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ORIGINAL ARTICLE

Does the cardioplegic solution have an effect on early outcomes following heart transplantation?†

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Abstract

OBJECTIVE: The choice of cardioplegic solution for myocardial preservation in heart transplantation (HT) remains debated. We analysed our experience with three different cardioplegic solutions in adult HT performed during past 5 years, in terms of non-immunological intraoperative biventricular graft failure (BVF) and in-hospital mortality.

METHODS: A total of 133 patients underwent HT at our hospital from January 2006 to December 2010. Patients were divided into three groups, according to the solution adopted in the donor: HTK-Custodiol ($n = 61$), Celsior ($n = 38$) and St Thomas ($n = 34$). For each patient, solution was chosen according to surgeon's preference.

RESULTS: Recipient and donor mean age was 48.2 ± 12.7 and 43.8 ± 13.6 years, respectively. Twenty-four patients (18.0%) were in Status 1 at the transplant. The mean ischaemic time was 187.9 ± 52.6 min. Intraoperative BVF was observed in 18 cases (13.5%). Patients with BVF, and their respective donors, were older than the other patients (patients: 53.3 vs 47.4 years, $P = 0.06$; donors: 49.4 vs 42.9 years, P 0.06), and experienced significantly higher in-hospital mortality (47.3 vs 7.8%, $P = 0.0001$). The combination of patients aged 60 years or older with donors aged 60 years or older carried a mortality of 66.6% (6 out of 9). The three groups of patients did not differ significantly in terms of preoperative and intraoperative features and outcomes, including biventricular graft failure and death. At multivariate analysis, predictors of in-hospital death were a combination of both a recipient and a donor aged ≥60 years (OR 27.9), intraoperative BVF (OR 14.8) and previous cardiac surgery (OR 13.0). Cardioplegic solution did not predict mortality.

CONCLUSIONS: We did not observe a significant effect of the kind of cardioplegic solution on the early HT outcomes. The combination between both a recipient and a donor aged ≥60 years, reoperation and BVF are strong predictors of in-hospital death.

Keywords: Heart transplantation • Myocardial preservation

INTRODUCTION

Heart transplantation (HT) remains the gold standard for the treatment of end-stage heart failure, offering excellent results on both the short and long term. Optimal myocardial preservation is a prerequisite to preserve early allograft function. Nevertheless, primary graft failure remains a leading cause of in-hospital death following HT [1, 2]. It is still debated which is the best preservation solution to protect the donor heart. Today, several different solutions are adopted in the clinical practice, according to the preferences of centres and surgeons. It has been reported that at least 167 different types of solutions are used for HT in USA [3]. We reviewed our last 5-year experience in HT to test the hypothesis whether the preservation solution has an effect on in-hospital outcomes.

PATIENTS AND METHODS

Study population

Between January 2006 and December 2010, 141 adult patients underwent orthotopic HT at Niguarda Ca' Granda Hospital. We reviewed their clinical data from the computerized database of the hospital. Before 2006, the clinical data about preservation solutions were inconsistently recorded. Eight patients were excluded from the study because the preservation solution adopted in the donor was not recorded. Therefore, 133 patients represented the study population. The study was approved by the Institutional Review Board of the hospital.

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Preservation solutions: clinical protocols

We adopted for HT three types of preservation solutions: intracellular HTK-Bretschneider (Custodiol®, Dr. Franz Kohler Chemie GMBH, Bensheim, Germany), extracellular Celsior® (Genzyme Corp., Boston, MA) and extracellular St Thomas (Plegisol®, Hospira, Inc., USA). The choice of the solution was left to surgeon's discretion. During the study period, nine surgeons performed all the HT.

Clinical protocols for preservation solutions were as follows. *HTK*: 40 ml/kg of solution (maximum dose: 3 l) at 5–8°C was administered into the ascending aorta after cross-clamping to obtain initially a perfusion pressure equal to 100 mmHg and, following cardiac arrest, reducing the pressure to 50 mmHg. *Celsior®* and *St Thomas*: 2 l of solution at 4°C administered into the ascending aorta after cross-clamping to obtain a perfusion pressure comprised between 60 and 80 mmHg. Heart harvesting was performed according to standard techniques [4]. Particularly, we discarded hearts with left ventricular ejection fraction of <50%, signs of right ventricular failure and/or with significant coronary artery stenosis at angiography; or intraoperative evidence of palpable coronary artery plaques, in case of angiography unavailablity. After excision, the heart was transported into sterile bags inside a storage container filled with ice. For HTK- and Celsior®-preserved organs, the hearts were immersed in 2 l of HTK and Celsior® solution at 4°C, respectively; 2 l of isotonic saline solution at 4°C was used for St Thomas-preserved hearts.

Intraoperative management and definition of biventricular failure

Anterograde cold (4°C) 4:1 blood cardioplegia was administered to hearts preserved by means of Celsior® and St Thomas solutions during surgical implantation every 20 min. With the exception of only one case, blood cardioplegia was not administered to HTK-preserved hearts during implantation; if the total ischaemic time was >180 min, half the dose of HTK solution was re-administered during implantation. After aortic declamping, to obtain full allograft recovery, the duration of circulatory support before weaning from cardiopulmonary bypass was calculated as follows: 20 min of support for each hour of organ ischaemia.

Criteria to identify the occurrence of intraoperative biventricular failure (BVF) were as follows: duration of circulatory support for allograft recovery >60 min when compared with the calculated time value; and inability to wean the patient from cardiopulmonary bypass because of cardiogenic shock associated with high values of both central venous pressure (>10 mmHg) and left atrial pressure (>15–20 mmHg); and visual and echocardiographic evidence of biventricular hypokinesis, in the absence of macroscopic signs of hyperacute rejection; and need of high-dose inotropes (e.g. epinephrine >0.1 μg/kg/min) and mechanical circulatory support (intra-aortic balloon pump [IABP] or veno-arterial extracorporeal oxygenation [VA-ECMO]), if implantable. All criteria must be satisfied to identify a case of BVF.

Data collection and statistical analysis

All data were collected retrospectively from the computerized database of the hospital. To identify predictors of in-hospital death following HT, general demographic data and intraoperative variables were recorded. Factors evaluated were: *preoperative recipient factors* (age, gender, weight, aetiology of heart disease, basal pulmonary vascular resistance, status 1 at HT [mechanical ventilation, IABP, VA-ECMO, retransplantation, complicated left ventricular assist device (LVAD) or total artificial heart, right ventricular assist device or biventricular assist device], IABP, VA-ECMO, LVAD, previous cardiac surgery); *donor factors* (age, gender, weight, length of stay in intensive care unit before donation, degree of inotropic support [high support if >10 μg/kg/min intravenous dopamine], kind of preservation solution) and *intraoperative data* (ischemic time, aortic cross-clamping time, cardiopulmonary bypass time, BVF, IABP, VA-ECMO). In Tables 1–5, continuous variables are shown as mean value ± SD; categorical data are shown as absolute values and percentages between parentheses. Normality of quantitative data has been verified by means of Kolmogorov–Smirnov test. *t* and Mann–Whitney tests were used to compare the means between two quantitative variables, as appropriate. Multiple comparisons between groups were performed by means of one-way analysis of variance, Kruskal–Wallis or 3 × 2 tables as appropriate. Fisher's exact test was

Table 1: Pre- and intraoperative features of the study patients

Variable	
Recipients	
Mean age (years)	48.2 ± 12.7
Females	42 (31.5%)
Mean weight (kg)	66.1 ± 12.8
Idiopathic dilated cardiomyopathy	68 (51.1%)
Ischaemic cardiomyopathy	37 (27.8%)
Hypertrophic cardiomyopathy	11 (8.2%)
Other aetiologies	17 (12.9%)
PVR (Wood Units)	2.7 ± 1.3
Postcardiotomy shock	3 (2.2%)
Status 1	24 (18.0%)
Preoperative IABP	12 (9.0%)
Preoperative VA-ECMO	6 (4.5%)
Preoperative LVAD	6 (4.5%)
Previous cardiac surgery	36 (27.0%)
Donors	
Mean age (years)	43.8 ± 12.7
Donor age ≥60 years	21 (15.7%)
Females	55 (41.3%)
Mean weight (kg)	75.3 ± 13.2
Mean LOS in ICU (days)	4.1 ± 4.6
No inotropes	15 (11.2%)
High-dose inotropes	5 (3.7%)
Norepinephrine infusion	51 (38.3%)
Recipient and donor aged ≥60 years	9 (6.7%)
Female donor/male recipient	23 (17.2%)
Weight <30% recipient	3 (2.2%)
Transplantation data	
Mean ischaemic time (min)	187.9 ± 52.6
Mean AXC time (min)	97.8 ± 25.5
Mean CPB time (min)	216.2 ± 79.7

High dose inotropes: intravenous dopamine ≥10 μg/kg/min. PVR: basal pulmonary vascular resistance; IABP: intra-aortic balloon pump; VA-ECMO: veno-arterial extracorporeal membrane oxygenation; LVAD: left ventricular assist device; LOS: length of stay; ICU: intensive care unit; AXC: aortic cross clamping; CPB: cardiopulmonary bypass.

Table 2: Comparison of pre- and intraoperative features between three groups of patients categorized according to the preservation solution

Variable	HTK (*n* = 61)	Celsior (*n* = 38)	St Thomas (*n* = 34)	*P*
Recipients				
Mean age (years)	47.7 ± 12.7	49.1 ± 13.1	48.0 ± 12.7	0.878
Females	21 (34.4%)	9 (23.6%)	12 (35.2%)	0.462
Mean weight (kg)	66.9 ± 14.7	66.4 ± 8.7	64.5 ± 12.9	0.690
PVR (Wood Units)	2.5 ± 1.2	3.0 ± 1.6	2.6 ± 1.1	0.264
Postcardiotomy shock	3 (4.9%)	7 (18.4%)	4 (11.7%)	0.228
Status 1	12 (19.6%)	5 (13.1%)	7 (20.5%)	0.647
Preoperative IABP	9 (14.7%)	1 (2.6%)	2 (5.8%)	0.093
Preoperative VA-ECMO	3 (4.9%)	0	3 (8.8%)	0.193
Preoperative LVAD	2 (3.2%)	2 (5.2%)	2 (5.8%)	0.813
Previous cardiac surgery	17 (27.8%)	9 (23.6%)	10 (29.4%)	0.846
Donors				
Mean age (years)	42.6 ± 12.9	45.7 ± 13.5	43.8 ± 15.1	0.536
Donor age ≥60 years	5 (8.1%)	8 (21.0%)	8 (23.5%)	0.083
Females	25 (40.9%)	14 (36.8%)	16 (47.0%)	0.678
Mean weight (kg)	76.0 ± 15.5	74.7 ± 11.2	74.7 ± 11.0	0.845
Mean LOS in ICU (days)	4.3 ± 5.2	4.1 ± 3.7	3.9 ± 4.6	0.913
No inotropes	11 (18.0%)	4 (10.5%)	0	0.028
High-dose inotropes	1 (1.6%)	1 (2.6%)	3 (8.8%)	0.192
Norepinephrine infusion	23 (37.7%)	14 (36.8%)	14 (41.1%)	0.922
Recipient and donor aged ≥60 years	3 (4.9%)	4 (10.5%)	2 (5.8%)	0.542
Female donor/male recipient	7 (11.4%)	9 (23.6%)	7 (20.5%)	0.248
Weight <30% recipient	2 (3.2%)	1 (2.6%)	0	0.577
Transplantation data				
Mean ischaemic time (min)	188.6 ± 54.3	192.1 ± 48.7	182.0 ± 54.6	0.714
Mean AXC time (min)	93.5 ± 25.3	104.9 ± 30.6	97.5 ± 17.2	0.098
Mean CPB time (min)	218.1 ± 87.3	229.1 ± 87.9	198.1 ± 48.6	0.250

High dose inotropes: intravenous dopamine ≥10 μg/kg/min.
PVR: basal pulmonary vascular resistance; IABP: intra-aortic balloon pump; VA-ECMO: veno-arterial extracorporeal membrane oxygenation; LVAD: left ventricular assist device; LOS: length of stay; ICU: intensive care unit; AXC: aortic cross clamping; CPB: cardiopulmonary bypass.

Table 3: Comparison of in-hospital outcomes between three groups of patients categorized according to the preservation solution

Variable	HTK (*n* = 61)	Celsior (*n* = 38)	St Thomas (*n* = 34)	*P*
Intraoperative BVF	9 (14.7%)	4 (10.5%)	5 (14.7%)	0.814
Intraoperative IABP	11 (18.0%)	8 (21.0%)	4 (11.7%)	0.570
Intraoperative VA-ECMO	3 (4.9%)	0	0	0.163
In-hospital death	10 (16.3%)	4 (10.5%)	5 (14.7%)	0.717

BVF: biventricular failure; IABP: intra-aortic balloon pump; VA-ECMO: veno-arterial extracorporeal membrane oxygenation.

used to assess differences between categorical variables. A *P*-value of <0.05 was considered significant. The stepwise forward selection logistic regression model was constructed to determine independent predictors of in-hospital death. Variables entered in the model were those exhibiting *P*-values <0.10 in the univariate analysis. We used SPSS 11.5 (SPSS Inc., Chicago, IL, USA) for Windows as statistical package for all the analyses.

RESULTS

Table 1 shows the preoperative and intraoperative data of all the study population. The three groups of patients, categorized according to the preservation solution adopted in the donor, did not differ significantly in terms of preoperative and intraoperative features (Table 2) and of BVF and in-hospital death (Table 3), albeit BVF incidence and mortality were lower in the Celsior® group. At univariate analysis, non-survivors were significantly older (55.6 ± 11.5 vs 46.9 ± 12.5 years, *P* = 0.006) and they underwent previous cardiac surgery more frequently when compared with patients discharged from the hospital (*P* = 0.0001) (Table 4). The ischaemic time did not differ significantly between patients with and without BVF (197.3 ± 48.1 vs 186 ± 53.3 min, respectively, *P* = 0.415). Donors for deceased recipients were older (49.3 ± 13.6 vs 42.9 ± 13.4 years, *P* = 0.056) (Table 4). Among non-survivors, donors aged 60 years or older (*P* = 0.013) and the combination of both a recipient and a donor aged ≥60 years (*P* = 0.0001) were significantly more prevalent. BVF and intraoperative need of IABP or VA-ECMO were also significantly more frequent in such groups. Logistic regression failed to identify predictors of BVF. However, at multivariate analysis, predictors of in-hospital death were combination between both a recipient and a donor aged ≥60 years (OR 27.9), intraoperative BVF (OR 14.8) and previous cardiac surgery (OR 13.0) (Table 5). The model classified correctly 91.7% of cases. Hosmer–Lemeshow

Table 4: Comparison of clinical features between both deceased and discharged patients (univariate analysis)

Variable	Non-survivors (n = 19)	Survivors (n = 114)	P
Recipients			
Mean age (years)	55.6 ± 11.5	46.9 ± 12.5	0.006
Females	8 (42.1%)	34 (29.8%)	0.210
Mean weight (kg)	63.8 ± 13.5	66.5 ± 12.6	0.401
PVR (Wood Units)	2.8 ± 1.1	2.7 ± 1.3	0.609
Postcardiotomy shock	2 (10.5%)	1 (0.8%)	0.026
Status 1	4 (21.0%)	20 (17.5%)	0.462
Preoperative IABP	3 (15.7%)	9 (7.8%)	0.234
Preoperative VA-ECMO	1 (5.2%)	5 (4.3%)	0.611
Preoperative LVAD	0	6 (5.2%)	0.389
Previous cardiac surgery	13 (68.4%)	23 (20.0%)	0.000
Donors			
Mean age (years)	49.3 ± 13.6	42.9 ± 13.4	0.056
Donor age ≥60 years	7 (36.8%)	12 (10.5%)	0.013
Females	9 (47.3%)	69 (60.5%)	0.204
Mean weight (kg)	77.7 ± 15.9	74.9 ± 12.7	0.392
Mean LOS in ICU (days)	4.0 ± 3.7	4.2 ± 4.8	0.866
No inotropes	14 (73.6%)	1 (0.8%)	0.331
High-dose inotropes	1 (5.2%)	4 (3.5%)	0.543
Norepinephrine infusion	8 (42.1%)	43 (37.7%)	0.451
Recipient and donor aged ≥60 years	6 (31.5%)	3 (2.6%)	0.000
Female donor/male recipient	4 (21.0%)	19 (16.6%)	0.424
Weight <30% recipient	0	3 (2.6%)	0.627
Transplantation data			
Mean ischaemic time (min)	188.6 ± 54.3	192.1 ± 48.7	0.448
Mean AXC time (min)	179.4 ± 63.9	189.3 ± 50.7	0.492
Mean CPB time (min)	285.0 ± 132.6	204.7 ± 60.8	0.018
In-hospital outcomes			
Intraoperative BVF	9 (47.3%)	9 (7.8%)	0.000
Intraoperative IABP	8 (42.1%)	15 (13.1%)	0.005
Intraoperative VA-ECMO	2 (10.5%)	1 (0.8%)	0.053

High dose inotropes: intravenous dopamine ≥10 μg/kg/min. PVR: basal pulmonary vascular resistance; IABP: intra-aortic balloon pump; VA-ECMO: veno-arterial extracorporeal membrane oxygenation; LVAD: left ventricular assist device; LOS: length of stay; ICU: intensive care unit; AXC: aortic cross clamping; CPB: cardiopulmonary bypass; BVF: biventricular failure.

Table 5: Risk factors for in-hospital death following heart transplantation (multivariate analysis)

Variable	Beta	SE	Wald	OR (95% CL)	P
Intraoperative BVF	2.701	0.783	11.9	14.8 (3.2–69.0)	0.001
Previous cardiac surgery	2.566	0.729	12.3	13.0 (3.1–54.2)	0.000
Recipient and donor aged ≥60 years	3.330	1.040	10.2	27.9 (3.6–214.5)	0.001
Constant	−3.966	0.676			

BVF: biventricular failure.

goodness-of-fit was 0.66. For the regression model, area under ROC was 0.869 ± 0.05. We performed post-hoc power analysis: assuming alpha being equal to 0.05, in one-sided test power (1 − β) resulted to be 0.69 to detect a 100% relative increase in mortality. Causes of death were: multiorgan failure in six patients (41.5%), BVF in five patients (26.3%), pulmonary complications in three patients (15.7%), acute rejection in one patient (5.2%) and other reasons in the remaining four (11.3%) patients. Postoperative acute allograft rejection was diagnosed in four patients (3.0%). The combination of patients aged ≥60 years with donors aged ≥60 years carried a mortality of 66.6% (six out of nine) and the cause of death was BVF in 50% of cases. However, excluding such subgroup of patients, overall mortality was 10.4% (13 of 124).

DISCUSSION

Analysing 133 patients who underwent HT, we found that the type of preservation solution for the donor heart did not influence significantly in-hospital outcomes, namely death and BVF. Predictors of in-hospital death were the combination of both recipient and donor >60 years, intraoperative BVF and previous cardiac surgery. Incidence of BVF and mortality were not significantly different between preservation solutions, albeit being lower in the Celsior® group.

Current strategies for heart preservation and storage during HT primarily involve hypothermia to decrease the metabolic rate of the myocardial tissue [5]. However, during last decades, many preservation solutions for HT have been developed and adopted clinically to achieve optimal myocardial protection [3]. They are classified according to the sodium concentration: in extracellular and intracellular solutions, the content of sodium is ≥70 mEq/l and <70 mEq/l, respectively. However, definitive data in favour of one solution with respect to the others in clinical practice are still lacking and current evidences remain somehow controversial. Moreover, deleterious effects of current methods of myocardial preservation and storage on the coronary endothelium has been demonstrated [6]. In a retrospective survey of United Network of Organ Sharing (UNOS), Demmy *et al.* [3] observed that intracellular solutions were associated with a reduced risk of in-hospital death following HT. In two randomized studies, Celsior® was demonstrated to be non-inferior to conventional preservation solutions in terms of safety and efficacy for HT, even in high-risk cases [7, 8]. Garlicki [9] reported better post transplant heart recovery in organs preserved with Celsior® when compared with intracellular solutions as HTK and University of Winconsin. Hernandez *et al.* [10] observed a lower rate of graft failure in marginal allografts preserved with Celsior® when compared with an undefined control. Good results have been reported also with HTK [11, 12], as longs as the ischaemic time was <4 h. However, Kofler *et al.* [13], in a retrospective analysis of 960 HT, observed significantly better patient survival up to 15 years from transplant with University Wisconsin when compared with HTK. Very recently, a retrospective review of 4910 HT performed in UNOS hospitals between 2004 and 2009 showed improved short-term survival with University of Wisconsin solution when compared with Celsior® (30 day, 96.7 vs 95.4%, P = 0.02; 1 year, 94.3 vs 84.1%, P = 0.005), even in high-risk allografts [2].

Primary graft failure still remains a leading cause of in-hospital mortality following HT (ISHLT 2010), leading to one-third of

early deaths. However, in literature, the definition of 'primary graft failure' is quite variable [14–17]. Often it includes acute right ventricular failure secondary to recipient pulmonary vascular disease that could be unrelated to organ preservation at least in some cases. Therefore, we preferred to investigate the incidence of intraoperative failure of both ventricles defined according to haemodynamic and echocardiographic criteria. In our opinion, overall non-immunomediated allograft failure is more likely related to the preservation status of the organ.

Obviously, the optimal preservation technique is mandatory to protect adequately the allograft and achieve satisfying clinical results. Nevertheless, evaluating HT outcomes, besides preservation methods, the interaction between recipient and donor features plays role that cannot be overstated. The donor age is a well-known risk factor for death and graft failure following HT [1, 14]. Recently, Bruschi *et al*. [18] reviewed experience in HT at our hospital and they observed a higher incidence of acute graft failure and in-hospital mortality (32%) among patients transplanted with donors aged ≥60 years when compared with those transplanted with younger donors (10.2%). In this study, non-survivors were significantly older than survivors (55.6 ± 11.5 vs 46.9 ± 12.5 years, $P = 0.006$) and they received older allografts (49.3 ± 13.6 vs 42.9 ± 13.4 years, $P = 0.05$). Even more importantly, the combination of recipients and donors aged ≥60 years was associated with very high in-hospital mortality (66.6%) and BVF was the cause of death in 50% of cases. However, excluding such subgroup of patients, overall mortality was 10.4%. According to our data, perfusion solutions could have a minor role in determining HT outcomes as compared to characteristics of both patients and donors.

Several limitations must be considered in evaluating the results reported herein. First, the study was retrospective and patients were not randomly assigned to a specific preservation solution. Moreover, subclinical effects of the preservation solutions on allograft histopathology, cellular function, and performance cannot be excluded. Interestingly, we did not observe statistically significant differences between the three groups of patients in terms of preoperative and intraoperative features, with the exception of an higher number of donors without inotropes in the HTK group. Therefore, the three groups could be considered comparable. The choice of the preservation solution was left to the surgeon. The surgeon's choice could have introduced some hidden bias and confounders in the results. Nevertheless, each surgeon showed a strong and stable preference for one solution during the study period. With 19 events out of 133 patients, multivariate analysis could be somehow limited. Finally, our computerized archive was insufficient to evaluate long-term survival, because data on the preservation solution adopted in each patient have only been recorded consistently since 2006.

In conclusion, in our experience, the type of preservation solution was not a risk factor for in-hospital death following HT. The incidence of BVF was not significantly different between different solutions. Predictors of death were the combination of both recipient and donor aged >60 years, the development of intraoperative BVF and previous cardiac surgery.

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APPENDIX. CONFERENCE DISCUSSION

Dr D. Chambers *(London, UK)*: Mortality is actually a very crude outcome as a measurement for comparison of cardioplegic solutions, and I think it almost certainly requires significantly higher numbers of patients in each group to

be able to determine any differences between these three cardioplegic solutions. However, markers of myocardial injury such as troponin release over 24 h may have provided more insight into whether there were any differences between the solutions. You did not mention it in your manuscript or your talk, so I am assuming that you did not actually measure troponin release in these patients. So, I wonder why you had not considered it important to do that and whether it is part of any continuing studies that you may be conducting?

Dr Cannata: I agree with you that there are several markers for myocardial injury in cardiac surgery; troponins and others are quite good. In our standard clinical practice, we do not record the troponin during the early postoperative period in all patients. It could be partially confounded in some cases by the dissection of adhesions of the previous heart during reoperation. Then I do not know if the use of troponin could be biased by the recipient heart removal, whether there is a confounding effect on the levels of troponin by such a manoeuvre.

Dr Chambers: So, you do not plan to measure them?

Dr Cannata: No.

Dr Chambers: Okay. And my second question is that it seemed that the most interesting feature of this study was the fact that old donor hearts going to old recipients had a very poor outcome, and you probably knew that already from a previous study that you mentioned in your paper. So, I wondered whether you and your colleagues have changed your donor and recipient selection criteria on the basis of these findings and, if not, what are the factors that would make you continue to use this combination for transplantation?

Dr Cannata: Now we are very cautious with such a combination. The problem is really difficult to solve because, in our opinion, in half the cases the problem is related to the donor heart. In half of the cases, the cause of death of the patient was BVF.

Dr Chambers: Sure.

Dr Cannata: But in the other half of the cases, we have a very good donor heart, old donor heart, but the recipient may die because of comorbidities or because of being really very sick at the moment of the transplantation. Usually, they are patients who underwent previous cardiac surgery; they are at higher risk as compared to other patients, and then it is really a problem. I think that we have to be very cautious in the choice of such a combination because results are poor.

Dr Chambers: So, presumably from your study, you are going to continue using the three different solutions because you did not show any differences between them?

Dr Cannata: Our standard policy is for a liberal choice of preservation solutions, and at the moment, that is our strategy.

Dr Z. Ahmadi *(Tehran, Iran)*: I have two questions. First of all, about the interval of administration of the cardioplegic solutions. As you know, for HTK solution and UW solution, only one administration is sufficient, but with St Thomas's solution, it should be administrated every 20 min. You do not mention the interval and the quantity of administration of these solutions.

Dr Cannata: Our policy for administration of preservation solution and the cardioplegia during operation are: for HTK, usually we do not administer further doses of cardioplegia during implantation, but we repeat administration in the case of an ischaemic time of more than three hours. For Celsior, depending on the transplanting surgeon, we have two ways to protect the heart during the implantation. For fast implantations, we do not use any further dose of cardioplegia; with a very short cross-clamp of 40 min, you can perform the implantation without repeating the cardioplegia. Other surgeons use blood cardioplegia every 20 min during the implantation. And finally for St Thomas's solution, in every case we use blood cardioplegia every 20 min during the implantation phase.

Dr Ahmadi: And the second question is about the technique of transplantation. Are all of the techniques bicaval, or biatrial?

Dr Cannata: The great majority of the cases are bicaval. We have only three cases with the Shumway technique because of difficult reoperation or retransplantation, but most of our experience is with bicaval transplantation.

Dr M. Morshuis *(Bad Oeynhausen, Germany)*: Did you also look at the long-term follow-up, for example, the effect on the graft vasculopathy?

Dr Cannata: I think this is a very important question because it is addressed in the literature. Our study period is relatively recent. I think we have to perform a study on the follow-up of such patients in order to evaluate the incidence of rejection and survival in allograft coronary disease during the follow-up. We have to perform such a study in the coming months.

Dr Morshuis: And one other question. What is your opinion of the TransMedics system?

Dr Cannata: The TransMedics system is a very good system for protecting the heart. I think that we have two problems. The first one is the cost of the system, which is quite high. And the second, in Italy, we have a geographic distribution of recipients and donors with not so huge distances between them. I think that the most interesting use of TransMedics will be the regeneration or evaluation of marginal hearts, and we hope to start such experience during the coming months.

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EDITORIAL COMMENT

Improving donor heart preservation

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INTRODUCTION

The accompanying paper by Cannata *et al*. [1] identifies the important challenges for the continuing efforts of cardiac surgeons to improve donor heart preservation. To expand the benefits and spurred by remarkable successes, transplantation has been offered to older and sicker patients and, to increase the donor pool, older hearts have been accepted. As indicated by the accompanying paper, the current methods of donor heart protection and transport have produced impressive results. However, cold storage can delay the recovery of ventricular function, induce at least transient endothelial injury [2] and