ASSOCIATION OF PATTERN OF MYOCARDIAL FIBROSIS WITH ADVANCED AND EARLY HEART FAILURE

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Abstract
Background: The cardiomyopathies are defined as “heterogenous group of diseases of the myocardium associated with mechanical or electrical dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilatation and are due to variety of causes that frequently are genetic. They usually present clinically with heart failure.
Methods: The cross sectional hospital based study was conducted in the Department of Radiodiagnosis in patients with heart failure with LVEF (Left Ventricular Ejection Fraction) of <45% without RWM(Regional Wall Motion) abnormality on echocardiography evaluated in department of cardiology at IGMC, Shimla over a period of one year.
Results: The myocardial fibrosis was seen in the 10 (47.62%) patients of advanced heart failure and 6(35.29%) patients of early heart failure with insignificant P value of 0.52 and odd ratio of 1.64. The subendocardial myocardial fibrosis in coronary territory was seen in the 3(14.29%) patients of advanced heart failure and 2(11.76%) patients of early heart failure with insignificant P value of 1.00 and odd ratio of 1.24.
Conclusion: The association of pattern of myocardial fibrosis with advanced and early heart failure was found statistically insignificant.
Keywords: MRI, Myocardial, Heart failure.

Introduction
Recent advances in non-invasive cardiac imaging, particularly magnetic resonance imaging (MRI), have made possible detailed tissue characterization and identification of diverse patterns of myocardial fibrosis in patients presenting with heart failure.

Multiple complex and overlapping pathways including inflammation, neuro-hormonal activation and ongoing myocardial injury orchestrate the process of cardiac remodeling that leads to myocardial Fibrosis. Despite pharmacotherapeutic advances in targeting traditional risk factors and blockades of the renin-angiotensin-aldosterone and adrenergic systems, the incidence of heart failure (HF) is still high. Additionally, disappointing results for the treatment of HF with preserved ejection fraction highlights that the current therapeutic paradigm for HF is missing one or more key pathophysiological mechanisms. Exploring alternate novel pathways associated with interstitial myocardial fibrosis and myocardial remodeling will allow us to better understand the pathogenesis of HF and develop more successful and targeted therapeutic interventions.

Material and methods
Study design and patient population and sample size: The cross sectional hospital based study was conducted in the Department of Radiodiagnosis in patients with heart failure with LVEF (Left Ventricular Ejection Fraction) of <45% without RWM(Regional Wall Motion) abnormality on echocardiography evaluated in department of cardiology at IGMC, Shimla over a period of one year. Coronary angiography was done in all eligible patient of dilated cardiomyopathy in the department of Cardiology and CT coronary angiography was planned in patients where coronary angiography was not possible in the department of Radiodiagnosis IGMC, Shimla. The Radiologist who reported the cardiac MRI was blinded to the result of coronary angiography/CT coronary angiography. Comparison of cardiac MRI and coronary angiography was made in the end of the study to find out the accuracy of cardiac MRI in the diagnosis of ischemic cardiomyopathies and differentiating it from the non ischemic cardiomyopathies. Thereafter association between pattern of distribution of myocardial fibrosis with ischemic and non ischemic Cardiomyopathy was made. NYHA functional class I and II are taken as early heart failure and NYHA functional class III and IV are taken as advanced heart failure.

Every consecutive eligible patient was enrolled for the study and the research procedure was in accordance with the approved ethical standards of Indira Gandhi Medical College and Hospital, Shimla, Ethics Committee.
**Exclusion Criteria:**

- Patients having contraindication for MRI e.g. Pacemaker, Metallic implants.
- Patients with deranged renal function test with e GFR <15 ml/kg/minute
- Patients with documented myocardial infarction.
- Patients with hypersensitivity to Gadolinium.

**Data analysis**

Data was reported as counts and percentages for categorical variables and mean±SD for continuous variables. The association of pattern and distribution of myocardial fibrosis with ischemic cardiomyopathy was analyzed calculating odds ratio and 95% C.I. The statistical analysis was done using Epi info version 7 software. Two sided p value of <0.05 was taken as statistically significant.

**Result**

**Table 1: Association of pattern of myocardial fibrosis with advanced and early heart failure;**

<table>
<thead>
<tr>
<th></th>
<th>ADVANCED HF(n=21)</th>
<th>EARLY HF (n=17)</th>
<th>OR</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MYOCARDIAL FIBROSIS</td>
<td>YES</td>
<td>10 (47.62%)</td>
<td>6 (35.29%)</td>
<td>1.64</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>11 (52.38%)</td>
<td>11 (64.71%)</td>
<td></td>
</tr>
<tr>
<td>SUBENDOCARDIAL CT</td>
<td>YES</td>
<td>3 (14.29%)</td>
<td>2 (11.76%)</td>
<td>1.24</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>18 (85.71%)</td>
<td>15 (88.24%)</td>
<td></td>
</tr>
<tr>
<td>SUBENDOCARDIAL NCT</td>
<td>YES</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>21 (100%)</td>
<td>17(100%)</td>
<td></td>
</tr>
<tr>
<td>TRANSMURAL CT</td>
<td>YES</td>
<td>2 (9.52%)</td>
<td>3 (17.65%)</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>19 (90.48%)</td>
<td>14(82.35%)</td>
<td></td>
</tr>
<tr>
<td>TRANSMURAL NCT</td>
<td>YES</td>
<td>1(4.76%)</td>
<td>1(5.88%)</td>
<td>0.80</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>20(95.24%)</td>
<td>16(94.12%)</td>
<td></td>
</tr>
<tr>
<td>FIBROSIS IN CORONARY TERRITORY</td>
<td>YES</td>
<td>5(23.81%)</td>
<td>4(23.53%)</td>
<td>1.01</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>16(76.19%)</td>
<td>13(76.47%)</td>
<td></td>
</tr>
<tr>
<td>MIDMYOCARDIAL</td>
<td>YES</td>
<td>3(14.19%)</td>
<td>0</td>
<td>1.94</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>18(85.81%)</td>
<td>17(100%)</td>
<td></td>
</tr>
<tr>
<td>EPICARDIAL</td>
<td>YES</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>21(100%)</td>
<td>17(100%)</td>
<td></td>
</tr>
<tr>
<td>FOCAL PATCHY</td>
<td>YES</td>
<td>1(4.76%)</td>
<td>2(11.76%)</td>
<td>0.38</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CT-Coronary Territory, NCT-Non Coronary Territory, ICM-Ischemic Cardiomyopathy, NICM-Non Ischemic cardiomyopathy, OR-Odd Ratio,

- The myocardial fibrosis was seen in the 10 (47.62%) patients of advanced heart failure and 6 (35.29%) patients of early heart failure with insignificant P value of 0.52 and odd ratio of 1.64.
- The subendocardial myocardial fibrosis in coronary territory was seen in the 3 (14.29%) patients of advanced heart failure and 2 (11.76%) patients of early heart failure with insignificant P value of 1.00 and odd ratio of 1.24.
- The transmural myocardial fibrosis in coronary territory was seen in the 2 (9.52%) patients of advanced heart failure and 3 (17.65%) patients of early heart failure with insignificant P value of 0.63 and odd ratio of 0.50.
- The transmural myocardial fibrosis in non coronary territory was seen in the 1 (4.76%) patients of advanced heart failure and 1 (5.88%) patients of early heart failure with insignificant P value of 1.00 and odd ratio of 0.80.
- The myocardial fibrosis in coronary territory was seen in the 5 (23.81%) patients of advanced heart failure and 4 (23.53%) patients of early heart failure with insignificant P value of 1.00 and odd ratio of 1.01.
- The midmyocardial fibrosis was seen in the 3 (14.19%) patients of advanced heart failure and none of the patients of early heart failure with insignificant P value of 0.23 and odd ratio of 1.94.
- The focal patchy myocardial fibrosis was seen in the 1 (4.76%) patients of advanced heart failure and 2 (11.76%) patients of early heart failure with insignificant P value of 0.57 and odd ratio of 0.38.
- There were no patients of subendocardial myocardial fibrosis in non ischemic territory and epicardial myocardial fibrosis
- Graphical presentation of association of pattern of myocardial fibrosis with advanced and early heart failure;
Discussion

Dilated cardiomyopathy is associated with dilatation and dysfunction of the left ventricle or of both ventricles. Ventricles can have normal or thin walls but always have increased cavity volumes and low ejection fraction. The clinical presentation of dilated CMP is usually characterized by progressive cardiac failure. The cause is not well understood and commonly it is idiopathic. Other causes include ischemic, genetic or familial, viral, immune, or a toxic origin, or can be secondary to cardiovascular diseases with myocardial dysfunction that is not explained by ischemic damage or increased volumetric loads. The dilated cardiomyopathy is broadly divided into the ischemic and non ischemic cardiomyopathy. They have distinct radiological profile on MRI.

The main causes of mortality are due to pump failure, ventricular arrhythmias and sudden cardiac death. So it is of utmost importance to identify the risk predictors in dilated cardiomyopathy. Multiple studies over periods of time suggested that myocardial fibrosis is substrate for arrhythmias in patients with dilated cardiomyopathy. So identification of myocardial fibrosis is the primary goal of cardiac MRI in these patients. The pattern of fibrosis on cardiac MRI can also help in distinguishing ischemic cardiomyopathy from non ischemic cardiomyopathy. The detection of mid wall fibrosis by CE-MRI is important marker in dilated cardiomyopathy of non ischemic category as presence of mid wall fibrosis has adverse outcome amongst patients with non ischemic dilated cardiomyopathy. The left ventricle remodeling (increased left ventricle end diastolic volume and LV mass) and advance heart failure (NYHA functional class III/IV) are also associated with adverse outcome in patients with dilated cardiomyopathy.

Conclusion

The association of pattern of myocardial fibrosis with advanced and early heart failure was found statistically insignificant. It may be due to small sample size in our study.

References
