UCLouvain

Faculté de médecine et médecine dentaire

Posthepatecomy postoperative evolution in the context of a liver transplantation by living donation. Twenty years of experience at Cliniques universitaires Saint-Luc.

Auteure : Ingegerd Elisabeth Laima LILJEBERG
Promoteur : Prof. Eliano BONACCORSI-RIANI
Lecteurs : Prof. Erwin SCHROEDER
Prof. émérite Jan LERUT
Dr. Roberto TAMBUCCI
Année académique 2019-2020
Master [180] en médecine, à finalité spécialisée

Un grand merci au Docteur Bonaccorsi-Riani pour sa patience, ses conseils et son encadrement tout le long de ce travail.

Merci à Madame Chantal De Reyck pour avoir accordé son temps précieux afin de prendre contact avec les patients et envoyer les questionnaires.

Merci également à ma famille qui m'a soutenue et m'a inconsciemment poussée à donner tout de mon mieux.

Abstract

Data of 64 donors having undergone living donor liver transplantation at Cliniques universitaires Saint-Luc were analysed in order to gain perspective on postoperative evolution by collecting retrospective laboratory, radiology and clinical data. Psychosocial aspects were evaluated with three surveys. The influence of type of graft on the outcome was also analysed.

Significant differences were found in total bilirubin ($p = 0.023$) and INR ($p = 0.0008$) values between the right and left liver donors. At one year, platelets remained lower than baseline values in both groups. The remaining liver volume was significantly smaller in right liver donors ($p < 0.0001$) with a more intense hepatic regeneration. Various radiological anomalies were observed in most of the patients, although the vast majority of these were temporary and did not require any therapeutic intervention. The only significant difference concerned blood vessel abnormalities ($p = 0.0184$) and perfusion disorders ($p = 0.0032$), which occurred more frequently in left liver donors. Postoperative complications occurred in 62.5% of the patients, 7.8% being Clavien-Dindo grade IIIA, 7.8% grade IIIB and one patient grade IVA. There was no significant difference in complication rates between the two groups. SF-36 survey showed no significant difference from a German liver donor population, except in Physical functioning where Saint-Luc donors scored higher ($p = 0.0405$). Compared to the Norwegian general population, Saint-Luc donors scored significantly higher in Physical functioning ($p = 0.0237$) but lower in Emotional well-being ($p = 0.0014$). Significantly higher results were observed in all categories except for Emotional well-being ($p = 0.9653$) in comparison to the Medical Outcomes Study population. EULID survey results showed that donors were globally satisfied with the donation process and all would undergo the procedure again. However, financial loss due to the donation was stated by 26%. Complementary questions showed that the donation had almost no impact on change of civil status. The donation did not cause any changes in life for two thirds of the donors.

In order to improve the donors' experience, more attention could be paid to the care of the donor during hospitalisation since 8% did not feel well taken care of. Nevertheless, these results show that living liver donation is a relatively safe option for liver transplantation with no clinical differences between right and left liver donors.

Résumé

Les données de 64 donneurs ayant vécu une transplantation hépatique par don vivant aux Cliniques universitaires Saint-Luc ont été analysées afin d'obtenir une perspective de l'évolution postopératoire en collectant des données biologiques, radiologiques et cliniques. L'aspect psychosocial a été analysé avec trois enquêtes. L'influence du type de greffe sur les résultats a également été analysée.

Des différences statistiquement significatives ont été trouvées entre les donneurs du foie droit et gauche pour les valeurs de la bilirubine totale (p = 0.023) et l'INR (p = 0.0008). Dans les deux groupes les plaquettes restaient à un niveau plus bas à un an par rapport aux valeurs préopératoires. Le volume du foie restant était significativement plus petit chez les donneurs de foie droit (p <0.0001) avec une régénération hépatique plus intense. Différentes anomalies radiologiques ont été observées chez la plupart des patients, bien que la grande majorité étaient temporaires et n'ont pas nécessité de traitement. La seule différence significative concernait les anomalies des vaisseaux (p = 0.0184) et les troubles de perfusion (p = 0.0032) qui apparaissaient plus souvent chez les donneurs du foie gauche. Les complications postopératoires concernaient 62.5% des patients, 7.8% étant grade Clavien-Dindo IIIA, 7.8% grade IIIB et un patient grade IVA. Il n'y avait pas de différence significative entre les deux groupes pour le taux de complications. L'enquête SF-36 montrait aucune différence significative avec des donneurs hépatiques allemands, sauf pour Fonctionnement physique où les donneurs de Saint-Luc ont obtenu des résultats supérieurs (p = 0.0405). En comparaison avec la population générale norvégienne, les donneurs de Saint-Luc surpassaient dans Fonctionnement physique (p = 0.0237) mais avaient des résultats plus bas dans Bien-être émotionnel (p = 0.0014). Des résultats significativement supérieurs étaient observés dans toutes les catégories sauf Bien-être émotionnel par rapport à la population Medical Outcomes Study (p = 0.9653). L'enquête EULID montrait que les donneurs étaient globalement satisfaits du processus de don et tous le feraient de nouveau. Pourtant, des pertes financières à cause du don étaient signalés par 26%. Des questions complémentaires montraient que le don n'avait presque pas d'impact sur le changement d'état civil. Le don n'avait pas causé de changements de vie pour deux tiers.

Afin d'améliorer l'expérience des donneurs, plus d'attention devrait être accordée aux soins du donneur pendant l'hospitalisation comme 8% ne se sentaient pas bien pris en charge. Néanmoins, ces résultats montrent que le don vivant du foie est une option relativement sûre pour transplantation hépatique avec peu de différences entre les donneurs du foie droit et gauche.

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1. Introduction

1.1. Liver transplantation history

Liver transplantation has been evolving for more than 60 years already. It was first described in 1952 by Vittorio Staudacher who is known to have performed the first orthotopic liver transplantation in dogs. In 1955, Welch proposed a canine heterotopic transplantation. Jack Cannon described his experiment of orthotopic transplants in an unknown animal species in 1956 (1). Two years later Francis Moore published a report of experimental liver replacement in mongrel dogs after total hepatectomy with longest survival of 6 days (2). In 1960, Thomas Starzl described his experience with 79 dogs recounting a maximal survival of 20,5 days postsurgery and concluding that optimal portal flow is an important factor of success (3). Based on knowledge from canine experiments, in 1963 he published the first three human liver transplantations proposing the procedure as a treatment of liver disease (4). However, the first long term survival was reported only in 1968 when a 19-month-old girl with hepatocellular carcinoma survived 13 months posttransplantation (5). The same year Calne and Williams recounted 5 human liver allografts and the technical difficulties that they faced during the procedures (6).

All grafts were obtained from donors after cardiac death until 1968 when the United States recognized brain death as a new criterion of death. This permitted another source of organs for donation (7, 8).

Further advances in organ transplantation were made with the readjustment of immunosuppressive therapies by the introduction of cyclosporine. Cyclosporine-steroid therapy was started in 1980 in liver recipients and showed increased patient survival. One-year patient survival reached 69,7% compared with previous 32,9% obtained with conventional immunosuppressive agents, i.e. azathioprine and steroids. This discovery raised the number of liver transplantation cases worldwide (9). In 1994 tacrolimus was approved as a primary immunosuppressant (10) and showed even better results (11).

In the United States, National Institutes of Health recognized liver transplantation as a beneficial therapeutic approach for end-stage liver disease following a conference in 1983 (12). Since then the procedure has seen an important proliferation worldwide. Moreover, the indications for transplantation have expanded with time which explains why there is a current shortage of organs (5). Globally, every year 20200 liver transplants are carried out, 14.6% of

which come from a living donor (13). In 2018, in total, 26.78 per million inhabitants (pmp) liver transplants were performed in Belgium versus 6,26 pmp in the world (14).

1.2. Indications

The rate of liver transplantation and its indications vary by country though there is a general increase of procedure rates worldwide. It is especially developing at a fast pace in several emerging countries. Most transplants are performed basing on Model for End-Stage Liver Disease, 18 to 20 being the corresponding score for surgery with the exception of USA and Germany where transplantation occurs at a score of 25-35 (15).

Indications are grouped into acute liver failure, end-stage liver disease (cirrhosis due to chronic viral hepatitis and alcohol being the main cause) and malignant or benign tumors (16). All groups combined the number one indication is hepatitis C. Other common indications include alcohol-related liver disease, non-alcoholic steatohepatitis and autoimmune diseases such as primary sclerosing cholangitis and primary biliary cirrhosis (15). Malignant and metabolic liver conditions are also frequently treated this way (5). Hepatocellular carcinoma as an indication is regulated by the Milan criteria and currently accounts for 15-50% of all hepatic transplants (17).

1.3. Donor Shortage

Organ shortage is a challenge that we have to face in today's medical field of transplantation. There is a gap between the demand and supply of organs.

Belgium has one of the biggest rates of deceased donors per million inhabitants in Europe (27 deceased donors per million population in Belgium versus 10.7 in Germany) (18). The Belgian "Law on the Procurement and Transplantation of Organs", adopted in 1986, has increased transplantation rates in the country, which are higher than in other countries following an informed consent policy (19).

This presumed consent law, or opting out approach, allows postmortem organ and tissue removal unless the donor had explicitly objected against such donation during life. Relatives are usually informed about the organ procurement and they have the right to object but they are not asked to make a decision. This law applies to every Belgian citizen and foreigners who have lived for more than 6 months in Belgium. On the contrary, the informed consent

approach, or opting in, requires explicit consent from the donor or his relatives if the donor had not expressed his will during life (20).

Moreover, the number of Belgians voluntarily declaring themselves as donors has risen from 34000 in 2005 (21) to over 275000 in 2018 (+12% since the end of 2016) (22). However, the number of organs of cadaveric origin are still insufficient to cover all the needs and thus a waiting list is inevitable. The latter may form a risk of death for the patients. In 2016, 100 Belgians died because of a shortage of organs (21) and 1300 persons were on a waiting list for a transplant in 2018 (22).

Organ shortage and its consequences concern liver transplantation as well due to the progressive improvements of the procedure and thus its increasing popularity. There have been numerous attempts in order to amplify sources of grafts. The criteria for donor selection have become less severe, which have developed into the so-called "extended criteria donors" (23). These will be detailed in chapter 1.5. Moreover, new surgical methods have developed so as to increase the number of recipients who benefit from a single donor. This will be covered in chapter 1.4. Furthermore, living-donor liver transplantation (LDLT) is another example of coping with organ scarcity. Due to cultural reasons (5) this method has significantly developed in Asian countries in comparison to the western world where the number of these transplants has not changed much for over a decade (23).

1.4. Alternative techniques

The conventional liver replacement technique is based on the first experiments on dogs described above. It comprises hepatectomy with the complete removal of the recipient's retrohepatic vena cava and upper and inferior anastomosis of the donor's vena cava which includes the hepatic veins (24). This method caused complications such as damage of vital organs leading to a high incidence of renal failure and bleeding from venous collaterals due to the reduced venous return. This was improved by the development of a veno-venous bypass to be used during the anhepatic phase of surgery. The procedure turned out to be not so problem-free. It either caused the spread of emboli or excessive bleeding due to anticoagulation when pumps were used (25).

Since the development of the so-called piggy-back technique the use of the veno-venous bypass has become questionable (25). As opposed to the conventional technique the piggy-back is based on the preservation of the recipient's inferior vena cava by performing an anastomosis between the graft suprahepatic vena cava and an orifice created from the

recipient's hepatic veins. The inferior vena cava of the graft is ligated or sutured. It was fully detailed in 1989 by Tzakis et al. (24) and is currently the most commonly used technique (5).
Split liver is a technique developed in order to cope with organ shortage since it allows to obtain two grafts from a single donor. Pichlmayr was the first to describe this procedure in 1988, making transplantation possible for a child and an adult simultaneously. Soon Bismuth and his colleagues performed a full right/full left split supplying two adult recipients with grafts (26). Studies revealed that there is no difference between split and whole-graft procedures in terms of postoperative complications and patient and graft survival (27, 28).
Auxiliary partial orthotopic liver transplantation (APOLT) is increasingly used for the treatment of acute liver failure. It consists of implanting a partial liver graft in its natural position and preserving part of the host's liver, thereby allowing the native liver to regenerate and to possibly spare the long-term immunosuppressive treatment. APOLT is indicated in patients with a good hepatic regeneration potential, hence children and young adults of less than 40 years and patients with hyper-acute liver failure. Another factor to take into account is the patient's clinical condition which reveals whether the patient will be able to tolerate such a complex procedure (29).
The newest addition to the list as a valid option for overcoming organ shortage, living donor liver transplantation (LDLT), will be detailed further.

1.5. Extended criteria donors

The need for liver grafts has resulted in less strict donor selection. There are no specific criteria for extended donors but there are some characteristics that are more commonly accepted. These include advanced donor age, hepatic steatosis, donation after circulatory death, transmittable diseases and other clinical and biological conditions (30).
In 2009, 29% of European donors were over 60 years old. Graft survival revealed to be significantly lower in donors over 65 compared to younger than 55 years (65% and 57% after 5 years respectively) (31). Different studies have shown a higher rate of mortality and long-term graft loss with older donors (32-34). Nevertheless, other studies found that good outcomes can be achieved with older donors as long as they are selected carefully and have a good liver function (35, 36). Jimenez-Romero et al. (36) found no significant difference in patient and graft survival between three groups of recipients receiving liver from donors of less than 60, between 60 and 70, and older than 70 years of age.

Steatosis of the liver makes the graft more sensitive to cold ischemia and increases damage to the organ during transplantation (30). Yet, according to the Paris consensus meeting (37), mild steatosis (less than 30% of the parenchyma affected) only slightly impacts liver function after transplantation, on the condition that the cold ischemia time has been short. With moderate steatosis (30%-60%), complications are common reaching 15% for primary nonfunction of the graft and 35% for delayed function. Nonetheless, some studies have shown that moderate and severe steatosis can lead to good results when reducing other unfavorable factors in donors and as long as appropriate precautions are taken (38, 39).
Donation after cardiac death (DCD) has showed worse results than donation after brain death (DBD) (40, 41). However, it is making a comeback nowadays as studies have shown that outcomes can be equivalent to that of DBD with particular care. This means applying certain donor and recipient selection criteria associated with better results (42-44).

1.6. Living donor liver transplantation

1.6.1. History

In Brazil, Raia performed the first ever liver transplant from a living donor in 1988 (45, 46). The graft comprised the hepatic segments II and III. There were no immediate postoperative complications for the donor, however the 4-year-old recipient died 6 days after surgery (46).
The first successful transplant was accomplished soon after by an Australian team in July 1989 (45). At 6 days postsurgery an acute rejection was diagnosed in the recipient. Nevertheless, he could be discharged 40 days after the intervention and at 5 months no complications had occurred in the recipient nor the donor (47). In 1990, Broelsch et al. (48) described their experience with five LDLT by transplanting segments II and III in child recipients. They reported donor criteria of eligibility that they used in order to select the donors. The results showed complications in all three donors who had the totality of the left liver excised. These were classified into involuntary accidents and complications, which could be reduced by increasing experience. Four of the recipients suffered complications such as bile leakage, hematoma with ensuing hemorrhage and rejection. One of them needed a retransplantation. Otherwise, early graft function was noted as excellent and all five were in good health at two to six months after the intervention.
Hashikura et al. (49) reported an adult-to-adult transplantation of the left liver lobe in 1993. Both, the donor and recipient were in good health and without complications 6 months later.

In the same year the first pediatric LDLT in Belgium was carried out by Dr. Jean-Bernard Otte. Five years later, adult-to-adult living donor liver transplantations were begun under the leadership of Prof. J. Lerut (50).
In order to reduce the risk of small-for-size syndrome (when the graft is not able to fulfill the metabolic and synthetic needs of the recipient due to the relatively small size of the graft (51)), Lo et al. (52) carried out an extended right lobe transplantation in 1996. The donor didn't suffer any complications except for a transient hyperbilirubinemia. However, the recipient was discharged at 80 days postsurgery having endured temporary renal dysfunction, sepsis and appendicitis during hospitalization. The recipient and the donor had both normal liver function 4 months after the transplantation.

The use of pediatric LDLT has been steadily increasing and in 2013 one third of pediatric liver grafts were from living donors (53). In the Eurotransplant program (comprising Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, Netherlands and Slovenia as member countries (54)), 6,9% of all liver transplants were LDLT in 2019, as opposed to 7,2% in 2010. Concerning Belgium, 9,3% were LDLT in 2019 and 13,6% in 2010. Austria and the Netherlands are the two countries where the proportion of LDLT is increasing with time (55, 56).

1.6.2. Advantages of LDLT

The main reason for the development of LDLT was the scarcity of deceased donors for pediatric transplantation. With this additional method, the organ donor pool is expanded and deaths can be avoided while on the waiting list for a graft. Other facts mentioned that support LDLT are the possibility of planning the operation ahead of time and an organ of better quality as compared to organ procurement from deceased donors (57). Moreover, it has been shown that adult LDLT is beneficial in terms of mortality over waiting for or receiving a graft from a deceased donor liver transplantation (DDLT) (58). In Europe, 5-year graft survival was found to be similar when comparing LDLT to DDLT in adults (64% and 63% respectively), meanwhile it was better in children (78% vs. 72%) (31). No significant difference in cost has been found when comparing LDLT to DDLT in an experienced centre (59). In 2001, Takatsuki et al. (60) suggested that recipients receiving liver from living donors could be candidates for withdrawal of immunosuppressive drugs in order to reduce long-term side effects.

1.6.3. Disadvantages

It took some time for LDLT to gain popularity as a treatment for liver disease due to the more challenging and difficult surgical procedure (57, 61). Besides, ethical considerations have questioned its justification since it puts a healthy donor at risk (57). Also, some causes of graft loss have been more frequently associated with LDLT such as technical complications, infections, rejection and tumor recurrence (31).

1.6.4. Risks

Abecassis et al. and Adcock et al. found that approximately 40% of living donors experience one or more complications (62, 63). Infections, pleural effusion, psychological complications, bile leak, incisional hernia, ileus, neuropraxia and ascites being the most common (62). Nearly all complications occurred during the first year postdonation (63) and the vast majority were resolved by three months postdonation (62). However, hernias and psychological complications, which occurred more than one year postdonation, tended to take longer to resolve: complete resolution within one year after diagnosis was 75% and 42%, respectively. Some complications can develop five or more years after the donation (62). Moreover, some psychiatric complications (including depression, anxiety, substance abuse, bipolar disorder, insomnia, symptom exacerbation of an already existing disorder and suicide) have been reported in previous studies (63, 64). A systematic review estimated the donor mortality risk at 0,2% (65). As with cadaveric split grafts, the risk for the recipient is an insufficient size of the graft for correct function. Dahm et al. (66) defined the small-for-size syndrome as a graft dysfunction or failure, which occurs within the first few weeks after surgery, characterized by ascites, hyperbilirubinemia, coagulopathies, encephalopathy and infection. This condition usually occurs when the graft/recipient weight ratio is less than 0.8% and presents a higher mortality rate.

1.6.5. Selection and safety of donors

In order to select the best candidate for donation and to decrease the risk of consequent complications, numerous examinations should be performed though a universal consensus for selection doesn't exist (67). According to Organ Procurement and Transplantation Network (OPTN) (68), all living donors need to undergo a psychosocial and medical evaluations prior

to surgery. The medical screening should contain, apart from medical history and physical exam, a thorough blood test including liver-specific tests and blood type (this should preferably be compatible with the recipient though not mandatory (69)), chest x-ray, ECG, transmissible disease screening and cancer screening in accordance to protocols in place. An anatomical assessment is essential so as to determine the safety of the procedure on the donor. It should include an evaluation of the liver volume, including the considered graft and remaining volume, parenchyma steatosis and hepatic vascularization.

Sometimes complementary invasive investigations are needed in order to further clarify some abnormalities. Among others these may consist of a liver biopsy, angiography and endoscopic retrograde cholangio-pancreatography (ERCP) (69).

General exclusion criteria have been developed for living donors and contraindicate donation for those who are less than 18 years old and not capable of making an informed decision, infected by HIV, having an active or incompletely treated cancer, suspected of being externally forced to donate or rewarded financially by the recipient, having an acute infection or uncontrolled psychiatric condition (68).

Additional specific exclusion criteria for liver donors include prior liver donation, having an active hepatitis B and C infection, particular alpha-1-antitrypsin phenotypes and an estimated donor remnant volume of less than 30% of the native hepatic volume (68).

1.6.6. Follow-up

The safety of the donor is very important since a healthy adult puts his life at risk by submitting himself to a major intervention. Belgium is one of the leading European countries performing LDLT (18) (in 2018, 2.87 living donor liver transplants pmp versus 2.01 in Europe versus 1 globally (14)), therefore donor follow-up and appropriate care are critical.

Donor follow-up varies greatly from centre to centre: based on the A2ALL multi-centre cohort study (70), it was found that follow-up ranges from 57% to 97%. Usually, it is completed rigorously during the first months (in more than 90% of cases) postdonation and gradually decreases (reaching 62% at two years). Some predicting factors of follow-up completion have been identified. For example, for the first year postdonation, donors of white race are more likely to complete it. After the first year, among other factors, older donors are more active to follow-up.

In order to ensure appropriate care and long-term health of the donor, OPTN requests its members to do a follow-up of minimum two years and at least at six months, one and two

years. Each hospital is expected to deliver status and clinical information of 80% of donors and laboratory data for at least 75% of patients at six months postdonation and at least 70% at one year (68).

2. Materials and methods

The data of a series of 64 patients having undergone hepatectomy in the context of adult-to adult LDLT from 1998 to 2016 at Cliniques universitaires Saint-Luc were collected from electronic medical records in the Medical Explorer software. The data were reviewed in order to analyze the postoperative evolution of donors.

Since the intervention these patients have been evaluated by laboratory tests and from a radiological and clinical point of view for different time periods.

The analyzed laboratory data consisted of creatinine, total bilirubin, aspartate transaminase (AST), alanine transaminase (ALT), hemoglobin, hematocrit, platelets and INR values preoperatively, every day from the operation day until postoperative day 7, day 10, day 15, day 30, at six months and close to one year posttransplantation.

The radiological data included an initial preoperative assessment of the donor's anatomy, eventual abnormalities and liver volume. This consisted of abdominal ultrasonography, CT scan and MRI. The postoperative evaluation comprised data from abdominal ultrasonographies at day 1, before discharge, the first after discharge and, if available, the following one. Also, were included results from all undergone abdominal MRIs and CT scans with an evaluation of remaining liver volume, when estimated.

Information from all postoperative consultations was collected. Long term data for the latter, for the laboratory and radiological analysis was considered until the 1st of September 2019.

Furthermore, three surveys were sent by mail to our donors and the answers were analyzed anonymously (see **Appendix 1, 2, 3**): SF-36, a survey assessing the quality of life, EULID survey, focused on the living donor's personal experience of the donation and his/her psychosocial state after the donation, and a complementary survey assessing the impact on civil status, life and, more specifically, procreation in women. The analyzed data concerned 24 patients having answered and sent in the completed surveys up until 30th of March 2020.

Statistic tests used were Chi-squared test, t-test, Fisher's exact test and Mann-Whitney test.

The level of significance was fixed at P-value <0.05.

3. Results

3.1. Demographic data

From 1998 to 2006 the Abdominal Surgery and Transplantation unit of Cliniques universitaires Saint-Luc carried out 64 living donor hepatectomies. Twenty-five of those were left and 39 were right hepatectomies. Mean age of donors at the time of transplantation was 37.3. The majority of donors were women and the mean BMI was 24.16. Daughters were the most frequent donors.

Nevertheless, there was no significant difference in age (p = 0.726) and BMI (p = 0.258) between left and right liver donors. Moreover, no association was found between the type of hepatectomy and gender (p = 0.610), and the type of hepatectomy and type of relationship (p = 0.516). (**Table 1**)

The preoperative imaging modalities assessed anatomical variations of the portal veins, hepatic arteries, hepatic veins and bile ducts. Ultrasonography found variations in 7% of the donors, CT scan in 25% and MRI in 35%. Thus, MRI is probably the most precise modality in order to assess anatomical variations before surgery.

The estimated remaining liver proportion was significantly lower in the right liver donors (a mean of 32% versus 62% in left liver donors, p <0.001). Likewise, a significant difference was noted in the remaining liver-donor body weight ratio (a mean of 0.6% versus 1.21% in right and left liver donors, respectively). (**Table 2**)

None of the donors required allogenic blood transfusion.

Table 1: Description of donor demographic characteristics

Characteristics	Total (n=64)	Left hepatectomy (n=25)	Right hepatectomy (n=39)	*P*-value
Age (years)	37.3 (19-65)	38.1 (19-59)	36 (19-65)	0.726
Gender				0.610
• Male	30 (46.9%)	13 (52.0%)	17 (43.6%)	
• Female	34 (53.1%)	12 (48.0%)	22 (56.4%)	
BMI (kg/m^2)	24.16 (18-30)	26.6 (18-30)	23.87 (19-30)	0.258
Donor to recipient relationship				0.516
Father	2	2	0	
Mother	7	2	5	
Son	11	5	6	
Daughter	15	5	10	
Brother	5	3	2	
Sister	5	1	4	
Husband	3	1	2	
Wife	1	0	1	
Cousin	1	0	1	
Nephew	2	0	2	
Goddaughter	1	0	1	
Mother-in-law	2	2	0	
Sister-in-law	3	1	2	
Brother-in-law	2	0	2	
Son-in-law	1	0	1	
Boyfriend	1	1	0	
Friend	2	1	1	

Table 2: Surgery-related characteristics

Characteristics	Total (n=64)	Left hepatectomy (n=25)	Right hepatectomy (n=39)	*P*-value
Estimated remaining liver proportion (%)	44 (22-76)	62 (24-76)	32 (22-41)	<0.001
Remnant to BWR (%)	0.84 (0.37-1.98)	1.21 (0.37-1.98)	0.6 (0.38-0.89)	<0.001
Operation time (min.)	475.52 (310-955)	478.8 (310-955)	474.87 (330-744)	0.756
Donor autotransfusion	53 (82.8%)	19 (76%)	34 (87%)	0.251
Hospital stay (days)	10.83 (6-20)	10.6 (6-17)	10.95 (8-20)	0.873
ICU stay (days)	1.20 (0-3)	1.28 (1-3)	1.15 (0-3)	0.311
Follow-up period (mo)	30 (0.5-166)	24 (1.5-100)	33 (0.5-166)	0.6694

3.2. Biochemistry outcomes

Both, donors who underwent right and left hepatectomy had a maximal increase of creatinine levels on the operation day, an average increase of 0.07 mg/dL from baseline values. After that the levels gradually decreased below usual creatinine levels until day 10 when the values started returning to the baseline level. (**Figure 1A**)

A significant difference (p = 0.023) between the two groups was found for total bilirubin values during the whole postoperative period. Total bilirubin levels reached a peak at day 2 posttransplantation in both groups. Right hepatectomy donors reached maximal total bilirubin levels of 2.88 mg/dL, left donors reached 1.65 mg/dL. Levels returned to normal a year after transplantation for right hepatectomy group. For the left group it took more or less 7 days, though there was a new increase after the 30 postoperative days and the mean value at one year remained higher than the mean baseline value, although still within normal range (a mean of 1.0 mg/dL versus 0.6 mg/dL before surgery). (**Figure 1B**)

The tendency of AST and ALT levels was rather similar for both groups, arriving at maximal values of 269 IU/L and 258 IU/L on day 0 for AST, respectively for right and left group, and 261 IU/L and 269 IU/L on day 1 for ALT. The baseline levels were reached at 180 days after surgery for AST and ALT. The left liver donors had a surge of AST levels on day 6, and on days 6 and 10 for ALT. (**Figures 1C** and **1D**)

Hemoglobin and hematocrit levels also followed a similar evolution in both groups, dropping to lowest levels on day 2 and day 1, respectively. On average, hemoglobin levels dropped a maximum of 3.3 g/dL and 9.6% for hematocrit. The right group maintained a plateau until day 10 after which the values started climbing. The values began increasing earlier in the left group, as of day 6. (**Figures 1E** and **1F**)

Platelets decreased until day 3 and day 2 for right and left group, respectively, although not dropping below $150x10^3/\mu L$. The peak values were reached at 15 days for both groups, which gradually decreased again, staying below departing levels, however within the normal range, at one year postsurgery (a mean of $234x10^3/\mu L$ at one year versus $265x10^3/\mu L$ before surgery in right liver donors (a decrease of 12%) and $220x10^3/\mu L$ versus $243x10^3/\mu L$ in left liver donors (a decrease of 9.5%)). (**Figure 1G**)

INR values were significantly higher (p = 0.0008) in the right hepatectomy group than in the left group. Maximal values arrived at 1.46 on day 2 for the right group and 1.29 on day 1 in the left group. Both groups reached departing values at 180 days after transplantation. (**Figure 1H**)

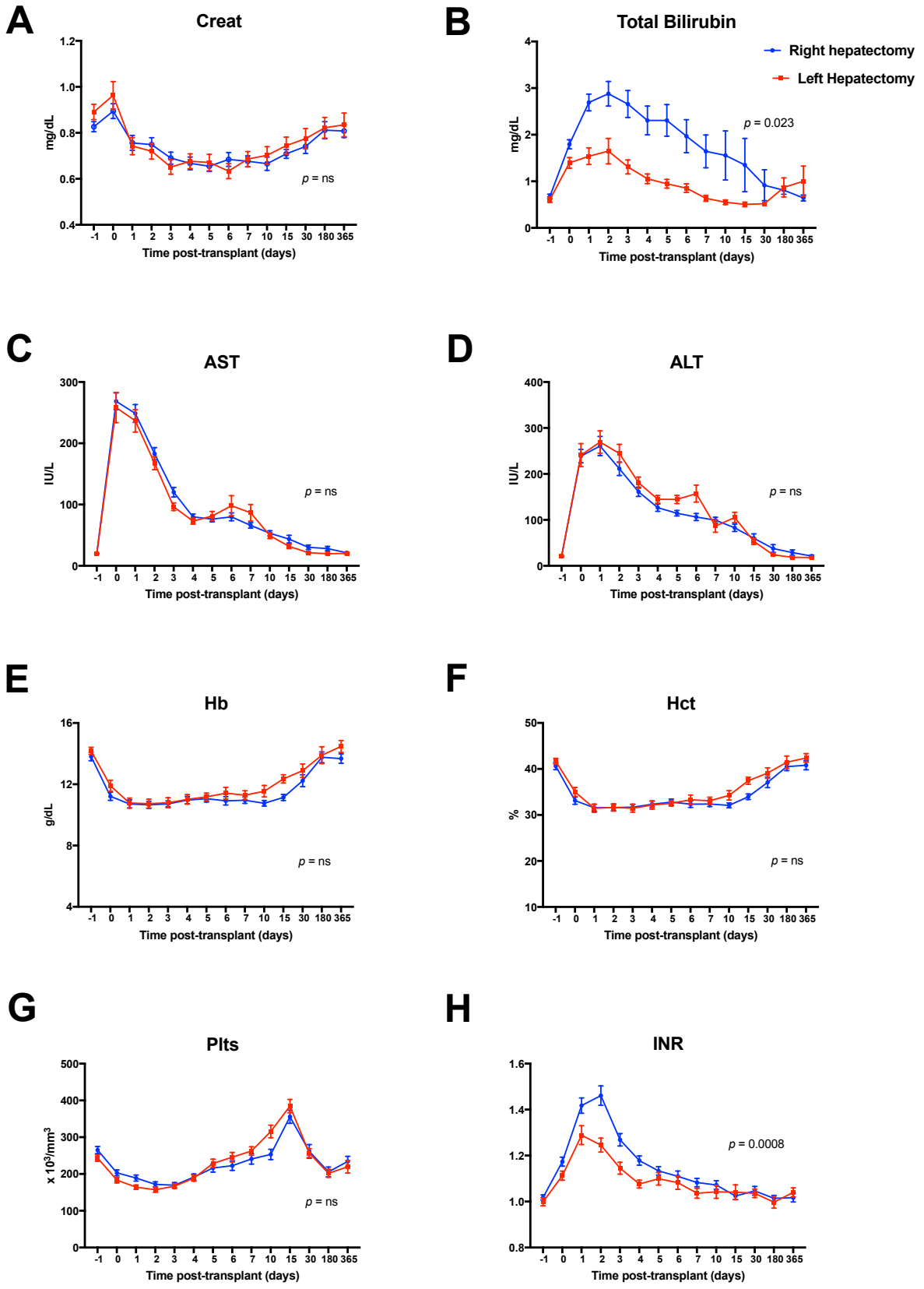


Figure 1: Pre- and posthepatectomy biochemistry outcomes

3.3. Imaging outcomes

The mean preoperative total liver volume was 1461 mL and 1590 mL in right and left liver donors, respectively (p = 0.0503). The right hepatectomy group had a significantly larger graft size than the left group (p < 0.0001). The remaining liver volume was 542.2 mL in the right group and 1063 mL in the left group (p < 0.0001) (**Figure 2**).

The first available liver volume in less than 60 days from the operation date showed a mean volume of 899 mL in right liver donors (n = 21) and 1385 mL in left liver donors (n = 15) (p < 0.0001) (**Figure 2**). These volumes represented 61.5% and 87.1% of the preoperative liver volume in both groups, respectively. The mean liver volume increase from the initial remaining liver was 96.48% and 23.88% in the right and left group, respectively (p = 0.0003) (**Figure 3**). The CT scan and MRI, whichever was used to estimate the volume, were realised at a range from 6 to 58 days postoperatively in the right hepatectomy group and 7 to 57 days in the left group.

The first volumetry after 60 postoperative days showed a mean volume of 1175 mL and 1393 mL, respectively in the right (n = 25) and left (n = 13) group (p = 0.0292) (**Figure 2**). These volumes represented 80.4% and 87.6% of the preoperative liver volume in both groups, respectively. The mean volume increase was 155.3% and 25.46% in both groups (p = 0.0009). (**Figure 3**) The time of the volumetry ranged from 84 to 1030 postoperative days for the right liver donors and from 85 to 654 days for the left liver donors.

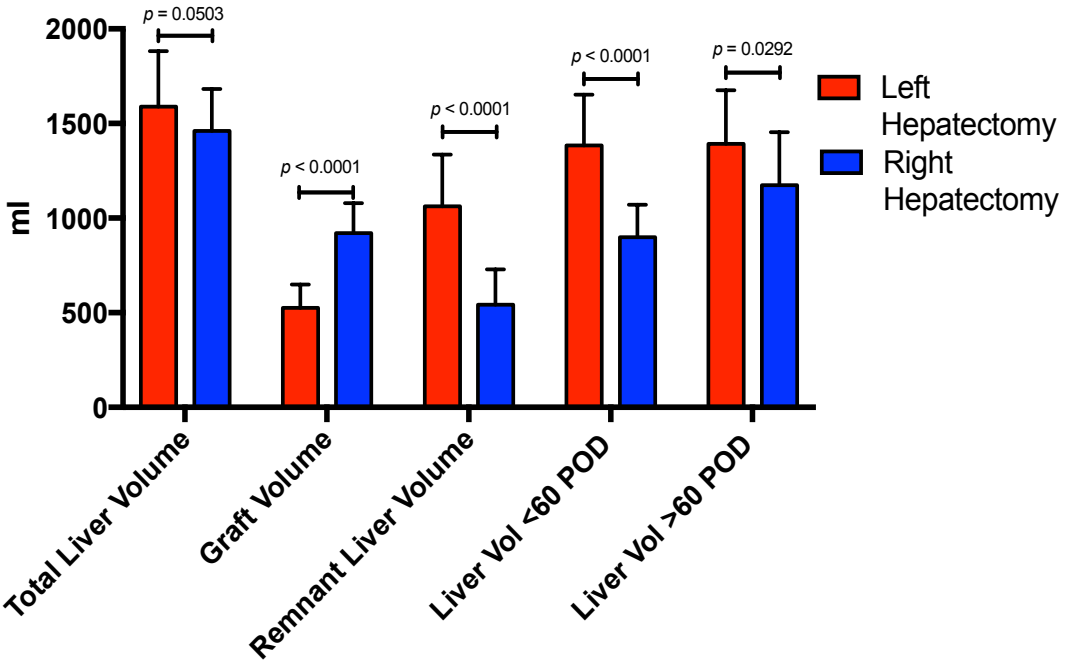


Figure 2: Liver volumes at different stages

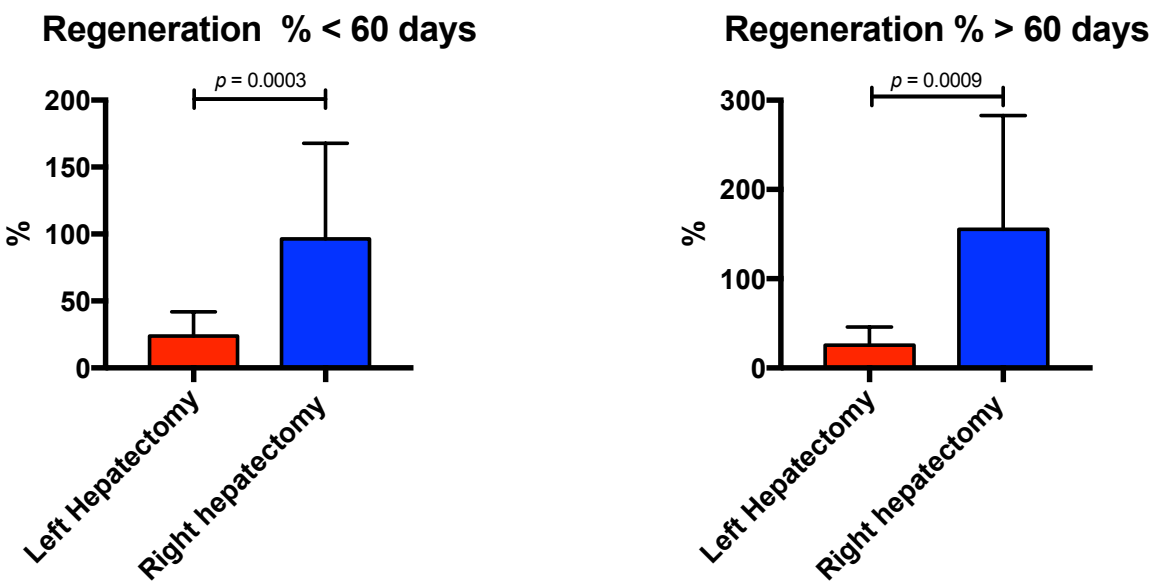


Figure 3: Regeneration of remaining liver before and after 60 days postsurgery

Many donors (70%) developed extrahepatic fluid collections of variable severity. One collection of the hepatectomy site had to be drained. Six collections were still present at 3 months postsurgery.

Slightly more than a half developed pleural effusions (56%), unilateral or bilateral, of which almost a half (n = 16) developed a concomitant adjacent lung parenchyma condensation. Two of the pleural effusions had to be drained and two were still present 3 months postsurgery.

Parietal collections or infiltrations were seen in almost a fourth of the donors (23%). One had to be drained and another was treated by wicking of the wound.

Intrahepatic bile duct dilatations appeared in 6% of the patients and extrahepatic bile duct distension was noted in 5%. None needed treatment.

A significant difference was found between left and right liver donors for blood vessel abnormalities (hepatic vein demodulation, slow or increased flow, flow inversion in a portal vein branch, low hepatic artery resistance index, thrombosis of a middle hepatic vein branch and portal trunk stenosis). The abnormalities were seen in fifteen left liver donors (60%) versus in eleven right liver donors (28%) ($p = 0.0184$). Similarly, hepatic perfusion disorders appeared in ten left liver donors (40%) and in three right liver donors (8%) ($p = 0.0032$). Four of the perfusion disorders were still present 3 months after hepatectomy. None required treatment.

New non specific hepatic lesions were noted in 5% of the donors.

Steatosis (either new or having increased considerably after the surgery) developed in 6% of the patients. Transient splenomegaly developed in 8% of the donors (**Table 3**).

Table 3: Postoperative radiological findings

Radiological findings	Total (n = 64)	Left hepatectomy (n = 25)	Right hepatectomy (n = 39)	*P*-value
Extrahepatic fluid collection	45 (70%)	21 (84%)	24 (62%)	0.0913
Pleural effusion	36 (56%)	15 (60%)	21 (54%)	0.7967
Parietal collection/infiltration	15 (23%)	6 (24%)	9 (23%)	1.000
Intrahepatic biliary dilatation	4 (6%)	2 (8%)	2 (5%)	0.6404
Extrahepatic biliary distension	3 (5%)	1 (4%)	2 (5%)	1.000
Blood vessel abnormalities	26 (41%)	15 (60%)	11 (28%)	0.0184
Perfusion disorders	13 (20%)	10 (40%)	3 (8%)	0.0032
New intrahepatic lesion	3 (5%)	0	3 (8%)	0.2746
Steatosis	4 (6%)	1 (4%)	3 (8%)	1.000
Splenomegaly	5 (8%)	1 (4%)	4 (10%)	0.6404

3.4. Clinical outcome

No significant difference in postoperative complications was found between the left and right liver donors.

A total of 40 donors (62.5%) experienced at least one complication.

Fifteen (23.4%) patients experienced a grade I complication and 14 (21.9%) a grade II complication.

Grade IIIA complications were present in 5 (7.8%) patients, which included two pleural effusion drainages (one of which also required drainage of a parietal collection), two prolene knot ablations and one drainage of collection at hepatectomy site.

Grade IIIB complications concerned 5 patients (7.8%). These consisted of three incisional hernias, which needed operation, and two biliary fistula correction surgeries.

A grade IVA complication occurred in one patient (1.6%), who suffered from a "small-for-size dysfunction" with total bilirubin levels up to 20.9 mg/dL during hospitalization. A conservative treatment was initiated by supplementation of magnesium, phosphorus, intravenous albumin and reduction of portal flow by an analogue of somatostatin.

Table 4: Postoperative complications, graded using the Clavien-Dindo classification

Clavien-Dindo grades	Total (n=64)	Left hepatectomy (n=25)	Right hepatectomy (n=39)	*P*-value
I	15 (23.4%)	6 (24%)	9 (23.1%)	0.770
II	14 (21.9%)	4 (16%)	10 (25.6%)	0.338
IIIA	5 (7.8%)	1 (4%)	4 (10.3%)	1.000
IIIB	5 (7.8%)	4 (16%)	1 (2.6%)	0.199
IVA	1 (1.6%)	0	1 (2.6%)	1.000
Total	40 (62.5%)	15 (60%)	25 (64.1%)	1.000

3.5. Donor mortality

No deaths have been observed in this donor population.

3.6. Donors' experience and psychosocial evolution

In total 24 patients had sent in their completed surveys, although some had not answered to all the questions.

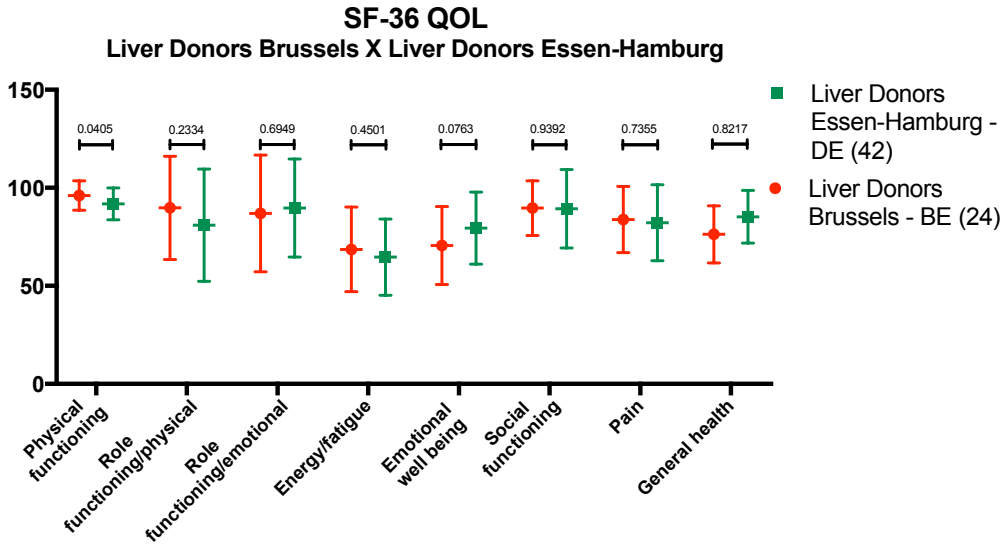
3.6.1. SF-36 survey

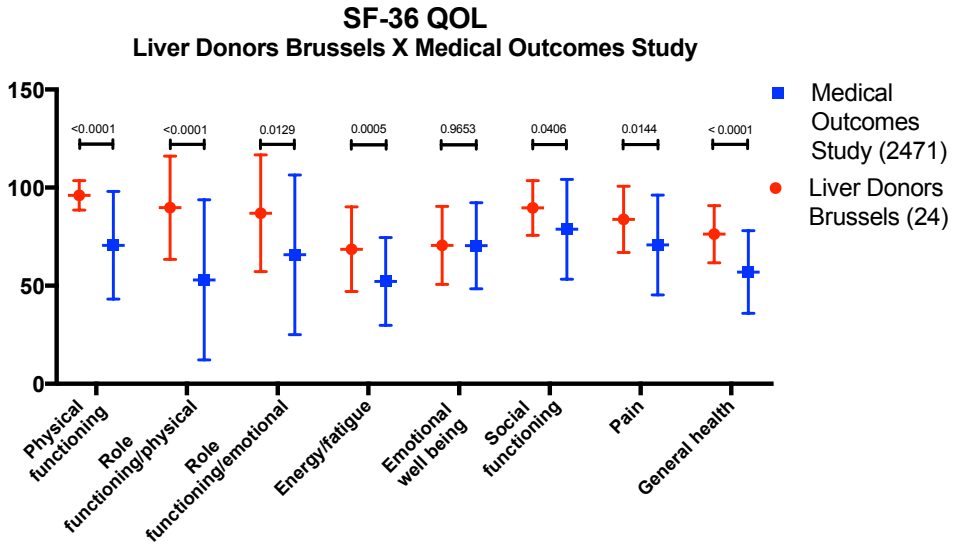
The results from the SF-36 survey were compared to three different populations: a German study of living liver donors (71), the Medical Outcomes Study (MOS) (72), which had studied patients with chronic conditions for two years (73), and a general population study in Norway (74). The different assessment categories contain Physical functioning, Role limitations due to physical health, Role limitations due to emotional problems, Energy/fatigue, Emotional well-being, Social functioning, Pain and General health. Higher scores mean a better quality of life in the particular category (72).

Saint-Luc's donor population showed similar results to the German donor study with only one category, Physical functioning, having a significant difference between the two studies. Saint-Luc's donors achieved a higher mean score of 96.08, meanwhile the Essen-Hamburg donors reached a score of 91.791 ($p = 0.0405$).

All categories showed significantly higher scores in Saint-Luc's donors in comparison to the MOS population, except for Emotional well-being ($p = 0.9653$). For Physical functioning this study's donors had a mean score of 96.08 and MOS of 70.61 ($p < 0.0001$), for Role limitations due to physical health a mean score of 89.77 versus 52.97 ($p < 0.0001$), for Role limitations due to emotional problems 86.95 versus 65.78 ($p = 0.0129$), for Energy/fatigue 68.62 versus 52.15 ($p = 0.0005$), for Social functioning 89.65 versus 78.77 ($p = 0.0406$), for Pain 83.8 versus 70.77 ($p = 0.0144$) and for General health 76.25 versus 56.99 ($p < 0.0001$).

In comparison to the Norwegian general population, the scores were significantly different only in two categories. For Physical functioning Saint-Luc's donors scored higher with 96.08 while the Norwegian study showed a mean score of 86.44 ($p = 0.0237$). On the other hand, the latter showed a higher score than Saint-Luc's donors for Emotional well-being, with 80.27 versus 70.58, respectively ($p = 0.0014$) (**Figure 4**).





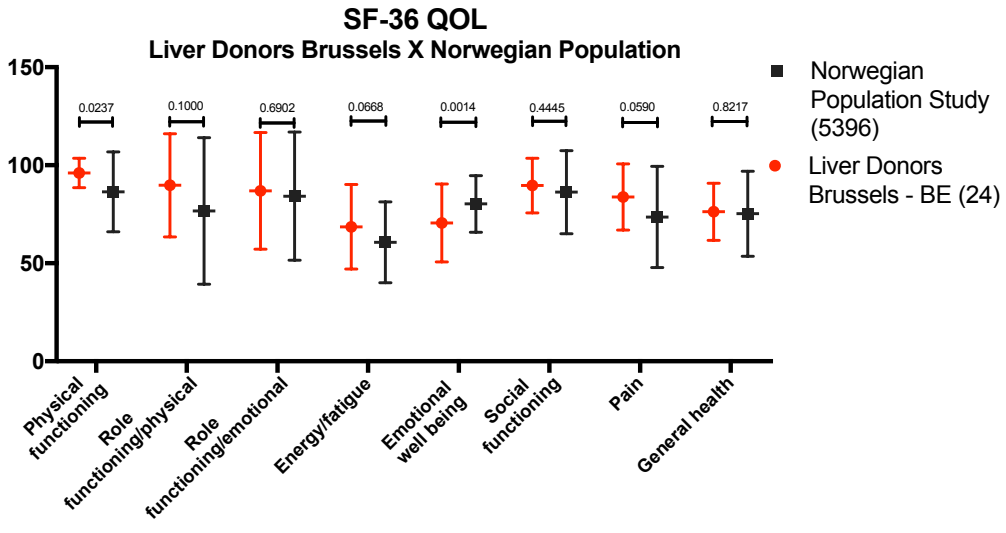


Figure 4: Comparison of results from SF-36 quality of life survey

3.6.2. EULID survey

Some questions being similar or identical to the ones in SF-36, only the most pertinent questions and answers are mentioned in this research.

The survey results showed that most (67%) of the donors felt happiness when they were told they could become donors. More than a third (38%) said they had a feeling of responsibility, 17% expressed fear and 13% insecurity. Most of the donors "strongly disagreed" (75%) or "disagreed" (21%) on being pressured to become a donor, while one patient (4%) "agreed".

When asked if information about surgery risks was clearly explained, 79% "strongly agreed" and all the rest (21%) "agreed". Concerning the medical tests to undergo in order to become a donor, 63% "strongly agreed" that they had received clear explanations while 33% "agreed" and 4% "disagreed". Meanwhile 12% felt that they had not received clear information about the hospitalization after surgery (including monitoring, catheters and pain).

Almost a half of the donors (46%) "strongly agreed" that the information given by the health professionals before the donation made them feel secure and the other half (54%) "agreed".

Whether well taken care of during hospitalization, 63% "strongly agreed", 29% "agreed" and 8% "disagreed".

None reported having thought about giving up the donation process at any moment and none regretted the donation during hospitalization.

It took more than three months to get back to a normal life again for 43% of the donors, between two and three months for 17%, between one and two months for 22% and less than a month for 13%. One patient reported not having recovered yet at the time of completion of the survey.

Most patients (57%) said the postoperative pain and recovery were less bothersome than expected and 35% thought they were as expected. The experience was more bothersome than expected for 9% of the donors.

When asked what are they most concerned about as a result of the donation, 62% reported having no concerns, 24% were concerned about the recipient's health and 14% about their own health.

Most donors (68%) reported their current health state as being more or less the same now as before donation, for 23% it was somehow worse now than before and for 9% it was somehow better than before.

For most patients (57%) the donation did not affect the working environment, a positive effect was noted by 30% and a negative effect by 4%.

The donation did not affect family and social life for 43%, while it had a positive impact for 52% and a negative impact for 4%.

A majority of the donors (82%) thought that being a living donor makes people value them more. Most (77%) felt admiration from others for having donated, 50% felt respect from others and one patient felt disapproval.

Most donors (68%) answered that the relationship with the recipient had not changed compared to before donation, 21% said it was better now than before and 11% said they had no relationship with the recipient. None of the relationships had become worse. From the 22 donors who had answered this question, three could not select any of the given answers due to the death of the recipient.

When asked whether being a donor had caused any personal financial loss, 22% "strongly agreed" and 4% "agreed", while half (52%) "strongly disagreed" and the rest "disagreed".

All of the donors answered that they would undergo the donation process again and all would recommend living donation to others, except for one who didn't know. When describing their feelings after being a donor, 32% answered "joy", 36% "pride", 32% "satisfaction", one patient expressed "indifference", another "regret" and 9% answered "other".

3.6.3. Complementary survey

The third survey containing questions about the impact of the donation on donor civil status showed that before the procedure 42% of donors were single, 46% were married, 8% were in cohabitation and one patient (4%) was widowed. After procedure, the percentage of married donors increased to 58% and the singles decreased to 21%. Furthermore, 17% of donors were in cohabitation and one donor (4%) separated.

If the civil status had changed, most donors (92%) answered that the donation had not had any impact on this change and 8% reported a moderate impact.

Whether the donation had caused any change in the donor's life (for example, in daily activities, habits, relationships, mood, emotional state etc.), 67% answered "no" and 33% answered "yes".

In order to assess the impact of the donation on female reproduction, some questions were dedicated to women only. Of the donors who had sent in the survey, 40% (n = 4) gave birth after donation, two of which gave birth twice. One needed reproductive assistance. Of the four women, one had two abnormal pregnancies and another had a spontaneous abortion besides a childbirth. Both of these women had not had children before donation.

All (n = 6) of the births occurred with a vaginal delivery and had no complications. One of them had already had a child before donation. Of those who did not have children after donation (n = 5, one being excluded due to menopause), none were considering pregnancy in the future.

4. Discussion

These results have shown, first of all, that although there is a significant difference in the remaining liver proportion between left and right liver donors, there is no such difference concerning the postoperative complications. Furthermore, no difference was noted between the left and right group for postoperative laboratory values, except for total bilirubin and INR values. Nevertheless, the same remark applies as there is no significant difference for postoperative complications. In addition, mean platelet values remained lower than baseline at one-year follow-up in both groups.

The hepatic regeneration was significantly more important in right liver donors than left donors, probably due to the significantly smaller remaining liver volume in the right group. However, on the first volumetric evaluation after 60 days at least 80% of the preoperative liver volume was reached in both groups.

Various abnormal radiological findings were observed in the donors but only a few required treatment. It should be noted that statistically more blood vessel abnormalities and perfusion disorders occurred in left liver donors.

In total, 62.5% of the donors experienced postoperative complications, 7.8% experiencing a grade IIIA and other 7.8% a grade IIIB complication. A grade IVA complication occurred in one patient.

The donors' quality of life via SF-36 survey was found to be similar to other living liver donors (71) and to the Norwegian general population (74). On the contrary, all scores, except for one category, were significantly higher in Saint-Luc's donor population in comparison to chronically ill patients from MOS study (72, 73).

Most donors reported having received clear information about the different aspects of the donation process. However, 8% were not satisfied with care provided during hospitalization. Although for a large proportion (43%) of the donors it took more than 3 months to return to a normal life, none regretted having donated and all would undergo the process again. Moreover, half of the donors thought the donation had a positive impact on their family and

social life; meanwhile almost a third said the working environment was positively impacted. Yet, a fourth of the study population experienced some degree of financial loss.
If a civil status change took place, a vast majority occurred without being influenced by the donation. For most, the process did not cause any change whatsoever in the donor's life.

Some limitations and possible bias of this research have to be mentioned.
First of all, although the research concerned a total of 64 donors, some had been lost to follow-up sooner or later. Consequently, the amount of accessible information at different follow-up time points was rather varied and incomplete, especially as time since surgery increased.
Concerning the radiological anomalies, the different findings were of different severity and, thus, could have been overestimated. Extrahepatic fluid collections ranged, for example, from minimal pelvic ascites to large hepatectomy site collections. Similarly, pleural effusions were of various dimensions in different donors but classified together regardless of the size. Therefore, the number of patients who needed treatment was mentioned in order to have a better view of the severity.
In regard to the surveys, only 24 donors had sent in their three surveys. As a consequence, the data concerned only 37.5% of all the donors and might not be representative. This applies especially to the questions directed to women specifically, since only a few gave birth after the intervention and the data was difficult to interpret. Moreover, some survey questions were not answered or could have been interpreted differently by each person. Some questions were answered by a written response instead of ticking the corresponding option. In this case, the seemingly most appropriate option was selected by the author of this research according to the written response. Also, since the surveys were analyzed anonymously it was not possible to interpret the answers in regard to time elapsed since surgery, which could have been helpful for interpretation.
More specifically about the SF-36 survey, nine did not answer to the question nr. 24 and no answers were received for nr. 25, which could have influenced the results for Emotional well-being category. In addition, the RAND scoring system was used, which is slightly different than the classic scoring procedure. However, only two categories are impacted by this scoring: Pain and General Health and the results have a correlation of 0.99 with the classic SF-36 (75).

We compared our results to the available literature. Trotter et al. (76) also reported lower platelet values at long term follow-up. At three years postsurgery the platelets were 19% lower than baseline values. Moreover, as in Saint-Luc's donor cohort, there was no significant difference in platelet values between left and right liver donors. Similarly, Lei et al. (77) found lower platelets at eight years postdonation in comparison to departing levels with a more important drop in their population (decrease of 29%) than Saint-Luc donors. Iida et al. (78) observed a significantly higher peak total bilirubin values in right liver donors. On the other hand, a significant difference was also found in peak AST and ALT levels, which was not observed in our study.

Similar hepatic regeneration results were reported by Klink et al. (79) with more important regeneration in right liver donors and occurring essentially in the first three months. Also, a considerable difference was noted in remaining liver volumes between the two groups (a mean of 522.0 mL or a proportion of 36.1% in right donors and 1181.5 mL or 72.0% in left donors). In contrast, abnormal radiological findings were discovered in 8.5% of the donors, which were fewer than in Saint-Luc's cohort. All consisted of fluid collections at the hepatectomy site and none required treatment. However, it must be noted that no radiological anomalies were observed in the study by Castedal et al. (80). The notably different results compared to our study could be explained by possible more specific inclusion criteria of the anomalies.

Regarding clinical postoperative complications, Lei et al. (77) observed a total complication rate of 25.3% (versus 62.5% or 40 patients in our study). Grade III complications were found in 17 donors, representing 5.7%, and grade IV in one donor (0.3%). An Italian study (81) reported an overall complication rate of 33.3%. Grade IIIA complications occurred in 15 donors (6.1%), grade IIIB in 13 donors (5.3%) and grade IVA in one donor (0.4%). Furthermore, in contrast to our study, Humphreville et al. (82) described a significantly higher complication rate in right liver donors than left liver donors (45.5% versus 27.8%, respectively) with a total complication rate of 42.5%. Iida et al. (78) also reported a significantly higher complication rate in right liver donors. A grade IIIA complication was observed in 15.4% of the right group versus 2% of the left, grade IIIB complication in 1.4% versus 0.5% and none grade IV versus one (0.13%) in the left group. Moreover, one perioperative donor (0.2%) death occurred in the right group. Similarly, one Asian study observed a higher complication rate in right liver donors with a rate of 28% versus 8.6% in left liver donors and a total complication rate of 15.8%. Although the complication rate was

lower than in our study, an additional variety of complications was described such as biliary strictures, intra-abdominal bleeding, pulmonary embolisms, small bowel obstructions and portal vein thrombosis (83).

In regard to the analysis of the quality of life, besides the already mentioned German liver donor study (71), other quality of life studies have published their results. For example, Lei et al. found similar SF-36 results, the biggest difference of scores concerning Role limitations due to emotional problems (86.95 in Saint-Luc donors versus 79.51 in the Chinese donors). Nevertheless, the follow-up ranged from 3 to 130 months whereas in our study the surveys were completed at a minimum of 3 years from the surgery (77). Thus the different timings might have had a different influence on the results. Dew et al. also reported comparable results with the exception of Emotional well-being, in which a higher score was achieved than in Saint-Luc's population (81.1 versus 70.58, respectively) (84).

Concerning their personal experience of the donation process, most donors (94%) from the study by Castedal et al. (80) stated as well having received highly satisfying information about the perioperative donor risks and none felt being pressured to donate. However, recovery time was reported longer in the same study with most donors needing more than three months to recover and more than a year for 11.8% (80). Moreover, 41% of donors from another study (85) experienced greater pain than expected versus 9% of Saint-Luc donors. With regard to the current health state versus before donation, Humphreville et al. (82) found it as being the same for the majority of donors, although worse health status was stated by 11.2%. Relationship with the family was improved in 25.9% of cases at two years after donation in the study by DiMartini et al. (86) while 52% of Saint-Luc donors said the donation had positively affected family and social life. Similarly to our study, two other studies found that the relationship with the recipient was improved or unchanged for most donors with only a small minority or none having become worse (85, 86). Financial expenses related to the donation were reported by 58% and they were burdensome for 15% of donors in the study by Dew et al. (84). Several other studies showed that the vast majority of donors had no regrets concerning the donation (77, 80) and would do it again (77, 80, 82, 84, 85).

5. Conclusion

All in all, the living donor liver transplantation experience at Cliniques universitaires Saint-Luc has been a positive one. If abnormalities occurred at a biochemistry or radiological level, the vast majority of these were transient changes and disappeared over time. Moreover,

although more than a half of donors experienced complications, they were serious in a small minority of patients. The surveys conducted, in spite of the low proportion of sent in answers, show that the donors have a similar quality of life not only with other liver donor populations but also with a Norwegian general population. The results equally reassure that these donors have more favorable results than chronically ill patients. Another indication of a successful experience is that all donors would be willing to undergo the process again if needed. However, closer attention could be paid to the donor while recovering at the hospital to improve their experience.

An important aspect of this research was to analyze the impact of the type of hepatectomy on different outcomes. Even though, some statistically significant differences were observed, most importantly, there was no difference between the clinical complications between right and left liver donors. In addition, the hepatic regeneration adapted correctly in each type of donation so as to reach similar proportions of the preoperative liver volume after 60 postoperative days.

This confirms that both procedures are equally safe options for living donor liver transplantation in spite of the significantly smaller remaining hepatic volume in right liver donors.

In order to ensure the safety of donors, a systematic preoperative screening and follow-up remain essential. Additionally, future studies could include a larger population of donors and could focus on exposing potential risk predictors of complications. Also, a deeper understanding of the donors' experience could be gained with systematic patient follow-up surveys. These could include personal suggestions for future improvement of the procedure.

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Appendix 1: SF-36 Quality of life questionnaire

Questionnaire SF-36

Sélectionnez une option pour chaque entité du questionnaire.

1. Dans l'ensemble, vous diriez que votre état de santé est :

- ○ 1 - Excellent
- ○ 2 - Très bon
- ○ 3 - Bon
- ○ 4 - Médiocre
- ○ 5 - Mauvais

2. **En comparant avec votre état de santé d'il y a un an**, comment l'évalueriez-vous **en ce moment**?

- ○ 1 - Bien meilleur maintenant qu'il y a un an
- ○ 2 - Plutôt meilleur maintenant qu'il y a un an
- ○ 3 - Plus ou moins le même
- ○ 4 - Plutôt pire maintenant qu'il y a un an
- ○ 5 - Bien pire maintenant qu'il y a un an

Les entités suivantes concernent des activités que vous êtes susceptible de faire pendant une journée typique. Est-ce que **votre état de santé actuel vous limite** dans ces activités? Si oui, à quel point?

	Oui, très limité(e)	Oui, un peu limité(e)	Non, pas du tout limité(e)
3. **Activités vigoureuses**, telles que courir, soulever des objets lourds, participer dans des sports intenses	○ 1	○ 2	○ 3
4. **Activités modérées**, telles que déplacer une table, passer l'aspirateur, faire du bowling ou jouer au golf	○ 1	○ 2	○ 3
5. Soulever ou porter les courses	○ 1	○ 2	○ 3
6. Monter **plusieurs** volées d'escaliers	○ 1	○ 2	○ 3
7. Monter **une** volée d'escaliers	○ 1	○ 2	○ 3
8. Se pencher en avant, s'agenouiller ou se baisser	○ 1	○ 2	○ 3
9. Marcher **plus d'un kilomètre**	○ 1	○ 2	○ 3
10. Marcher **plusieurs centaines de mètres**	○ 1	○ 2	○ 3
11. Marcher **une centaine de mètres**	○ 1	○ 2	○ 3
12. Se laver ou s'habiller	○ 1	○ 2	○ 3

Durant les **4 semaines passées**, est-ce que vous avez eu les problèmes suivants avec votre travail ou d'autres activités quotidiennes régulières **en raison de votre santé physique**?

	Oui	Non
13. Vous avez diminué la **quantité de temps** passée au travail ou à faire d'autres activités habituelles	○ 1	○ 2
14. Vous avez **accompli moins** de choses que vous ne l'auriez souhaité	○ 1	○ 2

15.	Vous avez été limité(e) dans le **type** de travail ou d'autres activités	○	1	○ 2
16.	Vous avez eu des **difficultés** pour effectuer votre travail ou d'autres activités (par exemple, cela vous a demandé plus d'effort)	○	1	○ 2

Durant les **4 semaines passées**, est-ce que vous avez eu les problèmes suivants avec votre travail ou d'autres activités quotidiennes régulières **en raison de problèmes émotionnels** (comme se sentir déprimé(e) ou anxieux(se))?

		Oui	Non
17.	Vous avez diminué la **quantité de temps** passée au travail ou à faire d'autres activités habituelles	○ 1	○ 2
18.	Vous avez **accompli moins** de choses que vous ne l'auriez souhaité	○ 1	○ 2
19.	Vous n'avez pas effectué votre travail ou d'autres activités aussi **soigneusement** que d'habitude	○ 1	○ 2

20. Durant les **4 semaines passées**, à quel point votre santé physique ou vos problèmes émotionnels ont-ils interféré avec vos activités sociales normales avec la famille, les amis, les voisins ou d'autres groupes de personnes?

    - ○ 1 - Pas du tout
    - ○ 2 - Légèrement
    - ○ 3 - Moyennement
    - ○ 4 - Beaucoup
    - ○ 5 - Enormément

21. Quelle intensité de douleur **physique** avez-vous présenté au cours de ces **4 dernières semaines**?

    - ○ 1 - Aucune
    - ○ 2 - Très légère
    - ○ 3 - Légère
    - ○ 4 - Moyenne
    - ○ 5 - Grande
    - ○ 6 - Très grande

22. Durant les **4 semaines passées**, à quel point des **douleurs** ont-t-elles interféré avec votre travail normal (travail à l'extérieur du domicile et travail ménager inclus)?

    - ○ 1 - Pas du tout
    - ○ 2 - Un peu
    - ○ 3 - Moyennement
    - ○ 4 - Beaucoup
    - ○ 5 - Enormément

Ces questions se rapportent sur la façon dont vous vous êtes senti(e) au cours des **4 semaines passées**. Pour chaque question, veuillez indiquer la réponse qui est la plus proche de la façon dont vous vous êtes senti(e).

Durant les **4 semaines passées**, combien de temps…

	Tout le temps	La plupart du temps	Une grande partie du temps	Une partie du temps	Un peu de temps	Jamais
23. Êtes-vous senti(e) plein(e) de vie?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
24. Êtes-vous senti(e) très nerveux(se)?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
25. Êtes-vous senti(e) si malheureux(se) que rien ne pouvait vous remonter le moral?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
26. Êtes-vous senti(e) calme et paisible?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
27. Avez-vous eu beaucoup d'énergie?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
28. Etes-vous senti(e) découragé(e) et triste?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
29. Êtes-vous senti(e) épuisé(e)?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
30. Êtes-vous senti(e) heureux(se)?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
31. Êtes-vous senti(e) fatigué(e)?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6

32. Durant les **4 semaines passées**, combien de temps **votre santé physique et vos problèmes émotionnels** ont-ils interféré avec vos activités sociales (comme voir les amis, les proches, etc.)?

- ○ 1 - Tout le temps
- ○ 2 - La plupart du temps
- ○ 3 - Une partie du temps
- ○ 4 - Un peu de temps
- ○ 5 - Jamais

Dans quelle mesure **chaque** affirmation est-elle VRAIE ou FAUSSE pour vous?

	Absolument vrai	Plutôt vrai	Je ne sais pas	Plutôt faux	Absolument faux
33. J'ai l'impression de devenir malade un peu plus facilement que d'autres personnes	○ 1	○ 2	○ 3	○ 4	○ 5
34. Je suis en aussi bonne santé que n'importe qui	○ 1	○ 2	○ 3	○ 4	○ 5
35. Je m'attends à ce que mon état de santé se dégrade	○ 1	○ 2	○ 3	○ 4	○ 5
36. Mon état de santé est excellent	○ 1	○ 2	○ 3	○ 4	○ 5

Appendix 2: EULID European Living Donor project questionnaire

Questionnaire EULID

1. **Que pensiez-vous du don d'organes <u>de donneur décédé</u> avant que vous ne soyez vous-même un donneur?**
   - o J'étais en faveur du don d'organes
   - o J'étais opposé au don d'organes
   - o Je n'avais jamais réfléchi à ce propos/Je n'en avais jamais entendu parler

2. **Que pensiez-vous du don d'organes <u>de donneur vivant</u> avant que vous ne soyez vous-même un donneur?**
   - o J'étais en faveur du don d'organes
   - o J'étais opposé au don d'organes
   - o Je n'avais jamais réfléchi à ce propos/Je n'en avais jamais entendu parler

3. **Qui vous a suggéré la possibilité de faire le don d'un organe de votre vivant?**
   - o Je me suis proposé moi-même sans avoir été sollicité
   - o Le receveur
   - o Un proche/Un ami
   - o Le médecin
   - o Autre

4. **Qu'avez-vous ressenti lorsqu'il vous a été dit que vous pouviez vous engager dans le processus pour être donneur?**
   - o De la peur
   - o De la joie
   - o De l'insécurité
   - o Un sentiment de devoir
   - o Autre

5. **Pensez-vous que les examens médicaux préalables au don vous ont été clairement expliqués?**
   - o Je suis entièrement d'accord
   - o Je suis d'accord
   - o Je ne suis pas d'accord
   - o Je ne suis pas du tout d'accord

6. **Ces examens médicaux ont-ils retenti sur votre vie quotidienne?**
   - o Je suis entièrement d'accord
   - o Je suis d'accord
   - o Je ne suis pas d'accord
   - o Je ne suis pas du tout d'accord

7. **Pensez-vous que les risques opératoires vous ont été clairement expliqués, y compris celui de risquer votre vie?**
   - o Je suis entièrement d'accord
   - o Je suis d'accord
   - o Je ne suis pas d'accord
   - o Je ne suis pas du tout d'accord

8. **Avez-vous pris votre décision après avoir bien réfléchi?**
   - o Je suis entièrement d'accord
   - o Je suis d'accord
   - o Je ne suis pas d'accord
   - o Je ne suis pas du tout d'accord

9. **Est-ce qu'il vous a été clairement expliqué qu'après l'opération vous alliez séjourner à l'hôpital, éventuellement isolé, avec des cathéters, sondes, appareils de surveillance, et que vous pourriez avoir des douleurs?**
   - o Je suis entièrement d'accord
   - o Je suis d'accord
   - o Je ne suis pas d'accord
   - o Je ne suis pas du tout d'accord

10. **Est-ce qu'il vous a été clairement expliqué que votre don ne garantissait pas l'évolution favorable de la greffe chez le receveur?**
    - o Je suis entièrement d'accord
    - o Je suis d'accord
    - o Je ne suis pas d'accord
    - o Je ne suis pas du tout d'accord

11. **Est-ce que vous avez été informé de la possibilité pour le receveur de bénéficier d'une greffe d'organe de donneur décédé?**
    - o Oui
    - o Non
    - o Je ne sais pas/Je ne me souviens plus

12. **Avez-vous demandé l'avis d'un proche ou d'un ami avant de prendre la décision de faire le don?**
    - o Oui
    - o Non
    - o Je ne sais pas/Je ne me souviens plus

13. **Si vous avez demandé l'avis de quelqu'un, pouvez-vous préciser de qui s'agissait-il?**
    - o Epoux(se)
    - o Frère ou sœur
    - o Père ou mère
    - o Enfant
    - o Ami
    - o Médecin
    - o Autre

14. **Si vous n'avez pas demandé l'avis d'une personne de votre entourage, pouvez-vous en préciser la raison?**
    - o Parce que je préfère prendre mes propres décisions sans demander l'avis de quelqu'un d'autre
    - o Parce que j'ai estimé que la personne risquait d'y être opposée
    - o Parce que je craignais une réponse négative
    - o Autre raison

15. **Est-ce que tous les membres de votre famille et vos amis proches ont été informés de votre décision?**
    - Oui, je les ai tous tenus informés
    - Non, je n'ai informé que les plus proches
    - Non, je ne l'ai dit à personne

16. **Est-ce que l'information qui vous a été délivrée par les professionnels de santé avant le don vous a rassuré?**
    - Je suis entièrement d'accord
    - Je suis d'accord
    - Je ne suis pas d'accord
    - Je ne suis pas du tout d'accord

17. **Quelle a été la première réaction du receveur lorsqu'il a été mis au courant de votre décision de devenir donneur?**
    - Il a été d'accord
    - Il n'a pas manifesté d'accord ni de désaccord
    - Il a refusé
    - Autre réaction

18. **Que pensez-vous des examens et tests médicaux que vous avez subi avant de faire le don?**
    - Ils ont été plus pénibles que je ne l'estimais
    - Ils ont été comme je l'estimais
    - Ils ont été moins pénibles que je ne l'estimais
    - Je ne sais pas/Je ne me souviens plus

19. **Aviez-vous l'impression qu'on s'occupait bien de vous pendant votre séjour à l'hôpital?**
    - Je suis entièrement d'accord
    - Je suis d'accord
    - Je ne suis pas d'accord
    - Je ne suis pas du tout d'accord
    - Je ne sais pas/Je ne me souviens plus

20. **Pensez-vous que les procédures et les étapes pour devenir donneur ont été appropriées?**
    - Je suis entièrement d'accord
    - Je suis d'accord
    - Je ne suis pas d'accord
    - Je ne suis pas du tout d'accord

21. **Vous êtes-vous senti contraint d'accepter de faire le don d'organe?**
    - Je suis entièrement d'accord
    - Je suis d'accord
    - Je ne suis pas d'accord
    - Je ne suis pas du tout d'accord

22. **Avez-vous songé à abandonner le processus de don, à un moment quelconque de son déroulement?**
    - Je suis entièrement d'accord
    - Je suis d'accord
    - Je ne suis pas d'accord
    - Je ne suis pas du tout d'accord

23. **Avez-vous pris des dispositions quelconques pour la prise en charge de votre famille, en cas de complications?**
    - Oui, je l'ai fait
    - En partie
    - Non, je ne l'ai pas fait

24. **Combien de temps a duré votre séjour à l'hôpital, après l'intervention?**
    - Moins d'une semaine
    - Entre une et deux semaines
    - Entre 2 semaines et un mois
    - Plus d'un mois

25. **Pendant combien de temps avez-vous dû arrêter vos activités (par exemple : travail ou études) en raison du don d'organe?**
    - Moins de 3 mois
    - 3-6 mois
    - 6-12 mois
    - Plus d'un an
    - Je n'ai pas encore repris mes activités

26. **Les explications sur le processus du don d'organe, qui vous ont été délivrées avant sa réalisation, ont-elles correspondu à votre propre expérience?**
    - Je suis entièrement d'accord
    - Je suis d'accord
    - Je ne suis pas d'accord
    - Je ne suis pas du tout d'accord
    - Je ne sais pas/Je ne me souviens plus

27. **Que ressentez-vous en ce qui concerne la douleur et la période post-opératoires?**
    - Ils ont été plus pénibles que je ne l'estimais
    - Ils ont été comme je l'estimais
    - Ils ont été moins pénibles que je ne l'estimais
    - Je ne sais pas/Je ne me souviens plus

28. **Pendant votre séjour à l'hôpital, avez-vous à un moment regretté d'avoir fait le don?**
    - Je suis entièrement d'accord
    - Je suis d'accord
    - Je ne suis pas d'accord
    - Je ne suis pas du tout d'accord

29. **Combien de temps avez-vous eu besoin pour retrouver une vie normale?**
    - Moins d'un mois
    - Entre un et deux mois
    - Entre deux et trois mois
    - Plus de trois mois
    - Je ne me suis pas encore remis

30. **Estimez-vous avoir eu des pertes financières en raison du don?**
    - Je suis entièrement d'accord
    - Je suis d'accord
    - Je ne suis pas d'accord
    - Je ne suis pas du tout d'accord

31. **Pensez-vous que le fait d'avoir été donneur a eu une influence sur votre environnement professionnel?**
    - Non, cela n'a eu aucune influence
    - Oui, une influence positive
    - Oui, une influence négative
    - Autre

32. **Pensez-vous que le fait d'avoir été donneur a eu une influence sur votre vie familiale et/ou sociale?**
    - Non, cela n'a eu aucune influence
    - Oui, une influence positive
    - Oui, une influence négative
    - Autre

33. **Si vous n'êtes pas couvert par la Sécurité Sociale, avez-vous eu des problèmes pour que votre assureur de santé vous rembourse les frais liés au don, et/ou au suivi médical après le don?**
    - Oui
    - Non
    - Autre

34. **Êtes-vous complètement remis du don d'organe?**
    - Je suis entièrement d'accord
    - Je suis d'accord
    - Je ne suis pas d'accord
    - Je ne suis pas du tout d'accord

35. **Est-ce que vous recommenceriez le processus de don?**
    - Je suis entièrement d'accord
    - Je suis d'accord
    - Je ne suis pas d'accord
    - Je ne suis pas du tout d'accord

36. **Comment estimez-vous votre qualité de vie après le don, par rapport à ce qu'elle était avant?**
    - Elle est meilleure qu'avant le don
    - Elle est identique
    - Elle est plus mauvaise qu'avant le don
    - Je ne sais pas

37. **Quel est le terme qui désigne le mieux vos sentiments après avoir été donneur?**
    - Joie
    - Fierté
    - Satisfaction
    - Indifférence
    - Regret
    - Autre

38. **Recommanderiez- vous le don d'organe du vivant à d'autres?**
    - Oui
    - Non
    - Je ne sais pas

39. **Est-ce que votre vie quotidienne et/ou vos passe-temps ont changé après le don?**
    - Oui
    - Non
    - Je ne sais pas
    - Autre

40. **Êtes-vous astreint à un suivi médical en raison de votre don?**
    - Oui
    - Non
    - Autre

41. **Si vous avez répondu "Oui" à la question précédente, quelle est la fréquence des visites médicales de suivi?**
    - Tous les 3 mois
    - Tous les 6 mois
    - Une fois par an
    - Autre

42. **Quel est votre principale préoccupation liée au don d'organe?**
    - Je n'ai aucune préoccupation
    - La détérioration de mon état de santé
    - L'aggravation de l'état de santé du receveur
    - Mon travail
    - Ma couverture sociale
    - Autre

43. **Que pensez-vous de votre état de santé actuel, <u>en comparaison avec ce qu'il était avant le don</u>?**
    - Bien meilleur qu'avant le don
    - Légèrement meilleur qu'avant le don
    - Plus ou moins identique
    - Un peu moins bon qu'avant le don
    - Bien pire qu'avant le don

44. **Avez-vous le sentiment que le receveur vous est redevable, ou assujetti à vous-même ou à votre famille parce que vous lui avez donné un organe?**
    - Je suis entièrement d'accord
    - Je suis d'accord
    - Je ne suis pas d'accord
    - Je ne suis pas du tout d'accord

45. **D'une façon générale, quel est le mot que vous emploieriez pour définir votre état de santé actuel?**
    - Excellent
    - Très bon
    - Bon
    - Médiocre
    - Mauvais

46. **Estimez-vous que vous tombez malade plus facilement que n'importe qui?**
    - Je suis entièrement d'accord
    - Je suis d'accord
    - Je ne sais pas
    - Je ne suis pas d'accord
    - Je ne suis pas du tout d'accord

47. **Estimez-vous être en aussi bonne santé que n'importe qui?**
    - Je suis entièrement d'accord
    - Je suis d'accord
    - Je ne sais pas

- Je ne suis pas d'accord
- Je ne suis pas du tout d'accord

48. Au cours des 4 dernières semaines, à quel point des problèmes de santé et/ou des problèmes émotionnels ont posé des difficultés dans vos relations sociales avec votre famille, vos amis, vos voisins ou d'autres personnes?

- Pas du tout
- Un peu
- Parfois
- Assez souvent
- Beaucoup

49. Pensez-vous que le don vous valorise vis-à-vis de votre entourage?

- Oui
- Je crois
- Je ne crois pas
- Non

50. Pensez-vous que le fait d'être un donneur d'organe a changé vos relations avec votre famille proche et/ou vos amis?

- Oui, elles se sont améliorées
- Oui, elles se sont détériorées
- Non, rien n'a changé
- Autre

51. Qu'est-ce que les gens manifestent lorsqu'ils apprennent que vous avez fait un don d'organe?

- Respect
- Admiration
- Indifférence
- Désapprobation
- Autres

52. Quels sont actuellement vos rapports avec le receveur?

- Meilleurs qu'avant le don
- Les mêmes qu'avant le don
- Plus mauvais qu'avant le don
- Nous n'avons pas de rapports

53. Comment avez-vous vécu le rétablissement du receveur après la transplantation, et comment se porte-t-il actuellement?

54. Si vous avez des commentaires à ajouter ou des sentiments à exprimer au-delà des questions déjà posées, vous pouvez les noter ici. Merci infiniment d'avoir accordé un peu de votre temps pour répondre à cette enquête.

Appendix 3: Complementary survey

1. Votre état civil AVANT la donation:

- Célibataire
- Marié(e)
- Divorcé(e)
- Veuf(ve)
- Séparé(e)
- Cohabitant(e)

2. Votre état civil APRES la donation:

- Célibataire
- Marié(e)
- Divorcé(e)
- Veuf(ve)
- Séparé(e)
- Cohabitant(e)

3. Si votre état civil a changé après la donation, quelle influence le fait d'avoir fait le don a-t-il eu sur ce changement?

- Aucune
- Légère
- Moyenne
- Grande
- Très grande

4. A votre avis, est-ce que la donation a engendré des changements dans votre vie quels qu'ils soient (par exemple dans les activités quotidiennes, les habitudes, les relations, l'humeur, l'état émotionnel etc.)?

- Oui
- Non

5. Si oui, veuillez indiquer ce qui a changé à cause de la donation:

6. Si vous avez un commentaire, vous pouvez l'écrire ci-dessous:

Des questions spécifiques pour les donneuses

7. Aviez-vous eu des grossesses avant la donation?

- Oui
- Non

8. Si oui, combien?

9. Avec de l'aide à la procréation?

- Oui
- Non

10. Votre (vos) grossesse(s) s'est-elle déroulée normalement?

- Oui
- Non

11.1. L'accouchement s'est-il passé par voie basse?

- Oui
- Non

11.2. Votre (vos) accouchement(s) s'est-il déroulé normalement?

- Oui
- Non

12. Votre (vos) enfant(s) était-il prématuré?

- Oui
- Non
- Poids et taille:

13. Aviez-vous eu des grossesses après la donation?

- Oui
- Non

14. Si oui, combien?

15. Avec de l'aide à la procréation?

16. Votre (vos) grossesses s'est-elle déroulée normalement?

17.1. L'accouchement s'est-il passé par voie basse?

17.2. Votre (vos) accouchement(s) s'est-il déroulé normalement?

18. Votre (vos) enfant(s) était-il prématuré?

- Oui
- Non
- Poids et taille:

19. Envisagez-vous une future grossesse?

- Oui
- Non

UNIVERSITÉ CATHOLIQUE DE LOUVAIN
Faculté de médecine et médecine dentaire
Avenue Mounier, 50 bte B1.50.04, 1200 Woluwe-Saint-Lambert, Belgique | **www.uclouvain.be/mede**