

Editorial

Can we improve the prognosis of postinfarction ventricular septal rupture?

¿Podemos mejorar el pronóstico de la rotura del tabique ventricular posinfarto?

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In recent decades, the incidence of mechanical complications has decreased in patients with acute myocardial infarction (AMI) in parallel to the increasing use of reperfusion strategies and, in particular, primary percutaneous coronary intervention (PCI).^{1,2} However, although this decrease has led to marked reductions in mortality due to these complications, their lethality remains very high^{2–4} and they are still among the most severe complications in AMI patients. The main risk factors for mechanical complications, in addition to the absence of effective reperfusion, are advanced age, the extent of the infarction, and delays in reaching the hospital.^{4,5}

Ventricular septal rupture (VSR) is probably the most feared mechanical complication of AMI that does not cause immediate patient death. On the one hand, patients with this complication treated conservatively have very low survival rates; on the other hand, surgical repair of the defect, with or without the concomitant exclusion of the infarcted territory, is a much more complex and aggressive intervention than that required in patients with free-wall rupture or papillary muscle rupture.⁶ Although the results of percutaneous closure of interventricular defect in selected patients are acceptable,⁷ the role of percutaneous closure of postinfarction VSR is not well established. Currently, this technique is typically reserved for patients who are poor candidates for surgery and who have an appropriate anatomy (anteroapical location, sufficient margins, absence of valvular involvement).

In addition to the intrinsic complexity of the procedure, the outcome of the surgical repair of VSR may be compromised by other factors. Firstly, VSR often results in severe hemodynamic deterioration with rapid progression to multiorgan failure, and many patients are either rejected for surgery or face the procedure with little chance of survival due to their precarious preoperative condition. Secondly, the friability of the infarcted tissue and difficulties in distinguishing it from healthy tissue in the first days of AMI are serious technical problems and favor suture dehiscence and consequent residual or recurrent ventricular septal defect, which is a frequent postoperative finding in these patients.⁶ To address this problem, and only if the patient is stable, interventions could be delayed for several days or even weeks by the use of vasodilator drugs and, if needed, intra-aortic balloon pump insertion to reduce afterload. In support of this strategy, 30-day

mortality after VSR surgery was lower in series with delayed interventions than in those with very early interventions, although it is clear that this difference may be partly due to survival bias.⁶ A recent systematic review and meta-analysis of 41 studies published between 1998 and 2020 included 6361 patients undergoing postinfarction VSR surgery. Overall postoperative mortality was 38.2% and the factors independently associated with higher mortality were intra-aortic balloon pump insertion, right ventricular dysfunction, posterior VSR, and emergency surgery.⁸

The use of mechanical circulatory support systems allows adequate tissue oxygenation to be maintained in patients with cardiogenic shock, thus preventing the onset of multiorgan failure or even reversing it once established. There are published reports of isolated cases and series of patients in which the preoperative use of venoarterial extracorporeal membrane oxygenation (VA-ECMO) managed to stabilize critically ill patients with VSR, who were then able to undergo surgery in better condition.^{9,10} Anecdotal reports have also been published on the use of rotary pump axial-flow left ventricular assist devices with the same objective.¹¹ Although VA-ECMO support may be the only survival option for patients with VSR in advanced degrees of shock, its role in the stabilization of less critically ill patients, as well as other aspects such as the optimal duration of preoperative support, remains to be determined, especially when these devices carry a significant risk of complications. Thus, a recent outcome analysis was published of the Extracorporeal Life Support Organization registry. It included 158 patients with postacute AMI mechanical complications, of whom 102 had VSR with VA-ECMO support (regardless of whether they underwent surgery and the timing of VA-ECMO in relation to surgery) with a median duration of 5.9 days. VA-ECMO complications occurred in 75.3% and in-hospital mortality was 62.7%, but patients with VSR had higher in-hospital mortality (64.7%).¹² Of note, 92.4% were in cardiogenic shock at the time of the indication for VA-ECMO, 25.9% had cardiorespiratory arrest prior to implantation, and 7.6% underwent VA-ECMO implantation during cardiorespiratory arrest.¹²

In a recently published article in *Revista Española de Cardiología*, Sánchez Vega et al. report the results of a Spanish multicenter registry, whose aim was to analyze changes in survival rates of patients with postinfarction VSR in the last decade and determine the factors associated with mortality, including those related to mechanical circulatory support systems.¹³ The study included 120 consecutive patients with postinfarction VSR admitted to 11 tertiary hospitals between January 2008 and December 2018. The sample was divided into 2 equal periods according to whether the date of admission was before or after June 30, 2013. Patient

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characteristics in both periods were compared, as well as 1-year VSR mortality, which was the main objective of the study, and in-hospital mortality. A multivariate survival analysis was performed with adjustment for the variables associated with mortality in the univariate analysis, as well as for other preselected variables influencing prognosis, such as AMI revascularization and VA-ECMO support.

In both periods, the patients' baseline characteristics were similar, although the patients were younger in the second period than in the first (69 ± 13 vs 75 ± 10 years; $P = .009$). With 1 exception, all patients had ST-elevation AMI with a similar distribution between groups in infarct location or culprit artery, which was almost always the left anterior descending artery or right coronary artery. In two-thirds of the patients, mean left ventricular ejection fraction was slightly reduced and the location of the VSR was apical, with no differences between the 2 periods. As expected, AMI was typically diagnosed beyond the optimal time window for reperfusion therapy, in almost half of the patients 24 hours after symptom onset. Coronary angiography was performed in 82.5% of the patients and PCI in 43.3%, with no differences between the 2 periods. The diagnosis of VSR was made on average 2 days after the diagnosis of AMI.

Intra-aortic balloon pumps were implanted in 75.0% of patients, with no differences between the 2 periods. The only significant difference in treatment was the increased use of VA-ECMO support in the second period than in the first period (27.0% vs 4.4%; $P = .001$). Surgical repair was performed in 65.8% of patients, percutaneous closure in 7.5%, combined VSR repair plus coronary artery bypass grafting in 16.6%, and heart transplant in 5.0%. Some degree of residual or recurrent shunt was detected in 25.8% of cases.

Total in-hospital mortality was 60.0% and 1-year mortality was 61.6%. Both percentages were significantly lower in the second period (total in-hospital mortality 52.7% vs 71.7%; $P = .038$; 1-year mortality 52.7% vs 75.6%; $P = .010$). In-hospital mortality was lower among patients who underwent surgery after at least 4 days of VA-ECMO support than among patients who underwent surgery before the fourth day. The multivariate analysis showed that older age was an independent predictor of in-hospital mortality and 1-year mortality, and patient inclusion in the second period was also an independent predictor of increased 1-year survival.

The authors should be congratulated for assembling a contemporary and large series of postinfarction VSR patients, for the thorough data analysis, and for the effort invested in identifying predictors of survival. The study provides valuable data on recent changes in the incidence and prognosis of this complication, all of which deserves comment.

First, the postinfarction VSR rate was low, ranging between 0.27% and 0.46% of AMI patients attended in each hospital. This rate is to be expected,⁶ but it is striking that over the course of the study period it tended to increase rather than decrease. Although the percentages are not given for both periods, 46 patients fulfilled the inclusion criteria (having post-AMI VSR) in the first period and 74 in the second, suggesting that there would have been an increase in the incidence of VSR if the number of patients with AMI had been similar in the 2 periods. The causes underlying these results are unclear, although they could be explained in part by the recent increased number of referrals of patients with AMI to tertiary centers (which is related to the implementation of primary coronary intervention networks in some hospitals) or by streamlining the diagnostic process, which would have allowed the early detection of VSR in patients who would otherwise have died without detection of this complication. Regardless of this consideration, the data suggest that the incidence of postinfarction VSR has a minimal threshold that will be difficult to reduce any further.

Another striking result is that the patients were on average 6 years younger in the second period than in the first. This difference could also be due in part to the underdiagnosis of VSR in the first period, which would have led to older patients being overrepresented during this period. If this were not the underlying reason, these data would be of concern, because they would suggest that an increasing proportion of relatively young patients are being diagnosed or receiving reperfusion treatment beyond acceptable times in a setting in which it is known that delays in effective reperfusion are one of the main risk factors for VSR in these patients.

On a different note, the main objective of the study was to analyze temporal trends in 1-year VSR mortality, which, along with in-hospital mortality, was significantly lower in the second period than in the first. Moreover, this reduction was maintained after adjustment for age and other potential confounding variables related to the patients and the therapeutic approach. These results are very encouraging, because they suggest that the recent advances in the care of these patients are beginning to improve their survival. It is plausible that much of this improved survival is due to the increasing use of preoperative VA-ECMO, which is the only treatment whose use increased significantly in the second period. However, it would be a little hasty to draw this conclusion using the available data, because uncontrolled confounding factors cannot be ruled out as having contributed to these differences. In favor of such caution is the fact that adjusted in-hospital mortality did not significantly decrease in the second period. The previously mentioned meta-analysis of patients with postinfarction VSR after surgery⁸ showed no trend toward greater survival in more recent years than in the earlier years, although it is very likely that there was little use of preoperative VA-ECMO in these patients. As emphasized by Sánchez Vega et al.¹³ the contribution of VA-ECMO to the survival of postinfarction VSR patients should be addressed in appropriate clinical trials, although it is clear that this is a difficult setting in which to conduct such studies. On the other hand, the results of this study suggest that it is better to wait several days after starting VA-ECMO before performing surgical repair, which seems reasonable from the point of view of pathophysiology: however, an experimental study designed for this purpose would also be needed to answer this question.

The results do not encourage enthusiasm for percutaneous VSR repair, because all the patients treated with this approach died. However, these patients were most likely rejected for surgery because of prohibitive risk. It should also be borne in mind that percutaneous closure may have a role to play in very well selected cases.^{6,7}

It would be desirable that the results of this study stimulate renewed efforts to reduce the incidence of VSR and other mechanical complications in patients with AMI, which would encourage the rapid diagnosis of AMI and immediate reperfusion (preferably with primary PCI), while guaranteeing appropriate concomitant treatment. Likewise, studies would be most welcome on the optimal timing of surgical VSR repair as well as the optimal role and timing of the use of circulatory support systems in the management of these patients, particularly in patients for whom implant could be considered elective. In the meantime, in the setting of this rare and severe condition that involves so many uncertainties regarding the most appropriate approach, it seems reasonable to promptly refer patients to centers experienced in the treatment of cardiogenic shock and the mechanical complications of AMI.^{14,15}

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CONFLICTS OF INTEREST

None declared.

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