COEXISTENT DIABETES IS ASSOCIATED WITH THE PRESENCE OF ADVERSE PHENOTYPIC FEATURES IN PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY

Background Type 2 diabetes mellitus (DM) is associated with worsened clinical outcomes in hypertrophic cardiomyopathy (HCM) patients. The reasons for this adverse prognostic association are incompletely understood. Although distinct entities both HCM and DM share common features of impaired myocardial energetics and coronary microvascular function.

Purpose We sought to test the hypothesis that co-existent diabetes is associated with greater reductions in myocardial energetics and perfusion, and higher scar burden in HCM. Research design and methods- Seventy-five age- and sex-matched participants with concomitant HCM and DM (HCM-DM, n=20), isolated HCM (n=20), isolated DM (n=20) and healthy volunteers (HV, n=15) underwent 31 phosphorus magnetic resonance spectroscopy and cardiovascular magnetic resonance imaging. The HCM groups were matched for HCM phenotype. The DM groups were matched for diabetes treatment, duration, HbA1c, body mass index and hypertension comorbidity.

Results ESC sudden cardiac death risk scores were comparable between the HCM groups (HCM:2.2±1.5%, HCM-DM:1.9±1.2%; p=NS) and sarcomeric mutations were equally common. HCM-DM had the highest NT-proBNP levels (HV:42ng/L[IQR:35–66], DM:118ng/L[IQR:53–187], HCM:298ng/L[IQR:157–837], HCM-DM:726ng/L[IQR:213–8695]; p<0.0001). Left-ventricular ejection fraction, mass and wall thickening were greater in HCM-DM compared with isolated HCM and DM.

Abstract 148 Table 1 CMR and 31P-MRS findings

|                      | HV n=15 | DM n=20 | HCM n=18 | HCM-DM n=20 | P value |
|----------------------|---------|---------|----------|-------------|---------|
| LV end-diastolic vol. | 83±18   | 72±14   | 82±19    | 76±22       | 0.03    |
| LV end-systolic vol. | 31±7†   | 29±10   | 28±15    | 26±14       | 0.03    |
| LV mass, g           | 99±27‡  | 87±23‡  | 173±63*  | 187±73      | <0.0001 |
| LV mass index, g/m²  | 54±11†  | 45±11‡  | 90±27*   | 92±40       | <0.0001 |
| LV mass to LV end-diastolic vol., g/mL | 0.65 | 0.64±0.15§ | 1.03±0.31* | 1.24±0.36 | <0.0001 |
| LV stroke vol., ml   | 95±23‡  | 82±17   | 118±21*  | 101±22      | <0.0001 |
| LV ejection fraction, % | 63±4‡  | 60±6†   | 70±9*    | 67±9        | <0.0001 |
| LV maximal wall thickness, mm | 10±1†   | 9±2‡    | 20±2*    | 21±4        | <0.0001 |
| RV end-diastolic vol. | 86±20†  | 71±12   | 79±14    | 66±13       | 0.0006  |
| RV end-systolic vol. | 35±10   | 29±8    | 30±10    | 28±13       | 0.35    |
| RV stroke vol., ml   | 95±23‡  | 78±17   | 94±16C   | 75±21       | 0.0006  |
| RV ejection fraction, % | 60±6    | 59±6    | 62±8     | 58±13       | 0.44    |
| LA bpline end-systolic vol., ml | 67±17†  | 64±20  | 100±28*  | 113±59      | <0.0001 |
| Bpline LA EF, %      | 62±7†   | 57±12   | 45±10    | 34±18       | <0.0001 |
| Global longitudinal strain, % | 14±3   | 16±5§   | 4±5      | 10±4        | <0.0001 |
| Peak systolic circumferential strain, % | 21±2‡  | 18±6    | 20±4     | 16±4        | 0.009   |
| Peak circumferential diastolic strain rate, s⁻¹ | 1.19 | 1.05±0.32 | 0.99±0.21 | 0.87±0.22 | 0.005   |
| Mean native T1, (ms) | 1211±81 | 1225±107| 1211±65 | 1209±69 | 0.9     |
| Extra cellular volume, (%) | 25[23-26]¶ | 22[21-24]§ | 27[22-29]‡ | 31[27-43] | <0.0001 |
| LGE scar percentage of LV mass (%) | 4±4    | 10±8    | 0.002    |              |         |
| Myocardial Energetics |
| PCR/ATP ratio        | 2.17    | 1.61    | 1.93     | 1.54±0.27   | 0.0003  |
| Myocardial Perfusion |
| Increase in RPP, %   | 37      | 39      | 33       | 32          | 0.3     |
| Stress MBF, ml/min/g | 2.06    | 1.78±0.45§ | 1.74    | 1.39±0.42   | 0.004   |
| Rest MBF, ml/min/g   | 0.68±0.03| 0.70±0.17| 0.59±0.19| 0.69±0.16   | 0.05    |
| MPR                   | 3.19    | 2.70±0.80§ | 3.09    | 2.04±0.82   | 0.0015  |

C £ signifies p<0.05 between HCM-DM and HCM with Bonferroni correction; § signifies p<0.05 between HCM-DM and HCM with Bonferroni correction; ¶ signifies p<0.05 between HCM-DM and DM with Bonferroni correction; * signifies p<0.05 between DM and DM with Bonferroni correction; † signifies p<0.05 between DM and HV with Bonferroni correction; ‡ signifies p<0.05 between HV and HV with Bonferroni correction; ‡‡ signifies p<0.05 between DM and HV with Bonferroni correction.

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thickness were similar between the HCM groups. HCM-DM displayed a greater degree of fibrosis burden with higher scar percentage, and lower global longitudinal strain compared to the isolated HCM. PCr/ATP was similarly decreased in the HCM-DM and DM (HV:2.17±0.49, DM:1.61±0.23, HCM:1.93±0.38, HCM-DM:1.54±0.27; p=0.0003). HCM-DM had the lowest stress myocardial blood flow (HV:2.06±0.42 ml/min/g, DM:1.78±0.45 ml/min/g, HCM:1.74±0.44 ml/min/g, HCM-DM:1.39±0.42 ml/min/g; p=0.004).

Conclusions We show for the first time that HCM patients with DM comorbidity display greater reductions in myocardial energetics, perfusion, contractile function and higher myocardial scar burden and serum NT-proBNP levels compared to patients with isolated HCM despite similar LV mass and wall thickness and presence of sarcomeric mutations. These adverse phenotypic features may be important components of the adverse clinical manifestation attributable to a combined presence of HCM and DM.

Conflict of Interest None

Abstract 149 Figure 1

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149 A NOVEL INTERNALLY VALIDATED RISK PREDICTION MODEL FOR ADVERSE CARDIAC OUTCOME IN FABRY DISEASE

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Abstract 149 Figure 2

Abstract 149 Figure 1

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Introduction The cardiac manifestations of Fabry disease are the leading cause of death, but risk stratification remains inadequate. Identifying patients who are at risk of adverse cardiac outcome may facilitate more evidence-based treatment guidance. Contemporary cardiovascular magnetic resonance imaging (CMR) biomarkers have become widely adopted but their prognostic value remains unclear. Our objective was to develop, internally validate, and evaluate the performance of, a prognostic model, including contemporary deep phenotyping, which can be used to generate individual risk estimates for adverse cardiac outcome in patients with Fabry disease.

Methods Longitudinal prospective cohort study of 200 consecutive patients with Fabry disease undergoing clinical CMR. Median follow-up 1,640 (987 – 2,293) days. Prognostic models were developed using Cox proportional hazards modelling. Outcome was a composite of adverse cardiac events. Model performance was evaluated.

Results The highest performing, internally validated, parsimonious multivariable model included age, native myocardial T1 dispersion (standard deviation of per voxel myocardial T1 relaxation times – Figure 1), and indexed left ventricular mass. Median optimism-adjusted c-statistic across 5 imputed model development datasets was 0.77. Model calibration was excellent across the full risk profile. A risk calculator, which provides 5-year estimated risk of adverse cardiac outcome for individual patients, including males and females, was generated (Figure 2 - survival free of the composite outcome according to predicted probability divided into three quantiles according to predicted probability).

Conclusion This study developed and internally validated a risk prediction model that accurately predicts 5-year risk of adverse cardiac outcome for individual patients with Fabry disease, including males and females, which could easily be integrated into clinical care. External validation is warranted.

Conflict of Interest None