Improved Outcome With Organs From Carbon Monoxide Poisoned Donors for Intrathoracic Transplantation

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Background. **The success of intrathoracic organ transplantation has lead to a growing imbalance between the demand and supply of donor organs. Accordingly, there has been an expansion in the use of organs from nonconventional donors such as those who died from carbon monoxide poisoning. We describe our experience with 7 patients who were transplanted using organs after fatal carbon monoxide poisoning.**

Methods. **A retrospective study of the 1,312 intrathoracic organ transplants between January 1979 and February 2000 was completed. Seven of these transplants (0.5%) were fulfilled with organs retrieved from donors after fatal carbon monoxide poisoning. There were six heart transplants and one single lung transplant. The history of carbon monoxide inhalation was obtained in all of these donors.**

Results. **Five of 6 patients with heart transplant are alive and well with survival ranging from 68 to 1,879 days (mean, 969 ± 823 days). One patient (a 29-year-old male) died 12 hours posttransplant caused by donor organ failure. The patient who had a right single lung transplant did well initially after the transplant, but died after 8 months caused by Pneumocystis carinii pneumonia. All those recipients who were transplanted from carbon monoxide poisoned donors and ventilated for more than 36 hours, survived for more than 30 days. Moreover, these donors were assessed and optimized by the Papworth donor management protocol.**

Conclusions. **Carbon monoxide poisoned organs can be considered for intrathoracic transplantation. In view of the significant risk of donor organ failure, a cautious approach is still warranted. Ideally, the donor should be hemodynamically stable for at least 36 hours from the time of poisoning and on minimal support. A formal approach of invasive monitoring and active management further improves the chances of successful outcome.**

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Currently, there are nearly 600 patients awaiting intrathoracic organ transplant in the United Kingdom. During the past year, only 390 such transplants were carried out in the 9 designated transplant centers [1]. Furthermore, up to 30% of patients on the waiting list are reported to die while waiting for an appropriate organ [2]. This is mainly caused by a shortage of donor organs, hence the need to explore nonconventional donors. One such group is the victims of carbon monoxide (CO) poisoning. In 1998, 744 deaths were registered from CO poisoning in the United Kingdom, most of which (80%) were within the accepted age group for organ donation [3].

Although there have been reports of successful solid organ transplantation using organs from CO-poisoned donors, there have also been reports of donor organ failure resulting in early recipient death. Thus, the use of these organs for transplantation remains controversial, as there is very little data to draw any firm conclusions. In a recent survey, el Oakley and colleagues [4] reported that only 25% of British surgeons would consider using intrathoracic organs from CO-poisoned donors for transplantation. Furthermore, a 35% mortality has been reported by Tsui and colleagues [5] when CO-poisoned organs were used for heart or lung transplants, or heart and lung transplants. We describe our single center experience with CO-poisoned organs and review the data reported in the literature so far.

Material and Methods

Methods

A retrospective review was carried out on prospectively collected data of all patients who had undergone intrathoracic organ transplantation at our institution. Since the conception of the program in 1979, 1,312 intrathoracic organ transplants have been completed, including six heart transplants and one right single lung transplant performed from donors who had fatal CO poisoning. The first CO-poisoned heart donor in our series was simply accepted on a reasonable blood pressure and visual inspection of the heart. All subsequent donors were

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Table 1. Minimum Transplant Acceptance Criteria

Mean arterial pressure	More than 60 mm Hg
Central venous pressure	Less than 12 mm Hg
Pulmonary capillary wedge pressure	Less than 12 mm Hg
Left ventricular stroke work index	More than 15 gm
Inotrope dosage	Less than 5 mcg/kg/min

rigorously assessed and managed according to the Papworth donor management protocol (Tables 1 and 2) [6].

Case Description and Results

The first heart transplant recipient who received a CO-poisoned organ died within 12 hours of operation despite maximal inotropic support. The donor was ventilated for only 8 hours before organ retrieval. The donor's heart rate was 100 beats per minute and blood pressure was recorded at 110/50 mm Hg with 5 μg/kg/min of dobutamine at the time of assessment. The donor's electrocardiogram was normal. In the immediate postoperative phase the recipient had episodes of multifocal ventricular ectopics that were controlled with intravenous lignocaine. A few hours later, the recipient developed severe right ventricular dysfunction, which was refractory to treatment with intravenous prostacyclin and isoprenaline. Postmortem examination revealed a flabby heart with dilated cardiac chambers.

The mean age of the 6 heart transplant recipient group was 38 $\pm$ 14.4 years, 5 of whom were males. Five of the recipients are still alive with survival ranging from 68 to 1,879 days (969 $\pm$ 823 days). Although the first donor was ventilated for only 8 hours before organ retrieval, the remaining donors were ventilated for at least 72 hours (96 $\pm$ 17 hours). Their electrocardiograms were normal. Postoperatively, the heart transplant recipients were extubated on average within 13 hours of their operation. Their hospital stay varied from 12 to 48 days (19.2 $\pm$ 15.9 days). The longest hospital stay was a result of postoperative complication of sternal wound infection.

The heart recipients have had an average of 10 cardiac biopsies, with grade 1A rejection occurring in two biopsies. There was no clinical or histologic evidence of tissue damage as a sequela of exposure to carbon monoxide.

The lung transplant patient was a 56-year-old male who had cryptogenic fibrosing alveolitis and underwent right single lung transplant in November 1998. The donor was ventilated for 36 hours and the gas exchange before organ explant, on 30% inspiratory oxygen, was PO_2 to 17.4 KPa and PCO_2 to 4.4 KPa. The donor chest radiograph was normal. The histology of the unused left lung revealed foci of mononuclear inflammatory cell infiltrate around the small airways, but clear alveolar spaces. These changes were nonspecific and were not directly related to carbon monoxide inhalation.

Postoperatively the patient was extubated within 3 hours with PO_2 to 12.0 KPa and PCO_2 6.1 KPa on 60% FiO_2. His transbronchial biopsies at 1 and 2 months were unremarkable. Unfortunately his 6-month biopsy revealed granulomatous changes, which were later confirmed to be caused by Pneumocystis carinii. He died at 227 days postoperatively of acute respiratory distress syndrome secondary to bronchopneumonia.

The data from the 7 transplant recipients and their respective donors are summarized in Tables 3 and 4.

Comment

Carbon monoxide is a colorless, odorless, and nonirritant toxic gas that is readily absorbed through the lungs [7]. Exogenously it is produced as a result of incomplete combustion of hydrocarbons, whereas endogenously it represents one of the breakdown products of the tetrapyrrole rings leading to a CO level of 0.7% in the body [8]. Levels as high as 15% have been recorded in smokers [9]. Its half-life, which is up to 6 hours when breathing room air, can be drastically reduced to 30 minutes by hyperbaric oxygen [10]. The affinity of CO for hemoglobin is 250 times that of oxygen [11] causing in a shift of the oxygen-dissociation curve to the left [12], resulting in a decrease in the delivery of oxygen at the tissue level.

Carbon monoxide directly damages the tissues by its effect on oxygen delivery leading to hypoxia and indirectly through the production of oxygen free radicals, which oxidize nucleic acids [13, 14]. Turino [15] suggested that the organs most sensitive to the CO damage are the brain and the myocardium. At the myocardial level, CO binds with myoglobin and interferes with the oxygen transport to muscle mitochondria [16]. At the cellular level, the injury to the myocardium can be summarized as mitochondrial swelling, loss of limiting membrane, necrosis of the myofibrils, separation of intercalated discs, increase in lipid droplets, and edema of small arteries with blister formation [17]. In the lungs CO damage leads to congestion, edema, hemorrhage [18], endothelial cells swelling, and depletion of lamellar bodies in type II cells [19]. Parving and colleagues [20] also demonstrated an increase in vascular permeability by using radiolabelled I^{131}.

There is, however, a poor correlation between blood carboxy-hemoglobin level, tissue carboxy-hemoglobin level, and the degree of organ damage [21]. Thus, the best way to assess the suitability of CO-poisoned organs is not the blood carboxy-hemoglobin level at admission and thereafter, but the pulmonary gas exchange and hemodynamic stability several hours after the injury.

There have been 12 reported cases of heart transplant [22–29] and 1 case of lung transplant [22] with CO-poisoned organs in the literature (Table 5). The lung

Table 2. Hormone Replacement Therapy

Triiodothyronine	Bolus	4 mcg
	Infusion	3 mcg/hr
Vasopressin	Bolus	1 unit
	Infusion	1–5 units/hr
Insulin	Minimum 1 mL/hr	
	Infusion to maintain normoglycemia	

Table 3. Recipient Data

Donor	Recipient Age (yrs)	Sex	Diagnosis	IT (min)	Ventilation (hr)	LOS (days)	Survival (days)	Outcome
Heart								
A	29	M	DCM	152	...	...	0	Death—donor organ failure
B	46	F	DCM	205	5	19	1,879	Alive
C	59	M	IHD	160	4	12	1,760	Alive
D	37	M	VCM	250	16	48	821	Alive
E	40	M	DCM	184	4	15	319	Alive
F	17	M	DCM	212	48	21	68	Alive
Lung								
E	56	M	CFA	295	3	36	227	Death—chest infection

CFA = cryptogenic fibrosing alveolitis; DCM = dilated cardiomyopathy; F = female; IHD = ischemic heart disease; IT = ischemic time; LOS = length of hospital stay; M = male; VCM = valvular cardiomyopathy.

transplant was successful, with improved clinical status in the patient who was still alive after 8 months [22]. Four early (30-day) and 2 late deaths were reported in the heart transplant group. Two of the early deaths were directly related to myocardial dysfunction secondary to carbon monoxide exposure. The first death was described by Karwande and colleagues [23] in 1989 when a 17-year-old male donor heart was used after CO poisoning. This heart showed clinical evidence of myocardial dysfunction with episodes of ventricular fibrillation and cardiac arrests requiring direct current cardioversion before explant. The electrocardiogram showed nonspecific changes. The recipient survived for 4 days but succumbed to poor ventricular function of the donor organ. The postmortem study of the heart revealed a dilated organ with petechial and confluent endocardial hemorrhages.

Coagulative necrosis and diffuse fatty infiltration of the myocyte were detected on histologic examination. These findings are indicative of myocardial anoxia secondary to CO exposure. The second fatal case was reported by Shennib and colleagues [22] when a diffusely hypokinetic heart was transplanted from a CO-poisoned donor to a moribund recipient who had suffered a massive myocardial infarction. The patient did not recover from this surgical insult. The remaining two early deaths were caused by a technical problem [24] and poor recipient selection [25].

The late deaths were reported by Koerner and colleagues [24] and caused by adenocarcinoma of the pancreas 4 months posttransplant in 1 patient and multiorgan fungal sepsis at 10 weeks postoperatively in another.

Successful heart transplants from CO-poisoned donors were described by Iberer and colleagues [26], Roberts and colleagues [27], and Smith and colleagues [28]. The latter [28] recommended that CO-poisoned hearts being considered as donor organs should adhere to the following criteria for maximum success: (1) normal electrocardiogram and satisfactory echographic finding, (2) minimal rise in cardiac enzymes, (3) minimal inotropic support, (4) short ischemic time, and (5) avoidance of recipients with high pulmonary vascular resistance.

In our series, 1 of 6 heart transplant recipients died as a result of donor organ failure. This procedure was carried out in 1988, which took place before the introduction of the Papworth donor management protocol [6, 30–33], which is based on counteracting the pathophysiologic changes caused by brain stem death. Hence, the

Table 4. Donor Data

Donor	Age (yr)	Sex	Ventilation (hr)	MAP (mm Hg)	HR (per min)	FiO_2 (%)	PO_2 KPa	PCO_2 KPa	ECG	CXR	Inotropes
Heart											
A	40	F	8	70	100	...	...	...	NAD	NAD	Dob
B	14	F	120	93	112	...	...	...	NAD	Right-sided shadow	Dob, ADH/T3
C	20	M	96	84	125	...	...	...	NAD	Bilateral shadows	Nil
D	25	M	96	83	105	...	...	...	NAD	NAD	...
E	15	M	96	80	116	...	...	...	NAD	NAD	ADH/T3
F	47	M	72	90	71	...	...	...	NAD	NAD	ADH/T3/ADR
Lung											
E	14	M	36	76	145	30	17.4	4.4	NAD	NAD	...

ADH = vasopressin; ADR = adrenaline; CXR = chest radiograph; Dob = dobutamine; ECG = electrocardiograph; F = female; FiO_2 = inspiratory oxygen; HR = heart rate; KP_a = kilopascals; M = male; MAP = mean arterial pressure; NAD = no abnormalities detected; PCO_2 = arterial partial pressure of carbon dioxide; PO_2 = arterial partial pressure of oxygen; T3 = thyroxine.

Table 5. Summary of Previous Case Reports of CO-Poisoned Organs and Outcome

Author	Number of Cases	Pretransplant Recipient Status	Outcome
Shennib et al [22]	One heart	Extremely unstable	One early death (recipient failure)
Karwande et al [23]	One heart	Stable	One early death (donor organ failure)
Koerner et al [24]	Five hearts	Stable	One early and two late deaths (technical problem, intestinal ischemia, pancreatic can)
Hantson et al [25]	One heart	Preoperative shock	One early death (recipient failure)
Iberer et al [26]	One heart	Stable	Successful
Roberts et al [27]	One heart	Stable	Successful
Smith et al [28]	Two hearts	Stable	Both successful
Shennib et al [22]	One lung	Stable	Successful

organ failure was probably caused by inadequate assessment and optimization. In the long-term survivors, the mean duration of ventilation of the donors (five hearts and one lung) was 86 ± 28 hours. This allowed time for irreversible organ damage to manifest when the donor was assessed for organ donation. These maneuvers provide a better assessment of the possible transplant organs. They also allow for better performance of borderline organs. Organs that fail to improve on this resuscitation protocol are rejected.

Organs from CO-poisoned donors can be used for intrathoracic transplantation. The decision to use these organs should not be based on the blood carboxyhemoglobin levels but rather on the duration between injury and expected time of explantation (duration of donor ventilation), along with the hemodynamic performance of the heart, and the gas transfer for the lungs after appropriate resuscitation. The latter can be optimized by the Papworth donor management protocol. Hearts that require significant inotropic support despite optimization can be more readily rejected, whereas those that perform adequately on minimal inotropic support can be safely used.

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The Forty-eighth Annual Meeting of the Southern Thoracic Surgical Association will be held November 8–10, 2001, San Antonio, Texas. The Postgraduate Course will be held the morning of Thursday, November 8, 2001, and will provide in-depth coverage of thoracic surgical topics selected primarily as a means to enhance and broaden the knowledge of practicing thoracic and cardiac surgeons.

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