surgery for BAV at our centre and compared long-term outcomes of AVR, either isolated or with ARR.

Methods Our in-hospital database was explored for patients who were treated for congenital BAV between 2004 and 2015. Patients with concomitant replacement of the ascending aorta and coronary artery bypass grafting (CABG) were left in the group, concomitant non-aortic heart valve procedures and patients with functional BAV were excluded. The remaining 242 patients were divided according to the treatment received, into patients receiving ARR (n = 59) or isolated AVR (n = 183). A sub-analysis of patients with pre-existing RD was performed.

Results ARR patients were significantly younger (58.3 ± 14.6 yrs vs. 64.3 ± 12.0 yrs, p < 0.01) and had a significantly higher logistic EuroSCORE (11.3 ± 10.3% vs. 6.1 ± 8.3%, p < 0.01). Mean ARD was 39.5 ± 7.1 mm in ARR vs. 34.5 ± 5.4 mm in AVR (p < 0.01). In the AVR group, 32.2% of patients had an ARD ≥ 40 mm (n = 59), from these, 8.2% (n = 15) had an ARD ≥ 45 mm prior to the procedure. Procedural times were significantly longer in ARR (Bypass time: 110.3 ± 36.2 mins in ARR vs. 78.2 ± 31.0 mins in AVR, p < 0.01), in 8.2% of AVR patients (n = 15) concomitant aortoplasty was performed. Perioperative complications were similar after both procedures, as stroke occurred in 1.7% (n = 1) after ARR and 2.2% (n = 4) after AVR (p = 1.0), dialysis was not necessary in any ARR patient and in 1.1% (n = 2) in AVR (p = 1.0). In ARR, survival at 30 days was 100% vs. 99.5% in AVR (p = 1.0). Median follow-up was 6.1 years. Survival at 5 years was 91.7% in ARR vs. 82.9% in AVR (p = 0.88). During the observational period, 3.4% (n = 2) of the AVR group needed repeat surgery on the ascending aorta due to an increase in ARD.

Conclusion Our experience shows, that one-third of patients receiving AVR for BAV is not treated according to current guidelines. Re-operations in this group were due to pre-existent RD. However, ARR does not increase perioperative risk and therefore we recommend ARR as the appropriate treatment in patients with pre-existent RD.

142 EFFECTS OF TRUNCATING VARIANTS IN TITIN ON CARDIAC PHENOTYPE AND LEFT VENTRICULAR REMODELLING IN DILATED CARDIOMYOPATHY

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Background The clinical course of dilated cardiomyopathy (DCM) is variable: while 20% of patients die within 5 years of diagnosis, up to 15% recover fully. DNA variants that truncate the sarcomeric protein titin (TTNtv) are found in up to 20% of DCM. We sought to characterise the phenotype of TTNtv DCM and evaluate the effect of TTNtv on left ventricular remodelling in DCM.

Methods 661 prospectively recruited DCM patients underwent targeted sequencing of TTN and cardiac MRI (CMR) scanning to evaluate left and right ventricular volumes, function, wall thickness and mass (Siemens scanners, 1.5T). TTNtv in constitutive exons were confirmed by Sanger sequencing or visual inspection of reads on IGV. Quantitative phenotypes were compared using t-tests or Mann-Whitney U tests as appropriate.

A subgroup of 122 patients underwent follow up CMR scanning. Linear regression analysis was used to determine the effects of TTNtv on interval change in left ventricular ejection fraction (LVEF), left ventricular volumes and mass.

Results Targeted sequencing of 661 patients with DCM (mean age 57.3 years, 68% male) identified 62 patients (9.4%) with confirmed truncating variants in TTN (A band, n = 48; I band, n = 11; M band, n = 3).

There was no difference in age at diagnosis between patients with and without TTNtv (54.1 yrs vs 57.7 yrs, p = 0.05). Patients with TTNtv had lower maximum and mean left ventricular wall thickness and lower indexed left ventricular stroke volume and mass (Table 1). There was no difference in baseline left or right ventricular ejection fraction between patients with and without TTNtv.

122 DCM patients (mean age 54.3 years, 66% male) underwent an additional CMR with a median follow-up interval of 2.6 years (IQR 1.4–4.6 years). Amongst these, 21 patients (16.9%) had TTNtv in constitutive exons (A band, n = 17; I band, n = 3; M band, n = 1).

67% of patients with TTNtv (14/21) showed an improvement in LVEF >5% compared to 50% of patients without TTNtv (51/101). The mean interval improvement in LVEF between baseline and follow up studies was 6.2% in patients with TTNtv compared to 4.6% in those without (p = 0.55). In regression analysis, the presence of a truncating variant in TTN was not predictive of the interval change in LVEF, indexed left ventricular end diastolic volume, end systolic volume, stroke volume and mass (Table 2).

Conclusion These data show that TTNtv DCM is phenotypically characterised by thinner left ventricular walls, lower left ventricular mass and indexed stroke volume in the absence of overt differences in ejection fraction or age at diagnosis. Notably, these data show that there is no evidence that DCM patients with TTNtv have a different pattern of left ventricular remodelling compared to patients without TTNtv. This

Abstact 142 Table 1 Comparison of baseline quantitative CMR phenotypes in patients with and without truncating variants in TTN (TTNtv)

Phenotype	Mean (sd) TTNtv+ (n = 62)	Mean (sd) TTNtv- (n = 599)	P value
LVEF (%)	38.3 (13.9)	39.3 (12.5)	0.62
LVSVi (mls)	43.2 (11.9)	47.7 (14.8)	0.03*
LVESVi (mls)	78.8 (38.2)	82.0 (39.1)	0.32
LVEDVi (mls)	122.9 (37.2)	129.6 (42.1)	0.17
LVMi (g)	82.8 (21.4)	93.3 (30.4)	0.002*
Max LV wall thickness (mm)	9.1(1.9)	10.1 (2.2)	<0.001*
Mean LV septal wall thickness (mm)	7.3 (1.6)	8.0 (1.9)	0.003*
Mean LV lateral wall thickness (mm)	5.0 (1.2)	5.7(1.6)	<0.001*
RVEF (%)	36.1 (14.5)	37.6 (13.9)	0.47
RVSVi (mls)	40.6 (13.7)	44.4 (14.8)	0.10
RVESVi (mls)	42.6 (17.7)	44.0 (22.8)	0.94
RVEDVi (mls)	83.2 (19.3)	88.4 (28.9)	0.44

* indicates significance at p < 0.05. LVEF/RVEF = Left/right ventricular ejection fraction. L/RVEDVi = indexed left/right ventricular end diastolic volume. L/RVESVi = indexed left/right ventricular end systolic volume. L/RVSVi = indexed left/right ventricular stroke volume. LVMi = indexed LV mass

Abstract 142 Table 2 Results of linear regression analysis to evaluate the effect of a truncating variant in TTN (TTNtv) on the interval change in left ventricular ejection fraction (LVEF), indexed left ventricular end diastolic volume (LVEDVi), end systolic volume (LVESVi), stroke volume (LVSVi) and mass (LVMi)

Interval change in outcome variable	Presence of TTNtv Unadjusted analysis			Presence of TTNtv Adjusted analysis (adjusted for age, gender, heart failure medication, resting heart rate and blood pressure, NYHA status)		
	Coefficient	P value	95% confidence interval	Coefficient	P value	95% confidence interval
LVEF (%)	1.6	0.60	-−4.3 to 7.5	1.2	0.73	−5.4 to 7.7
LVEDVi (mls)	2.9	0.75	−15.5 to 21.1	8.9	0.38	−11.0 to 28.8
LVESVi (mls)	-0.9	0.92	−18.8 to 17.1	3.5	0.73	−16.2 to 23.3
LVSVi (mls)	3.9	0.16	−1.47 to 9.37	5.3	0.08	−0.67 to 11.3
LVMi (g)	1.5	0.77	−8.3 to 11.3	1.6	0.78	−9.4 to 12.5

implies that the presence of a titin truncating mutation in a patient with DCM does not preclude the possibility of functional recovery.

143 CLINICAL AND GENETIC CHARACTERISTICS OF FAMILIAL DILATED CARDIOMYOPATHY IN A LARGE UK PROSPECTIVE COHORT

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Background Up to fifty percent of idiopathic dilated cardiomyopathy (DCM) has a familial basis. Variants can occur in over 40 genes, though truncating variants in the sarcomeric gene titin account for the largest proportion (~20%). At least half of familial DCM cases are genetically orphan. We sought to study whether familial DCM was associated with distinct clinical characteristics, independently of the underlying genetic variant.

Methods 595 prospectively recruited DCM patients underwent detailed phenotyping with cardiac MRI (Siemens scanners, 1.5T) and were sequenced using a customised panel of ~100 cardiomyopathy genes on Illumina and 5500xl platforms. Variants were identified and annotated using a customised bioinformatics pipeline. Clinical information including family pedigree data, ECG, and arrhythmia status at diagnosis (presence of confirmed ventricular or atrial arrhythmias) was collected on all patients. Familial DCM was defined as DCM occurring in 2 or more 1st or 2nd degree family members. Chi squared or Fisher's exact test was used to compare across categorical variables and t-tests or Mann-Whitney U tests across continuous variables as appropriate.

Results Overall, 16% of patients (95 out of 595) had familial DCM. Thirty individuals came from 13 families, the remaining were unrelated probands.

Patients with familial DCM had an earlier age of disease onset (49.8 years vs 58.8 years, $p < 0.0001$). Non-familial DCM was characterised by a male preponderance (71% vs 56%, $p = 0.004$).

Patients with familial DCM had less conduction disease at baseline (11% vs 36%, $p < 0.0001$). There was no difference in confirmed VT, NSVT or atrial fibrillation at baseline between groups.

Patients with familial DCM had a milder intermediate phenotype of DCM (left ventricular ejection fraction 45.2% vs 38.2%, $p < 0.0001$). Right ventricular ejection fraction was similar in both groups (39.1% familial vs 37.1% non-familial, $p = 0.14$). There was no difference in the presence of mid wall fibrosis detected on late gadolinium imaging ($p = 0.54$).

There were 44 potentially disease-causing variants in DCM genes in the familial DCM cohort (Table 1). Genetic testing had a yield of 44% in familial ($n = 42$), and 22% in non-familial DCM ($n = 117$). Five patients carried 2 variants. Truncating variants in titin were the most common variant ($n = 17$) and were over twice as common in patients with familial DCM compared to those without (18% vs 6.8%, $p < 0.001$). Truncating and missense variants in LMNA were ten times more frequent in familial DCM compared to non familial DCM ($p < 0.001$).

Conclusions Disease causing variants in TTN and LMNA were more commonly associated with familial DCM, but 56% of patients with familial DCM remain genetically unexplained. This highlights the need for further novel DCM disease gene discovery. Our data show that familial DCM is characterised by a younger age of disease onset and less severe ventricular dysfunction as compared to non-familial DCM.

Abstract 143 Table 1 Burden of variants in DCM genes in familial and non-familial DCM

Gene	Percentage of variants in familial DCM patients (N=95) (=total number of variants in cohort)	Percentage of variants in non familial DCM patients (N=500) (=total number of variants in cohort)	P value
Titin (TTN)	22.1% (21)	7.6% (38)	<0.001
Lamin A/C (LMNA)	6.3% (6)	1.2% (6)	0.006
Myosin heavy chain beta (MYH7)	6.3% (6)	4.2% (21)	0.42
Plakophilin 2 (PKP2)	4.2% (4)	4.0% (20)	1.0
Troponin T 2 (TNNT2)	3.2% (3)	1.2% (6)	0.16
RNA Binding Motif Protein 20 (RBM20)	2.1% (2)	4.4% (22)	0.40
Tropomyosin1 (TPM1)	1.1% (1)	0	0.16
BCL2-Associated Athanogene 3 (BAG3)	1.1% (1)	1.6% (8)	1