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A PROTEIN BIOMARKER MODEL FOR DETECTION OF CARDIAC ARRHYTHMIA AND PREDICTION OF ASSOCIATED HEART FAILURE

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Introduction Cardiac arrhythmia is strongly linked with heart failure (HF) and a primary cause of stroke. The condition affects around 37,000 people in Northern Ireland although it is estimated that many thousands more remain undiagnosed. It is important to be able to diagnose cardiac arrhythmia early, so that appropriate interventions can be made to reduce risk of subsequent stroke or HF. Currently, diagnosis and management of cardiac arrhythmia is reliant on assessment of clinical risk factors, however, routine monitoring of circulating biomarkers would significantly improve accuracy for prediction of arrhythmia and associated adverse events. The aim of this study was to (i) identify protein biomarkers, which can predict cardiac arrhythmia and (ii) identify protein biomarkers that are predictive of HF in patients with arrhythmia.

Methods Multiple Reaction Monitoring mass spectrometry-based assays were developed for measurement of a selection of candidate protein biomarkers of cardiovascular injury. Assays were developed using nanoflow reverse phase C18 chromatographic ChipCube based separation, coupled to an Agilent 6460 triple quadrupole mass spectrometer. Optimised MRM assays were applied, in a sample blinded manner, for analysis of a cohort of 410 serum samples. This included 112 patients with cardiac arrhythmia as well as matched controls without cardiac arrhythmia.

Results MRM assays were established for measurement of 25 proteins. Individually, a number of the biomarker proteins show significant differential expression between patients with and without cardiac arrhythmia. An 11-protein biomarker model was identified, which was comparable to BNP in prediction of HF within the cardiac arrhythmia subset of patients (Protein panel AUC = 0.856 vs BNP AUC = 0.838). Combination of the 11 proteins with BNP notably enhanced the predictive capacity of BNP (AUC = 0.898).

Conclusions/Implications Through this study, assays have been developed for robust, multiplexed measurement of 25 cardiovascular disease-associated proteins in patient serum samples. A number of proteins were identified, which show significant expression changes in association with cardiac arrhythmia and will be further explored. Importantly, a statistical model revealed a panel of 11 proteins, which can predict HF in patients with cardiac arrhythmia, with comparable accuracy to BNP. This panel will need to be further validated in independent patient cohorts.

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A MULTI-CENTRE ANALYSIS OF THE RATES OF GUIDELINE-DIRECTED IMPLANTABLE CARDIAC DEFIBRILLATOR IMPLANTATION FOR HEART FAILURE WITH REDUCED EJECTION FRACTION: COMPARING CENTRES WITH AND WITHOUT ELECTROPHYSIOLOGY SERVICES

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Introduction Implantable Cardiac Defibrillators (ICD) are a potentially lifesaving therapy inserted for multiple indications. The indications for insertion of ICDs are stated in the European Society of Cardiology guidelines, and American Heart Association guidelines. One of the most common indications is for implantation in heart failure with reduced ejection fraction (HFrEF). These include patients with New York Heart Association (NYHA) Class I-III in patients with ischaemic cardiomyopathy (ICM) and NYHA Class II-III in patients with non-ischaemic cardiomyopathy (NICM).

Purpose While ICDs are not exclusively implanted by electrophysiologists in the country of study, we hypothesised that a hospital having a dedicated electrophysiology service would lead to greater compliance with current guidelines.

Methods We compared two major tertiary referral centres, one of which has the largest Electrophysiology (EP) service in the country, with the other currently having no EP physician. We obtained a list of all patients who attended the respective Heart Failure Clinics for a year from the 1st of January 2018 to the 31st of December 2018. We then excluded patients with ejection fraction (EF) of >35% by examining the relevant patients' echocardiogram reports.

Results In Heart Failure Clinic in Hospital A (with an EP service), 172 patients attending the heart failure clinic had an EF less than or equal to 35%. Of those, 116 had an ICD (67.4%); 88 with an ICD and 28 with a Cardiac Resynchronisation Therapy – Defibrillator (CRT-D). 56 patients did not have ICD/CRT. In Hospital B (without an EP service), 174 patients attending the heart failure clinic had an EF less than or equal to 35%. 83 of these patients had an ICD (47.7%). Of those, 56 had an ICD and 27 had a CRT-D. We report a significant difference of 19.7% ($p=0.0002$) between two large tertiary referral centres in the rate of guideline-directed ICD implantation (figure 1).

Conclusion The availability of an electrophysiology service in a hospital may improve the rates of guideline-directed ICD implantation for heart failure with reduced ejection fraction. This hypothesis warrants further investigation in larger studies.

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A REVIEW OF MORTALITY IN PATIENTS WHO UNDERGO ICD INSERTION IN A SINGLE IMPLANTATION CENTRE

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Aims To review the ICD implantation rate in our institution, as well as to assess overall survival following ICD implantation, and to review the rate of early mortality (<1 year) following ICD insertion.

Methods Using the HeartRhythmIreland.com database, where all new ICD implants have been registered since 2005, we obtained information on demographics, implantation date, last registered visit, and notification of death. Date of death was confirmed with our own institution's electronic patient manager. Survival probability was calculated using the Kaplan-Meier method, using the most recent attended ICD check, or the date of death. Survival was defined as freedom from death at most recent check. (Figure 1).

Results 415 ICDs were implanted in our institution between 2005 and 2018. The mean (mean ($\pm$ SD)) age was 58.9 years ($\pm$ 14.00) and 333 (80.2%) of the patients were