

## SEXUAL DIMORPHISM IN CONGENITAL DIAPHRAGMATIC HERNIA

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**Background:** Congenital diaphragmatic hernia (CDH) is associated with pulmonary hypoplasia and pulmonary hypertension (PH), which is thought to be due to endothelial dysfunction. Sexual dimorphism in CDH-PH has yet to be examined from both clinical and cellular perspectives, in part due to lack of an appropriate model. However, we have previously demonstrated that human umbilical vein endothelial cells (HUVECs) provide a robust in vitro model for studying CDH-PH. We hypothesize that males have worse clinical PH outcomes than females, which may be attributed to endothelial dysfunction at the cellular level.

**Materials/Methods:** A single-center retrospective cohort study was performed for CDH patients from 2008-2020. Patients who underwent prenatal intervention were excluded. Patients were stratified by TOTAL trial definitions of CDH severity. Demographics, extracorporeal membrane oxygenation (ECMO) and inhaled nitric oxide (iNO) use, and outcomes (tracheostomy, survival at discharge, and PH resolution at one year) were measured. HUVECs were isolated from 6 CDH subjects, and scratch-wound migration and branching assays were performed. Statistical analyses were performed with logistic regression and unpaired t-tests.

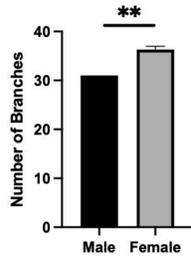
**Results:** 291 CDH patients were included in the study with male predominance (57%). When controlling for severity, there were no sex-based differences in iNO use ( $p=0.02$ ), survival ( $p=0.70$ ) or tracheostomy at discharge ( $p=0.39$ ), however, females were less likely to require ECMO ( $p=0.03$ ). Among 89 patients with available echocardiogram data, females had significantly more PH resolution ( $p=0.03$ ) on echocardiogram at one year. Female CDH HUVECs exhibited increased migration ( $p=0.04$ ) and branch formation ( $p<0.01$ ) relative to males(Figure1).

**Conclusions:** Using our database of patients treated under the same protocol, we show that males have worse CDH-PH-related outcomes. These differences were also seen at the cellular level, with males exhibiting increased endothelial dysfunction relative to females. Further understanding of this sexual dimorphism will help in the development of tailored therapies to treat CDH-PH.

**Images / Graph / Table**

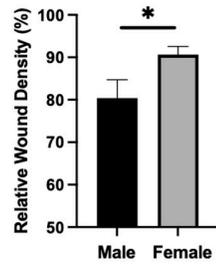
Figure 1  
A.

**CDH Male vs. CDH Female  
HUVEC Branch Formation**



B.

**CDH Male vs. CDH Female  
HUVEC Migration**



**A:** CDH Male vs. CDH Female HUVEC branch formation assay shows significantly increased number of branch formation compared to males. **B:** CDH Male vs. CDH Female HUVEC scratch-wound migration assay shows significantly increased migration among female CDH HUVECs compared to males.