Quality in liver transplantation: perspectives on organ procurement and allocation

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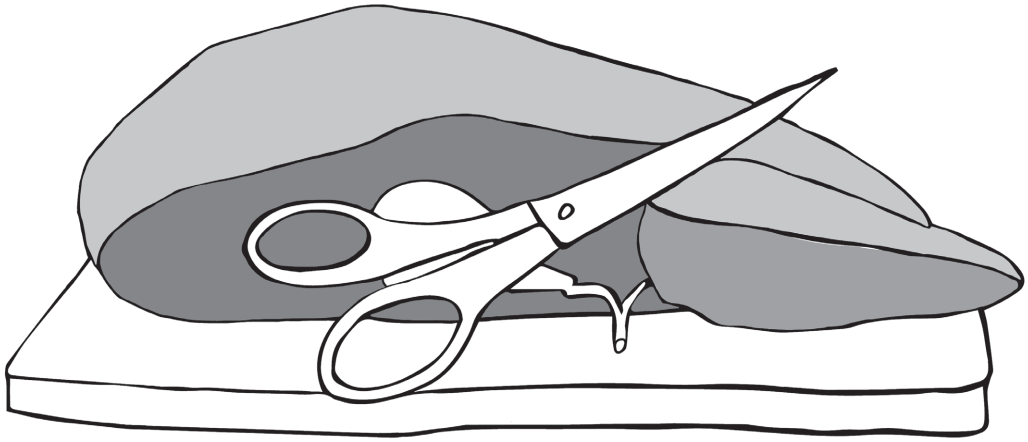

Chapter 3

Abdominal organ procurement in The Netherlands: an analysis of quality and clinical impact

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Abstract

Between March 2012 and August 2013, 591 quality forms were filled out for abdominal organs in The Netherlands. In 133 cases (23%) there was a discrepancy between the evaluation from the procuring and transplanting surgeons. Injuries were seen in 148 (25%) organs of which 12 (2%) led to discarding of the organ; one of 133 (0.8%) livers, five of 38 (13%) pancreata and six of 420 (1.4%) kidneys ($p<0.001$). Higher donor BMI was a risk factor for procurement related injury in all organs (OR 1.06, $p=0.011$) and donor after cardiac death (DCD) donation in liver procurement (OR 2.31, $p= 0.034$). DCD donation is also associated with more pancreata being discarded due to injury (OR 10.333, $p=0.046$). A higher procurement volume in a center was associated with less injury in pancreata (OR= -0.95, $p=0.013$) and kidneys (OR=-0.91, $p=0.012$). The quality form system efficiently monitors the quality of organ procurement. Although there is a relatively high rate of organ injury, the discard rate is low and it does not significantly affect 1-year graft survival for any organ. We identified higher BMI as a risk factor for injury in abdominal organs and DCD as a risk factor in livers. A higher procurement volume is associated with fewer injuries.

Introduction

The number of patients on the waiting list for organ transplantation clearly shows the need for more suitable organs in the Eurotransplant (ET) region(1). Complications during procurement may lead to the loss of organs or to inferior outcome (2-6). Therefore, optimal quality of organ procurement is essential. To reach this goal, combined efforts have been initiated to achieve this in The Netherlands.

One of these initiatives is the training and certification of procurement surgeons. The course 'Multi Organ Donor procurement surgery' (MOD training) was originally developed in The Netherlands and is organized yearly since 2005, by the European Society for Organ Transplantation (ESOT). The aim is to educate and train surgeons interested in abdominal organ procurement surgery (7). Currently, a step-by-step e-learning module is included as part of this course. Apart from the ESOT training, potential procurement surgeons in The Netherlands have to complete and register a set number of individual procurements and examinations under supervision before being certified (7). The Netherlands are divided in two regions (East and West) and five fully independent regional teams (ZUT-teams) cover these two regions and procure all abdominal donor organs. These teams consist of at least one certified procuring surgeon, an assistant surgeon, as well as two scrub nurses, an anesthesiology nurse and an anesthesiologist and carry all necessary instruments in order to perform the procedures independently on location. This results in better time management and it may also lead to more experienced surgeons, which will be beneficial to procurement quality of organs (2, 5, 8). The procurement teams (ZUTs) are based and related to their own center and in this study will be referred to as procurement center.

The idea of enabling feedback to improve and evaluate procurement quality has been suggested by several researchers (9, 10). In 2012, the Quality Form (QF) system was initiated in The Netherlands. This is a digital scoring program developed by the Dutch Transplant Foundation (NTS) for abdominal organs that are donated and accepted in The Netherlands. The system offers valuable information since a QF is filled out for each accepted organ by the procuring surgeon (QFD) and by the accepting surgeon (QFT).

Earlier studies investigated the quality of organ procurement and identified several, mostly donor related risk factors for procurement related injuries (2, 11, 12). The impact of these risk factors can differ between regions based on the different donor population characteristics. Within the Eurotransplant region for example, there is a higher mean donor age, stroke is reported more frequent as cause of death (COD) and there is more extra-regional allocation as compared to the United States. Even between countries within the Eurotransplant region substantial differences exist due to regulations and

protocols (e.g. in The Netherlands 45% of all donors (121/271) were from DCD donors in 2014 (1).

Known donor-specific risk factors for an increased number of procurement related injuries are higher donor age, higher BMI, donor after cardiac death (DCD) and male gender (2, 6, 12). Some risk factors have been identified as organ specific. In kidney procurements for example a higher injury rate was reported in case of a kidney-only procurement, compared to liver-kidney procurement. Also a kidney-only procurement performed by a surgeon with less experience (<30 organ procurements) is associated with more injuries whereas fewer injuries were seen in procurements where organs were procured by a center's own team, or in centers that perform more than 50 procurements annually (2, 8, 13).

A possible 'center effect' was also seen in pancreas procurement. Pancreata procured by non-pancreas transplanting centers were more often declined for transplantation, as were pancreata from centers with fewer procurements per year (14). Another study showed that locally procured liver grafts had less injuries than shipped ones (5).

Injuries in procured livers are reported in 10% to 34% (5, 10). The highest injury rate was reported in a study from The Netherlands, that revealed injury in 34% of all procured livers, of which 6.6% were clinically relevant (5). However, clinically relevant injury was not defined in this study. Lerut *et al.* report procurement related complications with a minor impact on the transplantation in 23% of all transplantations and problems with a major impact on the transplantation also in 23% (9). The lowest injury rate was reported in the UK, with injuries in 14% of the livers. The injury rate was based on information from the procuring team only (11).

Data on (non-critical) injuries related to pancreas procurement are sparse. However, the available data show that pancreas discard rates are the highest. Schulz reported that 8% of pancreatic grafts procured by teams that were not part of a pancreas transplant team were discarded for transplantation during back-table preparation(15). Decline after initial acceptance varies from 8% to 17% (10, 14, 15). Marang-Mheen *et al.* report that between 2002 and 2008 13% of pancreata in The Netherlands were declined after initial acceptance solely because of surgical injury(14).

Injuries in kidney procurement were reported between 7% and 21% (2, 12, 16, 17). The studies reporting the lowest incidences are often based on information of the procuring surgeon only and consequently might underestimate the actual number of injuries (2, 16). Anatomical injuries leading to disposal of kidneys was reported in the UK in 1% up to 3 % in the US (2, 18, 19).

This study aims to identify the incidence of procurement related injuries based on evaluations by both the procuring, as well as the accepting surgeon. Also, risk factors associated with procurement related injuries and 1- year graft survival of injured, but transplanted, grafts were investigated.

Methods

The data was derived from the QFs and provided by the NTS. The dataset includes all quality forms filled out between March 2012 and August 2013 for livers, pancreata and kidneys donated and accepted in The Netherlands. Organs procured for research or pancreata procured for islet-isolation were excluded. Organs that were accepted, but declined during procurement and subsequently not shipped, were also excluded. The data provided information about packaging, perfusion, arterial and venous anatomy, organ specific anatomy (gallbladder/ureter/duodenum) and parenchymal anatomy.

All possible graft quality assessment outcomes were labeled with scores. If no remarks and no injuries were reported, an organ was scored 'A'. In case there was a discrepancy between the forms filled out by both surgeons the judgement of the transplanting surgeon was considered leading. In these cases a 'B' score was given plus an additional score concerning the category of the discrepancy (packaging, damaging etc). A 'C' score indicates a possible preventable injury, such as; cut arteries, parenchymal tears, and injuries to the ureter. A 'D' score indicates a remark about an abnormality or damage like for example tumors, stenosis and trauma related injury of the organ. In both categories a distinction was made between transplantable organs (C1 and D1) and non-transplantable or discarded organs (C2 or D2) All other remarks, such as packaging issues or swapping of the kidneys, were labeled with an 'E' score (Table 1).

The response rate was determined and the available forms were labeled and these scores were counted as total and per center. The scores per organ were compared and analysed with a Chi-squared test to evaluate their performance. The possible association of injury and age, BMI, donor type and sex was analysed per organ and for all organs, using a logistical regression. A subgroup analysis was done for these factors and injury leading to discarding the organ (C2). Also, an analysis was performed by using a regression for the relation between a center's volume and the reported rate of injury (C1 + C2) in all organs and per organ. Standardized regression coefficients were shown.

Table 1. Quality Form scoring system

Category	Definition	Example
A	No abnormalities found by procurement surgeon and transplant surgeon	
B	Any differences on definitions or concerning anatomy	
C1	Possibly preventable injury, organ transplanted	Injured artery, vena or artery without patch
C2	Possibly preventable injury, organ not transplanted	Arterial or capsular injury or organ not properly flushed
D1	Abnormalities or non-procurement related damage, organ transplanted	Aneurysms, arterial stenosis
D2	Abnormalities or non-procurement related damage, organ not transplanted	Tumours, haematoma caused by initial trauma
E	Other remarks	Issues concerning packaging, number of bags, leakage.

The effect of procurement related injury on 1-year non death-censored graft survival was analysed using Kaplan-Meier estimates for all organs and for each organ separately (Log-rank testing). Graft failure was defined as the date of retransplant in liver, the date of re-start of exogenous insulin use in pancreas, the date of re-start of dialysis for kidney recipients or the date of death. Patients were considered lost to follow-up if there was no date of death, graft failure or 'last seen entered'. P-value below 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 22 or higher. The data used for this study is managed by the Dutch Transplant Foundation. The data management committee works according a protocol, focussing on the ethical principle of privacy protection. Approval of the use of the data is given by the data management committee of the Dutch Transplant Foundation on 28.05.2013.

Results

Between March 2012 and August 2013, 771 organs were accepted for transplantation. Of these, 17 organs were declined during procurement and subsequently not shipped (five livers, eight pancreata and four kidneys). Of all 754 accepted and shipped organs, 591 (78%) forms, both donation and transplantation, were filled out. These included 133 livers (23%), 38 pancreata (6%) and 420 kidneys (71%). Response rate for each organ was 87% (133 of 153) livers, 90% (38 of 42) pancreata and 75% (420 of 559) kidneys.

In 443 (75%) cases no procurement related injuries were reported (all scores except C1+C2). In 133 cases (23%) there was a discrepancy (score B) between the procuring and transplanting surgeons. Injuries leading to discarding of the organ were seen in 12 of 591 (2%) cases (score C2), or in 8% (12 of 148) of all injured organs (score C2 / score C1+C2). Scores are shown in Table 2.

Table 2. Scores per organ and as percentage of the number of organs

	Kidney (n)	%	Liver (n)	%	Pancreas (n)	%	Significancy (p)
A	270	64%	76	57%	28	74%	0.152
B	93	22%	30	23%	10	26%	0.946
C1	96	23%	35	26%	5	13%	0.134
C2	6	1%	1	1%	5	13%	**<0.001**
D1	11	3%	14	11%	0	0%	**0.001**
D2	5	1%	2	2%	1	3%	0.600
E	15	4%	4	3%	1	3%	0.710
Number of organs*	420		133		38		

*Multiple scores per organ were possible

Analysis of injury by organ group

In 136 cases (23%) injury was reported, not leading to discarding of the organ (C1 score). There was no significant difference between the organs. Score C2 (avoidable injury leading to organ discard) was registered in five of 38 (13%) in pancreas grafts, compared to six of 420 (1%) in kidneys and one of 133 (1%) in livers. This difference was statistically significant (p<0.001). Abnormalities or non-procurement related damages (D) were seen more often in liver grafts, compared to the other organs (p=0.001). All individual scores by organ group are shown in Table 3.

Risk factors associated with injury

Higher donor BMI was a significant risk factor for any procurement injury in all organs (OR 1.06, 95% CI 1.01 – 1.11, p=0.011). In a subgroup analysis, this effect remained significant only in kidney procurement (OR 1.06, 95% CI 1.01 – 1.11, p= 0.026). Furthermore, DCD donation appeared to be a risk factor for liver (OR 2.32, 95% CI 1.06 – 5.05, p= 0.034). Other OR's are shown in Table 3. Although not significant for all injuries in pancreas procurement (C1 + C2), DCD donation was a risk factor for injuries leading to discarding of the pancreas (C2 only) (OR 10.333, 95% CI 1.046 – 102.080, p=0.046).

Table 3. Odds ratios risk factors on injury per organ and for all abdominal organs combined

	Kidney		**Liver**		**Pancreas**		**Abdominal organs**	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
BMI	**1.059***	(1.007- 1.114)	1.065	(0.944-1.201)	1.207	(0.940-1.548)	**1.06****	(1.014-1.109)
Age	0.996	(0.981- 1.011)	0.999	(0.975-1.024)	1.002	(0.950-1.058)	0.997	(0.985-1.009)
Sex (F)	0.972	(0.617- 1.531)	0.598	(0.274- 1.304)	2.588	(0.461-14.529)	0.926	(0.636-1.348)
DCD	1.434	(0.797-2.015)	**2.316*****	(1.063- 5.045)	1.179	(0.392 -26.917)	1.434	(0.983-2.091)

* p=0.02; ** p=0.011; *** p=0.034

The relation between volume and injury

Centers that performed more procurements had fewer injuries (C category) in total. This relation was statistically significant for kidneys (C category) (OR=-0.91, p=0.012) and pancreata (OR= -0.95, p=0.013) (Table 4).

Table 4. Volume and injury percentage (C1+C2)

Center	All organs		Liver		Pancreas		Kidney	
	n	%	n	%	n	%	n	%
I	161	16%	37	22%	14	7%	110	15%
II	137	26%	29	31%	8	25%	100	24%
III	115	24%	30	30%	7	43%	78	21%
IV	97	25%	15	40%	5	40%	77	21%
V	76	45%	22	23%	4	50%	50	54%
VI	5	60%					5	60%
		r= -0.469		r= -0.672		r= -0.950		r= -0.910
		p= 0.067		**p= 0.214**		**p= 0.013**		**p= 0.012**

* The procurement teams (ZUTs) are based and related to their own center and are referred to as (procurement) center. The procurement team of center VI performed their last procurement in 2012.

Injury and outcome

Of all 591 included organs, 21 organs were not transplanted due to injury (C2, n=11), abnormalities or damage (D2, n=7), other reasons (E, n=2) or due to a combination of injury and non procurement related damage (C2+D2, n=1). 14 organs were excluded due to missing data. The remaining 556 organs were all transplanted, of which 131 organs had an injury (C1). Mean duration of follow up was 333 days. At 1 year, graft survival of repaired organs was 88.5% vs. 89.6% of unharmed and thus unrepaired organs (p=0.752). In the subset analysis of 408 kidneys (95 injuries) 1-year graft survival was 89.5% vs. 91.4% (p=0.550) and from 129 livers (34 injuries) survival was 85.3% vs. 83.2% (p=0.740).

Discussion

This is the first prospective study to include information on abdominal organs from both procuring and transplanting surgeons. It shows that a substantial number of organs are injured during procurement. The majority of these injured organs are however still repairable and do not have a significant decreased 1-year graft survival. Furthermore, several risk factors associated with procurement related injury were investigated.

There is a large discrepancy between the evaluation by the procuring and the transplanting surgeon (23%). The remarks from the transplanting surgeons are considered leading in this study since the procurement information can lead to an underestimation of injuries (2, 16, 17). There are several possible explanations for the frequent disagreement. The inspection performed by the accepting surgeon could be more thorough and is frequently performed under optimal circumstances. Vascular anomalies for example may only become apparent after removal of excessive, hilar fat. It is also possible that the accepting surgeon handles stricter evaluation criteria or that specific aspects are overlooked by the procuring surgeon when he/she has no or little experience with transplanting that organ. Failure to report injuries could be due to reporting bias, where negative results tend not to be reported.

We realize that the scoring system might be subjective and there could be an inter-observer variability between accepting surgeons or centers because the results are influenced by own preferences. The accepting surgeon however, may be seen as a more objective observer than the procuring surgeon himself. In 77% of all procured organs there was no discrepancy both surgeons. Both the dual evaluation, as well as the relatively high return rate (78%) adds to the reliability of the results (14, 17). The forms are to be filled out by the accepting surgeon after acceptance has been confirmed with Eurotransplant. Thus, forms could theoretically not be filled out because of decline during or before shipment or forgotten despite the system's reminders.

Injuries are reported in 25% of the organs, and are seen about equally in all organs (liver 27%, pancreas 26% and kidney 24%). The specific donor characteristics in The Netherlands with a high percentage of DCD (53% in this study) and older donors could have influenced the injury rates (1). The rather high number of injuries consists mostly of non-critical injuries (C1) and could well be a result of the strict criteria that we used. For example, missing of venous and/or arterial patches was considered non-critical injury.

Our results do not show inferior 1-year graft survival for patients transplanted with an injured (repaired) organ. The clinical significance of these non-critical injuries might therefore be questioned. Studies on post-transplantation outcome of injured organs are ambiguous. A German study showed that only 3.7% of all (non-critical) injuries led to clinically significant outcomes, such as extension of the surgical procedure and other complications. However, a study in the UK did not show any statistical significant differences in 1 or 3 year survival (2). Most studies focus on injury in general where there might be subgroups of injury associated with inferior outcomes. Arterial injuries for example might have a higher impact than parenchymal injuries. These findings underline the importance of a clear definition on procurement related injuries and consensus has to be achieved in the future.

As the definition of non-critical injuries(C1) and its effect on post-transplantation are not clear it would be logical to focus on the injuries leading to discarding of the organ (C2).

In this study 12 organs (2%) are discarded because of surgical injury. This indicates a high procurement quality, especially for the kidneys (1%) and livers (1%). Pancreata were significantly more often critically injured (13 %, $p<0.001$). These findings corroborate with international literature; injured and discarded organs are often procured from high-risk donors (10), and the pancreas is an easily, critically injured organ (20). This may be due to its retroperitoneal position and the unfamiliarity of pancreas transplantation by most (explanting) surgeons. Clearly, procurement of the pancreas requires special expertise (21).

The reported low discarding rate of these organs are based on the filled-out quality forms with a return rate of 78%. The remaining 22% missing quality forms include 163 organs (20 livers, 4 pancreata and 139 kidneys). Of these, eight organs (5%) are not transplanted, including 0 livers, two pancreata and six kidneys. Both pancreata and 5 kidneys were declined because of donor quality (score D2). One kidney was declined due to surgical injury to the ureter (score C2), however a quality form was not filled out. Sometimes, organs were declined during procurement and subsequently not shipped (five livers, eight pancreata and four kidneys). Of course, these organs were not inspected by a transplanting surgeon and evaluated solely by the procuring surgeon. This evaluation was potentially biased, and surgical injuries might be slightly underestimated.

We analysed the association of individual risk factors with injury during procurement. An increased donor BMI was associated with injury in general. This association was significant in kidney procurements, but did not reach significance in pancreas and liver procurements. Higher BMI might obstruct intra-operative view and subsequently lead to more injuries. Furthermore, donation after cardiac death (DCD) was a risk factor for injury to the liver during procurement, as was also shown by Ausania *et al.* (11).

This study also shows that a higher center procurement volume is protective for kidney and pancreas injuries related to the procurement. This finding is in concordance with previous results (2, 16, 17, 21). Most studies on this ‘center’ effect do focus however on outcome after transplantation. They mostly report an inferior outcome in the smallest transplantation centers and again a small decline in outcome in the very high volume centers. It could very well be that this inferior outcome in the low volume centers in procurement and transplantation is caused by the same ‘mechanism’. This could be the experience of the surgeons, the supporting OR-teams or the experience of the supportive physicians.

The number of procurement centers in The Netherlands has already been decreased from 7 procurement centers to 5 procurement teams prior to the studied period. Our results support this development and poses the question whether procurement surgery or expertise should be centralized even more.

Conclusions

This study shows a high standard of organ procurement quality in The Netherlands with low discard rates due to procurement related injuries. We identified higher BMI as a risk factor for injury in abdominal organs and DCD as a risk factor in livers. A higher procurement volume per center is associated with less injuries. The (repaired) injuries did not have a statistical significant effect on 1-year graft survival. The quality form system continues to monitor the procurement quality and may lead to further improvement of the whole process.

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