Original Article

Incidence of myocardial injury in coronavirus disease 2019 (COVID-19): a pooled analysis of 7,679 patients from 53 studies

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Background: Coronavirus disease 2019 (COVID-19) has become global pandemic and resulted in considerable morbidity and mortality since December 2019. Information on the incidence of myocardial injury remains scarce.

Methods: English-language databases (PubMed, Embase, Cochrane), Chinese-language databases (CNKI, VIP, WANFANG), and preprint platform were searched to identify studies that reported the myocardial injury data in COVID-19 patients. Random-effects meta-analyses were used to derive the pooled incidence and relative risks (RRs) of myocardial injury. Variations by disease severity were examined by subgroup analyses. Sensitivity analyses were performed to strengthen the results. Meta-regression was applied to explore the risk factors associated with myocardial injury.

Results: A total of 53 studies involving 7,679 patients were included. The pooled incidence of myocardial injury was 21% [95% confidence interval (CI), 17–25%; I^2, 96.5%]. The highest incidence of myocardial injury was found in non-survivors (66%; 95 CI%, 54–78%; I^2, 85.7%), followed by severe patients (43%; 95 CI%, 33–53%; I^2, 93.0%) and non-severe patients (11%; 95 CI%, 7–15%; I^2, 95.2%). Higher risk of myocardial injury was detected in severe patients than non-severe patients (RR, 5.74; 95% CI, 3.74–8.79; I^2, 86.8%). All the sensitivity analyses confirmed the robustness of primacy results.

Conclusions: This meta-analysis showed that myocardial injury occurred in 21% of COVID-19 patients. An elevated rate was observed in non-survivors (66%) and severe patients (43%). Severe patients had a 4.74-fold increase in the risk of myocardial injury than non-severe patients. Aggressive strategy may be considered for COVID-19 patients at high risk of myocardial injury.

Keywords: Severe acute respiratory syndrome coronavirus 2 (SAR-CoV-2); coronavirus disease 2019 (COVID-19); myocardial injury; incidence; meta-analysis

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Introduction

Since December 2019, coronavirus disease 2019 (COVID-19) caused by the newly discovered severe acute respiratory syndrome coronavirus 2 (SAR-CoV-2) has been recognized as a major public health issue due to rapidly global pandemic, resulting in 7,823,289 confirmed infections and 431,541 deaths worldwide by 15 June 2020 (1). Previous studies have described the main

findings of clinical and epidemiological characteristics in COVID-19 patients (2-4). With the increase of confirmed cases and the accumulation of clinical data, the cardiovascular manifestations caused by COVID-19 has raised concern. Myocardial injury, defined as elevated levels of troponin or creatine kinase isoenzyme (CK-MB) regardless of new abnormalities in electrocardiography and echocardiography, have been reported with the rate of 7.2% in the initial COVID-19 study (4). Two recent studies presented 19.7% to 27.8% of patients with COVID-19 had acute myocardial injury (5,6). Obviously, incidence of myocardial injury in this viral infection remains uncertain. The pathophysiology of COVID-associated myocardial injury have not well established but likely involve the direct damage to cardiomyocytes, systemic inflammation, myocardial interstitial fibrosis, interferon mediated immune response, exaggerated cytokine response, in addition to coronary plaque destabilization, and hypoxia (7). Apart from COVID-19 itself, there are other factors associated with myocardial injury in these patients, which include cardiovascular risk factors (smoking, hypertension, obesity, physical inactivity, advanced age), severe forms of the disease and medications such as hydroxychloroquine or chloroquine (7-9). Currently published meta-analyses have reported that more myocardial injury happened in severe COVID-19 patients, which was subsequently associated with deteriorative outcomes [mortality and need for intensive care unit (ICU) care] (10-12). Nevertheless, no study until now have given a full picture for myocardial injury incidence in patients with COVID-19. The present study therefore summarized all available evidence for a comprehensive and rigorous systematic review focused on myocardial injury incidence in COVID-19. In addition, to state the case-fatality rate related to cardiac injury, variations of myocardial injury incidence were also examined by disease severity (non-survivors, severe patients, and non-severe patients). We present the following article in accordance with the PRISMA reporting checklist (available at http://dx.doi.org/10.21037/cdt-20-535).

Methods

This systematic review and meta-analysis was established according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. The authors declare that all supporting data are available within the article and in the Supplementary file.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The ethical approval and consent are not required because no patient-level data is involved for this systematic review and meta-analysis.

Data sources and searches

Relevant studies were identified by performing English-language searches of PubMed, Embase, Cochrane Library databases (through April 24, 2020) as well as Chinese-language searches of China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (VIP), WANFANG databases (through April 23, 2020) using the search terms related to COVID-19. The full search strategy is outlined in *Table S1*. Preprint articles were retrieved from the websites of MedRxiv (https://www.medrxiv.org), BioRxiv (https://www.biorxiv.org), and SSRN (https://www.ssrn.com) (through April 24, 2020). Manual search was also conducted by screening the reference lists of inclusive studies and relevant meta-analysis.

Study selection and outcomes

Studies of any types [case series study, cross-sectional study, case control study, cohort study, or randomized controlled trial (RCT)] were eligible for inclusion if they included SARS-CoV-2 infected adult patients; reported the qualitative data of cardiac specific biomarkers (troponin or CKMB); or reported the data of myocardial injury with detailed definition. Studies were excluded if they did not report defined myocardial injury indexes or published in meta-analysis or case report. Because of the difficulty to estimate the potentially repetitive patients, all the studies met the inclusion criteria were available for meta-analysis. Two authors (ZG and CZ) independently reviewed each title and abstract, and assessed full texts of retrieved studies, with any disagreements being resolved via consultation with a third author (JP). The primary outcomes of this study were the incidence of myocardial injury in COVID-19 and corresponding relative risk (RR) in comparison between severe and non-severe patients. COVID-19 patients was the laboratory diagnosis using real time reverse transcription-polymerase chain reaction (RT-PCR) assay or clinical diagnosis based on the Guidance for COVID-19 (7th edition) released by the National Health Commission of China. Myocardial injury was defined as serum levels of troponin or CK-MB above the 99th percentile upper

reference limit, regardless of new abnormalities in electrocardiography and echocardiography. Severe patients were judged according to the Guidance for COVID-19 (7th edition) released by the National Health Commission of China (13).

Data extraction and quality assessment

Two authors (ZG and CZ) independently extracted the data using a priori designed form: which included study characteristics (study name, study source, regions, detailed hospital), patient characteristics (included period, illness severity, diagnosis standard for COVID-19, myocardial injury definition and its cut-off value), clinical characteristics (age, gender, smoking, and the comorbidities of hypertension, diabetes, cardiovascular disease (CVD), cerebrovascular disease, chronic pulmonary disease, chronic kidney disease, liver disease, and cancer), and data on cardiac injury (occurrence number and total number). The methodological quality of included RCTs was evaluated according to Cochrane Collaboration Risk of Bias Tool (14). The methodological quality of each included observational studies was assessed according to the Newcastle-Ottawa Scale (NOS) (15). To fit in our study design, the NOS was modified with totally 8 scores and the following 6 dimensions: representative of the sample; ascertainment of the exposure; ascertainment of the outcome; ascertainment of the outcome for quality control; control for factors of age and gender; and control for factors related to myocardial injury. A study can be awarded a maximum of 1 point for the first 4 dimensions and a maximum of 2 points for the last 2 dimensions (control for factors of age and gender: 1 point for age and 1 point for sex; control for factors related to myocardial injury: 1 point for reporting 1 or 2 comorbidities and 2 points for reporting ≥3 comorbidities). The total scores of ≥5 points represented a relatively good quality.

Data synthesis and statistical analysis

A random-effects (DerSimonian and Laird method) meta-analysis was used to calculate the pooled incidence of myocardial injury with 95% confidence intervals (95% CIs). Likewise, RRs of myocardial injury comparing severe with non-severe patients was performed. Heterogeneity among studies was assessed using the Cochran Q test and I^2 index, with I^2 >50% representing considerable heterogeneity (16). Subgroup analysis was conducted by the severity of illness (non-survivors, severe patients, and non-severe patients). The interaction analysis (P for interaction) using Cochran's Q test were applied to evaluate the risk difference of different illness severity (17). Interaction is referred to as effect modification, which investigates whether the effect of intervention in the primacy outcome varied between the subgroup such as disease severity. A leave-1-out sensitivity analysis for each meta-analysis was applied to explore whether a single study had an excessive influence on myocardial injury incidence. To strengthen the robustness of the results, further serial sensitivity analyses were conducted by including studies that real time RT-PCR assay was performed using a SARS-CoV-2 nucleic acid detection, or studies that used troponin or electrocardiography or echocardiography as definition of myocardial injury, or excluding studies that involved potentially repetitive patients in the same hospital with period within range of other studies; or excluding studies that sample size were <50. To address the potential risk factors associated with myocardial injury, all preexisting cardiovascular risk factors or established diseases will be taken into consideration in the meta-regression. As a rule, at least 25% data points should be available for each variable in univariable meta-regression. The presence of publication bias was evaluated qualitatively by funnel plots and quantitatively by Begg's test and Egger's test when more than 10 studies were available in a single analysis (18). Trim and fill method was used to deal with the publication bias. The trim and fill method requires no assumptions about the mechanism that lead to publication bias, provides an estimate of the number of missing studies, and also provides an estimated intervention effect to adjust the publication bias. Data were analyzed using Stata version 13.0 (StataCorp., College Station, TX, USA).

Results

Study selection and study characteristics

As outlined in *Figure 1*, initial search identified 5,449 records from English-language databases, 7,023 from Chinese-language databases, and 3,401 from preprint platform; 1,509 duplicates were removed and 14,077 records were excluded by screening titles and abstracts; the remaining 287 full-text articles were reviewed and 234 articles were excluded with the following reasons: studies were irrelevant (n=94), studies did not report outcome of myocardial injury (n=103), studies were meta-analyses, and studies was repetitive with other database (n=7). Finally, 53 studies involving 7,679

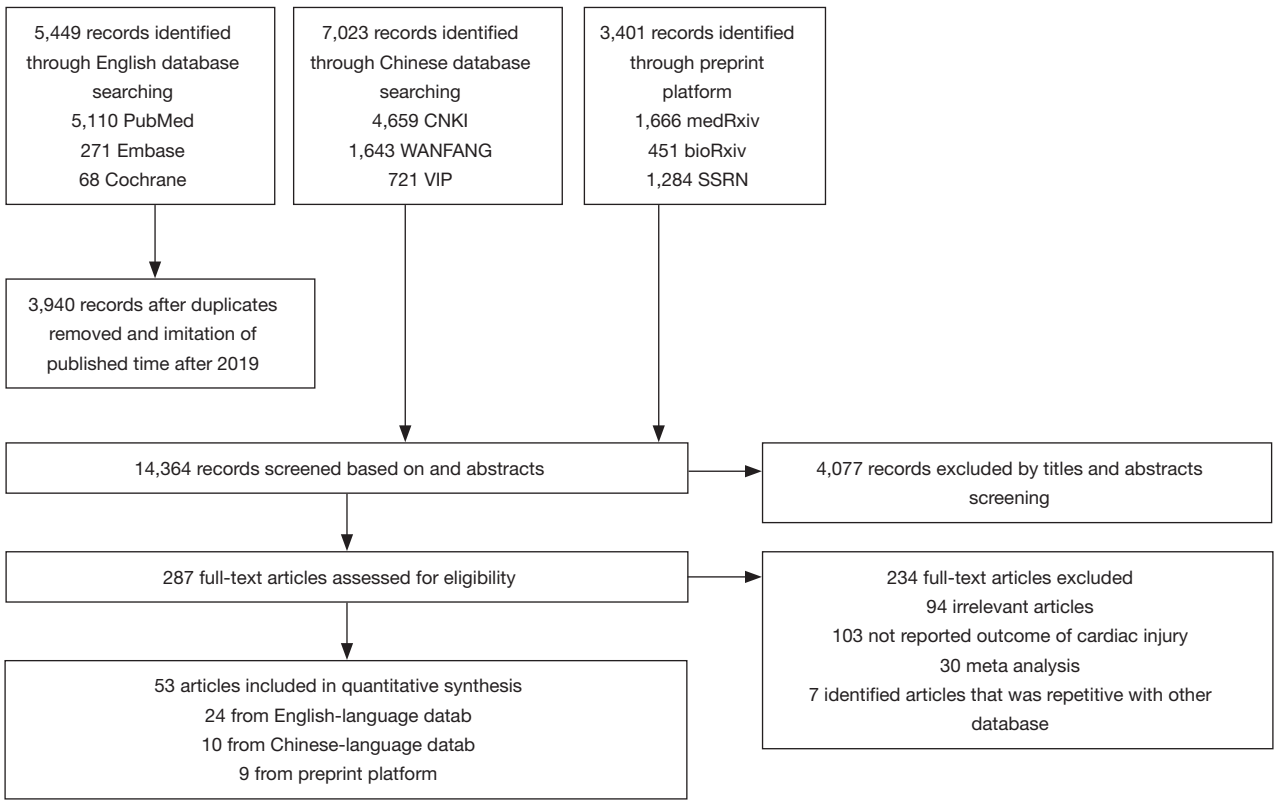

Figure 1 Flow diagram for the selection of eligible studies. CNKI, China National Knowledge Infrastructure; VIP, China Science and Technology Journal Database.

COVID-19 patients were included, with 24 from English-language databases, 10 from Chinese-language databases, and 19 from preprint platform. Among them, 21 studies (39%) were cross-sectional studies, 16 (30%) were case-series studies, 14 (26%) were case-control studies, and 2 (5%) were cohort studies. Twenty-eight studies (53%) were conducted in Hubei, 22 (41%) in regions outside Hubei, 2 (4%) in both Hubei and other regions, and 1 in New York (*Table S2*). The majority of studies (48/53, 91%) used RT-PCR method for confirming COVID-19. The remaining 5 studies used RT-PCR method or clinical diagnosis definition for confirming COVID-19. Thirty-three studies (62%) used troponin, 11 (21%) applied troponin or electrocardiography or echocardiography, and the remaining 9 (17%) employed CK-MB as cardiac injury definition (*Table S3*). The number of included COVID-19 patients varied from 8 to 1,327. The mean age was 54 years and the percentage of male was 54.1%. Other detailed information on comorbidities is summarized in *Table S4*.

Study quality

All included studies satisfied the following risk bias items: representative of the sample; ascertainment of the exposure; ascertainment of the outcome; and control for factors of age and gender. Twenty-three studies (43%) defined the myocardial injury in the text (ascertainment of the outcome for quality control); 37 studies (70%) reported more than 3 comorbidities (2 points) and 11 studies (21%) reported 1 or 2 comorbidities (1 point). Eventually, all 53 studies were rated as relatively good quality (*Table S5*).

Incidence of myocardial injury

Figure 2 gives the full picture of myocardial injury incidence. The overall pooled incidence of myocardial injury was 21% (95% CI, 17–25%; I^2, 96.5%; *Figure S1*). For severity of illness, the highest incidence of myocardial injury was found in non-survivors (66%; 95% CI, 54–78%; I^2, 85.7%; *Figure S2*), followed by severe patients (43%; 95% CI, 33–

Population	No. of studies	No. of patients	No. of cases	Incidence (95%CI)	I^2 (%)
Overall	53	7679	1353	0.21 (0.17-0.25)	96.5
Disease severity					$P_{interaction}$ <0.01
Non-survivors	8	380	255	0.66 (0.54-0.78)	85.7
Severe patients	29	1178	485	0.43 (0.33-0.53)	93.0
Non-severe patients	29	3257	333	0.11 (0.07-0.15)	95.2
Sensitivity analyses					
Patients detected with RT-PCR	48	7079	1189	0.20 (0.17-0.24)	96.2
Cases defined as troponin or EKG or Echo	44	6654	1295	0.23 (0.18-0.27)	96.8
Exclusion of potentially repetitive patients	36	5905	1003	0.20 (0.15-0.24)	96.6
Exclusion of studies that sample size <50	39	7326	1263	0.20 (0.16-0.25)	97.2

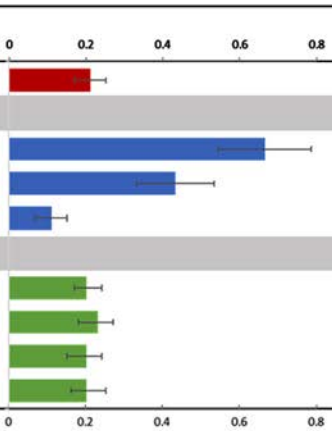

Figure 2 Incidence of cardiac injury. No., number; 95% CI, 95% confidence interval; EKG, electrocardiography; Echo, echocardiography.

Population	No. of studies	Severe patients cases/no.	Non-severe patients cases/no.	RR (95%CI)	I^2 (%)
Overall	29	445/1133	322/3100	5.74 (3.74-8.79)	86.8
Sensitivity analyses					
Patients detected with RT-PCR	28	398/989	301/3000	6.28 (3.97-9.93)	87.3
Cases defined as troponin or EKG or Echo	27	435/1025	317/2619	5.59 (3.62-8.64)	86.8
Exclusion of potentially repetitive patients	18	246/723	255/2095	4.34 (2.60-7.24)	85.5
Exclusion of studies that sample size <50	25	419/1092	317/3012	5.37 (3.42-8.43)	88.0

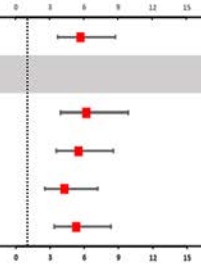

Figure 3 Cardiac injury risk of severe patients versus non-severe patients. No., number; RR, relative risk; 95% CI, 95% confidence interval; EKG, electrocardiography; Echo, echocardiography.

53%; I^2, 93.0%; *Figure S3*) and non-severe patients (11%; 95% CI, 7–15%; I^2, 95.2%; *Figure S4*), with significant difference (Pinteraction <0.01). Sensitivity analyses by removing a single study at 1 time; or including studies that patients were detected with RT-PCR assay; or including studies that cases were defined as troponin; or excluding studies that involved potentially repetitive patients or sample size were <50 confirmed the robustness of primacy results (*Table S6* and *Figures S5*,*S6*,*S7*,*S8*).

Comparison of myocardial injury risk with severe versus non-severe patients

Totally, 29 studies involving 4,233 patients were identified, and the incidence of myocardial injury was 39.3% in severe patients (445/1,133) compared with 10.4% (322/3,100) in non-severe patients (*Figure 3*), indicating that severe patients were associated with significantly higher risk of myocardial injury (RR, 5.74; 95% CI, 3.74–8.79; I^2, 86.8%; *Figure S9*). Leave-1-out sensitivity analyses as well as further serial sensitivity analyses were in consistence with the primacy results (*Figures S10*,*S11*,*S12*,*S13*,*S14*). Meta-regression failed to detect any clinical characteristics and comorbidities to impact the primacy results (*Table S7*).

Risk factors associated with myocardial injury

The association between various comorbidities and myocardial injury incidence is shown in *Table S8*. Eleven variables with more than 25% data points (age, gender, smoking, hypertension, diabetes, CVD, cerebrovascular disease, chronic pulmonary disease, chronic kidney disease, liver disease, and cancer) were assessed in univariable meta-regression. The results suggested that the incidence of myocardial injury were not associated with any of the above comorbidities.

Publication bias

The funnel plots for myocardial injury incidence in overall patients, in severe patients, and in non-severe patients were all asymmetrical on visual inspection, and the corresponding P values for the Egger's test were <0.001, 0.972, and 0.004, respectively (*Figure S15*). The trim and fill method was applied to handle publication bias, resulting in 9% (95% CI, 5–14%) for incidence in overall patients and 4% (95% CI, 1–7%) for incidence in non-severe patients (*Table S9*). Because of limited study number in non-survivors (8 studies), funnel plot was not performed.

Discussion

Major findings and interpretations

This systematic review and meta-analysis firstly provided a comprehensive overview of myocardial injury incidence based on 53 retrospective studies involving 7,679 COVID-19 patients. The major findings were as follows: (I) the overall incidence of myocardial injury was 21%; (II) considering the severity of disease, myocardial injury incidence progressively increased in non-survivors (66%), severe patients (43%), and non-severe patients (11%); (III) severe patients had a 4.74-fold increased risk of myocardial injury compared with non-severe patients. Previous study found that COVID-19 patients who were admitted to the ICU had higher plasma levels of cytokines (3). As cytokine storm is one of the potential mechanisms underlying myocardial injury, it is predictable that incidence of myocardial injury might be high among non-survivors and severe patients.

Comparison with previous studies

Currently, several systematic reviews and meta-analyses have been conducted to assess the risk of myocardial injury among COVID-19 patients. The earliest one, which pooled 4 studies of 341 patients, showed that the values of troponin were significantly increased in severe patients than that in non-severe patients [standardized mean difference (SMD), 25.6 ng/L; 95% CI, 6.8–44.5 ng/L] (10). Although this is the first meta-analysis to assess the myocardial injury risk in COVID-19, the limitation of study number and sample size may influence the robustness of results. Another meta-analysis addressed this issue by merging 28 studies of 4,189 patients and found that myocardial injury biomarkers were higher in severe patients compared with less severe patients (SMD, 0.69; 95% CI, 0.48–0.89) (11). Notably, this study used a broadly definition of myocardial injury (the combination of troponin, CK-MB, NT-proBNP, and myoglobin), which inevitably led to the overestimation of myocardial injury risk. The recent meta-analysis involving 2,389 patients from 13 studies reported that myocardial injury was associated with higher mortality (RR, 7.95; 95% CI, 5.12–13.34) and need for ICU care (RR, 7.94; 95% CI, 1.51–41.78) (12). This study used a precise definition of myocardial injury (troponin above the 99th percentile upper reference limit, regardless of new abnormalities in electrocardiography and echocardiography), whereas risk factors of myocardial injury as well as visible publication bias seemingly not to be well addressed. Given the above limitations, the present meta-analysis restricted the definition of myocardial injury and included all available evidence to comprehensively estimate the incidence and potential risk factors of myocardial injury in COVID-19 patients.

Potential mechanism of myocardial injury

The mechanisms underlying myocardial injury have not well established but likely involve viral myocarditis, cytokine storm, microvascular thrombosis, and unmasked CVDs. Evidence from autopsies found that 35% of heart samples in SAR-CoV infected patients presented the viral genome, which raised the possibility of direct impair of cardiomyocytes by the virus (19). SAR-CoV-2 might share the same mechanism as the highly homologous with SAR-CoV. Nevertheless, a recent pathological study failed to demonstrate the presence of SAR-CoV-2 within myocardial tissue (20). Therefore, the question of whether the SAR-CoV-2 could directly damage the heart requires further scientific verification. Guo *et al.* found that plasma troponin levels had a significantly positive linear correlation with plasma high-sensitivity C-reactive protein (hs-CRP) levels, indicating that myocardial injury may be associated with inflammatory pathogenesis during the disease progress (5). Besides hs-CRP, other cytokines, including interleukin (IL)-2, IL-7, IL-10, IgG-included protein 10, monocyte chemoattractant protein-1, macrophage inflammatory protein 1-alpha, and tumors necrosis factor, were proved to be involved in the inflammatory response of COVID-19 (3). The activation of these inflammatory cytokines after infection might cause endothelial dysfunction, coronary plaque destabilization, microvascular dysfunction, and subsequently contribute to myocardial

injury. Predictably, this marked inflammatory response could also lead to the development of disseminated intravascular coagulopathy (DIC) in critical patients. Tang *et al.* reported that coagulopathy was associated with high mortality and 71% of non-survivors met the criteria of DIC (21). As such, microvascular thrombosis of coronary vessels due to DIC is another potential mechanism that might contribute to myocardial injury. In addition, COVID-19 patients preexisting CVD and other comorbidities might be more likely to suffer from myocardial injury. Shi et al reported that approximately 30% and 60% of patients with myocardial injury had a history of coronary heart disease and hypertension, respectively, which were more prevalent than in those without myocardial injury (6). Although limited evidence exists for evaluating the association of myocardial injury with cardiovascular comorbidities, it is rational to presume that patients with underlying comorbidities are susceptible to myocardial injury through several mechanisms including virus-driven direct damage, systemic inflammatory response, coronary plaque destabilization, and hypoxia aggravation. Regrettably, we only obtained study-level information about comorbidities and failed to detect any risk factors associated with myocardial injury.

Clinical consideration for myocardial injury

Given the high incidence of myocardial injury among COVID-19 patients, it might be reasonable to triage patients according to cardiovascular comorbidities and myocardial biomarkers. The majority of patients with a mildly elevated troponin can be followed with expectant management until recovery from acute viral syndrome. However, patients whom are hemodynamically and electrophysiologically unstable with marked elevations of troponin should launch earlier and more aggressive intervention strategies.

Strengths and limitations

Strengths of this study mainly include the systematic and rigorous approach to estimate the incidence of myocardial injury. We performed a comprehensive search of English-language databases, Chinese-language, and preprint platform; restricted the definition of myocardial injury; used the revised NOS tool to suitably assess the study quality; conducted the subgroup analyses by disease severity to explore for differences on myocardial injury incidence; performed serial sensitivity analyses to strengthen the robustness of results; applied meta-regression to explore the risk factors associated with myocardial injury; and employed trim and fill method to handle the potential publication bias. Certainly, several intrinsic limitations should be recognized in this study. Firstly, all included studies were retrospective and there were differences on diagnosis criterion for COVID-19 and definition of myocardial injury. To account for these issues, we have conducted sensitivity analyses by only including studies that patients were detected with RT-PCR assay or cases were defined as troponin. The results of sensitivity analyses were in line with the primacy results. Secondly, given the difficulty of performing echocardiography or cardiac magnetic resonance imaging under strict isolation, the exact prevalence and nature of myocardial injury in COVID-19 may difficult to be fully illuminating. Thus, in the present study, we used myocardial enzymology indexes as the definition of myocardial injury. Thirdly, we did not obtain patient-level information about comorbidities and concomitant medication for exploring the potential risk factors of myocardial injury. Also, all the included studies did not report the adjusted RRs related to cardiac injury, thus the pooled RRs from crude data may introduce certain bias. Fourthly, there was significant heterogeneity among included studies and the sources of heterogeneity could be partly explained by disease severity. Finally, we did not assess the clinical diagnosis (angina, myocardial infarction, etc.) associated with elevated myocardial enzymes as well as the dynamic change of troponin and the association between myocardial injury and mortality.

Conclusions

This meta-analysis showed that 21% of patients undergoing myocardial injury in the setting of COVID-19. Higher incidence of myocardial injury was observed in non-survivors (66%) and severe patients (43%). Severe patients had a 4.74-fold increased risk of myocardial injury compared to non-severe patients. Aggressive intervention strategy might be considered for COVID-19 patients at high risk of myocardial injury.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at http://dx.doi.org/10.21037/cdt-20-535

Peer Review File: Available at http://dx.doi.org/10.21037/cdt-20-535

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/cdt-20-535). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The ethical approval and consent are not required because no patient-level data is involved for this systematic review and meta-analysis.

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Supplementary

Incidence of myocardial injury in COVID-19: a pooled analysis of 7,679 patients from 53 studies.

Table S1 Search strategy used in April 24, 2020

Literature databases	Search items	Items found
PubMed	COVID-19[Title/Abstract] OR 2019-nCov[Title/Abstract] OR novel coronavirus[Title/Abstract] OR Wuhan coronavirus[Title/Abstract] OR Wuhan pneumonia [Title/Abstract] OR SARS-CoV-2[Title/Abstract] OR coronavirus 2019[Title/Abstract]	5,110
Embase	'covid 19':ab,ti OR '2019 ncov':ab,ti OR 'novel coronavirus':ab,ti OR 'wuhan coronavirus':ab,ti OR 'wuhan pneumonia':ab,ti OR 'sars cov 2':ab,ti OR 'coronavirus 2019':ab,ti AND NOT ([embase]/lim AND [medline]/lim)	271
Cochrane	(COVID-19):ti,ab,kw OR (novel coronavirus):ti,ab,kw OR (Wuhan coronavirus):ti,ab,kw OR (Wuhan pneumonia):ti,ab,kw OR (SARS-CoV-2):ti,ab,kw OR (coronavirus 2019):ti,ab,kw	68
Overall	–	2,188
Duplication	–	3,940

Table S2 Characteristics of the included studies

Study name	Study source	Study design	Country	Region	Hospital in detail
Ai *et al.* (22)	Preprint platform	Cross-sectional	China	Hubei	Xiangyang No. 1 People's Hospital
Cai *et al.* (23)	English database	Cross-sectional	China	Hubei outside	Third People's Hospital of Shenzhen
Cao *et al.* (24)	English database	Cross-sectional	China	Hubei	Zhongnan Hospital of Wuhan University
Cao *et al.* (25)	Preprint platform	Cross-sectional	China	Hubei outside	Shanghai Public Health Clinical Centre
Chen *et al.* (26)	Chinese database	Case-control	China	Hubei	Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology
Chen *et al.* (27)	English database	Case-control	China	Hubei	Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology
Chen *et al.* (2)	English database	Case-control	China	Hubei	Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology
Chen *et al.* (28)	Preprint platform	Cross-sectional	China	Hubei outside	The first Hospital of Changsha and Loudi Central Hospital
Deng *et al.* (29)	English database	Case-control	China	Hubei	Renmin Hospital of Wuhan University
Fan *et al.* (30)	Preprint platform	Cross-sectional	China	Hubei	Wuhan Jinyintan Hospital
Fang *et al.* (31)	Chinese database	Cross-sectional	China	Hubei outside	Anhui Provincial Hospital
Feng *et al.* (32)	Chinese database	Case-series	China	Hubei outside	The First Hospital of Lanzhou University
Feng *et al.* (33)	English database	Cross-sectional	China	Hubei and other regions	Wuhan Jinyintan Hospital, Shanghai Public Health Clinical Center, and Anhui Tongling People's Hospital
Fu *et al.* (34)	English database	Case-control	China	Hubei	Union Hospital, Tongji Medical College, Huazhong University of Science and Technology
Fu *et al.* (35)	Preprint platform	Case-control	China	Hubei	Union Hospital, Tongji Medical College, Huazhong University of Science and Technology
Guo *et al.* (5)	English database	Case-control	China	Hubei	The Seventh Hospital of Wuhan
Han *et al.* (36)	English database	Cross-sectional	China	Hubei	Renmin Hospital of Wuhan University
He *et al.* (37)	Chinese database	Case-control	China	Hubei	Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology
Hong *et al.* (38)	Chinese database	Case-control	China	Hubei outside	The Fifth Affiliated Hospital of Sun Yat-sen University
Hu *et al.* (39)	English database	Cross-sectional	China	Hubei	Tianyou Hospital, Wuhan University of Science and Technology
Huang *et al.* (3)	English database	Case-series	China	Hubei	Wuhan Jinyintan Hospital
Huang *et al.* (40)	English database	Case-series	China	Hubei	Zhongnan Hospital of Wuhan University
Hui *et al.* (41)	English database	Case-series	China	Hubei outside	Beijing Youan Hospital
Jiang *et al.* (42)	Preprint platform	Case-series	China	Hubei outside	Wuxi Fifth People's Hospital
Li *et al.* (43)	Chinese database	Case-control	China	Hubei outside	Guangzhou Eighth People's Hospital
Li *et al.* (44)	Preprint platform	Case-series	China	Hubei	Renmin Hospital of Wuhan University
Liu *et al.* (45)	Preprint platform	Case-control	China	Hubei outside	Guangzhou Eighth People's Hospital
Ma *et al.* (46)	English database	Cross-sectional	China	Hubei outside	Chongqing Yongchuan Hospital
Petrilli *et al.* (47)	Preprint platform	Cross-sectional	U.S.A.	New York	NYU Langone Health
Qi *et al.* (48)	Preprint platform	Cross-sectional	China	Hubei outside	Qianjiang Central Hospital of Chongqing, Chongqing Three Gorges Central Hospital, and Chongqing Public Health Medical Center
Qiu *et al.* (49)	Preprint platform	Cross-sectional	China	Hubei outside	The First People's Hospital of Huaihua and the Central Hospital of Shaoyang
Shi *et al.* (10)	English database	Case-control	China	Hubei	Renmin Hospital of Wuhan University
Tian *et al.* (50)	Preprint platform	Cross-sectional	China	Hubei outside	The First Hospital of Jilin University, Changchun Infectious Disease Hospital and Siping Infectious Disease Hospital
Wang *et al.* (4)	English database	Cross-sectional	China	Hubei	Zhongnan Hospital of Wuhan University
Wang *et al.* (51)	English database	Cross-sectional	China	Hubei outside	The Second Xiangya Hospital of Central South University
Wang *et al.* (52)	English database	Cross-sectional	China	Hubei	Renmin Hospital of Wuhan University
Wang *et al.* (53)	Chinese database	Case-series	China	Hubei outside	Jinhua Municipal Central Hospital
Wu *et al.* (54)	English database	Cohort	China	Hubei	Wuhan Jinyintan Hospital
Wu *et al.* (55)	English database	Case-series	China	Hubei outside	The First People's Hospital of Yancheng City, The Fifth People's Hospital of Wuxi, The second People's Hospital of Yancheng City
Xiong *et al.* (56)	Chinese database	Case-series	China	Hubei	Renmin Hospital of Wuhan University
Xu *et al.* (57)	Preprint platform	Case-control	China	Hubei outside	West China Second University Hospital, Sichuan University
Xu *et al.* (58)	Preprint platform	Case-series	China	Hubei and other regions	Zhongnan Hospital of Wuhan University, Chinese PLA General Hospital, Peking Union Medical College Hospital, and affiliated hospitals of Shanghai University of Medicine & Health Sciences
Yan *et al.* (59)	Preprint platform	Cross-sectional	China	Hubei outside	The Second Affiliated Hospital of Hainan Medical University
Yang *et al.* (60)	Chinese database	Case-series	China	Hubei outside	Nanjing Public Health Medical Center
Yang *et al.* (61)	English database	Cross-sectional	China	Hubei	Wuhan Jinyintan Hospital
Zhang *et al.* (62)	Preprint platform	Case-series	China	Hubei	Renmin Hospital of Wuhan University
Zhang *et al.* (63)	English database	Case-control	China	Hubei	Wuhan No. 1 Hospital
Zhang *et al.* (64)	Chinese database	Case-series	China	Hubei	Wuhan Huo Shen-Shan Hospital
Zhao *et al.* (65)	Preprint platform	Case-series	China	Hubei outside	Beijing Youan Hospital
Zheng *et al.* (66)	Preprint platform	Case-series	China	Hubei outside	The First Affiliated Hospital, College of Medicine, Zhejiang University
Zhou *et al.* (67)	English database	Case-series	China	Hubei	Union Hospital, Tongji Medical College, Huazhong University of Science and Technology
Zhou *et al.* (68)	English database	Cohort	China	Hubei	Wuhan Jinyintan Hospital and Wuhan Pulmonary Hospital
Zhou *et al.* (69)	Preprint platform	Cross-sectional	China	Hubei	Yichang Central People's Hospital and Yichang Third People's Hospital

Table S3 Population, diagnosis, and cardiac injury definition of the included studies

Study	Population period	Population	Diagnosis standard	Definition	Cut-off value
Ai *et al.* (22)	NR–2020.2.9	NR	RT-PCR	CK-MB	24 U/L
Cai *et al.* (23)	2020.1.11–2020.2.9	Non-severe and severe patients	RT-PCR	CK-MB	NR
Cao *et al.* (24)	2020.1.3–2020.2.1	Survivors and non-survivors	RT-PCR	TNI	26 pg/mL
Cao *et al.* (25)	2020.1.20–2020.2.15	Non-ICU and ICU patients	RT-PCR	TNI	0.04 ng/mL
Chen *et al.* (26)	2020.1.1–2020.2.29	Non-severe and severe patients	RT-PCR	TNI	NR
Chen *et al.* (27)	2019.12–2020.1.27	Moderate and severe patients	RT-PCR	TNI or EKG or Echo	NR
Chen *et al.* (2)	2020.1.13–2020.2.12	Survivor and non-survivor patients	RT-PCR	TNI	15.6 pg/mL
Chen *et al.* (28)	2020.1.23–2020.2.14	Mild, Moderate, and Severe (critical) patients	RT-PCR	CK-MB	24 U/L
Deng *et al.* (29)	2020.1.6–2020.2.20	Non-severe and severe patients	RT-PCR	TNI	0.04 ng/mL
Fan *et al.* (30)	2019.12.30–2020.2.16	Non-ICU and ICU patients	RT-PCR or clinical diagnosis	TNI	10 U/L
Fang *et al.* (31)	2020.1.22–2020.2.18	Mild-moderate, severe, and critical patients	RT-PCR	TNI	0.3 μg/L
Feng *et al.* (32)	2020.1.23–2020.2.23	NR	RT-PCR or clinical diagnosis	CK-MB	NR
Feng *et al.* (33)	2020.1.1–2020.2.15	Moderate, severe, and critical patients	RT-PCR	TNI	0.04 ng/mL
Fu *et al.* (34)	2020.1.1–2020.1.30	Survivors and non-survivors	RT-PCR	TNI	NR
Fu *et al.* (35)	2020.2.9–2020.3.17	Good recovery and poor recovery patients	RT-PCR or clinical diagnosis	TNI	26.2 ng/L
Guo *et al.* (5)	2020.1.23–2020.2.23	NR	RT-PCR	TNT	NR
Han *et al.* (36)	2020.1.1–2020.2.18	Mild, severe, and critical patients	RT-PCR	TNI	0.04 ng/mL
He *et al.* (37)	2020.2.3–2020.2.24	Survivors and non-survivors	RT-PCR	TNI	34.3 ng/L
Hong *et al.* (38)	2020.1.17–2020.3.1	NR	RT-PCR	TNI	NR
Hu *et al.* (39)	2020.1.8–2020.2.20	Non-severe, severe, and critical patients	RT-PCR or clinical diagnosis	TNI	0.04 pg/mL
Huang *et al.* (3)	2019.12.16–2020.1.2	Non-ICU and ICU patients	RT-PCR	TNI or EKG or Echo	>28 pg/mL
Huang *et al.* (40)	2019.12.21–2020.1.28	NR	RT-PCR	TNI	NR
Hui *et al.* (41)	2020.1.21–2020.2.3	Mild, moderate, severe, and critical patients	RT-PCR	TNI	
Jiang *et al.* (42)	2020.1.23–2020.2.16	Non-severe and severe patients	RT-PCR	TNI or EKG or Echo	NR
Li *et al.* (43)	2020.1.20–2020.2.10	Mild, moderate, severe, and critical patients	RT-PCR	TNI	NR
Li *et al.* (44)	2020.1.14–2020.2.13	NR	RT-PCR	TNI	0.04 ng/mL
Liu *et al.* (45)	2020.1.10–2020.2.24	NR	RT-PCR	TNI	0.03 μg/L
Ma *et al.* (46)	2020.1.21–2020.3.2	Non-severe and severe patients	RT-PCR	TNI	0.034 ng/mL
Petrilli *et al.* (47)	2020.3.1–2020.4.2	NR	RT-PCR	TNI	0.1 ng/mL
Qi *et al.* (48)	2020.1.19–2020.2.16	Non-severe and severe patients	RT-PCR	TNT	14 pg/mL
Qiu *et al.* (49)	2020.1.22–2020.2.12	Imported and Indigenous patients	RT-PCR	TNI or EKG or Echo	NR
Shi *et al.* (10)	2020.1.20–2020.2.10	NR	RT-PCR	TNI	0.04 ng/mL
Tian *et al.* (50)	2020.1.21–2020.3.5	NR	RT-PCR	TNI	1.5 ng/mL
Wang *et al.* (4)	2020.1.1–2020.1.28	Non-ICU and ICU patients	RT-PCR	TNI or EKG or Echo	26.2 pg/mL
Wang *et al.* (51)	2020.1.17–2020.2.20	Non-severe and severe patients	RT-PCR	TNI	NR
Wang *et al.* (52)	2020.1.1–2020.2.6	Survivors and non-survivors	RT-PCR	TNI	0.04 pg/ml
Wang *et al.* (53)	2020.1.22–2020.2.7	Non-severe and severe patients	RT-PCR	CK-MB	NR
Wu *et al.* (54)	2019.12.25–2020.1.26	without and with ARDS patients	RT-PCR	CK-MB	24 U/L
Wu *et al.* (55)	2020.1.22–2020.2.14	Mild, moderate, severe, and critical patients	RT-PCR	CK-MB	25 U/L
Xiong *et al.* (56)	2020.1.17–2020.2.20	Mild, moderate, severe, and critical patients	RT-PCR	TNI	NR
Xu *et al.* (57)	2020.1.2–2020.2.14	NR	RT-PCR	TNT	28 pg/mL
Xu *et al.* (58)	2020.2.7–2020.2.28	Mild, severe, and critical patients	RT-PCR	TNI or EKG or Echo	28 pg/ml
Yan *et al.* (59)	2020.1.22–2020.3.14	Non-severe and severe patients	RT-PCR	TNI or EKG or Echo	NR
Yang *et al.* (60)	2020.1.23–NR	NR	RT-PCR	CK-MB	4.87 g/mL
Yang *et al.* (61)	2019.12.24–2020.1.26	Survivors and non-survivors	RT-PCR	TNI	28 pg/mL
Zhang *et al.* (62)	2020.1.11–2020.2.10	Non-survivors	RT-PCR	TNT	0.04 pg/mL
Zhang *et al.* (63)	2019.12.25–2020.2.15	Survivors and non-survivors	RT-PCR	TNI	0.026 μg/L
Zhang *et al.* (64)	2020.2.4–NR	Non-severe and severe patients	RT-PCR	CK-MB	NR
Zhao *et al.* (65)	2020.1.21–2020.2.8	Non-severe and severe patients	RT-PCR	TNI	0.05 ng/mL
Zheng *et al.* (66)	2020.1.22–2020.3.5	Noninvasive ventilation and invasive mechanical ventilation patients	RT-PCR	TNI or EKG or Echo	NR
Zhou *et al.* (67)	2020.2.5–2020.2.13	Non-severe and severe patients	RT-PCR	TNI	26.2 ng/L
Zhou *et al.* (68)	2019.12.29–2020.1.31	Survivors and non-survivors	RT-PCR	TNI or EKG or Echo	28 ng/mL
Zhou *et al.* (69)	2020.1.17–2020.2.26	Survivors	RT-PCR or clinical diagnosis	TNI or EKG or Echo	NR

NR, not reported; RT-PCR, reverse transcription-polymerase chain reaction; CK-MB, creatine kinase isoenzyme; TNI, troponin I; ICU, intensive care unit; EKG, electrocardiography; Echo, echocardiography; ARDS, acute respiratory distress syndrome.

Table S4 Clinical characteristics of the included studies

Study	Number	Mean age (y)	Male (%)	Smoking (%)	Hypertension (%)	Diabetes (%)	CVD (%)	Cerebrovascular disease (%)	Chronic pulmonary disease (%)	Chronic kidney disease (%)	Liver disease (%)	Cancer (%)
Ai *et al.* (22)	102	50.38	51	NR	NR	NR	NR	NR	NR	NR	NR	NR
Cai *et al.* (23)	298	47	50	NR	12.8	6.4	3.7	NR	NR	NR	2.7	1.4
Cao *et al.* (24)	55	54	52	NR	27.5	10.8	4.9	5.9	9.8	3.9	2	3.9
Cao *et al.* (25)	194	50.1	51	5.6	21.2	7.6	6	NR	NR	NR	3	2
Chen *et al.* (26)	150	59	56	NR	32.6	13.3	7.33	NR	NR	NR	NR	2
Chen *et al.* (27)	21	56	81	NR	NR	NR	NR	NR	NR	NR	NR	NR
Chen *et al.* (2)	203	62	62	13.9	33.9	17.2	8.4	1.5	6.6	1.5	4.0	2.6
Chen *et al.* (28)	291	46	49.8	NR	13.4	7.6	4.1	2.7	3.4	0.7	5.2	0.7
Deng *et al.* (29)	112	65	50.9	NR	32.1	17	13.4	NR	3.6	NR	NR	NR
Fan *et al.* (30)	101	65.46	64	NR	NR	NR	NR	NR	4.95	NR	NR	4.95
Fang *et al.* (31)	79	45.1	57	NR	20.3	14.5	3.8	3.8	0	3.8	3.8	1.3
Feng *et al.* (32)	8	40	62.5	NR	NR	12.5	NR	NR	NR	NR	NR	NR
Feng *et al.* (33)	384	53	56.9	13.4	23.7	10.3	8	3.6	4.6	0.8	NR	2.5
Fu *et al.* (34)	200		49.5	52.35	50.5	68.5	8	NR	4	NR	4.5	NR
Fu *et al.* (35)	50	64	54	20	20	24	22	NR	6	2	4	NR
Guo *et al.* (5)	187	58.5	48.7	9.6	32.6	15	15.5	NR	2.1	3.2	NR	7
Han *et al.* (36)	273	58.86	35.5	NR	NR	NR	NR	NR	NR	NR	NR	NR
He *et al.* (37)	54	68.18	62.96	NR	44.4	24.07	14.81	NR	3.7	NR	40.74	NR
Hong *et al.* (38)	18	63.5	50	NR	38.9	27.8	11.1	5.5	11.1	5.5	NR	5.5
Hu *et al.* (39)	244	61	51.4	11.8	32.5	14.6	NR	2.2	10.9	2.2	1.5	1.5
Huang *et al.* (3)	41	49	73	7	15	20	15	NR	2	NR	2	2
Huang *et al.* (40)	15	56.24	41.2	NR	23.5	11.8	17.6	NR	8.8	NR	2.9	8.8
Hui *et al.* (41)	20	32.8	46.3	NR	14.63	4.88	9.76	NR	NR	NR	NR	2.44
Jiang *et al.* (42)	55	45	49.1	NR	30.9	16.4	NR	1.8	NR	1.8	3.6	3.6
Li *et al.* (43)	66	51	43.94	NR	15.15	7.58	15.15	NR	NR	NR	NR	NR
Li *et al.* (44)	15	71.88	40	NR	60	36	32	12	12	20	4	8
Liu *et al.* (45)	291	48.1	45.7	NR	18.5	7.6	5.1	NR	NR	NR	NR	NR
Ma *et al.* (46)	84	48	57.1	8.3	14.3	11.9	6	4.8	6	1.2	13.1	1.2
Petrilli *et al.* (47)	1,327	61.7	63.34	25.92	36.47	24.6	54.11	NR	10.24	9.86	NR	6.95
Qi *et al.* (48)	76	48	55.8	19.9	7.5	9.7	NR	NR	9.4	NR	NR	NR
Qiu *et al.* (49)	104	43	47.12	3.85	14.42	11.54	6.73	NR	0.96	NR	NR	NR
Shi *et al.* (10)	416	64	49.3	NR	30.5	14.4	10.6	5.3	2.9	3.4	NR	2.2
Tian *et al.* (50)	28	41	57.63	NR	NR	NR	NR	NR	NR	NR	NR	NR
Wang *et al.* (4)	138	56	54.3	NR	31.2	10.1	14.5	5.1	2.9	2.9	2.9	7.2
Wang *et al.* (51)	242	45	49.17	7.9	14.9	6.2	3.7	2.5	0.4	NR	5	0.8
Wang *et al.* (52)	339	69	49	NR	40.8	16	15.7	6.2	6.2	3.8	0.6	4.4
Wang *et al.* (53)	17	42.1	58.82	NR	11.76	NR	NR	NR	NR	NR	NR	NR
Wu *et al.* (54)	198	51	63.7	NR	19.4	10.9	4	NR	2.5	1	3.5	0.5
Wu *et al.* (55)	38	46.1	48.75	NR	NR	NR	NR	NR	NR	1.25	1.25	1.25
Xiong *et al.* (56)	89	53	46.07	NR	29.2	15.7	NR	6.7	5.6	3.4	1.1	12.3
Xu *et al.* (57)	53	48.21	52.83	11.32	15.09	15.09	11.32	NR	5.66	NR	NR	NR
Xu *et al.* (58)	69	57	50.7	7.2	NR	NR	NR	NR	NR	NR	NR	NR
Yan *et al.* (59)	168	51	51.8	NR	14.3	7.1	7.1	NR	6	0.6	3.6	1.2
Yang *et al.* (60)	57	37	50.9	NR	NR	NR	NR	NR	NR	NR	NR	NR
Yang *et al.* (61)	52	59.7	67	4	NR	17	10	13.5	8	NR	NR	4
Zhang *et al.* (62)	60	72.5	65.9	NR	56.1	18.3	NR	12.2	14.6	4.9	2.4	7.3
Zhang *et al.* (63)	48	64.03	54.5	NR	51.8	17.3	14.5	16.4	NR	8.2	NR	NR
Zhang *et al.* (64)	16	54	60	8	28	11	11	3	0	2	8	NR
Zhao *et al.* (65)	77	52	44.2	NR	20.8	7.8	11.7	2.6	NR	6.5	NR	5.2
Zheng *et al.* (66)	34	66	67.6	NR	64.7	23.5	11.8	NR	5.9	5.9	11.8	NR
Zhou *et al.* (67)	34	63	50	NR	NR	NR	NR	NR	NR	NR	NR	NR
Zhou *et al.* (68)	191	56	62	6	30	19	8	NR	3	1	NR	1
Zhou *et al.* (69)	197	55.94	50.3	NR	NR	9.1	24.4	4.6	NR	1.5	NR	1.5

CVD, cardiovascular disease; NR, not reported.

Table S5 Quality scores of the included studies

Study	Representativeness of the cases	Ascertainment of exposure	Ascertainment of outcome	Ascertainment of outcome (quality control)[a]	Control for factors of age and sex[b]	Control for factors related to cardiac injury[c]	Total score
Ai *et al.* (22)	1	1	1	0	2	0	5
Cai *et al.* (23)	1	1	1	1	2	2	8
Cao *et al.* (24)	1	1	1	0	2	2	7
Cao *et al.* (25)	1	1	1	0	2	2	7
Chen *et al.* (26)	1	1	1	1	2	2	8
Chen *et al.* (27)	1	1	1	1	2	1	7
Chen *et al.* (2)	1	1	1	0	2	2	7
Chen *et al.* (28)	1	1	1	0	2	2	7
Deng *et al.* (29)	1	1	1	0	2	2	7
Fan *et al.* (30)	1	1	1	0	2	1	6
Fang *et al.* (31)	1	1	1	0	2	2	7
Feng *et al.* (32)	1	1	1	0	2	0	5
Feng *et al.* (33)	1	1	1	0	2	2	7
Fu *et al.* (34)	1	1	1	1	2	2	8
Fu *et al.* (35)	1	1	1	0	2	2	7
Guo *et al.* (5)	1	1	1	1	2	2	8
Han *et al.* (36)	1	1	1	0	2	2	7
He *et al.* (37)	1	1	1	1	2	2	8
Hong *et al.* (38)	1	1	1	1	2	2	8
Hu *et al.* (39)	1	1	1	0	2	2	7
Huang *et al.* (3)	1	1	1	1	2	2	8
Huang *et al.* (40)	1	1	1	0	2	2	7
Hui *et al.* (41)	1	1	1	0	2	2	7
Jiang *et al.* (42)	1	1	1	1	2	2	8
Li *et al.* (43)	1	1	1	1	2	1	7
Li *et al.* (44)	1	1	1	0	2	2	7
Liu *et al.* (45)	1	1	1	1	2	2	8
Ma *et al.* (46)	1	1	1	0	2	1	6
Petrilli *et al.* (47)	1	1	1	0	2	2	7
Qi *et al.* (48)	1	1	1	0	2	2	7
Qiu *et al.* (49)	1	1	1	1	2	1	7
Shi *et al.* (10)	1	1	1	1	2	2	8
Tian *et al.* (50)	1	1	1	0	2	0	5
Wang *et al.* (4)	1	1	1	1	2	2	8
Wang *et al.* (51)	1	1	1	0	2	2	7
Wang *et al.* (52)	1	1	1	0	2	2	7
Wang *et al.* (53)	1	1	1	0	2	1	6
Wu *et al.* (54)	1	1	1	0	2	2	7
Wu *et al.* (55)	1	1	1	0	2	1	6
Xiong *et al.* (56)	1	1	1	0	2	1	6
Xu *et al.* (57)	1	1	1	1	2	2	8
Xu *et al.* (58)	1	1	1	1	2	1	7
Yan *et al.* (59)	1	1	1	1	2	2	8
Yang *et al.* (60)	1	1	1	0	2	0	5
Yang *et al.* (61)	1	1	1	1	2	1	7
Zhang *et al.* (62)	1	1	1	0	2	2	7
Zhang *et al.* (63)	1	1	1	1	2	2	8
Zhang *et al.* (64)	1	1	1	1	2	2	8
Zhao *et al.* (65)	1	1	1	0	2	2	7
Zheng *et al.* (66)	1	1	1	1	2	2	8
Zhou *et al.* (67)	1	1	1	0	2	0	5
Zhou *et al.* (68)	1	1	1	1	2	2	8
Zhou *et al.* (69)	1	1	1	1	2	1	7

[a], one point for studies that reported the definition of cardiac injury; [b], one point for age, and one point for sex, totally 2 points for this section; [c], studies received 1 point for reporting 1 or 2 categories, received 2 points for reporting ≥3 categories related to cardiac injury (hypertension, diabetes, CVD, et al.). CVD, cardiovascular disease.

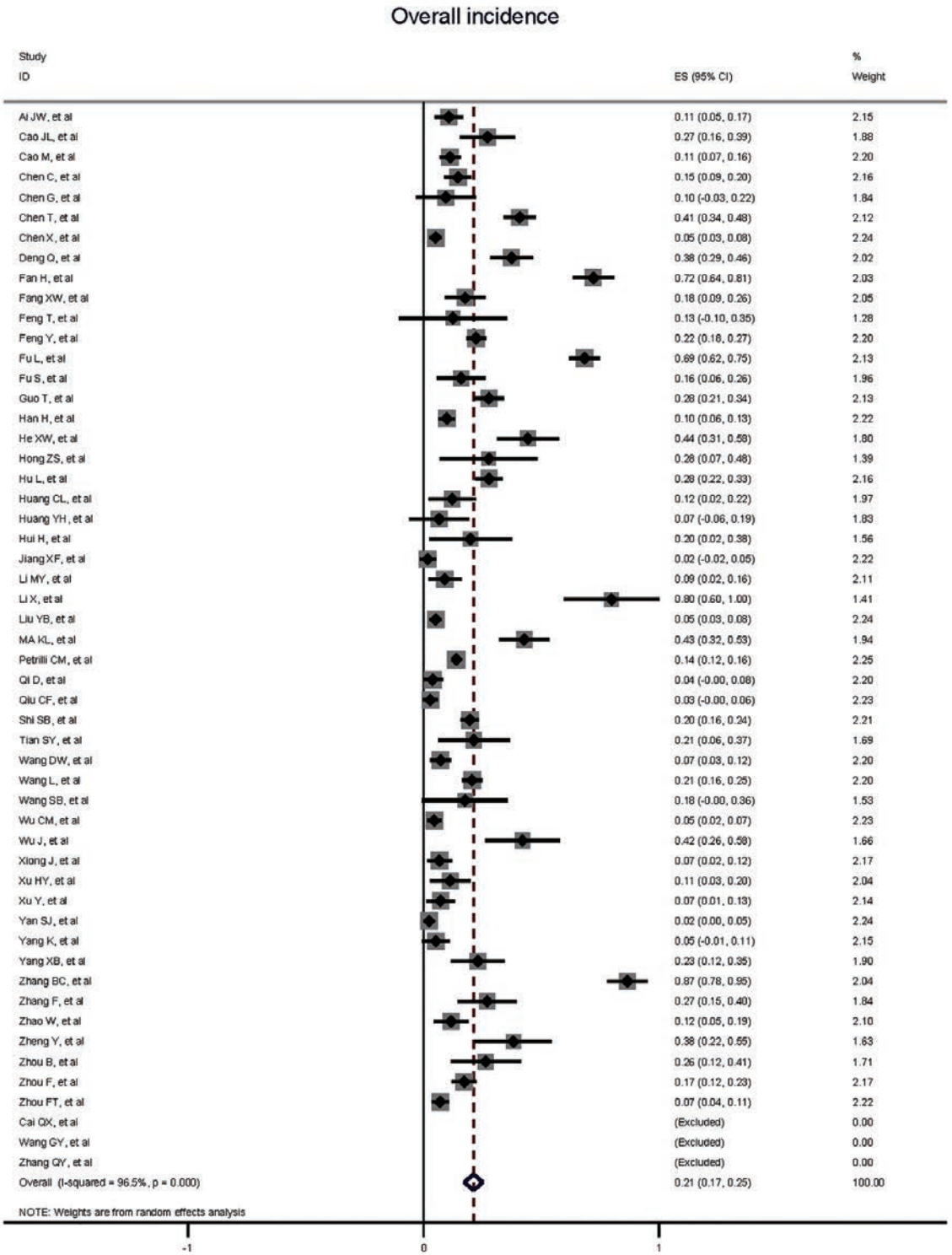

Figure S1 Overall incidence of cardiac injury.

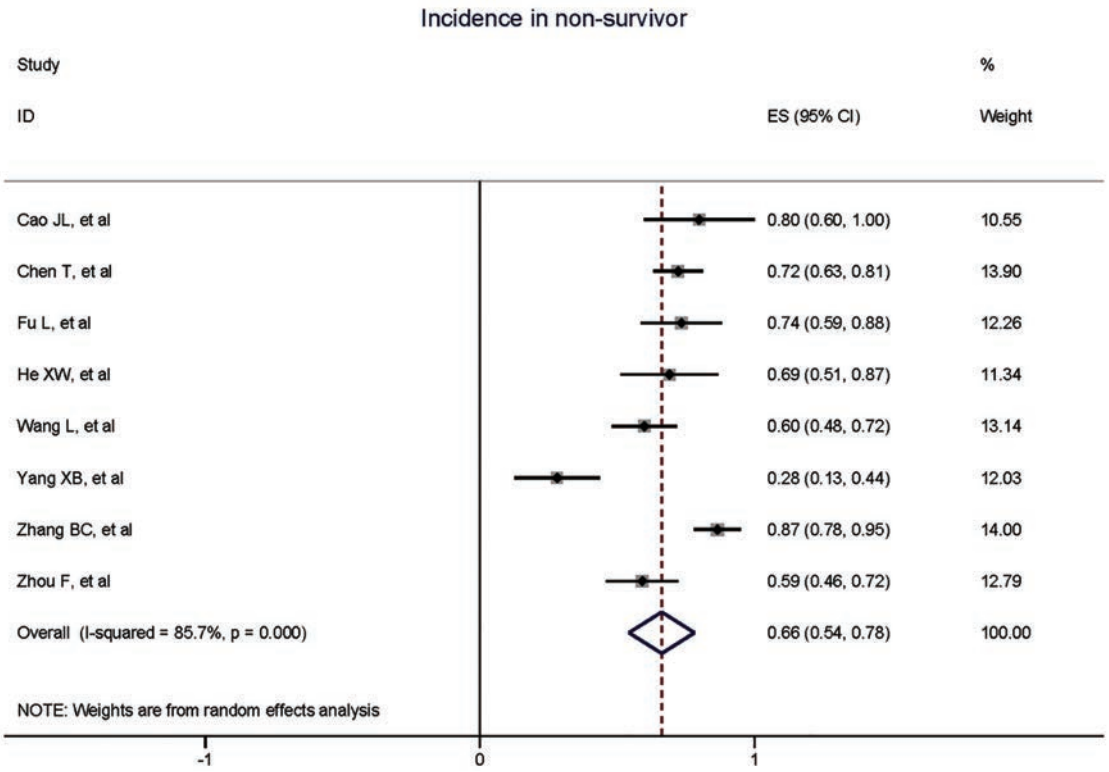

Figure S2 Incidence of cardiac injury in non-survivors.

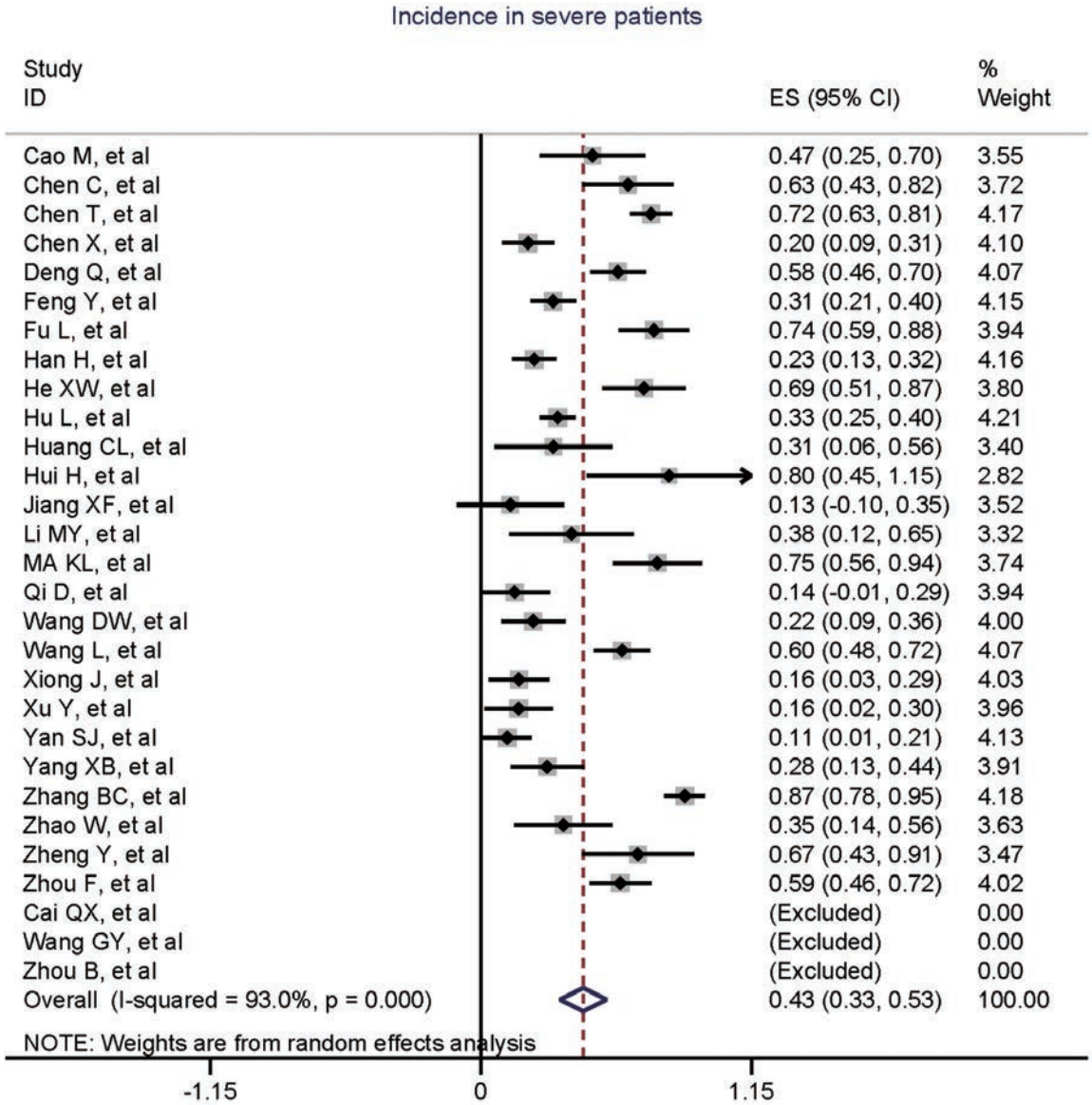

Figure S3 Incidence of cardiac injury in severe patients.

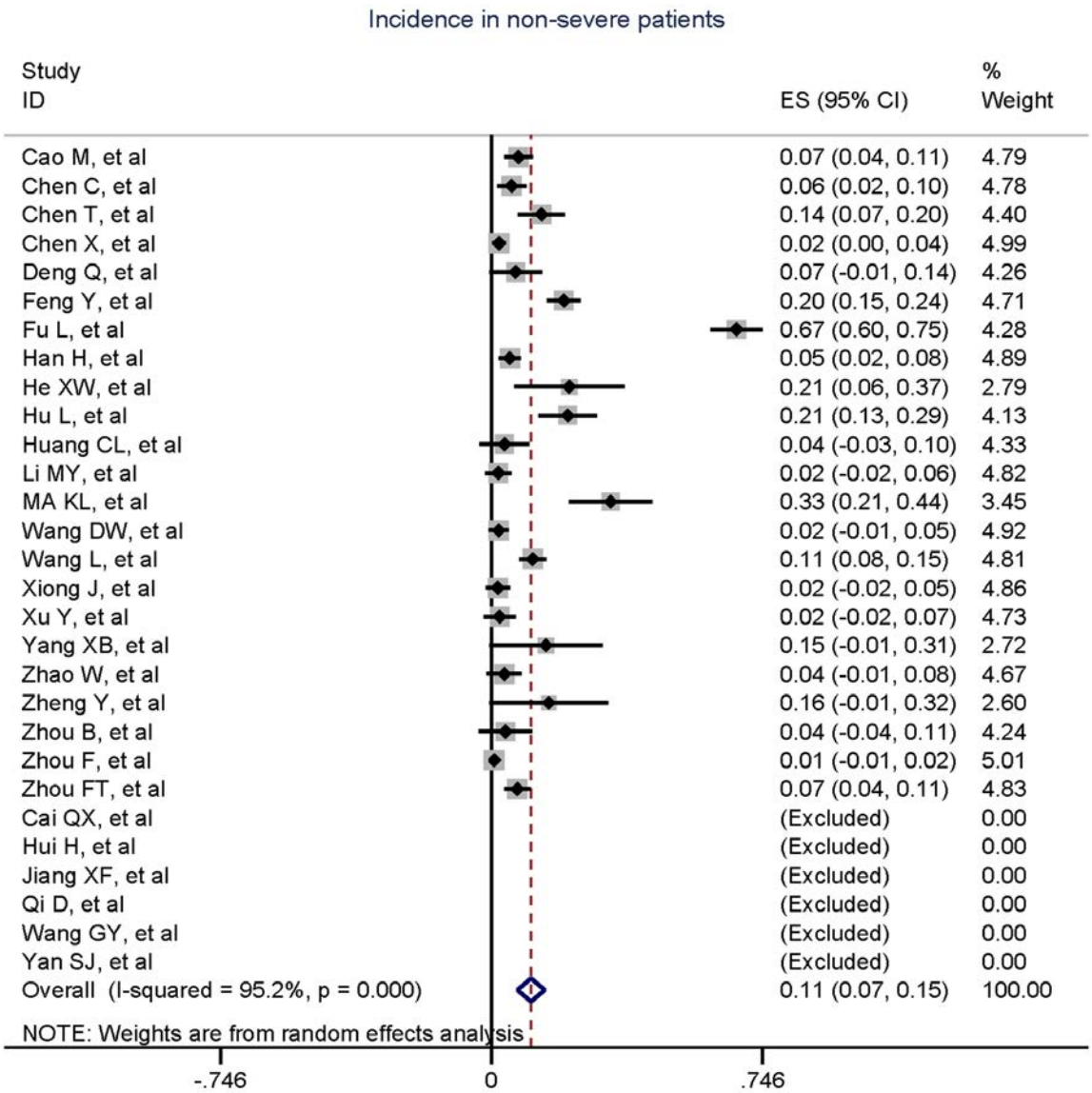

Figure S4 Incidence of cardiac injury in non-severe patients.

Table S6 Leave-1-out sensitivity analysis for cardiac injury incidence

Study omitted	Incidence (95% CI)			
	A. Overall	B. Non-severe patients	C. Severe patients	D. Non-survivors
Ai *et al.* (22)	0.21 (0.18–0.26)			
Cai *et al.* (23)	0.21 (0.17–0.25)	0.11 (0.07–0.15)	0.43 (0.33–0.53)	
Cao *et al.* (24)	0.21 (0.17–0.25)			0.65 (0.52–0.78)
Cao *et al.* (25)	0.21 (0.17–0.25)	0.11 (0.07–0.15)	0.43 (0.33–0.54)	
Chen *et al.* (26)	0.21 (0.17–0.25)	0.11 (0.07–0.15)	0.43 (0.33–0.53)	
Chen *et al.* (27)	0.21 (0.17–0.25)			
Chen *et al.* (2)	0.21 (0.17–0.25)	0.11 (0.07–0.15)	0.42 (0.32–0.52)	0.65 (0.51–0.80)
Chen *et al.* (28)	0.22 (0.18–0.26)	0.11 (0.07–0.16)	0.44 (0.34–0.55)	
Deng *et al.* (29)	0.21 (0.17–0.25)	0.11 (0.07–0.15)	0.43 (0.32–0.53)	
Fan *et al.* (30)	0.20 (0.16–0.24)			
Fang *et al.* (31)	0.21 (0.17–0.25)			
Feng *et al.* (32)	0.21 (0.17–0.25)			
Feng *et al.* (33)	0.21 (0.17–0.25)	0.10 (0.07–0.14)	0.44 (0.34–0.55)	
Fu *et al.* (34)	0.20 (0.16–0.24)	0.07 (0.05–0.10)	0.42 (0.32–0.52)	0.65 (0.52–0.79)
Fu *et al.* (35)	0.21 (0.17–0.25)			
Guo *et al.* (5)	0.21 (0.17–0.25)			
Han *et al.* (36)	0.21 (0.18–0.26)	0.11 (0.07–0.15)	0.44 (0.34–0.55)	
He *et al.* (37)	0.21 (0.17–0.25)	0.11 (0.07–0.14)	0.42 (0.32–0.53)	0.66 (0.53–0.79)
Hong *et al.* (38)	0.21 (0.17–0.25)			
Hu *et al.* (39)	0.21 (0.17–0.25)	0.10 (0.07–0.14)	0.44 (0.33–0.55)	
Huang *et al.* (3)	0.21 (0.17–0.25)	0.11 (0.07–0.15)	0.44 (0.34–0.54)	
Huang *et al.* (40)	0.22 (0.18–0.26)			
Hui *et al.* (41)	0.21 (0.17–0.25)	0.11 (0.07–0.15)	0.42 (0.32–0.53)	
Jiang *et al.* (42)	0.22 (0.18–0.26)	0.11 (0.07–0.15)	0.45 (0.34–0.55)	
Li *et al.* (43)	0.22 (0.18–0.26)	0.11 (0.07–0.15)	0.44 (0.33–0.54)	
Li *et al.* (44)	0.20 (0.17–0.24)			
Liu *et al.* (45)	0.22 (0.18–0.26)			
Ma *et al.* (46)	0.21 (0.17–0.25)	0.10 (0.06–0.14)	0.42 (0.32–0.52)	
Petrilli *et al.* (47)	0.22 (0.17–0.26)			
Qi *et al.* (48)	0.22 (0.18–0.26)	0.11 (0.07–0.15)	0.45 (0.35–0.55)	
Qiu *et al.* (49)	0.22 (0.18–0.26)			
Shi *et al.* (10)	0.21 (0.17–0.25)			
Tian *et al.* (50)	0.21 (0.17–0.25)			
Wang *et al.* (4)	0.22 (0.18–0.26)	0.11 (0.07–0.15)	0.44 (0.34–0.55)	
Wang *et al.* (51)	0.21 (0.17–0.25)	0.11 (0.07–0.15)	0.43 (0.33–0.53)	
Wang *et al.* (52)	0.21 (0.17–0.25)	0.11 (0.07–0.15)	0.43 (0.32–0.53)	0.67 (0.54–0.81)
Wang *et al.* (53)	0.21 (0.17–0.25)			
Wu *et al.* (54)	0.22 (0.18–0.26)			
Wu *et al.* (55)	0.21 (0.17–0.25)			
Xiong *et al.* (56)	0.22 (0.18–0.26)	0.11 (0.07–0.15)	0.45 (0.34–0.55)	
Xu *et al.* (57)	0.21 (0.17–0.25)			
Xu *et al.* (58)	0.22 (0.18–0.26)	0.11 (0.07–0.15)	0.45 (0.34–0.55)	
Yan *et al.* (59)	0.22 (0.18–0.26)	0.11 (0.07–0.15)	0.45 (0.35–0.55)	
Yang *et al.* (60)	0.22 (0.18–0.26)			
Yang *et al.* (61)	0.21 (0.17–0.25)	0.11 (0.07–0.15)	0.44 (0.34–0.54)	0.72 (0.63–0.80)
Zhang *et al.* (62)	0.20 (0.16–0.23)		0.41 (0.32–0.50)	0.63 (0.51–0.75)
Zhang *et al.* (63)	0.21 (0.17–0.25)			
Zhang *et al.* (64)	0.21 (0.17–0.25)			
Zhao *et al.* (65)	0.21 (0.17–0.25)	0.11 (0.07–0.15)	0.44 (0.34–0.54)	
Zheng *et al.* (66)	0.21 (0.17–0.25)	0.11 (0.07–0.15)	0.43 (0.32–0.53)	
Zhou *et al.* (67)	0.21 (0.17–0.25)	0.11 (0.07–0.15)	0.43 (0.33–0.53)	
Zhou *et al.* (68)	0.21 (0.17–0.25)	0.12 (0.07–0.16)	0.43 (0.32–0.53)	0.67 (0.54–0.81)
Zhou *et al.* (69)	0.21 (0.18–0.26)	0.11 (0.07–0.15)		

CI, confidence interval.

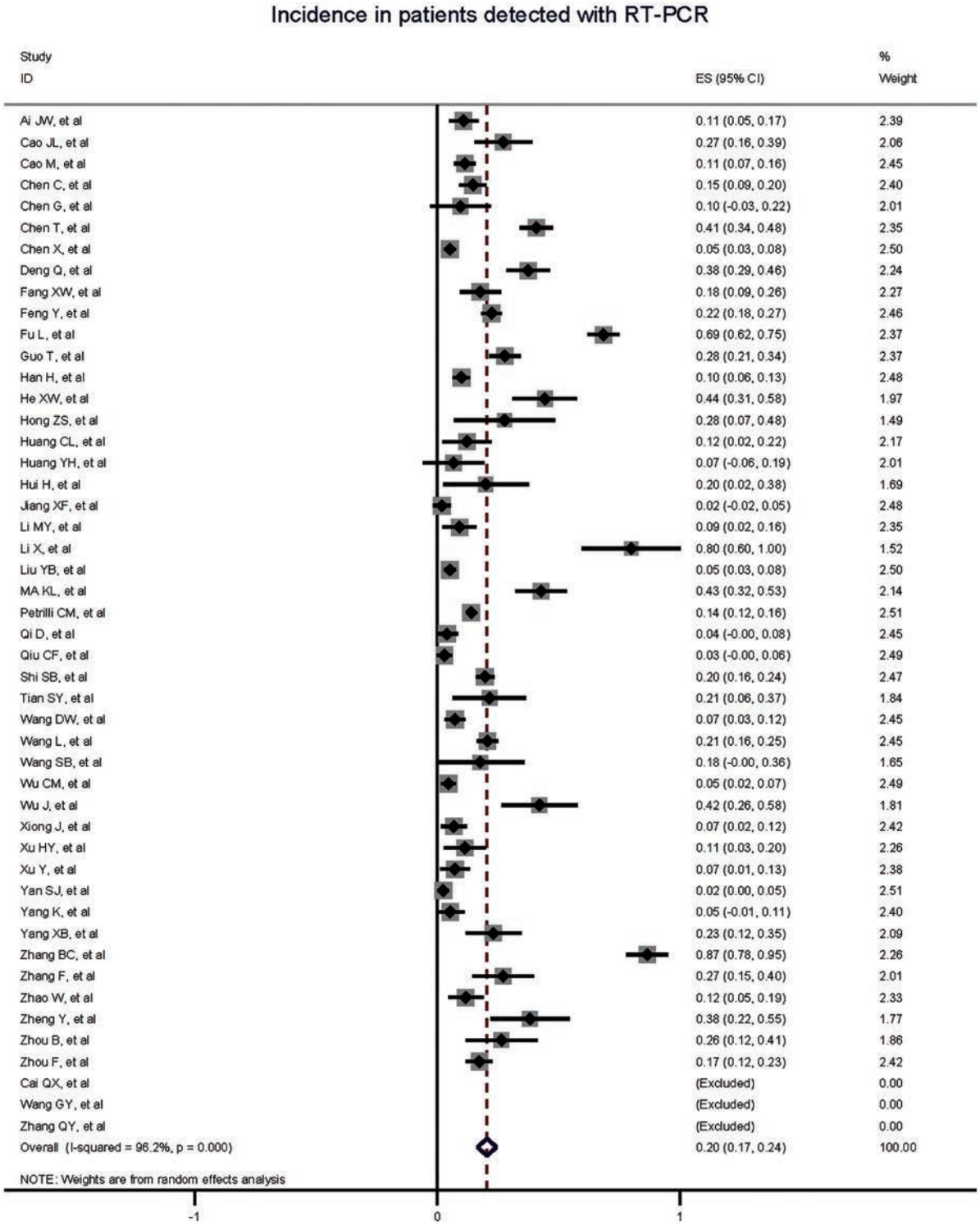

Figure S5 Incidence of cardiac injury in patients detected with RT-PCR method. RT-PCR, reverse transcription-polymerase chain reaction.

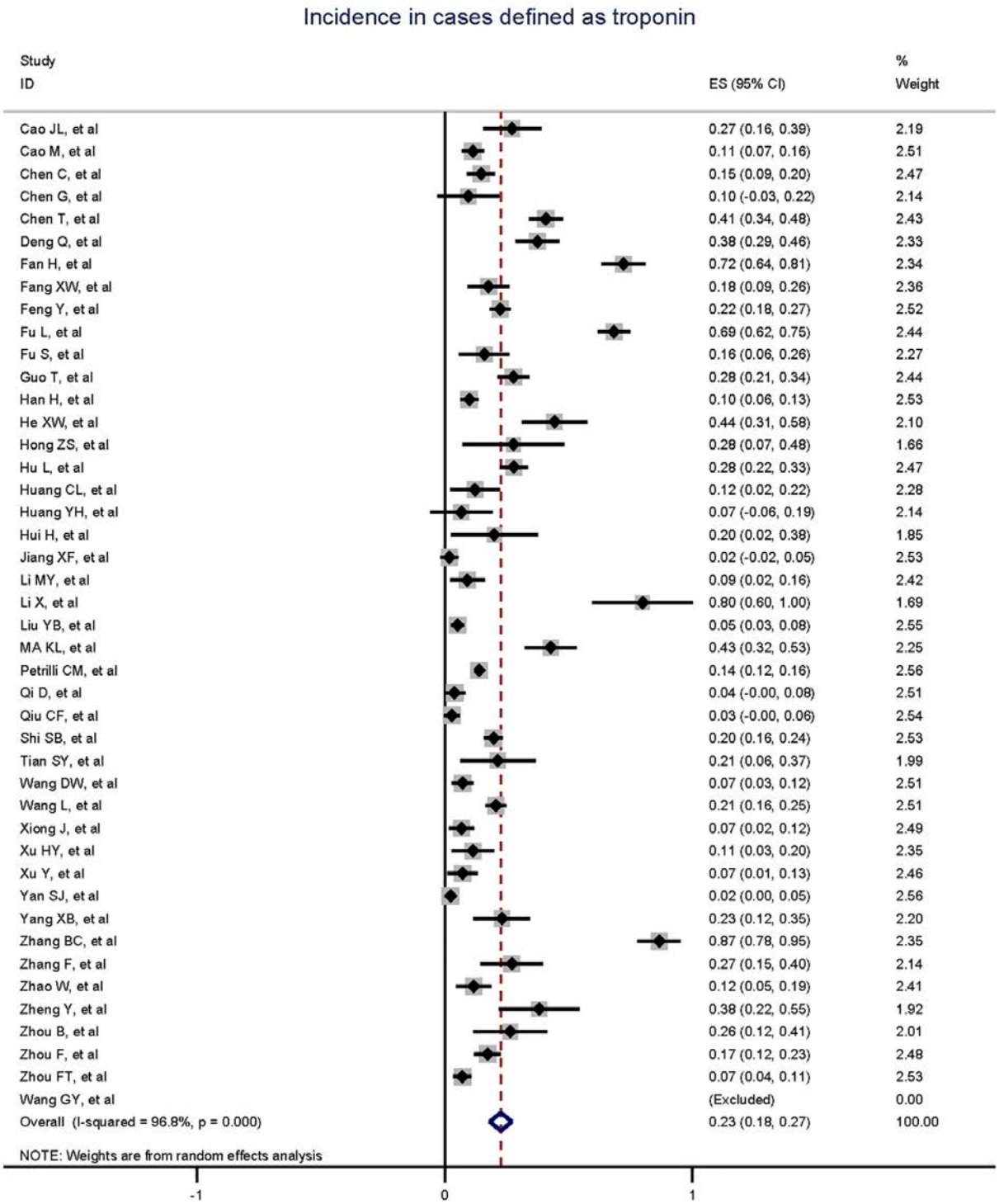

Figure S6 Incidence of cardiac injury in cases defined as troponin.

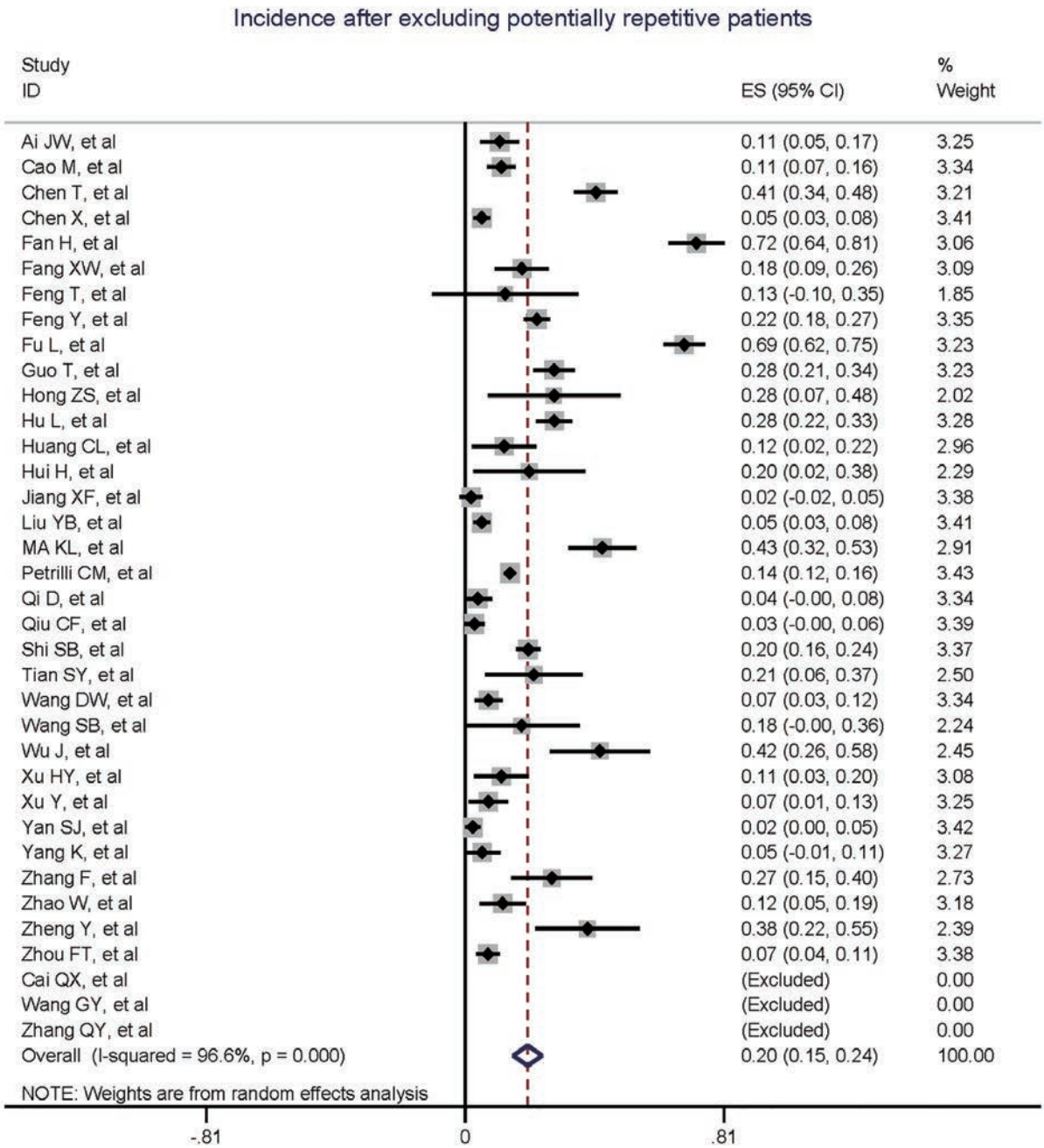

Figure S7 Incidence of cardiac injury after excluding potentially repetitive patients.

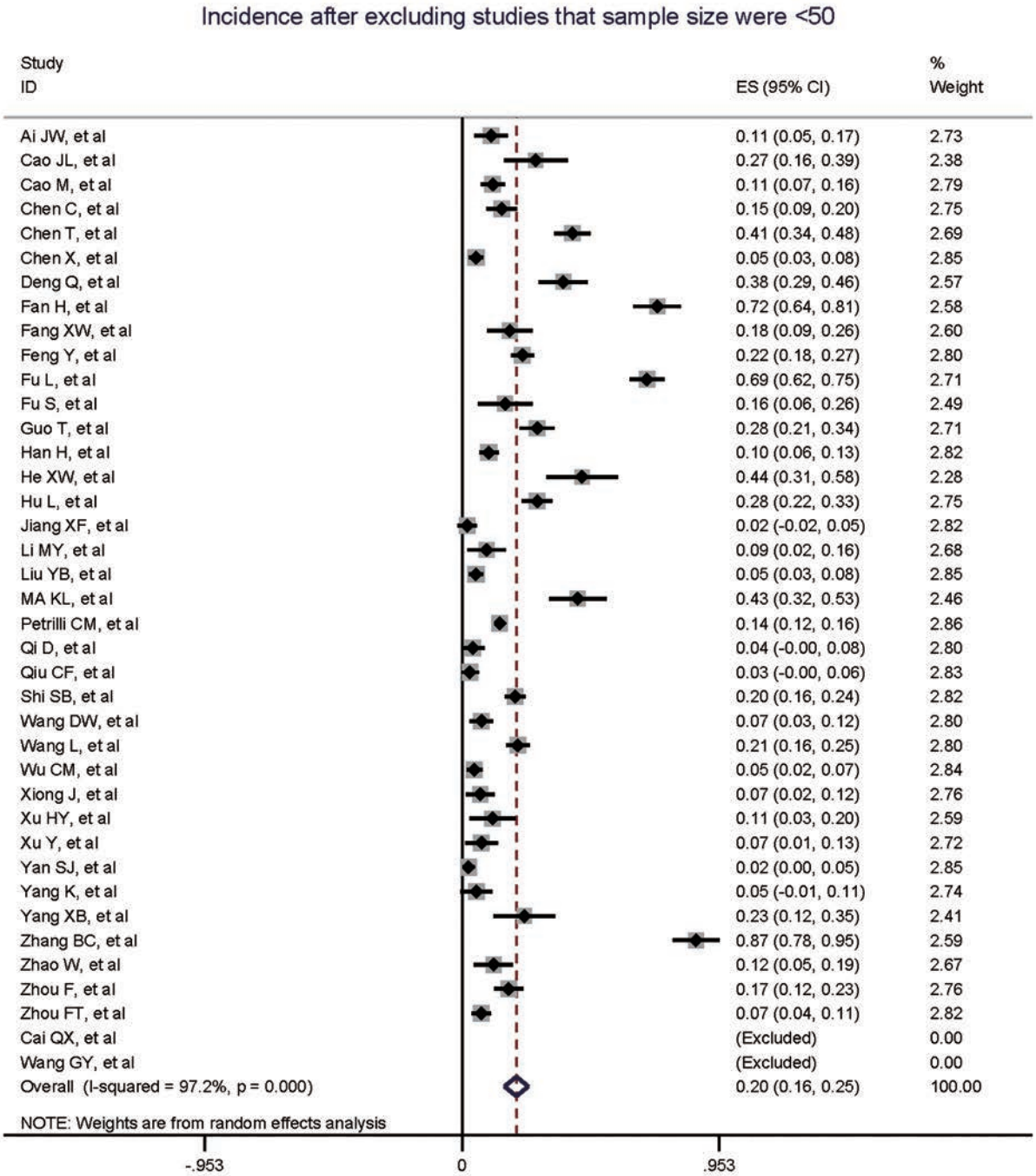

Figure S8 Incidence of cardiac injury after excluding studies that sample size <50.

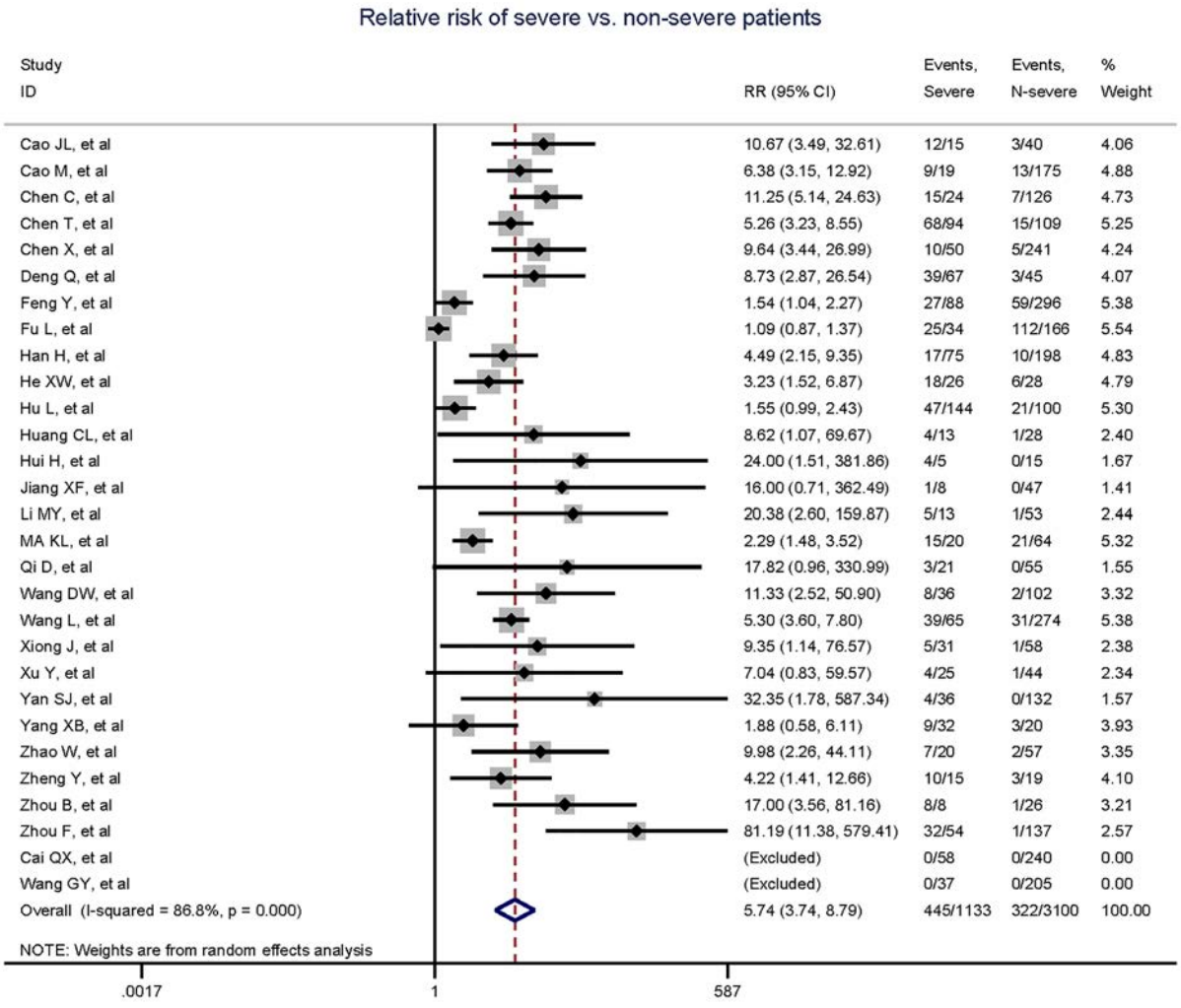

Figure S9 RR of cardiac injury with severe *vs.* non-severe patients. RR, relative risk.

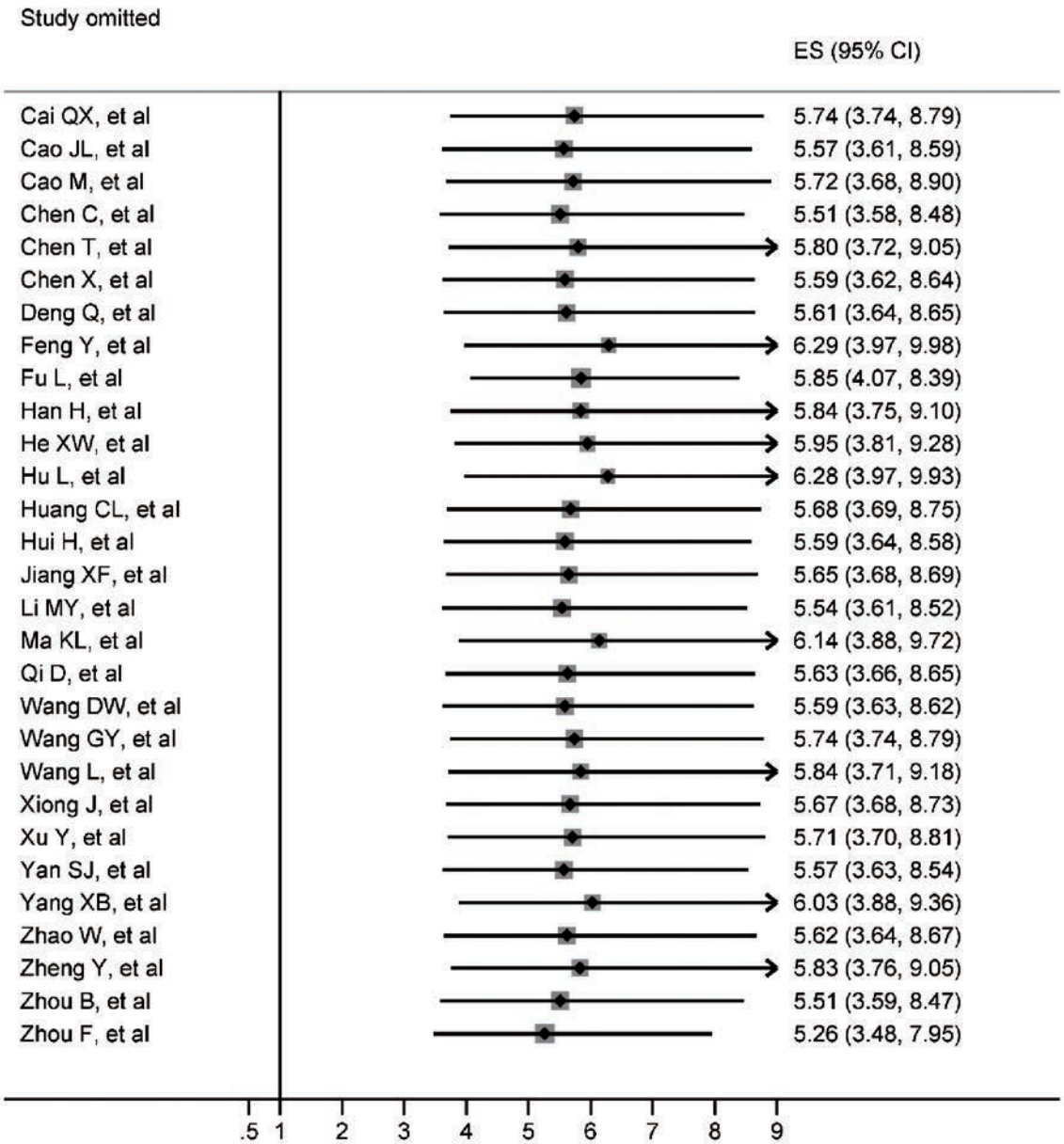

Figure S10 Leave-1-out sensitivity analysis for RR of severe patients vs. non-severe patients. RR, relative risk.

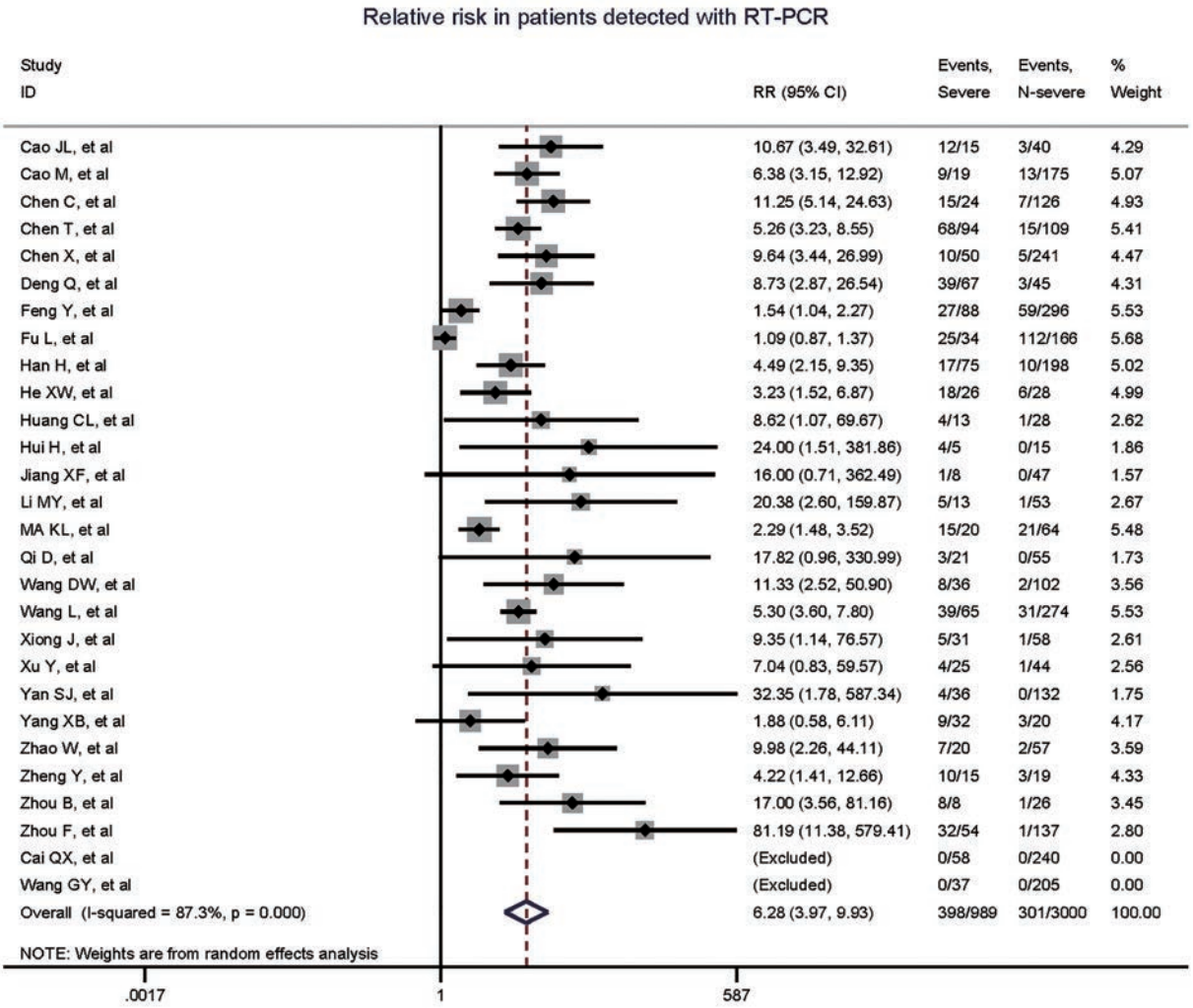

Figure S11 RR of cardiac injury with severe vs. non-severe patients (RT-PCR). RR, relative risk; RT-PCR, reverse transcription-polymerase chain reaction.

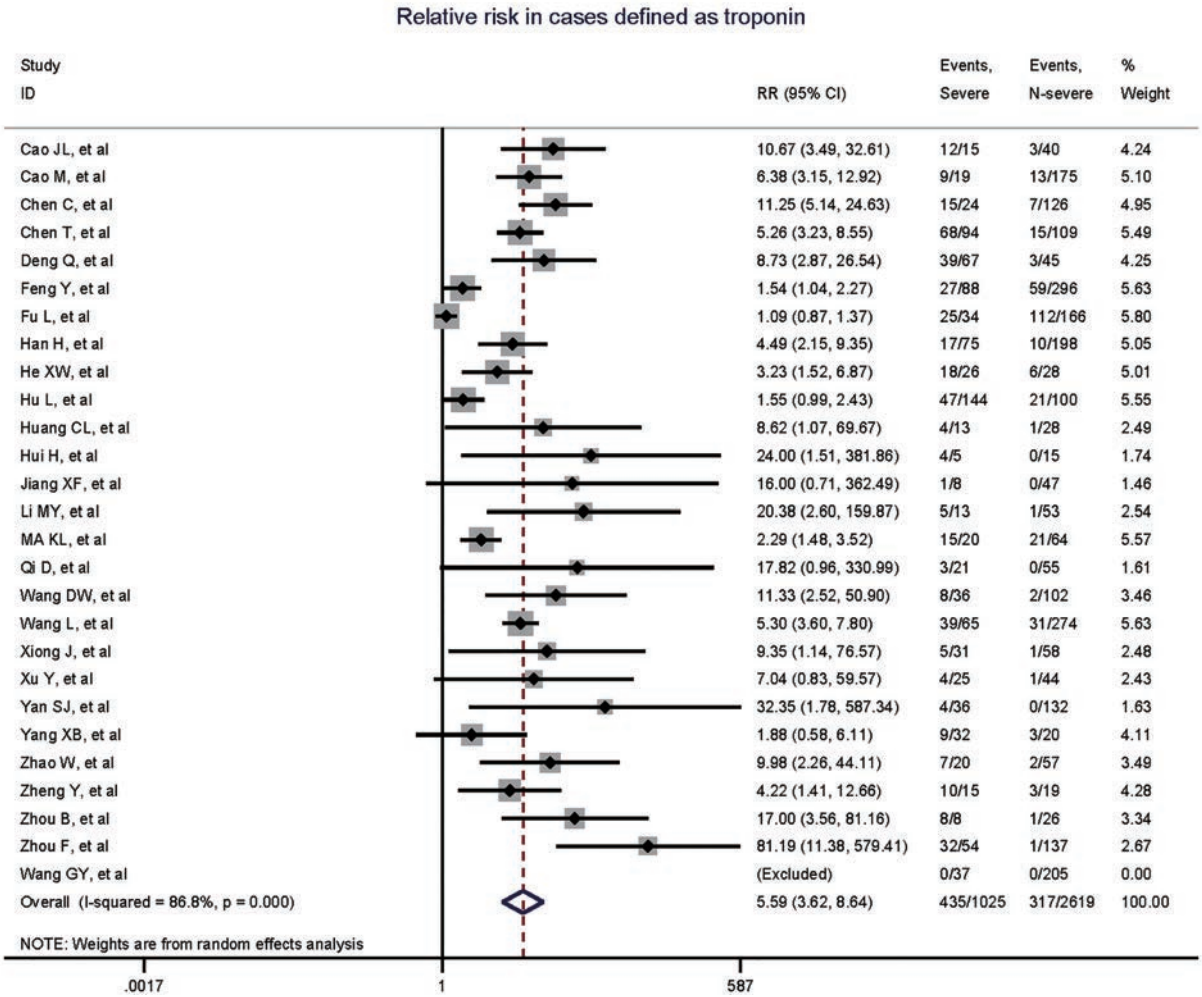

Figure S12 RR of cardiac injury with severe vs. non-severe patients (troponin). RR, relative risk.

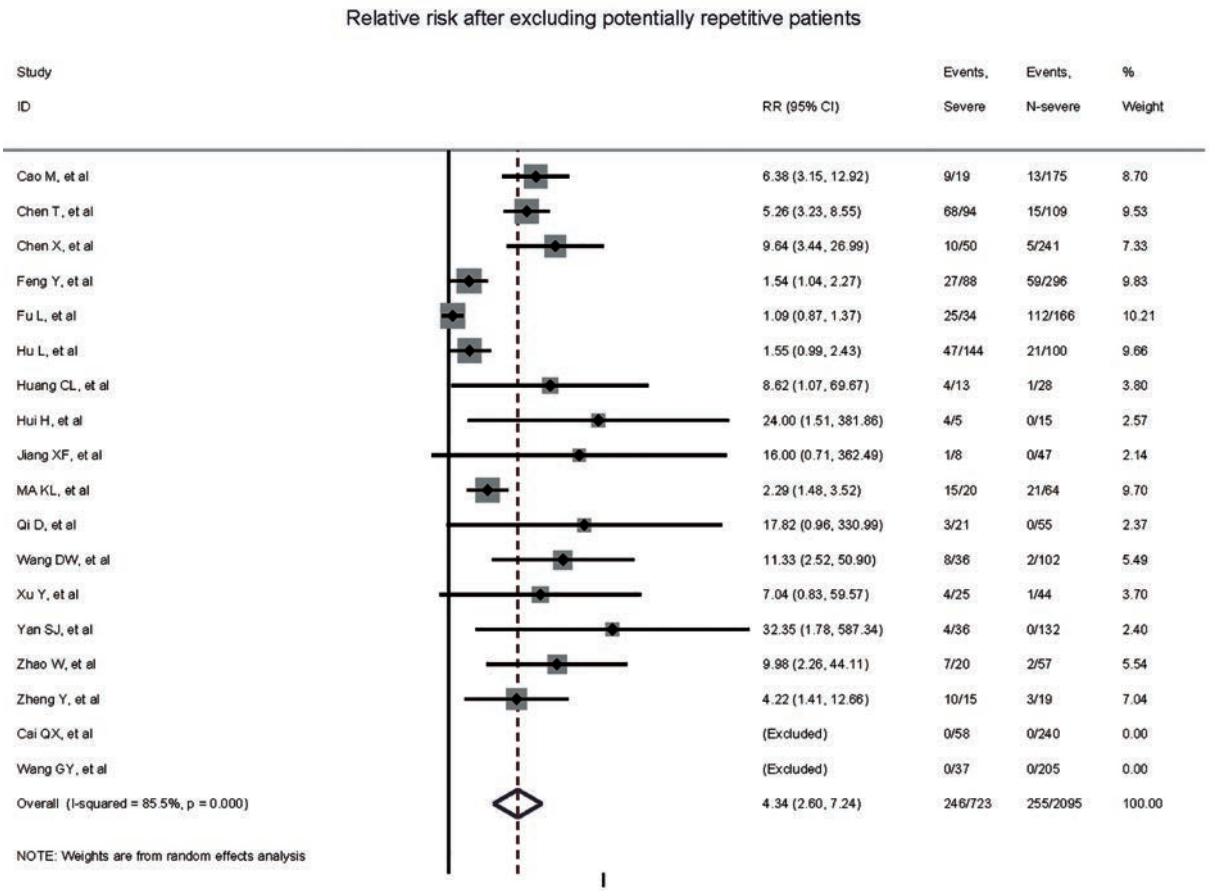

Figure S13 RR of cardiac injury with severe vs. non-severe patients after excluding potentially repetitive patients. RR, relative risk.

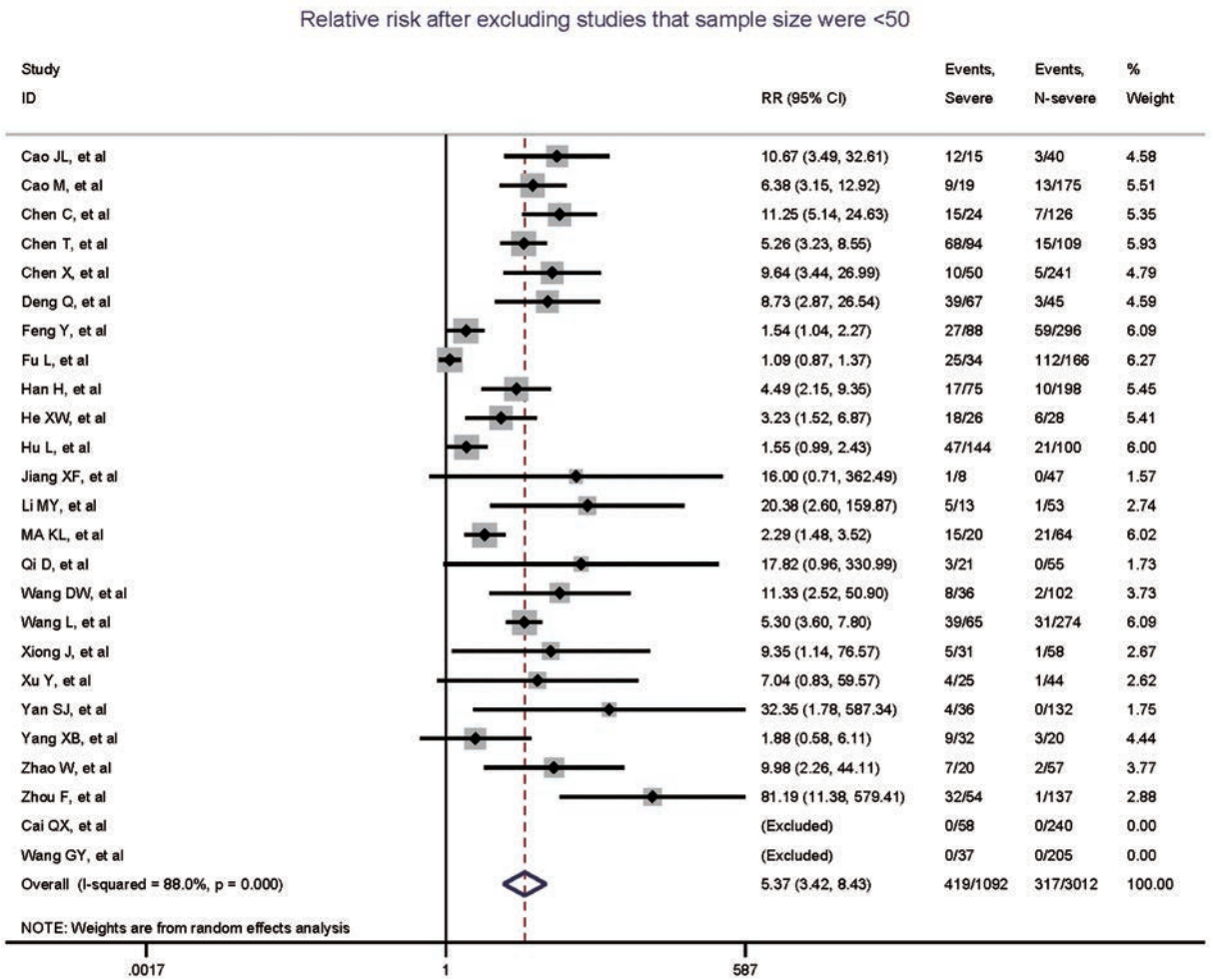

Figure S14 RR of cardiac injury with severe vs. non-severe patients after excluding studies that sample size <50. RR, relative risk.

Table S7 Meta-regression for RR of severe patients *vs.* non-severe patients

Variables	No. of reported studies	β coefficient (95% CI)	P value
Mean age	26	–0.0059 (–0.0275 to 0.0158)	0.583
Male	27	0.0053 (–0.0173 to 0.0278)	0.635
Smoking	11	–0.0040 (–0.0124 to 0.0044)	0.312
Hypertension	23	–0.0060 (–0.0165 to 0.0045)	0.249
Diabetes	24	–0.0037 (–0.0090 to 0.0016)	0.165
CVD	20	0.0090 (–0.0367 to 0.0546)	0.685
Cerebrovascular disease	12	0.0135 (–0.0787 to 0.1058)	0.750
Chronic pulmonary disease	18	0.0104 (–0.0585 to 0.0794)	0.752
Chronic kidney disease	14	0.0315 (–0.1087 to 0.1717)	0.633
Liver disease	15	0.0035 (–0.0173 to 0.0242)	0.723
Cancer	18	0.0315 (–0.0890 to 0.1520)	0.587

RR, relative risk; No., number; CI, confidence interval; CVD, cardiovascular disease.

Table S8 Univariable meta-regression for cardiac injury incidence

Population	Variables	No. of reported studies	β coefficient (95% CI)	P value
Overall	Mean age	41	–0.0062 (–0.0123 to –0.0002)	0.054
	Male	42	–0.0026 (–0.0079 to 0.0027)	0.322
	Smoking	14	–0.0020 (–0.0053 to 0.0014)	0.231
	Hypertension	33	–0.0023 (–0.0055 to 0.0009)	0.159
	Diabetes	35	–0.0015 (–0.0035 to 0.0006)	0.169
	CVD	32	–0.0007 (–0.0039 to 0.0026)	0.669
	Cerebrovascular disease	18	–0.0030 (–0.0164 to 0.0105)	0.646
	Chronic pulmonary disease	28	–0.0034 (–0.0137 to 0.0069)	0.504
	Chronic kidney disease	25	–0.0020 (–0.0149 to 0.0109)	0.754
	Liver disease	20	–0.0019 (–0.0064 to 0.0103)	0.632
	Cancer	28	–0.0115 (–0.0318 to 0.0088)	0.254
Non-survivors	Mean age	7	–0.0032 (–0.0165 to 0.0101)	0.559
	Male	8	–0.0028 (–0.0150 to 0.0093)	0.589
	Smoking	4	0.0002 (–0.0121 to 0.0125)	0.961
	Diabetes	8	0.0005 (–0.0047 to 0.0057)	0.832
	CVD	7	0.0017 (–0.0289 to 0.0322)	0.895
	Cerebrovascular disease	5	–0.0012 (–0.0250 to 0.0226)	0.883
	Chronic pulmonary disease	8	–0.0049 (–0.0218 to 0.0120)	0.503
	Chronic kidney disease	5	–0.0061 (–0.0737 to 0.0615)	0.792
	Liver disease	6	0.0016 (–0.0084 to 0.0116)	0.683
	Cancer	6	–0.0073 (–0.0476 to 0.0329)	0.639
Severe patients	Mean age	22	–0.0059 (–0.0130 to 0.0013)	0.101
	Male	23	–0.0053 (–0.0133 to 0.0027)	0.185
	Smoking	10	–0.0006 (–0.0069 to 0.0056)	0.820
	Hypertension	21	–0.0028 (–0.0071 to 0.0015)	0.195
	Diabetes	22	–0.0007 (–0.0049 to 0.0036)	0.749
	CVD	19	0.0013 (–0.0208 to 0.0234)	0.904
	Cerebrovascular disease	11	–0.0038 (–0.0194 to 0.0119)	0.598
	Chronic pulmonary disease	17	–0.0069 (–0.0202 to 0.0064)	0.287
	Chronic kidney disease	13	–0.0085 (–0.0482 to 0.0311)	0.644
	Liver disease	14	0.0017 (–0.0059 to 0.0093)	0.642
	Cancer	17	–0.0102 (–0.0357 to 0.0153)	0.407
Non-severe patients	Mean age	11	0.0020 (–0.0203 to 0.0242)	0.845
	Male	12	0.0064 (–0.0177 to 0.0305)	0.568
	Smoking	6	–0.0030 (–0.0096 to 0.0037)	0.283
	Hypertension	10	–0.0045 (–0.0127 to 0.0036)	0.233
	Diabetes	11	–0.0025 (–0.0061 to 0.0010)	0.142
	CVD	10	0.0096 (–0.0218 to 0.0411)	0.500
	Chronic pulmonary disease	8	0.0270 (–0.0415 to 0.0956)	0.372
	Liver disease	8	0.0066 (–0.0193 to 0.0325)	0.555
	Cancer	9	–0.0250 (–0.1880 to 0.1380)	0.727

No., number; CI, confidence interval; CVD, cardiovascular disease.

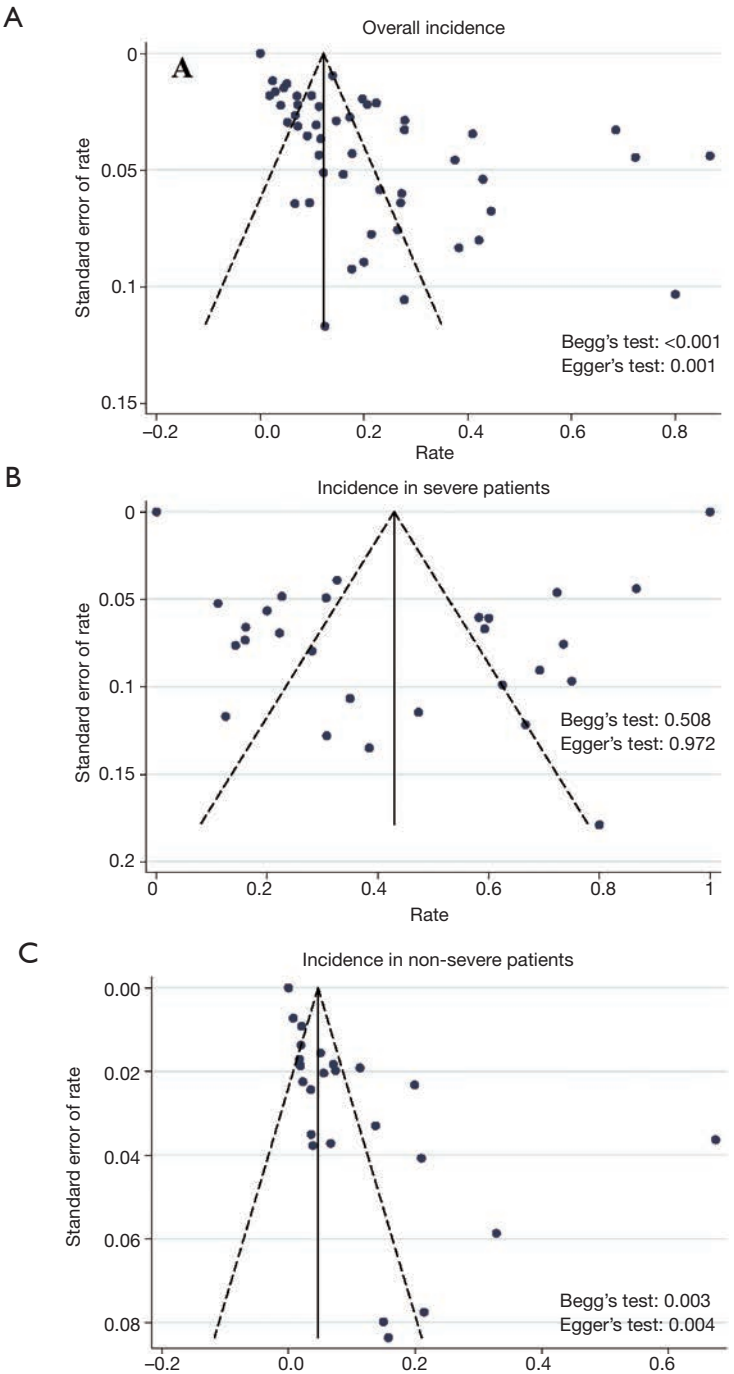

Figure S15 Publication bias on the incidence of cardiac injury [(A) overall; (B) severe patients; (C) non-severe patients].

Table S9 Trim and fill method to deal with publication bias

Population	Publication bias	Before trim and fill		After trim and fill	
	P for Egger's test	No. of studies	Incidence (95% CI)	No. of studies	Incidence (95% CI)
Overall	<0.001	50	0.21 (0.17–0.25)	69	0.09 (0.05–0.14)
Non-severe patients	0.004	23	0.11 (0.07–0.15)	33	0.03 (0.01–0.07)

No., number; CI, confidence interval.