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JACC FOCUS SEMINAR: MECHANICAL COMPLICATIONS OF ACUTE MYOCARDIAL INFARCTION, PART 1

JACC FOCUS SEMINAR

Right Ventricular Myocardial Infarction—A Tale of Two Ventricles

JACC Focus Seminar 1/5

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ABSTRACT

Right ventricular infarction (RVI) complicates 50% of cases of acute inferior ST-segment elevation myocardial infarction, and is associated with high in-hospital morbidity and mortality. Ischemic right ventricular (RV) systolic dysfunction decreases left ventricular preload delivery, resulting in low-output hypotension with clear lungs, and disproportionate right heart failure. RV systolic performance is generated by left ventricular contractile contributions mediated by the septum. Augmented right atrial contraction optimizes RV performance, whereas very proximal occlusions induce right atrial ischemia exacerbating hemodynamic compromise. RVI is associated with vagal mediated bradyarrhythmias, both during acute occlusion and abruptly with reperfusion. The ischemic dilated RV is also prone to malignant ventricular arrhythmias. Nevertheless, RV is remarkably resistant to infarction. Reperfusion facilitates RV recovery, even after prolonged occlusion and in patients with severe shock. However, in some cases hemodynamic compromise persists, necessitating pharmacological and mechanical circulatory support with dedicated RV assist devices as a "bridge to recovery." (J Am Coll Cardiol 2024;83:1779–1798) © 2024 the American College of Cardiology Foundation. Published by Elsevier. All rights reserved.

Thus it May Be Said, that the Purpose of the Right Ventricle is to Pump Blood to the Lungs, Not to Nourish Them.

—Sir William Harvey[1]

Right ventricular infarction (RVI) complicates 50% of cases of acute inferior ST-segment elevation myocardial infarction and is associated with higher in-hospital morbidity and mortality.[2] Although for many decades the right ventricle (RV) was thought to be unimportant in the circulation, the profound impact of RV systolic dysfunction was first appreciated in patients with inferior myocardial infarction (MI) developing hemodynamic compromise. This is characterized by hypotension with clear lungs and disproportionately elevated right heart filling pressure, despite intact global left ventricular (LV) systolic function.[3] The syndrome of predominant RV shock is a pathophysiologic "Tale of Two Ventricles": The RV is ischemic, dilated, and failing, whereas the LV is typically "dry" and contracting vigorously, unless damaged by previous ischemic insults.[4] Importantly, the term RV "infarction" is largely a misnomer, for in the vast majority of cases acute RV ischemic dysfunction represents viable myocardium, which recovers after reperfusion, even

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ABBREVIATIONS AND ACRONYMS

AMI = anterior myocardial infarction

AV = atrio-ventricular

ECMO = extracorporeal membrane oxygenation

IABP = intra-aortic balloon pump

LV = left ventricle

MCS = mechanical circulatory support

MI = myocardial infarction

PA = pulmonary artery

PAPi = pulmonary artery pulsatility index

pRVAD = percutaneous right ventricular mechanical assist devices

RA = right atrium

RCA = right coronary artery

RV = right ventricle

RVFW = right ventricular free wall

RVI = right ventricular infarction

after prolonged occlusion.[5] These responses are in marked contrast to the impact of acute coronary occlusion on LV myocardium, ominously so in those with LV shock.[6]

This paper reviews the insights and advances in the pathophysiology, hemodynamics, natural history, and treatment of patients with inferior myocardial infarction complicated by RVI. The evaluation and management are presented in trimodal pathophysiological and temporal context, from acute coronary occlusion in the emergency department, through catheterization laboratory reperfusion therapy, and to recovery in the coronary care unit. The review emphasizes the following:

1) differences between RV and LV with respect to structure, function, and metabolism that influence their disparate responses to ischemia and reperfusion;
2) relationship between the site of right coronary artery (RCA) occlusion and the presence and magnitude of right heart ischemia and intraprocedural complications;
3) pathophysiologic mechanisms leading to hemodynamic compromise and their relevance to pharmacologic and mechanical interventions;
4) arrhythmias and reflexes during acute occlusion and complicating reperfusion;
5) concept that RV "infarction" is a misnomer, for even severe acute ischemic RV dysfunction is nearly always reversible;
6) benefits of mechanical reperfusion therapy on hemodynamics and clinical outcome, even after prolonged occlusion and in patients with severe shock;
7) role of mechanical support as "hemodynamic bridge to recovery."

HIGHLIGHTS

- RVI results from proximal RCA occlusion, occurs in approximately 50% of patients with inferior MI, and is associated with increased in-hospital morbidity and mortality due to shock and arrhythmias.
- Augmented RA contraction optimizes RV performance. Reperfusion facilitates RV recovery and improves outcomes, even after prolonged occlusion and in patients with ventricular shock.
- Shock in patients with RVI reduces LV preload, and involvement of the interventricular septum adversely affects LV function. Patients with persistent hemodynamic compromise may benefit from pharmacological and mechanical circulatory support.

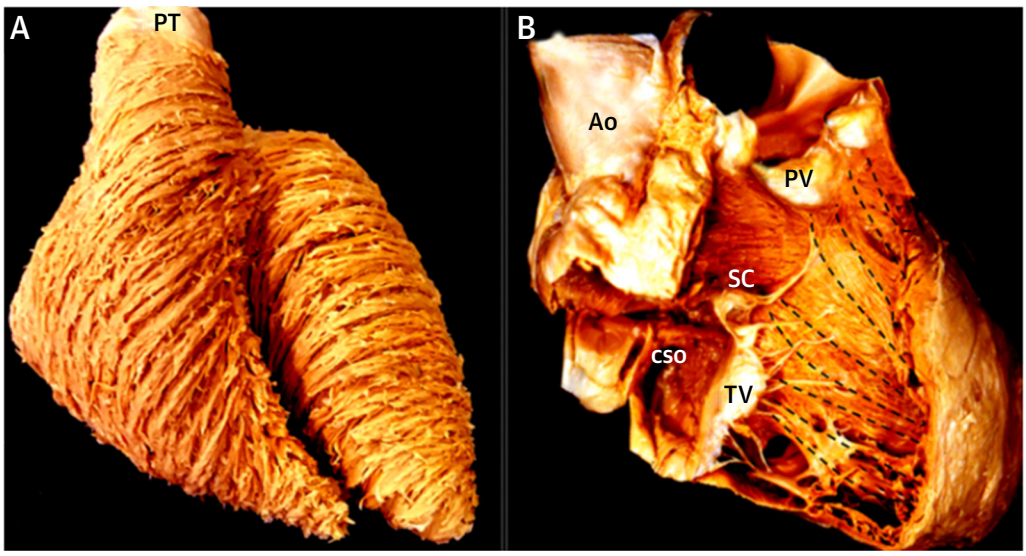
RV ARCHITECTURE, MECHANICS AND METABOLISM: BASIS FOR RESILIENCE

The RV and LV differ markedly in anatomy, mechanics, loading conditions, and metabolism; therefore, they have strikingly different O_2 supply-demand characteristics,[7] the basis for their markedly disparate responses to ischemia and reperfusion. The LV is a thick-walled pressure pump, perfused predominantly in diastole. In contrast, the pyramidal-shaped RV with its thin crescentic free wall is a volume pump ejecting into the lower resistance pulmonary circulation. The RV superficial circumferential layer constitutes 25% of wall thickness and spans the LV; the predominant subendocardial longitudinal layer is continuous with the septum, with longitudinal shortening contributing to 75% of RV contraction (Figure 1). RV systolic pressure and pulmonary flow are generated by the right ventricular free wall (RVFW) shortening and contraction toward the septum up to the outflow tract. As such, RV O_2 supply-demand profile is more favorable than the LV: demand is lower owing to lesser myocardial mass, preload, and afterload; lower intra-myocardial pressures facilitate RCA perfusion in both systole and diastole, and lower coronary resistance facilitates more favorable conditions for collateral development to the RCA. In aggregate, these factors render the RV remarkably resistant to infarction, as substantiated by its resilient response to reperfusion and the fact that even in the absence of RCA recanalization, in those who survive the initial complications, RV function eventually recovers.[5]

PATHOPHYSIOLOGY OF RV ISCHEMIC DYSFUNCTION AND HEMODYNAMIC COMPROMISE

RVI occurs almost invariably in association with inferior myocardial infarction, the culprit vessel nearly always proximal RCA occlusion compromising RV branch flow and RVFW perfusion (Figures 2 and 3). Occasionally, isolated RVI develops, typically from occlusion of a nondominant RCA or selective compromise of RV branches during percutaneous coronary interventions. RVFW ischemia results in

FIGURE 1 **RV Architecture**



The pyramidal-shaped right ventricle (RV) with thin crescentic free wall. RV superficial circumferential layer constitutes 25% of wall thickness and spans the left ventricle (LV) (A). The predominant subendocardial longitudinal layer is continuous with the septum (B), with longitudinal shortening contributing 75% of RV contraction. Ao = aorta; CSO = coronary sinus ostium; PT = pulmonary trunk; PV = pulmonary vein; SC = supraventricular crest; TV = tricuspid valve. Reproduced with permission by Sanz et al.[7]

RV systolic dysfunction, which diminishes transpulmonary delivery of LV preload, leading to decreased cardiac output despite intact LV contractility.[8] The ischemic RV is stiff and dilated, leading to rapid diastolic pressure elevation. Acute RV dilation and elevated diastolic pressure shift the interventricular septum toward the volume-deprived LV, further impairing LV compliance and filling. Abrupt RV dilation within the noncompliant pericardium elevates intrapericardial pressure, the resultant constraint further impairing RV and LV compliance and filling. Right atrial (RA) pressure is elevated and within 5 mm Hg of the pulmonary wedge pressure in patients with hemodynamically significant RVI. In aggregate, these effects contribute to the pattern of equalized diastolic pressures and RV "dip-and-plateau" characteristic of RVI (Figure 3).

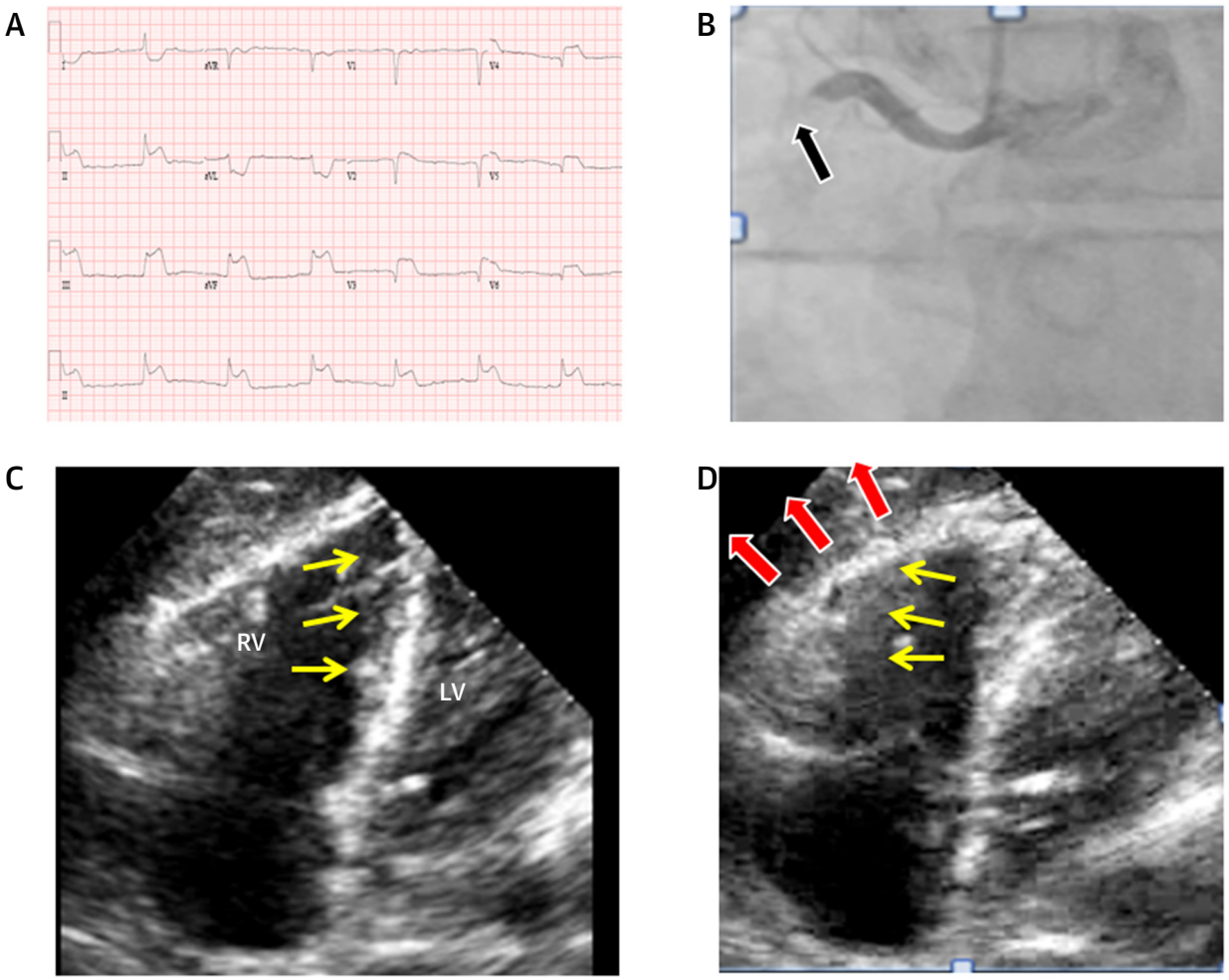
DETERMINANTS OF RV PERFORMANCE IN SEVERE RVI

SYSTOLIC VENTRICULAR INTERACTIONS. Under conditions of acute ischemia, the dyskinetic RVFW is stretched by neighboring contracting walls through regional intraventricular interactions. In early isovolumic systole, unopposed LV-septal pressure generation creates a left-to-right pressure gradient resulting in early systolic septal bulging into the RV cavity. This paradoxical displacement of the septum contributes to RV output and effective pulmonary flow (Figure 2).[8,9] Observations from experimental models demonstrate that inotropic stimulation enhances LV-septal contraction and thereby augments RV performance through compensatory systolic interactions.[9]

Although the magnitude of hemodynamic derangements is predominantly related to the extent of RVFW contraction abnormalities, some patients tolerate severe RV systolic dysfunction without hemodynamic compromise, whereas others develop life-threatening low output, emphasizing that additional factors modulate the clinical expression of RVI.

IMPORTANCE OF AUGMENTED RA CONTRACTION AND ISCHEMIA. The status of RA contraction is a key determinant of hemodynamic stability in RVI.[8-10] The ischemic RV imposes increased preload and afterload on the RA, the resultant enhanced RA contraction an important compensatory mechanism that optimizes RV filling and cardiac output (Figure 3). Augmented RA contractility inscribes a "W" pattern in the RA waveform characterized by a prominent A wave, sharp X descent reflecting enhanced atrial relaxation, and blunted Y descent owing to impaired passive

FIGURE 2 Proximal RCA Occlusion: Impact on Rhythm and RV Performance

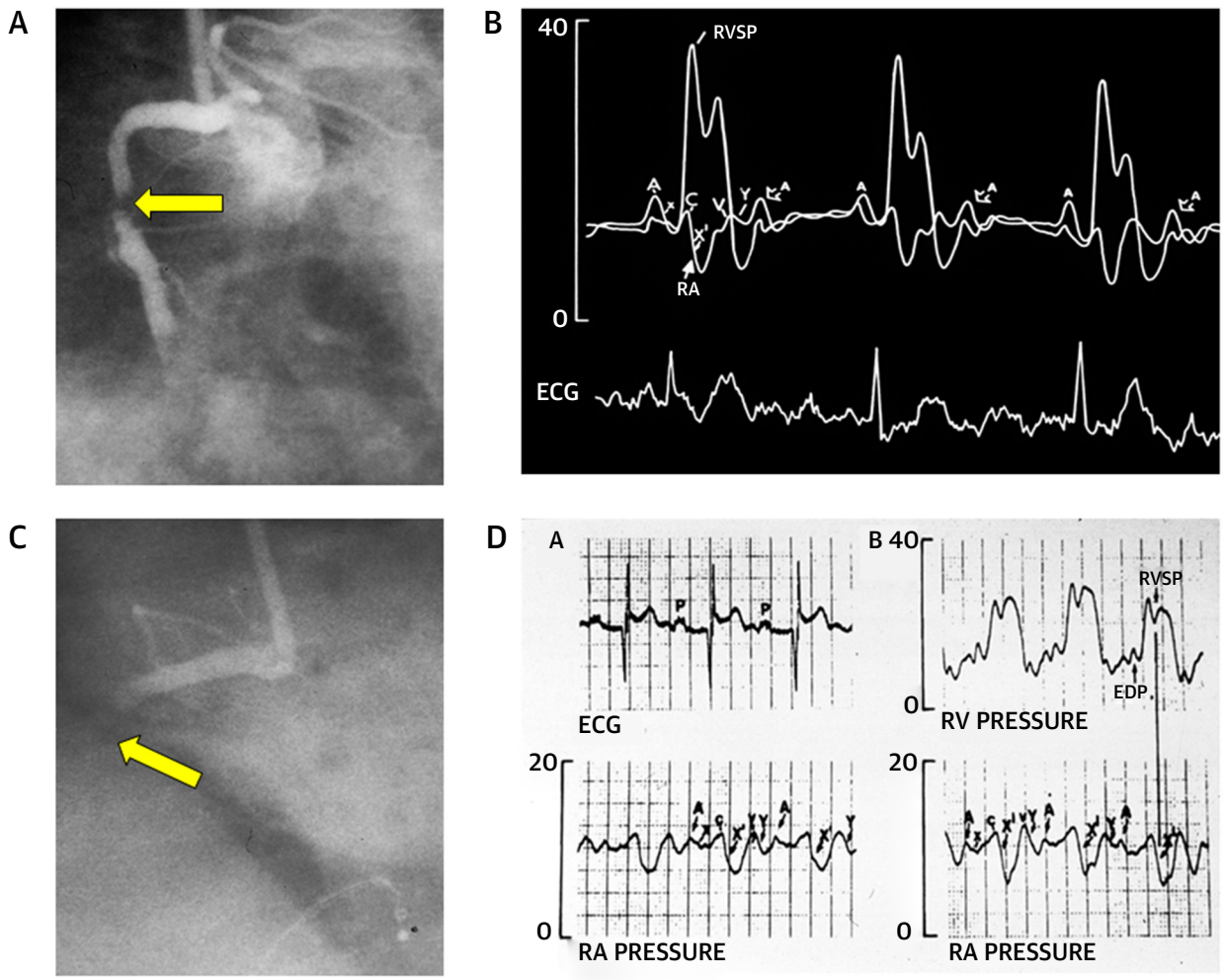


Patient with acute inferior ST-segment elevation myocardial infarction complicated by complete atrio-ventricular (AV) block (A) attributable to proximal right coronary artery (RCA) occlusion compromising the right ventricular (RV) branches (B, arrow). Echocardiographic images at end-diastole (ED) (C) and end-systole (ES) (D) demonstrate severe right ventricular infarction (RVI), characterized by severe RV dilation resulting in reversed septal curvature (yellow arrows) impinging on the volume-deprived left ventricle (LV). In systole, there is marked RV free wall dyskinesis (D, open red arrows) resulting in severely depressed global RV performance; the septum bulges paradoxically into the RV (D, yellow arrows) and reflects systolic ventricular interactions generating RV systolic performance.

emptying into the stiff dilated RV (Figures 3 and 4). This compensatory mechanism is lost when RVI develops from a very proximal RCA occlusion, compromising both RV and RA branches. Ischemic RA dysfunction decreases RV filling and performance, thereby resulting in more severe compromise of cardiac output and aortic pressure. In contradistinction to preserved RA perfusion, RA ischemia manifests hemodynamically as markedly elevated mean RA pressure and inscribes an "M" pattern in the RA waveform characterized by depressed A wave and X descent, as well as blunted Y descent (Figures 3 and 4). Arrhythmias inducing loss of the compensatory "atrial kick" may require restoration of physiologic rhythm, by atrioventricular (AV) pacing in complete heart block[11] and cardioversion for atrial fibrillation.

IMPACT OF LV SYSTOLIC DYSFUNCTION. LV function is a key determinant of hemodynamic stability and survival in patients with acute RVI. The compensatory contributions of LV-septal contraction to RV performance are emphasized by the deleterious effects of concomitant LV systolic dysfunction (acute and preexisting) associated with more severe hemodynamic compromise with RVI. In patients with RVI,

FIGURE 3 **Hemodynamics of Augmented RA Contractility vs Ischemic RA Dysfunction**

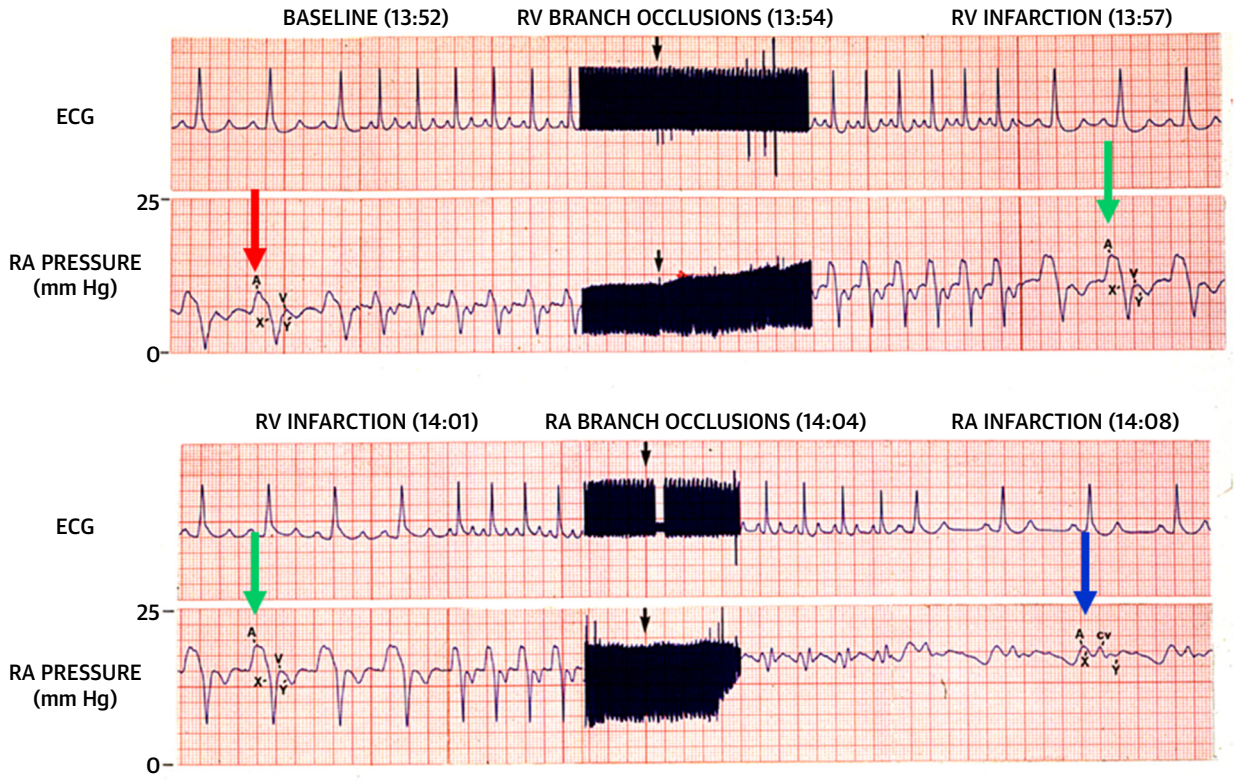


Comparative hemodynamic recordings of 2 patients with right ventricular infarction (RVI), one with augmented right atrial (RA) contraction vs case with RA ischemic dysfunction. Patient with RVI secondary to right coronary artery (RCA) occlusion proximal to the right ventricular (RV) branches but sparing the RA branches (A, arrow), manifested augmented RA contraction inscribing a "W" pattern in the RA pressure waveform (B). Peaks of the W are formed by prominent A waves with an associated sharp "X" systolic descent, reflecting enhanced atrial contraction and relaxation. RV systolic dysfunction is indicated by depressed peak RV systolic pressure (RVSP) and prolonged relaxation; RV diastolic dysfunction results in pattern of dip and rapid rise in diastolic pressure, as well as blunting of the RA Y descent. Patient with RVI from very proximal occlusion compromising RA as well as RV branches (C) resulting in ischemically depressed RA contractility inscribing an "M" pattern, characterized by markedly elevated mean RA pressure with diminished A waves (D). The RVSP waveform is markedly depressed characteristic of RVI. Reproduced with permission from Goldstein et al.[8] ECG = electrocardiogram.

concomitant depressed LV systolic function (ejection fraction <40%) is associated with greater hemodynamic compromise and higher in-hospital mortality.[12] Given the dependence of the ischemic RV on LV-septal contractile contributions, multivessel coronary disease and concurrent chronic total occlusions are associated with a worse outcome.[13,14] Not surprisingly, elderly patients with RVI have a particularly poor prognosis.[15]

ELECTROCARDIOGRAPHIC CHANGES AND RHYTHM DISORDERS ASSOCIATED WITH RVI. In patients with inferior myocardial infarction, obtaining right-sided electrocardiogram leads should be routine: ST-segment elevation and loss of R wave in V_{3R}/V_{4R} are sensitive indicators of the presence of RVI,[16] and correlates closely with occlusion of the proximal RCA, but is not predictive of the magnitude of RV dysfunction nor its hemodynamic impact.

FIGURE 4 Experimental Model of Augmented RA Contractility vs Ischemic RA Dysfunction

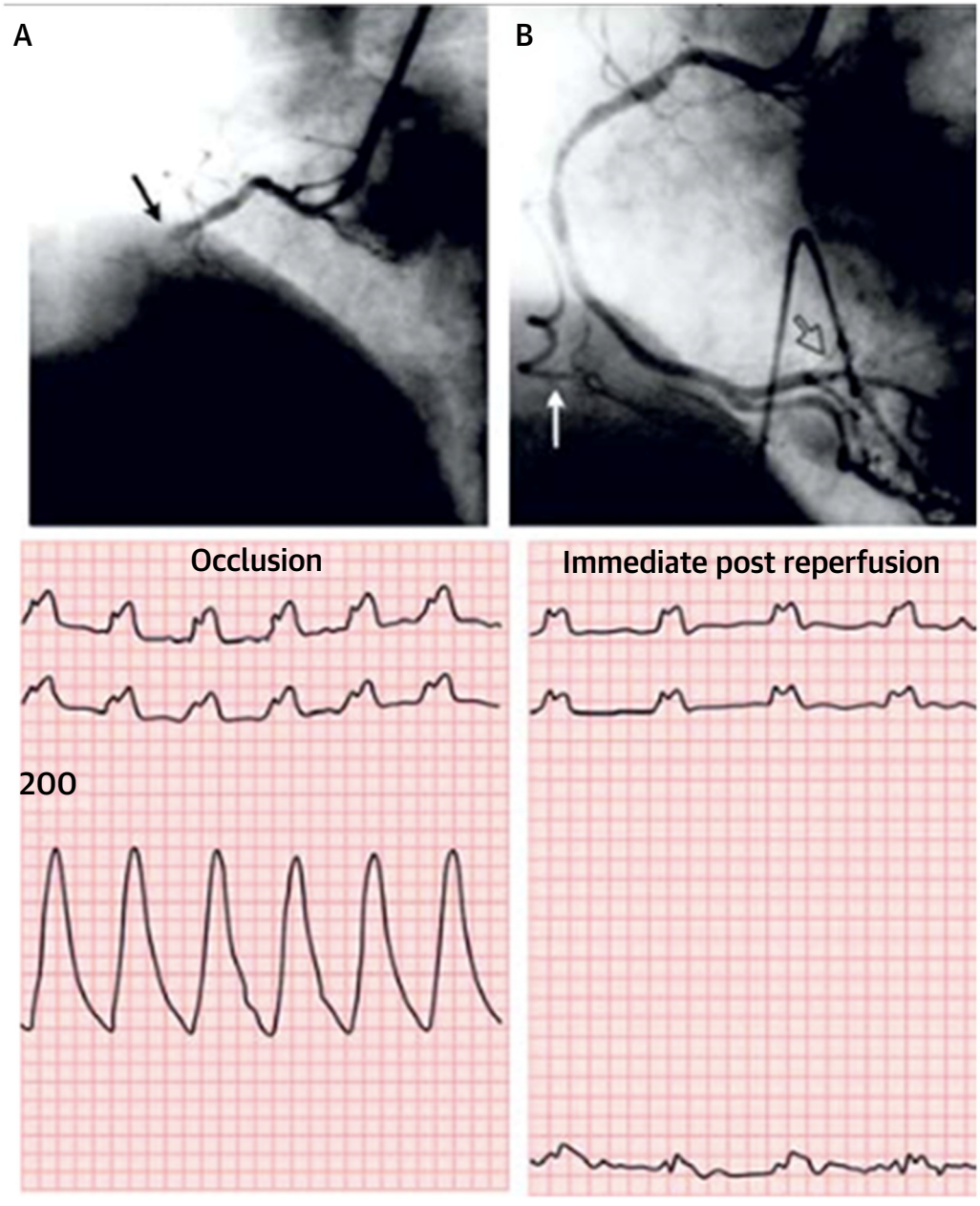


Hemodynamic recordings from an experimental model of right heart ischemia using selective sequential occlusion of right ventricular (RV) and then right atrial (RA) branches. At baseline RA pressure (RAP) and waveform are physiologic (red arrow). Occlusion of the RV branches alone induces RV infarction resulting in elevated mean RAP and compensatory augmented RA contractility, reflected in the "W" pattern (green arrow) characterized by prominent A waves with an associated sharp X descent indicative of enhanced atrial relaxation. Subsequent occlusion of the RA branches results in ischemic depression of RA contractility associated with further marked elevation of mean RAP and an "M" pattern characterized by depressed A waves (blue arrow). Reproduced with permission from Goldstein et al.[59]

ARRHYTHMIAS. Bradyarrhythmias. Bradycardia-hypotension and high-grade AV block commonly complicate inferior myocardial infarction, predominantly mediated by excess vagotonia in two-thirds of patients,[17-20] manifest clinically by nausea, vomiting, and diaphoresis. Originally attributed to the cardio-inhibitory Bezold-Jarisch reflex arising from the ischemic LV inferior-posterior wall,[19] it is now recognized that bradyarrhythmias are far more common in patients with RVI resulting from more proximal vs distal RCA occlusion, thereby implicating the RV as a source for such reflexes (Figure 2).[21] Bradycardia-hypotension and high-grade AV block during occlusion are thus "red flags" that RVI may be present, and may also be a harbinger of subsequent reperfusion-induced reflex arrhythmias.

Excess vagal tone exerts adverse hemodynamic effects mediated by both cardio-inhibitory (bradycardic) as well as vasodepressor responses. The hemodynamic impact in the setting of RVI may be markedly compromising. The depressed RV and preload deprived LV have fixed stroke volumes, thus rendering output heart rate dependent and aortic pressure sensitive to vasodilating influences. The vasodepressor input together with dampened compensatory sinus tachycardia thereby exacerbates hypotension. Of importance for interventional management, abrupt bradycardic-hypotensive reflexes may be elicited during reperfusion,[21,22] even "paradoxically" in patients whose rhythm and blood pressure were stable during RCA occlusion and otherwise successfully reperfused (Figure 5).

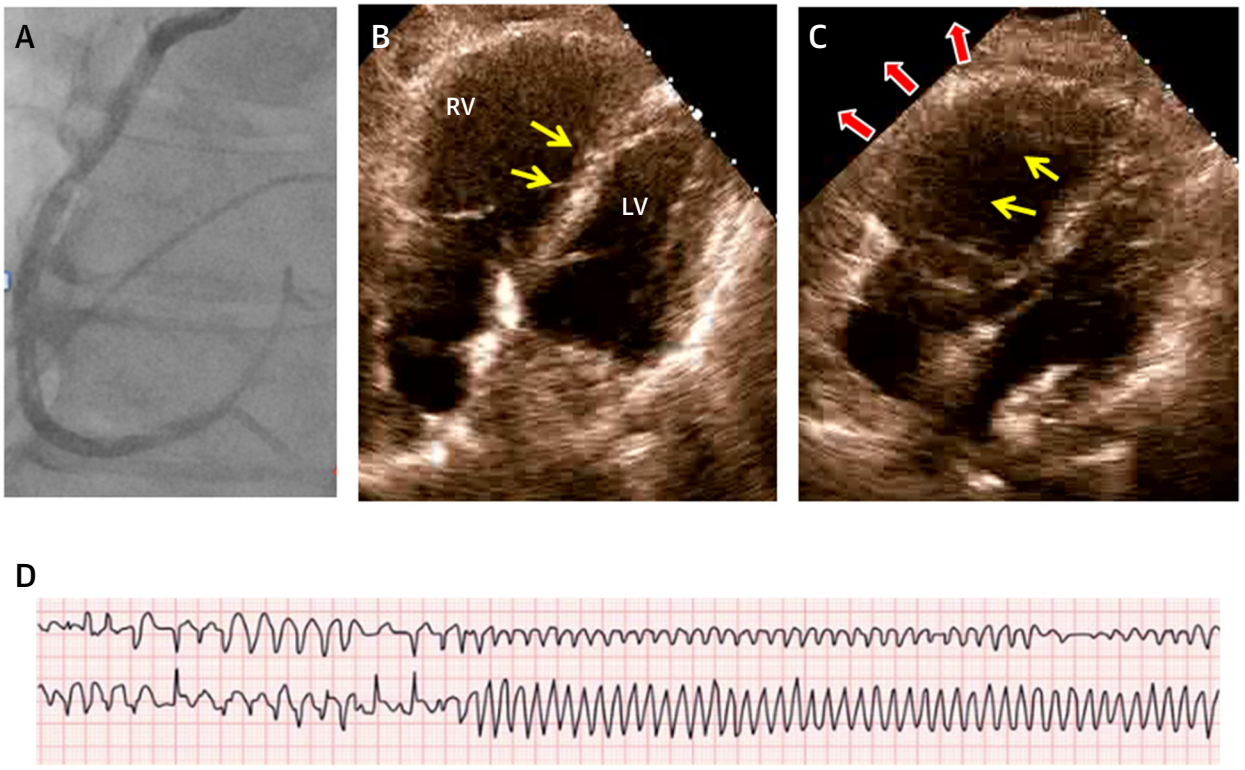
FIGURE 5 Reperfusion-Induced Reflex Bradycardia-Hypotension



Patient with acute inferior myocardial infarction and RVI due to proximal RCA occlusion (left panel, arrow) compromising the RV branches (A, black arrow) as well as the LV and atrioventricular nodal branches. During total occlusion there was sinus rhythm with intact aortic pressure resulting in abrupt sinus bradycardia with profound hypotension, that rapidly responded to atropine and brief vasopressor support. Reproduced with permission by Goldstein et al.[60] Abbreviations as in Figure 2.

VENTRICULAR TACHYCARDIA AND ELECTRICAL STORM. The ischemic dilated RV is prone to ventricular tachyarrhythmias,[23,24] which develop in a trimodal pattern, most commonly during the initial acute occlusion, occasionally abruptly with reperfusion, as well as subsequently if RV recovery lags.[14] Severe RV ischemic dilation may precipitate a ventricular tachycardia "electrical storm" (Figure 6).

FIGURE 6 Persistent RV Shock due to Coronary "No-Reflow"



Patient with acute RVI who suffered intractable coronary "no-reflow" due to persistent extensive intracoronary thrombus (A), resulting in persistent severe RV ischemic dysfunction characterized in diastole by persistent severe RV dilation with reversed septal curvature (B, yellow arrows) and severe systolic impairment with right ventricular free wall dyskinesis (C, open red arrows) and paradoxical septal motion (yellow arrows). (D) Course was complicated by recurrent malignant ventricular arrhythmias suppressed by amiodarone and which abated over 36 hours, as RV dysfunction and dilation improved. Abbreviations as in Figure 2.

Following successful mechanical reperfusion, late malignant ventricular arrhythmias are uncommon.

MECHANICAL COMPLICATIONS ASSOCIATED WITH RVI

Patients with acute RVI may experience additional mechanical complications that compound hemodynamic compromise and confound the clinical-hemodynamic picture. Ventricular septal rupture is a particularly disastrous complication, adding substantial overload stress to the ischemically dysfunctional RV.[25] Acute left-to-right shunting reduces effective forward LV output, precipitates pulmonary edema and elevates pulmonary pressures and resistance. In aggregate, these effects worsen RV dysfunction and conspire to further exacerbate low cardiac output and hypotension. Ventricular septal rupture complicating RVI is posterior in location, and with a serpiginous route that makes surgical repair complex. Posterior ventricular septal rupture is associated with a more unfavorable prognosis, usually due to a higher incidence of biventricular involvement and dysfunction. Surgery is technically difficult in these profoundly ill high-risk patients, owing to often extensive "Swiss cheese" necrotic damage of the inferior-posterior septum and contiguous RVFW, which precludes clean surgical lines for debridement and repair. An anchor for percutaneous closure is similarly challenging. RVFW rupture is a rare and usually disastrous complication.[26] Severe right heart dilation and diastolic pressure elevation associated with right heart ischemia may stretch open a patent foramen ovale, precipitating acute right-to-left shunting manifest as systemic hypoxemia and documented by echocardiographic contrast study.[27] After successful reperfusion, the shunt typically resolves as right heart pressures diminish with recovery of RV performance; occasionally some require closure. Severe tricuspid regurgitation occasionally

complicates RVI, a result of primary papillary muscle ischemic dysfunction, or rarely rupture.[28]

INFERIOR MI VS ANTERIOR MI: SAME GENUS, DIFFERENT SPECIES

The patterns and prevalence of electrophysiological and hemodynamic complications differ markedly in patients with inferior MI compared with anterior myocardial infarction (AMI). These manifestations can be considered according to a trimodal temporal pattern, including acute coronary occlusion, reperfusion, and recovery (Table 1).

ACUTE CORONARY OCCLUSION. Transmural ischemia may precipitate malignant ventricular arrhythmias, regardless of the culprit vessel and infarct location. Notably, bradyarrhythmias are common in the prereperfusion stage of inferior MI, but rare in patients with AMI who more commonly manifest sinus tachycardia (especially if LV ejection fraction is significantly impaired). Hemodynamically, patients with inferior MI are typically stable unless complicated by RVI resulting in hypotension with disproportionate right heart failure. In contrast, hemodynamic compromise in AMI is dominated by LV failure, initially as pulmonary congestion ("wet and warm"), but in more advanced stages frank cardiogenic shock ("wet and cold").

REPERFUSION. Immediate responses to flow restoration to the culprit vessel may differ dramatically. In inferior MI, RCA recanalization may induce abrupt reflex mediated bradycardia-hypotension, which may degenerate into ventricular tachycardia/fibrillation. In RVI, successful reperfusion typically results in early hemodynamic stabilization; pharmacological and mechanical circulatory support (MCS) may be required in some, but usually only briefly as reperfusion-mediated recovery of RV function ensues. In contrast, in AMI, reperfusion-induced arrhythmias are rare, unless severe coronary "no-reflow" occurs. Importantly, hemodynamic compromise resulting in cardiogenic shock imparts an ominous prognosis.

Hemodynamic recovery patterns may also differ markedly. In inferior MI, LV function is typically minimally depressed, hemodynamic compromise due to RVI typically recovers rapidly following successful reperfusion, the subsequent course typically smooth and short, and late prognosis excellent.[5] In contrast, in AMI, recovery of regional and global LV systolic dysfunction is slower and less complete, and such patients are at greater risk for persistent acute hemodynamic compromise, as well as later adverse remodeling including aneurysm formation with resultant ischemic cardiomyopathy and its consequences (especially in those presenting and reperfused later).

TABLE 1 Inferior vs Anterior ST-Segment Elevation Myocardial Infarction Same Genus, Different Species

Arrhythmias	Inferior MI	Anterior MI
Acute occlx	Bradycardias & VT/VF	VT/VF
Reperfusion	Bradycardias & VT/VF	Rare
Late	Rare	VT/VF
Hemodynamics		
Early	RV shock	Pulm edema shock
Late	Rare	CHF

CHF = congestive heart failure; MI = myocardial infarction; Pulm = pulmonary; RV = right ventricular; VT/VF = ventricular tachycardia/ventricular fibrillation.

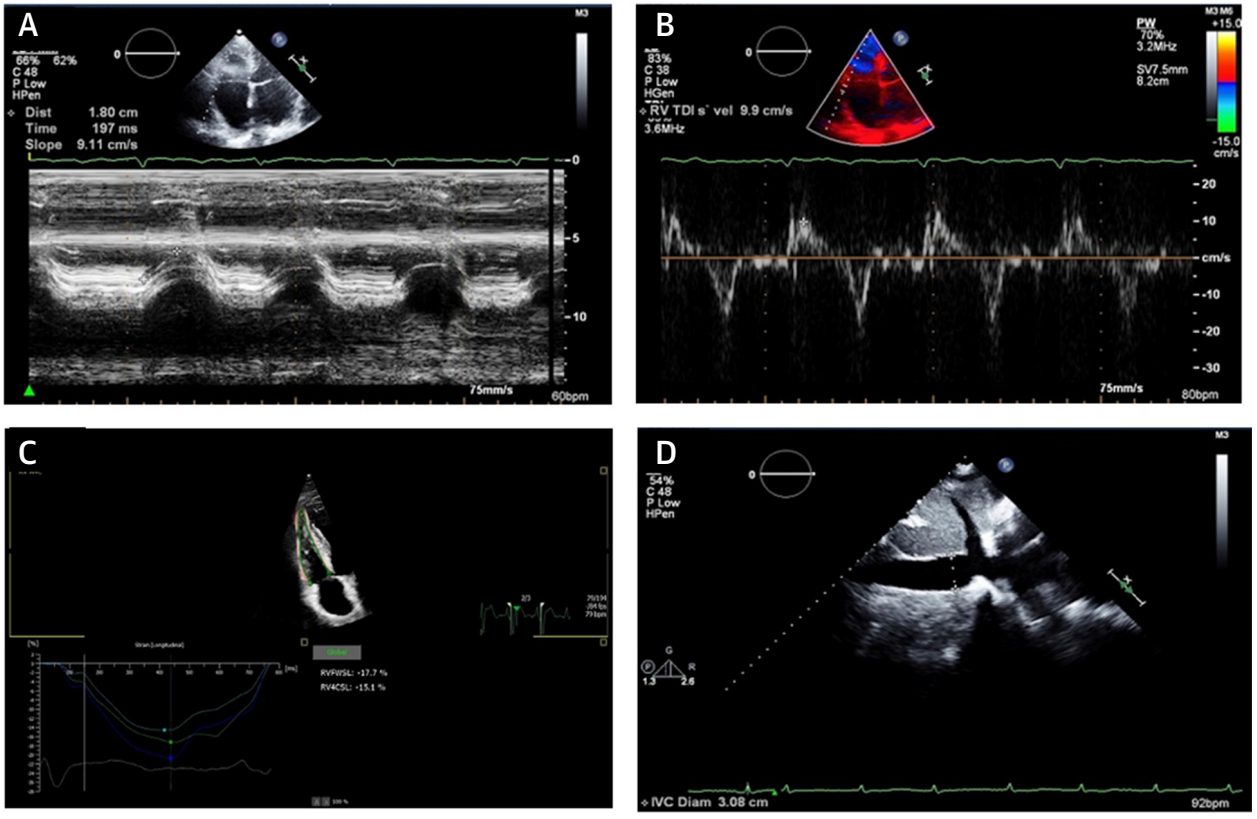
RVI: CLINICAL PRESENTATIONS

RVI typically presents with chest discomfort, although vagotonic manifestations (nausea, vomiting, and diaphoresis) may predominate.[2] In patients with inferior MI, RVI should be investigated in each and every case, first by electrocardiogram leads V3/4R (ST-segment elevation and loss of R-wave). The earliest clinical manifestation is elevated jugular vein pressure, with more severe RV dysfunction leading to frank hemodynamic compromise with systemic hypotension. When RVI develops in the setting of global LV dysfunction, the picture may be dominated by low output and pulmonary congestion, together with right heart failure. RVI may be initially hemodynamically silent, with hypotension precipitated by preload reduction attributable to nitroglycerin administration[29] or associated with bradyarrhythmias.

NONINVASIVE EVALUATION

ECHOCARDIOGRAPHY. Transthoracic echocardiography rapidly detects the presence and severity of RVI,[30] delineating RV dilation, RVFW dysfunction, diastolic reversed septal curvature, systolic paradoxical septal motion, and decreased tricuspid annular plane systolic excursion, a measure of RV systolic function (Figure 7A).[31] The RV-focused view facilitates evaluation of the RVFW and quantitation of fractional area change, tricuspid annular plane systolic excursion, systolic velocity on tissue Doppler imaging, free wall strain, and global longitudinal strain, all surrogate markers of RV function (Figures 7A to 7C). Severe RA enlargement suggests concomitant ischemic RA dysfunction, with elevated RA pressure reflected by the tricuspid E/A and the E/e' as well as intra-atrial septal bowing. These

FIGURE 7 Echocardiographic Parameters for the Evaluation of RV Function in RVI



(A) The M-mode cursor (white dashed line) aligned with the tricuspid annulus, allowing measurement of the Tricuspid Annular Plane Systolic Excursion (TAPSE) of 1.8 cm, which is lower than normal. (B) Tissue Doppler imaging (TDI) of the tricuspid annulus systolic velocity (S') of 9.9 cm/s, which is also lower than normal. (C) Right ventricular free wall strain measurement of −17.7%, which is also lower than normal and (D) plethora (dilated) inferior vena cava, which measures 3.08 cm in this patient. IVC = inferior vena cava.

features are predictive of cardiogenic shock, significant bradycardia, and higher mortality. Other important data include inferior vena cava plethora (Figure 7D) and tricuspid regurgitation. Of note, these findings are not specific for RVI, and importantly may be found in acute and chronic RV pressure overload.

In clinical practice, urgent limited echocardiography to rapidly assess RV and LV function can easily be performed as a "point-of-care" study at the bedside in the emergency room or in the catheterization laboratory without unduly delaying emergency percutaneous revascularization.

CARDIAC MAGNETIC RESONANCE. This imaging technique is the gold standard for noninvasive assessment of the RV. Late gadolinium enhancement indicative of necrosis is seen in 10% to 30% of RVI cases (Figure 8) and edema in up to 50%.[32] However, microvascular obstruction is rare.

CARDIAC COMPUTED TOMOGRAPHY. This imaging technique is crucial for evaluation of RV dysfunction in patients with acute pulmonary embolism in whom RV shock and echocardiographic findings overlap those with RVI. The presence of inferior MI by electrocardiogram is typically sufficient to establish the correct diagnosis.

INVASIVE ASSESSMENT

If echocardiography is insufficient to establish the presence of RVI, invasive hemodynamic evaluation by right heart catheterization confirms the diagnosis.[33] The hemodynamic patterns of RVI manifest in RV and RA waveforms have been previously discussed. Pulmonary artery (PA) pulse pressure reflects

RV pulsatile load and contractile strength; by normalizing it to RA pressure, this parameter thereby incorporates the influence of RV congestion. Emphasis should also be given to the pulmonary artery pulsatility index (PAPi) (PA pulse pressure systolic-diastolic)/RA pressure), an insightful parameter of RV performance.[34] The PAPi has gained significant value to risk-stratify patients with complicated RVI that may need MCS. Patients in the lowest PAPi quartile usually have significant tricuspid regurgitation and worse hemodynamic parameters of RV function. When compared with patients in the highest quartile, The PAPi is associated with moderate to severe tricuspid regurgitation. As a result, patients in the lowest PAPi quartile have a 60% higher risk of mortality and approximately twice the risk of major adverse events and heart failure hospitalization when compared with patients in the highest quartile.[35]

RVI TRIMODAL MANAGEMENT

Clinical approach to the patient with RVI can be considered according to 3 distinct time periods and hospital locales (Table 2): in the emergency department during acute coronary occlusion, in the catheterization laboratory during reperfusion interventions, and in the coronary care unit while recovery ensues.

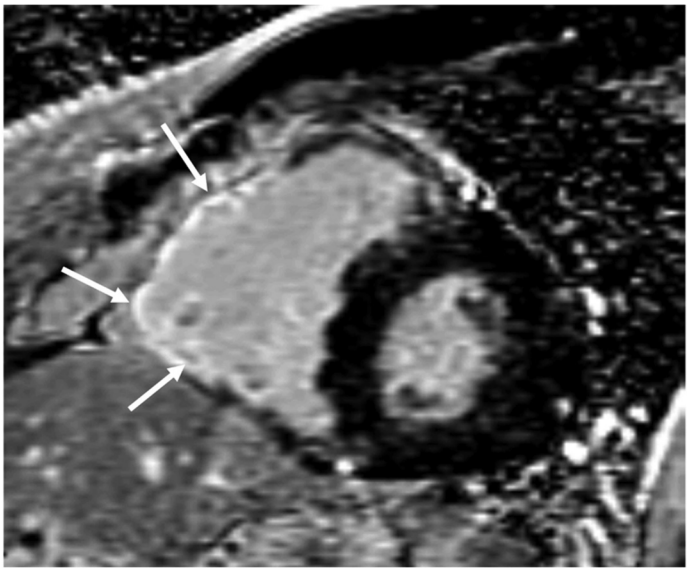
EMERGENCY ROOM

Early recognition of RVI and anticipation of its complications is key. In inferior MI, right-sided electrocardiogram leads should be standard. Recognition of clinical vagotonic stigmata, frank bradyarrhythmias-hypotension (or even sinus bradycardia alone) as well as elevated jugular venous pressure should raise suspicion. As noted, prompt bedside "point-of-care" echocardiography provides definitive insight regarding the presence of RVI as well as the status of LV ejection fraction. The importance of physiological rhythm has been discussed. Atropine should be considered for heart rate <50 beats/min even without hypotension and is the first therapy for frank bradyarrhythmias-hypotension; in some patients, transcutaneous pacing may be necessary.

OPTIMIZATION OF PRELOAD. The ischemic RV is dilated, noncompliant, and preload dependent, as is the ischemic LV, which is stiff but preload deprived. Although based on first principles it might be presumed that volume loading a distended RV would be adverse and would not by itself translate to enhanced LV filling and cardiac output. However, the detrimental effects of loss of augmented RA booster pump to RV filling have been explained as lowering the RV output generated by the compensatory LV-septal systolic interaction that generates RV power in the absence of RVFW motion, therefore optimal RV preload results in greater RV stroke volume for any given level of such systolic interaction.[9] Although experimental animal studies of RVI demonstrate hemodynamic benefit from volume loading, clinical studies have reported variable responses,[36,37] such conflicting results may reflect a spectrum of initial volume status, with patients relatively volume depleted benefiting, and those more replete manifesting a flat response. An initial volume challenge is reasonable for hypotension without pulmonary congestion, if the jugular vein pressure is <15 mm Hg. However, caution should be exercised to avoid excessive volume administration, because overdistension of the ischemically dilated RV may propel it to the "descending limb" of the Starling curve, resulting in further depression of RV pump performance as well as inducing severe systemic venous congestion. Abnormalities of volume retention and impaired diuresis may be related in part to impaired responses of atrial natriuretic factor.[38]

HEMODYNAMIC SUPPORT. In the emergency department, for hypotension not responsive to atropine and

FIGURE 8 CMR Imaging for RVI



Delayed enhancement cardiac magnetic resonance (CMR) imaging showing the infarcted RV wall (white arrows) and the dilated RV compared with the left ventricle. Abbreviations as in Figure 2.

TABLE 2 Inferior Myocardial Infarction-Right Ventricular Infarction: Trimodal Management Strategies

Emergency department
Delineate RVI: ECG V3/V4R
Point-of-care 2D echo: assess RV and LV function
Standard STEMI Rx: ASA and heparin; avoid IV NTG and BB
Establish physiologic rhythm: atropine, transcutaneous pacing
Optimize preload
Inotropes/vasopressors for low output-hypotension
Catheterization laboratory
Femoral venous access: "readiness" for TVP, inotropes/vasopressors
Restoration of coronary flow: primary catheter techniques
Consider catheter aspiration for extensive RCA thrombus
Anticipate reperfusion Bezold-Jarisch reflex bradycardia-hypotension
Persistent hemodynamic compromise
Hemodynamic monitoring via right heart catheter
Inotropes/Vasopressors
Mechanical support for persistent hypotension
Biventricular support based on echo and invasive hemodynamics
Coronary care unit
Hemodynamically stable, arrhythmia-free, intact LVEF: rapid ambulation
Persistent low output-hypotension:
Mild: brief but tapering inotropes/vasopressors
Severe, or escalating-prolonged pharmacological support: MCS

ASA = aspirin; BB = beta-blockers; ECG = electrocardiogram; IV = intravenous; LV = left ventricle; LVEF = left ventricular ejection fraction; MCS = mechanical circulatory support; NTG = nitroglycerine; STEMI = ST-segment elevation myocardial infarction; RCA = right coronary artery; RV = right ventricle; RVI = right ventricular infarct; TVP = transvenous pacemaker.

restoration of physiologic rhythm, pharmacological support should be promptly initiated with an agent that exerts sufficient vasopressor and inotropic effects to restore aortic perfusion pressure. The comparative benefits of pharmacological agents have been studied in LV shock, evidence showing norepinephrine conferring greater survival benefit compared with dopamine.[39] There is a paucity of data to inform the choice of drugs in predominant RV shock. The "pure" inotropic agents milrinone and dobutamine exert inotropy without vasopressor effects, and whereas both appear equally effective in RV shock,[40] they may not be sufficiently reliable to augment profoundly depressed aortic pressure. Further, the hypotensive effects of milrinone and dobutamine could be magnified in patients with RVI in whom there is failure to increase the LV preload.

First principles of cardiogenic shock dictate rapid stabilization of aortic pressure; therefore, an agent that exerts alpha agonist vasopressor properties together with inotropic properties (norepinephrine and dopamine) should be the initial agents of choices. The mechanisms by which inotropes improve low output and hypotension in RVI have been studied in experimental models of RVI, such observations documenting that inotropic stimulation of LV-septal mediated systolic ventricular interactions enhances RV performance, not via augmented RVFW contraction per se.[9] It is also important to consider the potentially beneficial effects of selective pulmonary vasodilators such as inhaled nitric oxide and prostanoids.

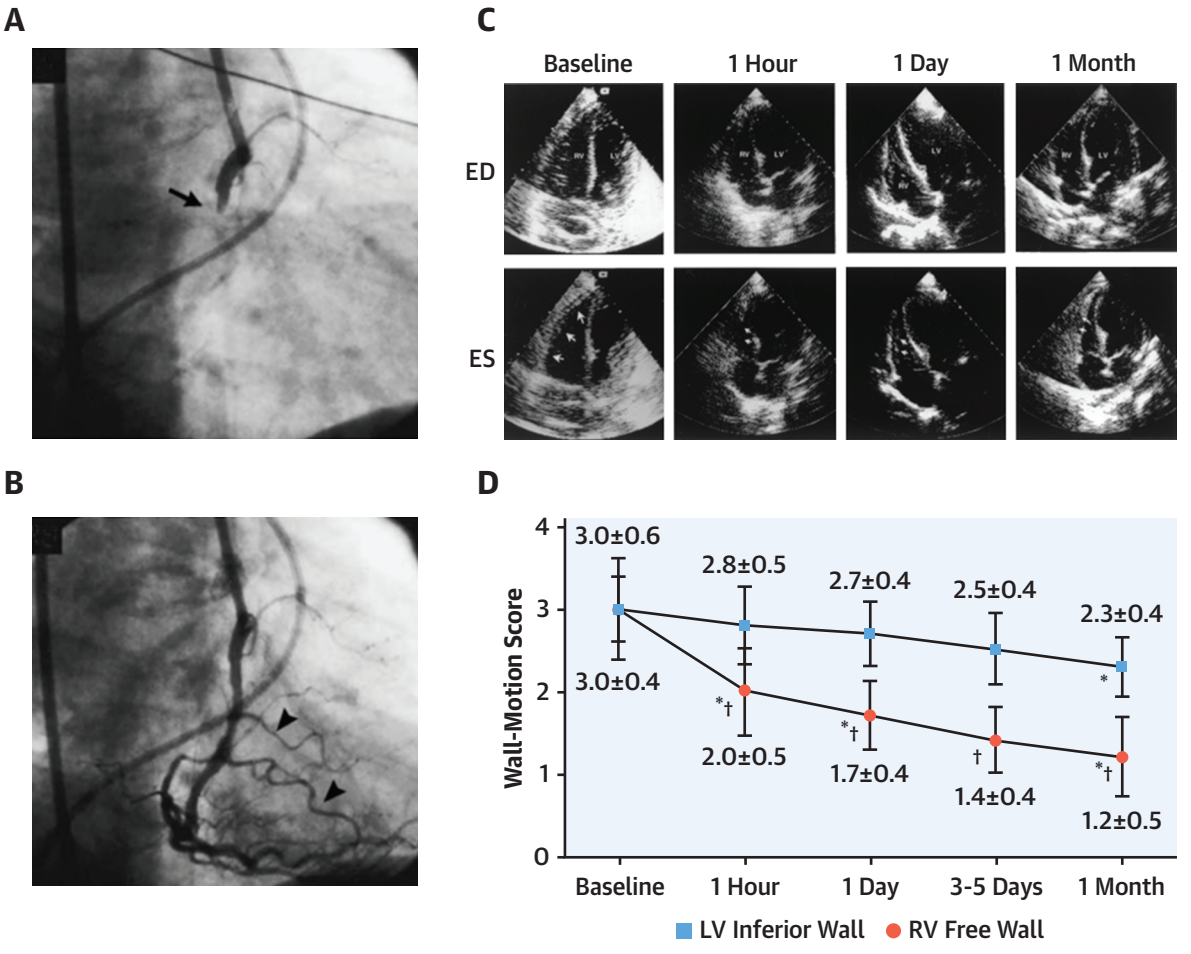
CATHETERIZATION LABORATORY

PREREPERFUSION. The interventional cardiologist must be prepared for the distinct arrhythmic complications of proximal RCA occlusion, as well as the hemodynamic consequences of RVI per se. In those with frank bradyarrhythmias, transvenous pacing is necessary. Further, even in the absence of frank bradycardia, anticipation of adverse reperfusion reflexes should prompt consideration of preemptive placement of a venous sheath to facilitate rapid transvenous pacing deployment and administration of parenteral vasopressors should they be necessary. RVI resulting in marked hypotension may require hemodynamic support before or after reperfusion, initially with pharmacological therapy. For refractory patients, MCS (to be discussed) may be needed.

REPERFUSION. In acute RVI, the salutary effects of reperfusion on recovery of RV performance, hemodynamics, and clinical outcomes are well established.[5] Observations in experimental animal models document rapid and complete recovery of RV function even after prolonged occlusions.[41] In RVI, primary percutaneous coronary intervention mediated successful complete reperfusion of the main RCA resulting in restoration of flow to the major RV branches similarly leads to immediate improvement in and later complete recovery of RVFW function (**Figure 9**) and consequently excellent clinical outcome (**Figure 10**). In contrast, failure to restore flow to the major RV branches is associated with lack of early recovery of RV performance associated with refractory hemodynamic compromise leading to high in-hospital mortality, even with successful reperfusion of the main RCA (**Central Illustration**). These findings emphasize the crucial relationship between reperfusion-mediated recovery of RV performance and clinical outcome.

Recovery of the RV even after prolonged ischemia occlusions differs strikingly from that of the LV, which suffers irreversible necrosis after ischemic insults of similar duration.[42] These disparate responses of the ventricles is emphasized by clinical observations documenting reperfusion-mediated complete recovery of RVFW motion, but persistent dysfunction in the concomitantly injured LV inferior wall

FIGURE 9 Recovery of RV Function After Successful Reperfusion

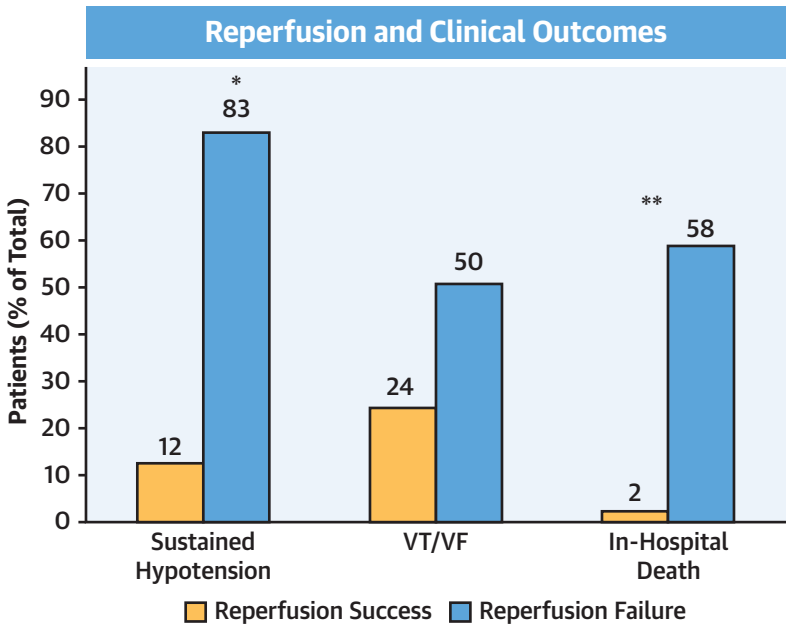


Patient with acute inferior myocardial infarction and RVI due to proximal RCA occlusion compromising RV branches (A, arrow), with successful primary reperfusion restoring flow to the RV (B, arrow) as well as LV branches. Echocardiographic images at baseline show severe RV dilation with reduced LV end-diastolic (ED) size (C). In systole, there was right ventricular free wall (RVFW) end-systolic (ES) dyskinesis (C, arrows), intact LV function, and compensatory paradoxical septal motion. One hour after reperfusion there was striking recovery of RVFW contraction (arrows), resulting in marked improvement in global RV performance and markedly reduced RV size and increased LV preload. At 1 day, there was further improvement in RV function (arrows), which at 1 month was normal. Bar graph comparing differential recovery of RVFW vs LV inferior wall following successful reperfusion (D). The RVFW recovers more rapidly and completely than the corresponding LV wall exposed to the same ischemic insult (wall motion score 1 = normal, 4 = dyskinetic). Reproduced with permission by Bowers et al.[5] Abbreviations as in Figure 2.

(Figure 9).[5] RV resilience has been demonstrated under conditions of chronic proximal RCA occlusion. In experimental animal models, collateralization promotes complete recovery of RV performance with trivial pathological evidence of infarction.[43] Clinically, even in those without successful reperfusion, in those surviving the acute complications, over time RV function returns to near normal at rest and with exercise.[44] Remarkably, chronic right heart failure attributable only to RVI is rare. Taken together, these results support the notion that the term RV "infarction" is largely a misnomer, the acutely ischemic RV is predominantly viable. RV resilience is undoubtedly attributable to more favorable O_2 supply-demand characteristics.

COMPLICATIONS DURING REPERFUSION. It is essential to recognize the potential abrupt complications associated with recanalization of the thrombotically occluded RCA. Such vessels may harbor extensive clot burden, the presence of which increases risks for no-reflow, which can be destabilizing and refractory, resulting in persistent RV dilation and

FIGURE 10 RVI: Superior Clinical Outcomes After Successful Reperfusion



Bar graphs demonstrating benefits of successful reperfusion vs reperfusion failure with respect to reduced arrhythmias, sustained hypotension, and in-hospital survival. Adapted from data in Bowers, et al.[5] *$P < 0.002$. **$P < 0.001$. VT/VF = ventricular tachycardia/ventricular fibrillation; other abbreviation as in Figure 2.

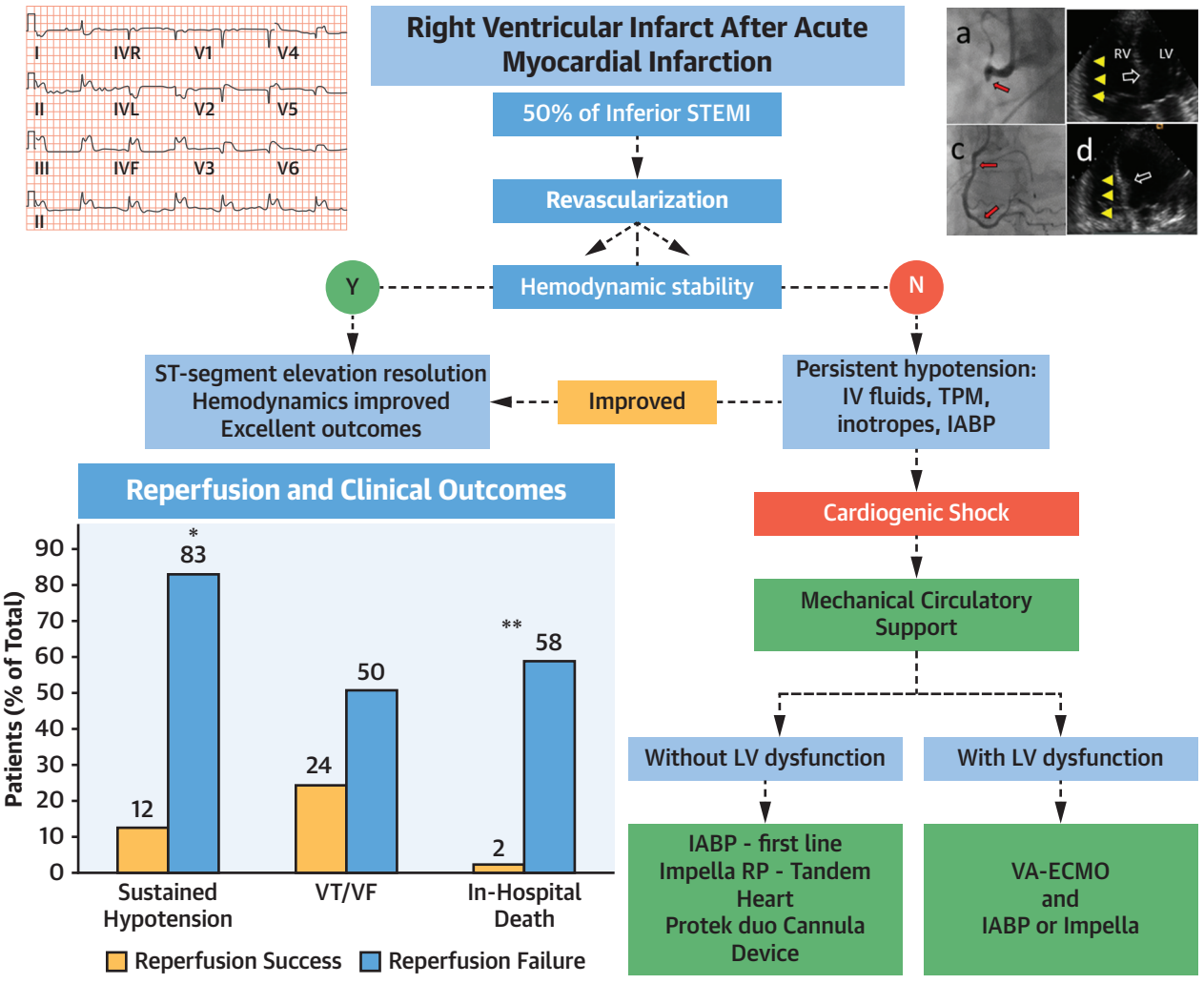
dysfunction associated with slower hemodynamic recovery. Although aspiration thrombectomy in MI is not routinely recommended, the presence of extensive coronary clot constitutes a reasonable and appropriate indication. In some cases, administration of intracoronary "no-reflow" medications may be necessary. Further, the interventionist must be prepared for reperfusion-induced reflex bradycardia-hypotension, most commonly seen abruptly following otherwise successful recanalization of proximal RCA occlusions;[21,22] this phenomenon is typically brief, but can be profoundly destabilizing. In anticipation, established venous access facilitates support with transvenous pacemaker and parenteral vasopressors.

PERSISTENT HEMODYNAMIC COMPROMISE: ROLE OF MECHANICAL CIRCULATORY SUPPORT

The advent of MCS support has transformed the management and outcomes of patients with RV as well as LV shock. Patients with acute MI resulting in severe hemodynamic compromise benefit from a "team approach,"[45-47] with a focus on invasive hemodynamic evaluation and utilization of MCS. Depending on the patient phenotype, the selection of MCS is informed by the severity of hemodynamic compromise, as well as need for monoventricular or biventricular support. The objective is to relieve congestion and improve cardiac output. RV preload, afterload, contractility, and the need for respiratory support are key. As some devices may increase systemic afterload, ventricular interdependency must be carefully considered to alleviate side effects and optimize performance. In aggregate, these considerations influence the selection of the MCS device most appropriate for an individual patient. Most commonly used devices include intra-aortic balloon pumping (IABP), Impella, Tandem Heart/Protek duo, and extracorporeal membrane oxygenation (ECMO).

INTRA-AORTIC BALLOON PUMPING. In "all-comers" with MI suffering cardiogenic shock, IABP use has not improved survival.[48] However, in select cases of RVI, utilization of IABP support can promptly stabilize aortic pressure.[49] The salutary effects of IABP on the RV are mediated by improving coronary perfusion, decreasing LV load, and enhancing LV-septal contractile contributions. IABP may be most appropriate as an initial stabilization step for "milder" cases of persistent hypotension and may be sufficiently

CENTRAL ILLUSTRATION Right Ventricular Infarct After Acute Myocardial Infarction



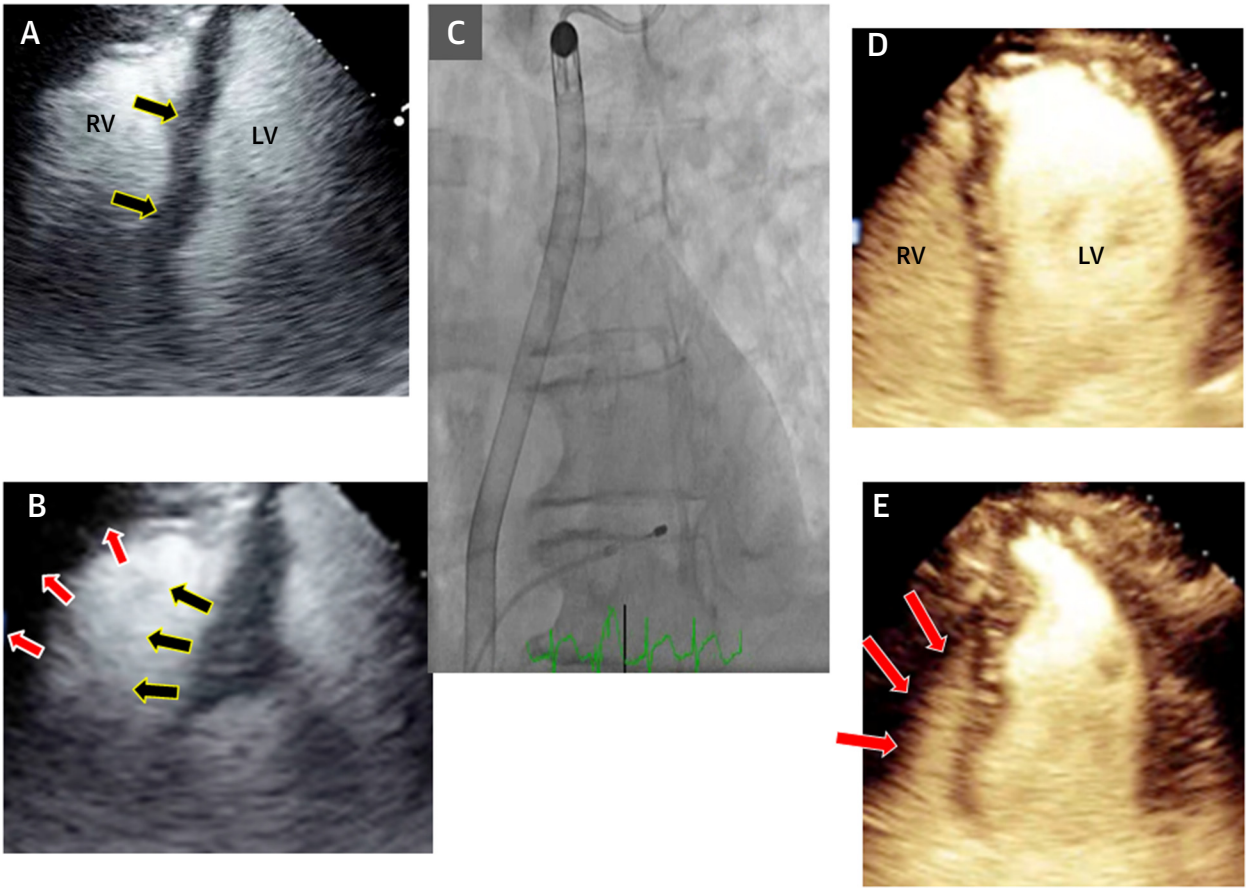
Goldstein JA, et al. J Am Coll Cardiol. 2024;83(18):1779–1798.

Revascularization with resolution of ST-segment elevation reduces sustained hypotension, malignant arrhythmias, and in-hospital death. Persistent hypotension and cardiogenic shock may require escalation of therapy, including right ventricular assist devices for clinical stabilization and preservation of end-organ perfusion. *$P < 0.002$. **$P < 0.001$. IABP = intra-aortic balloon pump; IV = intravenous; LV = left ventricle; RV = right ventricle; STEMI = ST-segment elevation myocardial infarction; TPM = temporary pacemaker; VA-ECMO = veno-arterial extracorporeal membrane oxygenation.

temporizing while RV and hemodynamic recovery ensues. As IABP efficacy depends on effective intra-aortic volume displacement, a certain degree of biventricular hydraulic power is needed to generate an appropriate ejection. In patients with chronic decompensated heart failure, LV power index >0.33 W/m^2 and RV cardiac power index >0.13 W/m^2 did better compared with patients with profound biventricular failure.[50] As such, IABP is not best suited for severe cases of RVI.

PERCUTANEOUS RV ASSIST DEVICES. The advent of dedicated percutaneous RV mechanical assist devices (pRVAD) has dramatically advanced the portfolio of hemodynamic support for more hemodynamically severe RVI, particularly refractory RV shock[45-47,51-58] (**Central Illustration**). pRVADs unload the dilated failing RV and directly generate RV output, and thereby reduce RA pressure, increase mean PA pressure, and augment transpulmonary delivery of LV preload. In the presence of preserved LV function,

FIGURE 11 RVAD Bridge for Persistent RV Shock Despite Successful Reperfusion



Acute RVI with persistent severe hypotension despite successful reperfusion. Postreperfusion echocardiographic images demonstrating persistent severe RV dysfunction characterized in diastole by persistent severe RV dilation with reversed septal curvature (A, yellow arrows) and severe systolic impairment with RVFW dyskinesis (B, open red arrows) and paradoxical septal motion (yellow arrows). Mechanical RV assist was instituted with Impella RP (C) resulting in increased stabilized hemodynamics with weaning of support over 48 hours as RV function completely recovered as indicated by normalization of RV diastolic size (D) and improved RVFW and global RV function (E). RVAD = right ventricular assist device; RVFW = right ventricular free wall; other abbreviations as in Figure 2.

cardiac output will increase while LV filling pressures will be normalized or remain unchanged. Although there are not well-established criteria for the initiation of pRVAD, these devices are indicated in patients with evidence of poor organ perfusion, a cardiac index of <2.2 L/min/m^2, a PAPi of <1.0, or a cardiac power output of <0.6.[45-47] Additional clinical considerations influencing the selection of pRVAD, device, and mode include the ventricle(s) that needs support, oxygenation, and local expertise. The escalation to pRVAD therapy, device selection and management benefit from the Heart Team approach.[45]

THE IMPELLA DEVICE. The percutaneous catheter-based Impella RP micro-axial pump (Impella RP, and Impella RP Flex, Abiomed Inc) provides direct RV bypass, drawing inflow from the inferior (RP) or superior (RP Flex) vena cava and outflow in the PA, generating up to 4.0 L/min of output.[51-53] The Impella RP is composed of a 22-F impeller bypassing blood from the cava system to the PA, bypassing the RV, and is usually inserted through a 23-F venous via transfemoral access. It promptly improves hemodynamics by direct combined unloading effects and RV output power, resulting in rapid decrement in central venous pressure and concomitant increment in cardiac index,[51-53] which thereby provides a hemodynamic "bridge to recovery" (Figure 11). The Impella RP Flex, an 11-F device, inserted via internal jugular access, exerts similar salutary hemodynamic effects while allowing for patient mobility.

The efficacy of the Impella RP device was first established by the prospective, multicenter, randomized RECOVER RIGHT (The Use of Impella RP Support System in Patients With Right Heart Failure) trial in patients with predominant RV shock due to RVI, postcardiotomy, or after LV assist device implantation.[51] The Impella RP resulted in immediate hemodynamic benefit and a 73% survival at 30 days. The most common adverse events were bleeding (60%) and hemolysis (13.3%). A subsequent prospective study of 60 patients with RV failure showed similar hemodynamic improvement and favorable survival at the time of discharge or after 30 days.[52]

THE TANDEM HEART/PROTEK DUO CANNULA DEVICE. The extracorporeal centrifugal flow Tandem Heart/Protek Duo support device (TandemLife) is an indirect RV bypass system delivered via the internal jugular vein and consisting of a dual-lumen catheter with inflow cannula drain from the RA into an extracorporeal centrifugal pump, which delivers blood back to the PA.[54] The system is based on a dual-lumen cannula for RV support, but there are 2 different types, the RA-PA dual cannula (ProtekDuo) and the RA/RV-PA dual cannula (Spectrum), each specifically designed to achieve distinctly different hemodynamic effects, depending on whether the patient has isolated RV failure or biventricular failure. Blood is removed from the proximal port (either RA or RA/RV) and returned distal from the pulmonic valve bypassing the RV. Furthermore, venous-venous extracorporeal oxygenation may be added if needed. The Tandem Heart pRVAD showed hemodynamic improvement within 48 hours, with best results in patients with RVI, and may improve survival rates.[54]

EXTRACORPOREAL MEMBRANE OXYGENATION DEVICE. Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) addresses both RV and LV dysfunction, systemic oxygenation, and acid-base balance via modulation of the partial pressure of CO_2. The device improves systemic arterial flow by unloading the right side of the heart.[54] The circuit employs a centrifugal pump such as the Centrimag (Thoratec), Rotaflow (Maquet), or TandemHeart (TandemLife) and a blood-gas exchange unit that includes a heat exchanger and a membrane oxygenator. As the blood transits through the membrane oxygenator, hemoglobin becomes fully saturated with oxygen and carbon dioxide is removed. The degree of oxygenation is determined by the flow rate and fraction of inspired oxygen. The circuit configuration permits the withdrawal and pumping of desaturated blood from the RA or a central vein, with non-pulsatile pump outflow directed toward the membrane oxygenator then guided via an outflow cannula to a systemic artery (eg, femoral or subclavian artery). Notably, VA-ECMO increases LV afterload, as reflected by the increase on effective arterial elastance. This contributes to an increase in LV filling pressures. In patients with significantly reduced ejection fractions at baseline, VA-ECMO may thereby increase wall stress and oxygen demand, which impedes myocardial recovery and may precipitate progressive pulmonary edema and acute lung injury. In these cases, strong consideration of biventricular mechanical support devices is mandatory.[56,57]

The application of these MCS devices in RVI can be summarized as follows: 1) RVI with mild hypotension, IABP may suffice; 2) severe predominant RV shock with preserved LV function, pRVAD alone; 3) RVI with shock due to biventricular failure, pRVAD and LV Impella indicated; and 4) profound hemodynamic collapse together with poor oxygenation, consider VA-ECMO. In this setting, the concomitant use of VA-ECMO and Impella (ECMELLA) provides a synergistic approach to simultaneously reduce LV filling pressures and improve cardiac output.[56,57]

WEANING AND COMPLICATIONS

Once the mechanisms responsible for right ventricular failure are under control, the hemodynamic parameters usually improve. At that time, consideration for de-escalation or weaning is appropriate. Recovery and anticipation to wean are indicated by reduction in central venous pressure, and improvements of PAPi, cardiac index, and RV systolic function, together with lesser requirements for pharmacologic support. Other parameters of interest include annular S'/systolic PA pressure (>0.33), a surrogate of RV to pulmonary circulation coupling.[58]

Major procedural complications of pRVAD are common to other such devices for the LV and include bleeding and perforation, dislocation, hemolysis, and consumed coagulopathy. Less frequently, differential hypoxemia, valvular damage, or limb ischemia are also seen.

CORONARY CARE UNIT

Recovery in the unit is determined by the status of RV and LV function. Following successful reperfusion, bradyarrhythmias including AV block typically resolve promptly. Hemodynamic compromise typically stabilizes and typically the RV recovers rapidly. Recurrent ventricular tachycardia/ventricular fibrillation can usually be suppressed with amiodarone and typically abates when reperfusion-mediated recovery lessens RV dilation. Thus, in most cases, the subsequent

course is smooth and short, and late prognosis excellent.[4] Even in those with marked hemodynamic instability, pharmacological and/or mechanical support is usually a sufficient "bridge" to recovery of RV function with resultant hemodynamic stabilization.

Finally, in RVI with severe hemodynamic compromise exacerbated by concomitant severe LV systolic dysfunction, early institution of biventricular mechanical support is essential and in those with severe multivessel coronary disease more complete revascularization may be beneficial.

CONCLUSIONS

Acute RCA occlusion proximal to the RV branches results in RVFW dysfunction. The ischemic, dyskinetic RVFW exerts mechanically disadvantageous effects on biventricular performance. Depressed RV systolic function leads to a decrease in transpulmonary delivery of LV preload, resulting in diminished cardiac output. The ischemic RV is stiff, dilated, and volume-dependent, resulting in pandiastolic RV dysfunction and septally mediated alterations in LV compliance, which are exacerbated by elevated intrapericardial pressure. Under these conditions, RV pressure generation and output are dependent on LV-septal systolic contributions mediated by paradoxical septal motion. When the culprit coronary lesion is distal to the RA branches, augmented RA contractility enhances RV performance and optimizes cardiac output. Conversely, more proximal occlusions result in ischemic depression of RA contractility, which impairs RV filling, thereby resulting in further depression of RV performance and more severe hemodynamic compromise. Bradyarrhythmias limit the output generated by the rate-dependent noncompliant ventricles. Patients with RVI and hemodynamic compromise may respond to gentle volume resuscitation and restoration of a physiologic rhythm. In some, parenteral inotropic/vasopressor support may be required. Beta-blockers and intravenous nitroglycerine should be avoided. The RV is remarkably resistant to ischemic injury and has a remarkable ability to recover even after prolonged occlusion. Therefore, the term RV "infarction" is largely a misnomer, the acutely ischemic RV predominantly viable and resilient. Although RV performance improves spontaneously even in the absence of reperfusion, recovery of function may be slow and associated with high in-hospital morbidity and mortality. Reperfusion enhances the recovery of RV performance and improves the clinical course and survival. Mechanical support may serve as a critical "bridge to recovery" in those with severe and refractory RV shock.

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