Are patients with mitral regurgitation being referred too late for surgery?

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In the current issue of *The Canadian Journal of Cardiology*, Toledano et al (pages 209-214) report an important study on cardiologists' thresholds for surgical referral in patients with mitral regurgitation (MR). The authors mailed a self-administered questionnaire containing seven different clinical scenarios to practising adult cardiologists in Canada. They observed relatively poor compliance with published clinical guidelines, as well as an inverse correlation between compliance and number of years in practice.

The current study is particularly timely, given the recent publication of the updated American College of Cardiology and American Heart Association (ACC/AHA) guidelines for the management of patients with valvular heart disease (1). However, Toledano et al used the previously published guidelines (2) to determine the correct recommendations for referral of patients with MR. A review of the earlier ACC/AHA guidelines reveals that patients with nonischemic MR should be referred for surgery under the following conditions:

- patients with heart failure symptoms (ie, New York Heart Association [NYHA] functional class II to IV) (class I evidence);
- asymptomatic patients with mild left ventricular (LV) dysfunction (ejection fraction [EF] of 50% to 60%) and mild LV dilation (end-systolic diameter 45 mm to 50 mm) (class I evidence);
- asymptomatic patients with moderate LV dysfunction (EF of 30% to 50%) and/or moderate LV dilation (end-systolic diameter 50 mm to 55 mm) (class I evidence);
- asymptomatic patients with atrial fibrillation or pulmonary hypertension (blood pressure greater than 50 mm Hg) (class IIa evidence);
- asymptomatic patients with mild LV dysfunction and normal LV dimensions, or normal LV function and mild to moderate LV dilation (class IIa evidence);
- patients with severe LV dysfunction (EF less than 30%) and/or severe LV dilation (end-systolic diameter of more than 55 mm) in whom chordal preservation is likely (class IIa). (Chordal preservation refers to the retention of annuloventricular continuity during mitral

valve [MV] surgery, and is associated with improved long-term LV function and survival [3]. Chordal preservation is always achieved in MV repair and is highly recommended during MV replacement surgery); or

- asymptomatic patients with normal LV function and dimensions in whom MV repair is likely (class IIb).

The updated version of the guidelines (1) makes similar recommendations, with the exception of LV dilation being defined as an end-systolic diameter of more than 40 mm, and MV repair in asymptomatic patients with normal LV function and diameter being a class IIa recommendation, provided that the likelihood of successful repair is greater than 90%.

Toledano et al presented seven different clinical scenarios and asked cardiologists to rate the parameters that were most important in deciding whether to refer their patients for surgery. The investigators found that only 57% of cardiologists would correctly refer an asymptomatic patient with an EF of 50% to 60%, and the remainder would wait for further deterioration in LV function. In addition, only 15% of cardiologists would correctly refer patients with NYHA class II symptoms and normal LV function. The investigators also found that guideline compliance was best among recent graduates and worst among long-time practising physicians. Somewhat surprising was that they did not observe any differences in compliance among the different cardiology subspecialties. The field of evaluation and monitoring of practice guideline compliance is in its early stages of development, and is beyond the scope of the present editorial. However, the topic is well covered by Toledano et al. Whatever method is used to improve clinician guideline compliance, it will inevitably involve improved education.

One limitation of the study by Toledano et al is that the survey response rate was only 45% (n=319) of practising cardiologists in Canada. The authors may have been able to improve their response rates with a variety of well-described techniques (4). It may be argued, therefore, that the results are not applicable to referring cardiologists across Canada. However, the response rate of the study is well within the normal range for physician surveys (5). In addition, the authors speculate that the cardiologists with a special interest in valvular disease would be more likely to return the questionnaire, and therefore, their results may represent an optimistic view of cardiologists' compliance with published guidelines. From a surgeon's standpoint, that is, at the receiving end of cardiologists' referral practice, the observations and conclusions of the study seem to have face validity.

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Why is it that cardiologists are reluctant to refer patients early in the MR disease process? While the answer to this question is not clear, a careful review of the literature reveals a substantial amount of data to support earlier patient referral. Several studies (6-8) have demonstrated that survival and congestive heart failure after MV repair and replacement surgery are closely related to preoperative LV function, LV diameter and clinical symptoms. In addition, several studies have demonstrated improved survival and event-free survival after MV repair, even in asymptomatic patients. Enriquez-Sarano et al (9) prospectively followed 456 patients with asymptomatic MR. Medical management was associated with increased risk of death and cardiac events, particularly in patients with more severe regurgitation, compared with expected rates in the general population. In contrast, surgery (91% of which was MV repair) was associated with significantly improved survival and freedom from congestive heart failure. David et al (10) followed 488 MV repair patients over an extended period of time. Survival 15 years postoperatively was 76% in the asymptomatic group, identical to that of the age- and sex-matched general population. However, 15-year survival in symptomatic patients was only 53%. NYHA class III or IV symptoms were an independent predictor of late death. We can surmise from these studies (6-10) that patients with nonischemic severe MR should be referred for surgery before they develop end-stage symptoms, LV dysfunction or LV dilation.

It is important to note that the most recent ACC/AHA guidelines clearly state that MV repair is preferable to MV replacement in patients with MR, and that patients should be selectively referred to those centres with extensive experience in MV repair surgery (1). In the study by Toledano et al, nearly all cardiologists stated that the experience of the cardiac surgeon had a large impact on their decision of whether to refer the patient. MV repair procedures range from the relatively simple and reproducible (eg, isolated annuloplasty for annular dilation or repair of a prolapsing P2 segment) to the complex and arduous (eg, bileaflet prolapse or repair of a Barlow's valve). MV repair, although more technically challenging, offers several well-described advantages over MV replacement, including better preservation of LV function, decreased risk of endocarditis, absence of anticoagulation in patients with sinus rhythm, and improved perioperative and long-term survival (11-13). Furthermore, MV repair eliminates the risk of structural valve dysfunction observed with bioprostheses. Although recurrent MR after MV repair does occur, it is infrequent and is usually related to intraoperative technical failure. The exception is in patients with ischemic MR, who have a substantial risk of recurrent MR (approximately 30%) after MV repair (14).

The number of MV repair operations reported in the Society of Thoracic Surgeons database (15) has increased by 150% over the past 10 years, despite a stable number of total cardiac procedures. The marked increase is probably due to many factors, including improved surgical techniques, minimal invasive operations, training and dissemination of knowledge within the surgical community, a decrease in the proportion of patients with rheumatic MV pathology and an increase in referrals from cardiologists. It is unlikely, however, that this last factor plays a large role because the total number of MV procedures (ie, repair and replacement) has increased by only 35% over the same time period (15).

Toledano et al state that approximately two-thirds of patients with MR are currently amenable to MV repair. Based

on our own experience, however, we estimate this proportion to be greater than 80% in centres that perform a large volume of MV repair operations. We perform all isolated MV repair and replacement operations through a minimally invasive right lateral minithoracotomy, using a 5 cm to 7 cm long muscle-sparing incision. We have performed over 1500 such procedures over the past 10 years with excellent results (16). We are firm believers that such techniques result in faster patient recovery, decreased pain and improved cosmesis (17). As a direct result of these techniques, we observed a 60% increase in the number of MV procedures performed at the Leipzig Heart Center (Leipzig, Germany) over a two-year period. Increasing acceptance of these techniques by surgeons, cardiologists and, most importantly, patients may result in a similar increase in referrals of MR patients in North America.

An interesting development on the horizon for patients with MR is percutaneous MV repair techniques. Such percutaneous MV repair techniques can be loosely divided into leaflet-based and coronary sinus-based approaches, with the largest clinical experience to date being with edge-to-edge 'Alfieri' technique (18). An avalanche of information is being presented at cardiology and cardiac surgery meetings on these procedures, with a very high level of interest among researchers, clinicians, device companies and investors. Indeed, the interpretation of the resulting data may be complicated by the fact that a large amount of capital has already been invested into the development of these devices and procedures. The ACC/AHA will soon be publishing a position paper on percutaneous valve procedures to clarify some of the issues regarding outcome reporting.

It will be interesting to see how percutaneous MV repair will affect cardiologists' referral patterns. Personal communication with several leading experts reveals that the device industry is expecting a substantial increase in the number of patients referred, with a shift toward referral earlier in the disease process. This would presumably be a result of clinicians' impressions that a percutaneous procedure would be less invasive and less risky than a standard MV repair operation. However, we should point out several possible limitations to this line of reasoning.

First, the percutaneous techniques will need to be as efficacious, or nearly as efficacious, as traditional MV repair surgery. Although early results may be very good for the percutaneous devices, their durability will need to be closely followed. Edge-to-edge procedures do not incorporate a mitral annuloplasty, an important determinant of durability in the Alfieri MV repair technique (19). Coronary sinus-based procedures do not account for the fact that the coronary sinus has no anatomical connections to the mitral annulus (it is, in fact, an intra-atrial structure), which may result in continued annular dilation and recurrent MR over time (20). Second, percutaneous MV repair should not preclude the subsequent possibility of open surgical repair. Although conventional MV repair early after failed percutaneous techniques has already been performed in several patients worldwide, it will be important to determine whether MV repair surgery is still possible many months after a percutaneous procedure, when scar tissue and adhesions have formed. Third, the risk in traditional MV repair is very low. Several large single-institution series (7-13,16) have reported very low rates of operative mortality and morbidity in patients with nonischemic MR. According to the Society of Thoracic Surgeons database (15), the risk of

operative mortality in isolated MV repair (n=4338) was only 1.3% in 2005. The bar has therefore been set very high for percutaneous MV procedures.

The study by Toledano et al in the current issue of the *Journal* is very interesting, important and timely. With the excellent perioperative and long-term results for MV repair surgery in patients with nonischemic MR, particularly in patients who are referred earlier in the disease process, we strongly encourage cardiologists to comply with the ACC/AHA guidelines. It is possible that percutaneous MV repair techniques may evolve into a viable option in such patients over the next decade, but significant data on efficacy and durability will be required before we can recommend widespread adoption of these procedures.

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