rial pressure (SPAP) was 86.5±20.2 mm Hg and resting PVR was 9.1±3.7 Wood units. After the initial targeted medical therapy, SPAP and PVR reduced significantly (SPAP, -10.1 mmHg, P<0.001; PVR, -4.5 Wood units, P<0.001), and the ratio of pulmonary to systemic blood flow increased (0.99, P<0.001). Right ventricular dimension increased (RVD, 2.7mm, P<0.001) associated with the decrease of left ventricular dimension (LVD, -2.2mm, P=0.003) and left atrial dimension (LAD, -2.1mm, P=0.004). The exercise capacity increased significantly (34.6 m, P<0.001). After transcatheter closure with F-ASO (33.8±3.7 mm), immediate SPAP further reduced (-17.0 mmHg, P<0.001) and the postoperative fenestration was 6.4±0.6 mm. The follow-up (7.8±2.3 months) demonstrated the reduction of RVD (-7.9mm, P<0.001) associated with the increase of LVD (6.9mm, P<0.001) and LAD (5.4mm, P<0.001). There were no related complications and the fenestration maintained patent in all patients. In addition, the further improvement was identified in the exercise capacity (46.0 m, P<0.001).

Conclusions: In ASD with severe PAH, the combination of F-ASO and targeted medical therapy was a safe and effective method. The fenestration remained patent in the short-to-medium follow up. Further research was required to evaluate the long-term result of the combined treatment.

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6013
Drug therapy in adult congenital heart disease: the burden of polypharmacy

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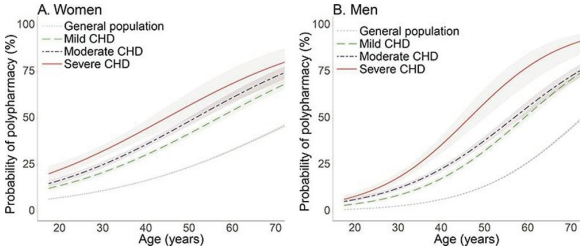
Background: Adult congenital heart disease (ACHD) increasingly includes frail individuals with more severe congenital heart defects (CHD), with sequelae and comorbidities requiring pharmacotherapy. Half of ACHD patients use chronic medication, which may cumulate over time.

Purpose: This study aims to investigate the prevalence, risk factors, and contributing drugs to polypharmacy, and its association with mortality in ACHD, compared to age- and sex-matched referents from the general population.

Methods: We identified patients from our nationwide ACHD registry and age- and sex-matched referents from the general population in a 1:10-ratio in the national Dispensed Drug Register and Cause of Death Register for the years 2006–2014. Drugs were classified according to the Anatomical Therapeutic Chemical classification, aggregated per year. Generalized estimating equations were used to determine associations between characteristics and polypharmacy, defined as ≥5 different dispensed drug types per year. Associations between baseline polypharmacy and mortality were analyzed in subjects surviving their baseline year using multivariable Cox regression.

Results: Overall, 14138 ACHD patients (49% male, median age 35 years) were included, of which 29% had baseline polypharmacy, compared to 13% of referents (P<0.001). Cardiovascular drugs were most prevalent (42% in patients vs 13% in referents, P<0.001), particularly antithrombotics (25% vs 4%, P<0.001), betablockers (21% vs 6%, P<0.001) and renine-angiotensin-aldosterone-system blockers (18% vs 5%, P<0.001). Female sex (OR=1.92 [95% CI 1.88–1.96], P<0.001), older age (OR=1.81/10years [95% CI 1.79–1.82], P<0.001) and ACHD with increasing OR for increasing severity (OR=2.51 [95% CI 2.40–2.61]. P<0.001 for mild, OR=3.22 [95% CI 3.06–3.40], P<0.001 for moderate, and OR=4.87 [95% CI 4.41–5.38], P<0.001 for severe CHD), were independently associated with polypharmacy during the study. Risk of polypharmacy increased more with age in men than women (Pinteraction<0.001) and in severe than moderate/mild CHD (Pinteraction=0.001). The proportion of subjects with polypharmacy remained similar from 2006 to 2014 (OR=0.97/year [95% CI 0.97–0.98], P<0.001). During 7 [IQR 5–8]years, 595 patients (4%) and 2375 referents (2%) died. Adjusted for age, sex, and defect severity, baseline polypharmacy was independently associated with mortality in ACHD (HR=2.90 [95% CI 2.42–3.49], P<0.001). Age- and sex-adjusted HR was similar in patients and referents (Pinteraction=0.077) and in moderate and severe compared to mild CHD (Pinteraction=0.79 and Pinteraction=0.74, respectively).



Probability of polypharmacy by age

Conclusion: Polypharmacy is common in ACHD. Female sex, CHD severity, and older age, especially in men and severe CHD, are associated with polypharmacy. Polypharmacy is associated with mortality. Polypharmacy is an easy marker of patients with worse outcome, underscoring that these patients require care of specialists with knowledge on appropriateness of polypharmacy.

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6014
Selective Heart Rate inhibition improves inadequate exercise response in Fontan Circulation

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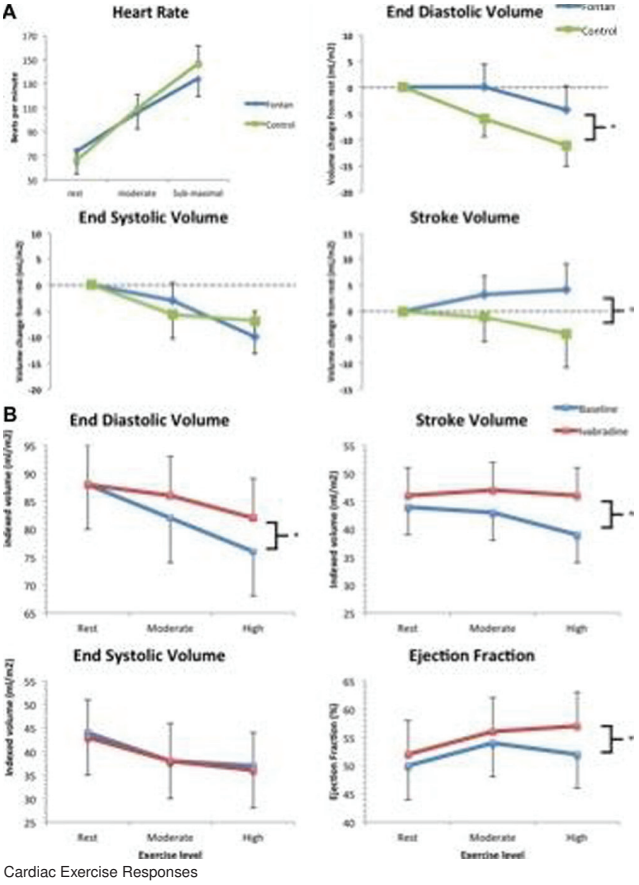
Introduction: Fontan patients experience a progressive decrease in cardiac performance throughout life, inevitable leading to development of heart failure. This failure seems to originate from inefficient haemodynamics, rather than ischaemic burden, but a clear pathway of failure remains to be elucidated. We have shown that in the biventricular heart, the RV is key in regulation of LV filling, optimizing energetic efficiency of the total cardiac contraction, especially during stress. The lack of a sub-pulmonary ventricle in Fontan patients is likely to impact LV filling regulation and ventricular efficiency, with increases in heart rate (HR). We propose that sub-optimal ventricular filling and CO augmentation during increases in HR significantly impact energetic efficiency of the heart.

Purpose: To explored the impact of HR on ventricular performance in the single ventricular Fontan circulation.

Methods: We used Exercise CMR and biomechanical modelling to compare the exercise response of Fontan patients to that of healthy volunteers. Secondly, we evaluated the impact of selective HR inhibition on ventricular performance in the Fontan circulation.

Results: See figure 1 and table 1 for our results. We showed that with increasing HR, ventricular filling rate is severely blunted in Fontan patients compared to healthy volunteers (peak 199ml/m^2/s vs 300ml/m^2/s, p<.01), resulting in a drop in end diastolic volume (EDV, p<.01) and stroke volume (SV, p<.01). As a consequence CO augmentation was severely blunted (p<.01). Using the biomechanical model, we showed that this drop in filling results in significant inefficiency of the single ventricle. Selective heart rate inhibition with Ivabradine (mean effect HR -7±3%, p<.01) significantly increased diastolic filling time, while filling rate was unchanged. As a result, EDV (mean effect +5±2%, p<.01) and SV (mean effect +10±5%, p<.01) increased, resulting in higher CO (mean HR effect -5±1%, p<.01), despite the lower HR. We than showed that the ventricle became sig-



Cardiac Exercise Responses