ings is that virtually all valved conduits except for cellular syngrafts resulted in significant sinus thrombus formation. This limitation of the model used could have been addressed in part by using a functional model in which blood flow and leaflet mobility can be demonstrated.² The significance of sinus thrombosis is not negligible, and it has been shown to become a nidus for inflammatory cells, potentially affecting neighboring cellular immune responses and any conclusions made from histologic examination.^{3,4}

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References

1. Grauss RW, Hazekamp MG, Vliet SV, Gittenberger-de Groot AC, DeRuiter MC. Decellularization of rat aortic valve allografts reduces leaflet destruction and extracellular matrix remodeling. *J Thorac Cardiovasc Surg.* 2003;126:2003-10.
2. Légaré JF, Nanton M, Bryan P, Lee TD, Ross DB. Aortic valve allograft implantation in rats: a new functional model. *J Thorac Cardiovasc Surg.* 2000;120:679-85.
3. Kranzhöfer R, Clinton SK, Ishii K, Coughlin SR, Fenton JW, Libby P. Thrombin potently stimulates cytokine production in human vascular smooth muscle cells but not in mononuclear phagocytes. *Circ Res.* 1996;79:286-94.
4. Libby P, Simon DI. Inflammation and thrombosis: the clot thickens. *Circulation.* 2001;103:1718-20.

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Reply to the Editor:

We thank Légaré and Ross for their comment on our article describing the in vivo behavior of decellularized rat aortic valve allografts. As they state in their letter, a complication of the model we used is the sinus thrombus formation observed in all decellularized syngrafts and allografts, as well as in the untreated allografts. They speculate that this is due mainly to a lack of leaflet mobility in a nonfunctional implantation model.¹

To overcome this difficulty Légaré and Ross suggest the use of a functional rat implantation model in which the creation

of native aortic valve insufficiency results in a significant diastolic flow reversal in the abdominal aorta, allowing leaflets to move and function.² Although we were aware of the existence of this model, we decided not to use it for our study. One reason is that the creation of aortic insufficiency results in progressive congestive heart failure from volume overload, making the model unsuitable for long-term follow-up studies. In addition, a rather high mortality is seen in the model (62.5% survival). We fully agree about the importance of having functional moving leaflets in the bloodstream in studying aortic valve failure; however, we look forward to new data that will encourage us to incorporate the model in our future studies.

We respectfully disagree with the assumption that a nonfunctional model is the main reason for the sinus thrombus formation. Interestingly, in our study none of the untreated (cellular) syngrafts displayed thrombus formation. This is consistent with earlier results in this model by Oei and colleagues,¹ who showed absence of thrombus formation in all syngrafts and even in some allografts. This indicates that loss of cellular structures, resulting in an absent blood-tissue barrier, from the treated syngrafts and allografts and untreated allografts is an essential condition in thrombus formation.

Our study suggests that decellularization reduces the recipient's immune response, resulting in a preservation of the extracellular matrix structure. We therefore believe in the feasibility of acellular allografts as scaffolds for tissue-engineering purposes and are performing seeding experiments at the moment to determine the best cell source.

Regarding the influence of thrombosis on the inflammatory response,³ seeding of acellular valves with autologous endothelium will result in a new blood-tissue barrier and is expected to protect against thrombus formation. We therefore believe that this model is suitable for further research in tissue engineering of aortic valves.

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References

1. Oei FB, Welters MJ, Bonthuis F, Vaessen LM, Marquet RL, Zondervan PE, et al. A size-matching heterotopic aortic valve implantation model in the rat. *J Surg Res.* 1999;87:239-44.
2. Légaré JF, Nanton M, Bryan P, Lee TD, Ross DB. Aortic valve allograft implantation in rats: a new functional model. *J Thorac Cardiovasc Surg.* 2000;120:679-85.
3. Libby P, Simon DI. Inflammation and thrombosis: the clot thickens. *Circulation.* 2001;103:1718-20.

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Which is the best surgical strategy for "complete" treatment of ischemic cardiomyopathy?

To the Editor:

We read with great interest the article published in the *Journal* by Maxey and associates¹ concerning surgery for ischemic cardiomyopathy. First of all, Maxey and associates are to be commended for outstanding results in a challenging cohort of patients. The study included 14 patients who underwent mitral valve repair (MVR) associated with coronary artery bypass grafting and left ventricular restoration (LVR), but Maxey and associates¹ did not mention the sequence of the surgical procedures. In a previous article, they reported performing coronary artery bypass grafting first, then MVR, and finally LVR.²

Ischemic mitral regurgitation is a functional disorder that is due mainly to changes in the geometric relationships between structurally normal valve components and a severely damaged ventricle. By changing ventricular volume and geometry, LVR may unpredictably result in mitral insufficiency that is absent before surgery³ or in an amelioration (sometimes disappearance) of mitral regurgitation.⁴ It therefore seems more rational to address MVR after completely rebuilding ventricular geometry. In addition, this strategy allows evaluation of valve competence after LVR and a check on leaflet apposition (in Bolling and associates' experience,⁵ in addition to the annuloplasty ring 54 of 100 patients required further mitral repairs). Moreover, after LVR with narrower configuration and papillary muscles realignment, the mitral incompetence may disappear, thus making mitral valve repair unnecessary. We could speculate that in the only patient who showed persistent mitral

regurgitation after surgery,¹ the evaluation of valve competence after LVR might have allowed coaptation, leak detection, and repair.

A transventricular approach to the mitral valve has also been recommended, affording an easier mitral annulus exposition and a faster repair. Likewise, through the ventriculotomy a papillary muscle narrowing can be attempted.³ In our opinion, through a transventricular approach only a “blind” rebuilding of mitral-ventricle geometry is possible. Moreover, the ventriculotomy approach forces the surgeon to elementary procedures, such as a suture annuloplasty, whereas visual valve evaluation and intraoperative coaptation adjustments seems unfeasible.

We think that in the setting of such a long and demanding procedure the best strategy is a valuable issue. We actually prefer first to perform beating-heart (or on-pump if required) coronary artery bypass grafting, then complete LVR under cardioplegic arrest, and finally accomplish transatrial MVR.

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References

1. Maxey TS, Reece TB, Ellman OI, Butler PD, Kern JA, Tribble CG, et al. Coronary artery bypass with ventricular restoration is superior to coronary artery bypass alone in patients with ischemic cardiomyopathy. *J Thorac Cardiovasc Surg.* 2004;127:428-34.
2. Maxey TS, Reece TB, Ellman PI, Kern JA, Tribble CG, Kron IL. The beating heart approach is not necessary for the Dor procedure. *Ann Thorac Surg.* 2003;76:1571-5.
3. Menicanti L, DiDonato M, RESTORE group. Surgical ventricular reconstruction and mitral regurgitation: what have we learned from 10 years of experience? *Semin Thorac Cardiovasc Surg.* 2001;13:496-503.
4. Kaza AK, Patel MR, Fiser SM, Long SM, Kern JA, Tribble CG, et al. Ventricular reconstruction results in improved left ventricular function and amelioration of mitral insufficiency. *Ann Surg.* 2000;235:828-32.
5. Bolling SF, Deeb GM, Bach DS. Mitral valve reconstruction in elderly, ischemic patients. *Chest.* 1996;109:35-40.

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Reply to the Editor:

I appreciate the comments by Fundarò and colleagues. They ask an important question. They wish to know the order of procedures to deal with mitral regurgitation in patients who require left ventricular restoration. Clearly, left ventricular restoration does reduce the distance between the papillary muscles and potentially the tethering of the posterior papillary muscle on the mitral leaflets. Therefore, how much can be done through the ventricle, and what is the best approach overall?

We have continued to change our approach to this problem. We have noticed that ventricular reconstruction alone can deal with some of the issues that relate to tethering in patients with mild and possibly moderate mitral regurgitation. In contrast, we have not been able to find a consistent way to deal with annular dilatation through the ventriculotomy. As Fundarò and colleagues have stated, it would be difficult to judge how much needs to be done through the ventriculotomy. Therefore, in situations where there is moderate to severe mitral regurgitation, we would add a left atrial incision as well. The order is as Fundarò and colleagues have stated. We do the coronary revascularization first, followed by the left ventricular reconstruction. We then perform an atriotomy and place a mitral ring at that point. I think it is difficult to go off-pump, check the transesophageal echocardiography after rewarming, and then determine whether a ring needs to be placed. Rather, in the case of severe regurgitation we make that decision before the operation. We are currently searching for a predictable technique to place a ring through the ventricle, but thus far we have not come up with an approach. I appreciate the opportunity to respond to this excellent question by Fundarò and colleagues.

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