Does Ex Vivo Perfusion Lead to Intimal Thickening in the First-Year Post-Heart Transplantation?

Takuma Sato, MD, Babak Azarbal, MD, Richard Cheng, Fardad Esmailian, MD, Jignesh Patel, MD, PhD, Michelle Kittleson, MD, PhD, Lawrence Czer, MD, Ryan Levine, BS, Sadia Dimbil, BS, Tamer Khayal, **Nena Musto, RN**, and Jon Kobashigawa, MD

Cedars-Sinai SMIDT Heart Institute, Los Angeles, CA

Abstract

Background: The Organ Care System (OCS), an ex-vivo heart perfusion system, is a physiologic alternative to cold organ storage (CS) for transport. In studies, OCS significantly shortened cold ischemic time compared to CS. However, OCS requires 2 short ischemic times when the heart is placed on and off the device. It is not known if this harms the coronary vascular bed. We examined patients (pts) placed on OCS with first-yr intravascular ultrasound (IVUS), as a sensitive and predictive assessment of early cardiac allograft vasculopathy (CAV).

Methods: Between 2011-2013, 39 heart transplant pts enrolled in the PROCEED 2 trial at our institution were randomized to CS or OCS. IVUS was performed at 4-6 weeks (baseline) and 1 yr (paired). Diagnosis of CAV was based on ≥0.5 mm increase in maximal intimal thickness (MIT) from baseline in a matched site. Clinical outcomes - 1-yr survival, 1-yr freedom from non-fatal major cardiac events (NF-MACE - myocardial infarction, new onset heart failure, coronary intervention, defibrillator/pacemaker implant, stroke), 1-yr freedom from rejection - were examined.

Results: Thirty-nine pts were randomized and underwent HTx by OCS (n=16) or CS (n=18). Of these, 18 pts (OCS: n=5, CS: n=13) with paired IVUS at baseline and 1 year post-transplant were examined. There was no significant difference in the proportion of pts with Δ MIT ≥ 0.5 mm between the two groups. The mean change in MIT from baseline to 1-year post-transplant was similar between the two groups. There was no significant difference in 1-year survival, 1-year freedom from NF-MACE or 1-year freedom from the various forms of rejection.

Conclusion: Development of CAV by IVUS in donor hearts preserved with OCS and CS is similar. This implies that OCS does not harm the coronary vascular bed and is a promising platform for donor heart transport. Larger sample sizes are needed to confirm these findings.

Background

- The Organ Care System (OCS), an ex-vivo heart perfusion system, is a physiologic alternative to cold organ storage (CS) for transport.
- In studies, OCS significantly shortened cold ischemic time compared to CS.
- However, OCS requires 2 short ischemic times when the heart is placed on and off the device.
- It is not known if this harms the coronary vascular bed.

Purpose

- To examine patients (pts) placed on OCS with first-yr intravascular ultrasound (IVUS), as a sensitive and predictive assessment of early cardiac allograft vasculopathy (CAV).

Methods

- Between 2011-2013, 39 heart transplant pts enrolled in the PROCEED 2 trial at our institution were randomized to CS or OCS
- IVUS was performed at 4-6 weeks (baseline) and repeated 1 yr after HTx.
- Diagnosis of CAV was based on a ≥ 0.5 mm increase in maximal intimal thickness (MIT) from baseline in any matched site.
- Endpoints included:
  - 1-yr survival
  - 1-yr freedom from non-fatal major cardiac events (NF-MACE: myocardial infarction, new onset heart failure, coronary intervention, defibrillator/pacemaker implant, stroke)
  - 1-yr freedom from any-treated rejection
  - 1-yr freedom from acute cellular rejection
  - 1-yr freedom from antibody-mediated rejection

Demographics

Demographics	OCS (n=5)	CS (n=13)	P-Value
Mean Recipient Age, Years ± SD	51.8 ± 15.5	59.1 ± 16.2	0.398
Mean Donor Age, Years ± SD	28.6 ± 14.8	30.8 ± 13.8	0.773
Body Mass Index, Mean ± SD	24.9 ± 7.7	22.1 ± 2.0	0.468
Female (%)	40.0%	30.8%	0.709
Previous Pregnancy in Females (%)	100.0%	100.0%	1.000
Ischemic Time, Mean Mins ± SD	121.6 ± 56.4	161.1 ± 31.5	0.074
Primary Reason for Transplant, Underlying Diagnosis of Coronary Artery Disease (%)	20.0%	38.5%	0.456
Status 1 at Transplant (%)	80.0%	76.9%	0.888
Cytomegalovirus Mismatch (%)	20.0%	38.5%	0.456
Diabetes Mellitus (%)	0.0%	30.8%	0.159
Treated Hypertension (%)	75.0%	66.7%	0.763
Insertion of Mechanical Circulatory Support Device (%)	20.0%	7.7%	0.456
Prior Blood Transfusion (%)	75.0%	57.1%	0.553
Pre-Transplant PRA ≥ 10% (%)	40.0%	23.1%	0.472
Pre-Transplant Creatinine, Mean ± SD	1.0 ± 0.2	1.3 ± 0.4	0.136

Outcomes

Endpoints	OCS (n=5)	CS (n=13)	P-Value
Mean Baseline MIT (mm) ± SD	0.1 ± 0.1	0.3 ± 0.4	0.294
Mean 1-Year MIT (mm) ± SD	0.3 ± 0.2	0.6 ± 0.5	0.218
Mean Δ MIT (mm) ± SD	0.2 ± 0.3	0.3 ± 0.5	0.684
Δ MIT ≥ 0.5 mm, %	20.0% (1/5)	23.1% (3/13)	1.000
1-Year Survival	100.0%	100.0%	1.000
1-Year Freedom from NF-MACE	100.0%	92.3%	0.535
1-Year Freedom from Any-Treated Rejection	60.0%	92.3%	0.075
1-Year Freedom from Acute Cellular Rejection	60.0%	92.3%	0.075
1-Year Freedom from Antibody-Mediated Rejection	80.0%	100.0%	0.107

Results Summary

- Thirty-nine pts were randomized and underwent HTx by OCS (n=16) or CS (n=18).
- Of these, 18 pts (OCS: n=5, CS: n=13) with paired IVUS at baseline and 1 year post-transplant were examined.
- There was no significant difference in the proportion of pts with Δ MIT ≥ 0.5 mm between the two groups.
- The mean change in MIT from baseline to 1-year post-transplant was similar between the two groups.
- There was no significant difference in 1-year survival, 1-year freedom from NF-MACE or 1-year freedom from the various forms of rejection.

Conclusion

- Development of CAV by IVUS in donor hearts preserved with OCS and CS is similar.
- This implies that OCS does not harm the coronary vascular bed and is a promising platform for donor heart transport.
- Larger sample sizes are needed to confirm these findings.

Author Disclosures

T. Sato: None. **B. Azarbal:** None. **R. Cheng:** None. **F. Esmailian:** G; C; TransMedics Inc. **J. Patel:** G; C; Alexion, Pfizer, Alnylam. O; C; Therakos. **M. Kittleson:** None. **L. Czer:** G; C; St. Jude Medical. **R. Levine:** None. **S. Dimbil:** None. **T. Khayal:** O; C; Transmedics. **J.A. Kobashigawa:** G; C; CareDx, Sanofi, CSL Behring.