recently come under the radar as a potential new biomarker for HF – one that is more cost-effective, less invasive, more convenient and acceptable for both patients and healthcare professionals, and one which could potentially reflect the information received from a standard blood NTproBNP test. One hurdle in measuring NTproBNP in saliva samples using standard point-of-care (POC) devices is the level of this protein in saliva. Measuring about 2000-fold lower, saliva NTproBNP is hardly measurable with standard POC devices. Here we present the KardiaTool platform, an integrated POC solution for non-invasive diagnosis and therapy monitoring of HF patients. The platform consists of two components, KardiaPOC (a highly sensitive portable device for non-invasive and simultaneous quantitative assessment of multiple HF related biomarkers from saliva samples, incorporating a functionalized magnetic nanoparticle approach) and KardiaSoft (a decision support software based on predictive modelling techniques that analyses POC and other patient data, and delivers information on HF diagnosis and therapy monitoring). The KardiaTool platform was developed as part of an ongoing collaborative Horizon 2020 project, KARDIATool.

Methods and Results The aim of this sub-study was to test the hypothesis that saliva NTproBNP levels correlate to blood NTproBNP levels. To achieve this, we recruited chronic heart failure patients attending the HF unit in St. Michael's Hospital (SVUH, Dublin). Patients underwent routine physical examination, including venepuncture, echocardiography and electrocardiography. NTproBNP was quantified in peripheral blood samples. Saliva was collected with the SalivaBio Oral Swab device and extracted following centrifugation at 5000 g for 5 min. Saliva samples were assessed with a modified immunoassay prior to the official KardiaPOC testing. Results from the first 46 HF patients show a significant and positive correlation between blood and saliva NTproBNP ($p < 0.05$). In addition, saliva NTproBNP correlated significantly with echocardiography parameters, including LA diameter ($r = 0.36$, $p = 0.02$) and E/A ratio ($r = 0.43$, $p = 0.01$).

Conclusions We were successfully able to quantify saliva NTproBNP levels in HF patients using a modified immunoassay approach, and these levels correlated with blood levels. The KardiaTool project is still ongoing, with patient recruitment in Ireland, Greece, and Italy. The next stage is to test the KardiaPOC device, which we envisage will have superior sensitivity for saliva NTproBNP quantification, and to determine the diagnostic test accuracy for acute and chronic heart failure.

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

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Background Through 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 tissue and shown that it correlates positively with the degree of cardiac tissue fibrosis. The purpose of this study was to expand our current knowledge of CLEC3B in the context of heart failure, with a specific emphasis on cardiac fibrosis.

Methods Left ventricular cardiac tissue samples from 30 patients with heart failure and 9 age/sex matched non-heart failure controls were studied to assess protein levels of CLEC3B and markers of cardiac fibrosis. 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 TGF β . 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 induced heart failure in CLEC3B knock out mice is currently ongoing to study the impact of CLEC3B on cardiac function and remodelling (echocardiography, histology, gene and protein analysis).

Results Protein levels of CLEC3B were significantly increased in cardiac tissue derived from patients with heart failure ($p < 0.01$), including in both HFrEF ($p < 0.001$) and HFpEF ($p < 0.01$) sub-sets, compared to non-failure controls. Levels of CLEC3B in cardiac tissue correlated significantly with markers of fibrosis, including collagen subtypes 1, 5, 6, 12, and 14, with the r-statistic ranging between 0.31 and 0.78, (all $p < 0.05$). RNAseq analysis of HCF cells showed significant changes in over 400 genes following both CLEC3B over-expression and knockdown, with different genes being modulated depending on TGF β stimulation of the HCF cells.

Conclusions/Implications These data show how CLEC3B has an important role in the fibrosis associated with cardiac remodelling in heart failure. Many candidate genes have been identified from RNAseq analysis which will help guide future investigations, alongside the in vivo CLEC3B knockout animal model of heart failure, to help elucidate the mechanisms involved in the role of CLEC3B in cardiac remodelling and disease progression.

42 RENAL SAFETY OF SGLT2 INHIBITORS IN THE REAL WORLD – AN OUTPATIENT HEART FAILURE CLINIC EXPERIENCE

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Background As recent evidence has emerged indicating the efficacy of sodium-glucose-co-transporter-2 inhibitors (SGLT2i) in reducing all-cause mortality as well as hospitalisations in patients with HFrEF, it has been widely and quickly adapted into Cardiology practice. However, given the comorbidities and polypharmacy associated with this patient cohort, the real-world initiation and monitoring can be challenging.

Aim To assess the renal biochemical effects of SGLT2i initiation, as well as effects on hospitalisation and side effects in a

cohort of patients commenced on SGLT2i at Beaumont Hospital HF unit.

Methods This is a retrospective observational study carried out through Heart Support Unit outpatient department. Demographic data available such as age, comorbidities, and concurrent medical therapies for HFrEF was obtained from PIPE and medical records [table 1]. Follow up biochemical markers of renal function and nt-Pro-BNP levels were obtained as well as data on any hospitalisations in the intervening period and changes in concomitant medications. Analysis was carried out to assess for any significant changes in renal function, electrolytes, nt-pro-BNP.

Results 86 patients were identified for SGLT2i (78 dapagliflozin and 8 empagliflozin), having started SGLT2i between July 2020 and March 2021. Of these 77 patients were available for analysis (59 male, 18 female). 9 patients were excluded due to contraindications, or lack of follow up data. Therapy was predominantly commenced at 10mg OD (96%). Mean follow up was 97 days post commencement of SGLT2i. Mean age was 68 (40-94). The treatment was well tolerated as a whole, 1 patient was discontinued due to hyponatremia (na 128). Mean creatinine prior to starting SGLT2 was 111.9

± 28 , mean eGFR 60.9ml/min/kg2 (male 63.5, female 51.8). Mean creat was 112.7 following observation. This was consistent even in patients with stage III and IV CKD, average creatinine rose just 1mmol in this patient cohort. No statistically significant difference (using paired t-tests) was noted in creat, Na, K, Mg or nt-pro-BNP. No clinically significant electrolyte abnormalities were identified at any follow up measurement. There were 9 cardiac hospitalisations during the study duration (11.5%). There were 7 non-cardiac admissions (9%). There was 1 death, caused by low output HF with euglycemic ketoacidosis.

Conclusion Consistent with published data, the introduction of SGLT2i was well tolerated in this cohort. There was no significant change in renal function. No clinically significant electrolyte disturbance was observed. Loop diuretic therapy was reduced or stopped in 23%. While a modest reduction in average nt-pro-BNP was seen, this was not statistically significant. The data is reassuring and consistent with literature, that these agents do not result in deterioration in renal function in these patients on complex polypharmacy regimens and there is no need to check renal profile unless clinically indicated.

Abstract 42 Table 1 Demographic data

	Number	Pre SGLT2i			Change post-SGLT2i			
		Mean Creat	eGFR	nt-Pro-BNP	Serum Na	Serum K	Creatinine	Serum nt-pro-BNP
Total patients	77	111.3	61.5	2332.3	0.52	0.14	2.51	-94.85
Male	59	113.62	63.65	1760.98	0.93	0.07	3.20	-7.77
Female	18	104.94	51.88	4150.35	-1	0	1	-417
CKD I	8	70.62	103.75	528.23	-0.57	0.14	6.00	-43.38
CKD II	26	97	72	942.26	1.00	-0.03	5.86	-341.95
CKD III	41	127	48	3391.1	0.70	0.34	0.78	63.53
CKD IV	2	198	23	2977	1.00	0.10	-15.50	-303.50

Abstract 42 Table 2

Demographic Data		
Male		59
Female		18
NYHA Class	I	13
	II	54
	III	10
Diabetes (n)		11
Mean EF		29% (± 8)
Percentage treated with	ARNI	67.50%
	ACEi	26%
	ARB	12%
	BB	84%
	MRA	71%
	Loop diuretic	73%