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Reperfusion Therapy Reduces the Risk of Myocardial Rupture Complicating ST-Elevation Myocardial Infarction

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The debate about the advantages of fibrinolytic therapy or primary percutaneous coronary angioplasty (PCI) as a superior reperfusion strategy for ST-elevation myocardial infarction (STEMI) has continued for 30 years. In the first decade, primary PCI was limited by first-generation equipment, inadequate radiographic imaging systems, suboptimal adjunctive antithrombotic therapy, and delays in time-to-treatment. Successful reperfusion rates were too low and infarct artery reocclusion and restenosis rates were too high, so fibrinolytic therapy was associated with better clinical outcomes.[1] Since then, fibrinolytic therapy improvements have included bolus administration of newer agents, adjunctive dual antiplatelet therapy with aspirin and clopidogrel, and cardiac catheterization as soon as possible for reperfusion failure and within 24 hours after successful reperfusion to maximize sustained infarct artery patency rates.[2] Perhaps more impressive has been the improvement in primary PCI that now makes it the preferred reperfusion strategy.[3] The PCI wires and catheters are well engineered, radiographic and intravascular imaging capability allows excellent visualization of the coronary arteries, antithrombotic medications decrease the risk of acute closure, and drug-eluting stents assure excellent long-term infarct artery patency rates. Most importantly, pre-hospital and in-hospital systems of care have been developed to decrease time-to-treatment and offer reperfusion therapy to almost all patients with STEMI unless treatment is deemed futile.[4]

Lost in the debate over which reperfusion strategy best reduces mortality rates is the important reduction in morbidity associated with both reperfusion therapies compared with historical controls. Hemodynamic, electrical, mechanical, and thrombotic complications have all been reduced by successful reperfusion therapy that restores microvascular perfusion, limits infarct size, and improves left ventricular remodeling. A leading cause of death before reperfusion therapy was myocardial rupture, defined for the purposes of this discussion as free-wall rupture or ventricular septal rupture and excluding papillary muscle rupture or left ventricular pseudoaneurysm formation from contained free-wall rupture.

The incidence of myocardial rupture is difficult to ascertain because death can occur before hospital admission, failed diagnosis is possible unless routine echocardiography is performed, and autopsy rates have been poor and variable. Some patients have certainly been misclassified as sudden cardiac death or cardiogenic shock due to myocardial necrosis. Rates as high as 6% for myocardial rupture and 3% for ventricular septal rupture were reported in the pre-reperfusion era. More recently, the risk in the reperfusion era appears to be approximately 2% for myocardial rupture and 0.3% for ventricular septal rupture.[5,6] The clinical diagnosis of free-wall rupture is suggested by the physical findings of cardiac tamponade (Beck's triad of hypotension, jugular venous distension, and muffled heart sounds; pulsus paradoxus), electrical mechanical dissociation in the absence of preceeding heart failure, or hypotension with at least a moderate pericardial effusion on echocardiography. The clinical diagnosis of ventricular septal rupture is suggested by a systolic murmur and confirmed by an abnormal oxygen saturation run during pulmonary artery catheterization, color flow Doppler echocardiography, or contrast left ventriculography. Pathologic confirmation of myocardial rupture can also be obtained during surgery or necropsy. Risk for myocardial rupture is increased with first myocardial infarction (MI), anterior MI, older age, female sex, absence of prior angina or MI, hypertension, no or unsuccessful reperfusion therapy, late reperfusion therapy, and one-vessel disease without collateral circulation. Prognosis is poor with mortality rates of 75% to

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90% with free-wall rupture and 40% to 75% with ventricular septal rupture.

It has previously been noted several times that reperfusion therapy has decreased the incidence of myocardial rupture. Figueras and collegues reported on 425 patients with myocardial rupture due to STEMI over a 30-year period from a single-center prospective MI registry including 6678 Spanish patients.[7] Free-wall rupture occurred in 280 patients and ventricular septal rupture occurred in 145 patients. The 6.2% incidence during the first 5 years decreased to 3.2% during the last 5 years as the use of reperfusion therapy increased from 0% to 75%. The rate of death declined from 94% to 75%, despite an increase in mean age from 66 to 75 years, in parallel with other improvements in medical therapy and the increasing delivery of primary PCI and surgical therapy.

In this issue of the *Journal of the American Heart Association*, Honda and colleagues investigated temporal trends in the incidence and clinical and pathological characteristics of myocardial rupture in patients with acute MI.[8] Their single-center prospective MI registry included 5699 Japanese patients who were divided into 3 cohorts by admission year: 1977-1989, 1990-2000, 2001-2011. There were 144 (2.5%) patients with myocardial rupture, with 45 survivors. The incidence of myocardial rupture decreased over time (3.3% to 1.7%) as reperfusion therapy rates increased (2.5% to 70.1%); mortality rates decreased over time (90% to 50%) as emergency surgical rates increased (39% to 74%). Risk factors for myocardial rupture included first MI, anterior MI, female sex, older age, and hypertension. The incidence of myocardial rupture declined from 3.3% without reperfusion therapy to 2.9% with fibrinolytic therapy to 1.2% with primary PCI, but in 64 autopsy cases, the myocardial hemorrhage rate was 83% with primary PCI, compared with 71% for fibinolysis and 18% with no reperfusion therapy. The authors concluded that reperfusion therapy, particularly primary PCI, has decreased the incidence of myocardial rupture and that surgical therapy has increased survival rates.

The change in baseline characteristics over time in the Japanese registry is stunning. If there was no ascertainment bias, the increase in the incidence of hypertension from 32% to 69%, hyperglycemia from 19% to 55%, and hyperlipidemia from 6% to 57% reflects a dramatic shift in atherosclerosis risk factors that portends a major increase in the risk for coronary artery disease in Japan. Similarly, the more recent use of primary PCI in almost 70% of patients and emergency surgery in a similar percentage of patients with myocardial rupture reflects increased utilization of invasive therapies.

The incidence of myocardial rupture in the Japanese registry was half that reported in the Spanish registry, perhaps because patients were younger, time-to-treatment was earlier, and patients with non-ST elevation MI were included. The outcomes over time trended similarly and both reports suggested that the benefit was due to increased use of reperfusion therapy, particularly primary PCI. The Japanese report more precisely shows the benefit with primary PCI versus fibrinolytic therapy and adds an important pathological observation.

Becker and van Mantgem defined 3 types of cardiac rupture after MI.[9] Type I rupture occurs within 24 hours as an abrupt, slit-like tear. Type II rupture occurs as a later tear from progressive myocardial erosion. Type III rupture occurs in older infarctions as a perforation within a thin walled aneurysm. In the pre-reperfusion era, Type III rupture was most common and required transmural myocardial necrosis with hemorrhagic transformation in the central region of necrosis where microvascular damage had resulted. It began either at the endocardial surface or within the myocardium and dissected through the infarct zone to the epicardial surface. The highest risk period was 3 to 5 days after MI. In the reperfusion era, Type I and Type II ruptures appear to be most common, with the highest risk in the first 1 to 2 days. Hemorrhage into a nontransmural infarction may weaken the supporting framework of the infarct zone and increase the risk of cardiac rupture through hemorrhagic dissection or delayed healing. The risk is increased with late administration of fibrinolytic therapy.[10] Thus, reperfusion therapy decreases the overall risk of myocardial rupture by decreasing the extent and transmurality of myocardial necrosis, but it may increase early risk due to intramyocardial hemorrhage. The risk of myocardial hemorrhage was previously attributed to fibrinolytic therapy as a unique complication and used as another point in the debate in favor of primary PCI.[11] The observation by Honda and colleagues that the risk for myocardial hemorrhage is similar with fibrinolytic therapy or primary PCI is new and challenging. Evidently, myocardial hemorrhage is present in at least 25% of patients after primary PCI, suggesting that new research is required to target potential therapies for this complication of reperfusion therapy.[12]

Emergency stabilizing therapy for myocardial rupture includes volume resuscitation, pressors, pericardiocentesis for free-wall rupture, and intra-aortic balloon counterpulsation for ventricular septal rupture. Beta-blockers were initially observed to decrease the risk of myocardial rupture in the first International Study of Infarct Survival (ISIS-1) trial, but the benefit is less clear now in the reperfusion era.[13] Myocardial rupture is usually rapidly fatal, but surgery can be undertaken in stabilized patients if feasible. Earlier surgery makes clinical sense, but cardiac surgeons prefer to operate later using natural history as a selection process to decrease the high surgical mortality rates. Better results would be predicted in patients younger than 80 years and without cardiogenic shock. The utility of other hemodynamic support devices and transcatheter ventricular septal closure devices remains to be determined.[14,15]

Disclosures

None.

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