We identified MINDBOMB1 (MIB1), encoding an E3 ligase, as a very good candidate gene for the pathophysiology of the disease. We analysed MIB1 in our cohort and found 3 nonsense and 3 missense variants: The nonsense variant R97* is leading to a loss of function, but is predicted damaging (Luxan et al. 2013). The last variant is of unknown function, but is predicted damaging (Luxan et al. 2013). The other variants were found in sporadic cases: The 3 nonsense variants R769*, R1001*, R97* are leading to a loss of function (Luxan et al. 2013). Cellular and molecular characterization of the 3 missense variants are ongoing to refine the impact of these variants in the NOTCH1 pathway deregulation.

In conclusion, our genetic approach led to the identification of MIB1 as the third most frequent gene for BAV, enhancing the role of NOTCH1 pathway in the pathophysiology of the disease.

P2600
The impact of pulmonary vascular resistance on fontan hemodynamics and outcomes
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Background: Central venous pressure (CVP) provides the driving force for pulmonary blood flow in Fontan physiology, and it is dependent on pulmonary vascular resistance index (PVRI), ventricular filling pressure and venous compliance. The relationship between CVP and PVRI in the Fontan physiology has not been studied. We hypothesized that in the absence of a subpulmonary ventricle in the Fontan physiology, PVRI becomes the primary determinant of CVP and Fontan related clinical outcomes.

Methods: Retrospective review of adult Fontan patients and non-congenital heart disease patients (non-CHD) that underwent cardiac catheterization at Mayo Clinic Rochester, Minnesota, 1990–2015. Fontan patients were matched to the non-CHD (1:1) by age at time of catheterization (±10 years) and body mass index (±2 kg/m²).

Results: There were 164 patients and 82 patients in the Fontan and non-CHD groups respectively. In comparison to the non-CHD group, the Fontan patients were younger (median age 36 vs 45 years, p<0.001), more likely to be on anticoagulation or antiplatelet therapy, and more likely to have atrial arrhythmia or cirrhosis. There was a good correlation between CVP and PVRI in the Fontan group (r=0.79, p<0.001) in contrast to the non-CHD group where CVP was independent of PVRI. There was a weak correlation between CVP and PAWP in the Fontan group (r=0.19, p=0.04). Elevated PVRI was an risk factor for FAD (protein losing enteropathy, cirrhosis, heart failure hospitalization, arrhythmia, thrombocytopenia) and FAD was assisted with death (odds ratio 8.2; 95% CI 6.6–10.1, p<0.001).

Conclusions: The current study demonstrates a direct correlation between CVP and PVRI in Fontan physiology. The data suggest that elevated CVP (systemic venous congestion), which is the primary factor in the pathogenesis of most FAD and death, may to a large extent, be driven by elevation in PVRI.

P2601
Asplenia patients after fontan suffer more hepatic impairment than non-asplenia

Background: Patients with asplenia do not possess spleen which is the largest levels of abdominal organs and able to impound large amounts of blood. So we predicted that asplenia patients after Fontan would hold more circulating blood volume and suffer more hepatic congestion than non-asplenia patients. We investigated hematological and cardiac status about asplenia patients after Fontan.

Methods: The medical records of 36 asplenia patients after Fontan were reviewed. Control was 168 non-asplenia patients after Fontan. They all underwent cardiac catheterization and blood test between 2010 and 2015. We compared routine hematological data and cardiac parameters between two groups.

Results: Asplenia patients got higher levels of gamma-glutamyl transpeptidase than non-asplenia (118 vs. 66 IU/l; p=0.00046). Similarly, the rate of patients with high levels of total bilirubin (≥0.9 mg/dl) was higher in asplenia (63% vs. 38%, p=0.016); that with high levels of alanine aminotransferase (≥32 IU/l) was higher (33% vs. 17%, p<0.001). However, platelet counts, which were decreased in patients with splenomegaly, were higher in asplenia patients (28.8 vs. 21.8 x10⁴/μl, p<0.00001). As for cardiac performances, asplenia patients possessed larger ventricular volume on end-systole (64% vs. 51%, p=0.013) and on end-diastole (125% vs. 106%, p=0.023); they did higher pressures of pulmonary capillary wedge (p=0.00082). They possessed regurgitation of atrio-ventricular valve (AVVR) more than asplenia (p<0.0001); they also did moderate or over AVVR more (p<0.0033). Other cardio-pulmonary factors were not significantly different between two groups. To investigate whether “asplenia” factor was related to hepatic impairment, we analyzed risk factors for GGT-elevation (>100 UI/l) by 5 performances above and “asplenia”. After multivariate analysis GGT-elevation was independently associated with odds ratio of 10.8 for existence of AVVR, 4.8 for ventricular volume on end-diastole (>150%; p=0.036), and 3.3 for “asplenia” (p=0.045). Explanatory coefficient for GGT-elevation was 0.42 by all these 6 factors.

Conclusion: Higher levels of total bilirubin and gamma-glutamyl peptide in asplenia indicates that asplenia patients, who do not own normal organ of spleen in abdomen, would have more congestive liver. We did not prove directly that liver was more congestive in asplenia than non-asplenia. However, “asplenia” factor was independently associated with GGT-elevation in Fontan patients. It is confirmed that the liver was more damaged in asplenia patients. We should keep track of liver damages more strictly in Fontan patients with asplenia.

P2602
Airway hyperresponsiveness is associated with secundum atrial septal defects in adults
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Background: Patients with secundum atrial septal defects (ASD) often present with asthma symptoms, potentially leading to delay in ASD diagnosis and subsequent treatment.

Purpose: Our aim was to study the association between ASD-based left-to-right shunting and asthma symptoms before and after percutaneous closure using bronchoprovocation testing.

Methods: A total of 31 ASD patients (65% female, median age 48 [IQR 38–59] years) underwent spirometry, methacholine challenge testing and the European Bronchoprovocation Testing protocol for ASD in adults.

Results: AF patients were younger (median age 36 vs 45 years, p<0.001), more likely to be on anticoagulation or antiplatelet therapy, and more likely to have atrial arrhythmia or cirrhosis. There was a good correlation between CVP and PVRI in the Fontan group (r=0.79, p<0.001) in contrast to the non-CHD group where CVP was independent of PVRI. There was a weak correlation between CVP and PAWP in the Fontan group (r=0.19, p=0.04). Elevated PVRI was an risk factor for FAD (protein losing enteropathy, cirrhosis, heart failure hospitalization, arrhythmia, thrombocytopenia) and FAD was assisted with death (95% CI 6.6–10.1, p<0.001).

Conclusions: The current study demonstrates a direct correlation between CVP and PVRI in Fontan physiology. The data suggest that elevated CVP (systemic venous congestion), which is the primary factor in the pathogenesis of most FAD and death, may to a large extent, be driven by elevation in PVRI.

Figure 1. Per-patient baseline dose-response curve of percentage FEV1 decline in response to cumulative inhaled methacholine dose (µg).

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