classified as a variant of uncertain significance, although in-silico prediction tools consider it deleterious. A second discussion was had with the patient explaining the additive risk of her genetic profile combined with the presence of scar in her septum. She agreed to ICD implantation. 8 months later, the patient received a shock for ventricular fibrillation during sleep.

Implications This case highlights the importance of an integrative risk assessment for each patient to include genetics. The ESC HCM-SCD risk prediction score is not impervious and, importantly, it does not include scar burden or genetics. It is established that patients with more than one mutation in candidate genes have an increased risk and although studies to this effect are few in number. An individualized approach needs to be taken in each HCM case.

**Abstract 54 Figure 2**

**EARLY DETECTION OF LATE ANTHRACYCLINE CARDIOTOXICITY IN ADULT SURVIVORS OF CHILDHOOD MALIGNANCY**

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**Abstracts**

**Background** Almost 60% of the 2,000 children diagnosed with cancer in the UK and Ireland every year are treated with anthracycline chemotherapy. Anthracyclines are WHO essential medicines, and 5-year childhood cancer survival rates are approaching 85%, but also carry a risk of cardiotoxicity, particularly for childhood cancer survivors (CCS) of whom 30% have left ventricular dysfunction at 10 years and 10% have heart failure at 40 years post treatment. Current guidelines advocate periodic screening every 1–5 years however this approach is both resource intensive and inadequate, diagnosing cardiotoxicity at a late and often irreversible stage. Consequently, ‘Defining Robust Predictors of Cardiotoxicity’ was deemed a top ten priority for the cardio-oncology field at the Global Cardio-Oncology Summit.

**Purpose** Our research aims to investigate novel imaging and blood biomarkers (established, novel and biomarker discovery) in the Northern Ireland population of childhood cancer survivors.

**Method** Consenting adult patients will have cardiovascular risk factor screening, a quality-of-life questionnaire, six-minute walk test (6MWT) and a 24-hour Holter monitor. Patients will undergo 3D echocardiography, Global Longitudinal Strain (GLS) and Right Ventricular (RV) Strain imaging. Magnetic Resonance Imaging (MRI) will be conducted with feature tracking, myocardial tagging and aortic distensibility. Blood will be analysed for established (NTproBNP, CRP, and Troponin) and novel (IL6, sST2, MPO) biomarkers. Biomarker discovery through proteomic and microRNA analysis will be explored in subgroups of patients with normal ventricular function, impaired strain and ejection fraction. The top differentially expressed biomarkers will subsequently be validated within the remaining cohort.

**Results** 50 patients have been recruited to date (33 female, mean age 26). Half were treated before the age of 5. Mean dose was 265mg/m2 (120–480). Time since treatment was mean 18 years (median 16.5, range 6–33). 7 patients had a blood pressure >140/90mmHg, 18 had an abnormal lipid profile, and 1 had an abnormal HbA1c. Mean BMI was 27.1kg/m2 (18–49) with 23 participants classed as overweight/obese. 21 (42%) patients had a 6MWT distance below the lower limit of normal for their age/sex/height/weight. Left ventricular dysfunction was detected in 22/50 (44%): 3D ejection fraction was <55% in 7/46, GLS was abnormal in 22/43 and RV strain was abnormal in 15/31 patients. Troponin was normal in all patients. NTproBNP was elevated (>125ng/L) in 10 patients (20%). Elevated NTproBNP was associated with higher anthracycline dose (P=0.004, r=0.42). NTproBNP, CRP and Troponin were not associated with abnormal echocardiographic parameters. MRI and novel biomarker analysis will be conducted on enrolment completion.

**Conclusion** Childhood cancer survivors are at increased cardiotoxicity risk. Current results indicate that CCS have increased cardiovascular risk and impaired 6MWT. Established biomarkers fail to correlate with imaging data and as such support ongoing biomarker research.

**Abstract 56**

**NOVEL HEART FAILURE BIOMARKER CLEC3B IS ASSOCIATED WITH CARDIAC FIBROSIS, AND IMPACTS CARDIAC FIBROBLAST CELL FUNCTION**

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**Background** Using a proteomics approach we have recently identified a novel blood-based biomarker for heart failure called CLEC3B, which exhibits improved diagnostic accuracy over BNP. We have previously investigated CLEC3B expression in human atrial and ventricular tissue and shown that it correlates positively with the degree of cardiac tissue fibrosis. The purpose of this study was to validate the diagnostic potential of CLEC3B within a symptomatic population containing both
cases and controls, and to determine its role in development of cardiac fibrosis and dysfunction associated with heart failure (HF).

**Methods** Through a HORIZON 2020 collaboration, 54 symptomatic patients were recruited from St Michael’s Hospital, Dublin and University Hospital of Ioannina (Greece), over a 6-month period. The recruited cohort consisted of 20 hypertensive or obese non-HF patients with symptoms of breathlessness, and 34 patients diagnosed with acute HF. Plasma samples were collected and CLEC3B was quantified using ELISA. As the primary cell type contributing to cardiac fibrosis is the fibroblast, parallel in vitro studies were carried out using primary human cardiac fibroblast cells (HCF). Both CLEC3B gene over-expression and gene knock-down studies were carried out in HCFs, in the presence or absence of stimulation with the pro-fibrotic growth factor TGFβ. The impact of modulating endogenous CLEC3B levels on gene and protein expression was studied, including by RNA sequencing, to identify the potential role of CLEC3B in fibroblast cells. An in vivo model of angiotensin II knockout on the expression of genes related to cardiomyopathy, histology, gene and protein analysis.

**Results** Within a breathless cohort, circulating CLEC3B levels were significantly reduced by approximately 30% in acute HF patients compared to non-HF patients (P<0.0001). Receiver operating characteristic (ROC) predictive modelling of plasma CLEC3B in non-HF vs. acute HF patients showed area under the curve, AUC=0.92. RNA sequencing analysis of HF cells showed significant changes in over 2000 genes following both CLEC3B over-expression and knockdown, with different genes being modulated depending on activation status of the HCF cells. Our mouse model of angiotensin II induced HF showed that there was an impact of global CLEC3B knockout on the expression of genes related to fibrotic processes.

**Conclusions/Implications** These data show that CLEC3B shows promise as a diagnostic tool that could help identify HF patients within a symptomatic breathless population. It also highlights that CLEC3B may have an important role in the development and progression of fibrosis associated with cardiac remodelling in heart failure, due to the impact on function of activated cardiac fibroblasts in both in vitro and in vivo experimental models. This aspect opens up the possibility of CLEC3B being a potential novel therapeutic target in diseases associated with cardiac fibrosis and remodelling.

**58 STRATEGIES TO OPTIMISE GUIDELINE-DIRECTED MEDICAL THERAPY IN HEART FAILURE PATIENTS WITH REDUCED EJECTION FRACTION BY IMPROVING SGLT2 INITIATION RATES IN NURSE-LED OUTPATIENT HEART FAILURE CLINICS**

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**Aims** Sodium-glucose Cotransporter-2 (SGLT2) Inhibitors are now advised as standard front line therapy for heart failure reduced ejection fraction (HFrEF) patients irrespective of whether diabetes is present or not. There has now been a multitude of positive trials in favour of SGLT2 inhibitor use with little information on how routine community HFrEF populations respond to this intervention in the setting of already taking maximum tolerated conventional disease modifying therapies. We therefore set out to assess the clinical response (using NYHA and NT-proBNP change) and tolerability of SGLT2 inhibitors in patients attending our outpatient heart failure unit.

**Methods** All patients commenced on SGLT2 inhibitors as additional medical therapy for HFrEF in a twelve-month period were included in the study. SGLT2 inhibitor therapy was initiated once patients were fully optimised on conventional medical therapy and stable from a heart failure perspective. For all patients commenced on an SGLT2 inhibitor as part of their HFrEF pharmacotherapy we then studied what effect this had on each patients NYHA functional class and NT-proBNP levels before and after initiation of SGLT2 inhibitor. For all patients we recorded whether a not a patient was still taking their SGLT2 inhibitor at most recent follow up appointment at our heart failure unit. Where patients were no longer prescribed SGLT2 inhibitors at follow-up, we analysed the reasons documented for this in the patients electronic patient record.

**Results** There were 184 patients commenced on SGLT2 in the 12-month period studied of which 78% (144 patients) were male and 26% (48 patients) were diabetic. The average age was 69 years old. Out of the 184 patients, 158 patients (86%) had their initial NYHA class documented in their patient record. The average NYHA functional class at time of commencing SGLT2 inhibitor for these patients was 1.9. At a subsequent follow-up review, 120 patients had a repeat NYHA documented and the average NYHA functional class at this time was 1.7 (with a mean time interval of 4.2months). 86 patients (72%) were in the same NYHA functional class, 28 patients (23%) were now in a lower NYHA functional class whilst 6 patients (5%) were in a higher NYHA functional class. The mean NT-proBNP was 2000pg/mL at initiation of SGLT2 inhibitor and it was 1830pg/mL at the follow-up visit with a mean time interval of 4months. The difference in NT-proBNP’s not meeting statistical difference. 166 patients (90%) were still prescribed their SGLT2 inhibitor at most recent follow up. The most common reasons patients had stopped their SGLT2 inhibitors during follow-up was due to urinary tract infections (3% of total patients) and symptomatic hypotension (3% of total patients).

**Conclusion** For the majority of patients there was no significant change in their reported NYHA class or NT-proBNP levels at follow-up. Overall, we found SGLT2 inhibitors to be a well-tolerated with high adherence rates (90%) at follow up and relatively few side effects warranting discontinuation.