Muscules (from the tensor tympani to the left ventricle [LV]) are in the business of generating force. In cardiac mechanics, the innate ability to generate force independently of preload is called contractility. A central tenet of cardiology is that the prognosis of most cardiac diseases is determined in large part by the health or disarray of the myocardium conferred by this property of contractility. Before the era of molecular biology, a search for the perfect index of contractility had become a Holy Grail of cardiology. Such an index would be independent of preload, afterload, and cardiac volume and mass; sensitive to changes in inotropy; reproducible; and easy to apply. Perhaps the most accurate of these is end-systolic stiffness (the modulus of systolic stress and strain), but the tedium of its clinical use is so daunting that it is rarely used. Thus, although dozens of indexes have been proposed, none fulfilled all of the above requisites, and the search was largely abandoned. Thus, the cardiology world has settled on none.

In prolonged severe mitral regurgitation (MR), contractility is depressed in both experimental animals and humans. Such depression is initially reversible but becomes irreversible at some point in the natural history of the disease, as evidenced by the poor prognosis of depressed EF that implies extensive myocardial damage. Contractile dysfunction in MR accrues from the loss of myocyte contractile elements and from abnormal calcium handling that alters myocardial excitation-contraction. In the early stages of disease, contractile dysfunction is reversible, preferably by mitral valve repair but also in part by β-adrenergic receptor blockade. Recently, β-blockade has been suggested to be protective in human MR, and with this finding taken together with other data, it appears that sympathetic overactivation plays a major role in the pathogenesis of myocardial injury in MR.

**The Present Study**

MR obviously effects a volume overload on the LV; therefore, the LV has been the target of most studies of MR. Increased preload, together with usually normal afterload, increases LV EF in MR so that the normal EF in patients with severe MR is probably ≥70%. By the time EF is reduced to 60% or even 64%, prognosis worsens, presumably because myocardial damage causing reduced contractility has ensued. The present study by Le Tourneau et al adds to our knowledge of the pathophysiology of MR in several ways. First, it confirms and emphasizes previous observations that right ventricular (RV) dysfunction plays a direct role in MR prognosis. Furthermore, it provides insight into the mechanism of RV dysfunction.

To reiterate, EF is determined by preload, afterload, wall thickness, and contractility, and all 4 factors vary from patient to patient. The increased LV filling pressure in MR, together with reflexive pulmonary vasoconstriction, often leads to pulmonary hypertension, thus afterloading the RV. It is often presumed that RV ejection performance, when impaired, is due to increased pulmonary pressure. Because the geometric vagaries of the RV make calculation of systolic wall stress (thought by many to be the gold standard of afterload) extraordinarily difficult, it is rarely measured and was not measured here. However, estimated pulmonary pressure barely correlated with RV EF, suggesting that RV afterload was not a major cause of reduced RV ejection performance. More important was the effect of MR on the interventricular septum. Reduced septal function played a major role in reduced RV function preoperatively, and its reversal helped explain improved postoperative RV function in patients in whom comparison studies were available. It is likely that impingement on the RV septum by the enlarged LV reduced preload in those fibers, reducing septal function, while a reduction in LV volume postoperatively allowed repreload of the RV septal fibers. However, in the Le Tourneau et al multivariable analysis, the combination of septal function, LV dimension, and pulmonary pressure had an R of 0.55 and an r² of 0.30, suggesting that much of the RV dysfunction remains unexplained by those factors. Thus, impaired contractility becomes likely to play a large role in the observed outcome, and irreversible contractile dysfunction of the LV and possibly the RV explains the poor 10-year survival of those patients with combined RV and LV dysfunction. Patients with isolated RV dysfunction probably had that finding based on the septal dysfunction and pulmonary hypertension but not contractile dysfunction because outcome was favorable in such patients. Patients with reduced LV EF had a modestly poor prognosis, almost certainly because of irreversible LV contractile dysfunction in those patients. On the other hand,
Figure. Schema showing how mitral regurgitation might cause ventricular dysfunction.

patients with reduced LV and RV EF probably had contractile dysfunction of both ventricles, a finding that again raises a neurohumoral hypothesis. Because both ventricles are bathed in the same humoral soup, if catecholamines can damage the LV, they likely could damage the RV as well, perhaps as shown in the Figure.

Mitral regurgitation creates an intricate interplay between LV volume overload, LV remodeling, RV–LV interaction, pulmonary hypertension, neurohumoral activation, and myocardial damage that should be avoided or intercepted before the LV or both ventricles become permanently damaged, points dramatically emphasized in this work by Le Tourneau et al.15

Disclosures
None.

References

Key Words: Editorials • heart valves • mitral valve insufficiency
The Myocardium in Mitral Regurgitation: A Tale of 2 Ventricles
Blase A. Carabello

Circulation. 2013;127:1567-1568
doi: 10.1161/CIRCULATIONAHA.113.002126

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2013 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/127/15/1567

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/