The power of ultrasound: treating secondary MR with sound waves

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Innovations in physics and its applications often enable medical advances. Collaboration between physicists who developed a high-frame-rate ultrasound system and cardiovascular investigators has allowed non-invasive measurement of vascular and myocardial stiffness. In this current issue of the European Heart Journal—Cardiovascular Imaging, members of these groups, using a related technology, have employed ultrasound to treat as well as to image the heart in mitral regurgitation (MR) secondary to myocardial infarction (MI) that causes mitral valve (MV) leaflet tethering mediated by chordae to the displaced papillary muscles (PMs). This is a condition for which a strong need is perceived for improved approaches.

Although there is evidence for adaptive MV growth in secondary MR, this extra leaflet tissue is often insufficient to compensate adequately for mitral annular (MA) enlargement and chordal tethering. The MV leaflets thus become increasingly taut, being pulled by the annulus towards the base, and by chordae towards the left ventricular (LV) apex. The normally convex MV closing configuration towards left atrium becomes concave, and the anterior MV leaflet appears like a ‘hockey stick’ on Echo. Once the necessary leaflet tissue redundancy for MV coaptation is exhausted, MR will develop, which will over time further advance annular remodelling and tethering by the collagen-based chordae and therefore MR (Figure 1A).

Current medical and surgical and transcatheter repair therapies for secondary MR thus aim to reduce overall leaflet tethering to restore leaflet coaptation by addressing the impaired LV (optimal medical heart failure therapy, revascularization, resynchronization, potential myocardial regeneration) and the mitral annulus (restoration of normal sinus rhythm, annuloplasty). Not as clinically established, but shown to be safe and effective is to directly target the chordal apparatus by cutting secondary chordae attaching to the leaflet bodies to relieve their tethering and to restore a greater surface for leaflet coaptation (Figure 1B). Such chordal cutting reduces both MR and chordal shortening, imposing additional restriction on the tethered leaflets, lend further support to the potential benefits of chordal cutting to relieve such MR.

The current paper reports a proof of concept for using pulsed cavitational focused ultrasound (histotripsy) to cut chordae non-invasively guided by real-time 3D echocardiography. The authors show that secondary anterior chordae can be selectively cut in vitro and in vivo in the beating sheep heart with a high-energy...
‘bubble cloud’ formed by very short, high-pressure ultrasound pulses. The amount of time required to cut a chord correlated with its thickness (average 20 min). After a learning curve, no significant anatomic damage to surrounding structures was noted. Arrhythmic events were rare and non-significant. It is important to point out that with the currently available technology, chordal cutting was guided non-invasively by 3D Echo, but a thoracotomy to expose the heart was needed to allow for adequate ultrasound energy penetration; the authors indicate transcutaneous delivery is being developed. All sheep had healthy hearts without MV disease, so chordal cutting effects on MR reduction could not be tested. Histotripsy has also been applied experimentally with the aim of palliating or treating congenital heart defects through non-invasive shunt creation. High-intensity focused ultrasound, previously applied in vitro, can likewise cut chordae but depends upon heating that may be difficult to maintain within the rapidly moving cardiac blood pool.

The authors should be congratulated on pushing the boundaries of ultrasound, as one can conceive a future where ultrasound is not only used for the diagnosis and guidance but also for the treatment of secondary MR! Based on the progress to date, we can anticipate some additional refinements: (i) demonstrating the absence of important embolization, a foremost need pointed out by the authors, and suggested by Xu et al. who found that >99% of total particles after myocardial histotripsy were < 6 μm in diameter, smaller than a red blood cell. (ii) Refining sample volume and precise chordal targeting. Interestingly, this may be easier after infarction, when chordal tension increases the separation between secondary and marginal chordae. The direct visualization of the microcavitation cloud can facilitate this process. (iii) Potential motion tracking to maximize target interaction with ultrasound energy, particularly for the thickened chordae following infarction. Immobility of the strut chordae relative to the LV in the normal heart, augmented by the increased chordal tension in secondary MR, makes these chordae particularly suitable targets for non-invasive section. Three-dimensional transoesophageal echocardiography may offer improved guidance. Application of cavitational focused ultrasound will need to be maximized and suggested by Xu et al. who found that >99% of total particles after myocardial histotripsy were < 6 μm in diameter, smaller than a red blood cell. (ii) Refining sample volume and precise chordal targeting. Interestingly, this may be easier after infarction, when chordal tension increases the separation between secondary and marginal chordae.

References