ISHLT September 2025 | Cardiothoracic Surgery
JOURNAL WATCH

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Lung transplant in patients with suspicious lung lesions

Begic M, Hillebrand C, Frommlet F, Benazzo A, et al. *JHLT* 2025 Jul 9:S1053-2498(25)02111-4. | DOI: 10.1016/j.healun.2025.07.005

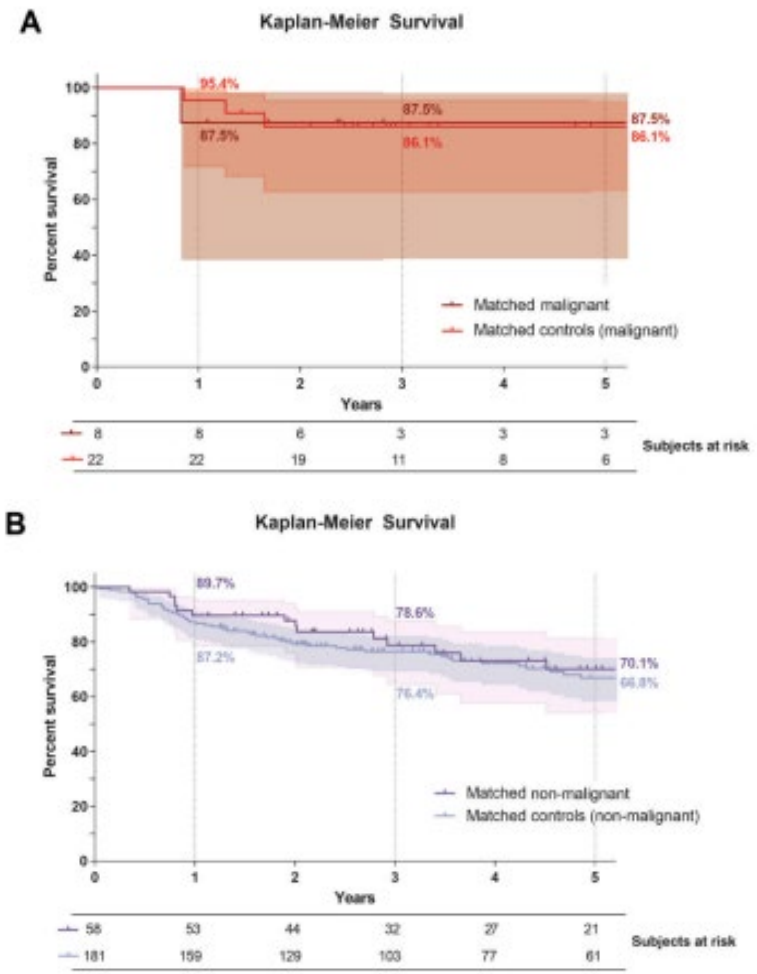
Study Highlights

Objective: To evaluate the significance of suspicious pulmonary lesions in patients who underwent lung transplantation.

Methods: This was a single-center retrospective analysis of all lung transplant patients with a suspicious lung nodule between January 2012 and October 2022. Characteristics of the lesion, and histology reports were assessed and compared to post operative outcomes and calculated overall survival at 1, 3, and 5- year intervals.
Suspicious lesions were defined as speculated radiographic features, growth of more than 2 mm in 3 months and/or maximum standard uptake value (SUVmax) above 2.5.

Results: 79 patients (7.4%) out of 1070 transplanted patients had a suspicious lung nodule on pre-transplant imaging. 83.5% were patients with COPD. Lung cancer was confirmed in the explanted lung in only 12 of the 79 patients (15.1%).
Adenocarcinoma was most common diagnosis, in 8 patients (66.7%). Stage I and II were most common, with 10 of 12 (83.3%), 2 patients were stage IIIA (16.6%) during post transplant work up.
Overall survival was similar between the malignant nodule group, the nonmalignant nodules groups, and a control group at 1 year (87.5% vs 89.7% vs 88.2%). 3 years (87.5% vs 78.6% vs 77.5%) and 5 years (87.5% vs 70.1% vs 68.6%). Cox proportional-hazard model determined that the nodules did not have significant impact on survival (hazard ratio: 0.828; 95% confidence interval: 0.451-1.519; p = 0.541).

Conclusions: Unverified suspicious lung nodules should not be an exclusion for transplant, only a small proportion are malignant. Long term survival is unaffected even in cases of early stage lung cancer.



Kaplan-Meier survival curves comparing propensity-score–matched patients with malignant (A) and nonmalignant lesions (B) with their respective matched controls.

Reviewer's Comments

- Patient selection is a critical component of transplantation and recent/active malignancy is a contraindication
- End stage lung disease is a significant risk factor for developing lung cancer compared to the general public
- Case series have demonstrated an incidence of unexpected lung cancer in explanted lung of 0.5% to 2.4%
- This study takes this a step further with a retrospective analysis of transplantation in patients with suspicious nodules.
- The findings of this study may help give confidence when evaluating patients with smaller lung nodules for transplantation.
- Most of the nonmalignant lesions were found to be necrotizing granulomas, organizing pneumonia, aspergilloma, chrondohyamartoma, and inflamed bronchogenic cysts, all which are expected findings in this patient cohort.

Limitations

- Single center retrospective study
- Aim was to analyze a rare finding which limited sample sizes.
- Lung cancer was confirmed in 12 out of 79 patients (15.1%), of these 12, 3 patients had advanced cancer recurrence (lung/pleura or liver & spine). 5 of these patients are deceased, 2 from cancer recurrence, 1 from another malignancy, and 2 from other causes.
- While the cox proportional hazard model determined that the malignant nodules did not impact survival overall, this incidence of recurrence is a reminder that the risk is not zero and judicious evaluation is important.

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Five-Year Experience of Heart Transplantation Following Donation After Circulatory Death

Benkert AR, Jawitz OK, Alvarez Lobo A, Casalinova S, et al. *J Thorac Cardiovasc Surg* 2025 Aug 19. | DOI: 10.1016/j.jtcvs.2025.08.013

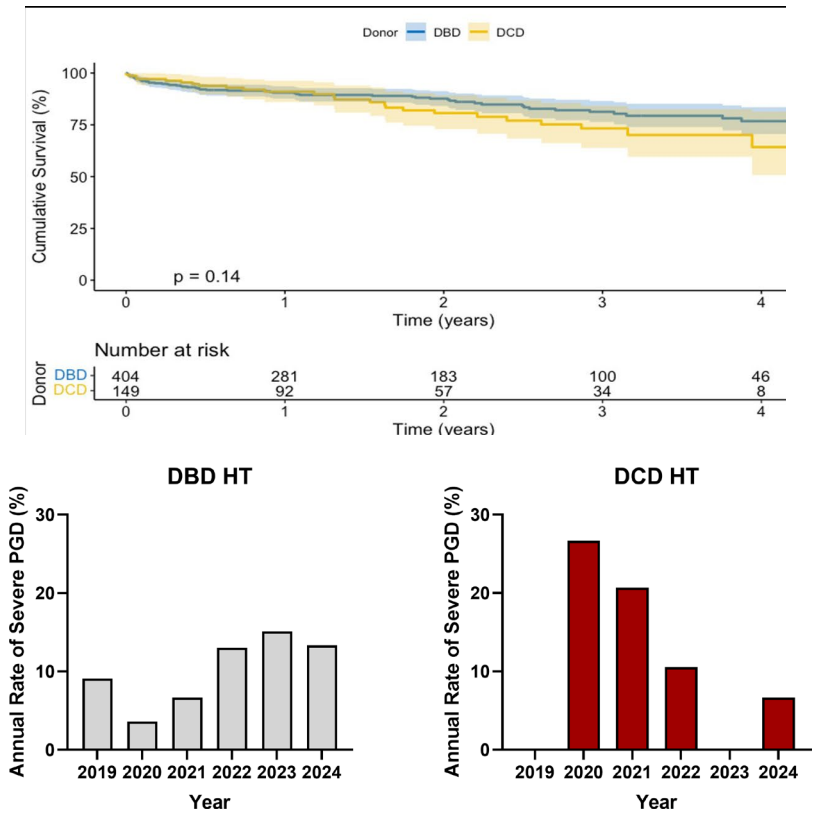
Study Highlights

Objective: A single institution's 5-year outcomes with DCD heart transplant.

Methods: The study period was January 2019 to October 2024. The instituition's medical records and the UNOS registry were used. The primary outcome was survival. Secondary outcome included primary graft dysfunction.

Results: 404 (73%) DBD and 149 (27%) DCD recipients were included. Baseline characteristics were similar. DCD recipients were less likely to have an IABP. DCD hearts had increased ischemic time (5.7 vs 3.7 hours). DCD hearts also had increased travel distances (381 vs 299 miles). Kaplan Meier survival rates and primary graft dysfunction rates were similar between the two groups.

Conclusions: The 5-year experience between DCD and DBD allografts seem to be similar with regards to overall survival and primary graft dysfunction.



Top: Kaplan-Meier graft survival estimate
Bottom: Annual rate of severe PGD following DBD HT and DCD HT.

Reviewer's Comments

- This study provides us with midterm outcomes following DCD heart transplants.
- The incidence of severe primary graft dysfunction (PGD) has decreased over the study period from 27% in 2020 to 6.7% in 2024 pointing towards improved processes and management of the donor heart.
- There is no significant difference in long term survival and severe PGD among the two groups of patients.

Limitations

- DPP and NRP cohorts could be analyzed separately, with the knowledge that the numbers are small in the NRP cohort.
- There is a divergence of the survival curve beyond 18 months, though not significant statistically, no clear reasons have been identified. This has been the trend with DCD transplants from published data.
- As outlined in the study, with the increase in DCD transplants across US from 3% to 14%, a multicenter analysis of data will provide higher volume of patients for analysis.
- The definition of ischemia time needs to be defined to provide a standardized method for comparison.

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Association of agonal phase duration with heart utilization and post-transplant outcomes in donation after circulatory death heart transplantation

Hong Y, Hess NR, Dorken-Gallastegi A, Iyanna N, et al. *JHLT* 2025 May;44(5):736-747. | DOI: 10.1016/j.healun.2024.11.011

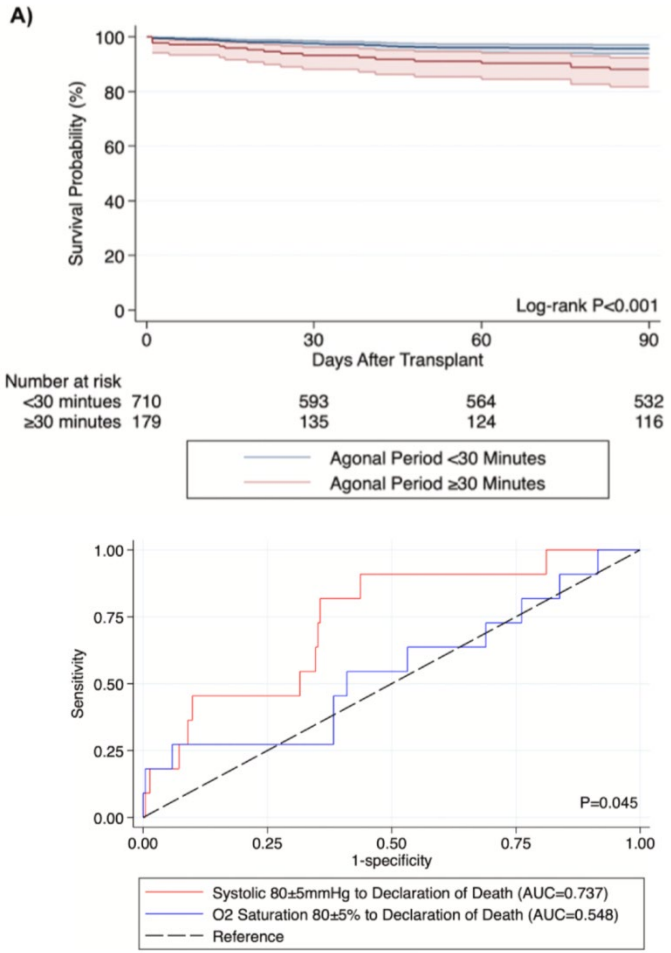
Study Highlights

Objective: Assess the impact of duration of agonal phase (from withdrawal of life sustaining treatment to circulatory arrest) and related hemodynamic measures on outcomes in donation after circulatory death (DCD) heart transplantation.

Methods: UNOS registry study of DCD heart transplantations between 2019 and 2023, stratified into two groups. One group with an Agonal period of >30 min the other < 30 min was compared for the primary endpoint of 90 day survival. Associations of different hemodynamic thresholds for onset of warm ischemia were assessed.

Results: 889 recipients included, with 179 (20.1%) from donors with an agonal time >30 minutes. 90 day survival was significantly lower in donor population with an agonal time >30 min (88.1% vs 95.6%, p<0.001). Time interval from systolic blood pressure of 80+/- 5 mm Hg exhibited higher association with 90-day mortality.

Conclusions: Utilization of donors with agonal period >30 min is associated with reduced post transplant survival. Hypotension is likely to be a more accurate indicator of myocardial ischemia compared to hypoxia.



Top: Kaplan-Meier graft survival estimate
Bottom: ROC curve illustrating the predictive accuracy stratified by hemodynamic parameter

Reviewer's Comments

- DCD heart transplantation has the ability to expand the donor pool for an incredibly scarce resource
- The study evaluates agonal times as a predictor for post-transplant survival at 90 days. Agonal times less than 30 min demonstrates improved post-transplant survival.
- Importantly it proposes a threshold of systolic BP of 80 ± 5 mmHg as an indicator of ischemia and onset of agonal time. This appears to be a much stronger predictor than oxygen saturation.
- While not reaching statistical significance there appears to be a difference between DPP and NRP survival despite controlling for the agonal phase time.

Limitations

- Retrospective study with non-randomized design – potential biases and confounders
- UNOS database has inherent flaws including lack of PGD data, post transplant tMCS, type of machine perfusion, procurement technique, perfusate used
- Agonal phase is defined by the withdrawal time to declaration of death. Variable standoff periods may have affected these results.

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Pig-to-human lung xenotransplantation into a brain-dead recipient

He J, Shi J, Yang C, Peng G, et al. *Nature Medicine (2025)* | DOI: 10.1038/s41591-025-03861-x

Study Highlights

Objective: While transplantation remains the gold-standard for management of end-stage lung disease, there is a shortage of organs compared to a growing need. Xenotransplantation is a promising solution that has been gaining attention given recent advances in both kidney and heart transplantation. The critical question of how to avoid hyperacute graft rejection as well as early graft failure remains.

Methods: : A Chinese Bama Xiang pig was edited with CRISPR-Cas9 to knock out GGTA1, B4GALNT2, CMAH and insert CD55, CD46, and TBM to create a six-gene-edited lung. A brain-dead decedent was used as a recipient and the left lung from the edited donor pig was transplanted. Clinical monitoring of physiologic parameters occurred throughout transplantation. Biopsies were collected at multiple time points via a left thoracotomy.

Results: The gene edited lung was transplanted and developed severe edema by 24 hours post-perfusion with an increase in cytokines, including interleukin-6 and interleukin-10 and increases in immune cells measured in XXX. Immunohistochemistry showed complement activation early after transplantation, including C4d deposition by 2 hours post-transplant. IgM and IgG levels were reported to markedly rise by post-operative day 6. Levels of porcine pathogens measured by transcriptomics were studied to determine the postoperative infection risk, with finding of negative to low levels of porcine viruses.

Conclusions: The authors report viability and functioning of the left lung transplanted from the gene-edited porcine donor into the human decedent, providing hope to the idea that xenotransplantation may be a feasible route. The optimism is tempered by the early onset of severe pulmonary edema and inflammation and significant graft damage.

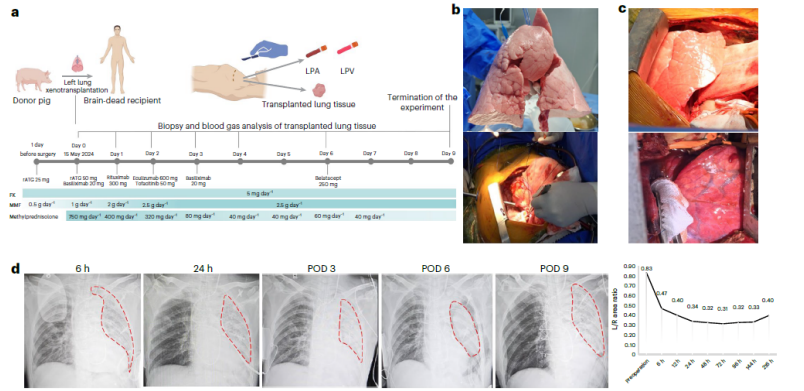

Fig. 1 | Experimental outline and surgical and clinical features of the pig-to-human lung xenotransplantation procedure. a, Outline of the experimental procedure, including the immune suppression regimen. In the schematic diagram above the timeline, the left lung from a gene-edited donor pig (*GTKO/B4GalNT2KO/CMAHKO/CD55/CD46/TBM*) was xenotransplanted into a brain-dead recipient, followed by lung biopsies and blood gas sampling from the anastomosed LPA and LPV. **b**, Surgical procedure, showing procurement of the left lung of the donor pig lung (top) and xenotransplantation (bottom). **c**, Photographs of the pig lung immediately after reperfusion and at 96 hours after reperfusion. **d**, Left: anterior–posterior chest radiographs at the indicated times after transplantation. Right: ratio of the area of the transplanted lung on the left side of the chest (L) to the area of the native lung on the right side of the chest (R), based on analysis of the radiographs. Illustrations in a created using BioRender.com. FK, tacrolimus; LPA, left pulmonary artery; LPV, left pulmonary vein; MMF, mycophenolate mofetil; rATG, rabbit anti-thymocyte globulin.

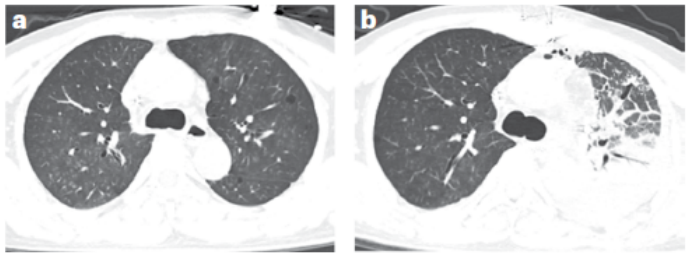

Fig. 2 | Changes in lung xenograft transparency after transplantation. a,b, Preoperative (11 May 2024) (**a**) and postoperative (16 May 2024) (**b**) chest computed tomography (CT). The postoperative CT obtained 24 hours after transplantation demonstrated consolidation in the dorsal region of the xenograft, whereas the anterior lung maintained good transparency.

Reviewer's Comments

- The study represents a bold move forward in the field of pulmonary xenotransplantation. It highlights the feasibility of building a gene-edited donor strain that can incorporate both gene knock-outs and insertions to develop a non-immunogenic graft.
- The results also underline how xenotransplantation of lungs remains in a premature stage with a need for further refinement before the technique is ready for living recipients.
- The publication also sparks interesting ethical questions that underlie all efforts at making xenotransplantation for any organ a reality

Limitations

- The lack of information on the clinical management of the decedent recipient makes interpretation of the results difficult to place in context.
- The physiologic conditions of using a brain-dead decedent presents an interesting confounding variable on understanding the true relationship between transplant of the porcine lung and onset of graft dysfunction. Brain death is associated with known pathophysiologic disruptions which themselves can introduce vasoplegia and inflammation.
- A decent model does not fully represent the physiologic conditions of a living recipient, however, does provide a model with greater ease of sampling and monitoring