

Lactate during ex-situ heart perfusion does not predict the requirement for mechanical circulatory support following donation after circulatory death (DCD) heart transplants

S. Cernic *et al.* | *J Heart Lung Transplant* Sep 2022 | [https://doi: 10.1016/j.healun.2022.02.003](https://doi.org/10.1016/j.healun.2022.02.003).

STUDY HIGHLIGHTS

Objective: Lactate levels are commonly utilized to assess heart function during *ex-situ* heart perfusion (ESHP) following donation after circulatory death (DCD). The association between lactate profiles during ESHP and the need for mechanical circulatory support (MCS) after transplant was investigated.

Methods: This single center, retrospective review examined all fifty-one recipients of DCD heart transplants from Mar 2015 - Jun 2020. Lactate levels were obtained over 3 hours of ESHP.

Results: There was no difference in arterial lactate profiles on ESHP for those dependent upon MCS post transplant. After 3 hours of ESHP, arterial lactate was >5mmol/L in 80% of cases requiring MCS vs 62% without ($p = 0.30$). There was also no difference in the frequency of rising lactate concentration: 15% MCS vs 13% non-MCS ($p = 1.00$).

Conclusion: For DCD hearts transplants utilizing ESHP, lactate profiles do not seem to be a reliable predictor of MCS requirements post-transplant.

CENTRAL FIGURE

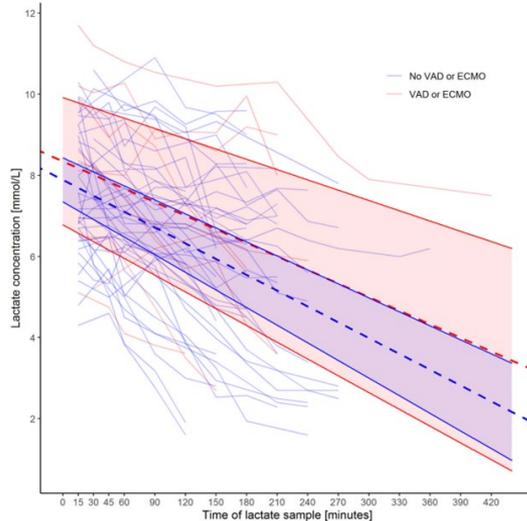


Figure 4
Arterial lactate trends of ESHP DCD hearts with requirement for post-transplant ECMO/VAD. Dashed lines represent the fitted models for each subgroup. The shaded areas between 2 solid lines represent the 95% confidence intervals for the fitted models.

REVIEWER'S COMMENTS

- The field of DCD heart transplantation is relatively young, with unanswered questions regarding ideal graft preservation and assessment.
- The evaluation of heart acceptability currently relies on echocardiogram prior to withdrawal of life sustaining therapy, lactate profiles and visual inspection of the heart during ESHP.
- Quantitative graft assessment is an area of active investigation to further improve outcomes.

LIMITATIONS

- The limitations of this study include its retrospective, single-center design, as well as the relatively small number of cases included in the analysis.
- Data on lactate profiles for hearts that were discarded were not included – only hearts that proceeded to transplant were included.
- Recipients' diagnosis differed significantly between the groups, which could contribute to the difference in their outcomes.

Prognostic Significance of the N-Terminal Pro-B-Type Natriuretic Peptide in Lung Transplant Candidates on the Waiting List

S. Izkhakian *et al.* | *Diagnostics* Aug 2022 | <https://doi.org/10.3390/diagnostics12092112>

STUDY HIGHLIGHTS

Objective: To retrospectively investigate the prognostic significance of N-terminal pro-B-type natriuretic peptide (NT-proBNP) in lung transplant (LTx) candidates at a single center.

Methods: Association of NT-proBNP levels with baseline characteristics and all-cause mortality analyzed from 205 LTx candidates added to waitlist Nov 17 – Dec 19.

Results: NT-proBNP correlated positively with age, FVC and MPAP, and negatively with DLCO and cardiac index. No correlation with 6MWT distance, FEV1, TLC, and PCWP. Optimal NT-proBNP to predict MPAP >35mmHg was >251pg/mL (Sens 58%, Spec 86%, PPV 45%, NPV 91%). On multivariate analysis, ↑ NT-proBNP strongly associated with ↑ mortality (HR 1.49, 95% CI 1.10–2.03, $p = 0.01$).

Conclusion: Strong association of ↑ NT-proBNP with severe PH and waitlist mortality. NT-proBNP is not currently factored into the lung allocation score (LAS)

CENTRAL FIGURE

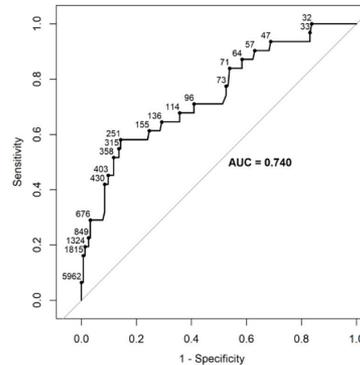


Figure 1: The relation of NT-proBNP levels and values of MPAP measured on RH catheterization. The receiver operator characteristic plot demonstrates sensitivity, specificity, and the area under the curve for the relation of NT-proBNP levels with values of MPAP measured on RH catheterization ≤ 35 or >35 mm Hg.

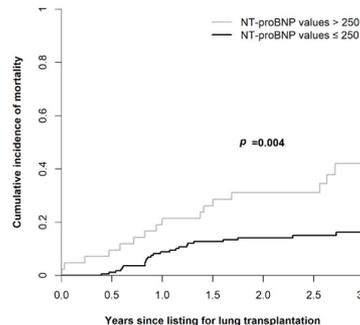


Figure 2: Cumulative incidence of mortality since listing for lung transplantation.

REVIEWER'S COMMENTS

- ↓ NT-proBNP level may identify LTx candidates with a low probability of significant PH, as a non-invasive alternative to right heart catheterization
- ↑ NT-proBNP level may warrant consideration of earlier listing for LTx.
- NT-proBNP may have a role as a biomarker to improve risk stratification in LTx candidates and add value to the LAS.

LIMITATIONS

- The limitations of this study include its retrospective, single-center design, which focused on only a single determination of NT-proBNP at the time of placement on the waiting list.
- Non-survivors waiting for LTx were more likely to have ILD; survivors were more likely to have COPD.
- Prospective larger studies are required for validation, and protocols for assessing NT-proBNP in a serial manner until LTx are necessary.

Successful 3-day lung preservation using a cyclic normothermic ex vivo lung perfusion strategy

A. Ali et al. | *EBioMedicine* Sep 2022 | <https://doi: 10.1016/j.ebiom.2022.104210>.

STUDY HIGHLIGHTS

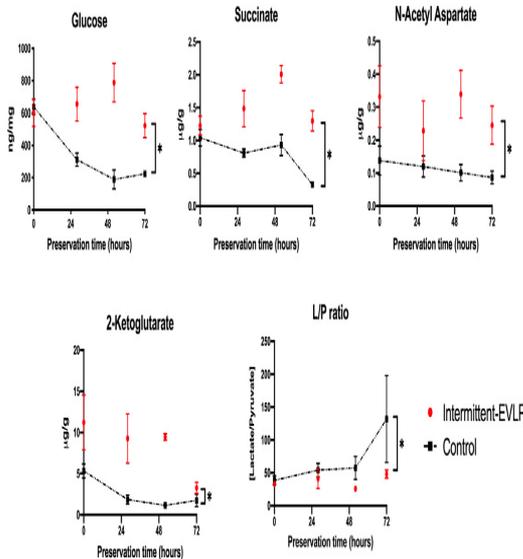
Background: Strategy of alternating 10°C cold static preservation (CSP) with *ex vivo* lung perfusion (EVLP) in repeated cycles was proposed to facilitate multi-day lung preservation.

Methods: Porcine lungs were preserved using 10°C CSP with a daily 4hr period of normothermic EVLP. After 72hrs, a single-left lung transplant was performed into a recipient animal. As negative controls, 2 lungs preserved for 72 hrs with 10°C CSP alone were transplanted. Lung function was monitored during a 4hr reperfusion period.

Results: Lung function and histological structures were stable in the EVLP group, whereas lungs stored with 10°C CSP alone failed immediately. Levels of glucose, succinate and N-acetyl aspartate, which support mitochondrial health, were better maintained using EVLP. Expression of the inflammasome activation marker CASP1 was ↓ after EVLP, and lower fold changes of mitochondrial injury markers were found in the EVLP treated grafts.

Conclusion: 3 days of successful lung preservation is achievable by combining 10°C CSP and intermittent normothermic EVLP.

CENTRAL FIGURE



Quantitative measure of central carbon metabolites during 3-day lung preservation with or without EVLP

REVIEWER'S COMMENTS

- >24hrs continuous perfusion has not previously been reported in *ex vivo* models.
- Continuous 10°C CSP is not a viable approach to 3-day preservation, resulting in a severe injury phenotype. Full metabolic activity at normothermia may mitigate cellular damage.
- This study demonstrates proof of concept that intermittent EVLP can improve preservation times, to potentially allow pre-implant therapy, to improve utilisation of lungs over long distances and help make lung transplantation a semi-elective procedure.

LIMITATIONS

- Sample size was small. The primary endpoint was restricted to 4 hours post transplantation. Cyclic EVLP using the current standard of care for lung preservation (4°C) was not evaluated. Lungs used were free from trauma, ventilator induced injury, aspiration, embolism or infective changes, which are commonly identified in routine transplantation.