The data by Drs Shingu and Matsui suggest the utility and need for procedures to address subvalvular tethering in patients with ischemic MR. Currently reported surgical procedures to address subvalvular tethering are conceptually reasonable and heterogeneous.³⁻⁵ A tailored and heterogeneous approach based on preoperative 3-dimensional evaluation of mitral valve geometry seems necessary to address patients' variability. Standardization is also necessary to perform subvalvular procedures in many institutions. This bidirectional improvement in therapeutic approach is required to achieve a favorable outcome in affected patients.

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References

1. Magne J, Sénéchal M, Mathieu P, Dumesnil JG, Dagenais F, Pibarot P. Restrictive annuloplasty for ischemic mitral regurgitation may induce functional mitral stenosis. *J Am Coll Cardiol*. 2008;51:1692-701.
2. Kubota K, Otsuji Y, Ueno T, Koriyama C, Levine RA, Sakata R, et al. Functional mitral stenosis after surgical annuloplasty for ischemic mitral regurgitation: Importance of subvalvular tethering in the mechanism and dynamic deterioration during exertion. *J Thorac Cardiovasc Surg*. 2010 Jan 30 [Epub ahead of print].
3. Terai H, Tao K, Sakata R. Surgical treatment for ischemic mitral regurgitation: strategy for a tethered valve. *Ann Thorac Cardiovasc Surg*. 2005;11:288-92.
4. Messas E, Guerrero JL, Handschumacher MD, Conrad C, Chow CM, Sullivan S, et al. Chordal cutting: a new therapeutic approach for ischemic mitral regurgitation. *Circulation*. 2001;104:1958-63.
5. Kron IL, Green GR, Cope JT. Surgical relocation of the posterior papillary muscle in chronic ischemic mitral regurgitation. *Ann Thorac Surg*. 2002;74:600-1.

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EFFECT OF CYCLOPHOSPHAMIDE ON MYOCARDIAL ISCHEMIA/ REPERFUSION INJURY IN RATS To the Editor:

Wang and associates¹ have recently published a very interesting and innovative origin of thought in which investigators have demonstrated the protective role of cyclophosphamide against myocardial ischemia/reperfusion injury in rats. In this study, cyclophosphamide showed a favorable effect on myocardial function in various parameters, which included improvement in left ventricular systolic pressure, left ventricular end-diastolic pressure, and maximum rate of rise or fall of left ventricular pressure. Apart from this, infarct size was reduced, along with improvement in histopathologic damage score, and plasma high-sensitivity C-reactive protein concentration, which is an inflammatory marker, was reduced significantly. However, we would like to highlight some of the points regarding this study

1. The study showed that cyclophosphamide decreased the C-reactive protein levels significantly, but it is not the proposed specific mechanism of action alone to have anti-inflammatory action. Other markers of inflammation, such as Cox inhibition, should also have been evaluated before making the final conclusion.
2. In this study, pretreatment with cyclophosphamide or saline was given before inducing ischemia/reperfusion. Thus, in this study design, investigators should have evaluated whether the drug cyclophosphamide or saline had any beneficial or detrimental effect before proceeding for ischemia and reperfusion or sham surgery.
3. The cardioprotective role of cyclophosphamide could have been evaluated on creatine kinase, myocardial band of creatine kinase, and tropinin I, which are the myocardial injury markers.^{2,3}

4. Various studies have evaluated the role of cytokines, which include interleukins 6 and 8, interferon-gamma, and tumor necrosis factor- α , which are upregulated after ischemia/reperfusion injury.^{4,5} In this present study, too, the expression of these cytokines, which are mediators of inflammation, could have been evaluated in comparison with saline or cyclophosphamide.

The present study provides useful information for more effective and targeted treatment for patients with ischemic heart disease, but the aforementioned points should be discussed for future therapeutic implication and reconfirmation in clinical studies.

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References

1. Wang QQ, Qui YG, Zhu YJ, Wang LH, Hu XSH, et al. Cyclophosphamide protects against myocardial ischemia/reperfusion injury in rats: one of the therapeutic targets is high sensitivity C-reactive protein. *J Thorac Cardiovasc Surg*. 2009;137:991-6.
2. Oksuz H, Senoglu N, Yasim A, Turut H, Tolun F, Ciralik H, et al. Propofol with N-acetylcysteine reduces global myocardial ischemic reperfusion injury more than ketamine in a rat model. *J Invest Surg*. 2009;22:348-52.
3. Arya DS, Bansal P, Ojha SK, Nandave M, Mohany I, Gupta SK. Pyruvate provides cardioprotection in the experimental model of myocardial ischemic reperfusion injury. *Life Sci*. 2006;79:38-44.
4. Cao Z, Xu X, Que L, Chan Q, Li Y. Dephosphorylation of cardiomyocyte CX43 is associated with myocardial ischemia and reperfusion injury. *J Narying Med Univ*. 2009;23:163-7.
5. Nosuli TO, Lakshminarayanan V, Baumgarten G, Taffeta GE, Ballantyne CM, Micheal LH, et al. A chronic mouse model of myocardial ischemia: essential in cytokine studies. *Am J Physiol Heart Circ Physiol*. 2000;278:1049-55.

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