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Organ transplantation in Switzerland: impact of the new transplant law on cold ischaemia time and organ transports

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Summary

Background: On 1 July 2007 a new transplant law came into force in Switzerland. The principal item of this new law is the change from centre-oriented allocation to patient-oriented national allocation of organs. The aim of the present study is to assess the impact on cold ischaemia time (CIT) and transport requirements.

Methods: From 1 July 2006 to 30 June 2008 168 brain-dead donors were registered by Swisstransplant in Switzerland. Donors have been analysed in a retrospective cohort study design. Donor characteristics, transportation requirements and CIT were assessed from the Necroreport.

Results: 74 donors (44%) were allocated in the period before the introduction of the new law (period A) and 94 donors (56%) after the new law. Donor characteristics were similar. In period A, 114 organs (37.9%) were allocated within the procurement centre, compared to 54 organs (15.5%) in period B. Transport time for liver and kidney was remarkably longer in period B. Overall, CITs remained largely stable except for a significant increase of nearly 115 minutes in the liver graft median CIT ($p < 0.01$).

Conclusions: The new Swiss transplant law clearly entails an increase in the frequency of organ transports. Overall CIT is not affected. However, liver transplantation is afflicted by an increase in transports and CIT. This may affect midterm outcome and should therefore be followed closely.

Key words: cold ischaemia; allocation modality; transplantation, organ

Introduction

In Switzerland, there are about 80 brain-dead organ donors each year, which is 10 to 12 brain-dead organ donors per million habitants per year (pmhb/y). The surrounding countries, in comparison, have 20 to 25 organ donors pmhb/y. Along with living donation and a small number of imported organs, this results in approximately 450 transplanted organs per year in Switzerland. Currently, around 1000 patients are listed on the national waiting list for organ transplantation (www.swisstransplant.org).

In 2004, a new transplant law was passed by the Swiss Federation and came into force on 1 July 2007. The principal item of this new law was the change from centre-oriented allocation to patient-oriented national allocation of organs. Before the introduction of this new law, patients on the waiting list of a centre with an organ donor were preferentially treated compared to patients on waiting lists in other hospitals.

This distribution practice led to the situation that patients from centres with many donors had shorter waiting lists and therefore shorter waiting times for organ transplantation than subjects from centres with small donor numbers.

In the context of the new law, different Swisstransplant organ working groups (experts from the involved organ transplantation programmes in Switzerland), have helped to define algorithms whereupon organs are assigned to patients. These algorithms consider medical urgency, medical benefit and time on the waiting list as the three most important criteria.

A specialised computer system, the Swiss Organ Allocation System (SOAS), was introduced at the time the new law came into effect. This contains the demographic and medical data of patients on the waiting list and potential donors are also entered into the system. The allocation of organs then takes place in accordance with the defined algorithm. Swisstransplant, as the Swiss National Foundation for organ transplantation, has the mandate of the Swiss Federation to carry out the allocation of organs in compliance with the law.

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On the basis of the new national allocation modalities, one must anticipate an increased transportation of organs that could have a negative impact on the cold ischaemia time (CIT) of the organs, which is one of the key aspects when looking at outcome data. It is well-known that a longer CIT has a direct negative influence on the outcome of the transplantation [1–4].

Patients and methods

In the period from 1 July 2006 to 30 June 2008, a total of 168 brain-dead donors were registered and allocated by Swisstransplant in Switzerland. Donors have been analysed in a retrospective cohort study design, based on the respective documents of Swisstransplant.

Alongside the demographic data, the cause of death that ultimately led to brain death was determined. For all of these donors, all organs and their associated medical diagnostics were examined and the allocation practice was analysed. Reasons for rejecting certain organs offered for transplantation were likewise evaluated for the individual transplantation centres.

The transport and ischaemia times were taken from the allocation dossiers, especially the Necroreport, in the period up to 30 June 2007. After that, all data were obtained from SOAS.

The results were examined for the total period, as well as for the 12 months before (1 July 2006 to 30 June 2007, period A) and the 12 months after (1 July 2007 to 30 June 2008, period B) the new transplant law came into effect.

Statistics

Variables for CIT did not show a normal distribution, and a non-parametric analysis was performed. Comparisons between period A and B were performed by Mann-Whitney test. A p-value <0.05 was considered significant.

Results

A total of 168 donors were analysed. 74 donors (44.0%) were announced and allocated in the 12 months before the introduction of the new law (period A) and 94 donors (56.0%) after the new law (period B). Donor characteristics did not differ between period A and B. Average age was 51.0 ± 17.6 (1 SD) years in period A, compared to 49.5 ± 19.5 years in period B. The underlying diagnosis for the cause of brain death was cerebral haemorrhage in around 50% of the patients in both time periods (table 1). There was no significant difference in the detection and procurement hospitals during the study period, with persistent regional differences in the incidence of donor detection in both time periods.

The number of removed organs per donor remained more or less stable in the examined time periods, with 4.1 organs per donor in period A, compared to 3.7 organs per donor in period B. Consent to donate organs was given almost exclusively by relatives (161 consents, 96%) in the entire period examined, although Switzerland's Federal Office of Public Health (FOPH) is making great efforts to encourage more citizens to fill in organ donor cards and declare their intentions in this way.

Overall, 650 organs were allocated: 301 organs in period A, out of which 114 organs (37.9%) were allocated within the procurement centre, and 349 organs in period B, out of which 54 organs (15.5%) were allocated within the procurement centre. Therefore, overall organ transport increased during the study period from 62.1% in period A to 84.5% in period B. While transport time for liver and kidney grafts was remarkably longer in period B, the overall CIT remained fairly stable, except for livers.

Table 1

Donor characteristics, causes of death and procurement and transport modality for period A (n = 74; 44%) and period B (n = 94; 56%).

	Period A		Period B	
	1.7.2006–30.6.2007		1.7.2007–30.6.2008	
No. of donors	74	44.0%	94	56.0%
Average age (y) (±1 SD)	51.0 ± 17.6		49.5 ± 19.4	
Male gender	40	54.1%	55	58.5%
Cause of death				
Intracranial haemorrhage	39	52.7%	46	48.9%
Craniocerebral trauma	17	23.0%	18	19.1%
Ischaemic-hypoxic brain damage	11	14.9%	14	14.9%
Cerebral infarction	4	5.4%	5	5.3%
Suicide	2	2.7%	1	1.1%
Tumours	0	0.0%	1	1.1%
Others	1	1.4%	9	9.6%
Procurement and transport				
No. of organs allocated	301	46.3%	349	53.7%
Transport of organs	187	62.1%	295	84.5%

Heart

In both time periods hearts were procured and transplanted from about one third of the donors. The average age of heart donors was 41.4 years in period A and 37.8 years in period B. Around three quarters of the donors were male. The causes of death did not differ substantially from that of overall donors. Echocardiography was performed in 82.1% of the donors in period A, compared to 77.4% in period B. Coronary angiography de-

Table 2

Results displayed by type of organ.

	Period A		Period B		*p-value*
	1.7.2006–30.6.2007		1.7.2007–30.6.2008		
Heart					
No. of hearts allocated	28	37.8%	31	33.0%	
Average age donor (y)	41.4		37.8		
Median CIT (min)	162 (IQR† 123–215)		179 (IQR 131–210)		0.596
Average duration of transport (min) (±1 SD)	39.3 ± 31.3		43.5 ± 33.7		
Tx at the site of procurement	5	15.2%	5	12.2%	
Average age recipient (y)	47.0		44.3		
Early mortality*	4	12.1%	4	9.8%	
Lungs					
No. of lungs allocated	33	44.6%	41	43.6%	
Average age donor (y)	45.7		43.7		
Median CIT (min)	285 (IQR 240.5–340.5)		272.5 (IQR 220–326.5)		0.420
Average duration of transport (min) (±1 SD)	53.5 ± 66.0		51.2 ± 34.6		
Tx at the site of procurement	7	21.2%	3	7.3%	
Average age recipient (y)	44.1		48.9		
Early mortality*	0	0.0%	1	2.4%	
Liver					
No. of livers allocated	67	90.5%	76	80.9%	
Average age donor (y)	51.7		49.6		
Median CIT (min)	363 (IQR 253–505)		477.5 (IQR 391.5–555.5)		0.005
Average duration of transport (min) (±1 SD)	26.7 ± 45.2		74.8 ± 57.7		
Tx at the site of procurement	33	49.3%	16	21.1%	
Average age recipient (y)	49.5		48.1		
Early mortality*	1	1.5%	3	3.9%	
Kidney left					
No. of left kidneys allocated	70	94.6%	88	93.6%	
Average age donor (y)	50.5		49.0		
Median CIT (min)	690 (IQR 533–900)		600.5 (IQR 490.5–832)		0.296
Average duration of transport (min) (±1 SD)	46.7 ± 74.5		96.0 ± 64.4		
Tx at the site of procurement	32	45.7%	12	13.6%	
Average age recipient (y)	52.1		50.5		
Return to dialysis	3	4.3%	7	8.0%	
Kidney right					
No. of right kidneys allocated	72	97.3%	88	93.6%	
Average age donor (y)	50.9		48.5		
Median CIT (min)	617 (IQR 500–773)		695 (IQR 527.5–889.5)		0.162
Average duration of transport (min) (±1 SD)	56.7 ± 78.1		95.2 ± 66.1		
Tx at the site of procurement	29	40.3%	13	14.8%	
Average age recipient (y)	52.5		50		
Return to dialysis	2	2.8%	11	12.5%	
Pancreas and Islets					
No. of pancreas and islets allocated	31	41.9%	25	26.6%	
Average age donor (y)	41.5		39.9		
Tx at the site of procurement	8	25.8%	5	20.0%	
Average age recipient (y)	49.2		46.7		

* 24–72 hours post transplantation
† IQR, interquartile range

creased slightly from 46.4% in period A to 35.5% in period B. The new law had no impact on the incidence of transports of hearts with 17.9% in period A and 16.1% in period B being transplanted in the procurement centre. Therefore, median CIT remained relatively stable with 162 min in period A, compared to 179 min in group B. Duration of transport, mostly by helicopter, was kept very low at 39.3 ± 31.3 min in group A and 43.5 ± 33.7 min in group B (table 2).

The average age of heart recipients decreased from 47.0 in period A to 44.3 years in period B. The youngest recipient in period A was 10 years old and the oldest 65. In period B, the youngest was 9 years old and the oldest 68. Three days after transplantation, 60.7% of recipients in period A were in a good to very good condition, 12.1% of heart recipients had died. The numbers were similar in period B with 67.7% in a good to very good condition, and 9.8% who had died (table 2).

Lung

The number of the transplanted lungs remained stable; lungs were retrieved from approximately 44% of all organ donors. No difference was found looking at age and the cause of death of lung donors. Less preprocurement investigations were performed in period B, with bronchoscopy in 19.5% compared to 30.3% in period A. Concerning organ transport, 21.2% of lungs were transplanted in the procurement centre in period A, while in period B only 7.3% of lungs remained in the same hospital. However, the transport time decreased on average by approximately 24 minutes; the CIT of the transported organs was likewise reduced by about 18 minutes (data not shown in table).

The average age of recipients of lung transplants climbed from period A to B, with an increase on average of 4.8 years. The minimum and maximum ages were approximately similar. The short-term outcome after transplantation was slightly worse in period B. Shortly after the operation, 78.8% of the patients' conditions were described as good to very good in period A, whilst in period B, 70.7% of the patients were in good to very good condition, and one patient had died.

Liver

The number of livers transplanted in relation to the number of donors decreased slightly in period B, but it remained higher than 80%, which makes the liver the most transplanted organ next to the kidney.

The average age of liver donors remained stable at approximately 50 years in both periods. There was an equal number of male and female liver donors in the first period, but in period B the ratio was 65% men and 35% women.

Preoperative diagnostic studies for liver transplantations primarily consist of ultrasounds and biopsies. A sonography was performed in 100% of the liver donors in period A and in 91% in period B. Biopsies were taken in approximately 15% of cases in both periods.

In Switzerland, liver allocation is mainly based on the MELD-system. The number of transported livers increased following the introduction of the new law with only 21.1% of the livers remaining in the donor centre in period B compared to 49.3% in period A.

The transport times increased from period A to period B on average from 26.7 to 74.8 minutes. The overall CIT of livers was 363 min in period A, compared to 477.5 min in period B ($p < 0.01$). The CIT of transported livers was also longer: on average 507.4 min in period B, as compared to 452.9 min in period A (data not shown in table).

The average age of recipients of liver transplants was close to 50 years in both time periods. With respect to the short-term results of the liver transplantation, an increase was seen in the number of patients described as staying in good condition. However, the number of deaths shortly after the operation increased from one patient (1.5%) in period A to three patients (3.9%) in period B (table 2).

Kidney

Kidneys were procured from almost all donors and subsequently transplanted; 95.9% in period A and 93.6% in period B.

The average age of kidney donors was around 50 years; the sex distribution showed a small predominance of male donors. Cerebral haemorrhage and traumatic brain injury again constituted the cause of death of a high proportion of kidney donors, and approximately 15% of kidney donors had died from anoxic brain damage in each period.

A sonography was conducted preoperatively in 100% of the cases in both periods. A CT-scan was carried out in 5% and biopsies were necessary in approximately 2% of kidney donors in both time periods.

The number of transported kidneys increased from period A to B. The proportion of kidneys transplanted in the same centre was 14.2% in period B, but in period A this was as high as 43% (percentage of right and left kidneys combined). The introduction of the new law had a considerable impact on the average transport time which nearly doubled from 51.7 min (period A) to 95.6 min (period B).

The average age of kidney recipients remained stable at approximately 50 years in the observed periods. The immediate postoperative short-term outcome showed 84.5% of the transplanted kidneys with a good function in period A and 72.7% in period B.

Pancreas

In relation to the number of donors, fewer pancreas transplantations were performed in period B (26.6%) than in period A (41.9%). Both, the number of whole organ pancreas transplantations and the number of the islet transplantations de-

creased. The ratio of islet vs pancreas transplantations decreased slightly from 61% to 56%, comparing period A to period B. The average donor age was approximately 40 years in both periods. CIT as well as average transport time decreased from period A to B (data not shown in table).

Recipients of pancreas or islets were on average approximately 47 years old. A few days postoperative, a good result was registered by transplantation centres in 83.9% of cases in period A and 75% in period B.

Discussion

The new Swiss transplant law, which came into force on 1 July 2007, primarily concerns organ allocation between Switzerland's six transplantation centres (Basel, Berne, Zurich, Geneva, Lausanne and St. Gallen). The key determining criteria for national organ allocation are the following: medical benefit, medical urgency and time on the waiting list. However, the transition from centre-oriented allocation to patient-oriented national organ allocation caused a considerable amount of debate. Therefore, a careful monitoring of this transition period is mandatory, because more than 1000 patients are presently on the waiting list and thus affected directly by the change in allocation policy. The data presented in this study, including characteristics of recipients, provide a unique opportunity to analyse the impact on organ allocation modality in the early stages of new law.

The geographical origin of donors is a topic that has been discussed for a long time in Switzerland since clear regional differences are obvious. There are strong donor cantons and/or transplantation centres, mainly Berne, Tessin and St. Gallen. Waadt and Geneva are average, while Zurich as the most populous canton and Basel have only few donated organs in the analysed time period. However, new structures that have been put in place together with the new transplant law are intended to increase the number of organ donors in Switzerland in the middle-term. Regional networks have been established with improved structures on intensive care units to improve donor detection and announcement.

Representatives of the Swiss Society of Intensive Medicine and regional networks have joined Swisstransplant in a national committee of organ donation (CNDO) with the objective of establishing national guidelines and structures to support organ donation in Switzerland.

No differences concerning donor characteristics were observed between the two study periods. This was to be expected as the new transplant law exerts no influence here.

Compared to other European countries, the number of procured organs per donor is very high in Switzerland, with an average of 4.1 organs per donor in period A and 3.7 in period B. This is probably due to a complete assessment of organ function, allowing an extended organ retrieval rate. The typical donor is a man of 50 years who has died from a cerebral haemorrhage or a traumatic brain injury.

Notably more organ transports were necessary under the new transplant law, rising from 62% in period A to 85% in period B. In order to keep CIT short, organ transports by helicopter were more often required in period B, leading to a pronounced increase in transportation costs. Yet, the new transplant law had no impact on the frequency of transports and CIT in heart transplantations. Median CIT remained relatively short (approx. 180 min), which is very important in order to improve the outcome [3]. More than 85% of all donor hearts in both periods required transportation, because procurement and transplant centres were different.

For lungs, a clear increase in transport requirement was observed (from less than 80% in period A to above 90% in period B). Despite this increase, average transport time and median CIT were slightly reduced. The increase of need for transportation for liver transplantation was even more pronounced. In period A, only 50% of the livers were transported; in period B, the transport requirement increased to nearly 80%. This is due to the fact that in period A, the centres with a liver transplant programme practiced centre-oriented allocation, which is no longer tolerated under the new law. However, as mentioned in a recent study, especially in older donors, expanding regional sharing of liver allografts should be regarded with caution [4, 5]. Median CIT in liver transplantation increased by nearly 115 minutes in period B, amounting to almost eight hours. Several studies have shown that CIT is an independent risk factor for the development of delayed graft function and primary nonfunction in liver transplantation [4, 5]. Recipient survival was shown to be adversely affected by a CIT of more than 12 hours in a European survey and more than 10 hours in a US survey [6, 7]. Liver grafts from elderly donors and/or donors with steatosis are even more affected by prolonged CIT and preservation injury. In this group, the best graft function can be achieved when CIT is kept below eight hours [8]. During the last decade, CIT has been reduced in European centres from 570 to 470 minutes on average, which is slightly below the reported range in period B. Looking at the average CIT of 507 minutes in transported livers in period B, CIT is fairly high, taking into account that Switzerland is a small country with excellent logistics. Combined with the increasing age of liver donors in Switzerland, outcome may be affected in non-

properly selected donors as mentioned in a recent study [9].

A similar shift in allocation practice was observed in kidney transplantation, where less than 60% of the kidneys were allocated to a different centre in period A, compared to over 85% in period B. Overall CIT in the two periods was similar, despite the remarkably higher need for transport in period B. No changes were observed in pancreas and islet transplantation.

It can therefore be concluded that the new Swiss transplant law clearly entails an increase in the frequency of organ transports. Overall CIT is not affected, which is mainly due to short distances and excellent logistics in Switzerland. However, liver transplantation is afflicted by an increase in transports and a significantly longer median CIT. This may affect mid-term outcome and should therefore be followed closely.

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