Background Dilated cardiomyopathy (DCM) is the leading cause of non-ischaemic heart failure. It causes approximately 10,000 deaths in Europe per year. Studies suggest that up to 50% of patients with DCM have a genetic predisposition and that mutations within one of 40 genes coding for structural and functional cardiac proteins accounts for up to 40% of familial disease. The relevance of genotype to clinical phenotype, treatment and prognosis is poorly understood. This study aimed to clinically and genetically characterise probands with familial DCM using next-generation sequencing technology (NGS) to determine specific genotype-phenotype correlations in DCM.

Methods 72 probands with DCM were consecutively recruited into this study within our centre. All received pre-test genetic counselling and provided written informed consent. All patients were clinically characterised using a standard phenotyping protocol. Genomic data isolated from peripheral blood lymphocytes using standardised protocols, was collected and screened for all major genes involved in cardiomyopathies and selected candidate genes using NGS. Eighty-six genes with 1528 exons representing 500kb of coding sequence, were studied using target enrichment methods (Agilent SureSelect System) followed by sequencing on the Illumina HiSeq 2000 platform. Clinical parameters were correlated with genotype findings.

Results Variant calling from 72 probands (male 54%, age 41 years (mean 40.7, range 14 to 68 years) generated 1415 exonic and splice-site calls. After filtering, 420 distinct candidate variants were reported, 253 of which were published pathogenic mutations, 112 of which were frameshift insertion/deletion or splice-site variants predicted to cause loss of function (thus likely to be pathogenic). A further 55 novel variants were considered potentially pathogenic on the basis of preliminary *in silico* analysis. Each proband, on average, carried 3 published pathogenic variants which included known mutations associated with DCM and other forms of cardiomyopathy. Up to two further variants predicted to be pathogenic were identified per DCM proband illustrating genetic heterogeneity. However, there was no simple correlation between a specific mutation or the number of mutations and the clinical phenotype. Moreover, there was no evidence of a 'poly-hit' theory of multiple mutations contributing to a worsened phenotype nor of specific variant demonstrating causality of phenotype suggesting that genotype-phenotype correlations in DCM are complex and may be influenced by both genetic and epigenetic factors.

Conclusion This study demonstrates the exciting potential for utilisation of next generation sequencing in routine clinical practice. However it highlights the genetic heterogeneity and high frequency of novel variants with uncertain effects on gene function in DCM. This presents considerable challenges for clinical interpretation. Large-scale phenotyping is therefore required to fully understand genotype-phenotype relations in DCM.

Imaging

125 DETERIORATION OF RIGHT VENTRICULAR FUNCTION ON EXERCISE DETECTED BY EXERCISE CARDIAC MAGNETIC RESONANCE IMAGING IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

[1]Shareen Jaijee*, [1]Marina Quinlan, Pawel Tokarczuk, [1]Benjamin Statton, [1]Alaine Berry, [1]Tamara Diamond, [2]Luke Howard, [2]Simon Gibbs, [1]Declan O'Regan. *[1]Robert-Steiner Unit, Hammersmith Hospital; [2]Pulmonary Hypertension Service, Hammersmith Hospital; *Presenting Author*

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Introduction Right ventricular (RV) function is a prognostic factor in patients with idiopathic PAH (iPAH). However at diagnosis, no factors differentiate those who will progress to RV dysfunction at 1 year. RV dysfunction in disease becomes more manifest on exercise and there is interest in the capacity of the RV to augment during exercise and its relationship with outcomes. Cardiac magnetic resonance imaging (CMR) is an accurate method of evaluating cardiac function during exercise. We aimed to study the ability of CMR to detect changes in RV and left ventricular (LV) function during exercise in healthy controls (HC) and patients with iPAH and hypothesised that RV dysfunction in iPAH becomes more apparent on exercise. Methods: Resting and exercise CMR was carried out on 10 HC (6 women, average age 36 ± 12) and 10 patients with iPAH (8 women, average age 37 ± 9) using a Philips 1.5T Achieva (Best, Netherlands) with a 32-channel cardiac coil. Supine exercise was performed using an MR compatible ergometer (Lode, Netherlands) at 40% of the watts achieved on cardiopulmonary exercise testing. Free breathing, real time LV short axis stack images were acquired during rest and exercise. LV and RV volumes were analysed using cvi42 (Circle Cardiovascular Imaging, Canada) using conventional endocardial surface segmentation. The Wilcoxon signed rank test was used to compare within groups and the Mann Whitney U test for between group analysis. Results: Results are summarised in Table 1. HCs exercised at a mean of 81 ± 25W and patients at a mean of 44 ± 11W. In HCs, RV and LV stroke volume (SV) increased on exercise, driven by a decrease in RV and LV end systolic volume (ESV). LV and RV

Abstract 125 Table 1 Resting and Exercise cardiac parameters, values are expressed as mean ± standared deviation

	Healthy controls			iPAH			Mann Whitney U value	
	Rest	Exercise	p value	Rest	Exercise	p value	Rest	Exercise
Heart rate	60±9	120±12	0.005	63±13	114±18	0.005	0.791	0.427
LVEDV	139±23	146±24	0.059	116±20	110±23	0.093	0.041	0.003
LVESV	48±7	38±10	0.013	39±10	26±8	0.005	0.028	0.016
LVSV	90±16	109±16	0.005	77±13	83±17	0.047	0.07	0.005
LVEF	65±2	74±4	0.005	66±5	76±5	0.005	0.545	0.257
RVEDV	152±34	151±23	0.575	146±22	158±23	0.022	0.762	0.364
RVESV	68±19	50±17	0.007	66±14	77±18	0.059	1	0.004
RVSV	85±16	101±10	0.007	79±11	81±19	0.386	0.496	0.023
RVEF	56±4	68 ± 6	0.005	55±4	51±10	0.333	0.545	0.001

ejection fraction (EF) increased. In patients, LVEDV and LVESV decreased on exercise, with an increase in LVSV and LVEF. RVEDV increased in size with a trend for ESV to be higher than at rest. RVSV and RVEF remained unchanged. Between groups, at rest, LVESV and LVSV were lower in patients with no significant differences in RV function. However, on exercise, patients had a significantly higher RVESV and lower RVSV and RVEF, compared to HCs. Conclusion: Exercise CMR is a sensitive, accurate test which can determine physiological changes in RV and LV function. We have shown that on exercise, when compared to HC, the LV in patients with iPAH decreases in size, the RV increases in size and RV dysfunction becomes apparent which was otherwise not present at rest. This could potentially be valuable in the assessment of response to treatment and prognosis in patients with iPAH.

126 THE ROLE OF CARDIAC MAGNETIC RESONANCE IMAGING IN PATIENTS WITH CARCINOID HEART DISEASE

Boyang Liu*, Manvir Hayer, Shanat Baig, Tahir Shah, Stephen Rooney, Nicola Edwards, Richard Steeds. *Queen Elizabeth Hospital Birmingham*; **Presenting Author*

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Introduction Carcinoid heart disease (NET-CHD) is a frequent and adverse complication of carcinoid syndrome due to right ventricular (RV) failure. Medical therapy alone has a 2-year survival of approximately 20% and while surgical valve replacement is effective in improving symptoms and may increase survival, peri-operative risk remains approximately 15–20%. Transthoracic echocardiography (TTE) is considered the gold standard for assessment of NET-CHD and data on the role of cardiac magnetic resonance imaging (CMR) are limited despite recognised advantages in assessment of the right heart. The aim of this study was to assess the role of CMR in assessment of NET-CHD.

Methods This is a retrospective cohort study of 50 consecutive patients with proven NET referred with elevated NT pro-BNP to the European Centre of Excellence for Neuroendocrine Tumours in Birmingham between 2005–2015. At referral, all subjects underwent comprehensive left ventricular (LV) and RV assessment with CMR (1.5T Siemens Avanto), including deformation (Tissue Tracking, cvi42® Circle Cardiovascular Imaging), and late gadolinium enhancement (LGE).

Results In total, 36 patients were diagnosed with NET-CHD and 14 without (CHD-neg). Right sided valve disease was universal in NET-CHD: severe tricupid regurgitation (97%), severe pulmonary regurgitation (86%). On CMR, RV end-diastolic volume (EDV) and end-systolic volume (ESV) were increased (120 ± 30ml/m^2 vs. 67 ± 14 ml/m^2, $p < 0.01$; 49 ± 20ml/m^2 vs. 11 ± 3ml/m^2, $p < 0.01$) but with no difference in RVEF (60 ± 14% vs. 60 ± 9% $p = 0.92$). There was early evidence of ventricular-ventricular interaction, with reduction in both LVEDV (53 ± 16ml/m^2 vs. 72 ± 16 ml/m^2, $p < 0.01$) and LVESV (19 ± 10 ml/m^2 vs. 28 ± 16ml/m^2, $p < 0.05$) in NET-CHD, but no difference in LV ejection fraction (67 ± 8% vs. 63 ± 14%, $p = 0.3$). There was no difference in LV global longitudinal strain (GLS) or circumferential strain (GCS) between groups. RV LGE indicative of endocardial plaques was present in 6/36 (17%) but not observed in CHD-neg. Diffuse LV LGE was present 5 NET-CHD patients. Over follow up (median 1.3 years [0.6–3.1]), 20 patients with NET-CHD died. These patients had a lower GCS (14.8 ± 4.6% vs. 18.2 ± 4.4%, $p < 0.05$) and lower GLS (14.7 ± 4.7% vs. 18.3 ± 4.4%, $p < 0.05$) on CMR but no difference in LVEF, RVEF, LV volumes, RV volumes or NT-proBNP. In a logistic regression model, LV GLS remained an independent predictor of death.

Conclusion Significant increase in RV size and the presence of RV plaques are measurable on CMR early following referral with NET-CHD. This is sufficient to adversely affect LV filling and global deformation, which may contribute to effort intolerance and adverse cardiovascular outcomes.

127 SERIAL MONITORING OF LEFT VENTRICULAR EJECTION FRACTION IN PATIENTS WITH HAEMATOLOGICAL MALIGNANCIES RECEIVING ANTHRACYCLINE-BASED CHEMOTHERAPY

Polyvios Demetriades*, Emily Ho. *Sandwell and West Birmingham NHS Hospitals Trust*; **Presenting Author*

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Introduction Anthracyclines are one of the most widely used chemotherapeutic agents. However, their use has been limited due to significant risk of cardiotoxicity. This has been reported in 6.2% of adult patients with haeamatological malignancies. Early-onset cardiotoxicity is by far the commonest, occurs within the first year following treatment and manifests as a form of dilated cardiomyopathy. Early detection with imaging, even in asymptomatic patients, and appropriate treatment with anti-failure medication leads to recovery of left ventricular function (LVEF) in up to 82% of patients. This highlights the need for a consensus strategy to guide monitoring frequency and duration in the long-term management of these patients. We conducted a quality improvement project to review the current practice in the Haematology department of our Trust.

Methods We identified patients with haematological malignancies that were commenced on anthracycline-based chemotherapy regimens between March 2014 and August 2015.

We collected data regarding pre and post-chemotherapy imaging with echocardiograms and compared our findings against the recommendations of the "ESMO Clinical Practice Guidelines". These suggest that all patients should have serial monitoring of their LVEF at baseline and at 3-monthly intervals for the first year post-treatment.

In addition, we performed a qualitative analysis to review the management of the patients with abnormal echocardiograms both pre and post-chemotherapy.

Results We identified a total of 83 patients, of which 74.7% were treated with doxorubicin-based chemotherapy.

The majority of patients (96.4%) had a baseline echocardiogram to assess LVEF prior to chemotherapy. However, only 29 patients (34.9%) had imaging post-chemotherapy. Unfortunately, in the majority (n = 18) this was requested due to symptoms rather than as part of serial monitoring.

Of our cohort, six patients had a degree of left ventricular systolic dysfunction (mild to moderate) prior to chemotherapy but proceeded without any cardiology input. Of these, only 50% had an echocardiogram post-chemotherapy.