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The Journal of Heart and Lung Transplantation

http://www.jhltonline.org

Recipient Outcomes With Extended Criteria Donors Using Advanced Heart Preservation: An Analysis of the GUARDIAN-Heart Registry

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KEYWORDS:
Cardiac transplantation;
Primary graft dysfunction;
Hypothermic storage;
Preservation system;
Extended donors

BACKGROUND: The prevalence of end-stage heart failure and patients who could benefit from heart transplantation requires an expansion of the donor pool, relying on the transplant community to continually re-evaluate and expand the use of extended criteria donor organs. Introduction of new technologies such as the Paragonix SherpaPak Cardiac Transport System aids in this shift. We seek to analyze the impact of the SherpaPak system on recipient outcomes who receive extended criteria organs in the GUARDIAN-Heart Registry.

METHODS: Between October 2015 and December 2022, 1,113 adults from 15 US centers receiving donor hearts utilizing either SherpaPak (n = 560) or conventional ice storage (ice, n = 453) were analyzed from the GUARDIAN-Heart Registry using summary statistics. A previously published set of criteria was used to identify extended criteria donors, which included 193 SherpaPak and 137 ice.

RESULTS: There were a few baseline differences among recipients in the 2 cohorts; most notably, IMPACT scores, distance traveled, and total ischemic time were significantly greater in SherpaPak, and significantly more donor hearts in the SherpaPak cohort had >4 hours total ischemia time. Posttransplant mechanical circulatory support utilization (SherpaPak 22.3% vs ice 35.0%, p = 0.012) and new extracorporeal membrane oxygenation/ventricular assist device (SherpaPak 7.8% vs ice 15.3%, p = 0.033) was significantly reduced, and the rate of severe primary graft dysfunction (SherpaPak 6.2% vs ice 13.9%, p = 0.022) was significantly reduced by over 50% in hearts preserved using SherpaPak. One-year survival between cohorts was similar (SherpaPak 92.9% vs ice 89.6%, p = 0.27).

CONCLUSIONS: This subgroup analysis demonstrates that SherpaPak can be safely used to utilize extended criteria donors with low severe PGD rates.

J Heart Lung Transplant xxxx;xxx:xxx–xxx

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https://doi.org/10.1016/j.healun.2023.12.013

Heart transplantation remains the gold-standard treatment for patients with end-stage heart failure. Over the past decade, heart transplants in the United States increased by 67.4%; however, a record 4,373 new patients were added to the waiting list in 2021, resulting in a waitlist exceeding 7,000 patients, highlighting a shortage of donor hearts.[1,2] Nevertheless, recipient centers often decline donor hearts that do not meet stringent acceptance criteria. Consequently, the possibility to safely utilize extended criteria donor hearts to expand the donor pool is an area of immediate and growing interest.

With prior data showing that the risk of primary graft dysfunction (PGD) increases by 5% for every 10 minutes of ischemic time,[3] distance from the transplant center is one of the primary concerns when considering donor risk factors. PGD has been reported in 7.4% to 31% of heart transplant recipients,[4-7] accounting for 23.4% of all deaths within 90 days of transplantation,[8] and is associated with a significantly higher rate of in-hospital, 30-day, and 1-year mortality.[4] While the causes of PGD are multifactorial, controlled hypothermic preservation during organ transport is a recommended precaution to prevent PGD.[5]

During transit, organs have historically been stored in a preservation solution and submerged in ice.[9] The International Society of Heart and Lung Transplant (ISHLT) consensus statement advocates the preparation and packaging of donor hearts in a preservation solution at 4°C while minimizing direct organ contact with ice to reduce the risk of hypothermic freezing injury, which may lead to graft dysfunction.[10] The authors further recommend maintenance of donor hearts during organ transport ideally between 5°C and 10°C, a range that is difficult to achieve through traditional ice storage methods.[10] Despite these precautions, within 60 to 75 minutes of ice storage, the myocardial temperatures may fall below 1°C.[11,12] This is not surprising considering that ice is in fact 0°C or colder, as it is in liquid form above 0°C. Direct contact of materials and solutions with ice is therefore contact at freezing temperatures. Studies have shown that prolonged exposure to freezing temperature causes myocardial cell swelling and edema[11] and prevents the recovery of mechanical functioning.[12] Accordingly, the time spent in ice directly correlates with the risk of ischemic reperfusion injury or graft dysfunction, and consequently, patient mortality.[13,14] Nicoara et al found that each hour of cold ischemic time resulted in 1.8 times greater odds of PGD.[4] The use of an organ preservation system with stable hypothermic control may significantly reduce the risk of PGD associated with extended cold ischemic storage time and allow for an expanded geographic scope and consequent longer ischemic times when considering candidate transplant recipients.

The Food and Drug Administration–cleared and CE-marked Paragonix SherpaPak® Cardiac Transport System (Paragonix Technologies, Cambridge, MA) uses innovative phase-change material panels to provide a stable 4°C to 8°C environment for up to 40 hours with no external power source.[15] An early analysis of propensity-matched data from the multicenter GUARDIAN registry study from 12 US cardiac transplant hospitals found that, relative to ice, the SherpaPak preservation of donor hearts during transport reduced severe PGD incidence by 65% (16.1% vs 5.7%, $p = 0.03$) and reduced the need for posttransplant mechanical circulatory support (MCS) by 46% (40.2% vs 21.8%, $p = 0.009$).[16] Compared to SherpaPak organ preservation, patients receiving transplants after ice transport spent more days in intensive care units with a higher need for MCS during intensive care unit stay, incurring an average additional cost of $25,694 per patient.[16] The average cost savings observed per patient when the SherpaPak was used to transport donor hearts is greater than the average cost of the SherpaPak by almost $10,000. Moreover, a 3-year single-center study showed similar postoperative outcomes in patients receiving SherpaPak transplants with a significantly higher (4.10 hours) allograft ischemic time compared to patients receiving ice transplants (3.64 hours) and a significantly reduced requirement for intraoperative or postoperative blood units after patient matching.[17]

In this study, we utilize the recently established multicenter Global Utilization And Registry Database for Improved heArt preservatioN (GUARDIAN-Heart) to assess the clinical outcomes of patients undergoing heart transplants following the use of the SherpaPak Cardiac Transport System in extended criteria donors. This analysis summarizes the rate of MCS utilization and severe PGD after SherpaPak heart transport, relative to ice transport, in patients receiving donor hearts after > 4-hour ischemic time or > 2-hour ischemic time with at least one other disqualifying factor (> 55 years of age, downtime > 20 minutes, left ventricular ejection fraction 40%-50%, left ventricle posterior wall thickness 12-16 mm, or luminal irregularities).

Materials and methods

We performed a retrospective sub-analysis of the GUARDIAN-Heart Registry (NCT04141605), which includes data on heart transplant donors and recipients from 9 US transplant centers. GUARDIAN-Heart is funded and administered by Paragonix Technologies (Cambridge, MA, USA). The registry has been described previously,[18] but briefly, informed consent and approvals were obtained by the institutional review boards of each center. The database included donor and recipient demographics and medical history, as well as recipient outcomes up to 1-year posttransplant.

Subjects from the GUARDIAN-Heart Registry transplanted between October 2015 and December 2022 were included in this study. The definition for extended criteria donors was based on the OCS (Organ Care System) Heart EXPAND trial[21] and is characterized by (1) a total ischemic time ≥4 hours or (2) a total ischemic time ≥2 hours with one or more of the following: over 55 years of age, over 20 minutes of downtime, left ventricular ejection fraction (LVEF) 40% to 50%, left ventricular posterior wall thickness 12 to 16 mm, or luminal irregularities. Cohorts of transplant patients who received an extended donor after organ transport using ice and SherpaPak were compared. All donor hearts were recovered from donation after brain death. The choice of preservation solution used was at the discretion of the transplanting center.

Table 1 Clinical Parameters of Extended Criteria Donors Included in the Two Study Cohorts

Variables	Ice (n = 137)	SherpaPak (n = 193)	p-value
Donor inclusion criteria			
> 4-hour total ischemic time	**64/137 (46.7%)**	**131/193 (67.9%)**	**< 0.001**
> 2-hour total ischemic time AND			
Age > 55 years	4/137 (2.9%)	10/193 (5.2%)	0.41
Downtime > 20 minutes	26/137 (19.0%)	36/193 (18.7%)	> 0.99
LVEF 40%-50%	38/137 (27.7%)	39/193 (20.2%)	0.12
LVPW 12-16 mm	18/137 (13.1%)	15/193 (7.8%)	0.14
Luminal irregularities	5/137 (3.6%)	9/193 (4.7%)	0.79

LVEF, left ventricular ejection fraction; LVPW, left ventricular posterior wall thickness.

We compared differences in the baseline characteristics of extended donor heart transplants between ice and SherpaPak cohorts based on donor, recipient, and matched characteristics using summary statistics. Baseline donor characteristics analyzed included age and body mass index. Recipient baseline characteristics analyzed included age, body mass index, baseline LVEF, implantable ventricular assist device (VAD), intra-aortic balloon pump (IABP), and extracorporeal membrane oxygenation (ECMO) or temporary VAD. Donor-recipient match characteristics analyzed included female/male mismatch, predicted heart mass mismatch, distance to organ, total ischemic time, and era.

To compare posttransplant outcomes in ice and SherpaPak cohorts, summary statistics were used to compare 24-hour LVEF and the rate of posttransplant MCS, new posttransplant IABP, new posttransplant ECMO or VAD, cardioversion, PGD, and severe PGD. Severe PGD was defined as PGD requiring MCS (excluding IABP) within 24 hours posttransplant according to the 2014 ISHLT consensus statement[5]. Postoperative survival was also summarily compared in-hospital, at 30 days, and 1 year after the transplant. Survival was compared at these time points using the Cox proportional hazards model after adjusting for baseline differences of ischemic time, baseline left ventricular assist device (LVAD), re-do sternotomy, and recipient age. Additionally, survival probability through the first year after transplantation was analyzed by means of Kaplan-Meier analysis, with the survival curves being compared using the log-rank test.

Continuous variables were reported as mean ± standard deviation and analyzed by unpaired t-test with Welch's correction, and categorical variables were reported as counts and percentages and analyzed using Fisher's exact test. Univariate logistic regressions were performed to determine whether either preservation modality or certain categories of extended criteria donors were independently associated with the odds of severe PGD in this study. A multivariate logistic regression analysis was performed to assess the relationship between preservation modality and severe PGD while adjusting for ischemic time, baseline LVAD, re-do sternotomy, and recipient age. Statistical analyses were performed using R (version 4.2.2; The R Foundation for Statistical Computing, Vienna, Austria). A two-sided p-value of < 0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 330 extended donor heart transplant recipients (SherpaPak, n = 193; ice, n = 137) were analyzed, and the qualifying criteria were well matched between the 2 cohorts with the exception of significantly more donor hearts transported with the SherpaPak having ischemic times exceeding 4 hours (SherpaPak 67.9% [131/193] vs ice 46.7% [64/137], $p < 0.001$; see Table 1). Complete data were available through discharge on the entire study cohort, while 27 patients did not yet have completed 1-year data at the time of the analysis (n = 25/193 SherpaPak vs n = 2/137 ice). These missing data were reflected in the denominator of 1-year survival, as well as censored in the Kaplan-Meier analysis at 1 year. A review of the baseline demographics of the 2 cohorts revealed comparable baseline characteristics (Table 2). Although the majority of the baseline characteristics were similar in both cohorts, a trend toward higher donor age (SherpaPak 56.3 ± 12.5 years vs ice 54.0 ± 11.3 years, p = 0.07) and increased rates of temporary ECMO/VAD in the SherpaPak cohort (SherpaPak 15.0% vs ice 8.0%, p = 0.06) was observed. Patients in the ice cohort had a significantly higher rate of pretransplant implantable VAD (SherpaPak 24.9% vs ice 47.4%, $p < 0.001$) and were significantly more likely to have resternotomy (SherpaPak 50.3% vs ice 63.5%, p = 0.018), although the patients in the SherpaPak cohort were sicker, with a significantly higher IMPACT score (SherpaPak 7.4 ± 5.1 vs ice 6.2 ± 4.8, p = 0.036). Notably, a significantly higher proportion of patients in the SherpaPak cohort received a heart transplant after changes to the 2018 UNOS Donor Heart Allocation policy (SherpaPak 98.4% vs ice 76.6%, $p < 0.001$). Consequently, extended donor hearts in the SherpaPak cohort were significantly farther from transplant recipients (SherpaPak 609 ± 377 miles vs ice 340 ± 289 miles, $p < 0.001$) and had a significantly higher total ischemic time (SherpaPak 251 ± 51 minutes vs ice 222 ± 55 minutes, $p < 0.001$). The average temperature in the SherpaPak cohort during donor heart preservation and transport was 5.3°C, with a median of 5.1°C.

Posttransplant outcomes

Despite a longer transport distance and ischemic time in extended donors from the SherpaPak cohort, we observed a significant improvement in several clinical metrics of posttransplant outcomes in these patients relative to the ice cohort (Table 3). Patients in the SherpaPak cohort had a significantly

Table 2 Baseline Demographics of Donors and Recipients in the Two Study Cohorts

Variables	Ice (n = 137)	SherpaPak (n = 193)	p-value
Donor characteristics			
Age (years)	33.1 ± 10.4	34.9 ± 10.9	0.14
BMI (kg/m^2)	28.9 ± 7.1	28.6 ± 7.4	0.79
Recipient characteristics			
Age (years)	54.0 ± 11.3	56.3 ± 12.5	0.07
BMI (kg/m^2)	28.3 ± 4.5	27.8 ± 4.7	0.28
LVEF at baseline (%)	22.6 ± 13.4	21.7 ± 11.7	0.52
Implantable VAD	65/137 (47.4%)	48/193 (24.9%)	< 0.001
Temporary IABP	26/137 (19.0%)	46/193 (23.8%)	0.34
Temporary ECMO/VAD	11/137 (8.0%)	29/193 (15.0%)	0.06
Previous cardiac surgery	112/137 (81.8%)	149/192 (77.6%)	0.41
Number of prior cardiac surgeries	2.1 ± 1.1	1.9 ± 1.5	0.21
Re-do sternotomy	87/137 (63.5%)	97/193 (50.3%)	0.018
IMPACT score	6.2 ± 4.8	7.4 ± 5.1	0.036
Match characteristics			
F/M mismatch	17/137 (12.4%)	29/193 (15.0%)	0.52
PHM mismatch	0.03 ± 0.17	0.01 ± 0.17	0.23
Distance to organ (miles)	340 ± 289	609 ± 377	< 0.001
Total ischemic time (minutes)	222 ± 55	251 ± 51	< 0.001
Era (% post change)	105/137 (76.6%)	190/193 (98.4%)	< 0.001

BMI, body mass index; ECMO, extracorporeal membrane oxygenation; F/M, female to male; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction; PHM, predicted heart mass; VAD, ventricular assist device.

reduced requirement for any posttransplant MCS (SherpaPak 22.3% vs ice 35.0%, p = 0.012), new posttransplant ECMO/VAD (SherpaPak 7.8% vs ice 15.3%, p = 0.033), and a significantly higher LVEF 24 hours posttransplant (SherpaPak 57.1 ± 12.5% vs ice 53.0 ± 14.0%, p = 0.012). Furthermore, transplant recipients in the SherpaPak cohort had a significantly lower rate of PGD (SherpaPak 14.5% vs ice 25.5%, p = 0.015) and severe PGD (SherpaPak 6.2% vs ice 13.9%, p = 0.022) compared to the ice cohort.

In-hospital, 30-day, and 1-year survival were numerically higher in the SherpaPak cohort (in-hospital: SherpaPak 97.9% vs ice 94.9%; 30-day: SherpaPak 98.4% vs ice 96.4%; 1-year: SherpaPak 92.9%, n = 168 vs ice 89.6%, n = 135), but these differences were not statistically significant. Cox proportional hazards regression analyses found no statistical differences after adjusting for baseline covariates. While in-hospital survival showed a trend favoring the SherpaPak cohort (hazard ratio [HR] 0.29, 95% confidence interval [CI] 0.08-1.10, p = 0.069), 30-day (HR 0.34, 95% CI 0.08-1.51, p = 0.16), and 1-year survival (HR 0.64, 95% CI 0.28-1.47, p = 0.29) were statistically similar. Kaplan-Meier survival analysis through 1 year also failed to show a statistical difference in survival between the 2 cohorts (Figure 1).

Table 3 Posttransplant Outcomes After Extended Donor Heart Transplants in the Two Study Cohorts

Variables	Ice (n = 137)	SherpaPak (n = 193)	p-value
Time to first wean	77.4 ± 79.7	75.8 ± 88.0	0.87
Number of attempts to wean	1.1 ± 0.44	1.2 ± 0.70	0.30
All post-Tx MCS	48/137 (35.0%)	43/193 (22.3%)	0.012
New post-Tx IABP	20/137 (14.6%)	19/193 (9.8%)	0.23
New post-Tx ECMO/VAD	21/137 (15.3%)	15/193 (7.8%)	0.033
PGD	35/137 (25.5%)	28/193 (14.5%)	0.015
PGD severe[a]	19/137 (13.9%)	12/193 (6.2%)	0.022
LVEF at 24 hours (%)	53.0 ± 14.0	57.1 ± 12.5	0.012
In-hospital survival	130/137 (94.9%)	189/193 (97.9%)	0.21
30-day survival	132/137 (96.4%)	190/193 (98.4%)	0.28
1-year survival	121/135 (89.6%)	156/168 (92.9%)	0.41

ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; PGD, primary graft dysfunction; Tx, transplant; VAD, ventricular assist device.

[a]Note: Severe PGD is defined by the need for new ECMO/VAD use initiated within the first 24 hours posttransplant.

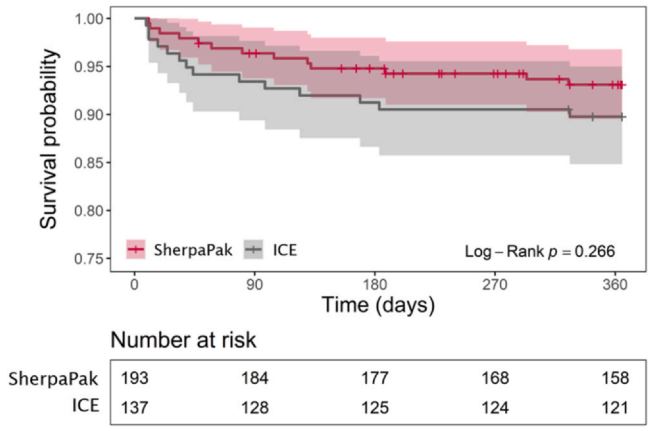

Figure 1 KM survival for recipients receiving hearts from extended criteria donors.

Severe PGD risk

Since we observed a significant reduction in severe PGD in patients receiving an extended donor heart after SherpaPak transport relative to ice transport, we sought to determine whether heart transport modality impacted the risk of severe PGD in the individual extended donor subcategories. We found that severe PGD risk (OR) was significantly reduced in the SherpaPak cohort relative to the ice cohort (OR = 0.41, 95% CI = 0.19-0.88, $p = 0.022$; Figure 2). Additionally, the ORs for 4 of the subcategories favored SherpaPak, where > 4-hour ischemic time and > 2-hour ischemic time combined with 40%-50% LVEF were significantly better, with ORs of 0.40 and 0.10, respectively (Figure 2). The sample sizes were too small to assess the OR for > 2-hour ischemic time combined with either older age (> 55 years) or luminal irregularities. A multivariate logistic regression analysis further found that after adjusting for baseline differences, the odds of severe PGD were significantly reduced when the SherpaPak was used to preserve the donor hearts, with an OR of 0.38 (95% CI 0.17-0.86, $p = 0.019$; Table 4).

Discussion

Although the hypothermic preservation and transportation of donor hearts using ice has historically been the standard of care, there are several detrimental effects of the resulting uncontrolled hypothermia and freezing temperatures, such as progressive ischemic cellular injury, calcium overload leading to extracellular edema, development of lactic acidosis, reperfusion injury, and endothelial injury. The recently published ISHLT consensus statement suggests the 3-bags technique for donor heart transportation as an option to prevent freezing injuries by avoiding direct contact.[10] Several studies have demonstrated that the temperature in donor hearts decreases fastest within the first hour of cold storage by ice and a progressive increase in cellular edema occurs in the first 4 hours of ice storage.[11] The most effective storage temperatures with the least cold-induced injury have been identified to be between 4°C and 8°C, as the ventricular function and high energy stores are well preserved at these temperatures.[9,19,20]

The present study utilized the prospective multicenter randomized OCS Heart EXPAND trial's suggested definition for extended criteria donors, which advocates for the higher utilization of extended criteria donor hearts by expanding the acceptance criteria to include hearts, which would have been rejected due to issues such as storage times.[21] While the study is still ongoing, preliminary data suggest promising outcomes in regard to posttransplant PGD and survival of the study group.[21] Nevertheless, utilizing the OCS Heart system may present logistical complications, as it requires trained personnel and specialized transportation solutions and resources. To provide a cost-effective and simple technological alternative for the preservation and transportation of donor hearts while eliminating the detrimental effects of progressive cold injuries, Paragonix has developed the SherpaPak Cold Storage System, which maintains hearts at controlled temperatures between 4°C-8°C throughout the entire donor heart preservation interval without the risk of direct contact with ice.[15]

In the present study, we compared the outcomes of the SherpaPak organ preservation and conventional ice storage in transporting 330 extended criteria donor hearts as defined by the modified extended donor criteria used in the EXPAND study.[21] Modifications of the EXPAND extended donor criteria were made by omitting the following inclusion criteria, which were unavailable in the GUARDIAN registry: alcoholism, carbon monoxide as a cause of death, diabetes, and donor age 45 to 55 years with no coronary catheterization data. In the EXPAND trial, subjects included under these criteria accounted for only 17.3% of the total subjects. Our study included 330 subjects under the modified EXPAND criteria, representing 32.6% of the total subjects in the GUARDIAN-Heart Registry. Although the extended criteria donors in the ice cohort had significantly more patients bridged with an LVAD, the SherpaPak cohort were significantly sicker, with a statistically significantly higher IMPACT score. Additionally, the SherpaPak cohort also had a trend toward higher donor age and increased rates of temporary ECMO/VAD when compared to the ice cohort. However, the SherpaPak donor hearts were procured from significantly further geographic distances

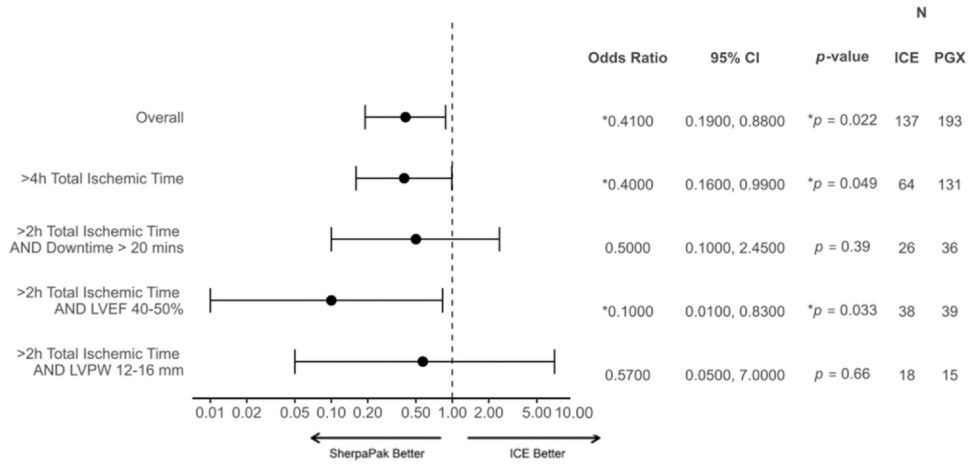

Figure 2 Univariate logistic regression analysis of the impact of preservation modality on the risk of severe PGD in extended criteria donors in the US Adult GUARDIAN-Heart Registry. Overall refers to the overall extended donor criteria subgroup population. Note: due to small cohort sizes, the confidence intervals exceeded the limits of the analysis for criteria > 2-hour ischemic time in combination with either age > 55 years or presence of luminal irregularities.

Table 4 Multivariate Logistic Regression Analysis for Risk of Severe PGD

Variables	OR	Severe PGD 95% CI	*p*-value
SherpaPak	0.38	0.17, 0.86	0.019
Recipient age	1.00	0.96, 1.03	0.78
Use of durable LVAD at baseline	1.58	0.62, 4.00	0.34
Total ischemic time	1.01	1.00, 1.01	0.16
Resternotomy	0.99	0.38, 2.59	0.99

CI, confidence interval; LVAD, left ventricular assist device; OR, odds ratio; PGD, primary graft dysfunction.

(SherpaPak 609 ± 377 miles vs ice 340 ± 289 miles, $p < 0.001$) and had a significantly higher total ischemic time (SherpaPak 251 ± 51 minutes vs ice 222 ± 55 minutes, $p < 0.001$).

The presence of a greater number of ice patients with durable LVADs at baseline requires consideration for bias due to heart transplantation in recipients bridged with durable LVADs tending to be more surgically complex, thus resulting in longer total ischemic times. Recent ISHLT registry data reports demonstrate that previous surgery and the use of MCS devices are risk factors associated with a significant increase in posttransplant 1-year mortality.[2] However, it is important to note that posttransplant survival after MCS therapy has significantly improved over the last 2 decades. According to the 38th ISHLT adult heart transplantation report, compared to patients transplanted between 2000 and 2005, the 1-year posttransplant survival of patients bridged to transplant via VAD between 2010 and 2018 has improved and approached the 1-year survival rates of patients without VAD support.[22] Improved device technology, careful recipient selection, and experience in surgical and perioperative care are possible reasons for these outcome rate improvements.[22] A preliminary retrospective subgroup analysis of the GUARDIAN Registry evaluated the influence of the SherpaPak on posttransplant outcomes in recipients bridged to transplant via LVAD. Lerman et al demonstrated that in patients with a durable LVAD at baseline, those receiving hearts preserved using the SherpaPak had a 61% lower rate of posttransplant severe PGD when compared to traditional ice storage ($p = 0.01$). This is despite a significantly longer total ischemic time in the SherpaPak cohort,[23] a known risk factor for severe PGD.[4]

When comparing posttransplant outcomes, we found that SherpaPak utilization resulted in a 37% reduction in all posttransplant MCS ($p = 0.012$), a 33% reduction in new posttransplant IABP ($p = 0.23$), a 49% reduction in new posttransplant ECMO/VAD ($p = 0.033$), a 43% reduction in PGD ($p = 0.015$), and a 55% reduction in severe PGD ($p = 0.022$). These findings may be attributed to reduced ischemic injury during heart preservation, which is a known risk factor for PGD,[24] the main cause of death in the first 30 days after heart transplant.[25] In fact, logistic regression revealed that use of the SherpaPak resulted in greater than 60% reduced odds of severe PGD. The reduced rate of severe PGD, new MCS, and new ECMO/VAD in recipients of hearts from extended criteria donors utilizing SherpaPak heart preservation is consistent with a previous study, which found a decreased incidence of these adverse events in a propensity-matched analysis from nonextended criteria donors and donors with ischemic time > 4 hours.[18] Although PGD is a relatively common (7.4%-31%) posttransplant complication,[4,5,26] the etiology of PGD is considered multifactorial. Previous studies have demonstrated that a longer ischemic time is a significant predictor of PGD,[25,26] with every hour of ischemic time having increased the odds of developing severe PGD 1.8-fold.[25] We observed that within our pool of extended criteria donor hearts, SherpaPak vs ice preservation was the only significant predictor of severe PGD. Notably, the significantly increased risk of PGD in the ice cohort was observed, despite a significantly longer average ischemic time and travel distance in the SherpaPak cohort. Collectively, these findings suggest that the utilization of the SherpaPak system

significantly reduces the risk of adverse posttransplant outcomes relative to traditional ice preservation.

While several improved methods of heart preservation have been proposed, only a few studies have directly investigated transplant outcomes in extended criteria donors utilizing these systems. In this analysis, we are the first to describe posttransplant outcomes after the utilization of the SherpaPak with extended criteria donor hearts. The reduced incidence of severe PGD in extended criteria donors using the SherpaPak reported here is in line with the incidence reported in the EXPAND trial (SherpaPak = 6.2%, ice = 13.9%, OCS = 10.7%).[21] While caution is needed when comparing noncontemporaneous and nonrandomized trials and cohorts, it is interesting to note that these data suggest that the utilization of the SherpaPak reduces the risk of severe PGD even further in extended donors compared to traditional ice storage. Future analyses of the GUARDIAN-Heart study are needed to assess if SherpaPak preservation may similarly improve outcomes in NRP DCD (normothermic regional perfusion in donation after circulatory death) donors.

The data presented in this study suggest that the utilization of the SherpaPak in extended criteria heart donors may be a viable method for expanding the available donor pool while reducing the risk of adverse posttransplant events associated with extended criteria donors. Our results are particularly encouraging for European extended criteria donor considerations, although further clinical evaluation in Europe is warranted.

Several limitations should be considered when interpreting this study. Protocols for ice storage differ among transplant centers, and the specific preservation solution and cardioplegia used in the SherpaPak were not protocolized. Moreover, the utilization of the SherpaPak or ice was not randomized. When both options were available, onsite clinicians made the judgment for utilization. It is interesting to note that although severe PGD was significantly reduced in the SherpaPak cohort, and severe PGD is a risk factor for mortality, we did not observe any statistically significant difference in survival between the 2 cohorts. As survival is a multifactorial event in the transplant population, having immunologic, infectious, and cardiac contributions, a larger N and longer follow-up is likely required to assess any potential impact on survival. Finally, centers differed in the volumes of heart transplants and access to donor hearts, which may impact clinical decisions on donor heart utilization and clinical outcomes. Continued enrollment in the GUARDIAN-Heart study and further investigation may address some of these limitations and better inform clinical guidelines.

Conclusion

Utilization of the Paragonix SherpaPak Cardiac Transport System for extended criteria donor heart preservation and transportation significantly reduced the rate of all posttransplant MCS, new posttransplant ECMO/VAD, PGD, and severe PGD when compared to static cold storage in ice. Moreover, SherpaPak utilization significantly reduced the odds ratio of severe PGD in extended criteria donor heart transplants. These findings demonstrate that the SherpaPak can be safely utilized for heart preservation during transportation of organs from extended criteria donors, a particularly relevant application, given the need for an expanded donor pool to keep pace with the demand for heart transplants. The Paragonix SherpaPak Cardiac Transport System provides a simple, cost-effective solution to safely increase donor heart utilization while minimizing adverse posttransplant events.

Financial conflict of interest statement

There is no financial conflict of interest.

Acknowledgments

This study is registered at www.clinicaltrials.gov with the Unique Identifier NCT04141605 and is funded and administered by Paragonix Technologies. The authors gratefully acknowledge the assistance of Aarti Urs of ALKU (Andover, MA) for his medical writing assistance, the assistance of Michael Tajima and Mary V. Jacoski of Paragonix Technologies with analysis and editing of the manuscript, and Julia Kobe and Salina Moon, also of Paragonix Technologies, for their assistance with statistical analyses.

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