**Table 2. Clinical trials of iNO in Adult Transplant, LVAD implantation**

| CITATION | STUDY DESIGN | N | SETTING | COMPARISON | MEASURES | PRIMARY RESULTS | SAFETY |
|---|---|---|---|---|---|---|---|
| **Kieler Jensen** et al. [34] | Randomized | 12 | PH after transplant; | iNO, sodium nitroprusside (SNP), prostacyclin | systemic or pulmonary AP, cardiac output, RVF, or systemic VR. PCWP, transpulmonary pressure gradient | iNO is a selective pulmonary vasodilator | Arterial and pulmonary arterials levels of nitrate increased during INO and this increase was paralleled by an increase in MetHb levels to ~2%. |
| **Argenziano M** et al.[35] | Randomized, double blind | 11 | PH after LVAD | iNO or $N_2$ | pulmonary hemodynamics + LVAD flow | iNO 20 ppm on weaning from CPB (vs N) induced significant reduction in mPAP and increase in LVAD flow | No systemic hypotension, hypoxia or other adverse events. Ventilator failure precipitated abrupt iNO cessation in 1 patient → reversible hemodynamic collapse and VF. |
| **Rajek A** et al. [36] | Randomized | 68 | transplant; | PGE1 vs iNO (20ppm) | hemodynamics and "successful" weaning off CPB | PGE1 vs iNO 4ppm and titrated to reduce PVR during transplant; iNO aided weaning from CPB more successfully than PGE1 | Arterial and pulmonary arterials levels of nitrate increased during inhalation of NO and was paralleled by an increase in MetHb levels to about 2%. |
| **Ardehali A** et al. [37] | Prospective, open | 16 | Xplant; | | systemic and pulmonary hemodynamics, RV function | Post-transplant iNO 20ppm started before term of CPB significantly reduced RV stroke work and PVR. | No MetHb. $NO_2$< 0.5 ppm in all pts. RV dysfunction in 1iNO vs. 6 controls. |
| **Radovancevic B** et al. [38] | Randomized, crossover | 19 | Pre-Xplant | PGE1 vs iNO | pulmonary hemodynamics; systolic PAP, PCWP, right atrial pressure, cardiac output | PGE1 vs iNO in testing for PH reversibility in heart transplant candidates; comparable dilatory effects in PH | No mention of adverse events. No significant decrease in cardiac index. |
| **Potapov E** et al. [39] | Randomized, double blind **(INOT41)** | 150 | Management of RVF with LVAD on CPB; | INO 40ppm or placebo for 48h, then cross-over if no response | RV function, time on MV, requirement for RVAD, LOS, 28-day mortality | iNO decreased (non-significantly) incidence of failures, Secondary endpoint (time on MV) significantly better with iNO | No major safety issues were identified |
| **Khan TA** et al. [40] | Randomized, crossover | 25 | Heart, lung transplant | iNO vs prostacyclin | primary endpoint: mean PA pressure, secondary endpoints: CVP, CI, mixed venous $O_2$ saturation ($SvO_2$), mean systemic arterial pressure, and oxygenation index | In heart transplant and lung transplant recipients, iNO and prostacyclin similarly reduce PAP and central venous pressure, and improve CI and $SvO_2$.<br>Median ICU stay was 3 days. | No patient required invasive treatment to manage PHT or RV dysfunction. |

BP=blood pressure, CI=cardiac index, CO=cardiac output, CPB= cardiopulmonary bypass, CVP=central venous pressure, HR=heart rate, ICU= intensive care unit, iNO=inhaled nitric oxide, i-PGi2=inhaled prostacyclin, LAP=left atrial pressure, MAP=mean arterial pressure, metHB=methemoglobin, MPAP=mean pulmonary arterial pressure, MV=mechanical ventilation, NTP=nitroprusside, $O_2$=oxygen, PCWP= pulmonary capillary wedge pressure, PH=pulmonary hypertension, PGE1=IV prostaglandin E1, PVR=pulmonary vascular resistance, PVRI= pulmonary vascular resistance index, RV=right ventricular, RVAD=right ventricular assist device, RVEF=right ventricular ejection fraction, SVRI=systemic vascular resistance index, $SvO_2$=mixed venous oxygen saturation.