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.1,2 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 heart3 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).4 This is a condition for which a strong need is perceived for improved approaches.5

Although there is evidence for adaptive MV growth in secondary MR,6,7 this extra leaflet tissue is often insufficient to compensate adequately for mitral annular (MA) enlargement and chordal tethering.8 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.9 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 chordae6,7,10 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 coaptation11,12 (Figure 1B). Such chordal cutting reduces both MR and its associated LV remodelling13 and has been successfully applied by several surgical groups.14–16 The pathological changes observed in chordae post-infarction7 and the recent reported relation between secondary 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.17

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.3 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

Figure 1  (A) Functional/Ischaemic MR: the PM is displaced posteriorly, laterally, and apically because of local LV dilatation and remodelling (arrows) caused by MI (shaded area). This LV wall-PM displacement tethers the anterior mitral leaflet apically and changes its shape relative to the annulus (dashed redline). Chordal and annulus tethering limits coaptation, resulting in MR. Targeted cutting of secondary chords (B) restores the normal geometry of the anterior leaflet (convex towards the left atrium). The reduction of systolic leaflet tenting area/volume (compare intra-leaflet area above dashed redlines A vs. B) provides enough leaflet tissue for adequate leaflet coaptation (B, red circle).

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is encouraging and with further animal investigations along the lines the proof of concept for this ingenious therapeutic use of ultrasound as annular dilatation and thus should effectively restore MV leaflet less-invasive MV repair approach will target leaflet tethering as well MitraClip or the Cardioband. Such a combined and complementary procedure with transcatheter MV repair strategies such as the 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 MRI. 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. (iv) Application of cavitation focused ultrasound will need to be achieved without thoracotomy. Optimally, a transoesophageal or gastric window may prove to be sufficient. (v) Acute and long-term durability of MR reduction will need to be demonstrated as this non-invasive approach of chordal cutting does not address the dilated mitral annulus, although in vivo data so far indicate that it relieves progressive LV remodelling.

Cutting chords by this technique may also be a beneficial partner procedure with transcatheter MV repair strategies such as the MitraClip or the Cardioband. Such a combined and complementary less-invasive MV repair approach will target leaflet tethering as well as annular dilatation and thus should effectively restore MV leaflet coaptation; the less-invasive approach can allow more patients to benefit from relief of tethering than is currently possible. Overall, the proof of concept for this ingenious therapeutic use of ultrasound is encouraging and with further animal investigations along the lines noted can lead to potential human application.

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