Editorial

Cardiac rupture after ST-elevation myocardial infarction (STEMI): a 'Stitch' in time?

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Over the past decades, wider adoption of revascularization techniques, specifically percutaneous coronary intervention (PCI) has improved overall morbidity and mortality associated with ST-elevation myocardial infarction (STEMI) (1). Despite increases in the rates of PCI and administration of fibrinolysis in the absence of PCI availability and/or delay in transfer to a PCI-capable facility, patients with STEMI carry a small yet significant risk of mechanical complications (1-3). These potentially fatal complications include papillary muscle rupture (PMR), ventricular septal defect (VSD), and free wall rupture (FWR) (1,3). Compared to the pre-reperfusion era, global incidence of cardiac rupture (CR) in the current era of pharmacological, catheter-based, and surgical reperfusion, has declined, from an 1.7% in 1980s (pre-reperfusion era) to 0.27% in the last decade, thereby emphasizing the importance of reperfusion (1,4). However, within this contemporary era of evolving reperfusion techniques, CR continues to plague STEMI outcomes making timely identification of predisposing factors relevant.

In this issue of the journal, Xu *et al.* aim to identify risk factors for CR in their patient population by describing nearly 200 patients with CR out of a total of 22,016 patients with STEMI and comparing their characteristics with 390 STEMI patients who did not have CR (5). In this study, 66 patients with CR accepted PCI as a management option for STEMI. Subsequently, the investigators included 132 patients who accepted PCI from the control group in a predefined ratio of 1:2 to serve as controls for this subset. The incidence of CR was 0.89% in the study population. Female sex, older age, smoking, total chest pain time, myocardial infarction (MI) in the high lateral wall, acute heart failure and N-terminal pro-B type natriuretic peptide (NT-proBNP) levels were reported as significant predictors for CR. Among those who received PCI, non-single lesion, and pre- and postoperative Thrombolysis In Myocardial Infarction (TIMI) grades predicted CR.

The findings reported by the authors should be considered with its strengths and limitations. Among baseline clinical characteristics, age and sex were comparable to previous reports of STEMI patients who suffered mechanical complications, wherein patients with CR were more likely to be older and women (6-9). It is currently unknown why women are more likely to develop CR after STEMI. Data on race and/or ethnicity are not reported and the study population was derived entirely from two hospitals in China, limiting the generalizability of the authors' findings. Prevalence of hypertension, diabetes, history of MI, and history of PCI were similar between the cohort with CR and the one without. In their analyses,

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the authors also reported some variables that have poor statistical association with wide confidence intervals and questionable statistical association, notably NT pro-BNP. In contrast to the study by Xu *et al.*, in an evidently large study of 3,951,861 patients with STEMI between 2003 and 2015, Elbadawi *et al.* found the prevalence of each of these factors, including a history of smoking to be unanimously lower in patients with STEMI complicated by CR compared to STEMI patients without mechanical complications (6).

While the authors from the index study report the incidence of CR in their patient population, presentation of data on the proportion of patients who received other forms of reperfusion therapies (fibrinolysis, fibrinolysis followed by PCI, or surgical reperfusion) within the overall study population is crucial to be able to truly interpret the incidence of CR in STEMI patients, especially in the context of contemporary reperfusion era. Similarly, an incidence of CR of 0.53% when PCI was performed within 12 hours of symptom onset to manage STEMI raises the likelihood of a significantly lower incidence of CR had PCI been performed been earlier in the STEMI course. The role of early reperfusion in reducing the likelihood of mechanical complications after STEMI has stood the test of time and has significantly lowered the incidence of CR (4,6,8,9). Tripathi *et al.* in their assessment of 2,034,153 patients admitted for STEMI between 2003 and 2017 reported a remarkably lower incidence of CR of 0.32%, wherein 93.5% had primary PCI, 3.2% had fibrinolysis alone, and 3.3% had fibrinolysis followed by PCI (2). These data reflect the incidence of CR in the contemporary era, wherein most patients receive some form of reperfusion therapy. Recent data have also shown that rates of CR do not significantly differ from one reperfusion strategy to other, although there are reports of lower incidence of CR with PCI when compared with fibrinolysis (2,10). The American Heart Association consensus guidelines recommend a door-to-balloon time of 90 minutes or less for STEMI patients undergoing primary PCI based on the association between shorter times to reperfusion and lower mortality after STEMI (11). By curtailing the extent and transmurality of myocardial necrosis, timely and adequate reperfusion therapy decreases the overall risk of myocardial rupture (12).

Other findings noted in the index study that are of interest include the presence of single angiographic lesion which was less commonly associated with CR. This could be secondary to greater myocardium under jeopardy and cessation of perfusion in a significant territory when compared to isolated lesions, especially with high lateral wall MI. Additionally, presence of high lateral wall location could portend occult involvement of left main stem. Of note, the authors did not distinguish the different forms CR while presenting their results, although acquired VSD and PMR are likely to have a different presentation, and a more benign prognosis than FWR (2).

Cardiac rupture typically occurs within the first 24–96 hours after MI, of which FWR is the most commonly reported form and is rapidly fatal, even with surgery (1). Although FWR of the left ventricle often presents as sudden cardiac death occurring in the out-of-hospital setting, it commonly involves the anterior wall followed by the lateral wall as observed in studies conducted in both living subjects and autopsies (6,13-15). A major contributing factor for FWR is a first anterior or lateral wall MI in the absence of collateral flow and should be suspected in any patient with sudden hemodynamic instability with signs of cardiac tamponade after acute MI (1,15). PMR presenting as acute severe mitral regurgitation occurs most often within days after acute MI. Risk factors consist of older age, female sex, history of heart failure, chronic renal dysfunction, and delayed presentation after a first MI (1). PMR is most commonly associated with lateral or inferior wall STEMI and subsequently involves the posteromedial papillary muscle due to single arterial bloody supply. Although, the incidence of PMR has significantly declined in the reperfusion era (0.05–0.26%), in-hospital mortality remains high (1,16). Risk factors for developing VSD after STEMI are similar to those of other forms of CR. With a wide spectrum of presentation, ranging from an incidental murmur to florid circulatory collapse, ventricular septal rupture most often occurs 3–5 days after STEMI (1). Anterior location of infarct is most commonly associated with VSD complicating STEMI with corresponding total occlusion of the left anterior descending artery, compared to inferior (accompanied by posterior VSD) or lateral infarcts. Despite treatment, 30-day mortality remains higher in patients who develop VSD than those who do not develop this complication after STEMI (17).

Considering the widespread adoption of reperfusion therapy to manage STEMI in the current era, Rencuzogullari *et al.*, as an effort to identify patients with STEMI managed exclusively with primary PCI who were at high risk of CR, calculated SYNTAX Score and SYNTAX Score II (SS II) in a retrospective, single-center case-control study of 1,663 patients with STEMI who underwent PCI (18). Originally developed for patients with stable

ischemic disease, these scores aimed to predict the complexity of coronary lesions and prognosis of patients undergoing PCI, and guide decision making between coronary artery bypass grafting and PCI in patients with left-main or three vessel coronary artery disease, respectively. The investigators found SS II to be a multivariable predictor of CR in these patients and noted an uptrend in the risk of CR with increasing SS II scores. Randomized controlled trials evaluating the effect of proactive surveillance of patients with high SS II scores on patient outcomes after CR will help understand the utility of these prediction models in cardiac rupture complicating STEMI.

The overall incidence of cardiac rupture after STEMI remains low across different populations around the world as timely reperfusion within regionalized systems of care develop (1,2,6,12). However, considering the high mortality rate associated with these mechanical complications, prompt identification of specific risk factors that place STEMI patients at elevated risk is recommended and serves as a first step towards limiting the catastrophic sequalae. Areas of further research include identifying why women are at higher risk of suffering CR and developing accurate models using large data sources, comprising ethnically diverse populations, to verify whether distinct risk factors exist for the three subtypes of CR. Evaluating the role of risk-stratification models and periodic screening with modalities such as echocardiography for early identification of CR and their effect on patient outcomes after rupture is also required. Although, the incidence of CR has decreased compared to the pre-reperfusion era, mortality continues to remain high despite advances in surgical techniques and mechanical circulatory support. Besides identifying risk factors for CR, developing effective treatment strategies is essential to improve patient outcomes after cardiac rupture.

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Footnote

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