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LETTER TO THE EDITOR

Moderate to severe ischemic mitral regurgitation: More data to guide the choice. Why not consider the use of subvalvular repair?

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In a recent issue of *Cardiology Journal*, Li et al. [1] described long-term outcomes of mitral valve surgery in patients with ischemic mitral regurgitation (MR). Using a propensity-score matched analysis with 77 pairs of patients and a median follow up of 53 months, their results indicate that subvalvular-sparing mitral valve replacement leads to reduced hospitalization for heart failure and improved ventricular remodeling, with no differences in mortality. This study encourages scientific debate on this topic as an optimal treatment in patients with ischemic MR, which is far from being established.

Moving from anatomic details to mechanical aspects, the importance of restoring a functional mitral subvalvular apparatus has been increasingly considered a determinant for optimal treatment of ischemic MR. In fact, the Papillary Muscle Approximation Trial reported the safety and effectiveness of valvular and subvalvular repair (associated with complete myocardial revascularization), in patients with moderate to severe ischemic MR [2–4]. This "paradigm shift" in the concept of mitral valve repair is responsible for a flourishing of literature in recent years [1, 2, 5, 6], but awareness of the results of clinical trials and reproducibility of surgical techniques are crucial for future studies.

The natural history of ischemic MR is heterogeneous and is largely determined by the severity of mitral failure, as a majority of patients with mild to moderate regurgitation remain asymptomatic and may have a near-normal life expectancy [7].

The untreated moderate ischemic mitral valve (with a restrictive mitral annuloplasty) by preferring coronary artery bypass grafting (CABG) alone did not lead to significant differences in left ventricular reverse remodeling at 2 years [8]. As demonstrated by the CTSN trial [8] in patients with combined restrictive mitral annuloplasty (RMA) and CABG, mitral-valve repair provided a more durable correction of MR but did not significantly improve survival (hazard ratio [HR] in combined-procedure, 0.90; 95% confidence interval [CI] 0.45–1.83; p = 0.78) or reduce overall adverse events (major adverse cardiac and cardiovascular events [MACCE], HR 0.89; 95% CI 0.60–1.34; p = 0.58) or improve readmissions for heart failure (CABG-alone vs. combined-procedure; p = 0.84). Conversely, the patients who underwent RMA combined to CABG were associated with an early hazard of increased neurologic events (combined-procedure vs. CABG-alone p = 0.02) and supraventricular arrhythmias (combined-procedure vs. CABG-alone p = 0.04), at 2 years.

In patients with severe ischemic MR, expert consensus favors simultaneous correction of MR at the time of CABG operation [7]. Revascularization without mitral valve surgery does not significantly reduce moderate-to-severe MR, as described by investigators reporting recurrent moderate to severe ischemic MR in 77% of patients [9]. However, the central question remains under debate [4, 8, 10]: which strategy for mitral valve surgery is the most effective?

In support of mitral-valve repair achieved with a restrictive annuloplasty combined to papillary muscle approximation (PMA), recent studies showed a relatively lower perioperative morbidity and mortality, associated with improvements in left

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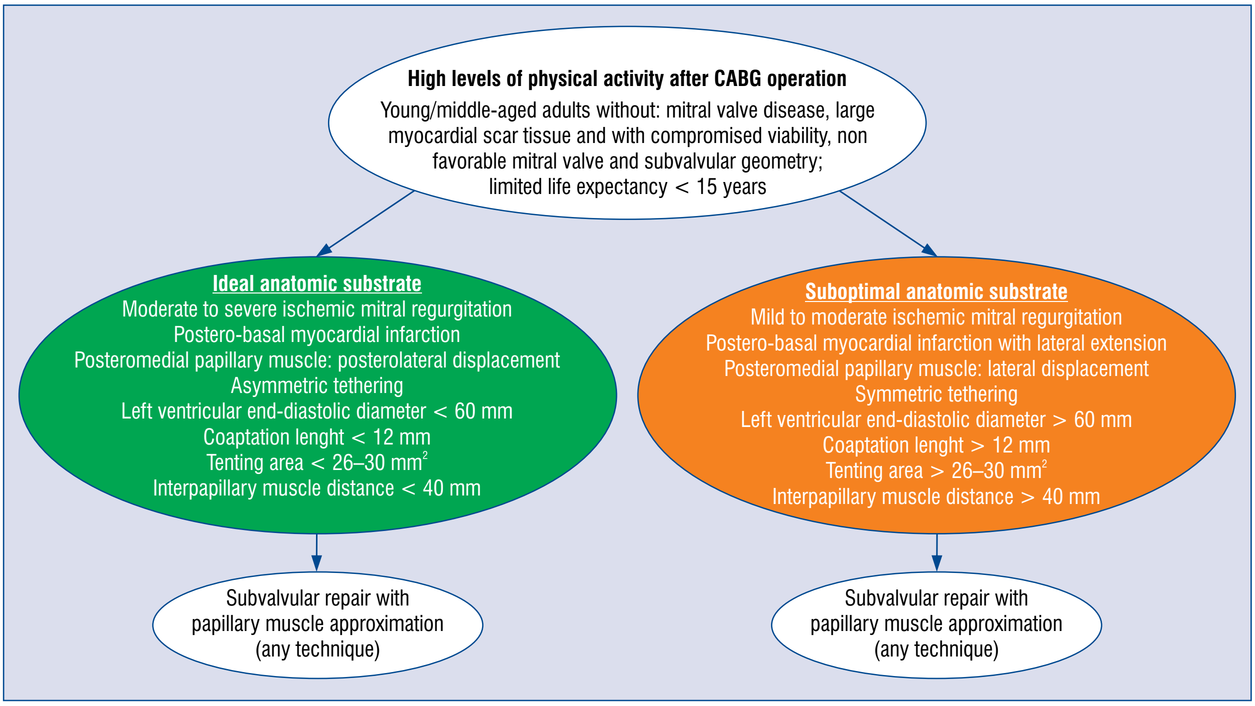

Figure 1. Indications and contraindications for papillary muscle approximation. This proposed algorithm remains to be further validated and supported by practice guidelines; CABG — coronary artery bypass grafting.

ventricular remodeling that is related to the preservation of the subvalvular apparatus [2–4]. On the other hand, the benefit of chordal-sparing mitral valve replacement (CS-MVR) is providing a more durable correction of MR with favorable ventricular remodeling [1, 10], albeit in association with no significant difference in cumulative mortality rates of major adverse cardiac or cerebrovascular events between patients who underwent CS-MVR or RMA [1, 10].

One study included 251 randomized patients to RMA or CS-MVR and reported no significant reduction in 2 year mortality with CS-MVR. The rate of death was 19.0% in the repair group and 23.2% in the replacement group (HR for RMA of 0.79, 95% CI 0.46–1.35; $p = 0.39$) [10].The proportion of patients with recurrent moderate-to-severe MR at some point during the 2-year period was significantly higher in recipients of RMA than in those who had CS-MVR (58.8% vs. 3.8%, $p < 0.001$). Li et al. [1] reported a significant reduction of hospitalization for heart failure in patients in the propensity score-matched RMA group than in the CS-MVR group ($p = 0.015$).The incidence of MR recurrence was significantly higher in the patients who received RMA ($p < 0.001$) while there were no significant differences in overall survival, freedom from cardiac death or MACCE for patients belonging to the two groups. Finally, multivariable analysis showed the use of RMA or CS-MVR was not a significant predictor of late overall death or MACCE ($p = 0.997$ and $p = 0.260$, respectively) [1].

Evidence from randomized controlled trial studies and meta-analysis strongly suggests that surgical intervention on the subvalvular apparatus is beneficial. RMA alone has been associated with a higher rate of recurrent MR compared with RMA associated with subvalvular procedures (such as PMA) [1–4, 10]. One study evaluated the effect of surgery on long-term outcomes in patients who had combined RMA and PMA ($n = 48$) or RMA ($n = 48$) alone for moderate-to-severe ischemic MR. No significant difference in terms of survival was found (HR for PMA 0.76; 95% CI 0.35–1.68; $p = 0.502$; log rank = 0.496) and in MACCE (HR for PMA 0.66; 95% CI 0.42–1.04; $p = 0.073$; log rank = 0.069). However, PMA patients had a significantly better 5-years rate of recurrent MR than those managed with RMA alone (27% vs. 55.9%; $p = 0.013$). At 5 years, recurrence of severe MR, rehospitalization for heart failure and worsening of New York Heart Association class were lower among the PMA group [2–4]. The Papillary Muscle Approximation Trial has also demonstrated that the subvalvular procedure allows restoration of valve geometry by correcting three crucial dimensions: interpapillary muscle distance, coaptation length, and anteroposterior annular diameter [2–4]. In another randomized controlled trial, 101 patients with moderate-to-severe ischemic MR were evaluated (subvalvular repair n = 51; RMA n = 50) over 1 year; the rate of freedom from MR grade > 2 was 98% in subannular repair vs. 86.7% in RMA (p = 0.045), associated with an improvement in survival rate for subannular repair (100% vs. 90%, p = 0.025) [5].

Differences in results of clinical trials should be interpreted considering the heterogeneity in terms of surgical techniques of subvalvular repair. A standardization of procedures is warranted to produce comparable results. Successful valvular and subvalvular mitral-valve repair encompasses four general principles. First, combined repair must restore an adequate surface of coaptation of both leaflets in the systole with an adequate papillary muscle approximation [4]. Second, full leaflet motion must be restored with no restrictive movements of the leaflet related to subvalvular procedures. Third, to reduce the anteroposterior diameter, a restrictive annuloplasty ring with a "two-size downsized" ring is used to adapt the geometry of mitral anulus to the dimension of the left ventricle. Last, but not least, the surgeon should ensure that no more than trivial MR is present at the completion of the repair to guarantee greater improvement of left ventricular remodeling and long-term durability of the repaired valve (Fig. 1).

Conflict of interest: None declared

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