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Yaron Fridman, University of Pittsburgh Medical Center
Timothy C. Wong, University of Pittsburgh Medical Center
Kayla M. Piehler, University of Pittsburgh Medical Center
KArolina M. Zareba, University of Pittsburgh Medical Center
James Moon, University College of London
Martin Ugander, Karolinska University Hospital
Daniel Messroghli, Deutsches Herzzentrum Berlin
John M. Jakicic, University of Pittsburgh
Uma Valeti, University of Minnesota Twin Cities
Chung-Chou Chang, University of Pittsburgh Graduate School of Public Health

Only first 10 authors above; see publication for full author list.

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Myocardial fibrosis is associated with subsequent death and hospitalization for heart failure in obese adults

Yaron Fridman¹,², Timothy C Wong¹,², Kayla M Piehler¹,², Karolina M Zareba¹,², James Moon³, Martin Ugander⁴, Daniel Messroghli⁵, John M Jakicic¹³*, Uma Valeti⁶, Chung-Chou Chang⁷, Sanjeev G Shroff⁸, Christopher A Miller⁹, Matthias Schmitt⁹, Peter Kellman¹⁰, Javed Butler¹¹, Mihai Gheorghiade¹², Erik B Schelbert¹,²

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Background
Cardiac imaging in obese adults poses significant technical challenges, yet the prognostic value of diffuse myocardial fibrosis in obese adults quantified with cardiovascular magnetic resonance (CMR) extracellular volume fraction (ECV) measures is unknown. This issue is important because obesity increases the risks of death and hospitalization for heart failure (HHF). Myocardial fibrosis measured in obese adults with ECV may indicate vulnerability to death and HHF.

Methods
We enrolled 480 consecutive obese patients with a BMI >30 referred for cardiovascular magnetic resonance (CMR) without amyloidosis, stress cardiomyopathy, or hypertrophic cardiomyopathy. We quantified myocardial fibrosis with CMR ECV measures in noninfarcted myocardium. Patient data, BMI, hematocrit, were collected on the day of CMR, and we tracked outcomes prospectively.

Results
Median BMI was 35 (IQR 32-41), and median ECV was 27.7% (IQR 25.6%-30.9%, range). BMI and ECV were not related (p=0.90). Over a median 1.5 years (IQR 0.9-2.5yrs), 27 HHF events and 28 deaths occurred after CMR in 50 individuals. Adjusting for age, gender, renal function, myocardial infarction size, ejection fraction, hospitalization status, and heart failure stage, ECV in obese adults was associated with HHF (HR1.92 95%CI 1.40-2.65 for every 5% increase in ECV (ECV range: 16.6-45.8), death (HR 2.50 95%CI 1.59-3.95) or both (HR1.97 95%CI 1.44-2.70). ECV improved the classification of obese adults at risk and improved model discrimination for the composite outcome: e.g., HHF or death [continuous net reclassification improvement (NRI) 0.429, 95%CI 0.063-0.758; p=0.02; integrated discrimination improvement (IDI) 0.069, 95% CI 0.016-0.132; p=0.02].

Conclusions
Despite the challenges of cardiac imaging in obese adults, diffuse myocardial fibrosis quantified by ECV is associated with HHF, death, or both. Myocardial fibrosis may represent a principal marker of cardiac vulnerability that improves risk stratification even in the setting of obesity. Since myocardial fibrosis can be reversible, myocardial fibrosis and the fibroblast that regulates it may be attractive therapeutic targets in obese patients.

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In multivariable models, EC in noninfarcted myocardium in obese patients remained associated with the combined endpoint of HHF/death. The addition of ECV improved the classification of individuals at risk (new reclassification improvement, NRI) and the discrimination of the model (integrated discrimination improvement, IDI).

<table>
<thead>
<tr>
<th>Multivariable Cox regression model</th>
<th>Hazard Ratio for every 5% increase in ECV (95% CI; p value)</th>
<th>Category free NRI (95% CI; p value)</th>
<th>Categorical NRI 0.05, 0.10 risk categories (95% CI; p value)</th>
<th>IDI (95% CI; p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modeling composite of HHF or death, stratified by heart failure stage and hospitalization status, adjusted for EF, age, glomerular filtration rate, myocardial infarction size, and gender</td>
<td>1.97 (1.44-2.70; p&lt;0.001)</td>
<td>0.43 (0.06-0.76; p=0.02)</td>
<td>0.04 (0.005-0.079; p=0.02)</td>
<td>0.069 (0.016-0.132; p=0.02)</td>
</tr>
</tbody>
</table>

Authors' details

1Cardiology, Heart and Vascular Institute, UPMC, Pittsburgh, PA, USA. 2UPMC Cardiovascular Magnetic Resonance Center, Pittsburgh, PA, USA. 3University College of London, Heart Hospital Imaging Centre, London, UK. 4Clinical Physiology, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden. 5Congenital Heart Disease and Pediatric Cardiology, Deutsches Herzzentrum Berlin, Berlin, Germany. 6Cardiology Division, University of Minnesota, Minneapolis, MN, USA. 7Biostatistics, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, USA. 8Biomedical Engineering, University of Pittsburgh, Pittsburgh, PA, USA. 9Centre for Imaging Sciences and Biomedical Imaging Institute, University of Manchester, Manchester, UK. 10National Heart, Lung, and Blood Institute, Bethesda, MD, USA. 11Cardiology Division, Emory University, Atlanta, GA, USA. 12Center for Cardiovascular Innovation, Northwestern University Feinberg School of Medicine, Chicago, IL, USA. 13Health and Physical Activity, University of Pittsburgh, Pittsburgh, PA, USA.

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