Heart failure's effects in cells can be reversed with a rest

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Structural changes in heart muscle cells after heart failure can be reversed by allowing the heart to rest, according to research at Imperial College London. Findings from a study in rats published today in the *European Journal of Heart Failure* show that the condition's effects on heart muscle cells are not permanent, as has generally been thought. The discovery could open the door to new treatment strategies.

Heart failure means that the heart muscle is too weak or stiff to pump blood as effectively as it needs to, and it is commonly the result of a heart attack. Around 750,000 people in Britain are living with heart failure. Severe heart failure carries a risk of death within one year which is worse than most cancers, and new heart failure treatments are badly needed.

Patients with advanced heart failure are sometimes fitted with a left ventricle assist device (LVAD). The LVAD is a small pump that boosts the function of the heart and reduces strain on the left ventricle, the biggest chamber of the heart, which pumps blood around the body's main circulation.

In 2006, researchers at Imperial led by Professor Magdi Yacoub showed that resting the heart using an LVAD fitted for a limited time can help the heart muscle to recover. The new study is a major step in understanding the mechanisms for this improvement at the level of heart muscle cells.

The Imperial researchers studied the changes that occur in heart muscle cells during heart failure in rats, and whether "unloading" the heart can reverse these changes.

"If you injure a muscle in your leg, you rest it and this allows it to recover," said Dr Cesare Terracciano, from the National Heart and Lung Institute (NHLI) at Imperial, who supervised the study. "The heart can't afford to rest - it has to keep beating continuously. LVADs reduce the load on the heart while maintaining the supply of blood to the body, and this seems to help the heart recover. We wanted to see what unloading does to heart muscle cells, to see how this works."

To study the effect of unloading, they transplanted a failing heart from one rat into another rat alongside that rat's healthy heart, so that it received blood but did not have to pump. After the heart was able to rest, several changes in the structure of heart muscle cells that impair how well they can contract were reversed.

"This is the first demonstration that this important form of remodelling of heart muscle cells induced by heart failure is reversible," said Michael Ibrahim, also from the NHLI at Imperial, who conducted the research for his PhD funded by the British Heart Foundation. "If we can discover the molecular mechanisms for these changes, it might be possible to induce recovery without a serious procedure like having an LVAD implanted."

The most profound cellular effects observed in this study concerned structures called t-tubules. These allow electrical signals to travel deep into the muscle cells so that all of the fibres contract simultaneously. T-tubules are densely packed and regular in healthy heart cells, enabling efficient muscle contraction, but they become sparse and irregular after heart failure. Unloading the heart led to the t-tubules returning to normal.

More information: M. Ibrahim et al. 'Mechanical unloading reverses transverse tubule remodelling and normalizes local Ca2+-induced Ca2+ release in a rodent model of heart failure.' *European Journal of Heart Failure*, published online 2 April 2012.

Provided by Imperial College London