Donor Lung Preservation at 10 °C: Clinical and Logistical Impact

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Abstract

Introduction: Cold static donor lung preservation at 10 °C appears to be a promising method to safely extend the cold ischemic time (CIT) and improve lung transplant (LTx) logistics. The inclusion criteria for 10 °C preservation were suitable grafts for LTx without any donor retrieval concerns. Primary endpoint: primary graft dysfunction (PGD) grade-3 at 72-h. Secondary endpoints: clinical outcomes, cytokine profile and logistical impact.

Results: Thirty-three out of fifty-seven cases were preserved at 10 °C. Donor and recipient characteristics were similar across the groups. Total preservation times (h:min) were longer (p < 0.001) in the 10 °C group [1st lung: median 12:09 (IQR 9:23–13:29); 2nd: 14:24 (12:00–16:20)] vs. standard group [1st lung: median 5:47 (IQR 5:18–6:40); 2nd: 7:15 (6:33–7:40)]. PGD grade-3 at 72-h was 9.4% in 10 °C group vs. 12.5% in standard group (p = 0.440). Length of mechanical ventilation (MV), ICU and hospital stays were similar in both groups. Thirty and ninety-day mortality rates were 0% in 10 °C group (vs. 4.2% in standard group). IL-8 concentration was significantly higher 6-h post-LTx in the standard group (p = 0.025) and IL-10 concentration was increased 72-h post-LTx in the 10 °C group (p = 0.045).

Conclusions: Preservation at 10 °C may represent a safe and feasible strategy to intentionally prolong the CIT. In our center, extending the CIT at 10 °C may allow for semi-elective LTx and improve logistics with similar outcomes compared to the current standard preservation on ice.

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concept of lung preservation at 10 °C is being re-explored, given
cytoprotective metabolites are produced and mitochondrial health
is maintained when lungs are preserved at this temperature. Ali et al. investigated the effects of prolonged static cold storage on pig lungs exposed to 36 °C of static cold storage at either 10 °C or
on ice, followed by a 12-h evaluation on EVLP. The results showed
that lungs stored at 10 °C had less injury and improved pulmonary
function compared to those stored on ice. Based on these findings,
the concept of extending static cold preservation was tested clini-
cally in five human patients with excellent outcomes. Preclinical
data also published by the Toronto Lung Transplant Program sug-
gested that the combination of 10 °C storage with two cycles of 4-h
normothermic EVLP may result in excellent graft function after a
total of 3 days of preservation.

A clinical trial has recently been conducted to evaluate the fea-
sibility of using 10 °C lung preservation to enable semi-elective LTx
(ClinicalTrials.gov Identifier: NCT04616365). The primary end-
point of this study was to demonstrate the safety of 10 °C lung
preservation in a cohort of patients who underwent delayed trans-
plantation, while avoiding nighttime procedures. The secondary
endpoint was to compare the outcomes of these patients to those
who underwent transplantation using standard preservation dur-
ing a contemporaneous period of time. The study demonstrates that
extended preservation at 10 °C is both safe and efficient, resulting
in low rates of PGD and showing comparable early and mid-term
outcomes to those of lungs preserved using standard methods. The
potential to extend cold static preservation time by up to 12–24 h
at 10 °C could revolutionize the field of LTx.

The ability to reliably extend preservation periods could offer
several benefits beyond avoiding overnight transplantation. These
include overcoming current geographical limitations in
organ donation, creating more time for immunological matching
between donors and recipients, and the potential for perform-
ing LTx in a semi-elective manner. The successful implementation
of semi-elective LTx has significant advantages, particularly in
medium-size LTx programs, where both optimal OR scheduling and
the well-being of health care professionals are important factors
with regard to maintaining the surgical activity at the best possible
level. Other advantages might include improved OR logistics or the
acceptance of two simultaneous donors.

Our study aims to compare the outcomes and the logistical
impact of LTx using extended donor lung preservation at 10 °C to
the current standard of cold storage on ice.

**Material and methods**

**Study design and inclusion criteria**

This is a prospective non-randomized study including patients
who underwent LTx between November 2021 and February 2023
at our center, comparing prolonged preservation at 10 °C versus a
simultaneous cohort of patients using standard preservation on ice.

Our study protocol was adapted from the recently published
clinical trial evaluating the feasibility of using 10 °C lung preser-
vation to enable semi-elective LTx (ClinicalTrials.gov Identifier:
NCT04616365). The donor inclusion criteria for prolonged preservation at 10C
were lung grafts from both DBD or controlled DCD suitable for direct
transplantation when expected crossclamp was later than 6:00 pm.
The parameters used for evaluating the donor lungs were P/F ratio,
chest X-ray, bronchoscopy findings and donor history. The donor
exclusion criteria were: any concern during graft procurement,
doubts about the perfusion of the organ with the preservation solu-
tion, need for EVLP evaluation, an objective evidence of air leak that
prevented the lungs from being inflated during the storage time,
donor age greater than 70 years. Age was subsequently eliminated as exclusion criteria six months after the start of the study. The decision
was based on an internal analysis of outcomes using donors
older than 70 years old that did not show statistical significance when compared with younger donors.

The recipient inclusion criteria were patients older than 18
years old with signed informed consent and listed for primary lung
transplantation. Redo lung transplantation or urgent status was
considered as exclusions. However, after a few months, the investig-
gators decided to eliminate the urgent status as an exclusion criteria
because these patients might be more complex than elective cases
(for instance, patients with extracorporeal membrane oxygenation
(ECMO) as bridge to transplant). Consequently, the study team
decided to avoid overnight transplantation due this complexity.

The decision of prolonged preservation at 10 °C was made by the
transplant team in order to intentionally extend the CIT for any
logistical purpose once the retrieved grafts met the aforemen-
tioned criteria. Reasons for deciding to extend the CIT at 10C were
the following: avoidance of night-time surgeries, delaying com-
plex LTx cases to the morning, need for specific intervention that
is only available during daytime or waiting for histopathological
findings. On the other hand, reasons to follow the standard protocol
on ice to go straight to transplant were: donor cross-clamp times
before 6:00 p.m., risk of lung deflation during prolonged storage,
donor concerns, absence of informed consent, avoiding cancelation
of morning elective cases and procurements performed by other
programs.

Recipient selection was conducted according to blood type, size,
and LAS, regardless of the selected preservation method.

**Donor procurement and preservation procedures**

All lungs were retrieved from donors after brain death or after
controlled circulatory death. Organ procurement was performed
according to our standard protocols described elsewhere. Lung
preservation was performed by antegrade pulmonary artery flushing
with a low-potassium dextran-based solution after inject-
ing prostaglandin E1 through the pulmonary artery. Subsequently,
retrograde flush through the pulmonary veins was performed.
Lungs were stored on ice after mild inflation with 50% oxygen and
transported to the recipient hospital in the ice cooler.

At the end of the retrieval, any grafts meeting the criteria
for 10 °C preservation and with a donor cross-clamp time after
6:00 p.m. were transferred to a specific incubator located at the
entrance of the recipient OR, which maintained uniform temper-
atre at 10 °C (MYTEMP™65HC, Benchmark Scientific, NJ, USA).
There was a maximum of 12 h from the donor cross-clamp time
to the arrival of the recipient to the OR. Grafts following the stan-
dard preservation method were stored in the same ice cooler
used for transport. Fig. 1 illustrates the study design and preservation
procedures.

**Outcomes**

The primary endpoint was to compare the incidence of PGD
grade 3 at 72 h according to the 2016 ISHLT consensus, using dif-
f erent methods of preservation (10 °C versus standard on ice). The
secondary endpoints were the comparison of days of recipient MV,
length of ICU and hospital stay, as well as 30 and 90-day mortality
rates. We also performed a survival analysis of both groups.

The reasons for deciding upon prolonged preservation at 10 °C
or standard preservation on ice were also collected.

The histologic acute lung injury (ALI) score was analyzed com-
paring both preservation groups using lung biopsies performed
30-min after reperfusion. Our biopsy protocol includes a biopsy
in the donor before cross-clamp, before implantation during graft

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Fig. 1. Study design and preservation procedures. *After meeting inclusion criteria and providing informed consent unless there was any concern in the retrieval or the need for EVLP evaluation.

preparation on the back table, and 30 min to 1 h after the reperfusion of that lung. The three samples are usually taken from the same lung and the same lobe (usually right middle lobe or lingula). We decided to focus on the 3rd sample because it was the most consistent biopsy. The AIL score evaluates three items (neutrophils, alveolar edema, and interstitial infiltrates), with each one receiving a score between 0 and 3 points, where 0 was no presence of the histological change, 1 was mild, 2 moderate and 3 severe (Table S1, Supplementary material).

The cytokine expression profile (Interleukin-8, Interleukin-10) was analyzed using ELISA (Enzyme-Linked Immunosorbent Assay) measuring the following blood serum samples: the recipient before transplant (T1); 6-h post-transplant (T4); 24-h post-transplant (T5); and 72-h post-transplant (T6).

Statistical analysis

Categorical variables were analyzed using the Chi-square test while the Mann-Whitney U test was used for numerical variables. Overall survival was defined as the time from surgery to death from any cause. Patients who were lost to follow-up or who were alive at the end of the study were censored at the last visit date. Survival analysis was performed using Kaplan-Meier curves, and the comparison between the curves was performed via a log-rank test. The level of significance was set at 0.05. Stata v17 software was used for the analysis.

Results

From November 2021 to February 2023, 57 LTx were performed at our institution (excluding redo-LTx and EVLP cases). Of these, 33 cases (57.9%) were transplanted after a prolonged preservation at 10 °C, and 24 cases (42.1%) were preserved following the standard method on ice. Fig. 2 shows the study flowchart. The main reason for using 10 °C storage was to intentionally extend the CIT to avoid overnight surgeries by performing LTx as a semi-elective procedure (N = 20). Other logistical reasons for choosing prolonged preservation at 10 °C included delaying complex LTx cases to the next morning (N = 11), need for intraoperative plasmapheresis (N = 1) or waiting for donor histopathological findings (N = 1). Standard preservation on ice was carried out due to donor cross-clamp times before 6:00 p.m. (N = 9), donor concerns including a MSSA (Methicillin-sensitive Staphylococcus aureus) positive donor BAL and two cases with suspected air leak that might lead to deflation during the prolonged preservation storage (N = 3), absence of informed consent (N = 2), decision to avoid canceling morning elective OR schedule (N = 6) or other reasons (3 urgent status cases prior to urgency being eliminated as an exclusion criteria and 1 case retrieved by another program [n = 4]).

Donor and recipient characteristics were comparable between groups (Table 1). Most donors were female with a mean age of 58 years in the 10 °C group vs. 61 years in the standard group. The donor P/F ratio was similar between groups (463 in the 10 °C group vs. 475 in the standard group), as was the donor smoking history (12% in the 10 °C group vs. 17% in the standard group). Seventy-nine percent of the recipients in the 10 °C group were male (vs. 54% in the standard group; p = 0.056). Bilateral transplants were performed in 90.9% cases in the 10 °C group, and 18.2% in urgent status. Idiopathic Pulmonary Fibrosis (IPF) was the most frequent indication for LTx in both groups (30% in the 10 °C group vs. 29% in the standard group), with a median LAS score of 37 and 38.5, respectively.

Total preservation times (h:min) from donor cross-clamp to recipient reperfusion were statistically longer (p < 0.001) in the 10 °C group [1st lung: median 12:09 (IQR 9:23–13:29); minimum 5:32; maximum 17:15]; 2nd lung: median 14:24 [IQR 12:00–16:20; minimum 8:20; maximum 18:40] in comparison to the standard group [1st lung: median 5:47 (IQR 5:18–6:40; minimum 5:20; maximum 6:40); 2nd lung: median 7:15 (IQR 6:33–7:40; minimum 6:30; maximum 7:40)]. Median lung transport time (h:min) in the ice cooler was 3:15 in the 10 °C group (IQR 2:30–3:55). 10 °C preservation time (h:min) represents the period of intentional extension of the CIT [1st lung: median 6:50 (IQR 2:00–12:58); 2nd lung: median 8:35 (IQR 3:40–14:19)]. The CIT (h:min) for both the first and second implanted lungs were also significantly longer in the 10 °C group [1st lung: median 11:40 (IQR 9:50–13:25); 2nd lung: median 13:36 (IQR 11:20–15:20)] in comparison to the standard group [1stlung: median 5:05 (IQR 4:32–5:58); 2nd lung: median 10:36 (IQR 7:15–14:28)].
Table 1
Demographics and transplant outcomes comparing prolonged preservation at 10°C vs. standard preservation on ice.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Standard preservation on ice (n=24)</th>
<th>Prolonged preservation at 10°C (n=33)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Donor</strong></td>
<td></td>
<td></td>
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<tr>
<td>Age donor (mean ± SD)</td>
<td>61 ± 12.3</td>
<td>58 ± 10.7</td>
<td>0.166</td>
</tr>
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<td>Gender, female (%)</td>
<td>15 (65.2)</td>
<td>22 (66.7)</td>
<td>0.910</td>
</tr>
<tr>
<td>Smoking history (%)</td>
<td>4 (17)</td>
<td>4 (12)</td>
<td>0.698</td>
</tr>
<tr>
<td>Type of donor:</td>
<td></td>
<td></td>
<td>0.088</td>
</tr>
<tr>
<td>DBD (%)</td>
<td>13 (54.2)</td>
<td>25 (75.8)</td>
<td></td>
</tr>
<tr>
<td>DCD (%)</td>
<td>11 (45.8)</td>
<td>8 (24.2)</td>
<td></td>
</tr>
<tr>
<td>MV donor, days (median, IQR)</td>
<td>2 (1–11)</td>
<td>1 (1–11)</td>
<td>0.758</td>
</tr>
<tr>
<td>P/F ratio (median, IQR)</td>
<td>475 (415–504)</td>
<td>463 (396–512)</td>
<td>0.677</td>
</tr>
<tr>
<td><strong>Recipient</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age recipient (mean ± SD)</td>
<td>60.3 ± 6.5</td>
<td>56.4 ± 10.6</td>
<td>0.056</td>
</tr>
<tr>
<td>Gender, male (%)</td>
<td>13 (54)</td>
<td>26 (79)</td>
<td>0.048</td>
</tr>
<tr>
<td>Indication (%)</td>
<td></td>
<td></td>
<td>0.761</td>
</tr>
<tr>
<td>COPD</td>
<td>7 (29)</td>
<td>7 (21)</td>
<td></td>
</tr>
<tr>
<td>IPF</td>
<td>7 (29)</td>
<td>10 (30)</td>
<td></td>
</tr>
<tr>
<td>ILD</td>
<td>7 (29)</td>
<td>8 (24)</td>
<td></td>
</tr>
<tr>
<td>CF</td>
<td>1 (4)</td>
<td>2 (6)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2 (9)</td>
<td>5 (19)</td>
<td></td>
</tr>
<tr>
<td>LAS score (median, IQR)</td>
<td>38.5 (35–41)</td>
<td>37 (35–44)</td>
<td>0.576</td>
</tr>
<tr>
<td>BMI (median, IQR)</td>
<td>25.8 (24.2–28.4)</td>
<td>25 (22.1–26.8)</td>
<td>0.251</td>
</tr>
<tr>
<td>6MWT (median, IQR)</td>
<td>344 (296–425)</td>
<td>374 (270–416)</td>
<td>0.969</td>
</tr>
<tr>
<td>mPAP mmHg (median, IQR)</td>
<td>21 (18–25)</td>
<td>22.5 (16–30)</td>
<td>0.928</td>
</tr>
<tr>
<td>Ratio pTLC donor/Rec (median, IQR)</td>
<td>0.9 (0.6–1.0)</td>
<td>0.8 (0.7–1.0)</td>
<td>0.078</td>
</tr>
<tr>
<td><strong>Transplant</strong></td>
<td></td>
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</tr>
<tr>
<td>Bilateral LTx (%)</td>
<td>23 (95.8)</td>
<td>30 (90.9)</td>
<td>0.651</td>
</tr>
<tr>
<td>Urgent status (%)</td>
<td>2 (8.3)</td>
<td>6 (18.2)</td>
<td>0.291</td>
</tr>
<tr>
<td>Intraoperative ECLS (%)</td>
<td></td>
<td></td>
<td>0.327</td>
</tr>
<tr>
<td>ECMO</td>
<td>17 (70.8)</td>
<td>25 (75.8)</td>
<td></td>
</tr>
<tr>
<td>CPB</td>
<td>0</td>
<td>2 (6)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>7 (29.2)</td>
<td>6 (18.2)</td>
<td></td>
</tr>
<tr>
<td>Total preservation time 1st lung (h:min)</td>
<td>5:47 (5:18–6:40)</td>
<td>12:09 (9:23–13:29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total preservation time 2nd lung (h:min)</td>
<td>7:15 (6:33–7:40)</td>
<td>14:24 (12:00–16:20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CIT 1st lung (h:min)</td>
<td>5:05 (4:32–5:58)</td>
<td>11:40 (9:50–13:25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CIT 2nd lung (h:min)</td>
<td>6:31 (5:34–7:28)</td>
<td>13:36 (11:20–15:20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Postoperative outcomes</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>PCG grade 3 at 72 h (%)</td>
<td>3 (12.5)</td>
<td>3 (9.4)</td>
<td>0.440</td>
</tr>
<tr>
<td>Postoperative ECMO (%)</td>
<td>4 (16.7)</td>
<td>4 (12.1)</td>
<td>0.626</td>
</tr>
<tr>
<td>MV recipient, days (median, IQR)</td>
<td>2 (1–11)</td>
<td>1 (0.8–10.5)</td>
<td>0.758</td>
</tr>
<tr>
<td>ICU stay, days (median, IQR)</td>
<td>9 (6–23)</td>
<td>8 (6–18)</td>
<td>0.814</td>
</tr>
<tr>
<td>Hospital stay, days (median, IQR)</td>
<td>45 (35–75)</td>
<td>42 (36–54)</td>
<td>0.297</td>
</tr>
<tr>
<td>30-d mortality (%)</td>
<td>1 (4.2)</td>
<td>0</td>
<td>0.237</td>
</tr>
<tr>
<td>90-d mortality (%)</td>
<td>1 (4.2)</td>
<td>0</td>
<td>0.237</td>
</tr>
<tr>
<td>Best post-op FEVi (median, IQR)</td>
<td>2380 (1595–2740)</td>
<td>2170 (2020–2680)</td>
<td>0.913</td>
</tr>
<tr>
<td>Acute cellular rejection (%)</td>
<td>8 (34.8)</td>
<td>9 (28.1)</td>
<td>0.598</td>
</tr>
</tbody>
</table>

DBD: brain death donor; DCD: donor after controlled circulatory death; MV: mechanical ventilation; P/F: arterial oxygen partial pressure/ fractional inspired oxygen; LTx: lung transplantation; COPD: chronic obstructive pulmonary disease; IPF: idiopathic pulmonary fibrosis; ILD: interstitial lung disease; LAS: lung allocation score; BMI: body mass index; 6MWT: 6 min walking test; mPAP: median pulmonary artery pressure; pTLC: predictive total lung capacity; CIT: cold ischemia time; ECLS: extracorporeal oxygenation; CPB: cardiopulmonary bypass; PGD: primary graft dysfunction; FEVi: forced expiratory volume 1 s.
Similarly, 258 (257–254) methods 254 (249–241). The preservation times are displayed in Fig. 3a and b.

No statistically significant differences were detected regarding PGD grade 3 at 72-h (9.4% in the 10°C group vs. 12.5% in the standard group) or the need for postoperative ECMO (12.1% in the 10°C group vs. 16.7% in the standard group). The median length of MV (1 vs. 2 days), ICU stay (8 vs. 9 days) and hospital stay (42 vs. 45 days) were similar in both groups (Table 1). No deaths were observed at 30 and 90 days in the 10°C group. One patient (4.2%) from the standard preservation group passed away 28 days post-operation due to sepsis. The median follow-up time was 15.36 months (IQR 12.5–17.1). Survival outcomes for the 10°C group were similar compared to the standard group (100% vs. 95.8% at 90 days; 97% vs. 92% at 180 days, 93% vs. 87% at 1 year, respectively; log-rank 253 p = 0.363). Fig. 4 shows the Kaplan–Meier survival curves.

The median ALI score for postreperfusion biopsy was 1 point for the 10°C group (IQR 0–1) and 0 for the standard group (IQR 0–1). The histopathological findings of two cases carried out by different methods of preservation are illustrated in Fig. 5.

Regarding the cytokine expression profile (Table 2), there was a significantly higher IL-8 concentration 6 h after transplant (T4) with standard preservation on ice (p = 0.025) and a significantly increased IL-10 concentration 72 h after transplant (T6) in the 10°C group (p = 0.045). The graphs comparing cytokine profiles are displayed in Fig. 6.

**Fig. 3.** Transport, cold ischemia and preservation times. (a) Preservation times for both groups. Median times for the first and second lung respectively [minimum–maximum]. (b) Box plot showing the different preservation times.

**Fig. 4.** Kaplan–Meier survival curves.

**Discussion**

Despite the continuous efforts on improving donor and recipient management, 10 PGD remains a significant source of early morbidity and mortality. 18,20 Similarly, the maximum CIT of 6–8 h has traditionally been associated with the occurrence of PGD. 21,22 Although recent studies suggest that current preservation techniques allow for a safe extension of the CIT without increasing the risk of developing PGD grade 3, 23,24 transplant surgeons are normally conservative while using the standard preservation approach. Therefore, despite the available evidence, the maximum safe CITs are still uncertain. Following the new evidence on the safety and feasibility of extending the CIT to the temperature of 10°C, 25,26 our results support the fact that prolonged preservation at 10°C provides comparable early outcomes to the standard method, specifically in terms of the incidence of PGD grade 3 at 72-h. In this study, by extending the preservation times at a temperature of 10°C we did not observe a negative impact on donor lung histopathology but we saw a superior inflammatory profile.

Incidence of severe PGD at 72-h was the primary endpoint of this study based on evidence suggesting that it has a strong impact on early and late outcomes 19,20 and this is influenced by organ preservation strategies. The incidence of PGD grade 3 at 72-h in the study group (9.4%) did not differ from the control group, despite total preservation times of up to 18 h. Secondary endpoints, such as...
as length of MV, hospital stay, and ICU stay were similar in both groups. All patients in the study group survived to the 30th and 90th day post-LTx. Clinical outcomes of this study are consistent with those recently published by the multicenter clinical trial on 10 °C preservation.22

The impact of the preservation strategy on the post-LTx cytokine expression profile has recently been analyzed. An animal study concluded that extending the CIT from 6 to 12 h using the standard preservation method on ice did not modify the expression of pro-inflammatory cytokines (IL-1β, IL-6, IFN-gamma).23 Additionally, the metabolomic benefits of 36-h preservation at 10 °C has been described in experimental animal models showing significantly lower concentrations of IL-1β and IL-8 in the EVLP perfusate for lungs stored at 10 °C versus those stored on ice.7 Moreover, in the setting of injured porcine lungs, 12-h preservation at 10 °C showed reduced histological damage and lower tissue concentrations of IL-1β, in comparison to those immediately implanted after standard preservation on ice.24 Our results are in keeping with the previous studies, revealing a significant increase in the proinflammatory profile using the standard approach (IL-8 serum concentration 6 h after LTx) and a protective anti-inflammatory benefit when preserved under 10 °C (IL-10 serum concentration 72 h after LTx).

While IL-8 has been shown to be associated with early onset inflammation and PGD, IL-10 might have positive effects on allograft outcomes by inhibiting inflammatory responses.25 In fact, treating injured human donor lungs with IL-10 may enhance lung function, potentially making injured lungs suitable for LTx.26 These findings in the cytokine profile expression are aligned with other markers such as a low AIR score and less severe PGD incidence, pointing out that there is no significant inflammatory insult when prolonging the CIT using 10 °C preservation.

An additional important issue is the observation made in several studies that surgical procedures performed at nighttime appear to be associated with a higher risk of surgical complications.27,28 Specifically, in the context of transplantation, some authors have linked the time of implantation to early morbidity and mortality outcomes.29 More specifically, in the field of LTx, Yang et al. suggested that LTx performed at nighttime, between 6:00 p.m. and 6:00 a.m. were associated with a higher risk of major adverse events in the postoperative period.30 Exploring the concept that performing procedures during daytime may result in a safer outcome is what has motivated these studies to intentionally extend preservation times under 10 °C to achieve a semi-elective procedure. However, it is not only to avoid nighttime procedures; there are many other reasons behind this decision, such us delaying complex cases to the next morning. For instance, recipients in

**Table 2**

<table>
<thead>
<tr>
<th>Cytokines (concentration mcg/dL)</th>
<th>Standard preservation on ice</th>
<th>Prolonged preservation at 10 °C</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-8 (median, IQR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T4 (6 h post-transplant)</td>
<td>58.8 (9.4–83.4)</td>
<td>35.2 (24.5–54.7)</td>
<td>0.025</td>
</tr>
<tr>
<td>IL-10 (median, IQR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T6 (72 h post-transplant)</td>
<td>11.4 (9.3–28.5)</td>
<td>41.1 (22.1–64.9)</td>
<td>0.045</td>
</tr>
</tbody>
</table>

**Fig. 5.** Histopathological findings. (A) Normal lung biopsy performed after reperfusion following extended 10 °C preservation. (B) Mild interstitial infiltrate constituted by lymphocytes in a case with standard preservation on ice.

**Fig. 6.** Box-plot showing cytokine expression profile comparing both preservation methods.
an urgent status with ECMO as a bridge or for whom long dis-
section is expected due to previous surgeries could benefit from
a morning OR start time when the majority of hospital person-
nel are present.\textsuperscript{12} Prolonged preservation at 10°C also facilitate
pre-transplant treatments in pre-sensitized recipients and enabled
us to perform intraoperative plasmapheresis at our site, which is
only logistically possible in the mornings on working days. Another
logistical benefit has been the opportunity to accept two or more
donors at the same time and delaying one of the cases in order
to spread the workload between transplant teams.\textsuperscript{11} In fact, wait-
ing for a frozen section to rule out a malignancy in donors with
a suspicious nodule has classically been a reason for declining a
graft in our institution due to a possible prolonged CIT before the
10°C preservation strategy became available. Among the demand
and scarcity of suitable donors, another potential opportunity for
our program could be assessing donor lungs in distant regions and
improving organ sharing thanks to 10°C preservation. We strongly
believe that the aforementioned logistical benefits have a critical
impact on LTx programs, particularly in those programs located in
medium-sized hospitals, as it could increase flexibility with regard
to the scheduling of LTx operations and lead to a greater focus on
patient safety.

This study has several limitations, mainly the relatively small
case number. However, it provides both contemporary and
comparable groups of patients showing promising outcomes and
increases knowledge surrounding the novel strategy of 10°C preser-
vation. Nevertheless, conducting a randomized trial comparing
10°C to standard cold storage on ice would help to definitively
clarify whether preservation at 10°C leads to equal or better out-
comes when intentionally extending CIT. Transporting the lungs
on ice before being transferred to the 10°C device represents
another limitation of our study, diminishing the hours the grafts
could be beneficially preserved at 10°C. Furthermore, the inability
to constantly monitor the temperature during both preservation
strategies might be another weakness of this study. In contrast,
this study has several strengths, such as having performed a non-
matched analysis between groups, which provides a raw analysis
but a close approximation of what happens in real life.

Conclusion

In conclusion, our study reinforces that LTx after extended
preservation at 10°C yields a low incidence of PGD and comparable
early outcomes to the standard method with significantly longer
preservation times. Extending preservation times by up to 18 h at a
temperature of 10°C greatly improved logistics at our site and has
the potential to revolutionize the field of LTx.

Statement of IRB/ethics board approval

This study was approved by the Ethics Committee of our institu-
tion, in accordance with the Declaration of Helsinki (Project Code:
118/21, 29 September 2021).

Statement of informed consent

All patients enrolled in the study provided a signed informed
consent.

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