

# Prognostic impact of right ventricular involvement in patients with acute myocardial infarction: Meta-analysis

Martial Hamon, MD; Denis Agostini, MD, PhD; Olivier Le Page, MD; John W. Riddell, MD; Michèle Hamon, MD

## LEARNING OBJECTIVES

On completion of this article, the reader should be able to:

1. Describe the criteria to identify patients with acute myocardial infarction who have right ventricular involvement.
2. Explain the impact of right ventricular involvement on outcomes of acute myocardial infarction.
3. Use this information in a clinical setting.

The authors have disclosed that they have no financial relationships with or interests in any commercial companies pertaining to this educational activity.

All faculty and staff in a position to control the content of this CME activity have disclosed that they have no financial relationship with, or financial interests in, any commercial companies pertaining to this educational activity.

Lippincott CME Institute, Inc., has identified and resolved all faculty conflicts of interest regarding this educational activity.

Visit the *Critical Care Medicine* Web Site ([www.ccmjournal.org](http://www.ccmjournal.org)) for information on obtaining continuing medical education credit.

**Objective:** The objective of this study was to examine the relationship between right ventricular involvement (RVI) in acute myocardial infarction (AMI) and the increase in mortality and morbidity frequently suggested in the last two decades.

**Design:** The authors conducted a systematic review and meta-analysis.

**Setting:** This study was conducted at an academic medical center.

**Data Source:** The authors reviewed PubMed, BioMedCentral, and the Cochrane database and conducted a manual review of article bibliographies.

**Study Selection and Data Extraction:** Using a prespecified search strategy, 22 relevant studies involving a total of 7,136 patients with AMI at baseline, of whom 1,963 had RVI (27.5%), were included in a meta-analysis using a random effects model. Pooled relative risks of the impact of RVI on patient mortality and morbidity were calculated.

**Main Results:** An overall pooled relative risk mortality increase of 2.59 (95% confidence interval, 2.02–3.31) was found ( $Z = 7.57$ ;  $p < .00001$ ). RVI in AMI was also associated with a statistically significant increase in all secondary end points assessed, including cardiogenic shock, ventricular arrhythmias, advanced atrioventricular block, and mechanical complications.

**Conclusions:** Our results support the view that early recognition of RVI, namely by means of right electrocardiographic leads in acute myocardial infarction, may have prognostic value. Whether or not this recognition will permit improvement of outcomes through more aggressive percutaneous coronary intervention would need to be tested in future studies. (*Crit Care Med* 2008; 36:2023–2033)

**KEY WORDS:** Acute myocardial infarction; right ventricular infarction; mortality; meta-analysis

The relationship between right ventricular involvement (RVI) in acute myocardial infarction (AMI) and the increase in mortality and morbidity has frequently been

suggested in the last two decades (1–22). However, the magnitude of this increased risk has been debated. Some authors suggest that risk increases in relation to the baseline characteristics of the study popu-

lation, namely in relation to the advanced age (15, 16, 18–20). Other studies have found that the increased mortality may be restricted to patients with atrioventricular block (6, 9). More recently, the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications risk score, which predicts mortality after primary percutaneous coronary intervention (PCI) for AMI, did not report RVI as an independent risk factor for increased mortality (23). It remains unclear whether the worse prognosis of patients with RVI observed by some authors is simply related to the more extensive left ventricular infarction or is the result of the RVI itself. Be-

### \*See also p. 2194.

Cardiologist (Ma.H.), Department of Cardiology, University Hospital of Caen & INSERM 744, Institut Pasteur de Lille, Caen, France; Nuclear Physician and Cardiologist (DA), Department of Nuclear Medicine, University Hospital of Caen, Caen, France; Cardiac Surgeon (OLP), Department of Cardiac Surgery, University Hospital of Caen, Caen, France; and Radiologist (Mi.H.), Department of Radiology, University Hospital of Caen, Caen, France; and Cardiologist (JWR), Altnagelvin Hospital, Londonderry, UK.

The authors have not disclosed any potential conflicts of interest.

For information regarding this article, E-mail: [hamon-m@chu-caen.fr](mailto:hamon-m@chu-caen.fr)

Copyright © 2008 by the Society of Critical Care Medicine and Lippincott Williams & Wilkins

DOI: 10.1097/CCM.0b013e31817d213d

cause right ventricular ejection fraction has been shown to be a predictor of survival in heart failure independent of, and additive to, left ventricular dysfunction, it is plausible that RVI can significantly affect prognosis after AMI (24).

To elucidate the prognostic significance of RVI in AMI, we have conducted a systematic review and meta-analysis.

## METHODS

The report of this meta-analysis is in accordance with "Meta-Analysis of Observational Studies in Epidemiology: A Proposal for Reporting" (25).

### Study Selection and Data Collection

Relevant studies were identified by systematic searches of the scientific literature for all reported observational studies of AMI and RVI. The databases searched to find articles were PubMed, Cochrane library, and BioMedCentral. Ideally, AMI in the included studies should be defined according to the World Health Organization criteria, but we included studies that gave no explicit definition of AMI (26). Any study, either prospective or retrospective, assessing the impact of RVI in patients with AMI was included if: a) right ventricular infarction or involvement was assessed by means of specific electrocardiographic leads (including V4R) and/or echocardiography or with established radionuclide techniques; b) in-hospital and/or more follow-up was ensured; and c) the study reported all-cause mortality as an outcome measure. Studies focusing on the specific subgroup of patients in cardiogenic shock at hospital arrival were excluded from our review.

The search was not restricted to English language articles and included all articles up to June 2007. The search strategy used both key words and the MeSH term searches for AMI, RVI, and mortality or prognosis and took the form of the following protocol in PubMed database: (acute [all fields] AND ("myocardial infarction" [MeSH terms] OR myocardial infarction [text word]) AND (right [all fields] AND ("heart ventricles" [all fields] OR "heart ventricles" [MeSH terms] OR ventricular [text word]) AND ("infarction" [MeSH terms] OR infarction [text word]) AND ("mortality" [sub-heading] OR "mortality" [MeSH terms] OR mortality [text word]) OR ("prognosis" [MeSH terms] OR prognosis [text word])). To identify additional studies, reference lists of retrieved articles were inspected.

Based on careful study of the abstracts of identified articles, studies were excluded if the inclusion criteria were clearly not met. Two

reviewers (MH and MH) independently assessed studies to determine eligibility and independently carried out data extraction using a standardized form. Any discrepancy was resolved by consensus.

### Outcome Measures

The primary outcome was in-hospital total mortality rate comparing patients with AMI with and without RVI. Secondary outcomes included any further cardiovascular event either fatal or nonfatal: cardiogenic shock, sustained ventricular tachycardia or ventricular fibrillation, advanced atrioventricular block, and mechanical complications.

### Criteria to Assess Quality

Unlike randomized, controlled trials, no generally accepted lists of appropriate quality criteria for observational studies are available. Rather than producing a simple arbitrary quality score, specific quality aspects were used to assess the studies such as control of confounding factors, minimization of selection bias, method used for the diagnosis of RVI in AMI, the reperfusion treatment used, if any, the year of publication, and the sample size.

Assessing control of confounding factors was carried out independently by two reviewers using prespecified criteria. These criteria included age, gender, reperfusion treatment, coronary heart disease risk factors, history of previous myocardial infarction, comorbidities, and severity of the AMI (left ventricular ejection fraction). Control of confounding factors

was classified as poor if little or no attempt was made to measure or control for known basic confounders such as age and gender. Adequate control considered at least these basic confounders, and good control considered the majority of the clinical variables previously mentioned.

### Data Synthesis and Statistical Analysis

Studies were pooled using the DerSimonian and Laird random-effects model. The weighted mean difference and 95% confidence interval were used for continuous variables. Heterogeneity between studies was analyzed with chi-square and  $I^2$  statistics. Statistically significant heterogeneity was considered present at  $p < .10$  and  $I^2 > 50\%$ . Pooled relative risks were reported with 95% confidence intervals. Statistical significance was set at the .05 level on the basis of two-way Z-tests. Publication bias was explored visually by using funnel plot constructions both for prospective and retrospective studies. A sensitivity analysis was carried out using the following criteria: a) a sample size of at least 150 patients at baseline; b) prospective study; and c) with immediate RVI diagnosis based on electrocardiogram and/or echocardiography at admission. Other sensitivity analyses included separate analyses performed on prospective and retrospective studies and according to quality of control of confounding factors. All analyses were carried out using RevMan 4.2.9 software (27).

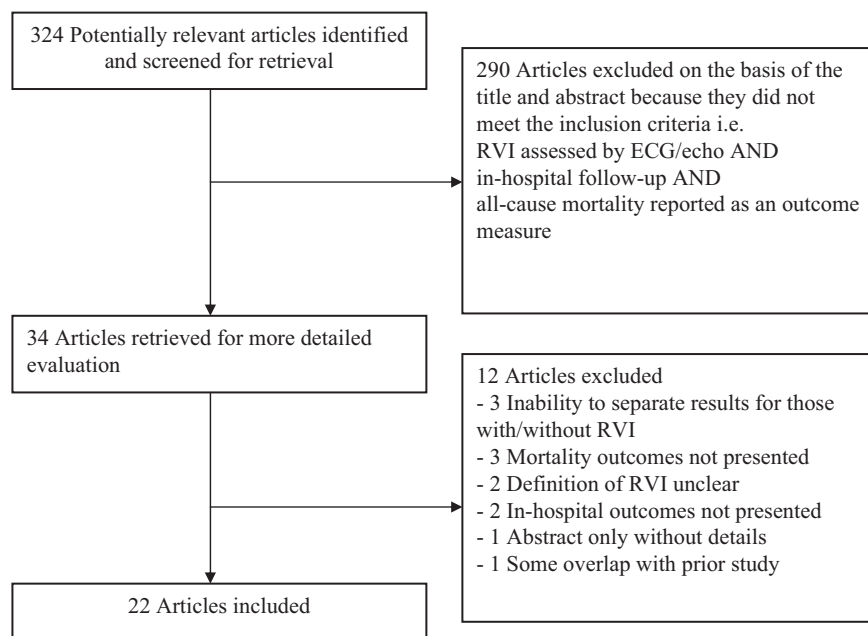


Figure 1. Flow chart of the study selection process. RVI, right ventricular involvement; ECG, electrocardiogram; echo, echocardiogram.

Table 1. Characteristics of the included studies

Study	Total Patients	Sex, (% male)	Age (Mean yrs)	Years of Enrollment	RVI Diagnostic	Follow-up	Study Results
Prospective Berger et al., 1993 (1)	1,110	87	56	1990	Radionuclide ventriculogram	1 year	RV dysfunction occurs infrequently after thrombolytic therapy of patients with AMI. Among surviving patients who undergo predischARGE radionuclide ventriculography, RVI is not associated with increased mortality in the following year
Giannitsis et al., 2000 (2)	88	—	62	1999	ECG with ST-segment elevation $\geq 0.1$ mV in V <sub>3R</sub> or V <sub>4R</sub> lead	In-hospital 10 days	Patients with RVI had larger infarct sizes, more frequent AV block but similar in-hospital mortality compared to patients without RVI
Haines et al., 1985 (3)	74	88	52	1984–1985	Right ventricle scintigraphy	In-hospital 5 years	RV dysfunction after inferior MI is not associated with higher risk for recurrent cardiac events
Khan et al., 2004 (4)	100	86	56	2000–2001	ECG with ST-segment elevation $\geq 0.1$ mV in V <sub>3R</sub> or V <sub>4R</sub> lead	In-hospital	RVI was associated with increased morbidity and mortality in patients with inferior MI
Marwick et al., 1991 (5)	168	72	60	1988–1990	Radionuclide ventriculography	In-hospital 1 year	RVI is an independent adverse prognostic factor in patients with inferior MI particularly in those with impaired left ventricular function
Mavric et al., 1990 (6)	243	68	64	1987–1988	ECG with ST-segment elevation $\geq 0.1$ mV in V <sub>3R</sub> or V <sub>4R</sub> lead	In-hospital	RVI is associated with a higher mortality in patients with complete atrioventricular block
Mehta et al., 2001 (7)	1129	76	59	1995–1996	ECG with ST-segment elevation $\geq 0.1$ mV in V <sub>4R</sub> lead	In-hospital	Patients with inferior MI and RVI were at increased risk of death, shock and arrhythmias independently of left ventricular infarct size
Pereira et al., 2006 (8)	183	69	—	1998–2000	ECG with ST-segment elevation $\geq 0.1$ mV in V <sub>3R</sub> or V <sub>4R</sub> lead	In-hospital	Higher rates of heart failure, electrical and hemodynamic complications, and death in patients with RVI
Ramires et al., 1993 (9)	107	85	64	1990–1991	ECG with ST-segment elevation $\geq 0.1$ mV in V <sub>3R</sub> or V <sub>4R</sub> lead and/or right ventricle scintigraphy	In-hospital	Infarct extension from inferior wall to the right ventricle is associated with atrioventricular block and does not increase mortality
Rodrigues et al., 1986 (10)	51	75	59	1985–1986	ECG with ST-segment elevation $\geq 0.1$ mV in V <sub>3R</sub> or V <sub>4R</sub> lead and Radionuclide ventriculogram	In-hospital 2 months	RVI persists after inferior MI and is associated with considerable morbidity and mortality
Zehender et al., 1993 (11)	200	76	62	1985–1990	ECG with ST-segment elevation $\geq 0.1$ mV in V <sub>4R</sub> lead	In-hospital	RVI during AMI, accurately diagnosed by ST-segment elevation in lead V <sub>4R</sub> , is a strong, independent predictor of major complications and in-hospital mortality
Zeymer et al., 1998 (12)	522	76	60	1996	ECG with ST-segment elevation $\geq 0.1$ mV in V <sub>4R</sub> lead	30 days	Similar mortality but higher 30-day cardiac mortality in patients with RVI related to larger infarct size. RVI is not an independent predictor of survival
Zornoff et al., 2002 (13)	416	82	59	1990–1991	Echocardiographic study (between 3 and 16 days after AMI)	671–946 days	RV function was an independent predictor of death and the development of heart failure in patients with left ventricular dysfunction after MI

Table 1.—Continued

Study	Total Patients	Sex, (% male)	Age (Mean yrs)	Years of Enrollment	RVI Diagnostic	Follow-up	Study Results
Retrospective Assali et al., 2007 (14)	337	82	61	2001–2005	ECG with ST-segment elevation $\geq 0.1$ mV in $V_{3R}$ or $V_{4R}$ lead and/or 2D Echo.	In-hospital 30-day	RVI was an independent predictor of mortality
Bueno et al., 1997 (15)	188	52	79	1989–1995	ECG with ST-segment elevation $\geq 0.1$ mV in $V_{3R}$ or $V_{4R}$ lead and/or 2D Echo.	In-hospital	In patients with RVI death rate was higher as all major cardiac complications. In elderly patients RVI is a powerful independent predictor of in-hospital death
Bueno et al., 1998 (16)	798	78	64	1991–1995	ECG with ST-segment elevation $\geq 0.1$ mV in $V_{3R}$ or $V_{4R}$ lead and/or 2D Echo.	In-hospital	Patients with RVI had higher incidence of major complications. RVI is an independent predictor of death in elderly patients
Gumina et al., 2002 (17)	580	56	68	1988–1998	ECG with ST-segment elevation $\geq 0.1$ mV in $V_{3R}$ or $V_{4R}$ lead and/or 2D Echo.	In-hospital	RVI is associated with increased in-hospital mortality and morbidity and also increased long-term mortality
Hanzel et al., 2006 (18)	54	48	76	1994–1997	2D Echocardiography	In-hospital	Elderly patients with inferior MI with RVI suffer greater morbidity and mortality than those without RVI
Kukla et al., 2006 (19)	159	70	64	2000–2001	ECG with ST-segment elevation $\geq 0.1$ mV in $V_{4R}$ lead	In-hospital	RVI is associated with worse prognosis and increased rate of in-hospital complications
Ribeiro et al., 2003 (20)	373	54	65	1996–2000	ECG with ST-segment elevation $\geq 0.1$ mV in $V_{4R}$ lead	In-hospital	RVI by univariate analysis is associated with death but not by multivariate analysis
Saw et al., 2001 (21)	136	76	63	1995–1998	ECG with ST-segment elevation $\geq 0.1$ mV in $V_{4R}$ lead	In-hospital	RVI increased in-hospital mortality in AMI. ST elevation in lead III $>$ II is more sensitive than $V_{4R}$ in diagnosing RVI
Vagas-Barron et al., 2002 (22)	122	88	56	—	ECG with ST-segment elevation $\geq 0.1$ mV in $V_{4R}$ lead	In-hospital 22 $\pm$ 17 months	RVI is a major determinant of cardiovascular events during the acute phase of inferior MI. Long-term prognosis of those who survive is excellent if immediate reperfusion is achieved

RVI, right ventricular involvement; ECG, electrocardiogram; AV, atrioventricular block; AMI, acute myocardial infarction; RV, right ventricle; MI, myocardial infarction; mV, millivolt; Echo., echocardiogram.

## RESULTS

### Description of Studies

Of the 324 articles screened, 34 were considered in depth for inclusion, but 12 were excluded because they did not meet inclusion criteria (Fig. 1). Twenty-two studies met all inclusion criteria and had sufficient data available (1–22). Agreement between the two reviewers for study eligibility was very high ( $\kappa = .9$ ). These studies had a total sample size of 7,136 patients with AMI at baseline, of whom 1,963 had RVI (27.5%). Thirteen studies were prospective studies corresponding to a total number of 4,391 patients with AMI, of whom 1,184 had RVI (27%), and nine studies were retrospective studies with a total of 2,745 AMI with

779 RVI (28.4%). Seventeen studies used electrocardiogram with ST-segment elevation  $\geq 0.1$  mV in  $V_{3R}$  or  $V_{4R}$  lead for diagnosis of RVI during AMI (Table 1). Two studies used only echocardiography to define RVI and three studies used mainly radionuclide ventriculography or right ventricular scintigraphy. The reperfusion method was frequently thrombolysis. In-hospital mortality, the primary end point of the present meta-analysis, was clearly stated in all studies. In nine studies, left ventricular ejection fraction was reported according to RVI. No significant difference was observed (weighted mean difference  $-0.77$ , 95% confidence interval [CI],  $-3.66$  to  $2.11$ ,  $p = .60$ ).

The number of patients at baseline in the primary studies varied from 51 to

1,129. Most studies had a small sample size and only nine studies contained more than 200 AMI. The RVI varied from 5.2% to 53.5% with an average of 31.7%. Follow-up for in-hospital mortality was exhaustive. Control of confounding factors was poor in six studies, adequate or good in 16, and only 11 studies provided adjusted estimates of the mortality increase related to RVI (Table 2).

### Total Mortality

A random-effects meta-analysis was carried out, and the pooled relative risk (RR) was 2.13 (95% CI, 1.51–3.01) and 3.31 (2.63–4.17) for the 13 prospective and the nine retrospective studies respectively. For all 22 studies, an increase in

Table 2. Quality assessment of the included studies

Study	Total Patients	RVI (%)	Clear Definition of MI	Clear Definition of RVI	Control of Confounding Factors	Reperfusion Method (%)	Minimization of Selection Bias
<b>Prospective</b>							
Berger et al., 1993 (1)	1,110	5.2	Yes	No	Adequate	Thrombolysis: 100%	70% of original cohort (main exclusion criteria related to technical problems during radionuclide ventriculogram and 42 deaths prior to inclusion)
Giannitsis et al., 2000 (2)	88	30.7	Yes	Yes	Poor	Primary PCI: 98.8%	Complete case series
Haines et al., 1985 (3)	74	36.5	Yes	No	Poor	Not assessable	74 consecutive inferior AMI uncomplicated during acute phase and <65 yrs old
Khan et al., 2004 (4)	100	34.0	Yes	Yes	Poor	Thrombolysis: 90%	Consecutive series with exclusion of patients with prior AMI, valvular heart diseases, or cardiomyopathy
Marwick et al., 1991 (5)	168	20.8	Yes	No	Good	Not assessable	Complete case series from a 80% original cohort
Mavric et al., 1990 (6)	243	18.5	Yes	Yes	Adequate	None	Complete case series
Mehhta et al., 2001 (7)	1129	43.5	Yes	Yes	Good	Thrombolysis: 96%	71% of original cohort (RV status unknown in 470 excluded patients)
Pereira et al., 2006 (8)	183	20.8	Yes	Yes	Adequate	Thrombolysis: 67.2%	95% of eligible patients (183/192)
Ramires et al., 1993 (9)	107	45.8	Yes	Yes	Adequate	Not assessable	Unclear, but some patients excluded because of circumflex artery lesions, prior reperfusion or CABG, use of drugs that influence AV conduction, atrial flutter, or fibrillation
Rodrigues et al., 1986 (10)	51	49.0	Yes	No	Poor	Not assessable	Consecutive and nonselected case series, implies 100%, but unclear
Zehender et al., 1993 (11)	200	53.5	Yes	Yes	Good	Thrombolysis: 35.5%	Consecutive series of 200 inferior AMI patients
Zeymer et al., 1998 (12)	522	32.4	Yes	Yes	Good	Thrombolysis: 100%	Complete series of 522 patients with inferior AMI from an randomized trial testing new thrombolytic regimens in AMI
Zornoff et al., 2002 (13)	416	19.0	Yes	Yes	Good	Thrombolysis: 34.6%	81% of a substudy analysis from the SAVE trial. Patients with LVEF <40% and without heart failure who were 21 to 80 yrs old included between 3 and 16 days after MI
<b>Retrospective</b>							
Assali et al., 2007 (14)	337	21.7	Yes	Yes	Good	Primary PCI: 100%	Consecutive series of inferior AMI who underwent primary PCI
Bueno et al., 1997 (15)	188	41.0	Yes	Yes	Good	Thrombolysis: 20.7% Primary PCI: 4.4%	94% of a consecutive series of patients >75 yrs with inferior AMI
Bueno et al., 1998 (16)	798	37.1	Yes	Yes	Good	Thrombolysis: 46% Primary PCI: 9%	97% of a consecutive series of patients with inferior AMI
Gumina et al., 2002 (17)	580	17.6	Yes	Yes	Good	Primary reperfusion: 43.8% (thrombolysis or PCI)	Complete series of 580 patients with inferior or lateral AMI
Hanzel et al., 2006 (18)	54	33.3	Yes	Yes	Poor	Primary PCI: 100%	Selection of patients >70 yrs with inferior AMI from a database where 50% of patients excluded because echocardiography images non adequate for RVI diagnosis
Kukla et al., 2006 (19)	159	40.9	Yes	Yes	Adequate	Thrombolysis: 53%	88% of a consecutive series of patients with inferior AMI
Ribeiro et al., 2003 (20)	373	9.9	Yes	Yes	Poor	Thrombolysis: 51.5%	Consecutive series of AMI
Saw et al., 2001 (21)	136	43.4	Yes	No	Good	Thrombolysis: 70%	78% of a consecutive series of inferior AMI
Vagas-Barron et al., 2002 (22)	122	42.6	Yes	Yes	Good	Thrombolysis: 36.1% Primary PCI: 29.5%	60% of a consecutive series of patients with inferior AMI

RVI, right ventricular involvement; MI, myocardial infarction; PCI, prothrombin consumption index; AMI, acute myocardial infarction; RV, right ventricle; CABG, coronary artery bypass graft; AV, atrioventricular; LVEF, left ventricular ejection fraction.

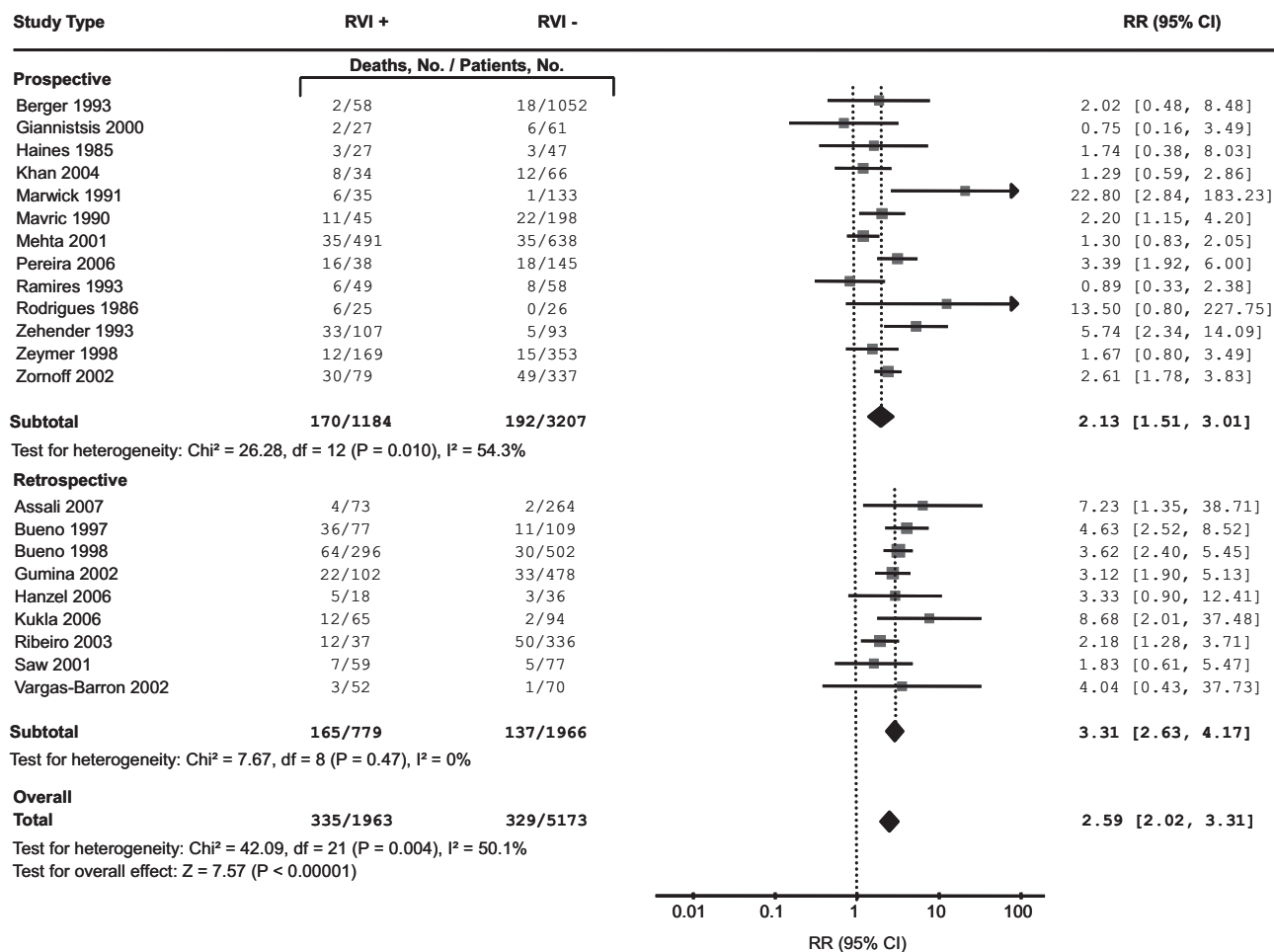


Figure 2. Pooled relative risks of mortality increase in patients with acute myocardial infarction and right ventricular involvement (RVI): random-effects meta-analysis of 22 studies. CI, confidence interval; RR, relative risk.

mortality rate from 6.3% without RVI to 17% when RVI was observed, corresponding to an overall pooled RR mortality increase of 2.59 (95% CI, 2.02–3.31) was found (Fig. 2). Although most 95% CIs for the primary studies overlapped, some heterogeneity was observed in prospective studies ( $\chi^2$  for heterogeneity,  $p = .01$ ), hence the need for the random-effects meta-analysis. However, the overall effect was highly significant ( $Z = 7.57$ ;  $p < .00001$ ) and the results did not differ when the analysis was limited to prospective or retrospective studies. Funnel plots were created to compare the SE of the log odds ratio with the log odds ratio for the prospective and retrospective studies, revealing possible publication bias in prospective studies (Fig. 3). Larger, more precise studies with smaller SEs tended to find smaller mortality rises in patients with RVI than did smaller studies with more deaths and therefore larger SEs (Fig. 3).

### Sensitivity Analyses

The sensitivity analysis using the following criteria: a) a sample size of at least 150 patients at baseline; b) prospective studies; and c) with immediate RVI diagnosis based on electrocardiography and/or echocardiography at admission included only five studies that met all these criteria (6, 7, 8, 11, 12). However, the pooled RR for these five studies (RR, 2.32; 95% CI, 1.41–3.84; test for heterogeneity:  $\chi^2 = 12.36$ ,  $df = 4$ ;  $p = .01$ ;  $I^2 = 67.6\%$ ) was essentially the same as for all 22 studies (RR, 2.59; 95% CI, 2.02–3.31).

Four studies recruited patients during the in-hospital stay and not in the acute phase of myocardial infarction because they used either echocardiography or radionuclide ventriculography for RVI diagnosis. In those studies, only two reported how many patients died before entry into the study. A sensitivity analysis was carried out including only

those studies that were able to ascertain RVI during the acute phase of myocardial infarction. The increase in mortality rate estimated by this analysis (RR, 2.54; 95% CI, 1.92–3.37) and the analysis including all 22 studies (RR, 2.59; 95% CI, 2.02–3.31) did not differ significantly.

Finally, according to the control of confounding factors (poor, adequate, and good), pooled RR in mortality was also similar between three groups delineated (RR, 1.90; 95% CI, 1.27–2.84; RR, 2.64; 95% CI, 1.36–4.40; RR, 3.30; 95% CI, 2.50–4.34, respectively) with a trend to have an increased impact of RVI on mortality among studies with better control of confounding factors.

### Morbidity Outcomes

Fifteen studies presented information on cardiogenic shock occurrence (15.7% versus 6%) during the hospital stay according to initial RVI or not in patients

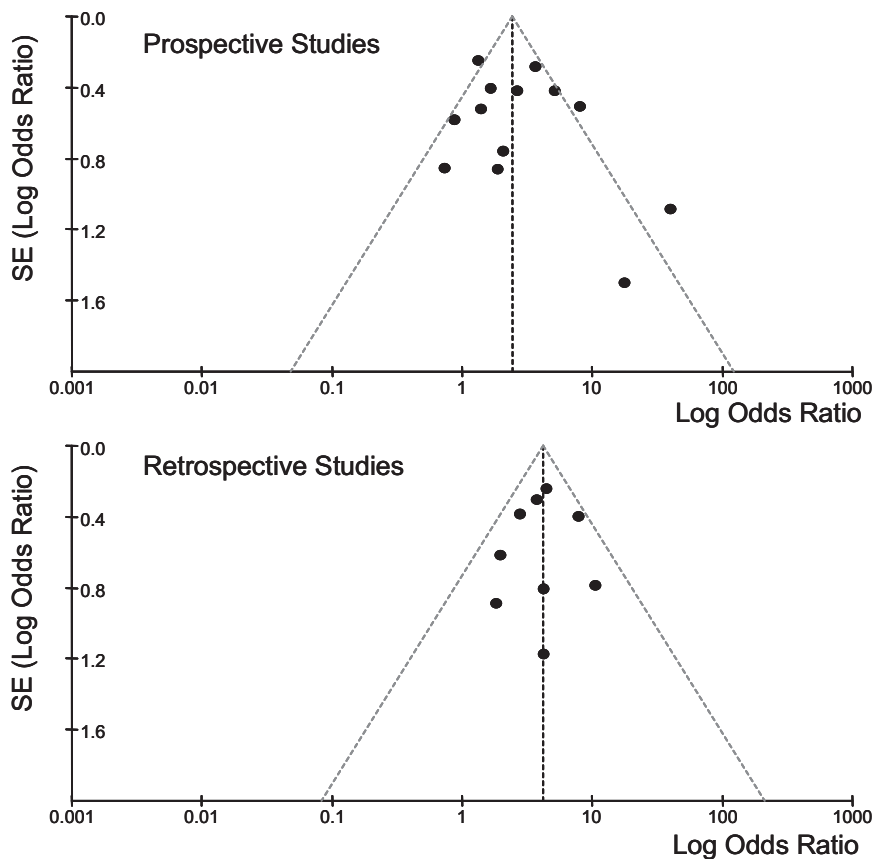


Figure 3. Funnel plots of prospective (top) and retrospective studies (bottom).

with inferior myocardial infarction (Fig. 4). The corresponding pooled RR for cardiogenic shock was 2.90 (95% CI, 2.12–3.96). Thirteen studies presented information on severe ventricular arrhythmias (ventricular tachycardia or ventricular fibrillation) with an increase of severe ventricular arrhythmias from 6.1% to 16.8% when RVI was found corresponding to a pooled RR of 2.29 (95% CI, 1.92–2.73) (Fig. 5). Ten studies presented data on the occurrence of atrioventricular block, which increased from 8.2% to 22.6% with RVI corresponding to a pooled RR of 3.27 (95% CI, 2.28–4.70) (Fig. 6). Only seven studies presented information on the rate of mechanical complications (cardiac rupture, papillary muscle rupture, or septal perforation), which increased from 1.2% to 4% corresponding to a pooled RR of 3.01 (95% CI, 1.90–4.76) (Fig. 7). All aforementioned pooled RR estimates for morbidity outcomes were highly significant ( $p < .0001$ ).

## DISCUSSION

The present meta-analysis indicates that RVI in patients with AMI is associated with a significantly worse prognosis.

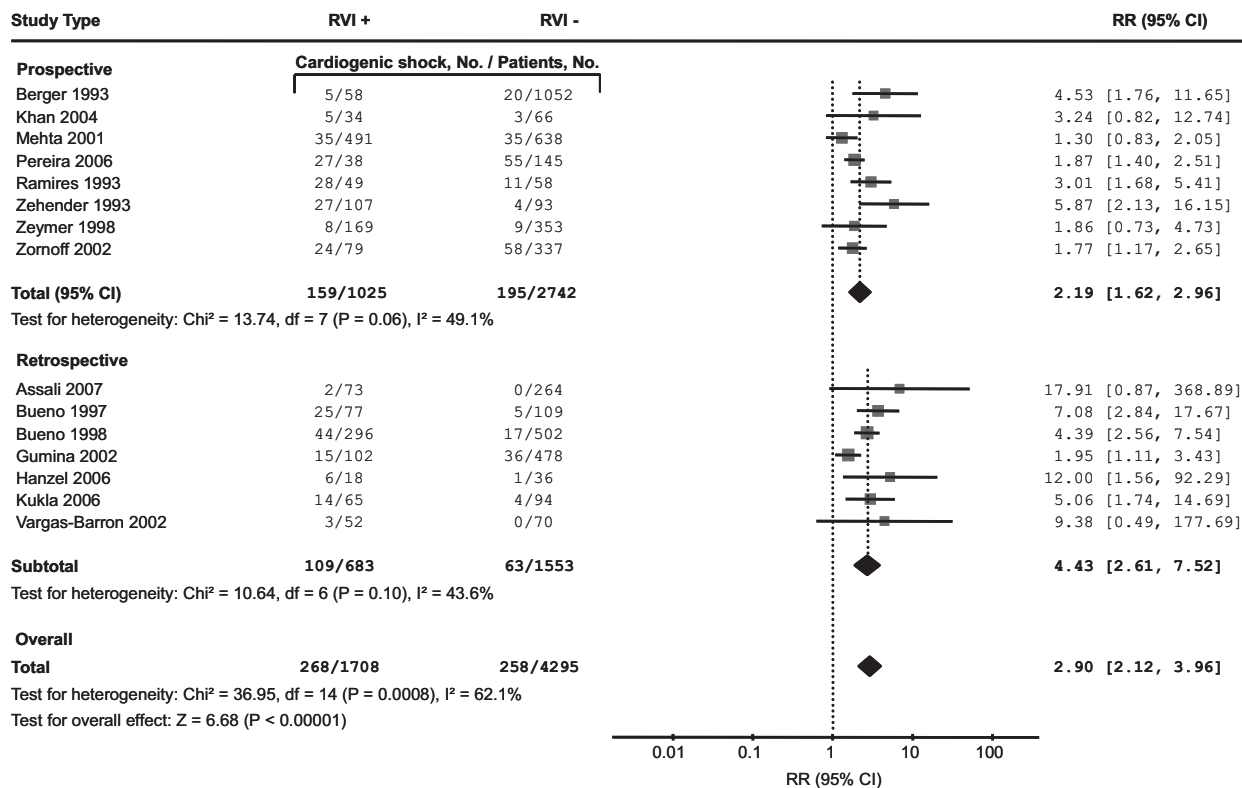


Figure 4. Pooled relative risks of cardiogenic shock increase in patients with acute myocardial infarction and right ventricular involvement: random-effects meta-analysis of 15 studies. RR, relative risk; RVI, right ventricular involvement; CI, confidence interval.

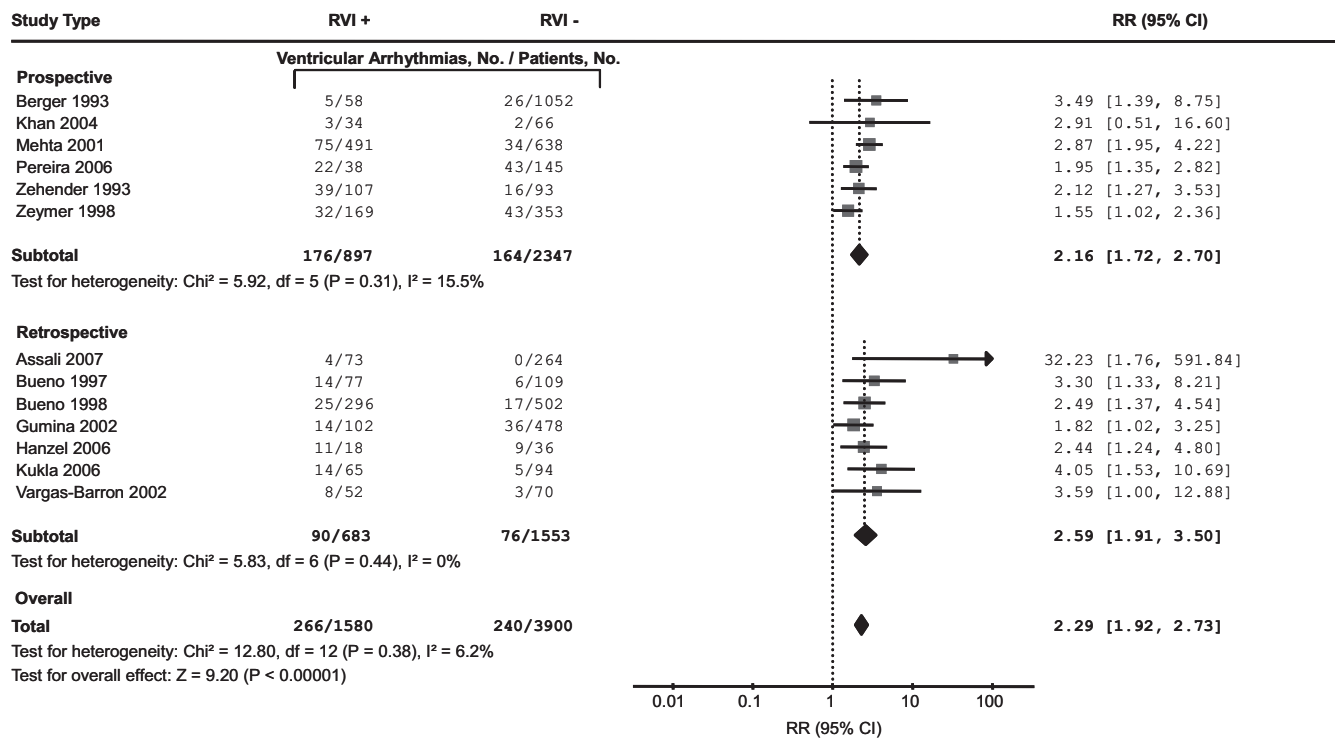


Figure 5. Pooled relative risks of ventricular arrhythmias increase in patients with acute myocardial infarction and right ventricular involvement: random-effects meta-analysis of 13 studies. *RR*, relative risk; *RVI*, right ventricular involvement; *CI*, confidence interval.

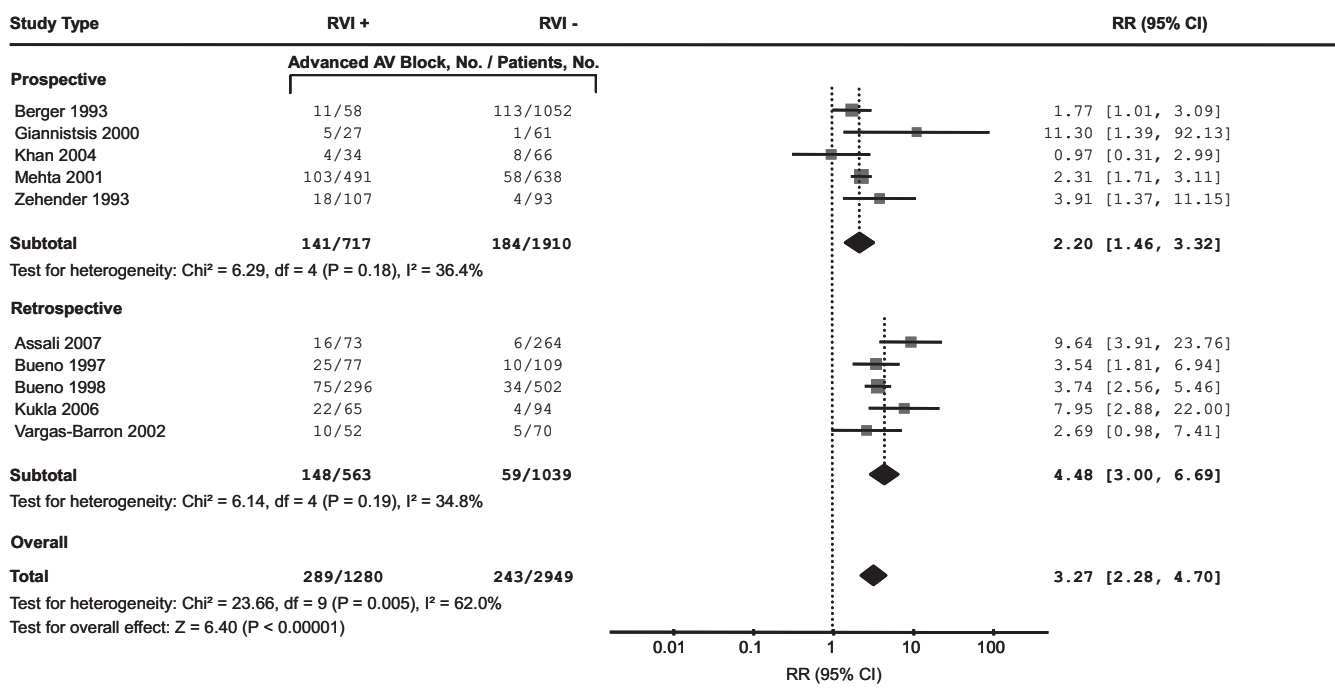


Figure 6. Pooled relative risks of advanced atrioventricular block increase in patients with acute myocardial infarction and right ventricular involvement: random-effects meta-analysis of ten studies. *RR*, relative risk; *RVI*, right ventricular involvement; *CI*, confidence interval.

The mechanisms that underlie this excess in mortality in patients with RVI are unclear but could relate to an increased propensity to develop life-threatening ventricular arrhythmias in these patients.

Whether or not the right ventricle may be more arrhythmogenic than the left ventricle as previously suggested (7–24) warrants further investigation. In the studies included in the present meta-analysis,

left ventricular infarct size and function were similar between patients with and those without RVI. These findings suggest that RVI by itself is independently associated with mortality and morbidity

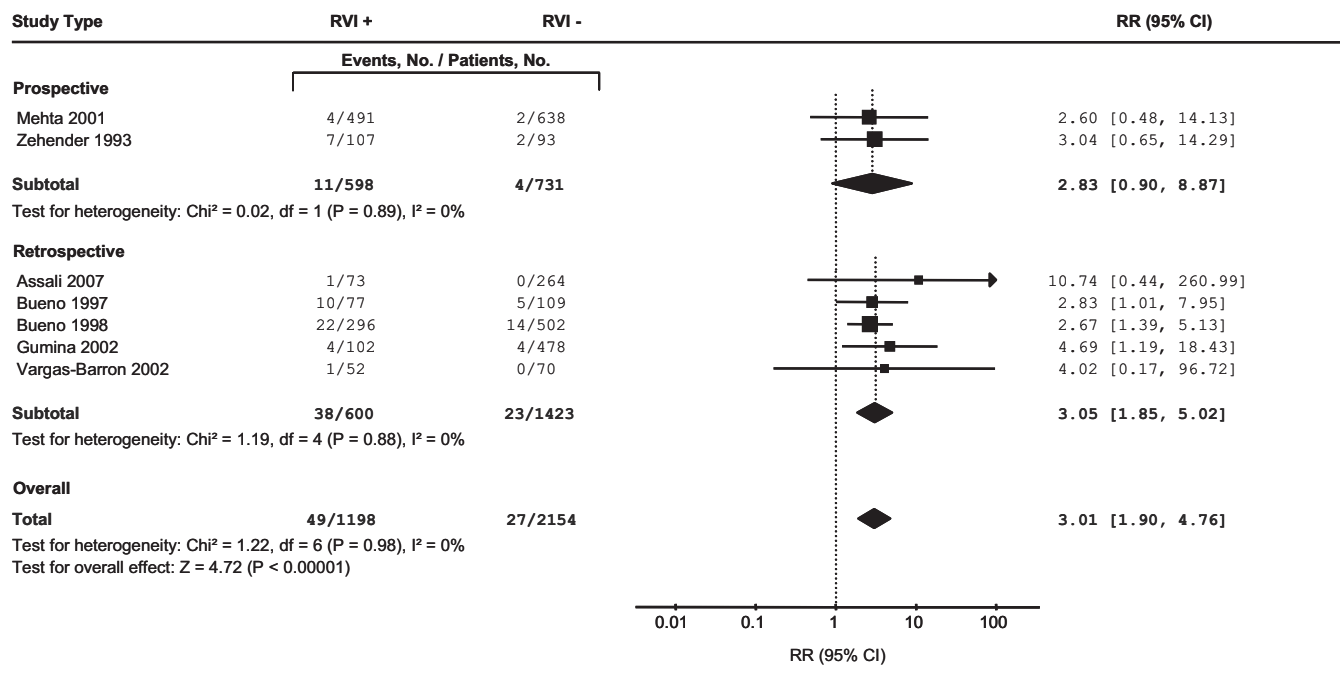


Figure 7. Pooled relative risks (RRs) of mechanical complications increase in patients with acute myocardial infarction and right ventricular involvement (RVI) random-effects meta-analysis of seven studies. CI, confidence interval.

in these patients. Sensitivity analyses show that the analysis restricted to prospective studies lead to the same results of deleterious impact of RVI on patient outcomes.

Previous studies examining the prognostic impact of RVI in patients with inferior AMI have involved small or moderately high numbers of patients with low rate of outcome events leading to wide CIs in the point estimates provided (1–22). Our pooled estimates with narrow limits support the concept that early recognition of RVI during AMI, easily done with electrocardiography and/or echocardiography, is of critical importance in attempting to limit by intervention the deleterious impact of this diagnosis. Indeed, as shown by Bowers et al. in patients with RVI, early and complete reperfusion of the right coronary artery by angioplasty (including major right ventricular branches) results in the dramatic recovery of right ventricular performance and an excellent clinical outcome (28). In contrast, unsuccessful reperfusion was associated with impaired recovery of right ventricular function and a high mortality rate. PCI with stenting in this perspective seems to be the most effective technique and as soon as RVI is suspected in AMI, prompt primary PCI should be proposed (2, 14, 29), particularly in those with severe hemodynamic compromise (30). However, we must acknowledge

that there are not enough data available to date to be sure that aggressive primary PCI would be more efficient than early thrombolysis to decrease the rate of major complications associated with RVI. Further attempts are necessary in future trials to focus on this subgroup of patients with inferior AMI and RVI. In the meantime, it seems reasonable to strongly recommend systematically searching for RVI in AMI, and therefore electrocardiographic assessment of right ventricular infarction should be routinely performed in all patients with AMIs. Recent studies suggest that contrast-enhanced cardiac magnetic resonance imaging could be useful to improve diagnostic accuracy of RVI in patients with acute inferior myocardial infarction (31). Further studies are warranted to determine the prognostic relevance of late enhancement cardiac magnetic resonance imaging in this setting. The obligatory delay for such assessment makes electrocardiography and echocardiography the methods of choice in routine practice for the acute phase assessment of RVI.

### Limitations

**Observational Data.** This review has a number of limitations. First, we are considering observational data. Patients with AMI and RVI may well differ from those

without RVI in a number of ways, including their age, gender, risk factors, and acute treatment that they received because of the AMI. However, the direction of these potential confounding factors is not obvious. Some studies found that the subsequent mortality risk with RVI was restricted to elderly patients (15, 16, 18–20) or patients with atrioventricular block (6, 9), whereas others suggested that RVI is an independent and strong predictor of mortality (4, 5, 7, 11–14, 21, 22). The present meta-analysis was carried out using crude estimates. The 11 studies that presented adjusted outcome measures for total mortality used markedly different adjustment methods to consider different covariates and were measured in varying ways. However, results of these 11 studies found surprisingly only small differences between adjusted and nonadjusted estimates. In fact, the RR increase appeared greater after adjustment in some studies, suggesting that our estimates may be conservative and may slightly underestimate the true risk increase associated with RVI in patients with inferior AMI.

**Diagnostic Performance of Electrocardiography for Right Ventricular Involvement.** Electrocardiographic sensitivity and specificity for RVI in inferior AMI has been studied in autopsy patients with AMI and 12-lead plus leads  $V_{3R}$  and  $V_{4R}$  electrocardiography (32). Although it

seems that ST elevation in the right precordial leads is able to reach the highest sensitivity and specificity especially in lead  $V_{4R}$  for posterior RVI (100% and 68.2%, respectively), no reliable electrocardiographic criteria were found to identify anterior RVI. It has been also suggested that in some patients with inferior AMI caused by the occlusion of the right coronary artery proximal to the first right ventricular branch, no ST-segment elevation in lead  $V_{4R}$  can occur because of concomitant posterior left ventricular involvement (33). In such patients, the incidence of RVI may be underestimated on the basis of ST-segment elevation in lead  $V_{4R}$ . Therefore, in addition to the prompt performance of 12-lead plus leads  $V_{3R}$  and  $V_{4R}$  electrocardiography, a systematic echocardiography is highly recommended in AMI to identify more accurately RVI.

**Publication Bias.** Like with any systematic review, there is always a possibility of publication bias, as suggested, at least for prospective studies, by the funnel plots (Fig. 3). However, exclusion of the smaller studies in a sensitivity analysis made essentially no difference to the pooled RR. Finally, we must also acknowledge that a majority of studies have been conducted during the “thrombolytic era” and data related to the prognostic impact of RVI when primary PCI is performed remain limited.

## CONCLUSION

Our results support that early recognition of RVI, namely by means of right electrocardiographic leads in AMI may have prognostic value. Whether or not this recognition will permit improvement of outcomes through more aggressive PCI intervention remains theoretical and would need to be examined prospectively in future studies.

## ACKNOWLEDGMENT

We appreciate the critical review of this manuscript by Dr. Rémy Morello from the Unité de Recherche Clinique, University Hospital of Caen, Caen, France.

## REFERENCES

- Berger PB, Ruocco NA, Ryan TJ, et al; TIMI Research Group: Frequency and significance of right ventricular dysfunction during inferior wall left ventricular myocardial infarction treated with thrombolytic therapy (re-

- sults from the thrombolysis in myocardial infarction [TIMI] II trial). *Am J Cardiol* 1993; 71:1148–1152
- Giannitsis E, Hartmann F, Wiegand U, et al: Clinical and angiographic outcome of patients with acute inferior myocardial infarction. *Z Kardiol* 2000; 89:28–35
- Haines DE, Beller GA, Watson DD, et al: A prospective clinical, scintigraphic, angiographic and functional evaluation of patients after inferior myocardial infarction with and without right ventricular dysfunction. *J Am Coll Cardiol* 1985; 6:995–1003
- Khan S, Kundi A, Shariiff S: Prevalence of right ventricular myocardial infarction in patients with acute inferior wall myocardial infarction. *Int J Clin Pract* 2004; 58:354–357
- Marwick TH, Birbara TM, Allman KC, et al: Prognostic significance of right ventricular ejection fraction following inferior myocardial infarction. *Int J Cardiol* 1991; 31: 205–212
- Mavric Z, Zaputovic L, Matana A, et al: Prognostic significance of complete atrioventricular block in patients with acute inferior myocardial infarction with and without right ventricular involvement. *Am Heart J* 1990; 119:823–828
- Mehta SR, Eikelboom JW, Natarajan MK, et al: Impact of right ventricular involvement on mortality and morbidity in patients with inferior myocardial infarction. *J Am Coll Cardiol* 2001; 37:37–43
- Pereira AC, Franken RA, Scharzwälder Sprovier SR, et al: Impact on hospital mortality and morbidity of right ventricular involvement among patients with acute left ventricular infarction. *Sao Paulo Med J* 2006; 124:186–191
- Ramires JF, Solimene MC, Savioli RM, et al: Mortality is not increased with inferior infarction associated with right ventricular infarction and atrioventricular block. *Coron Artery Dis* 1993; 4:965–970
- Rodrigues EA, Dewhurst NG, Smart LM, et al: Diagnosis and prognosis of right ventricular infarction. *Br Heart J* 1986; 56:19–26
- Zehender M, Kasper W, Kauder E, et al: Right ventricular infarction as an independent predictor of prognosis after acute inferior myocardial infarction. *N Engl J Med* 1993; 328: 981–988
- Zeymer U, Neuhaus KL, Wegscheider K, et al; for the HIT-4 Trial Group: Effects of thrombotic therapy in acute inferior myocardial infarction with or without right ventricular involvement. *J Am Coll Cardiol* 1998; 32: 876–881
- Zornoff LM, Skali H, Pfeffer MA, et al; for the SAVE Investigators: Right ventricular dysfunction and risk of heart failure and mortality after myocardial infarction. *J Am Coll Cardiol* 2002; 39:1450–1455
- Assali AR, Teplitsky I, Ben-Dor I, et al: Prognostic importance of right ventricular infarction in acute myocardial infarction cohort referred for contemporary percutaneous

- reperfusion therapy. *Am Heart J* 2007; 153: 231–237
- Bueno H, Lopez-Palop R, Bermejo J, et al: In-hospital outcome of elderly patients with acute myocardial infarction and right ventricular involvement. *Circulation* 1997; 96: 436–441
- Bueno H, Lopez-Palop R, Perz-David E, et al: Combined effect of age and right ventricular involvement on acute inferior myocardial infarction prognosis. *Circulation* 1998; 98: 1714–1720
- Gumina RJ, Wright RS, Kopecky SL, et al: Strong predictive value of TIMI risk score analysis for in-hospital and long-term survival of patients with right ventricular infarction. *Eur Heart J* 2002; 23:1678–1683
- Hanzel GS, Merhi WM, O’Neil WW, et al: Impact of mechanical reperfusion on clinical outcome in elderly patients with right ventricular infarction. *Coron Artery Dis* 2006; 17:517–521
- Kukla P, Dudek D, Rakowski T, et al: Inferior wall myocardial infarction with or without right ventricular involvement—treatment and in-hospital course. *Kardiol Pol* 2006; 64:6
- Ribeiro DG, de Andrade PJ, Paes Junior JN, et al: Acute myocardial infarction. Acute myocardial infarction: predictors of mortality at a public hospital in the city of Fortaleza. *Ceara state Arq Bras Cardiol* 2003; 80:614–620
- Saw J, Davies C, Fung A, et al: Value of ST elevation in lead III greater than lead II in inferior wall acute myocardial infarction for predicting in-hospital mortality and diagnosing right ventricular infarction. *Am J Cardiol* 2001; 87:448–450
- Vargas-Barron J, Castillo-Mora G, Lopez-Meneses M, et al: Comparison of short- and long-term benefits of reperfusion in single-vessel inferior wall acute myocardial infarction with and without right ventricular wall infarction. *Am J Cardiol* 2002; 90:144–146
- Halkin A, Singh M, Nikolsky E, et al: Prediction of mortality after primary percutaneous coronary intervention for acute myocardial infarction. The Cadillac Risk Score. *J Am Coll Cardiol* 2005; 45:1397–1405
- Pfisterer M, Emmenegger H, Soler M, et al: Prognostic significance of right ventricular ejection fraction for persistent complex ventricular arrhythmias and/or sudden death after first myocardial infarction: relation to infarct location, size and left ventricular function. *Eur Heart J* 1986; 7:289–298
- Stroup DF, Berlin JA, Morton SC, et al: Meta-analysis of observational studies in epidemiology: A proposal for reporting. *JAMA* 2000; 283:2008–2012
- Project WM. *MONICA Manual*, Vol. part IV (a). Geneva, World Health Organization, 1990
- Review Manager 4.2.9. The Cochrane Collaboration. Available at: <http://www.cc-ims.net/RevMan/download.htm>. Accessed January 30, 2007
- Bowers TR, O’Neill WW, Grines C, et al: Effect of reperfusion on biventricular function

- and survival after right ventricular infarction. *N Engl J Med* 1998; 338:933–940
29. Antman EM, Anbe DT, Armstrong PW, et al: American College of Cardiology; American Heart Association Task Force on Practice Guidelines; Canadian Cardiovascular Society ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction). *Circulation* 2004; 110:e82–292; erratum in *Circulation* 2005; 111:2013–2014
  30. Jacobs AK, Leopold JA, Bates E, et al: Cardiogenic shock caused by right ventricular infarction. A report from the SHOCK registry. *J Am Coll Cardiol* 2003; 41:1273–1279
  31. Kumar A, Abdel-Aty H, Kriedemann I, et al: Contrast-enhanced cardiovascular magnetic resonance imaging of right ventricular infarction. *J Am Coll Cardiol* 2006; 48: 1969–1976
  32. Lopez-Sendon J, Coma-Canella, Alcasena S, et al: Electrocardiographic findings in acute right ventricular infarction: sensitivity and specificity of electrocardiographic alterations in right precordial leads  $V_{4R}$ ,  $V_{3R}$ ,  $V_1$ ,  $V_2$  and  $V_3$ . *J Am Coll Cardiol* 1985; 6:1273–1279
  33. Kosuge M, Kimura K, Ishikawa T, et al: Implications of the absence of ST-segment elevation in lead V4R in patients who have inferior wall acute myocardial infarction with right ventricular involvement. *Clin Cardiol* 2001; 24:225–230