal perfusion of the donor and from all management strategies with particular respect of the hemodynamic stability. Allograft renal function after transplantation may be influenced by donor management. Although the use of dopamine as a renal protective agent in the general critical care population is inappropriate, Schnuelle and colleagues demonstrated in a European multicenter trial that donor pretreatment with low-dose dopamine can reduce the need for dialysis after kidney transplantation [107]. Absolute kidney donor exclusion criteria (Table 3.5) shared by the donors of other organs are the same as those for other organs and include HIV infection, malignant neoplasms (including in the central nervous system), sepsis, disseminated infections uncontrolled with antimicrobial

Table 3.5 Kidney and pancreas exclusion criteria

Kidney and pancreas exclusion criteria: absolute contraindications
HIV (or risk group)
Sepsis or uncontrolled disseminated infection (bacteria, viruses, fungi)
Multiorgan failure
Malignant tumor disease with metastasizing capacity
Creutzfeldt-Jakob, Kuru, Gerstmann-Straussler-Scheinker, fatal familial insomnia
Diabetes type I
Chronic pancreatitis
Pancreatic trauma (only for pancreas)
Patients treated with cadaver-derived pituitary hormones
Chronic kidney failure (structural damage)
Age >80 for kidneys and >45 for pancreas
Arterial hypertension
Diabetes type II
Acute renal failure
Chronic alcohol abuse
Prolonged warm ischemia
Glomerulonephritis and other nephropathies in normal renal function phase
Donors with positive serology for hepatitis B and C viruses unless for patients with hepatitis HBV and HCV

therapy (including bacteria, viruses, and fungi), multiorgan failure, and uncommon diseases such as Creutzfeldt-Jakob and those caused by prions such as Kuru. Donors with hepatitis B and C may be accepted for donation to recipients who are carriers of the same viruses. Thus, kidneys from AgHBs carrier donors may be used in AgHBs(+) recipients. Additionally, the use of renal grafts from donors with HCV-positive antibodies in HCV-positive recipients can be considered without apparently increasing major morbidity or mortality. Chronic renal failure is also an absolute renal donor exclusion criterion.

3.7 Pancreas Donor Exclusion Criteria

The pancreas shares the same donor selection criteria with the kidney, with the specific characteristic that pancreatic donors cannot have a personal background of alcoholism, a personal or familiar background of diabetes, significant alterations in the serum amylase values, or an age greater than 45–50 (Table 3.5). The best indication of the suitability of a pancreas allograft for transplantation is the appearance of the organ at the time of procurement. After completing the surgical maneuvers, the pancreatic parenchyma should be carefully evaluated for its procurement in terms of fat content, edema, or fibrosis and for quality of the vasculature. All aspects of the pancreas should be inspected for injury to the pancreatic parenchyma and for the presence of hematomas, masses, or nodular areas. Most centers avoid transplanting organs with calcifications, extensive fibrosis, fatty infiltration, severe edema, or significant visceral atherosclerosis. Depending from different center policies, pancreas procurement may be cancelled for technical reasons such as abnormal arterial vascularization between the liver and the pancreas, which may occur with a right replacing hepatic artery originating from the superior mesenteric artery and would render a successful and correct split and the transplantation of both organs difficult. Surgical injuries that occur during pancreas procurement may lead to complications after transplantation, impaired function of the allograft, graft loss, or even death of the patient. These injuries may be so dangerous that the pancreas harvesting must be considered an absolute contraindication. In such cases, pancreatic islet transplantation can be considered. Proper procurement and the constant training of surgeons for pancreatic procurement are therefore very important to maintain high-quality pancreas procurement. Some recent reports show that vascular lesions are observed in 16.7 % of pancreatic grafts and suggest that surgical procedures of pancreas procurement may be improved by better surgical training and the standardization of the surgical technique. Some studies have shown that pancreatic allografts have been frequently refused during back-table inspection, partly because of multiple surgical injuries to the artery, veins, and duodenum [108]. Donor age and procurement by centers not performing pancreas transplantations were both found to significantly increase the probability of pancreas refusal. The quality of pancreas procurement may thus be improved by the specific training of surgeons who specifically perform pancreas transplantations.

3.8 Intestinal and Multiorgan Exclusion Criteria

There are very few absolute contraindications to intestinal donation, and they can be grouped into four broad categories: (1) severe intestinal trauma, (2) malignancy outside of the central nervous system (CNS), (3) active infections, and (4) inflammatory bowel disease (IBD) or the same contraindications for liver procurement in the case of combined liver and intestinal transplantation. Ideal donors are preferably younger (<45 years) and with little or no use of vasoactive drugs.

Patients with short bowel syndrome present with the abdominal cavity retracted, thus requiring smaller donors (30–40 % less of the calculated body surface area). Preference is given to ABO identity. With the development of effective drugs for prophylaxis and the treatment of cytomegalovirus, seropositive donors are accepted and are avoided only for recipients with negative serology. The decontamination of the gastrointestinal tract and the use of antibodies in donor lymphocytes showed no benefits related to infection, rejection episodes, or incidences of graft versus host disease. Typically, in these donors

Table 3.6 Intestinal and multiorgan exclusion criteria

Donor criteria	Exclusion criteria
All donors evaluable at a standard risk	Abdominal trauma especially when operative procedures have been performed
Age <45 years	Asphyxia or CO intoxication
Intensive care <5 days	Resuscitation after long period of hypotension
Enteral nutrition during stay in ICU	Prolonged shock
BMI <25	Blood losses with large RBC transfusion
Size matching with recipient	Alcoholism or drug abuse
Cold ischemia <6 h	Arteriosclerosis
Crossmatch negative	Malignancy outside of the central nervous system (CNS), active infections, or IBD

also liver and pancreas are retrieved. Due to the shared bloodstream, the simultaneous harvesting of these grafts can be a challenge but is possible to perform the procedure without compromising other grafts [109] (Table 3.6).

References

1. Akyol M, Tswen Wen VL (2013) Cap. 1. Organ retrieval logistics. 1–8. In: Oniscu GC, Forsythe JL, Fung J (eds) Abdominal organ retrieval and transplantation bench surgery. Wiley-Blackwell, West Sussex. UK
2. Keegan MT, Wood KE, Coursin DB (2010) cap. XVIII. An Update on ICU Management of the Potential Organ Donor. 547–559. In Vincent J-L Yearbook of Intensive Care and Emergency Medicine. Springer-Verlag Berlin Heidelberg
3. Rosendale JD, Chabalewski FL, Mc Bride MA, Garrity ER et al (2002) Increased transplanted organs from the use of a standardized donor management protocol. Am J Transplant 2:761–768
4. Matesanz R, Miranda B (1996) Organ donation: the 'Spanish model'. Transplant Proc 28(1):11
5. Journalist Workshop on Organ donation and transplantation Recent Facts & Figures 26 November 2014 – Brussels. http://ec.europa.eu/health/blood_tissues_organs/docs/ev_20141126_factsfigures_en.pdf
6. Wolach B, Sazbon L, Gavrieli R, Broda A, Schlesinger M (2001) Early immunological defects in comatose patients after acute brain injury. J Neurosurg 94:706–711
7. Kane TD, Johnson SR, Alexander JW, Craycraft TK (1997) Bacterial translocation in organ donors: clinical observations and potential risk factors. Clin Transplant 11:271–274
8. Ison MG, Hager J, Blumberg E, Burdick J, Carney K, Cutler J et al (2009) Donor-derived disease transmission events in the United States: data reviewed by the OPTN/UNOS Disease Transmission Advisory Committee. Am J Transplant 9:1929–1935
9. Ison MG, Nalesnik MA (2011) An update on donor-derived disease transmission in organ transplantation. Am J Transplant 11:1123–1130
10. Ison MG, Grossi P (2013) Donor-derived infections in solid organ transplantation. Am J Transplant 13:22–30
11. Nanni Costa A, Grossi P, Gianelli Castiglione A, Grigioni WF (2008) Quality and safety in the Italian donor evaluation process. Transplantation 85(8 Suppl):S52–S56
12. The CNT/European risk classification system. http://www.edqm.eu/en/Search-519.html
13. Guidelines for prevention of transmission of infectious diseases from organ donors to recipients. http://www.scandiatransplant.org/organ-allocation/ScandtxInfGuidelines2014.pdf
14. Sözen H, Fidan K, Mahli A, Singin E, Buyan N, Sindel S et al (2008) Successful solid organ transplantation from septicemic cadaveric donors: case report. Transplant Proc 40:299–301
15. Grossi PA, Fishman JA, The AST Infectious Disease Community of Practice (2009) Donor-derived infections in solid organ transplant recipients. Am J Transplant 9(Supp. 4):S19–S26
16. Freeman RB, Giatras I, Falagas ME, Supran S, O'Connor K, Bradley J et al (1999) Outcome of transplantation of organs procured from bacteremic donors. Transplantation 68:1107–1111
17. Lumbreras C, Sanz F, Gonzalez A, Perez G, Ramos MJ, Aguado JM et al (2001) Clinical significance of donor unrecognized bacteremia in the outcome of solid-organ transplant recipients. Clin Infect Dis 33:722–726
18. Cerutti E, Stratta C, Romagnoli R, Serra R et al (2006) Bacterial- and fungal-positive cultures in organ donors: clinical impact in liver transplantation. Liver Transpl 12:1253–1259
19. Ydreborg M, Westin J, Lagging M, Castedal M, Friman S (2012) Impact of donor histology on survival following liver transplantation for chronic hepatitis C virus infection: a Scandinavian single-center experience. Scand J Gastroenterol 47:710–717
20. Wood KE, Becker BN, McCartney JG, D'Alessandro AM, Coursin DB (2004) Care of the potential organ donor. N Engl J Med 351:2730–2739
21. Lund LH, Edwards LB, Kucheryavaya AY, Benden C et al (2014) The registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report—2014; focus theme: retrasplantation. J Heart Lung Transplant 33:996–1008
22. Copeland JG (1995) Only optimal donors should be accepted for heart transplantation: protagonists. J Heart Lung Transplant 14:1038–1042
23. Wittwer T, Wahlers T (2008) Marginal donors grafts in heart transplantation: lessons learned from 25 years of experience. Transplant Int 21:113–125

24. Costanzo MR, Augustine S, Bourge R, Bristow M, O'Connell JB, Driscoll D, Rose E (1995) Selection and treatment of candidates for heart transplantation. A statement for health professionals from the Committee on Heart Failure and Cardiac Transplantation of the Council on Clinical Cardiology, American Heart Association. Circulation 92:3593–3612
25. Zaroff JG, Rosengard BR, Armstrong WF, Babcock WD, D'Alessandro A, Dec GW, Edwards NM, Higgins RS, Jeevanandum V, Kauffman M, Kirklin JK, Large SR, Marelli D, Peterson TS, Ring WS, Robbins RC, Russell SD, Taylor DO, Van Bakel A, Wallwork J, Young JB (2002) Consensus conference report: maximizing use of organs received from cadaver donor-cardiac recommendations, March 28-29, 2001, Crystal City, VA. Circulation 106:836–841
26. Dronavalli VB, Banner NR, Bonser RS (2010) Assessment of the potential heart donor: a role for biomarkers? J Am Coll Cardiol 56:352–361
27. Bombardini T, Ghrerardi S, Sicari R, Picano E (2013) Transplant of stunned donor hearts rescued by pharmacological stress echocardiography: a "proof of concept" report. Cardiovasc Ultrasound 11:27
28. Loebe M, Potapov EV, Hummel M et al (2000) Medium-term results of heart transplantation using older donor organs. J Heart Lung Transplant 19:957–963
29. Blanche C, Kamlot A, Blanche DA et al (2002) Heart transplantation with donors fifty years of age and older. J Thorac Cardiovasc Surg 123:810–815
30. Potapov EV, Loebe M, Hubler M et al (1999) Medium-term results of heart transplantation using donors over 63 years of age. Transplantation 8:1834–1838
31. Gupta D, Piacentino V, Macha M et al (2004) Effect of older donor age on risk for mortality after heart transplantation. Ann Thorac Surg 78:890–899
32. Bourge RC, Naftel DC, Costanzo-Nortdin MR et al (1993) Pretransplantation risk factors for death after heart transplantation: a multiinstitutional study. The Transplant Cardiologists Research Database Group. J Heart Lung Transplant 12:549–562
33. Young JB, Naftel DC, Bourge RC et al (1994) Matching the heart donor and heart transplant recipient. Clues for successful expansion of the donor pool: a multivariable, multiinstitutional report. The Cardiac Transplant Research Database Group. J Heart Lung Transplant 13:353–365
34. Fernandez Lucas M, Miranda B, Matesanz R et al (1997) Donor characteristics and hospital survival in cardiac transplantation. The Spanish Groups of Heart Transplantation. Transplant Proc 29: 3384–3385
35. Boehmer JP (1993) Expanding the donor pool: how far is too far? J Heart Lung Transplant 12:816–818
36. Omoto T, Minami K, Böthig D, Scütt U, Tenderich G, Wlost S, Körfer R (2003) Risk factor analysis of orthotopic heart transplantation. Asian Cardiovasc Thorac Ann 11:33–36
37. International Society for Heart and Lung Transplantation guidelines for the care of heart transplant recipients task force 1: peri-operative care of the heart transplant recipient (4 Aug 2010). http://www.jsht.jp/uploads/ISHLT_GL_TaskForce1_080410.pdf
38. Lamour JM, Kanter KR, Naftel DC, Chrisant MR, Morrow WR et al (2009) The effect of Age, diagnosis, and previous surgery in children and adults undergoing heart transplantation for congenital heart disease. J Am Coll Cardiol 54:160–165
39. Bourge RC, Kirklin JK, Thomas K et al (2001) The emergence of co-morbid diseases impacting survival after cardiac transplantation, a ten year multi-institutional experience. J Heart Lung Transplant 20:167–168
40. Young JB, Hauptman PJ, Naftel DC et al (2001) Determinants of early graft failure following cardiac transplantation, a 10-year, multi-institutional, multivariable analysis. J Heart Lung Transplant 20:212
41. Hoecher K, Young JB, McCarthy PM, Smedira N, Price LL, Stewart KW (1998) Long term mortality and morbidity with use of older donors in cardiac transplantation: a single center experience (abstr). Transplantation 65(Suppl):S104
42. McCarthy JF, McCarthy PM, Massad MG et al (1998) Risk factors for death after heart transplantation: does a single center experience correlated with multicenter registries? Ann Thorac Surg 65:1564–1569
43. Livi U, Bortolotti U, Luciani GB et al (1994) Donor shortage in heart transplantation: is extension of donor age limits justified? J Thorac Cardiovasc Surg 107:1346–1355
44. Drinkwater DC, Laks H, Blitz A et al (1996) Outcomes of patients undergoing transplantation with older donor hearts. J Heart Lung Transplant 15:684–691
45. Pflugfelder PW, Singh NR, McKenzie FN, Menkis AH, Novick RJ, Kostuk WJ (1991) Extending cardiac allograft ischemic time and donor age: effect on survival and long-term cardiac function. J Heart Lung Transplant 10:394–400
46. Tenderich G, Koerner MM, Stuettgen B, Arusoglu L, Bairaktaris A, Hornik L, Wlost S, Mirow N, Minami K, Koerfer R (1998) Extended donor criteria: hemodynamic follow-up of heart transplant recipients receiving a cardiac allograft from donors > or = 60 years of age. Transplantation 66:1109–1113
47. Hosenpud JD, Bennett LE, Keck BM, Fiol B, Boucek MM, Novick RJ (1999) The registry of the international society of heart and lung transplantation: sixteenth official report—1999. J Heart Lung Transplant 18:611–626
48. Lietz K, John R, Mancini DM, Edwards NM (2004) Outcomes in cardiac transplant recipients using allografts from older donors versus mortality on transplant waiting list; implications for donor selection criteria. J Am Coll Cardiol 43:1553–1561
49. Kauffmann MH, McBride MA, Shield CF, Daily OP, Wolf JS, Kirklin JK (1999) Determinants of waiting time for heart transplants in the United States. J Heart Lung Transplant 18:414–419

50. Bennett LE, Edwards EB, Hosenpud JD (1998) Transplantation with older donor hearts for presumed 'stable' recipients: an analysis of the Joint International Society for Heart and Lung Transplantation/United Network for Organ Sharing Thoracic Registry. J Heart Lung Transplant 17:901–905
51. Isner JM, Chokshi SK (1991) Cardiovascular complications of cocaine. Curr Probl Cardiol 16(2): 89–123
52. Rongione AJ, Steg PG, Gal D, Isner JM (1988) Cocaine causes endothelium-independent vasoconstriction of vascular smooth muscle. Circulation 78:II-436. Abstract
53. Kloner RA, Hale S, Alker K, Rezkalla S (1992) The effects of acute and chronic cocaine use on the heart. Circulation 85:407–419
54. Houser SL, MacGillivray T, Aretz HT (2000) The impact of cocaine on the donor heart: a case report. J Heart Lung Transplant 19(6):609–611
55. Rubin E (1979) Alcoholic myopathy in heart and skeletal muscle. N Engl J Med 301:28–33
56. Houyel L, Petit J, Nottin R, Duffet JP, Mace L, Neveux JY (1992) Adult heart transplantation: adverse role of chronic alcoholism in donors on early graft function. J Heart Lung Transplant 11(6):1184–1187
57. Freimark D, Aleksic I, Trento A et al (1996) Hearts from donors with chronic alcohol use: a possible risk factor for death after heart transplantation. J Heart Lung Transplant 15:150–159
58. Shea KJ, Sopko NA, Ludrosky K, Hoercher K, Smedira NG, Taylor DO, Starling RC, Gonzalez-Stawinski GV (2007) The effect of a donor's history of active substance on outcomes following orthotopic heart transplantation. Eur J Cardiothorac Surg 31:452–456
59. De La Zerda DJ, Cohen O, Beygui RE, Kobashigawa J, Hekmat D, Laks H (2007) Alcohol use in donors is a protective factor on recipients' outcome after heart transplantation. Transplantation 83(9):1214–1218
60. Goldbaum LR, Orellano T, Dergal E (1976) Mechanism of the toxic action of carbon monoxide. Ann Clin Lab Sci 6:372–376
61. Rodrigus IE, Conraads V, Amsel BJ, Moulijn AC (2001) Primary cardiac allograft failure after donor carbon monoxide poisoning treated with biventricular assist device. J Heart Lung Transplant 20(12):1345–1348
62. Karwande SV, Hopfenbeck JA, Renlund DG, Burton NA, Gay WA Jr (1989) An avoidable pitfall in donor selection for heart transplantation. Utah Heart Transplant Program. J Heart Transplant 8:422–424
63. Fortin JL, Ruttimann M, Capellier G, Bigorie A, Ferlicot S, Thervet E (2007) Successful organ transplantation after treatment of fatal cyanide poisoning with hydroxocobalamin. Clin Toxicol 45:468–471
64. Barkoukis TJ, Sarbak CA, Lewis D, Whittier FC (1993) Multiorgan procurement from a victim of cyanide poisoning. A case report and review of the literature. Transplantation 55:1434–1436
65. Snyder JW, Unkle DW, Nathan HM, Yang SL (1993) Successful donation and transplantation of multiple organs from a victim of cyanide poisoning. Transplantation 55:425–427
66. Wood DM, Dargan PI, Jones AL (2003) Poisoned patients as potential organ donors: postal survey of transplant centres and intensive care units. Crit Care 7:147–154
67. Saito S, Matsumiya G, Ueno T et al (2009) Bench replacement of donor aortic valve before orthotopic heart transplantation. J Heart Lung Transplant 28:981–983
68. Prieto D, Antunes P, Antunes MJ (2009) Donor mitral valve repair in cardiac transplantation. Transplant Proc 41:932–993
69. Massad M, Smedira NG, Hobbs R et al (1996) Bench repair of donor mitral valve before heart transplantation. Ann Thorac Surg 61:1833
70. Coskun KO, Coskun ST, El Arousy M et al (2007) Cardiac surgery after heart transplantation: coronary artery bypass grafting and heart valve replacement. Heart Surg Forum 10:E110
71. Sandler D, McKenzie FN, Menkis AH et al (1991) Early death after cardiac transplantation – the role of unsuspected donor coronary artery disease. J Heart Lung Transplant 29:623
72. Gao SZ, Hunt SA, Alderman EL et al (1997) Relation of donor age and preexisting coronary artery disease on angiography and intracoronary ultrasound to later development of accelerated allograft coronary artery disease. J Am Coll Cardiol 29:623
73. Wong CK, Yeung AC (2001) The topography of intimal thickening and associated remodelling pattern of early transplant coronary disease: influence of preexistent donor atherosclerosis. J Heart Lung Transplant 20:858
74. Grauhan O, Patzurek J, Hummel M et al (2003) Donor-transmitted coronary atherosclerosis. J Heart Lung Transplant 22:568
75. Marelli D, Laks H, Bresson S et al (2003) Results after transplantation using donor hearts with preexisting coronary artery disease. J Thorac Cardiovas Surg 126:821–825
76. Kuppahally SS, Valantine HA, Weisshaar D et al (2007) Outcome in cardiac recipients of donor hearts with increased left ventricular wall thickness. Am J Transplant 7:2388–2395
77. Grande AM, Viganò M (2004) Myxoma in a donor heart. Texas Heart Inst J 31:106–107; de Boer HD, de Jonge N, de Boer WJ (1999) Mitral valve myxoma: an unusual reason for rejecting a donor heart. J Heart Lung Transplant 18:924–925
78. McKeown DW, Bonser RS, Kellum JA (2012) Management of the heartbeating brain-dead organ donor. Br J Anaesth 108(S1):i96–i107
79. Venkateswaran RV, Steeds RP, Quinn DW, Nightgale P, Wilson IC et al (2009) The haemodynamic effects of adjunctive hormone therapy in potential heart donors: a prospective randomized double-blind factorially designed controlled trial. Eur Heart J 30:1771–1780

80. Koo KKY, Sun JCJ, Zhou Q et al (2011) Pulmonary artery catheters: evolving rates and reasons for use. Crit Care Med 39:1–6
81. Shemie SD, Ross H, Pagliarello J et al (2006) Organ donor management in Canada: recommendations of the forum on medical management to optimize donor organ potential. Can Med Assoc J 174:S13–S30
82. Laks H, Scholl FG, Drinkwater DC et al (1997) The alternate recipient list for heart transplantation. Does it work? J Heart Lung Transplant 16:735–742
83. Patel J, Kobashigawa JA (2004) Cardiac transplantation: the alternate list and expansion of the donor pool. Curr Opin Cardiol 19:162
84. Felker GM, Milano CA, Yager JEE et al (2005) Outcomes with an alternate list strategy for heart transplantation. J Heart Lung Transplant 24:1781
85. Lima B, Rajagopal K, Petersen RP et al (2006) Marginal cardiac allografts do not have increased primary graft dysfunction in alternate list transplantation. Circulation 114(Suppl I):I27–I32
86. Chen JM, Russo MJ, Hammond KM et al (2005) Alternate waiting list strategies for heart transplantation maximize donor organ utilization. Ann Thorac Surg 80:224
87. Theodore J, Robin ED (1976) Speculations on Neurogenic Pulmonary Edema (NPE). Am Rev Respir Dis 113:405–411
88. Davison DL, Terek M, Chawla LS (2012) Neurogenic pulmonary edema. Crit Care 16:212–218
89. Naik PM, Angel LF (2011) Special issues in the management and selection of the donor for lung transplantation. Semin Immunopathol 33:201–210
90. Meyer DM, Bennett LE, Novick RJ, Hosenpud JD (2000) Effect of donor age and ischemic time on intermediate survival and morbidity after lung transplantation. Chest 118:1255–1262
91. Fischer S, Gohrbandt B, Struckmeier P, Niedermeyer J, Simon A, Hagl C, Kallenbach K, Haverich A, Stru¨ ber M (2005) Lung transplantation with lungs from donors fifty years of age and older. J Thorac Cardiovasc Surg 129:919–925
92. De Perrot M, Waddell TK, Shargall Y, Pierre AF, Fadel E, Uy K, Chaparro C, Hutcheon M, Singer LG, Keshavjee S (2007) Impact of donors aged 60 years or more on outcome after lung transplantation: results of an 11-year single-center experience. J Thorac Cardiovasc Surg 133:525–531
93. Maccherini M, Keshafjee SH, Slutsky AS, Patterson GA, Edelson JD (1991) The effect of low-potassium dextran versus Euro-Collins solution for preservation of isolated type II pneumocytes. Transplantation 52:621–626
94. Bins OAR, DeLima NF, Buchanan SA, Cope JT, King RC, Marek CA et al (1996) Both blood and crystalloid-based extracellular solutions are superior to intracellular solutions for lung preservation. J Thorac Cardiovasc Surg 112:1515–1521
95. Weill D, Dey GC, Young KR, Zorn GL et al (2002) A positive donor gram stain does not predict outcome following lung transplantation. J Heart Lung Transplant 21:555–558
96. Pelaez A, Mitchell PO, Shah NS, Force SD, Elon L, Brown LAS, Guidot DM (2015) The role of donor chronic alcohol abuse in the development of primary graft dysfunction in lung transplant recipients. Am J Med Sci 349:117–123
97. Oto T, Griffiths A, Levvey B, Withford H, Kotsimbos TC, Rabinov M et al (2004) Donor history of asthma is not a contraindication to lung transplantation: 12-year single-center experience. J Heart Lung Transplant 23:309–316
98. Steen S, Ingemansson R, Budrikis A, Bolys R, Roscher R, Sjöberg T (1997) Successful transplantation of lungs topically cooled in the non-heart-beating donor for 6 hours. Ann Thorac Surg 63:345–351
99. Steen S, Liao Q, Wierup PN, Bolys R, Pierre L, Sjöberg T (2003) Transplantation of lungs from non-heart-beating donors after functional assessment ex vivo. Ann Thorac Surg 76(1):244–252; discussion 252
100. Steen S, Sjöberg T, Pierre L, Liao Q, Eriksson L, Algotsson L (2001) Transplantation of lungs from a non-heart-beating donor. Lancet 357(9259): 825–829
101. Machuca TN, Cypel M (2014) Ex vivo lung perfusion. J Thorac Dis 6(8):1054–1062
102. Aseni P, De Feo TM, De Carlis L et al (2014) A prospective policy development to increase split-liver transplantation for 2 adult recipients: results of a 12-year multicenter collaborative study. Ann Surg 259:157–165
103. Cuende N, Grande L, Sanjuan F, Cuervas-Mons V (2002) Liver transplant with organs from elderly donors: Spanish experience with more than 300 liver donors over 70 years of age. Transplantation 73:1360
104. Takada Y, Haga H, Ito T, Nabeshima M, Ogawa K, Kasahara M et al (2006) Clinical outcomes of living donor liver transplantation for hepatitis C virus (HCV)-positive patients. Transplantation 81:350–354
105. Hong JC, Yersiz H, Kositamongkol P, Xia VW, Kaldas FM, Petrowsky H, Farmer DG, Lipshutz G, Markovic D, Hiatt JR, Busuttil RW (2011) Liver transplantation using organ donation after cardiac death. Arch Surg 146:1017–1023
106. Varma V, Mehta N, Kumaran V, Nundy S (2011) Indications and contraindications for liver transplantation. Int J Hepatol 2011:121862. doi:10.4061/2011/121862. Epub 2011 Oct 5
107. Schnuelle P, Gottman U, Hoeger S et al (2009) Effects of donor pretreatment with dopamine on graft funetion after kidne y tr ansplantation. JAMA 302:1067–1075
108. Marang-van de Mheen PJ, Hilling DE, Dirkes MC, Baranski AG (2011) Surgical injuries of pancreatic allografts during procurement. Clin Transplant 25(5):737–743
109. Abu-Elmagd K, Fung J et al (2000) Logistics and technique for procurement of intestinal, pancreatic, and hepatic grafts from the same donor. Ann Surg 232:680–687

Part II

Principles of Brain Death Diagnosis and Optimal Management for Organ Retrieval

Brain Death Diagnosis

4

Antonino M. Grande and Paolo Aseni

I know when one is dead and when one lives.
She's dead as earth. Lend me a looking-glass.
If that her breath will mist or stain the stone,
Why then, she lives.

W. Shakespeare, King Lear, Act V, Scene III

During Shakespeare's time in the late sixteenth and early seventeenth century, not breathing and the absence of blood circulation were universal criteria to declare someone dead. For almost two centuries, doctors have been using the stethoscope to diagnose death. In the twentieth century, the discovery of cardiopulmonary resuscitation, defibrillation, and pharmacologic therapies to counteract heart arrest changed the definition; cardiac arrest could be established as a clinical death, giving rise to the possibility of post-arrest resuscitation. For almost 50 years, doctors have thus been diagnosing death by applying neurological criteria.

The brain is anatomically divided into the cerebrum, with its outer shell, the cortex; the cerebellum; and the brain stem, composed of the midbrain, the pons, and the medulla oblongata. Traditionally, the cerebrum has been considered the "higher brain" because it has primary control of consciousness, thought, memory, and feeling. The brain stem is the "lower brain," because it organizes spontaneous, vegetative functions such as swallowing, yawning, and sleep–wake cycles. At the same time, "higher brain" functions such as cognition or consciousness are not mediated strictly by the cerebral cortex, but they result from complex interactions between the brain stem and the cortex. Breathing is controlled in the brain stem, particularly the medulla. Neural impulses originating in the respiratory centers of the medulla stimulate the diaphragm and intercostal muscles, which cause lung inflation and deflation. Generally, respiratory centers adjust the rate of breathing to maintain the correct levels of carbon dioxide and oxygen. During heavy exercise, sighing, coughing, or sneezing, other areas of the brain regulate the activities of the respiratory centers or even briefly take direct control of respiration. The destruction of the brain's respiratory center stops respiration, thus causing a sudden loss of oxygen to the heart that causes it to cease functioning. Therefore, the traditional signs of life, respiration and heartbeat, disappear: the person is considered dead.

The irreversible loss of the capacity for consciousness combined with the irreversible loss of

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I. - Une c devant un

Pomme de discorde: la politique extérieure

Fig. 4.1 From the first page of "La Libre Belgique," August 10–11, 1963. "Two patients survive several weeks after transplantation of a kidney previously removed from a cadaver. Important contribution of a young Belgian investigator"

the capacity to breathe is acknowledged globally as death. Death is a result of the irreversible loss of both these functions in the brain [1]. Specifically a brain stem failure can originate from an intracranial lesion (trauma, hemorrhage, ischemia) or from an extracranial cause (cardiorespiratory arrest, cerebral anoxia). The idea of brain death arose in the 1950s when physicians began sustaining patients who lacked brain function by mechanical ventilation; these patients appeared "alive" based on regular heart rhythm and blood pressure. It was clear that the advent of mechanical ventilation halted the unavoidable circulatory breakdown that always follows respiratory arrest. Therefore, in those cases, it became necessary to diagnose death with neurological criteria. In 1959, Wertheimer et al. [2] described the "death of the nervous system." And in the same year, the French neurophysiologists Mollaret and Goulon [3] defined a state of coma in which the brain appeared irreparably damaged and ceased to function but in which the heart and lung function could be maintained artificially. They called this state "coma depassè." A few years before, in 1954, Joseph Murray, Nobel Laureate in 1990, performed the first human organ transplant by taking a kidney from an identical twin, and in 1962; he performed the first successful kidney transplant from a human cadaver [4]. One year later, Starzl et al. [5] performed the first liver transplant, and Hardy et al. [6] performed the first lung transplant. For all these transplants, donors were transferred into the operating room, and mechanical ventilation was stopped; organ retrieval could start only when the donor's heart stopped beating. At this time, donors were declared dead by classic cardiorespiratory criteria [7]. In 1963, Guy Alexandre, a Belgian surgeon at the Catholic University of Louvain, performed the first transplantation using a heart-beating, brain-dead donor (Fig. 4.1). Mechanical ventilation was not

Table 4.1 Dr. Alexandre's criteria for brain death diagnosis

Precondition: severe craniocerebral injury
Criteria for brain death diagnosis:
1. Complete bilateral mydriasis
2. Complete absence of reflexes, both natural and in response to profound pain
3. Complete absence of spontaneous respiration, 5 min after mechanical respiration has been stopped
4. Falling blood pressure, necessitating increasing amounts of vasopressor drugs (adrenaline) or Neo-Synephrine (phenylephrine hydrochloride)
If all conditions are met, observation is <6 h, and EEG must be flat

Table 4.2 Harvard criteria for brain death diagnosis

Precondition:	Irreversible cerebral damage
	Exclusion of two conditions: hypothermia (below 90 °F) and central nervous system depressants, such as barbiturates
Criteria:	Pupil fixed and dilated and will not respond to a direct source of bright light
	Non-receptivity and unresponsiveness to even the most intensely painful stimuli
	Ocular movement (to head turning and to irrigation of the ears with ice water) and blinking are absent
	No evidence of postural activity (decerebrate or other)
	Swallowing, yawning, vocalizations are absent
	Corneal and pharyngeal reflexes are absent
	Stretch of tendon reflexes cannot be elicited; plantar or noxious stimulation gives no response
	No movements or breathing
	Observations covering a period of at least 1 h by physicians are adequate to satisfy the criteria of no spontaneous muscular movements or spontaneous respiration [established by turning off the respirator for 3 min] or response to stimuli such as pain, touch, sound, or light
	All of the above tests shall be repeated at least 24 h later with no change
	Flat EEG

discontinued, and the team did not wait for the donor's heart to stop beating [8, 9].

The graft worked immediately after transplant, and serum creatinine levels were normal after a few days; however, the recipient died of sepsis on postoperative day 87 [8]. Dr. Alexandre's criteria for brain death criteria are shown in Table 4.1.

In 1966, Richard Lillehei and William Kelly et al. performed the first successful pancreas transplant [10, 11]. In 1967, Dr. Christiaan Barnard, in Cape Town, South Africa, performed the first heart transplant [12]. The surgical team brought a brain-dead donor into the operating room with the recipient; the mechanical ventilation was stopped, and everyone waited for the donor's heart to stop beating. Technically, the donor was not "brain dead" at the time of organ retrieval, but he was declared dead by classical cardiorespiratory criteria [13]. Even Barnard [12] stated, "As soon as the donor had been certified dead (when the electrocardiogram had not shown activity for 5 minutes and there was absence of any spontaneous respiratory movements and absent reflexes)… the donor chest was then opened rapidly."

The following year in the United States, due to organ transplantation's worldwide diffusion, the "Ad Hoc Committee of the Harvard Medical School" established criteria for brain death before organ retrieval [14]. In a comatose patient, the Commission defined brain death as a condition characterized by unresponsiveness, a lack of receptivity, and the absence of movements, breathing, and brain stem reflexes (Table 4.2).

Furthermore, the declaration of death should be performed by physicians that were not involved in transplantation procedures and would not participate in the process of transplantation.

Table 4.3 Declaration of Sydney

Determining the time of death is in most countries the legal responsibility of the physician and should remain so. Usually the physician will be able without special assistance to decide that a person is dead, employing the classical criteria known to all physicians. Two modern practices in medicine, however, have made it necessary to study the question of the time of death further: 1—the ability to maintain by artificial means the circulation of oxygenated blood through tissues of the body which may have been irreversibly injured, and 2—the use of cadaver organs such as heart or kidneys for transplantation. A complication is that death is a gradual process at the cellular level, and tissues vary in their ability to withstand oxygen deprivation. However, clinical interest lies not in the preservation of isolated cells but in the fate of a person. Here, the point of death for the different cells and organs is not as important as the certainty that the process has become irreversible by whatever techniques of resuscitation may be employed. This determination will be based on clinical judgment supplemented if necessary by a number of diagnostic aids, of which the electroencephalograph is currently the most helpful. However, no single technological criterion is entirely satisfactory in the present state of medicine, nor can any one technological procedure be substituted for the overall judgment of the physician. If transplantation of an organ is involved, the decision that death exists should be made by two or more physicians, and the physicians determining the moment of death should in no way be immediately concerned with the performance of transplantation. Determining the point of death of the person makes it ethically permissible to cease attempts at resuscitation and, in countries where the law permits, to remove organs from the cadaver provided that prevailing legal requirements of consent have been fulfilled.

The same day, on August 5, 1968, the 22nd World Medical Assembly, meeting in Sydney, Australia, announced the Declaration of Sydney [15] (Table 4.3). In this document, it was stated not only that "Death is a gradual process at the cellular level with tissues varying in their ability to withstand deprivation of oxygen" but also that death "lies not in the preservation of isolated cells but in the fate of a person."

4.1 Brain Stem Damage

In 1971, Mohandas and Chou [16] described lesions to the brain stem as a critical constituent in brain damage. This consideration was later confirmed by the Conference of Medical Royal Colleges and their Faculties in the United Kingdom [17], where brain death was stated as an overall irreversible loss of brain stem function. This announcement, made in 1981, allowed the subsequent conclusions and guidelines of the President's Commission for the Study of Ethical Problems in Medicine and Behavioral Research [18] that enacted the Uniform Determination Death Act [19] (UDDA): "An individual who has sustained either (1) irreversible cessation of circulatory and respiratory functions, or (2) irreversible cessation of all functions of the entire brain, including the brain stem, is dead. A determination of death must be made in accordance with accepted medical standards." In other words, "death is a unitary phenomenon which can be accurately demonstrated either on the traditional grounds of irreversible cessation of heart and lung functions or on the basis of irreversible loss of all functions of the entire brain [18]." The UDDA defines that "for legal and medical purposes an individual who has sustained irreversible cessation of all functioning of the brain, including the brain stem, is dead."

Neurological criteria can indicate death by attesting the loss of the whole brain, including, but not limited to, the brain stem [20]. A subject may be artificially supported for respiration and circulation after all brain functions irreversibly cease, but physicians have developed techniques for diagnosing the loss of brain functions while cardiorespiratory support is given.

Once the brain is deprived of adequate stores of oxygen and glucose, its neurons will irreversibly lose any activity. In the adult, this deprivation for more than a few minutes causes some neuron loss [21]. Thus, even in the absence of direct trauma and edema, brain activity can be lost if its circulation is disrupted. If blood flow is discontinued, the nervous tissue damage is characterized by complete self-digestion (autolysis) patterns over the ensuing days. If the brain lacks

all functions, consciousness is gone. Whereas some spinal reflexes often persist in such patients (because circulation to the spine is separate from that of the brain), all reflexes controlled by the brain stem, as well as cognitive, affective, and integrating functions are absent. Respiration and circulation in these bodies may be made by a mechanical ventilator together with massive medical management. In adults who had irreversible cessation of the functions of the entire brain, this artificial performance can last a short time, but the heart usually stops beating within 2–10 days. However, a small child who has lost all brain functions will have a cardiac arrest within several weeks [22].

A less severe injury to the brain can cause mild to profound damage to the cortex, lower cerebral structures, cerebellum, brain stem, or some combination thereof. The cerebrum, especially the cerebral cortex, is damaged first and more easily than the brain stem by the loss of blood flow; a 4–6 min loss of blood flow caused by a cardiac arrest will create permanent damage in the cerebral cortex, whereas the relatively more resistant brain stem may continue to function [21]. In this case, the main functions of the cerebrum are irrevocably lost, and the patient remains in a "persistent vegetative state" [23]; the patient may show spontaneous, involuntary movements such as yawns or facial grimaces, their eyes may be open, and they may be capable of breathing without assistance. However, lacking the superior cerebral function, any patient's movement does not mean that he is aware of himself or his environment. This was the case for Karen Ann Quinlan, for whom medical and nursing care, including feeding through intravenous or nasogastric tubes, and antibiotics for recurrent pulmonary infections allowed a survival longer than 10 years [24].

The cranial nerves, except I, II, and the spinal component of XI, originate in the brain stem, and the diagnosis of their functional loss confirms irreversible damage to this structure and by association to the reticular activating system and medulla oblongata. The following cranial nerve reflexes must be examined to diagnose their absence (Fig. 4.2).

- Pupils should be fixed in diameter and unresponsive to light (midposition with respect to dilation, 4–6 mm), absence of papillary reflex to light: cranial nerves II and III.
- When each ear is instilled with iced water, nystagmus or any eye movements are absent (vestibuloocular reflex): cranial nerves II, IV, VI, VIII.
- Absence of corneal reflex: cranial nerves V, VII.
- No facial or limb movement when supraorbital pressure is applied: cranial nerves V, VII.
- Oculocephalic reflex: eyes remain midline when the head is turned rapidly horizontally and vertically: afferent limbs labyrinth, vestibular nerve, neck proprioceptors, efferent limbs cranial nerves III and VI.
- Absence of response to painful stimuli on supraorbital pressure or deep pressure on both condyles of the temporomandibular joint: afferent limb V nerve, efferent limb VII nerve.
- Absence of coughing in response to tracheal suctioning and absence of gag reflex after stimulation of the posterior pharynx: cranial nerves IX and X.
- Apnea testing positive.

When all cranial nerve reflexes are absent, the apnea testing is performed to establish the clinical diagnosis of brain death.

In apnea testing, the patient is disconnected from the respirator, and a cannula, supplying pure oxygen at a rate of 4–10 l/min, is carried into the endotracheal tube down to the level of the carina. The cannula will ensure sufficient alveolar ventilation and the transport of oxygen to the blood in absence of respiratory movements. Before testing, preoxygenation with 100 % O_2 should be performed for at least 10 min to avoid hypoxia. Preoxygenation arterial PO_2 values should be ≥200 mmHg, which helps avoid possible hypocapnia that may be caused by hyperventilation or by high tidal volume settings on the mechanical ventilator. The corporeal temperature should be ≥32 °C, and it is important to ensure that the arterial PCO_2 or $PaCO_2$ is normal or greater than

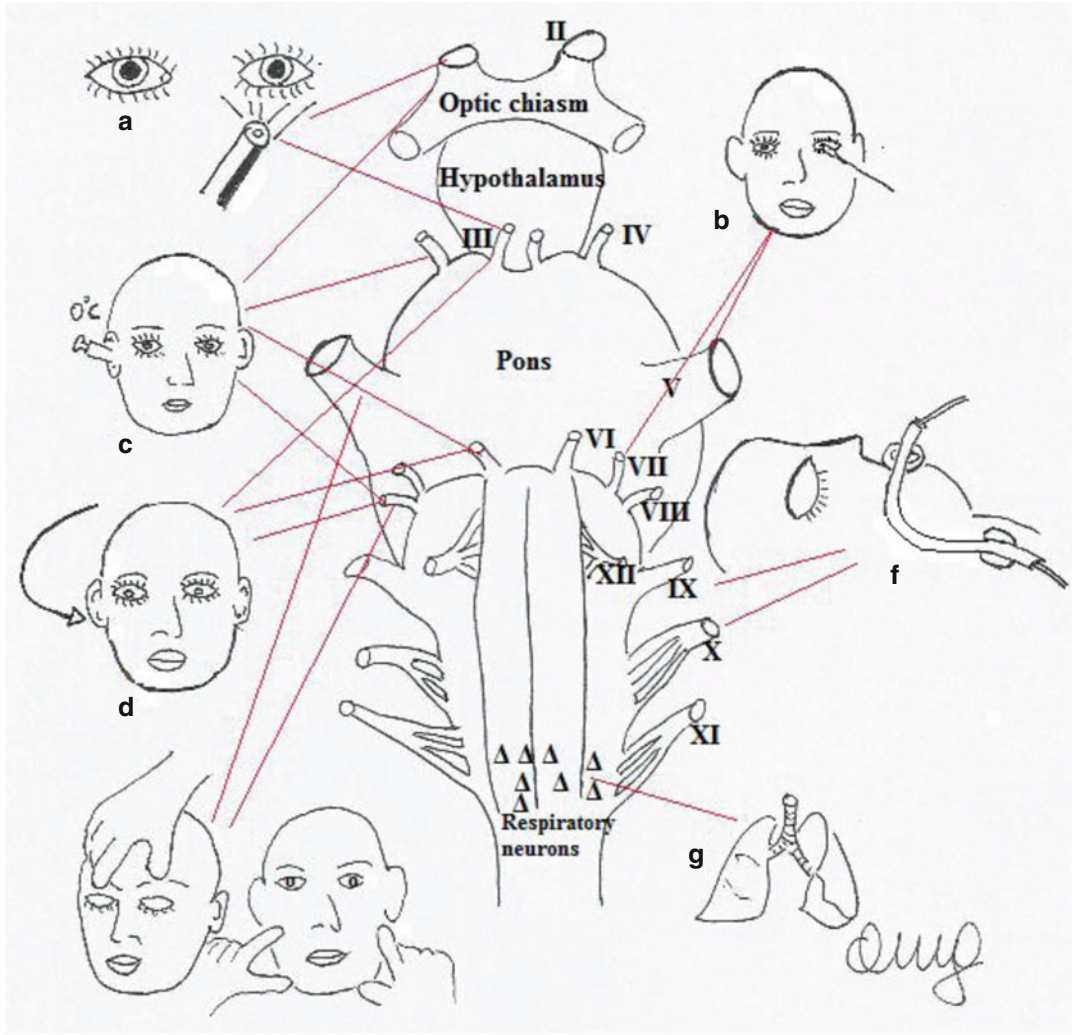

Fig. 4.2 Brain stem reflexes in brain death (**a**) Light reflex. (**b**) Corneal reflex. (**c**) Vestibuloocular reflex. (**d**) Oculocephalic reflex. (**e**) Absent response to pain stimuli. (**f**) Cough reflex. (**g**) No breathing

40 mmHg. A systolic blood pressure of at least 90 mmHg is recommended. Apnea testing is completed when no breathing effort is observed at a $PaCO_2$ of 60 mmHg or with a 20 mmHg increment from baseline; in this case, the test result is positive and confirms the diagnosis of brain death [25].

When the clinical examination establishes a diagnosis of brain death, it is fundamental to exclude the possibility of misdiagnosis, and confirmatory tests are recommended [26].

The misdiagnosis of brain death is possible in the following conditions: hypothermia, drug intoxication, and locked-in syndrome. In hypothermia, the brain stem reflexes are not present if the core temperature is <28 °C; these deficits can be reversible [27].

Many sedative and anesthetic drugs can imitate brain death status, but some aspects of brain stem function, for instance, the pupillary response to light, are preserved. If ingested in large doses, many drugs can cause a partial

Table 4.4 Confirmatory testing for brain death diagnosis

Cerebral angiography (conventional, computerized tomography, magnetic resonance, and radionuclide): absence of intracerebral filling at the level of carotid bifurcation or the circle of Willis
Electroencephalography: absence of electrical activity during at least 30 min of recording (note that the intensive care setting can result in an altered reading due to electronic artifacts)
Transcranial Doppler ultrasonography: small systolic peaks in early systole without diastolic flow showing very high vascular resistance associated with abnormal increased intracranial pressure (~10 % of patients may not have temporal insonation windows because of skull thickness)
Nuclear brain scanning: brain death is confirmed by the absence of isotopic uptake in cerebral parenchyma

loss of brain stem reflexes. A practical approach to drug/toxin exposure can be as follows:

(a) Drug or poison is known, but the substance cannot quantified: patient should be observed for a period at least four times the elimination half-life of the substance.
(b) Drug not known, but there is high suspicion: patient should be observed for 48 h to observe any change in brain stem reflexes; if there is no change, a confirmatory test must be performed [28].

The locked-in syndrome is usually due to the destruction of the base of the pons. The patient cannot move the limbs, grimace, or swallow, but blinking and vertical eye movements are preserved because the upper rostral mesencephalic structures are not involved. Consciousness persists because the tegmentum and the reticular formation are not damaged [26, 29]. This syndrome is often caused by an acute embolism of the basilar artery. Another pathology that mimics brain death is the reversible Guillain–Barré syndrome involving all the peripheral and cranial nerves. The progression can be recorded over a period of days [30].

Confirmatory testing is required by law in several European, Central and South American, and Asian countries; in Sweden, only cerebral angiography is required, and in the United States, the selection of tests is up to the physician [26]. In Italy, brain death is diagnosed according to the following criteria established by Italian law [31]: (a) deep coma; (b) absence of brain stem reflexes; (c) absence of motor responses after painful stimuli in trigeminal areas; (d) apnea ($PaCO_2 > 60$ mmHg); (e) flat electroencephalogram; (f) observation lasting 6 h for adults, 12 h for children younger than 5 years of age, and 24 h for newborns and infants younger than 2 months of age; and (g) cerebral blood flow test to demonstrate the arrest of cerebral circulation when factors affecting clinical evaluation and/or electroencephalography are present (e.g., toxic, metabolic factors, or sedative administration). Table 4.4 shows the main confirmatory testing for brain death diagnosis.

Two models of brain death are widely accepted: whole brain death and the death of the brain stem. For this reason, there are different brain death criteria in different countries: whole brain death is accepted by the United States, Italy, and most European countries, whereas brain stem death has been adopted first by the United Kingdom [31–37]. When whole brain death is considered, only cerebral flow examinations (angiography and SPECT) are suitable and are considered the gold standard [35].

When the clinical criteria of brain death have been diagnosed, the physician should inform the close relatives and discuss organ donation with them. After the first clinical examination of the patient, an observation period, usually 6 h for adults and children >1 year old, is organized to rule out any clinical signs that are incompatible with brain death. A clinical assessment is repeated. In some individuals, cranial or cervical lesions, hemodynamic instability, or other reasons may preclude a definitive clinical assessment. In these cases, a confirmatory test is mandatory to diagnose brain death.

Different legal definitions of death have evolved in different countries over time. In Europe, the United States, and almost worldwide,

the following two types of donation after death are commonly employed: (a) donation after brain death (DBD) and (b) donation after circulatory death (DCD).

Although kidney transplantation in the 1950s and 1960s was primarily from live donors, at the dawn of transplantation, all organs were retrieved from patients immediately after cardiorespiratory arrest, i.e., from "non-heart-beating" donors (NHBDs) that are recently better defined DCD. Upon the acceptance of the brain death definition, "heart-beating" donors rapidly became the primary source of organs for transplantation. However, the number of heart-beating donors is now progressively decreasing due to the great improvements in the diagnosis and treatment of severe brain injuries, and fewer young people are dying from severe trauma or catastrophic cerebrovascular events [7, 38, 39]. The number of DCD is slowly increasing worldwide, and in the United Kingdom, a steady increase in DCD activity from 5.6 % (42/745) in 2001/02 to 36.93 % (373/1010) in 2010/11 was reported [39, 40].

References

1. Gardiner D, Shemie S, Manara A, Opdam H (2012) International perspective on the diagnosis of death. Br J Anaesth 108(Suppl 1):i14–i28
2. Wertheimer P, Jouvet M, Descotes J (1959) A propos du diagnostic de la mort du systeme nerveux dans les comas avec arrêt respiratoire traites par respiration artificielle. Presse Med 67:87–88
3. Mollaret P, Goulon M (1959) The depassed coma (preliminary report). Rev Neurol (Paris) 101:3–15
4. Merrill JP, Murray JE, Takacs FJ, Harger EB, Wilson RE, Dammin GJ (1963) Successful transplantation of kidney from a human cadaver. JAMA 185:347–353
5. Starzl TE, Marchioro TL, Vonkaulla KN, Hermann G, Brittain RS, Waddell WR (1963) Homotransplantation of the liver in humans. Surg Gynecol Obstet 117:659–676
6. Hardy JD, Webb WR, Dalton ML Jr, Walker GR Jr (1963) Lung homotransplantation in man. JAMA 186:1065–1074
7. Machado C (2005) The first organ transplant from a brain-dead donor. Neurology 64:1938–1942
8. Squifflet JP (2003) The history of transplantation at the Catholic University of Louvain, Belgium 1963–2003. Acta Chir Belg 103(3 Spec No):10–20
9. Alexandre GPJ (1991) From the early days of human kidney allotransplantation to prospective xenotransplantation. In: Terasaki PI (ed) History of transplantation: thirty-five collections. U.C.I. Tissue Typing Laboratory, Los Angeles, pp 337–348
10. Lillehei RC, Idezuki Y, Feemster JA et al (1967) Transplantation of stomach, intestine, and pancreas: experimental and clinical observations. Surgery 62:721–741
11. Kelly WD, Lillehei RC, Merkel FK et al (1967) Allotransplantation of the pancreas and duodenum along with the kidney in diabetic nephropathy. Surgery 61:827–837
12. Barnard CN (1967) The operation. S Afr Med J 41:1271–1274
13. Machado C (2007) The first organ transplant from a brain-dead donor. In: Brain death. A reappraisal. Springer, New York, cap.2: 21–31
14. A definition of irreversible coma. Report of the Ad Hoc Committee of the Harvard Medical School to examine definition of brain death (1968) JAMA 205:337–340
15. Gilder SS (1968) Twenty-second world medical assembly. Br Med J 3:493–494
16. Mohandas A, Chou SN (1971) Brain death: a clinical and pathological study. J Neurosurg 35:211–218
17. Diagnosis of brain death: statement issued by the honorary secretary of the Conference of Medical Royal Colleges and their Faculties in the United Kingdom on 11 October 1976 (1976) BMJ 2:1187–1188
18. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research (1981) Defining death: a report on the medical, legal and ethical issues in the determination of death. Government Printing Office, Washington, D.C
19. Uniform Determination Death Act. www.law.uppen.edu/bll/archives/ulc/finact199/1980s/udda80.pdf
20. Smith M (2012) Brain death: time for an international consensus. Br J Anaesth 108(S1):i6–i9
21. Cranford RE, Smith HL (1979) Some critical distinctions between brain death and persistent vegetative state. Ethics Sci Med 6:199–209
22. Korein J (1980) Brain death. In: Cottrell J, Turndorf H (eds) Anesthesia and neurosurgery. C.V. Mosby & Co, St. Louis, at 282, 284, 292–293
23. Jennett B, Plum F (1972) The persistent vegetative state after brain damage: a syndrome in search of a name. Lancet 1(7753):734–737
24. Mc Fadden RD. Karen Ann Quinlan, 31, dies; Focus of'76 right to die case. New York Times 12 June 1985
25. Machado C, Perez J, Scherle C, Areu A, Pando A (2009) Brain death diagnosis and apnea test safety. Ann Indian Acad Neurol 12:197–200
26. Wijdicks EFM (2001) The diagnosis of brain death. N Engl J Med 344:1215–1221
27. Danzl DF, Pozos RS (1994) Accidental hypothermia. N Engl J Med 331:1756–1760
28. Henderson GV. Coma, Head Trauma, and Spinal Cord Injury. Chapter 1 p 27. In Samuel's manual of neurologic therapeutics, 8th edn (2010) Lippincot Williams & Wilkins, Philadelphia, PA, USA
29. Patterson JR, Grabois M (1986) Locked-in syndrome: a review of 139 cases. Stroke 17:758–764

30. Kotsoris H, Scheifler L, Menken M, Plum F (1984) Total locked-in state resembling brain death in polyneuropathy. Ann Neurol 16:150, abstract
31. Ministero della Sanità: Regolamento recante le modalità per l'accertamento e la certificazione di morte (1994) Decreto 22/8/1994 n. 582
32. Abdel-Dayem HM, Bahar RH, Sigurdsson GH (1989) The hollow skull: a sign of brain death in Tc-99m HM-PAO brain scintigraphy. Clin Nucl Med 14:912–916
33. Royal Colleges and Faculties of the United Kingdom (1976) Diagnosis of brain death. BMJ 2:1187–1188
34. Editorial. Brain death criteria. Ned Tijdschr Geneeskd (1983) 127:2293
35. Le Ministre Delegue charge de la Sante. Decret n. 90–844 du 24 septembre 1990.
36. Wissenschaftlicher Beirat der Bundesärtzekammer, "Kriterien des Hirntodes." Kriterien des Hirntodes (1991) Dtsch Artzebl Mitteilg 87:2855–2860
37. Munari M, Zucchetta P, Carollo C, Gallo F, De Nardin M, Marzola MC, Ferretti S, Facco E (2005) Confirmatory tests in the diagnosis of brain death: comparison between SPECT and contrast angiography. Crit Care Med 33:2068–2073
38. Death rate trends for RTAs and CVAs. WHO European Health for All database – http://www.euro.who.int/hfadb
39. Ridley S, Bonner S, Bray K, Falvey S, Mackay J, Manara A, Intensive Care Society's Working Group on Organ and Tissue Donation. (2005) UK guidance for non-heart-beating donation. Br J Anaesth 95:592–595
40. Akoh JA (2012) Kidney donation after cardiac death. World J Nephrol 6;1(3):79–91

Movements in Brain Death

5

Antonino M. Grande

Key points

1. Spontaneous movements and reflexes in brain death can occur and these movements arise from spinal cord neurons.
2. They do not preclude the diagnosis of brain death and are considered spinal reflexes.
3. Plantar responses, muscle reflexes by stretching, and jerking movements of the fingers; abdominal contraction is present in 60 % of donors when the peritoneum is incised.
4. Reflex movements originate from the spinal cord starting from the C1 metamer, and they involve a variable number of inferior metamers.
5. A pathophysiological explanation could be the occurence of superior control loss of phylogenetically more recent structures over the inferior, spinal cord, more archaic. When the subject is treated by ventilatory support and pharmacological therapy, spinal cord neurons are oxygenated by the blood supply. In this way, spinal cord shock is resolved, and neuronal function recovery can trigger reflex movements.
6. Sensational headlines where the donor just before the "execution" suddendly recovered are presented and discussed. It should be clear that there is a complete discrepancy between a coma and a vegetative state, and the headlines confusing the two situations are significantly hindering organ donation.

In Milan, in an old hospital made of red bricks, at 1 a. m., a stretcher is pushed by two porters through the double doors of an aged operating room where urgent cases were once treated but that is now used only for multiorgan retrieval procedures. The incessant beeping of a monitor is heard in the room; the anesthesiologist is ventilating the donor with the Ambu bag. The man died of a cerebral hemorrhage, is tall, and has a muscular body. Suddenly, a scream of a fellow echoes through the room: "It's moving, he wants to get up!" The donor has just moved his right arm and is lifting his right thigh from the stretcher. The panic spreads among the nurses, but some doctors also appear perplexed; the anesthesiologist spends at least 15 min calming tempers in the operating room. He protests loudly, excitedly

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waving a piece of paper—the death certificate—and then he explains more calmly that all examinations and tests have established the cerebral death of the man. The donor is taken again to the operating room after a momentary hesitation that was useless for all; the man died "again," and the multiorgan harvesting procedure could begin.

In another instance, a donor was ready for the last phase in organ retrieval in the operating room. All vascular structures emerging from the heart were isolated and encircled, and just when the ascending aorta was clamped, the donor moved and delivered with his left arm a powerful punch to the abdomen of my assistant. After a moment of hesitation, the aortic clamp was released, and the blood flow was resumed in the aorta; the donor was still moving—this time his right leg. With a thousand thoughts in my mind, seconds felt like hours. The glazed look in the scrub nurse's eyes and the echoing nurses excited words, somebody screams that this is a desperate act of a man against the donation. The abdominal surgeon appears extremely resolute and exclaims, "clamped the aorta, we start the perfusion," and in an automatic way, I do the same, without hiding my anxiety and nervousness.

5.1 Historical Background

Movements after death have been described many times; perhaps Descartes in 1637 first wrote of this phenomenon in his work *Discourse on the Method*, where "heads of animals, a little after decapitation, are still observed to move and bite the earth, notwithstanding that they are no longer animate…" [1]. In 1887, two French doctors, Regnard and Loye [2], witnessed an execution by guillotine and reported: "Two seconds after decapitation, the cheeks were still rosy, the eyes wide open, with moderately dilated pupils, the mouth firmly closed. No fibrillary contractions could be observed. When the finger was placed close to one eye, no change of expression took place; but on touching an eye or the tips of the lashes, during the first five seconds, the lids closed just as in life. This reflex action could not be elicited from the sixth second after decapitation. The jaws were tightly clenched and could not be opened by manual force; no similar muscular contraction could be detected in the trunk or extremities.

One minute after death, the face began to turn pale, the trunk remained flaccid, the carotids continuing to throw out blood remaining in the circulatory area. At the end of four minutes the face was quite pale, the upper lids were half closed, the jaws less firmly clenched than before.

Irritation of the cut surfaces of the spinal cord failed to produce reflex movements either in the trunk or on the face. For twenty minutes there was no change; then the necropsy was begun. There were signs of old pleurisy and alcoholism. The heart beat actively. On opening the pericardium, the ventricles and auricles continued to pulsate for twenty-five minutes; the former then ceased to beat, but the auricles went on for forty minutes longer. Thus the heart beat for an hour after decapitation. Then, its chambers were laid open; the left ventricle was firmly contracted, the right relaxed. There was emphysema at the edges of the left lung, as is nearly always observed after death by the guillotine. There were bubbles of air in the vessels of the pia mater, and much air in the subarachnoid space. The knife had passed through the lower part of the fourth cervical vertebra."

5.2 Pathophysiology of Spinal Cord Movement

It is well known that spontaneous movements and reflexes can occur in brain death subjects. These movements arise from spinal cord neurons, do not preclude the diagnosis of brain death, and are considered spinal reflexes—plantar responses, muscle reflexes by stretching, and jerking movements of the fingers. Abdominal contraction is present in 60 % of donors when the peritoneum is incised [3]. In the past, death has always been synonymous with immobility, but the idea of brain death has led to an evolution of this concept, because different types of movement have been described in this condition.

In 1982, Medel et al. [4] reported the case of a 28-year-old brain-dead man who spontaneously

presented extension movements of both upper limbs; the hands were held in a praying pose and arms flexed at the elbow, and this was followed by abduction, separation of the hands, and the falling of the arms alongside the trunk. The man also had flexion/extension activity in the lower limbs and walking-like movements. These movements could also be caused by harmful stimulation of the limbs, flexion of the neck, or plantar stimulation. Ropper [5] reported five cases of the classic Lazarus' sign in brain-dead heart-beating donors during apnea testing when a ventilator was disconnected: bilateral arm flexion to the trunk, shoulder abduction, and hand raising above the chest and moving up the neck. Similar episodes were also reported in non-hypoxic situations such as arterial hypertension, tachycardia, and facial flushing [6, 7].

The head can also be involved in these spontaneous movements, as described by Christie et al. [8] and Wu and Balaguer [9]. The head movements are controlled by the sternocleidomastoid, trapezium, and anterior vertebral muscles, and the nerves involved are the accessory nerve (cranial nerve XI) and the direct branches of the cervical plexus (C1–C2 for the sternocleidomastoid muscle; the trapezium is innervated by the branches of the ansa cervicalis and the spinal accessory nerve from 3rd and 4th cervical roots; the anterior vertebral muscles receive innervation from the second to seventh cervical nerves). It is well understood that the head movements are primarily regulated by spinal cord innervation, which explains the nature of these reflexes.

Saponisk et al. [10] examined 107 patients with brain death and found that plantar withdrawal responses, muscle stretch reflexes, abdominal contractions, Lazarus' sign, and respiratory-like movements, which are all considered spinal reflexes, were present in as many as 40–50 % of heart-beating cadavers. Table 5.1 shows the various documented spontaneous movements in brain-dead individuals.

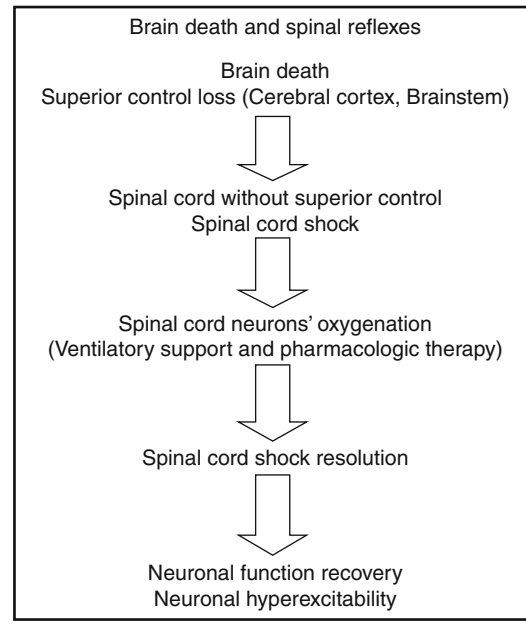
There are many explanations for the reflex movements exhibited by brain-dead patients, but the mechanisms that underlie these movements remain unclear.

Table 5.1 Movements found in brain-dead heart-beating cadavers

Flexor/extensor plantar responses
Triple flexion response
Abdominal reflex
Cremasteric reflex
Tonic-neck reflexes
Isolated jerks of the upper extremities
Unilateral extension-pronation movements
Asymmetric opisthotonic posturing of trunk
Undulating toe flexion sign
Myoclonus
Lazarus sign
Respiratory-like movements
Quadriceps contraction
Eye opening response
Leg movements mimicking periodic leg movement
Facial myokymia

From Saponisk et al. [10]

Fig. 5.1 Mechanism responsible for reflex movements



Reflex movements originate from the spinal cord starting from the C1 metamer, and they involve a variable number of inferior metamers. A pathophysiological explanation is still speculative; the mechanism shown in Fig. 5.1 is a reasonable explanation of the phenomenon: there is a superior control loss of phylogenetically more

recent structures is favored over the inferior, more archaic spinal cord. When the subject is treated by ventilatory support and pharmacological therapy, spinal cord neurons are oxygenated by the blood supply. In this way, spinal cord shock is resolved, and neuronal function recovery can trigger reflex movements.

5.3 Anesthesia in Organ Donors

In June 1999, the recommendation of the Intensive Care Society (UK) regarding anesthesia and clinical management during the donation operation was: "Brainstem dead patients do not require analgesia or sedation …" for surgery for the retrieval of donor organs [11]. However, the report states that in the operative phase, neuromuscular blocking agents should be given to prevent reflex muscle contraction and that systemic arterial hypertension may be treated with sodium nitroprusside or a volatile anesthetic agent such as isoflurane. It is well recognized that systemic arterial pressure often increases when the donor's skin is incised and when sternotomy is performed; inotropic drugs can be decreased and also withheld. The systemic hypertension and tachycardia that accompanies the donation operation can be distressing for operating theater personnel to witness, and for this reason, anesthesia or agents to control these reflexes should always be administered. Wetzel et al. [12] reported that the retrieval procedure can induce a mean increase in blood pressure of 31 mmHg and a mean heart rate increase of 23 beats min^{-1}. This effect on blood pressure and heart rate most likely indicates an organism in distress and most likely occurs at a spinal level, but we are unaware of EEG studies during organ collection to confirm this idea [13]. Therefore, anesthesia during organ retrieval is performed for the preservation of hemodynamic stability, for neuromuscular blocking, and possibly for ischemic preconditioning of the retrieved organs, but not for the benefit of the deceased patient [14].

Anesthesia in brain-dead heart-beating donors is not practiced to block pain perception, which is not felt at the cortical level, but to abolish neurovegetative reflexes that can stabilize the blood pressure, pulse frequency, and peripheral circulation.

5.4 Newspaper Headlines

It is easy to find newspaper articles in which the donor is described as a man waiting to be executed. Readers will certainly be shocked to learn that just before the "execution," the donor suddenly and miraculously recovered. Therefore, for those who work every day in transplant surgery, it is not rare to read sensational headlines such as, "The boy who came back from the dead: experts said that car crash teen was beyond hope. His parents disagreed… His devastated parents were even asked to consider donating his organs" [15], "Man who was declared dead feels 'pretty good'" [16], "Poised to Donate Organs, 21-year-old Emerges From Coma" [17], and "Syracuse hospital patient awakens just before organs were to be harvested" [18]. In the latter case, "Doctors at a Syracuse hospital came within inches of harvesting the organs of a live woman who woke on the operating table, despite previous reports by nurses indicating she was alive" [18]. Here, briefly, is her story. C. S. B., a 41-year-old woman, had overdosed on alprazolam, diphenhydramine, and a muscle relaxant and slipped into a deep coma as it would later be revealed. She was declared brain dead by hospital doctors, and a relative gave permission to take her off life support and retrieve her organs. The day before the organ harvesting operation, a nurse noticed that her toes curled when performing a simple reflex test of running a finger along her foot. This and several other signs that followed were shockingly ignored by doctors, and before surgery, the woman's nostrils were flared as though she was breathing independent of her respirator. Her lips and tongue were also moving. Despite these signs, the doctor's notes show no acknowledgement of the woman's movements, and in the

operating room, when the harvesting procedure was starting, she opened her eyes and gazed up at the bright lights hanging over her. The lady was later discharged after a 2-week stay. It is important to note that neither the woman nor the family filed a lawsuit against the hospital or the doctors. Nonetheless, the hospital was fined $6000 by the New York Department of Health. The state also ordered the hospital to hire a consultant to review the facility's quality assurance program, to implement that consultant's recommendations, and to hire a consulting neurologist to teach the staff how to accurately diagnose a brain death [18]. What happened in Syracuse was truly exceptional, due mainly to the physicians' negligent behavior that allowed an incredible misdiagnosis. Despite this case, nobody who is accurately declared brain dead ever wakes up or is sometimes "feeling pretty good" [16]; moreover, it should be clear that there is a complete discrepancy between a coma and a vegetative state, and the headlines confusing the two situations are significantly hindering organ donation.

The vegetative state is a clinical status of complete unawareness of the self and the surrounding environment; it is associated with sleep-wake cycles and with either complete or partial preservation of hypothalamic and brain stem autonomic functions. Therefore, an individual in a vegetative state does not have evidence of sustained, reproducible, purposeful, or voluntary behavioral responses to visual, auditory, tactile, or noxious stimuli; they exhibit no evidence of language comprehension or expression, and they show bowel and bladder incontinence. However, there are variably preserved cranial nerve and spinal reflexes [21]. This condition is called a persistent vegetative state 1 month after acute traumatic or nontraumatic brain injury or degenerative/metabolic disorders. In other words, an individual can spontaneously breathe, open his eyes, and look aware, but he will not respond in any way; he is not brain dead. This explains the confusion and mystification that create the sensational headlines and stories (Table 5.2).

Table 5.2 Sensational headlines

The boy who came back from the dead: experts said that car crash teen was beyond hope. His parents disagreed… His devastated parents were even asked to consider donating his organs [15]
Man who was declared dead feels "pretty good" [16]
Poised to Donate Organs, 21-year-old Emerges From Coma [17]
Syracuse hospital patient awakens just before organs were to be harvested [18]
Le donneur d'organes n'était pas mort [19] (The organ donor is not dead)
Pronto per l'espianto, chiede una sigaretta (Ready for organ harvesting, asks for a cigarette) [20]

References

1. Descartes R (1637) Discourse on the method. Oxford University Press, Oxford 2006
2. Regnard P, Loye P (1887) Death by decapitation. BMJ ii:195
3. Conci F et al (1986) Viscero-somatic and viscero-visceral reflexes in brain death. J Neurol Neurosurg Psychiatry 48:695–698
4. Mandel S, Arenas A, Scasta D (1982) Spinal automatism in cerebral death (Letter). N Engl J Med 307:501
5. Ropper AH (1984) Unusual spontaneous movement in brain-dead patients. Neurology 34:1089–1092
6. Jordan JE, Dyess E, Cliett J (1985) Unusual spontaneous movements in brain-dead patients. Neurology 35:1082, Letter
7. Heytens L, Verlooy J, Gheuens J, Bossaert L (1989) Lazarus sign and extensor posturing in a brain-dead patient. J Neurosurg 71:449–451
8. Christie JM, O'Lenic TD, Cane RD (1996) Head turning in brain death. J Clin Anesth 8:141–143
9. Wu Y, Balaguer PO (2013) Spontaneous and reflex head turning in brain death. Crit Care 17:440
10. Saponisk G, Maurino J, Saizar R, Bueri JA (2005) Spontaneous and reflex movements in brain death. Am J Med 118:311–314
11. Morgan G, Morgan V, Smith M (1999) Donations of organs for transplantation. The management of the potential organ donor. A manual for the establishment of local guidelines. The Alden Group, Intensive Care Society, Oxford
12. Wetzel RC, Setzer N, Stiff JL et al (1985) Hemodynamic responses in brain dead organ donor patients. Anesth Analg 64:125–128
13. Young PJ, Matta BF (2000) Anaesthesia for organ donation in the brainstem dead – why bother? Anaesthesia 55:105–106
14. McKeown DW, Bonser RA, Kellum JA (2012) Management of the heart-beating brain-dead organ donor. Br J Anaesth 108(Suppl 1):I96–I107

15. Eccles L (2012) The boy who came back from the dead: expert said that crush teen was beyond hope. The Daily Mail on line April 24, 2012
16. Levy M and agencies (2008) Man who was declared dead feels 'pretty good'. The Telegraph March 24, 2008
17. Donaldson James S (2011) Poised to donate organs, 21-year-old emerges from coma. ABC news http://abcnews.go.com/Health/arizona-accident-victim-emerges-coma-poised-donate-organs/story?id=15208351
18. Golgowsky N (2013) Syracuse hospital patient awakens just before organs were to be harvested. New York Daily News July 9, 2013
19. Nau J-Y, Le Monde (2008) Le donneur d'organes n'était pas mort. p. 11
20. Il Giorno (1999) Pronto per l'espianto, chiede una sigaretta. p. 1
21. The Multi-Society Task Force on PVS (1994) Medical aspects of the persistent vegetative state. N Engl J Med 330:1499–1508

6 Management of Hemodynamic and Metabolic Impairments in Heart-Beating Donors

Antonino M. Grande and Paolo Aseni

Key Points

- Transplantation results are significantly better when organs are obtained from live donors compared with organs from brain-dead and from non-heartbeating donors.
- This outcome is closely related to acute and widespread physiological changes occurring during brain death that, if untreated, cause organic deterioration and cardiac arrest.
- Inflammatory and hormonal changes, if not carefully diagnosed and treated, may adversely affect donor organ function after transplantation and susceptibility to rejection.
- In brain death, the impairments eventually developed are initially caused by the physiological response and then aggravated by the lesion/injury and the medications given.
- Cardiovascular changes in the donor during the observation period and the harvesting procedure may jeopardize the functionality of potential transplantable organs.
- The increasing intracranial pressure produces a compensatory arterial hypertension that is followed by sympathetic overactivity, which in turn induces a "catecholamine storm" with increased cardiac output, heart rate, and systemic vascular resistance.
- Treatment algorithms for donor management in some common clinical settings are shown.
- Management of glycemic homeostatic derangements, acid-base alterations, fluid, electrolyte changes and pulmonary changes are discussed.

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Transplantation results are significantly better when organs are obtained from live donors compared with organs from brain-dead and from non-heart-beating donors [1–3]. This outcome is closely related to acute and widespread physiological changes occurring during brain death that, if untreated, cause organic deterioration and cardiac arrest. Furthermore, inflammatory and hormonal changes, if not carefully diagnosed and treated, may adversely affect donor organ function after transplantation and susceptibility to rejection [4–7].

In brain death, the impairments eventually developed are initially caused by the physiological response and then aggravated by the lesion/injury and the medications given. Table 6.1 shows the main physiological impairments in brain-dead donors.

Table 6.1 Main physiological impairments in brain-dead donors

Impairment	Possible cause
Hypothermia	Hypothalamic damage, ↓ metabolic rate, vasodilation and heat loss
Hypotension	Vasoplegia, hypovolemia, ↓ coronary blood flow, myocardial dysfunction
Diabetes insipidus	Posterior pituitary damage
D.I.C.[a]	Tissue factor release, coagulopathy, platelet function initiation by catecholamines
Cardiovascular	Cathecholamine storm, myocardial damage, ↓ coronary blood flow
Pulmonary edema	Acute blood volume diversion, capillary damage
Electrolytes	Cellular membrane permeability alteration, diabetes insipidus
Glucose	↓ Insulin, insulin resistance
TSH	Irreversible damage to hypothalamus and pituitary gland
Pulmonary	Pneumonia risk, aspiration of gastric contents, neurogenic pulmonary edema

[a]*D.I.C.* disseminated intravascular coagulation

6.1 Cardiovascular Changes and Management

Irreversible damage to the central nervous system leads to severe systemic disturbances [8]. The pathophysiologic mechanism can be explained by considering that the cerebrum, brain stem, spinal cord, cerebrospinal fluid (CSF), and blood are inside a noncompliant skull and vertebral canal. All these components form a nearly incompressible system with the exception of a small compressibility in the intervertebral spaces. The normal combined volume of the intracranial contents is approximately 1450 mL distributed as follows: 1300 mL of brain, 65 mL of CFS, and 110 mL of blood.

The pressure within the dura and skull is called the intracranial pressure (ICP). Normal ICP is usually 5–15 mmHg [9, 10]. The Monroe–Kellie hypothesis asserts that the sum of intracranial volumes (brain, CSF, blood) should be constant [11, 12]. Consequently, an increase in any of these components must be counterbalanced by a decrease in another constituent to prevent an increase in ICP. The cerebral perfusion pressure (CPP) depends on the mean systemic arterial pressure (MAP) and ICP:

$$CPP = MAP - ICP$$

where MAP = 1/3 systolic blood pressure + 2/3 diastolic blood pressure [13], remembering that diastole counts twice as much as systole because 2/3 of the cardiac cycle is in diastole. An MAP of approximately 60 is necessary to perfuse coronary arteries, brain, and kidneys.

According to this formula, CPP reduction can be made by an increase in ICP or by a decrease in MAP. An increase in ICP is caused by an expanding intracranial volume distributed uniformly inside the skull. Normally, these changes are well compensated, and the cerebral blood flow (CBF) is preserved when CPP ranges from 50 to 150 mmHg. However, at some point, even a small

change in intracranial volumes results in a considerable change in ICP. There are homeostatic mechanisms that elevate MAP to overcome an increase in ICP, but these mechanisms eventually fail when the CPP falls under 50 mmHg, resulting in cerebral ischemia. The brain autoregulatory mechanism causes a vasodilation of cerebral vessels when CPP decreases to ensure adequate CBF. However, persistent vasodilation may cause an increase in ICP that, in turn, reduces CPP (vasodilatory cascade). Increasing the CPP causes a vasoconstriction of cerebral vessels that can reduce ICP.

ICP elevation eventually causes cerebral ischemia. Considering the brain damage, it is possible to identify the following situations:

- Mesencephalon ischemia causes parasympathetic activation and sinus bradycardia.
- Ischemia of the pons results in excessive sympathetic stimulation and hypertension (Cushing's reflex).
- Abnormalities in the blood supply to the medulla oblongata enhance the tension of the sympathetic system, which coexists with an inhibition of baroreceptor reflexes. Sympathetic stimulation results in high concentrations of circulating endogenous catecholamines [14], which creates a "vegetative storm"—vasoconstriction, hypertension, tachycardia, and a negative oxygen balance of the myocardium. The spasm of coronary vessels reduces oxygen supply to the myocardium, which results in subendocardial ischemia, myocytolysis, necrosis of contractile proteins, subendocardial hemorrhages, edema, and leukocyte infiltrations.

Brain death is often characterized by the onset of arrhythmias and conduction abnormalities, which are well-known direct consequences of decreased vagal nerve tonus, excessive sympathetic stimulation, myocardial ischemia, or electrolyte disturbances caused by the increase in the total amount of drugs administered. Moreover, brain death induces hormonal disturbances: hypophysis insufficiency, which causes diabetes insipidus, a condition that develops in more than 80 % of all donors.

Cardiovascular changes in the donor during the observation period and the harvesting procedure may jeopardize the functionality of potential transplantable organs. The increasing intracranial pressure produces a compensatory arterial hypertension [15] that is followed by sympathetic overactivity, which in turn induces a "catecholamine storm" [16, 17] with increased cardiac output, heart rate, and systemic vascular resistance. There is a simultaneous central redistribution of blood volume, increased afterload, and visceral and myocardial ischemia. The severity of changes is associated with the speed of brain death onset; an experimental canine model showed circulating epinephrine concentrations increased more than 1000-fold when the ICP increased rapidly. Slower increases in ICP resulted in diminished increases in catecholamine concentrations (200-fold) and a lower incidence of myocardial ischemic damage (93 % and 23 % in the rapid ICP increase and slower ICP increase groups, respectively) [18]. In man, myocardial injury occurs in 20–25 % of brain death, and myocardial dysfunction is verified by echocardiography in ~40 % of brain-dead donors [19, 20]. After the catecholamine storm, there is a loss of sympathetic tone and peripheral vasodilation that, if untreated, can cause hypoperfusion and ischemia in all potential transplantable organs.

Repeated measurements of troponin levels are recommended in this phase and are very important when evaluating a potential donor. Elevated troponin levels indicate myocardial damage and may determine graft dysfunction after heart transplantation. Therefore, the troponin level should always be considered during the selection of recipients: a value significantly exceeding normal is a risk factor for postoperative cardiac failure, especially in conjunction with long-term ischemia (>4 h) [21].

In case of hemodynamic instability with an inability to maintain adequate systemic blood

Table 6.2 Intensive care management for hemodynamic instability

Rules of 100s
Maintain systolic blood pressure >100 mmHg
Maintain heart rate <100/min
Maintain Hb >100 g·L
Maintain urinary output >100 mL/h
Maintain PaO_2 >100 mmHg

pressure, aggressive fluid resuscitative therapy directed at restoring and maintaining intravascular volume that can be achieved applying the "Rule of 100" [22] (Table 6.2): systolic blood pressure greater than 100 mmHg, urine output greater than 100 $mL \cdot h^{-1}$, PaO_2 greater than 100 mmHg, hemoglobin concentration greater than 100 g·L. Fluid replacement should be administered, using isotonic crystalloids and colloid, fresh frozen plasma (FFP), and red blood cells (RBCs), to attain a satisfactory central venous pressure (CVP) of 8–10 mmHg. Note that if the lungs are evaluated for retrieval, starch-based colloids should be avoided. Monitoring the central or mixed venous oxygen saturation is indicated in all donors with hemodynamic instability.

Medications should be administered and tailored with a targeted SVO2 ≥60 %.

6.1.1 Hypotension

Hypotension is defined as a mean arterial blood pressure (MAP) of <60 mmHg measured from an indwelling arterial catheter. Donor organs are likely at more risk from hypotension than hypertension [23]; this condition may be a direct consequence of all pathologies that have determined a shock state, or it may occur after brain death because the lost function of the cerebral vasomotor centers causes vasodilation, reduced cardiac contractility, and hypovolemia related to the diabetes insipidus.

During the retrieval procedure, one of the main causes of hypotension is related to the surgical maneuvers; prolonged upward tilting of the right liver lobe can cause torsion of the abdominal vena cava, which causes deep hypotension. Torsion of the small bowel and of the mesenteric vascular pedicles during the Cattell–Braasch maneuver can cause severe hypotension due to the pooling of a large volume of venous blood in the splanchnic viscera. These surgical maneuvers should be avoided or their duration limited when donors are hemodynamically unstable.

6.1.1.1 Treatment

A MAP <60 mmHg is dangerous and for this reason avoid surgical maneuvers that can cause deep and prolonged hypotension. Check medical records to rule out hemorrhagic anemia due to a previous acute hemorrhage; test hematocrit and coagulation to determine if coagulopathy is present. If hematocrit is <28 %, blood transfusion is mandatory, and RBCs and FFP are required.
Treat polyuria if present.

Check medical records for evidence of severe infection, drugs, other allergic reactions, or cardiac tamponade (after echocardiography) and pneumothorax (chest x-ray).

ECG should be repeated to rule out myocardial ischemia or infarction.

If the donor, after volemic correction and attaining a CVP of 8–10 mmHg, is still unstable, it is time to consider the insertion of a Swan–Ganz catheter to direct the therapy. At this point, it is possible to understand the following hemodynamic parameters: pulmonary artery pressure, wedge pressure, cardiac output, cardiac index, systemic vascular resistance, left ventricular stroke work index, and pulmonary vascular resistance. Knowing these hemodynamic data makes it possible to titrate the most appropriate therapy.

Below we consider treatment algorithms for donor management in some common clinical setting.

- A donor presents hypotension (MAP <60 mmHg). After controlling any blood loss source (external, gastroenteric tract, urinary, abdominal), the first therapeutic action is volume replacement if preload is low according to the Swan–Ganz catheter. CVP is 10 mmHg, pulmonary capillary wedge pressure is 15 mmHg, cardiac index <3.2 $L \cdot min \cdot m^2$, left ventricular

stroke work index 50 g/m^2, and systemic vascular resistance (SVR) >1800 dyn·s·cm^{-5}. In this case, vasodilator infusion should be started together with a moderate inotropic support using dopamine infusion. In this clinical setting, a vasopressor such as norepinephrine should be avoided, because a peripheral vascular resistance increase can cause severe hypotension and decrease splanchnic organ perfusion with major damage, especially to the bowel and to the liver.

- In another clinical setting, a donor shows a low systemic vascular resistance <1100 dyn·s·cm^{-5}, and a vasopressor (e.g., norepinephrine, phenylephrine) is the vasoactive drug of choice that is titrated to maintain the MAP >60 mmHg. If the left ventricular stroke work index (LVSWI) is low (<35 g·m/m^2), a positive inotropic agent (e.g., dopamine, dobutamine) should be used. Vasoactive therapy should be diminished and removed as soon as possible if an MAP >60 mmHg is attained, because vasoactive therapy decreases splanchnic organ perfusion. Subsequent deviations may require a return to the algorithm application [22].
- If we consider a donor showing wedge pressure >25 mmHg, cardiac index <2.2 L·min·m^2, left ventricular stoke work index <45 g/m^2, and systemic vascular resistance >2000 dyn·s·cm^{-5}, this individual should not be considered as an organ donor for thoracic organs. These hemodynamic data reflect the worst prognosis in an intensive care patient [23, 24].
- When a donor presents hypotension, MAP <60 mmHg, CVP <10 mmHg, and wedge pressure <12 mmHg. Treatment should be as follows:
  - Low CVP and wedge pressure, high SVR: increase volemia (Table 6.3), perform preload optimization, and avoid epinephrine and norepinephrine if SVR is high.
  - Endpoints reached: observe hemodynamic data.
  - Endpoints still not reached: start vasopressor protocol (Table 6.4).
  - Endpoints reached: titrate vasopressor to minimum effective dose.
  - MAP still <60 mmHg: echocardiography; evaluate vasopressin and/or epinephrine infusion if SVR is low or normal.

Table 6.3 Control of volemia by CVP and recommended amount of infusion

CVP/wedge mmHg	Volume (cc)
<5	1000
5–10	500
10–15	250
>15	0

Table 6.4 Hemodynamic algorithm

Vasopressor protocol
Start dopamine 5 mcg/kg/min
Titrate dopamine to MAP endpoint
Maximum dopamine dose: 10 mcg/kg/min
Add norepinephrine 0.05 up to 0.15–0.2 mcg/kg/min (if heart considered)
Titrate norepinephrine to maximum dose 2.0 mcg/kg/min (if heart not considered)

Table 6.5 Causes of organ impairment

1. Primary organ pathology
2. Chronic comorbidities
3. Brain resuscitation therapy
4. Pathophysiology of brain death

As matter of fact, harvested organs may deteriorate after transplantation, and marginal grafts (see Chap. 3) are more at risk for failure. However, we should be aware that the organs' function might deteriorate even before retrieval for several reasons, as shown in Table 6.5.

In Table 6.5, points 1 and 2 indicate that organ function is correlated to its pre-harvesting status, and each organ must be accurately studied and evaluated before its acceptance. From point 3, we know that therapy for an acutely injured brain causes organ alterations. To maintain cerebral perfusion, the following methods are commonly used:

- Sedatives (barbiturates and propofol) [25] are given for cerebral metabolic suppression to induce a pharmacological coma and are particularly potent in hypovolemic patients; they cause hypotension corrected with vasoconstrictor agents, which, in turn, can lead to subendocardial ischemia.

- Osmotherapy [26] can cause cardiovascular collapse and respiratory failure.
- Inotropic agents are given to increase MAP, which may damage the heart but have no consequences on kidney function [27].

6.1.2 Hypertension

Hypertension is rare after brain death but can occur before an established diagnosis. MAP should be kept <90 and >60–65 mmHg.

6.1.2.1 Treatment

Diminish or stop any inotropic or vasopressor drug. Start therapy if MAP is >95 mmHg for 30 min after brain death; start labetalol 20 mg IV bolus and repeat every 20 min, controlling the heart rate. If after two doses MAP is still high, start nicardipine IV 5 mg/h titrating up to 15 mg/h.

6.2 Hormonal Changes and Replacement Therapy

Various functional components of the pituitary and hypothalamic regulatory systems may become affected as brain ischemia spreads, causing a drop in the circulating levels of triiodothyronine (T3), cortisol/adrenocorticotrophic hormone (ACTH), insulin, and arginine vasopressin. Recently, hormonal replacement therapy was reported to result in the rapid recovery of cardiac function in both experimental animals and humans and to enable significantly more organs to be transplanted [28, 29]. Mi et al. Cooperative Studies Program Coordinating Center, VA Maryland, U S A performed an important retrospective and epidemiologic study [30] on this topic using data from the United Network for Organ Sharing (UNOS) in a total of 71,571 potential organ donors during the 10-year period, from January 1, 2000 to December 31, 2009. Data were analyzed from a subset of 40,124 deceased subjects who were not donors after cardiac death (donation after cardiac death, DCD) and for whom complete data on the hormonal therapy administered (if any) were available. The study found that thyroid hormone (T3 or T4), a corticosteroid, and antidiuretic hormone played important roles in the management of the donor if transplantation was to be maximized, and the combination of thyroid hormone, a corticosteroid, antidiuretic hormone, and insulin was the optimal hormonal therapy to maximize multiple organ procurement. In contrast, considering pancreas transplantation alone, insulin administration was detrimental. Authors stated that livers were retrieved from a significantly greater number of donors (>80 %) compared with any other organ (considering a pair of kidneys or lungs as a single organ) ($P<0.0001$) irrespective of the hormonal treatment that the donor received. Thus, the liver (even when the donor is untreated) is perhaps more resistant to brain death-associated injury than other organs and shows a greater adaptability to chemical, nutritional, and immunogenic stimuli than other vital organs. Furthermore, corticosteroids are not always beneficial to the procurement of the heart, perhaps because T3/T4 is particularly effective in increasing myocardial energy stores and in reducing the inflammatory response, which may counteract the weaker effect provided by corticosteroids [29].

6.3 Management of Glycemic Homeostatic Derangements

Both hypoglycemia and hyperglycemia can be harmful to donor organs [31]. Serum glucose should be checked every 4 h, and finger-stick glucose should be measured every 2 h.

6.3.1 Hypoglycemia

Treat if glycemia <75 mg/dL by administering preloaded dextrose 50 % (D50) syringes containing 25 g of dextrose in 50 mL of water (0.5 g/mL). If D50 syringes are not available, use a dextrose vial or alternative dextrose concentration D10 W and give 250 mL of this fluid (25 g of dextrose). Check glycemia again in 30 min; if <75 mg/dL, repeat D50.

Table 6.6 Algorithm to control glycemia in brain death donors

Glucose mg/dL	Subcutaneous insulin units
100–150	No
151–175	7
176–200	12
201–225	16
>225	must add IV insulin
226–250	5 IV insulin
251–275	8 IV insulin
276–300	10 IV insulin
>300	Consider insulin infusion

6.3.2 Hyperglycemia

Hyperglycemia may be determined by infused glucose and by elevted circulating "stress" hormones like cortisol, glucagone and catecholamine that cause insuline resistance.

Treat if serum glucose >150 mg/dL. Check and remove glucose infusion in all IV fluids unless required by administered drugs. Start subcutaneous insulin every 4 h (see algorithm, Table 6.6); if glycemia ≥225 mg/dL, supplemental intravenous insulin is administered hourly following Table 6.6. If glucose remains >250 mg/dL, insulin infusion should be started.

6.4 Acid–Base Alterations and Therapeutic Management

Acid–base monitoring in the donor and the correction of all the imbalance states is paramount for a good organ perfusion and preservation without exception for any organ.

6.4.1 Assessment

The blood indicates the acid–base status of the tissues, respiratory function through the release of volatile carbon dioxide from the lungs, and the interaction of serum electrolytes and proteins. An acid–base imbalance in the blood is revealed by a modification in the blood pH. Because local tissue factors influence venous blood pH, an arterial blood gas (ABG) test should be performed. Arterial pH (normally 7.36–7.44) is a logarithmic calculation of the concentration of hydrogen ions within the arterial blood sample.

Altered blood acid–base balance is always a symptom of an underlying metabolic or respiratory condition that causes changes in ABG. It is very important to consider that alterations initiated by a change in $PaCO_2$ are referred to as respiratory disorders; those initiated by a change in plasma bicarbonate concentration are known as metabolic disorders. Regardless, a change in the acid–base status alone can cause its own symptoms, and the treatment should be directed not only to treat acidemia or alkalemia but also to identify the origin of the disorder [32].

Alkalemia may cause [32]:
- Coronary artery constriction
- Reduced ionized calcium (arrhythmias and decreased cardiac contractility)
- Decreased potassium (arrhythmias, ammonia production, and polyuria)
- Increased production of lactic and keto acids
- Reduced magnesium and phosphorus (arrhythmias)
- Increased binding between hemoglobin and O_2 (reduced O_2 deliver to tissues).

Acidemia may cause:
- Reduced cardiac contractility
- Cardiac arrhythmias
- Increased pulmonary artery constriction
- Increased blood volume
- Reduced blood flow to kidneys and liver
- Reduced response to catecholamines
- Insulin resistance
- Increased potassium
- Inhibition of phosphofructokinase and decreased glycolytic flux and O_2 consumption

Acid–base modifications can be caused by respiratory and metabolic causes; therefore, the treatment of ABG alterations should first be directed toward changing parameters on the mechanical ventilator, using the $PaCO_2$ to modify

pH. When $PaCO_2$ is <35 mmHg, usually hyperventilation should be controlled; conversely, $PaCO_2$ >45 mmHg can indicate hypoventilation.

Respiratory alkalemia is a frequent situation caused by treatment. Cerebral blood flow is reduced in the case of head injury, and if still present after brain death is established, appropriate corrective actions are made in ventilator tidal volume or respiratory rate to augment $PaCO_2$ following the reaction: $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3$.

The hydrogen ions formed in this reaction will reduce pH. Donor CO_2 elimination depends on the following reaction: *ventilation* = (*tidal volume – dead space*) × *respiratory rate*. Therefore, increasing dead space or reducing tidal volume or respiratory rate will augment CO_2 retention and $PaCO_2$.

Modifications in tissue and organ metabolism can cause metabolic alkalemia or acidemia. Considering ABG bicarbonate, it is possible to comprehend the acid–base imbalance: bicarbonate values >28 mmol/L reveal metabolic alkalosis; values <20 mmol/L indicate metabolic acidosis. Moreover, base excess or base deficit specifies the amount of strong acid or base to add for pH normalization when $PaCO_2$ is normal. Base excess (and deficit) is normally zero, and this value is preceded by a – or +. The amplitude of the value shows the level of metabolic imbalance; the plus sign indicates metabolic alkalosis, and the minus sign indicates an acidotic status [32].

Metabolic alkalosis can be caused by hypovolemia caused by the administration of diuretics and mannitol for high intracranial pressure treatment. Furthermore, alkalemia is found in the case of a large loss of gastric acid contents or when potassium is low.

Hydrochloric acid or sodium bicarbonate may be administered to correct the calculated metabolic acid–base deficit. In the case of metabolic alkalosis, the amount of HCl to be administered is calculated as follows: mEq HCl needed = (103 – donor Cl^-) × 0.5 (donor weight in kg).

In metabolic acidosis, which is usually more common in donors, bicarbonate administration can be calculated by this equation: mEq HCO_3^- needed = (24 – donor HCO_3^-) × 0.4 (donor weight in kg).

Always try to ascertain and treat the metabolic alkalosis causes, not only by administering bicarbonate but also by controlling potassium and diuretic suspension (if previously prescribed).

Blood lactate monitoring: serial lactate measurements should be taken. Normal blood lactate concentration is 1–0.5 mmol/L. Lactic acid is the endpoint of the anaerobic breakdown of glucose in the tissues. The lactate exits the cells and is transported to the liver, where it is oxidized back to glucose. With tissue hypoxia, lactic acid is produced in the anaerobic cycle and utilized for energy production. If the organism remains in the clinical state of a persistent oxygen debt, therefore overcoming the body's buffering abilities, lactic acidosis will ensue. Hyperlactatemia is defined as mild to moderate when the blood lactate concentration is between 2 and 4 mmol/L without metabolic acidosis, and lactic acidosis is characterized by persistently high blood lactate levels, usually >4–5 mmol/L, in association with metabolic acidosis [33]. If lactate levels are high or increasing, the etiology should be discovered (see above, acid–base alterations).

6.5 Fluid and Electrolyte Changes and Therapeutic Management

6.5.1 Assessment

Electrolyte levels should be maintained within the normal limits; therefore, the laboratory testing of sodium (Na), potassium (K), chloride (Cl), bicarbonate (HCO_3), magnesium (Mg), phosphorous (P), and ionized Ca (Ca^{++}) should be performed every 4 h (Table 6.7, normal electrolyte values), remembering that any testing should be delayed

Table 6.7 Normal electrolyte levels

Na 136–142 mEq/L (mmol/L)	Mg 1.5–2.3 mg/L (0.65–1.05 mmol/L)
K 3.5–5.0 mEq/L (mmol/L)	P 2.3–4.7 mg/dL (0.74–1.52 mmol/L)
Cl 96–106 mEq/L (mmol/l)	Ca (ion.) 2.3–2.54 mEq/L (1.15–1.27 mol/L)
HCO_3 21–28 mEq/L (mmol/L)	

30 min after electrolyte administration. The human body is placed within a water-based medium, the solvent. The total body water (TBW) is divided into the intracellular (IC) (60 % of TBW) and extracellular (EC) (40 % of TBW) spaces. EC spaces are then divided into the intravascular (plasma) (8 % TBW), interstitial (around the cells but outside capillaries) (28 % TBW), and transcellular (4 % TBW) areas [33, 34]. Ions, glucose, hormones, and other substances are dissolved in TBW as solutes. They are spread unevenly in the various compartments of the TBW because of a variety of cellular membrane permeability differences, active ionic pumps, molecular size considerations, osmolar gradients, and electrochemical or hormonal factors [34].

6.5.2 Treatment of Sodium Abnormalities

Disorders of the serum sodium concentration present particular problems in cadaveric organ donors with brain death. Severe hypernatremia, sometimes up to 180 mmol/L, can be observed.

6.5.3 Hypernatremia

Polyuria and hypernatremia are common problems during the pre-transplant care of brain-dead donors. They not only have important role in hemodynamic stability but also may influence organ transplantation outcomes. The negative influence of donor hypernatremia in liver transplantation has been reported, and several studies have also shown that elevated serum sodium in the donor can have adverse effects on kidney allograft function [35].

Hypernatremia should be treated when Na is >150 mEq/L. If polyuria is present, (>250 cc of urine above intake per h; see below polyuria treatment). Without polyuria, administer 1 L 0.2 % saline, hypotonic solution as a rapid infusion and replace the same amount of urine output with 0.2 % saline. All medications must be mixed in 0.45 % or 0.2 % saline if pharmaceutically possible and any maintenance IV is dextrose 5 % and 0.2 % saline; avoid diuretics.

6.5.4 Hyponatremia

If Na is <125 mEq/L, NaCl 3 % (513 mEq/L) 30–40 mL/h x 3 h should be infused (central line is preferred); all medications administered by IV should be in 0.9 % (154 mEq/L) saline solutions when possible. In this way, natremia can increase ~ 10–15 mEq/L in 24 h.

If hyperglycemia is present, the serum Na may be low because of the high blood glucose. Increasing blood sugar (>300) causes a contemporary rise in osmolality; water shifts from the intracellular to the extracellular compartment and causes hyponatremia. In this case, insulin administration is mandatory rather than correcting hyponatremia. Remember that as a rule of thumb in clinical medicine, the serum sodium concentration decreases by 1.6 mEq/L for every 100 mg/dL increase in glucose concentration [36].

6.5.5 Potassium Abnormalities

Potassium is mainly an intracellular electrolyte and its regulation is impaired in in organ donor. While hyperkalemia is rare, hypokalemia is found in about 90 % of cases.

6.5.6 Hyperkalemia

Hyperkalemia (>7.0 mmol/L) is commonly associated with acute renal failure, concerns the cardiac conducting tissue, and can cause arrhythmia including ventricular fibrillation and asystolic arrest. The ECG changes include tall T waves >5 mm (K 6–7), small broad P waves or absent P waves, wide QRS complex (K 7–8), sinusoidal QRST (K 8–9), and atrioventricular dissociation or ventricular tachycardia/fibrillation (K >9) [37]. If renal failure is present, an urgent hemodialitic treatment is the only available therapeutic option.

If K is ≥5.8 mEq/L, it should be treated unless the laboratory reports the specimen "hemolyzed" and repeats the test. First, remove K from all infusions, and control K every hour.

Administer D50 (prefilled syringe, 25 g dextrose) and insulin 15 units IV, $NaHCO_3$ 50 mEq IV, 20 milliliters 10 % Ca gluconate is given intravenously in adults (0.5 mL/kg in children) over 5–10 min and may be repeated as necessary. The onset of action is immediate, but its duration is only a few minutes [38, 39]. Control K with 1–2 h intervals and readminister the above medications if hyperkalemia is still present; consider sodium polystyrene sulfonate resin for binding K in the intestinal lumen, especially the large bowel and ileum.

6.5.7 Hypokalemia

Start treatment when K is ≤3.9 mEq/L and stop diuretic therapy.

Consider that the maximum rate of intravenous replacement is 20 mEq/h with continuous ECG monitoring (the maximum rate should be increased to 40 mEq/h in emergency situations):

- K 3.6–3.9 mEq/L, administer potassium chloride 20 mEq IV over 2 h; central catheter is preferred.
- K 3.4–3.5 mEq/L, administer 20 mEq over 2 h plus 10 mEq in 1 h × 1.
- K 3.1–3.3 mEq/L: 20 mEq over 2 h × 2 and recheck potassium at the end of infusion.
- K 2.6–3 mEq/L, start KCl 20 mEq IV over 2 h × 2 and 10 mEq IV over 1 h; control potassium level at the end of infusion.
- K 2.3–2.5 mEq/L, administer KCl 20 mEq IV over 2 h × 3.

6.5.8 Magnesium Abnormalities

Magnesium is the second most abundant intracellular cation after potassium and the fourth most abundant cation of the body after calcium, potassium, and sodium. Mg is involved in hundreds of enzymatic reactions, is essential for life, is an important cofactor for many biologic processes, and has an important role in controlling parathyroid hormone (PTH) activity.

6.5.9 Hypermagnesemia

This disorder has a low incidence because the kidney can eliminate excess magnesium by rapidly reducing its tubular reabsorption to almost negligible amounts. The most common cause of hypermagnesemia is renal failure, and when there is a breakdown or destruction of cell body, the electrolyte magnesium shifts outside the cell wall and causes the decreased excretion of potassium. It is usually concurrent with hypocalcemia and/or hyperkalemia, and if so, intravenous calcium gluconate can be used, because the effects of magnesium in neuromuscular and cardiac function are antagonized by calcium. Intravenous diuretics, in the presence of normal renal function and in the absence of polyuria, can also be employed.

6.5.10 Hypomagnesemia

Mg reduction decreases the release of PTH and causes skeletal resistance to PTH and severe hypocalcemia. Therefore, Mg depletion causes tetany, cardiac arrhythmias, and bone instability. The normal adult level of magnesium is 1.5–2.5 mg/dL. Hypomagnesemia should be treated when Mg is <1.5 mg/dL.

- Administer 4 g $MgSO_4$ in 2 h; if still low, repeat.
- Often, Mg depletion is associated with other abnormalities such as hypoalbuminemia, hypophosphatemia, and hypokalemia; in these cases, management should be considered in conjunction with the treatment of the associated electrolyte abnormalities [40].

6.5.11 Calcium Abnormalities

Almost 98 % of the total body calcium is in the bones; in serum, calcium is bound to protein or other anions as ionized calcium, which is the biologically active form. Normal values for calcium are as follows: ionized (preferable to control), 1.0–1.4 mmol/L (4.0–5.6 mg/dL), and total calcium, 2.12–2.62 mmol/L (8.5–10.5 mg/dL).

6.5.12 Hypercalcemia

This is rare and is commonly caused by a preexisting parathyroid gland disorder, kidney failure, malignancy, or the use of thiazide diuretics; hypercalcemia may increase polyuria or increase the potential for toxic side effects from digitalis.

6.5.13 Hypocalcemia

This condition is often observed in organ donors, and the most frequent causes are chronic kidney failure, parathyroid disease, rhabdomyolysis, and sepsis. Consider that alkalemia increases calcium–protein binding and thus decreases ionized calcium; hypocalcemia is also present in hypomagnesemia and may produce dangerous cardiac arrhythmias, decreased cardiac contractility, and hypotension. Treatment is as follows: one 10 mL ampule of 10 % calcium gluconate IV bolus over 10 min (in emergency, the administration may be as quickly as over 4 min [41]); one 10 mL ampule of 10 % calcium chloride via slow IV bolus over 15 min. In 1 h, recheck ionized Ca and readminister calcium gluconate.

6.5.14 Phosphorus Abnormalities

Normal levels of phosphorus are 0.89–1.44 mmol/L (2.5–4.5 mg/dL). It is primarily an intracellular ion (85 %).

6.5.15 Hyperphosphatemia

Hyperphosphatemia is rare in donors, and it is found in advanced or chronic renal failure and may occur with severe muscle or red blood cell breakdown and acidosis; it can favor the development of hypocalcaemia.

6.5.16 Hypophosphatemia

Hypophosphatemia is frequent in donors and may be a consequence of diuretic effects or a loss of fluid content from the gastrointestinal tract; it may also be a consequence of respiratory alkalemia during dextrose or insulin administration. The effects are as follows: decreased cardiac contractility, red blood cell and muscle breakdown (rhabdomyolysis), low platelet levels (induce thrombocytopenia), and reduced white blood cell function [32]. Treatment is as follows: if $P < 2.2$ mg/dL (0.71 mmol/L), 30 mmol potassium phosphate IV over 2–3 h, or 30 mmol sodium phosphate IV over 2–3 h (preferred if serum potassium >4.0 mmol/L) and repeat (total 2 doses); if P is still low, administer 30 mmol potassium phosphate IV over 2–3 h.

Chloride is largely present in the EC space, and its changes are not treated (do not require specific treatment).

Bicarbonate is usually not treated unless as an adjunct therapy in selected cases of hyperkalemia.

6.5.17 Polyuria Treatment

Polyuria is defined as a urine output >3 L/day in adults or 2 L/m^2 in children and may lead to severe metabolic and hemodynamic changes during organ harvesting. In this case, replacement with common electrolyte solutions can create fluid and electrolyte balance disturbances (edema, hyperosmolarity, hypernatremia, and hypokalemia) with a deterioration of cell membranes and ultimately of the organs that should be harvested [43, 44]. Almost half of the donors present with polyuria (urine output greater than 125 mL/h) and hypernatremia. Polyuria and hypernatremia could be induced by central diabetes insipidus resulting from insufficient blood levels of antidiuretic hormone from the posterior pituitary gland of brain-dead patients. Polyuria inducing hypovolemia and an impairment of the balance in electrolytes causes a decrease in blood pressure and impairment in organ perfusion. To avoid the latter, it is necessary to evaluate urine output and serum electrolytes every 2–4 h.

6.5.18 Assessment

- Evaluate blood sugar by laboratory or fingerstick measurement. Glucose values >200 mg/dL may contribute to polyuria.
- Discontinue any prescribed diuretic therapy.
- Calculate recent fluid intake/output balance and adjust intake to be 100 mL/h less than total output. If urine output over the last 3 h averaged approximately 400 mL/h, total IV fluid intake should be approximately 300 mL/h.
- Monitor serum Na and glucose levels at 2-h intervals.
- Serum Na > 148 mEq/L indicates water loss.
- If Na 135–147 mEq/L, control urine output and maintain hourly fluid intake 100 mL less than urine output.

6.5.19 Treatment

- Discontinue unnecessary fluid intake (maintain intake 100 cc less than output until intake and output are equal and then maintain intake = output).
- If urine output >250 cc above IV intake for the last 2 h and serum Na > 145 mEq/L when last measured, give 1 μg desmopressin (DDAVP) IV.
- Begin the replacement of urine output each hour cc/cc with 0.2 % saline hypotonic solution.

If urine output has not declined below 200 mL above intake (urine out >200 mL above fluid intake) in the next hour, give an additional 1 μg of DDAVP intravenously [42].

6.6 Pulmonary Changes and Management

A pulmonary impairment is frequent in the brain-dead donor and may be due to pneumonia, especially in long-term patients, the aspiration of gastric contents, neurogenic pulmonary edema, or pulmonary trauma causing a massive pulmonary contusion.

Table 6.8 Mechanical lung ventilation in potential donors

1. Peak airway pressure (AWP) < 40 cm H_2O
2. Plateau AWP < 35 cm H_2O
3. FIO_2 the lowest to keep $SpO_2 > 92$ % and $PaO_2 > 70$ mmHg
4. PEEP ≤ 5 cm H_2O; if lungs not considered, adjust to maintain $PaO_2 > 70$ mmHg.
5. Auto PEEP should be avoided
6. Tidal volumes 6–8 mL/kg body weight
7. Rate adjusted to maintain minute ventilation of approximately 8–10 l/min or to maintain PaCO2 > 16 mmHg and <60 mmHg to maintain arterial pH at 7.35–7.45.
8. Flow rate – usually approximately 60 L/min; adjust to minimize peak AWP; beware of auto PEEP as flow rate is slowed; a higher flow rate may be needed to minimize auto PEEP.
9. Inspiratory pressure setting – to limit peak airway pressure at 35–40 cm H_2O, consult with respiratory care practitioner for final pressure limit setting due to various ventilator types.
10. Adequate suctioning of excessive sputum.
11. Bronchodilators are administered if wheezing or a peak airway pressure – plateau airway pressure gradient of >10 cm H_2O.

It is very important to adopt a protective ventilatory strategy in potential lung donors that involves the following: small tidal volumes, PEEP of 5 cm H_2O, alveolar recruitment maneuvers after each disconnection of the ventilator, and bronchial suctioning of the secretion using a closed system (Table 6.8). Tidal volumes passed [45] from 10–15 mL kg^{-1} to 6–8 mL kg^{-1}, because lower tidal volume ventilation has shown an improved outcome in acute lung injury and its introduction has been associated with a greater number of transplantable lungs [46]. Tracheal cuff pressure should be 25 cm H_2O, and the head of the donor should be elevated to avoid aspiration [18].

Considering pulmonary infections, quantitative cultures of specimens obtained with bronchoscopic or nonbronchoscopic techniques, such as bronchoalveolar lavage (BAL) and/or protected specimen brush (PSB), could improve the identification of patients with true ventilator associated pneumonia and facilitate decisions whether to treat and thus to improve clinical outcome [47, 48].

6.7 Management of Hypothermia

Hypothalamic collapse after brain death also impairs temperature regulation. A decreased metabolic rate and the absence in muscular activity further contribute to reduced heat production. Thus, heat dispersal due to peripheral vasodilation should be considered. This condition is predictable, and consequently, the heat loss should not be allowed by using these therapeutic maneuvers:

- Administering warmed intravenous fluids
- Warming blankets
- Using heated and humidified inspired gases
- Warming splanchnic viscera by using heated abdominal surgical swabs
- Increasing the ambient temperature

6.8 Management of Anemia and Coagulation Abnormalities

These conditions are mainly due to hemorrhage, but the requirements of various harvesting teams for blood draws for laboratory testing may also play a significant role.

6.8.1 Assessment

First, a low hematocrit value, 28–30 %, can be caused by overhydration that increases the plasmatic level and decreases the relative volume of hematocrit.

If anemia is confirmed, control for and exclude bleeding sources, including external wounds and IV sites; examine gastric contents, observe urinary tract, and exclude hematochezia and intra-abdominal bleeding (sometime after percutaneous liver biopsy). If hematocrit is <28–30 %, transfuse 2 units red blood cells, and 1 h after the last unit, repeat hematocrit; if still <30 %, transfuse again 2 units red blood cells.

If no active bleeding sites are found, check for a possible coagulopathy; order PT, PTT, fibrinogen, and a platelet count. Disseminated intravascular coagulation (DIC) or a massive transfusion is a consequence of post-traumatic and surgical hemorrhage. Bleeding following massive transfusion may be due to hypothermia, dilutional coagulopathy, platelet dysfunction, fibrinolysis, or hypofibrinogenemia; the transfusion of 15–20 units of blood products causes dilutional thrombocytopenia, and platelet transfusions may be required, especially if platelet counts fall below 20,000/microL [49].

Coagulation alterations causing bleeding in brain death donors are primarily caused by the following issues: plasminogen activator and thromboplastin (largely available in the brain) released by brain tissue lesions, platelet function altered by catecholamine increase, and low platelet count due to consumption in DIC platelets and hypothermia [50–53].

References

1. Wilhelm MJ, Pratschke J, Beato F, Taal M, Kusaka M, Hancock WW, Tilney NL (2000) Activation of the heart by donor brain death accelerates acute rejection after transplantation. Circulation 102(19): 2426–2433
2. Zweers N, Petersen AH, Van Der Hoeven JA, De Haan A, Ploeg RJ, De Leij LF, Prop J (2004) Donor brain death aggravates chronic rejection after lung transplantation in rats. Transplantation 78(9): 1251–1258
3. Pratschke J, Wilhelm MJ, Laskowski I, Kusaka M, Beato F, Tullius SG, Neuhaus P, Hancock WW, Tilney NL (2001) Influence of donor brain death on chronic rejection of renal transplants in rats. J Am Soc Nephrol 12(11):2474–2481
4. Barklin A (2009) Systemic inflammation in the brain-dead organ donor. Acta Anaesthesiol Scand 53:425–435
5. Avlonitis VS, Wigfield CH, Kirby JA, Dark JH (2005) The hemodynamic mechanisms of lung injury and systemic inflammatory response following brain death in the transplant donor. Am J Transplant 5(4 Pt 1):684–693
6. Bos E, Leuvenink H, van Goor H, Ploeg RJ (2007) Kidney grafts from brain dead donors: inferior quality or opportunity for improvement? Kidney Int 72: 797–805
7. Weiss S, Kotsch K, Francuski M et al (2007) Brain death activates donor organs and is associated with a worse I/R injury after liver transplantation. Am J Transplant 7:1584–1593

8. Kutsogiannis DJ, Pagliarello G, Doig C, Ross H, Shemie SD (2006) Medical management to optimize donor organ potential: review of the literature. Can J Anaesth 53:820–830
9. Rangel-Castillo L, Gopinath S, Robertson CS (2008) Management of intracranial hypertension. Neurol Clin 26:521–541
10. Docze T (1993) Volume regulation of the brain tissue – a survey. Acta Neurochir (Wien) 121:1–8
11. Langfit TW, Weinstein JD, Kassell NF (1965) Cerebral vasomotor paralysis produced by intracranial hypertension. Neurology 15:622–641
12. Miller JD, Sullivan HG (1979) Severe intracranial hypertension. Int Anesthesiol Clin 17:19–75
13. Sesso HD, Stampfer MJ, Rosner B, Hennekens CH, Gaziano JM, Manson JE, Glynn RJ (2000) Systolic and diastolic blood pressure, pulse pressure, and mean arterial pressure as predictors of cardiovascular disease risk in men. Hypertension 36:801–807
14. Smith M (2004) Physiologic changes during brain stem death – lessons for management of the organ donor. J Heart Lung Transplant 23:217–222
15. Agrawal A, Timothy J, Cincu R, Agarwal T, Waghmare LB (2008) Bradycardia in neurosurgery. Clin Neurol Neurosurg 110:321–327
16. Bugge J (2009) Brain death and its implications for management of the potential organ donor. Acta Anaesthesiol Scand 53:1239–1250
17. Smith M (2004) Physiologic changes during brain stem death—lessons for management of the organ donor. J Heart Lung Transplant 23(Suppl 9):S217–S222
18. McKeown DW, Bonser RS, Kellum JA (2012) Management of the heartbeating brain-dead organ donor. Br J Anaesth 108(suppl 1):i96–i107
19. Dujardin KS, McCully RB, Wijdicks EF et al (2001) Myocardial dysfunction associated with brain death: clinical, echocardiographic, and pathologic features. J Heart Lung Transplant 20:350–357
20. Venkateswaran RV, Townend JN, Wilson IC, Mascaro JG, Bonser RS, Steeds RP (2010) Echocardiography in the potential heart donor. Transplantation 89:894–901
21. Potapov EV, Ivanitskaja EA, Loebe M, Mockel M, Muller C, Sodian R, Meyer R, Hetzer R (2001) Value of cardiac troponin I and T for selection of heart donors and as predictors of early graft failure. Transplantation 71:1394–1400
22. Gelb AW, Robertson KM (1990) Anaesthetic management of brain dead for organ donation. Can J Anaesth 37:806–818
23. Powner DJ, Crommett JW (2003) Advanced assessment of hemodynamic parameters during donor care. Prog Transplant 13:249–257
24. Unverferth DR, Magorien RD, Moeschberger ML, Baker PB, Fetters JK, Leier CV (1984) Factors influencing the one-year mortality of dilated cardiomyopathy. Am J Cardiol 54:147–152
25. Rosner MJ (1993) Pathophysiology and management of increased intracranial pressure. In: Andrews BT (ed) Neurosurgical intensive care, International Edition. New York :McGraw Hill
26. Harukuni I, Kirsch JR, Bhardwaj A (2002) Cerebral resuscitation: role of osmotherapy. J Anesth 16:229–237
27. Schunelle P, Berger S, De Boer J, Persijn G, Der Wonde FJ (2001) Effects of catecholamine application to brain-dead donors on graft survival in solid organ transplantation. Transplantation 72:455–463
28. Rosendale JD, Kauffman HM, McBride MA, Chabalewski FL, Zaroff JG, Garrity ER, Delmonico FL, Rosengard BR (2003) Aggressive pharmacological donor management results in more transplanted organs. Transplantation 75:482–487
29. Novitzky D, Cooper DK (2014) Thyroid hormone and the stunned myocardium. J Endocrinol 223(1):R1–R8
30. Mi Z, Novitzky D, Collins JF, Cooper DKC (2015) The optimal hormonal replacement modality selection for multiple organ procurement from brain-dead organ donors. Clin Epidemiol 7:17–27
31. Powner DJ, Kellum JA, Darby JM (2000) Abnormalities in fluids, electrolytes, and metabolism of organ donors. Prog Transplant 10:88–96
32. Powner DJ, Kellum JA (2000) Maintaining acid–base in organ donors. Prog Transplant 10:98–105
33. Mizock BA, Falk JL (1992) Lactic acidosis in critical illness. Crit Care Med 20:80–93
34. Oh MS, Carroll HJ (2000) External balance of electrolytes and acids and alkali. In: Seldin DW, Giebisch G (eds) The kidney: physiology & pathophysiology. Lippincott Williams & Wilkins, Philadelphia, pp 33–60
35. Kazemeyni SM, Esfahani F (2008) Influence of hypernatremia and polyuria of brain-dead donors before organ procurement on kidney allograft function. Urol J 5:173–177
36. Katz MA (1973) Hyperglycemia-induced hyponatremia–calculation of expected serum sodium depression. N Engl J Med 289:843–844
37. Mandal AK (1997) Hypokalemia and hyperkalemia. Med Clin North Am 81:611–639, - Wrenn KD, Slovis CM, Slovis BS. The ability of the physician to predict hyperkalemia from the ECG. Ann Emerg Med. 1991;20:1229–1232
38. Allon M (1993) Treatment and prevention of hyperkalemia in end-stage renal disease. Kidney Int 43:1197–1209
39. Ahee P, Crowe AV (2000) The management of hyperkalaemia in the emergency department. J Accid Emerg Med 17:188–191
40. Martin KJ, Gonzalez EA, Slatopolsky E (2009) Clinical consequences and management of hypomagnesemia. J Am Soc Nephrol 20:2291–2295
41. Bushinsky DA, Monk RD (1998) Calcium. Lancet 352:306–311
42. Hirschl MM, Matzner MP, Huber WO et al (1996) Effect of desmopressin substitution during organ procurement on early renal allograft function. Nephrol Dial Transplant 11:173–176

43. Shah V, Bhosale G (2006) Organ donor problems and their management. Indian J Crit Care Med 10:29–34
44. Ramos HC, Lopez R (2002) Critical care management of the brain-dead organ donor. Curr Opin Organ Transplant 7:70–75
45. Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000; 342(18):1301–1308
46. Mascia L, Pasero D, Slutsky A et al (2010) Effect of a lung protective strategy for organ donors an eligibility and availability of lungs for transplantation. JAMA 304:2620–2627
47. Chastre J, Fagon JY (2002) Ventilator-associated pneumonia. Am J Respir Crit Care Med 165:867–903
48. Bonten MJ, Bergmans DC, Stobberingh EE, van der Geest S, De Leeuw PW, van Tiel FH, Gaillard CA (1997) Implementation of bronchoscopic techniques in the diagnosis of ventilator-associated pneumonia to reduce antibiotic use. Am J Respir Crit Care Med 156:1820–1824
49. Levy JH (2006) Massive transfusion coagulopathy. Semin Hematol 43(1 Suppl 1):S59–S63
50. Talving P, Benfield R, Hadjizacharia P, Inaba K, Chan LS, Demetriades D (2009) Coagulopathy in severe traumatic brain injury: a prospective study. J Trauma 66:55–61, discussion 61–62
51. Barklin A, Tønnesen E, Ingerslev J, Sørensen B, Fenger-Eriksen C (2009) Coagulopathy during induced severe intracranial hypertension in a porcine donor model. Anesthesiology 110:1287–1292
52. Hefty TR, Cotterell LW, Fraser SC, Goodnight SH, Hatch TR (1993) Disseminated intravascular coagulation in cadaveric organ donors. Incidence and effect on renal transplantation. Transplantation 55:442–443
53. Valdivia M, Chamorro C, Romera MA, Balandín B, Pérez M (2007) Effect of posttraumatic donor's disseminated intravascular coagulation in intrathoracic organ donation and transplantation.Transplant Proc. Sep;39:2427–8

Non-Heart-Beating Donors

7

Antonino M. Grande and Carlo Pellegrini

Key Points

- Since the dawn of transplantation organs have been retrieved from patients immediately after circulatory arrest, specifically from "non-heartbeating" donors.
- When the Harvard Medical Committee in 1968 defined the concept and the diagnostic criteria of brain-death, organ retrieval began to be performed in "heart-beating" donors that will soon become the main source of organs for transplantation.
- The number of heart-beating donors is now declining because fewer young people are dying from severe head trauma or catastrophic cerebrovascular events and the diagnosis and management of brain injuries have improved.
- The constantly increasing gap between donors and patients on waiting lists has prompted donation after circulatory death (DCD) or "non-heart-beating donors" (NHBDs) that represent a valid source of organs for transplantation utilizing mechanical support with Extracorporeal Membrane Oxygenator (ECMO).
- ECMO may be used as a bridge to organ donation in NHBDs.

Since the dawn of transplantation organs have been retrieved from patients immediately after circulatory arrest, specifically from "non-heart-beating" donors. When the Harvard Medical Committee [1] in 1968 defined the concept and the diagnostic criteria of brain-death, organ retrieval began to be performed in patients whose death was ascertained after brainstem testing. These "heart-beating" donors have become the main source of organs for transplantation. However, the number of heart-beating donors is now declining because fewer young people are dying from severe head trauma or catastrophic cerebrovascular events [2], and the diagnosis and management of brain injuries have improved. Therefore, the scarcity of donor organs is the primary limiting factor of transplantation worldwide, and this condition causes an increased time span between listing and transplantation and prevents the

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Table 7.1 Maastricht classification for DCD donors

I	Dead on arrival	Uncontrolled
II	Unsuccessful resuscitation	
III	Awaiting cardiac arrest following withdrawal of care	Controlled
IV	Cardiac arrest after brainstem death	
V	Cardiac arrest in a hospital inpatient	Uncontrolled

death rate on the waiting list from improving. For this reason, selection criteria for organ donors have changed, and grafts from "marginal donors" have been used. These are older than optimal donors or present mild to moderate grade of organ dysfunction (such as diabetes mellitus, hypertension, renal insufficiency) or may transmit infectious diseases (CMV or HCV hepatitis). However, "marginal donors" do not affect outcomes in selected cases. Finally, the constantly increasing gap between donors and patients on waiting lists has prompted donation after circulatory death (DCD) or "non-heart-beating donors" (NHBDs). A substantial number of patients with brain death after cardiac arrest represent a valid source of organs for transplantation. Therefore, aggressive medical management of brain-death donors has significantly increased the number of transplanted organs by preventing cardiovascular collapse and the subsequent loss of organs, thus enhancing the number of potential organ donors [3, 4]. Extracorporeal membrane oxygenation (ECMO) has been increasingly used in patients with acute cardiac failure and in patients after cardiac arrest, both in and out of the hospital [5, 6].

At the same time, it is well known that donors often present hemodynamic instability despite maximal inotropic administration; therefore, mechanical circulatory support with ECMO may prevent loss of organs through haemodynamic stabilization of donor. Several reports have recently shown the use of ECMO as a bridge to organ donation [7, 8].

DCD donors are usually identified according to Maastricht classification [9] based on the circumstances of death and, consequently, the warm ischemic time (Table 7.1). Donors in categories I, II, and V are considered "uncontrolled" because they are unplanned and often present in the emergency department; donors in categories III and IV are considered "controlled".

7.1 Controlled Donors

Controlled donors primarily consist of terminally ill patients whose relatives ask for the discontinuation of life-sustaining treatments. After informed consent for organ donation is obtained, life-sustaining measures are withdrawn in a controlled setting. When respiration and circulation cease and do not return spontaneously within a few minutes, the patient is declared dead, and organ preservation can be initiated. Because the suspension of treatments is controlled, the warm ischemic damage is minimized.

7.2 Uncontrolled Donors

Uncontrolled donors are usually people who have had unexpected cardiac arrest. The unpredictable occurrence of the fatal event and the potential delay and/or the inadequate implementation of cardiopulmonary resuscitation are responsible for the very low level of survival, which is <10 % with a return of spontaneous circulation (ROSC) and <1 % without ROSC. After the declaration of circulatory death (in most countries, this is after a 5-min "no touch" period of asystole, whereas in Italy, the ascertainment is performed with a 20-min continuous EKG registration), authorization for donation is requested from relatives, and if consent is obtained, interventions to preserve organs are performed.

The use of organs from DCD donors implies two consequences:

- Limited warm ischemic damage (see Box 7.1)
- Organ function evaluation, especially for uncontrolled categories

Box 7.1. Warm Ischemia

The interruption of blood flow to an organ or tissue produces ischemia and the following reperfusion causes an acute inflammatory response that may create significant cellular damage and organ dysfunction. For instance, warm ischemia/reperfusion injury of the liver has been shown in a large number of clinical settings, including hepatic resectional surgery, liver transplantation, and hemorrhagic shock with fluid resuscitation [9, 10]. In transplantation, two distinct periods of warm ischemia are usually considered: (1) ischemia during organ retrieval, the time from cross clamping (or from cardiac arrest in non-heart-beating donors) until cold perfusion is commenced and (2) ischemia during implantation, the period from removal of the organ from ice until reperfusion. These periods of warm ischemia differ in their nature and the magnitude of their pathophysiologic consequences. The term "warm ischemia" is used to describe both of these periods in much of the medical literature [11].

Consequences of ischemia/reperfusion injury include liver failure in association with remote organ failure in more severe cases, both of which have significant rates of morbidity and mortality. Experimental models of warm hepatic ischemia/reperfusion injury have provided a greater understanding of the events that contribute to the pathogenesis of this syndrome and have prompted several clinical approaches to the prevention and treatment of organ dysfunction caused by hepatic ischemia/reperfusion.

Cold in situ perfusion (ISP) is among the first techniques used for the preservation of donor kidneys, cooling the organs without adding oxygen to the circuit [12]. The temperature decrease is not homogeneous, and organs from DCD suffer from longer warm ischemia (starting from the suspension of circulation to the administration of cold preservation solution or the institution of regional perfusion). Delayed graft function (DGF) [13] and primary nonfunction (PNF) [14] occur frequently after transplantation, and depending on the severity of the ischemic damage, DGF and PNF may affect 20–80 % and 15–25 % of kidney transplants from DCD, respectively [15]. Therefore, it is of utmost importance to decrease the ischemia–reperfusion injury as this will reduce the incidence of DGF and PNF and will allow a significant expansion of the donor pool.

ECMO has been suggested to minimize the effects of warm ischemia resulting from cardiocirculatory arrest.

To evaluate the function of organs from DCD, different procedures for the normothermic perfusion of isolated kidneys or lungs have entered clinical transplantation practice in the last few years [16, 17].

7.3 ECMO Technique

ECMO is a device that can replace both the heart and the lung function; oxygen is added to the donor's blood circulating in a closed circuit. It is composed of a centrifugal pump, an oxygenator, venous and arterial cannulas, and tubing. An additional component of ECMO is the heat exchanger to regulate the blood temperature during perfusion (i.e., hypothermic or normothermic perfusion) (Fig. 7.1).

The centrifugal pump, by the transfer of kinetic energy, allows the blood to flow through the oxygenator, the tubing, and the arterial cannula. The movement of the rotating part of the pump also causes a negative pressure that facilitates the drainage of venous blood through the venous cannula. Hollow fiber oxygenators are currently used. In the last 10 years, silicone fibers have been replaced by methyl-pentane fibers, thus allowing longer supports and less frequent plasma leakage.

Donor acceptance criteria are as follows: witnessed cardiac arrest, maximum no-flow period of 15 min, low flow time (cardiopulmonary resuscitation length) less than 150 min, age less than 60

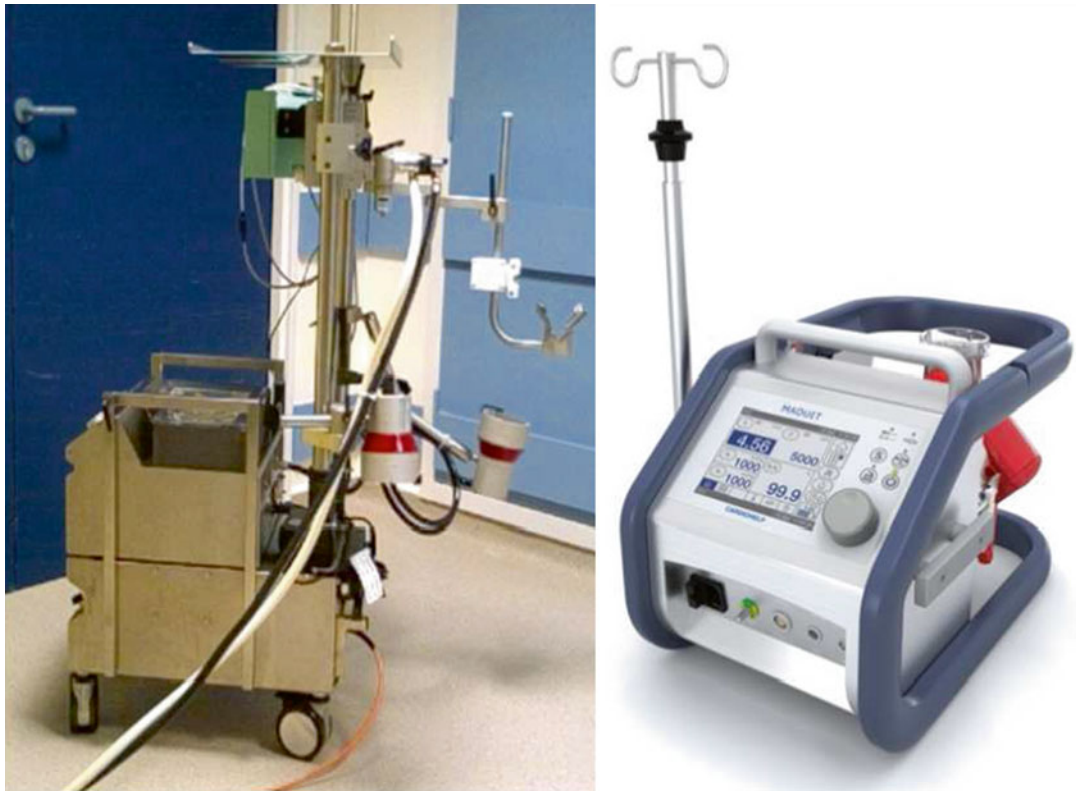

Fig. 7.1 ECMO systems

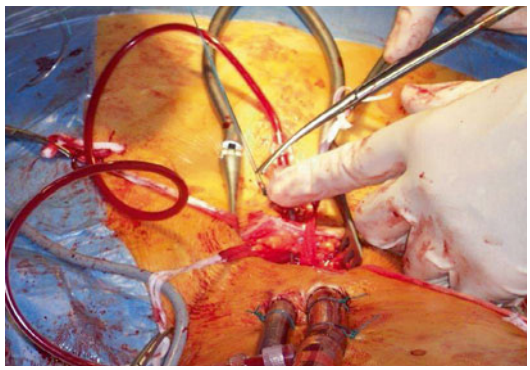

Fig. 7.2 Surgical cannulation of femoral vessels

years, no recent history of cancer or drug abuse, and no aortic dissection. Depending on the country's laws and/or institutional ethics committee authorization, donor cannulation and the initiation of perfusion may be allowed before donation consent has been obtained. In our experience, we obtain donation consent from relatives first.

The cannulation of femoral vessels can be performed either surgically or percutaneously. At the beginning of our experience, surgery represented the preferred choice for ECMO implantation. While automated chest compression is being conducted, a groin incision is performed on either the right or left side (Fig. 7.2).

After the dissection of subcutaneous tissue, both the femoral artery and vein are isolated. Purse-string sutures are performed on both vessels with 5/0 polypropylene suture. After vessel incision and the progressive enlargement of the path, a cannula is introduced and connected to the respective tubing (venous or arterial part). Heparin is administered (5000 IU), and extracorporeal circulation is started (ECMO flow = 2.4 L/min/m^2 of body surface). On the site opposite of cannulation, another incision is performed, and the femoral artery is isolated. After performing a purse-string suture to control bleeding, an occluder balloon catheter is introduced into the vessel and brought to approximately the diaphragmatic hiatus. After the inflation of the cath-

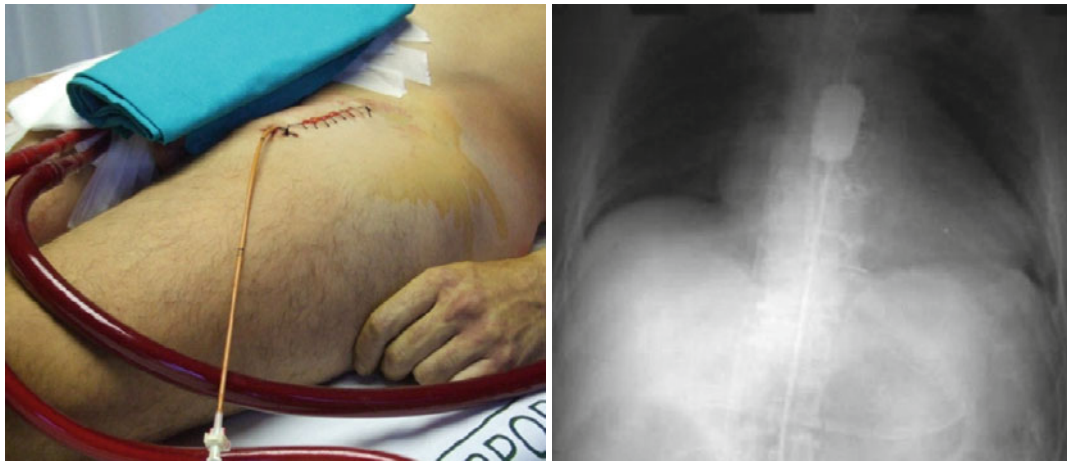

Fig. 7.3 The occlusion balloon catheter is inserted in the femoral artery opposite to ECMO arterial cannula (*left*); chest x-ray showing occlusion balloon position (*right*)

eter balloon (with a mix of saline and radiopaque dye that allows visualization on radiographs), the thoracic aorta is occluded, and both femoral arteries are ligated around the ECMO arterial cannula and the balloon catheter. In this way, the ECMO constitutes a recirculating closed circuit system that will not perfuse the superior district of the body and the lower limbs. ECMO flow is reduced to 2.2–2.4 L/min (Fig. 7.3). The proper positioning of the occlusion balloon immediately above the diaphragm is confirmed by a chest radiograph.

There are two different approaches, depending on the perfusate temperature:

1. Organs are immediately cooled; this technique is called total body cooling.
2. Organs are perfused in normothermia, and circulating blood is heated to maintain the temperature of approximately 37 °C; this is normothermic ECMO (N-ECMO).

In both cases, blood samples are withdrawn to determine activated clotting time (>160 s < 200 s) and biochemical (including acid–base status) and hematological parameters.

Alternatively, femoral artery and vein cannulation can be performed percutaneously under ultrasound control (Fig. 7.4).

In this case, a vascular linear probe is used to puncture the vessels, and by Seldinger's technique, a 1.5-m metal wire is inserted in each vessel. After enlarging the subcutaneous path with increasing dilators, cannulas are introduced both in the artery and the vein, and the extracorporeal circulation is started.

The donor is then taken to the operating room with the ECMO running. The maximum length of ECMO is 240 min. A standard surgical operation is performed, because there is no urgency to cool the organs for preservation. Because the usual preoperative donor diagnostic screening is not performed, thorough abdominal and thoracic cavity exploration is mandatory.

After organ isolation, ECMO is stopped, and the arterial cannula is used to perfuse 3–4 L of a cold preservation solution. Organ protection is enhanced by topical cooling with sterile ice and cold saline.

7.4 Advantages of ECMO in Organ Preservation

Normothermic circulation with ECMO allows a partial restoration of the energetic status of the organs, which severely declines during warm ischemia.

In brain-dead patients, high serum catecholamine reduces β-adrenergic receptor density, which can increase the possibility of graft dysfunction. Conversely, the use of ECMO could

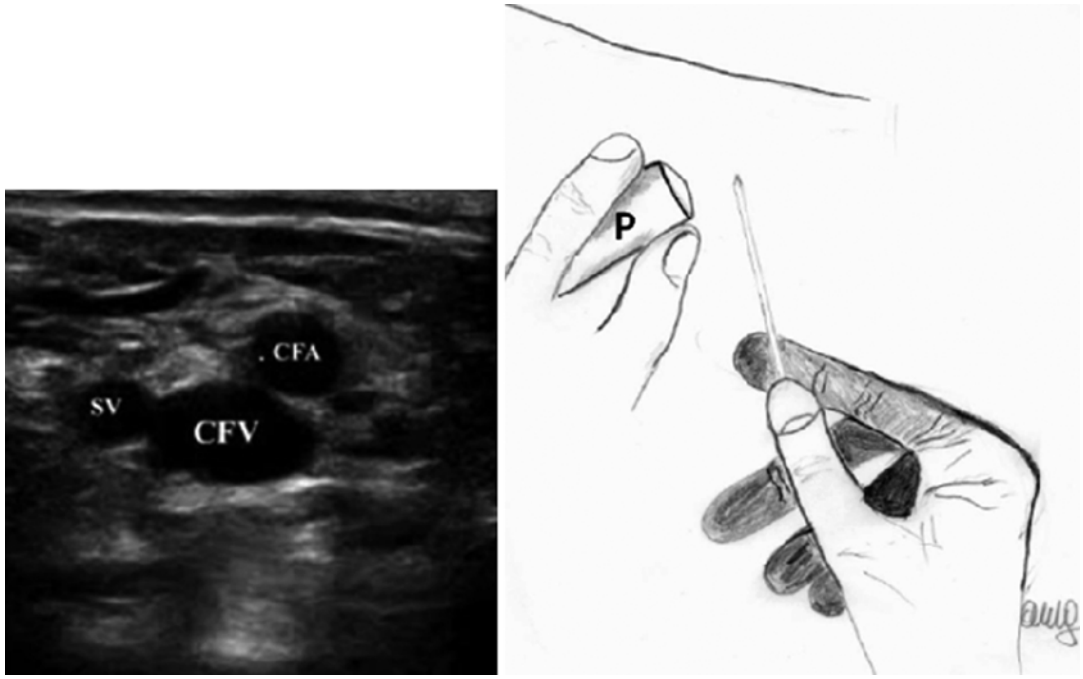

Fig. 7.4 Femoral vessels puncture technique under ultrasound control, *CFA* common femoral artery, *CFV* common femoral vein, *SV* saphenous vein, *P* ultrasound probe

better preserve the organs limiting catecholamine administration [18].

Experimental Studies As demonstrated by Arias-Diaz et al. [19], normothermic recirculation allowed the partial restoration of the adenine nucleotide (ATP) and reduced glutathione (GSH) content in pig liver and kidneys exposed to 30 min of warm ischemia followed by both 30 min of normothermic perfusion and 100 min of hypothermic flow. The restored ATP and GSH levels were retained after the period of hypothermic perfusion.

In the study by Net and colleagues, cardiocirculatory arrest and the subsequent normothermic recirculation were considered to be similar to ischemic preconditioning, and its efficacy was attributed to the maintenance of adequate levels of ATP and xanthine levels. After the start of normothermic recirculation, the mean arterial blood pressure immediately increased and continued to increase during the subsequent hours. Moreover, tissue oxygen saturation, blood CO_2 content, plasma potassium concentration, and blood pH recovered to pre-arrest levels in a few minutes [20].

Finally, the normothermic perfusion of organs after cardiocirculatory arrest provides significantly better short-term graft survival compared to hypothermic circulation. In the study published by Garcia Valdecasas et al. [21], graft survival after 5 days was compared in three groups of pig liver transplants (group 1 = heart-beating donor, no warm ischemia; group 2 = 20 min of warm ischemia and hypothermic extracorporeal recirculation for 15 min; group 3 = 20 min of warm ischemia and normothermic extracorporeal recirculation for 30 min). Organ preservation before harvesting was obtained by in situ cooling. Graft survival in groups 1 and 3 was 100 %, and it was 0 % in group 2 ($p < 0.03$). Normothermic recirculation had a significant effect on endothelial damage decrease ($p < 0.05$) and on the reduction of histological changes after reperfusion ($p < 0.04$).

Clinical Practice In 1989, Koyama published the first description of the clinical use of hypothermic ECMO in DCD to preserve the kidneys [22]. In the early cases, the extracorporeal support was not limited to the abdomen. The first application of normothermic reperfusion

Table 7.2 Main studies on kidney transplantation in ECMO in DCD

Center	Type of study	Type of preservation	Significant results	Drawbacks	References
Barcelona (Spain)	Non-randomized retrospective comparative	N-ECMO H-ECMO vs. cold ISP	1. Incidence of PNF and DGF lower in N-ECMO vs. H-ECMO and ISP 2. Duration of DGF shorter in H-ECMO compared to ISP organs	Both ECMO groups were small ($N=8$)	[24]
Madrid (Spain)	Non-randomized retrospective comparative	N-ECMO H-ECMO vs. DBD	1. 1- and 5-year graft survival of DCD organs was comparable with young (< 60 years) DBD donors and was better than older (> 60 years) DBD donors	No comparison between hypothermic and normothermic perfusion	[25–27]
St. Petersburg (Russia)	Retrospective	N-ECMO	1. Absence of PNF despite long warm ischemia time (mean = 76 ± 16 min) 2. 30 % of immediate resumption of function 3. Nearly normal creatinine level 3 months after transplantation	No control group	[28]
La Pitiè-Salpetriere	Non-randomized retrospective comparative	N-ECMO vs. cold ISP	1. Earlier function recovery in the N-ECMO group 2. Lower level of serum creatinine 1 month after transplantation	Retrospective study	Presented at the first International Meeting in Ischemia Reperfusion in Transplantation (2012)
Taipei (Taiwan)	Retrospective comparative	MC II, III, IV vs. DBD and living donors	1. 5-year graft survival identical in the three groups 2. The longer the ECMO was run, the longer the DGF	Retrospective study	[29–31]
Winston-Salem (USA)	Retrospective comparative	N-ECMO vs. DCD direct aortic perfusion	1. N-ECMO donors had reduced DGF rate ($p<0.016$)	Retrospective study Organ harvested locally	[32]
University of Michigan (USA)	Retrospective comparative	N-ECMO vs. DBD	1. N-ECMO donors had reduced DGF rate (no significant), 1 case PNF in DBD group	Small numbers	[33]

N-ECMO normothermic ECMO, *H-ECMO* hypothermic ECMO, *ISP* in situ perfusion, *DBD* brain-death donor, *DCD* cardiac-death donor, *PNF* primary nonfunction, *DGF* delayed graft function, *MC* Maastricht donor category

in humans was performed with kidney transplantation from uncontrolled DCD [12]. Several reports have shown that ECMO can be safely utilized to hemodynamically sustain and secure systemic oxygenation in patients with cardiac or respiratory failure. Thus, ECMO represents a bridge to organ donation after brain or circulatory death for optimal organ perfusion until procurement [23]. Several groups reported their experience with either the hypothermic or normothermic extracorporeal perfusion of uncontrolled donors.

The results of the main studies on kidney transplantation are summarized in Table 7.2.

Although not all studies in the medical literature are double blind, and they are often performed on a limited number of donors, it can be observed from these data that ECMO techniques have the possibility to expand the supply of organs for transplantation. Considering these methodological limitations, ECMO techniques must be further studied to ameliorate graft survival and transplantation outcome.

References

1. A definition of irreversible coma. Report of the Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death (1968) JAMA 205:337–340
2. Death rate trends for RTAs and CVAs, WHO European Health for All database – http://www.euro.who.int/hfadb
3. Lee JH, Hong SY, Oh CK, Hong YS, Yim H (2012) Kidney transplantation from a donor following cardiac death supported with extracorporeal membrane oxygenation. J Korean Med Sci 27:115–119
4. DuBose J, Salim A (2008) Aggressive organs donor management protocol. J Intensive Care Med 23:367
5. Deakin CD, Nolan JP, Soar J et al (2010) European Resuscitation Council guidelines for resuscitation 2010 section 4. Adult advanced life support. Resuscitation 81:1305–1352
6. Massetti M, Gaudino M, De Paulis S, Scapigliati A, Cavaliere F (2014) Extracorporeal membrane oxygenation for resuscitation and cardiac arrest management. Heart Fail Clin 10:S85–S93
7. Isnardi DI, Olivero F, Lerda R, Guermani A, Cornara G (2013) Extracorporeal membrane oxygenation as a bridge to organ donation: a case report. Transplant Proc 45:2619–2620
8. Ke H-Y, Lin C-Y, Tsai Y-T, Lee C-H, Hong G-C, Lee C-H, Tsai C-S (2010) Increase the donor pool: transportation of a patient with fatal head injury supported with extracorporeal membrane oxygenation. J Trauma 68:E87–E88
9. Kootstra G, Daemen JHC, Oomen APA (1995) Categories of non-heart beating donors. Transplant Proc 27:2893–2895
10. Bellingham JM, Santhanakrishnan C, Neidlinger N et al (2011) Donation after cardiac death: a 29-year experience. Surgery 150:692
11. Halazun KJ, Al-Mukhtar A, Willis S, Ahmad N (2007) Warm ischemia in transplantation: search for a consensus definition. Transplant Proc 39:1329–1331
12. Garcia-Rinaldi R, Lefrak EA, Defore WW et al (1975) In situ preservation of cadaver kidneys for transplantation: laboratory observations and clinical application. Ann Surg 182:576–584
13. Perico N, Cattaneo D, Sayegh MH, Remuzzi G (2004) Delayed graft function in kidney transplantation. Lancet 364:1814–1827
14. Wijnen RM, Booster MH, Stubenitsky BM et al (1995) Outcome of transplantation of non heart-beating donor kidneys. Lancet 345:1067–1070
15. Yarlagadda SG, Coca SG, Formica RN Jr et al (2009) Association between delayed graft function and allograft and patient survival: a systematic review and meta-analysis. Nephrol Dial Transplant 24:1039–1047
16. Nicholson ML, Hosgood SA (2013) Renal transplantation after ex vivo normothermic perfusion: the first clinical study. Am J Transplant 13:1246
17. Cypel M, Yeung JC, Machuca T et al (2012) Experience with the first 50 ex vivo lung perfusions in clinical transplantation. J Thorac Cardiovasc Surg 144:1200
18. Fukushima N, Sakagoshi N, Ohtake S, Sawa Y, Kawata H, Shirakura R et al (2002) Effects of exogenous adrenaline on the number of the beta-adrenergic receptors after brain death in humans. Transplant Proc 34:2571–2574
19. Arias-Díaz J, Álvarez JM, Gómez M, Del Barrio R, García-Carreras C, González P, Balibrea JL (1997) Changes in adenine nucleotides and lipid hydroperoxides during normothermic cardiopulmonary bypass in a porcine model of type II non-heart-beating donor. Transplant Proc 29:3486–3487
20. Net M, Valero R, Almenara R, Barros P, Capdevilla L, Lopez-oado MA, Ruiz A et al (2005) The effect of normothermic recirculation is mediated by ischemic preconditioning in NHBD liver transplantation. Am J Transplant 5:2385
21. García-Valdecasas JC, Tabet J, Valero R, Taurá P, Rull R, García F, Montserrat E et al (1998) Liver conditioning after cardiac arrest: the use of normothermic recirculation in an experimental animal model. Transpl Int 11:424–432
22. Koyama I, Hoshino T, Nagashima N, Adachi H, Ueda K, Omoto R (1989) A new approach to kidney procurement from non-heart-beating donors: core cooling on cardiopulmonary bypass. Transplant Proc 21:1203–1205
23. Barrou B, Billault C, Nicolas-Robin A (2013) The use of extracorporeal membranous oxygenation in donors after cardiac death. Curr Opin Organ Transplant 18:148–153
24. Valero R, Cabrer C, Oppenheimer F et al (2000) Normothermic recirculation reduces primary graft dysfunction of kidneys obtained from non-heart-beating donors. Transpl Int 13:303–310
25. Sanchez-Fructuoso AI, Prats D, Torrente J et al (2000) Renal transplantation from non-heart beating donors: a promising alternative to enlarge the donor pool. J Am Soc Nephrol 11:350–358
26. Sanchez-Fructuoso AI, de Miguel Marques M, Prats D, Barrientos A (2003) Non-heart-beating donors: experience from the Hospital Clinico of Madrid. J Nephrol 16:387–392

27. Sanchez-Fructuoso AI, Marques M, Prats D et al (2006) Victims of cardiac arrest occurring outside the hospital: a source of transplantable kidneys. Ann Intern Med 145:157–164
28. Reznik O, Skvortsov A, Loginov I et al (2011) Kidney from uncontrolled donors after cardiac death with one hour warm ischemic time: resuscitation by extracorporeal normothermic abdominal perfusion 'in situ' by leukocytes-free oxygenated blood. Clin Transplant 25:511–516
29. Lee CY, Tsai MK, Ko WJ et al (2005) Expanding the donor pool: use of renal transplants from non-heart-beating donors supported with extracorporeal membrane oxygenation. Clin Transplant 19:383–390
30. Chen KH, Tsai MK, Ko WJ et al (2000) Renal transplantation from non-heart-beating donors with extracorporeal membrane oxygenation: preliminary results. Transplant Proc 32:1743–1744
31. Ko WJ, Chen YS, Chen RJ et al (2002) Non-heart-beating donors under extracorporeal membrane oxygenation support. Transplant Proc 34:2600–2601
32. Farney AC, Hines MH, al-Geizawi S et al (2011) Lessons learned from a single center's experience with 134 donations after cardiac death donor kidney transplants. J Am Coll Surg 212:440–451; discussion 451–453
33. Gravel MT, Arenas JD, Chenault R 2nd et al (2004) Kidney transplantation from organ donors following cardiopulmonary death using extracorporeal membrane oxygenation support. Ann Transplant 9:57–58

8 Multiple Organ Retrieval: General Principles, Organ Preservation, and New Strategies

Riccardo De Carlis, Raffaella Sguinzi, Antonino M. Grande, and Paolo Aseni

Key Points

- Organ procurement is the first stage of the transplant procedure, and it decisively contributes to transplantation success or failure.
- In stable donors, we recommend first gaining access to the retroperitoneal space with control of the inferior vena cava and the abdominal aorta, and soon after, we recommend accurate dissection of the hepatic hilum and the recognition of any vascular abnormalities before in situ cooling.
- The purpose of organ preservation is to slow the unavoidable biological deterioration and damage that occurs between harvesting and reperfusion, thus buying time to organize staff and facilities, to transport organs, and, when necessary, to perform histological examinations.
- Simple cold storage is the most widely used preservation method, which relies on the effects of hypothermia supplemented by the use of special preservation solutions.
- Machine perfusion provides the unique opportunity to evaluate the functional performance of the graft prior to transplantation, likely allows a longer and safer cold ischemia time, and, in the near future, will allow the administration in the perfusion system of innovative pharmacological agents for ex vivo organ damage repair.

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8.1 General Principles

8.1.1 Organizational and Preoperative Aspects

Organ procurement has been defined as "the lifeblood of organ transplantation." It is the first part of the whole transplant procedure and decisively contributes to its success or failure, because every mistake at this stage can render an organ unsuitable for transplantation or lead to serious complications in the recipient [1].

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Ideally, the retrieval team should be self-sufficient and not require any support from the donor hospital other than an operating theater and a local staff member. In practice, most retrieval teams also require a donor hospital anesthetist and a scrub nurse to be present during the procedure. Surgical teams from the transplant center to which the graft will be transplanted usually harvest the organs. Teams from cardiothoracic transplant centers almost always perform cardiothoracic organ retrievals. For the retrieval of all other organs, ideally a single abdominal organ retrieval team should be available. The presence of a single retrieval team, rather than individual organ teams, streamlines the process and ensures a uniform approach to the abdominal retrieval, which is an important factor, particularly when operating in different environments. Local teams sometimes retrieve kidneys for other transplant centers [2]. The donor transplant coordinator plays an important role in organizing organ procurement, arranging the transport of the surgical team to and from the donor hospital, and performing much of the administrative tasks [1, 3]. All retrieval teams should be equipped with a bag containing surgical instruments needed for the procedure. Perfusion solutions are kept refrigerated with ice in proper thermal containers. Some instruments are not always available in the donor hospital, and therefore, the contents of the bag should be checked periodically, in particular before leaving from the transplant center. The bag should also contain drugs that may be difficult to obtain in the donor hospital, for example, prostacyclin, antifungal agents, and some antibiotics for the decontamination of the duodenal lumen during pancreas procurement [2]. Surgical instruments vary according to the necessities and preferences of each retrieval team. Table 8.1 shows a representative list of the retrieval team equipment.

Table 8.1 Retrieval team equipment

Gigli saw (or sternal saw)
Finochietto rib retractor
Autostatic abdominal retractors
Overholt forceps
Monopolar forceps
Aortic clamp
Sterile aortic and sterile venous cannulae
One-way and two-way rapid perfusion system
Gastrointestinal anastomosis (GIA) linear stapler (for pancreas procurement)
Vascular stapler
Multi-fire clip applier (with medium and small clips)
Histological biopsy needle
Toomey syringe
Blunt needle (for bile duct flushing)
Sterile bags for organ packing
Sterile containers (urine collection type) for vascular grafts
Impermeable plastic aprons
Sterile gloves
Prostacyclin
Amphotericin B (for gastroduodenal decontamination in the case of pancreas procurement)
Preservation solution (in thermal containers with ice)

Organ procurement should be performed in a peaceful and dignified atmosphere. In general, a respectful treatment of the organ donor is a condition *sine qua non* for each person involved in the organ donation, and the remaining wishes of the donor or the relatives must be respected. Communication is essential to ensure that a smooth retrieval process is achieved. Competition or a lack of communication between the members of organ retrieval teams may lead to surgical injury of the organs or inadequate preservation [1, 3]. After arrival in the donor hospital, the procurement surgeon should introduce himself or herself and the procurement team. If different surgical teams are involved in the procurement, they must discuss the details of the technique and sequence they want to adopt before starting the procedure [3]. Every organ is important and must be removed from the donor without jeopardy to any of the individual grafts, especially in the case of anatomical or vascular conflict detected during preliminary dissection. In general, the order of multiple organ procurement gives priority to the heart and lungs; then the liver, pancreas, and small bowel; and finally to the kidneys, vascular grafts, and tissues [2, 4].

The key responsibility and an absolute imperative for the lead surgeon of the retrieval team is the correct identification of the donor prior to the

Table 8.2 Checklist for the lead surgeon and specific responsibilities of the retrieval team

Identify the donor
Brainstem death tests performed and documented appropriately
Consent for organ donation
Blood group
Virology status, medical history, and other blood tests
All of the following conditions should be reported to the transplant coordination center and to all centers involved in organ transplantation:
If the donor is contaminated with microorganisms
Systemic sepsis or endocarditis
HCV, HBsAg (with some exceptions), and HIV-positive donors
Malignancies (with some exceptions: low-grade prostate cancer, some brain tumors, and nonmelanoma cutaneous neoplasm)
Coronary heart disease
Valvular heart disease
Inadequate ventricular function
Systemic vascular disorders
Hypotensive and hypertensive episodes, necessity to give amines
Documentation of key retrieval events
Completion of appropriate documentation
Completion of procedure summary in medical notes
Correct labeling of the organs, blood, and tissue samples

operation and the check of its blood group compatibility. The lead surgeon must also check that the diagnosis of death has been made appropriately and documented correctly and that the consent or authorization for donation has been obtained and documented. Preoperative checks should also ensure that all other necessary information about the donor is available, as summarized in Table 8.2. Clinical examination of the donor should be performed, including inspection of the entire body for any skin lesions, palpation of the breast (in both male and female donors!), and digital rectal examination to identify possible malignancies.

8.1.2 Preventable Errors in Organ Procurement

Severe adverse events in organ transplantation are quite rare. Nevertheless, the scientific literature and the media have reported a small number of cases where organ recipients died or had serious injuries as a result of errors during the transplantation process [5]. Clinicians and surgeons traditionally equate medical errors with human shortcomings and often fail to understand the importance of redesigning the systems and processes of care to anticipate potential failures that can lead to errors. Organ transplantation is a particularly complex procedure of healthcare and routinely stresses nearly all of the systems and processes of surgical care, offering a unique opportunity to proactively identify vulnerabilities and potential failures. Initial steps have been taken to understand these issues through the United Network for Organ Sharing (UNOS) Operations and Safety Committee, which has collected data about preventable errors in organ transplantation and shown that 55 % of reported adverse events are due to miscommunication and errors in documentation and data entry. Separate data about kidney and liver transplantation have confirmed that failures in communication and the coordination of care are significant contributors to preventable errors. Moreover, errors with labeling and packing have been reported by the UNOS Operations and Safety Committee as a recurrent problem across transplant centers, and between 2006 and 2010, they accounted for 38 % of the reported errors [6]. A national commission instituted in Italy after three cases in 2007 of transplant-related human immunodeficiency virus (HIV) transmission released some recommendations to improve transplant safety: automatic transcription of test results from laboratory instruments to laboratory information systems and donors' medical records, centralization of donor laboratory tests, and training to develop a proactive quality and safety culture in regional donation and transplantation networks [5]. Checklists can play an important role in surgery; the World Health Organization (WHO) released its surgical safety checklist in June 2008 and demonstrated its impact in a 2009 study of eight international hospitals. The rate of death was 1.5 % before the checklist was introduced and declined to 0.8 % afterward; inpatient complications occurred in 11 % of

patients at baseline and in 7 % after the introduction of the checklist. However, each transplant center has its own systems and checklists for procedures, because at this point there are no international standard guidelines specific to transplantation [7].

8.1.3 High Infectious Risk Donors

High infectious risk donors (HRDs) are non-ideal donors that are considered suboptimal because they are thought to carry an increased risk of infectious transmission. The definition of HRDs was introduced in 1994 when the Centers for Disease Control and Prevention (CDC) developed guidelines to identify persons at risk of transmitting infectious disease through transplantation. HRDs are defined as persons meeting one of the following behavioral criteria:

- Men who had sex with other men (MSM) in the preceding 5 years
- Persons who report the nonmedical intravenous, intramuscular, or subcutaneous injection of drugs in the preceding 5 years
- Persons with hemophilia or related clotting disorders who have received clotting factor concentrates
- Commercial sex workers (CSWs) who have engaged in sex in exchange for money or drugs in the preceding 5 years
- Persons who have had sex in the preceding 12 months with any person described above or with a person known or suspected to have HIV infection
- Persons exposed in the preceding 12 months to known or suspected HIV-infected blood
- Inmates of correctional systems (incarcerated donors)

All donors are tested for infectious disease; thus, the HRD designation is currently used to identify those donors at risk of acquiring an infection in the weeks or months before death and those likely to have false-negative serologic tests due to the associated window period. Despite controversy surrounding their use, organs from HRDs benefit the transplant community as a whole by expanding the supply of available organs and decreasing waiting times for patients with high waitlist mortality. Special informed consent use can mitigate legal risk. Communicating infectious risk to patients is extremely difficult because the true infection risk is unknown and varies widely depending on individual donor risk factors. Putting the issue in terms the patients can understand is also challenging. Nucleic acid testing (NAT) mitigates infectious risk by decreasing the window period, and it is therefore recommended for HRDs to reduce the risk of infectious transmission [8].

8.1.4 Surgical Technique: Main Principles

The surgical technique for multiple organ procurement will be extensively discussed in the following dedicated chapters. Here we only focus on some essential general aspects of the procedure. Regardless of the technique adopted, the first operative step must include a careful exploration of the thoracic and abdominal cavities to exclude gross pathological conditions that contraindicate the procedure. This inspection completes the preoperative evaluation of the donor and helps minimize the risk of disease transmission to the recipient.

The guiding principle of all procurement techniques is the avoidance of warm ischemia. This can be achieved with in situ organ cooling by the carefully timed and controlled intravascular infusion of cold preservation solutions at the time of circulatory arrest [4]. Therefore, the organ procurement procedure is generally divided into two parts (called “warm” and “cold” phases), depending on which comes before or after in situ flushing.

The surgical techniques for multiple organ procurement have undergone progressive changes over time. The first techniques used during the 1970s and early 1980s required the exposure and complete dissection of each organ while the heart was still beating, during the warm phase. This was obviously time consuming, particularly as

less experienced surgeons were increasingly involved in the procedure and become a deterrent to collaboration between abdominal and cardiac teams [9, 10]. Starzl and colleagues described the "flexible technique" for organ procurement in 1984, in which all donor organs to be procured were rapidly cooled in situ, simultaneously removed in a bloodless field, and further dissected on a back table [4, 9, 11]. Several teams subsequently introduced the in situ flush and cold dissection technique, initially recommended for instable donors, as a rapid procurement method for all multiorgan retrievals [9]. Thus, surgical techniques for abdominal organ procurement can be roughly divided in two main categories: the warm dissection technique and the rapid retrieval technique ("dissection in the cold"). In the warm dissection technique, organ dissection takes place before the cannulation of the aorta and cold perfusion. Conversely, the rapid retrieval technique aims first to achieve control of the aorta and its cannulation to rapidly start cold perfusion. Sometimes, isolated kidney retrieval needs to be performed if no other organ is suitable for transplantation [3].

We think that donor surgeons must be familiar with both the cold and warm dissection techniques, because they have complementary roles. We recommend the rapid retrieval technique only if the donor becomes unstable, because this procedure minimizes warm ischemic times during hemodynamic instability and can be safely performed in critical situations by non-expert surgeons. However, one well-known disadvantage of this rapid technique is the difficulty in recognizing any possible accessory or replacing blood vessels, which during the cold phase turn into non-pulsating, non-bleeding structures. Thus, a rapid perfusion is usually obtained at the expense of the subsequent cold phase and back table surgery, which consequently requires more time and increases the risk of injury to cooled grafts [2, 10]. In stable donors, we recommend instead a combined technique, which first involves gaining access to the retroperitoneal space and the control of the abdominal aorta (to easily convert to the rapid technique if the donor suddenly becomes unstable during the procedure) and is followed by an accurate dissection of the hepatic hilum and the recognition of any vascular abnormalities before in situ cooling. In our experience, this technique is instructive for the surgeon in training and minimizes the risk of not recognizing vascular abnormalities in exchange for a negligible number of graft injuries during the warm phase if a well-trained surgeon assists the procedure. Moreover, additional time for warm dissection does not hamper collaboration between different transplantation teams if the donor remains stable. There is little evidence that manipulation and dissection prior to perfusion can cause vasospasm and increase oxygen consumption of the abdominal organs (especially the liver), leading to poor preservation [3, 9]. In our opinion, this effect is insignificant and may be overcome by the faster cold phase and back table surgery, which expose the graft for a shorter time to a temperature that is greater than the optimum for proper preservation.

8.2 Organ Preservation

8.2.1 Ischemia-Reperfusion Injury Physiopathology

The exact underlying mechanisms of both primary nonfunction and delayed graft function remain unclear but most likely involve ischemia-reperfusion injury, which develops soon after transplantation [12]. Once removed from the donor, the organ undergoes a period of ischemia and incurs subsequent damage. The longer the organ is removed from blood, oxygen, and nutrients, the less likely it will be able to return to normal function after transplantation. The injury process that begun during hypothermia is exacerbated by the rewarming as the organ is being implanted [13]. A wide range of pathological processes contributes to ischemia and reperfusion-associated tissue injury.

The ischemic period in particular is associated with significant alterations in the control of gene expression. For example, ischemia is associated with the inhibition of oxygen-sensing

prolylhydroxylase (PHD) enzymes, because they require oxygen as a cofactor. The hypoxia-associated inhibition of PHD enzymes leads to the posttranslational activation of hypoxia and inflammatory signaling cascades, which control the stability of the transcription factors, hypoxia-inducible factor (HIF) and nuclear factor-κB (NF-κB), respectively [14]. Changes in gene expression seem to be the earliest indicators of ischemia-reperfusion-related injury that are measurable in the graft, and quantitative gene expression analysis in postreperfusion biopsies may be a valuable tool to postoperatively identify patients at risk of early clinical allograft dysfunction after transplantation [12]. Several studies have suggested a functional role for microRNAs in ischemia and reperfusion. Pharmacological approaches to inhibit microRNAs seem likely to become treatment modalities for patients in the near future [14].

Once the oxygen supply has been exhausted, the cells transfer from aerobic to anaerobic metabolism, which quickly becomes self-limiting due to the production of lactate and protons. Membrane ion transport begins to shut down without excess adenosine triphosphate (ATP) to fuel the pumps, and passive redistribution occurs, resulting in cellular swelling as water osmotically corrects the imbalance. Taken together, these and other changes lead to the activation of cell death programs, including apoptosis and necrosis [13].

Necrotic cells are highly immunostimulatory and lead to inflammatory cell infiltration and cytokine production. Ischemia and reperfusion activate a host immune response in a sterile environment. This sterile immune response involves signaling events through pattern recognition molecules such as Toll-like receptors (TLRs), which can be activated by endogenous molecules in the absence of microbial compounds, particularly in the context of cell damage or death. Many studies suggest that inhibitors of TLR signaling could be effective for the treatment of sterile inflammation induced by ischemia and reperfusion. Ischemia and reperfusion also elicit a robust adaptive immune response that involves, among other cell types, T lymphocytes. In contrast, regulatory T cells appear to have a protective role in ischemia and reperfusion injury. A series of studies have shown that neo-epitopes expressed on ischemic tissues are targets for natural antibody binding during the reperfusion phase with subsequent complement activation, neutrophil recruitment, and tissue injury. The production of reactive oxygen species (ROS) at sites of sterile inflammation alters cellular proteins, lipids, and ribonucleic acids, leading to cell dysfunction and death [14].

Oxidative stress associated with reperfusion results in further free radical damage to the organs [13]. Xanthine oxidase may serve as the initial source of free radical generation in ischemia-reperfusion injury. With the onset of ischemia, ATP is degraded to hypoxanthine. Simultaneously, xanthine dehydrogenase is converted by ischemia to xanthine oxidase. Although the concentrations of substrate and enzyme are high during ischemia, the absence of oxygen prevents purine oxidation until reperfusion. During reperfusion, oxygen becomes available, suddenly and in excess, and the oxidation of hypoxanthine proceeds rapidly, generating a burst of superoxide radical by-products [2]. In this way, reperfusion-dependent events further aggravate ischemia-induced parenchymal injury either by prolonging focal ischemia (due to direct free radical damage on pericytes) or from the release of proinflammatory mediators that promote leukocyte infiltration and local activation [13]. Attenuated vascular relaxation after reperfusion due to injured pericytes can result in a no-reflow phenomenon characterized by the increased impedance of microvascular blood flow after reperfusion [14].

8.2.2 Strategies for Organ Preservation

The transplant process requires the retrieval of an organ from the donor and the preservation of it throughout its implantation in the recipient. Preservation is logistically essential for organ transplantation because it buys time to organize staff and facilities, transport organs, and perform

necessary laboratory tests. The purpose of organ preservation is to slow extracorporeal biological deterioration that occurs in organs during the time between harvesting and reperfusion, providing a viable graft with primary function after transplantation [11, 15]. Good organ preservation has proven to be a major determinant of graft outcome after revascularization [12].

Clinical organ transplantation has moved forward from an experimental procedure in the early 1950s to the current treatment of choice for patients with end-stage organ disease, and the development of organ preservation techniques has flanked and supported the success of this procedure. With the shortage of organs available for transplant, "marginal donors" have become an important source to expand the donor pool. For these organs, preservation is of even greater importance and remains a subject of ongoing research [11].

There are currently two approaches of preservation for most transplantable organs: static or dynamic. Both preservation modalities are preceded by the donor procurement phase, in which access to the required organs is surgically achieved by introducing chilled solutions in sufficient volumes into the major vascular channels to wash out the blood and achieve moderate cooling before final removal from the body [11].

Simple cold storage (SCS) is the easiest and most widely used preservation method in organ transplantation. SCS relies on the effects of hypothermia supplemented by the use of special preservation solutions that are aimed at inhibiting the unavoidable deterioration. Hypothermia represents a compromise between the benefits and detriments of cooling. The standard recommended temperature for SCS is 4 °C. Below this point, organs can freeze, which will result in coagulative necrosis upon reperfusion. Temperatures above 4 °C are associated with increased metabolic activity, ATP depletion, lactic acid buildup, and mitochondrial disturbances, resulting in severe parenchymal and endothelial injury. Clinical hypothermia slows total cellular metabolism, reduces the requirements for oxygen, and inhibits the activity of hydrolytic enzymes to prevent tissue injury [11, 13].

In contrast, machine perfusion constitutes a method for dynamic preservation in which the organ, after an initial washout of blood, is connected to a perfusion device, and a solution is pumped through its vasculature [16]. This continuous perfusion permits the delivery of oxygen and nutrients to the parenchyma and the removal of toxic metabolites. Various temperatures have been used from hypothermic perfusion at 4 °C to normothermic perfusion at 37 °C; the latter maintains the organ in a more physiological and metabolically active state. With normothermic perfusion, organs resume their function. Solutions used as perfusate also vary from low potassium crystalloid solutions to blood-based solutions. The flow can be continuous or pulsatile, mimicking the physiological variation in systolic and diastolic pressure [17].

Although machine perfusion was the original preservation technique used for organ transplantation, the early perfusion devices required significant resources and customized vans to transport them between donor and recipient hospitals. The introduction of conventional preservation solutions for SCS overshadowed for years the more complicated use of machine perfusion in clinics [13]. In an era of donor shortage and the increased use of suboptimal grafts and organ exchange across sometimes distant geographical areas, SCS has reached its limits. Machine perfusion has reemerged, and new portable devices have been developed, with the largest clinical experience acquired in kidney and lung transplantation [17]. In kidney transplantation, several studies including an international randomized controlled trial have shown a reduced rate of delayed graft function and better graft survival after hypothermic machine perfusion versus static cold perfusion [16, 18]. One clinical study has been published comparing 20 adult liver recipients after hypothermic machine perfusion with a historically matched group of recipients after SCS with a reduction in early allograft dysfunction [19]. The results of an international

multicenter trial randomizing standard donor lungs for preservation with SCS versus machine perfusion are awaited [20].

8.2.3 Most Common Cold Static Preservation Solutions

The most common solutions used for cold static preservation are compared in Table 8.3. When cold ischemic times are limited, most studies in the liver, kidney, and pancreas transplantation found equivalent outcomes for histidine-tryptophan-ketoglutarate and Celsior versus University of Wisconsin solution [21].

8.2.3.1 Collins' Solution

Developed in 1969, Collins' solution was based on a combination of high-potassium ion content, to mimic intracellular composition, and osmotic barrier supported by glucose, to suppress cell swelling [11]. Magnesium was added to act as a

Table 8.3 Comparison of the most common cold static preservation solutions

	Euro-Collins	UW	HTK	Celsior
Electrolytes				
Na^+ (mmol/L)	10	25–30	15	100
K^+ (mmol/L)	115	125–130	10	15
Ca^{2+} (mmol/L)	–	–	0.015	0.25
Mg^{2+} (mmol/L)	–	5	4	13
Cl^- (mmol/L)	15	–	50	41.5
Buffers				
Phosphate(mmol/L)	57.5	25	–	–
Bicarbonate(mmol/L)	10	–	–	–
Sulfate (mmol/L)	–	5	–	–
Histidine(mmol/L)	–	–	198	30
Impermeants				
Mannitol(g/L)	–	–	30	60
Raffinose(mmol/L)	–	30	–	
Lactobionate(mmol/L)	–	100	–	80
Hydroxyethyl starch (g/L)	–	50	–	–
Glucose(mmol/L)	198	–	–	–
Energetic substrates				
Adenosine (mmol/L)	–	5	–	–
Alpha-ketoglutarate(mmol/L)	–	–	1	–
Tryptophan(mmol/L)	–	–	2	–
Glutamate(mmol/L)	–	–	–	20
Antioxidants				
Allopurinol (mmol/L)	–	1	–	–
Dexamethasone (mg/L)	–	16	–	–
Glutathione(mmol/L)	–	3	–	3
Others				
Insulin (U/L)	–	40	–	–
Penicillin G (U/L)	–	200,000	–	–
General properties				
pH	7.0	7.4	7.2	7.3
Osmolarity (mOsm/L)	375	320	310	320
Viscosity (cP at 4 °C)	N/A	5.7	1.8	1.15

HTK histidine-tryptophan-ketoglutarate, *UW* University of Wisconsin

membrane stabilizer, but in the presence of phosphate, the magnesium phosphate formed crystal precipitates, which was reported when using the original solution. To eliminate this problem, a modified Collins' solution was developed in Europe (named Euro-Collins) that omitted the magnesium and used mannitol in place of glucose [13]. Collins' solution and its more recent variant Euro-Collins were widely distributed for organ preservation until the advent of the University of Wisconsin solution in the late 1980s [11, 21].

8.2.3.2 University of Wisconsin (UW) or Belzer Solution

Originally developed by Belzer and Southard for pancreas preservation in 1987, the University of Wisconsin (UW) solution is currently the most commonly used static cold preservation solution for abdominal organs [21]. It is a potassium-rich, sodium-depleted, osmotically active solution that is supplemented with a precursor of ATP (adenosine) and antioxidant agents (allopurinol, reduced glutathione). Osmotically active substances (raffinose and lactobionate) prevent cellular swelling but generate high viscosity. The colloid hydroxyethyl starch permits more effective flushing [11, 21]. Potential risks include hyperkalemic cardiac arrest at reperfusion, ischemic-type biliary complications, and microcirculatory disturbances as a result of particle formation. These disadvantages are not clinically relevant in most cases because UW solution yields prolonged safe preservation for abdominal organs [21].

8.2.3.3 Histidine-Tryptophan-Ketoglutarate (HTK) Solution

Originally designed as a cardioplegic solution in 1980 by Bretschneider, histidine-tryptophan-ketoglutarate (HTK) solution represents an alternative to UW solution. It is a crystalloid solution with an osmolarity slightly higher than that of the intracellular space [12, 21]. Its major components are a strong buffer (histidine), osmotic barrier (mannitol), and low-permeability amino acids (tryptophan and alpha-ketoglutaric acid), which help to stabilize cell membranes and may be substrates for anaerobic metabolism. The electrolyte composition is characterized by low concentrations of potassium, which therefore allow a safe, direct release into the recipient's blood circulation. The lower viscosity of HTK solution provides more effective flushing and the rapid cooling of organs. Because HTK is less expensive and lower preservation costs per donor can be obtained, it has become increasingly popular over the last 20 years, especially in developing countries [11]. HTK solution has been reported to have less biliary complications than UV solution, but contrary to most clinical trials, US national registry data in the kidney, pancreas, and liver transplantation demonstrate more detrimental effects and earlier graft loss after preservation with HTK versus UW solution [21, 22].

8.2.3.4 Celsior Solution

Initially formulated specifically for heart preservation in 1995, Celsior solution is now widely utilized for abdominal and thoracic organ storage [21]. It adopts many of the principles of UW solution (impermeants lactobionate and mannitol) and the strong buffer of HTK solution (histidine), but in contrast with UW solution, reduced glutathione is the only antioxidant agent included. Celsior solution contains relatively lower potassium levels compared with UW solution and Euro-Collins' solution. It has the advantage of being less viscous than UW solution and can rapidly perfuse large parenchymal volumes, such as the liver and lungs [2, 11].

8.2.4 Some Special Considerations on Perfusion Preservation of the Heart Graft[1]

Perfusion preservation provides oxygen and metabolic substances to harvested donor organs, thus improving their reperfusion function and the survival of the transplanted patient. If we

[1] Written by A.M. Grande.

consider the heart graft, the transplant procedure remains consistently feasible for only 4–6 h. In fact, even beyond 3 h of storage, recipient mortality has been demonstrated to increase exponentially [23]. Therefore, current research is directed to improve the existing perfusion solutions by adding or omitting various components. The composition of the preservation solution is intended to represent some important variables that affect graft survival. Preservation solutions are frequently classified into two broad categories on the basis of electrolyte content:

- *Intracellular* type, characterized by high potassium and low sodium (Celsior solution, Euro-Collins' solution)
- *Extracellular* type, low potassium and high sodium (UW solution, HTK solution, Belzer-Machine Perfusion solution)

Intracellular-type storage solutions may decrease the ATP requirements of the preserved organ by reducing the energy production needed to maintain membrane Na^+/K^+ ATPase activity [24]. However, the mere fact that more than 150 different organ preservation solutions are used in the United States alone explains that the optimal heart preservation solution remains to be defined [25]. As a matter of fact, the initial cellular and functional preservation of the myocardial tissue is achieved with hypothermia and mechanical arrest. ATP is consumed at a minor level, even during mechanical cardiac arrest, allowing the breakdown of ATP, which is produced by anaerobic glycolysis during the ischemic time. If the ATP reserve is depleted irreversibly, myofiber contracture may occur [26]. The perfusion solutions should also maintain ion homeostasis, and even though Na^+/K^+ ATPase activity is significantly reduced by hypothermia, ions flow down their concentration gradient; intracellular hydrogen ions are exchanged for extracellular sodium ions that, in turn, are replaced by calcium ions. This process increases the concentration of calcium ions inside the sarcolemma, thus damaging cardiac myofibers during reperfusion.

8.3 New Strategies

8.3.1 Machine Perfusion and Ex Vivo Graft Conditioning

Machine perfusion creates a window between procurement and transplantation during which functional performance and the viability of the organ can be evaluated prior to transplantation. Different physiological parameters can be measured, and various biochemical markers released in the perfusate can be analyzed, but the exact value of these markers to predict functional performance after transplantation is not clear and needs to be further investigated [17]. For the kidneys, vascular resistance correlates with delayed graft function and 1-year graft failure, but the predictive value is low, making this information inadequate as a stand-alone viability parameter to accept or discard a given kidney. More accurate prediction of graft outcome will require the integration of perfusion parameters and biomarker concentrations into multifactorial graft quality scoring systems [27]. Machine perfusion provides a unique opportunity to administer innovative pharmacological agents for ex vivo repair and the improvement of graft quality prior to transplantation. Few papers have been published on organ therapy during machine perfusion, and they are generally limited to preclinical large animal models; however, the potential for this approach is great because important graft improvements can be accomplished through the relatively simple addition of a specific pharmaceutical agent to the preservation solution [28]. The use of mesenchymal stem cells (MSCs) has gained attention in the field of organ transplantation because of their pro-regenerative, anti-inflammatory, and immunomodulatory properties. The administration of MSCs has been shown to enhance recovery from ischemia-reperfusion-induced acute renal failure in rats. The role of autologous MSCs as an induction therapy to promote graft acceptance has also been studied in a randomized controlled trial after living-related kidney transplantation. Machine perfusion offers a unique platform to

selectively administer these MSCs directly into the donor organ, overcoming the issues of homing, trafficking, and safety [17].

8.3.2 Donation After Cardiac Death

The use of non-heart-beating donors, today better known as donation after cardiac death (DCD), has been extensively discussed elsewhere in a dedicated chapter. Here we only focus on some essential aspects. The potential of DCD has been recognized since the early days of kidney transplantation and has recently undergone a resurgence of interest to expand the donor pool. In DCD, the cessation of circulatory and respiratory function happens first, leading to warm ischemia during the period between circulatory dysfunction and subsequent cold perfusion by the procurement team. This is in contrast with the heart-beating cadaver donor, defined by the irreversible cessation of all brain functions but with full circulatory and respiratory functions until cold perfusion, resulting in minimal organ ischemia or preservation injury. Thus, in DCD, the effects of injury sustained during warm ischemia are superimposed on subsequent cold preservation injury [29]. DCD can be controlled or uncontrolled. In the uncontrolled situation, the donor is declared dead on the arrival at the hospital or fails to respond to cardiopulmonary resuscitation after circulatory arrest. This is an unplanned situation, and there is no opportunity to organize the process of organ donation in advance; true organ ischemia and damage occur before procurement. In controlled DCD, the donor experiences circulatory arrest after a process of planned withdrawal of support when further treatment is deemed futile. There is usually an opportunity to obtain family consent and mobilize the retrieval team prior to the withdrawal of support, and for this reason, the warm ischemia time is usually shorter [29, 30]. The outcomes for organs transplanted after cardiac death are similar to those for organs transplanted after brain death. However, the length of time that organs can be deprived of oxygen and still be transplanted successfully varies; it is best to retrieve the liver less than 30 min after the withdrawal of life-sustaining measures, whereas the kidneys and pancreas can often be recovered up to 60 min after this withdrawal [31]. A femoral cannula can be placed after or before cardiac arrest; organs are cold flushed after the declaration of death and retrieved as in the aforementioned rapid technique [29].

References

1. Baranski A (2009) Surgical technique of abdominal organ procurement: step by step. Springer, London
2. Aseni P, De Carlis L (2011) Prelievomultiorgano a scopo di trapianto. Ghedimedia, Milano
3. Wunderlich H, Brockmann JG, Voigt R et al (2011) DTG procurement guidelines in heart beating donors. Transpl Int 24(7):733–757
4. Starzl TE, Hakala TR, Shaw BW Jr et al (1984) A flexible procedure for multiple cadaveric organ procurement. Surg Gynecol Obstet 158(3):223–230
5. Bellandi T, Albolino S, Tartaglia R et al (2010) Unintended transplantation of three organs from an HIV-positive donor: report of the analysis of an adverse event in a regional health care service in Italy. Transplant Proc 42(6):2187–2189
6. Ison MG, Holl JL, Ladner D (2012) Preventable errors in organ transplantation: an emerging patient safety issue? Am J Transplant 12(9):2307–2312
7. Pondrom S (2011) The AJT report: news and issues that affect organ and tissue transplantation. Am J Transplant 11(7):1345–1346
8. Kucirka LM, Singer AL, Segev DL (2011) High infectious risk donors: what are the risks and when are they too high? Curr Opin Organ Transplant 16(2):256–261
9. Brockmann JG, Vaidya A, Reddy S et al (2006) Retrieval of abdominal organs for transplantation. Br J Surg 93(2):133–146
10. Vegeto A, Berardinelli L (1999) Il trapianto di rene. UTET, Milano
11. Guibert EE, Petrenko AY, Balaban CL et al (2011) Organ preservation: current concepts and new strategies for the next decade. Transfus Med Hemother 38(2):125–142
12. Anaya-Prado R, Delgado-Vázquez JA (2008) Scientific basis of organ preservation. Curr Opin Organ Transplant 13(2):129–134
13. Henry SD, Guarrera JV (2012) Protective effects of hypothermic ex vivo perfusion on ischemia/reperfusion injury and transplant outcomes. Transplant Rev (Orlando) 26(2):163–175
14. Eltzschig HK, Eckle T (2011) Ischemia and reperfusion – from mechanism to translation. Nat Med 17(11):1391–1401
15. McLaren AJ, Friend PJ (2003) Trends in organ preservation. Transpl Int 16(10):701–708

16. Moers C, Smits JM, Maathuis MH et al (2009) Machine perfusion or cold storage in deceased-donor kidney transplantation. N Engl J Med 360(1):7–19
17. Van Raemdonck D, Neyrinck A, Rega F et al (2013) Machine perfusion in organ transplantation: a tool for ex-vivo graft conditioning with mesenchymal stem cells? Curr Opin Organ Transplant 18(1):24–33
18. Moers C, Pirenne J, Paul A et al (2012) Machine perfusion or cold storage in deceased-donor kidney transplantation. N Engl J Med 366(8):770–771
19. Guarrera JV, Henry SD, Samstein B et al (2010) Hypothermic machine preservation in human liver transplantation: the first clinical series. Am J Transplant 10(2):372–381
20. Warnecke G, Moradiellos J, Tudorache I et al (2012) Normothermic perfusion of donor lungs for preservation and assessment with the organ care system lung before bilateral transplantation: a pilot study of 12 patients. Lancet 380(9856):1851–1858
21. Parsons RF, Guarrera JV (2014) Preservation solutions for static cold storage of abdominal allografts: which is best? Curr Opin Organ Transplant 19(2):100–107
22. Stewart ZA, Cameron AM, Singer AL et al (2009) Histidine-Tryptophan-Ketoglutarate (HTK) is associated with reduced graft survival in deceased donor livers, especially those donated after cardiac death. Am J Transplant 9(2):286–293
23. Taylor DO, Edwards LB, Mohacsi PJ et al (2003) The registry of the International Society for Heart and Lung Transplantation: twentieth official adult heart transplant report – 2003. J Heart Lung Transplant 22(6):616–624
24. Belzer FO, Southard JH (1988) Principles of solid-organ preservation by cold storage. Transplantation 45(4):673–676
25. Demmy T, Biddle JS, Bennett LE et al (1997) Organ preservation solutions in heart transplantation – patterns of usage and related survival. Transplantation 63(2):262–269
26. Costanzo MR, Dipchand A, Starling R et al (2010) The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients. J Heart Lung Transplant 29(8):914–956
27. Jochmans I, Moers C, Smits JM et al (2011) The prognostic value of renal resistance during hypothermic machine perfusion of deceased donor kidneys. Am J Transplant 11(10):2214–2220
28. Bon D, Chatauret N, Giraud S et al (2012) New strategies to optimize kidney recovery and preservation in transplantation. Nat Rev Nephrol 8(6):339–347
29. Reddy S, Friend P (2005) Liver transplantation outcomes using donors after cardiac death. Curr Opin Organ Transplant 10:95–100
30. Manzarbeitia C, Reich DJ (2005) Non-heartbeating donors: special considerations for procurement and preservation in liver transplantation. Curr Opin Organ Transplant 10:101–104
31. Steinbrook R (2007) Organ donation after cardiac death. N Engl J Med 357(3):209–213

Part III

Surgical Technique for Thoracic Organ Procurement

Thoracic and Mediastinal Inspection, Heart Procurement

9

Antonino M. Grande

Tips, Tricks, and Pitfalls in Heart Retrieval

- Evaluate wall motion; check carefully for scars or contusions.
- Palpate and control coronary arteries for atherosclerosis and calcifications.
- Avoid manipulating sinoatrial area.
- If you do not remain at the operating table during the abdominal surgery period, scrub before the aorta and inferior vena cava are cannulated and ligated by the liver/kidney team.
- Determine whether abdominal surgeons want to vent into the pericardium or through the infrarenal inferior vena cava.
- Administer heparin i.v. before aortic crossclamping.
- Secure cardioplegic cannula via a purse string.
- Be sure that liver/kidney/lung teams do not start their perfusions until the heart is satisfactorily vented.
- Tie or clamp superior vena cava.
- Anteriorly incise inferior vena cava.
- Cut left inferior pulmonary vein or, if lungs are being retrieved, the left atrial appendage to vent the left ventricle.
- Crossclamp ascending aorta above cardioplegic cannula insertion.
- Start cardioplegic infusion.
- Pour crushed ice over the heart, and place a sucker into the inferior vena cava to draw the warm runoff.
- During cardioplegia infusion, always control the ascending aorta pressure and prevent left ventricular distention.
- Left ventricular distention can be controlled by releasing the aortic crossclamp for a few seconds.
- Avoid right and/or left ventricle distension, thus controlling possible insufficient venting, especially if the lungs are retrieved In this case, the lung perfusate returning in the left atrium must be vented.
- When cardioplegic infusion is completed, the heart is excised. Divide inferior vena cava, right and left pulmonary veins and arteries, superior vena cava, and the aorta at the arch level; if the lungs are being retrieved, an atrial cuff must be tailored along the pulmonary veins (see Chap. 10).

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- Bench surgery: prepare the heart by dividing the pulmonary trunk at the bifurcation, inspect the valves for defects or vegetations, check for atrial septal defects or patent foramen ovale, and check for adequate rim of atrial tissue along the coronary sinus.
- Maintain the cardioplegic cannula; this will facilitate cardioplegic infusion at the time of heart implantation.
- Pack the heart in cold saline solution or in iced cardioplegic solution.

9.1 Introduction

Legal restrictions, such as safety belts, helmets for motorcycle drivers, and speed limits, and improvements in car design, have reduced the number of serious brain injuries, and roadside and emergency room resuscitation have become more aggressive, lessening the degree of injuries. Over a 10-year period, we have examined 153 hearts and 118 pairs of lungs; 106 hearts (69.28 %) and 38 pairs of lungs (47.5 %) were considered suitable for transplantation. However, when we compare the years 1995–1999 (period A) with the years 2000–2005 (period B), it is interesting to note that 14 % of hearts (13/92) in period A vs. 56 % (34/61) in period B were unsuitable and 41 % of lungs (21/51) in period A vs. 88 % (59/67) in period B were unsuitable (both $p<0.001$, Fisher's exact test) [1]. We examined all the organs of this series in the operating room, applying the same criteria that, as years pass, become less strict. Consequently, it is not rare to examine unsuitable donors offered by intensive care and transplant coordination centers. Therefore, in thoracic transplantation, it is necessary not only to increase and widen the donor pool (considering older subjects aged over 65 years and those with systemic disease, infections, etc.) but to identify donors suitable to perform the transplant procedure safely; the relaxing of donor eligibility criteria allows not only more donors but also creates more risk for recipients. The number of patients requiring heart transplants is continuously increasing, but surgeons have become more demanding about the organs they are willing to use. Khush et al. [2] analyzed Organ Procurement and Transplantation Network (OPNT) data evaluating all potential adult cardiac organ donors between 1995 and 2010; there were more than 80,000 potential donors, and of these, 34 % were accepted and 48 % refused. There was a significant decrease in donor heart acceptance from 44 % in 1995 to 29 % in 2006, which was followed by an increase to 32 % in 2010. Older donor age, female sex, and medical comorbidities predicted nonacceptance. Donor age and comorbidities increased during the study period, with a concomitant decrease in the acceptance of hearts from donors with undesirable characteristics. This is quite understandable, and it is mandatory to support all efforts aimed at ascertaining evidence-based criteria for donor heart evaluation and acceptance for cardiac transplantation. Consequently, heart harvesting is the most important and delicate portion of the cardiac transplantation procedure.

9.2 Donor Evaluation

When a patient is pronounced brain dead and the next of kin has given consent for organ donation, medical evaluation will start, including the acquisition of complete medical and social history from the family of the deceased. The assessment of a potential donor heart is accomplished by echocardiography and coronary angiography, especially in older male candidates (>40 years). Furthermore, donors should not present an active infectious process or malignancy and should not have had a prolonged cardiac arrest. Other donor factors should also be considered, including age, the presence of diabetes or lung disease, cigarette smoking, and alcohol or drug abuse. Moreover, the surgeon must reexamine all the clinical information in the chart to guarantee that no relevant medical findings were unreported or unappreciated by the coordinator center. The key responsibility for the lead surgeon of the retrieval team is the correct identification of the donor prior to the operation and to check its blood group compatibility.

It is very important to evaluate the recipient status. If the recipient had previous heart surgery,

more time will be required for the implanting surgeon, and precision timing should be individually determined by the coordinator. Moreover, in most cases anesthesia induction is delayed until the donor heart is considered suitable for transplantation. Therefore, good communication between harvesting teams is obligatory to reduce donor organ ischemic time [3].

When the donor is older than 40 with a hypertensive and cigarette smoking history, coronary angiography is mandatory. Occasionally, coronary angiography can initially appear normal, but a careful study can show irregularities and flow impairment. It is not infrequent to see coronary angiographies within the accepted normal range but upon surgical inspection to find atherosclerotic plaques and calcifications. Figure 9.1 shows coronary angiography in a 48-year-old man who died of cerebral hemorrhage; angiography reported diffuse coronary narrowing as "coronary irregularities." At surgical inspection (Fig. 9.2), coronary arteries were diffusely calcified.

Therefore, aspects that could be regarded as normal in subjects over the age of 40 should not always be considered normal in donors. Figure 9.3 shows cardiac inspection in a 48-year-old woman who died of cerebral hemorrhage during surgery; there is an important left anterior descending coronary calcification. In this case, coronary angiography showed a slowing of coronary flow that could hide alterations in coronary vessels.

9.3 Surgical Technique

It is important to underline that chest inspection is essential to prevent infective or neoplastic transmission to recipients.

The mediastinum is checked for nodules immediately before incising the pericardium. The same control must be performed for the pleural cavity, especially if a chest CT was not available preoperatively. The inspection of lungs for nodules, particularly in heavy smokers, and the inspection of parietal pleura for malignant mesothelioma should also be performed.

The most common malignancies transmitted are as follows: renal cell carcinoma, adenocarcinoma of the lung, glioblastoma multiforme, and lymphoma. Therefore, an accurate inspection of the chest cavity should be performed to discover any suspicious lesion or nodule that could be either a primitive or secondary neoplasm. Additionally, infective nodules can be a source of infectious disease. Every suspicious node should be biopsied.

Most drugs (anticonvulsants, pain medications, gastrointestinal motility agents, eyedrops, antihypertensive and antinausea agents, subcutaneous heparin, osmotic agents) are unnecessary during donor operation and should be discontinued.

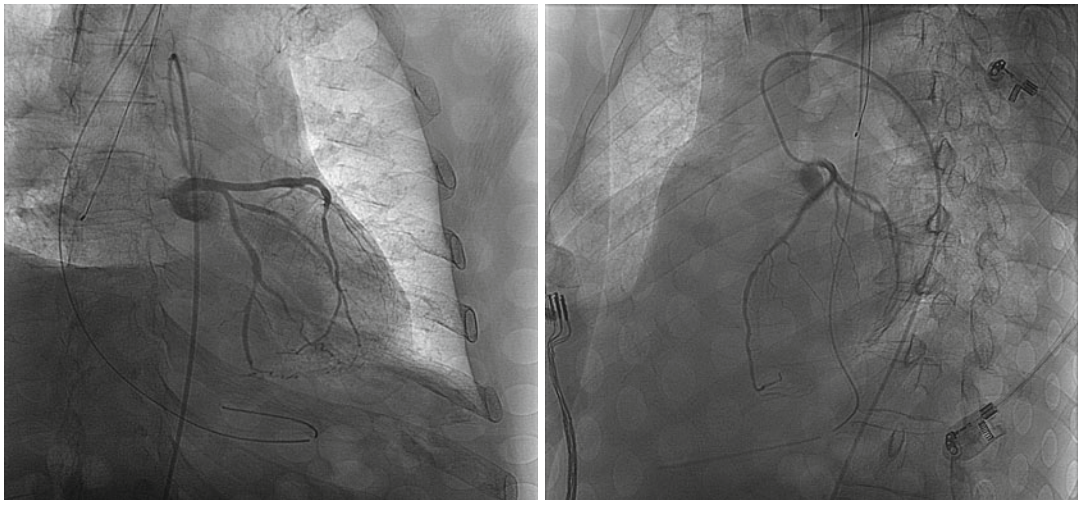

Fig. 9.1 Coronary angiography showing diffuse narrowing

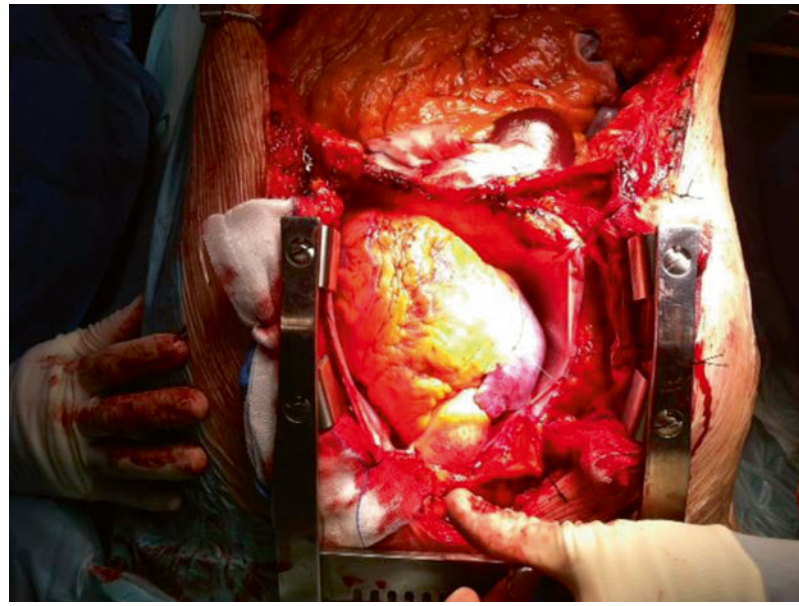

Fig. 9.2 Surgical inspection. Left anterior descending (LAD) coronary results calcified (same case as Fig. 9.1)

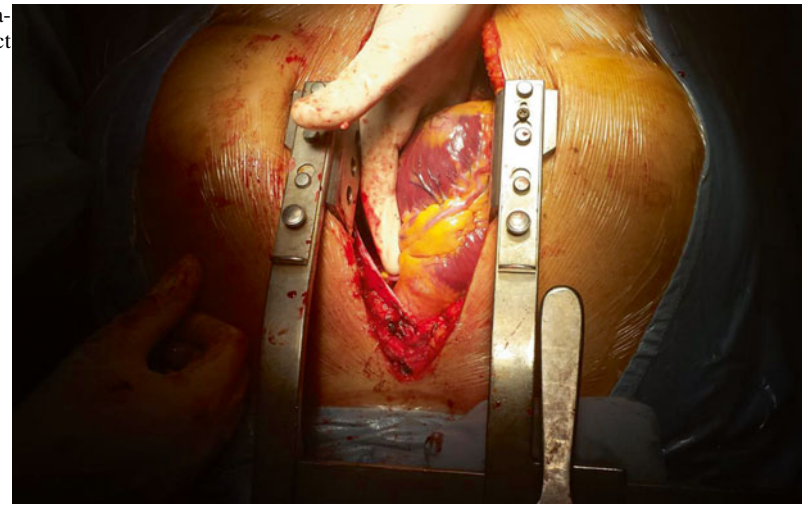

Fig. 9.3 Coarse calcifications on the medium tract of the LAD coronary artery

The donor is transferred in the operating room, and invasive monitoring is mandatory for checking systemic blood pressure, pulmonary pressures, and right atrial pressure; these parameters are useful in guiding fluid therapy and administering vasoactive drugs. The administration of fluids can limit the excessive intake of inotropic drugs at high doses and may have deleterious effects and an ischemic action on the myocardium and the other organs. Therefore, especially when hemoglobin is approximately 10 g/dL, it is preferable to transfuse 1–2 units of packed red cells in case of possible bleeding during the surgical procedure.

We believe that the heart-harvesting procedure represents the last and also one of the most defined chances to evaluate the capability of the organ before transplantation.

The donor is placed in a supine position, and his skin is prepped and draped. The procedure is always started by the heart surgeon with a midline incision through the skin from the jugular

notch to the xiphoid process. Hemostasis is achieved using electrocautery; subcutaneous tissue and presternal fascia are incised, and the bone is divided using a sternal saw. The thymus gland residue is divided to facilitate the exposure of the mediastinal structures. The anterior pericardium is incised on the midline and then suspended.

At this point, it is possible to perform a careful inspection of the donor heart through the following sequence of steps:

- Evaluate left and right ventricle contractility.
- Evaluate right heart volume overload assessed by pulmonary trunk distension.
- Evaluate hypovolemia by assessing pulmonary trunk collapse.
- Perform epicardial inspection for ecchymosis and hematoma caused by trauma.
- Carefully inspect coronary artery and palpate to find any arterial calcifications and atherosclerosis.
- Evaluate valvular disease by assessing valvular bruits.
- Look for congenital defects.

In the case of right heart overload, which causes right ventricular distension and depressed right ventricular function, the anesthesiologist can force diuresis by diuretic administration. In contrast, hypovolemia is corrected by fluid infusion or red blood cell transfusion in the case of anemia. Ecchymosis and hematomas can reduce heart contractility; coronary artery disease, especially if the coronary angiogram was not performed, can severely threaten the subsequent transplant.

When the donor is unstable and inotropic agents are administered for pressure support, it is mandatory to monitor central venous pressure (CVP). CVP provides a window into the right ventricular response to various loading conditions; an elevated CVP indicates a high right end diastolic pressure. A Swan-Ganz catheter may be placed to measure donor pulmonary pressure and vascular resistance, which can be elevated with neurologic pulmonary edema or acute respiratory distress syndrome (ARDS) caused by trauma. In these cases, the harvesting team should try to increase the inotropic support, force the diuresis, and turn off the positive end-expiratory pressure (PEEP) on the respiratory ventilator. After all, if in the donor the CVP remains high and the right ventricular distension is still observed, the same aspects will most likely be present in the recipient, especially in the case of elevated pulmonary pressure.

Another important issue is the inability to wean the donor heart from high doses of inotropic agents, which sometimes is unrelated to cardiac insufficiency but instead caused by the loss of sympathetic tone after brain death. In this case, high-dose inotropic agents are necessary for their vasoconstrictive effects on systemic blood pressure. In other cases, myocardial dysfunction may be due to a contusion or subendocardial damage from trauma or hypotension. At this time a Swan-Ganz catheter will be helpful; an abnormal high cardiac output and a low systemic vascular resistance will reveal the preservation of cardiac function.

After careful evaluation, if the donor heart is considered suitable for transplantation, the aorta is divided from the pulmonary trunk and encircled with an umbilical tape. The superior vena cava (SVC) is also encircled with two heavy silk ligatures or a tourniquet is passed around it; we do not routinely encircle the inferior vena cava (IVC).

When abdominal surgeons are ready, the donor is heparinized, and a cannula is inserted into the ascending aorta and connected to a pressurized bag of crystalloid cardioplegia. The SVC is doubly ligated or the tourniquet previously passed around is tightened, and the IVC is cut while the abdominal surgeon is pushing the liver toward the donor's feet (this maneuver avoids damage to the suprahepatic veins; Fig. 9.4). A suction tube is inserted inside the IVC that was just incised, and the heart is allowed to beat for five or six cardiac cycles to accomplish cardiac emptying and to avoid distension. Then, the aortic clamp is applied, and cardioplegic solution is instilled in the ascending aorta. The next step is to incise the left inferior pulmonary vein (Fig. 9.5) and to pour cold saline solution at 4 °C in the pericardial sac for topical cooling. Blood is sucked; the heart should rapidly stop in diastolic phase, and the surgeon controls aortic valve

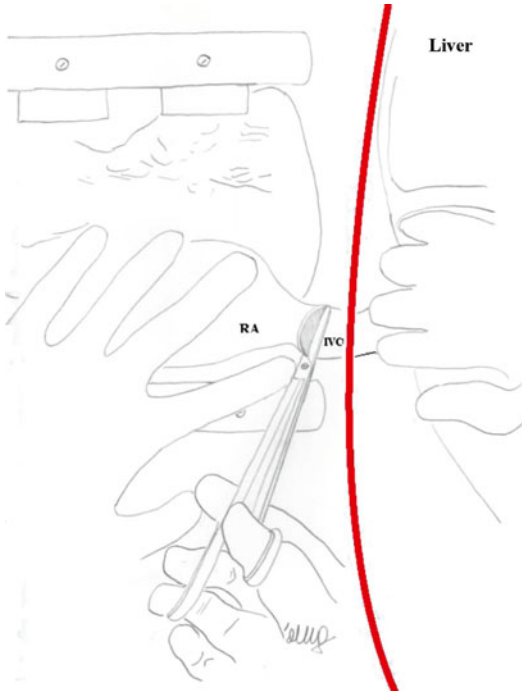

Fig. 9.4 Inferior vena cava (*IVC*) is incised while the abdominal surgeon is pulling down the liver to avoid suprahepatic vein lesions; the *red line* represents schematically the diaphragm (*RA* right atrium)

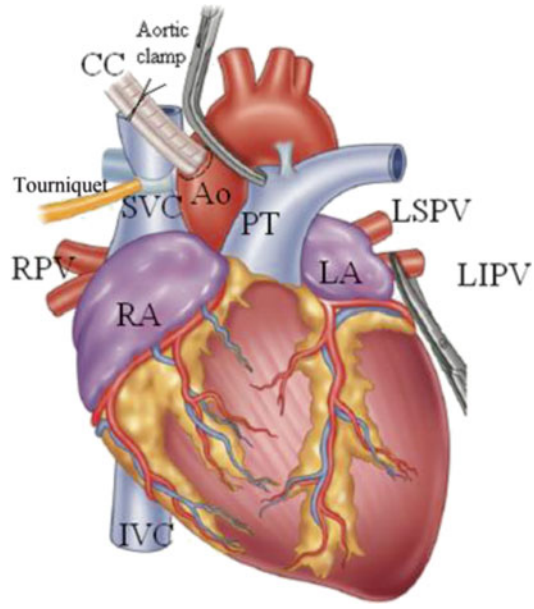

Fig. 9.5 Heart retrieval, starting the procedure: SVC tourniquet is tightened, IVC is cut, aorta is crossclamped, cardioplegic solution is instilled, and LIPV is incised in order to avoid left ventricular distension. *SVC* superior vena cava, *IVC* inferior vena cava, *CC* cardioplegic cannula, *LIPV* left inferior pulmonary vein, *LSPV* left superior pulmonary vein, *RPV* right pulmonary veins, *LA* left atrium, *RA* right atrium, *Ao* aorta, *PT* pulmonary trunk

competence. The cardioplegic solution should always create distension and high pressure in the aortic portion between the aortic clamp and the valve.

When cardioplegia is completely instilled, the cardioplegic cannula can be removed, and the purse string can be tied. Many surgeons keep the cardioplegic cannula because it will facilitate cardioplegic infusion at the time of heart implantation. The aorta is divided just below the crossclamp, the SVC is resected, and the IVC division is completed. Then, the heart is lifted upward, the pulmonary veins are separately divided, and finally the pulmonary trunk is divided near its bifurcation. The harvested heart (Fig. 9.6) is placed in a basin and inspected. In case an open foramen ovale is found, it is closed using a 5–0 polypropylene suture from either the right or left side. The heart is then placed in a sterile bag containing cold saline solution (some surgeons use cardioplegia); this bag is placed in a second one filled with cold saline. The organ is placed in a plastic container filled with saline and crushed ice, avoiding the inclusion of any air (which would interfere with insulation and cause warming), and is transported in this insulated bag.

9.4 Heart Procurement for Heterotopic Heart Transplantation

This technique was introduced by Losman and Barnard and connects the donor heart in parallel with the recipient heart [4, 5]. There are anastomoses between the donor and recipient left atria, the right atria, and the aorta and the pulmonary arteries; the latter is accomplished by the insertion of a tubular prosthesis. The retrieval procedure is quite similar to the one described for orthotopic transplantation with the exception of leaving a long tract of superior vena cava.

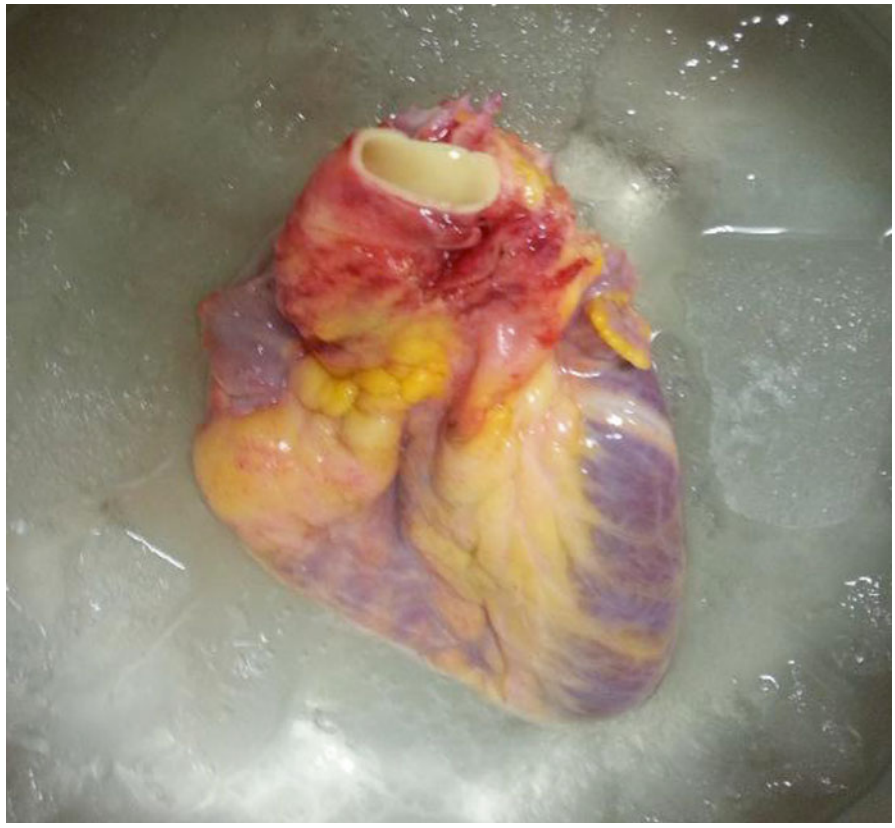

Fig. 9.6 The harvested heart

References

1. Grande AM (2006) Supply and demand of organs for donation. Intensive Care Med 32:342
2. Khush KK, Zaroff JG, Nguyen J, Menza R, Goldstein BA (2015) National decline in donor heart utilization with regional variability: 1995–2010. Am J Transplant 15(3):642–9
3. Camp PC Jr (2010) Heart transplantation: donor operation for heart and lung transplantation. Oper Tech Thorac Cardiovasc Surg 15:125–37
4. Barnard CN, Losman JG (1975) Left ventricular bypass. S Afr Med J 49:303–12
5. Novitzky D, Cooper DKC, Barnard CN (1983) The surgical technique of heterotopic heart transplantation. Ann Thorac Surg 36:476–82

Lung and Heart-Lung Procurement

10

Antonino M. Grande

Tips, Tricks, and Pitfalls in the Lung Retrieval Operation

- Avoid manipulating the sinoatrial area.
- Do not eviscerate the lungs from the pleural cavity.
- Provide the dissection of the interatrial sulcus, or Waterston's groove, to obtain a larger left atrial cuff.
- Direct pneumoplegia cannula toward the pulmonary valve.
- Incise the left atrial appendage first and the inferior vena cava next to obtain complete decompression of both ventricles; perform this step before the pericardial cavity is flooded by blood vented from the incised inferior vena cava.
- Cut directly left atrial appendage without the previous application of a vascular clamp (which carries a risk of lacerating the appendage and damaging the circumflex coronary artery).
- Just before aortic cross clamping, administer prostaglandin E1 bolus in the pulmonary trunk
- Once the heart is empty, cross clamp the ascending aorta.
- Start cardioplegia and pneumoplegia solutions.
- During cardioplegia infusion, always control the ascending aorta pressure.
- Left ventricular distention can be controlled by releasing the aortic cross clamp for a few seconds.
- Control possible pneumoplegic cannula displacement.
- During pneumoplegia infusion lungs should turn white: if a color mismatch is present, the solution went preferentially into one lung.

10.1 Introduction

Donor lung shortage represents the major factor limiting lung transplantation, and lung organ procurement rates have consistently been significantly lower than those for the kidney, liver, and heart. One of the main factors further limiting increases in the number of lung transplantations is the shortage of donor lungs, and even in the most active centers, the median number of lungs retrieved represents only 15 % of all cadaver donors, whereas the kidneys and livers are har-

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vested from 88 % of donors and hearts are harvested from 30 % of deceased donors [1]. This is most likely due to the high susceptibility of the lungs to complications arising before donor brain death, such as thoracic trauma and the aspiration of gastric contents, and to other complications after brain death, such as ventilator-associated lung injury, pneumonia, or neurogenic pulmonary edema [2].

10.2 Donor Evaluation

Arriving at the hospital where a potential lung donor has been reported, the retrieval team must take the following steps.

10.2.1 Chest Imaging Studies

The harvesting surgeon should oversee all chest imaging studies. If CT of the chest is not available, a chest X-ray should be carefully evaluated; donors with important unilateral abnormalities should not be excluded for donation of the contralateral lung [3]. Diffuse bilateral lung infiltrates indicate a developing pneumonia, especially in a patient with high temperature and purulent secretions. These lungs should not be retrieved if important, pneumonic infiltrates are confirmed at surgical inspection [4]. In trauma donors, not all chest radiographic abnormalities are caused by pulmonary parenchymal injury, and at the same time, overlying chest wall contusion can sometimes mask an adequate donor lung [5].

10.2.2 Gram Stains and Bronchoscopy Findings

Sputum Gram stains and cultures are routinely performed on all lung donors either by suction catheter or bronchoscopy. A positive donor Gram stain is not necessarily correlated with posttransplant pneumonia, insufficient oxygenation, or the duration of posttransplant mechanical ventilation [6–8]. The incidence of donor infection was reported to be 52 %, and transmission to the recipient occurred in 8.1 % of cases despite appropriate antibiotic prophylaxis [9]. The Newcastle group reported poor early graft function and decreased survival in patients with positive cultures of donor bronchoalveolar lavage (BAL), indicating that lower airway colonization may be indicative of an increased risk of postoperative graft infection and dysfunction [10].

10.2.3 Donor Age

Given the lack of organ donors, lungs from donors aged 60 years or more are commonly considered for transplantation. Previous studies have shown that older donor age had lower early and late survival [11, 12], and when combining older donor age with graft ischemic times longer than 6 h, this effect is augmented. Nonetheless, de Perrot (Toronto Lung Transplant Program) [13] did not find a difference in hospital mortality related to donor age, but reported a lower 10-year survival related to older donor age and more recipients from older donors dying from bronchiolitis obliterans. Considering the analysis of the International Society for Heart and Lung Transplantation (ISHLT) registry data between 1995 and 2005, donor age is only a borderline risk factor ($p = 0.083$) for 1-year mortality but is still a significant factor ($p = 0.008$) for 5-year mortality [14]. These data were confirmed by 2014 ISHLT report that indicates advanced donor age is a risk factor for 1-year mortality in adult heart-lung transplant recipients (p-value = 0.00195) [15].

10.2.4 Gender

A recent analysis showed that female to male transplantation, even after adjusting for size mismatch and diagnosis, was associated with higher 30-day mortality; instead, female to female was beneficial, and donor and recipient sex mismatch was significantly associated with decreased long-term survival [14, 16, 17].

10.2.5 Graft Ischemic Time

Most transplant centers perform lung transplants with an ischemic time between 4 and 6 h. A negative effect on survival with ischemic times beyond 5 h has been reported [18], but according to ISHLT registry data, graft ischemic time is not an increased risk factor for 1- and 5-year survival after lung transplantation [14, 15]. Most transplant centers using extracellular solution for lung preservation report good results with ischemic times greater than 10 h. Therefore, an expected long ischemic time is not considered an absolute contraindication for a long-distance donor when the donor lungs are in good condition [4].

10.2.6 Gas Exchange

Good oxygenation is the most important marker for evaluating the functional efficiency and characteristics of the donor lung. Arterial blood gas analysis in a donor is easily repeated to follow the gas exchange evolution. It is very important to evaluate the PaO_2/FiO_2 ratio (arterial oxygen tension/fractional inspired oxygen); marginal donor lungs are usually indicated when the PaO_2/FiO_2 ratio is less than 320 [19]. However, good oxygenation is not always a criterion for lung donor assessment. Sometimes in young donors gas exchanges may be satisfactory also in case of severe chest trauma, but chest CT can show important massive, bilateral pulmonary contusions, pneumopericardium and hemopneumothorax (see Chap. 3). Moreover, extravascular lung water (EVLW) has also been used as a sensitive prognostic indicator of pulmonary edema and to control arterial blood gases and the lung functional status [20]. Active hemodynamic management is performed to achieve a cardiac index exceeding 2.5 L/min/m^2 with central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP) at 10 mmHg or less and mean arterial pressure (MAP) at 65–85 mmHg. At the same time, fluid administration should be restricted to small amounts of blood (to achieve a hemoglobin level ≥ 10 g/dL); diuretics are administered to decrease CVP and PCWP, and gelatin colloid is used to maintain CVP/PCWP. Systemic vascular resistance must be kept in the range of 800–1200 dyn · cm/s by actively substituting, for instance, vasopressin for norepinephrine [19].

10.3 Surgical Technique

After median sternotomy and cardiac evaluation, the pleural spaces are bilaterally opened without electrocautery to avoid unintentional burn injury to the lungs. It is mandatory to conduct an accurate inspection of the lungs and of the pleural wall for nodules. Every suspicious nodule should be biopsied.

The lungs are palpated and visually examined. The recruitment of all atelectatic lung segments is obtained by gentle massage of both lungs as the anesthesiologist inflates them to a sustained 30 cm H_2O pressure and a positive end-expiratory pressure of 15 cm H_2O.

Lung compliance is mandatory, and it is evaluated under direct vision through the "collapse test": the endotracheal tube is disconnected from the ventilation, and if the lungs are inflated or slowly collapse, the test is positive. This is an indirect sign that the lungs are infiltrated and have fluid accumulation, infective diseases, emphysema, or bronchial plugging. It is advised not to eviscerate the lungs from the pleural cavity for the precise purpose of recruiting the atelectatic portions of the lungs; otherwise, there may be severe lung hyperinflation and injury to hilar structures, and the hemodynamic status may worsen and also compromise multiple organ retrieval [21]. The inspection of the lung is a very delicate and important act: a large hematoma or multiple parenchymal contusions can jeopardize the transplantation outcome (Fig. 10.1).

The pulmonary trunk and the right pulmonary artery are cautiously dissected from the aorta using electrocautery; then the superior vena cava is mobilized dividing the attachments between the latter and right pulmonary artery. It is important to avoid grasping with forceps the periauricular tissue of the right atrium containing the sinoatrial node. Start from the right side in the

previous area dissected for mobilizing the right pulmonary artery; the superior vena cava is dissected free all the way to its bifurcation into the left innominate vein and encircled with a heavy silk. Identify and ligate the azygous vein, and do not divide it—it is unnecessary and may cause hemorrhage and damage to the adjacent upper lobe branch of the right pulmonary artery [21]. The left innominate vein is mobilized free and encircled, and the same procedure is performed on the innominate artery. The anterior aspect of the trachea is found immediately underneath the innominate artery (Fig. 10.2). The pretracheal fascia is opened longitudinally, and gentle dissection is performed on both sides of the trachea along the cartilaginous rings to the posterior membranous tissue; by gentle digital dissection or using a blunt right-angle instrument, it is possible to mobilize and encircle the upper portion of the trachea [22].

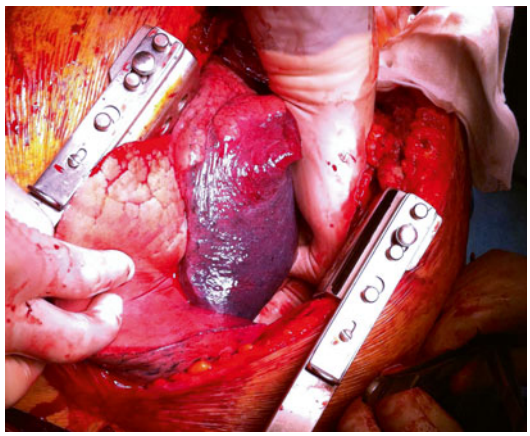

Fig. 10.1 Posterior aspect of right inferior lobe showing a large hematoma

Then, the following step at this preparatory stage is the dissection of the interatrial sulcus, or Waterston's groove, to obtain a larger left atrial cuff; the interatrial sulcus is opened longitudinally along the atrial axis, and the right atrium is tractioned and pulled to the left, thus exposing a portion of the left atrial wall that had been covered by the right atrium (Fig. 10.3a).

The cardioplegia cannula is inserted in the anterior midportion of the ascending aorta and secured by a 4-0 polypropylene purse string. In the distal pulmonary trunk, a cannula for pneumoplegia is secured in the same way. Note that the tip of the cannula should be pointed toward the pulmonary valve to prevent a selective perfu-

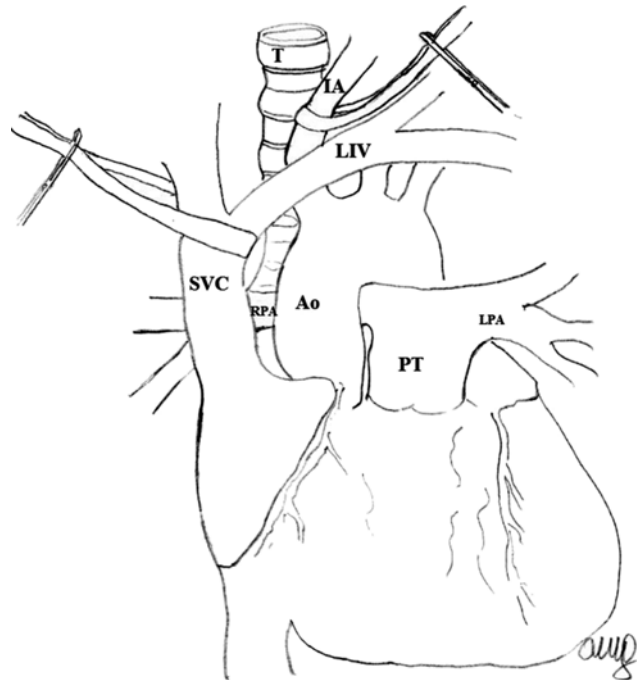

Fig. 10.2 Left innominate vein (*LIV*) and superior vena cava (*SVC*) are pulled toward the right; the innominate artery (*IA*) is gently mobilized to the left: underneath the IA the trachea can be easily visualized (*T* trachea, Ao aorta, *PT* pulmonary trunk, *RPA* right pulmonary artery, *LPA* left pulmonary artery, *RA* right atrium)

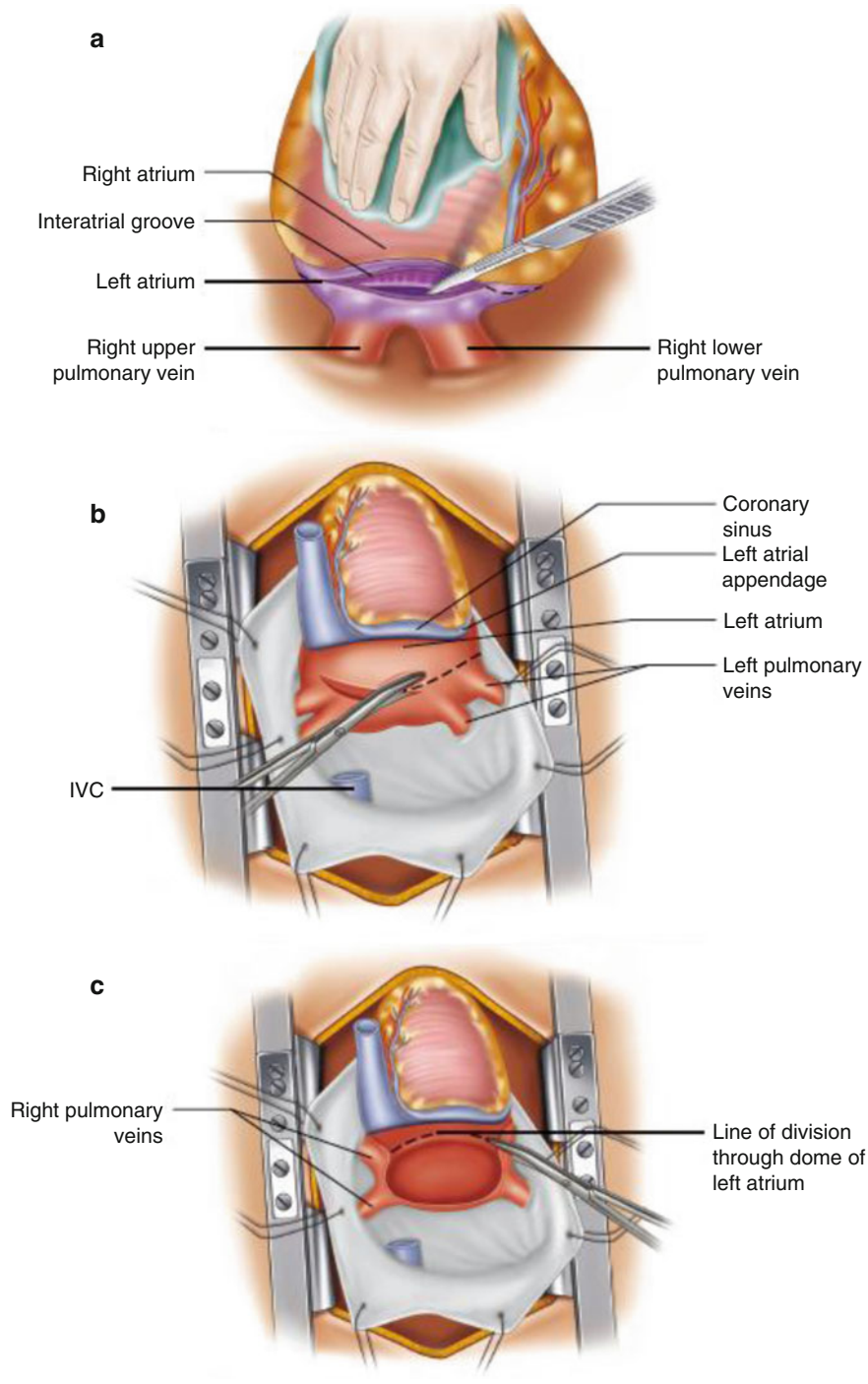

Fig. 10.3 Right and left pulmonary cuff preparation. (**a**) The interatrial groove is exposed using a No. 11 scalpel or sharp scissors; the left atrium is entered leaving at least 1 cm of atrial tissue around the right pulmonary veins. (**b**) The heart is elevated, and the entry of the left pulmonary veins is exposed into the pericardium; the incision is continued to the left, halfway between the coronary sinus and the origin of the pulmonary veins from the left atrium, and extended to the base of the left atrial appendage. (**c**) The incision is then carried around the superior portion of the left atrium, reaching the incised interatrial groove on the right

sion of one lung (often the left lung because the left pulmonary artery rises directly from the trunk).

Once the dissection of all donor organs has been accomplished, heparin is administered followed by the prostaglandin E_1 500 μg bolus into the pulmonary trunk. Note that the lungs are continuously ventilated with low rate and low volume until the trachea is divided.

The superior vena cava is ligated, and the left atrial appendage is resected to vent the left atrium and to decompress the left ventricle. Never clamp the atrial appendage, due to the risk of atrial lacerations and circumflex coronary artery damage. Afterward, incise the inferior vena cava to obtain complete decompression of the right ventricle. Once the heart is empty, cross clamp the ascending aorta, and immediately start cardioplegia and pneumoplegia infusions. Cardioplegia is infused at a pressure of 80–100 mmHg, and pneumoplegia is infused at gravity pressure.

At the end of pneumoplegia infusion, both lungs should turn white; if there is a color mismatch, the solution went preferentially into one lung.

The inferior vena cava is completely divided; the heart is then retracted to the left to expose the previous dissection in the interatrial groove. Using a No. 11 scalpel or sharp scissors, the left atrium is entered leaving at least 1 cm of atrial tissue around the right pulmonary veins (Fig. 10.3a). Next the heart is elevated, and the entry of the left pulmonary veins is exposed into the pericardium; the incision is continued to the left halfway between the coronary sinus and the origin of the pulmonary veins from the left atrium (Fig. 10.3b). This incision is extended to the base of the left atrial appendage, taking care to tailor an adequate left pulmonary vein cuff. The incision is then carried around the superior portion of the left atrium, reaching on the right the incised interatrial groove (Fig. 10.3c).

The superior vena cava and the azygous vein are divided; the innominate and left carotid arteries are divided, and the aortic arch is cut after the origin of the left carotid artery. The pulmonary trunk is transected at the pneumoplegia cannulation site. At this point, the heart can be disconnected and placed in a sterile plastic bag.

After heart excision, some surgeons complete lung protection by performing an additional retrograde pneumoplegia infusion. The lungs are still ventilated with low rate and low volume. The pericardium is incised at the diaphragmatic level, and both inferior pulmonary ligaments are transected, taking care to avoid damaging the lower lobes. Next, the pericardium is divided on the midline and will act as a guide behind which to perform the remaining dissection. The right lung is carefully pulled out of the pleural cavity and put into the left hemithorax; the avascular plane above the aorta and esophagus is dissected, and the same action is performed for the left lung. Afterward, the lungs are repositioned in their anatomical site, and all the mediastinal tissue localized above the trachea is transected on both sides. Next, the trachea is pulled forward. The lungs are gently inflated to approximately 80 % of their volume, and the endotracheal tube is removed. The trachea is stapled twice and it is transected between the staple lines; the division should be performed two rings above the carina. At this point, the lungs can be pulled outside the thoracic cavity, inspected, and accurately packaged using a three-bag technique: the inner bag contains the lungs and pneumoplegic solution, and the other two are filled with slush ice and 0.9 % saline. The packed lungs are then positioned in a cool box.

10.4 Heart-Lung Block Retrieval

The harvesting team should check donor hemodynamic and ventilatory parameters, reports on the chest X-ray, chest CT, echocardiography, electrocardiogram, and coronary angiography when available. Heart-lung retrieval is technically easier than harvesting separately heart and lungs. After sternotomy and pericardial opening, the superior vena cava (above the azygous vein)

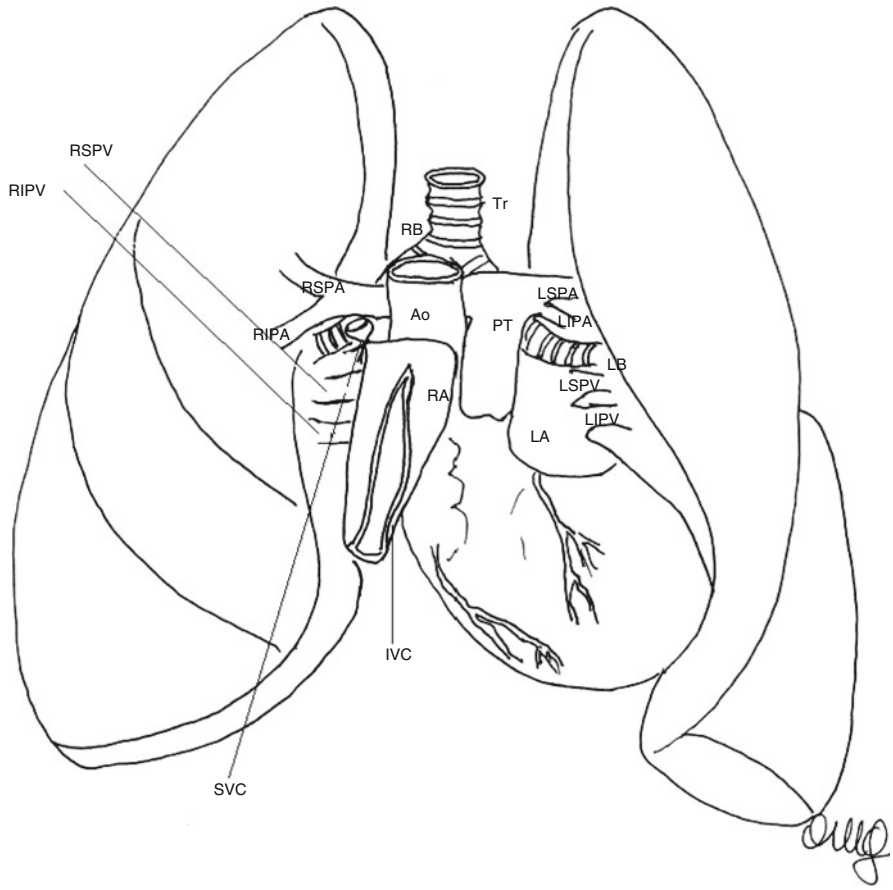

Fig. 10.4 Anterior view of heart-lung block (Tr trachea, Ao aorta, PT pulmonary trunk, RB right bronchus, LB left bronchus, RSPA right superior pulmonary artery, RIPA right inferior pulmonary artery, LSPA left superior pulmonary artery, LIPA left inferior pulmonary artery, RA right atrium opened, LA left atrium, RSPV right superior pulmonary vein, RIPV right inferior pulmonary vein, LSPV left superior pulmonary vein, LIPV left inferior pulmonary vein, IVC inferior vena cava, SVC superior vena cava ligated)

and the trachea are isolated. After aortic cross-clamping, administer prostglandin E1 bolus in the pulmonary trunk and start cardioplegia and pneumoplegia infusions. The left ventricle is vented by incising the left atrial appendage; the superior vena cava and the inferior vena cava are divided, the trachea is stapled and it is transected between the staple lines. The heart and lung block is then mobilized from its mediastinal attachments in the same fashion as described above (Fig. 10.4).

Then, the block is checked for any missed pathology (e. g., patent foramen ovale, atrial septal defect, lung mass, iatrogenic injury).

References

1. Division of Transplantation, Bureau of Health Resources Development (2005) Annual report of the US Scientific Registry for Transplant Recipients and the Organ Procurement and Transplantation Network – transplant data: 1995–2004. Health Resources and Services Administration; US Department of Health and Human Services, Rockville
2. Ware LB, Wang Y, Fang X et al (2002) Assessment of lungs rejected for transplantation and implications for donor selection. Lancet 360(9333):619–620
3. Puskas JD, Winton TL, Miller DJ, Scavuzzo M, Patterson GA (1992) Unilateral donor lung dysfunction does not preclude successful contralateral single-lung transplantation. J Thorac Cardiovasc Surg 103:1015–1017

4. Van Raemdonck D, Neyrinck A, Verleden GM, Dupont L, Coosemans W, Decaluwé H, Decker G, De Leyn P, Nafteux P, Lerut T (2009) Lung donor selection and management. Proc Am Thorac Soc 6(1):28–38
5. Lau CL, Patterson GA (2003) Current status of lung transplantation. Eur Respir J 22(Suppl 47):57s–64s
6. Weill D, Dey GC, Young KR, Zorn GL, Early LJ, Hicks RA, Kirklin J, McGiffin DC (2001) A positive donor gram stain does not predict the development of pneumonia, oxygenation or duration of mechanical ventilation following lung transplantation [abstract]. J Heart Lung Transplant 20:255
7. Zenati M, Dowling RD, Dummer JS, Paradis IL, Arena VC, Armitage JM, Kormos RL, Hardesty RL, Griffith BP (1990) Influence of the donor lung on development of early infections in lung transplant recipients. J Heart Lung Transplant 9:502–509
8. Bonde PN, Patel ND, Borja MC, Allan SH, Barreiro CJ, Williams JA, Thakur NA, Orens JB, Conte JV (2006) Impact of donor lung organisms on post-lung transplant pneumonia. J Heart Lung Transplant 25:99–105
9. Ruiz I, Gavaldà J, Monforte V, Len O, Román A, Bravo C, Ferrer A, Tenorio L, Román F, Maestre J et al (2006) Donor-to-host transmission of bacterial and fungal infections in lung transplantation. Am J Transplant 6:178–182
10. Avlonitis VS, Krause A, Luzzi L, Powell H, Phillips JA, Corris PA, Gould FK, Dark JH (2003) Bacterial colonization of the donor lower airways is a predictor of poor outcome in lung transplantation. Eur J Cardiothorac Surg 24:601–607
11. Novick RJ, Bennett LE, Meyer DM, Hosenpud JD (1999) Influence of graft ischemic time and donor age on survival after lung transplantation. J Heart Lung Transplant 18:425–431
12. Meyer DM, Bennett LE, Novick RJ, Hosenpud JD (2000) Effect of donor age and ischemic time on intermediate survival and morbidity after lung transplantation. Chest 118:1255–1262
13. de Perrot M, Waddell TK, Shargall Y, Pierre AF, Fadel E, Uy K, Chaparro C, Hutcheon M, Singer LG, Keshavjee S (2007) Impact of donors aged 60 years or more on outcome after lung transplantation: results of an 11-year single-center experience. J Thorac Cardiovasc Surg 133:525–531
14. ISHLT Registry slides. Available from: http://www.ishlt.org/downloadables/lung_adult.ppt. Accessed 18 Aug 2008.
15. Yusen RD, Edwards LB, Kucheryavaya AY, Benden C, Dipchand AI, Dobbels F, Goldfarb SB, Levvey BJ, Lund LH, Meiser B, Stehlik J, International Society for Heart and Lung Transplantation (2014) The Registry of the International Society for Heart and Lung Transplantation: thirty-first adult lung and heart–lung transplant report—2014; focus theme: retransplantation. J Heart Lung Transplant 33:1009–1024
16. Sato M, Gutierrez C, Kaneda H, Liu M, Waddell TK, Keshavjee S (2006) The effect of gender combinations on outcome in human lung transplantation: the International Society of Heart and Lung Transplantation Registry experience. J Heart Lung Transplant 25:634–637
17. Thabut G, Mal H, Cerrina J, Dartevelle P, Dromer C, Velly JF, Stern M, Loirat P, Bertocchi M, Mornex JF et al (2005) Influence of donor characteristics on outcome after lung transplantation: a multicenter study. J Heart Lung Transplant 24:1347–1353
18. Snell GI, Rabinov M, Griffiths A, Williams T, Ugoni A, Salamonsson R, Esmore D (1996) Pulmonary allograft ischemic time: an important predictor of survival after lung transplantation. J Heart Lung Transplant 15:169–174
19. Venkateswaran RV, Patchell VB, Wilson IC, Mascaro JG, Thompson RD, Quinn DW, Stockley RA, Coote JH, Bonser RS (2008) Early donor management increases the retrieval rate of lungs for transplantation. Ann Thorac Surg 85:278–286
20. Hu W, Lin C-W, Liu B-W, Hu W-H and Zhu Y. Extravascular lung water and pulmonary arterial wedge pressure for fluid management in patients with acute respiratory distress syndrome. Multidiscip Respir Med. 2014;9:3. http://www.mrmjournal.com/content/9/1/3.
21. Pasque MK (2010) Standardizing thoracic organ procurement for transplantation. J Thorac Cardiovasc Surg 139:13–17
22. Camp PC Jr (2010) Heart transplantation: donor operation for heart and lung transplantation. Oper Tech Thorac Cardiovasc Surg 15:125–137

Part IV

Surgical Technique for Abdominal Organ Procurement

11 Detailed Abdominal Organ Inspection and Early Surgical Steps for Abdominal Organ Procurement

Paolo Aseni, Anna Mariani, Riccardo De Carlis, Vincenzo Emanuele Buscemi, and Giacomo Concone

Tips, Tricks, and Pitfalls

- Sternotomy is a mandatory surgical step for carefully inspecting the thorax and mediastinum.
- Accurately inspect all abdominal organs.
- Perform liver biopsy whenever liver steatosis is evident to have a better evaluation of macroscopic and microscopic steatotic components.
- Try to recognize an accessory or replaced right hepatic artery from the superior mesenteric artery and consider that it is present in approximately 18 % of cases.
- Preserve a left accessory or replaced left hepatic artery from the left gastric artery running throughout the lesser sac.
- Polar renal arteries arising from the iliac arteries should be carefully checked. If present, care should be taken to preserve polar renal arteries; iliac cannulation before the origin of the polar artery must be performed.
- When the supraceliac abdominal aorta is difficult to control, consider cross-clamping the thoracic aorta as an alternative to supraceliac aortic cross-clamping.
- In case of rapid donor destabilization during the procedure, consider quick cannulation of the inferior abdominal aorta above the iliac vessels and a blind cross-clamping of the descending thoracic aorta.
- Before perfusion, remember to flush the gallbladder and clear the common bile duct of retained bile.

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11.1 Abdominal Exploration and Evaluation

The key responsibility for the lead surgeon of the retrieval team is the identification of the donor prior to the operation and to check its blood group compatibility. According to medical

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literature about organ procurement [1–10], this can be divided into three steps:

(a) Accurate surgical inspection
(b) The identification and preparation of the all vessels with respect to specific surgical requirements for flushing and organ preservation
(c) The final "cool phase" characterized by the harvesting of the different organs

A correct position of the donor on the operating table should be selected according to different technical requests from cardiothoracic and abdominal teams. Usually an ideal position for all teams requires the arms at the sides and the head reclined; the limits of the operative field extend from the neck, jugulum, the central part of the thorax and abdomen, and pubic symphysis down to the upper third of the thigh, which should be left uncovered by the sterile drapes and free from all monitoring devices and infusion cannulae. A midline incision from the sternal notch to the pubis provides maximal exposure. Sternotomy is always a mandatory surgical step, even when the cardiothoracic team is not involved for heart and lung procurement. In the case of kidney-only retrieval, thoracic and mediastinal exploration should be performed by the kidney-harvesting team. Sternotomy allows the abdominal surgeon to carefully inspect the thorax and the mediastinum and to vent the suprahepatic inferior vena cava (IVC) when perfusion is started above the diaphragm; it also allows an easier cross-clamping of the thoracic aorta as an alternative to supraceliac aortic cross-clamping. This maneuver can be helpful when the supraceliac abdominal aorta is difficult to control, such as in some overweight patients or when the left hepatic artery arises from the left gastric artery. A sternal saw is not always available in the donor operating room; thus, it can be helpful if the abdominal surgeons are equipped with a Gigli saw, and abdominal surgeons should be trained to use it.

After sternotomy, the hemostasis of the spongy bone of the sternum is achieved with electrocautery; hemostasis with bone wax is unsafe due to the risk of small wax fragments migrating inside the lumen of the suprahepatic veins during organ perfusion. The positioning of the auto-static sternal retractor (Finocchietto) between two surgical pads can often simply and rapidly achieve hemostasis of the spongy bone by simple compression. After sternotomy, a longitudinal or "Mercedes shape" pericardiotomy is performed to completely inspect the mediastinum and to control the intrapericardial portion of the IVC.

If the donor has previously undergone sternotomy, it would be better to perform a thoraco-phreno-laparotomy at the level of the seventh right intercostal space; this approach can avoid massive bleeding and cardiac damage during redo-sternotomy, which would require a much longer time. Thoraco-phreno-laparotomy incision allows the full exploration of the right thorax, and after flushing the abdominal organs, the surgeon can than extend and complete a manual inspection of the mediastinum and the left thorax.

If the cardiothoracic team is present, the first step is always a median sternotomy with the exploration and evaluation of the heart and lung functions for the final evaluation of thoracic organs' suitability for transplantation. After the cardiothoracic evaluation, a wide median laparotomy extending the incision from the xiphoid to the pubis is then performed (Fig. 11.1).

After median laparotomy, the ligamentum teres is divided and double ligated; the falciform ligament is also dissected to explore the anterior and diaphragmatic surface of the right and left lobe of the liver. This maneuver allows the first impression of the suitability of liver retrieval and transplantation by visual inspection and by palpation.

To evaluate the suitability of all the abdominal organs for transplantation, an accurate anatomical inspection should be performed utilizing all other information previously obtained from the donor's clinical report, including biochemical parameters and radiological imaging. The first step requires an accurate exploration of all the abdominal quadrants, searching for pathological nodules or tissue swelling that, when found, are to be sampled and immediately sent for histopathological evaluation.

At this time, the abdominal surgeon should express his decision to harvest the liver for transplantation. Touching the liver by gentle palpation

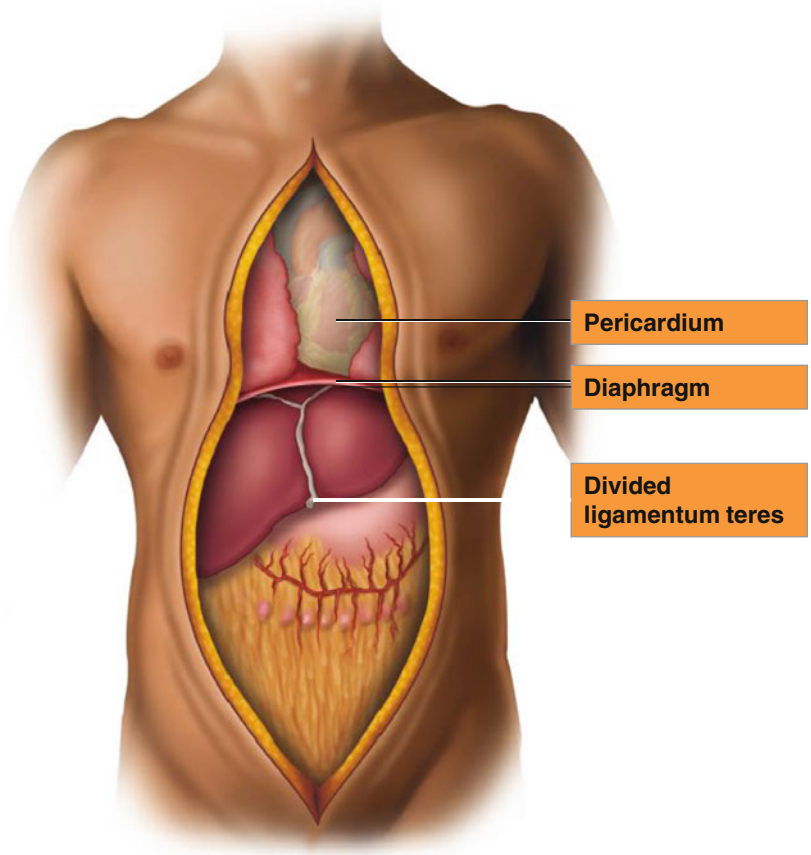

Fig. 11.1 Extending median sternotomy to median laparotomy with full thoracic and abdominal organ exposure

can reveal nodularities that must be sampled and gives information about parenchymal consistence.

The normal color of the liver is reddish brown. A pale color or an increased parenchymal consistency may be detected in those donors with large amine infusion with hemodynamic instability. In donors with a prolonged amine administration and hardening of the parenchyma, a liver biopsy should be performed.

A yellowish liver parenchyma, usually more evident by gentle finger compression on the liver surface, and a smoothed liver edge may suggest marked steatosis. In such case, a liver biopsy must be performed to better evaluate liver damage and the percentage of micro- and macrosteatotic components. The criteria for evaluating the viability of liver grafts with steatosis are variable among centers and depend on several clinical factors. However, the decision to retrieve steatotic liver can sometimes be difficult and involves two different considerations: the risk of primary graft dysfunction of the graft and the risk of lost opportunity to save the life of a cirrhotic patient. Usually, in the absence of other risk factors, macro-steatosis not greater than 50 % is the upper limit usually accepted by the majority of centers in the absence of other risk factors.

A murky parenchyma and its hardening by finger palpation may reveal fibrotic changes or a venous stasis. Also in this case, a liver biopsy can offer some useful information. In all HCV-Ab-positive donors, liver biopsy is mandatory. Sometimes, liver biopsy by a percutaneous technique should be performed before taking the donor to the operating room. Percutaneous liver biopsy in donors is not free from complications, such as parenchymal hematoma or even hemoperitoneum, which can lead the donor to hemodynamic instability. After negative exploration of the abdomen, the

liver, pancreas, intestine, and kidneys are considered for final judgment of suitability for transplantation. The donor is than considered at "standard risk", and the surgeon can alert the transplant centers and proceed with the identification and preparation of all the vascular anatomical structures for abdominal organ perfusion and for a more rapid retrieval technique after organ perfusion.

There is some experimental evidence that dissection prior to perfusion can cause vasospasm by increasing the oxygen consumption of the abdominal organs (especially of the liver). Usually, the time needed by the thoracic retrieval team (20–30 min) will allow the full reversal of these changes. However, if thoracic organs are not being allocated, a recovery period of 20–30 min for compensation of the induced vasospasm can be helpful before perfusion is started. In a warm dissection technique, while preparing the perfusion system and equipment, leaving the abdominal field untouched for 20 min can allow and restore a full circulatory compensation. There are two basic techniques to retrieve abdominal organs: (1) the "warm dissection technique," in which the dissection of all organs takes place before cannulation and perfusion; and (2) the rapid technique, or "dissection in the cold" (mandatory for hemodynamically unstable donors), which minimizes operating time during the warm phase, prolonging the organ retrieval during the cool phase.

11.2 Warm Dissection: Basic Surgical Strategy for the Control of Thoracic and Abdominal Aortae

A self-retaining retractor is used to widen the opening of the abdominal wall. The control of major abdominal vessels requires an extended Kocher plus Cattell and Braasch maneuver [11], moving the ascending colon toward the left across the midline and completely mobilizing the distal small bowel, right colon, and duodenum. The correct line of dissection continues among Gerota's fascia, Toldt's fascia, and the preduodenopancreatic fascia or Fredet's area [12].

If bowel procurement must be performed without pancreas procurement, a complete duodenal mobilization with Kocher's maneuver should extend to the third and fourth portion of the pancreas to gain the Treitz ligament and the retro-pancreatic fascia. The Cattell and Braasch maneuver, when complete, provides full exposure of the infrahepatic vena cava and complete control of the left renal vein (Fig. 11.2).

The infrahepatic vena cava is then dissected and doubly encircled with an umbilical tape below the origin of the right renal vein and above the iliac bifurcation. A simple fingertip touch of the distal aorta can reveal atherosclerotic plaques; in case of diffuse atherosclerotic aortic calcifications, ligation and cannulation of the abdominal aorta should be avoided, and iliac arteries' cannulation is preferred. If the aorta has no diffuse calcifications, an upward dissection of the distal aorta above the iliac bifurcation for a tract of 5 cm is performed up to the origin of the inferior mesenteric artery (IMA). When the intestine is not retrieved, the IMA can be doubly ligated and dissected to allow better control of the distal aorta and easier introduction of the perfusion cannula. However, sometimes the preservation of the inferior mesenteric artery (IMA) is recommended, because it can be useful for pediatric recipients during split-liver procedures; in such cases, the

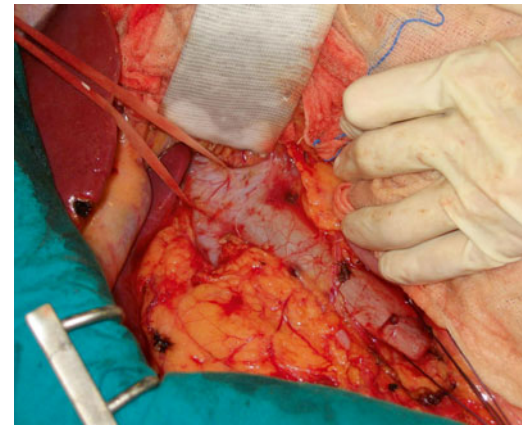

Fig. 11.2 After extended Kocher plus Cattell and Braasch maneuver, the right colon, distal small bowel, and duodenum are mobilized toward the left side across the midline exposing completely the IVC and left renal vein

IMA can be retrieved with an aortic patch for arterial reconstruction of the pediatric liver graft.

The abdominal aorta immediately above iliac bifurcation is then encircled with umbilical tape and a silk thread. Some 2–3 retro-aortic lumbar arteries can be ligated to avoid backflow during cannulation. One or more inferior polar renal arteries arising from the iliac arteries should be carefully assessed. If present, care should be taken to preserve the polar renal artery. Cannulation of the distal iliac artery 4–5 cm below the origin of the polar renal artery is mandatory to ensure a complete perfusion of the kidney. If the iliac artery cannulation is performed, the contralateral iliac artery should be controlled and occluded by a vascular clamp before perfusion. If the abdominal aorta presents diffuse atherosclerotic damage, the distal iliac artery and a thoracic aortic cross-clamping are highly recommended. In such cases, organ perfusion depends almost totally on a good portal vein perfusion. In some patients with a devastating and diffuse abdominal aortic atherosclerotic barrage, a retrograde cannulation of the ascending or descending thoracic aorta is theoretically the only available option for systemic organ perfusion [13, 14]. The control of the descending thoracic aorta can be obtained by opening the left pleural space, retracting the left lung anteriorly and upward. The visualization of the descending thoracic aorta is quite difficult without squashing the heart and causing hemodynamic instability in the donor. For this reason, either cross-clamping or the retrograde thoracic aortic cannulation must be the final steps before organ perfusion is started. In the case of rapid donor destabilization, a blind cross-clamping of the descending thoracic aorta is also possible and faster than supraceliac aortic cross-clamping.

11.3 Warm Dissection: IVC and IMV for Portal Perfusion

During the IVC dissection phase and during control with tape, attention must be paid not to encircle for ligation the right ureter, which may run attached to the right lateral border of the IVC. In the majority of older donors and in the absence of intestinal and pancreatic retrieval, we prefer to perfuse the liver by double perfusion throughout the aortic and portal vein. This can be advantageous in elderly donors with diffuse atherosclerotic arterial damage in whom the possible coexistence of various degrees of celiac trunk stenosis may hamper homogeneous liver perfusion. The cannulation of the portal vein is obtained through access of the inferior mesenteric vein (IMV). The IMV lies in or adjacent to the ligament of Treitz and passes below the lower border of the pancreas to join the splenic vein. Once recognized, the IMV is dissected and double encircled with two 3/0 silk ties 10 cm distally from the ligament of Treitz. The IMV is now prepared for quick cannulation by a Bardic cannula (14–16 Fr), which should be advanced just before the portal vein bifurcation during the next phase of perfusion (Fig. 11.3).

11.4 Warm Dissection: Control of Supraceliac Abdominal Aorta

To obtain control of the supraceliac aorta, the left hepatic lobe should be fully mobilized; the left triangular ligament is dissected with a complete subdiaphragmatic mobilization until the left suprahepatic vein is visible. While the second operator is retracting the stomach on the left side, the gastrohepatic ligament is examined by the help of the operating light, searching for an accessory or replaced left hepatic artery from the left gastric artery running throughout the lesser sac. If one is noted, it will be preserved. After the dissection of the lesser sac, *pars flaccida* and *pars condensa*, the supraceliac aorta can be identified by palpation. To reach the supraceliac aorta, the caudate lobe is displaced upward to the right side by Leriche's valve. The diaphragmatic crura with some muscular bundles and the periaortic neuro-fibromatous tissue should be dissected by electrocautery. The esophagus is then retracted to the left side (Fig. 11.4). After the incision of periaortic serosa, the aorta can be dissected for 2–3 cm and encircled with a right angle blunt O'Shaughnessy with a thick silk wire. Care should be taken to avoid damage to the diaphragmatic veins and the esophagus. If a left

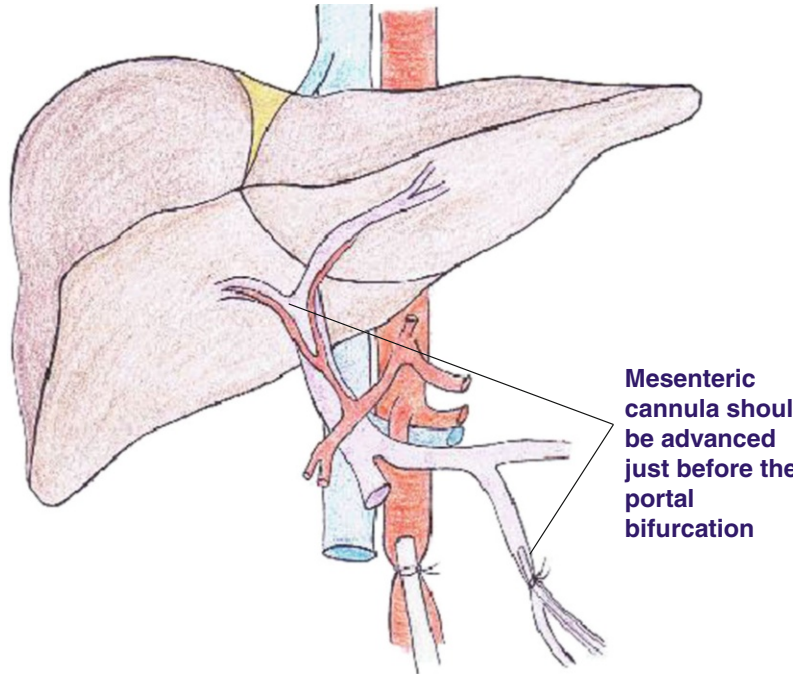

Fig. 11.3 Positioning of portal and aortic cannula for perfusion

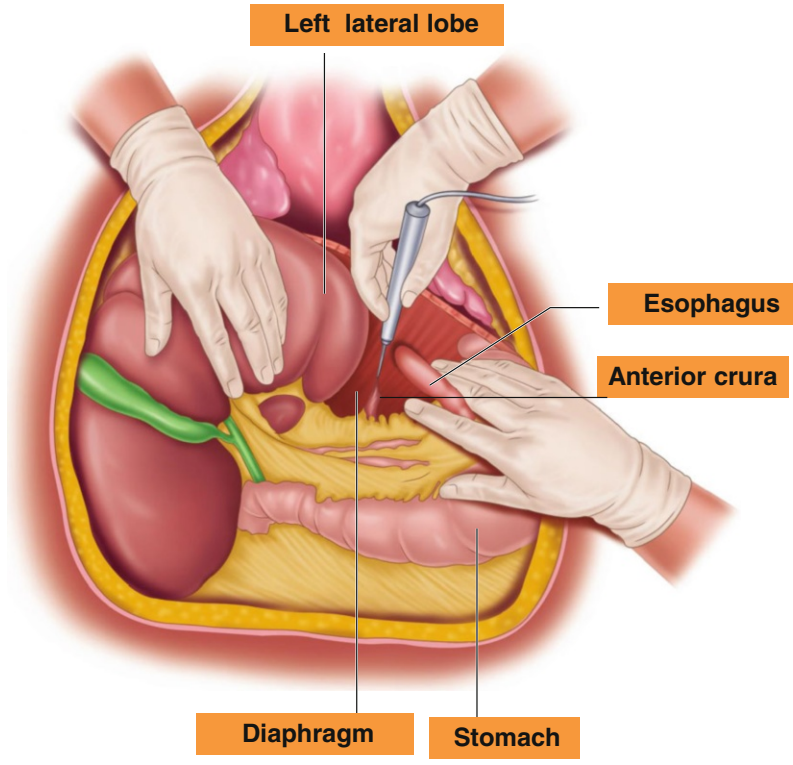

Fig. 11.4 Warm dissection: control of supraceliac abdominal aorta

hepatic artery from the left gastric artery is found, we suggest the dissection and preparation of the left hepatic artery during the warm phase by ligating all of the very thin and short arteries for the greater gastric curve. When a left accessory hepatic artery is found, the risk to damage this small vessel during the supraceliac aorta dissection is very high. In such case, we prefer to perform the cross-clamping of the descending thoracic aorta.

11.5 Dissection and Control of the Thoracic Aorta

The parietal pleura should be widely opened. To cross-clamp the descending thoracic aorta, the left lung should be fully mobilized by dividing the left inferior pulmonary ligament. To avoid arrhythmia and hemodynamic instability, this maneuver should be performed at the end of the surgical procedure, unless hemodynamic instability will occur. The left lung should be retracted anteriorly and upward; however, the direct visualization of the descending thoracic aorta is almost impossible with the donor in a supine position. The descending thoracic aorta lies posterior and medially in the left chest, running along the left paravertebral space and anteriorly to the thoracic spine; it is easily felt by two fingers when the esophagus is recognized for the presence of the nasogastric tube. This allows the blind identification of the adjacent aortic wall. The parietal pleura that cover the descending aorta should be grasped with forceps to create a first small incision; this small incision can be widened with the fingers by bluntly dissection of the pleura for 3–4 cm, and the aortic cross-clamping can be easily obtained. To maintain hemodynamic stability, the blind clamping of the thoracic aorta is only possible at the end of the surgical procedure when the left lung can be retracted medially and upward.

11.6 Identification and Control of All the Elements of the Hepatic Hilum

The portal triad is now examined, and an aberrant (accessory or replaced) right hepatic artery, if present, should be identified on the right edge of the porta hepatis, posteriorly to the bile duct and on the right side of the portal vein. The hilum dissection can be limited to the division of the common bile duct when the donor is unstable.

The dissection of the peritoneum around the hilum is the first step. The dissection of the anterior portion of the duodenum and of the pancreatic head is performed by the ligation of the pyloric vein and the ligation of the left gastric vein, which will later allow easy control of the splenic artery.

Mascagni's lymph node is easy to identify, and it is used to expose the main bile duct. The bile duct is minimally dissected and ligated in the preduodenal portion. The distal common bile duct is then transected by the cold scalpel, and the terminal orifice is left open (Fig. 11.5). Two choledochal arteries are identifiable in the bile duct wall; hemostasis by electrocautery should be performed at minimal electric power to avoid ischemic damage to the biliary duct.

The identification and encircling of the gastroduodenal artery (GDA) (Fig. 11.6) 2 cm from the origin of the common hepatic artery may allow its utilization as a conduit for bench reconstruction of an accessory right hepatic artery from the superior mesenteric artery (SMA).

The GDA is identified and encircled. A check for the GDA is always advisable. Encircling the GDA by a 3/0 silk tie, which is pulled up, the pulse of the hepatic artery should be appreciable by the operator's fingers (Rio-Branco maneuver); if the pulse of the hepatic artery disappears, it may be caused by stenosis or even by obstruction of the celiac trunk with a retrograde flow of the hepatic artery provided from the SMA through the GDA. In the case of a replaced infrapancreatic right hepatic artery from the SMA, celiac trunk atherosclerotic stenosis or a median arcuate ligament syndrome can be other possible causes of hepatic artery pulse absence and should carefully be excluded.

If there is no pulse on the hepatic artery without any aberrant artery from the SMA, the GDA must be preserved along with the entire SMA axis with an aortic Carrel patch until the anatomical condition can be recognized during bench surgery.

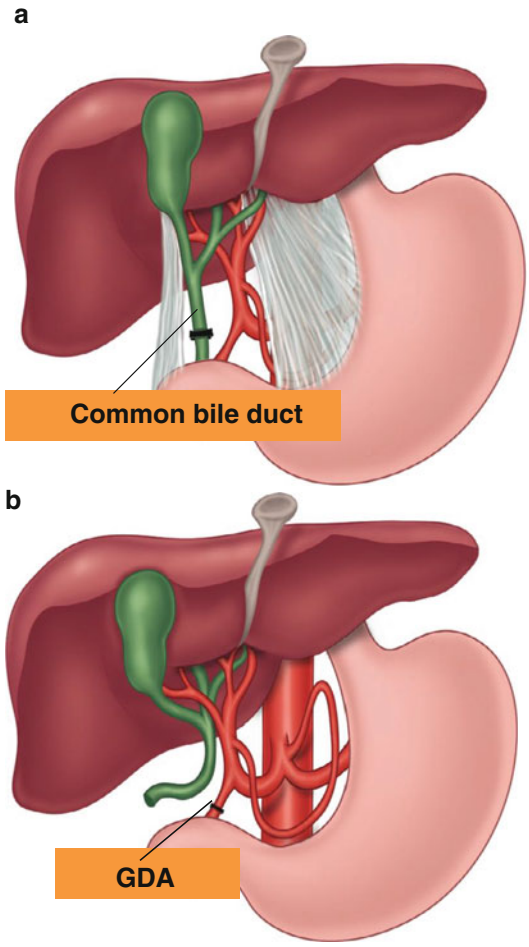

Fig. 11.5 Section of the common bile duct (**a**) and identification of the GDA (**b**)

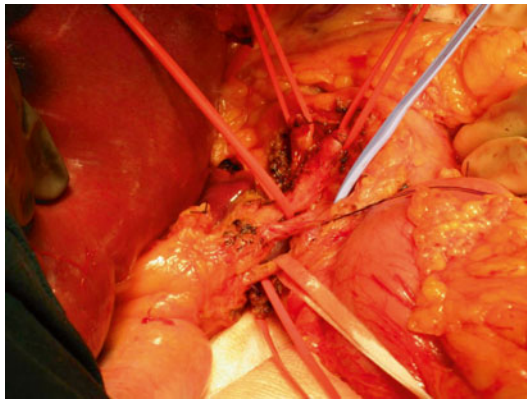

Fig. 11.6 Identification and control of the portal vein, GDA, splenic, and left gastric arteries

Usually, portal venous perfusion is abandoned during pancreas procurement according to the majority of pancreas procurement teams who consider the risk to induce pancreatic edema very high. However, in the presence of aortic atherosclerotic findings, when there is a consistent risk of suboptimal liver perfusion, portal perfusion with a portal vent technique may be considered. In such case, the portal vein can be identified, gently dissected, and encircled with a rubber tape. It is then possible to use a tourniquet around the portal vein; a small venotomy below the portal tourniquet can induce the venting of the splanchnic blood flow, which avoids pancreatic edema. A small resection of the splenic inferior pole can also be useful to maintain a low perfusion pressure in the splanchnic area.

After the ligation of the coronary (left gastric) vein located in the inferior part of the lesser omentum, the hilum dissection is continued along the pre-pancreatic lymphnodal plane located in the upper border of the pancreas where the splenic artery runs deeper by a 90° direction from the common hepatic artery; the splenic artery is dissected and then encircled.

The left gastric artery is also identified near the lesser curve of the stomach. If an aberrant (accessory or replaced) left hepatic artery from the left gastric artery (Hyrtl's artery) is present, this should be dissected during the warm phase. The ligation of all the small collaterals after the origin of the left accessory hepatic artery during the warm phase can be advantageous. We prefer to perform this phase of identification and the dissection of all small collaterals during the warm phase of the surgical procedure to reduce the time of cold ischemia during the cool phase and during bench surgery. Many other centers prefer to perform the dissection and ligation of small collaterals after flushing during bench surgery to minimize manipulation during the warm phase. An incision in the gallbladder fundus is performed, and the gallbladder is flushed with Ringer solution to clear the common bile duct of retained bile. This step can be important, because biliostasis is known to increase the risk of developing non-anastomotic stenosis during prolonged ischemia, especially when adequate

flushing of bile from the bile ducts is not achieved [15].

At this time, the warm dissection has been completed, and we have encircled by different ties the following arteries and veins:

- Infrahepatic IVC above the right renal vein
- Infrarenal IVC
- Supraceliac abdominal aorta
- Distal aorta before the iliac bifurcation or iliac arteries
- IMV
- All the elements of hepatic hilum (GDA, left gastric, splenic artery, portal vein) (Fig. 11.6)

11.7 Rapid Retrieval Technique or Cold Dissection

Some centers prefer to use this technique with the assumption that less manipulation of the anatomical structures could be advantageous during reperfusion [8, 16, 17]. We use this technique only in unstable donors, because major evidence for the superiority of the cold technique versus the conventional warm technique by controlled prospective studies is lacking. The initial steps are the same as in the warm technique with less blunt dissection in favor of a wider use of diathermy transection to gain time for hemostasis.

The following steps are quickly performed:

- Sternotomy and laparotomy.
- Longitudinal opening of the pericardium from the apex of the heart to the venous brachiocephalic trunk.
- Exploration of all abdominal and thoracic organs; careful checking for all pathologies and judgment for suitability of organs for transplantation.
- Self-retaining retractor for the thorax and abdomen is rapidly placed.
- Quick cannulation and retrieval preparation by exposure of the abdominal aorta and common iliac arteries; at this time if major instability of the donor is present, the perfusion line should be prepared and perfusion started.
- If the donor is hemodynamically stable, the exposure of the abdominal aorta, the common iliac arteries, and the IVC should be performed.
- Incision of peritoneal duplicature of the distal ileum and cecum (Cattell-Braasch and Kocher's maneuver).
- Complete exposure of the infrahepatic IVC from the aortic bifurcation to the upper margin of the left and right renal veins.
- Identification of aortic bifurcation and proximal common iliac arteries with particular attention to the renal lower pole arteries originating from the common iliac arteries (1–3 % of all donors); in such case, cannulation of the iliac arteries below the origin of polar arteries is mandatory.
- Dissection and encircling of the distal abdominal aorta by two large ties for later fixation of the perfusion cannula.

11.8 Last Step: Perfusion of the Abdominal Organs

In both warm and cold techniques, the final steps are identical; nevertheless one should remind that the cold technique requires an extra time for organ dissection after perfusion. Two perfusion lines are set up, and a careful control of two perfusion lines should be organized to minimize the risk of air introduction in the perfusion system. The line for the aortic perfusion is brought to the height of 120–150 cm, and the line for the portal perfusion is elevated to 50–60 cm. The two lines are filled with perfusion solution, avoiding air bubble formation. Systemic heparin is administered i.v. (300 units/kg body weight).

A Bard cannula 14–16 Fr. is inserted through a small venotomy (3 mm) into the lumen of the inferior mesenteric vein (Fig. 11.7) where it is introduced and advanced into the portal vein up to 2 cm before its bifurcation and securing by a double silk tie.

After distal clamping of the aorta, the pre-iliac aortic tract is ligated, and a large-bore cannula is introduced through a transversal arteriotomy (Fig. 11.8) into the distal aorta and connected to

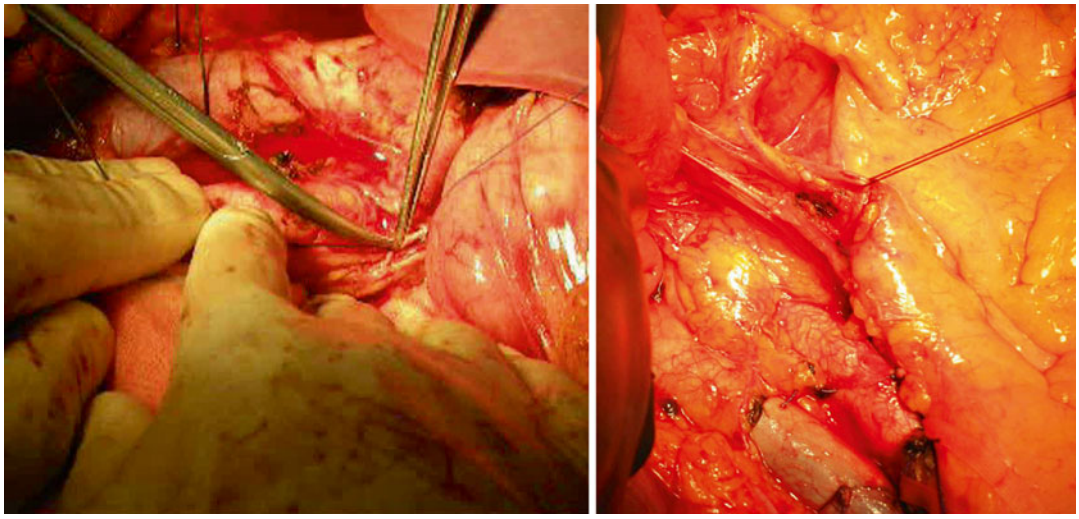

Fig. 11.7 Small venotomy on IMV for cannulation and portal perfusion

a large syringe filled with Ringer solution. The correct intraluminal position of the aortic cannula should be checked by refilling blood into the syringe. The cannula is then fixed with silk tie and connected to the perfusion aortic line, avoiding the introduction of air bubbles.

The two abdominal perfusion lines (the aortic and portal) (Fig. 11.9) are connected, and the abdominal and thoracic teams are ready for perfusion.

Soon after the aortic cross-clamping of the thoracic team, the inferior suprahepatic vena cava should be completely transected for wide venting. Consider that heart transplantation almost never requires a bicaval anastomotic technique; for this reason, a gentleman's agreement between abdominal and cardiothoracic surgeons usually involves leaving at least 5 mm of vena cava cuff to the liver for the suprahepatic anastomosis of the liver graft [18]. The cardiothoracic surgeon starts the cardioplegic perfusion. The supraceliac aorta is now ligated (or the descending thoracic aorta is clamped). The IVC upon the iliac bifurcation is ligated, and the perfusion of the abdominal organs can now begin.

The abdomen is filled with a large quantity of slushed ice mixed with cold Ringer solution to achieve the best hypothermic condition for all the abdominal anatomical compartments.

We usually use 4–5 L of low viscosity solution introduced through the aorta and 2 L introduced through the portal vein. Effective suction of all the warm blood effluent can help to more quickly achieve good hypothermic conditions. After flushing the thoracic organs, heart procurement will be performed first; then the lungs, liver, pancreas or small intestine, kidneys, and finally vascular grafts are procured.

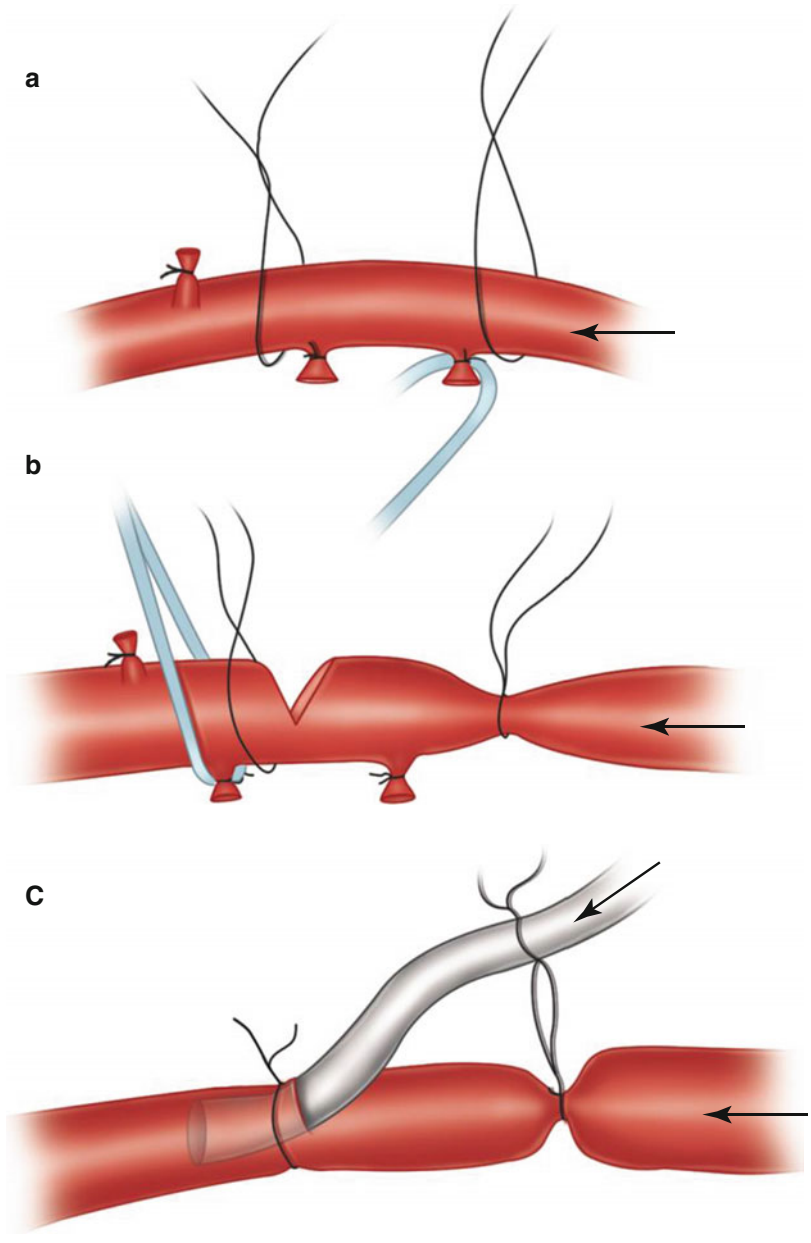

Fig. 11.8 The pre-iliac aorta is ligated and a large-bore cannula is introduced through a transversal arteriotomy. (**a**) Some lumbar arteries are ligated and distal aorta encircled with ties. (**b**) Transverse aortotomy. (**c**) Positioning of the cannula

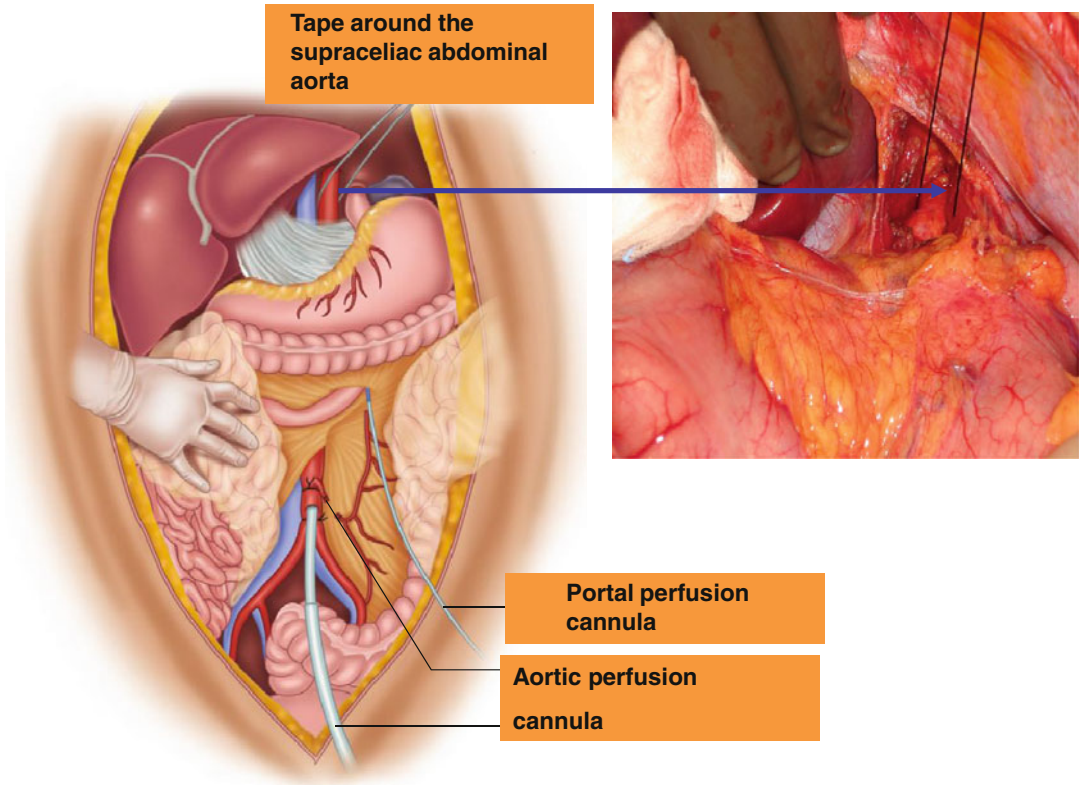

Fig. 11.9 Preparation of the abdominal organs' perfusion: after cannulation of abdominal aorta and IMV organ perfusion can start

References

1. Forti D, Rondinara GF, Aseni P (1997) Il prelievo multi-organo a scopo di trapianto. Fogliazza Editore, Milano
2. Baranski A (2009) Surgical technique of abdominal organ procurement: step by step. Springer, London
3. Aseni P, De Carlis L (2011) Il prelievo multiorgano a scopo di trapianto. Ghedimedia, Milano
4. Pang P, Houssin D (1992) Le prèlevement d'organes. Masson, Paris
5. Kremer B, Broelsch CE, Henne-Bruns D (1994) Atlas of liver, pancreas, and kidney transplantation. Thieme Medical Publishers, New York
6. Belzer FO, Southard JH (1988) Principles of solid-organ preservation by cold storage. Transplantation 45(4):673–676
7. Starzl TE, Hakala TR, Shaw BW Jr et al (1984) A flexible procedure for multiple cadaveric organ procurement. Surg Gynecol Obstet 158(3):223–230
8. Starzl TE, Miller C, Bronznick B et al (1987) An improved technique for multiple organ harvesting. Surg Gynecol Obstet 165(4):343–348
9. Van Burden CT, Barakat O (1994) Organ donation and retrieval. Surg Clin North Am 74(5):1055–1081
10. Gubernatis G (1989) Techniques of organ procurement and preservation of liver and pancreas. Baillieres Clin Gastroenterol 3(4):799–811
11. Cattell RB, Braasch JW (1960) A technique for the exposure of the third and fourth portions of the duodenum. Surg Gynecol Obstet 111:378–379
12. Fredet P (1905) Le péritoine in Traité d'Anatomie humaine de Poirier et Charpy. Masson, Paris
13. Benedetti E, Massad MG, Kisthard JA (1997) Aortic cannulation in organ donors with pathology of the infrarenal aorta. J Am Coll Surg 185(5):488–489
14. Molmenti EP, Molmenti H, Marubashi S et al (2001) Cannulation of the aorta in organ donors with infrarenal aortic pathologies. Dig Dis Sci 46(11):2457–2459
15. Op den Dries S, Sutton ME, Lisman T et al (2011) Protection of bile ducts in liver transplantation: looking beyond ischemia. Transplantation 92(4):373–379
16. Boggi U, Vistoli F, Del Chiaro M et al (2004) A simplified technique for the en bloc procurement of abdominal organs that is suitable for pancreas and small-bowel transplantation. Surgery 135(6):629–641
17. Van Buren CT, Barakat O (1994) Organ donation and retrieval. Surg Clin North Am 74(5):1055–1081
18. Delgado DH, Rao V, Ross HJ (2002) Donor management in cardiac transplantation. Can J Cardiol 18(11):1217–1223

Whole-Liver Procurement

12

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Tips, Tricks, and Pitfalls

- After perfusion, avoid prolonged time during organ retrieval.
- Hepatoduodenal and gastrohepatic ligaments should be dissected as near as possible to the lesser curve, avoiding damage to the accessory (or replaced) left hepatic artery from the left gastric artery.
- Excessive tractions or rotations of the liver can cause tearing of the Glisson's capsule and liver parenchyma.
- Transection of the right adrenal gland suggests the correct plane of division of the infrahepatic vena cava, thus avoiding injury of the right renal vein.
- Avoid any manipulation of the pancreatic parenchyma.
- Remember to rinse the common bile duct with perfusion solution shortly after liver retrieval.
- Flush the liver again through the portal stump at the back table soon after retrieval.

12.1 Hepatic Hilum Dissection and Hepatectomy

Abdominal organs are always retrieved after the removal of the thoracic organs [1–4]; soon after heart and lung procurement, the surgical procedures for procuring each abdominal organ can begin.

All maneuvers must be essential and fast to avoid prolonged cold ischemia during multi-organ retrieval [5, 6]. When the essential organ dissection and the recognition of all vascular pedicles are performed during the warm phase, it is easier to proceed quickly during the final steps of liver procurement.

Opening the esophageal hiatus with a wide incision on the right and left crura of the diaphragm facilitates the subsequent surgical steps (Fig. 12.1).

The hepatoduodenal and gastrohepatic ligaments should be dissected as near as possible to

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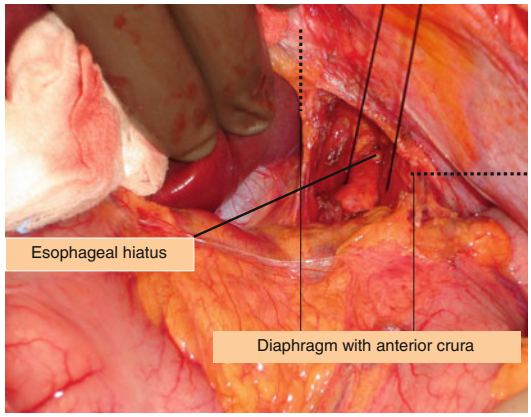

Fig. 12.1 Opening the esophageal hiatus with a wide incision on the right and left crura of the diaphragm facilitates the subsequent surgical steps

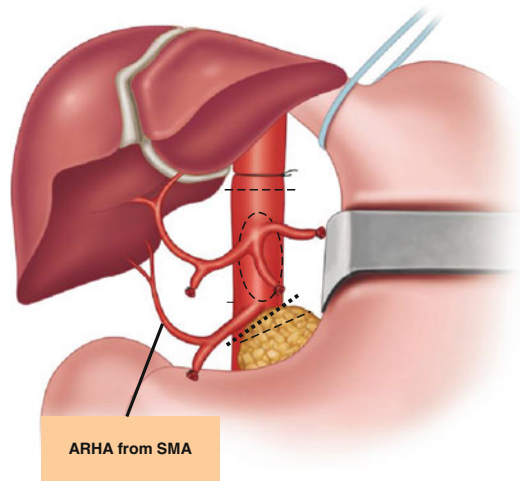

Fig. 12.2 Care should be exercised during the dissection and division of the SMA not to damage a previously unrecognized ARHA from the SMA. Even if unrecognized, an ARHA from the SMA should be suspected until proven otherwise after a detailed surgical inspection of the hepatic hilum

the lesser gastric curve, avoiding possible damage to an accessory (or replaced) left hepatic artery (ALHA) from the left gastric artery (LGA). The LGA is divided and tied distally from the origin of the ALHA. The gastroduodenal artery (GDA) should also be divided; its distal stump can be suture marked with a 6/0 Prolene stitch if its revascularization is planned during pancreas transplantation. However a proximal stump of the GDA of at least 0.5 cm is helpful for bench reconstructions with an accessory (or replaced) right hepatic artery if present (ARHA).

The bowel is displaced upward in the thorax, and the root of mesentery is identified. Taking as reference the aortic axis, the superior mesenteric artery (SMA) is easily found deep in the fibro-fatty tissue of the mesenteric root of the small bowel. When the pancreas is not harvested, the SMA can be encircled, ligated, and taken together with the liver for a length of 8–10 cm. Care should be exercised during the dissection and division of the SMA not to damage a previously unrecognized ARHA from the SMA. Even if unrecognized, an ARHA from the SMA should be suspected until proven otherwise after a detailed surgical inspection of the hepatic hilum (Fig. 12.2). The SMA can then be dissected up to its aortic origin; after cleaning the aortic wall of fibromuscular tissue, the aorta can be divided along a 45° plane of dissection with particular care not to damage the renal arteries that run a few millimeters below the origin of SMA. The distal end of the SMA is tied and retracted on the right side and upward by the second operator, who will also displace the head of the pancreas and duodenum on the left side and downward.

If portal perfusion has been utilized in combination with aortic perfusion, the perfusion cannula is removed, and transection of the portal vein at the spleno-mesenteric confluence is done. If a long portal vein is needed, such as in recipients with portal vein thrombosis, it is possible to transect the pancreatic isthmus, thus dividing the portal vein beyond the spleno-mesenteric confluence, provided the pancreas will not be procured.

During liver and pancreas procurement, a 2-cm segment should remain with the pancreatic graft. The short cuff of the pancreatic portal vein can be suture marked with a 5/0 Prolene stitch to facilitate its identification during the bench surgery of the pancreas [7–9].

In case of liver procurement without pancreas procurement, a 5–6-cm segment of the splenic artery can be taken with the liver for possible reconstruction during bench surgery with an ARHA. A gentle traction of the GDA and the

splenic and left gastric arterial stumps on the right side will allow an easier identification and dissection of the celiac trunk at its origin from the infradiaphragmatic portion of the aorta. Once the celiac trunk is recognized, a wide section of the posterior diaphragmatic crura allows the dissection of the aorta up to the vertebral plane. A final 5-cm length aortic patch will then be made available by cutting the supraceliac aorta above the diaphragmatic hiatus. This aortic patch (oval or cylindrical) includes the SMA, any ARHA from the SMA, the celiac trunk with the common hepatic artery, and a 4–5-cm stump of both the splenic and left gastric arteries with any ALHA from the LGA. The complete excision and removal of the liver requires the dissection of the right inferior pulmonary ligament and the transection of a wide diaphragmatic patch anteriorly and posteriorly to the vena cava following a line that should cross through the right adrenal gland (Fig. 12.3). During this phase, heavy tractions or rotations of the liver can cause tearing of the Glisson's capsule and liver parenchyma. To minimize venous vascular damage during this phase, the left index finger of the operator should be placed within the lumen of the vena cava to protect the vena cava and the suprahepatic veins.

After the transection of the right adrenal gland, the infrahepatic vena cava should be divided above the renal veins where a tie was previously placed. Diaphragmatic dissection is concluded with the transection of all remaining lower diaphragmatic crura attached to the liver. The graft is now freed from any adjacent anatomical structures and placed in a bag previously filled with cold perfusion solution; the bag should lie in a large bowl with ice and cold Ringer solution. Soon thereafter, the graft should receive an additional 1 liter of cold perfusion through a cannula inserted into the portal vein on the back table. The common bile duct is also gently rinsed with 100 cc of the same solution. The liver will be packed in three different bags; the internal one is filled with perfusion solution, and the others are filled with minced ice. No ice rocks should remain in contact with the liver due to the risk of ice burns to the liver parenchyma.

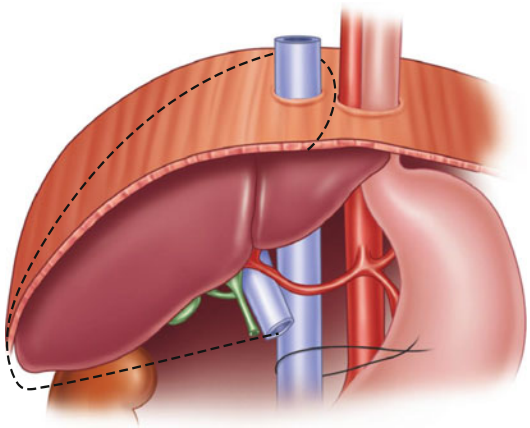

Fig. 12.3 Complete excision and removal of the liver with the transection of a wide diaphragmatic patch anteriorly and posteriorly to the vena cava following a line that should cross through the right adrenal gland

12.2 En Bloc Liver and Pancreas Procurement

If both the liver and pancreas have to be procured, the so-called en bloc procurement is a procedure sometimes adopted by some centers [8, 9]; the procedure is obviously mandatory when a combined liver and pancreas transplantation is planned for the same recipient. Otherwise, they can be retrieved with the en bloc technique and then divided during bench surgery, especially when both grafts are allocated to the same transplant center.

When the combined liver and pancreas procurement procedure is adopted, the sterilization of the gastroduodenal contents is required; gastrointestinal decontamination is achieved through the nasogastric tube with a solution containing saline, 10 % Betadine, and one ampule of amphotericin B, colimycin, and vancomycin.

The warm dissection proceeds with the same technique. Care should be taken to avoid any manipulation of the pancreatic parenchyma. Portal perfusion should be avoided; in a few cases where it is strongly advised, such as in donors with atherosclerotic vessels, a vent for pancreatic venous outflow should be created to avoid pancreatic edema during organ perfusion. However,

we suggest the aortic perfusion only, whenever possible, to avoid pancreatic edema. At the end of the organ perfusion, the gastrocolic ligament will be opened and dissected from the right colic flexure to the left colic flexure reaching the lesser sac with the subsequent division and ligation of the right gastroepiploic and right gastric artery.

The transection of the gastrosplenic and spleno-colic ligaments of the pancreas is performed, using the spleen as a handle ("le poignet du pancreas") (Fig. 12.4). After the ligation of short gastric vessels, the dorsal side of the pancreas and the spleen is mobilized and dissected. The mesocolon is then dissected with separate ligation of all mesenteric vessels. A section of proximal duodenum is obtained by stapling distally to the pylorus using a GIA stapler device.

The inferior border of the pancreas is dissected, and mesenteric veins and all collaterals are divided and sutured quite distally from the inferior pancreatic border with multiple ties or with a mechanical suture stapler device; care must be taken to avoid even small lesions of the pancreatic capsule. The distal duodenum is now stapled 10 cm from Treitz's angle using a mechanical stapling GIA device (Fig. 12.5). After the complete dissection of the posterior border of the pancreas from the prevertebral plane, the aorta will be divided immediately below the SMA ostium with a caudo-cranial section plane of 45°. Care should be taken not to damage the orifices of both renal arteries.

At this time, the maneuvers and surgical techniques are exactly the same as for liver procurement alone with the exception of the vasculo-biliary elements of the hepatic hilum, which should remain untouched for their identification and separation during the back-table procedure when transplanted for two recipients. However, in the case of simultaneous liver and pancreas transplantation, the hepatic hilum can remain intact depending on the specific technique of combined organ transplantation utilized. Prevertebral muscular and fibro-connective tissue is than divided with the proximal aorta including both the celiac and SMA trunk, and the release of the liver and pancreas is completed. At the end of the procedure, the liver, duodenum, and pancreas are removed en bloc with the spleen and all vascular elements (Fig. 12.6).

An additional 1 liter cold perfusion should be added throughout the celiac trunk and through the SMA during bench perfusion. Remember that during perfusion a 5 cm vent incision on the lower pole of the spleen can be useful to improve the perfusion outflow and minimize the risk of pancreatic edema.

12.3 Multivisceral Procurement

A dedicated chapter in this textbook by Di Benedetto and Tarantino [10] will describe the detailed surgical procedure of the intestinal and multivisceral procurement for "cluster transplantation." Beyond the isolated intestinal transplantation, there are at least three types of multivisceral transplantation: (a) the combined liver and intestinal transplantation; (b) the multivisceral transplant which includes the liver, stomach, duodenum, pancreas, and small bowel; and (c) the modified multivisceral transplant in which the liver is not included and the stomach may or may not be included (Fig. 12.7). We summarize here only the main surgical of the first two procedures. During the observation of the donor, the gastrointestinal tract should be irrigated through a nasogastric tube with 500 ml of saline solution containing Betadine (10 %), two vials of vancomycin, two vials of colimycin, and two vials of amphotericin B.

The initial maneuvers of liver dissection are the same as those for whole-liver procurement. After the dissection of the ligamentum teres hepatis and the falciform ligament, a definitive decision for small bowel procurement should be made by evaluating the macroscopic appearance of the splanchnic organs; desirable criteria include minimal intestinal edema, the absence of intestinal wall congestion, normal intestinal motility, the absence of intestinal adhesions, no hematoma, and no signs of recent intestinal contusion.

Some unique steps in the technical procedure for the en bloc procurement of the liver, stomach, duodenum, pancreas, and small intestine are required [9, 11, 12].

The hepatic hilum should remain untouched, and the common bile duct, the gastroduodenal artery, and portal vein should not be dissected.

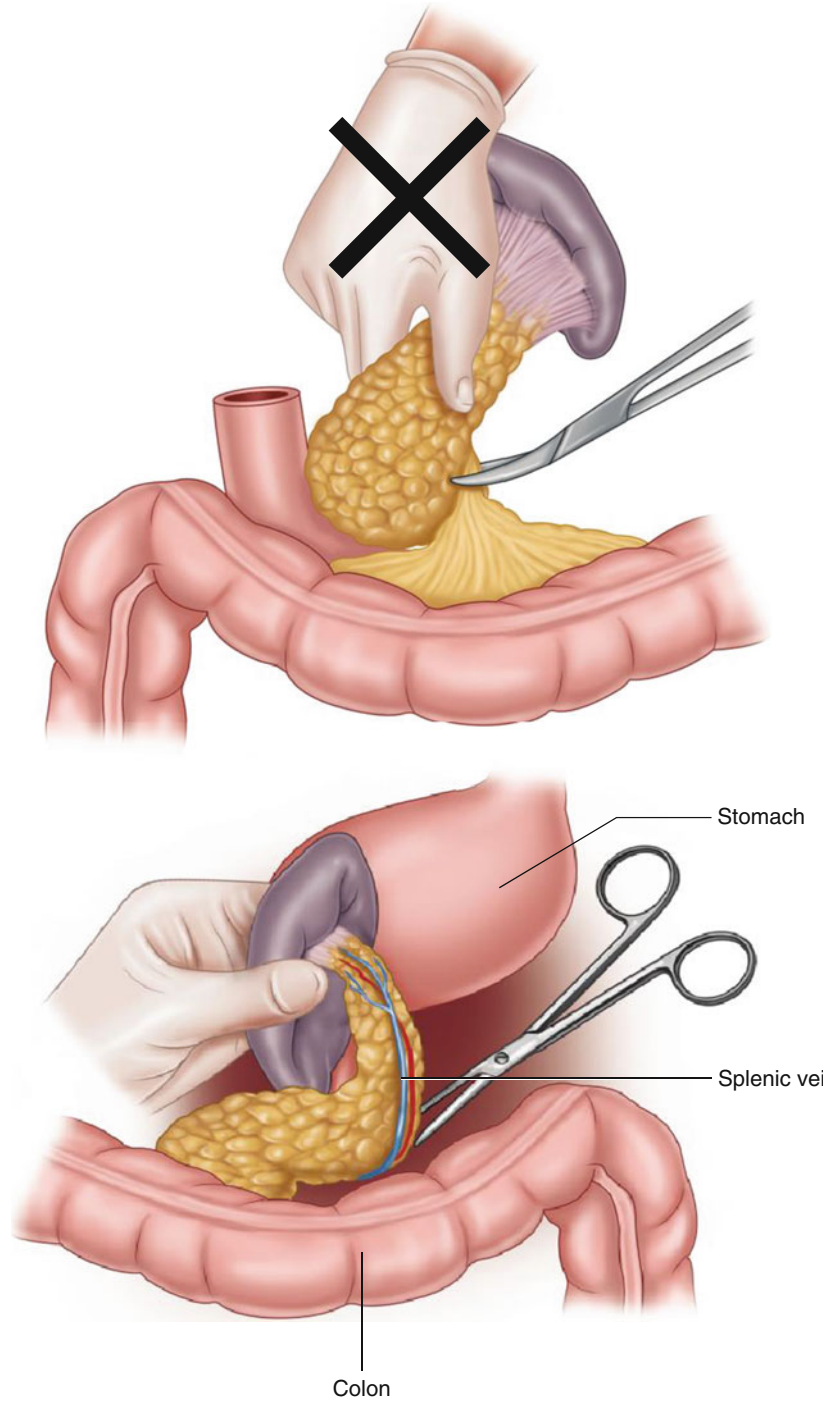

Fig. 12.4 Care should be taken to avoid any manipulation of the pancreatic parenchyma. The spleen is used as a handle ("le poignet du pancreas")

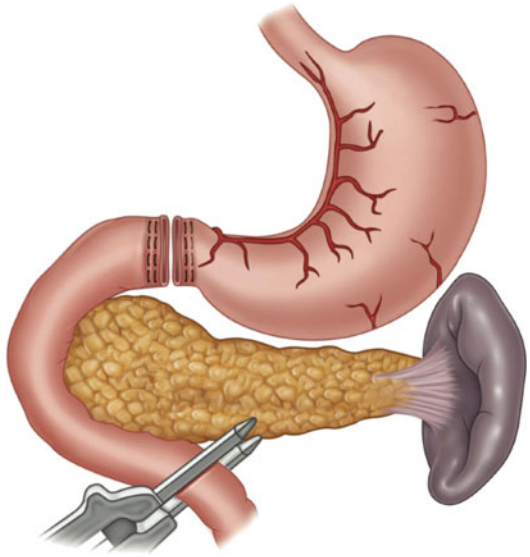

Fig. 12.5 Section of proximal duodenum is obtained by stapling distally to the pylorus using a GIA stapler device. Distal duodenum is also stapled 10 cm from Treitz's angle

The following steps are necessary:

- A Cattell-Braasch maneuver is necessary to displace the whole bowel to the root of the mesentery.
- A wide Kocher maneuver.
- The dissection of the gastrocolic ligament (with the preservation of an ALHA), the spleno-colic ligament, and the reno-colic ligament.
- The mobilization of the distal duodenum and sectioning of the ligament of Treitz.
- The celiac and inferior mesenteric artery is included in the aortic patch.
- The inferior mesenteric vein is preserved with the portal vein.
- The aorta and IVC are encircled twice.
- The division of the gastrocolic omentum.
- The mobilization of the left colon.
- The dissection with the complete colon and the exposure of all colic vessels.

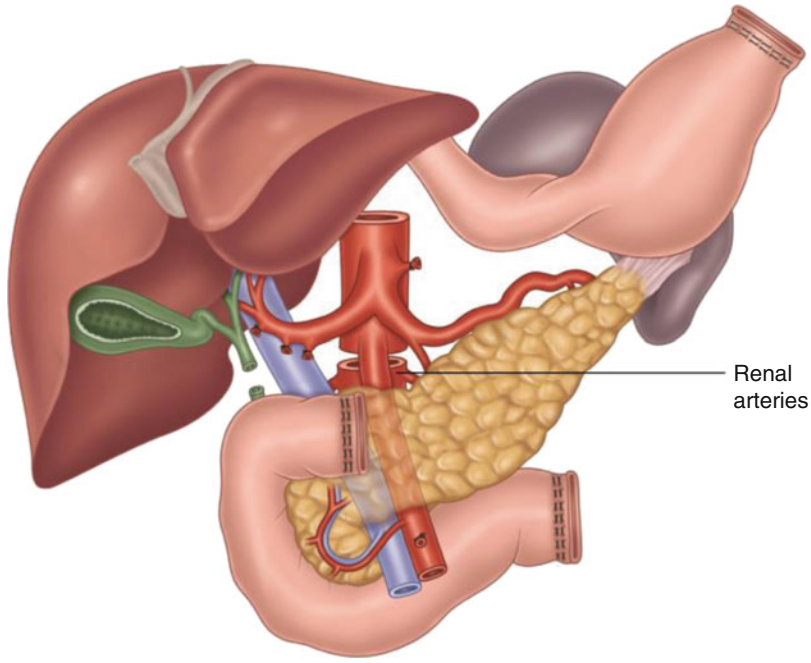

Fig. 12.6 The liver, duodenum, and pancreas are removed "en bloc" with the spleen and all vascular elements: the aortic patch includes the celiac trunk and SMA

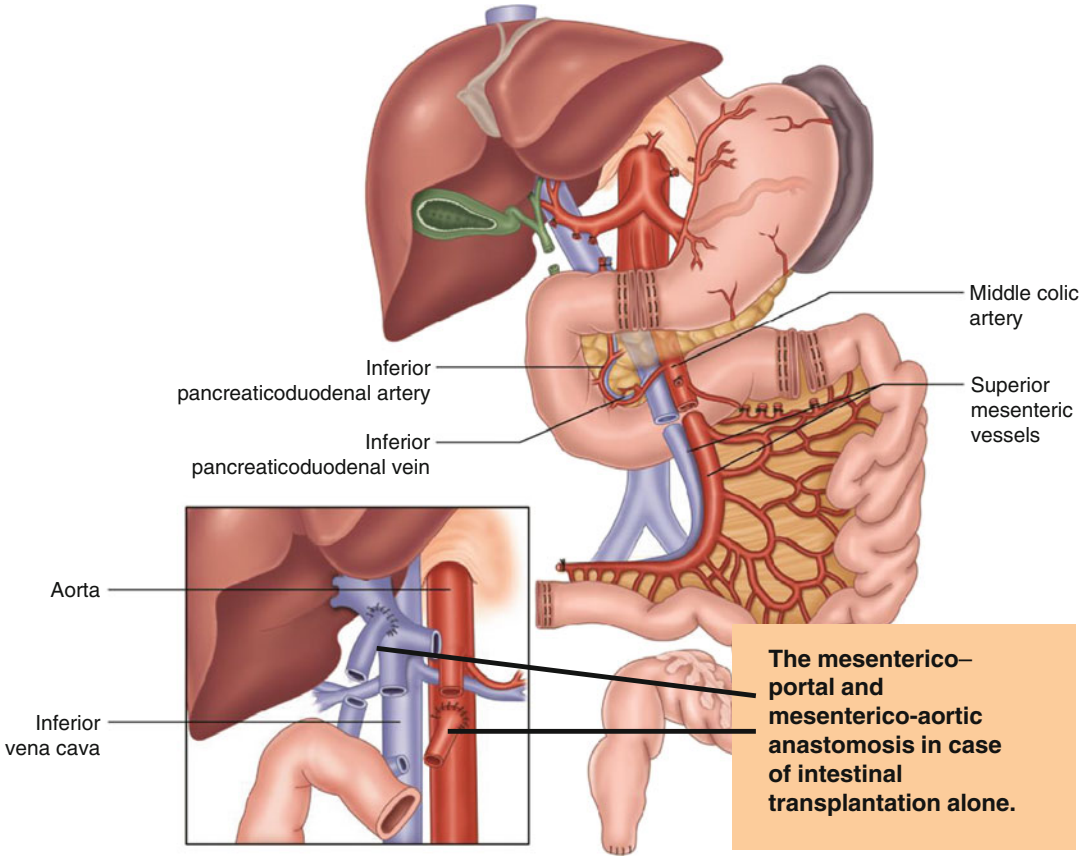

Fig. 12.7 The multivisceral procurement includes the liver, stomach, duodenum, pancreas, and small bowel: this technique can be modified in the combined liver and intestinal procurement or in a modified multivisceral procurement in which the liver is not included and the stomach may or may not be included

- The decompression of the intestine as proposed by some centers should be discouraged due to the risk of mechanical damage caused by this traumatic manouvre.
- The dissection proceeds laterally and distally along the mesocolon outside of the ileocolic and superior mesenteric arterial arcade until the inferior mesenteric vein (no cannulation of the inferior mesenteric vein is performed for portal perfusion).
- Complete colectomy (or left hemicolectomy if the right hemicolon is to be procured with the small intestine).
- The isolation of the cardia and the terminal ileum (or transverse colon) exposing the entire mesenteric root.
- The medial visceral rotation and the mobilization of the pancreatic tail and spleen.
- The transection of lesser omentum and the preservation of the ALHA.
- All collaterals from the SMA are identified and respected.
- Complete isolation of the proximal and distal part of the abdominal aorta (for cross-clamping) and flush the gallbladder.

- The perfusion is performed only through an aortic cannula after systemic heparinization. Hyperperfusion of the intestine should be avoided by the redistribution of liquid perfusion by gentle manual compression.
- Intraluminal perfusion is recommended by some centers; however, data on the benefits are inconsistent.
- En bloc removal of the liver, stomach, duodenum, pancreas, jejunum, and distal ileum (with or without the right colon) is performed with the upper section of the esophagogastric junction after establishing GIA stapler mechanical sutures and with the lower section of the terminal ileum. Donor thoracic aorta is used to create a conduit for the anastomosis with the recipient abdominal aorta. The vascular pedicle of this multivisceral en bloc procurement consists of 12 cm of thoracoabdominal aorta above the renal arteries, including the celiac trunk ostium, the SMA ostium, the inferior vena cava above the renal veins' confluence, and a cuff of the suprahepatic inferior vena cava.

References

1. Starzl TE, Hakala T, Shaw BJ et al (1984) A flexible procedure for multiple cadaveric organ procurement. Surg Gynecol Obstet 158:223–230
2. Starzl TE, Miller C, Bronznick B, Makowka L (1987) An improved technique for multiple organ harvesting. Surg Gynecol Obstet 165:343–348
3. Van Burden CT, Barakat O (1994) Organ donation and retrieval. Surg Clin North Am 74:1055–1081
4. Pang P, Houssin D (1992) Le prèlevement d'organes. Masson, Paris
5. Boggi U, Vistoli F, Del Chiaro M et al (2004) A simplified technique for the en bloc procurement of abdominal organs that is suitable for pancreas and small-bowel transplantation. Surgery 135:629–641
6. Halazun KJ, Al-Mukhtar A, Aldouri A, Willis S, Ahmad N (2007) Warm ischemia in transplantation: search for a consensus definition. Transplant Proc 39:1329–1331
7. Gubernatis G (1989) Techniques of organ procurement and preservation of liver and pancreas. Baillieres Clin Gastroenterol 3:799–811
8. Dunn DL, Morel P, Schlumpf R et al (1991) Evidence that combined procurement of pancreas and liver grafts does not affect transplant outcome. Transplantation 51:150–157
9. Wunderlich H, Brockmann JG, Voigt R, Rauchfuss F, Pascher A, Brose S, Binner C, Bittner H, Klar E (2011) Commission of Organ Donation and Removal German Transplantation Society. DTG procurement guidelines in heart beating donors. Transpl Int 24:733–757
10. Di Benedetto F, Tarantino G (2016) Small-bowel and multivisceral procurement. In: Multiorgan procurement for transplantation. A guide to surgical technique and management. Switzerland: Springer International Publishing
11. Abu-Elmagd K, Fung J, Bueno J et al (2000) Logistics and technique for procurement of intestinal, pancreatic, and hepatic grafts from the same donor. Ann Surg 232:680–687
12. Casavilla A, Selby R, Abu-Elmagd K, Tzakis A, Todo S, Reyes J, Fung J (1992) Logistics and technique for combined hepatic-intestinal retrieval. Ann Surg 216:605–609

Split Liver: Surgical Techniques for Adult and Pediatric Recipients and for Two Adult Recipients

13

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Abbreviations

DD	Deceased donor
FLG	Full left graft
FRG	Full right graft
GW/RW	Graft weight to recipient weight boby ratio
LHV	Left hepatic vein
LLG	Left lateral graft
LDLT	Living donor liver transplantation
LG	Left graft
LHV	Left hepatic vein
MHV	Middle hepatic vein
NITp	North Italy Transplant program
RHV	Right hepatic vein
RLT	Reduced liver transplantation
REG	Right extended graft
RG	Right graft
S	Segment
SLT	Split-liver transplantation
SFSS	Small-for-size syndrome
TH	Transhilar
TU	Transumbilical

Tips, Tricks, and Pitfalls

- Three different standard types of liver bipartition producing six different types of grafts can be created with different hepatic segments (S):
  - Splitting for adult and pediatric recipients with left lateral graft, S II-III (LLG) and right extended graft, S I, IV–VIII (REG)
  - Splitting for two adult recipients or for adult and pediatric recipient of large size recipients with creation of right graft, S I, V–VIII (RG) and left graft, S II–IV (LG)
  - Splitting for two adult recipients with creation of full left graft, S I–IV (FLG) and full right graft, S V–VIII (FRG)
- The absence of an extrahepatic portal vein bifurcation is an absolute contraindication to liver splitting.
- Division of the portal branches to S I optimizes the freeing/lengthening of the left portal vein for the implantation

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- Identifying the portal tract entering the caudate process at its lower aspect is helpful in preparing for the division of the hilar plate.
- Early dissection of the Arantius remnant allows a safe encircling and control of the left hepatic vein (LHV)
- In the adult and pediatric in situ splitting technique, a 1–2-min selective clamping of the LHV may provide assurance that the hepatic venous drainage of S IV is not jeopardized.
- Recognition of independent S II and III suprahepatic venous outflow (<5 % of cases) is crucial in the adult and pediatric splitting procedure.
- Segment IV hypoperfusion is a potential pitfall during liver splitting for adult and pediatric recipients.
- During adult and pediatric split-liver procedure, parenchyma transection can be achieved according to the transhilar approach or the transumbilical approach.
- In the liver-splitting technique for two adult recipients, the "hanging maneuver" can be helpful in defining the correct plane of transection.
- In the rare cases of remarkable MHV dominancy during split-liver procurement, for two adult recipients, the ex situ splitting of the vena cava and/or MHV can be considered possible options to avoid the complex reimplantation of all tributaries of the MHV and the congestion of S IV, V, and VIII.

13.1 Introduction

The shortage of liver grafts available for transplantation from deceased donors (DD) prompted several transplant centers during the early 1990s to seek alternatives to conventional liver transplantation such as split-liver transplantation and partial grafts from living donors.

Waiting list mortality is approximately 15–20 % in Europe and 14 % in the United States [1, 2], and approximately 2,500 patients die every year in the United States for lack of a suitable liver donor. Split-liver transplantation (SLT), a procedure in which one donor liver is divided into two hemilivers, is an important method to overcome organ shortage. To date, the principal beneficiaries of this procedure have been adult/pediatric pairs, and excellent outcomes have been reported by the majority of pediatric transplant centers; where the waiting list mortality has been approximately 0 % in the last few years.

13.2 Historical Background

The transplantation of partial-liver allografts in children was initially advocated by Smith, who in 1969 proposed that the left lateral graft was suitable for children [2]. This technical option was revisited in the 1980s when the increasing demand for pediatric liver transplantation resulted in an insufficient pool of deceased donors (DD) and an increased waiting list mortality.

Initial attempts to reduce pediatric waiting list mortality targeted the surgical reduction of an adult DD liver to fit the abdominal cavity of a child, a procedure called "reduced-liver transplantation" (RLT). Split-liver transplantation (SLT) began in the 1980s as a response to the disparity between adult and pediatric recipients; the waiting list mortality in the pediatric population exceeded 25 % at major transplant referral centers.

The first successful RLT was simultaneously reported by Bismuth [3] and Broelsh [4] in 1984. Later studies demonstrated that the use of RLT grafts in children achieved success rates equal to or better than those of whole cadaver organs. However, the simple surgical reduction of a liver graft from an adult deceased donor (DD) failed to expand the donor pool and simultaneously increased competition problems between adult and pediatric transplant candidates. After substantial ethical debate [5–8], the surgical reduction techniques were also extended to adults of small size.

In 1989, Pichlmayr et al. and Bismuth et al. [9, 10] almost simultaneously reported the successful ex situ division of a deceased donor liver into a left

lateral graft (LLG), segments (S) II and III, for transplantation into a pediatric recipient, and a right extended graft (REG), S I, IV–VIII for transplantation into an adult. As a prerequisite of this new SLT surgical procedure, a dedicated "benching" period was required for further dissection, which substantially increased the organ cold ischemia time. Goss and colleagues at University of California, Los Angeles (UCLA) proposed in situ separation as a procedure to reduce cold ischemia time and enhance the identification of biliary and vascular structures. During this procedure, the liver was divided within the adult DD during procurement without any special equipment. The in situ technique was initially performed at UCLA in 1992. Important clinical reports in 1997 by Goss [11], Azoulay [12], and Rogiers [13] showed the significant advantages of this technique in avoiding the period of bench surgery necessary to perform the ex situ splitting procedure with the related complications of the prolonged cold ischemia time of the graft. Performed on selected DDs, the in situ liver-splitting procedure offered the benefits of pediatric living donor liver transplantation (LDLT) without the donor risk, and this has now become the first choice for the transplantation of infants and small children in the majority of centers.

In 1999, Colledan et al. reported the first successful in situ split liver procedure from a deceased donor for two adults, obtaining a full right graft (FRG) and a full left graft (FLG).

13.3 Anatomic Principles

Any technical description of split, reduced, or living donor liver transplantation must begin with the acknowledgment of the anatomic classification of the liver described by Couinaud [13] and refined by Bismuth [14] (Fig. 13.1), which has been universally accepted by the transplant communities of Europe, Asia, and North America as the reference for describing different portions of partial-organ allografts. The liver is divided into eight functional units, termed "segments" which receive separate hilar pedicles. Each pedicle contains a portal venous branch, hepatic arterial branch, and a bile duct pedicle

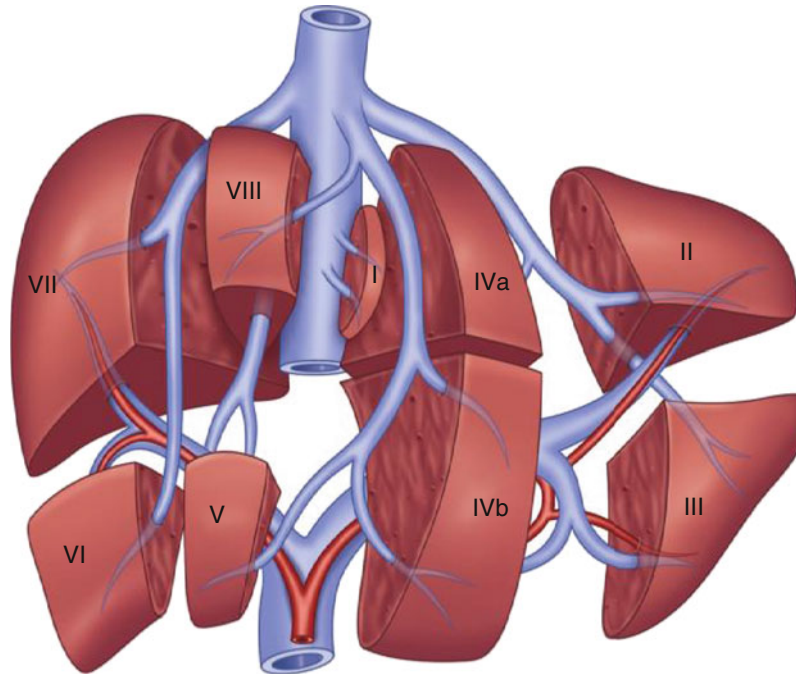

Fig. 13.1 The segmental anatomy of the liver as described by Couinaud and Bismuth. Each anatomic segment receives a unique portal pedicle consisting of a portal venous branch, hepatic arterial inflow, and bile duct. Each segment is drained by unique hepatic venous outflow branches and separated by connective tissue scissurae

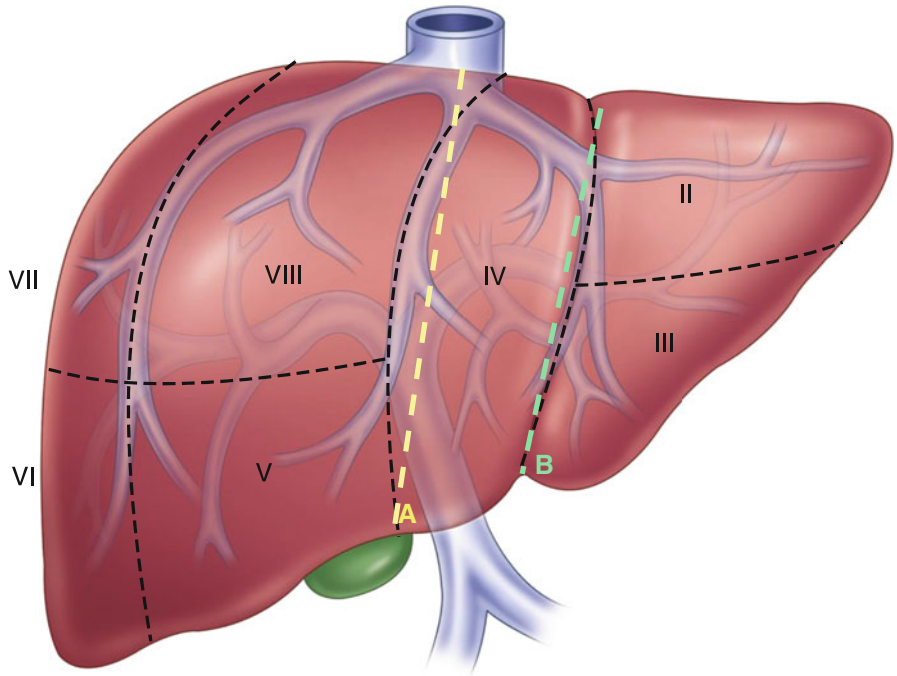

Fig. 13.2 Surgical division of the liver along the middle hepatic vein (yellow line labeled "A") yields a full left graft (FLG) S I–IV and full right graft (FRG) S V–VIII that can be utilized in SLT for two adults. Division along the falciform ligament (green line labeled "B") yields the pediatric left lateral graft (LLG) S II–III and the remnant, adult right extended graft (REG) S I, IV–VIII

with unique drainage through individual venous branches. Hepatic parenchyma transection corresponds so called to "scissurae," connective tissue planes that separate each individual liver "segment".

Couinaud's classification permits the creation of functionally distinct partial-organ allografts (Fig. 13.2). The division of the hepatic parenchyma at the falciform ligament yields an S II/III left lateral graft (LLG), which is 25 % of the total liver volume and approximately 250–350 cc, for pediatric recipients, and a remnant right extended graft (REG) (Couinaud S I and IV–VIII) of approximately 900–1100 cc, for transplantation into adults. The LLG can be further reduced to a "monosegment graft" (S III) for very small infants and neonates.

In order to transplant two recepients from one adult DD, the liver can be divided along a sagittal plane directed to the right or to the left side of the middle hepatic vein. The parenchyma transection along the chosen specific plane is able to create three types of liver bipartition with different percentages of parenchyma volume for the two hemigrafts (Fig. 13.2). Depending on the recipient's body weight, there are three standard techniques to split the liver and six different potential grafts:

(a) Split liver for adult and pediatric recipients with a LLG (S II, III) of approximately 25 % of total volume and a REG (S I, IV–VIII) of approximately 75 % of total volume. (Fig. 13.3a).
(b) Split liver for two adult or for an adult and pediatric recipients of large size of about 25–35 kg) with the creation of a left graft (LG) including S II, III, and IV, with approximately 35 % of total volume, and a right graft (RG) (S I, V–VIII) with approximately 65 % of total volume.
(c) Splitting for two adult recipients with the creation of a full left graft (FLG) including S I–IV with approximately 40 % of total volume and a

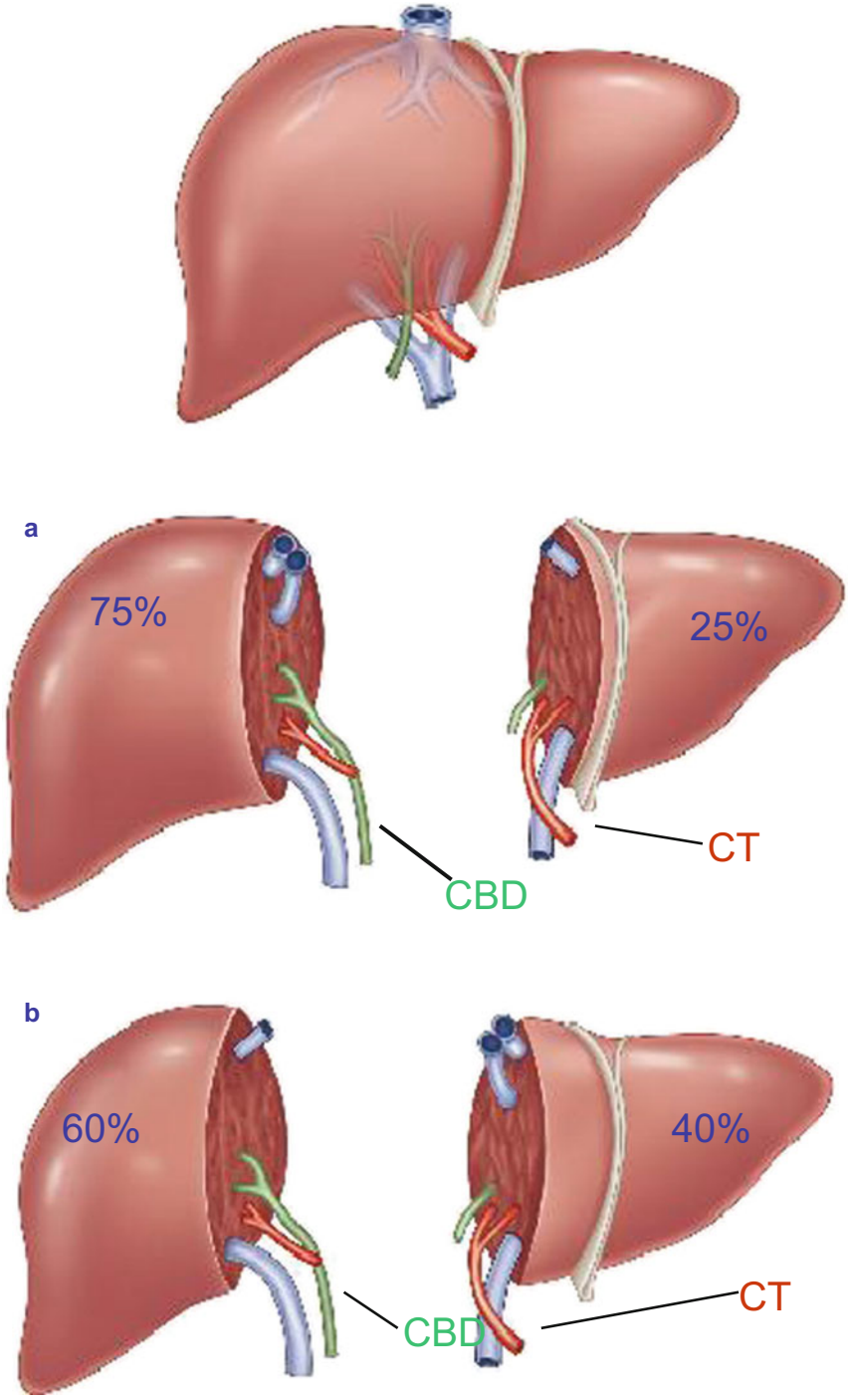

Fig. 13.3 Schematic representation of split liver for adult and pediatric recipients (**a**) and split liver for two adults (**b**). For simplification and to expose details of the supra-hepatic veins the vena cava has not been drawn. In our experience in NITp area, the common bile duct (*CBD*) is usually retained with the right extended graft and with the full right graft. The celiac trunk (*CT*) is usually retained with the left lateral graft and with the full left graft whereas the main portal trunk is retained with the right extended graft (**a**) and with full left graft (**b**)

Table 13.1 Six different types of grafts with estimated graft weight for a standard body weight of 70 kg

Type of graft	Couinaud segments	Percentage of total volume (%)	Estimated graft weight in g or ml (for a female-male of 65–70 Kg of BW)
Right extended graft (REG)[a]	S I, IV–VIII	75	900–950
Left lateral graft (LLG)[a]	S II–III	25	300–350
Right graft (RS) with caudate lobe[b]	S I, V–VIII	65	800–850
Left graft (LG) without caudate lobe[b]	S II–IV	35	400–450
Full right graft (FRG)[c]	S V–VIII	60	750–800
Full left graft (FLG)[c]	S I–IV	40	450–500

[a]For adult and pediatric recipient
[b]For adult and pediatric recipient of larger size
[c]For two adults

full right graft (FRG) including S V–VIII with approximately 60 % of total volume (Fig. 13.3b).

Liver graft volume can be roughly estimated preoperatively. Its volume is about a 1.8 % and a 2.2 %, for female and male respectively (Table 13.1), of the total body weight of the donor. A more accurate formula taking into account the body surface and gender can give more accurate values of estimated liver volume [15]. Because a remarkably close correlation exists between the liver weight and the volume of water at 25 ° C, liver volume can be converted to liver weight on a one-to-one basis.

Partial-liver graft recipients with a graft weight to recipient weight ratio (GW/RW) less than 0.8–1 % are reported to have a higher incidence of postoperative complications [16], including small-for-size syndrome (SFSS) especially in patients with portal hypertension.

The decision whether to split a DD liver and whether to perform the procedure in situ or ex situ depend on a number of variables that have different degrees of impact on decision-making [5, 17–22]. These variables include formal donor-related data, the given anatomical situation, the macroscopic appearance of the liver, the weight and clinical status of the potential recipients; moreover we have to take into account the availability of an experienced surgeon and logistics. An ideal liver to be split (Table 13.2) would be from a young donor with no history of liver disease, normal liver values (particularly the γ-glutamyl-transpeptidase), and short intensive care stay. The optimal donor should be hemodynamically stable before and during the donor operation. The ideal liver should have a macroscopically soft consistency, with sharp edges, and preferably with a large left lateral lobe (unless the recipient of this part is a small child); a separate right or left replaced hepatic artery can be advantageous. Whenever possible and in consideration of optimal logistics, the donor should be submitted to multiorgan procurement in the transplant center itself, thus providing the best conditions for in situ splitting. However, this condition is rarely achievable

Table 13.2 Optimal donor parameters for liver splitting

Young, healthy donor (<40–50 years of age)
No history of liver disease/injury
Normal liver enzymes (AST, ALT, γGT)
Hospitalization < 5 days, short ICU stay (≤2 days)
Hemodynamic stability
Macroscopically normal liver
Multiorgan heart-beating deceased donor
Minimal to moderate vasopressors (dopamine < 15 mcg/kg/min)

13.4 Split-Liver Transplantation: General Aspects

Split-liver transplantation for adult and pediatric recipients has become a standard procedure with results equivalent to those with whole liver transplantation (Figs. 13.3 and 13.4).

Two different techniques can be distinguished: split liver ex situ, i.e., performed on the backtable in the ice bath after the perfusion and

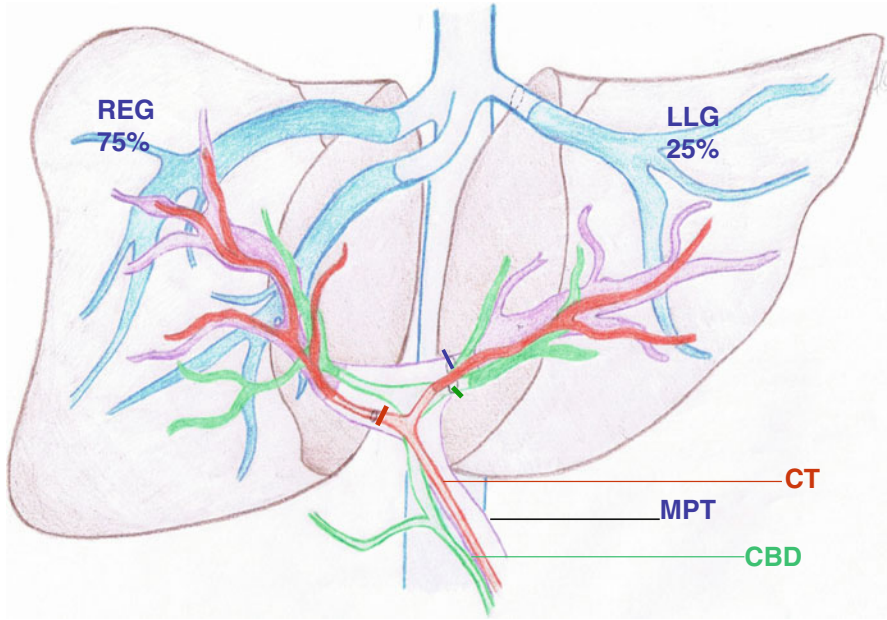

Fig. 13.4 Schematic drawing of split liver for adult and pediatric recipients. The parenchyma transection line is immediately lateral to the falciform ligament, yielding a left lateral graft (LLG, S II/III) for pediatric recipients of approximately 250–300 cc (25 %) and a right extended graft (REG S I, IV–VIII) of approximately 900–950 cc (75 %). Usually in NITp area the celiac trunk (*CT*) is retained with LLG (S II–III); the main portal trunk (*MPT*) and common bile duct (*CBD*) are retained with REG (S I, IV–VIII)

harvesting of the whole liver; in situ split liver, i.e., preformed inside the heart-beating donor prior to the perfusion and harvesting of the liver.

All types of splitting procedures can principally be performed ex situ as well as in situ. Because contrast-enhancement scans are rarely available for the majority of DDs, the anatomy of the biliary and hepatic vein system remains unknown until the liver is surgically divided. The liver's extrahepatic vascular anatomy should be determined during the procedure by recognizing the different types of the vascular anatomical pattern. Identifying an extrahepatic left portal vein or a variant, the presence of multiple or a standard single hepatic arterial supply and their branching modality into the right and left arterial supply are the most important early surgical steps. Surgeons are sometimes required to modify the transection line according to their intraoperative observations and their personal knowledge of the liver's anatomy and its variations [21, 23].

13.4.1 Ex Situ Split-Liver Technique for Adult and Pediatric Recipients

In the ex situ split-liver technique, the whole organ is retrieved according to the standard techniques of multiple organ procurement and whole liver procurement. The whole liver is preserved with the preferred perfusion solution. Grafts are usually prepared at the recipient transplant center and placed in an ice bath of perfusion solution. Predissection, cholangiography and arteriography can be performed at the back table during the ex situ technique in order to delineate the anatomy more precisely, but these procedures are time consuming. Otherwise, a thin metal cannula may be used to gently probe the hepatic artery and the bile duct to facilitate the detection of aberrant anatomy. As a general rule a successful liver division should share vascular and biliary structures between the two sides but without handicapping either and, when

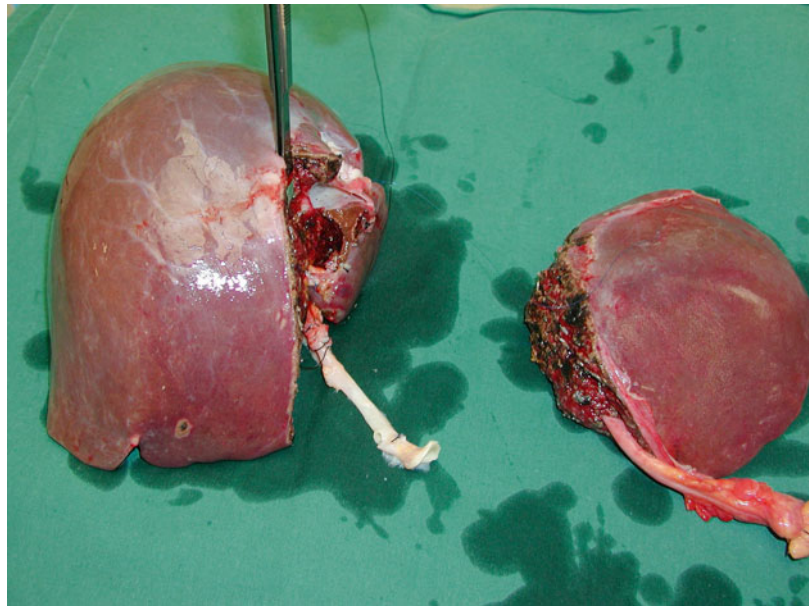

Fig. 13.5 Ex situ split liver for adult and pediatric recipient at the end of parenchyma transection: many centers prefer to retain the celiac trunk with the REG (Courtesy of Dr. Roberto Troisi, Ghent University Hospital and Medical School)

possible, provide either graft with single first order arterial and biliary elements. Dissection of the portal triad is performed to separate the branches of the hepatic artery, portal vein, and right and left hepatic ducts. It is matter of debate which half of the liver should retain the entire hepatic/celiac trunk and the main trunk of the portal vein. In the majority of cases, the common bile duct is retained with the right graft. The rationale for determining which graft should receive the major vascular pedicle is explained by the anatomy of the components of the porta hepatis [24]. In the majority of cases, the left portal vein, the right hepatic artery, and the left bile duct should be sectioned because they are anatomically longer than the contralateral pedicles, thus facilitating the anastomoses to the recipient vessels. The absence of extrahepatic portal vein bifurcation is a contraindication to liver splitting. Because microsurgical hepatic artery reconstruction is now commonly performed, retaining the sectioned left hepatic artery with the LLG is usually preferred and is more commonly performed in North Europe centers during in situ splitting (Fig. 13.5). Biliary anatomy can be carefully explored by probing the main bile ducts, because an extensive dissection of the bile ducts may hamper the peri-biliary vascular plexus. The left hepatic duct is preferably sectioned because it is usually single. When the left hepatic duct is absent, the left lobe drains S IV and S II–III, thus configuring with the right duct a bile duct trifurcation; this allows a favourable plane of transection between S IV and S II–III in cases of liver splitting for adult and pediatric recipient. With regard to the possible extension of the arterial graft, interposition grafts by allogeneic iliac, splenic, superior, or inferior mesenteric arteries are usually employed. For portal vein extension, donor iliac veins can be used to extend both the right and left sides. Dissection of the hepatic hilum should be performed only from the left side keeping the right side untouched. After completing the resection of the gallbladder, the portal vein, the hepatic artery, the bile duct, and the hepatic vein are identified as well as the segment IV artery. After transaction of the left hepatic artery distally to the origin of segment IV artery, the small portal branches from the left portal vein supplying S IV are ligated and transected. In case of an adult and pediatric liver transplant recipients, the line of parenchyma transection extends from the confluence of the middle and left hepatic veins 0.5 cm on the right side of the falciform ligament to approximately 1 cm until the right side of the umbilical fissure up to the hilar plate. Splitting the liver parenchyma step by step along with

umbilical scissure is continued from downward to upward ligating all tiny vessels. Parenchyma dissection can usually be performed with the mosquito or Kelly fracture technique or with scalpel transection with ligation of the single elements of the intrahepatic portal triad structures. The left bile duct is finally transacted as well as the left portal vein and the left hepatic vein close to suprahepatic inferior vena cava, leaving a suitable stump. The left hepatic vein is retained with the left graft. The right and middle hepatic veins in continuity with the vena cava are retained with the REG. Infusion of cold preservation solution via portal vein and hepatic artery can help to check for leaks. In order to reduce bleeding from the surfaces of the grafts, the majority of surgeons use sealing products such as fibrin glue, collagen, or polyglactin mesh.

In early experience and until the late 1990s, the ex situ liver split procedure was the most widely used method to transplant two patients with one liver [25]. Recently, few centers are still using this approach [26–28]. The ex situ splitting of the liver allograft on the bench is considered a time-consuming procedure and usually results in a long ischemic time. During the splitting procedure into right and left grafts, some allograft rewarming occurs; even if slight, it can be associated with increased susceptibility to hepatic ischemic/reperfusion injury. When a second recipient operating room is not immediately available, or if one of the hemiliver grafts must be transported to another center, the prolonged ischemic time can hamper the recipient outcome. Prolonged ischemia and rewarming during the ex situ split procedure exposes the graft to injury, with a higher incidence of poor graft function unless the split-liver transplant is organized in a very favourable environment and conditions. Thus, the ex situ technique may be restricted to some elective and selective cases, particularly for adult and pediatric recipients who can be simultaneously transplanted in the same transplant centers [17–20] or when a donor becomes unstable during the in situ procedure. Some authors [29] have reported encouraging results with the ex situ split technique for two adult recipients by splitting the vena cava and the middle hepatic vein (see below Sect. 13.4.3).

13.4.2 In Situ Splitting Technique for Adult and Pediatric Recipients

In situ splitting in the heart-beating DD is a modification of the ex situ splitting technique; it is an extension of the techniques established for living related donor procurement, which is associated with a lower rate of biliary complications, intra-abdominal hemorrhage, and primary nonfunction of the graft compared with other series of ex situ splitting techniques [26, 27]. As for the ex situ technique, only hemodynamically stable DDs are considered suitable for in situ splitting. It is important that donor hospitals and other procurement teams are notified as soon as possible of the decision to split the liver in situ, and the decision to proceed should be unanimous among different organ teams. No special equipment is needed; standard surgical facilities for a multiorgan procurement are usually used. The procedure requires an extra 2–3 h compared to the standard multiorgan technique. Before starting the splitting procedure, the standard surgical steps of abdominal organ procurement, including supraceliac and infrarenal aortic dissection and cannulation of the inferior mesenteric vein, should be completed. With this strategy, if a donor becomes unstable, the splitting procedure could be aborted with quick aortic cannulation, aortic cross-clamping, and organ cold perfusion.

Isolation of the Left Hepatic Vein (LHV) Segments II and III of the liver are mobilized. The dissection is always initiated with the division of the umbilical ligament, which is tied and gently held up to expose the umbilical fissure. Dissection of the falciform ligament is prolonged to the level of the diaphragm, with identification of the hepatic veins. By opening the gastrohepatic ligament and pulling up the left lobe (Fig. 13.6), it is possible to identify and section the fibrotic remnant of the ductus venosus Arantii which connects the left portal vein to the root of the left hepatic vein. Section and division of the fibrotic remnant near to the LHV enable isolation and encircling of the LHV with a vessel loop; this manoeuvre becomes easier and safer if directed

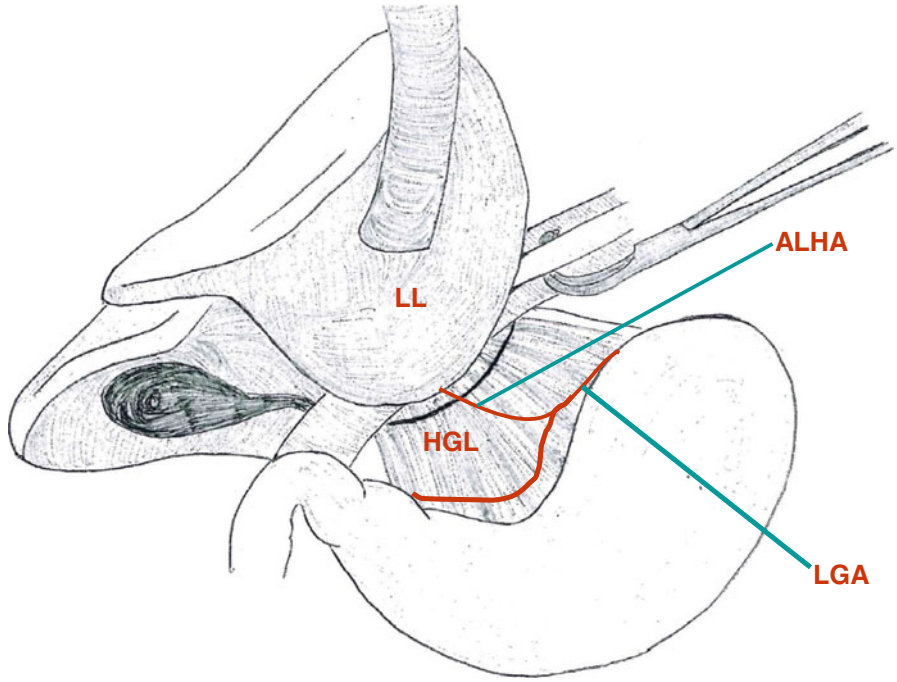

Fig. 13.6 The left lobe (*LL*) is pulled upward and the hepatogastric ligament (*HGL*) is divided to expose the ligamentum venosum Arantii. Care must be taken to preserve an accessory left hepatic artery (*ALHA*) from left gastric artery (*LGA*)

both ventrocranially and dorsocaudally by an Overholt dissector. A 1–2 min selective clamping of the LHV can ensure that the middle hepatic venous drainage of S IV, V, and VIII is not jeopardized. Occasionally, S II and III have independent orifices to the vena cava. The recognition of independent S II and S III veins is critical, and inadvertent injury to these veins should be carefully avoided. However, this condition requires that both orifices are incorporated on a common caval patch. A common middle and left hepatic vein requires careful separation after 1–2 cm of parenchyma division.

Parenchyma Dissection and Division of the Umbilical Plate There are two primary ways to dissect and divide the umbilical plate: (a) the transhilar division and (b) the transumbilical division. Both techniques have been well described by Broelsh [30] and more recently by J. De Ville De Goyet [31], and their use has largely depended on the surgeon's education and personal preference.

(A) In the transhilar (TH) approach, the LLG should be prepared beginning with hilar dissection at the base of the round ligament, with isolation of the left hepatic artery, the left portal vein branch, and the left bile duct. During the last decade, a significant debate has developed around how and when to preserve the artery for S IV (Fig. 13.7). The segment IV artery originates very near the arterial bifurcation, rarely from the right and more commonly from the left hepatic artery with some anatomical variability as follows:

(a) A unique branch from left hepatic artery (80 %)
(b) As a middle trunk of trifurcation of the hepatic artery (middle hepatic artery)
(c) From the right hepatic branch when a replaced left artery arises from the left gastric artery
(d) From the right hepatic branch when a replaced right hepatic artery arises from SMA
(e) Multiple small branches, the main from the left hepatic artery

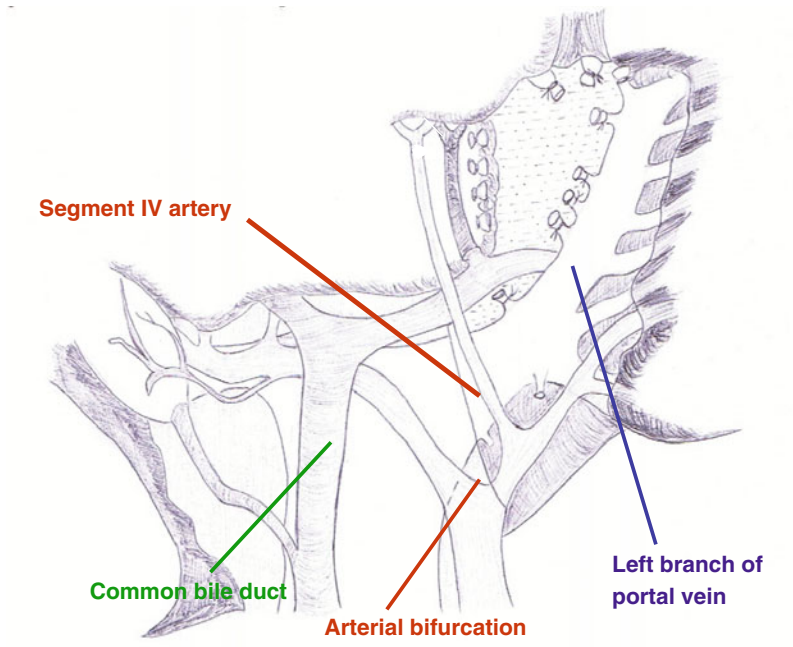

Fig. 13.7 The segment IV artery originates very near the arterial bifurcation, rarely from the right and more commonly from the left hepatic artery

However, one should be aware of the fact that the majority of S IV artery branches are functionally accessory branches rather than replaced arteries and that intrahepatic collateral circulation exists with a valuable supply. As a result, when the S IV artery arises from the left hepatic artery and do not appear to provide significant arterial inflow, it can be tied and sacrificed. In some particular cases, when the S IV artery shows a caliber ≥ 2 mm or if partial discoloration of segment IV is produced after 1–2 min occlusion of the same artery, it is better to preserve it, leaving the celiac trunk with REG or cutting the S IV branch at its origin of the left hepatic artery and re-anastomosing it with a microvascular technique with the gastroduodenal artery. Some concerns have also been raised for S I, the caudate lobe: when the right hepatic artery is divided at its origin and the celiac trunk is retained with the LLG, the vascular elements for the caudate lobe are removed with the left graft. In our experience during several hundred adult and pediatric split liver procurements in the North Italy Transplant program (NITp) area, the celiac trunk was usually retained with the LLG, and the S IV artery has been ligated and sacrificed if considered functionally an accessory branch. Only in some few cases when the S IV artery was considered functionally relevant (discoloration after clamping test or diameter ≥ 2 mm), the celiac trunk was retained with the REG. This technical option of keeping the celiac trunk usually with the LLG still remains a common agreement among surgeons of the NITp area and was never considered in our experience a possible cause of graft loss for ischemic necrosis of S I or S IV. Furthermore, one should be aware that the ultimate evaluation of S IV and S I viability can be better obtained after graft reperfusion during the transplant procedure. When REG reperfusion shows some areas of marked discoloration in S IV or S I, removing the segments or a portion of them it is an option that can be weighed against the high risk of ischemic necrosis and possible biliary fistula.

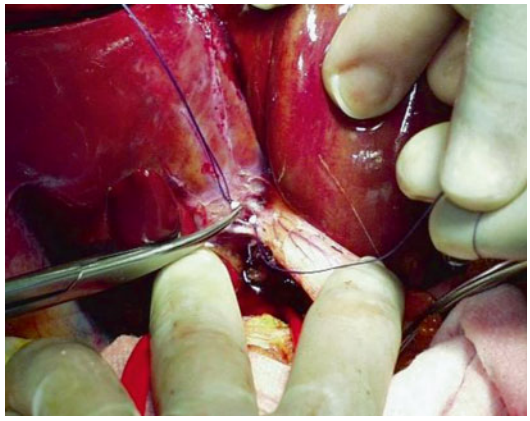

Fig. 13.8 Ligation and transection of the portal branches to segment IV (transumbilical approach) [32]

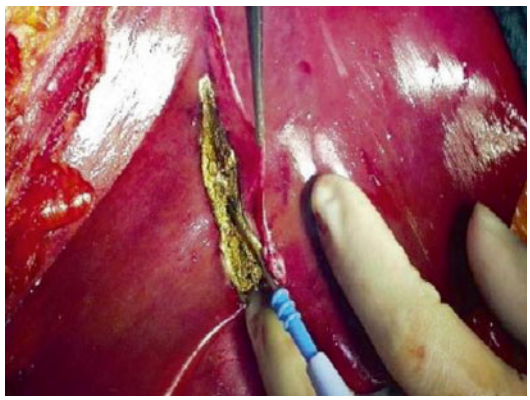

Fig. 13.9 Transection line of the liver parenchyma during split liver for adult and pediatric recipient runs 5 mm on the right side of the falciform ligament [32]

The TH phase continues with the dissection of small portal venous branches to S IV (usually 6–8), which are ligated with 5–6/0 Prolene suture and divided laterally to the umbilical fissure to isolate the entire left portal branch (Fig. 13.8). Some small portal branches to segment I should be preserved, because they originate from the main and not the left portal vein. When total vascular control of the left lateral segments is completed, parenchyma transection should began by marking with electrocautery the liver capsule 5 mm to the right side of the falciform ligament (Fig. 13.9). The parenchyma division proceeds until the hilar plate is divided at the right side of the umbilical fissure line (0.5–1 cm to the right) and ends precisely at the Arantius remnant line with the exclusion of the caudate segment (S I), which is not included in the graft. Dissection of the anterior liver parenchyma is obtained by a Harmonic scalpel, by CUSA, by bipolar electrocautery and water sealing, or by simply electrocautery and gentle Kelly fracture. The dissection is directed between the LLG and S IV and should be carried out to 1 cm above the ductal plate surrounding the left bile duct in the umbilical fissure. The MHV is retained with the right graft. Some small penetrating vessels draining S IV in the left venous system and some small biliary orifices should be divided and suture ligated as required. However, if any large vein from S IV is draining in the LHV, a short test clamping of 1–2 min of the LHV can be helpful to test the functional relevance of the same vessel.

The main advantage of the TH approach is that the surgeon can easily move the division line to the right providing a larger LLG including S II, III, and the small part of S IV). This flexibility can be helpful when the LLG is relatively small or when there is a need to provide a larger liver mass. The parenchyma division should proceed until the hilar plate is divided at the right of the umbilical fissure line (0.5–1 cm), and it should end precisely at the Arantius remnant line. In this way, S I is not included in the graft. It is necessary to divide the plate and the portal pedicle for S I to completely free the hilar plate and the LLG not only from the caudate lobe but also from its paracaval portion by ligating some very small ascending portal branches. Finally, a sharp division of the hilar plate is performed between the main bifurcation of the hepatic vascular structures and the umbilical fissure; this allows to obtain a single biliary orifice in the majority of cases.

(B) In the transumbilical (TU) approach, the *Rex recessus* (the distal portion of the left portal vein running after a sharp bend between S IV and the LLG) should be exposed soon after the preparation of the extrahepatic structures. The peritoneum of the umbilical fissure is opened from the umbilical ligament to the porta hepatis. All venous branches of the *Rex recessus* draining into S IV are divided. The left portal

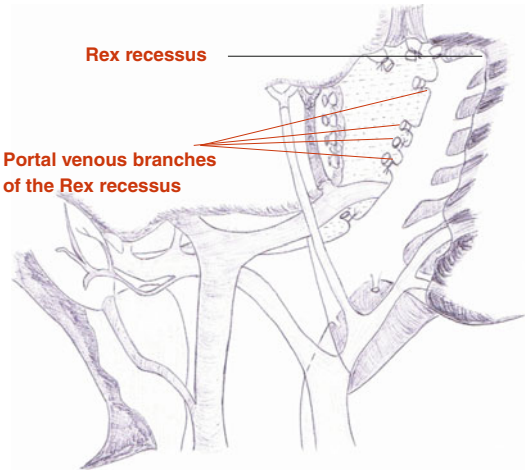

Fig. 13.10 In the transumbilical (*TU*) approach, the *Rex recessus* should be exposed soon after the preparation of the extrahepatic structures. All venous branches of the *Rex recessus* draining into S IV are divided

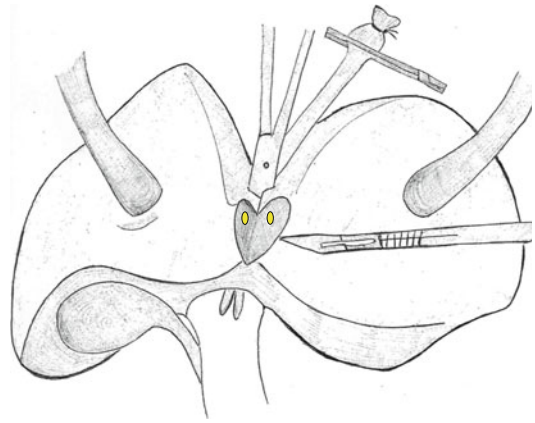

Fig. 13.11 Division of the hilar plate: a blunt right-angle dissecting forceps is passed to encircle the hilar plate. The left hepatic duct(s) is visible within the hilar plate

vein at the Rex *recessus* is shifted to the left until the umbilical plate where division for S II and S III will take place and then fully exposed (Fig. 13.10). The left hepatic artery is also progressively mobilized during the latter manoeuvre; eventually, the artery for S IV is divided, and the plate attached to S IV will go with the right split graft. The division of the S IV artery, arising more often from the left hepatic artery, follows the same general rules described for the TH approach. After a common agreement among different surgical teams of the NITp area, the celiac trunk is always retained with the LLG unless different anatomical evidence for possible ischemia of S IV is recognized (Fig. 13.4). The division of the liver parenchyma exactly follows the line of insertion of the falciform ligament at first and ends at the convergence between the LHV and MHV. In the same manner as for TH, the parenchyma division is guided to reach anteriorly the middle line of the umbilical plate, previously prepared, and along the Arantius remnant posteriorly. This approach results in dividing the plate more to the left compared with the TH technique, leaving in place the portal pedicle supplying the caudate lobe process. The remaining left hilar plate and bile duct are sharply transected with scissors or a scalpel close to the liver surface (Fig. 13.11), and biliary drainage to segment IV should be preserved. Vascularization and the perfusion of S IV can be more easily evaluated during the in situ procedure in the heart-beating DD. Hypoperfusion of S IV is a potential pitfall, and segmentectomy or subsegmentectomy of S IV may sometimes be considered. At the end of the parenchyma dissection, the LLG is separated from the remaining extended right liver graft parenchyma with its own vascular pedicle and venous drainage.

At the end of the dissection, two liver grafts are procured, each with a preserved vascular pedicle and venous drainage in a bloodless field. Some microfibrillar collagen sheets or a hemostatic sponge can be applied to the cut surfaces, and organ procurement continues with a subsequent perfusion phase and cooling of the donor organs. After organ perfusion and cooling, the right hepatic artery, the left portal vein, and the left hepatic veins are divided. At the end of the procedure, the main portal vein, the common bile duct, and the right hepatic artery stay with the right graft unless some particular anatomical conditions are evident as discussed before. The right graft is removed in the usual fashion, retaining the entire vena cava, while the LLG retains the left suprahepatic vein. The left bile duct and the common bile duct are gently flushed with 50 ml of perfusion solution prior to the storage of both grafts.

Main Steps for Bench Surgery The transplantation of the LLG retaining the LHV requires the preservation of the native inferior vena cava in the recipient. After further flushing with the perfusion solution throughout the portal vein, the parenchyma surface is carefully inspected during back-table preparation for possible vascular and biliary leaks that are oversewn. Bench surgery depends on the particular technique of transplantation of the LLG. During recipient operation, the right hepatic vein orifice to the vena cava is suture ligated, as are all the smaller accessory hepatic veins along the inferior vena cava. The left and middle hepatic vein orifices are opened in order to form a large common trunk for hepatic venous anastomosis. Anastomosis of the portal vein will be performed end-to-end utilizing nonabsorbable monofilament suture. For infants and neonates, the anastomosis may be a running (continuous) suture on the posterior wall and interrupted suture anteriorly. If the celiac trunk has not been retained with the LLG, the donor left hepatic artery can be anastomosed to the recipient common hepatic artery provided a long branching of the left artery can be obtained in the recipient. Otherwise, the anastomosis can be performed with the infrarenal aorta by artery interposition of a graft harvested from the DD. Biliary anastomosis is occasionally performed duct-to-duct but is more frequently performed by an end-to-side Roux-en-Y hepaticojejunostomy.

Preparation of the REG during bench surgery for transplantation includes the removal of remnant diaphragm from the liver bare area, ligature of phrenic vein origins, and closure of the orifices of the left hepatic vein, left portal vein, and left hepatic artery origin in those cases where the celiac trunk is retained with the right graft. In some cases of an S IV relevant artery, its revascularization, using the recipient gastroduodenal artery, can be considered; the left bile duct remnant is oversewn. Gently flushing each structure may help to identify small vascular orifices. The orifice of the LHV is finally sutured by a transverse oversewn. The REG is ready for transplantation, utilizing standard whole-organ techniques.

13.4.3 Split-Liver Procedure for Two Adult Recipients

The initial steps in the donor operation are performed as in any other multiple organ harvesting procedure. One should remember that before pereforming any split procedure, the standard techniques of abdominal organ procurement, including supraceliac and infrarenal aortic dissection and cannulation of the inferior mesenteric vein, should be completed. In this way if a donor becomes unstable, the splitting procedure can be aborted with rapid progression to aortic cannulation, aortic cross-clamping, and organ cold perfusion.

The right hepatic pedicle is first dissected with the usual extrahepatic intra-Glissonean approach, and the right hepatic artery and right branch of the portal vein are isolated and encircled with different colored vessel loops (Fig. 13.12). The right liver lobe should be fully mobilized, and all the short hepatic veins to the retrohepatic vena cava are isolated and saved to preserve adequate venous outflow. The parenchyma bridge, when present, from S IV to S III around the IVC must be divided. The right hepatic vein is isolated and taped with a vessel loop. After the isolation of all short hepatic veins, a tape can be positioned from the groove between the RHV and MHV to the groove between the right and left Glissonean sheaths via the posterior hepatic surface (hanging maneuver). The lateral end of the tape is carried behind all the retrohepatic vein branches draining from the right liver lobe. To complete the hanging maneuver, the end of the tape is passed ventral to the right hepatic artery and right portal vein. In this way, the vessel loop defines a transection plane leading from the bifurcation of the hepatic artery and portal vein to a point between the right and middle hepatic veins. Before transection, ultrasound can be performed intraoperatively, whenever possible, to detect major S V and S VIII veins crossing the transection plane at the line of Cantlie. The "tape-assisted" parenchyma transection leads the surgeon more easily to the anterior wall of the inferior vena cava, potentially with better preservation of the caudal

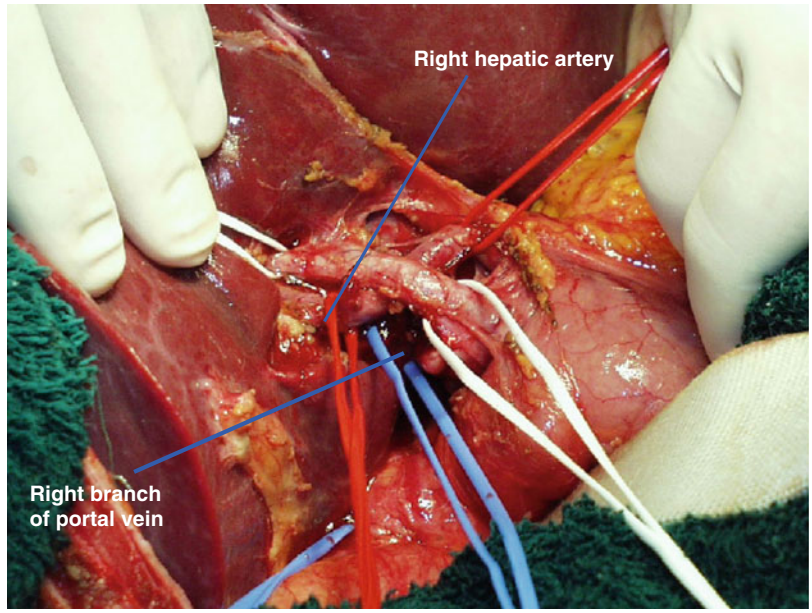

Fig. 13.12 The right hepatic pedicle is dissected with the extrahepatic intra-Glissonean approach; the right hepatic artery and right branch of the portal vein are isolated and encircled with different colored vessel loops [32]

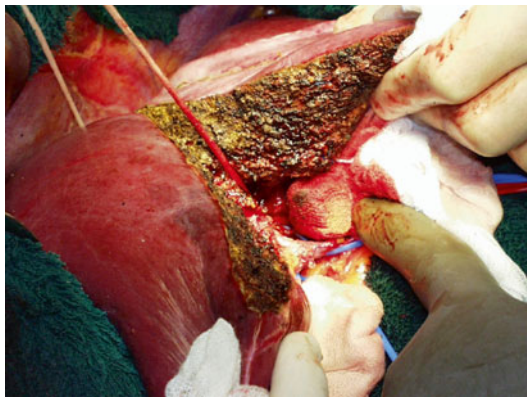

Fig. 13.13 The "tape-assisted" parenchyma transection leads more easily to the anterior wall of the inferior vena cava, with better preservation of the caudal lobe venous outflow [32]

lobe venous outflow (Fig. 13.13). At the end of the parenchyma transection and division of the right bile duct, the organ-procurement procedure is continued with the standard technique, and organ perfusion and cooling can be initiated. The right hepatic vein, right hepatic artery, and right portal vein are divided at the end of organ perfusion, usually leaving the right hepatic branch, the right portal vein, and the common bile duct with the right graft. A FRG and a FLG are obtained, and the left and right bile ducts are gently flushed with the perfusion solution prior to the storage of both grafts. Almost all centers in the NITp area typically retain the common bile duct with the right graft and the common trunk of the portal vein and the celiac trunk with the left graft. However, in particular anatomical situations concerning both the donor and the recipient, some variations from the standard technique can be discussed. There are three modalities for liver-splitting techniques for two adults: (a) liver splitting into FLG S I–IV and FRG S V–VIII which is the most used in our experience, (b) liver splitting into FLG S II–IV and FRG S I, V–VIII, and (c) ex situ splitting with standard technique or splitting the vena cava and middle hepatic vein (FLG S I–IV and FRG S V–VIII).

(a) *Split Liver for Two Adult Recipients with Creation of FLG S I–IV and FRG S V–VIII*

This is the technique most frequently used for adult recipients, and it has developed in parallel with the one of the right lobe living donor procurement [31–34] (Fig. 13.14). Usually, left lobe grafts of approximately 450–500 g with S I–IV are used for adults weighing from 45 to 50 kg and

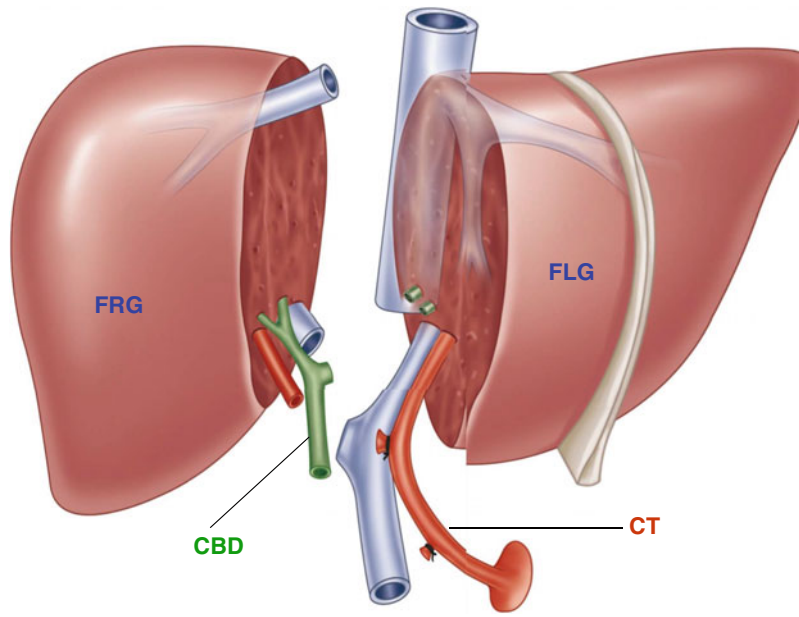

Fig. 13.14 In split liver for two adults, the common bile duct (*CBD*) is usually retained with the FRG. The celiac trunk (*CT*) is usually retained with the FLG to maximize arterial supply to S IV

in select circumstances, depending on donor size, for heavier recipients. The FRG, S V–VIII, of approximately 750–800 g, generally allows donor graft-to-recipient body weight ratios of more than 1.0 %. The procedure is similar to the one described earlier (Sect. 13.4.3). The hepatic veins are identified, and the right hepatic vein is encircled with a vessel loop. All diaphragmatic attachments to the liver are released, and the dissection proceeds from the right lobe to the inferior vena cava. There is no need to dissect the left border of the inferior vena cava. Minor and major accessory hepatic veins are usually encountered in about one half of DDs; these are individually preserved with a small caval patch for implantation only if ≥ 5 mm in diameter.

The hepatoduodenal ligament is opened to expose the hilum after retrograde cholecystectomy. The right hepatic artery is identified and exposed lateral to the common hepatic duct. Lateral exposure can avoid skeletonization of the proper hepatic bifurcation, thereby preserving any possible arterial supply to S IV from the right hepatic artery. The right portal vein should be approached from the lateral right side of the hilum and dissected to the level of the bifurcation where it is encircled with a vessel loop. A short and selective Pringle maneuver of the left hilum is then performed to create a demarcation line for parenchyma division. Once the hilar plate has been identified, the left bile duct (unique or double duct orifices) is sharply divided, and the remnant orifice is closed with a 6/0 monofilament; bleeding from hilar plate points can be secured with 5–0 nonabsorbable monofilament suture. Parenchyma division will continue along the main portal fissure with the surgeon's left fingertips positioned behind the right lobe anterior to the inferior vena cava. The hanging maneuver can be helpful and leads the surgeon more easily to the anterior wall of the inferior vena cava, with better preservation of the caudal lobe venous outflow. The MHV is retained with the FLG; for this reason, some S V and S VIII venous tributaries draining in the MHV are sharply divided and ligated when of small diameter (≤4 mm) (Fig. 13.15). Later revascularization of some venous tributaries to the MHV can be evaluated for vessels with a diameter larger than 5 mm or when a Makuuchi 5-min clamping test indicates its utility. In living donor liver transplantation (LDLT), Makuuchi [35] advocates aggressive reconstruction of all veins draining the right paramedian sector in the living donor right lobe when the MHV is not harvested with the right lobe. This author suggests the use of intraoperative

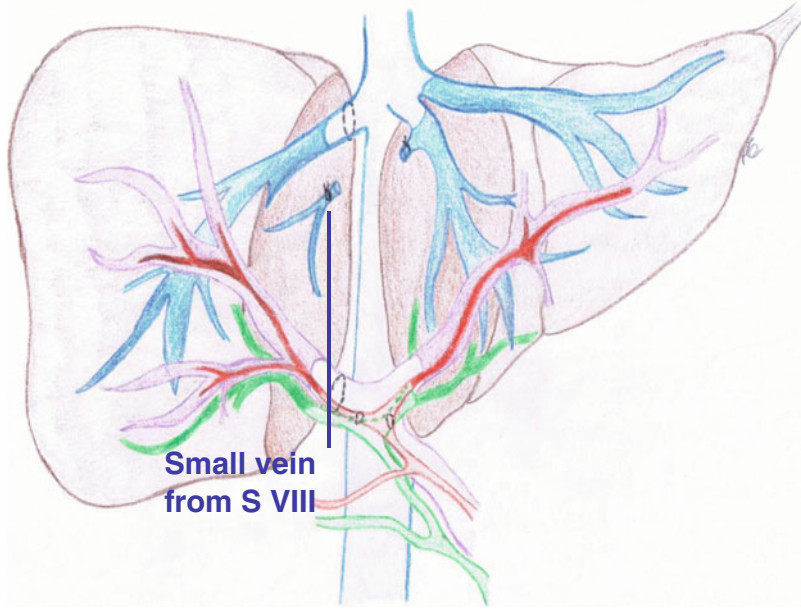

Fig. 13.15 Split liver for two adults: FRG and FLG with creation of FLG S I–IV and FRG S V–VIII; some S V and S VIII venous tributaries draining in the MHV are divided and ligated when of small diameter

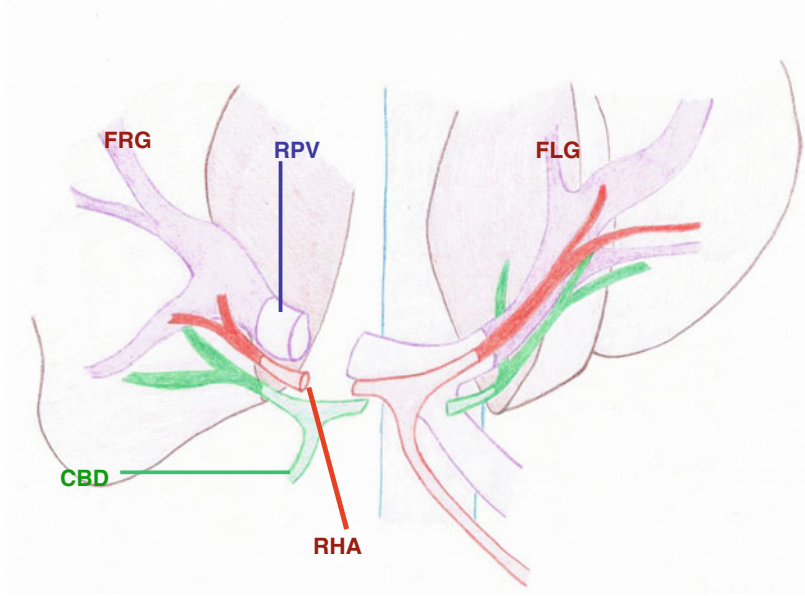

Fig. 13.16 Split liver for two adults. FRG and FLG. Graft separation should be performed including sharp division of the right portal vein (*RPV*) immediately distal to the bifurcation and transection of the right hepatic artery (*RHA*) immediately distal to its takeoff from the proper hepatic artery. The common bile duct (*CBD*) is retained with FRG

ultrasound Doppler evaluation after a 5-min test by clamping both the hepatic artery and the branches of the MHV; the evidence of a portal hepatofugal flow in the paramedian portal branch will suggest the reconstruction of the occluded paramedian venous branch. After the completion of parenchyma division, the right hepatic vein, right portal vein, and right hepatic artery remain intact for organ cold perfusion. At this point, heparin is administered and aortic cannulation is achieved. At the end of cool perfusion, graft separation should be performed including sharp division of the right portal vein immediately distal to the bifurcation and transection of the right hepatic artery immediately distal to its takeoff from the proper hepatic artery (Fig. 13.16). The rationale for preserving the

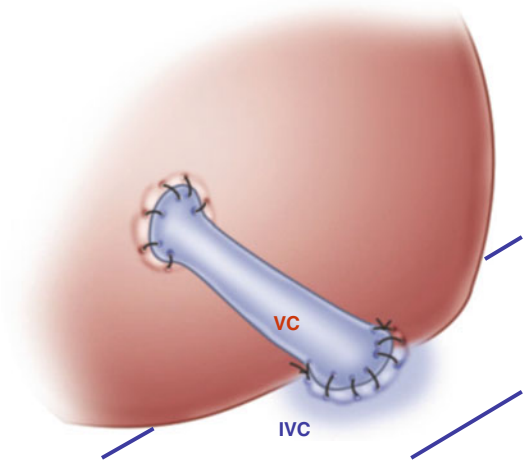

Fig. 13.17 FRG presents large accessory hepatic vein from S VII larger than 5 mm in diameter: an anastomosis with the inferior vena cava (*IVC*) is performed utilizing a venous conduit (*VC*) harvested from the donor

celiac axis with the left graft is to maximize arterial supply to S IV as its arterial supply is routinely derived more from branches of the left than from branches of the right hepatic artery. The right hepatic vein is divided from the suprahepatic vena cava as a patch, and the FRG S V–VIII is removed. Because more common biliary variants are described in the right lobe, the common bile duct is retained with FRG (Fig. 13.16) and is flushed prior to cold storage in the cold perfusion solution. The FLG S I–IV graft is also removed, utilizing standard organ recovery techniques followed by the irrigation of the left bile duct and storage in cold preservation solution.

(a1) *Main steps of bench surgery and recipient operation*

The *ex situ* preparation of the FRG S V–VIII graft includes suture ligature of small biliary radicles and the potential restoration of all MHV branches draining S IV, S V, and S VIII to avoid congestion of the paramedian sector. Additionally, large accessory hepatic veins from S VI and S VII, when larger than 5 mm in diameter, should be anastomosed either directly to the vena cava or more optimally to some other venous conduit harvested from the donor (Fig. 13.17). This anastomosis can be performed with different techniques by employing donor iliac venous grafts and their secondary branches or the donor mesenteric vein. *Ex situ* preparation includes closure of the right portal vein orifice, the right hepatic vein orifice, and the right hepatic artery orifice from the common hepatic artery of the FLG S I–IV. All small parenchyma biliary orifices should be recognized and ligated. The FRG S V–VIII requires the recipient's inferior vena cava. The FRG is positioned orthotopically with a graft hepatic vein anastomosis to the recipient right hepatic vein orifice or to a common trunk formed by the recipient's remnant left, middle, and right hepatic vein orifices. End-to-end anastomosis of the portal vein is frequently possible, as the anastomosis of the right hepatic artery with the recipient common hepatic artery. Donor iliac arteries or veins may also be used for interposition grafting. Biliary drainage may be achieved in the recipient with an end-to-end anastomosis to the common bile duct. The FLG can be transplanted in the standard orthotopic manner with or without venovenous bypass or by a piggyback technique; biliary drainage is usually obtained with the left bile duct by Roux-en-Y bilio-jejunostomy or by an end-to-end anastomosis of the left duct with the donor common or left duct.

(b) *Split Liver for Two Adult Recipients or for Adult and Pediatric Recipient of Large Size with the Creation of a LG S II–IV and an RG S I, V–VIII*

Grafting of the left lobe S II–IV weighing approximately 400–450 g is usually performed for smaller adults or for larger pediatric recipients weighing 35–45 kg. This procedure is technically more difficult than the previous ones and requires particular skill and experience in splitting the liver [28]. The middle and left hepatic veins should be retained together with the FLG; they are encircled together with a vessel loop to guide parenchyma dissection. In this procedure, the "hanging manoeuvre" by retrohepatic tape can also be helpful to guide parenchyma dissection. Unlike the previous technique, the tape should be passed not on the right but on the left side of the caval border, leaving the caudate lobe with the RG S I, V–VIII. For this purpose, the tape should be positioned from

the groove between the right and middle veins to the groove between the right and left Glissonean sheaths along the posterior hepatic surface of the LLS and lying on the remnant of the *ductus Arantii*. The left bile duct, left hepatic artery, and left portal vein are identified and encircled by a vessel loop. The dissection should be performed distally along the entire extrahepatic length to the level of the round ligament. Left hepatic artery branch (or branches) servicing S IV must be preserved. The main difference in this technique is that the left portal vein should be freed along its entire length, and careful division of some small portal branches for caudate lobe (usually 1–5) is paramount to completely free the LG from the caudate lobe, which should be retained with RG S I, V–VIII. However, because some small portal branches are servicing the caudate lobe from the posterior wall of the portal vein, a complete dissection of these posterior small branches from the left portal vein can be better and safely performed only after cool perfusion and during bench surgery when their orifices can be suture ligated.

A temporary left pedicle occlusion, of both the left portal vein and the left hepatic artery, generates a clear demarcation plane for parenchyma transection. The plane is marked by electrocautery on the Glissonean capsule, and dissection proceeds to the hilar plate with the available surgical tools (CUSA, Harmonic Scalpel, monopolar electrocautery, and water cooling or simply by Kelly fracture and bipolar electrocautery). During this step, some parenchyma vessels are encountered and ligated. The left bile duct is sharply transected at the level of the hilar plate, whereas the left hepatic artery and left portal vein are preserved to ensure organ cold perfusion. After the administration of heparin, aortic cannulation, cross-clamp, and organ cold perfusion are started. Post-perfusion time requires the procedure to continue rapidly with sharp transection of the left portal vein immediately distal to the bifurcation and with transection of the right hepatic artery immediately distal to its takeoff from the proper hepatic artery. This technique requires that the common trunk of the portal vein and common hepatic duct are maintained with the right graft while preserving the celiac axis with the left graft as in the adult-to-pediatric technique. Because less collateral circulation is available in a small left lobe, the preservation of the celiac axis with the left graft can be paramount to maximize arterial supply to S IV, although some small branches can originate both from the left and from the right hepatic artery. The vena cava is retained with the RG S I, V–VIII. The left and middle hepatic veins are taken from the suprahepatic vena cava as a common venous cuff, and the left bile duct retained with the LG is flushed with perfusion solution prior to cold storage. This technique increases the risk of vascular and biliary complications because the perfusion of S IV may be sometime suboptimal. Complete dissection of the left portal vein can sacrifice some small portal branches to S IV; this manoeuvre associated with the arterial hypoperfusion of the same segment can lead to partial necrosis and bile leakage in that area.

(b1) *Main Steps for Bench Surgery and Recipient Operation*

Ex situ graft preparation of LG S II–IV only requires the identification and repair of cut-surface biliary orifices. For both FLG S II–IV and FRG S I, V–VIII, after standard organ recovery, the irrigation of the common bile duct should be performed, and grafts should be stored in cold perfusion solution. Vascular reconstruction with donor-derived conduit vessels may be required for the FRG.

The implantation of RG S I, V–VIII into an adult is accomplished in the standard orthotopic manner with or without venovenous bypass with a piggyback technique. An oversewing of the common vein orifice of the left and middle hepatic vein can compromise the suprahepatic vena caval cuff in width; the orifice can be kept open for a running suture to the recipient caval cuff using the piggyback technique. The right hepatic artery and the common trunk of the portal vein are anastomosed end-to-end with the recipient hepatic artery and portal vein. Interposition vascular venous and arterial grafts must be used for anastomosis to a suitable source of arterial inflow. Biliary reconstruction can be performed by

choledochocholedochostomy for RG with a T-tube, which reduce the biliary back pressure in order to prevent some bile leakage from the cut surface of the liver. The LG can be transplanted into a child or small adult with the preservation of the recipient vena cava. The middle and left hepatic vein cuff is anastomosed to the suprahepatic vena cava of the patient. However, because of size discrepancy, various venoplasty maneuvers must be often performed to avoid graft kinking. The majority of these techniques have been described by several authors [31–34]. Portal vein reconstruction must be individualized to the recipient's anatomy. In some cases, a direct end-to-end anastomosis is contraindicated, and anastomosis to the confluence of the splenic and superior mesenteric veins is required. In some cases, an extension venous graft is necessary to provide a tension-free anastomosis, but the use of venous grafts should be limited while the longest recipient portal axis should be preserved during hepatectomy. Hepatic artery reconstruction can be performed either to the hepatic artery of the recipient or to the aorta with a transmesocolic infrarenal iliac graft arterial conduit. If the left hepatic artery is retained with the LG, a microsurgical reconstruction by end-to-end anastomosis to the proper hepatic artery of the recipient should be performed. The left graft biliary tract reconstruction is usually accomplished by a Roux-en-Y left hepaticojejunostomy, and in one fourth of LG S II–IV, there are two or more separate bile ducts.

(c) *Ex Situ Splitting for Two Adult Recipients: Standard Technique and Splitting of the Retrohepatic Vena Cava and Middle Hepatic Vein*

The main surgical steps for ex situ splitting technique have been described above in paragraph Sect. 13.4.1. Only the lack of an extraepatic portal vein biforcation can be considered an absolute barrier to ex situ splitting. The liver can be divided through the middle of segment IV, retaining the MHV with the right graft. In some cases, the liver can be divided along the Cantlie line (the main portal scissure) separating the right and the left lobes and obtaining a FRG (S SV–VIII) and a FLG (SI, S II–IV) (Figs. 13.18, 13.19, 13.20); in this case all portion of S IV is allocated to the left graft to increase the graft-to-recipient body weight ratio. The middle hepatic vein can be kept on the left in continuity with the common trunk of the left and middle hepatic veins. The cutting lines are the same as for left hemihepatectomy in living donors. In this case, ex situ splitting may offer the advantage of full anatomical access to create the best optimal venous outflow in both grafts.

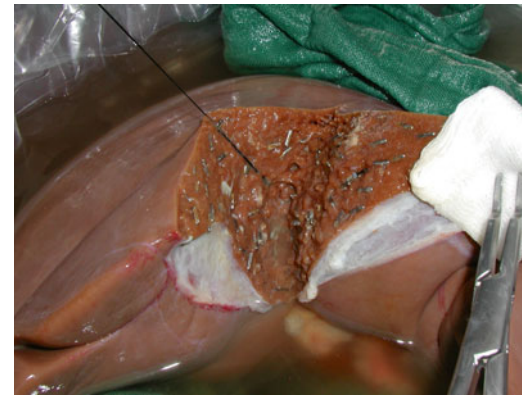

Fig. 13.18 Ex situ split liver for two adult recipients: parenchyma transection (Courtesy of Dr. Roberto Troisi, Ghent University Hospital and Medical School)

Sometimes the main problem associated with liver splitting for two adults is the possible congestion of the paramedian segments, S V, S VIII, and S IV, which can be evident only after revascularization; all these segments have some venous effluent to the MHV. Congestion of one or more than one segment with a higher probability of "small-for-size syndrome" and post transplant liver failure can be clearly evident during parenchyma division during in situ technique. In ex situ technique the lack of optimal blood flow in the paramedian segments can be recognized only after revascularization. At this regard some Authors have proposed the possibility to split longitudinally the inferior vena cava (IVC) into two parts [29]. Hilar dissection should start by the usual identification and preparation of the hepatic artery bifurcation

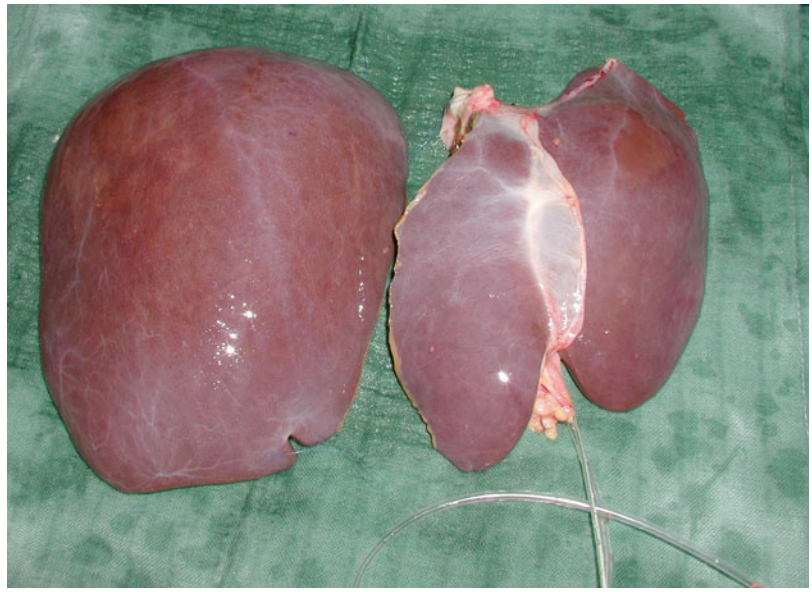

Fig. 13.19 Anterior view of split liver for two adults at the end of the procedure: the full right and full left liver graft (Courtesy of Dr. Roberto Troisi, Ghent University Hospital and Medical School)

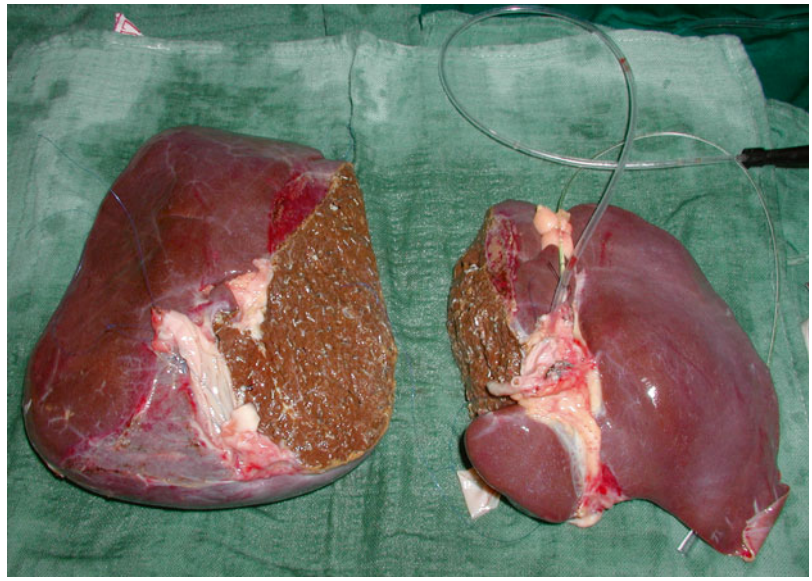

Fig. 13.20 Ex situ split liver for two adults at the end of the procedure, view of the inferior surface of the full right and full left liver graft (Courtesy of Dr. Roberto Troisi, Ghent University Hospital and Medical School)

and the S IV artery. The artery transection will depend on the origin of the S IV artery and on its functional relevance. The portal vein is dissected down to the main bifurcation, and the main portal vein is retained, as usual, with the left hemiliver to preserve the S I branches. The division of the bile duct retains the main bile duct with the right liver lobe due to the frequency of more biliary variants in the right hemiliver. Before starting the parenchyma transection, the dorsal and ventral wall of the IVC is cut along the midline, acquiring two hemicava patches (Fig. 13.21). Transection of the dorsal and ventral wall of the IVC in the midplane to conceive two hemicava patches is performed before starting the parenchyma

transection, which is conducted later by the sharp knife technique along the line of Cantlie.

The MHV is then cut from inside the IVC, preserving the half of the MHV for each of the two hemilivers. The parenchyma can be cut outside the IVC from S VIII 1–2 cm on the right side of the MHV, thus leaving its main orifice for the left graft and two portions of the MHV for each graft. At the end we will have two graft each of them with a large hemicava patch including two halves of the MHV with orifices of all draining veins (Fig. 13.22). Then, the split portion of the MHV of the left hemiliver is reconstructed with half an iliac artery, and for the right portion, an entire iliac vein graft is used (Fig. 13.23). Implantation of the grafts is performed using the standard techniques. For the venous outflow, a large venous anastomosis is performed using a cavo-cavostomy technique. The hemicava patch of the right graft can also be anastomosed by longitudinal extension of the opening of the recipient's right hepatic vein. Splitting of the MHV requires extra time for the ex situ venoplasty reconstruction with a longer ischemic time, which may increase the recipient morbidity, especially for biliary complications. For this reason, in our opinion this technique has a very

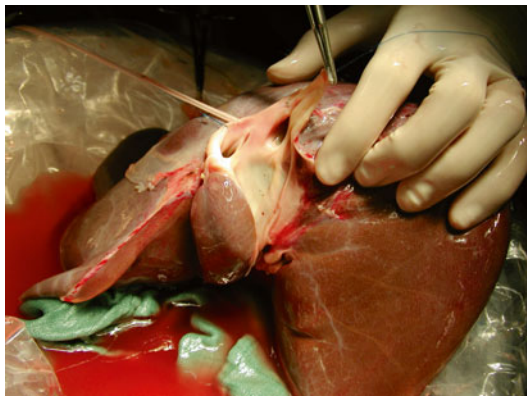

Fig. 13.21 Splitting of the vena cava: the posterior wall of the vena cava is divided longitudinally (Courtesy of Dr. Roberto Troisi, Ghent University Hospital and Medical School)

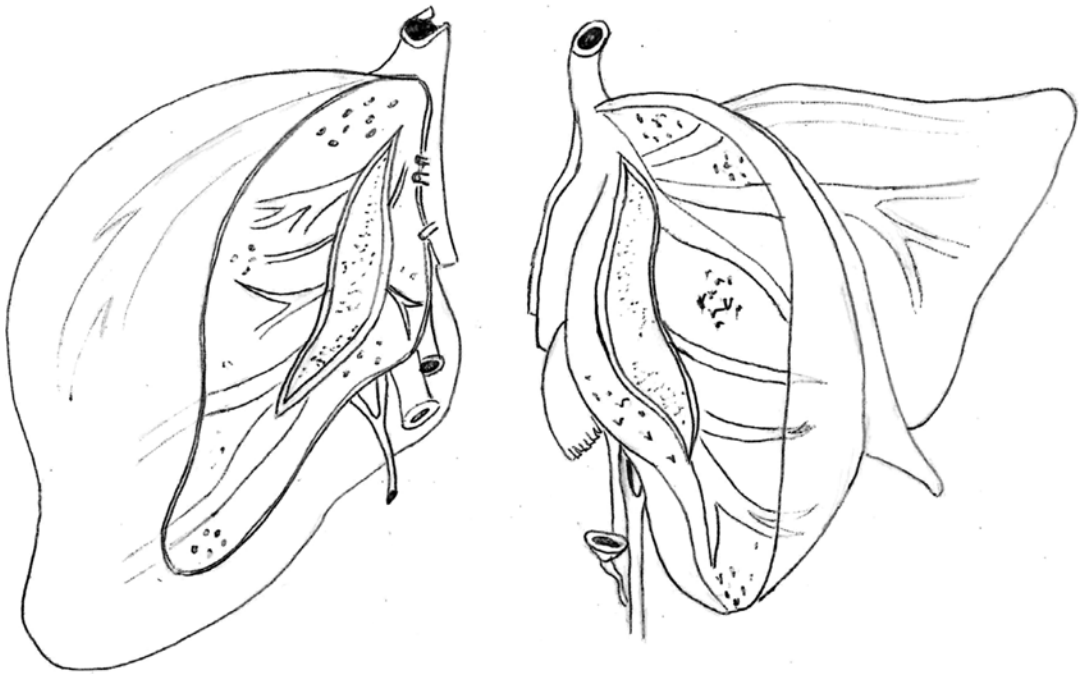

Fig. 13.22 Splitting of the vena cava and MHV: the MHV is cut from inside the IVC, preserving the half of the MHV for each of the two hemilivers

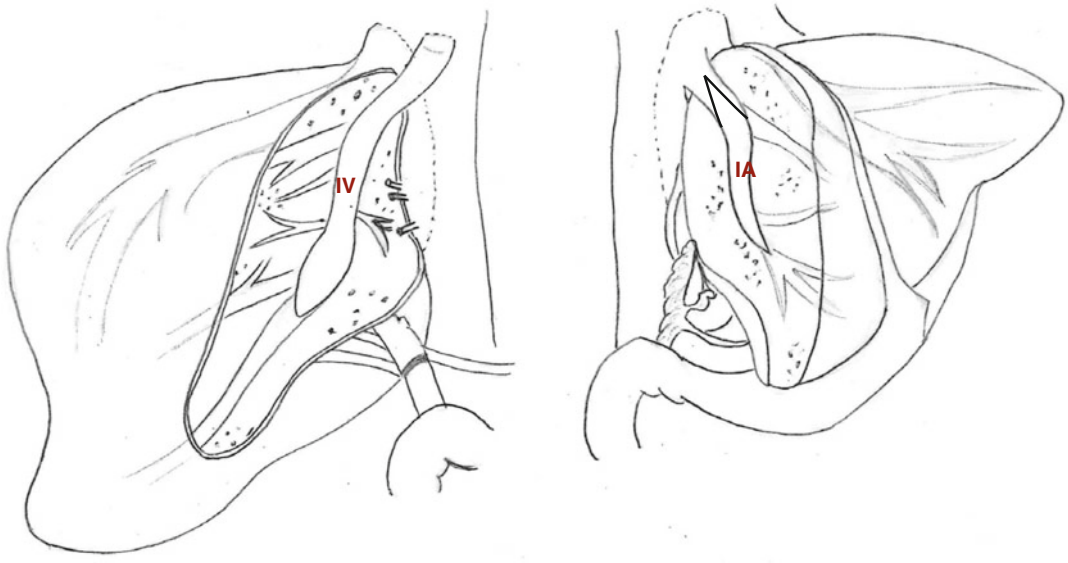

Fig. 13.23 Splitting the vena cava and the MHV: the split portion of the MHV of the left hemiliver is reconstructed with half an iliac artery (*IA*), and for the right portion, with an entire iliac vein (*IV*) graft

limited application in clinical practice. It can be taken into consideration when a high number of accessory hepatic veins from S IV, S V and S VIII are draining into the MHV with a strong dominance which may hamper the vascularization the right paramedian sector and S IV.

13.5 Conclusions

The widespread utilization of split-liver transplantation is hampered by difficulties in sharing liver grafts between centers, especially when the liver is split for two adults. Most centers agree to partial-liver grafts from deceased donors only when shared between adult and pediatric recipients, as excellent outcomes have been described [26]. Considering the good results in a large series of split-liver transplantation for adult and pediatric recipients and the excellent results also reported in living donor liver transplants [26–28], many centers are questioning the value of split-liver procedures for two adults in light of the difference between the benefit of the transplant community and the cost to the individual transplant recipients. As a matter of fact, a higher risk of morbidity and mortality for patients after liver transplantation exists with marginal whole organs compared to optimal split-liver grafts, although no randomized studies exist or will most likely ever exist on this issue. Some concern remains about the significant learning curve for the splitting procedures for two adults, and some questions remain unanswered about the risk of low volume of the split grafts, which can put the recipient at risk of small-for-size syndrome with subsequent liver failure, in particular for those patients with portal hypertension. However, a multicenter study has recently reported encouraging results when donors and recipients are carefully selected and meticulous techniques are adopted [1, 26–28, 33, 34]. A cooperative split-liver transplant program among different centers may investigate better allocation policies and most likely will allow better results provided that close supervision is ensured by more experienced centers.

References

1. Aseni P, De Feo TM, De Carlis L, Valente U, Colledan M, Cillo U, Rossi G, Mazzaferro V, Donataccio M, De Fazio N, Andorno E, Burra P, Split-Liver Study Group. A prospective policy development to increase split-liver transplantation for 2 adult recipients: results of a 12-year multicenter collaborative study. Ann Surg. 2014;259:157–65.

2. Smith B. Segmental liver transplantation from a living donor. J Pediatr Surg. 1969;4:126–32.
3. Bismuth H, Houssin D. Reduced-sized orthotopic liver graft in hepatic transplantation in children. Surgery. 1984;95:367–70.
4. Broelsch CE, Neuhaus P, Burdelski M. Orthotopic transplantation of hepatic segments in infants with biliary atresia. In: L K, Klinische Forschung, editors. Chirurgisches Forum '84f. Experim U. Berlin: Heidelberg-Springer; 1984.
5. Rogiers X, Malago M, Gawad K, Jauch KW, Olausson M, Knoefel WT, Gundlach M, Bassas A, Fischer L, Sterneck M, Burdelski M, Broelsch CE. In situ splitting of cadaveric livers. The ultimate expansion of a limited donor pool. Ann Surg. 1996;224:331–9.
6. Vulchev A, Roberts JP, Stock PG. Ethical issues in split versus whole liver transplantation. Am J Transplant. 2004;4:1737–40.
7. Busuttil RW, Goss J. Split liver transplantation. Ann Surg. 1999;229:313–21.
8. Giacomoni A, Lauterio A, Donadon M, De Gasperi A, Belli L, Slim A, Dorobantu B, Mangoni I, De Carlis L. Should we still offer split-liver transplantation for two adult recipients? A retrospective study of our experience. Liver Transpl. 2008;14:999–1006.
9. Pichlmayr R, Ringe B, Gubernatis G. Transplantation of a donor liver to two recipients (splitting transplantation) – a new method in the further development of segmental liver transplantation. Langenbecks Arch Chir. 1989;373:127–30.
10. Bismuth H, Morino M, Castaing D, Gillon MC, Descorps Declere A, Saliba F, Samuel D. Emergency orthotopic liver transplantation in two patients using one donor liver. Br J Surg. 1989;76:722–4.
11. Goss JA, Yersiz H, Shackleton CR, Seu P, Smith CV, Markowitz JS, Farmer DG, Ghobrial RM, Markmann JF, Arnaout WS, et al. In situ splitting of the cadaveric liver for transplantation. Transplantation. 1997;64: 871–7.
12. Azoulay D, Astarcioglu I, Bismuth H, Castaing D, Majno P, Adam R, Johann M. Split-liver transplantation. The Paul Brousse policy. Ann Surg. 1996;224:737–46.
13. Couinaud C. Le Foie. Paris: Masson; 1957.
14. Bismuth H. Surgical anatomy and anatomical surgery of the liver. World J Surg. 1982;6:3–9.
15. See Ching C, Chi Leung L, Chung Mau L, Lam BK, Lee EW, Yik W, Sheung Tat F. Estimating liver weight of adults by body weight and gender. World J Gastroenterol. 2006;12:2217–22.
16. Hill MJ, Hughes M, Jie T, Cohen M, Lake J, Payne WD, Humar A. Graft weight/recipient weight ratio: how well does it predict outcome after partial liver transplants? Liver Transpl. 2009;15:1056–62.
17. Rela M, Voregas V, Miniesan P, et al. Split liver transplantation: King's College Hospital experience. Ann Surg. 1998;227:282–8.
18. Yersiz H, Renz JF, Hisatake GM, Farmer DG, Busuttil RW. The conventional technique of in-situ split-liver transplantation. J Hepatobiliary Pancreat Surg. 2003;10:11–5.
19. Renz JF, Yersiz H, Reichert PR, Hisatake GM, Farmer DG, Emond JC, Busuttil RW. Split-liver transplantation: a review. Am J Transplant. 2003;3:1323–35.
20. Humar A, Ramcharan T, Sielaff TD, et al. Split liver transplantation for two adult recipients: an initial experience. Am J Transplant. 2001;1:366–72.
21. Broering DC, Wilms C, Lenk C, Schulte am Esch 2nd J, Schönherr S, Mueller L, Kim JS, Helmke K, Burdelski M, Rogiers X. Technical refinements and results in full-right full-left splitting of the deceased donor liver. Ann Surg. 2005;242:802–12; discussion 812–813.
22. Xavier Rogiers, Henri Bismuth, Ronald W. Busuttil, Dieter C. Broering, Daniel Azoulay (Eds). Split liver transplantation. Springer Edition. Heidelberg 2002. ISBN: 978-3-7985-1256-6 (Print) 978-3-642-57523-5.
23. Chaib E, Bertevello P, Saad WA, Pinotti HW, Gama-Rodrigues J. The main hepatic anatomic variations for the purpose of split-liver transplantation. Hepatogastroenterology. 2007;54:688–92.
24. Broering DC, Schulte am Esch J, Fischer L, Rogiers X. Split liver transplantation. HPB. 2004;6:76–82.
25. Emond JC, Whitington PF, Thistlethwaite JR, Cherqui D, Alonso EA, Woodle IS, Vogelbach P, Busse-Henry SM, Zucker AR, Broelsch CE. Transplantation of two patients with one liver. Analysis of a preliminary experience with 'split-liver' grafting. Ann Surg. 1990; 212:14–22.
26. Hong JC, Yersiz H, Farmer DG, Duffy JP, Ghobrial RM, Nonthasoot B, Collins TE, Hiatt JR, Busuttil RW. Long term outcomes for whole and segmental liver grafts in adult and pediatric liver transplant recipients: a 10-year comparative analysis of 2,988 cases. J Am Coll Surg. 2009;208:682–9; discusion 689–691.
27. Hashimoto K, Quintini C, Aucejo FN, Fujiki M, Diago T, Watson MJ, Kelly DM, Winans CG, Eghtesad B, Fung JJ, Miller CM. Split liver transplantation using hemiliver graft in the MELD Era: a single center experience in the United States. Am J Transplant. 2014;14:2072–80.
28. Lee WC, Chan KM, Chou HS, Wu TJ, Lee CF, Soong RS, Wu TH, Lee CS. Feasibility of split liver transplantation for 2 adults in the model of end-stage liver disease era. Ann Surg. 2013;258:306–11.
29. Broering DC, Pamela B, Lars M, Christian W, Xavier R. Splitting of the middle hepatic vein in full-right -full-left splitting of the liver. Liver Transpl. 2005;11: 350–2.
30. Broelsch CE, Whitington PF, Emond JC, Heffron TG, Thistlethwaite JR, Stevens L, Piper J, Whitington SH, Lichtor JL. Liver transplantation in children from living related donors surgical techniques and results. Ann Surg. 1991;214:428–37.
31. de Ville de Goyet J, di Francesco F, Sottani V, Grimaldi C, Tozzi AE, Monti L, Muiesan P. Splitting livers: trans-hilar or trans-umbilical division? Technical aspects and comparative outcomes. Pediatr Transplant. 2015;19:517–26.

32. Forti D. Transplantul cu ficat redus (“reduced size”) si impartit (“split”). Capitolul 2004;48:1098–1110. In: Irinel Popescu.Chirurgia Ficatului, Vol II. Editura Universitara “Carol Davila”
33. Yersiz H, Renz JF, Hisatake G, Reichert PR, Feduska NJ Jr, Lerner S, Farmer DG, Ghobrial RM, Geevarghese S, Baquerizo A, Chen P, Busuttil RW. Technical and logistical considerations of in situ split-liver transplantation for two adults: part I. Creation of left segment II, III, IV and right segment I, V-VIII grafts. Liver Transpl. 2001;7:1077–80
34. Yersiz H, Renz JF, Hisatake G, Reichert PR, Feduska Jr NJ, Lerner S, Farmer DG, Ghobrial RM, Geevarghese S, Baquerizo A, Chen P, Busuttil RW. Technical and logistical considerations of in situ split-liver transplantation for two adults: part II. Creation of left segment I–IV and right segment V–VIII grafts. Liver Transpl. 2002;8: 78–81
35. Makuuchi M, Sugawara Y. Technical progress in living donor transplantation for adults. HPB. 2004;2:95–8

Small-Bowel and Multivisceral Procurement

14

F. Di Benedetto and G. Tarantino

Tips, Tricks and Pitfalls

1. Careful selection must be paid to donor selection and size matching of donor with recipient.
2. Exploration of the abdominal cavity is a fundamental step during small-bowel and multivisceral procurement.
3. Attention must be paid after Kocher plus Cattell–Braasch manoeuvre, isolating the inferior mesenteric vessels for possible injuries to the right ureter, especially if there are anatomical variants.
4. Utmost attention should be paid to the possible presence of a right branch for the liver from the superior mesenteric artery, and/or of a left hepatic artery from the left gastric artery.
5. Henle's trunk (when present), or the inferior pancreaticoduodenal vein itself, must be preserved so as not to damage pancreatic vascularization. At the same time, it is possible to damage the jejunal branches of the superior mesenteric artery, thus compromising the first part of the bowel graft.
6. After perfusion, the graft should be wrapped inside a towel, to prevent ice burns.

14.1 Introduction

The constant progress in intestinal transplantation (ITx) over the last decade is secondary to a combination of several factors: a better definition of the indications and timing of referral for transplant; improved immunosuppression strategies based on both induction therapy and calcineurin inhibitors; the introduction of different methods to monitor bowel graft status such as zoom ileoscopy, cytoscan and intestinal biopsies and finally better control of infectious complications and post-transplant lympho-proliferative disease (PTLD) [1]. The combination of all these factors determined an increase in both patient and graft survival, as well as an increase in the number of organs transplanted and centres performing this type of complex procedure worldwide.

The history of ITx goes back about a century referring to the innovative work of Alexis Carrel with experimental animal studies [2], and later in

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the middle of the twentieth century by Lillehei et al. [3] as an isolated graft, and then by Starzl and Kaupp [4] as part of a multivisceral homotransplantation in a canine model. During the following decades, poor results came from various attempts to perform ITx because of the onset of technical complications, sepsis or rejection. Only a few sporadic successful cases at the end of the 1980s included the first successful multivisceral transplant in Pittsburgh, USA, in 1987 [5], followed by the first successful isolated ITx in 1989 in Germany [6], then in France [7] and in Canada [8].

Only after the introduction of calcineurin inhibitors, namely, tacrolimus, in the early 1990s, was ITx an available therapeutic option for patients affected by intestinal insufficiency [9], and thus increasing patient and graft survival rates.

These results were further improved with advances in induction protocols, post-transplant care, and operative techniques.

The definition of types of intestinal grafts originates from the 'cluster' approach first described Starzl [4, 5, 8] in his manuscripts that reported the use of intestinal and multivisceral grafts (Fig. 14.1). There is general consensus to define isolated ITx as the implantation using the jejunoileal axis alone, with vascular anastomoses based on the superior mesenteric vessels, as well as the use of the term liver–intestine for grafts that include a hepatic graft with the small bowel. The latter can be defined as 'non-composite liver–intestine transplant' when separate vascular

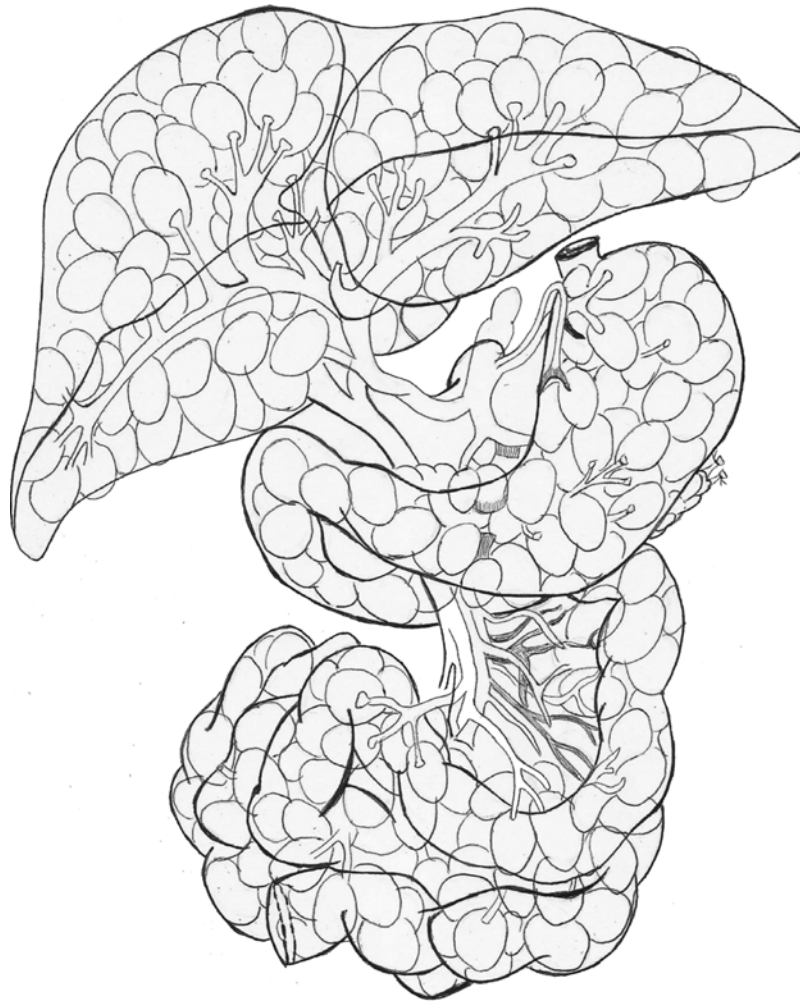

Fig. 14.1 Cluster theory for intestinal and multivisceral procurement and transplantation (From Casavilla et al. [19])

anastomoses are performed for each of the hepatic and intestinal grafts. On the other hand, while these kinds of transplantations represent exact descriptions, the term 'multivisceral transplantation' is used for the transplantation of any small bowel-contained visceral allograft (liver, pancreas, duodenum, small bowel) which includes 'stomach'. This can be 'full' or 'modified' according to the inclusion or exclusion of donor liver, respectively. A full multivisceral graft is usually defined when the liver, stomach, pancreas, duodenum and small bowel are included. Also right colon and ileocecal valve implantation has been reported by some authors [10], in particular in recipients affected by dysmotility disorders and minimal native rectosigmoid colon.

14.2 Donor Selection

Harvest begins with a careful selection of the donor in each case, paying utmost attention particularly to body weight and residual abdominal cavity of the recipient: size-matching donor with recipient is the first pitfall in intestinal transplantation and probably one of the most important ones, because a mistake can lead to transplant failure.

The management of the abdominal wall closure is considered to be a fundamental step in the process of ITx that reflects the importance of careful candidate selection, during the matching of donor/recipient and during the planning of the surgical procedure. Nowadays, several tools are available to help with a lack of abdominal domain and can mainly be divided into two groups. The first aims to reduce the abdominal content (using small donors, or reduced grafts) and the second focuses on enlarging the abdominal domain. Examples of these strategies are the use of rotational flaps [10]; the use of permanent non-biological re-absorbable or non-reabsorbable meshes [11] and the use of the acellular dermal matrix from donated human skin. More recently, a new technique has been developed using a vascularized composite tissue graft from the donor's abdominal wall used as a free flap. This process is known as 'abdominal wall transplant' [12]. The wall graft can be implanted into the recipient iliac vein and artery or directly to the recipient epigastric vessels by using microsurgical anastomosis. This procedure presents different advantages such as a low immunogenicity and the possibility to be performed during the transplant or later from a different donor. Another possibility is to use the fascia of the rectum muscle as a non-vascularized graft for abdominal wall closure. This procedure can be easily performed, does not present any extra cost and presents low immunogenicity. The fascia is then covered by the recipient skin closure, integrating to the abdominal wall, and thus creating a firm scar tissue that would substitute the original fascia tensile strength avoiding the development of incisional hernias.

Donor obesity is a relative contraindication to harvest, because the fatty and heavy mesentery can cause thrombosis of the vascular anastomoses of the recipient.

Donors with negative serology for cytomegalovirus (CMV) have been, for a long time, preferred to CMV-positive donors; however, nowadays the increasing need for transplantation and the shortage of donors have made the use of CMV-positive donors into CMV-positive or naive recipients common. In fact, the use of viral pre-emptive therapy determines no significant difference in outcome compared with the use of negative donors; thus, CMV matching is not considered mandatory anymore [13].

Cause of death is nowadays still considered essential in donor selection: even though a trauma donor should not be eliminated from selection because most abdominal traumas affect liver and spleen while the bowel can be protected by its natural relative mobility inside the abdomen.

Heart-beating donors are still the preferred cadaveric donors. Donation after cardiac death is currently not utilized for the retrieval of intestinal grafts. On the other hand, the possibility to use donors with previous cardiopulmonary resuscitation is still a matter of debate and, however, is seen as a contraindication. Nevertheless, a recent study [14] reported that the utilization of these kinds of donors showed no differences compared with ideal donors in terms of recipient length of

hospital stay, graft survival, time for total parenteral nutrition discontinuation or incidence and degree of rejection. The use of amine is historically considered controversial, but the fine vessels composing the arterial arcades of the jejunal and ileal loops are particularly sensitive to ischemia induced by pressors.

Blood group identical donors are preferred, but compatible mismatch donors have been successfully used in isolated and multi-organ transplant recipients in urgent need of transplantation [15]. Furthermore, patients undergoing ITx are likely to have up to 30 % chance of having high-panel-reactive antibody titres. Until recently, ITx was not indicated in those cases with a positive T-cell cross-match, but this limit can nowadays be overcome with the application of immunomodulation strategies.

Ideally most of donors should be under 40 years of age, died of cerebrovascular accident, be haemodynamically stable and with minimal or no vasoactive amine support: the importance of age can be questionable, but younger donors have statistically less possibilities to have bowel polyps (or cancer) than older ones.

If judged suitable, the donor undergoes selective bowel decontamination, performed through a nasogastric tube, with antibacterial and antifungal drugs, to avoid bacterial overgrowth and subsequent translocation during cold ischemia time.

After laparotomy, we carefully evaluate the liver (in case of multivisceral harvest with liver) and all the digestive tract and, if there is any doubt, we always do not proceed with the operation: the presence of bowel mass should exclude the use of the donor, such as mesenteric hematomas; reperfusion of the intestine can be, in those last cases, disastrous.

14.3 Surgical Technique

During inspection of the bowel, utmost attention should be paid to colour, oedema, peristalsis and pulses. The presence of Meckel diverticula does not compromise the harvest. The first step of intestinal or multivisceral procurement is isolation of the superior mesenteric artery (SMA) origin from the aorta: to achieve this, we perform a Kocher plus Cattell–Braasch manoeuvre, mobilizing the ascending colon toward the left (Fig. 14.2), cutting the Treitz ligament and all the mesenteric ligaments as well and tying the inferior mesenteric vessels [16]. The main pitfall during this manoeuvre can be injury to the right ureter, especially if there are anatomical variants. In this way, discovering completely the left renal vein and the mesenteric root, we can isolate the SMA origin, cutting part of the celiac ganglion surrounding the artery. Utmost attention should be paid to the possible presence of a right branch for the liver from the SMA [17]. The second step is the dissection of the coloepiploic ligament and the opening of the lesser sac with isolation of the middle colic vein: this is mandatory during isolated intestinal harvest to reach and isolate the superior mesenteric vein (SMV), and it is necessary for multivisceral harvest as well to create the distal part of the graft, represented by the transverse colon with the middle colic vein. For this purpose, a GIA 75 linear stapler can be used to cut the transverse colon on the left anatomical side of the middle colic vein, thus preserving it with the graft.

The colon is necessary to properly orientate the graft and can also be used as part of isolated or multivisceral transplant.

During this manoeuvre, it is possible to injure Henle's trunk (when present) or the inferior pancreaticoduodenal vein itself, damaging pancreatic vascularisation. At the same time, it is possible to damage the jejunal branches of the SMA, often running parallel to the SMV main trunk, thus compromising the first part of the bowel graft (Fig. 14.3).

The third step is the isolation of the proximal part of the graft, duodenum for the isolated small bowel and oesophagus for the multivisceral; the duodenum should be cut using a GIA 75 stapler in its 4th part, already isolated in previous steps. Cutting the left triangular ligament of the liver and the diaphragmatic crura, we reach the

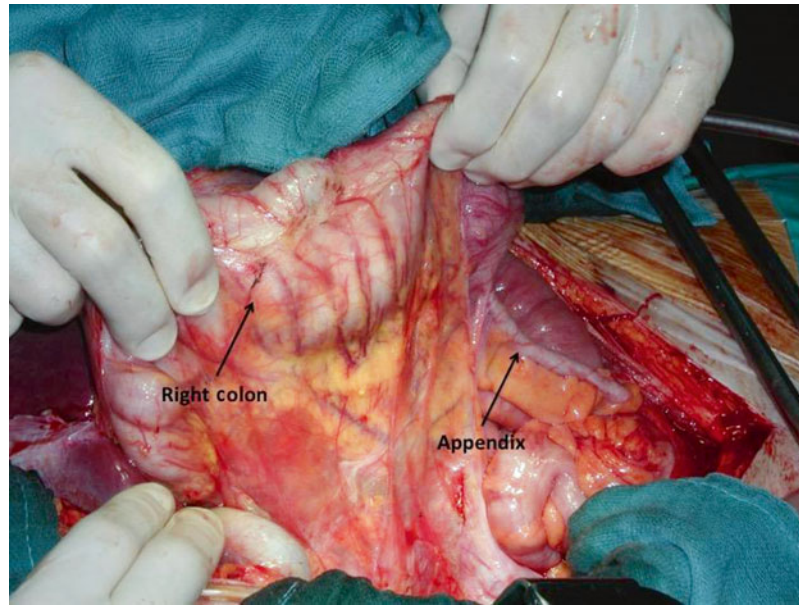

Fig. 14.2 Cattell–Braasch manoeuvre: mobilization of the ascending colon toward the left till the hepatic flexure

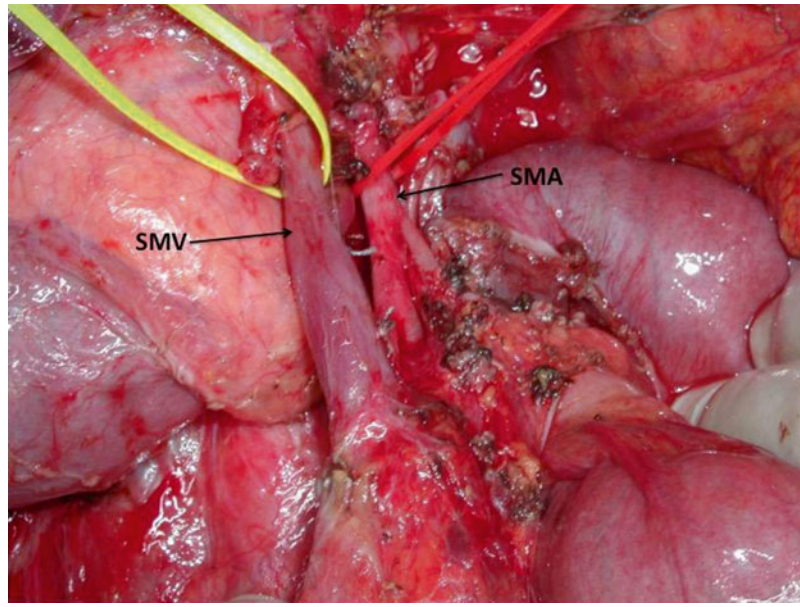

Fig. 14.3 Isolation of superior mesenteric vein (*SMV*) and superior mesenteric artery (*SMA*)

oesophagus, dividing the distal part of the oesophagus again with the aid of a GIA 75 linear stapler: attention should be paid to not damaging a possible left branch of the liver arising from left gastric artery. Then the warm phase can be ended by complete mobilization of the graft from distal oesophagus (or duodenum if isolated small bowel) to transverse colon, cutting all the ligaments with electrocautery: bleeding from these small mesenteric vessels at reperfusion can lead to tedious haemostasis and should be avoided. The last step of the warm phase during multivisceral harvest is the isolation of the pancreas and the aortic origin of the celiac trunk: to

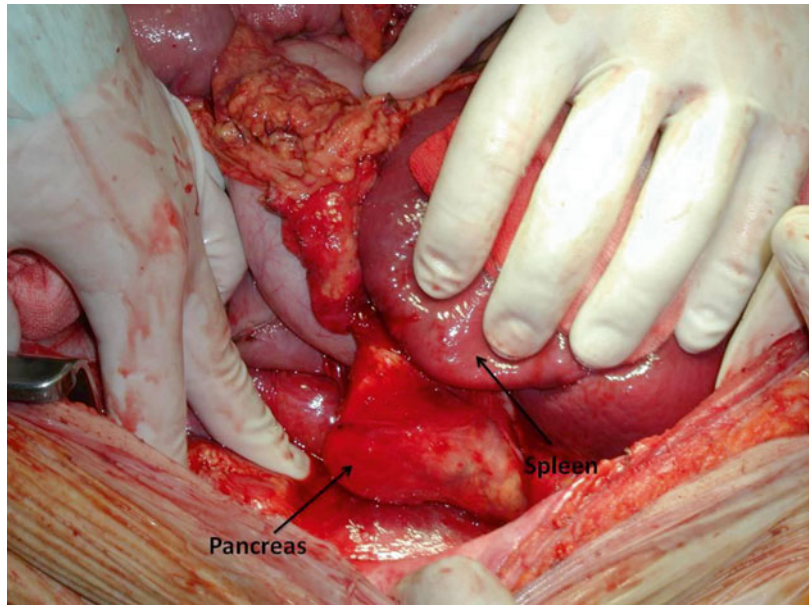

Fig. 14.4 Mobilization of the spleno-pancreatic block

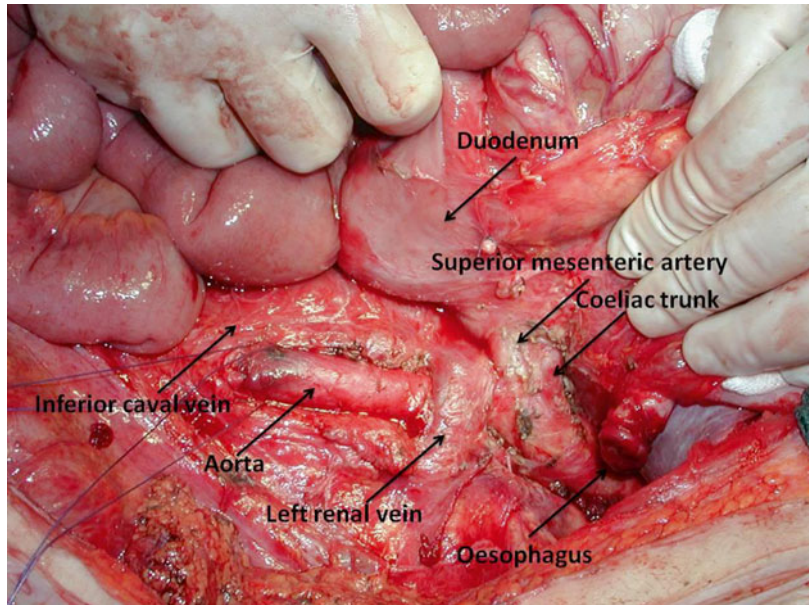

Fig. 14.5 Complete exposition of retroperitoneal vessel and isolation of SMA and coeliac trunk

obtain this, we mobilize the spleen from the retroperitoneum (Fig. 14.4), and, working on a surgical plane above the left Gerota's fascia, we completely mobilize the tail and the body of the pancreas and the pancreaticoduodenal block, thus reaching the origin of the celiac trunk (Fig. 14.5). Attention should be paid not to injure the spleen itself and the left kidney. The celiac trunk must be freed from the celiac ganglia surrounding it. Then we complete isolation of the

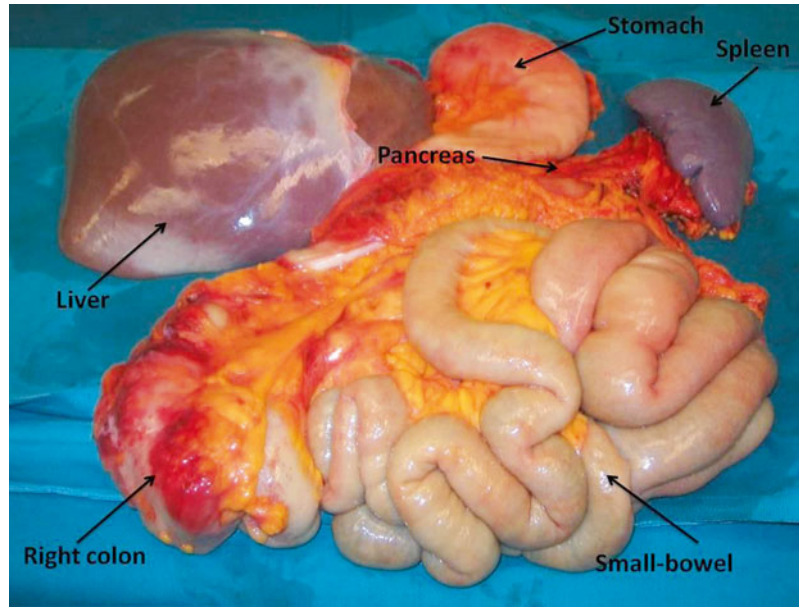

Fig. 14.6 Multivisceral graft

proximal and distal part of the abdominal aorta (for cross-clamping) and flush the gallbladder.

The graft should be wrapped inside a towel, to prevent ice burns. After cross-clamping and cold perfusion, the intestine should blanch homogenously. Avoiding portal cannulation is mandatory. During multivisceral harvest, we create an enlarged aortic patch including the origin of the SMA and the celiac trunk, paying attention not to damage the renal arteries. On the SMA and SMV origins, a Prolene suture should be placed (usually in the right vascular wall) for orientation of the bowel graft. In case of multivisceral retrieval without the liver, earlier in the 'warm' phase we prepared the hepatic hilum [18], isolating the main biliary duct, proper hepatic artery and portal vein: these structures must be shared with the liver team, and usually the main biliary duct is cut just above the duodenum, proper hepatic artery close to the gastroduodenal artery (GDA) origin and portal vein is shared with the liver team. In cases of the right branch from the SMA or the left branch from the left gastric artery, the multivisceral harvest should be aborted in favour of the liver, even if some vascular reconstructions at the back table are still possible. Theoretically right hepatic artery can be reconstructed on donor's GDA, if both vessels show comparable calibre. On the other hand, SMA could alternatively be cut just below the right hepatic accessory artery. This procedure should be discussed among the liver and small-bowel procurement teams. Indeed, the presence of the right branch does not exclude the simultaneous multi-organ harvest of the liver, pancreas and isolated small bowel. If multivisceral harvest with liver is necessary, a total hepatectomy is associated to the procedure, cutting the inferior vena cava above the diaphragm and above the origin of the renal veins, being careful not to damage them (Fig. 14.6). The operation must be concluded harvesting the iliac vessels as vascular grafts, watching both ureters. An aortic conduit (in cases of multivisceral transplantation) can be created harvesting the thoracic aorta. In this way, we minimize the 'cold' part of the harvest and the ischemia time, and the back table is a fast procedure, requiring only preparation of the origin of the vessels for anastomosis purposes (Fig. 14.7).

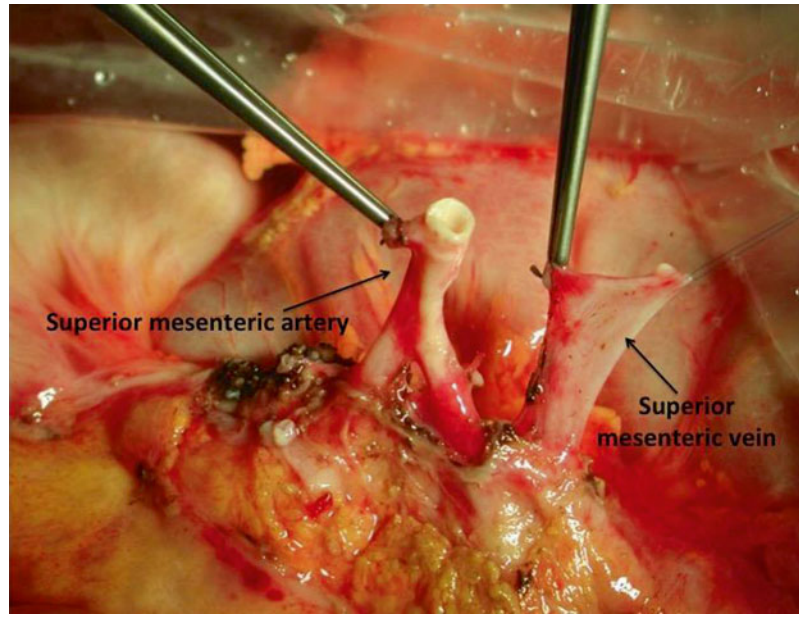

Fig. 14.7 Back table and preparation of SMA and SMV

References

1. Di Benedetto F, Quintini C, Lauro A et al (2004) Outcome of isolated small bowel and pancreas transplants retrieved from multiorgan donor: the In Vivo technique. Transplant Proc 36:437–438
2. Carrel A (1902) La technique des anastomese vasculaires et la transplantation des visceres. Lyon Med 98:859
3. Lillehei RC, Goott B, Miller FA (1959) The physiological response of the small bowel of the dog to ischemia including prolonged in vitro preservation of the bowel with successful replacement and survival. Ann Surg 150:543–560
4. Starlz TE, Kaupp HA Jr (1960) Mass homotransplantations of abdominal organs in dogs. Surg Forum 11:28
5. Starlz TE, Rowe MI, Todo S et al (1989) Transplantation of multiple abdominal viscera. JAMA 261:1449
6. Deltz E, Schroeder P, Gebhardt H, Gundlach M, Engemann R, Timmermann W (1989) First successful clinical small intestine transplantation. Tactics and surgical technic. Chirurg 60:235
7. Goulet O, Re Villon Y, Jan D et al (1990) Small-bowel transplantation in children. Transplant Proc 22:2499
8. Starzl TE, Todo S, Tzakis A et al (1991) The many faces of multivisceral transplantation. Surg Gynecol Obstet 172:335–344
9. Di Benedetto F, Lauro A, Masetti M et al (2005) Outcomes after adult isolated small bowel transplantation: experience from a single European centre. Dig Liver Dis 37(4):240–246
10. Gondolesi G, Fauda M (2008) Technical refinements in small bowel transplantation. Curr Opin Organ Transplant 13(3):259–265
11. Di Benedetto F, Lauro A, Masetti M et al (2005) Use of prosthetic mesh in difficult abdominal wall closure after small bowel transplantation. Transplant Proc 37:2272–2274
12. Levi AG, Tzakis AG, Kato T et al (2003) Transplantation of the abdominal wall. Lancet 361:2173–2176
13. Selvaggi G, Tzakis AG (2009) Small bowel transplantation: technical advances/updates. Curr Opin Organ Transplant 14(3):262–266
14. Matsumoto CS, Kaufman SS, Girlanda R et al (2008) Utilization of donors who have suffered cardiopulmonary arrest and resuscitation in intestinal transplantation. Transplantation 86:941–946
15. Grant W, Langnas A (2002) Pediatric small bowel transplantation: techniques and outcomes. Curr Opin Organ Transplant 7:202–207
16. Nickkholgh A, Contin P, Abu-Elmagd K et al (2013) Intestinal transplantation: review of operative techniques. Clin Transplant 27(Suppl 25):56–65
17. Abu-Elmagd K, Fung J, Bueno J et al (2000) Logistics and technique for procurement of intestinal, pancreatic, and hepatic grafts from the same donor. Ann Surg 232:680–687
18. Di Benedetto F, De Ruvo N, Masetti M et al (2006) Hepatic hilum management in 250 liver-multivisceral procurements. Transplant Proc 38(4):1068
19. Casavilla A, Selby R, Abu-Elmagd K, Tzakis A, Todo S, Reyes J, Fung J, Starzl TE (1992) "Logistics and technique for combined hepatic-intestinal retrieval". Ann Surg 216(5):605–609

Pancreas Procurement

15

Silvio Nadalin, Ivan Capobianco, and Stefan Hulik

Abbreviations

BDD	Brain-dead donor
CHA	Common hepatic artery
CT	Celiac trunk
DCD	Donor after circulatory death
DD	Deceased donor
DPA	Dorsal pancreatic artery
GDA	Gastroduodenal artery
HA	Hepatic artery
HTK	Histidine-tryptophan-ketoglutarate
IPDA	Inferior pancreaticoduodenal artery
LT	Liver transplantation
MO	Multiorgan
MOP	MO procurement
PT	Pancreas transplantation
RHA	Right hepatic artery
RRHA	Replaced right hepatic artery
SA	Splenic artery
SMA	Superior mesenteric artery
SMV	Superior mesenteric vein
SPDA	Superior pancreaticoduodenal artery
SV	Splenic vein
UW	University of Wisconsin

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Tips, Tricks, and Pitfalls

- The technique and quality of pancreas procurement significantly influence the outcome of pancreas transplantation.
- The quality of the procurement of the pancreas is a multifactorial reality essentially influenced by donor quality, excellent and experienced procurement surgeon, and precise standardized technique.
- After accurate donor selection and donor management at ICU, a perfect pancreas procurement is based on a wide anatomical knowledge, an accurate inspection of the graft, a gentle and precise preparation of the pancreas, and adjacent vascular structures in different phases.
- Prolonged time to remove the organs after cold perfusion increases the risk of rewarming and could lead to organ dysfunction posttransplantation.
- Every pancreas procurement surgeon should be aware of the complex vascular anatomy of the pancreas including its potential anatomical variations.
- Because of the potential risks of duodenal distension and enteric contamination in vivo, it is advisable to delay stapling of the distal duodenum/proximal jejunum until just prior to start with the removal of the pancreas.

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- Shortening the portal vein has the advantages of both preventing a kink and conferring protection from compression by the surrounding tissues.
- Minimizing cold ischemia (<12 h) is one of the single most important predictors of success in pancreas transplantation irrespective of donor quality or method of preservation.
- Pancreas should be mobilized medially up to the aorta taking care not to injure the left renal vein, SA, or SV using the spleen as a handgrip (no-touch technique).
- Iliac graft vessels for bench reconstruction should be procured by an experienced surgeon since improper technique or traction injuries may affect the outcome of the transplant procedure.

15.1 Introduction

The pillars of successful pancreas transplantation in chronological sequence are represented by (1) donor selection, (2) pancreas procurement, (3) logistic and shipping, (4) pancreas recipient, (5) preparation of the pancreas graft at back table, and (6) implantation of the pancreas graft.

Among the above-reported factors, the quality of the procurement of the pancreas plays a central role in the outcome of pancreas transplantation. It is a multifactorial reality essentially influenced by donor quality, excellent and experienced procurement surgeon, and precise standardized technique.

In this chapter, we will mainly concentrate on single pancreas procurement from brain dead donors, and we will go through the following aspects influencing the quality of pancreas retrieval and consequently the outcome of pancreas transplantation:

1. Pancreas donor profile
2. Anesthesiological and ICU management of pancreas donor
3. Pancreas procurement surgeon
4. Anatomical backgrounds
5. Isolated pancreas procurement operation
6. Other aspects:
   - En bloc pancreas and liver procurement
   - Pancreas procurement from DCD donors

15.2 Pancreas Donor Profile

There are different ways and different parameters used to define the ideal pancreas donor. Age, BMI, cause of death, sodium, and pancreas enzymes are the most used variables with different ranges. Although most of the authors consider 50 years as the older age for acceptance, Stegall proposed to extend the acceptance over 50 years [1]. On the opposite side, Brockmann [2] and Biglarnia [3] demonstrated the feasibility of pancreas transplantation even with small pediatric donors.

In general, the "ideal" pancreas donor ranges in age from 10 to 40 years, has a BMI <27 kg/m^2, and is a brain-dead donor as a result of trauma rather than cerebrovascular disease [4].

Other centers consider also additional parameters like the presence/absence of abdominal trauma, signs of pancreatitis or pancreas edema at imaging [5], or the amount of blood substitution occurred before pancreas procurement [6].

The most used scores actually used for identification of ideal pancreas donor are represented by the pre-procurement pancreas suitability score P-PASS (Table 15.1) and by the pancreas donor risk index (P-DRI) (Table 15.2).

The P-PASS was introduced in Eurotransplant area 2008 by Vinkers et al. [7, 8] in order to identify/select the ideal pancreas donor who is usually characterized by a score ≤17. Although the P-PASS was able to influence the acceptance/refusal rates of pancreas grafts [7], it did correlate with the postoperative outcome but did not correlate with the long-term outcome [9].

Axelrod et al. [10] introduced in 2010 the pancreas donor risk index (P-DRI), a more reliable score than the P-PASS which has been now

Table 15.1 Pre-procurement pancreas suitability score (P-PASS) [8]

Donor characteristics	One point	Two points	Three points
Age (year)	<30	30–40	≥40
BMI (kg/m^2)	<20	20–25	≥25
ICU stay (day)	<3	3–7	≥7
Cardiac arrest (min)	No	Yes, <5	Yes, ≥ 5
Sodium (mmol/L)	<155	155–160	≥160
Amylase (U/L)	<130	130–390	≥390
Lipase (U/L)	<160	160–480	≥480
(Nor)adrenaline	No	<0.05 gamma	≥0.05
Dobuta-/dopamine	No	<10	≥10
Total points	9	18	27

Table 15.2 Pancreas donor risk index (P-DRI) [10]

Donor characteristics	Reference donor (*DRI* = 1.00)	Change factor value to	DRI
Gender	Male	Female	0.87
Age	28	45	1.56
Black race	No	Yes	1.27
Asian race	No	Yes	1.17
BMI	24	30	1.17
Height (cm)	173	190	0.90
Cause of death: CVA/stroke	No	Yes	1.23
Cause of death: CVA/stroke in PAK	No	Yes	0.93
Pancreas preservation time (h)	12	20	1.13
DCD	No	Yes	1.38
SCr >2.5	No	Yes	1.22

From Axelrod et al. [10].
BMI body mass index, *CVA* cardio vascular accident, *DCD* donor after circulatory death, *PAK* pancreas after kidney

$$\begin{aligned}\text{pDRI} = \exp(&-0.13792 \times I\left[\text{Female Donor}\right] - 0.034455 \times I\left[\text{Donor Age} - 20\right] \\ &+ 0.026149 \times \left[\text{Donor Age} \quad 28\right] + 0.19490 \times I\left[\text{Donor Creatinine} > 2.5\right] \\ &+ 0.23951 \times I\left[\text{Donor Black Race}\right] + 0.15711 \times I\left[\text{Donor Asian Race}\right] - 0.000986347 \times \left[\text{Donor BMI} - 24\right] \\ &+ 0.0033274 \times I\left[\text{Donor BMI} > 25\right] \times \left[\text{Donor BMI} - 25\right] - 0.006073879 \times \left[\text{Donor Height} - 173\right] \\ &+ 0.21018 \times \left[\text{Donor COD CVA}\right] - 0.28137 \times I\left[\text{Donor COD CVA for PAK txp}\right] \\ &+ 0.014678 \times \left[\text{Preservation Time} - 12\right] + 0.33172 \times I\left[\text{DCD}\right])\end{aligned}$$

adopted US wide and in most of Western world. According to Axelrod et al., a P-DRI <1,57 represents an ideal pancreas donor.

However, many centers do not consider any of the above mentioned parameters and use their own selection criteria. For example, in Innsbruck [5], the following parameters have been considered: age 5–55 (high risk >45), BMI <30, ICU stay <7 days, no signs of pancreatitis (acute/chronic), no abdominal trauma, no intra-abdominal infection, and no severe pancreas edema or lipomatosis (based on imaging findings).

If from one side one could be tempted to extend the selection criteria, from the other side it would be advisable to be more restrictive as possible. At this regard, the intestinal donor profile reported by Fischer-Frohlich et al. [11]. Table 15.3 may represent a sort of super selected ideal pancreas donor as well.

Table 15.3 Currently proposed standard inclusion criteria for intestinal and multivisceral donors

Donor data	Range in an ideal donor
Age	0–50 years
Donor-recipient size match	DRWR and DRHR compatible
BMI	<28
ICU Stay	<1 week
Enteral nutrition	Initiate within 25 h after admission
CPR	<10 min
Trauma mechanism	Absence of direct or blunt abdominal trauma
Sodium	Most recent <155 mmol/L peak (last 24 h) <165 mmol/L
Transfusions	No significant ongoing requirements at time of procurement
Medication	Standard donor therapy
Preservation solution	HTK or UW (HTK should be preferred)
Blood	Identical or compatible

From Fischer-Frohlich et al. [11]
CPR cardio pulmonary resuscitation, *QRWR* donor-recipient weight ratio, *DRHR* donor-recipient height ratio, *ICU* stay intensive care unit

Table 15.4 Summary of target perioperative parameters in multiorgan donors

Systolic blood pressure	>90 mmHg
Mean arterial pressure	>60 mmHg
Heart rate	<100 bpm
Central venous pressure	8–10 mmHg
Systemic vascular resistance	>1000 dyne per s per cm
Arterial saturation	>90 %
PaO_2	>60 mmHg (>8 kPa)
FiO_2	<40 %
Positive end-expiratory pressure	>7.5 cmH_2O
Peak inspiratory pressure	<30 cmH_2O
Tidal volume	6–8 mL/kg
pH	7.35–7.40
PCO_2	35–45 mmHg (4.67–6.0 kPa)
Na+	<155 mEq/dL
Urine output	0.5–2.5 mL/kg/h
Blood glucose target concentrations	4–8 mmol/L

15.3 Management of Pancreas Donor at ICU

General anesthesiological and ICU management of BDDs is in the meanwhile a standardized procedure mainly focused on restoration of physiological and metabolic homeostasis of the transplantable organs and tissues [12, 13].

The actual targets of perioperative parameters in multiorgan BDDs are summarized in Table 15.4.

With special regard to pancreas donation, particular care should be taken in the following conditions:

- Review fluid balance and correct hypovolemia; be aware that vascular tone may be impaired. Use cardiac output monitoring if possible to titrate fluids and inotropic or pressor drugs to intended goals as guided by retrieval team. In the setting of low systemic vascular resistance and hypotension, vasopressin or norepinephrine may be considered, especially in combination with infusion of an inotrope such as epinephrine [2] although the use of high doses of vasopressors can induce unpredictable effects in the splanchnic circulation with reduced portal flow and intestinal ischemia.
- Administer maintenance fluids (enteral route can be used), but avoid positive balance and hypernatremia. Correct electrolyte abnormalities to normal values. Correction of serum sodium levels to <155 mEq/dL is recommended.
- Maintain and start enteral feeding as soon as possible.
- For treatment of diabetes insipidus, replace first the free water deficit, and second, give desmopressin short thereafter. Inadequate treatment of this condition causes severe hypernatremia, hypocalcemia, hypokalemia, hypophosphatemia, and hypomagnesemia. The use of desmopressin in pancreas donors is controversial; univariate analysis of a large series showed a significantly higher risk of pancreas graft thrombosis if the organ came from a desmopressin-treated donor.

- Hormonal therapy with triiodothyronine, insulin, and steroids in BDDs has been shown to lead to metabolic and hemodynamic stability, reducing wastage of organs and improving function after transplantation [2]. Intravenous infusion of insulin (1 unit/h minimum) is recommended for rapid correction of hyperglycemia and avoidance of islet cell exhaustion. However, hyperglycemia, unless due to preexisting diabetes, in a brain-dead donor does not appear to affect pancreas function after transplantation.
- In case of imaging studies that show evidence of pancreatic edema, one may consider administering intravenous mannitol and colloids [4].

15.4 Pancreas Procurement Surgeon

The procurement surgeon does represent a pivotal role in pancreas retrieval. In fact, it is extremely regrettable when a pancreas graft that is otherwise appropriate for transplantation is not retrieved either because of avoidable surgical damage, atypical anatomy, or the lack of availability of an experienced pancreas procurement surgeon [4].

The pancreas procurement surgeon should be preferably an experienced pancreas transplant surgeon him/herself. His/Her quality and reliability should be guaranteed through specific trainee/fellowship (see UK and US model), audits, and analysis of quality reports.

It would be preferable if the procurement surgeon belongs to the same recipient's transplant center [4, 5, 14, 15].

As demonstration of the high relevance of this topic, J. Loss et al. [16] published recently about the different criteria that play a role when deciding to accept/reject a pancreas graft. The lack of confidence in the donor surgeon's competence might influence the decision-making to accept/refuse a pancreas offer. One of the main parameters in this context was the confidence of the recovery team in evaluating the quality of the pancreas (i.e., pancreas macroscopy) and technical quality of pancreas procurement.

15.5 Anatomical Backgrounds

Every pancreas procurement surgeon should be aware of the complex vascular anatomy of the pancreas including its potential anatomical variations. Here are some essential points of vascular anatomy to be taken in consideration when performing a pancreas procurement procedure [17].

15.5.1 Arterial Supply of the Pancreas

15.5.1.1 Normal Anatomy

The head and uncinate process are supplied by the pancreaticoduodenal arcade, which consists of two to several loops of vessels that arise from the superior pancreaticoduodenal artery (SPDA) (branch of GDA, which usually arises from the common hepatic artery (HA) as it crosses the portal vein (PV) above the pancreas border and the dorsal pancreatic artery (DPA), arising from the splenic artery (SA)) and inferior pancreaticoduodenal artery (IPDA) (branch of the SMA). The arcades run on the anterior and posterior surface of the pancreas next to the duodenum, and the anterior arcade is lying somewhat closer to the duodenum (Fig. 15.1).

The body and the tail of the pancreas are mainly supplied by a second system arising from the splenic artery (SA), which gives rise to three arteries into the dorsal surface of the gland. The dorsal pancreatic artery (DPA) is the most medial of the three and the most important. It anastomoses with the pancreaticoduodenal arcade in the neck of the pancreas.

15.5.1.2 Anatomical Variations

In approximately 25 % of individuals, the right hepatic artery (RHA) arises partially or completely from the superior mesenteric artery. In such cases, we talk about accessory or replaced right hepatic artery (RRHA) (Fig. 15.2).

Rarely, the right or left hepatic arteries originate independently from the celiac trunk or branch after a very short common hepatic artery origin from the celiac, and the GDA may originate from the right hepatic artery.

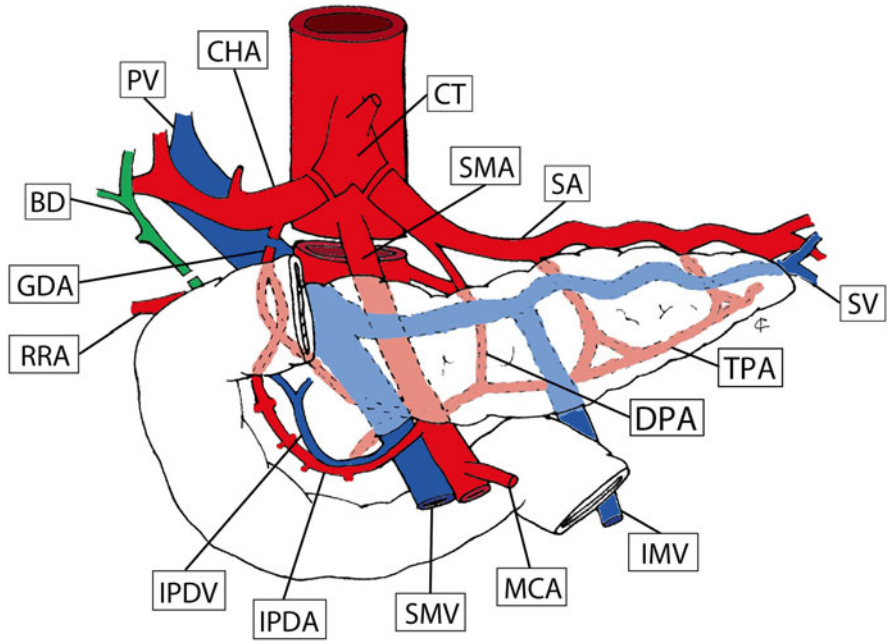

Fig. 15.1 Vascular anatomy of the pancreas. *CT* coeliac trunk, *SMA* superior mesenteric artery, *SA* splenic artery, *SV* splenic vein, *TPA* transverse pancreatic artery, *DPA* dorsal pancreatic artery, *IMV* inferior mesenteric vein, *MCA* middle colic artery, *SMV* superior mesenteric vein, *IPDA* inferior pancreato-duodenal artery, *IPDV* inferior pancreato-duodenal vein, *RRA* right renal artery, *GDA* gastro-duodenal artery, *BD* bile duct, *PV* portal vein, *CHA* common hepatic artery

The presence of an RRHA should not represent a contraindication either to pancreas retrieval or pancreas acceptance. It is important not to prepare the RRHA along its course behind the pancreas head but to identify and divide it as it emerges from superior border of pancreatic head [18, 19].

The IPDA can arise alone from the SMA or can share a common trunk with the jejunal artery, with the RRHA, or with the dorsal pancreatic artery. A relevant anatomical variation which should be taken in serious consideration is when the DPA arises from CHA (Fig. 15.3).

15.5.1.3 Venous Anatomy of the Pancreas

Venous drainage generally follows arterial supply (Fig. 15.1). The veins of the body and the tail of the pancreas drain into the splenic vein, where it lies partly embedded in the posterior surface of the gland. These veins are short and fragile. The head and uncinate process veins drain into the superior mesenteric vein (SMV) and portal vein on the right lateral side of these structures. Uncinate veins often drain into a large first jejunal tributary vein, which then empties into the SMV. This vein usually passes behind the SMA. A nearly constant posterior superior pancreaticoduodenal vein enters the right lateral side of the portal vein at the level of the duodenum [17].

The superior mesenteric vein (*SMV*) at the root of the lesser omentum is usually a single trunk; two or sometimes even three branches may join as the vessel enters the tunnel beneath the neck of the pancreas (shaded in Fig. 15.1) to form a superior mesenteric trunk. This trunk ascends behind the neck of the pancreas and is joined by the splenic vein (*SV*), which enters it from the left to form the portal vein (*PV*), which emerges from the retroperitoneal upper border of the neck of the pancreas and ascends toward the liver within the free edge of the lesser omentum, lying behind the

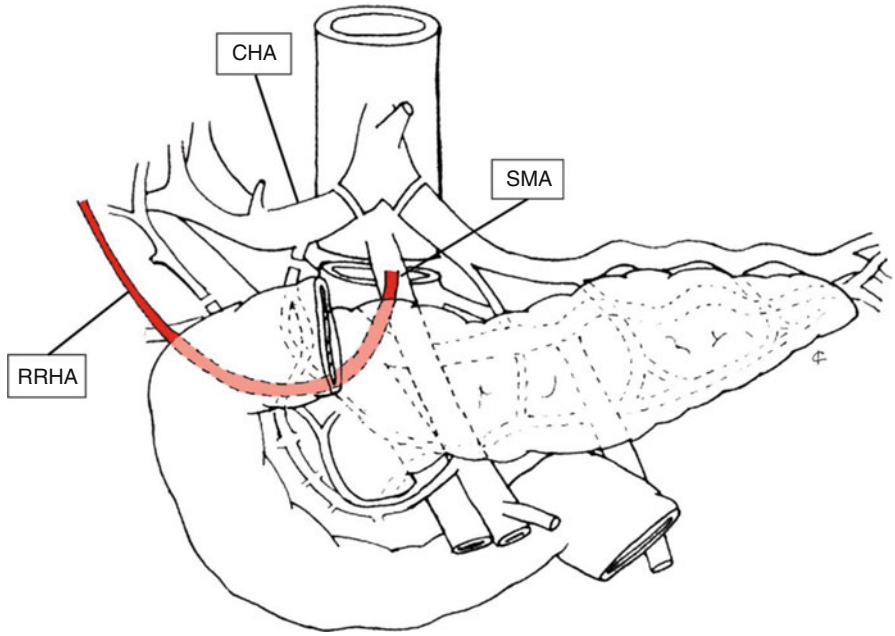

Fig. 15.2 *RRHA* replaced right hepatic artery, *CHA* common hepatic artery, *SMA* superior mesenteric artery

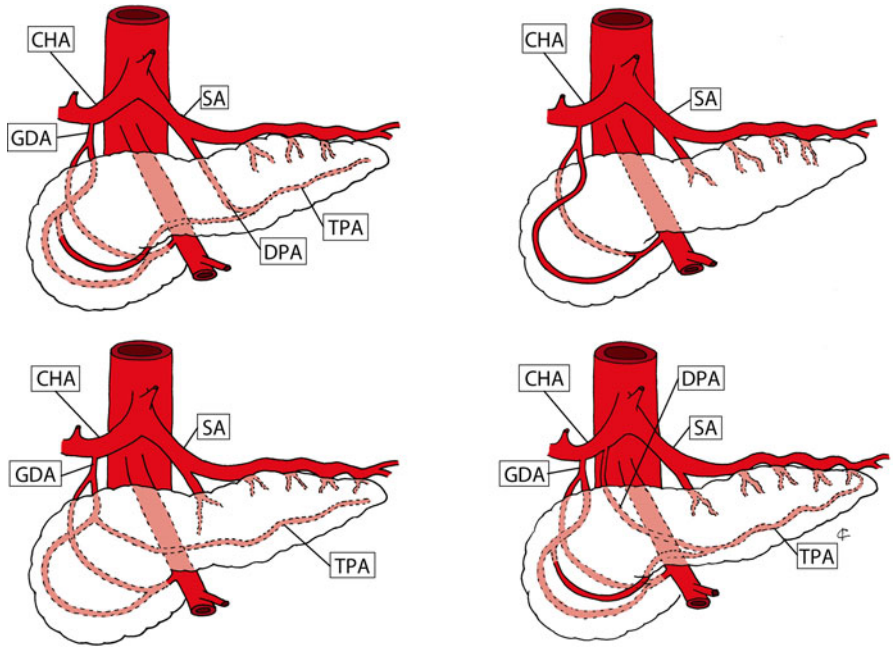

Fig. 15.3 Variation of the arterial blood supply of the pancreas from Wunderlich et al. [24]. *CHA* common hepatic artery, *GDA* gastro-duodenal artery, *SA* splenic artery, *TPA* transverse pancreatic artery, *DPA* dorsal pancreatic artery

bile duct and the hepatic artery and surrounded by the lymphatics and nodes of the lesser omentum. During this course, it receives blood through the coronary vein (*CV*), which communicates with esophageal venous collaterals, which connect with the gastric vein and the esophageal plexus. Sometimes a separate right gastric vein enters the PV in this area. A superior pancreaticoduodenal vein often enters the PV just above the level of the pancreas, and several smaller veins enter the SMV and PV from the right side beneath the neck of the pancreas. It must be noted that there is little variation in the portal venous anatomy [17].

15.6 Surgical Procedure

15.6.1 Exploration

After opening the abdomen (usually through a midline incision extended to median sternotomy), the procurement surgeon should perform a general exploration of the abdominal cavity and the organs followed by an accurate inspection of each single abdominal organ planned to be procured.

Before starting any organ preparation and manipulation, the cannulation accesses (i.e., subdiaphragmatic aorta, distal aorta, and iliac arteries) must be secured and prepared to be ready at any time for a crash perfusion and procurement in case of acute hemodynamic decompensation of the donor. For a rapid and almost complete exposure of distal aorta and infrahepatic IVC, a Cattell–Braasch maneuver (i.e., medial mobilization of the right colon with distal ileum and the duodenum) and an extended Kocher maneuver are usually performed.

After that, the entire root of the small bowel mesentery is mobilized up to the superior mesenteric artery (SMA) and inferior border of the pancreas.

Additional exposure of the pancreas can be obtained by transecting the gastrohepatic ligament to gain access to the lesser sac, which allows for inspection of the superior border of the pancreas and visualization of the splenic artery (SA). Care must be taken to identify and preserve an accessory left hepatic artery from the left gastric artery. Further exposure of the pancreas is obtained by transecting the gastrocolic ligament along the greater curvature of the stomach to permit full inspection of the anterior wall of the pancreas.

In general, the presence/absence of the following parameters should be considered during a detailed pancreas exploration to judge its quality and transplantability:

- Edema
- Pancreatitis (acute/chronic)
- Injury
- Fat content
- Hematoma
- Fibrosis
- Texture (firm, hard, woody)
- Tumor
- Quality of vessels (i.e., visceral arteriosclerosis)
- Congenital abnormalities (e.g., like duodenal diverticula)

The vascular anatomy (see above) may also represent a critical factor for pancreas transplantation or acceptance in case of:

- Replaced RHA from SMA
- Contemporaneous isolated intestinal procurement (see below, preparation of mesenterial root)

Finally, it is of paramount importance to communicate these findings in details as well as the general impression of transplantability of the graft not only to the local organ procurement organization but mainly to the recipient center, directly by phone or even through multimedia support (e.g., submission of digital pictures via Internet/smartphones) [4].

15.6.2 Preparation of the Pancreas In Situ (Vessels, Borders, Mesenteric Root)

The procurement surgeon has two possibilities to dissect and prepare the pancreas in situ:

1. Dissection with intact circulation ("warm" preparation)
2. Dissection after cross-clamp and cold perfusion ("cold" preparation)

The advantages/disadvantages of the two procedures have been summarized in Table 15.5.

But, independently from when the preparation of pancreas graft has being performed, it is essential to remember that this phase is based on the principle of a "no-touch" procedure, i.e., extremely cautious handling of pancreas graft and the neighboring organs and vascular structures.

15.6.2.1 Preparation of the Arteries

1. Gastroduodenal artery (GDA):

   The belonging of an adequate long stump of GDA (to the liver or to the pancreas) may be a matter of debate between liver and pancreas transplant centers.

   The GDA should be prepared to guarantee enough of its length in both directions (i.e., CHA and the pancreas head); this is to avoid to cut the GDA directly at its origin from CHA with consequent impairment of the vascular pedicle for the liver (Fig. 15.4). Additionally, in case of compromised perfusion of the pancreas head via IPDA (e.g., due to anatomical variations, simultaneous intestinal procurement, lesions) or in case of the absence of cross-circulation between the SA and SMA, a well-prepared distal stump of GDA may allow the revascularization of the pancreas head through a so-called "triple" arterial reconstruction in conjunction with the GDA, SMA, and SA at the back table (Fig. 15.5) [20, 21].
2. Common hepatic artery (CHA):

   The CHA should be prepared only along its upper border avoiding consequently any risk of injuries of the pancreatic parenchyma.

   In this phase, it is also important to exclude the presence of dorsal pancreatic artery as branch of CHA (Fig. 15.3d). In such a case, the pancreas surgeon should also consider the possibility of later dividing the CHA before the CT. This is only after feedback with liver surgeon and according to the need of liver recipient center.
3. Splenic artery (SA) and coeliac trunk (CT):

   Similarly to what reported above about the GDA, SA should be prepared long enough to later guarantee a safe cut few mm after its branching from CT without compromising the utilization of CT by the liver transplant surgeon (Fig. 15.4). On the other side, the SA should not be prepared to much along the pancreas body due to the high risk of associated parenchyma injuries. However, it is important to remember that after division close to its celiac origin, the SA should be marked with a fine vascular suture because it tends to retract into the pancreatic tissue.

   It would be desirable, after communication with the liver procurement surgeon, if the CT and SMA could be so prepared to be lately procured in a single common aortic patch together with the pancreas in order to avoid risky vascular reconstructions and consequent vascular complications (Fig. 15.6). In fact, in case of standard liver transplantation, the integrity of the CT is not required anymore since the arterial anastomosis is usually performed at the bifurcation of CHA with GDA.
4. Superior mesenteric artery (SMA):

   The SMA should be identified at its origin under the inferior pancreas border already

Table 15.5 Pros (+) and cons (–) of warm vs. cold preparation in situ of the pancreas

Parameter	Warm preparation	Cold preparation
Vasospasm	–	+
Time-consuming	–	+
Parenchyma and vascular injuries	–	+
Bleeding control	+	–
Identification of vascular Anatomy	+	–
Length of first warm ischemia	+	–

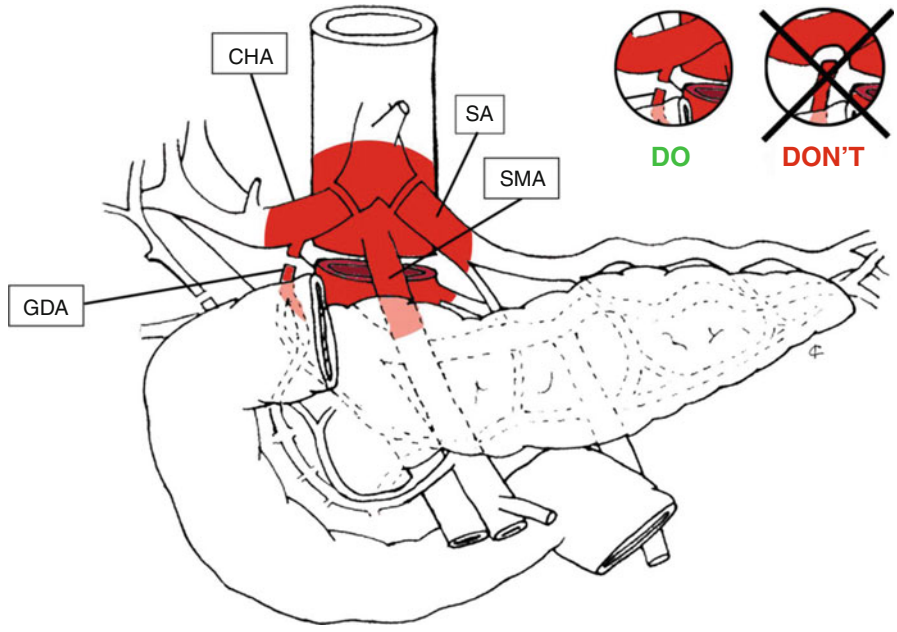

Fig. 15.4 Preparation of the gastroduodenal artery (*GDA*). *CHA* common hepatic artery, *SA* splenic artery, *SMA* superior mesenteric artery

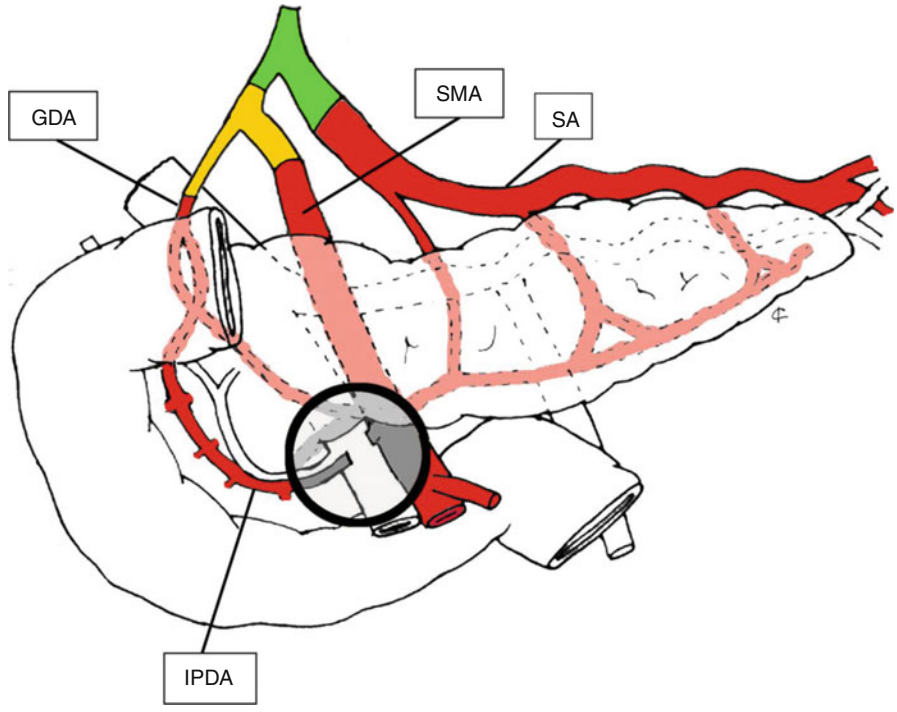

Fig. 15.5 Triple arterial reconstruction after conjunction with the *GDA*, SMA, and SA

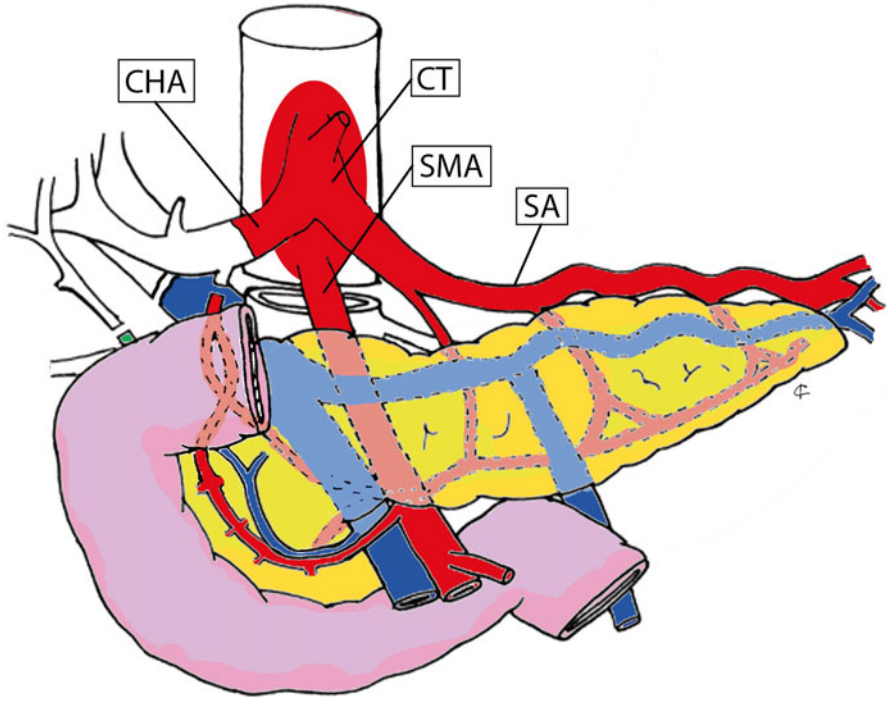

Fig. 15.6 Single common aortic patch. (*CHA* common hepatic artery, *CT* common trunk, *SMA* superior mesenteric artery, *SA* splenic artery)

during the preparation of big vessels for cannulation. A too wide dissection and encircling of SMA with vessels loops should be avoided in order to minimize damage to the parenchyma and SMA itself. It is not advisable to look for a replaced RHA (RRHA) from SMA at this place and this time. Eventually, the presence/absence of RRHA can be demonstrated by means of an "SMA test" which consists in clamping the SMA at its origin with microvascular clamp for a very short time. In case of the presence of an RRHA, the arterial pulse at hepatoduodenal ligament may disappear, or an ischemic demarcation of the right liver lobe can be observed.

15.6.2.2 Preparation of Superior Mesenteric Vein (SMV) and Portal Vein (PV)

The pancreas and liver allografts both require an appropriate length of portal vein. From a pancreas perspective, it is preferable that the portal vein be transected halfway between the superior border of the pancreas and the inferior border of the liver. Most recovery surgeons transect the portal vein in situ at the level of the coronary or left gastric vein, which may or may not allow an adequate length of portal vein with the pancreas allograft. As long as the venous confluence is intact, however, the pancreas can usually be transplanted. Rarely, donor iliac vein may be required for venous lengthening if the portal vein stump is <1 cm in length depending on the venous anatomy in the recipient. At the back table, an elongation of PV can be performed: the portal vein is placed on gentle traction with fine sutures and dissected back toward the confluence of the SMV and SV, ligating and dividing the superior pancreaticoduodenal and coronary veins if present. Some centers prefer to shorten the portal vein as much as possible by dividing it just distal to the confluence of the SV and SMV. Although it becomes technically more difficult to perform the venous anastomosis in the recipient, shortening the portal vein has the advantages of both preventing a kink and conferring protection from

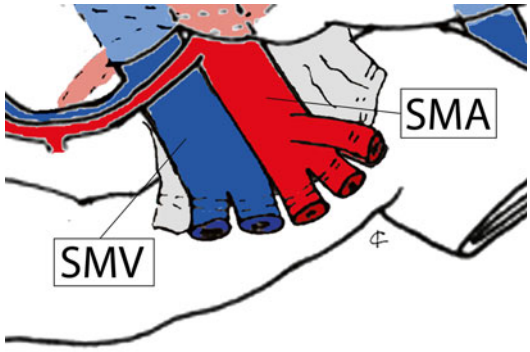

Fig. 15.7 Division of the mesenteric root by stapler (*SMV* superior mesenteric vein, *SMA* superior mesenteric artery)

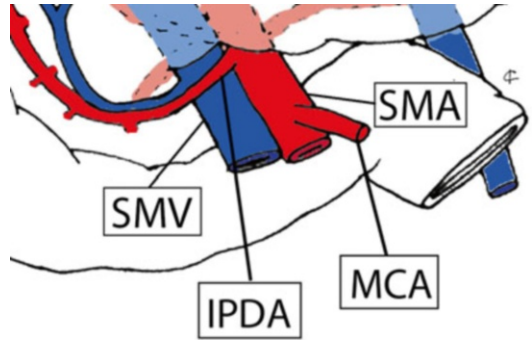

Fig. 15.8 Emerging of the middle colic artery (*MCA*) and inferior pancreaticoduodenal artery (*IPDA*) (*SMV* superior mesenteric vein, *SMA* superior mesenteric artery)

compression by the surrounding tissues, which acts almost like a tortoise shell around the venous anastomosis.

However, since the length of PV still represents a matter of major conflict between the liver and the pancreas surgeon, the communication between procurement surgeons and recipient centers is essential to find a friendly agreement.

During the Cattell–Braasch maneuver, the IMV should be doubly ligated beyond the inferior border of the pancreas near the ligament of Treitz, taking care not to narrow the SV.

15.6.2.3 Preparation of the Mesenteric Root

The mesenteric root should not be divided until most of the aortic flush is complete to allow passive portal flush via mesenteric venous return. In fact, a premature ligation and division of the base of the mesentery may cause bowel infarction, which could result in bacterial translocation and portal endotoxemia.

At the time of pancreas retrieval, the line of transection of mesenterial root is defined by "scoring" the visceral peritoneum above and below the mesenteric root along the proposed line of transection which should be at least 2 cm away from the head of the pancreas and uncinate process to avoid injury to the inferior pancreaticoduodenal arcade. After that, the mesenteric root is usually divided by using vascular staplers (Fig. 15.7, stapler). Due to the fact that such staplers do not always provide adequate hemostasis, it is advisable to oversew the mesenteric staple line at the back table. Alternatively, another technique is to individually ligate and divide the mesenteric vessels in situ as the base of the mesentery is dissected and serially transected [4].

The colonic mesentery, consisting primarily of the right and middle colic vessels, is divided in similar technique and timing as reported above for the mesenteric root of the small bowel.

Following transection of the root of the mesentery, the small bowel can be eviscerated to further improve exposure of the retroperitoneum.

In case of separate donation of pancreas and intestinal allograft, the base of the small bowel mesentery just distal to the pancreas must be carefully dissected taking maximal care of maintaining the integrity of IPDA. This danger particularly occurs when the colon is included in the intestinal graft. In this case, the middle colic artery – emerging from SMA only few millimeters after the IPDA – should be also procured (Fig. 15.8) [4]. The reason of this problem is that the SPDA is the terminal branch of the GDA that is ligated while removing the liver. The additional loss of the IPDA will devascularize the head and part of the uncinate process of the pancreas. In case of isolated small bowel procurement, the risk of damaging the IPDA is minimized by limiting the dissection of the SMA to a level just proximal to the origin of the first jejunal trunk [4, 14].

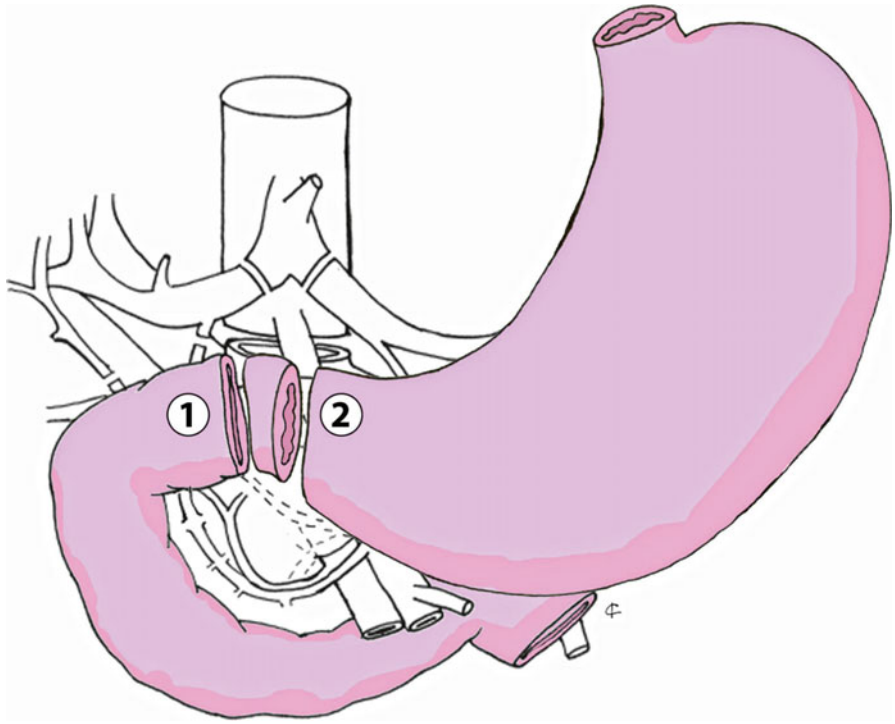

Fig. 15.9 Division of the proximal duodenum distal (*1*) or proximal (*2*) to the pylorus

15.6.2.4 Preparation of Duodenum

The pancreas is procured en bloc with the duodenum, which acts as a reservoir and allows the anastomosis to the recipient bowel or bladder for exocrine drainage.

The duodenum is usually exposed with an extended Kocher maneuver during the initial phase of exploration of the abdominal cavity and retroperitoneum.

During the retrieval procedure, the proximal duodenum is typically stapled and divided just distal or proximal to the pylorus (Fig. 15.9) and again at the fourth portion of the duodenum or the proximal jejunum near the ligament of Treitz.

Dividing the pancreas before the pylorus may reduce the risk of injury of the pancreas head at procurement. Anecdotally, it could be suggested to let the duodenal stumps as long as possible giving the transplant surgeon to adapt the length of duodenum at back table according to the local needs and surgical procedure typical of recipient's center.

Because of the potential risks of duodenal distension and enteric contamination in vivo, it is advisable to delay stapling of the distal duodenum/proximal jejunum until just prior to start with the removal of the pancreas. In this context, it is helpful to "milk" or decompress the contents of the duodenum distally before applying the distal staple line to prevent duodenal distension prior to removal.

In the past, recovery surgeons routinely flushed the donor duodenum (prior to cross-clamping) through a nasogastric tube with amphotericin B solution and/or iodine solution as an intraluminal sterilization maneuver. However, this step may not be necessary for enteric-drained allografts and has become a less common practice.

Finally, the pancreas allograft side of the common bile duct must be ligated during the portal triad dissection of the liver and eventually oversewn at back table [4].

15.6.2.5 Preparation of the Spleen

It is advisable not to prepare and mobilize the spleen from retroperitoneum during the warm

phase in order to avoid unpleasant spleen laceration and consequent bleeding which may compromise the whole MOP procedure. The mobilization of the spleen and dissection of vasa brevia from the stomach should be performed lately during the cold phase at pancreas removal.

15.6.2.6 Perfusion

Static cold storage procedures remain the preservation technique used for the vast majority of pancreas transplants performed worldwide [22].

There are many controversies about the "ideal" preservation solution during pancreas procurement as pointed out by Barlow AD [22]. In a retrospective analysis performed by Becker et al. [23], there was no significant difference between histidine–tryptophan–ketoglutarate (HTK) and University of Wisconsin (UW) solution. Both solutions have been shown to be safe for pancreas preservation. So, in Western Europe, the routinely used HTK solution seems to have no impact on the posttransplant pancreas graft function [24].

On the contrary, in the USA, the UW solution is still the preferred one since some investigators have reported a higher incidence of reperfusion pancreatitis and early pancreas graft failure associated with using HTK solution for pancreas preservation, particularly with higher in situ flush volumes and longer cold ischemic times (above 12–14 h) [4].

Preliminary experiences using other extracellular preservation solutions such as Celsior (a low-viscosity, colloid-free preservation solution) and IGL-1 (similar to UW except for inversion of the sodium and potassium content and replacement of hydroxyethyl starch with polyethylene glycol) in clinical pancreas transplantation have yielded acceptable results, particularly for cold ischemia times below 12–14 h [25–28].

The total amount of infusate is guided by blanching of the organs and estimation by palpation of the degree of cooling. It is important to avoid both venous hypertension and overperfusion of the intestine and pancreas. Clinical experience has demonstrated that this high-volume flush may not be necessary and in fact may be detrimental, particularly for pancreas preservation. Limiting the flush volume until the venous effluent is clear may be more practical and cost-effective. Furthermore, in situ perfusion through the portal vein or one of its tributaries is not recommended [14].

Also flushing of the pancreas ex vivo is probably not necessary and may be harmful to the microcirculation

However, it is become increasingly apparent that minimizing cold ischemia (<12 h) is one of the single most important predictors of success in pancreas transplantation irrespective of donor quality or method of preservation [29].

15.6.2.7 Removal of the Pancreas from Abdominal Cavity

The removal of the isolated pancreas occurs generally after the removal of the intestine and liver based on the abovementioned "no-touch" procedure.

After division of vascular structures and division of proximal and distal duodenum, the stomach is usually rotated cranially to further improve exposure of the pancreas. Now the spleen can be carefully mobilized medially by dividing the short gastric vessels and its ligamentous attachments to the colon and diaphragm, allowing for mobilization and elevation of the tail of the pancreas from its retroperitoneal bed. Using the spleen as a handle, the tail and body of the pancreas can be mobilized medially up to the aorta taking care not to injure the left renal vein, SA, or SV (Fig. 15.10). Because the SA may be tortuous and is often extrapancreatic and cephalad to the superior border of the pancreas, one must specifically avoid surgical damage or traction injury to this vessel.

After the complete mobilization of the pancreas from retroperitoneum, the graft can be now completely removed from the abdominal cavity and placed in a bowl containing ice cold water at back table.

It is important to consider that the spleen should be kept with the pancreas. Material for crossmatch needed for organ allocation can be taken from upper and lower pole of the spleen.

At the back table, the pancreas graft is finally accurately explored to check the vascular anatomy, to exclude relevant injuries and to confirm the transplantability of the graft.

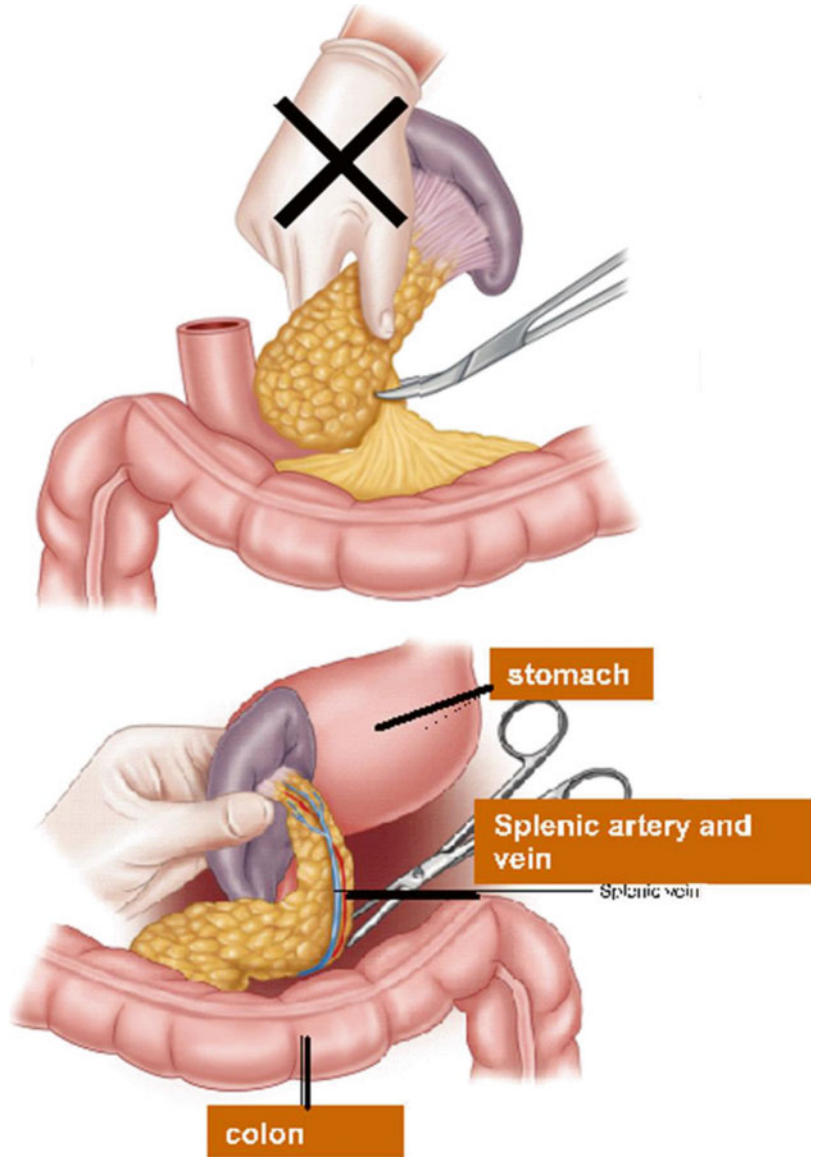

Fig. 15.10 "Spleen handle": removal of the pancreas from the abdominal cavity using the spleen as a handle

Finally, the pancreas is packed according the standardized guidelines in a three-bag system [24] and prepared to be shipped to the recipient's center together with the vascular grafts needed for vascular reconstruction.

15.6.2.8 Procurement of Iliac Vessels ("Y-Grafts")

Currently, the most common technique for arterial reconstruction is to retrieve a naturally bifurcating artery from the donor to be used as an arterial "Y"-graft. The most commonly used bifurcation is that of the common iliac artery into the internal and external iliac arteries, which are anastomosed to the SA and SMA, respectively (Fig. 15.11) [4].

Alternative "Y"-grafts include the brachiocephalic trunk, the aortic cross, carotid artery Y-graft, and either the donor or recipient internal iliac artery [30–32]. It is essential that also these vessels are procured by an experienced surgeon because the failure to identify atherosclerotic vascular disease or surgical damage to these vessels

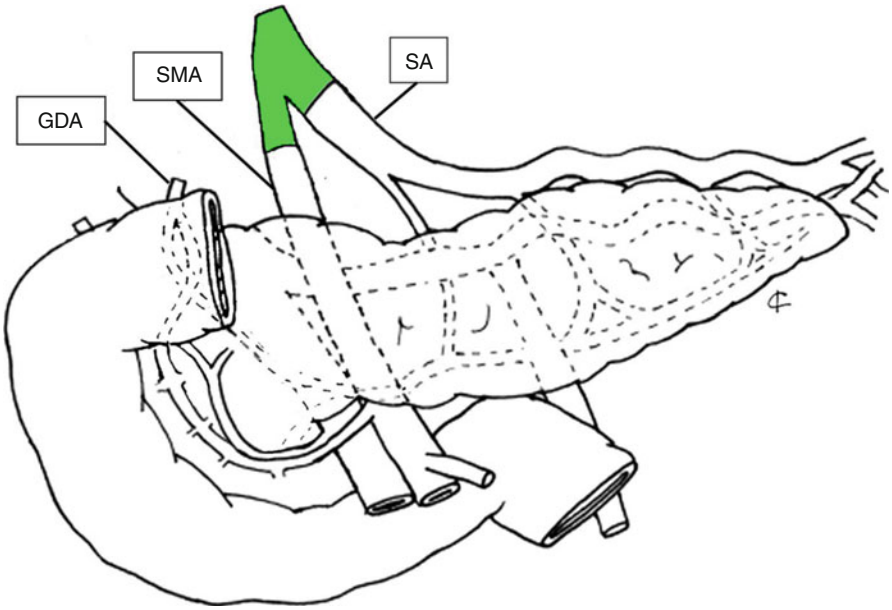

Fig. 15.11 Arterial reconstruction with "Y-graft"

from improper technique or traction injuries may affect the outcome of the transplant procedure.

15.7 Other Techniques

15.7.1 En Bloc Procurement

Traditionally, organs are removed individually in a fixed sequence (the heart, lungs, intestine, liver, pancreas, and kidneys). There is evidence that intra-abdominal temperature does not drop as rapidly as previously thought, despite intravascular as well as topical cooling. Additionally, a prolonged time to remove the organs after cold perfusion increases the risk of rewarming (especially of the pancreas) and could lead to organ dysfunction posttransplantation. Therefore, to avoid these potential problems, the *en bloc procurement of the liver and pancreas* has been advocated. This reduces the dissection and removal time, is associated with fewer procurement-related injuries, and may be associated with a better initial organ function [4].

Published for the first time in 1992 by Nakazato et al. [33], different technical variations of the en bloc procurement of visceral organs have been proposed up to now [14, 26]. Wunderlich et al. described in detail the procedure of "en bloc liver and pancreas removal" [24]:

- Incision of the diaphragm on the left side until the esophagus and on the right side until the adrenal gland with much care not to cause lesions to the right liver capsule due to traction.
- Division of the right gastroepiploic and right gastric artery using ligation.
- Stapling of the proximal duodenum directly distally to the pylorus.
- Ligation of the left gastric artery and vein.
- Clipping and ligating of the inferior mesenteric vein at the distal border of the pancreas.
- Dissection and transection of the superior mesenteric artery and vein at the third portion of the duodenum next to the inferior part of the head of the pancreas. The mesenteric root can be transected using a GIA stapler. The stapler line should not be too close to the lower part of the uncinate process to avoid incidental injury/closure of the pancreaticoduodenal artery.

- Stapling of the proximal jejunum distal to the ligament of Treitz.
- Transection of the splenocolic ligament while lifting up the tail of the pancreas using the spleen as a handgrip.
- Mobilization of the dorsal side of the pancreas using electrocautery.
- Dissection of the aortic part of the superior mesenteric artery under visualization of the left and right renal arteries.
- Freeing of the infrahepatic IVC displaying the origins of the right and left renal veins and transection of the IVC just above the renal veins.
- Division of the right paravertebral muscle layer and transection of the right adrenal gland.
- Division of the left paravertebral muscle layers and transection of the left adrenal gland up to the sling/clamp of the proximal aorta.
- Release of the bloc is complete once the prevertebral connective tissue is divided and the SMA is cut out with the proximal aorta including the coeliac trunk. Special care must be taken here not to injure the main renal arteries because of their proximity to the SMA.
- Accurate separation of the organs at back table according the technical and anatomical pitfalls mentioned above for the standard procurement.

15.7.2 Pancreas Procurement from DCD Donors

The technique for pancreas retrieval in DCD donors is a combination of standard retrieval techniques and protocols for achieving rapid cross-clamp in the unstable brain-dead donor setting. Aberrant arterial vasculature is particularly vulnerable since dissection is performed in a cold field without blood flow or pulses evident to assist inidentification of the vascular anatomy. The liver and pancreas are usually removed en bloc and separated on the back table.

With short periods of warm and cold ischemia in the setting of young, thin, and otherwise stable individuals without aforementioned risk factors, excellent results can be obtained in DCD donor pancreas transplantation, particularly in SPK transplantation.

In recent years, organ recovery from DCD donors has increased steadily. It should be noted, however, that pancreas transplantation from DCD donors has yet to gain widespread acceptance especially in the USA and in UK [4, 34, 35].

Since DCD grafts are subjected to greater ischemic damage, improved preservation techniques are likely to improve outcomes. At this regard, there are a number of preservation techniques already in clinical use for other organs that could potentially have benefits in DCD pancreas transplantation. These include the "two-layer method," persufflation, hypothermic machine perfusion, and ex vivo normothermic perfusion [22].

Conclusions

The technique and quality of pancreas procurement significantly influence the outcome of pancreas transplantation.

After accurate donor selection and donor management at ICU, a perfect pancreas procurement is based on a wide anatomical knowledge, an accurate inspection of the graft, a gentle and precise preparation of the pancreas, and adjacent vascular structures in different phases.

In order to minimize the risk of surgical errors, it is essential that an experienced pancreas transplant surgeon performs such a detailed procedure.

References

1. Stegall MD, Dean PG, Sung R et al (2007) The rationale for the new deceased donor pancreas allocation schema. Transplantation 83(9):1156–1161
2. Brockmann JG, Vaidya A, Reddy S et al (2006) Retrieval of abdominal organs for transplantation. Br J Surg 93(2):133–146
3. Biglarnia AR, Bennet W, Nilsson T et al (2014) Utilization of small pediatric donors including infants for pancreas and kidney transplantation: exemplification of the surgical technique and the surveillance. Ann Surg 260(2):e5–e7
4. Fridell JA, Powelson JA, Kubal CA et al (2014) Retrieval of the pancreas allograft for whole-organ transplantation. Clin Transplant 28(12):1313–1330

5. Ollinger R, Margreiter C, Bosmuller C et al (2012) Evolution of pancreas transplantation: long-term results and perspectives from a high-volume center. Ann Surg 256(5):780–786; discussion 6–7
6. Fellmer PT, Pascher A, Kahl A et al (2010) Influence of donor- and recipient-specific factors on the postoperative course after combined pancreas-kidney transplantation. Langenbecks Arch Surg 395(1): 19–25
7. Vinkers MT, Rahmel AO, Slot MC et al (2008) Influence of a donor quality score on pancreas transplant survival in the Eurotransplant area. Transplant Proc 40(10):3606–3608
8. Vinkers MT, Rahmel AO, Slot MC et al (2008) How to recognize a suitable pancreas donor: a Eurotransplant study of preprocurement factors. Transplant Proc 40(5):1275–1278
9. Schenker P, Vonend O, Ertas N et al (2010) Preprocurement pancreas allocation suitability score does not correlate with long-term pancreas graft survival. Transplant Proc 42(1):178–180
10. Axelrod DA, Sung RS, Meyer KH et al (2010) Systematic evaluation of pancreas allograft quality, outcomes and geographic variation in utilization. Am J Transplant 10(4):837–845
11. Fischer-Frohlich CL, Konigsrainer A, Schaffer R et al (2012) Organ donation: when should we consider intestinal donation. Transpl Int 25(12):1229–1240
12. MacPhee I, Fronek J (eds) (2012) Handbook of renal and pancreatic transplantation. Hoboken, Wiley-Blackwell
13. McKeown DW, Bonser RS, Kellum JA (2012) Management of the heartbeating brain-dead organ donor. Br J Anaesth 108(Suppl 1):i96–i107
14. Abu-Elmagd K, Fung J, Bueno J et al (2000) Logistics and technique for procurement of intestinal, pancreatic, and hepatic grafts from the same donor. Ann Surg 232(5):680–687
15. Sollinger HW, Odorico JS, Becker YT et al (2009) One thousand simultaneous pancreas-kidney transplants at a single center with 22-year follow-up. Ann Surg 250(4):618–630
16. Loss J, Drewitz KP, Schlitt HJ et al (2013) Accept or refuse? Factors influencing the decision-making of transplant surgeons who are offered a pancreas: results of a qualitative study. BMC Surg 13:47
17. Jarnagin WR, J Belghiti, Büchler MW, Chapman WC, D'Angelica MI, DeMatteo RP, Hann LE (eds) (2012) Blumgart's surgery of the liver, pancreas and biliary tract, 5th edn. Philadelphia, Elsevier Saunders
18. Huang Y, Li J, Qi H (2013) Management of the accessory or replaced right hepatic artery (A/R RHA) during multiorgan retrieval when the inferior pancreaticoduodenal artery shares a common origin with A/R RHA. Transplant Proc 45(1):20–24
19. Molmenti EP, Klein AS, Henry ML (2004) Procurement of liver and pancreas allografts in donors with replaced/accessory right hepatic arteries. Transplantation 78(5):770–771
20. Nghiem DD (2008) Revascularization of the gastroepiploic artery in pancreas transplant. Transpl Int 21(8):774–777
21. Socci C, Orsenigo E, Zuber V et al (2006) Triple arterial reconstruction improves vascularization of whole pancreas for transplantation. Transplant Proc 38(4): 1158–1159
22. Barlow AD, Hosgood SA, Nicholson ML (2013) Current state of pancreas preservation and implications for DCD pancreas transplantation. Transplantation 95(12):1419–1424
23. Becker T, Ringe B, Nyibata M et al (2007) Pancreas transplantation with histidine-tryptophan-ketoglutarate (HTK) solution and University of Wisconsin (UW) solution: is there a difference? JOP 8(3):304–311
24. Wunderlich H, Brockmann JG, Voigt R et al (2011) DTG procurement guidelines in heart beating donors. Transpl Int 24(7):733–757
25. Baertschiger RM, Berney T, Morel P (2008) Organ preservation in pancreas and islet transplantation. Curr Opin Organ Transplant 13(1):59–66
26. Boggi U, Vistoli F, Del Chiaro M et al (2004) Pancreas preservation with University of Wisconsin and Celsior solutions: a single-center, prospective, randomized pilot study. Transplantation 77(8):1186–1190
27. Codas R, Petruzzo P, Morelon E et al (2009) IGL-1 solution in kidney transplantation: first multi-center study. Clin Transplant 23(3):337–342
28. Manrique A, Jimenez C, Herrero ML et al (2006) Pancreas preservation with the University of Wisconsin versus Celsior solutions. Transplant Proc 38(8):2582–2584
29. Maglione M, Ploeg RJ, Friend PJ (2013) Donor risk factors, retrieval technique, preservation and ischemia/reperfusion injury in pancreas transplantation. Curr Opin Organ Transplant 18(1):83–88
30. Bandlien KO, Mittal VK, Toledo-Pereyra LH (1988) Procurement and workbench procedures in preparation of pancreatic allografts. Factors essential for a successful pancreas transplant. Am Surg 54(9): 578–581
31. Ciancio G, Olson L, Burke GW (1995) The use of the brachiocephalic trunk for arterial reconstruction of the whole pancreas allograft for transplantation. J Am Coll Surg 181(1):79–80
32. de Miranda MP, Genzini T, Gil AO et al (1998) Use of a donor aortic cross for arterial reconstruction of the pancreaticoduodenal allograft. Clin Transplant 12(3): 165–167
33. Nakazato PZ, Concepcion W, Bry W et al (1992) Total abdominal evisceration: an en bloc technique for abdominal organ harvesting. Surgery 111(1):37–47
34. Kandaswamy R, Skeans MA, Gustafson SK et al (2015) OPTN/SRTR 2013 annual data report: pancreas. Am J Transplant 15(Suppl 2):1–20
35. Muthusamy AS, Mumford L, Hudson A et al (2013) Pancreas transplantation from donors after circulatory death from the United Kingdom. Am J Transplant 13(3):824

Kidney Procurement

16

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Tips, Tricks, and Pitfalls

- *Tip*: Preserve long ureters.
  - *Trick*: Keep the ureters away from the operating field when not working on them.
  - *Pitfall*: It is easy to damage the ureters when dissecting the anatomical structures close to them.
- *Tip*: Preserve the left renal vein carefully.
  - *Trick*: Before splitting the aorta, suspend, cut, and retract the left renal vein.
  - *Pitfall*: It is easy to damage the left renal vein when splitting the aorta if the vein is not dissected and retracted sufficiently.
- *Tip*: Preserve the renal pedicles carefully.
  - *Trick*: When dissecting the great vessel after perfusion, stay close to the prevertebral muscular plane.
  - *Pitfall*: It is easy to damage the renal pedicles when dissecting them from the posterior plane.
- *Tip*: Preserve polar arteries.
  - *Trick*: Explore the aorta and the iliac vessels for any polar arteries.
  - *Pitfall*: It is easy to cut polar arteries, if not clearly identified previously, while conducting the mediolateral dissection.
- *Tip*: Try to not dissect the plane between the aorta and vena cava and the kidneys.
- *Tip*: Mobilize medially the kidneys from the perinephric tissue preserving the Gerota's fascia.
- *Tip*: Preserve the renal capsule.
  - *Trick*: When examining the kidney after its procurement, find the right plane to dissect in order to avoid damage to the kidney capsule.
  - *Pitfall*: Especially in old donors, the perirenal fat may not be dissociable from the kidney capsule.

Kidneys could be retrieved in the following different conditions:

- From brain-dead donor during multi-organ recovery procedure
- From brain-dead donor donating kidneys alone
- From non-heart-beating donors
- From living donor

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The purpose of this chapter is to describe the surgical techniques adopted in all these conditions; the kidney procurement from a living donor using a laparoscopic or robotic approach will be discussed later in Chap. 22.

16.1 Kidney Procurement During Multi-organ Recovery

Kidneys are removed from brain-dead multi-organ donors after the liver and pancreas [1–3]. The entire dissection is performed in a cold and bloodless surgical field. First, ureters should be identified at the cross with iliac vessels (on the left side, the sigmoid mobilization should be performed previously). Ureters should be dissected, preserving the surrounding fatty tissue to avoid devascularization and cut close to the urinary bladder. Hemostat such as light *mosquitoes* could be applied to the periureteral fat at the distal end of the ureters in order to allow gentle traction. The dissection should be conducted up to the kidney lower pole. When ureteral dissection is completed, the ureters should be kept away from the operative field in order to avoid injury during the following maneuvers. The two kidneys can be retrieved singularly or en bloc.

In the first case, the inferior vena cava is cut just above the iliac bifurcation, and the left renal vein is cut and detached at its origin in order to expose the aorta. The inferior vena cava remains with the right kidney and could be useful to extend the right renal vein on the back table (Fig. 16.1).

The aorta is than transected just above the iliac bifurcation and dived in two parts on a longitudinal plane. The renal artery origins should be carefully identified and preserved during this maneuver. Special care should be taken to avoid damage in the presence of polar arteries originating from the aorta or from the iliac branches. Dissecting cranially and caudally the perinephic fat from the Gerota's fascia the right kidney can be easily mobilized medially and then removed; with the left hand, the surgeon should lift the veva cava and the right hemi-aorta and dissect them from the vertebral plane. The dissection continues to the right on the psoas anterior face until the right vascular pedicle is completely freed. Then the surgeon can mobilize the left kidney and its fat from the left to right, always lifting the organ and its vascular-ureteral pedicle and

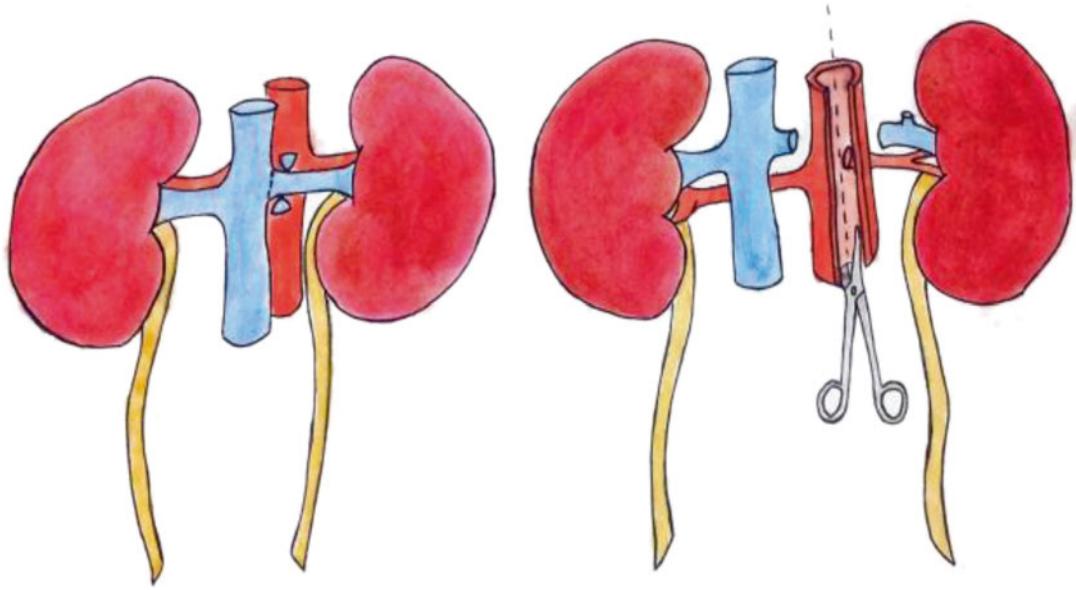

Fig 16.1 The inferior vena cava remains with the right kidney and could be useful to extend the right renal vein on the back table

completing the dissection along the prevertebral plane to avoid injury.

Before removing the left kidney, the left colon should be medialized. The line of Toldt is incised, and the colon is retracted medially until the left perirenal fat is completely exposed. The left ureter should be find lateral to the sigmoid colon near the pelvic inlet where it cross the iliac artery and than divided. If an accurate mobilization is performed. After distal transection, the ureter and the mesoureter can also be medialized throughout the left mesocolon with the left gonadal vein. The splenic and diaphragmatic ligaments are severed. Thereafter the removal of the left kidney proceeds as described for the right kidney.

16.2 En Bloc Removal Technique

When retrieving the two kidneys en bloc, the aorta and inferior vena cava (IVC) are severed transversely just above the iliac bifurcations; the left renal vein is not detached from the IVC, and the aorta is not split (Fig. 16.2). The dissection from the vertebral plane is conducted by lifting the great vessels until the renal vascular pedicle is free; the two kidneys are mobilized laterally as described previously, and the removal is completed [4].

This technique is particularly useful in marginal donors when usually one have to perform a dual kidney transplant. In such cases, bilateral renal biopsies are mandatory to determine whether the two kidneys could be transplanted in different recipients (classic kidney transplant) or in a single recipient (dual kidney transplant) or whether they could be rejected for transplantation. On one hand, this technique allows to save time during the procurement and the splitting of the kidneys, tailoring them to the needs of the dual kidney transplantation; on the other hand, this technique requires a slightly longer back-table time to split them.

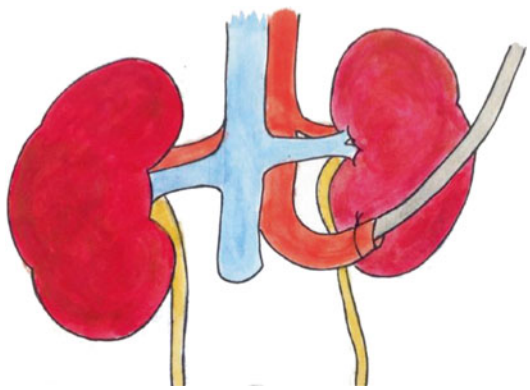

Fig. 16.2 En bloc removal technique: the aorta and inferior vena cava (IVC) are severed transversely just above the iliac bifurcations; the left renal vein is not detached from the IVC, and the aorta is not split

Once the organs are removed from the donor's abdomen, they should be examined carefully, and biopsies should be performed on the superior pole when necessary. This procedure should be performed by plunging the kidney in cold Ringer's solution or in the preferred perfusion solution.

16.3 Kidney Procurement Alone

For some donors, kidneys are the only harvestable organs. In such cases, the same incision for multi-organ donation (from the sternal notch to the pubis) is performed to allow accurate exploration and the best exposure. The right colon, small bowel, and duodenum are mobilized as described in Chap. 11.

The inferior mesenteric artery is ligated and cut, and the aorta and IVC are isolated and suspended just above the iliac bifurcation. The small bowel is retracted upward to expose the superior mesenteric artery, which is identified and encircled just above the left renal vein. The supraceliac aorta is suspended. The hepatic pedicle is also suspended as for Pringle maneuver. If convenient, the celiac trunk can be clamped to save perfusion liquid later on.

After systemic heparinization with 300-U/kg body weight, the lower aorta is cannulated, the lower IVC is ligated at the iliac bifurcation level, incised above the diaphragm just below the right atrium and the perfusion is started. The supraceliac aorta is cross-clamped or ligated. To perfuse both kidneys selectively, the superior mesenteric artery is ligated, and the previously suspended hepatic pedicle can be as for Pringle manoeuvre. Ice and cold saline are packed in the abdomen to refrigerate both kidneys. When the perfusion

ends, the aorta and the IVC are cut transversely above the renal vessel origin. The removal of the kidneys proceeds as previously described for multi-organ procurement.

16.4 Kidney Procurement from Non-heart-Beating Donor (Table 16.1) (donation after circulatory death)

Non-heart-beating donors [5–8] are grouped according to the Maastricht classification. Kidneys can be harvested from donors in class II or above. Once the cardiac death is assessed, CPR and mechanical ventilation should start. This procedure allows the flow of oxygenated blood, thus reducing the damage the organs will suffer. Careful recording of the warm ischemic time (time from the cardiac arrest to resuscitation procedures and from resuscitation procedures to the cool perfusion starts) should be registred. Heparinization (300-U/kg body weight) should start as soon as possible. Some authors recommend the use of phentolamine (0.125 mg/kg) to induce vasodilatation of the renal vessels before the infusion and thus to facilitate a rapid decrease in temperature. Surgical dissection and cannulation of the femoral vessels are performed; then the cold perfusion starts.

The perfusion can be performed completely in situ or with the help of a cardiopulmonary bypass (CPBP) machine.

In the first case, a three-chamber catheter with two balloons is inserted into the aorta through the femoral artery. The two balloons are inflated to isolate the abdominal aorta. The perfusion starts, and the solution mixed with blood is removed by the cannula in the femoral vein. Anaise [9] reports that 70 mmHg of pressure increases the drop in temperature (up to 15 °C in 5 min); lower pressure would permit the release of renin-angiotensin and would increase the renal vascular resistance, promoting a decrease in renal blood flow and poor hypothermia.

Using the CPBP machine, the extracorporeal circulation is connected to the femoral cannulas [10]. Cannulating the contralateral femoral artery allows the placement of a Fogarty into the aorta. The Fogarty balloon is inflated above the renal arteries, excluding the celiac and supraceliac aorta. The main difference between the in situ perfusion technique and body cooling with cardiopulmonary bypass is that in the latter case, the blood volume of the donor is maintained without exsanguination. The CPBP ensures the reversibility of the process and the ability to wait longer if further authorization is necessary to confirm the deceased as an organ donor.

In both cases (in situ and bypass perfusion), continuous hypothermic peritoneal saline infusion should be performed to refrigerate the surface of the abdominal organs.

Once the donor is taken to the operating room, the removal of kidneys is performed as described for brain-dead donors.

Table 16.1 Maastricht classification for non-heart-beating donor

Group	Category	Description
Uncontrolled death	I	Includes victims of accident and suicide (some centers exclude suicide victims from their programs) who are found dead at the scene and for whom resuscitation is deemed pointless (e.g., fatal cervical spine fracture). These are the worst group of potential donors because of the unknown primary warm ischemic time
	II	Donors who are victims of unsuccessful resuscitation after sudden cardiac (the majority) or cerebral catastrophe who either are brought to emergency departments while being resuscitated by ambulance personnel or who died in the department. Other sources include patients suffering isolated brain injury, anoxia, stroke and victims of major trauma who died soon after hospital admission
Controlled death	III	Encompasses patients who are dying, often in an intensive care unit; they are not eligible for any other treatment of resuscitation
	IV	Patients who develop unexpected cardiac arrest during or after the diagnosis of brain death

16.5 Kidney Procurement by Open Access from Living Donor

Seldom, a minimally invasive approach for a living kidney donor is not suitable [11, 12]. In these cases, lombotomic, minilombotomic or transperitoneal nephrectomy could be considered appropriate.

Lombotomic and minilombotomic Nephrectomy The donor is placed in the lateral position (lombotomic position); the operating table is flexed to expose the flank completely. A 15-20 cm incision is performed on the flank, between the lower margin of the 12th rib and the lateral edge of the rectus abdominis. The external and internal oblique muscles are sectioned as are the transversus abdominis to access the retroperitoneum. The kidney is dissected gently. The ureter is identified and sectioned distally. The renal vessels should be identified close to their origins from the aorta and IVC. On the left side, careful dissection should be performed to identify, ligate, and cut the adrenal and gonadic veins (originating from the left renal vein). At this point, after mild heparinization, an excellent urine flow should be evident from the severed ureter (diuretic stimulation could be helpful). After clamping and cutting the renal vessels (possibly artery first and vein afterward), the kidney can be removed and flushed with cold preservation solution through the artery for the next step of bench surgery.

Transperitoneal Nephrectomy The donor is placed in a supine position. A 20-cm, J-shaped paramedian transrectal incision is performed 3 cm from the right or left subcostal margin and up to 3 cm from the pubis. On the right side, the right colon is mobilized medially, and the IVC is exposed after an appropriate Kocher maneuver. The right renal vein is encircled to show the right renal artery. The ureter should be identified at the cross with the iliac vessels and severed distally in the prevesical tract. The right kidney is mobilized and removed after clamping and cutting the pedicle as described above.

On the left side, the left colon is mobilized medially and freed from the spleen ligament until the perirenal fat is exposed. The kidney should be mobilized from the lateral side. The ureter is identified and severed as described for the right kidney. The left renal vein is identified, suspended, and detached from the adrenal and gonadic veins. The left renal artery is encircled close to its aorta origin. As for the right kidney, an excellent urine flow should be assessed before proceeding with the renal vessel clamping and cutting.

Sistemic heparinization (5000 UI) is administered. Once the right or left kidney is removed, immediate flushing with cold perfusion throughout the artery should be performed.

Before wound closure, drainage is placed.

References

1. Starzl T, Hakala T, Shaw B, Hardesty R, Roshental T, Griffith B, Iwatsuki S, Bahnson H (1984) A flexible procedure for multiple cadaveric organ procurement. Surg Gynecol Obstet 158:223–230
2. Starzl T, Miller C, Broznick B, Makowka L (1987) An improved technique for multiple organ harvesting. Surg Gynecol Obstet 165:343–348
3. Starzl T, Todo S, Tzakis A, Alessiani M, Casavilla A, Abu K, Fung J (1991) The many faces of multivisceral transplantation. Surg Gynecol Obstet 172: 335–344
4. Nakazato P, Concepcion W, Bry W, Limm W, Tokunaga Y, Itasaka H, Feduska N, Esquivel CO, Collins GM (1992) Total abdominal evisceration: an en bloc technique for abdominal organ harvesting. Surgery 111:37–47
5. Szostek M, Danielewicz R, Lagiewska B, Pacholczyk M, Rybicki Z, Michalak G, Adadynski L, Walaszewski J, Rowinski W (1995) Successful transplantation of kidneys harvested from cadaver donors at 71 to 259 minutes following cardiac arrest. Transplant Proc 27:2901–2902
6. Anaya F (1996) Innovaciones tecnológicas en la donación en asistolia. Nefrologia 16:96–106
7. Booster M, Wijnen R, Ming Y, Vroemen J, Kootstra G (1993) In situ perfusion of kidneys from non-heart beating donors: the Maastricht protocol. Transplant Proc 25:1503–1504
8. Bell MDD (2003) Non-heart beating organ donation: old procurement strategy—new ethical problems. J Med Ethics 29:176–181
9. Anaise D, Yland MJ, Waltzer WC, Frischer Z, Hurley S, Eychmuller S, Rapaport FT (1988) Flush pressure requirements for optimal cadaveric donor kidney preservation. Transplant Proc 5:891–894

10. Ko WJ, Chen YS, Tsai PR, Lee PH (2000) Extracorporeal membrane oxygenation support of donor abdominal organs in non-heart-beating donors. Clin Transplant 14:152–156
11. Nicholson M, Kaushik M, Lewis G, Brook N, Bagul A, Kay M, Harper S, Elwell R, Veitch P, Hosgood SA (2011) Health-related quality of life after living donor nephrectomy: a randomized controlled trial of laparoscopic versus open nephrectomy. Transplantation 91:457–461
12. Nanidis T, Antcliffe D, Kokkinos C, Borysiewicz C, Darzi A, Tekkis P, Papalois VE (2008) Laparoscopic versus open live donor nephrectomy in renal transplantation: a meta-analysis. Ann Surg 247:58–70

Vascular Homograft Procurement

17

Paola Tracanelli and Federico Romani

Tips, Tricks, and Pitfalls

- During cannulation for organ cooling, section the aorta next to renal arteries origin and perform an atraumatic distal aortic clamping.
- During organ procurement, pay attention that liver and kidney surgeons limit their dissection, preserving the most extended part of aorta that they can.
- Before vessel harvesting, carefully observe their morphological features, avoiding vessels not suitable for reimplantation.
- During vessel isolation, don't pull them strongly, to prevent dissection and intimal lesions.
- Try always to get the longest segment of a vessel, in order to have many chances of use.

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Homograft is a tissue graft obtained from an organism of the same species of the recipient.

In vascular surgery, homograft is the name used for transplanted cadaveric vascular segments, also called allografts.

Allografts have been used for more than a century. In 1903 Hopner tried to replace the carotid artery of a dog with the femoral one of another.

In 1912 Carrell introduced aortic replacement using cadaveric artery allograft and Gross in 1948 treated an aortic coarctation using a human arterial allograft.

Then in 1952 Dubost replaced the infrarenal aorta with a fresh aortic allograft.

In the 1960s, the development and success of synthetic prostheses led homograft fell into disuse: the use of synthetic grafts became a standard vascular procedure, thanks to their long-term stability and their industrial manufacturing that made them widely available.

A new interest in allografts came back since 1988, thanks to a French surgeon, E. Kieffer, who employed aortofemoral allografts in the treatment of abdominal aortic infected prostheses. Kieffer et al. at the beginning used fresh allografts; thereafter, they preferred cryopreserved arterial segments due to structural pathological changes that led to reoperation in 9 % of patients [1–3].

In fact all the first allografts used to replace infected infrarenal aortic synthetic prostheses were fresh aortic homografts, stored at 4 ° C for 48 hours [2].

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Fresh allografts are destined to devitalization, with alterations as a result of noncalcific medial degeneration that caused spontaneous ruptures, thrombosis, and late aneurysmal formation [2].

A new inspiration came from the favorable experience with cryopreserved allograft heart valves: these were used with success in septic heart pathologies, such as endocarditis or aortic root abscesses. Why don't try to extend their positive results to the whole vascular tree?

In fact cryopreserved allograft heart valves proved their durability (up to 7 years from surgery) and resistance to infection, maybe because they contained viable fibroblasts, produced collagen and seemed able to continuous self-repairing.

Even today clinical data showed that cryopreserved homografts won the challenge with the fresh ones, because the latter show early postoperative mortality caused by allograft rupture and allograft-related late death, involving 5 % of the patients treated for aortic graft infection.

In 2011 Vogt et al. found that cryopreserved arterial homografts were safer, cheaper and more effective in treating mycotic aneurysms and infected vascular prosthesis than conventional grafts.

The allograft-treated group showed statistically significant better results in mortality (both surgical or infection related), disease-related survival free of reoperation, duration of ICU stay, global hospitalization, postoperative antibiotic therapy, complication rate and eradication of infection and cost-effectiveness (with an overall cost-reduction of 40 %) [2].

In literature, cryopreserved allografts have been particularly useful in the treatment of patients with aortoenteric, aortoesophageal or aortobronchial fistula, leading to 1-year mortality rate reduction, from 34 % of conventional techniques to 9 % after allograft implantation in two consecutive studies of the same institution [4, 5].

Due to the reduced frequencies of these life-threatening conditions, at the moment the versatility and potential of cryopreserved allografts have been showed by small series and case reports.

Homografts have been used with success in the treatment of peripheral vascular infections, too.

Cases of replacement of arterial segments with homograft and in contemporary vertebral stabilization have been described in patients where a polysegmental spondylitis coexisted with infected abdominal aorta aneurysm.

At last homografts have been used also in patients undergoing simultaneous gastrointestinal and aortic surgery, in those at risk of infection due to long-term immunosuppression or in case of surgery for thoracic malignancies involving major intrathoracic vessels, in order to reduce the incidence of infection of prosthetic material.

Table 17.1 shows some indications adopted for allografts in vascular surgery [6].

Using homografts the main advantages are:

- allografts allow in situ replacement of infected vascular or prosthetic segments, avoiding complex extra-anatomic reconstructions and their possible disadvantages (mainly aortic stump blowout syndrome, reinfection of implanted new graft, almost lifelong antibiotic treatment).

  For certain sites of infection (transverse aortic arch, proximal ascending aorta, upper abdominal aorta), they represent the optimal solution, because extra-anatomic reconstructions here are difficult or impossible.
- allografts can restore the natural direction of blood flow.
- some authors propose in limited prosthetic vascular infections (involving just an anastomosis or a branch of a prosthetic graft,

Table 17.1 Main indications used for allografts in vascular surgery [6]

Indication	Implanted arterial allografts	%
Infected prosthetic material	1373	54.8
Infected native artery	72	2.9
Mycotic aneurysm	119	4.8
Critical ischemia	372	14.8
Arterial injury	48	1.9
Prosthetic graft thrombosis	40	1.6
Entero-vascular fistula	47	1.9
Aneurysm of native artery	15	0.6
Allograft failure	22	0.9
Tumor	10	0.4
Aortic coarctation	3	0.1
Congenital cardiac surgery	378	15.1
Heart transplantation	4	0.2
Intolerance of vascular prosthesis	3	0.1

such as in aortobifemoral reconstructions) the substitution just of the infected prosthetic segment, in order to be less invasive and reduce reinfection rate.
- allografts don't cause perigraft fluid accumulation and scar formation around the implanted graft, reducing the risk of local wound problems or reinfections.
- antifungal and antibiotic therapy can be limited in time: it can be stopped after 3–6 months post surgery, avoiding long-term or lifelong administration even for microbiological aggressive pathogens like *Pseudomonas aeruginosa*, *Candida albicans* or *Aspergillus fumigatus*, well known for their multidrug resistance [2].

Main disadvantages of allografts are:

- the prolonged time necessary to the acquisition of the optimal homograft for any individual case; in fact, they cannot be stocked in every single hospital and so it's impossible to face emergency situations.
- long-time preparation: for the correct use of cryopreserved grafts is necessary to follow a precise protocol of thawing and washing before implantation.

  Furthermore, in case of long vascular segment substitution, homografts required a long surgical preparation, such as ligation of side branches or end-to-end anastomosis of two or several short allograft segments.
- they are more expensive than prosthetic grafts.
- cryopreserved homografts are not an everlasting vascular graft: explanted arterial allografts were fibrotic, acellular, nonvital and without endothelial cells, with weak and focal T-cell infiltrations, while the only fibrous tissue was preserved.

Vogt et al. observed the narrowing over time of allografts with smaller diameter, like a sign of chronic rejection [2].

This observation was previously supported also by other authors, such as A.D. Callow, who noticed that the larger smooth muscle cells composition in muscular arteries (such as the femoral or the popliteal ones) and, on the other hand, the greater elastic content of iliac and aortic segments, make the former more antigenic than the latter. The antigenicity of muscular and elastic arteries must be greatly reduced by the process of cryopreservation; antigenicity caused also the unsuccess of vein allografts, affected by immunologically induced thrombosis as a consequence of endothelial damage [3].

Nowadays, the indications for cryopreserved arterial allografts are few and limited to complicated thoracic cases, and in abdominal aorta the occurrence of complications of conventional surgical techniques can be treated with cryopreserved grafts [2].

In conclusion, as Vogt et al. state, "cryopreserved arterial and aortic allografts represent an additional powerful biological tool in patients with life-threatening vascular infection, improving early and late mortality and reducing the incidence of late complications and reoperations in patients with major aortic infections [2]."

In alternative to arterial homografts autologous venous segments were proposed: they showed increased operating times, the same morbidity of arterial ones, with sacrifice of healthy tissue.

Cryopreserved venous grafts also showed to be resistant to infections, thrombosis and aneurysm formation, but without the same durability of arterial segments [2].

As established in the CVHG[1] protocol, vessel procurement begins after organ harvesting.

Donor exclusion criteria are the same adopted in NITp[2] for organ and donors and are also recommended by the Europe General Standards for Tissue Banking:

- risk factors for HIV, hepatitis and other transmissible diseases in donor anamnesis
- actual signs of symptoms of transmittable diseases (malignancies included)
- donor serology positive for HIV-1, HIV-2, HbsAg, HCV or syphilis [1]

[1] CardioVascular HomoGraft.

[2] North Italy Transplant program, a transplant organization (the first Italian one) that coordinated organ procurement and transplantation activity since 1972 and serves an area of about 19 milion of inhabitants in Lombardia, Liguria, Veneto, Friuli-Venezia Giulia, Marche and Trento.

Vessels retrieved are sections of thoracic aorta, the abdominal aortoiliac tract and femoral arteries (both deep and superficial) [1].

Finding surgical strategies for procurement of vascular segments is important to reach a compromise between the need of organs and vascular structure harvesting [7].

In fact on one hand, we have to preserve the vascular peduncle of every single organ to make possible transplantation; on the other hand, we have to try to collect the longest vascular segment from every organ removal.

The first concern is cannulating for organ cooling: generally it's used an infrarenal aortotomy to cannulate aorta, clamping at the thoraco-abdominal passage.

Section of the aorta should be near to renal arteries origin.

Distal aortic clamping should be atraumatic for the vessel's wall; it can be used a tourniquet. Some surgeons suggest an endoluminal clamping with a double-balloon catheter, in order not to pinch the artery wall.

This device can be introduced through a section on the descending aorta (anterograde access) or through a hypogastric artery (retrograde access).

The latter permits to avoid section on the aortic wall, and it's easiest to perform because the donor is supine and the approach is a median sternotomy.

After aorta cannulating and perfusion of splanchnic organs and kidneys, the first step is procurement of heart and then lungs, liver and pancreas and kidneys.

Liver surgeons have to try to limit aorta dissection in a cranio-caudal direction, respecting the right renal artery and vein. Kidney surgeons have to limit aorta dissection too, in order to preserve the largest aortic segment as they can.

At last vessel harvesting can be performed, previously exploring them in order to avoid those with extended involvement of atheromasic lesions.

First, the thoracic descending aorta is isolated on a periadventitial plane, then intercostal arteries are divided at 0.5 cm from their origin.

By gently pulling the aorta anteriorly, these collaterals can be seen, avoiding to create lesions of the wall that could cause dissection after the implant.

Collateral branches are not sutured until the moment of their use, after cryopreservation.

Even the aortic arch is harvested and it's useful for reconstruction of bifurcated tracts. For this purpose, its branches are dissected the most distally as it's possible.

After the section of the left anonymous vein, it's possible to dissect in a cranial direction and harvesting a long trait of common carotid artery up to its bifurcation. These arterial segments can be useful in liver transplant for vascular reconstruction, preserving infrarenal aorta and common iliac arteries, including their bifurcation.

Even if the liver surgeon prefers to harvest iliac arteries, these should be isolated together with infrarenal aorta up to its carrefour and properly conserved; in this way, if the harvested vascular segments won't be used within 48 hours, they should be sent to the homograft bank for cryopreservation and storing.

Iliac axes have to be harvested for all their extension, including the first tract of hypogastric artery, till their first collateral branch, in order to get used during a transplant or for reconstruction of another bifurcation [7].

The same technique is used for superficial femoral arteries, sectioning their collaterals at one centimeter after their origin [7].

A series of procedures are necessary to preserve homograft. Banking of the tissues is the name given to all these procedures that include isolation, preparation, conservation and distribution of the homograft.

The harvested homografts are kept into a transport solution at 4 °C till their arrival at the bank.

Allograft dissection and evaluation have to be performed as soon as it's possible, within 24 hours after procurement.

This is the moment where a first classification of homografts is realized, based on macroscopical analysis of the graft collected.

They are divided into:

- first class: for arterial grafts, the existence of aneurismatic lesions or two blisters in the arterial wall, transmural calcification for more

than 50 % of diameter, intimal ulcers make them not acceptable.

For venous segments, they are completely unuseful if they look frankly varicose veins or with an extended wall fibrosis.

- second class: arteries are considered "acceptable with reserve" if they are ectatic or in presence of fibrocalcific thickening or calcific atheromas without ulcerative areas. Venous allografts with focal ectasia or thickened segments are also defined in this way.
- third class: normal arteries for diameter and morphology, with small traces of atherosclerosis and veins without pathological lesions can be considered acceptable [8].

As following step, the homografts are kept at 4 ° C for 96 hours on average with antibiotics; after this phase of sterilization, the tissue has to be frozen, thanks to a homogenous and controlled thermic decrease. Storing takes place at −150/−180 ° C in fumes of liquid nitrogen till homograft employment; this technique allows long-term conservation.

All these procedures of cryopreservation aim to maintain the structural and functional integrity of cells and tissues; the thermic decrease has to avoid damages to cellular vitality and function and especially of tissue structure in toto.

Some cryoprotector agents are employed to reduce the concentration of solutes, the cellular dehydration and the formation of micro–macro crystals.

The next step is establishing the adequacy of the homograft, studying bacteriological and viral aspects. Viral screening is performed on the donor's blood and the bacteriological tests are performed on tissues and fluids.

In every step of banking, information about the donor and tissues are recorded on paper and database, allowing a detailed collection of data for every single homograft [7].

An important and large experience was the one of the European Homograft Bank, in activity since 1991.

They have prepared, stored in liquid nitrogen vapor below −130 °C and distributed different kinds of arterial allografts throughout Europe and elsewhere [6].

All the tissues are prepared according to the European regulations and standards.

From 1991 to 2011, 1428 batches of cryopreserved arteries were distributed all over European countries; the most important indications for allograft (Table 17.1) implantation were infections (65 %), critical limb ischemia (15 %) and congenital cardiac malformations (15 %). Two percent of homografts were used for repairment of arterial injury, 1.5 % for prosthetic graft thrombosis, 0.4 % for tracheal replacement in case of cancer.

The upper age limit for artery donors was 55 years for males and 60 years for females without cardiovascular risk factors.

Donors with a history of malignant, bacterial, viral or other transmittable diseases weren't accepted; also arteries with morphological alterations were excluded. Morphological features leading to artery exclusion were atheroma or calcifications, luminal stenosis, ulcerative lesions, dilatation or aneurysms, important wall hematomas, wall infections and tears during recovery or preparation.

Allografts came from heart-beating multiorgan donors in brain death or non-heart-beating deceased donors recovered within 24 hours after cardiac arrest with a warm ischemia time of 6 hours (before the refrigeration of the body at +2 to +8 °C). The process must begin as soon as possible, with a maximum delay of 24 hours. In fact, the total ischemia time should not be more than 72 hours.

Once tissues (heart and arteries) had been explanted, they were rinsed with sterile saline and packed in triple sterile plastic bags, filled with cold saline (+4 °C), closed and put into a polystyrene box on wet ice bed, together with blood samples for serology evaluation of the donor. Then they were transferred to EHB within 24 hours from tissue recovery or cardiac arrest. When the material arrived at EHB, the technical staff verified the packaging, labeling and transport conditions of the tissues and blood samples. Then the donor/tissue record was created after anonymization and coding of the donor and tissue.

In the same way also for the EHB, the first morphological evaluation was the following stage, with measurement of proximal and distal

diameters and performing histological exam at both extremities of the conduit.

All the morphologically acceptable tissues were put into a solution of three antibiotics (vancomycin, polymixin B and lincomycin) for 48 hours at 4 ° C, then they passed to the second morphological analysis.

The allograft was put in 100 ml of a cryoprotectant solution of 10 % dimethyl sulfoxide in medium 199.[3]

Cryopreservation was achieved with a controlled-rate freezing program of 1 °C/min, down to −40 °C, and of 5 °C/min down to −100 °C by means of liquid nitrogen.

The cryopreserved tissues were stored in a permanently monitored storage tank in liquid nitrogen at temperatures below −130 °C.

All donor blood samples were routinely screened for hepatitis B and C, HIV, HTLV, syphilis, malaria, viral myocarditis, Q fever and tuberculosis.

Bacteriological cultures were taken for aerobic and anaerobic organisms, yeasts and fungi from transport solution with tissue samples (control A), a decontamination solution with tissue samples (control B) and a preservation solution (control C).

Histological examination of the extremities of the artery was performed in order to exclude malignancies and active infections.

EHB is responsible of the selection of the proper allograft: depending on indications, degree of emergency, and availability of the allografts, the EHB proposed a specific allograft for every request.

Even the shipment of the allograft was organized by EHB, through two kinds of shipment: in a dry shipper in liquid nitrogen at temperature below −130 °C or in dry ice at −78 °C. The first one was preferable because it allowed the safe return of the biological material in case of no implantation.

The last step was the implanting surgeon's evaluation of allograft morphology and quality of tissue preservation, with a complementary bacteriological evaluation, too, to exclude any possible contamination.

[3]A nutritional source with different components, created in 1950s by Morgan et al.

After implantation, a traceability form had to be filled and sent back to EHB.

In 20 years, EHB collected an increasing number of arteries, as shown in Fig. 17.1, reaching a maximum number of 138 batches of arteries per year in 2011. Not all the explanted arteries could be turn into cryopreserved allograft: only 68 % of arteries could be accepted, while 32 % of them were discarded mainly because of bias in morphology (58 %) and positive bacteriology (31 %) (Fig. 17.2). The most frequently implanted were femoral arteries, followed by descending aorta (Fig. 17.3) [6].

The following table (Table 17.2) shows the most common complications of the EHB's arterial allografts that didn't allow the use of the same grafts.

Even in Italy the experience of homograft banking has been realized: one of the most important tissue banks is Centro Cardiologico Monzino, where vascular (arteries and veins) and cardiac tissues (aortic, mitral, and pulmonary valves) are harvested.

This bank was founded in 1993 with the name "BIO" (Banca Italiana Omoinnesti); it was part of the hospital called "Centro Cardiologico Monzino," and its aim at the beginning was just to harvest cardiac tissues for the hospital itself.

In 1994 the activity was enlarged, including vascular tissues and involving other hospitals, allowing them to use the harvested homografts. In the same year, the bank began its collaboration with NiTp.

In 1997 the BIO became member of the European Association of Tissue Bank (EATB).

In 2000 the Italian Health Ministry approved BIO's procedures as national guidelines for procurement and transplant of cardiovascular tissues.

From 2003 the bank was certified according to UNI EN ISO 9001, and from 2005 BIO was recognized as a "certified tissue bank" within the program of CNT (Centro Nazionale Trapianti) for its activities of harvesting, processing, storing and distribution of cardiac and vascular tissues.

Since that time, the bank continues its activity of vascular and cardiac tissue procurement and storing, satisfying the needs of almost all Northern Italy [9].

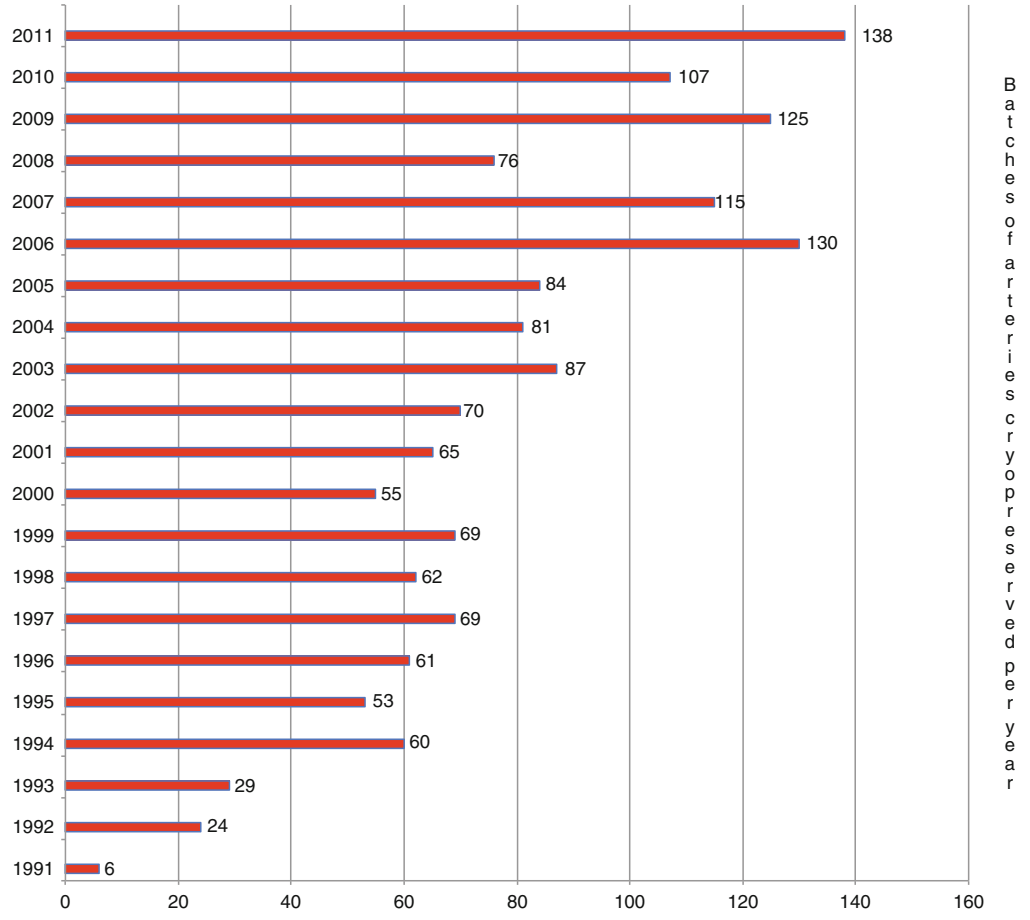

Fig. 17.1 Batches of arteries harvested and treated between 1991 and 2011 in EHB

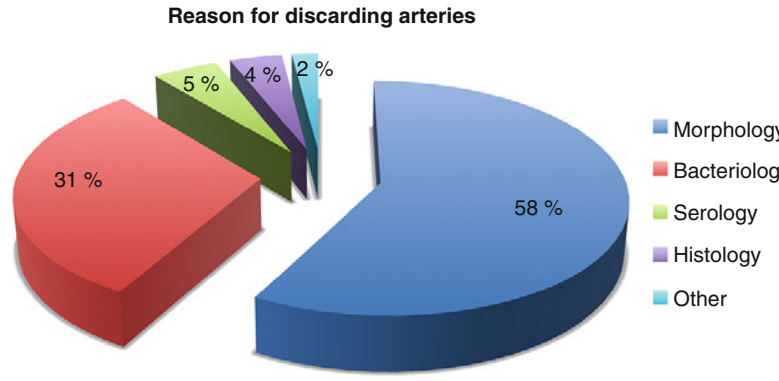

Fig. 17.2 Main causes of discarding harvested arteries between 1991 and 2011 in EHB

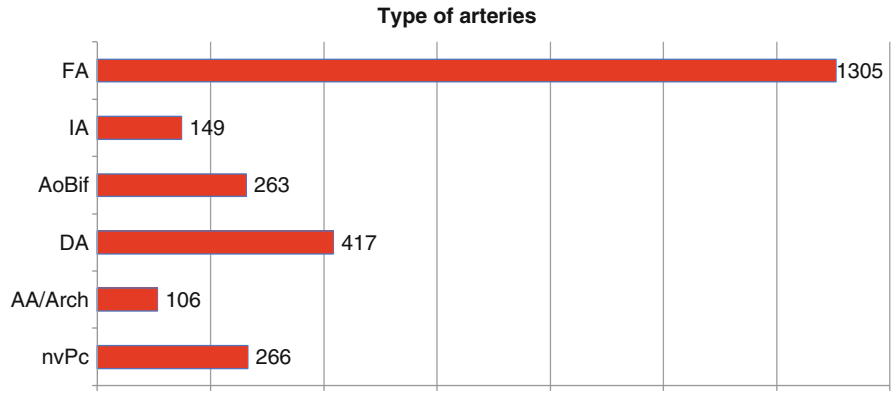

Fig. 17.3 Types of arteries used for implants. *FA* femoral artery, *IA* iliac artery, *AoBif* aortic bifurcation, *DA* descending aorta, *AA/Arch* ascending aorta/arch, *nvPC* pulmonary bifurcation without valve

Table 17.2 Complications occurred to the EHB's arterial allografts that made them unuseful for surgery

Complications	Number	%
Thawed, not implanted	36	83.7
Allograft tear during thawing	5	11.6
Bag rupture	1	2.3
Temperature fluctuation	1	2.3

References

1. Agrifoglio G, Bonalumi F et al (1997) Aortic allograft replacement: North Italy Transplant Programme (NITp). Eur J Vasc Endovasc Surg 14(Suppl A):108–110
2. Vogt PR (2011) Arterial allografts in treating aortic graft infections: something old, something new. Semi Vas Surg 24:227–233
3. Callow AD (1996) Arterial homografts. Eur J Vasc Endovasc Surg 12:272–281
4. Vogt PR, Pfammatter TH et al (1997) In situ repair of aortobronchial, aortoesophageal, and aortoenteric fistulae with cryopreserved aortic homografts. J Vasc Surg 26:11–17
5. Von Segesser LK, Tkebuchava T et al (1997) Aortobronchial and aortoesophageal fistulae as risk factors in surgery of descending thoracic aortic aneurysms. Eur J Cardiothorac Surg 12(2):195–201
6. Jashari R, Van Hoeck B et al (2013) Banking of cryopreserved arterial allografts in Europe: 20 years of operation in the European Homograft Bank (EHB) in Brussels. Cell Tissue Bank 14:589–599
7. Ponzio F, Merlo M (2001) Prelievo dei Segmenti Vascolari, Annali Italiani di Chirurgia. LXXII 2:121–123
8. Polvani GL, Guarino A et al (2001) Banking degli Omoinnesti Vascolari. LXXII 2:125–128
9. Guarino A Requisiti Normativi e Strutturali per Banche di Tessuti, Relazione del 26 Marzo 2014 alla quarta "Round Table" di Arisla- Fondazione Italiana di Ricerca per la SLA (Sclerosi Laterale Amiotrofica)

Transplantation Bench Surgery of the Abdominal Organs

18

Sguinzi Raffaella, Riccardo De Carlis, Maurizio Vertemati, Ornella Rossetti, and Paolo Aseni

Tips, Tricks and Pitfalls

Liver

- Carefully dissect the donor inferior vena cava, especially in the suprahepatic region, where the adventitia is firmly adherent to the surrounding diaphragm, and on the posterior side to avoid uncontrollable posterior bleeding during implantation.
- Recognize hepatic artery variations (Michel's classification) when examining the superior mesenteric artery.
- Dissect the hepatic artery from the aortic patch to the level of bifurcation of the gastroduodenal artery, cleaning off the celiac plexus and fibrofatty tissue enveloping the vessels.
- Do not ligate the small collaterals too near to the vascular ostia, especially in atheromasic arteries.

Kidney

- Carefully remove the perinephric fat without skeletonizing the ureters; avoid extensive opening and massive cleaning of perinephric fat in kidneys from older donors.
- Mark and subtend both the ureters with light mosquito forceps to avoid their accidental shortening and injury.
- Cut the left renal vein along the left margin of the vena cava.
- Choose the right renal vein elongation technique that is most appropriate according to the shape of the vein.
- Pay special attention to the inferior polar arteries, which often originate far from the main renal artery, from the inferior abdominal aorta, or from the iliac axis.

Pancreas

- Manipulate the pancreas parenchyma very carefully to minimize edema, injuries, and bleeding, factors which increase the risk of acute pancreatitis of the graft.

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The back-table procedure constitutes the final stage of organ procurement and requires definitive inspection, careful dissection, and preparation of the retrieved organ. It is important to maintain adequate cold preservation during the surgical maneuvers. The first step is macroscopic organ inspection to detect any injury or suspected lesion; then vascular preparation is performed. This technique requires a precise knowledge of physiological and anatomical variations in vascular patterns and an accurate dissection of all elements to perform the anastomosis on the recipient. Vascular reconstructions with homologous or heterologous grafts may be necessary. The tightness of every vascular element is systematically verified. In this chapter liver kidney and pancreas technical features of the back table are described with particular attention to anatomical descriptions of vascular patterns and surgical techniques.

18.1 Liver Back-Table Surgery and Vascular Graft Preparation

18.1.1 General Principles

The back-table surgery for the liver graft is an important step before orthotopic liver transplantation (OLTx); it constitutes the final stage of liver procurement and is the first back-table procedure in the recipient operating room when back-table should be performed by the same surgical team. The total operation time for organ harvesting and the consequent warm and cold ischemia can affect the success of the subsequent liver transplant procedure. Cold storage of the organ by dipping in cold preservation solution, a fast bench surgery and fast implantation are also important factors to reduce the overall ischemic time and to maintain graft quality by reducing the "preservation injury" (PI). PI can occur at any time during the agonal phase of the cardiocirculatory activity, after aortic cross clamping and cardiac arrest, during the cold phase of organ harvesting, and finally during the implantation of the graft into the recipient. Multiple potential factors leading to primary graft dysfunction (PGD) can contribute to the graft damage of PI. These include donor diseases, drug toxicity, prolonged hypotension, unrecognized trauma of the graft, metabolic abnormalities triggering graft edema and an improper perfusion technique.

It is important to keep the liver as fully immersed in the cooled preservation solution as possible during the entire bench surgical procedure and to limit exposure to the relevant anatomy. Large pieces of ice in the liver bag should also be avoided, because they can damage the liver.

The surgeon performing the back-table procedure (an assistant is desirable) creates a cold solution fluid with a fine ice slurry bath from four 1 liter bags of frozen lactated Ringer's solution added to the perfusion fluid in the back-table basin, maintaining the solution temperature of approximately 4 °C. The donor liver graft is then covered with cold wet swabs to protect the organ from direct contact with ice and to avoid freezing damage of the surface liver tissue.

After perfusion, the exsanguinated liver graft is further inspected to confirm its degree of steatosis and suitability for transplantation.

18.1.2 Inferior Vena Cava Preparation

One important step during the back-table procedure is the careful dissection and preparation of the donor inferior vena cava (IVC) to identify and ligate its tributaries. Failure to control these veins or to identify any iatrogenic injury to the IVC and hepatic veins will result in troublesome hemorrhage after reperfusion and require difficult maneuvers for the mobilization of the graft to identify and suture the bleeding sites. This maneuver increases the risk of ischemia to the new liver and strains the vascular anastomotic sites, which can result in further bleeding.

The IVC of the donor liver is prepared for transplantation on the bench. Dissection is started on the posterior aspect of the suprahepatic IVC and continues down to the infrahepatic IVC,

dissecting and dividing the left hepatocaval ligament at the level of the left edge of the caudate lobe. Sufficient width of the posterior vena cava is mobilized to facilitate the cavo-cavostomy and this can usually be achieved without dividing any venous tributaries that drain the caudate lobe. The diaphragmatic and fatty tissue around the suprahepatic IVC is carefully dissected; there are usually 1–2 small phrenic veins on the right and 1–2 larger veins on the left that must be tied at this stage. A Watson-Cheyne probe can help identify these branches. The left hepatic vein is thin-walled and is prone to injury during this dissection.

The cut ends of the suprahepatic and infrahepatic IVC are stretched out by the assistant surgeon. The posterior aspect of the IVC and the right lobe of the liver are dissociated from all extraneous tissue including pieces of diaphragm and the right adrenal tissue. The right adrenal vein and the inferior phrenic veins, usually 2–4, require ligation. Great care should be taken in the region of the suprahepatic IVC, because the adventitia of the right and left hepatic veins adheres firmly to the surrounding diaphragm. Inappropriate dissection can lead to the injury of these veins which, following repair, may compromise hepatic venous outflow. The caudate lobe is partially dissected from the IVC by first dividing the right hepatocaval ligament (Makuuchi's ligament) where it inserts into the right edge of the caudate lobe. Some very small hepatic veins may need to be ligated and divided near to the superior caval outflow to obtain an adequate caval patch. The IVC should be inspected for defects that require oversewing with Prolene 6/0 or 7/0. Water tightness is confirmed by applying a vascular clamp subsequently to both ends of the IVC and flushing with 20–30 mL of Celsior solution from the free side using a 50-mL catheter-tipped syringe. It is very important to verify the tightness of the vena cava wall and to maintain the vena cava length to allow the surgeon to determine its length during graft implantation. In the case of the piggyback anastomotic technique, excess infrahepatic vena caval tissue should be removed (Fig. 18.1). The inferior edge of the IVC is then closed and sutured with 4-0 Prolene running sutures or with a vascular stapler device.

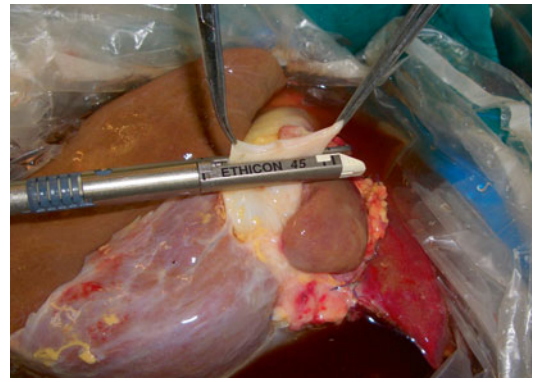

Fig. 18.1 Suture of the distal IVC (vascular stapler)

18.1.3 Portal Vein Preparation

The portal vein is dissected free for an adequate length, almost 3–5 cm to the level of its bifurcation, and 1–2 small tributaries (coronary left gastric vein) are ligated. The portal vein must be confirmed as watertight: Some perfusion solution is flushed with a catheter-tipped syringe, using two fingers to close the hilar side filled with bath fluid and test for any points of leakage. Every injury of the vein must be repaired with 6/0 Prolene stitches [1–3].

18.1.4 Hepatic Artery Variations

During liver transplantation, the recognition of hepatic artery variations (HAV) is mandatory for the safety of the graft and of the recipient (Fig. 18.2).

There are ten types of anatomical pattern presentation according to *Michel's classification* [4–9]:

- Type 1 (70 %): classic anatomical pattern in which the common hepatic artery arises from the celiac trunk to form the gastroduodenal and proper hepatic arteries, the latter dividing distally into right and left branches.
- Type 2 (9.7 %): a replaced left hepatic artery arises from the left gastric artery.
- Type 3 (7.8 %): a replaced right hepatic artery originates from the superior mesenteric artery.
- Type 4 (3.1 %): a replaced left hepatic artery arises from the left gastric artery and a

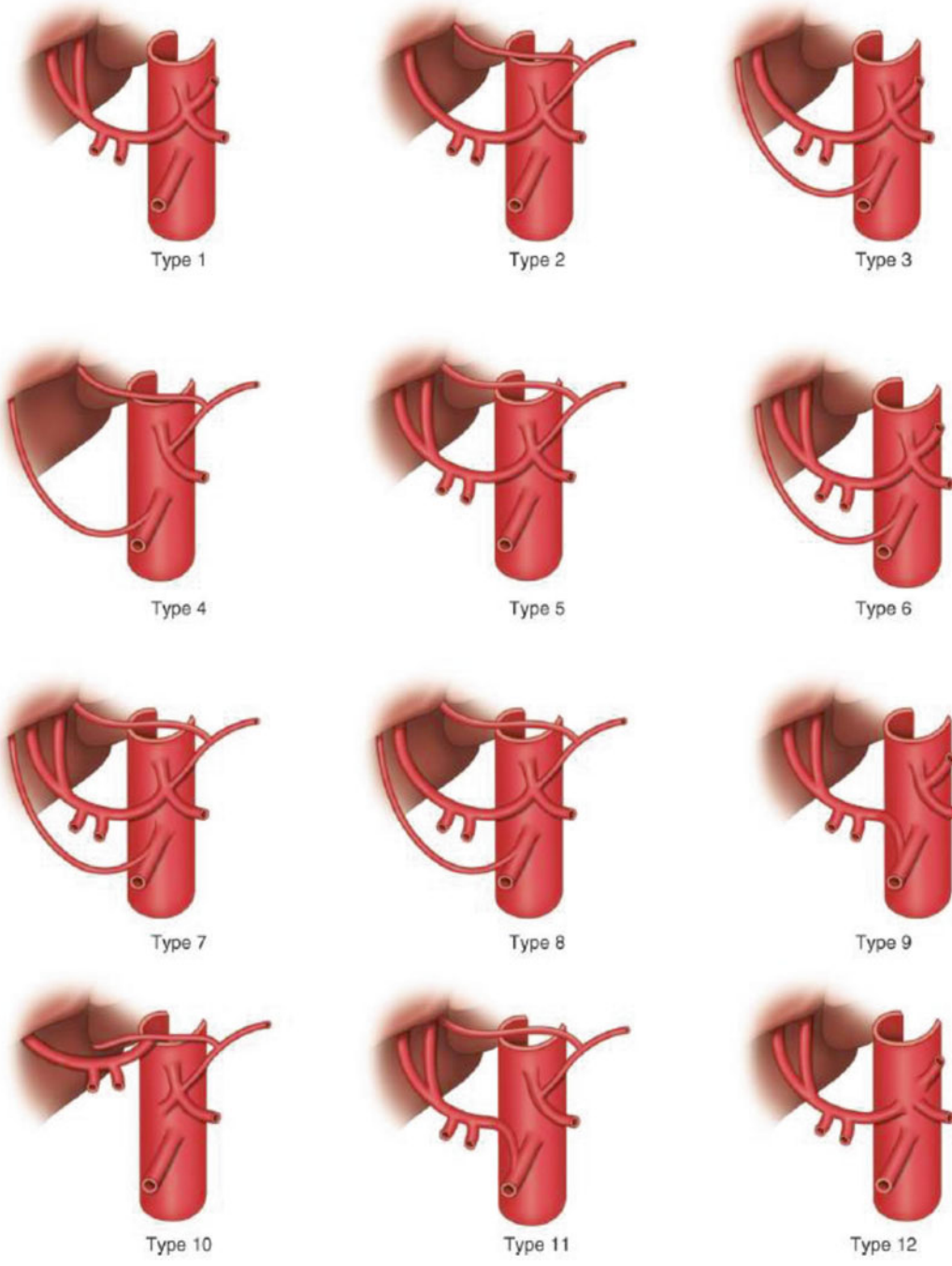

Fig. 18.2 Michel's classification: ten types of hepatic artery variations according to Michel's classification with two new types not previously included

replaced right hepatic artery originates from the superior mesenteric artery.
- Type 5 (3.9 %): an accessory left hepatic artery originates from the left gastric artery.
- Type 6 (0.6 %): an accessory right hepatic artery arises from the superior mesenteric artery.
- Type 7 (0.6 %): an accessory left hepatic artery originates from the left gastric artery, and an accessory right hepatic artery originates from the superior mesenteric artery.
- Type 8 (0.3 %): a replaced left hepatic artery originates from the left gastric artery and an accessory right hepatic artery originates from the superior mesenteric artery or vice versa.
- Type 9 (2.5 %): the common hepatic artery originates from the superior mesenteric artery.
- Type 10: the common hepatic artery arises from a left gastric artery.

The two new types not included in Michel's classification are as follows:

- Type 11 (0.3 % of cases in the literature): the common hepatic artery arises from the superior mesenteric artery and an accessory left hepatic artery is a branch from the left gastric artery.
- Type 12 (0.7 % of cases in the literature): the common hepatic artery originates directly from the aorta.

In 1971, Suzuki et al. contributed an article on the surgical importance of anatomic variants of the hepatic arteries; it emphasized the detailed hepatic arterial variation at the hepatic hilum. Suzuki presented a new classification based on the hepatic arterial pattern at the hilar region; according to *Suzuki's classification*, the numbers of hepatic arteries constitute the primary factor in classifying variations of the artery.

These are classified into three groups:

Group I has one hepatic artery (proper hepatic artery).
Group II has two independent hepatic arteries with four presentation patterns.
Group III has three or more hepatic arteries entering the liver at the hilar region.

Each group is divided into three types in correspondence with the arteries from which the hepatic artery originates.

In the celiac type, the hepatic artery is derived from the celiac trunk or its branches.
In the mesenteric type, the hepatic artery arises from the SMA or its branches.
In the mixed type, the hepatic artery originates from both the celiac and superior mesenteric arteries or, very rarely, from the celiac and abdominal aorta.

18.1.5 Hepatic Artery Preparation

Aberrant hepatic arteries should be sought and, if present, dissected for an appropriate length. Once the variations are recognized, the second step is performed during back-table surgery; an optimal arterial supply must be assured for the liver graft by adequate harvesting of the vascular donor graft. Only accurate microvascular technique with the help of magnifying glasses can assure the patency of the anastomoses and minimize the risk of immediate arterial thrombosis and organ failure. The hepatic artery is then evaluated and cleared of adventitia, celiac plexus nerves, and lymphatic tissue. The celiac trunk is prepared and the distal end of the donor SMA is dissected along its longitudinal axis to identify the right accessory (Type 4) or replaced artery (Type 9). In the case of a classic anatomical pattern with a unique hepatic artery, the arterial inflow is dissected from the aortic patch to the level of bifurcation of the gastroduodenal artery, cleaning off the celiac plexus and fibrofatty tissue enveloping the vessels and avoiding the skeletonization of the arterial axis. A small quantity of fibrous tissue around the proper hepatic artery will prevent vascular kinking or twisting of the artery in that area. The superior mesenteric artery should be examined carefully to detect an accessory or replaced right hepatic artery. Finally, an aortic patch of approximately 2.0 cm × 1.5 cm is created. The splenic artery, the left gastric artery, and the origin of the gastroduodenal artery are ligated. Especially in atheromasic arteries, it is important

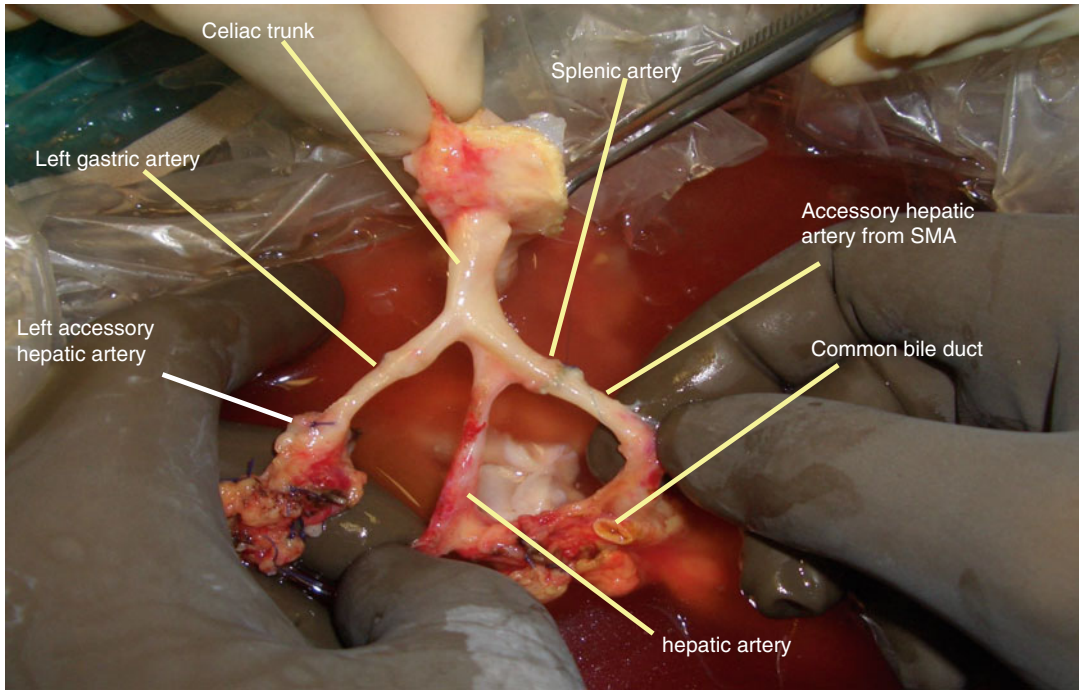

Fig. 18.3 Reconstruction of an accessory right hepatic artery (from SMA) on the splenic artery (7/0 monofilament) and preservation of accessory left hepatic artery from the left gastric artery

not to ligate small collaterals too near to the vascular ostia to avoid the danger of forming intimal flaps. If an accessory left hepatic artery originating from the left gastric artery is present, it is dangerous to explore its patency with a blunt needle, because it has very small caliber. In this case, it will be better to leave some adventitial fibrofatty tissue to avoid the skeletonization of the artery and subsequent kinking or twisting. All small collaterals (vasa gastrica breviora) must be carefully ligated, and the left hepatic artery should be hydro-pneumatically tested by injecting a small quantity of solution from the ostium of the celiac trunk [2, 3]. If an accessory hepatic artery originating from the SMA is present, there is no standard technique of vascular reconstruction; the goal of reconstruction is to obtain a unique celiac common trunk to be anastomosed with the recipient's hepatic artery with a satisfactory result at bench time. After more than 300 cases of hepatic artery reconstruction performed in over 1800 liver transplantations (from 1985 to 2015), we were able to outline some general principles about bench surgery reconstructive techniques. If the accessory right hepatic branch diameter is sufficiently large (>2 mm), an end-to-end reconstruction with the splenic artery may be the best choice to achieve a unique arterial inflow from the celiac trunk (Fig. 18.3). If the accessory right hepatic branch diameter has a small caliber (<2 mm), an anastomosis with the stump of the gastroduodenal artery can be realized (Fig. 18.4).

In the case of accidental sectioning of the right accessory branch, two possibilities of reconstruction are available according to our experience:

(a) If the residual stump is very short, an end-to-end anastomosis between the right accessory hepatic branch and the gastroduodenal artery (also utilizing an interposition graft by a short arterial segment of adequate diameter, as splenic or left gastric artery) can be performed.
(b) If the section is proximal to the mesenteric branch, an end-to-end anastomosis with the splenic, left gastric artery or with the gastroduodenal artery is always possible.

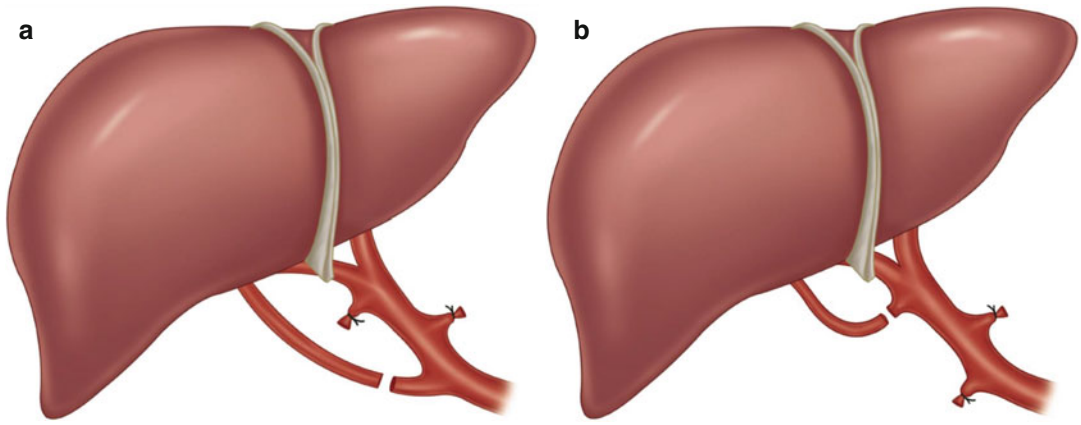

Fig. 18.4 Two most common types of reconstruction for the accessory right hepatic artery depending on caliber and length (**a**) with the splenic stump and (**b**) with the GDA stump

In Fig. 18.5 some other possible reconstruction techniques are shown; every case is different and must be analyzed according to each individual arterial segment in consideration of its length and different angulations of vascular insertion relative to the longitudinal axis. Sometimes due to the recipient's arterial damage (stenosis or flapping), an interposition jumping graft with the iliac donor artery graft on the recipient's aorta is necessary during the transplant procedure or, more frequently, during liver retransplantation (Fig. 18.6).

18.1.6 Biliary Tract Identification and Completion of Liver Back-Table Transplantation

It is better to prepare the biliary tract directly on the recipient after the reperfusion of the graft, thus avoiding any dissection at the back table to prevent common bile duct devascularization of the graft.

Depending on the delay from the completion of the back-table procedure to implantation, the liver should either be re-bagged and placed in another thermostatic container with ice or kept in a cool room until the time of reimplantation. In the case of early implantation, the liver should be wrapped in a pack and kept fully immersed in the same basin with perfusion solution and slush ice packed all around it but not directly in contact with the graft. When ready, just before implantation, the graft can be flushed with 500 mL of Ringer's solution to dilute the excess potassium [10–13].

18.1.7 Arterial Graft Preparation

After the liver back-table preparation, it is important to prepare donor iliac arterial and venous grafts, not only for a scheduled retransplantation procedure but also in case of any unexpected damage or thrombosis of the recipient's hepatic artery or portal vein. Donor iliac arteries may be used as a conduit between the recipient's infrarenal aorta and the donor's graft hepatic artery. Occasionally, the right common/external iliac artery or the suprarenal aorta may be used for inflow to the conduit. The recipient's hepatic artery can be unsuitable to provide a correct hepatic inflow. In these cases, the hepatic artery is implanted into the recipient's infrarenal aorta with the interposition of an iliac "jumping graft" with an end-to-side anastomosis between the common iliac artery graft on the recipient's aorta and an end-to-end anastomosis of the external iliac artery on the recipient's hepatic artery at the level of the origin of the gastroduodenal artery (internal iliac artery graft is sectioned and ligated at its origin). Sometimes in the case of portal vein thrombosis, donor iliac veins may be used as

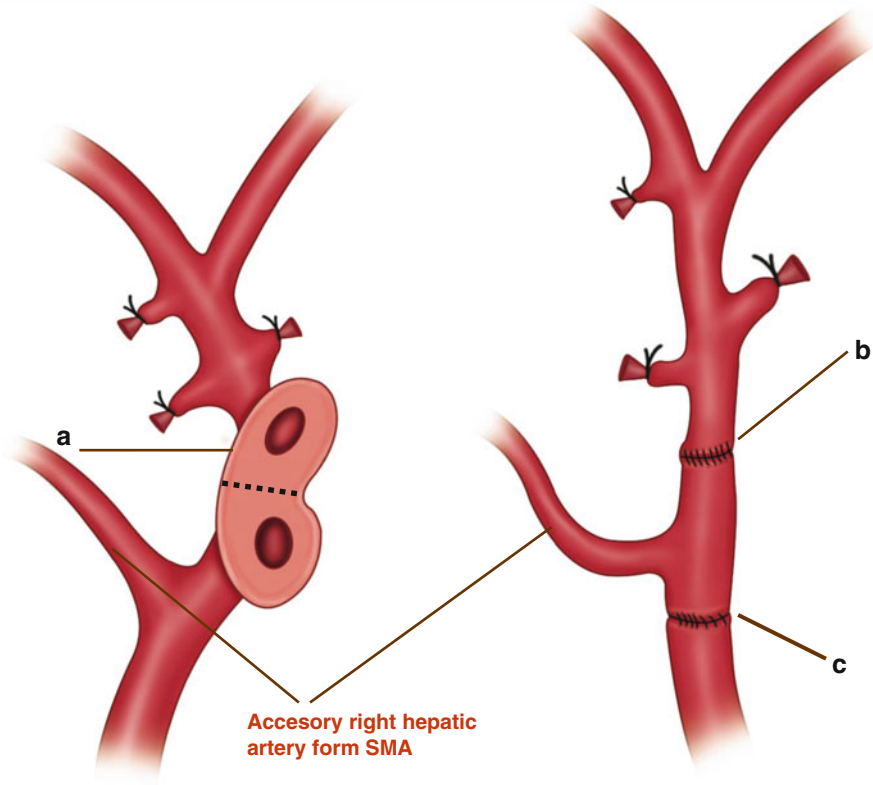

Fig. 18.5 Arterial reconstruction techniques in the presence of an accessory right hepatic artery: (**a**) aortic patch with celiac trunk and SMA can be divided, obtaining two single patches for end-to-end anastomosis; (**b**) end-to-end anastomosis performed between the common hepatic artery and the SMA of the graft; and (**c**) end-to-end anastomosis between SMA and recipient's hepatic artery

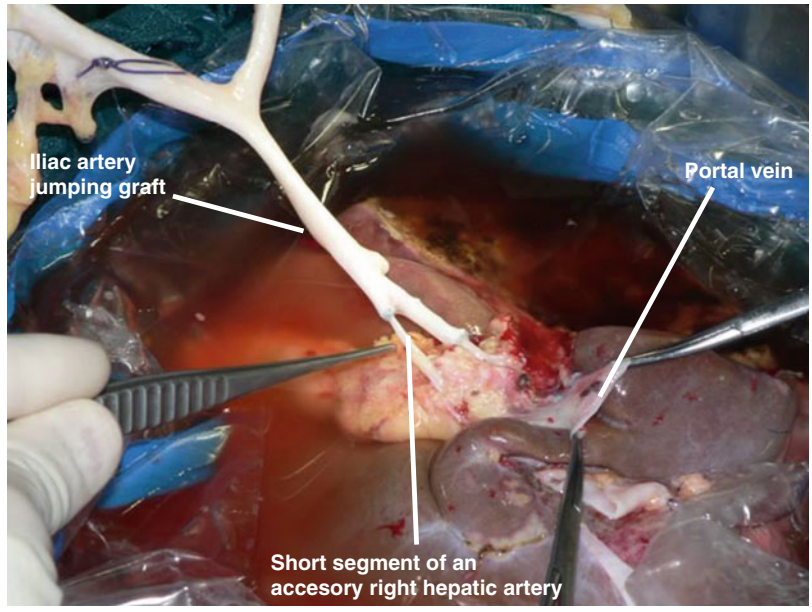

Fig. 18.6 Right accessory hepatic artery with a short section line too near to hepatic hilum: arterial reconstruction with an iliac jumping graft of the same donor during a liver retransplant

conduits between the recipient's superior mesenteric vein (SMV) and the donor's portal vein with an end-to-side anastomosis. Iliac arterial and venous graft preparation must be meticulous, removing all connective tissue around the vascular walls and suturing with 7/0 monofilament all small collaterals and all the little venous and arterial holes along the vascular conduits [14, 15].

18.2 Kidney Back-Table Surgery

18.2.1 General Principles

The kidney back-table procedure can sometimes be the last procedure of bench surgery; it is often performed by surgeons who have been involved in the liver back-table surgery for many hours. It is important to be systematic in organ preparation to minimize the possibility of mistakes that may compromise the implantation. The purpose of the back table for the explanted kidneys is to examine the organ under hypothermic conditions in a cold fluid prepared with frozen lactated Ringer's solution added to the preferred perfusion solution in a basin at a temperature of approximately 4°C. A living-donor kidney must be immediately perfused with 500–600 cc of UW or perfusion solution and usually no more preparation is needed after living-donor nephrectomy, unless double or multiple renal arteries are present; organs from deceased donors require meticulous preparation prior to transplantation.

18.2.2 Systematic Macroscopic Exploration of Kidney

The opening of Gerota's fascia soon after harvesting the kidney is a standard kidney donor procedure to exclude the presence of renal tumors and to evaluate the perfusion status of both kidneys. However, extensive opening and massive cleaning of perinephric fat should be avoided in kidneys from older donors, in which the perinephric fat is strongly adherent to the renal surface and capsular damage can be easily produced. Perinephric fat should also be carefully removed to maintain the ureteral vascular supply without skeletonizing the ureters. Both the ureters are then marked and subtended with light mosquito forceps laterally. The vascular pedicle for the vascular anastomosis is then prepared; renal arteries and veins and vascular patches must be dissected from perivascular tissue [3, 16]. If the kidneys have been harvested en bloc, they should be separated; the aortic segment is cut along the midline of its longitudinal axis, taking care not to get too close to the renal aortic ostia. A wide aortic patch should be provided for both kidneys (Fig. 18.7). The left renal vein should be cut along the left margin of the vena cava. The vena cava is usually kept with the right kidney for elongation venoplasty of the short right renal vein. However, some centers cut the vena cava into two hemi-veins along the longitudinal axis leaving one venous patch for each kidney.

18.2.3 Renal Vein Preparation

After the separation of the right and left renal grafts, the first step is renal vein dissection. The left kidney renal vein is prepared by ligating all venous collaterals, in particular the adrenal vein and the gonadic vein with the intention not to dissect close to the hilum. For the right kidney, the right renal vein must also be reconstructed and elongated.

Three techniques of right renal vein reconstruction are usually employed; the "standard technique" consists of lengthening the vein and reshaping the adjacent vena cava to the right renal vein using two transverse incisions directed toward the ostium of the left renal vein, which are joined with continuous sutures of nonabsorbable material (Fig. 18.8a). This technique is the most commonly used for its simplicity and ease to perform; it provides an elongated segment that is more similar to the renal vein. The second technique consists of elongating the right renal vein through an oblique section of the cava that runs from the right upper edge of the right renal vein ostium to the lower edge of the left renal vein, forming a type of "pipe" (Fig. 18.8b). A disadvantage of this technique is that the distal part of

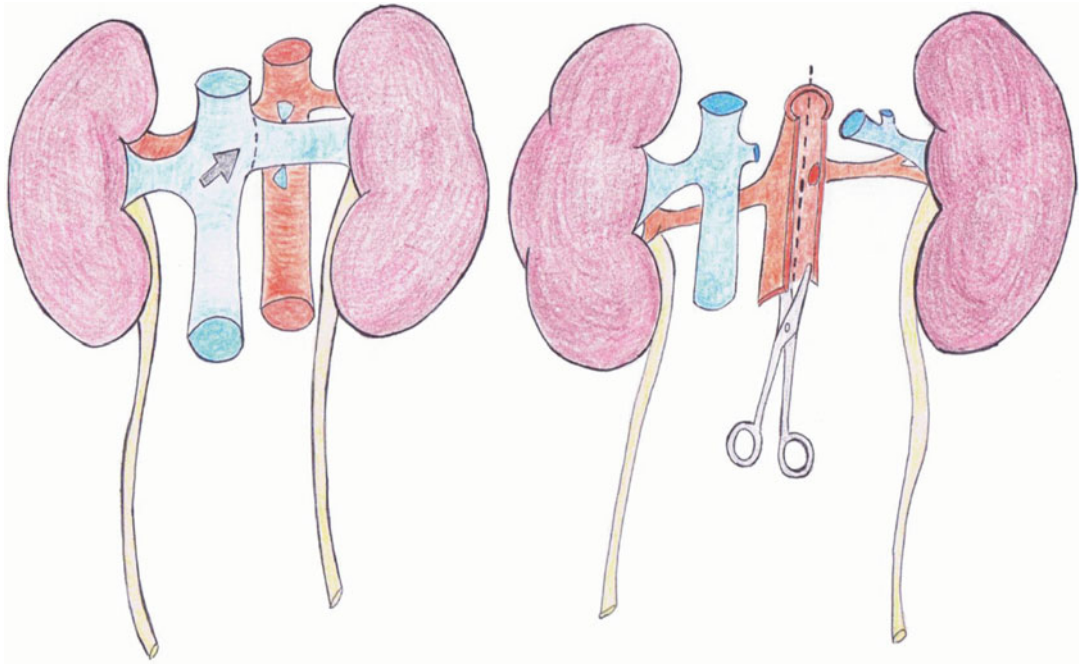

Fig. 18.7 If the kidneys have been explanted en bloc, they should be separated; the inferior vena cava remains with the right kidney and could be useful to extend the right renal vein; the aortic segment is cut along the midline of its longitudinal axis, taking care not to get too close to the renal aortic ostia

the elongated segment is broad, and the reno-iliac anastomosis could be too large. The third elongation technique is used when the right kidney brings only half of the vena cava, which is cut longitudinally during the removal of the kidneys. In this case, both vena cava flaps can be joined along the longitudinal axis of the right renal vein [17, 18] (Fig. 18.8c).

18.2.4 Preparation of Renal Arteries

Arterial branches are completely dissected with the intention not to dissect too close to the hilum. Small collaterals from the renal artery, such as a lower adrenal gland artery, must be ligated or overstitched. Multiple renal transplant arteries or accessory polar arteries must be identified. Special attention should be paid to the inferior polar arteries, which often originate far from the main renal artery, especially from the inferior aorta or from the iliac axis. The use of grafts with multiple renal arteries can pose a challenge to the transplant surgeon. Various reconstruction techniques are described in the case of multiple renal arteries, differing according to the surgeon's experience and the arteries' anatomical position and orientation. Two main arterial sectioning techniques at procurement are described: the first is commonly used when the renal arteries' ostia are near and consists of dissecting and separating the emergence of both renal vessels from the aorta, leaving behind a wide aortic Carrel patch.

An alternative approach is to cut the artery and perform a second end-to-side anastomosis in the main renal artery of the graft without a Carrel patch (Fig. 18.9). The latter option is mandatory in living-donor nephrectomy when the aortic "patch" cannot be obtained. If a common patch is impossible to preserve, we suggest patches for each artery. Preferably, all arteries should be located on a single patch by suturing the two hemi-patches (Fig. 18.10). However, when the distance between the arteries is sufficiently short (no more than 2 cm), no further reconstruction is

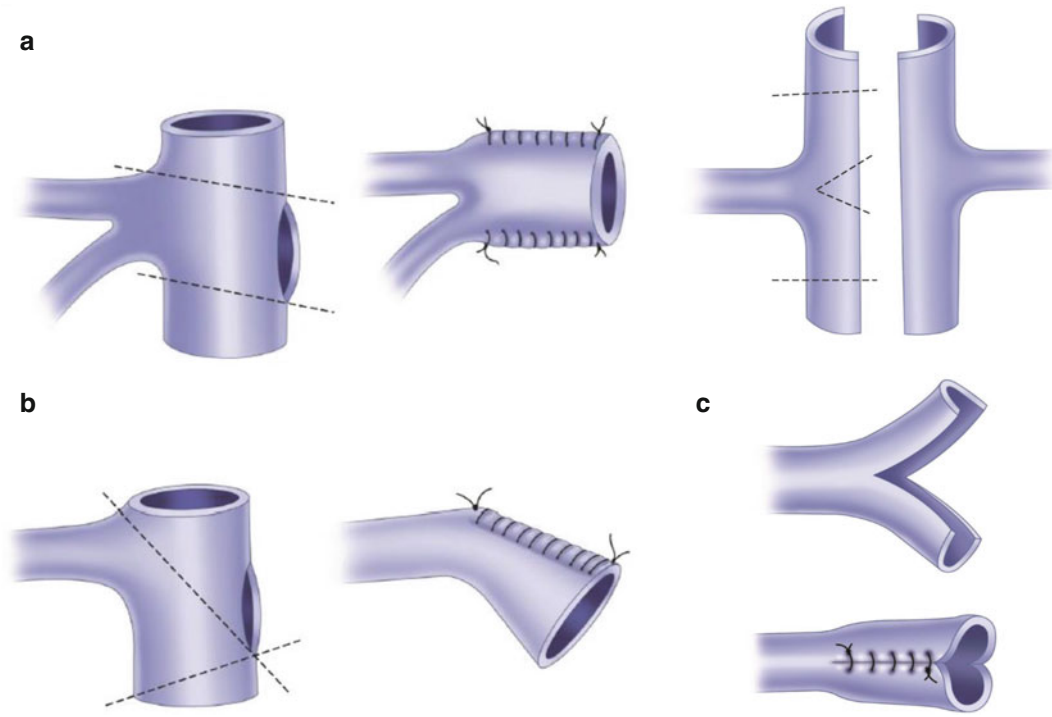

Fig. 18.8 Three different types of right renal vein reconstruction and elongation. (**a**) "standard technique": consists of lengthening the vein and reshaping the adjacent vena cava to the right renal vein using two transverse incisions directed toward the ostium of the left renal vein, which are joined with continuous sutures of non-absorbable material. (**b**) "second technique": consists of elongating the right renal vein through an oblique section of the cava that runs from the right upper edge of the right renal vein ostium to the lower edge of the left renal vein, forming a type of "pipe". (**c**) "third technique": used when the right kidney brings only half of the vena cava, which is cut longitudinally during the removal of the kidneys. In this case, both vena cava flaps can be joined along the longitudinal axis of the right renal vein

needed, and a unique end-to-side anastomosis is performed between the donor aortic patch and the recipient's common iliac artery in the lower right iliac abdominal quadrant, if possible.

Several other possible techniques [19–22] have been described when there is great distance between the arteries: aortic patch can be divided into two for sequential anastomosis, or it can be shortened by a segment resection with side-to-side anastomosis using 7–8/0 stitches. Truncated accessory or polar renal arteries during harvesting or bench surgery should be reconstructed by end-to-end anastomosis by microsurgical technique. Alternatively, the truncated vessel should be used for sequential end-to-side anastomosis to the recipient without a patch. If possible, we usually do not perform end-to-side anastomosis to the main renal artery because of the high risk of vascular thrombosis of both vessels leading to graft loss. Small polar arteries showing a strong backflow when perfused by the main artery can be closed if sequential anastomosis seems unreasonably difficult or dangerous, remembering that a lower polar artery may be crucial for the perfusion of the ureter and renal pelvis. Cutting a lower polar artery may lead to distal necrosis of the ureter followed by urinary leakage.

Atherosclerosis is frequently found in donor organs; while mild, it has no effect on the technique. However, when severe, it requires special attention. Along with atherosclerosis, the risk of renal dysfunction and vascular occlusion is augmented due to preexisting renal artery stenosis of the donor and intimal injury. The renal artery should be analyzed for proximal stenosis; the

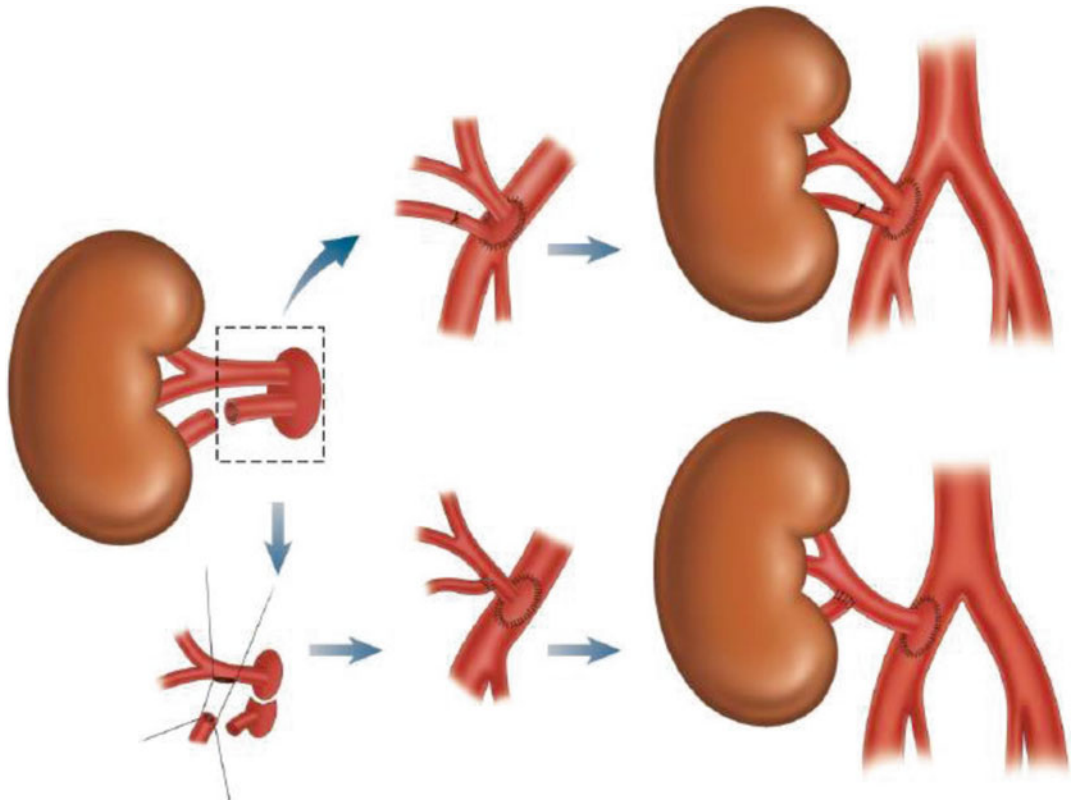

Fig. 18.9 Alternative approach in the case of double renal artery when a Carrel patch is too large (wide distance between two arteries); the inferior artery is cut and an end-to-side anastomosis to the main renal artery of the graft is performed

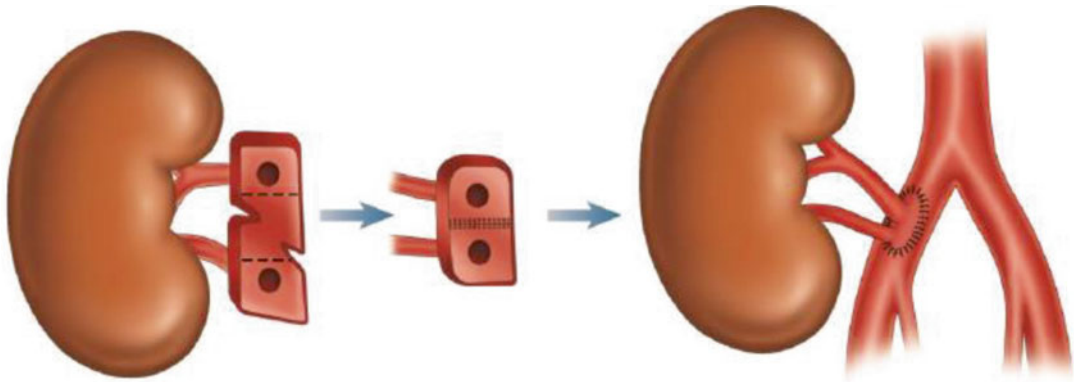

Fig. 18.10 Arterial anastomosis with unique patch

presence of stenosis or intimal desquamation within the patch or proximal artery requires shortening of the renal artery. Due to this risk, we avoid a further back-table perfusion in the case of atherosclerotic plaques near the renal ostium. In affected areas where atherosclerotic plaques cannot be safely removed, some "Kunlin" stitches can be used to minimize the

risk of ongoing dissection and vascular occlusion by the intimal flap. However, aortic patches with severe atherosclerosis and intimal lesions should instead be removed and the shortened artery finally anastomosed end to side without a patch. When a donor kidney has two arteries of unequal size, it is preferable to anastomose them individually rather than perform an end-to-side or side-to-side bench surgery, which has the potential risk of compromising the lumen of the larger renal artery. The larger of the two arteries is anastomosed first. A distal side-to-side anastomosis is favored for two vessels of similar diameter, whereas an end-to-side anastomosis is preferred for vessels showing discrepancies in diameter. We suggest sequential anastomosis if one common aortic patch is lacking. Whenever possible, sequential end-to-side anastomoses are prepared with patches. However, a suitable length of the arteries is even more important than the existence of patches. Common and external iliac arteries may be used for up to three or more sequential anastomoses.

As another option, damaged or supernumerary renal arteries can be anastomosed end to side to a biological vascular patch, which is then anastomosed to the recipient's iliac artery [23].

Multiple renal arteries are found unilaterally in 25 % and bilaterally in 10 % of the population. The existence of multiple renal arteries (more than two) has been considered a relative contraindication because of the incidence of vascular and urologic complications. Recently, multiple studies have shown that despite technical difficulties, grafts with multiple arteries present similar indexes of surgical complications and outcome compared to grafts with a single artery [19, 20].

Venous and arterial water tightness must be confirmed by flushing with perfusion solution. A test for any points of leakage should be performed with a 30-mL syringe filled with bath fluid gently inserted in the renal artery and vein after finger clamping the distal hilar side. It is very important to take care not to damage the intimal side of vessels, and we prefer blunt tip needles for arteries and conic needles for veins. Every injury or leak of the renal vein and artery must be repaired with Prolene 7/0 stitches. The kidney can finally be rebagged, wrapped in a pack, and kept well immersed in the preferred perfusion solution with slush packed all around it.

18.3 Living Donor Kidney Back-Table Surgery

Living donor kidney back-table surgery is a very important step for the implementation and success of renal transplantation and it needs special attention.

The kidney must be immediately perfused with 600–800 cc of low viscosity perfusion solution with the perfusion bag 90 cm above the organ. A careful dissection of some small clusters of perirenal fat can be removed; care must be taken around the ureter, the renal pelvis and their vascularization. The renal hilum must be prepared by dissecting the renal vein and tying together the adrenal vein and the gonadic vein for the left kidney. Some small collaterals of the main renal vein can be safely ligated and sectioned because of the presence of multiple collaterals in the venous system. In the case of a short right renal vein, it can be elongated with a caval patch using a venous homograft procured within 48 h from deceased donors or from the tissue bank when correctly preserved.

In the case of multiple renal arteries, the technique should be individualized on the basis of the caliber and length of the multiple renal arteries. It becomes more challenging when there are more than two arteries, because there is no vascular graft available from a living-donor kidney unless recently (less than 48 h) retrieved and correctly preserved from a deceased donor. Depending on the vascular graft available from a tissue bank or from recent deceased donor graft procurement, various operative techniques can be utilized for the vascular reconstruction of kidneys with multiple arteries. In the majority of cases, separate anastomoses of the renal arteries to the common, to the external and/or to the internal iliac artery can be performed. The most common arterial reconstructive technique without an available vascular graft is a side-to-side

reconstruction (syndactylization) performed on the back table by "spatulating" both arteries and joining them to form a common ostium for the anastomosis to the recipient iliac artery. Some allografts have small accessory arteries near the upper renal pole that do not supply the ureter or pelvis and are less than 1 mm in diameter; these can be safely ligated as they most likely supply less than 10 % of the kidney parenchyma. Other techniques involve two separate anastomoses to the recipient artery; a smaller accessory renal artery can be anastomosed end to side to the main renal artery [21]. The inferior epigastric artery can be also used as inflow to lower pole accessory arteries [22]. Some cases with three arteries and in the absence of atherosclerotic damage, the internal iliac artery with the two main collaterals from the recipient can be harvested, thus allowing three distal branches for bench reconstruction.

A novel technique described in the literature allows multiple renal arteries to be anastomosed to the gonadal vein Carrel patch, which is anastomosed to the side of the external iliac artery [24]. This technique enables multiple renal arteries to be parallel to each other to avoid the risk of kinking. The gonadal vein can be obtained with the ureter during live donor nephrectomy; it can also be considered a technical resource during live donor kidney transplantation. The gonadal vein has also been used to extend the right renal vein using a spiral fashion vein or as a conduit for an end-to-end anastomosis to the renal vein when the gonadal vein is larger, particularly in female donors. Recent improvements in surgical techniques with laparoscopic or robotic equipment have made the recovery of renal allografts with multiple arteries safe feasible, and therefore more common; a proper reconstruction does not increase the risk of renal artery thrombosis [25]. After kidney preparation, vascular water tightness must be confirmed by flushing with perfusion solution using a blunt tip needle as previously described. A basic training in vascular surgery and creative problem solving with the ability to provide solutions to unforeseen scenarios are usually required for transplant surgeons.

18.4 Pancreas Back-Table Surgery

The back-table preparation of the pancreas is best performed at the recipient hospital, because the procedure requires special surgical precision and attention. Sometimes, the liver and pancreas are retrieved en bloc by surgical teams and should be transported to different transplantation centers; in that case, the ex vivo separation of the two organs must be performed at the donor hospital (Fig. 18.11). A cold fluid bath is prepared with frozen lactated Ringer's solution added to the usual perfusion solution in a basin at 0–4 °C. A whole pancreaticoduodenal graft that includes the whole pancreas and the first, the second and a segment of the third duodenal portions should be fully immersed in the cold bath solution because the bench procedure can sometimes require more than one hour. The ends of the duodenal segments are further stapled with a GIA stapler 60 to form a 14–15 cm segment starting from the lower pylorus and arriving to the second duodenal tract. Encroachment upon the ampulla of Vater must be avoided. Both extremities of the suture can be reinforced with 4/0 reabsorbable purse-string sutures according to the surgeon's experience. Every small arterial and venous vessel at the head of the pancreas is closed with sutures to prevent bleeding during reperfusion of pancreas, especially in diabetic recipients who suffer from parasympathetic dysfunction and who will not have an adequate full adrenergic response to blood loss. A second 4/0 Prolene ligature on the distal bile duct as well as on the distal tract of the gastroduodenal artery can be useful, although some centers use the revascularization of the gastroduodenal artery. Ligatures must not be too near the intersection with the pancreaticoduodenal artery. The distal splenic artery and the distal splenic vein are ligated separately and the spleen is then removed. Finally, a donor Y graft from the common iliac axis and its bifurcation of the external and internal iliac branches is usually employed to create a single arterial pedicle, by anastomosing their peripheral branches to the SMA and to the splenic artery of the graft (Fig. 18.12) with end-to-end 6-0 Prolene running sutures. In case of compromised perfusion of the head of the pancreas due to

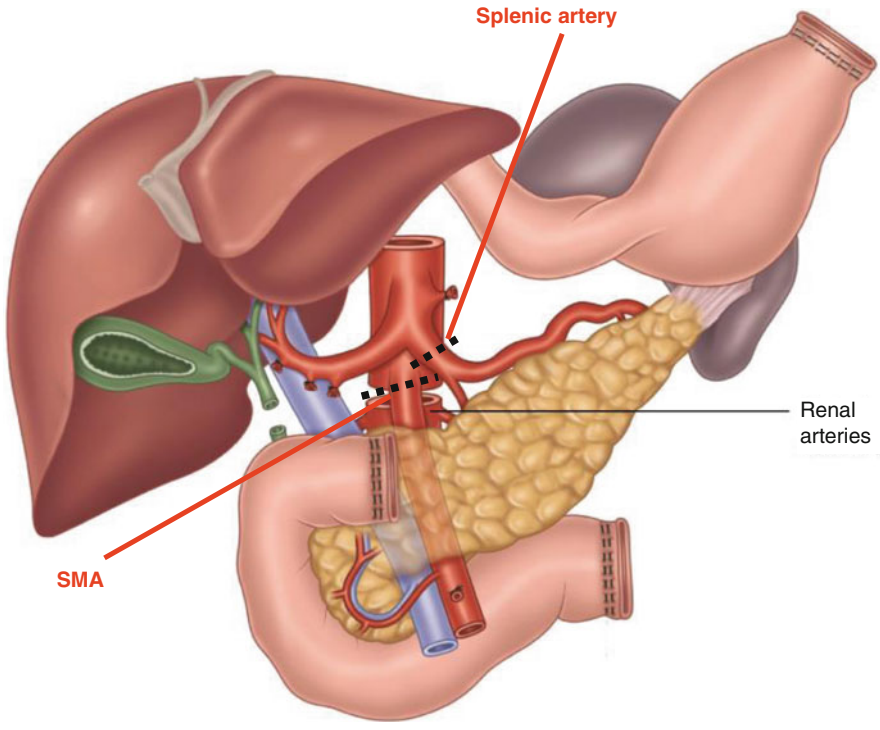

Fig. 18.11 Separation of liver and pancreas after "en bloc" liver and pancreas procurement

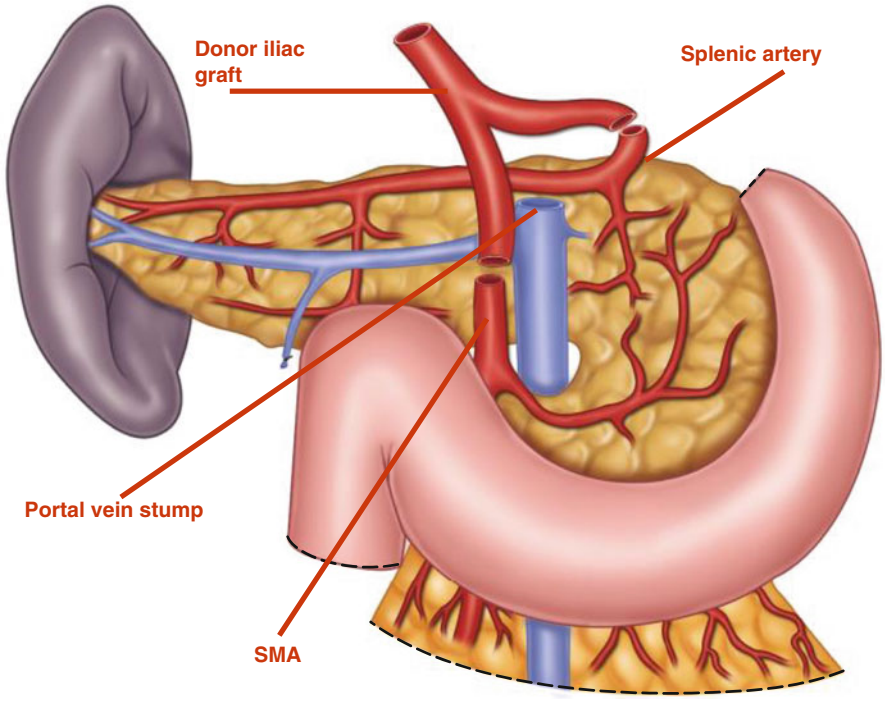

Fig. 18.12 Posterior view of spleno-duodeno-pancreatic graft before bench reconstruction with the Y-shaped donor iliac graft

anatomical variations, a correct preservation of the GDA may allow the revascularization of the pancreas head through a so-called "triple" arterial reconstruction (for details see Chap. 15).

In the case of donors with atheromasic lesions on the iliac vascular graft that seem unsuitable for anastomoses, a donor carotid axis with internal/external bifurcation, usually with lower incidence of atheromasic lesions, can be retrieved and used to create the "Y" vascular conduit. A section of the portal vein of the pancreatic graft is then completed, leaving a portal vein cuff not longer than 1.5–2 cm; the pancreatic portal segment should be sufficiently long to permit its anastomosis on the recipient common iliac vein, but it should not be so long that it increases the risk of venous kinking and consequent thrombosis. A final low pressure tight test is necessary and is performed by the gentle injection of 100 mL of cold perfusion solution in the common iliac conduit of the graft; this will allow the identification and the tying of all vascular orifices of small vessels. The pancreatic graft can now be considered suitable and ready for implantation [3, 26].

References

1. Oniscu CG, Forsythe JL, Fung J (2013) Abdominal organ retrieval and transplantation bench surgery. Wiley, Chichester
2. Currie I (2014) Edimbourg transplant unit annual report. Scottish Organ Retrieval Team 2013/2014
3. Abu-Elmagd K, Fung J, Bueno J et al (2000) Logistics and technique for procurement of intestinal, pancreatic, and hepatic grafts from the same donor. Ann Surg 232(5):680–687
4. Lopez-Andújar R, Moya A, Montalvá E et al (2007) Lessons learned from anatomic variants of the hepatic artery in 1,081 transplanted livers. Liver Transpl 13(10):1401–1404
5. Bhardwaj N (2010) Anomalous origins of hepatic artery and its significance for hepatobiliary surgery. J Anat Soc India 59(2):173–176
6. Hiatt JR, Gabbay J, Busuttil RW (1994) Surgical anatomy of the hepatic arteries in 1000 cases. Ann Surg 220(1):50–52
7. Chiang KH, Yang Chang P, Lee SK et al (2005) Angiographic evaluation of hepatic artery variations in 405 cases. Chin J Radiol 30:75–81
8. Li GM, Zhu JY, Huang L et al (2005) The analysis for the variation of hepatic arteries of the donor livers. Zhonghua Wai Ke Za Zhi 43(7):447–449
9. Chen H, Yano R, Emura S et al (2009) Anatomic variation of the celiac trunk with special reference to hepatic artery patterns. Ann Anat 191(4):399–407
10. Melada E, Maggi U, Rossi G et al (2005) Back-table arterial reconstructions in liver transplantation: single-center experience. Transplant Proc 37(6): 2587–2588
11. Hevelke P, Grodzicki M, Nyckowski P et al (2003) Hepatic artery reconstruction prior to orthotopic liver transplantation. Transplant Proc 35(6):2253–2255
12. Andraus W, Haddad LB, Ducatti L et al (2013) Artery reconstruction in liver transplantation: the best reconstruction of right artery variation. Arq Bras Cir Dig 26(1):62–65
13. Lee CC, Jeng LB, Li PC et al (2008) Innovative technique to reconstruct two branches of the right hepatic artery in living donor liver transplantation. Transplant Proc 40(8):2525–2526
14. Dong JH (2005) Management of vascular anomalies and complication in liver tranplantation. Hepatobiliary Pancreat Dis Int 4(3):330–331
15. Soliman T, Bodingbauer M, Langer F et al (2003) The role of complex hepatic artery reconstruction in orthotopic liver transplantation. Liver Transpl 9(9): 970–975
16. Ayala-Garcia MA, Ramirez-Barba EJ, Encalada JMS, Yebra BG (2011) Renal Explantation Techniques. In: Renal Transplantation -Updates and Advances (eds) . Long L. pp 49-75. e-book: www.intechopen.com
17. Valeriani G, Cerbone V, Russo E et al (2010) Bench surgery in right kidney transplantation. Transplant Proc 42(4):1120–1122
18. Arango O, Lorente JA, Bielsa O et al (2013) Elongation of the right renal vein in 120 consecutive transplant patients: a comparative analysis. Actas Urol Esp 37(3):135–141
19. Beckmann JH, Jackobs S, Klempnauer J (2008) Arterial reconstruction in kidney transplantation. Tx Med 20:7–12
20. Hwang JK, Kim SD, Park SC et al (2010) The long-term outcomes of transplantation of kidneys with multiple renal arteries. Transplant Proc 42(10):4053–4057
21. He B, Mou L, Mitchell A et al (2013) Meticulous use of techniques for reconstruction of multiple renal arteries in live donor kidney transplantation. Transplant Proc 45(4):1396–1398
22. Antonopoulos IM, Yamaçake KG, Oliveira LM et al (2014) Revascularization of living-donor kidney transplant with multiple arteries: long-term outcomes using the inferior epigastric artery. Urology 84(4): 955–959
23. Berardinelli L (2006) Best results in living donor transplantation using an aggressive policy in microsurgical bench reconstruction of nonoptimal arterial supply. Transplant Proc 38(4):991–993
24. He B, Mitchell A (2012) A novel technique for reconstruction of multiple renal arteries in live donor kidney transplantation: a case report and literature review. Transplant Proc 44(10):3055–3058
25. Yildirim M, Kucuk HF (2011) Outcomes of renal transplantations with multiple vessels. Transplant Proc 43(3):816–818
26. Chaib E, Macedo RA, Santos VR et al (2013) Pancreas transplantation-surgical technique. Pancreatic Dis Ther 3(2):120–123

Part V

Surgical Technique for Liver and Kidney Living Donor

Right Hemihepatectomy for Living Donor Liver Transplantation in Adults (Open Technique)

19

Luciano De Carlis, Paolo Aseni, Stefano Di Sandro, Iacopo Mangoni, Raffaella Sguinzi, and Andrea Lauterio

Abbreviations

AHV	Accessory hepatic vein
DD	Deceased donor
HVTs	Hepatic vein tributaries
LDLT	Living donor liver transplantation
LH	Left hepatectomy
LLS	Left lateral segment
MHV	Middle hepatic vein
RH	Right hemihepatectomy
RHV	Right hepatic vein
SI-VIII	Segment (roman numeration refers to each segment)
SLT	Split liver transplantation
SFSS	Small-for-size syndrome
V 1-8	Vein (hepatic accessory or tributary; Arabic numeration refers to each single segment)

Tips, Tricks, and Pitfalls

- Successful donor outcome and the recipient's hope for the highest probability of a successful transplant are relevant factors that ethically support the choice for LDLT.
- The absence of an extrahepatic portal vein bifurcation is an absolute contraindication to living donor liver procurement.
- Living donor liver transplantation should fulfill the same minimal criteria established for deceased donors liver transplantation.
- The liver's extrahepatic vasculobiliary anatomy should be carefully determined by recognizing preoperatively all different types of the anatomical pattern.
- Graft weight/recipient weight (GW/RW) ratio >0.8 % and a graft volume/standard liver volume (GV/SLV) ratio >40 % are the safe limits for donor graft size to avoid a small for size syndrome (SFSS).
- During right hemihepatectomy leave untouched the left triangular ligament or the gastrohepatic ligament, because their section may result in excessive

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mobility of the left lobe with possible torsion or kinking and outflow occlusion of the remnant graft.
- Throughout the hilar dissection, extreme care should be employed to avoid the devascularization of the common bile duct with possible ischemic biliary stricture in the donor.
- The preservation of the mean hepatic vein avoids the congestion of S IV and subsequent liver dysfunction in the donor.
- Try to perform extensive revascularization of all hepatic vein tributaries of the mean hepatic vein (V5, V8) and all accessory hepatic veins (V6 and V7) when with caliber >4 mm.
- To maintain the correct parenchyma transection plane, the "hanging maneuver" may be useful.

19.1 Basic and Ethical Principles of Living Liver Donor Transplantation

Since the late 1980s, the shortage of livers for transplantation has prompted several transplant centers to seek alternatives to conventional deceased donor (DD) liver transplantation, such as split liver transplantation from DD, livers from non-hearth beating donors or donation after cardiac death (DCD) and partial grafts from living donors. Living donor liver transplantation (LDLT) has become an alternative to conventional liver transplantation due to the refractory shortage of DD organs. The procedure requires a major hepatectomy to be performed on a healthy individual who has no medical indication other than the desire and willingness to offer a part of his/her liver to a sick recipient. If there is a DD organ available, the benefit to the recipient of living donation is inconsequential because the recipient risk of morbidity rate for the procedure is higher than 30 % [1], and the risk of donor death is estimated at around one fatal event for every 500 procedures. However, in some geographic areas, such as in Asia where there is almost no alternative to living donation, recipient benefit from LDLT is maximal, and donor risk is acceptable. In the USA, the higher the mean MELD (model for end-stage liver disease) score in a specific area, the higher the presence of active living donor programs [2]. According to the World Health Organization, approximately 20 % of all solid organ transplantations are livers, and about one-fifth of these are from living donors [3]. However, LDLT poses some challenging ethical and technical questions. "Equipoise" (the equilibrium of risk to the recipient and the donor) and "double equipoise" (from both points of view) are some of the many facets of the current ethical debate. When a donor takes the risk to provide the recipient with a benefit, the donor hopes for the highest probability of a successful recipient outcome and a successful donation; the recipient hopes to minimize donor risk. Successful donor outcome and the recipient's hope for the highest probability of a successful transplant are relevant factors that ethically support the choice for LDLT [4, 5]. However, LDLT is a complex surgical procedure that requires significant surgical expertise and planning to allow good outcomes for both donors and recipients. Although the recipient benefit from LDLT is well documented, with 5-year survival after transplantation ranging from 80 to 85 %, the successful application of LDLT imposes unique surgical and medical restraints and particular donor considerations; the procedure has a significant complication rate (from 30 to 50 %) resulting from anatomic variations that require prompt and technically challenging solutions to allow the transplantation of a partial liver graft.

19.2 Historical Background

The first liver transplantation in the pediatric population was reported by Raia et al. in Brazil in 1989; however, the first two recipients died due to medical complications within the early perioperative period [6]. In 1990, the first successful case was published by Strong et al. from Australia concerning a 15-month-old child who received

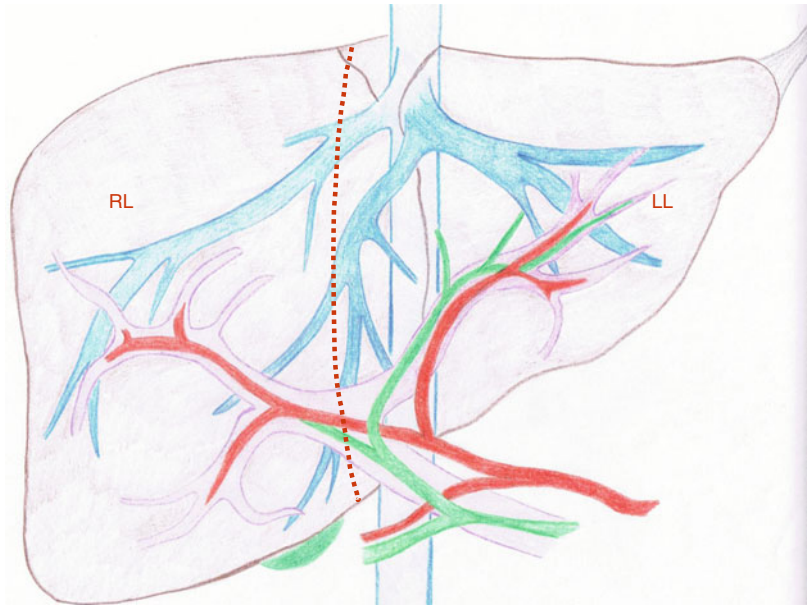

Fig. 19.1 Right lobe liver donation from a living donor: right lobe (*RL*) and left lobe (*LL*) with the relevant vascular and biliary anatomy

living related liver donation from his mother [7]. In the early 1990s, Broelsch et al. established the first program for living related liver transplantation at the University of Chicago. He reported the first series of 20 cases under prospective scrutiny and was able to demonstrate the benefit of this procedure for both donor and recipient [8]. Equivalent results were obtained by Tanaka et al. in Kyoto, providing evidence of the clinical effectiveness of LDLT in children [9]. The procedure was gradually adopted more widely, especially in Asian countries, where DD were rarely available. In 1994, Yamaoka et al. first reported the use of a right lobe for transplantation, and Marcos et al. demonstrated in their first series of 30 patients that right lobe LDLT can be performed with minimal risk to the donor and recipient [10–12] (Fig. 19.1).

19.3 General Rules to Accept Living Donor Liver Donation and Preoperative Assessment

At present, most experts agree that recipients considered for LDLT should fulfill the same minimal criteria established for DD liver transplantation.

To optimize the ratio of donor risk to recipient benefit, a careful preoperative assessment of the donor is mandatory for each individual patient. Clinical examinations, imaging studies, special examinations, biochemical parameters, and psychosocial evaluation prior to donation vary among centers.

Liver anatomy is first assessed by standard ultrasound (US) and Doppler US with special emphasis on the liver parenchyma. The US evaluation enables the first assessment for steatosis and any lesion, the distribution, number and caliber of hepatic veins and the presence of accessory hepatic veins (AHVs) and all relevant hepatic veins tributaries (HVTs) of the mean hepatic vein (MHV) [13]. Triphasic computed tomography (CT) is then performed with a serial coronal section view that is especially useful for evaluating the hepatic veins (Figs. 19.2 and 19.3) and portal vein variants (Figs. 19.4 and 19.5) and the volumetric of the graft and remnant liver. Magnetic resonance (MR) angiography can allow vascular evaluation, and magnetic resonance cholangiopancreatography (MRCP) is useful for biliary anatomy evaluation. All efforts are made to detect all biliary abnormalities especially for distribution of the posterior biliary branch from S VI and S VII (Fig. 19.6). A recent study has reported a

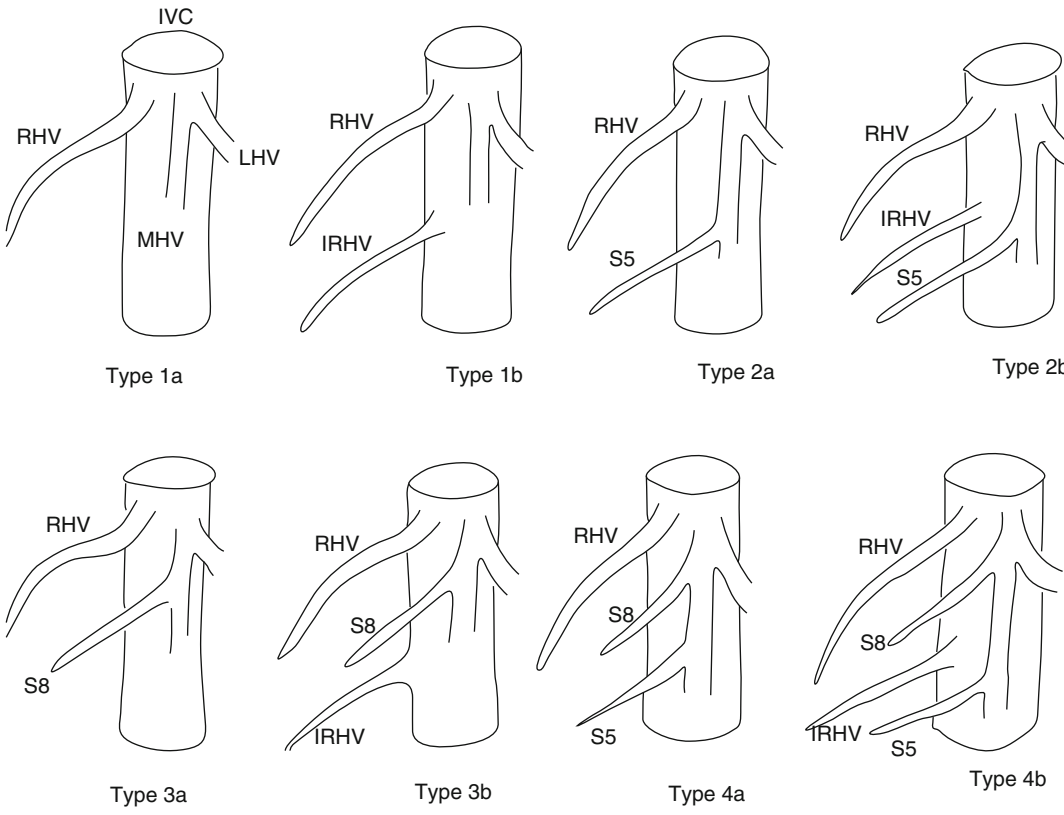

Fig. 19.2 Anatomical variations and classification in four patterns of hepatic veins in right living donors according to Varotti et al. [13] (*RHV* right hepatic vein, *LHV* left hepatic vein, *MHV* mean hepatic vein, *IRHV* inferior right hepatic vein, *S5* vein from segment V, *S8* vein from segment VIII)

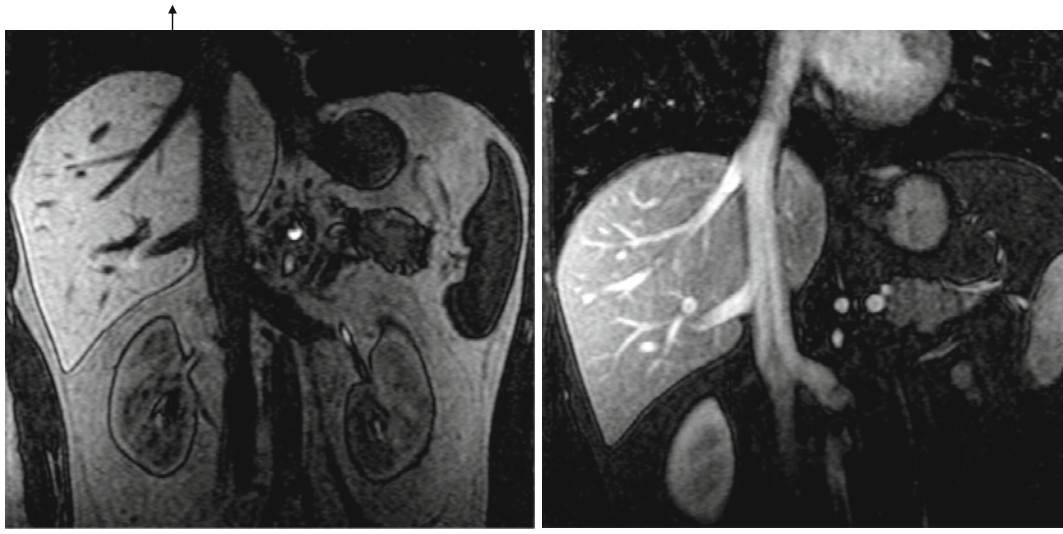

Fig. 19.3 Triphasic computer tomography for vasculobiliary anatomical evaluation: a very large AHV V6 (right inferior hepatic vein)

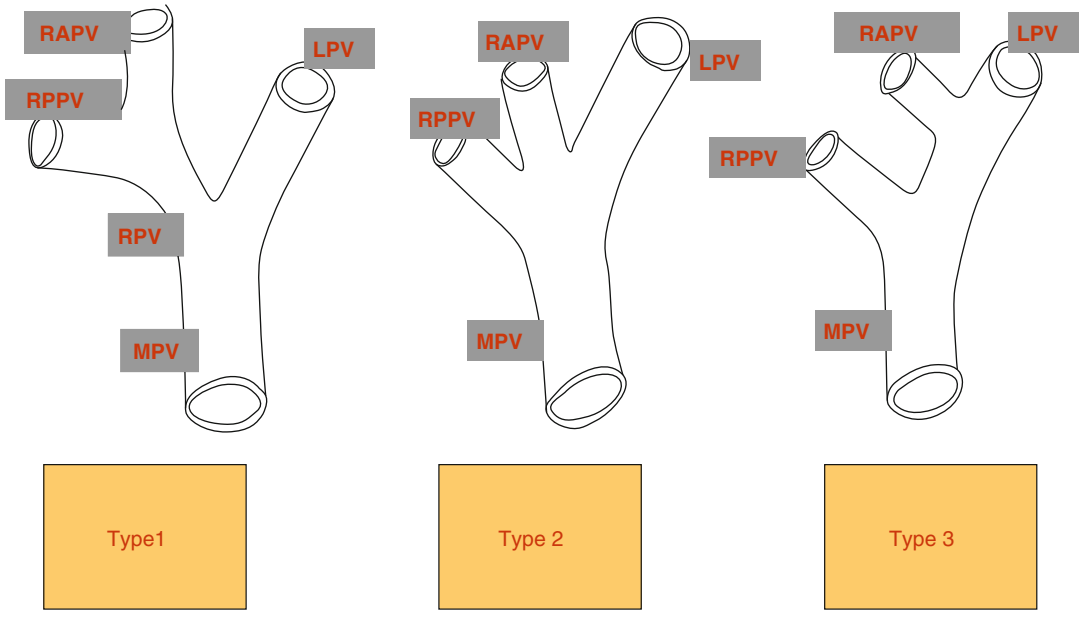

Fig. 19.4 Anatomic variations of donor portal vein in right lobe living donor procurement: three patterns. *RAPV* right anterior portal vein, *RPPV* right posterior portal vein, *MPV* main portal vein, *LPV* left portal vein

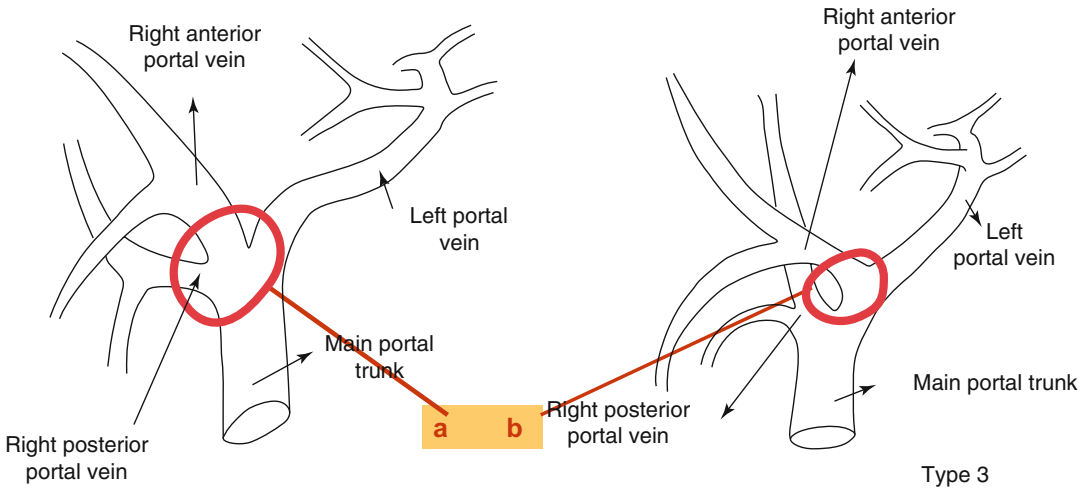

Fig. 19.5 Schematic representation of some challenging portal anatomical variations in right lobe procurement from living donors. (*a*) Portal vein trifurcation. (*b*) Right anterior portal vein from the left portal branch

new classification of biliary pattern which can be of clinical relevance since it can predict the specific risk to develop biliary complications in relation to the pattern of the right bile duct (RBD) anatomy. In this study the infra-portal and long RBD variants showed 0 % biliary complications, whereas supra-portal with a short caudal segment showed the highest complication rate of 52.6 % [14].

The liver's extrahepatic vasculobiliary anatomy should be carefully determined by recognizing all different types of the anatomical pattern. The absence of extrahepatic portal vein bifurcation is the only unquestionable anatomical

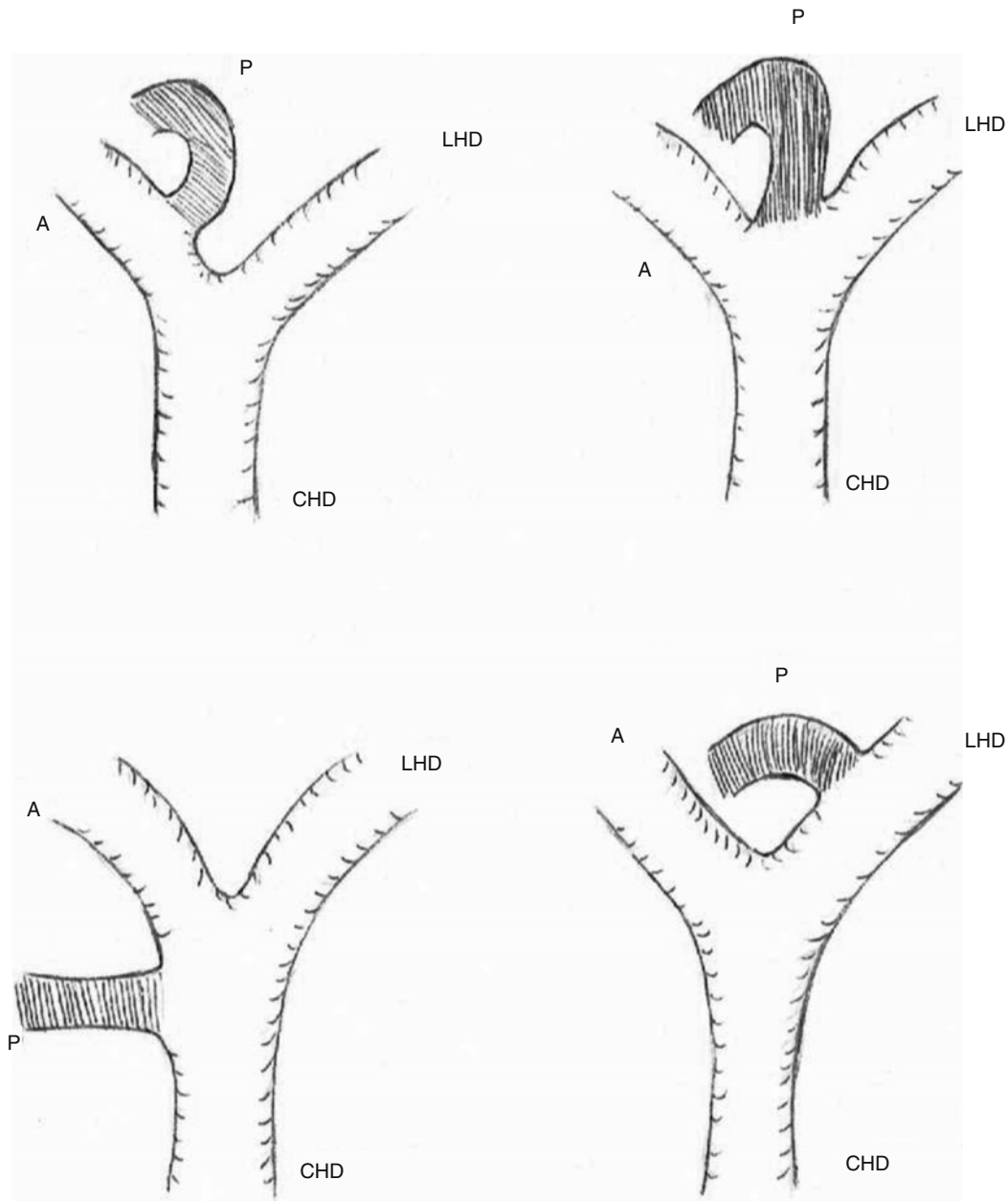

Fig. 19.6 Most common types of biliary anatomical distribution of posterior (*P*) biliary branch from segments S VI and VII (according to Nakamura [26])

contraindication to right lobe hemihepatectomy. However, the study of the intrahepatic portal vein pattern, the multiple or standard single hepatic arterial supply, the branching modality of the artery into the right and left arterial supply, and a detailed examination of the biliary branching pattern are all paramount to ensure the donor safety.

At the end of radiological workup, a review of the images with radiologists for complex cases with multiple anatomical variations allows surgeons to plan the possible parenchyma divi-

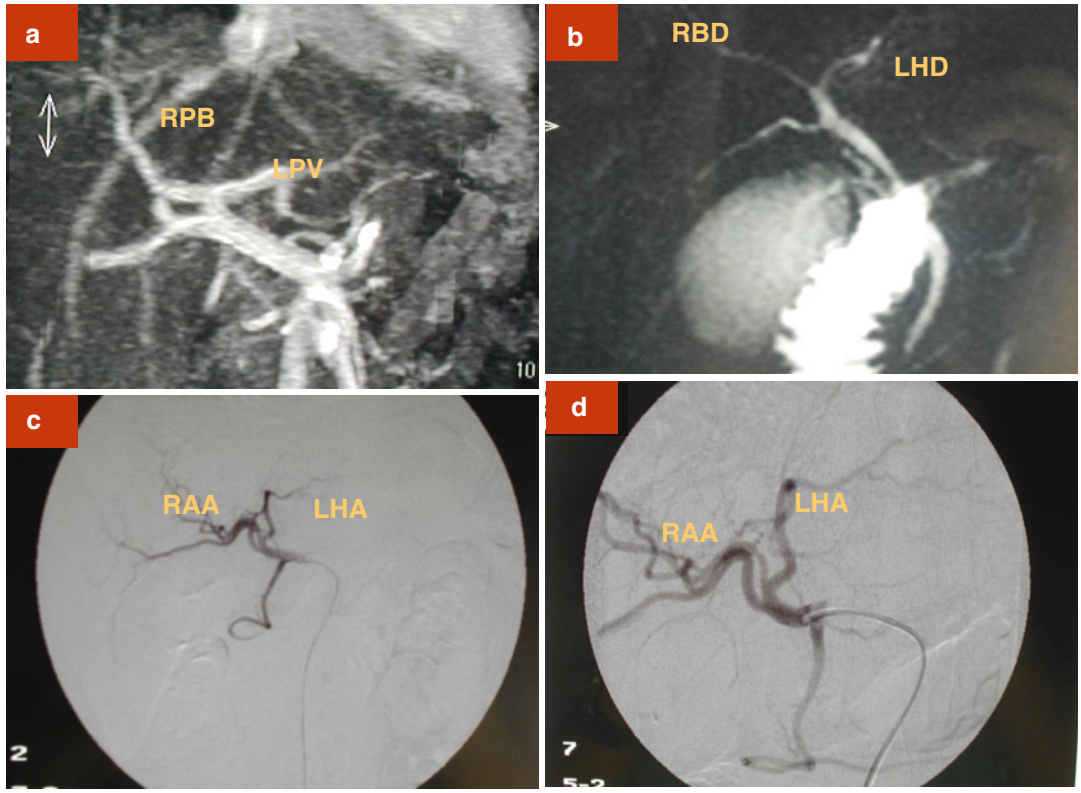

Fig. 19.7 Multiple portal, biliary, and arterial anatomic variations in this patient were considered a contraindication to LDLT: (**a**) right portal branch (*RPB*) arising from left portal vein (*LPV*), (**b**) right bile duct (*RBD*) to left hepatic duct (*LHD*), (**c**, **d**) right accessory artery (*RAA*) from left hepatic artery (*LHA*)

sion or vascular reconstruction strategy according to preoperative observations. In some particular cases, the multiple anatomical variations preclude a safe liver resection (Fig. 19.7).

19.4 Right Graft Versus Left Liver Graft

During the early experience, efforts in LDLT focused on left lateral segment (LLS) grafts in pediatric recipients, because they were initially disadvantaged on the waiting list.

Right hemihepatectomy (RH) performed for adult-to-adult LDLT has a higher risk of morbidity and mortality compared with the resection of the left lateral segment (LLS) employed for children. A higher rate of complications is also reported in recipients when RH is compared to left hemihepatectomy (LH) for adults. However, when the competing risk for the recipient receiving RH or LH is fully evaluated, a higher incidence of SFSS occurs, and a higher risk of death has also been documented when using smaller grafts from LH [15]. CT scan volumetry and 3D reconstruction are routinely utilized in clinical practice to calculate the standard liver volume. Previous literature has suggested that a graft weight/recipient weight (GW/RW) ratio >0.8 % and a graft weight/standard liver volume (GV/SLV) ratio >40 % are the safe limits for donor graft size to avoid SFSS. The incidence of SFSS is also dependent on several other factors related to the presence of significant portal hypertension. Recipients with a hepatic venous pressure gradient >15 mmHg seem at higher risk [16, 17]. However, because the donor safety of RH was confirmed in several studies, in our center we will continue to advocate the use of RH grafts whenever possible, since in our experience the calculated GW/RW and GW/SLV ratios was almost always >1 % and >40 %, respectively, for all recipients.

19.5 Right Hemihepatectomy: Open Surgical Technique

RH in LDLT is a nearly standardized procedure worldwide, but some points of discussion are still open. During the first decade of experience, one important point of debate was whether the MHV should be harvested during RH. Careful technical evaluation is therefore mandatory and should be based on a detailed preoperative study of the relevant liver anatomy for each single donor, including the artery, portal vein, hepatic veins, and bile duct [18–20]. Multiple and small arteries and portal vein pattern requiring reconstruction (Fig. 19.4) are relative contraindications, whereas the absence of extrahepatic portal bifurcation (nondivision of the main portal vein with the absence of a separate left main portal vein) is an absolute contraindication for LDLT.

The donor's abdomen is opened through a right subcostal incision with a vertical extension to the xiphoid. The falciform ligament is divided, and the sulcus between the right hepatic vein (RHV) and MHV is clearly defined by clearing the surrounding connective tissue. No attempt is made to divide either the left triangular ligament or the gastrohepatic ligament, because this may result in excessive mobility of the residual left lobe with possible torsion or kinking and outflow occlusion of the remnant graft. Cholecystectomy is routinely performed; then an intraoperative cholangiogram is considered to be useful in many centers to provide anatomical information about any biliary abnormalities, particularly regarding the level of confluence of the common hepatic duct and the presence, number, and size of any aberrant segmental bile ducts from the right lobe draining into the left hepatic duct. Multiple ducts, depending on their size and number, may necessitate additional biliary anastomosis or reconstruction during bench surgery. Some other centers prefer to place a plastic probe inside the right hepatic duct as an anatomical guide to prevent unnecessary dissection in this area. The right hepatic artery is exposed and mobilized from the hepatic parenchyma to the right border of the common hepatic duct. Throughout the hilar dissection, especially where the right hepatic artery comes into contact with the bile duct, extreme care should be employed to avoid the devascularization of the common bile duct with possible ischemic biliary stricture in the donor. After mobilizing the right hepatic artery, the portal vein is identified, encircled with a vessel loop and completely mobilized to the maximum length to permit a comfortable placement of vascular clamps (Fig. 19.8).

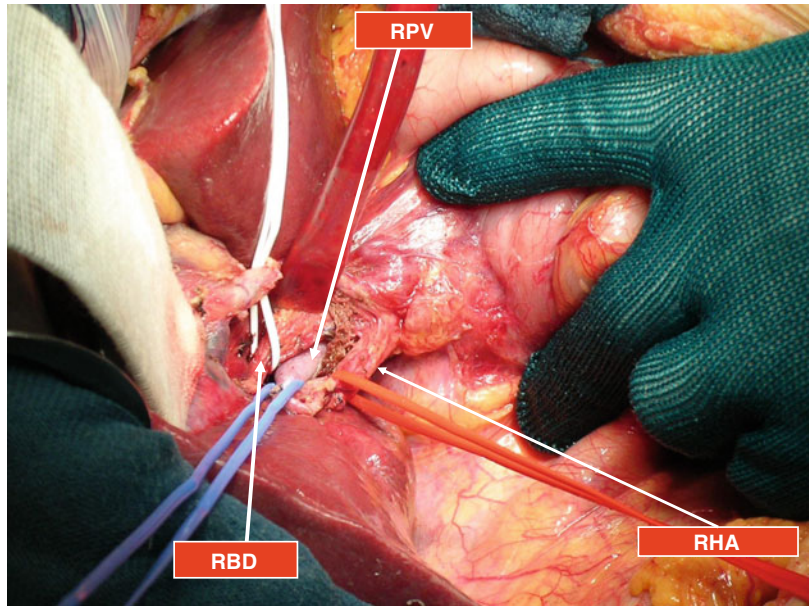

Fig. 19.8 The portal vein is identified, encircled with a vessel loop and completely mobilized to the maximum length to permit a comfortable placement of vascular clamps. Right portal vein (*RPV*), right hepatic artery (*RHA*), and right bile duct (*RBD*)

The right lobe of the liver is mobilized by sectioning its diaphragmatic attachments and right triangular and coronary ligaments. The dissection of the hepato-caval ligament, which is present in two-thirds of cases, allows total control of the right hepatic vein, which is encircled with tape. The retrohepatic vena cava is exposed and dissected, preserving all significant AHVs draining the right lobe, in particular those with a caliber greater than 4 mm (Fig. 19.9). Intraoperative ultrasound (US) is used to define the course and relationship of the MHV to the RHV as they drain into the inferior vena cava. It is also paramount to detect the presence and hemodynamic relevance of all HVTs draining the right anterior segment S V and S VIII into the MHV (Fig. 19.10) and all AHVs draining S VI and S VII (posterior segments) into the vena cava. These veins may contribute significantly to the venous drainage of the right lobe, and their division and ligation may result in venous congestion after the implantation of the graft. During this time, temporary clamping

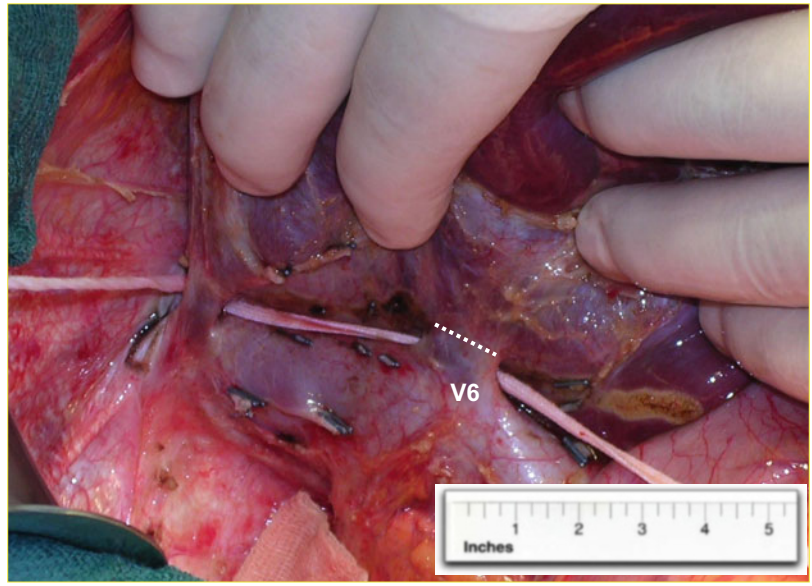

Fig. 19.9 A large inferior right hepatic vein V6 of 1 cm is preserved for revascularization

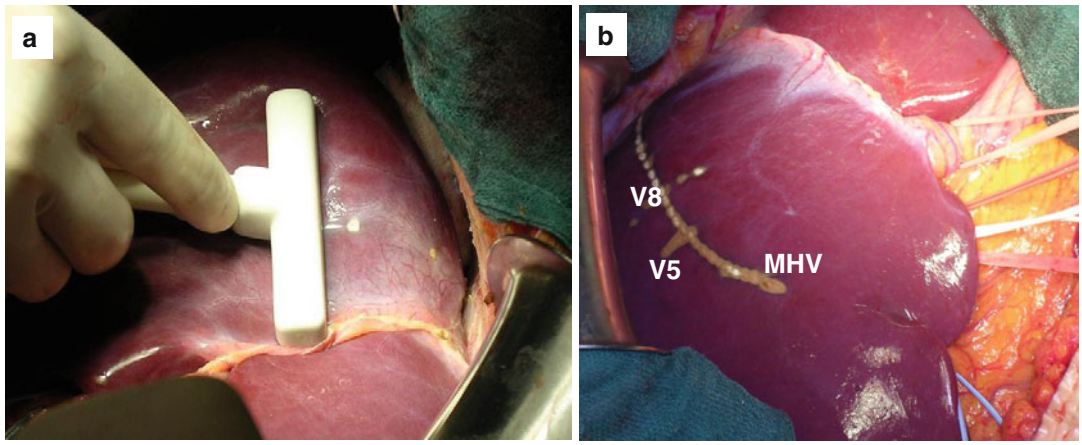

Fig. 19.10 (**a**) Intraoperative US is used to define the course and relationship of the MHV. (**b**) It is paramount to detect the presence and hemodynamic relevance of tributary veins draining the right lobe, particularly those draining segment S V and S VIII into the MHV

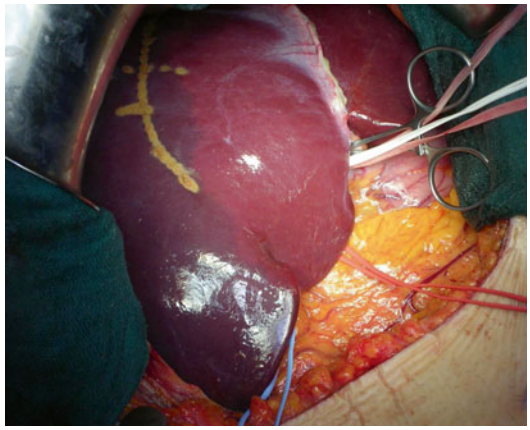

Fig. 19.11 Line of demarcation after 1-min clamping of the right vascular pedicle is evident: on the left side of the Cantlie's line, an area of mild congestion of the left remnant liver (S IVa) can be observed as a temporary phenomenon

of AHVs from S VI and S VII followed by the evaluation of the surface color of the right lobe should be assessed to determine whether the vessels could be safely divided or should be preserved. If venous congestion occurs in S VI or S VII, separate hepatic vein anastomoses must be performed to ensure adequate venous outflow of the graft. Otherwise, all irrelevant short AHVs draining the posterior sector of the right lobe are then ligated and divided.

The line of parenchyma transection is determined, occluding the right hepatic artery and the right portal vein with an atraumatic bulldog clamp for approximately 1 min to delineate a demarcation area between the right and left lobes that is marked with electrocautery (Fig. 19.11). A mapping of the course of the middle hepatic vein is identified with US, and the line of transection is consequently adjusted at 1 cm to the right of the middle hepatic vein. The MHV is kept with the left remnant lobe, where it provides venous drainage for S IVa and S IVb. The preservation of the MHV avoids the congestion of S IV and subsequent liver dysfunction in the donor. A considerable discrepancy of the demarcation surface between the right and left lobes associate to a small caliber RHV may suggest an important dominance of the MHV with the possibility of harvesting the MHV which has never been performed in our experience. In such case, we prefer the extensive revascularization of all HVTs of the MHV (V5, V8) and all AHVs (V6 and V7) [19, 21, 22].

Parenchyma transection is performed at the anterior edge of the liver and proceeds cranially toward the hilar plate and posteriorly to the RHV; no vascular occlusion is performed to avoid ischemia and organ dysfunction in the donor and recipient livers. The cavitron ultrasonic surgical aspirator (CUSA) is useful to expose the blood vessels within the hepatic parenchyma. Smaller vessels are then coagulated using the harmonic scalpel, and vessels smaller than 4 mm are ligated and divided. Bipolar coagulation can provide additional hemostasis to the surface of the cut edge. Using this combination of instruments, the parenchyma transection can be performed in less than 2 h with minimal blood loss. To maintain the correct parenchyma transection plane, the "hanging maneuver" (Fig. 19.12) is performed; an umbilical tape is passed between the RHV and MHV (anteriorly) and then behind the posterior of the right lobe along the anterior vena cava wall. The tape is then brought out at the level of the hilum behind the hilar plate. This technique is useful to keep the vessels down and out of the transection plane. Parenchyma division will continue along the main portal fissure with the surgeon's left fingertips positioned behind the right lobe anterior to the inferior vena cava. By this technique, the MHV should be retained with the left lobe. Venous tributaries from S V and S VIII draining into the MHV are evaluated and preserved after tape encircling. A 1- to 2-min clamping test without parenchyma discoloration may suggest that they are insignificant for the outflow (Fig. 19.13), and they can be divided and ligated. The hemodynamic evaluation of all AHVs and HVTs can also be achieved with a 5 min clamping test as suggested by Makuuchi and Sugawara [21]; the author advocates the aggressive reconstruction of all veins draining the right paramedian sector in the living donor right lobe when the MHV is not harvested with the right lobe. The use of intraoperative US Doppler can be helpful in the evaluation of the draining relevance of a single AHV after a 5 min test by clamping both

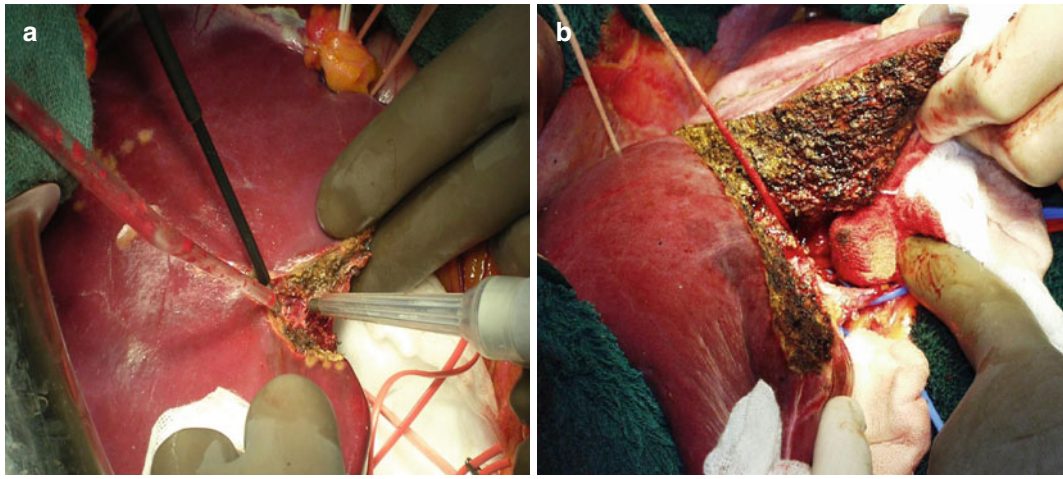

Fig. 19.12 (**a**) Parenchyma transection employing CUSA. (**b**) Tape-assisted (hanging maneuver) parenchyma transection is useful to keep the vessels down and out of the transection plane and leads more easily to the anterior wall of the inferior vena cava

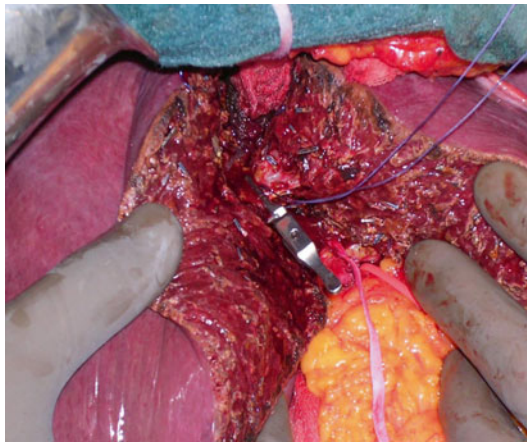

Fig. 19.13 Evaluation of the surface color of the right lobe by temporary clamping of all HVTs and AHVs with or without the Makuuchi test enables to determine whether the vessels could be safely divided or should be preserved

the hepatic artery and venous branches of the MHV; the evidence of a hepatofugal portal flow in the paramedian portal branch will strongly suggest the reconstruction of the occluded paramedian vein.

All significant vessels and bile ducts are closed with surgical clips or fine Prolene suture. Before completing the parenchyma transection, the right hepatic duct is again identified and sharply divided with scissors, avoiding the encroachment of the confluence and left hepatic duct. Monopolar or bipolar coagulation is generally not used to prevent burn injury and consequent stricture. The bile duct stump remaining with the donor is sutured with a 5-0 Prolene suture.

After the parenchyma and the bile duct are divided, the right lobe of the donor is attached by only the right hepatic vein, portal vein, hepatic artery (Fig. 19.14), and one or two preserved tributaries of the MHV or AHVs to the retrohepatic vena cava. At this point, 40 IU/kg heparin is administered to the donor, and the right hepatic artery, right portal vein, right hepatic vein, and all AHVs are clamped and divided, allowing the removal of the right lobe graft from the donor. The RHA is clamped and divided, leaving adequate length for the closure of the proximal stump. The distal transected portion of the RHA is left to back bleed. Next, the RPV is clamped, stapled by linear endovascular stapler, and divided leaving a bulldog clamp on the graft side. It is very important to not apply the stapler too close to the portal vein bifurcation. All the AHVs and HVTs are ligated and divided after applying clips or divided and preserved as previously indicated. The RHV is then clamped, stapled by endovascular staple, and divided. The graft is passed off the back table and perfused with low-viscosity cold perfusion (Fig. 19.15).

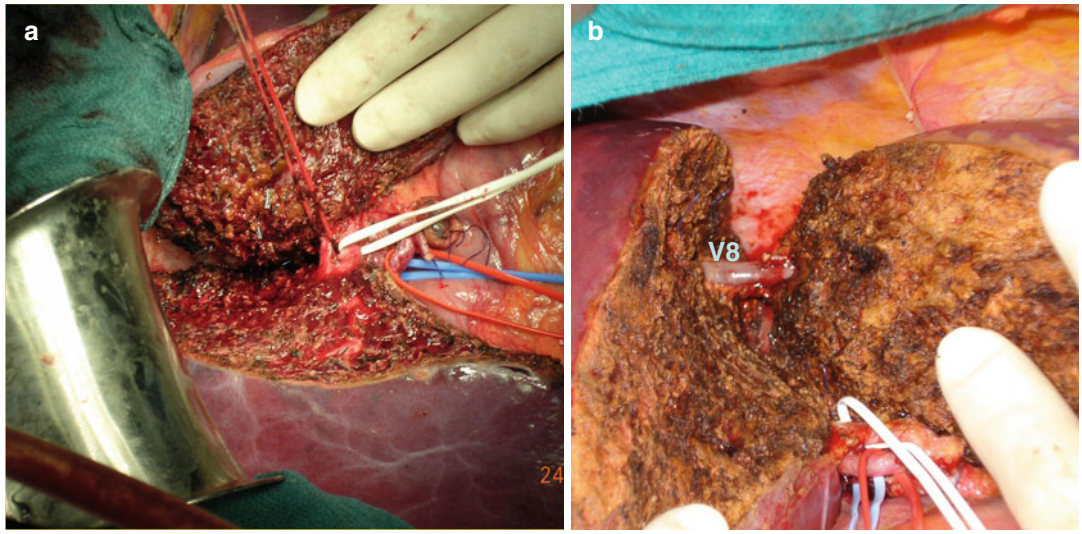

Fig. 19.14 (**a**) The parenchyma transection is completed and a double biliary duct is evident. (**b**) The right lobe of the donor is attached by only the RHV, portal vein, hepatic artery, and a preserved V8 tributary to the MHV

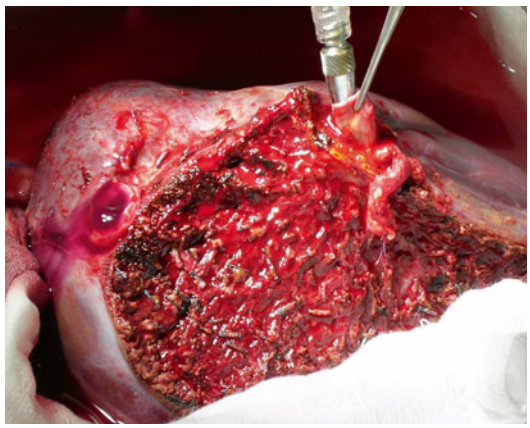

Fig. 19.15 Back table: the right lobe graft is flushed with low-density perfusion solution via the portal vein

The stump of the right hepatic artery is sutured. RHV and portal vein of the donor remnant liver are sutured whenever vascular stapler devices are not used. The bile duct stump of the donor is closed with 5-0 monofilament in running sutures. After complete hemostasis, 10 ml of physiologic (or indigo carmine) solution is injected via the cystic duct tube into the biliary system. When physiologic solution (or dye) leakage is identified, additional monofilament sutures are placed and the solution injection is repeated to confirm the leakage is repaired. One or two drains are placed at Winslow's foramen or the cut surface of the liver.

19.6 Back Table Reconstruction

The right hepatic duct is flushed with a syringe containing perfusion solution and the graft is weighed or its volume is measured by water displacement. At the back table, the graft is usually immersed in ice sludge and flushed with a low-viscosity preservation solution through the portal vein. Perfusion of the bile duct should gently be performed without damaging the bile lumen.

19.6.1 AHV Reconstruction

The major controversy with right lobe LDLT lies in the necessity of including the MHV in the graft and the concerns for the safety of the donor. The MHV collects important venous drainage for the right anterior segments and is essential for perfect graft function of right lobe LDLT [19, 20, 23]. In the absence of the MHV with the right lobe, we attempt to reconstruct all relevant HVTs of the anterior sectors with a diameter larger than

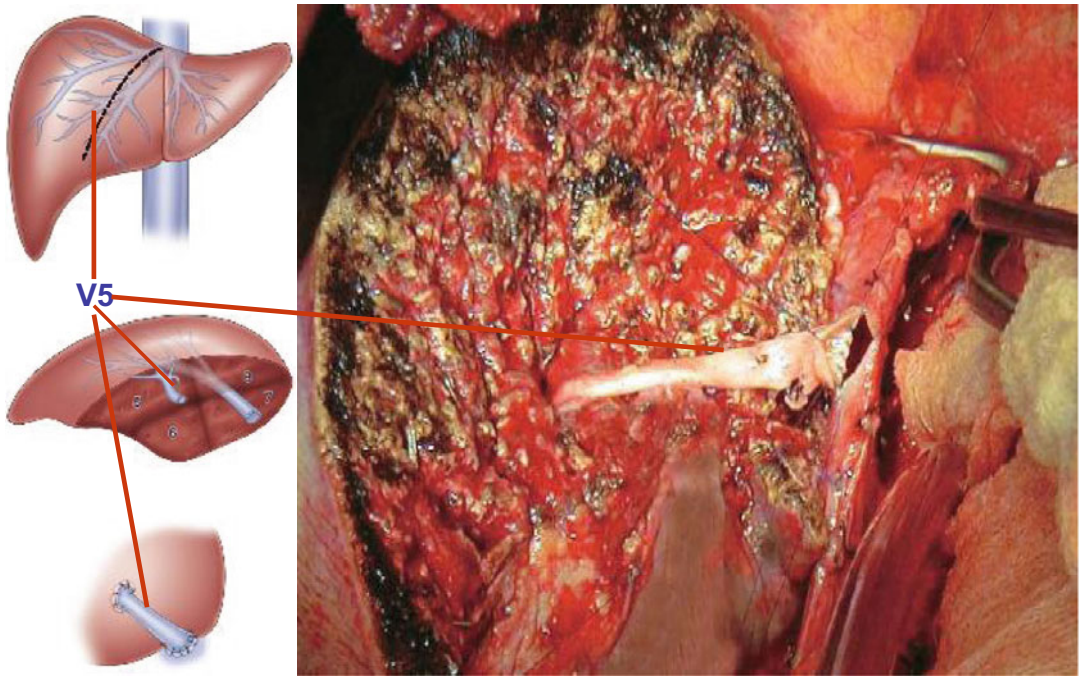

Fig. 19.16 Reconstruction of HVTs V5: a jumping venous graft from V5 to recipient IVC. The interposition allograft is anastomosed end-to-end to the V5 (on the back table) and end-to-side (during LDLT) to recipient IVC using two continuous 6-0 polypropylene suture

4 mm. In our center in the presence of consistent MHV dominancy and with a Makuuchi positive test [18], various interposition venous grafts have been used for reconstruction of all tributaries of the MHV. These interposition grafts have included autologous vein grafts harvested from the recipient's dilated venous collaterals or from the greater saphenous vein or eterologous venous graft, when available from a DDs, within 48 h of the retrieval (Fig. 19.16). Usually interposition grafts were anastomosed end-to-end to the V5 and/or V8 on the back table using two continuous 6-0 polypropylene sutures. The reconstructed HVTs are then anastomosed to the MHV and LHV vein stump or retrohepatic vena cava in the recipient. When a V8 is located near the RHV orifice, a common orifice with the RHV is usually obtained. In the case of double V5 branches, venoplasty of the two V5 is performed to achieve a large, single orifice; if venoplasty cannot be performed, the largest of the V5 can be anastomosed to the interposition graft in end-to-end fashion and then anastomosed to the IVC in an end-to-side fashion [22]. In some cases, when complex multiple reconstructions of relevant AHVs are required, new solutions can be suggested to overcome specific problems by innovative surgical techniques.

19.6.2 Hepatic Artery Reconstruction

Hepatic artery reconstruction is a crucial step in LDLT [23]. The selection of the recipient artery is critical for successful anastomosis. The artery is chosen according to the patency, size, match, length, and direction. To solve the discrepancy in size, different techniques have been described, and single stitch or running sutures are debated. High hilar dissection has the advantage of providing distal small arteries, providing the luxury of a choice in terms of optimal size match with the recipient stump. To overcome the risk of intimal dissection, the use of a microclamp instead of ligation to occlude the vessel is recommended. We use the "parachute" technique,

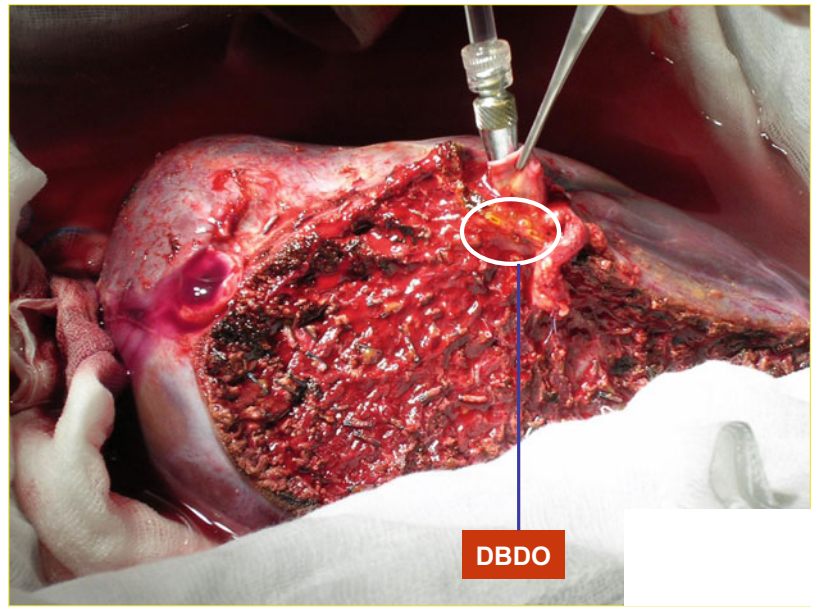

Fig. 19.17 Anatomical variation of the right hepatic duct. *DBDO* double biliary duct opening

maintaining the two distant arterial stumps, with one running 8-0 polypropylene suture and using (2.5×) loupe magnification. Arterial flow is reestablished before the suture is tied to allow further expansion. A Doppler US is routinely performed at the end of the anastomosis, at the end of surgery, and daily until po day 7. The "parachute" technique with running suture compared with interrupted suture can avoid repeatedly tied and excessive vessel manipulation. The use of a microscope allows more precise and easy arterial anastomosis; however, an accurate surgical technique using 2.5× loupe magnification can afford remarkable results.

19.6.3 Biliary Reconstruction

The overall early and late biliary complication rate remains high in LDLT, ranging from 5.3 to 40.6 % [24]. In the last few decades, the technical aspects of biliary reconstruction have been debated for their impact on biliary complications and they remain the "Achilles heel" of the procedure. The "best surgical technique" is still debated; direct duct-to-duct biliary reconstruction is the first technical choice even in case of multiple ducts. However, when two bile duct orifices are very near (approximately 20 % of cases) (Fig. 19.17), a common orifice can be obtained to provide an end-to-end anastomosis with the recipient's common bile duct. In case of distant bile duct double orifices, a bilio-jejunostomy on a Roux-en-Y loop should be performed in the recipient (Fig. 19.18). At the end of the back table procedure, the graft is packed in sterile chilled solution until implantation.

In conclusion, the major task in LDLT is related to difficulty to balance the donor risk in relation to the recipient outcome. Further studies should be addressed for early and long-term donor safety such as hypercoagulable states in donors after hepatectomy, small-for-size grafts, venous outflow obstruction, and hepatic artery thrombosis and impact of long-term steatosis [25]. As allocation systems evolve to ensure that limited organs from DD can be given to those recipients with maximal transplant benefit, LDLT should be considered a significant therapeutic resource.

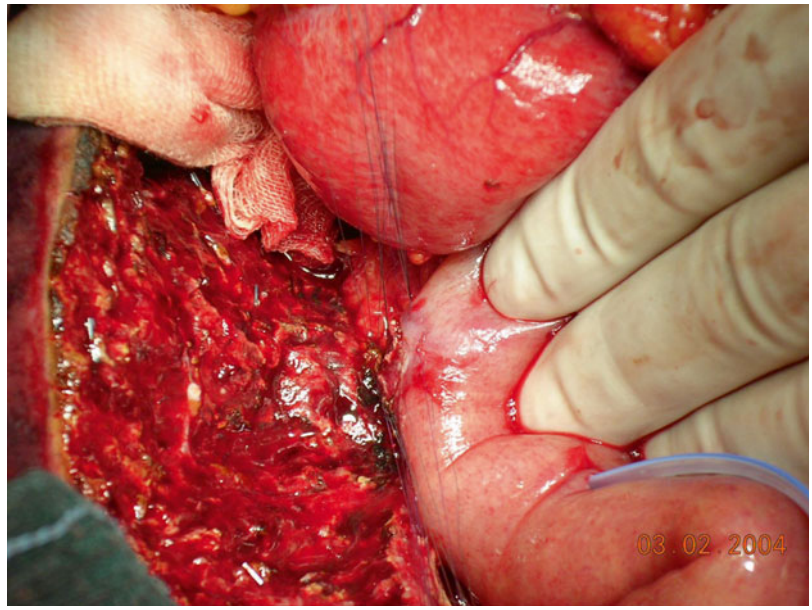

Fig. 19.18 LDLT: in case of distant double bile duct orifices, a Roux-en-Y bilio-jejunostomy can be performed

References

1. Marsh JW, Gray E, Ness R, Starzl TE (2009) Complications of right lobe living donor liver transplantation. J Hepatol 51:715–724
2. Mathur AK, Ashby VB, Fuller DS, Zhang M, Merion RM, Leichtman A, Kalbfleisch J (2014) Variation in access to the liver transplant waiting list in the United States. Transplantation 98:94–99
3. Global observatory on donation and transplantation. Organ donation and transplantation activities, 2012. 1 July 2014. http://issuu.com/o-n- t/docs/2012ad. Accessed 6 July 2015
4. Miller CM, Smith ML, Diago Uso T (2012) Living donor liver transplantation: ethical considerations. Mt Sinai J Med 79:214–222
5. Siegler M, Simmerling MC, Siegler JH, Cronin DC 2nd (2006) Recipient deaths during donor surgery: a new ethical problem in living donor liver transplantation (LDLT). Liver Transpl 12:358–360
6. Raia S, Nery JR, Mies S (1989) Liver transplantation form live donors. Lancet 2:497
7. Strong R, Ong TH, Pillay P, Wall D, Balderson G, Lynch S (1988) A new method of segmental orthotopic liver transplantation in children. Surgery 104:104–107
8. Broelsch CE, Whitington PF, Emond JC, Heffron TG, Thistrlethwaite JR, Stevens L et al (1991) Liver transplantation in children from living related donors. Ann Surg 214:428–439
9. Tanaka K, Uemoto S, Tokunaga Y, Fujita S, Sano K, Nishizawa T, Sawada H, Shirahase I, Kim HJ, Yamaoka Y et al (1993) Surgical techniques and innovations in living related liver transplantation. Ann Surg 217:82–91
10. Yamaoka Y, Washida M, Honda K, Tanaka K, Mori K, Shimahara Y, Okamoto S, Ueda M, Hayashi M, Tanaka A et al (1994) Liver transplantation using a right lobe graft from a living related donor. Transplantation 57:1127–1130
11. Marcos A, Fisher RA, Ham JM, Shiffman ML, Sanyal AJ, Luketic VA, Sterling RK, Posner MP (1999) Right lobe living donor liver transplantation. Transplantation 68:798–803
12. Nadalin S, Bockhorn M, Malagó M, Valentin-Gamazo C, Frilling A, Broelsch CE (2006) Living donor liver transplantation. HPB (Oxford) 8:10–21
13. Varotti G, Gondolesi GE, Goldman J, Wayne M, Florman SS, Schwartz ME, Miller CM, Sukru E (2004) Anatomic variations in right liver living donors. J Am Coll Surg 198:577–582
14. Jeon YM, Lee KW, Yi NJ, Lee JM, Hong G, Choi Y, Park MS, Kim H, Suh KS (2013) The right posterior bile duct anatomy of the donor is important in biliary complications of the recipients after living-donor liver transplantation. Ann Surg 257:702–707
15. Roll GR, Parekh JR, Parker WF, Siegler M, Pomfret EA, Ascher NL, Roberts JP (2013) Left hepatectomy versus right hepatectomy for living donor liver transplantation: shifting the risk from the donor to the recipient. Liver Transpl 19:472–481
16. Chan SC, Liu CL, Lo CM, Lam BK, Lee EW, Wong Y, Fan ST (2006) Estimating liver weight of adults by body weight and gender. World J Gastroenterol 12:2217–2222
17. Hill MJ, Hughes M, Jie T, Cohen M, Lake J, Payne WD, Humar A (2009) Graft weight/recipient weight

ratio: how well does it predict outcome after partial liver transplants? Liver Transpl 15:1056–1062
18. Ghazaly M, Badawy MT, El-Din Soliman H, El-Gendy M, Ibrahim T, Davidson BR. Venous outflow reconstruction in adult living donor liver transplant: outcome of a policy for right lobe grafts without the middle hepatic vein. HPB Surg 2013, Article ID 280857, 11 pages http://dx.doi.org/10.1155/2013/280857
19. Radtke A, Schroeder T, Sotiropoulos GC, Molmenti E, Schenk A, Paul A, Nadalin S, Lang H, Saner F, Peitgen HO, Broelsch CE, Malagò M (2005) Anatomical and physiological classification of hepatic vein dominance applied to liver transplantation. Eur J Med Res 10:187–194
20. Grewal HP, Shokouh-Amiri MH, Vera S, Stratta R, Bagous W, Gaber AO (2001) Surgical technique for right lobe adult living donor liver transplantation without venovenous bypass or portocaval shunting and with duct-to-duct biliary reconstruction. Ann Surg 233:502–508
21. Makuuchi M, Sugawara Y (2004) Technical progress in living donor liver transplantation for adults. HPB (Oxford) 6(2):95–98
22. Kim JD, Choi DL, Han YS (2014) Simplified one-orifice venoplasty for middle hepatic vein reconstruction in adult living donor liver transplantation using right lobe grafts. Clin Transplant 28:561–568
23. Amin AA, Kamel R, Hatata Y, Attia H, Marawan I, Hosney A, El-Malt O, Tanaka K (2009) Crucial issues of hepatic artery reconstruction in living donor liver transplantation: our experience with 133 cases at Dar Al-Fouad Hospital, Egypt. J Reconstr Microsurg 25:307–312
24. Wang SF, Huang ZY, Chen XP (2011) Biliary complications after living donor liver transplantation. Liver Transpl 17:1127–1136
25. Shimul A, Shah MD, Gary A, Levy MD, Lesley D, Adcock MD, Gary Gallagher RN, David R, Grant MD (2006) Adult-to-adult living donor liver transplantation. Can J Gastroenterol 20:339–343
26. Nakamura (2002) Anatomical variations and surgical strategies in right lobe living donor liver transplantation: lesson from 120 cases. Transplantation 73:1896–1903

20 Pure Laparoscopic Left Lateral and Full Left Hepatectomy Including the Middle Hepatic Vein in Living Donors

Roberto Ivan Troisi and Andrea Gatti

20.1 Introduction

Minimally invasive liver surgery has been widely used for the treatment of different liver diseases. In comparison with standard liver surgery, the laparoscopic approach has the advantage of reducing surgical morbidity, postoperative pain, and recovery time [1–3]. Further developments in laparoscopic surgery have demonstrated its technical feasibility in living donor hepatectomy [4–6]. The first laparoscopic living donor liver transplantation (LDLT) procedure was described in 2002, and since then, this procedure has taken some time to be accepted, most likely because of inherent technical difficulties and the highly demanding surgical skills required to performing it [4]. Later on, specialized units have performed minimally invasive living donor hepatectomy with either the pure (full laparoscopic) technique or the hybrid technique (including hand-assisted procedures and single-port incision [5–9]. Different types of graft harvesting, including left lateral sectionectomy and left and right hepatectomy, have been performed [10–13]. Comparative analyses of conventional surgery and minimally invasive techniques for living donor hepatectomy have previously been described [14–16]. However, because of the limited number of reports comparing both techniques and especially because of the low number of patients, it is still not yet clear which method is more beneficial to the donor. According to the 2nd International Consensus Conference on Laparoscopic Liver Surgery, such procedures are classified as Balliol 2b, meaning the need for institutional oversight and a registry to determine short- and long-term outcomes in both donor and recipient (balance of harms) [17].

20.2 Surgical Technique

(a) Left Lateral Sectionectomy procedure
The donor is placed in a supine position with the legs apart. Usually, four trocars are placed on the upper abdominal quadrants; an 8–10-cm suprapubic incision is done and a GelPort device (Applied Medical, USA) is used to maintain the pneumoperitoneum (Fig. 20.1). After localization of the middle hepatic vein by ultrasonography, dissection of the hilum to expose the left hepatic artery and the left portal vein is performed with scissors and bipolar forceps. The left triangular ligament is divided and the Arantius ligament is dissected and cut,

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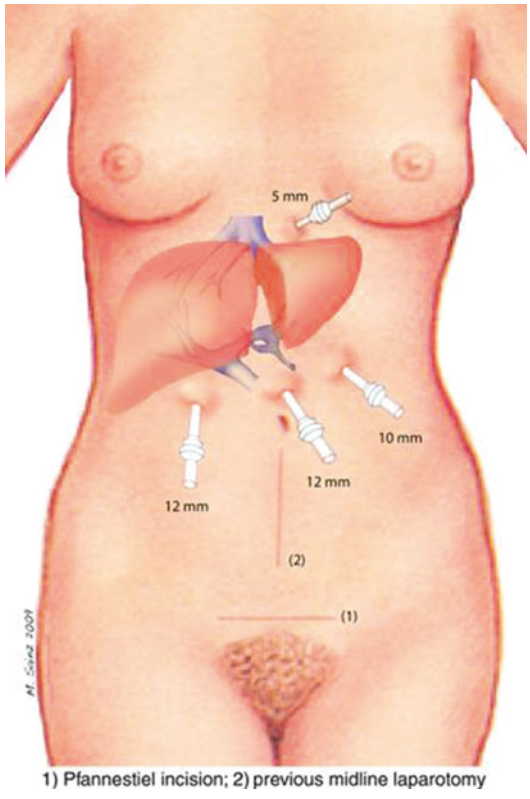

Fig. 20.1 Trocar position for laparoscopic LLS. (1) Pfannenstiel incision; (2) previous midline laparotomy (Reproduced with permission from Troisi et al. [25])

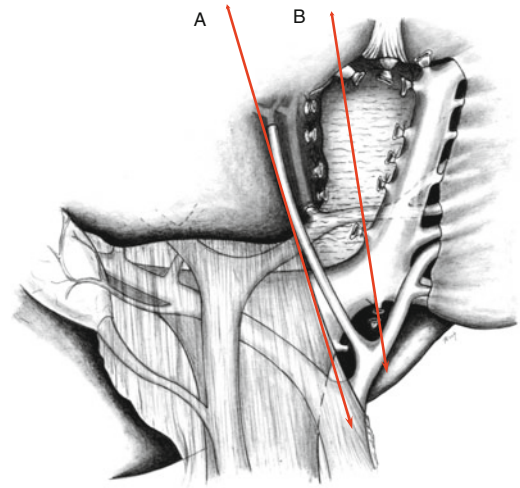

Fig. 20.2 Left lateral split and resection lines: (*a*) Tanaka technique; (*b*) Hamburg technique (Reproduced with permission from Rogiers and Troisi [26])

exposing the space below the common trunk of the middle and left hepatic veins. The cholecystectomy is usually not performed. The hilum is gently dissected using scissors and bipolar device aiming to free the left hepatic artery eventually preserving the branch for segment IV. Parenchymal dissection is performed with the laparoscopic ultrasonic dissector and without Pringle maneuver. The transection line could be done at the level of ligamentum teres (Hamburg technique) or 1 cm on the medial side of this (Tanaka technique). Approaching the ligamentum teres allows to preserve in most of the cases the SIV artery and the SIV duct [2, 3] for biliary anastomosis is higher (Fig. 20.2). Non-resorbable clips (Hem-o-Lok, TFX Medical Ltd., Durham, USA) are systematically placed on intrahepatic vessels while dissecting the parenchyma. The site of transection of the left hepatic duct is close to the Rex recessus and is not requiring the real-time cholangiography because the site is at the distance of the S IV duct (especially when using the Hamburg technique). The left hepatic bile duct is secured by a couple of titanium clips or, alternatively, by closing it with non-resorbable stitches. Afterward, we divide and cut the portal vein and bile duct tributaries to the caudate lobe originating from the left portal branch. Following the administration of systemic heparin (5000 units), the left hepatic artery is clipped and divided. Then, a prompt linear stapler division of the left portal vein (Endo TA 30 mm, Covidien, Mansfield, USA) and the common left and middle hepatic vein trunk (Endo GIA60 mm curved, Covidien) is placed and fired, allowing a manual graft extraction through the suprapubic incision. The graft is flushed on the back table with 2 L of HTK solution:

(b) Pure Full Left Hepatectomy including the Middle Hepatic Vein

Preoperative liver donor evaluation is much more demanding for a fully laparoscopic living donor left hepatectomy (LLDLH) for adult LDLT. The preoperative evaluation is completed by means of the 3D reconstruction of donor graft volume and vascular

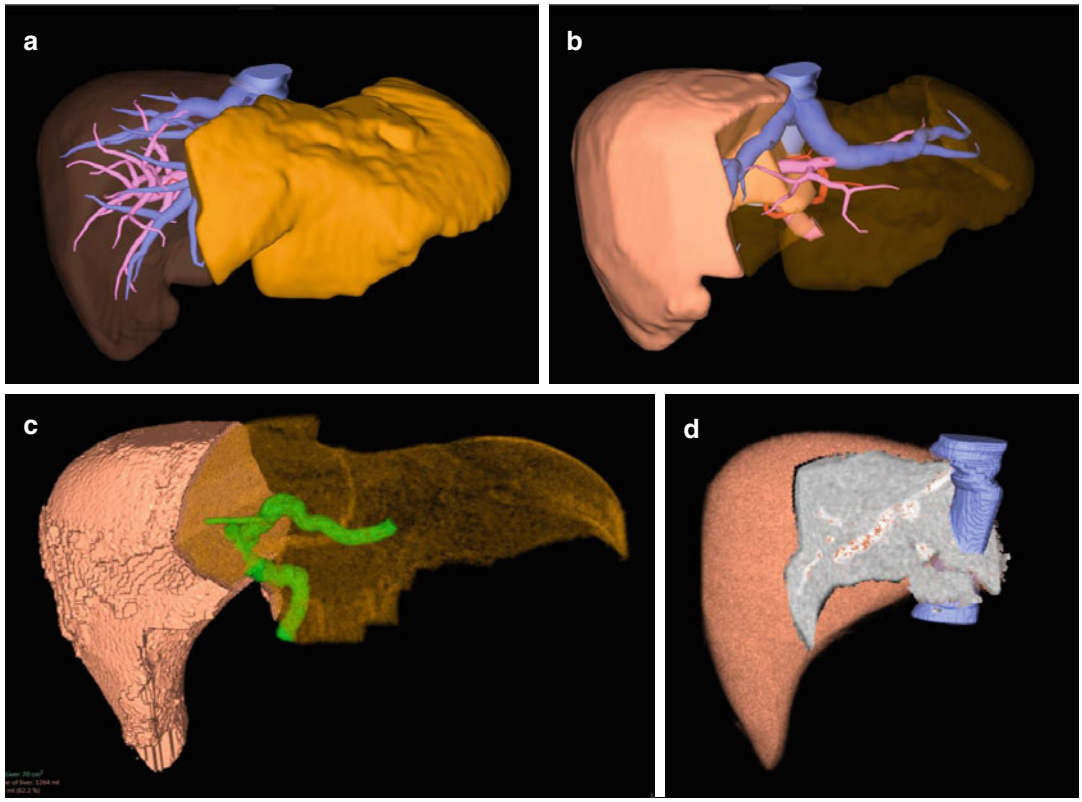

Fig. 20.3 Synapse Vincent 3D evaluation of donor anatomy; (**a**) graft measuring 485 ml; (**b**) intrahepatic anatomy plus remnant –63.6 %-; (**c**) biliary anatomy; (**d**) cutting edge including the MHV

Table 20.1 Donor demographics and operative data

Sex (M/F)	Age (y)	BMI	Anesth Time (min)	OP Time (min)	Res Time (min)	Bleeding (ml)	WIT (min)
4/7	41 ± 9[a]	24 ± 3.8	516 ± 83	476 ± 64	149 ± 29	105 ± 81	4 ± 2.3

[a]Data are in mean ± SD

Table 20.2 Graft characteristics

Double HA	Formal bile anat	GV[a]	Actual GV	Remnant (%)	GW (g)	Actual GRBWR
3/8	5/6	434 ± 92	395 ± 84	69 ± 5	348 ± 67	0.73 ± 0.3

Data in mean ± SD
[a]Estimated graft volume

anatomy. We use the Vincent Synapse 3-D Fuji (Japan) (Fig. 20.3). Donor demographics and graft characteristics are summarized on Tables 20.1 and 20.2. Usually five trocars are used (four 12 mm and one 5 mm) due to the need for exchanging the CUSA instrument according to the angle of the resection line (Fig. 20.4). Differently from the procedure (a), the trunk of the middle and left hepatic vein is encircled with a tape using the Goldfinger device (Ethicon Endo Surgery, Cleveland, USA), which will be successively used, for a "hanging over" maneuver at the completion of the parenchyma liver division close to the caval vein (Fig. 20.5). There is an absolute need for a

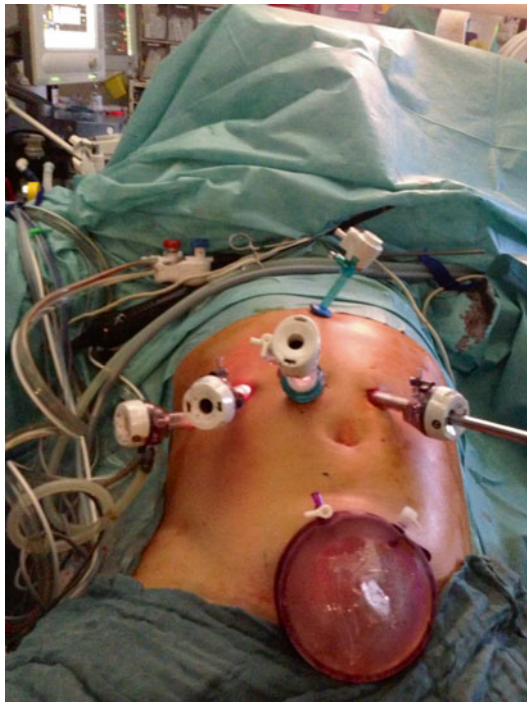

Fig. 20.4 Trocar position for laparoscopic full left hepatectomy. The gel port system through a Pfannenstiel incision is positioned just before graft extraction

real-time cholangiography to exactly localize the cut point of the left hepatic duct. In some cases we try to understand the role of indocyanine green near-infrared fluoroscopy in helping us to identify this point. In any case, the point is marked with a titanium clip as landmark [18, 19]. The resection is done after cholecystectomy and US evaluation of the MHV and tributaries coming from the anteromedian sector along to the Cantlie's line. The MVH is preserved until the trunk, which has been previously dissected and prepared with a tape. Final phases are identical as that of procedure (*a*). At the end of the procedure, a cholangiogram with methylene blue test is routinely performed to check the integrity of the biliary anatomy of the right lobe, and a combined methylene blue test is associated (Fig. 20.6).

A video clip showing a pure laparoscopic full left hepatectomy is added to this chapter (Video 20.1).

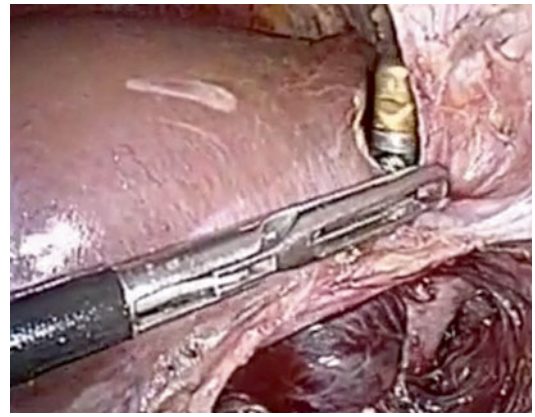

Fig. 20.5 Dissection between the IVC and the trunk of the middle hepatic vein with the Goldfinger dissector in order to achieve a hanging over maneuver

20.3 Results

Eleven donors reported in this series are, to date, alive and well. Conversion has been recorded in one case due to unclear exposure of the left hepatic duct (short median incision). Neither bleedings episodes nor biliary fistulas have been recorded so far. Late reoperation has been done in another one due to an increased in cholestatic enzymes with normal serum bilirubin (type C1 biliary anatomy). The cholangio-MRCP confirmed a sectoral dilatation of the right posterior duct. Although no symptoms where present, we decided to drain this duct with a Roux-en-Y loop following unsuccessful percutaneous dilatation [11]. Overall median length of hospital stay is 4–5 days. Donor and graft characteristics are reported on Tables 20.1 and 20.2.

20.4 Discussion

According to our systematic review with meta-analysis of laparoscopic live donor hepatectomy, we found no difference in donor safety between minimally invasive and open approaches and found lower blood loss associated with laparoscopic LLS for pediatric transplant [20]. In a recent publication, comparative postoperative outcomes of liver and kidney donors showed a significantly lower number of minor complications

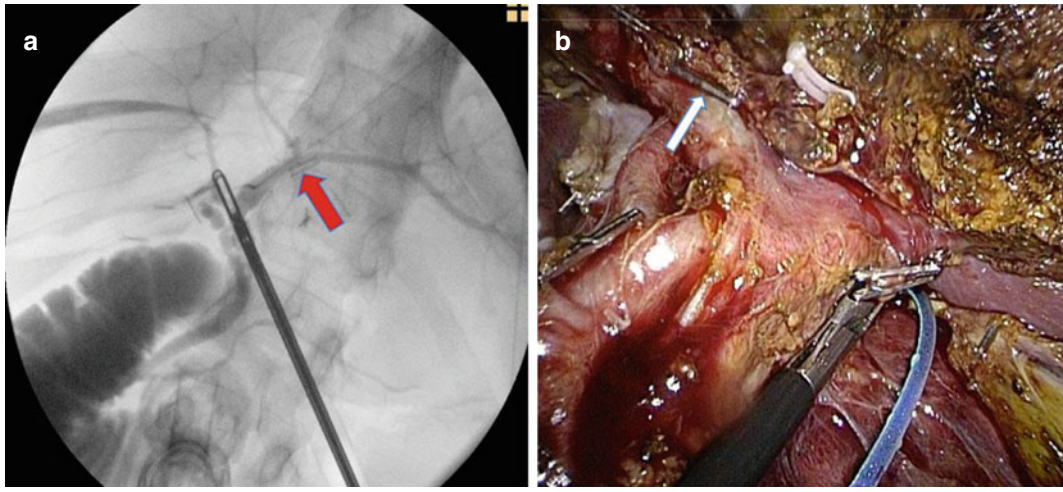

Fig. 20.6 Standard intraoperative donor cholangiogram: (**a**) landmark clips before cutting the biliary duct in the donor (*red arrow*); (**b**) methylene blue test at the end of the donor procedure showing no contrast leak on the cutting edge and on the biliary stump (*white arrow*) (Adapted from Troisi et al. [11])

in liver donors, as compared to kidney donors, and an identical number of major complications in both groups. A comparable comprehensive complication index was observed between liver and kidney donors with complications [21]. This study is the first validation of laparoscopic donor hepatectomy and suggests that the laparoscopic approach along the open should become, similarly to laparoscopic donor nephrectomy, a standard of care.

A different situation is concerning the full LLDH. To our best knowledge, our group has firstly showed the procedure during the IHPBA 2012 in Paris [22]. Left hepatectomy donor morbidity and mortality is well known to be associated with an overall decreased risks compared to that of right hepatectomy [23, 24]. For this reason, advocating shifting the risks from the donor to the recipient side by proposing left lobe adult LDLT could be an option. Donor morbidity is indeed intensely scrutinized in Western countries where liver transplantation from a living donor is not considered a first choice treatment. The concept of applying a laparoscopic technique is attractive because it can potentially further reduce donor morbidity. Unfortunately, two main disadvantages have to be anticipated: the long learning curve of laparoscopy and the specific experience of partial liver transplants from living donors. LLDH must be considered as the ultimate evolution of the laparoscopic technique. The learning curve also depends on the background in general laparoscopic surgery that would facilitate laparoscopic HPB procedures (provided one has already gained experience in open HPB and transplant surgery). The rationale behind the concept of pure laparoscopic fully left living donor hepatectomy for calculated small-for-size living donor liver transplantation is based on the possibility that the laparoscopic technique could further reduce donor morbidity, enabling a successful transplantation in selected recipients. In our opinion there are two critical points for fully laparoscopic procurement: the small size of the left hepatic artery and the exact localization of the cutting place of the left bile duct. The first condition can increase the risk of intima damage during dissection while the second can induce late biliary stenosis in the donors, especially in case of anatomical variations. A relation between these complications and the laparoscopic approach can neither be confirmed nor denied at this point but living donor safety may possibly suffer in this type of procedure. The major problematic issue during laparoscopic donor operations is the optimal intraoperative visualization of the biliary duct anatomy and the cutting point. The real-time cholangiogram is in our opinion mandatory to confirm the cut point of

the biliary ducts. Additionally, ICG near-infrared fluoroscopy could be of utility; however, doses, injection route, and time are to date not yet well defined [19].

In conclusion, our small experience proves the feasibility of laparoscopic full left lateral sectionectomy for pediatric LDLT and also the left liver procurement for adult LDLT. Although it seems that laparoscopic LLS could be the standard of care in highly specialized centers, full LLDH is still far from a standardization of the procedure with unknown risks for the donors. Full LLDH is a consistent attempt to reduce donor morbidity: the potential of this technique and the long-term results in donors and recipients but especially its reproducibility must be validated.

References

1. Koffron AJ, Auffenberg G, Kung R, Abecassis M (2007) Evaluation of 300 minimally invasive liver resections at a single institution: less is more. Ann Surg 246:385–392
2. Montalti R, Berardi G, Laurent S, Sebastiani S, Ferdinande L, Libbrecht LJ et al (2014) Laparoscopic liver resection compared to open approach in patients with colorectal liver metastases improves further resectability: oncological outcomes of a case–control matched-pairs analysis. Eur J Surg Oncol 40:536–544
3. Simillis C, Constantinides VA, Tekkis PP, DarziA LR, Jiao L, Antoniou A (2007) Laparoscopic versus open hepatic resections for benign and malignant neoplasms—a meta-analysis. Surgery 141:203–211
4. Cherqui D, Soubrane O, Husson E, Barshasz E, Vignaux O, Ghimouz M et al (2002) Laparoscopic living donor hepatectomy for liver transplantation in children. Lancet 359:392–396
5. Koffron AJ, Kung R, Baker T, Fryer J, Clark L, Abecassis M (2006) Laparoscopic-assisted right lobe donor hepatectomy. Am J Transplant 6:2522–2525
6. Kurosaki I, Yamamoto S, Kitami C, Yokoyama N, Nakatsuka H, Kobayashi T et al (2006) Video-assisted living donor hemihepatectomy through a 12-cm incision for adult-to-adult. Surgery 139:695–703
7. Scatton O, Katsanos G, Boillot O, Goumard C, Bernard D, Stenard F et al (2015) Pure laparoscopic left lateral sectionectomy in living donors: from innovation to development in France. Ann Surg 261:506–512
8. Suh KS, Yi NJ, Kim T, Kim J, Shin WY, Lee HW et al (2009) Laparoscopy-assisted donor right hepatectomy using a hand port system preserving the middle hepatic vein branches. World J Surg 33:526–533
9. Choi HJ, You YK, Na GH, Hong TH, Shetty GS, Kim DG (2012) Single-port laparoscopy-assisted donor right hepatectomy in living donor liver transplantation: sensible approach or unnecessary hindrance? Transplant Proc 44:347–352
10. Yu YD, Kim KH, Jung DH, Lee SG, Kim YG, Hwang GS (2012) Laparoscopic live donor left lateral sectionectomy is safe and feasible for pediatric living donor liver transplantation. Hepatogastroenterology 59: 2445–2449
11. Troisi RI, Wojcicki M, Tomassini F, Houtmeyers P, Vanlander A, Berrevoet F et al (2013) Pure laparoscopic full left living donor hepatectomy for calculated small-for-size LDLT in adults: proof of concept. Am J Transplant 13(9):2472–2478
12. Soubrane O, Perdigao Cotta F, Scatton O (2013) Pure laparoscopic right hepatectomy in a living donor. Am J Transplant 13:2467–2471
13. Samstein B, Adam Griesemer A, Cherqui D, Mansour T, Pisa J, Yegiants A, Fox AN, Guarrera JV, Kato T, Halazun KJ, Emond J (2015) Fully laparoscopic left-sided hepatectomy is safe and associated with short hospital stay and earlier return to work: a comparative study. Liver Transpl 21:768–773
14. Kasahara M, Sakamoto S, Shigeta T et al (2012) A 7-cm upper midline incision for living donor left lateral hepatectomy: single-center consecutive 7O donor experience. Transplantation 93(8):e33–e34
15. Han HS, Cho JY, Yoon YS et al (2015) Total laparoscopic living donor right hepatectomy. Surg Endosc 29:184
16. Zhang X, Yang J, Yan L et al (2014) Comparison of laparoscopy-assisted and open donor right hepatectomy: a prospective case-matched study from china. J Gastrointest Surg 18(4):744–750
17. Wakabayashi G, Cherqui D, Geller DA, Buell JF, Kaneko H et al (2015) Recommendations for laparoscopic liver resection. A report from the Second International consensus conference held in Morioka. Ann Surg 261(4):619–629
18. Troisi RI, Elsheikh YM, Shagrani MA, Broering D (2014) First fully laparoscopic donor hepatectomy for pediatric liver transplantation using the indocyanine green near-infrared fluorescence imaging in the Middle East: a case report. Ann Saudi Med 34(4): 354–357
19. Tomassini F, Scarinci A, Elsheik Y, Scuderi V, Broering D, Troisi RI (2015) Indocyanine green near-infrared fluorescence in pure laparoscopic living donor hepatectomy: a reliable road map for intrahepatic ducts? Acta Chir Belg 115:2–7
20. Berardi G, Tomassini F, Troisi RI (2015) Comparison between minimally invasive and open living donor hepatectomy: a systematic review and meta-analysis. Liver Transpl 21(6):738–752. doi:10.1002/lt.24119
21. Soubrane O, de Rougemont O, Kim KH, Samstein S, Mamode N, Boillot O, Troisi RI et al (2015) Laparoscopic living donor left lateral sectionectomy: a new standard practice for donor hepatectomy. Ann Surg 262:757–763

22. Troisi R (2012) Adult LDLT with intentional small for size graft following fully laparoscopic living donor left hepatectomy including the middle hepatic vein. IHPBA2012com; NSVT06: 281
23. Umeshita K, Fujiwara K, Kiyosawa K, Makuuchi M, Satomi S, Sugimachi K, Tanaka K, Monden M (2003) Operative morbidity of living liver donors in Japan. Japanese Liver Transplantation Society. Lancet 362(9385):687–690
24. Iida T, Ogura Y, Oike F, Hatano E, Kaido T, Egawa H, Takada Y, Uemoto S (2010) Surgery-related morbidity in living donors for liver transplantation. Transplantation 89(10):1276–1282
25. Troisi RI, Van Huysse J, Berrevoet F, Vandenbossche B, Sainz-Barriga M, Vinci A, Ricciardi S, Bocchetti T, Rogiers X, de Hemptinne B. Evolution of laparoscopic left lateral sectionectomy without the Pringle maneuver: through resection of benign and malignant tumors to living liver donation. (2011) Surg Endosc. 25(1):79–87. doi: 10.1007/s00464-010-1133-8. Epub 2010 Jun 8
26. Rogiers X, Berrevoet F, Troisi R. Comment on outcomes in right liver lobe transplantation: a matched pair analysis by G.K. Bonney et al. in Transplant International 21(2008) 1045–1051: Technical details matter

Totally Laparoscopic Right Hepatectomy for Living Donors

21

Choon Hyuck David Kwon and Jae-Won Joh

Tips, Tricks, and Pitfalls

- Only patients without any anatomical variations of the artery, portal vein, and bile duct should be selected.
- For easy dissection and mobilization of the right liver, dissect the coronary ligament and inferior triangular ligament first and have the patient tilted left side down and retract the liver using both the ligamentum teres and the gallbladder in addition to a gentle push using a snake retractor.
- Check the division plane of the bile duct with a radiopaque marker and cholangiogram. Have two bulldog clamps applied on both sides before cutting the bile duct to prevent troublesome bleeding.
- Do not hesitate to apply intermittent inflow occlusion and increase the intra-abdominal pressure to balance the CVP whenever necessary to control major bleeding events.
- Place the right liver inside a plastic bag and have the end lace of the bag drawn out through the wound incision before ligating the vessels to decrease warm ischemic time.

Living donor liver transplantation (LDLT) has been proposed as an alternative source of organs and is an accepted treatment strategy especially in regions where deceased donors are scarce. However, the donors, despite their altruistic action, suffer substantially from medical and psychological burden [1, 2]. Laparoscopic approach for liver resection is known to decrease pain, reduce hospital stay, offer early recovery to normal life, and is more cosmetically acceptable and has gained much popularity in recent years [3]. However, due to the technical difficulty of the operation and the concern of safety in living donors, it has not been performed widely [4]. There have been several reports with left side donors and its acceptance as a possible alternative to open hepatectomy is gaining momentum [5]. However, despite the fact that the right liver is more often used for adult LDLT due to the graft size, because right hepatectomy is known to be more technical demanding and more dangerous compared to left side, very few centers are performing laparoscopic right hepatectomy for donors, and most reports are just case reports [6]. Currently more evidence with larger numbers of cases will be necessary and for the time being, laparoscopic right donor hepatectomy will not be accepted widely among the surgeons in this field. Nevertheless with the development of new instruments and accumulation of experience in the laparoscopic field, laparoscopic right hepatectomy will probably gain wider acceptance than the present time.

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Before describing in more detail, I would like to note that all the comments concerning the operative technique described in this chapter are solely based on personal experience, and there may be other variations in performing this operation. Also, it is very important that the surgeon should be experienced in both living donor hepatectomy and laparoscopic liver resection before proceeding laparoscopic donor hepatectomy since no mistakes is allowed during the operation of the donor.

21.1 Selection of Patient

It is important to select the proper patient for laparoscopic donor hepatectomy. Selection of patients with anatomic variations that requires additional technical sophistication should not be done.

21.1.1 Patient's Clinical Characteristics

Most centers experienced in LDLT remain very strict in the selection process of the donors. At our institution, all donors (1) should not have other comorbidity which may hinder the safety of the donor, (2) should be less than 65 years of age, (3) should have macrosteatosis of less than 30 %, and (4) should have an expected remnant liver of more than 30 %. However, for safety reasons, the selection criteria for laparoscopic approach is more conservative, and we only select patients under 60 years old and with a remnant of more than 35 %.

21.1.2 Hepatic Artery

Bleeding from hepatic artery stumps in donors have been reported and may have very serious consequences. Clips or Hem-o-Lok, by nature, is removed more easily compared to open surgical ties, so it is important to leave enough end stump during division of the hepatic artery. Therefore patients with early bifurcation of the right anterior and posterior hepatic artery with a short right hepatic artery should not be selected for laparoscopic donor hepatectomy.

21.1.3 Portal Vein

We have experienced two cases of portal vein complication out of 40 cases done so far. Both of them had portal vein variation, one type 2 and one type 3. In patients with early division of anterior and posterior portal veins, the right glissonian trunk is usually wide and thick which increases the difficulty of the operation and is not recommended for laparoscopic approach.

21.1.4 Bile Duct

Even in open donor hepatectomy, division of the bile duct is one of the most critical and stressful step during donor hepatectomy. Therefore, we recommend laparoscopic approach only for patients with normal biliary anatomy. According to our experience, patients with bile duct variation had postoperative biliary complication rate of over 40 % compared to less than 10 % in normal anatomy. Additionally, in order to increase the safety of the operation and improve outcome, we perform an intraoperative cholangiogram to all donors before and after the division of the bile duct.

21.2 Surgical Procedure

21.2.1 Anesthesia and Position of the Patients

Good collaboration and teamwork between the surgical team and the anesthesiologist are very important for a smooth and safe operation. We do not routinely insert a central venous line but less than 500 mL per hour of crystalloid is given throughout the operation to maintain low-volume anesthesia. Under these circumstances, if excessive bleeding occurs or the intra-abdominal pressure is increased for a pro-

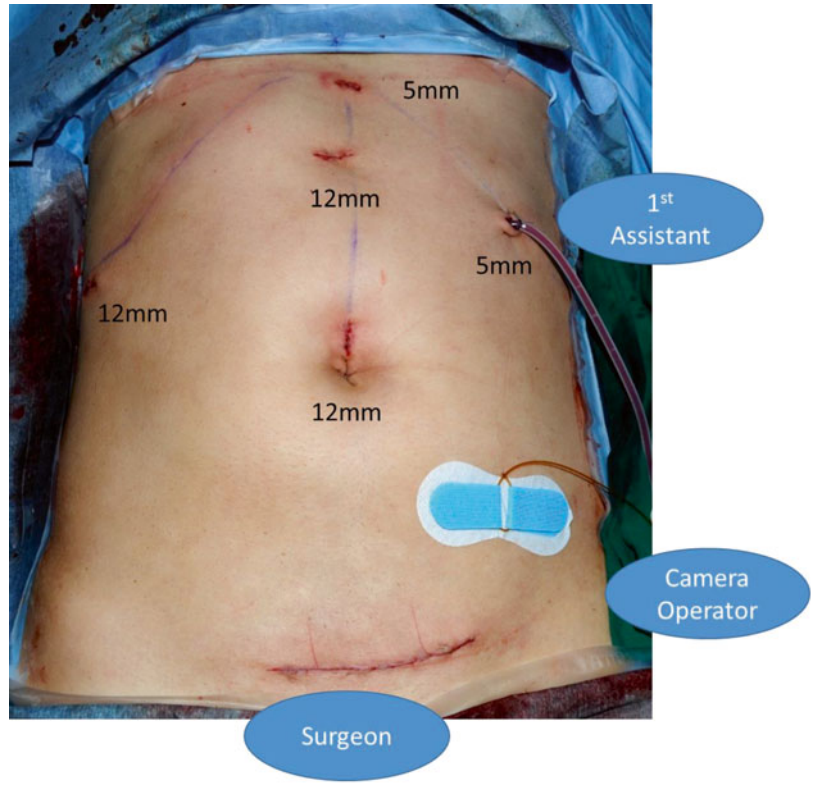

Fig. 21.1 Position of the trocar ports and surgeons. The umbilical port is used to insert the camera, two 12 mm ports are used by the operator and two 5 mm ports by the assistant

longed period, circulatory collapse may easily happen. Therefore, it is very important that the anesthesiologist is informed of any events during the operation so that precautious may be taken beforehand.

Serious complications have been reported on donors after epidural anesthesia, so intrathecal morphine injection in addition to local pain control (Fig. 21.1) is used instead of epidural anesthesia. Early recovery after surgery protocol may be applied using this method of pain control.

The patient is placed in a modified lithotomy position, so-called "French" position, and the operator stands between the patient's legs while the camera operator and first assistant stand on the left side of the patient. Generally three 12 mm and two 5 mm trocar ports are used as shown in Fig. 21.1. The camera is placed through the umbilical port. I recommend using a flexible camera because it provides a better view, especially of the upper area around the coronary ligaments compared to rigid scope, which is vital for the safety of the donor. The intraperitoneal pressure is maintained at 11 mmHg. After pneumoperitoneum is established, a wedge liver biopsy is done for final confirmation of the liver histology.

21.2.2 Mobilization of the Liver

The round ligament and falciform ligament is first dissected using either an advanced bipolar device or ultrasonic shear until the IVC is visualized. Then the right coronary ligament is dissected from left to right as far as possible followed by dissection of the inferior side of the right triangular ligament. Having the upper and lower ligaments dissected first before dissecting the right side of the triangular ligament makes the mobilization of the liver easier. Instruments used for retraction during laparoscopic approach are usually sharper compared to the hand or instruments used in open hepatectomy and may result in a tear of the liver. So it is important to simultaneously have the patient tilted left side down

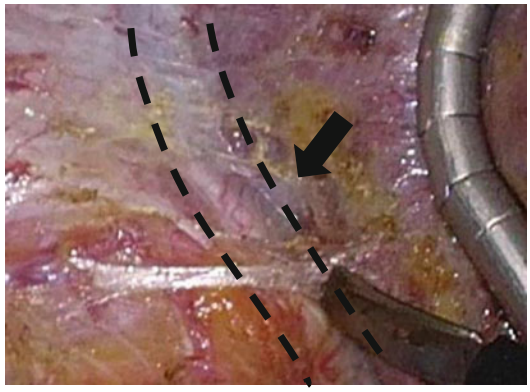

Fig. 21.2 Right side mobilization is done only until the caval ligament (*black arrow*) and IVC (*dotted line*) is visualized. The liver is retracted to the left side using a snake retractor in addition to left down tilt of the patient and retraction of the liver using ligamentum teres and the gall bladder

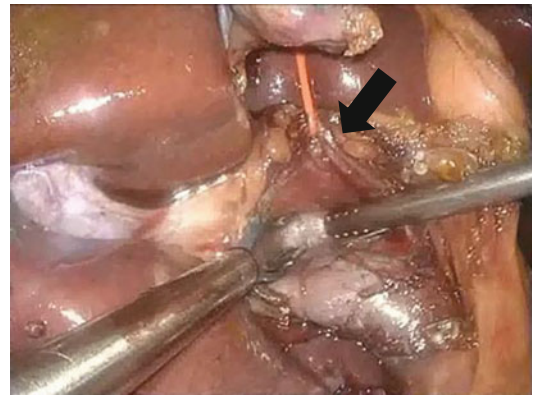

Fig. 21.3 Dissection of the hepatic artery and portal vein is done by blunt dissection using bipolar forceps and suction tip. The hepatic artery (*black arrow*) is looped with vessel sling or the soft tissue around perihilar area is retracted cephalad and leftward to gain a better view during portal vein dissection

(15 to 30 degree), retract the liver using both the ligamentum teres and the gallbladder, and finally apply a gentle traction using a snake retractor.

Unlike in open donor hepatectomy where the caval ligament is divided at the initial stage, the angle of approach is not safe in laparoscopic approach, so I recommend mobilizing the liver only until the caval ligament is exposed and divide the caval ligament after the parenchymal division has been finished (Fig. 21.2).

21.2.3 Dissection of the Hilar Plate

After the cystic artery and duct is clipped and divided, the right hepatic artery is dissected followed by the portal vein. Left cephalad traction of the plate using the cystic duct by the assistant helps gain a better operative view. I prefer using a blunt bipolar forceps and suction tip to dissect the vessels (Fig. 21.3). Division of the caudal portal branch eases the dissection around the right portal vein. After the right hepatic artery and portal vein is isolated, it is temporarily clamped with a bulldog, and the demarcation line between left and right liver is marked using a monopolar electrocautery. Unexpected bleeding requiring inflow control may occur at any stage of the operation, so the hepatoduodenal ligament should be looped for possible application of inflow control (Pringle maneuver) before proceeding with the parenchymal transection.

21.2.4 Parenchymal Transection

Before starting parenchymal transection, laparoscopic USG is used to verify the location of the middle hepatic and the main hepatic vein branches (V5 and V8). Usually division of the parenchyma up to 2 cm from the capsule does not require fine dissection and may be carried out using either advanced bipolar device using Kelly crush technique or ultrasonic shear. When dissecting the deeper area where main hepatic vein branches may be present, cavitron ultrasonic surgical aspirator (CUSA) or gentle dissection using ultrasonic shear is recommended. The CUSA is one of the best instruments for precise parenchymal transection and most frequently used among surgeons performing donor hepatectomy. However, its maintenance for optimal function requires much work from the nursing side and the hand piece is heavy and not very ergonomic. The ultrasonic shear, along with suction, may be used like the CUSA to dissect the liver parenchyma, and this has become my preferred method.

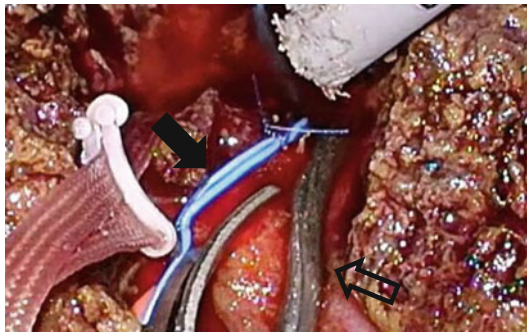

Fig. 21.4 Division of the bile duct. The Glisson branch after dissecting the hepatic artery and portal vein is encircled with a tape, and a bulldog clamp (*open arrow*) is applied on the remnant side. Bile duct is divided along the radiopaque mark (*black arrow*) after confirming with intraoperative cholangiogram

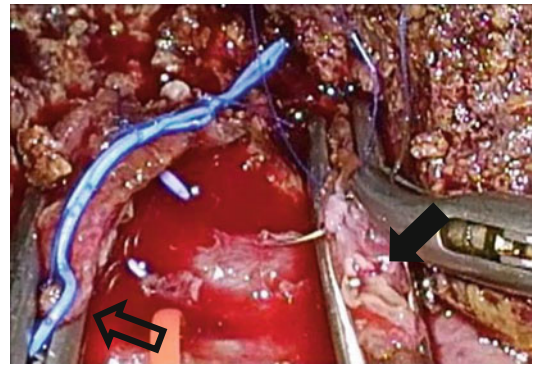

Fig. 21.5 Suture of the remnant bile duct. The Glisson, including the right bile duct (*black arrow*), is sutured using Prolene 5-0 or PDS 5-0 by continuous running method. The graft side bulldog is left clamped (*open arrow*) and removed at the back table

Small branches (less than 2 mm) are usually divided with energy devices and branches between 2 and 5 mm are clipped. When hepatic vein branches requiring reconstruction at the back table are encountered, they are double clipped on both sides and divided.

After the anterior area of the parenchyma is transected so that the entire glissonian branch is exposed, the caudate is transected. The assistant should have the hilar plate retracted gently cephalad to obtain a good surgical field, and the surgeon should transect the caudate as much as possible from the inferior side of the glissonian branch. This will greatly facilitate transection of the remnant superior area of the caudate lobe which will be done after the bile duct division.

21.2.5 Bile Duct Division

The whole glissonian structure other than the dissected artery and portal vein is left intact to preserve the microcirculation around the biliary tree to decrease the bile duct complication of the recipient. After a radiopaque marker is sutured at the expected line of division, an intraoperative cholangiogram is taken to verify the correct division plane. One bulldog clamp is applied on each side of the glissonian structure before dividing the bile duct since troublesome bleeding usually occurs (Fig. 21.4). The remnant bile duct stump is sutured using a back and forth continuous running suture with Prolene 5-0 or PDS 5-0 (Fig. 21.5). After suturing the bile duct, the bulldog clamp is removed and additional bleeding control is done with Prolene 5-0 sutures. Monopolar and/or bipolar coagulation is generally not used to prevent burn injury which may result in bile duct stricture. The bulldog clamp on the graft side is left clamped and is removed at the back bench. The minor bleeding control around the graft bile duct is performed on the recipient side after reperfusion.

21.2.6 Final Steps and Retrieval of the Graft

After dividing the bile duct, the remnant parenchymal transection is performed. Care must be taken when dissecting along the IVC where there may be unexpected short hepatic veins. After the right hepatic vein has been exposed, the liver is placed inside the plastic bag. The abdomen is deflated, and a Pfannenstiel incision of 10–15 cm long is made at the suprapubic area (Fig. 21.1). After the lace of the plastic bag is drawn out through the incision, a wet gauze and 5–6 towel clips are applied at the wound area to prevent air leak, and the abdomen is inflated again.

The hepatic artery is double clipped and divided. The remnant side of the right portal vein

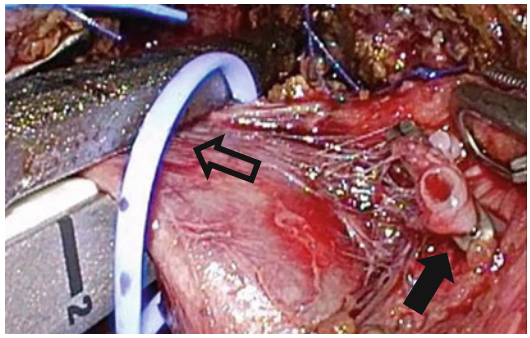

Fig. 21.6 Division of hepatic artery and portal vein. The hepatic artery is double clipped and divided (*black arrow*). The portal vein is stapled using a vascular TAE. Care must be taken not to apply the stapler too close to the remnant portal vein since stricture may occur (*open arrow*). The liver has already been placed inside the plastic bag

is stapled using endo-TAE, a bulldog clamp is applied on the graft side portal vein and the portal vein is divided. It is important to not apply the stapler too close to the left side since portal vein stricture may occur (Fig. 21.6). Then the remnant side of the right hepatic vein is stapled with endo-TAE and divided. The caval ligament is divided at this point either after applying clips or using a vascular endo-GIA. The right liver, which has been already placed inside the plastic bag, is now gently taken out of the abdomen by pulling the lace of the plastic bag through the incision. By having the right liver placed in the plastic bag and the end of the lace brought out through the incision before starting vessel ligation, warm ischemic time may be reduced, usually to less than 5 min. The graft is perfused using HTK solution mixed with 2000–3000 IU of heparin at the back table. All clips of the V5 and V8 branches are removed, and the hepatic artery is also flushed gently taking care not to injure the intimal layer of the artery.

Irrigation and hemostasis is performed. Bile leakage test using indigo carmine dye is done to verify open bile ducts or leakage points at the suture site. A final intraoperative cholangiogram is performed to confirm presence of stricture in the remnant bile duct. Two Jackson-Pratt drains are placed in the right fossa and at the perihilar area.

21.2.7 Management of Major Bleeding Event

Major bleeding, especially from hepatic vein branches and/or IVC has always been a big challenge during major liver resection. The surgeon should try to best of his or her ability to prevent any injury of the veins which may lead to massive bleeding or transfusion. However in case of major bleeding event, there are two important strategies that I use. First is the application of intermittent inflow occlusion (Pringle maneuver). Although frequent application of inflow control may increase the postoperative liver enzyme especially in patients with macrosteatosis, survival of the recipient is not affected, and one should not hesitate to use intermittent inflow occlusion in case of bleeding events [7]. The second strategy is the flexible application of intra-abdominal pressure. The intra-abdominal pressure is kept as low as possible, usually at 11 mmHg, during the whole operation to minimize the consequences of prolonged increased intra-abdominal pressure such as acidosis or elevated PCO_2. However, in case of large vein injury resulting in profuse bleeding, it may be sequentially increased up to 15 mmHg until balance is achieved with the CVP. This balancing process allows the operator sufficient time to repair the injury with minimal bleeding. Simultaneously, only a small amount of gas embolism occurs so the side effects related to gas embolism may be prevented. We have used this method routinely in over 200 cases of major liver resection without experiencing any adverse effect related to massive gas embolism.

21.3 Postoperative Recovery

Intrathecal morphine injection in addition to local pain control with bupivacaine using commercially available catheter (Fig. 21.1) usually offers sufficient pain control, so early recovery after surgery protocol may be applied. Oral fluid is started on day 1 and soft diet on day 2. Total

bilirubin level of the drains and routine DISIDA scan is taken on day 5 before removal of the drains to evaluate possible biliary leakage. The patient is discharged on day 7 and Doppler USG and abdomen CT is done at the outpatient during follow-up.

Total laparoscopic right hepatectomy for living donors is still a very challenging procedure requiring the cutting-edge techniques of HBP surgery. Surgeons willing to perform this operation should be experienced both in living donor hepatectomy and laparoscopic liver resection. However, according to our results after more than 40 cases, it may be performed relatively safely with major complication rate of less than 10 % and now takes up about 25 % of our living donor program. This operation will provide liver donors, who are not patients per se, to recover with less pain, have a more cosmetically satisfying wound, and return to normal life earlier.

References

1. Shin M et al (2012) Donor morbidity including biliary complications in living-donor liver transplantation: single-center analysis of 827 cases. Transplantation 93(9):942–948
2. Verbesey JE et al (2005) Living donor adult liver transplantation: a longitudinal study of the donor's quality of life. Am J Transplant 5(11):2770–2777
3. Dagher I et al (2009) Laparoscopic versus open right hepatectomy: a comparative study. Am J Surg 198(2):173–177
4. Troisi RI (2014) Open or laparoscopic living donor liver hepatectomy: still a challenging operation! Am J Transplant 14(3):736
5. Yu YD et al (2012) Laparoscopic live donor left lateral sectionectomy is safe and feasible for pediatric living donor liver transplantation. Hepatogastroenterology 59(120):2445–2449
6. Han HS et al (2015) Total laparoscopic living donor right hepatectomy. Surg Endosc 29(1):184
7. Park JB et al (2012) Effect of intermittent hepatic inflow occlusion with the Pringle maneuver during donor hepatectomy in adult living donor liver transplantation with right hemiliver grafts: a prospective, randomized controlled study. Liver Transpl 18(1):129–137

Laparoscopic and Robot-Assisted Nephrectomy

22

Alessandro Giacomoni, Lucrezia Furian, Giacomo Concone, and Paolo Rigotti

Tips, Tricks and Pitfalls

- Examine carefully the position of the donor preoperatively, to avoid discomfort for the patient and for the surgeons.
- Communicate with all the members of the surgical team, including anaesthesiologists and nurses, to clarify the main phases of the operation.
- Get ready for a rapid open conversion, drawing on the body of the donor the midline incision.
- Remind that hand-assisted technique can become useful to manage unexpected difficulties.
- Avoid the use of non-tissue affixing ligation technique for renal vessels.
- Plan a strategy to maximize the length of renal vessels, using Endoscopic GIA or TA stapling device, keeping away from early bifurcations.
- Note the advantages of using a Ligasure™ vessel sealing for dissection, to shorten operative time and to avoid clips interfering with the stapling suture line.
- Pay a lot of attention to haemostasis of the Pfannenstiel incision, since the heparin bolus effect may result in subcutaneous hematoma.

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The scientific community has largely demonstrated that living donor kidney transplantation (LDKT) is a valid alternative for patients with end-stage renal disease (ESRD). When considering long-term patient and graft survival, the results of LDKT are significantly better than the ones obtained with deceased kidney transplantation [1, 2]. Moreover, LDKT offers several advantages when compared to deceased kidney donations as the recipient experiences better quality of life and better immediate graft outcome. Moreover, LDKT offers the possibility of transplanting patients either pre-emptively or after a shorter dialysis period.

Over the last decade, the United Network for Organ Sharing (UNOS) has reported that LDKT is performed more and more frequently, so as to

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exceed the number of transplantation with deceased donors. The reasons for fostering the living kidney donations may depend on the demonstrated advantages of the LDKT when compared to deceased donor transplantations as well as on the diffusion of minimally invasive surgical procedures for kidney harvesting. Minimally invasive techniques appear to be more acceptable for the donors, most likely because of the significant reduction in postoperative pain, decreased length of hospital stay, rapid patient rehabilitation and better cosmetic results. Because of that, the laparoscopic approach for living donation nephrectomy, first reported by Ratner in 1995 [3], has been performed in increasing number of cases, both for hand-assisted and for totally laparoscopic procedure.

22.1 Preoperative Evaluation and Intraoperative Management of Living Donor

Besides the nephrological and psychosocial evaluations, which have to be made in accordance with the clinical practice guidelines, the study of the surgical and anaesthesiologic risk of the living donor has to be cautiously considered, allowing for only those subjects ASA Class I or II (American Association of Anaesthesiologists Physical Status Classification) to become donors.

Moreover, as with the open procurement procedure, preoperative considerations of anatomy and functional status of the donor kidneys are crucial for the side of the nephrectomy procedure. It is mandatory to clarify whether one kidney has a lower function (through a nuclear scan with split renal function), abnormalities of the parenchyma (cysts, angiomyolipoma, ptosis) or of the urinary tract (lithiasis, ureteral duplicity, pyelectasis) through ultrasound and urographic exams or vascular abnormalities (multiple renal arteries, circumaortic or retroaortic renal veins) through three-dimensional spiral CT or magnetic resonance angiography.

The kidney with worse or imperfect features will be harvested, although in case of absence of significant abnormalities, generally the left kidney is preferentially used, because of the anatomically longer renal vein at this side.

The contraindications to laparoscopic donor nephrectomy are the same as those established for open nephrectomy, although a previous abdominal surgery may increase the complexity of the procedure through a transperitoneal approach. Nevertheless, overweight or slightly obese subjects should preferentially undergo laparoscopic procedures, because of the minor risk of wound complications, better postoperative respiratory performance and early mobilization [4, 5].

Donors are at moderate risk of developing venous thromboembolism and should receive prophylactic low-molecular-weight heparin (starting before surgery and continuing for at least 5 days or until discharge), supplemented with graduated stockings and/or intermittent pneumatic compression devices. Since pneumoperitoneum increases intra-abdominal pressure, causing a decrease in renal blood flow and glomerular filtration rate resulting in oliguria, administration of IV fluids the night before surgery may be useful.

Fasting before operation and induction of anaesthesia lead to relative hypovolemia and the goal is to compensate this before pneumoperitoneum is started. To counterbalance the increased intra-abdominal pressure, vigorous IV hydration during laparoscopic donor nephrectomy is nowadays recommended in an attempt to optimize preload and promote diuresis [5]. The adequacy of intravascular volume expansion can be monitored by the turgor of the renal vein; a collapsed renal vein signals the need for more liberal use of intravenous fluids. A brisk diuresis is stimulated throughout the procedure by an 80 mL bolus administration of mannitol. Just before removing the kidney, the donor is given 20 mg of furosemide and 5000 UI of heparin. When the kidney has been removed, protamine is generally given to reverse completely the anticoagulant effect of heparin. Moreover, the role of the anaesthesiologist is to obtain a sufficient laparoscopic working space; therefore the patient must be kept completely relaxed.

In the postoperative analgesia, non-steroidal anti-inflammatory drugs (NSAIDs) are generally

avoided because of their potential nephrotoxicity; intravenous analgesia (paracetamol) is limited to the first postoperative day, and patients should be converted to oral analgesic when clear liquids are introduced on the second postoperative day. Special attention should be paid to the prevention of complications related to lateral position (nerve damage, airway compromise, pressure sores, venous access compromise).

22.2 Laparoscopic Living Donor Nephrectomy: Operative Procedure

Before proceeding with the positioning of the patient, it is useful and recommended to mark with a dermographic pen the midline, the suprapubic Pfannenstiel line and the standard position of the trocars. The line marks will become very helpful in case of need of a rapid open conversion or, more frequently, to achieve a better cosmetic result for the Pfannenstiel incision, which is made when the rotation of the patient may lead to a distorted incision (Fig. 22.1). The marks for the trocar introduction are particularly convenient for patients with global abdominal enlargement.

The positioning of the patient is a modified lateral decubitus position, with the hips rotated back and the arms extended above the head (Fig. 22.2). The table is only slightly flexed, to expand the area between the costal margin and the pelvis. It is important to make sure that the sternal support of the surgical table is placed cranially enough in order to not interfere with the actions of the hand of the first operator. The arm of the patient lays over the contralateral, and no supports are needed, since they could hamper free movements of the surgeon. A 12 mmHg pneumoperitoneum is established with the Hasson open technique. Instead of the traditional periumbilical incision, a 2 cm paramedian incision slightly above the umbilicus (between the umbilicus and the Palmer's point) can lead to some advantages, because it is a safe incision with no muscle cutting, with low risk of incisional hernia. The fascia is incised and the peritoneum is grasped and opened. Care is taken to ensure that there is no bowel attached. Two stay sutures are placed in the fascia around the opening to secure the Hasson cannula that is placed into the peritoneal cavity in order to avoid leakage of the CO_2 gas used for insufflation. We consider safer and recommend the open approach, although the Cochrane Database of Systematic Reviews 2012 concluded that the open entry technique is associated with a significant reduction of failed entry (compared to the closed entry technique), with no difference in the incidence of visceral or vascular injury [6]. The videoendoscope is inserted in this first port, and three more operative ports are placed: a 12 mm in the iliac fossa on the middle clavicular line (between the umbilicus and the anterior superior iliac spine), a 5 mm in the hypochondrium on the middle clavicular line (two fingerbreadths below the costal margin) and a fourth 5 mm trocar for the assistant in the flank (Fig. 22.3). As far as the left sided procedure is concerned, after the exploration of the abdominal cavity, the ascending and sigmoid colon are taken down starting from the splenic flexure by dividing the lateral attachments with DeBakey graspers and curved scissors. The colon is reflected medially with exposition of the Gerota's fascia. The dissection can subsequently be accomplished bluntly, reducing the risk of

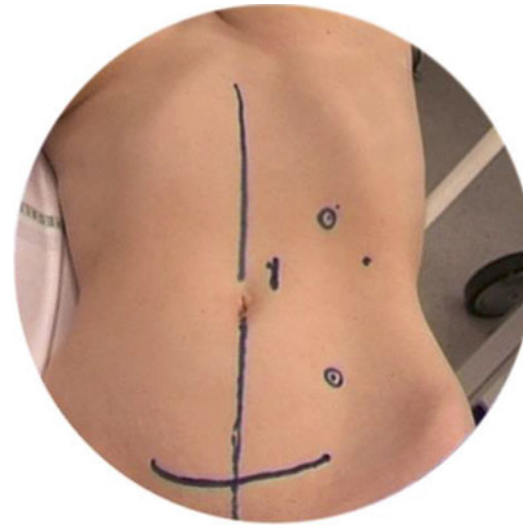

Fig. 22.1 Midline, suprapubic line marks and position of the trocars

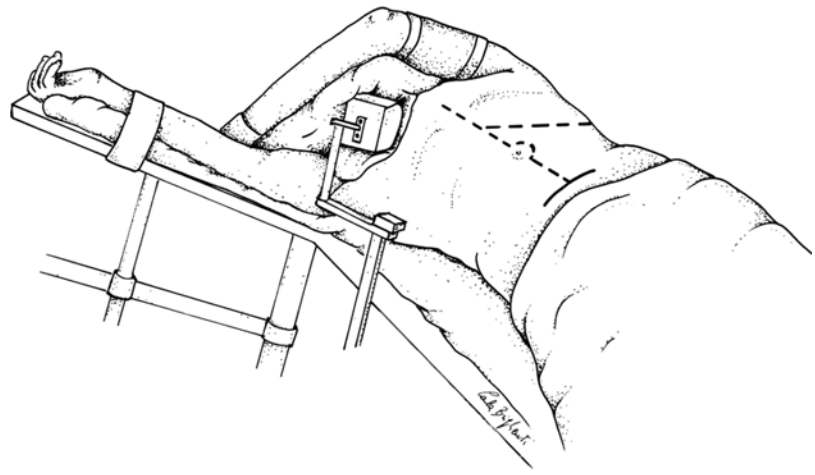

Fig. 22.2 Modified lateral decubitus position

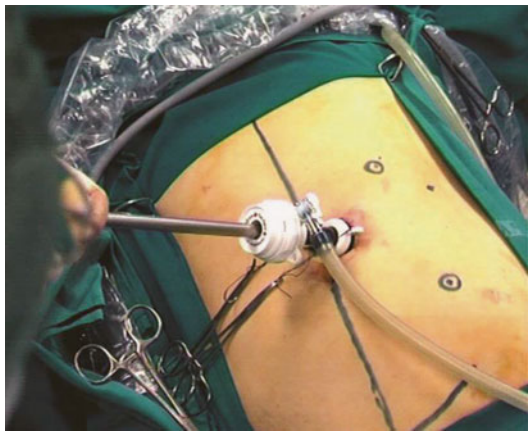

Fig. 22.3 Introduction of the laparoscope and sites of operative trocars

buttonholing the mesocolon, sweeping the tissue medially and developing a natural plane between the mesocolon and Gerota's fascia. Once the colonic mobilization has been completed, the left ureter and gonadic vessels are easily identified. The next step is full mobilization of the ureter and the gonadic vessels, which will be separated from the surrounding structures but not divided. By tracing the gonadal vein in a cephalad direction, the renal vein is exposed. Through the fourth port, a retractor is manoeuvred by the third operator gently pushing the tail of the pancreas away from the upper margin of the renal vein. The renal vein has to be cleared completely of the surrounding tissue, and the adrenal, gonadal and lumbar branches are cut. The first branch to be cut is the adrenal vein, which is kept in light traction by the integrity of the gonadal vein. The use of a bipolar, vessel-sealing device (Ligasure™) instead of clips-and-cuts allows to shorten the operative time and avoids the presence of clips in the stapling suture line of the renal vein, but it seals vessels less than 7 mm in diameter; therefore it cannot be used for hypertrophic branches. The first operator can introduce the device through the flank port in order to obtain an optimal direction for reaching the adrenal vein (Fig. 22.4).

The gonadal vein can be easily divided with the same device through the hypochondrium 5 mm port, whereas much attention needs to be paid for the dissection and division of the lumbar vein, which is often short and with early bifurcations. To expose the lumbar vein, it is necessary to elevate and pull towards the hilum the lower pole of the kidney with DeBakey grasper, in order to proceed with its ligation (Fig. 22.5).

The renal artery, which lies posterior to the vein, can be exposed through such elevation of the lower pole of the kidney and has to be separated from the surrounding nervous plexus at the level of its origin form the aorta. To complete the dissection, the adrenal gland is separated from the upper pole of the kidney, using Ligasure™ device, to avoid bleeding from the small arterial adrenal

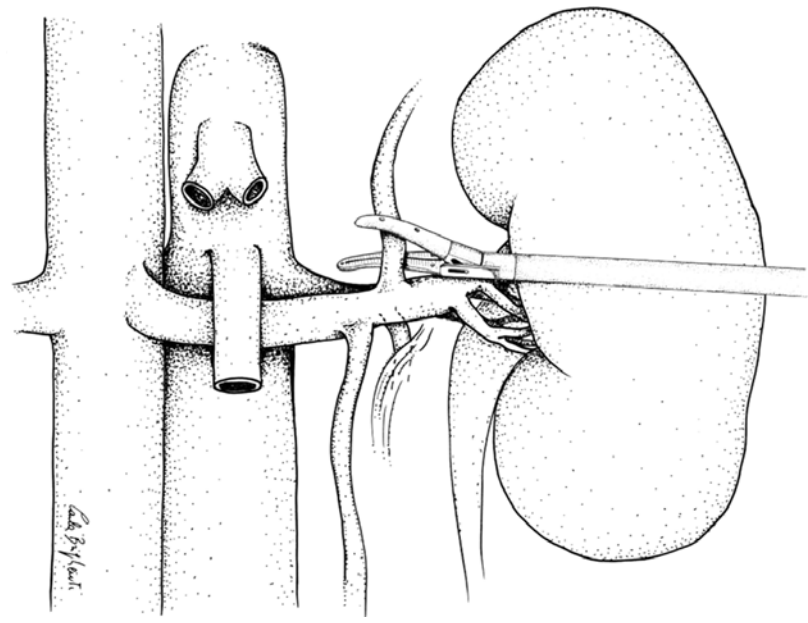

Fig. 22.4 Section of the left adrenal vein by a Ligasure™ device inserted through the flank 5 mm port

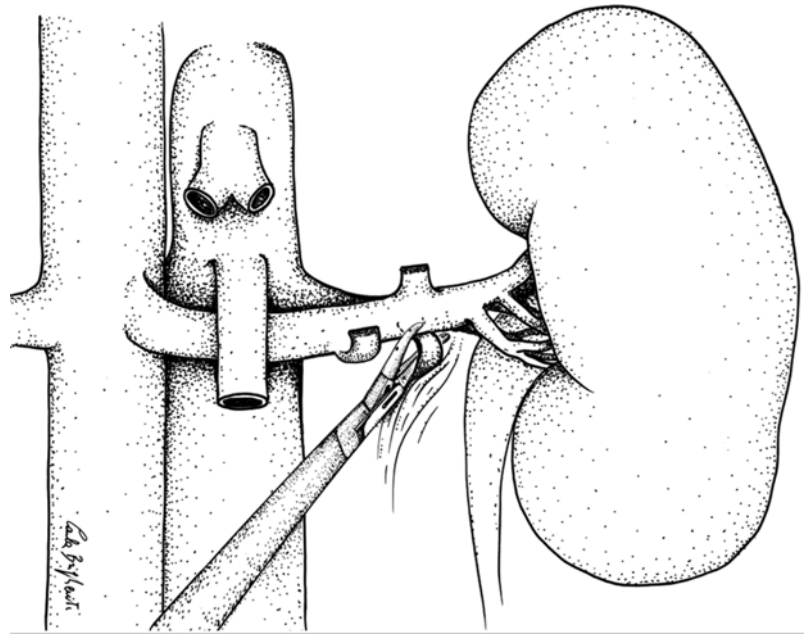

Fig. 22.5 Ligation of the lumbar branch by Ligasure™ device

branches and to obtain an effective synthesis of the lymphatic tissue on the cephalic side of the renal artery, otherwise causing lymphatic extravasation and chyloperitoneum. Once the main renal vessels are fully dissected, the procedure continues with full mobilization of the kidney from the Gerota's fascia starting from the lower pole upward, along the lateral surface of the kidney, completely mobilizing the kidney except for the renal pedicle. The gonadal vein, ureter and mesoureter are then separated from the psoas muscle and dissected free, and the ureter is cut. A flow of urine is expected to

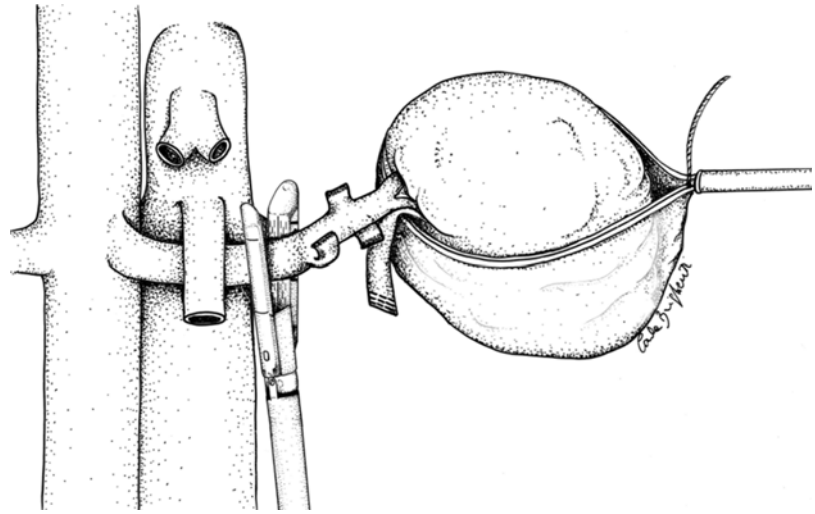

Fig. 22.6 Kidney loaded into the Endobag and Endo GIA stapler division of the renal vein

be seen from the ureter, demonstrating a good perfusion of the kidney during the procedure. In case such flow should not be observed, a 10–15 minutes resting with interruption of the pneumoperitoneum is advisable.

At this point of the surgical procedure, the 7 cm Pfannenstiel incision just above the pubis is made, and the Endo Catch™, a retriever pouch device, is introduced. To ensure the persistence of pneumoperitoneum without leak of gas, a pure string using size 0 monofilament suture is placed to surround the device's entry, and some wet lap sponges are positioned around. The kidney is loaded in the bag and then lifted with some stretching of the renal vessels, heparin 5000 UI is administered and a vascular endoscopic GIA stapler is used to divide the renal artery followed by the vein (Fig. 22.6). It is necessary to retain that using a non-tissue affixing ligation technique is no longer acceptable and that hem-o-lock® ligation system is contraindicated for ligation of the renal artery during laparoscopic nephrectomy by a FDA recall since 2006 [7].

The kidney, fully loaded inside the endobag, is removed through the Pfannenstiel incision, and protamine is usually given to reverse completely the anticoagulant effect of heparin.

For right-sided procedures, port placement is a mirror image of that used for the left-sided procedure as well as the other surgical steps; the main variations of the technique are aimed to preserve maximal renal vein length. After the institution of pneumoperitoneum and the exploration of the abdominal cavity, the cecum is mobilized and reflected medially, the liver is lifted away from the upper pole of the kidney using a retractor through the fourth flank port. Isolation of the ureter and gonadal vein does not differ from that described for the left-sided procedure. The gonadal vein can be divided from the vena cava between clips, far enough from the renal vein, without troubling the stapler section of the main vessels. Usually no branches of the renal vein are present, although much attention has to be paid to lumbar veins originating from the inferior vena cava, during the isolation of the renal artery. Separation of the adrenal gland can be obtained by Ligasure™ device, as in the left-sided procedure, allowing the isolation of the upper margin of the renal vein. Aiming to maximize the length of the renal vein, the introduction of a hand port at the level of the Pfannenstiel incision would allow the kidney to be lifted on its pedicle under stretch, before the division of the vessels. Moreover, in case of early artery bifurcation, the hand port would allow to mobilize the kidney medially, facilitating the full control of the artery proximally to its origin.

The division of the renal vein has to be performed in a plane parallel to the inferior vena cava, introducing the endoscopic GIA device into the right lower quadrant port. The skill of Endo GIA to articulate allows achieving such parallel plane (Fig. 22.7a, b).

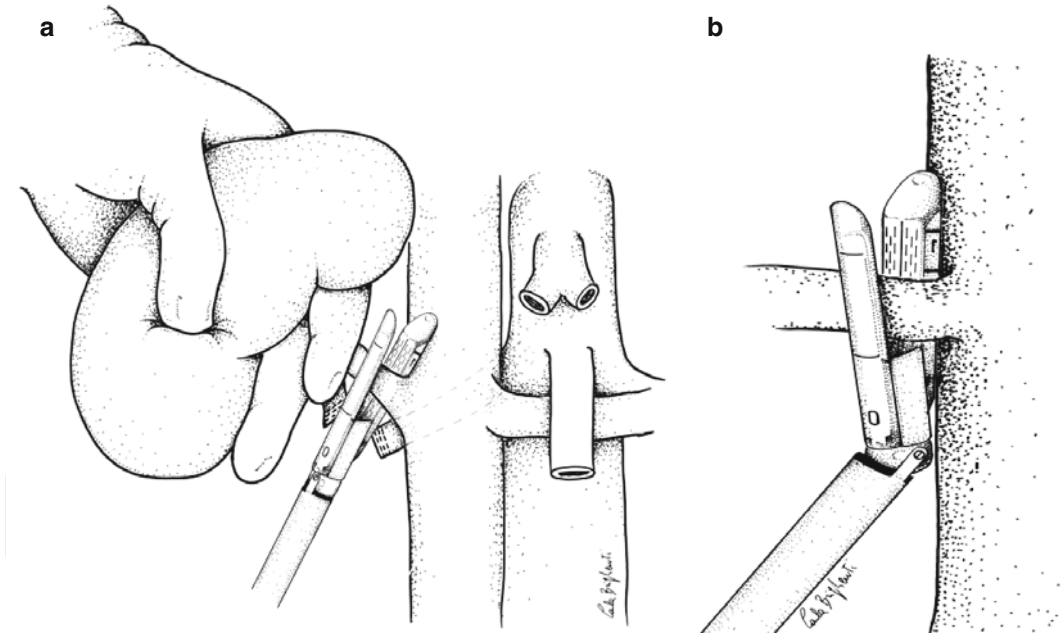

Fig. 22.7 Insertion (**a**) and appropriate direction parallel to the inferior vena cava (**b**) can be obtained with the articulating Endo GIA

Considering that such device results in the loss of approximately 1–1.5 cm of length of renal vein, the use of an Endo-TA can be planned. Nevertheless, with this device, no articulation is possible; therefore a decision has to be taken in choosing between the advantage of sparing few millimetres of the vein length with the TA stapler or optimizing the direction of the suture line, based on the anatomical situation during surgery.

The peritoneum and the fascia of the Pfannenstiel incision are closed with absorbable sutures. The operative field is checked for bleeding and a drain is left in place; the 12 mm port site has to be verified to make sure that no lesions of the epigastric vessels are present, and no suture is needed if bladeless trocars are used, otherwise a figure-of-eight absorbable suture aided by the Carter-Thomas instrument is recommended.

The technique described is essentially a pure laparoscopic approach, although the availability of a hand-assisted device should always be equipped, not only in the right side nephrectomy, to better attain the length of the vessels, but also in the left-sided procedures. As a matter of fact, in case of a lack of gas pressure of the pneumoperitoneum after the Pfannenstiel incision, or to retract the colon for some moderately obese patients, or finally to handle some complications, the introduction of the operator hand may prevent the need for open conversion. Although the hand-assisted technique is an available option, in our experience, pure laparoscopic approach is feasible for both left and right nephrectomies [8].

22.3 Robotic-Assisted Technique for Kidney Living Donation

Tips, Tricks and Pitfalls

- Do not put metallic clips where you will need to use staplers.
- Place the patient in order to avoid collisions among robotic arms and between robotic arms and the patient itself.
- For donor safety concerning renal artery:
  - It's better to use TA instead of GIA stapler to avoid the risk of stapler malfunctioning.

  - The section should be done with robotic scissors after placement of an hem-o-lock on the arterial stump.
- Always administer one bolus of curare together with heparin to facilitate the kidney extraction.

Left Nephrectomy

- Extend the dissection of the splenopancreatic block up to the left diaphragmatic crura.
- Renal vein should be encircled with an elastic tape after the section of gonadic and adrenal veins in order to:
  - Easily recognize it during posterior isolation of the kidney
  - Modulate robotic arm's strength with adequate traction during dissection manoeuvres and staplering.

In 2002 Horgan S. et al. described the first series of robotic-assisted nephrectomy (RAN) for living donor kidney transplantation [9]. Since then, few reports described this procedure with various changes of the surgical technique [10–15]. No matter how the different techniques adopted for this procedure, all articles confirmed the safety and feasibility of the RAN [16–19].

Robotic-assisted surgery is often replacing traditional surgery because it seems to offer clear advantages when compared to traditional laparoscopy. Robotic assistance provides various comforts to the surgeon, such as 3D stable view of the operative field, endowrist instruments that are easy to use and the possibility to reduce the postural fatigue which is very common among surgeons performing laparoscopy. Those comforts play an important role in a successful outcome of the surgical procedures [20]. As a result, robotic instruments allow the surgeon to replicate movements of the traditional open technique in a minimally invasive environment. Knots and sutures, for instance, can be very easily performed using the robot while they represent a crucial issue in the traditional laparoscopy. All these factors represent a valuable advantage when compared to the long and complex laparoscopic surgical operations which induce mental and physical stress and may well lead to a progressive decrease of the surgeon's lucidity and concentration. The simplification of surgical procedure determines an increased safety for the patient, this being the main reason to adopt this kind of technique for living donors. Comparing the different series of RAN, various surgical strategies exist, from the hand-assisted to the totally robotic nephrectomy, depending on the centre-by-centre experience [9–19, 21]. Robotic technology is evolving. In the next future robotic stapler will be available making the last "laparoscopic" step of this procedure safer and under robotic control. Probably a smaller robotic Ligasure will be commercialized along with a new surgical bed that could be moved without undocking the robot.

22.4 Totally Robotic Nephrectomy

22.4.1 Donor Selection

Donor selection criteria do not differ from the general accepted criteria for laparoscopic surgery. Previous multiple abdominal surgery can be considered a relative contraindication to minimally invasive donor nephrectomy (with case-by-case analysis). According to literature evidence, the left kidney has to be considered the first choice even in the presence of vascular anomalies [13].

The left kidney harvesting guarantees a longer stump of the renal vein as well as the absence of liver interposition.

The choice of harvesting the right kidney depends on the preoperative radiological detection of a clear functional dominance of the left kidney that has to be preserved in order to guarantee the donor safety. All candidates need to be informed about the risk of the conversion to the open approach.

22.4.2 Patient Positioning

After general anaesthesia, the patient is placed in completely right lateral 90° decubitus. In order to obtain an adequate exposure of the kidney region,

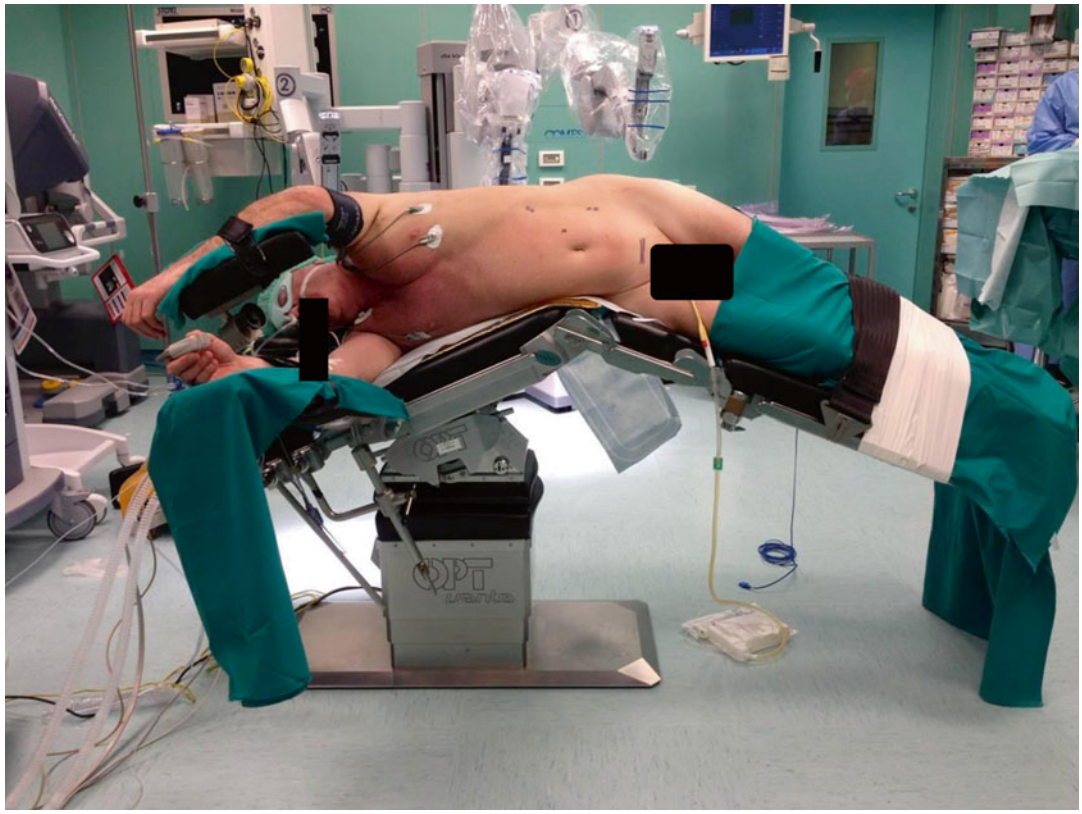

Fig. 22.8 Patient's position in totally robotic technique

the break of the surgical bed has to lay on the transtubercular plane. In order to avoid conflicts with the robotic arms, the lower leg of the patient should be bent at 90 °, while the upper leg must be completely stretched (Fig. 22.8).

22.4.3 Incision and Trocar Placement

The first surgical step is a Kustner preparatory incision of around 8–10 cm, with opening the fascia and the peritoneum.

A camera trocar (12 mm) is placed using the intra-abdominal hand control throughout the Kustner incision about 5–6 cm off the umbilical scar (on the mid-clavicular line ipsilateral to the side of the nephrectomy).

Afterwards the surgeon closes the muscle and peritoneum incision with a running suture while placing an endo-bag instrument (Endo Catch II–15 mm) throughout the fascia access and attaching it to the pelvis of the patient with adhesive strips.

It's important to leave the free margins of the running suture long enough to be easily and rapidly pulled for its cutting when extracting the kidney or in case of emergency bleeding control.

Therefore, the 12 mmHg pneumoperitoneum is induced and two 8 mm robotic trocars are placed under camera vision into the omolateral anterior axillary line, respectively, in subcostal and flank region (Fig. 22.9). Another 12 mm trocar for the assistant surgeon has to be placed in the left extreme side of the Kustner incision (Fig. 22.10).

At this time, the robotic cart is docked to the trocars from the patient's back side.

Basic access and first connected robotic instruments are a bipolar Maryland forceps controlled by the left robotic arm, a monopolar hook on the right robotic arm and a 30° videoscope. A complete summary of robotic and laparoscopic

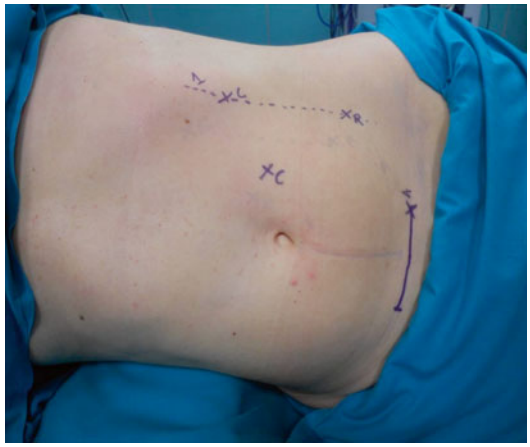

Fig. 22.9 Totally robotic technique: trocars positioning

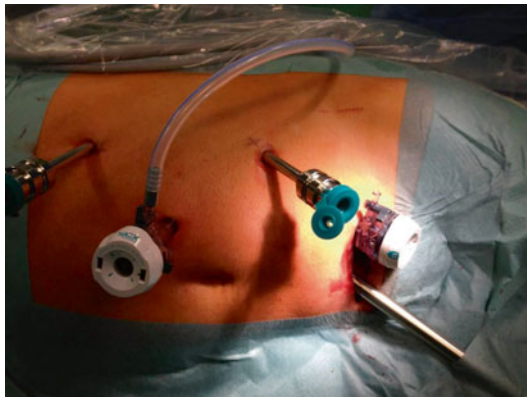

Fig. 22.10 Final trocars placement

instruments needed for the procedure is shown in Table 22.1.

Table 22.1 Laparoscopic and robotic instruments

Three robotic trocars (one 12 mm for the 30 °robotic videoscope and two 8 mm for the robotic arms)
One 12 mm trocar for the assistant surgeon at the table (plus another 5 mm trocar for right nephrectomy)
One Endo Catch II (15 mm)
Robotic instruments
Fenestrated bipolar forceps (type Maryland)
Permanent cautery hook
Precise bipolar forceps
Needle holder
Large clip applier
Round tip scissors
Laparoscopic instruments
Large grasper
Straight tip scissor
Medium metallic clip applier
Staplers
Vein : Endopath Stapler–Echelon 45
Artery : Endo-TA Stapler 30 mm

22.4.4 Left Nephrectomy

The following step is the dissection of the left colon with the exposure of the renal region followed by the dissection of the spleno-pancreatic block from the upper renal pole up to the left diaphragmatic crura.

This manoeuvre will simplify the further approach to the vessels making it also safer in case of bleeding. The ureter is detected and marked by an elastic tape. Following the gonadal vessels, the left renal vein is identified. The left renal vein has to be isolated and respectively separated from the adrenal, gonadal and lumbar veins that are cut after distal and proximal placement of metallic clips or hem-o-lock according to size. Finally, the renal vein can be encircled by an elastic tape. The upper renal pole is then dissected from the adrenal gland: the anterior and posterior kidney surface are completely dissected from the perirenal fat tissue. The dissection of the renal artery can be better obtained by approaching it from below, lifting up the inferior renal pole and can be easily completed throughout a posterior approach keeping the kidney in a medial position after its complete dissection from the posterior Gerota's tissue. Once the whole kidney is isolated from the surrounding tissues and the vessels are dissected, the ureter is cut approximately at the iliac vessels crossing side after closing its distal stump by hem-o-lock, while the proximal stump is left open. Intravenous (IV) heparin is then administered at a dose of 80 UI/kg together with a bolus of curare in order to ease the kidney extraction. At this point the left kidney is introduced into the endo-bag previously placed by the assistant surgeon who loads the kidney, leaving out only the vascular pedicles gently pulled upwards. The renal artery is stapled by

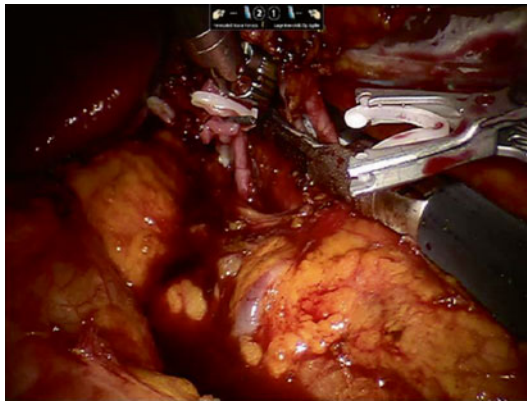

Fig. 22.11 Renal artery stapling by Endo-TA 30

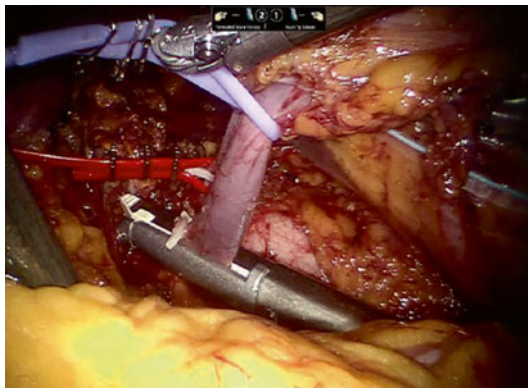

Fig. 22.12 Renal vein section by Endopath stapler (Echelon 45)

Endo-TA stapler with vascular charge at the origin from the aorta. Before cutting the renal artery with scissors, a hem-o-lock is placed on the already stapled line and the artery is finally interrupted (Fig. 22.11). Hereinafter, the renal vein is stapled and cut by a GIA Endopath stapler (Fig. 22.12).

Kidney extraction occurs by closing the endobag, undocking the robot cart, cutting the running suture of the fascia and finally pulling the kidney outside the abdomen. The last check of the left renal loggia and trocar access holes can be performed with laparoscopy after closing the minilaparotomy and after the induction of the pneumoperitoneum. At this point a bolus of protamine can be given to the patient to reverse the anticoagulant effect of heparin. The robot has to remain sterile until the end of the check, as it can be useful sometimes to stop a possible bleeding with stitches positioning. One tubular 21 French drain is finally placed on the renal bed and skin repair is usually obtained with absorbable intradermic suture (Fig. 22.13).

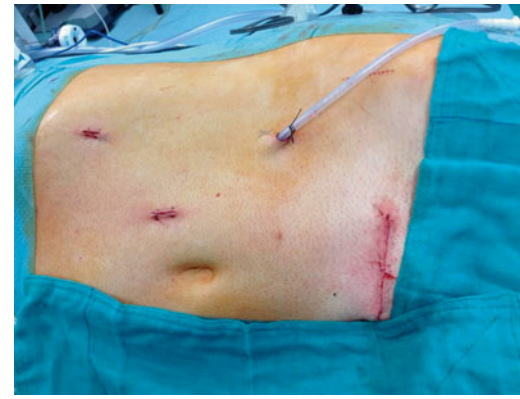

Fig. 22.13 Procedure completed

22.4.5 Right Nephrectomy

In right nephrectomy port placement is a mirror image of the one used for the left-sided procedure but the often needed positioning of a further 5 mm trocar in the epigastric region for hepatic lobe lifting. The right renal vessel anatomy differs from the left one. The renal vein is short and particular care has to be taken while isolating the right renal artery. It is probably safer to dissect the artery after keeping the kidney in a medial position in order to avoid damages to the vein or to its rare collateral branches.

22.5 Hand-Assisted Nephrectomy

22.5.1 Patient Positioning, Incision and Trocar Placement

After a general anaesthesia, the patient is placed in right 60° lateral decubitus position.

First surgical step is to perform a minilaparotomy by sub-umbilical midline incision of around 8 cm or a Kustner incision.

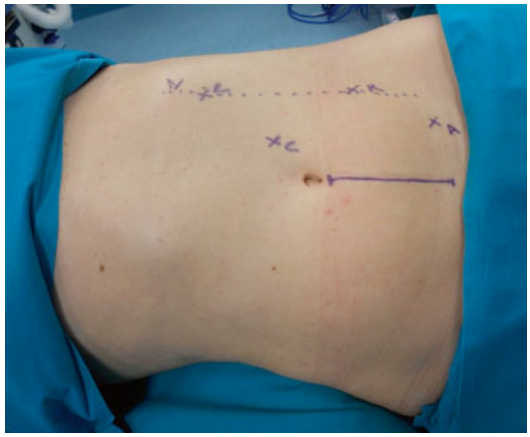

Fig. 22.14 Hand-assisted technique: trocars positioning

The 12 mm trocar for 30° videoscope is placed in the peri-umbilical region, in front of the renal hilum identified by the assistant hand, around 3 cm above the umbilicus and left lateral.

Two 8 mm robotic trocars are placed in the left lateral abdominal wall along the hemi-clavear line while another 12 mm trocar is placed in the left inguinal region for the assistant. At this time, the robotic cart is docked to the trocars from the back of the patient (Fig. 22.14). The assistant surgeon should wrap up his arm with a steri-drape in order to decrease the surgical site infection rate. The first connected robotic instruments are a bipolar Maryland forceps controlled by the left robotic arm and monopolar hook on the right robotic arm.

22.5.2 Surgical Console Time: Left or Right Nephrectomy

Kidney mobilization as well as vessels and ureter preparation and section are performed exactly in the same way, with hand-assisted or totally robotic technique. More than the expected advantage in case of a sudden need for haemostatic control, the main difference between hand-assisted and totally robotic technique lays on the extraction of the specimen that is done directly from the assistant surgeon at the surgical table. The hand can be also useful in opening the operative field by pulling away the bowel during surgery.

References

1. Hariharan S, Johnson CP, Bresnahan BA, Taranto SE, McIntosh MJ, Stablein D (2000) Improved graft survival after renal transplantation in the United States, 1988 to 1996. N Engl J Med 342(9):605–612
2. Ibrahim HN, Foley R, Tan L, Rogers T, Bailey RF, Guo H, Gross CR, Matas AJ (2009) Long-term consequences of kidney donation. N Engl J Med 360(5): 459–469
3. Ratner LE, Ciseck LJ, Moore RG, Cigarroa FG, Kaufman HS, Kavoussi LR (1995) Laparoscopic live donor nephrectomy. Transplantation 60(9): 1047–1049
4. Leventhal JR, Kocak B, Salvalaggio PR et al (2004) Laparoscopic donor nephrectomy 1997 to 2003: lessons learned with 500 cases at a single institution. Surgery 136:881
5. Mertens zur Borg IR, Di Biase M, Verbrugge SJ et al (2008) Comparison of three perioperative fluid regimes for laparoscopic donor nephrectomy. A prospective randomized dose-finding study. Surg Endosc 22(1):146–150
6. Ahmad G, O'Flynn H, Duffy JM et al (2012) Laparoscopic entry techniques. Cochrane Database Syst Rev (2):CD006583
7. Friedman AL, Peters TG, Jones KW et al (2006) Fatal and nonfatal hemorrhagic complications of living kidney donation. Ann Surg 243(1):126–130
8. Saad S, Paul A, Treckmann J et al (2008) Laparoscopic live donor nephrectomy for right kidneys: experience in a German community hospital. Surg Endosc 22: 674–678
9. Horgan S, Vanuno D, Sileri P, Cicalese L, Benedetti E (2002) Robotic-assisted laparoscopic donor nephrectomy for kidney transplantation. Transplantation 73(9):1474–1479
10. Galvani CA, Garza U, Leeds M, Kaul A, Echeverria A, Desai CS, Jie T, Diana R, Gruessner RW (2012) Single-incision robotic-assisted living donor nephrectomy: case report and description of surgical technique. Transpl Int 25(8):e89–e92
11. Oberholzer J, Tzvetanov I, Mele A, Benedetti E (2010) Laparoscopic and robotic donor pancreatectomy for living donor pancreas and pancreas-kidney transplantation. J Hepatobiliary Pancreat Sci 17(2): 97–100
12. Pietrabissa A, Abelli M, Spinillo A, Alessiani M, Zonta S, Ticozzelli E, Peri A, Dal Canton A, Dionigi P (2010) Robotic-assisted laparoscopic donor nephrectomy with transvaginal extraction of the kidney. Am J Transplant 10(12):2708–2711
13. Gorodner V, Horgan S, Galvani C, Manzelli A, Oberholzer J, Sankary H, Testa G, Benedetti E (2006) Routine left robotic-assisted laparoscopic donor nephrectomy is safe and effective regardless of the presence of vascular anomalies. Transpl Int 19(8):636–640

14. Giacomoni A, Di Sandro S, Lauterio A, Mangoni I, Mihaylov P, Concone G, Tripepi M, Poli C, Cusumano C, De carlis L (2013) Initial experience with robot assisted nephrectomy for living donor kidney transplantation: feasibility and technical notes. Transplant Proc 45(7):2627–2631
15. Horgan S, Benedetti E, Moser F (2004) Robotically assisted donor nephrectomy for kidney transplantation. Am J Surg 188(4A Suppl):45S–51S
16. Horgan S, Galvani C, Gorodner MV, Jacobsen GR, Moser F, Manzelli A, Oberholzer J, Fisichella MP, Bogetti D, Testa G, Sankary HN, Benedetti E (2007) Effect of robotic assistance on the "learning curve" for laparoscopic hand-assisted donor nephrectomy. Surg Endosc 21(9):1512–1517
17. Giacomoni A, Di Sandro S, Lauterio A, Concone G, Mangoni I, Mihaylov P, Tripepi M, De Carlis L (2014) Evolution of robotic nephrectomy for living donation: from hand assisted to totally robotic. Int J Med Robot 10(3):286–293
18. Hubert J, Renoult E, Mourey E, Frimat L, Cormier L, Kessler M (2007) Complete robotic-assistance during laparoscopic living donor nephrectomies: an evaluation of 38 procedures at a single site. Int J Urol 14(11):986–989
19. Liu XS, Narins HW, Maley WR, Frank AM, Lallas CD (2012) Robotic-assistance does not enhance standard laparoscopic technique for right-sided donor nephrectomy. JSLS 16(2):202–207
20. Giacomoni A, Concone G, Di Sandro S, Lauterio A, De Carlis L (2014) The meaning of surgeon's comfort in robotic surgery. Am J Surg 208(5):871–872. doi:10.1016/j.amjsurg.2014.04.012, Epub 2014 Jun 27
21. Giacomoni A, Di Sandro S, Lauterio A, Concone G, Buscemi V, Rossetti O, De Carlis L (2015) Robotic nephrectomy for living donation: surgical technique and literature systematic review. Am J Surg. pii: S0002-9610(15)00538-3. doi: 10.1016/j.amjsurg.2015.08.019. [Epub ahead of print]

Appendix

A Narrative: A Difficult Case of Organ Procurement

Dis aliter visum
(Gods have deemed otherwise)
Vergilius, Aeneid

June 23, *2008*, *approximately mid-day*, *Niguarda Hospital*, *Milan*

I am hurriedly crossing the driveway in my large hospital, in my usual fashion. A nurse in blue scrubs uniform appears to follow me and suddenly tells me: "Doctor, hey, Doctor! What happened 10 years ago?" I hear a cheerful voice that I am supposed to recognize. "Hey, Doctor, I am speaking to you. Do you remember anything? What exactly happened 10 years ago?" "Sorry, are you speaking to me?" I reply, watching the nurse who I really cannot remember having ever met before. "I really don't know what the hell happened 10 years ago!" I say. I look in total amazement at the nurse, who is smiling at me and who I am still failing to recognize. "Why should I know what happened 10 years ago? Maybe my favorite soccer team, the Inter won the UEFA Cup? I utter the first nonsense that comes to mind. "Hey you! Try to remember what really happened exactly 10 years ago." She replies with a big smile. "I guess many things happened in 1998," I add cautiously. "I will tell you what happened 10 years ago," she replies again. "My mom received a wonderful liver, and you risked your life in a bad crash." In a split second, I understand, and I see everything with the flashback to my car accident on June 23, 1998. I immediately ask her, "How is your mother now?" "She's very good, she's really in wonderful shape and much better than me." Would you like to see her again for a check-up?" "Why not? I'd be happy to see her again; but during the last 10 years, why have I never seen her?" "Doctor, we were a little ashamed of my gaffe, and we preferred to be followed up by other doctors, but mom always asks about you." "The most important thing is that your mother is doing well and that the liver function is good," I add smiling. "The liver works fine," says the nurse with emphasis, waving her hand affectionately and adds, "Thanks, Doctor, you are all really wonderful doctors." I ponder on what she says, and I try to remember exactly what kind of gaffe she's talking about.

June 23, *1998*, *5 am*, *Highway Brescia-Milan* [1]

Dozing could be a good approach to regain a little bit of energy, which we needed to work a few more hours on bench surgery in the operating room at our anticipated arrival time of 6:30 am. It was 5:15 am, and we started on the Brescia-Milano Highway for only a few minutes. A liver and a pancreas, retrieved from a donor who had died of cerebral hemorrhage, were stored in two separate bags and were cooled in the typical blue and white organ containers. Our blue Mercedes, silent and proud, was traveling fast in the passing lane to bring us as quickly as possible to the hospital. My young and brilliant fellow of Persian origin, who I had nicknamed Avicenna, had just reminded me that we had been starving for nearly 24 h. Because of the speed with which the donation was reported, we had to quickly prepare everything we needed for the organ procurement

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in the early afternoon, and although both hungry we had no time to eat; at 5 pm, we left the hospital for "Spedali Civili di Brescia." The surgical procedure of organ procurement was delayed for several hours relative to the expected schedule, which often occurs during the organ procurement. I was thinking how to organize the bench surgery at our arrival in Milan and the likelihood of finding some coffee and a croissant before diving into the delicate work of organ preparation before the transplant procedure. On June 23, 1998, a cloudless, sunny day was forecast, and the bright sky allowed us to see beyond the hills of Brescia at the first light of dawn. Suddenly, there was first a dry and intense explosion, then a flash of sparks, followed by a frightening screech of metal scraps and sheets. I felt a sudden, searing pain in my chest and neck, which finally burst into my head. I remember my last thought before losing consciousness: "Lord, You have created this beautiful blue sky, have mercy on me." I don't remember how long I was unconscious. I tried to get out from the cabin of the Mercedes, which was reduced to a crumpled box; however, the throbbing pain in my chest did not allow me to move even one centimeter. I could see slumped on the grass, next to the emergency lane, our driver, who in a weak voice was trying to call for help by dialing 118, the emergency number. I believed that I was severely injured and began to fear that I would not receive help in time. Then, the appearance of my young collaborator, Avicenna, limping but upright, gave me strength, and I regained a little bit of confidence. "Hey, doc! How are you?" he said with a firm voice. "Don't worry! I managed to call the operating room, and I stopped the intervention on the recipient. The liver and pancreas are there on the asphalt. They bounced out from the trunk, but they are still in their plastic bags in the middle lane. Unfortunately, my phone has turned off and only now was I able to find that one of the drivers is trying to call for help. Don't move from there." "Good stuff," I thought. This fool wants to be a hero. First, he alerts the operating room and afterwards, he tries to call for help. We are wasting time and the next donor might be myself. Instinctively, I dismissed that horrible thought with the usual "apotropaic" gesture of a perennially superstitious surgeon. The piercing trumpeting of the horns of huge trailer trucks that passed without stopping, both on the right and left sides, was terrifying. Several trucks, like true monsters, carelessly sped past the crumpled car, in which I was trapped in the middle of the road, and threatened to give me the "coup de grace." After some hesitation, the brave Avicenna entered the crumpled car, turned the keys to start the engine and moved it 6 m from the middle lane to the emergency lane. Approximately 50 endless minutes passed before the ambulances with blaring sirens arrived. When the rescuers proceeded to extract me from the cabin, I began to lose consciousness; however, when I heard a nurse give an order to transport me to the nearest small hospital, I tried to cry out with a whisper: "Please transport me to a big hospital that is well equipped; I could have serious chest injuries." With all my strength, I used a mobile phone to try to convince my colleague at the operative emergency coordination center that sending me to a small hospital without thoracic surgery and neurosurgery departments could be a fatal decision for me. Meanwhile, I had learned about the car accident. A gang of thugs in a stolen Alfa Romeo rammed our Mercedes in an attempt to stop and hijack the car. Surprised by the violence of the car crash, the criminals fled without a trace. This type of theft of luxury cars was widespread during that year along the Milano-Venezia Highway. After 20 min, with piercing and excruciating thoracic pain, we arrived in three different ambulances at the emergency room of the same "Spedali Civili di Brescia" where we had started an hour earlier. I remember that the young fellow who initially examined us, who was very sleepy, hospitalized all three of us in the same room of the emergency department. At that point, my injuries were reported to be six fractured ribs with pleural effusion, head and cervical trauma, and two dorsal vertebral fractures, and in my heart, I thought that maybe someone had decided that my "time" had not yet come. The liver and pancreas, although they were thrown from the vehicle during the impact, had been rescued by the police. As suggested by Avicenna, the liver was quickly

transferred to my hospital and the pancreas was transported to a nearby hospital, which was waiting for it. In the operating room, the liver was well wrapped in the usual three plastic bags, each containing cool perfusion solution. On careful inspection in the operating room, my colleagues observed that the organs appeared to be incredibly intact, without any damage, and were subsequently successfully transplanted to the scheduled recipients.

I returned to work in my department one morning at the beginning of September 1998, although I felt a little unsteady after less than 2 months since the accident. I struggled to climb two flights of stairs to reach my surgical department. I had tried to restore the muscle tone that had been lost during my convalescence. Down the hall, I could see a lady who was ranting and complaining to my colleagues: she had been waiting for more than 30 min for the doctor on duty to take care of outpatients, and he was still absent. In her opinion, this was a disgrace! She wanted to talk to the Director of the Department to express her anger over the regrettable delay. Her mother had been submitted to liver transplantation 2 months before and was waiting for that rascal of a doctor to examine her and change a simple surgical wound dressing. They were in a hurry and could not spend the entire day waiting for Mister Doctor to conveniently show up. My director was severe with me in support of the complaints of the relative and the transplanted patient and reprimanded me for being more than 30 min late in meeting with an outpatient in front of my colleagues who had otherwise greeted me smiling on my return to work. The young lady strutted, satisfied that I was humiliated and added "And now let's goes and don't waste any more time! I have worked in this hospital for many years, and I never put up with loafers!" I felt very dazed and upset to hear these unexpected words upon my return to work. A woman just over 50 years of age, lying on the bed, was waiting for a simple dressing for a wound that had finally healed. Reviewing the medical report, I noted the date of her liver transplant. It was the same date as my car accident. I realized that I was in the presence of the patient for whom I risked my life. At first, I had to stifle a slight hint of the anger, but this was soon overcome by a strong feeling of depression. Noticing my visibly wet eyes, the patient observed that I was very emotional and uncomfortable. After I finished applying the new dressing, she asked me, "Doctor, is there anything wrong?" "Don't worry, Ma'am, it's all right," I replied. "I was only thinking that I will remember the date of your transplantation for the rest of my life." The patient, in turn, immediately felt that maybe she was in the presence of the person who had risked his life for having procured her a new liver and about whom she had heard the story that appeared in several newspapers. The patient and her daughter, also visibly uncomfortable, apologized profusely for the sad episode that had occurred earlier. I apologized, too, for my delay, and smiling, I waved goodbye. After only a few months, I had resumed my work as a surgeon, with some bone crunching, but all in all with a renewed enthusiasm that helped me to find myself again. I saw Avicenna that morning and I told him about the nurse's unbelievable gaffe. He hugged me, quite moved, because he was transferring to another hospital. "Really, we were very lucky, Doc!" was all he said. "Avicenna, you're right! It all turned out for the best," I replied. Avicenna, the driver and I, we can tell our story.

Reference

1. Englesbe MJ, Merion RM (2009) The riskiest job in medicine: transplant surgeons and organ procurement travel. Am J Transplant 9:2406–2415