Background IMR is a simple invasive measure of microvascular function available at the time of pPCI. T2-weighted non-contrast CMR can reveal myocardial oedema, and in the post-infarct population this represents the ischaemic area at risk (AAR). Contrast-enhanced CMR delineates the area of myocardial infarction. The volume of myocardium within the AAR, but not contained within the infarct area is salvaged myocardium.

Methods 108 patients with STEMI underwent invasive coronary physiology measurements during pPCI and had a subsequent CMR scan at a median of 19 h post pPCI. Short axis non-contrast T2-weighted images were acquired and delayed enhancement imaging was performed following administration of intravenous gadolinium (0.1 mmol/kg). AAR was determined and myocardial salvage was calculated as AAR—infarct area.

Results IMR was 29 (21), AAR 52% (15%) and myocardial salvage 6% (9%)—all mean (SD). Spearman rank correlation between IMR and AAR was 0.27 (p 0.02) and between IMR and salvage was 6% (9%).

Conclusions IMR measured acutely correlates with AAR and correlates negatively with myocardial salvage as determined by MRI.
Conclusions HARP and SinMod methods show a high level of agreement for assessment of global mid-ventricular transmural circumferential strain, with good reproducibility for both individual methods. Agreement is much lower for segmental measurements; poor reproducibility for segmental measurements using both techniques probably reflects user variability in identification of right ventricular septal insertion points and contour tracing.

132 NON-SYNONYMOUS SMAD6 MUTATIONS IMPAIRED INHIBITION OF BMP SIGNALLING IN PATIENTS WITH CONGENITAL CARDIOVASCULAR MALFORMATION

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Introduction Congenital cardiovascular malformation (CVM) exhibits familial predisposition but the specific genetic factors involved are unknown. Bone morphogenetic proteins (BMPs) regulate many processes during development, including cardiac development. Five genes of the BMP signalling were surveyed for novel variants predisposing to CVM risk. One of the genes, SMAD6, functions as an inhibitory SMAD which preferentially inhibits BMP signalling. The SMAD6 knockout mouse is characterised by cardiac valve and outflow tract defects, including aortic ossification. We hypothesised that rare functional variation in SMAD6 could predispose to congenital cardiovascular malformation (CVM).

Methods The coding regions of BMP2, BMP4, BMPR1A, BMPR2 and SMAD6 were sequenced in 90 unrelated Caucasian cases of CVM. The MH2 domain of SMAD6 were further sequenced in additional 346 CVM patients. Functional effects of the wild-type and variant SMAD6 proteins were expressed in C2C12 cells and their capacity to inhibit ALK3 activated expression of a BMP-responsive reporter, or to inhibit osteogenic differentiation (using an alkaline phosphatase assay) was assessed.

Results We identified two novel non-synonymous variants, P415L and C484F, that were not present in 1000 ethnically-matched controls. P415L was identified in a patient with congenital aortic stenosis and C484F was identified in a patient with coarctation and calcification of the aorta. Both mutations are in evolutionarily conserved amino acid residues and are predicted to be damaging by silico analysis. This was confirmed in functional assays as both SMAD6 variants failed to inhibit BMP signalling compared with wild-type SMAD6. The P415L mutant appeared to be hypomorphic whereas C484F appeared to be a null allele in the luciferase assay. The C484F mutant had a significantly (p<0.05) lower capacity to inhibit alkaline phosphatase generation in response to BMP signalling.

Conclusions This is the first time that functional mutations in SMAD6 have been described in patients with CVM, specifically those with calcific aortic malformations. Our data suggest that adequate inhibition of BMP signalling pathway due to genetic variation in SMAD6 may be an important factor in CVM.

133 ACTIVITY AND PSYCHOSOCIAL HEALTH IN ADOLESCENTS WITH CONGENITAL HEART DISEASE (CHD)

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Many patients with CHD are now adolescents. Like other patients with chronic illnesses they may be at higher risk of psychological/emotional problems. Ability to exercise is an important quality of life measure and indicator of physical health. We aimed to ascertain if activity and psychosocial health were reduced in adolescents with major CHD compared to those with a minor diagnosis. Patients aged 12–20 years were identified using the Northern Ireland regional database (HeartSuite). Participants were categorised as having major or minor CHD and divided into four diagnostic...