

Assessing the potential of international organ exchange – the Swiss experience

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Received 8 June 2010; received in revised form 10 January 2011; accepted 4 February 2011; Available online 12 March 2011

Abstract

Objective: Little is known about the impact of international organ exchange on national transplant programmes. This study evaluates the relevance of hearts and lungs offered by the European Organ Exchange Organisations to Swisstransplant, Switzerland's national organ procurement organisation. **Methods:** The study is a retrospective analysis of donor characteristics of 290 hearts and 199 lungs, offered by the European Organ Exchange Organisations between 1 January 2004 and 31 December 2008 to Swisstransplant. It assesses the responses (acceptance/reasons for refusal) from the Swiss heart and lung transplant centres. **Results:** Among the 290 hearts offered by the foreign transplant organisations, eight (2.8%) were accepted by a Swiss transplant centre. This corresponds to 5.8% of the Swiss heart transplant activity during the observation period. In the lung group ($n = 199$), five (2.5%) were accepted, equalling 2.8% of the transplant activity. As for the reasons for refusal, approximately one-fifth and one-sixth of both the heart and lung offers were refused for medical and logistic reasons, respectively. For more than half of the offers, there was either no compatible recipient on the Swiss waiting list, or the reason for refusal was not specified. Notably, 47.6% of the offers in the heart group and 46.7% of the lung offers originated from donors aged less than 16 years. **Conclusions:** International organ exchange is a very valuable and effective way to allocate a maximum of medically suitable organs to recipients on the waiting list. Organ exchange is lifesaving, especially in children, and also in patients with rare blood groups. A professional structure within the national organ procurement organisations, and a close cooperation between them on an international level, is crucial to achieve organ exchange on a high-quality level in Europe.

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Keywords: Transplantation; International organ exchange; Switzerland; Heart; Lung

1. Introduction

Sometimes it is said that organ transplantation is a victim of its own success, as demand of organs exceeds supply by far. While organ donation rates remain mostly stable (even though they vary greatly among different countries), the number of patients on national waiting lists is steadily growing. In terms of an optimal use of scarce organs, international organ exchange seems to be a valuable way to partially alleviate organ shortage and reduce waiting list mortality [1]. Regrettably, cold ischaemia time in thoracic organs remains one of the major limiting factors in transplantation and, hence, restricts the feasibility of long-distance procurements [2–4]. In the future, advances in machine perfusion techniques may permit longer preservation times, thus enabling prolonged transportation.

Organ exchange among the European Organ Exchange Organisations (EOEO) takes place if there is no suitable recipient on the offering country's waiting list. Yet, little is known about the impact of organ exchange on national transplant programmes [1,5,6]. Thus, the purpose of our study was to evaluate the relevance of the so-called 'foreign offers' (FOs) for the Swiss heart and lung transplant programmes. We therefore analysed the quota of effectively transplanted grafts, as well as the transplant centres' reasons for refusal of the offered organs.

2. Materials and methods

We retrospectively analysed donor characteristics of 290 hearts and 199 lungs, offered by the EOEO between 1 January 2004 and 31 December 2008 to Swisstransplant (Switzerland's national organ procurement organisation). The EOEO is a group of organisations from within a number of countries in Europe that agree to offer organs, for which no recipient in the country of origin can be found, to other European countries. The members of the EOEO are UK Transplant

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(United Kingdom), ABM (Agence de la biomédecine, France), ONT (Organización Nacional de Trasplantes, Spain), OPT (Organização Portuguesa de Transplantação, Portugal), CNT (Centro Nazionale Trapianti, Italy), Swisstransplant (Switzerland), Eurotransplant (Austria, Belgium, Croatia, Germany, Luxemburg, the Netherlands and Slovenia), Scandiatransplant (Denmark, Finland, Iceland, Norway and Sweden), Poltransplant (Poland), HNOT (Greece), Balttransplant (Estonia, Latvia and Lithuania), Hungary, the Czech Republic and Romania.

During the study period, heart transplantations were carried out in Switzerland in the following University hospitals: Basel, Bern, Geneva, Lausanne and Zürich; and lung transplantations in Geneva, Lausanne and Zürich.

Data were extracted from the archived donor information forms. The donor characteristics included age, sex, blood group, height, weight, cause of death and serologies. Information about echocardiography and coronary angiography of the hearts were included. Among the lungs, additional data consisted of chest X-ray, chest computed tomography (CT) scan, information about lung diseases, blood gas values and laboratory tests.

As the age of the heart and lung donors did not show a Gaussian distribution, we decided to perform separate analyses for offers from donors aged <16 years and ≥16 years.

Finally, the offers were classified as transplanted, revoked or refused. As international allocation takes place according to the 'first come, first served' principle, the revoked group contains the offers that were accepted by another country's transplant organisation before the Swiss transplant centres had decided whether to accept the offer or not. In the 'refused offers' group, we evaluated three reasons for refusal:

(1) Medical reasons:

This category consists of organs that were not accepted either because of their bad quality or due to a lack of

additional investigations, such as echocardiography or percutaneous coronary angiography (PCA).

(2) Logistic reasons:

Offers in this category were not accepted either because the transport distance was too long, if meteorological conditions prevented flying, or because no operating team was available.

(3) No compatible recipient/no data available:

This category contains offers that were refused either because there was no suitable recipient on the Swiss waiting list or if the transplant centres had not specified the reason for refusal.

If the transplant centres gave divergent reasons for refusal of an offered organ, the offer was counted once in each category. Due to the considerable amount of missing data, we refrained from statistically analysing the 'no compatible recipient/no data available' category.

2.1. Description of the offering procedure

The members of the EOEO offer organs, for which there is no suitable recipient on the offering country's waiting list, to the other organisations. The offers are received by fax, which is transmitted to all organisations simultaneously. The national transplant organisations then contact the transplant centres, which decide whether to accept the offer or not. If the probability of an acceptance of the offer is high, the transplant coordinator may express the enhanced interest in allocation by a so-called 'interest call' to the offering organisation, to intensify collaboration. As mentioned above, the organ is finally allocated to the transplant organisation that accepts the offer first.

Table 1. Heart offers: donor characteristics and reasons for refusal.

	Heart offers			Reasons for refusal	
	Total	Transplanted	Revoked	Medical	Logistic
Number	290	8 (2.8%)	12 (4.1%)	58	45
Age (years; median, IQR ^a)	16 (IQR 4–45)	23 (IQR 15–33.3)	22.5 (IQR 10.8–38.8)	44.5 (IQR 29.3–54.8)	47 (IQR 37–54)
<16 years (n, % of n in category)	138 (47.6%)	3 (37.5%)	5 (41.7%)	7 (12.1%)	4 (8.9%)
≥16 years (n, % of n in category)	148 (51.0%)	5 (62.5%)	7 (58.3%)	51 (87.9%)	41 (91.1%)
n/a	4 (6.0%)				
Sex (number, % of number in category)					
m	117 (40.3%)	3 (37.5%)	4 (33.3%)	23 (39.7%)	13 (28.9%)
f	159 (54.8%)	5 (62.5%)	8 (66.7%)	35 (60.3%)	32 (71.1%)
n/a	14 (4.8%)				
Height (cm; median, IQR)	158 (IQR 112.5–166)	165.5 (IQR 146.8–67)	158.5 (IQR 145–165)	167 (IQR 160–175.3)	165 (IQR 160–170)
Weight (kg; median, IQR)	50 (IQR 17–70)	55 (IQR 48.7–70)	47.5 (IQR 38.3–60)	70 (IQR 55–9.3)	65 (IQR 58–0)
Blood type (n, % of n in category)					
A	113 (39.0%)	1 (12.5%)	7 (58.3%)	21 (36.2%)	22 (48.9%)
AB	62 (21.4%)	2 (25.0%)	0 (0.0%)	7 (12.1%)	7 (15.6%)
B	59 (20.3%)	2 (25.0%)	1 (8.3%)	9 (15.5%)	6 (13.3%)
O	54 (18.6%)	3 (37.5%)	4 (33.3%)	21 (36.2%)	10 (22.2%)
Cardiovascular risk factors (yes/no/not available, in % of n in category)					
Nicotine abuse	20.7%/30.0%/49.3%	25%/62.5%/12.5%	8.3%/16.7%/75%	39.7%/20.7%/39.7%	44.4%/20.0%/35.6%
Hypertonia	6.9%/29.0%/64.1%	12.5%/37.5%/50%	0%/16.7%/83.3%	3.4%/41.4%/55.2%	11.1%/22.2%/66.7%
Diabetes mellitus	2.1%/33.1%/64.8%	0%/62.5%/37.5%	0%/16.7%/83.3%	5.2%/43.1%/51.7%	4.4%/24.4%/71.2%

^a IQR, interquartile range.

2.2. Statistics

Results are shown as mean values and first standard deviation (± 1 SD), if not otherwise specified.

3. Results

3.1. Heart

3.1.1. Donor characteristics

The donor characteristics of the heart offers are displayed in Table 1. Notably, 138 (47.6%) of the donors were aged <16 years versus 148 (51%) ≥ 16 years (in four donors, no record of the age was available).

3.1.2. Serologies and checks

Table 2 shows the serological findings of the offered hearts, whilst Table 3 provides information on whether the donors were reanimated, if inotropic support was required, and whether an echocardiogram and/or a PCA was available.

3.1.3. Transport distance

The distribution of the transport distances of the offered hearts is shown in Table 4. All hearts allocated to the Swiss transplant centres came from a radius of <1000 km, and six out of eight organs were procured within a radius of <500 km. The accepted offers originated from the German (Euro-transplant), French (ABM), Italian (CNT) and UK (UK Transplant) transplant organisations.

3.1.4. Accepted offers

Among the 290 hearts offered by the foreign transplant organisations, eight (2.8%) were accepted by the Swiss transplant centres (Table 1). This corresponds to 5.8% of the Swiss heart transplant activity during the observation period [7].

Table 2. Heart offers: serologies.

HIV		
pos	0	(0.0%)
neg	215	(74.1%)
n/a	75	(25.9%)
HBV		
pos	5	(1.7%)
neg	211	(72.8%)
n/a	74	(25.5%)
HCV		
pos	12	(4.1%)
neg	205	(70.7%)
n/a	73	(25.2%)
CMV		
pos	84	(29.0%)
neg	101	(34.8%)
n/a	105	(36.2%)
EBV		
pos	6	(2.1%)
neg	2	(0.7%)
n/a	282	(97.2%)
Troponin		
Normal level	43	(14.8%)
Increased level	26	(9.0%)
n/a	221	(76.2%)
CK/CK-MB		
Normal level	24	(8.3%)
Increased level	23	(7.9%)
n/a	243	(83.8%)

Abbreviations: HIV, human immunodeficiency virus; HBV, hepatitis B virus; HCV, hepatitis C virus; CMV, cytomegalovirus; EBV, Epstein-Barr virus; CK, creatinine kinase; CK-MB, creatinine kinase myocardial type.

3.1.5. Refused offers

Table 1 also shows the number and donor characteristics of the heart offers refused for medical or logistic reasons. Due to the substantial share of missing data, the 'no compatible recipient/no data available' category has not been analysed statistically, and it therefore does not appear in the table.

Table 3. Heart offers: checks.

	Total (n = 290)		Transplanted (n = 8)	
Reanimation				
Yes	59	(20.3%)	3	(37.5%)
No/not available	231	(79.7%)	5	(62.5%)
Inotropic support				
Yes	200	(69.0%)	7	(87.5%)
No/not available	90	(31.0%)	1	(12.5%)
Echocardiogram				
Available	179	(61.7%)	8	(100%)
Not available	111	(38.3%)	0	(0%)
Ejection fraction available	100	(34.5%)	7	(87.5%)
Ejection fraction not available	190	(65.5%)	1	(12.5%)
Ejection fraction; median in %, IQR*		63 (IQR 60–70)		65 (IQR 61–67.5)
Pathological findings	30	(10.3%)	2	(25%)
Percutaneous coronary angiography				
Available	6	(2.1%)	1	(12.5%)
Not available	284	(97.9%)	7	(87.5%)
Ejection fraction available	4	(1.4%)	1	(12.5%)
Ejection fraction not available	2	(0.7%)	7	(87.5%)
Ejection fraction; median in %, IQR		62.5 (IQR 58.8–67.3)		65
Pathological findings	1	(0.3%)	0	(0%)

* IQR, interquartile range.

Table 4. Heart offers: provenance.

0–499 km		
Offers	94	(32.4%)
Transplanted	6	(2.1%)
500–999 km		
Offers	120	(41.4%)
Transplanted	2	(0.7%)
1000–1499 km		
Offers	48	(16.6%)
Transplanted	0	(0.0%)
>1500 km or n/a		
Offers	28	(9.7%)
Transplanted	0	(0.0%)

3.1.6. Revoked offers

Due to the 'first come, first served' modality of the offering procedure, 12 (4.1%) heart offers for which, in principle, there could have been a recipient in Switzerland, were withdrawn before a Swiss transplant centre had accepted them (Table 1).

3.2. Lung

3.2.1. Donor characteristics

The donor characteristics of the lung offers are displayed in Table 5. As in the heart group, nearly half (46.7%, $n = 93$) of the offered lungs came from donors aged <16 years versus 53.3% ($n = 106$) ≥ 16 years.

3.2.2. Serologies and checks

Table 6 shows the serological findings for the offered lungs, and Table 7 provides information regarding the duration of mechanical ventilation, cardiac and/or respiratory arrest, as well as partial pressure of oxygen in the blood (PaO_2), partial pressure of carbon dioxide in the blood ($PaCO_2$) and pH values.

3.2.3. Transport distance

The distribution of the transport distances of the offered lungs is displayed in Table 8. Four (80%) of the lungs allocated

Table 6. Lung offers: serologies.

HIV		
pos	0	(0.0%)
neg	143	(71.9%)
n/a	56	(28.1%)
HBV		
pos	1	(0.5%)
neg	144	(72.4%)
n/a	54	(27.1%)
HCV		
pos	6	(3.0%)
neg	135	(67.8%)
n/a	58	(29.1%)
CMV		
pos	58	(29.1%)
neg	60	(30.2%)
n/a	81	(40.7%)
EBV		
pos	7	(3.5%)
neg	2	(1.0%)
n/a	190	(95.5%)

Abbreviations: HIV, human immunodeficiency virus; HBV, hepatitis B virus; HCV, hepatitis C virus; CMV, cytomegalovirus; EBV, Epstein-Barr virus.

to the Swiss transplant centres originated from within a radius of 500–1000 km, and one (20%) was procured within a radius of 1500 km. The accepted offers came from the French and UK transplant organisations.

3.2.4. Accepted offers

Among the 199 lung grafts offered by the foreign transplant organisations, five (2.5%) were accepted by the Swiss transplant centres (Table 5). This corresponds to 2.8% of the Swiss lung transplant activity during the observation period [7].

3.2.5. Refused offers

Table 5 also shows the number and donor characteristics of the lung offers refused for medical or logistic reasons. Due to the substantial share of missing data, the 'no compatible recipient/no data available' category has not been analysed statistically, and it therefore does not appear in the table.

Table 5. Lung offers: donor characteristics and reasons for refusal.

	Lung offers			Reasons for refusal	
	Total	Transplanted	Revoked	Medical	Logistic
Number	199	5 (2.5%)	7 (3.5%)	36	32
Age (years; median, IQR [*])	22 (IQR 3.3–46)	38 (IQR 35–54)	32 (IQR 12.8–38)	42 (IQR 27–56.5)	52.5 (IQR 38.3–59.5)
<16 years (n , % of n in category)	93 (46.7%)	0 (0.0%)	2 (28.6%)	4 (11.1%)	0 (0.0%)
≥ 16 years (n , % of n in category)	106 (53.3%)	5 (100.0%)	5 (71.4%)	32 (88.9%)	32 (100.0%)
Sex (number, % of number in category)					
m	112 (56.3%)	4 (80.0%)	5 (71.4%)	23 (63.9%)	23 (71.9%)
f	80 (40.2%)	1 (20.0%)	1 (14.3%)	13 (36.1%)	9 (28.1%)
n/a	7 (3.5%)		1 (14.3%)		
Height (cm; median, IQR)	162 (IQR 106–175)	180 (IQR 177–185)	174 (IQR 134–181)	173 (IQR 165–182)	179.5 (IQR 170–183.3)
Weight (kg; median, IQR)	56 (IQR 15–75.4)	85 (IQR 80–87)	75 (IQR 38–82.5)	75 (IQR 65–90)	77.5 (IQR 69.8–90)
Blood type (n , % of n in category)					
A	83 (41.7%)	3 (60.0%)	4 (57.1%)	19 (52.8%)	19 (59.4%)
AB	42 (21.1%)	0 (0.0%)	0 (0.0%)	3 (8.3%)	3 (9.4%)
B	32 (16.1%)	1 (20.0%)	1 (14.3%)	5 (13.9%)	4 (12.5%)
O	42 (21.1%)	1 (20.0%)	2 (28.6%)	9 (25.0%)	6 (18.8%)
Cardiovascular risk factors (yes/no/not available, in % of n in category)					
Nicotine abuse	18.6%/39.7%/41.7%	40%/40%/20%	0%/42.9%/57.1%	25%/27.8%/47.2%	46.9%/31.3%/21.9%
Hypertonia	6.0%/24.1%/69.9%	20%/20%/60%	0%/14.3%/85.7%	2.8%/30.6%/66.7%	15.6%/15.6%/68.8%

* IQR, interquartile range.

Table 7. Lung offers: mechanical ventilation, cardiac/respiratory arrest.

	Total (n = 199)	Transplanted (n = 5)
Duration of mechanical ventilation (days)	2.6 ± 2.0	2.0 ± 1.4
Cardiac arrest (number, percentage)		
Yes	30 (15.1%)	0 (0%)
No	110 (55.3%)	5 (100%)
Not available	59 (29.6%)	0 (0%)
Respiratory arrest (number, percentage)	10 (5.0%)	0 (0%)
PaO ₂ (in FiO ₂ 100%; in mmHg)	428.5 ± 107.3	414.7 ± 41.9
PaCO ₂ (in mmHg)	37.0 ± 10.3	33.4 ± 4.3
pH	7.4 ± 0.1	7.5 ± 0.1

Abbreviations: PaO₂, arterial blood oxygen tension; FiO₂, fraction of inspired oxygen; mmHg, millimetre of mercury; PaCO₂, arterial blood carbon dioxide tension; pH, potential for hydrogen ion concentration.

Table 8. Lung offers, provenance.

0–499 km	
Offers	35 (17.6%)
Transplanted	0 (0.0%)
500–999 km	
Offers	58 (29.1%)
Transplanted	4 (2.0%)
1000–1499 km	
Offers	77 (38.7%)
Transplanted	1 (0.5%)
>1500 km or n/a	
Offers	29 (14.6%)
Transplanted	0 (0.0%)

3.2.6. Revoked offers

Due to the 'first come, first served' modality of the offering procedure, seven (3.5%) lung offers for which, in principle, there could have been a recipient in Switzerland, were withdrawn before a Swiss transplant centre had accepted them (Table 5).

4. Discussion

The feasibility of international organ exchange and its benefits for the patients on the waiting list are still too little known. It is not only legal, but also essential, as it guarantees an optimal usage of the scarce organs, seeing that grafts for which there is no recipient on the national waiting list may be offered to a suitable recipient in another country. International organ exchange thus prevents the wasting of precious organs that are lost locally, if no recipient can be found. This is achieved by enlarging the donor pool and, hence, reducing the mismatch between donors and recipients. Such a strategy is especially valuable for smaller countries where the number of donors is insufficient to obtain a suitable organ for high-priority patients in time, as well as for patients who belong to a rare blood group or who have particular anatomical characteristics. Clearly, this particularly applies to children, who suffer from the highest waiting list mortality among heart and lung transplant candidates [8,9].

When considering the donor characteristics of the offered thoracic organs, it is particularly striking that nearly half of the donors (47.6% in the heart group and 46.7% in the lung group) are 16 years of age or younger. This high proportion of offered paediatric hearts and lungs can be explained by the

relatively low number of children awaiting heart or lung transplantation on the respective national waiting lists, which, in turn, increases the risk of donor–recipient mismatch. To avoid the loss of precious donor organs due to lack of suitable recipients on national heart waiting lists, Swisstransplant initiated a web-based register, the European Children Heart List (www.childrenhearts.org), for European children up to 12 years awaiting a heart transplant. The aim of this register is to facilitate the exchange of information on potential recipients and to enlarge the donor pool, thereby reducing waiting time and waiting list mortality as well as loss of donor organs due to lack of suitable recipients on national waiting lists.

Regardless of the fact that the overall mortality for the heart and lung waiting lists in Switzerland is comparable with other European countries [10,11], it remains a major concern. For the comprehensive study period, the total number of patients, who died whilst waiting for a heart or lung transplant in Switzerland, was 31 (10%) and 21 (6%), respectively [7]. In a heart-allocation simulation model for the Eurotransplant region, van den Hout et al. estimated that organ exchange among the Eurotransplant countries reduces waiting list mortality by 1.9–12.4%, depending on the country [1]. However, an assessment of the impact of the FO on the Swiss heart and lung waiting lists mortality was unfeasible because the rate of accepted FO, as compared with the comprehensive heart and lung transplant activity, was too small (5.8% and 2.8%, respectively). Notably, the study by Pretagostini et al., who evaluated the impact of the Italian national coordinating centre for the exchange of organs with other European countries revealed that in Italy, 15.4% of the offered hearts and 7.9% of the offered lungs were transplanted [6]. However, the period assessed (15 months) is rather short, and may therefore provide only limited statistical evidence. Nevertheless, and considering the heart and lung offers in the 'revoked' category (4.1% and 3.5%, respectively), it seems reasonable to assume that the percentage of effectively transplanted organs could be enhanced by the implementation of a more straightforward decision procedure with shorter response times in the Swiss transplant centres.

Although international organ exchange aims to reduce donor–recipient mismatch, for about half of both the heart and lung offers, there was no compatible recipient with regard to blood group, age, height or weight on the Swiss waiting list. This, in turn, reflects the fact that these organs originated from donors with very particular or rare donor characteristics, for which, even in large organ procurement organisations (such as ABM or Eurotransplant), no suitable recipient could be found. In order not to waste precious grafts, expanding the recipient pool on an international level is thus of vital importance. One of the major limiting factors for international organ exchange, however, remains cold ischaemia time, as it restricts transport time and thus prohibits long transport distances. This is reflected by the fact that, on the one hand, 75% of the accepted hearts were procured within a radius of <500 km, and 80% of the accepted lungs originated from within a radius of <1000 km. On the other hand, roughly one-sixth of both the offered hearts and lungs were refused for logistic reasons. In the future, machine perfusion of heart and lung grafts may permit longer

preservation times and longer transport distances [12,13], which is of major importance so as not to lose good-quality organs. In a recently published study, median cold ischaemia time in Switzerland ranged from 162 to 179 min for the heart, and from 272.5 to 285 min for the lung [14].

In the 'refusal for medical reasons' group, which comprises approximately of one-fifth of the heart (58/290) and lung (36/199) offers, the main reason for refusal was the poor functionality of the organs. Offers are also refused more often, if additional investigations, such as echocardiography or PCA, were not performed. Donor assessment and availability of further investigations, such as PCA, vary widely between the different European countries. PCA, which is feasible under machine perfusion, may furthermore allow to increase the number of heart transplantations from FO.

One limitation of our study lies in the considerable amount of missing data due to the non-standardised modality of the FO. Another shortcoming stems from the small number of transplantations carried out in Switzerland, which disallows solid statistical interpretation.

In conclusion, international organ exchange is a very valuable way to allocate as many organs as possible to recipients on the waiting list. Organ exchange is life-saving, especially in children, and also in patients with rare blood groups. A professional structure within the national organ procurement organisations, and a close co-operation between them on an international level, is crucial to achieve organ exchange on a high-quality level in Europe.

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