RESULTS: Mice that received metformin had lower circulating levels of IL-6 and MCP-1 when compared to control mice (P=0.02 and P=0.04, respectively, Figure). There was no difference in the adipokines, leptin or resistin and no difference in circulating insulin or PAI-1 levels.

CONCLUSION: Prophylactic administration of Metformin lowers the circulating pro-inflammatory cytokines IL-6 and MCP-1 in an obese mouse model of PE. Studies are ongoing to further investigate additional mechanisms by which metformin may ameliorate known dysfunctional pathways associated with PE.

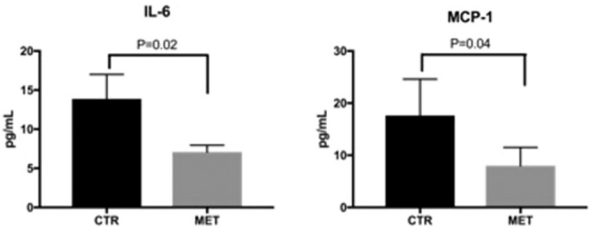

Figure. Concentrations of IL-6 and MCP-1 in serum from obese mice with sFlt-1-induced preeclampsia and treated (MET) or nontreated (CTR) with metformin. Mean ± SEM.

428 Preeclampsia is characterized by decreased expression of endothelin converting enzyme-1 in the placenta

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OBJECTIVE: Endothelin-converting enzyme 1 (ECE-1) is a key regulatory enzyme in the proteolytic processing of Endothelin-1 (ET-1), a potent vasoactive peptide. In most vascular beds, ECE-1 localizes to endothelial cells, but has not been extensively studied in the human placenta. We sought to evaluate the expression and cellular localization of ECE-1 in normal and preeclamptic placentas.

STUDY DESIGN: Placentas from normal (n=6) and preeclamptic (n=6) women, matched for gestational age, were collected and serially sectioned for immunofluorescence (IF) studies to localize ECE-1 expression. Cell type specific markers were used to identify the following cell types: endothelial, trophoblast, macrophage, smooth muscle and fibroblast cells. The samples were stained with antibodies for ECE-1 and tissue markers and counterstained with DAPI. Negative controls were stained with secondary antibodies and DAPI. Quantitative analysis of ECE-1 within placenta samples was performed by western blot and ELISA.

RESULTS: Immunofluorescence studies confirmed ECE-1 expression within the stroma and villous spaces of intermediate and stem villi of human placentas. Localization of ECE-1 occurred occasionally with endothelial cells but not with the other cell types evaluated (Figure 1). IF studies suggested less ECE-1 expression in preeclamptic placentas. Western blot and ELISA showed significantly less ECE-1 in preeclamptic compared with normal placentas (Figure 2).

CONCLUSION: ECE-1 is expressed in the villous spaces of the human placenta. There is significantly less ECE-1 expression in preeclamptic versus normal placentas. ECE-1 likely plays an important role in vascular homeostasis in the placenta and may be protective against disorders of vascular dysfunction, such as preeclampsia. The lack of colocalization of ECE-1 suggests a secreted form of the enzyme, however further study is needed to confirm this.

Figure 1.

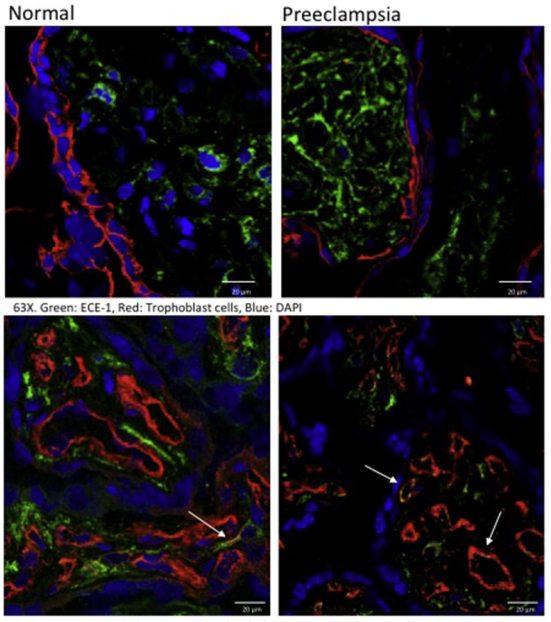
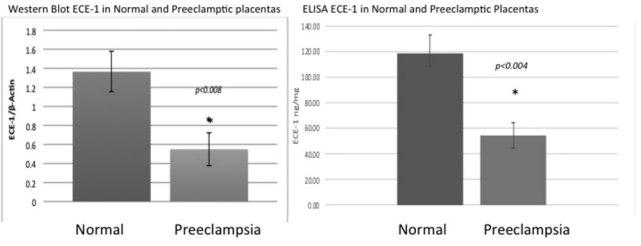


Figure 2



429 Echocardiographic markers aid in risk stratification of women with persistent hypertension after preeclamptic pregnancy

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OBJECTIVE: Women diagnosed with preeclampsia (PEC) have a higher incidence of chronic hypertension (HTN), heart failure, stroke, and other forms of cardiovascular disease. We hypothesized parameters on echocardiography (ECHO) performed at diagnosis of PEC would be associated with subsequent cardiovascular risk.

STUDY DESIGN: Women with PEC were prospectively recruited from the Johns Hopkins Health System between September 2014 – December 2015. We included singleton pregnancies > 23 weeks and diagnosis of PEC with severe features (PEC-SF) or PEC-SF superimposed on chronic HTN and excluded known maternal heart valve disease, previous cardiac surgery, known cardiomyopathy, pulmonary hypertension, history of pulmonary embolism, or interstitial lung disease. ECHO was performed at time of PEC-SF diagnosis. Participants were assessed for HTN 3 years after delivery, defined as systolic blood pressure (BP) >130 mmHg, diastolic BP > 80 mmHg, or on anti-hypertensive therapy. Outcome data were collected via phone and electronic medical records. Baseline differences were tested using parametric or non -parametric tests as appropriate; significance was defined as p-value < 0.0007 using Bonferroni's correction.

RESULTS: 17 women were without HTN at 3 years and 28 women had HTN 3 years after diagnosis of PEC-SF. The groups did not differ in age, race, or gestational age. There were significantly more women with pre-pregnancy HTN in the HTN group and a trend towards higher body mass index (Table 1). Women with HTN 3 years after PEC-SF diagnosis had increased left ventricular (LV) septal wall thickness when compared to women without HTN (Table 1). A restricted, sensitivity analysis including only women without pre-pregnancy HTN continued to show significantly increased LV septal wall thickness in PEC-SF with HTN at 3 years versus PEC-SF without HTN (Figure 1).

CONCLUSION: In our cohort of 45 women with PEC-SF, 62% had HTN 3 years after delivery. Among women with persistent HTN, 16/28 (57%) had no history of HTN prior to pregnancy. Women who had HTN 3 years after PEC-SF diagnosis had thicker LV septal wall thickness on ECHO at PEC diagnosis than women without HTN, regardless of history of pre-pregnancy HTN. ECHO at PEC diagnosis may aid in risk stratifying women at risk of developing cardiovascular disease.

Figure 1: Compares Left ventricular (LV) septal wall thickness in women with preeclampsia with severe features (PEC-SF) with and without hypertension after 3 years of diagnosis.

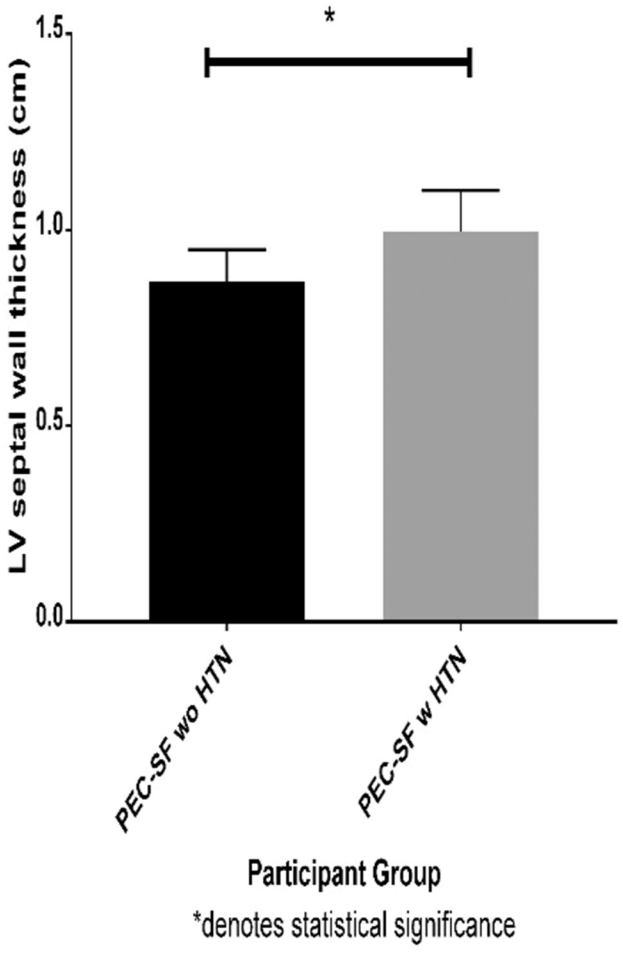

Table 1: Demographic and echocardiographic data in women with preeclampsia with or without a diagnosis of hypertension by the end of the third post-natal year

	[illegible]	[illegible]	p-value
Age (years)	[illegible]	[illegible]	[illegible]
Gestational age at diagnosis (weeks)	[illegible]	[illegible]	[illegible]
Body Mass Index	[illegible]	[illegible]	[illegible]
Race (%)			[illegible]
Asian	[illegible]	[illegible]	
Black	[illegible]	[illegible]	
Other	[illegible]	[illegible]	
White	[illegible]	[illegible]	
Ethnicity (%)			[illegible]
Hispanic	[illegible]	[illegible]	
Non-Hispanic	[illegible]	[illegible]	
History of pre-pregnancy hypertension (%)	[illegible]	[illegible]	[illegible]*
Highest Systolic BP (mmHg)	[illegible]	[illegible]	[illegible]
Highest Diastolic BP (mmHg)	[illegible]	[illegible]	[illegible]
Echocardiographic measurements			
IVSd (mm)	[illegible]	[illegible]	[illegible]
RA area (cm^2)	[illegible]	[illegible]	[illegible]
RV TAPSE (cm)	[illegible]	[illegible]	[illegible]
SV (cm^3)	[illegible]	[illegible]	[illegible]
TAPSE (cm)	[illegible]	[illegible]	[illegible]
LA area (cm^2)	[illegible]	[illegible]	[illegible]
LV septal wall thickness (cm)	[illegible]	[illegible]	[illegible]*
LV posterior wall thickness (cm)	[illegible]	[illegible]	[illegible]
LVEF (%)	[illegible]	[illegible]	[illegible]
Mitral E (cm/s)	[illegible]	[illegible]	[illegible]
Mitral septal e' (cm/s)	[illegible]	[illegible]	[illegible]
Mitral E/e' ratio	[illegible]	[illegible]	[illegible]
Mitral DT (msec)	[illegible]	[illegible]	[illegible]

[illegible]

[illegible]

*denotes statistically significant difference between groups