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The prognostic value of normal stress cardiovascular magnetic resonance imaging -A systematic review and meta-analysis-

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None of the authors have any conflicts of interest associated with this study.

Abstract

Objectives

The purpose of our study was to determine the prognostic value of normal stress cardiovascular MRI (CMR) by a systematic literature review and meta-analysis.

Methods

A comprehensive literature search of published studies through November 2011 in MEDLINE database and Cochrane Library, regarding prognostic value of stress CMR in patients with known or suspected coronary artery disease (CAD), was performed.

Results

Ultimately, we identified 11 studies. The summary relative risk ratio for major adverse cardiac events (MACE) was 0.50 (95% confidence interval (CI): 0.44 to 0.58) for normal cine CMR and 0.09 (95% CI: 0.02 to 0.35) for normal perfusion CMR. The summary relative risk ratio for hard cardiac events was 0.36 (95% CI: 0.16 to 0.8) for normal cine CMR and 0.22 (95% CI: 0.07 to 0.66) for normal perfusion CMR.

Conclusion

Normal stress CMR for patients known or suspected of having CAD has good prognostic value in predicting cardiac events.

Keywords

Magnetic resonance imaging, Prognosis, Cardiac imaging techniques, Systematic review, Meta-analysis

Introduction

In clinical practice, myocardial perfusion and cardiac wall motion are usually assessed with non-invasive imaging modalities such as single-photon emission computed tomography (SPECT) or stress echocardiography. Recent advances in cardiac magnetic resonance imaging (cardiac MRI: CMR) have enabled dynamic first-pass contrast-enhanced imaging of the entire left-ventricular myocardium and cardiac wall motion imaging with improved image quality. Against this background, reports on the evaluation of coronary artery disease (CAD) and prognosis of patients suspected of having CAD by CMR have been increasing [1–4]. Recently, several prognostic studies with various follow-up periods using CMR have been reported [5–8]. Prognostic information is useful in cardiac risk stratification and subsequent clinical management. Also, accurate risk stratification has become increasingly important in optimizing patient outcomes and containing rapidly escalating medical care costs [9]. Similarly, it is important to assess the prognostic value of negative stress CMR from possibility of decreasing unnecessary additional tests and interventions. Although these studies were well-conducted and documented the good prognostic value of CMR, most studies were based on small populations or were single-center trials.

The purpose of our study was to obtain consolidated data about the prognosis of patients diagnosed to be negative in stress CMR by a systematic literature review and meta-analysis combining the results of currently available published studies.

Materials and Methods

Search for published data

A literature search was performed using the Medline database and the Cochrane Library [10] to identify articles published from January 1990 to November 2011 as part of a larger review of the prognostic value of CMR. The following search terms were used: magnetic resonance imaging, cardiac, prognosis, prognostic value, and outcome. In a manual search, we also scanned references in the eligible articles and review articles that were retrieved.

Inclusion and exclusion criteria

Studies were included if they met the following criteria:

1) Prospective cohort studies of subjects who underwent exercise CMR for known or suspected CAD.
2) Provided primary data on clinical outcomes of major adverse cardiac events (MACE) or hard cardiac events.
3) Stress myocardial perfusion MRI (p-MRI) or stress cine MRI (cine MRI) were performed as CMR.
4) Provided primary data on the presence or absence of abnormal findings in CMR.
5) Full peer-reviewed journal papers.
6) Provided appropriate data on MACE or hard cardiac events at a follow-up period of not less than 6 months.

Studies were excluded if they met the following criteria:
1) CMR was performed exclusively in patients with chronic heart failure, after myocardial infarction, percutaneous angioplasty, or coronary bypass surgery (did not include normal patients).
2) Exclusively duplicated or overlapping data.
3) Meeting abstracts (they did not provide adequately detailed data).

As definition of clinical outcomes, hard cardiac events were nonfatal myocardial infarction or cardiac death, MACE was a composite of adverse cardiac events such as hard cardiac events, revascularization and hospitalization due to unstable angina or heart failure. After an initial search, two investigators applied these inclusion and exclusion criteria and selected articles for data extraction. The selection was carried out independently and disagreements were resolved by consensus.

Data abstraction

Two investigators (K.I. and S.N.), blinded to the journal, author, year of publication, and institution, independently reviewed the full text of each potentially eligible study and abstracted data, including characteristics of the study, participant characteristics, test characteristics, and mean follow-up time. The occurrence of first outcome (MACE) and second outcome (hard cardiac events) were recorded. Results including the number of events or event rates based on positive or negative tests were abstracted. Results stratified by type of CMR examination or clinical outcome were abstracted separately when provided. Disagreements were resolved by

consensus.

Methodological quality assessment

Methodological quality assessment was performed independently by the two reviewers using the Newcastle–Ottawa Scale (NOS) [11]. Disagreements were resolved by consensus. The NOS checklist was developed as a tool for quality assessment of non-randomized studies to be used in a systematic review. The NOS contains eight items, categorized into three dimensions: selection; comparability; and, depending on the study type, outcome (cohort studies) or exposure (case-control studies). A star system is used to allow a semi-quantitative assessment of study quality, such that the highest quality studies are awarded a maximum of one star for each item, with the exception of the item related to comparability, which allows the assignment of two stars. The NOS ranges from zero to nine stars [12].

Data synthesis and statistical analysis

The primary analysis was performed based on the 2×2 event data for patients with the presence or absence of abnormal findings in CMR. For purpose of our study, the risk ratio was defined as the probability of an event in the negative result (absence of abnormal findings) group of CMR divided by the probability of an event in the positive result (presence of abnormal findings) group of CMR. The modified 2x2 table for purpose of our study is shown in Fig. 1. Individual and summary relative risk ratios, negative predictive value, and 95% confidence intervals (CIs) for prognosis of MACE or hard cardiac events were calculated for each study. The method of calculating the summary relative risk ratios was determined based on homogeneity using a Q statistic. For data synthesis, we used the individual study results and applied the fixed-effects model [13] (if homogeneity could not be rejected) or the random-effects model [13] (if homogeneity could be rejected). A p value of less than 0.05 was considered statistically significant. Also, in the test of homogeneity, when the p value was greater than 0.05, the summary negative predictive value and summary event rate after negative test were calculated, together with their 95% CIs.

For summary relative risk ratios, we compared those of cine MRI and p-MRI. When there was no overlap of the 95% CIs, we determined that there was a statistically significant difference. Publication bias toward the

relative risk ratios was determined using data extraction in each of the articles and was assessed by the rank correlation test described by Begg and Mazumdar [14]. If publication bias was present, trim and fill method was performed in order to adjust for publication bias. A p value of less than 0.05 was considered statistically significant.

Our statistical analyses were performed by using R (V. 2.12.1 package:metafor) [15,16] and Meta-Disc (V. 1.4) [17]. Also, our study did not require the approval of the Ethical Review Board.

Results

Search results

The search process and results are shown in the flowchart in Fig. 2. Eventually, 11 studies [5,6,8,18–25] fulfilled all inclusion criteria and were eligible for meta-analysis. All eligible studies had been published in peer-reviewed journals between 2004 and 2011.

Characteristics of the included studies

The 11 stress CMR studies included 4,907 patients (3,221 men) with a mean age of 61.2 years (Table 1). These patients were followed for 0.8 to 6.2 years (Table 1). For prognostic utility, six studies evaluated stress cine MRI [5,6,8,19,21–22] and seven studies evaluated stress p-MRI [6,18,20,22-25]. Three studies evaluated both stress cine MRI and stress p-MRI in the same patient groups [6,21,22]. Five studies reported data on both hard cardiac events and MACE [5,6,8,18,23], three studies hard cardiac events only [19,22,24], and three studies MACE only [20,21,25]. Methodological quality assessment by NOS was 5–6 stars (Table 1). Several articles described that the patients received intervention, such as pharmacological treatment for hypertension or hyperlipidaemia, in the follow-up period of stress CMR [6,8,21,22,24,25].

Prognostic value of negative result in stress cine MRI for predicting MACE

There were four studies assessing the prognostic value of stress cine MRI for MACE (Table 2) [5,6,8,21]. These patients were followed for 1.8 to 6.2 years to check for the occurrence of MACE. Overall, these studies included a total of 1,715 patients (59% men), of whom 1,314 patients (77%) were

negative in stress cine MRI. Overall, 251 of the 1,314 patients (19%) who were negative in stress cine MRI had a MACE during the follow-up period, compared with 228 of the 401 patients (57%) who were positive in stress cine MRI. The summary relative risk ratio for MACE (negative versus positive results in stress cine MRI) was 0.50 (95% CI: 0.44 to 0.58) (Fig. 3). The Q statistic for the summary relative risk ratio was not significant (3.8, p=0.43). In the assessment of publication bias, there was little evidence to suggest the presence of publication bias (Kendall's tau = -1.0, p = 0.04).

Prognostic value of negative result in stress p-MRI for predicting MACE

There were six studies assessing the prognostic value of stress p-MRI for MACE (Table 3) [6,18,20,21,23,25]. These patients were followed for 0.8 to 5.3 years to check for the occurrence of MACE. Overall, these studies included a total of 2,630 patients (60% men), of whom 1,834 patients (70%) were negative in stress p-MRI. Overall, 178 of the 1,834 patients (9.7%) who were negative in stress p-MRI had a MACE during the follow-up period, compared with 324 of the 796 patients (41%) who were positive in stress p-MRI. The summary relative risk ratio for MACE (negative versus positive results in stress p-MRI) was 0.09 (95% CI: 0.02 to 0.35) (Fig. 4). The Q statistic for the summary relative risk ratio was significant (Q=58.8, p<0.001). In the assessment of publication bias, there was no evidence of significant publication bias (Kendall's tau = -0.47, p = 0.19).

Prognostic value of negative result in stress cine MRI for predicting hard cardiac events

There were five studies assessing the prognostic value of stress cine MRI for hard cardiac events (Table 4) [5,6,8,19,22]. These patients were followed for 1.4 to 6.2 years to check for the occurrence of hard cardiac events. Overall, these studies included a total of 2,551 patients (73% men), of whom 1,775 patients (70%) were negative in stress cine MRI. Overall, 96 of the 1,775 patients (5.4%) who were negative in stress cine MRI had hard cardiac events during the follow-up period, compared with 86 of the 776 patients (11%) who were positive in stress cine MRI. The summary relative risk ratio for hard cardiac events (negative versus positive results in stress cine MRI) was 0.36 (95% CI: 0.16 to 0.8) (Fig. 5). The Q statistic for the summary relative risk ratio was significant (Q=27.6, p<0.001). In the assessment of publication bias, there was no evidence of significant

publication bias (Kendall's tau = -0.40, p = 0.32).

Prognostic value of negative result in stress p-MRI for predicting hard cardiac events

There were five studies assessing the prognostic value of stress p-MRI for hard cardiac events (Table 5) [6,18,22–24]. These patients were followed for 1.0 to 5.3 years to check for the occurrence of hard cardiac events. Overall, these studies included a total of 2,630 patients (61% men), of whom 1,714 patients (65%) were negative in stress p-MRI. Overall, 61 of the 1,714 patients (3.5%) who were negative in stress p-MRI had hard cardiac events during the follow-up period compared with 110 of the 916 (12%) who were positive in stress p-MRI. The summary relative risk ratio for hard cardiac events (negative versus positive results in stress p-MRI) was 0.22 (95% CI: 0.07 to 0.66) (Fig. 6). The Q statistic for the summary relative risk ratio was significant (Q=30.9, p<0.001). In the assessment of publication bias, there was no evidence of significant publication bias (Kendall's tau = -0.60, p = 0.14).

Assessment of summary negative predictive value and summary event rate after negative test

A homogeneity test on all cases (Tables 2–5) rejected the homogeneity (p<0.05). Thus, negative predictive value and event rate after negative test in each study, together with their 95% CIs, were calculated; however, the summary negative predictive value and summary event rate after negative test, together with their 95% CIs, were not calculated (Tables 2–5).

Comparison of stress cine MRI and stress p-MRI in the summary relative risk ratio

According to the articles that compared the prognostic value of stress CMR in the same patient groups [6,21,22], the difference in prognostic value of a negative result in stress CMR did not have a significant tendency (Table 6). Using the summary relative risk ratios for each cardiac event, we compared stress cine MRI and stress p-MRI (Figs. 3-6). Those of stress p-MRI were lower than those of stress cine MRI. Moreover, in comparing the summary relative risk ratio of MACE, there was a significant difference because there was no overlap in the 95% CIs. For hard cardiac events, there was no significant difference and there was overlap in the 95% CIs.

Discussion

Our systematic review and meta-analysis of the published data demonstrated the summarized prognostic value for patients who had a negative result in stress CMR though were suspected of having CAD, using the summary relative risk ratio, negative predictive value, and event rate after negative test. The results suggested that a negative result in stress CMR has good prognostic value in predicting cardiac events. In particular, when the endpoint was defined as a hard cardiac event, patients who were negative in stress CMR had a markedly decreased risk of events than patients who were positive in stress CMR (Figs. 5 and 6). Also, when the endpoint was defined as MACE, patients who were negative in stress p-MRI had a markedly decreased risk of events than patients who were positive in stress p-MRI (Fig. 4). In the comparison between stress cine MRI and stress p-MRI, summary relative risk ratios for each cardiac event in stress p-MRI were lower than those in stress cine MRI (Table 7).

The development of myocardial ischemia begins with coronary stenoses, which lead initially to hypoperfusion, followed by wall motion abnormalities, a temporal sequence known as the ischemic cascade [9]. The later development of wall motion abnormalities in this sequence suggests that stress p-MRI may be more sensitive in detecting CAD, and therefore more useful for prognosis than stress cine MRI. In diagnostic opportunities, several authors suggested that perfusion markers are more sensitive and wall motion abnormalities more specific for the detection of CAD [26,27]. In comparing the predictive power of positive stress test results, adenosine perfusion and dobutamine wall motion imaging were equally high [6]. Although articles comparing the prognostic value of stress CMR in the same subject group [6,21,22] did not show any significant tendency in the difference of the prognostic value of a negative result in stress CMR, our analysis suggested that the prognostic value of a negative result in stress p-MRI is superior to that of stress cine MRI (Table 7).

In the current systematic review and meta-analysis of other imaging modalities, Sarwar et al. [28] have reported that the cumulative relative risk ratio for cardiovascular event in patients without and with coronary artery calcium (CAC) symptoms in computed tomography angiography (CTA) is 0.09 (95% CI: 0.04 to 0.20). Our result was similar, in terms of the prognostic value of a normal result in stress p-MRI in predicting MACE (Fig. 3). Metz et al. [9] have reported summary estimates of event rate after

negative test and negative predictive value for hard cardiac events in stress myocardial perfusion SPECT and exercise echocardiography (SPECT: 1.21 (95% CI: 0.98 to 1.48) and 98.8 (95% CI: 98.5 to 99.0), respectively; echocardiography: 1.56 (95% CI: 1.14 to 2.07) and 98.4 (95% CI: 97.9 to 98.9), respectively). Although we were not able to calculate summary estimates of event rate after negative test and negative predictive value, the individual studies of stress MRI that we analyzed had approximately the same results as those of Metz et al. (Table 5).

There are several limitations in our study. First, there is a limited number of analyzed articles available when considering external validation. This was because the inclusion criteria were determined in order to minimize the analysts' bias. The limited number of analyzed articles forced us to give up subgroup analyses by patient gender, type of pharmacological stress, follow-up period and so on. To overcome this limitation, we may need to perform additional analyses using cumulative meta-analysis [29].

The second limitation is that the data we extracted from the literature and analyzed had insufficient homogeneity. Therefore, we were not able to calculate summary negative predictive value and summary event rate after negative test. Possible reasons for the lack of homogeneity include: 1) The observation period is different for every study; therefore, there is a tendency for the occurrence ratios of MACE and hard cardiac events after a negative result in stress CMR to be higher in studies with a long observation period. In addition, we were not able to obtain prognostic data that depended on the observation period from each study. 2) Even if the characteristics of the patients (Table 1-a: sample type) are approximately the same, the real pretest probability is different in each study. 3) A limited number of articles was analyzed (same as the first limitation described above).

The third limitation is that our analysis included several studies in which patients received intervention, such as pharmacological treatment for hypertension or hyperlipidaemia. In other words, our results may not observe the pure natural history of a negative result in stress CMR.

Recently, guidelines for medical practice have been developed in Japan. To achieve this, evidence assessment is required using articles collected through a comprehensive search; therefore, investigation of evidence will be increasingly important in diagnostic imaging [30]. Stress CMR has

added value for predicting cardiac events in terms of improved differentiation between high-risk and low-risk patients [19]. Accurate prognosis evaluation from risk stratification by non-invasive procedures will contribute to a reduction in unnecessary hospitalizations and invasive coronary angiography. Also, it will provide cost savings in diagnosis and treatment. Under the situation that we described above, prognostic evaluation of stress tests, including CMR, will become more and more important.

In conclusion, our systematic review demonstrates that a negative result in stress CMR has good prognostic value in predicting cardiac events. In particular, when the endpoint was defined as a hard cardiac event, patients who were negative in stress CMR had a markedly decreased risk of events than those who were positive in stress CMR. However, a limited number of articles was analyzed. It is necessary to continue studying stress CMR to establish evidence that it is useful for prognostic evaluation.

Potential conflicts of interest

The authors declare that there are no relevant potential conflicts of interest.

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Figure captions and legends

Fig. 1 Modified 2x2 table

Event: MACE or hard cardiac event
CMR: p-MRI or cine MRI

Fig. 2 Flow chart of the search process and results.

N = Number

Fig. 3 Forest plot of the summary relative risk ratios for MACE in patients with negative and positive results in stress cine MRI.

MACE: Major adverse cardiac events
RR: Relative risk ratio
CI: Confidence interval

Fig. 4 Forest plot of the summary relative risk ratio for MACE in patients with negative and positive results in stress perfusion MRI.

MACE: Major adverse cardiac events
RR: Relative risk ratio
CI: Confidence interval

Fig. 5 Forest plot of the summary relative risk ratio for hard cardiac events in patients with negative and positive results in stress cine MRI.

RR: Relative risk ratio
CI: Confidence interval

Fig. 6 Forest plot of the summary relative risk ratio for hard cardiac events in patients with negative and positive results in stress perfusion MRI.

RR: Relative risk ratio
CI: Confidence interval

First Author	Ref.	Year	Sample type	Total population	Mean Age (yrs)	Men (n)
Kuijpers D	5	2004	Suspected CAD	214	63	179
Jahnke C (a)	6	2011	Suspected or known CAD	679	61	471
Jahnke C (b)	6	2011	Suspected or known CAD	679	61	471
Wallace EL	8	2009	Suspected or known CAD	221	63	0
Bingham SE	18	2011	Suspected CAD	908	65	532
Kelle S	19	2011	Suspected or known CAD	1017	62	961
Ingkanisorn WP	20	2006	Suspected CAD	135	56	75
Bodi V (a)	21	2009	Suspected or known CAD	601	64	360
Bodi V (b)	21	2009	Suspected or known CAD	601	64	360
Bodi V (a)	22	2007	Suspected or known CAD	420	64	255
Bodi V (b)	22	2007	Suspected or known CAD	420	64	255
Pilz G	23	2008	Suspected CAD	218	63	122
Coelho-Filho OR	24	2011	Suspected CAD	405	57	237
Hartlage G	25	2011	Suspected CAD	89	56	29

Table 1-a Characteristics of the included studies.

CAD: Coronary artery disease

First Author	Ref.	Mean or median follow-up (years)	Cine or perfusion	NOS (stars)	Definition of end points
Kuijpers D	5	2.0	Cine	5	MACE and hard cardiac events
Jahnke C (a)	6	5.3	Cine	5	MACE and hard cardiac events
Jahnke C (b)	6	5.3	Perfusion	5	MACE and hard cardiac events
Wallace EL	8	6.2	Cine	6	MACE and hard cardiac events
Bingham SE	18	2.6	Perfusion	5	MACE and hard cardiac events
Kelle S	19	3.7	Cine	5	Hard cardiac events
Ingkanisorn WP	20	1.3	Perfusion	5	MACE
Bodi V (a)	21	1.8	Cine	5	MACE
Bodi V (b)	21	1.8	Perfusion	5	MACE
Bodi V (a)	22	1.4	Cine	5	Hard cardiac events
Bodi V (b)	22	1.4	Perfusion	5	Hard cardiac events
Pilz G	23	1.0	Perfusion	5	MACE and hard cardiac events
Coelho-Filho OR	24	2.5	Perfusion	5	Hard cardiac events
Hartlage G	25	0.8	Perfusion	5	MACE

Table 1-b Characteristics of the included studies.

MACE: Major adverse cardiac events

First Author	Ref.	Negative test (n)	Stress	Scanner type (T)	Negative predictive value (%) (95% CI)	Event rate after negative test (%) (95% CI)
Kuijpers D	5	214	Dobutamine	1.0	92.8 (88.5–95.9)	7.2 (4.1–11.5)
Jahnke C (a)	6	679	Dobutamine	1.5	67.3 (62.5–71.8)	32.7 (28.2–37.5)
Wallace E.L	8	221	Dobutamine	1.5	68.2 (60.4–75.3)	31.8 (24.7–39.6)
Bodi V (a)	21	601	Dipyridamole	1.5	90.0 (87.2–92.4)	10.0 (7.6–12.8)

Table 2 Studies of the value of cine MRI in predicting MACE.

MACE: Major adverse cardiac events

CI : Confidence interval

First Author	Ref.	Negative test (n)	Stress	Scanner type (T)	Negative predictive value (%) (95% CI)	Event rate after negative test (%) (95% CI)
Jahnke C (b)	6	363	Adenosine	1.5	67.4 (62.4–72.2)	32.6 (27.8–37.6)
Bingham SE	18	610	Adenosine	1.5	93.2 (90.9–95.1)	6.8 (4.9–9.1)
Ingkanisorn WP	20	107	Adenosine	1.5	99.5 (95.8–100)	0.5 (0–4.2)
Bodi V (b)	21	454	Dipyridamole	1.5	96.2 (94.0–97.7)	3.8 (2.2–6.0)
Pilz G	23	218	Adenosine	1.5	98.9 (96.4–99.8)	1.1 (0.2–3.6)
Hartlage G	25	82	Adenosine	1.5	99.4 (94.5–100)	0.6 (0–5.5)

Table 3 Studies of the value of perfusion MRI in predicting MACE

MACE: Major adverse cardiac events

CI : Confidence interval

First Author	Ref.	Negative Test (n)	Stress	Scanner type (T)	Negative predictive value (%) (95% CI)	Event rate after negative test (%) (95% CI)
Kuijpers D	5	214	Dobutamine	1.0	97.9 (95.0–99.4)	2.1 (0.6–5.0)
Jahnke C (a)	6	404	Dobutamine	1.5	87.8 (84.2–90.8)	12.2 (9.2–15.8)
Wallace E.L	8	161	Dobutamine	1.5	92.3 (87.0–95.9)	7.7 (4.1–13.0)
Kelle S	19	716	Dobutamine	1.5	96.9 (95.3–98.0)	3.1 (2.0–4.7)
Bodi V (a)	22	280	Dipyridamole	1.5	96.6 (93.8–98.4)	3.4 (1.6–6.2)

Table 4 Studies of the value of cine MRI in predicting hard cardiac events.

CI : Confidence interval

First Author	Ref.	Negative Test (n)	Stress	Scanner type (T)	Negative predictive value (%) (95% CI)	Event rate after negative test (%) (95% CI)
Jahnke C (b)	6	351	Adenosine	1.5	90.2 (86.6–93.1)	9.8 (6.9–13.4)
Bingham SE	18	610	Adenosine	1.5	97.8 (96.3–98.8)	2.2 (1.2–3.7)
Bodi V (b)	22	239	Dipyridamole	1.5	96.5 (93.3–98.4)	3.5 (1.6–6.7)
Pilz G	23	218	Adenosine	1.5	100	0
Coelho-Filho OR	24	296	Adenosine or Dipyridamole	1.5 or 3.0	97.8 (95.4–99.2)	2.2 (0.8–4.6)

Table 5 Studies of the value of perfusion MRI in predicting hard cardiac events.

CI : Confidence interval

First Author (Ref. #)	Cine or perfusion	Definition of end points	Relative risk ratio (95% CI)	Negative predictive value (%) (95% CI)	Event rate after negative test (%) (95% CI)
Jahnke C (6)	Cine	MACE	0.52 (0.44–0.61)	67.3 (62.5–71.8)	32.7 (28.2–37.5)
Jahnke C (6)	Perfusion	MACE	0.55 (0.46–0.65)	67.4 (62.4–72.2)	32.6 (27.8–37.6)
Jahnke C (6)	Cine	Hard cardiac events	1.18 (0.77–1.83)	87.8 (84.2–90.8)	12.2 (9.2–15.8)
Jahnke C (6)	Perfusion	Hard cardiac events	0.74 (0.49–1.13)	90.2 (86.6–93.1)	9.8 (6.9–13.4)
Bodi V (21)	Cine	MACE	0.41 (0.25–0.66)	90.0 (87.2–92.4)	10.0 (7.6–12.8)
Bodi V (21)	Perfusion	MACE	0.11 (0.07–0.18)	96.2 (94.0–97.7)	3.8 (2.2–6.0)
Bodi V (22)	Cine	Hard cardiac events	0.33 (0.15–0.73)	96.6 (93.8–98.4)	3.4 (1.6–6.2)
Bodi V (22)	Perfusion	Hard cardiac events	0.42 (0.18–0.94)	96.5 (93.3–98.4)	3.5 (1.6–6.7)

Table 6 Studies of the prognostic value of CMR in the same patient group.

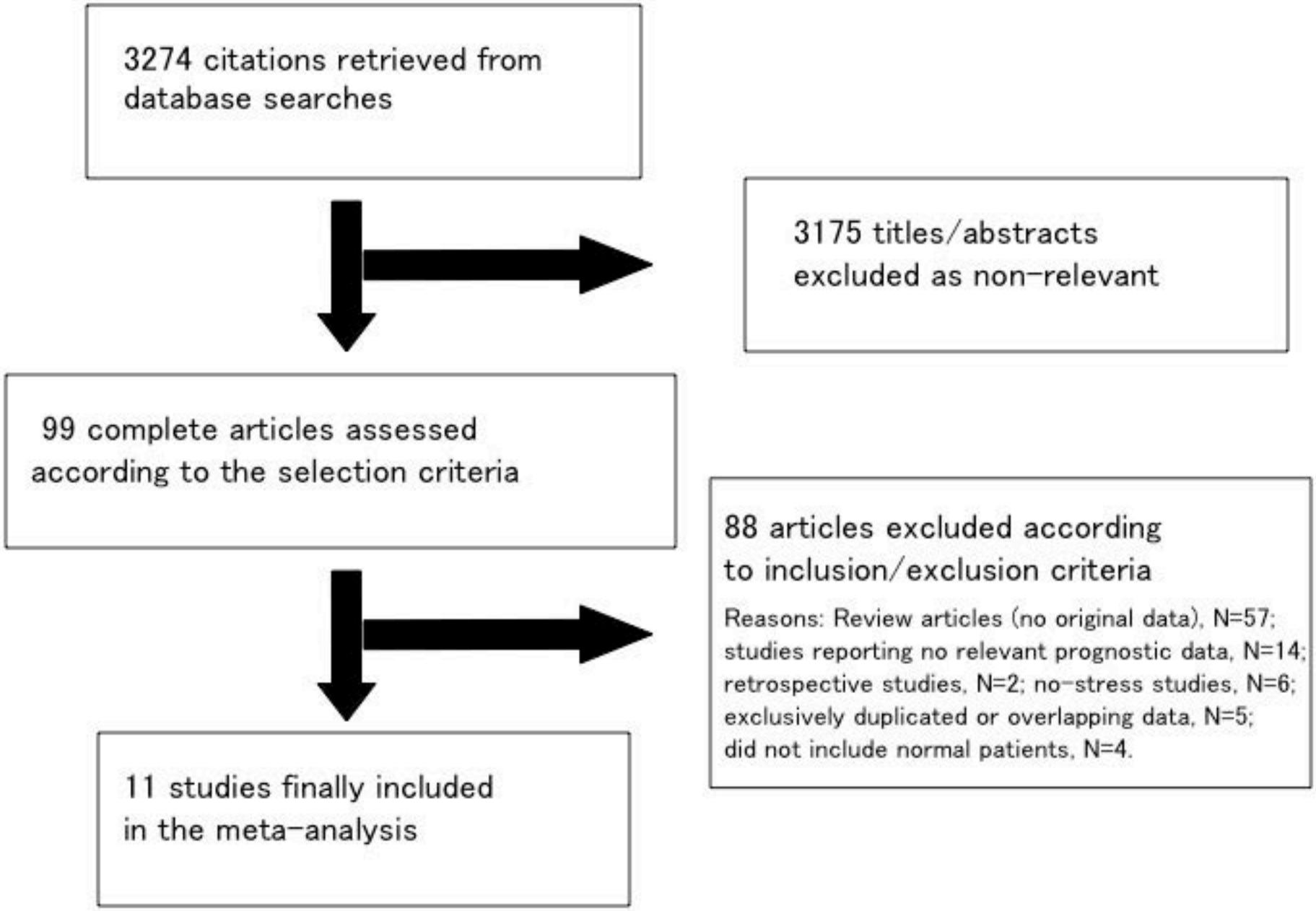
MACE: Major adverse cardiac events

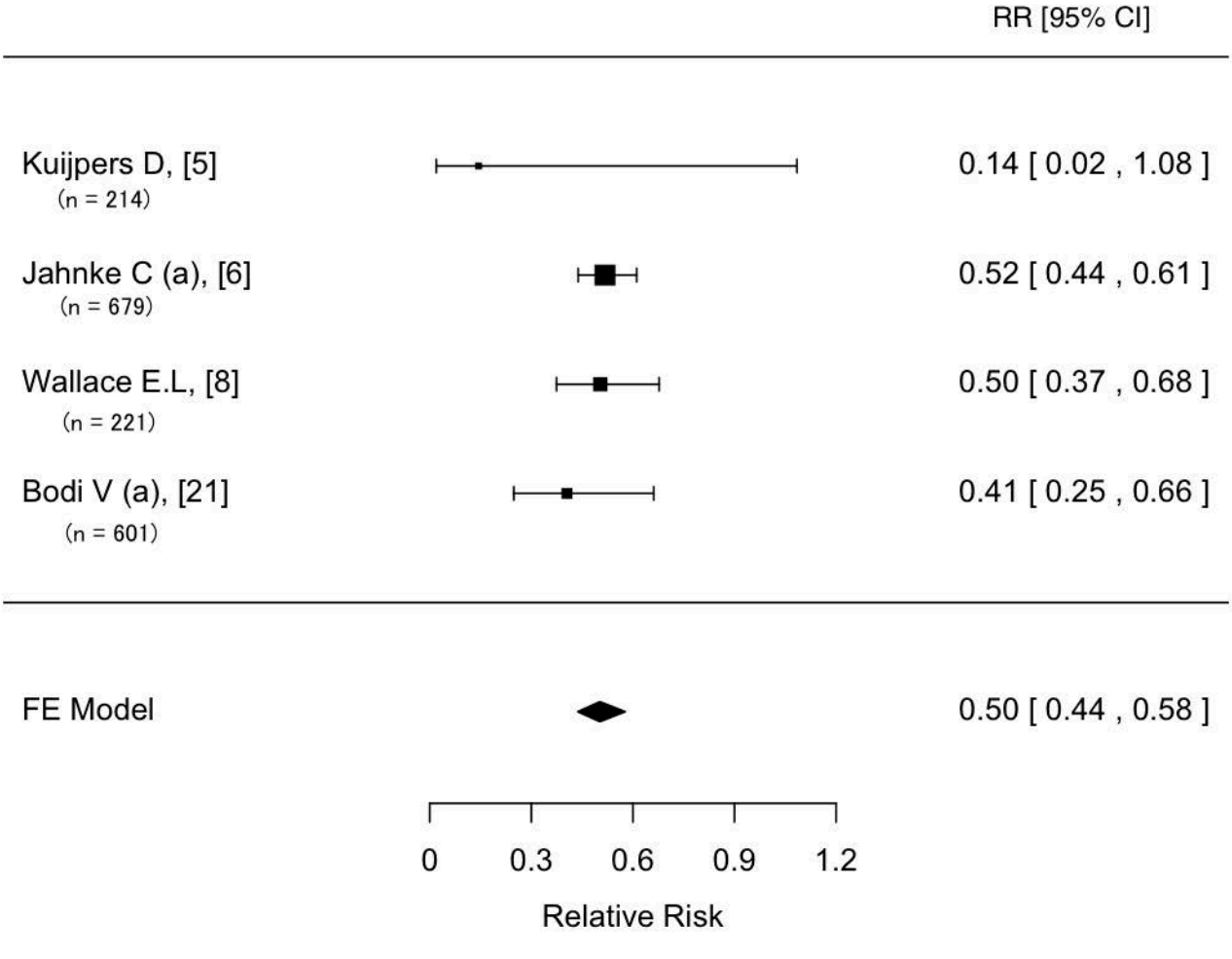
CI : Confidence interval

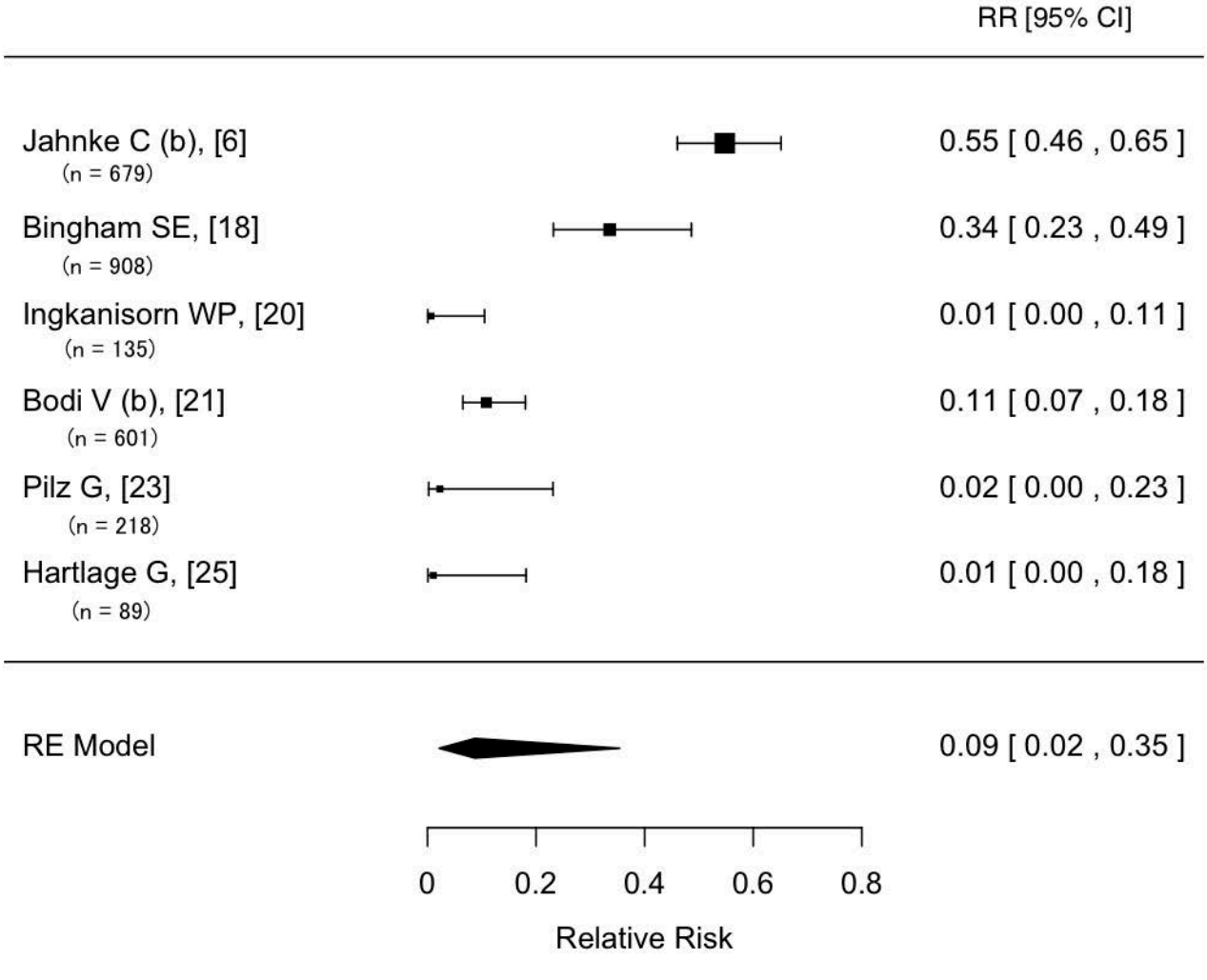
	Event (+)	Event (−)
Negative CMR	a	c
Postive CMR	b	d

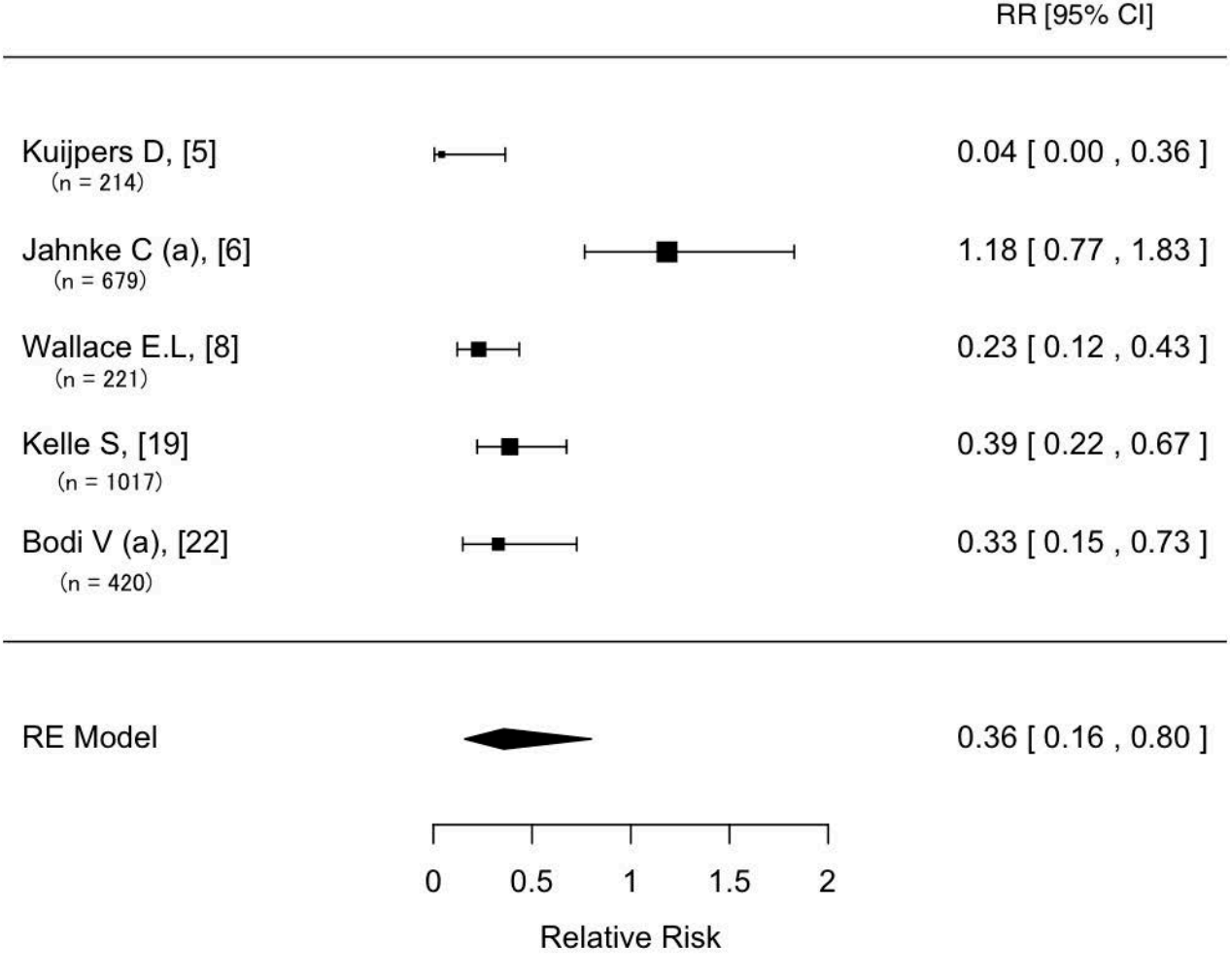
Risk ratio = a(b+d)/b(a+c) (Prospective study)

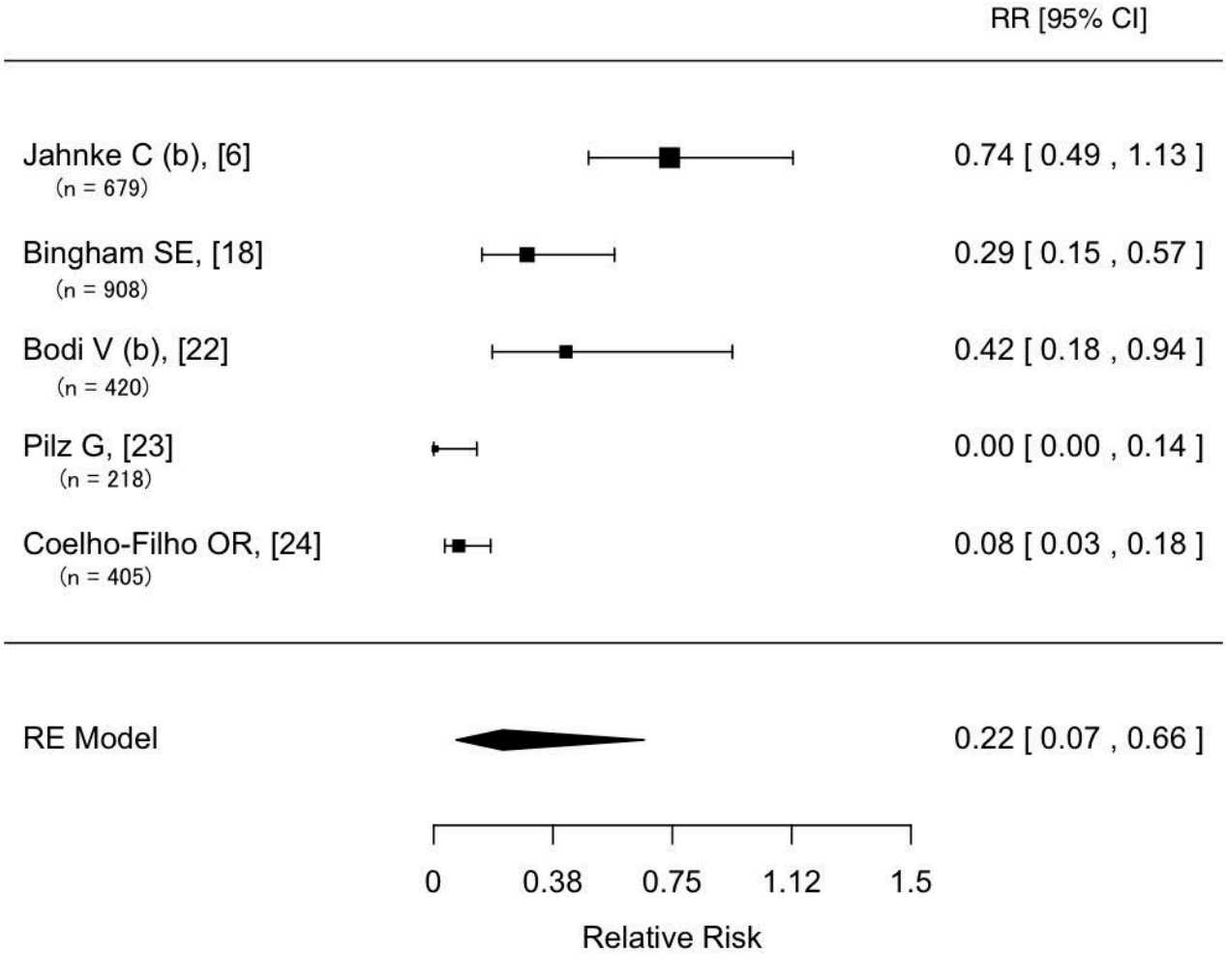
Negative predictive value = c/(a+c)


3274 citations retrieved from database searches
3175 titles/abstracts excluded as non-relevant
99 complete articles assessed according to the selection criteria
88 articles excluded according to inclusion/exclusion criteria
Reasons: Review articles (no original data), N=57; studies reporting no relevant prognostic data, N=14; retrospective studies, N=2; no-stress studies, N=6; exclusively duplicated or overlapping data, N=5; did not include normal patients, N=4.
11 studies finally included in the meta-analysis


RR [95% CI]
Kuijpers D, [5]
(n = 214)
0.14 [0.02 , 1.08]
Jahnke C (a), [6]
(n = 679)
0.52 [0.44 , 0.61]
Wallace E.L, [8]
(n = 221)
0.50 [0.37 , 0.68]
Bodi V (a), [21]
(n = 601)
0.41 [0.25 , 0.66]
FE Model
0.50 [0.44 , 0.58]
0
0.3
0.6
0.9
1.2
Relative Risk


RR [95% CI]
Jahnke C (b), [6]
(n = 679)
0.55 [0.46 , 0.65]
Bingham SE, [18]
(n = 908)
0.34 [0.23 , 0.49]
Ingkanisorn WP, [20]
(n = 135)
0.01 [0.00 , 0.11]
Bodi V (b), [21]
(n = 601)
0.11 [0.07 , 0.18]
Pilz G, [23]
(n = 218)
0.02 [0.00 , 0.23]
Hartlage G, [25]
(n = 89)
0.01 [0.00 , 0.18]
RE Model
0.09 [0.02 , 0.35]
0
0.2
0.4
0.6
0.8
Relative Risk


RR [95% CI]
Kuijpers D, [5]
(n = 214)
0.04 [0.00 , 0.36]
Jahnke C (a), [6]
(n = 679)
1.18 [0.77 , 1.83]
Wallace E.L, [8]
(n = 221)
0.23 [0.12 , 0.43]
Kelle S, [19]
(n = 1017)
0.39 [0.22 , 0.67]
Bodi V (a), [22]
(n = 420)
0.33 [0.15 , 0.73]
RE Model
0.36 [0.16 , 0.80]
0
0.5
1
1.5
2
Relative Risk


RR [95% CI]
Jahnke C (b), [6]
(n = 679)
0.74 [0.49 , 1.13]
Bingham SE, [18]
(n = 908)
0.29 [0.15 , 0.57]
Bodi V (b), [22]
(n = 420)
0.42 [0.18 , 0.94]
Pilz G, [23]
(n = 218)
0.00 [0.00 , 0.14]
Coelho-Filho OR, [24]
(n = 405)
0.08 [0.03 , 0.18]
RE Model
0.22 [0.07 , 0.66]
0
0.38
0.75
1.12
1.5
Relative Risk