in the first days of life. IHs undergo a predictable natural history, beginning with a rapid proliferative phase, followed by a period of stabilization, and finally involution. Hemangioma endothelial cells (HemECs) are distinct from normal ECs: HemECs express Glut1 and are hyperproliferative. The mechanisms governing the progress from proliferation, to stabilization, and finally to involution is not understood. Our laboratory found, on a preliminary screen, that involuting IHs endothelium had loss of VECADHERIN (VECAD) expression. VECAD is a cell adhesion protein specific to ECs. VECAD plays a key role in angiogenesis and cell cycle progression, as well as EC survival. We thus hypothesize that loss of VECAD in IH endothelial cells contributed to cell death that may contribute to IH involution.

Methods: IHs from different stages (proliferating, stable, and involuting) were used in this study. Resected IH samples were clinically evaluated and categorized as proliferating (n=2), stable (n=5), or involuting (n=3) based on age and histological appearance. All samples were from patients who did not receive propranolol or other systemic treatment. Dermal vasculature in neonatal dermal tissues were used as controls (n=4). All specimens were embedded in paraffin and sectioned. Immunofluorescent staining was done using antibodies against VECAD and EC marker, CD31. Apoptosis was assessed with terminal deoxynucleotidyl transferase-mediated dUTP nick end-labeling (TUNEL) assay. The mean fluorescent intensity for endothelial VECAD and CD31 were quantified using ImageJ software (NIH) over 18 regions of interests per IH or control sample. Data is presented as a ratio of VECAD/CD31 mean intensity. Statistical analysis with one-way ANOVA and post-hoc t-test was performed with Graphpad and a p-value of <0.05 was considered statistically significant.

Results: Proliferating IHs had high cell density with poorly defined vascular spaces; stable IHs had well defined, tightly packed vascular channels, and involuting samples had large vascular channels that were interspersed with fatty infiltrates. Proliferating HemECs had weak CD31 and weak VECAD staining when compared to stable IHs; but relative VECAD/CD31 expression ratios were similar to stable IH and control vessels. VECAD expression was significantly decreased in involuting HemECs with the lowest VECAD/CD31 ratio, even as CD31 intensity was comparable to stable IHs. As expected, the number of TUNEL+ ECs were significantly higher in involuting IHs when compared to proliferating or stable IHs (p<0.0001).

Conclusion: Loss of VECAD expression in IH endothelium corresponded to IH involution and increased apoptosis in IH endothelium. It is unclear whether loss of VECAD is causative of IH involution; further studies are needed to elucidate the role of VECAD function in EC survival.

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A Novel Therapeutic Target To Improve Tissue Oxygenation And Increase The Number Of Viable Organs/vascular Composite For Transplant: Prospective Study On Brain Dead Donors

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Background: S-nitrosothiols (SNOs) are chemicals in the body that regulate a wide range of activities including blood flow, oxygen delivery, responses to disease or pollution, muscle performance, and metabolism. Our laboratory has demonstrated that brain death is associated with a decrease in SNO leading to a decrease in tissue micro perfusion. We hypothesized that SNO levels directly correlate with donor tissue/organ viability.

Methods: In a prospective cohort study of brain dead donors (n=63), serial measurements of S-nitrosohemoglobin (SNO-Hb) were collected and tissue oxygenation were monitored by tissue oxygen monitor (TStat). SNO levels were then correlated to microcirculation, organs failure rate, and lactate levels. The data was analyzed using R software.

Results: SNOHb levels decrease immediately after brain death. Increasing SNO-Hb levels inversely correlated with lactate levels (p<0.001) (R=0.61). Increasing SNO-Hb levels directly correlated with increasing tissue oxygenation (p<0.001). Regression analysis identified SNO-Hb as a strong primary predictor variable of percentage of organs recovered and as a direct predictor of quality of donor tissue (P=0.015) (R=0.4).

Conclusion: Our study demonstrated SNO-Hb levels after brain death directly correlate with tissue perfusion and ultimately organ viability. Therapies to increase SNO-Hb after brain death in the donor is a possible therapeutic target to improve microcirculation and the number of organs/VCA available for transplant.