Abstracts

S193

Table 1.

<table>
<thead>
<tr>
<th>All-cause mortality</th>
<th>OR AF vs no AF</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>3.7</td>
<td>1.1 - 13.0</td>
<td>0.04</td>
</tr>
<tr>
<td>Median follow-up (1.8 yrs.)</td>
<td>2.7</td>
<td>1.2 - 6.2</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Conclusions: AF is common, frequently paroxysmal and, associated with worse prognosis in HFPEF. Whilst the role of AF ablation in HFPEF remains uncertain, proactive strategies to identify, risk stratify and treat AF in HFPEF are critical to optimise outcomes of patients with HFPEF.

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139

The Role of Cardiac Biomarkers in the Prediction of Cardiotoxicity in Patients Treated for Cancer: A Systematic Review

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Background: The adverse morbidity and mortality due to cardiotoxicity in patients treated for cancer has prompted a move for earlier diagnosis of myocardial injury. Current guidelines recommend biomarker screening during cardiotoxic treatment. However, the risk conferred by biomarker elevations in this subgroup remains unclear.

Methods: A systematic search of MEDLINE, PubMed and EMBASE was conducted for studies utilising cardiac biomarkers for detection of LV dysfunction in adults treated for cancer. Cardiotoxicity was defined as a reduction of the LVEF of ≥ 5% points to <55% with symptoms of heart failure or an asymptomatic reduction of ≥10% points to <55%.

Results: 782 studies were screened and twenty-two studies reporting of biomarkers is imperative to assess their clinical utility and cost-effectiveness in screening of patients following cancer therapy.

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139

The Role of Extracellular Matrix Stiffness on Cardiac Metabolic Activity

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The cardiac L-type Ca 2+ channel (LTCC) can regulate mitochondrial metabolic activity via calcium-independent mechanisms. The sarcomeric network plays an important role in this response: Hypertrophic cardiomyopathy (HCM) occurs due to mutations in sarcomeric proteins. Using murine models of human HCM, we have shown that mutations in sarcomeric proteins are associated with altered LTCC kinetics, impaired structural-functional communication between LTCC and mitochondria, and increased metabolic activity (consistent with the human phenotype). However, the mechanisms by which mutations in sarcomeric proteins lead to alterations in metabolic activity remain unknown.

Cardiomyocytes can ‘sense’ extracellular matrix (ECM) mechanics via a process called mechanotransduction. This involves conversion of mechanical stimuli into biochemical events that can alter myocardial function. Since human HCM is characterised by a stiff myocardium, we developed an in vitro model to determine the role of increased ECM stiffness on metabolic activity.

Wild-type cardiomyocytes were cultured on hydrogels with stiffnesses mimicking healthy (10 kPa) or HCM (40 kPa) myocardium. Cardiomyocytes on 40 kPa hydrogels exhibited increased stiffness versus 10 kPa (atomic force microscopy; 3.8 ± 0.4 kPa, n = 53 versus 1.5 ± 0.2 kPa, n = 31; p < 0.05). Cardiomyocytes on 40 kPa hydrogels also exhibited a larger increase in metabolic activity in response to activation of LTCC (Flavoprotein autofluorescence; 40 kPa: 64.6 ± 4.3% increase, n = 35 versus 10 kPa: 20.3 ± 1.8%, n = 27 p < 0.05), that was attenuated by sarcomeric protein depolymerising agents latrunculin A (F-actin) or colchicine (β-tubulin).

We conclude that ECM stiffness may regulate cardiac metabolic activity. Increased ECM stiffness may contribute to increased metabolic activity and development of HCM.

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