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Prognostic value of C-reactive protein levels in pulmonary infections

A systematic review and meta-analysis

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Abstract

Background: C-reactive rotein (CRP) has been extensively studied as a biomarker that can predict mortality in patients with acute lung disease and our study aimed to elucidate the prognostic value of CRP levels for mortality in patients with various airway diseases, accounting for these differences and potential confounding factors accounts.

Methods: An extensive literature search was conducted in several databases including PubMed, Embase, Web of Science, Scopus, and ProQuest to ensure the inclusion of up-to-date evidence from studies published between January 2019 and December 2024. Both fixed-effects and random-effects models were used to calculate pooled mean hazard ratios (HR) and odds ratios (OR) for mortality.

Results: For mortality, the fixed effects model revealed a HR of 1.0065 (95% CI: 1.0054–1.0075, $P < .0001$), indicating a slightly increased risk of death associated with higher CRP levels. However, the random effects model, considering study heterogeneity, suggested an HR of 1.0488 (95% CI: 0.9978–1.1024, $P = .0608$), with significant heterogeneity ($Q = 135.31$, $P < .0001$). The OR analysis under the random effects model showed a more substantial increase in mortality risk with an OR of 1.2033 (95% CI: 1.0635–1.3614, $P = .0033$). Regarding ICU admissions and ventilation needs, substantial heterogeneity was also observed. The analysis did not find a statistically significant association between elevated CRP levels and ICU admission (OR = 1.1108, 95% CI: 0.9604–1.2847, $P = .1568$) or the necessity for ventilation (OR = 1.8981, 95% CI: 0.9651–3.7331, $P = .0633$), although both indicated trends towards increased risk.

Conclusion: CRP levels show a potential yet inconsistent association with mortality risk in patients with pulmonary infections. While elevated CRP levels suggest an increased risk of mortality, the results should be interpreted cautiously due to potential overestimation of the effect and the presence of publication bias.

Abbreviations: CI = confidence interval, CRP = C-reactive protein, HR = hazard ratios, OR = odds ratios.

Keywords: C-reactive protein, meta-analysis, mortality, pulmonary infections, systematic review

1. Introduction

A growing body of research highlights the growing interest in the prognostic value of C-reactive protein (CRP) levels in patients with lung disease. This interest stems from the potential to use this readily available biomarker to improve clinical outcomes. As a known inflammatory marker, CRP has been extensively studied in a variety of contexts, including its association with mortality and severe morbidity in pulmonary diseases.[1] Recent research shows an increasing focus on improving CRP accuracy and predictive power. In addition, the study examines how CRP interacts with other parameters to improve both assessment and prognosis of patients. Specifically, Futai et al, 2019 used a multicenter prospective registry-based observational study to assess the efficacy of CRP and procalcitonin in predicting outcome for septic stroke patients, emphasizing continued improvement in biomarker utility in intensive care emphasis.[2] Researchers have focused increasingly on understanding the dynamic interactions between white cell counts, inflammatory markers, and CRP levels and how all of these factors affect patient outcomes.[3]

Differences in the predictive power of CRP, as reflected in threshold values in patient populations, have led policymakers to reconsider their reliance on this biomarker Despite extensive research, there is uncertainty the clinical use of CRP remains uncertain, and some studies reveal low to moderate sensitivity and specificity. These changes in CRP levels highlight the importance of considering them in the broader clinical context, rather

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than as independent indicators of severity and prognosis This review will examine the importance of CRP levels is of prognostic importance in patients with pneumonia well. We aim to synthesize recent findings and acknowledge the limitations and clarify the prognostic role of CRP in this setting. The goal is to promote informed clinical decision making and ultimately improve patient outcomes.

2. Material and methods

2.1. Search strategy

A systematic literature search was conducted in content-based databases, including PubMed, EMBASE, Web of Science, Scopus, and ProQuest, covering publications from January 2019 to December 2024. To maximize the search's comprehensiveness and reliability, MeSH terms and up-to-date keywords were employed to ensure the inclusion of relevant data across these platforms. Keywords were refined through an iterative process involving pilot searches and expert consultation. Pilot searches using broad terms were conducted to evaluate their effectiveness in capturing relevant studies. Based on the results, terms were adjusted to address gaps or redundancies. Peer consultation further ensured the relevance and inclusivity of the selected keywords, enhancing the comprehensiveness of the search strategy. These included:

- Primary terms: "Pulmonary Infections," "Respiratory Infection," "Pneumonia," "Nosocomial Infections."
- COVID-19 related terms: "COVID-19," "SARS-CoV-2," "Coronavirus Infections."
- Additional terms: "Inflammatory Markers," "Comorbidities."

Boolean operators ("OR") were used to combine terms together, ensuring that multiple related studies were captured. This approach was aimed at covering various manifestations of pneumonia, inflammatory markers, their association with COVID-19 and its complications, and possible interactions with comorbidities. By considering various keywords and conditions, we sought to comprehensively assess the multifaceted relationships between these factors and their impact on patients with pulmonary infections.

2.2. Study selection process

A systematic and multi-phased approach ensured unbiased selection of studies for this meta-analysis. Duplicate records were removed initially, followed by independent title and abstract screening against pre-defined inclusion/exclusion criteria. Studies clearly not meeting the criteria (investigating other diseases, insufficient sample size, missing data, or unavailable for full-text review) were excluded.

Further evaluation through full-text review was conducted on studies potentially meeting the criteria (patients with diagnosed pulmonary infections, sample size ≥ 30, reported CRP values for both groups). Two independent reviewers assessed eligibility, resolving discrepancies through discussion or involving a third reviewer as a tiebreaker. This rigorous process minimized selection bias and ensured the inclusion of relevant and high-quality studies. Eligible studies included those reporting detailed patients' characteristics, such as age, gender distribution, and comorbidities, ensuring a comprehensive understanding of the populations studied. These criteria were essential to ensure that the meta-analysis captured the potential influence of demographic and clinical variables on the relationship between CRP level and mortality risk.

2.3. Data extraction

A pre-designed checklist was used for data extraction, ensuring comprehensive capture of crucial study details. This included: author, publication date, country, participant demographics (sample size, age, comorbidities), and mortality risk. Data were extracted independently by 2 reviewers, which improved accuracy and reduced bias. Discrepancies between reviewers were resolved through discussion or, if necessary, consultation with a third reviewer. This careful approach provides confidence in the data extraction process and strengthens the reliability of the meta-analysis. While participants' demographics, such as age, comorbidities, and sample size, were systematically extracted, variations in CRP measurement methods were inconsistently reported across studies, limiting their potential inclusion in subgroup analysis. In addition to extracting general study characteristics, participants' demographics, including mean age, gender proportions, and prevalence of key comorbidities (e.g., cardiovascular disease, diabetes, or obesity), were specifically recorded. These variables were collected to assess the representativeness of the study populations and to evaluate their potential impact on the observed association between CRP levels and mortality risk.

2.4. Quality assessment

We rigorously assessed the quality of included studies using the review tool and cutoff review developed by the National Heart, Lung, and Blood Institute (NHLBI). This comprehensive instrument ensures a thorough examination of internal validity, which is important for the reliability and validity of any meta-analysis. Two independent reviewers evaluated each study using a criterion scale ("yes," "no," "new CD," "new NR," and "new NA") Through discussion or discussion with a third investigator controlled as necessary. This qualitative study provided valuable insights into the methodological strengths and weaknesses, ultimately guiding decisions during data collection and informing our meta-analysis the strength of all of our findings increased. The designation of "Fair" to "Good" for study quality reflected the methodological rigor and reliability of the included studies, as evaluated using the NHLBI tool. This tool assessed study quality based on criteria such as study design, sample size justification, blinding, and the handling of confounders. Each study was rated as "Good," "Fair," or "Poor" depending on its adherence to these standards. A "Good" rating indicated high methodological rigor with minimal risk of bias, signifying robust methodologies and well-documented procedures that enhanced reliability. Conversely, a "Fair" rating signified acceptable quality with moderate confidence in validity, though some limitations, such as incomplete blinding or potential selection bias, might be present. Studies rated as "Poor" were excluded from the meta-analysis due to significant methodological flaws that could compromise reliability. These quality ratings were integral to interpreting the findings of the meta-analysis, ensuring that the included data were sufficiently credible to support meaningful conclusions. By incorporating a rigorous quality assessment, variability in study design or execution was minimized, thereby providing a balanced perspective on the relationship between study outcomes and prognostic factors under investigation.

2.5. Statistical analysis

Statistical analyses were performed using the R software metapackage developed by Schwarzer, Carpenter, and Rücker (2015). This comprehensive package allowed for in-depth statistical analysis of study outcomes and potential biases, ensuring a robust and reliable meta-analysis.[4] This software facilitated the calculation of pooled effect sizes, assessment of heterogeneity, construction of various data visualization plots, and bias evaluation through tools like Egger's test (Egger et al, 1997) for a comprehensive meta-analysis[5] and Begg's tests referenced from Begg & Mazumdar's 1993 publication,[6] We visually assessed the symmetry of funnel plots to identify potential publication

bias. Additionally, we employed Galbraith and Baujat plots to gain deeper insights into the sources of heterogeneity among studies. Specifically, Galbraith plots aided in visualizing the extent of heterogeneity and identifying outlier studies contributing to it, as described by Bax et al.[7] The Baujat plot is another valuable tool for visualizing the sources of heterogeneity in meta-analysis. It allows us to identify studies that significantly contribute to the overall heterogeneity, providing insights into the potential reasons for variation in study results.

Our meta-analysis employed various statistical measures to evaluate the association between CRP levels and mortality risk in patients with pulmonary infections, while simultaneously assessing the consistency and reliability of findings across included studies.

- *P* value: This statistic measures the probability that observed data would happen by chance under the null hypothesis which is typically the hypothesis that there is no effect in This context (no association between CRP levels and mortality). A *P* value less than .05 is commonly considered statistically significant, indicating strong evidence against the null hypothesis. This is a statistical measure representing the number of standard deviations of a data point from the mean.

- *z* value: The *z* value is used to assess the significance of the overall effect size in the context of meta-analysis. A higher absolute value of *z* indicates A stronger deviation from the null hypothesis values typically compared against standard normal distribution thresholds are typically used to determine significance.

- *Q* test: The *Q* test is used to assess heterogeneity among the studies included in a meta-analysis. It tests whether observed differences in study results are greater than what would be expected by chance alone. A high *Q* value (with a correspondingly low *P* value) suggests significant heterogeneity, meaning that the study outcomes vary more than expected from sampling error alone.

- Tau² (τ^2): This is an estimate of the between-study variance in a random-effects meta-analysis. It reflects the extent of variation in true effect sizes across studies, beyond what would be expected from random error within studies. A higher τ^2 indicates greater heterogeneity among the true effects being estimated by the different studies.

- Tau (τ): This represents the standard deviation of the underlying effects across studies in a random effect meta-analysis. It is the square root of and provides an estimate of the average deviation of the true effect size from the total effect size estimated in the meta-analysis.

- I^2: This statistic describes the percentage of variation in studied studies due to heterogeneity rather than chance. I^2 values 25%, 50%, and 75% are typically considered to represent moderate low heterogeneity and high heterogeneity respectively. It provides a measure of the extent to which the variance in observed effects reflects the variance in true effects rather than the sampling error.

Due to inconsistencies in the reporting of CRP measurement techniques, meta-regression analyses to explore their influence on the results were not feasible. Nevertheless, subgroup analysis based on available study characteristics was conducted where possible to address heterogeneity. A CRP threshold of > 100 mg/L was used as it is a commonly reported cutoff in clinical studies for indicating severe inflammation and poor outcomes in pulmonary infections. This consistent use across studies allowed for standardized data pooling and facilitated comparability. While a random-effects model was employed to account for study heterogeneity, it is acknowledged that the high I^2 values (exceeding 90%) suggest substantial variability across studies. To further explore the sources of this heterogeneity, a range of potential factors were considered, including CRP measurement methods, patients' characteristics (such as age, gender, and comorbidities), and disease severity. However, due to the limitations of the available data, meta-regression analysis was not conducted in this study. The variability could be attributed to differences in study populations, methodologies, and reporting practices, which are common challenges in meta-analyses. Future research, particularly with more homogenous data, will benefit from employing meta-regression to more directly examine these potential sources of heterogeneity.

While publication bias was assessed through funnel plot symmetry, Begg's and Egger's tests, the Trim-and-Fill method was not employed to adjust for potential bias. The decision was based on the scope and concentration of the current study, which prioritized identifying the presence of publication bias rather than adjusting effect estimates retrospectively. It is recognized that the Trim-and-Fill method could provide additional insights by estimating and imputing potentially missing studies due to publication bias. However, limitations in the reporting and characteristics of the included studies restricted its application. Future analyses incorporating this method will yield more precise pooled effect estimates, thereby addressing potential distortions caused by publication bias.

3. Results

3.1. Search results

This study conducted a comprehensive meta-analysis to pool data from studies on the topic at hand (Fig. 1). The first step consisted of a comprehensive search of several major databases, such as PubMed, EMBASE, Web of Science, Scopus, and ProQuest, yielding a total of 7831 records. To narrow down this broad database in 2010, duplicates were identified and removed, resulting in 3349 records being removed from the original set. This work reduced the number of records to 4482, and then a preliminary analysis was performed. During the search phase, titles and abstracts were thoroughly screened, resulting in the exclusion of 3210 records for irrelevance or noncompliance with search criteria. These articles were screened extensively to ensure that they met the stringent inclusion criteria established for the meta-analysis. A significant number of these full-length articles have been omitted for a variety of reasons. 49 were excluded because they were exploratory or meta-analyses, not original research studies. An additional 32 cases were excluded from analysis due to sample sizes of less than 10 participants, which could compromise the robustness and reliability of findings A substantial portion of the total of 682 cases were excluded due to cases a was therefore insufficient, indicating that the detailed data required for inclusion in the meta-analysis were not obtained. Poor study design was the reason for excluding 321 articles, highlighting the importance of methodological rigor in research considered for meta-analysis. Additionally, 145 articles were not included due to language barriers, which prevented a thorough evaluation of their content. After this rigorous selection and exclusion process, only 43 studies met all the criteria and were included in the meta-analysis.

3.2. Characteristics of included studies

This meta-analysis compiles a wide range of studies published between 2019 and 2024 focusing on the relationship between various diseases and patient outcomes, with a significant number of studies concentrating on COVID-19. The research encompasses a global perspective, including data from countries such as China, Serbia, the USA, Spain, Turkey, Portugal, India, Egypt, Iran, France, Mozambique, Japan, the UK, Austria, Finland, Kazakhstan, Italy, Germany, Brazil, Switzerland, Pakistan, Lebanon, and Poland. The conditions investigated are diverse, ranging from obesity and pneumonia to more specific instances such as hemodialysis, peritoneal dialysis, and surgical patients with COVID-19, as well as those with nosocomial carbapenem-resistant Acinetobacter baumannii pneumonia. Comorbidities with COVID-19 such as cancer, cardiovascular

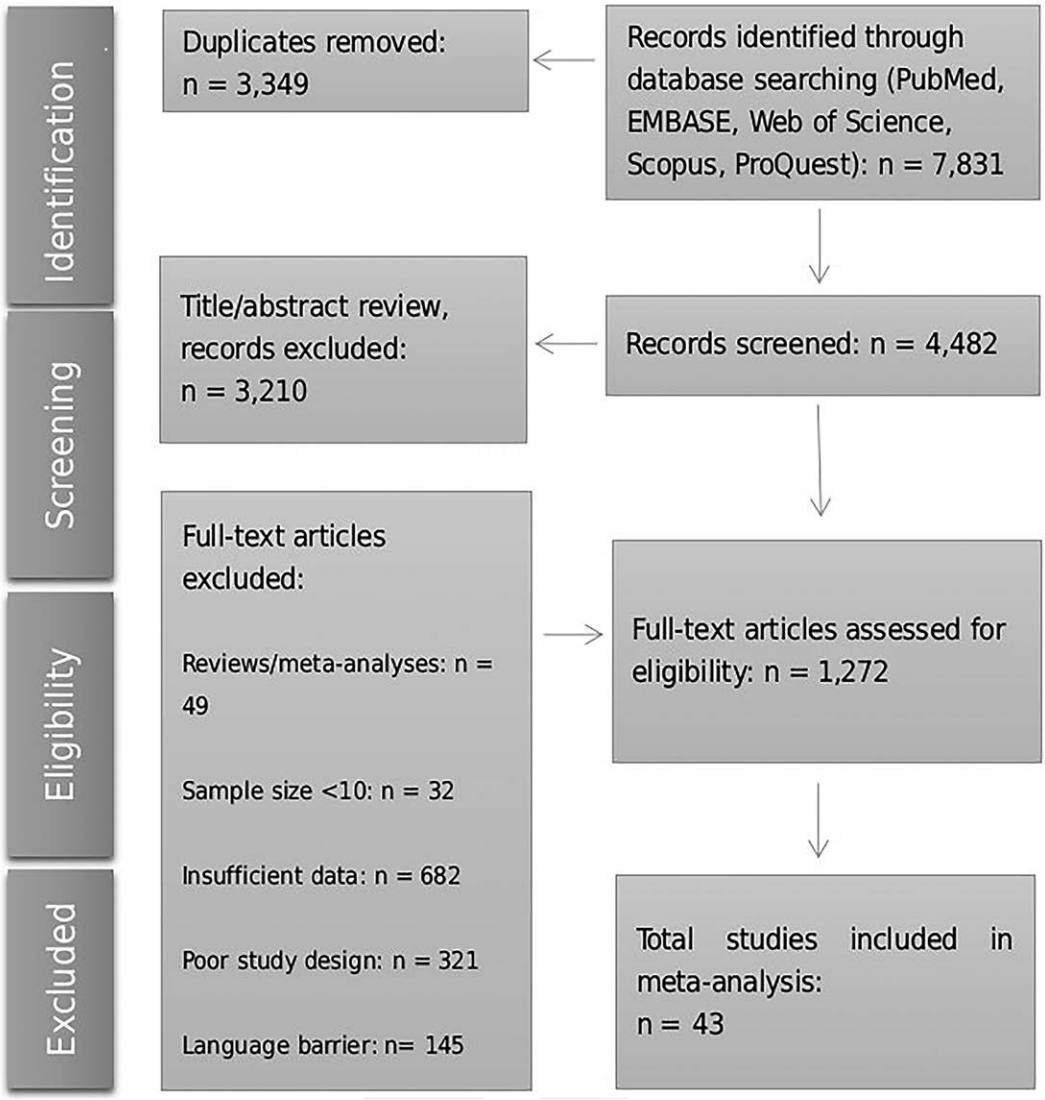

Figure 1. Flow diagram of study selection process.

disease, diabetes, and chronic kidney disease are also well-represented in the study selection[8–50] (Table 1).

3.3. Quality assessment

The quality of the studies has been assessed as "Fair" to "Good," indicating a reasonable level of confidence in the data provided (Table 1). This collection of data from such a varied array of sources provides a comprehensive foundation for the meta-analysis, aiming to discern the prognostic significance of different diseases and patient characteristics on outcomes, especially in the context of the COVID-19 pandemic.

3.4. Analysis of CRP levels and mortality risk in pulmonary infection patients with HR value

We investigated the association between CRP levels and mortality in patients with pulmonary infections across the datasets with HR value (Fig. 2A). Elevated CRP level was associated with a slight but significant increase in mortality risk, as shown by the fixed effects model (HR: 1.0065, 95% CI: [1.0054–1.0075], $P < .0001$). However, the high variability among studies ($Q = 135.31$, $P < .0001$) necessitated the use of a random effects model, which provided a less definitive HR of 1.0488 (95% CI: [0.9978–1.1024], $P = .0608$). The heterogeneity in our meta-analysis was quantified using tau^2 (0.0064 [0.0044–0.1264]) and tau (0.0798 [0.0661–0.3555]), with the Q test for heterogeneity confirming the presence of significant variability across studies ($Q = 135.31$, df = 10, $P < .0001$). The funnel plot depicted in Figure 2B which showed the majority of studies are clustered at the top of the plot, indicating a concentration of studies with high precision and smaller standard errors, which are typically associated with larger sample sizes. Notably, one study, Chen et al., 2019, is an outlier located at the bottom right of the plot. This position indicates that it has a relatively larger effect size with a lower precision.

Egger's linear regression test, corresponding to Figure 3A, indicated potential funnel plot asymmetry, with a calculated t value of 2.68 and 9 degrees of freedom, resulting in a P value of .0251. This suggests that there is a statistically significant linear relationship between the effect estimates and their standard errors, typically interpreted as evidence of publication bias. The regression analysis estimated a bias of 3.2228 with a standard error of 1.2017, and an intercept of 0.0025 with a standard error of 0.0021. The presence of multiplicative residual heterogeneity (tau^2) was substantial at 8.3561, which implies that there is considerable variability between the study effects that is not solely

Table 1

Characteristics of the included studies

Study	Country	Disease	Number	Age	Mortality	Quality assessment
Chen et al, 2019[8]	China	Obese with pneumonia	909	72 (57–83)	12 mo	Fair
Brkovic et al, 2023[9]	Serbia	Hemodialysis with COVID-19	442	63 ± 13.7	N/A	Fair
Li et al, 2023[10]	China	COVID-19	3545	63.7	N/A	Fair
Wang et al, 2023[11]	USA	COVID-19	456	63 (51–73)	1 & 2 mo	Good
San Martín-López et al, 2023[12]	Spain	COVID-19	5510	65 (53–76)	3 mo	Fair
Koc et al, 2023[13]	Turkey	COVID-19	283	61 ± 13 and 60 ± 18	N/A	Fair
Niu et al, 2023[14]	China	Nosocomial carbapenem-resistant Acinetobacter baumannii pneumonia	159	67.90 ± 14.54	28 d	Fair
Cidade et al, 2023[15]	Portugal	COVID-19	136	63.7 ± 9.3	28 d	Good
Kajal et al, 2023[16]	India	COVID-19	5865	55 ± 15.18	N/A	Fair
Ali et al, 2023[17]	Egypt	COVID-19	200	59.25 ± 12.96	N/A	Good
Ertekin et al, 2023[18]	Turkey	COVID-19	619	69 (57–76)	N/A	Fair
Sivri et al, 2023[19]	Turkey	COVID-19	640	59.5 ± 18.04 (Living) and 67.6 ± 14.1 (Deceased)	N/A	Fair
Siavoshi et al, 2023[20]	Iran	COVID-19	11,944	59.4 ± 18.0	N/A	Good
Abensur et al, 2023[21]	France	COVID-19	1035	69.0 (58.0–79.0)	N/A	Good
Balanza et al, 2023[22]	Mozambique	Pneumonia	472	14.1 (6.1–27.1)	28 d, and 90 d	Good
Gohda et al, 2022[23]	Japan	COVID-19	80	70 (61–76)	N/A	Fair
Gursu et al, 2022[24]	Turkey	Peritoneal Dialysis with COVID-19	142	52 (42–61)	N/A	Fair
Yilmaz et al, 2022[25]	Turkey	Surgical patients with COVID-19	38	55.03 ± 19.04	30 d	Fair
Carbonell et al, 2022[26]	Spain	ICU COVID-19	4635	64 (55–71)	N/A	Fair
Aziz et al, 2022[27]	Austria	Diabetes Mellitus, Prediabetes with COVID-19	747	70.3 ± 13.3	N/A	Fair
Forsblom et al, 2022[28]	Finland	COVID-19	585	over 65 years	N/A	Fair
Pya et al, 2021[29]	Kazakhstan	COVID-19	205	57.3 ± 12.7	N/A	Fair
Masotti et al, 2022[30]	Italy	COVID-19	223	69.4 ± 13.3	N/A	Fair
Akingboye et al, 2021[31]	UK	Cancer with COVID-19	80	77.8 ± 12.3	90 d	Fair
Cremer et al, 2020[32]	Germany	Cardiovascular comorbidities with COVID-19	2147	N/A	N/A	Fair
Sharifpour et al, 2020[33]	USA	COVID-19	203	63 ± 15	N/A	Fair
de Oliveira et al, 2021[34]	Brazil	Cancer with COVID-19	155	60.9 ± 13.4	N/A	Fair
Tessitore et al, 2021[35]	Switzerland	Cardiovascular disease with COVID-19	839	67 (54–81)	N/A	Good
Nasir et al, 2021[36]	Pakistan	COVID-19	445	53 (40–64)	N/A	Good
Sadeghi et al, 2021[37]	Iran	COVID-19	214	59	N/A	Good
Sharma et al, 2022[38]	India	COVID-19	255	5.21 (1.40–10.00)	N/A	Good
Ocak et al, 2021[39]	Turkey	COVID-19	130	53.44 ± 12.38	N/A	Fair
Leoni et al, 2022[40]	Italy	COVID-19	98	66 (56–73)	28 d	Good
Dagher et al, 2022[41]	Lebanon	COVID-19	761	60.81 ± 16.93	N/A	Good
Peng et al, 2022[42]	China	COVID-19	611	57.00 (41.00–68.00)	N/A	Good
Keri et al, 2022[43]	India	COVID-19	209	49 (35–63)	N/A	Fair
Assandri et al, 2022[44]	Italy	COVID-19	96	64 (36–88)	N/A	Fair
Lei et al, 2022[45]	China	Diabetes with COVID-19	288	48.5 (34.3–62.0)	N/A	Fair
Mostaghim et al, 2020[46]	USA	Obesity with COVID-19	791	65 ± 20	N/A	Fair
Vasbinder et al, 2024[47]	USA	COVID-19	1137	60 ± 18	N/A	Good
Shanmugavel et al, 2023[48]	USA	Chronic kidney disease with COVID-19	118	> 60 years	N/A	Fair
Kania et al, 2023[49]	Poland	Diabetes with COVID-19	5191	64 (51–74)	N/A	Fair
Kamjai et al, 2022[50]	Thailand	COVID-19	474	54 (19–87) (Mild cases) | 60 (22–92) (Severe cases)	N/A	Fair

due to sampling error. Complementing the Egger's test, we also used Begg's rank correlation method, presented in Figure 3B. The Begg's test yielded a z value of 3.04, with an accompanying P value of .0024, reinforcing the presence of asymmetry in the funnel plot. The rank correlation statistic (ks) was 39.0000 with a standard error of 12.8452, further indicating the presence of publication bias or other systematic differences between smaller and larger studies.

The Baujat analysis shown as Figure 4A has presented notable findings within its graph representation. Notably, the studies by Brkovic et al, 2023, both the univariate and multivariate analyses during admission, are positioned at the upper left corner of the graph. In contrast, the study by Li et al, 2023 is found on the far right side of the graph, indicating a different influence or heterogeneity level. The bulk of the literature appears to cluster towards the lower left

quadrant of the graph, which may point to a lower influence and heterogeneity.

The Galbraith plot shown as Figure 4B provides a visual representation of the dispersion and potential influence of included studies in a meta-analysis. We can discern that studies are distributed across four distinct regions. The first region, from the top down, includes the studies by Li et al, 2023, Chen et al, 2019, Wang et al, 2023, and Akingboye et al, 2021. Notably, the study by Li et al, 2023, is positioned at the uppermost right corner, indicating it has the largest standard error inverse and the highest standardized treatment effect. This uppermost positioning suggests that the Li et al, 2023 study could have a substantial impact on the meta-analysis due to its larger effect size or higher variance. The other publications are distributed in the second and third regions of the plot, moving downwards.

In an effort to understand the sources of high heterogeneity within a meta-analysis, a re-analysis was performed after stratifying the studies into outlier and non-outlier groups, based on Baujat's analysis as shown Figure 5A. The subgroup of non-outliers, which consists of seven studies, showed a HR of 1.0077 with a 95% CI ranging from 1.0049 to 1.0104 under the common effect model. This subgroup presented a heterogeneity I^2 of 73.9%, a substantial reduction compared to the overall heterogeneity but still indicating considerable variability among the studies. The Q test for heterogeneity within this non-outlier group was significant ($P < .0001$), suggesting that variance among these studies is present but less pronounced.

The meta-analysis, also reevaluated by dividing studies into Multivariate and Univariate groups using the R package "meta," presents insightful findings as shown Figure 5B. The Multivariate subgroup, comprising seven datasets, shows a reduction in heterogeneity to 75.8%, indicated by an I^2 value, yet this percentage still reflects a high level of variability among the studies' results. The Univariate group maintains an even higher level of heterogeneity, at 97.3%, despite comprising a smaller number of four studies. The common effect model yields a HR of 1.0057 with a 95% CI of [1.0033; 1.0082] for the Multivariate subgroup, and an HR of 1.0066 with a 95% CI of [1.0055; 1.0078] for the Univariate subgroup. These results indicate a slight increase in the effect size when using a common effect model. In the random effects model, which takes into account the variability among studies, the Multivariate subgroup displays an HR of 1.0155 with a 95% CI of [1.0026; 1.0285] and a very low tau-squared (τ^2) of 0.0002, suggesting minor between-study variance. Conversely, the Univariate subgroup shows a higher HR of 1.0735 with a wider 95% CI of [0.9460; 1.2182] and a considerably higher τ^2 of 0.0165, indicating a significant level of variance among the included studies.

In this meta-analysis, studies were also stratified into subgroups based on pneumonia infection combined with other diseases and reassessed using the R package "meta" shown as Figure 5C. The subgroups considered were "Obese & COVID-19," "Hemodialysis & COVID-19," "COVID-19," and "Cancer & COVID-19." The "COVID-19" subgroup, which did not account for additional diseases. This subgroup maintained a very high heterogeneity, with an I^2 of 96.5%, and an HR of 1.0102 (95% CI: 1.0065–1.0140) under the common effect model. Under the random effects model, the HR slightly increased to 1.0693 (95% CI: 0.9707–1.1779) due to the adjustment for between-study variability.

3.5. Analysis of CRP levels and mortality risk in pulmonary infection patients with OR value

In this meta-analysis shown as Figure 6A exploring the prognostic significance of CRP levels in patients with pulmonary infection, data on mortality OR were extracted from various studies and analyzed. Given the high heterogeneity among the studies, indicated by an I^2 statistic of 89.9%, the use of random effects models was deemed more appropriate for the analysis. The common effect model, which assumes a single underlying effect size, yielded an OR of 1.0075 with a 95% CI ranging from 1.0064 to 1.0085, and this result was highly significant with a z value of 13.99 and a P value of less than .0001. However, due to the significant heterogeneity observed, which suggests a substantial variation in effect sizes across studies, the random effects model provided a more reliable estimate. This model showed an OR of 1.2033, with a 95% CI of 1.0635–1.3614, and was also statistically significant ($z = 2.94$, $P = .0033$). The heterogeneity was quantified with a tau-squared (τ^2) value of 0.1444 and a tau value of 0.3800, indicating a considerable spread of effect sizes. The confidence intervals for tau-squared ranged from 0.1254 to 0.4504, and for tau from 0.3541 to 0.6712, underscoring the variability among the included studies. The test for heterogeneity confirmed the presence of significant variability with a Q value of 436.46 for 44 degrees of freedom, reinforcing the choice of the random effects model over the common effect model for this analysis. In the analysis presented in Figure 6B, we observe a funnel plot that predominantly exhibits a regular inverted funnel shape, indicative of a symmetric distribution of studies around the effect size. However, a notable feature of this funnel plot is the asymmetry manifested by the presence of studies on the right side without corresponding studies on the left. This pattern suggests a potential publication bias, where studies with positive or significant findings are more likely to be published, while those with negative or non-significant results are underrepresented or absent.

The Begg rank correlation test shown as Figure 7A is utilized to assess funnel plot asymmetry. The outcome of this test yields a z value of 0.85 with a P value of .3947. This result suggests that there is no statistically significant evidence of asymmetry within the funnel plot according to this test. The sample estimates provided are a Kendall's score (ks) of 87.0000 and its standard error (se.ks) of 102.2204. Conversely, Figure 7B shows the results from an Egger linear regression test. The test results in a t value of 4.56 with degrees of freedom (df) set at 43, and a highly significant P value of less than .0001. This indicates a strong evidence of funnel plot asymmetry, suggesting the presence of publication bias or other factors leading to an uneven distribution of study effects. The sample estimates detail a bias of 2.0902 with a standard error (se.bias) of 0.4584, and an intercept of 0.0035 with its standard error (se.intercept) of 0.0016. Additionally, the analysis notes a multiplicative residual heterogeneity variance (tau^2) of 6.8417.

In the observed Baujat plot as shown Figure 8A, the study by Abensur et al, 2023, under the univariate analysis, is positioned at the very top left corner of the plot. This placement suggests that the study not only contributes significantly to the heterogeneity of the meta-analysis but also has a relatively low effect size variance compared to other studies included in the analysis. On the other end of the spectrum, the study by Ertekin et al, 2023, finds itself at the extreme right, indicating it has a high effect size variance but its contribution to heterogeneity might not be as pronounced as its position might initially suggest. The majority of the included studies cluster in the lower left corner of the Baujat plot. The clustering of studies reveals that some have both less impact on the overall variation and smaller differences in effect sizes. This points to a more consistent effect size across these studies. However, certain studies (Peng et al, 2022 (Univariate), Abensur et al, 2023 (Multivariate), Dagher et al, 2022, and Akingboye et al, 2021) stand out as relatively significant contributors to the heterogeneity of the meta-analysis, despite not being as influential as the study in the top left corner.

The analysis is shown as Figure 8B, the studies included in the meta-analysis are divided into four distinct regions, indicating different effects on overall heterogeneity The first region, at the top of the plot, holds Ertekin et al., 2023, and Peng et al, 2022 (Univariate). The observations found above the Galbraith plot are very diverse and contribute significantly to the overall variability

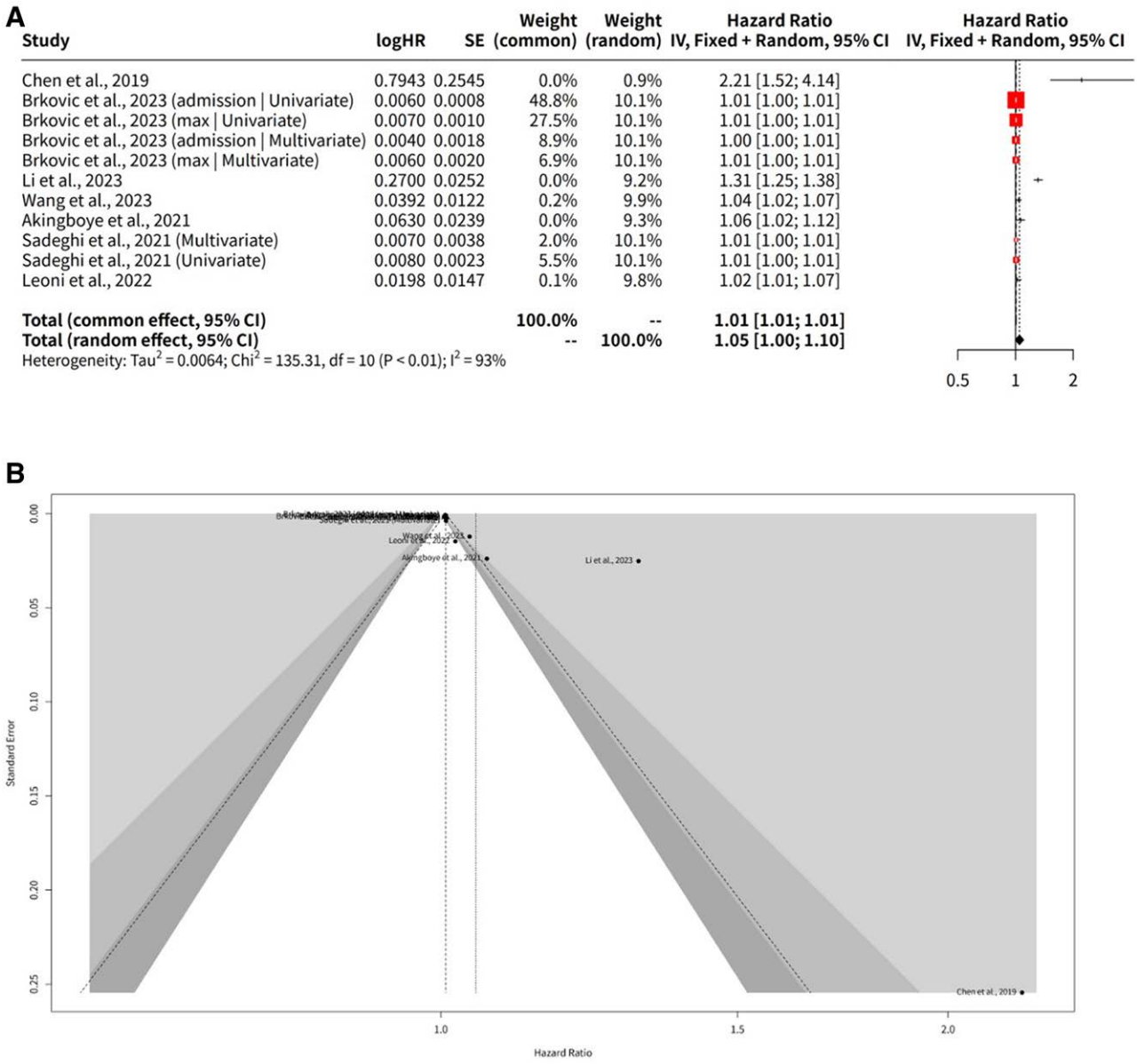

Figure 2. Forest plot of CRP levels and mortality risk and funnel plot analysis. (A) Forest plot of CRP levels and mortality risk in pulmonary infection patients. (B) Funnel plot of study precision and effect sizes for CRP levels. CRP = C-reactive protein.

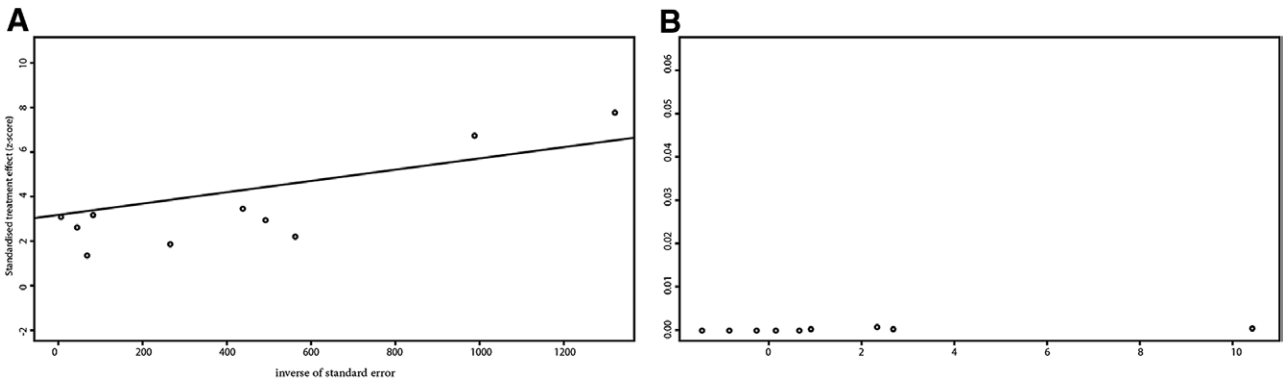

Figure 3. Egger's test for funnel plot asymmetry and Begg's test for publication bias detection. (A) Egger's test for funnel plot asymmetry. (B) Begg's test for publication bias detection.

of the observations. These studies may be overrepresented, potentially influencing meta-analysis results due to their high variability. In contrast, the lower part of the plot contains studies with relatively few variables, such as Abensur et al, 2023 (Univariate) and Abensur et al, 2023 (Multivariate). Residual analyses are clustered in the middle sections plot between the upper areas.

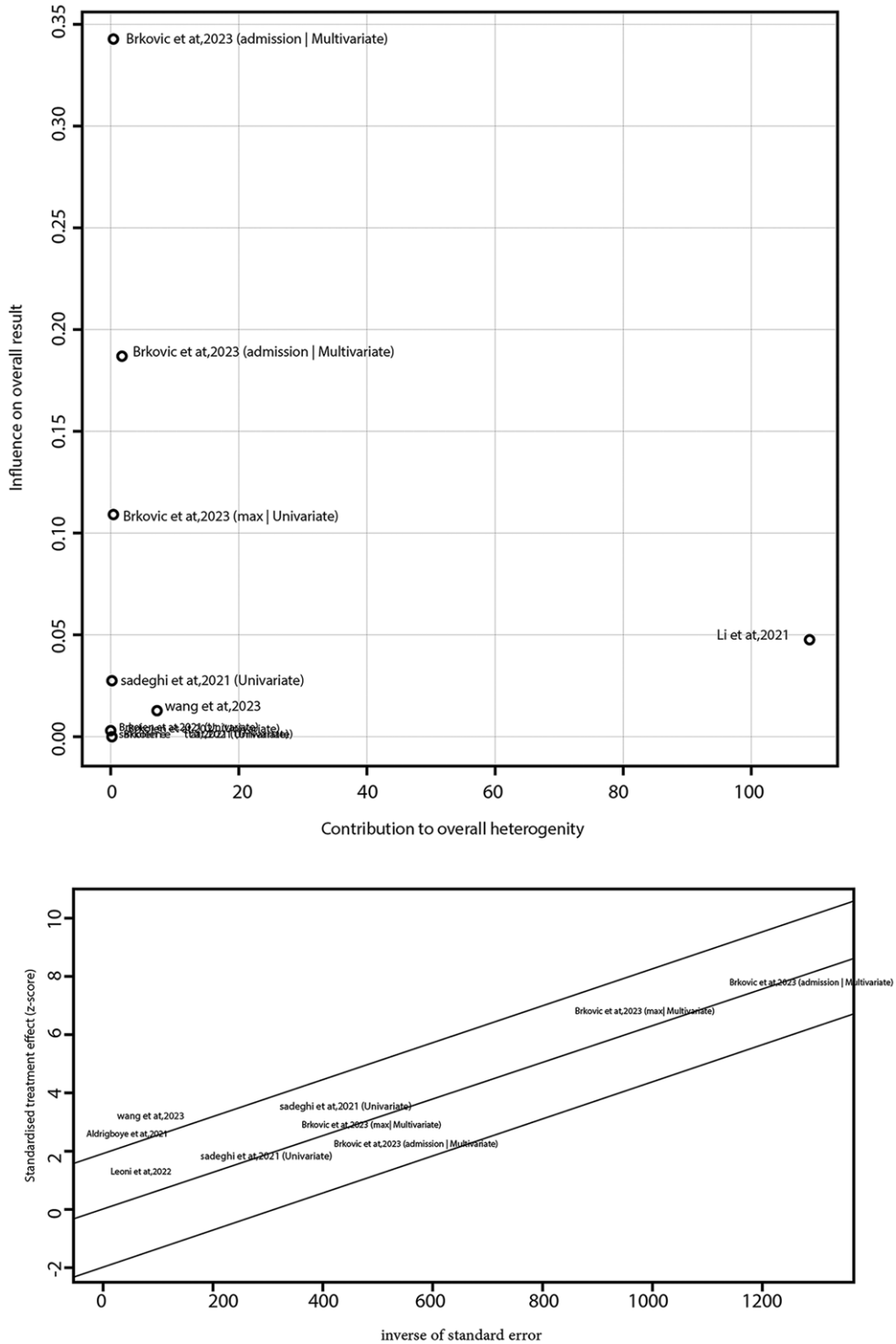

Figure 4. Baujat analysis of study influence and heterogeneity and galbraith plot analysis. (A) Baujat analysis of study influence and heterogeneity. (b) Galbraith plot of study dispersion in meta-analysis.

3.6. Distinguishing between univariate and multivariate analyses in heterogeneity exploration

To better understand the wide differences in the results of the meta-analysis, the studies were divided into two groups: single-variable and multi-variable analyzes were conducted separately for each group. The variable group (Fig. 9A) of 15 studies was analyzed using both common-effects and random-effects models. In the common effect model, the OR was 1.0071 (95% CI: 1.0054–1.0088), with a z-score of 8.29 ($P < .0001$). This signifies a small but highly significant effect. However, the random effects model, accounting for variation in study effects, showed an OR of 1.4230 (95% CI: 1.0178–1.9895), with a z-score of 2.06 ($P = .0391$). This indicates a larger effect size, but with less statistical significance. This model suggests a larger effect size that remains statistically significant, acknowledging the between-study heterogeneity. The quantification of heterogeneity revealed substantial inconsistency across studies with an I^2 of 94.4% and a heterogeneity (H) value of 4.21, indicating very high variance among study outcomes. The tau^2 value was calculated at 0.3922, further corroborating the

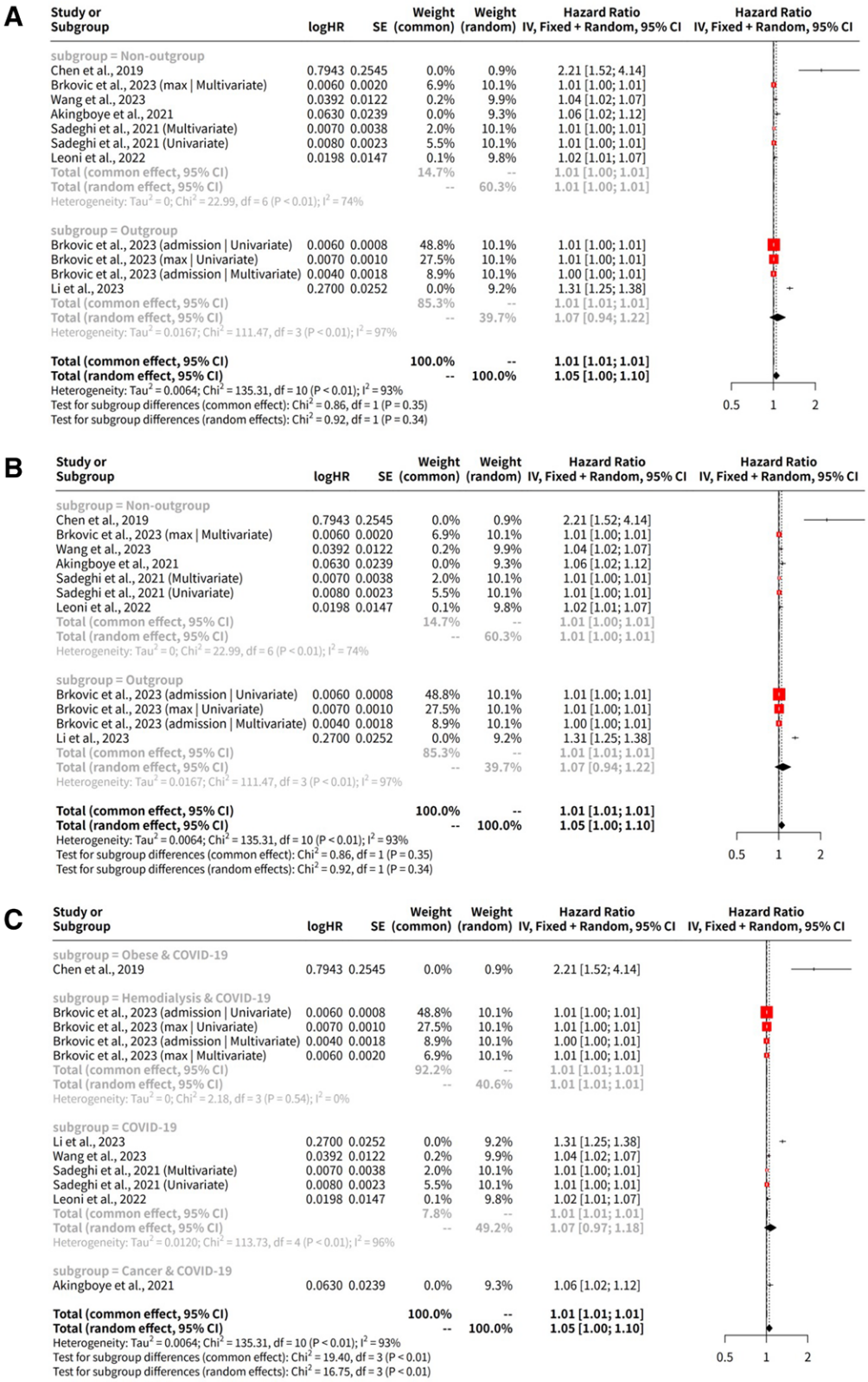

Figure 5. Stratification based on Baujat's analysis for outliers and subgroup analysis by comorbidities. (A) Stratification based on Baujat's analysis for outliers in meta-analysis. (B) Comparison of multivariate and univariate studies in meta-analysis. (C) Subgroup analysis by comorbidities in pneumonia patients.

significant heterogeneity observed, which was supported by a highly significant test of heterogeneity (Q = 247.79, df = 14, *P* value < .0001).

In the Multivariate subgroup shown as Figure 9B, which included 30 datasets, the common effect model estimated an OR of 1.0077 with a 95% CI between 1.0064 and 1.0091, and an even higher z-score of 11.28, leading to a *P* value of less than .0001. This indicates a consistently small but significant effect size across studies. The random effects model in this subgroup presented an OR of 1.0274 with a 95% CI from 1.0141 to 1.0409,

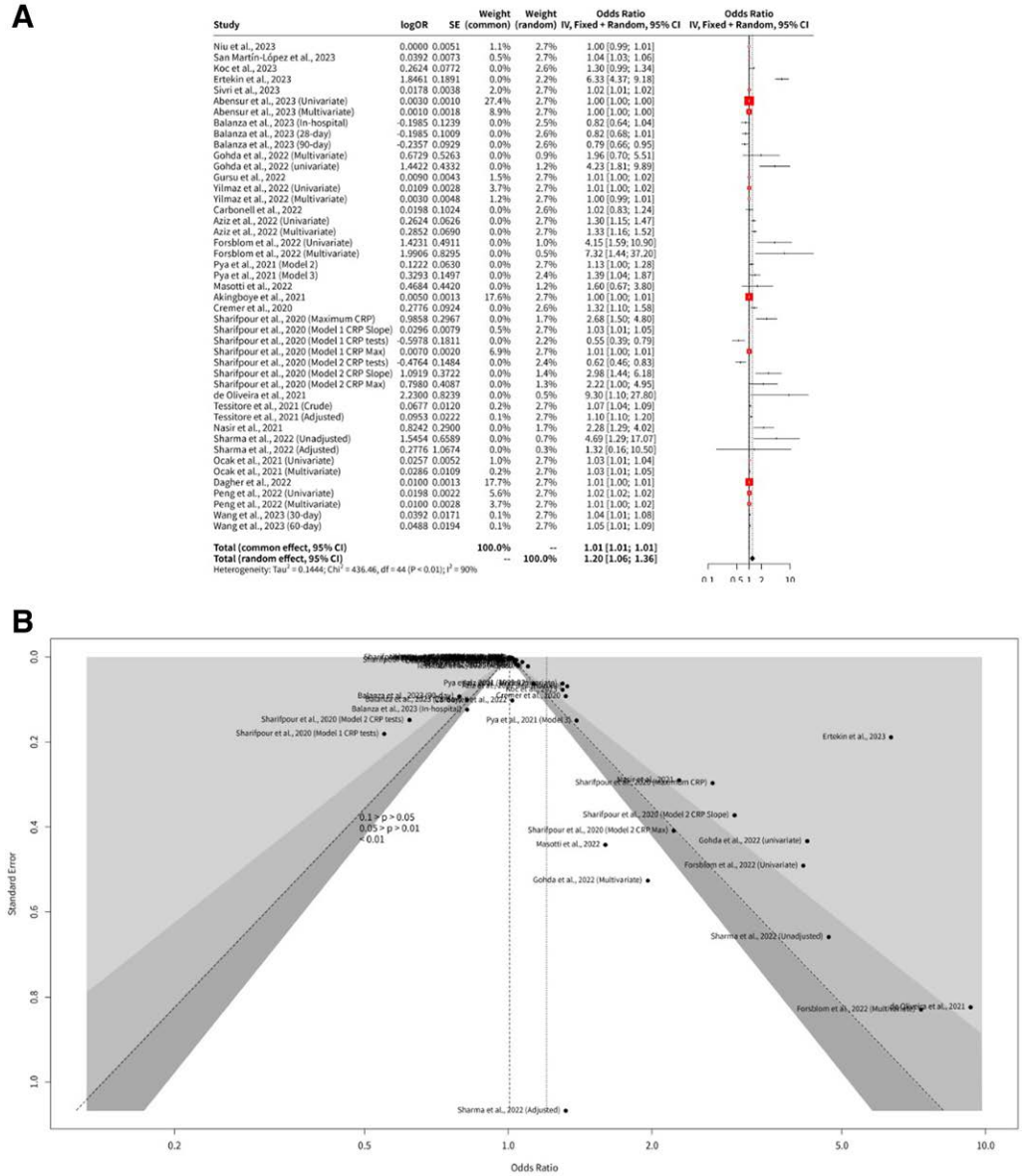

Figure 6. Analysis of CRP levels and mortality and funnel plot for publication bias in CRP level. (A) Analysis of CRP levels and mortality in pulmonary infections with OR value. (B) Funnel plot for publication bias in CRP level in meta-analysis. CRP = C-reactive protein.

and a z-score of 4.06, also resulting in a statistically significant *P* value of less than .0001. Despite the Acknowledgments of heterogeneity among studies, the effect size remains significant but is smaller compared to the Univariate group under the random effects model. Heterogeneity within the Multivariate group was still notable but less pronounced than in the Univariate group, with an I^2 of 84.6% and an H value of 2.55. The tau^2 value was significantly lower at 0.0006, indicating lesser variability among the study effects compared to the Univariate subgroup. The heterogeneity was also statistically significant (Q = 188.33, df = 29, $P < .0001$).

3.7. Mortality variations over different follow-up intervals

In an effort to elucidate the reasons behind high heterogeneity observed in a meta-analysis focusing on mortality rates over different follow-up times, studies were grouped based on the duration of mortality tracking into 1-month, 2-month, and 3-month mortality subgroups (Fig. 10). This reanalysis involved only literature that provided usable data, totaling nine studies across the subgroups. The results from the random effects model revealed an OR of 1.0140 with a 95% CI ranging from 1.0006 to 1.0276, which was statistically significant ($P = 0.0409$). This model highlighted the substantial heterogeneity across studies, quantified by a τ^2 of 0.0003 and an I^2 value of 82.4%, indicating that 82.4% of the variability in effect estimates was due to heterogeneity rather than chance. A heterogeneity test further confirmed this with a Q-value of 45.39 and a *P* value of less than .0001.

Subgroup analysis under the random effects model showed distinct outcomes for each follow-up duration. For the 1-month mortality subgroup, which included five studies, the OR was 1.0068 with a 95% CI of 0.9994 to 1.0142, suggesting a minimal but non-significant increase in mortality. The 3-months mortality subgroup, comprising three datasets, presented an OR of 0.9633 (95% CI: 0.8392–1.1058), indicating no significant difference in mortality, albeit with substantial variation (tau-squared = 0.0129). The single study in the 2-months mortality subgroup reported an OR of 1.0500 (95% CI: 1.0107–1.0908), showing a noticeable increase in

mortality. Tests for differences among these subgroups yielded a Q value of 4.92 with a *P* value of .0853 in the random effects model, suggesting that while there were observable trends, the differences between the subgroups did not reach statistical significance.

3.8. Evaluating mortality risks with high CRP levels greater than 100 mg/L

To understand why different studies have come up with different results about the link between CRP and mortality, a meta-analysis was done. Eleven datasets were chosen based on having CRP levels higher than 100 mg/L. These datasets were used to look for a possible link between CRP and death rates (Fig. 11). The study found significant differences between the included studies, as evidenced by a high I-squared value of 94.1%. This indicates that most of the variation in the results is primarily due to differences between the studies themselves, rather than random chance or chance findings. Researchers found significant variation among studies, as measured by a high $\tau 2$ (0.6579) and tau (0.8111) value with a wide confidence interval (CI). This was confirmed by a Q test (Q value 168.93, *P* value < .0001). However, when combining the studies, the overall effect showed a statistically significant odds ratio (OR) of 1.0086 (95% CI: 1.0047–1.0125, *P* value < .0001). This indicates that the overall effect was small and consistent across studies. However, the random effects model, which is more appropriate in the presence of such high heterogeneity, presented a more variable and elevated OR of 1.8651 with a 95% CI between 1.1130 and 3.1256, maintaining statistical significance at a *P* value of .0180.

3.9. Impact of comorbidities on pneumonia patients' outcomes

In this comprehensive meta-analysis investigating the reasons for high heterogeneity in studies examining pneumonia patients with various comorbidities, the studies were re-grouped according to the specific comorbid conditions (Fig. 12). Overall, the random effects model was found to be more applicable, yielding an OR of 1.0442 and a 95% CI of 0.9652 to 1.1297, although this was not statistically significant (*P* value = .2815). The subgroup analysis revealed varying effects based on the comorbid conditions of the patients. For non-COVID-19 pneumonia patients across four datasets, the random effects model for this subgroup suggested a lower OR of 0.8779, which approached significance (95% CI: 0.7666–1.0054). Patients on peritoneal dialysis with COVID-19, surgical patients with COVID-19, and those with cardiovascular disease and COVID-19 showed a slight increase in ORs in both common and random effects models, with the latter accounting for variability among studies. Notably, the subgroup with diabetes or prediabetes combined with COVID-19 exhibited a significantly higher OR of 1.3135 (95% CI: 1.1994–1.4384). The cancer with COVID-19 subgroup presented a stark difference between models. While the common effect model indicated a slight increase in OR (1.0050; 95% CI: 1.0025–1.0075), the random effects model revealed an extremely high OR of 2.6247 (95% CI: 0.3027–22.7563), highlighting a significant variability (tau-squared = 2.1359, tau = 1.4615) possibly due to the small number of studies and wide confidence intervals.

3.10. Meta-analysis of ICU admission trends

The meta-analysis under discussion focused on examining the OR of the necessity for ICU admission (Fig. 13). Given the substantial heterogeneity among the studies, indicated by an I-squared value of 92.4%, the random effects model was deemed more appropriate for this analysis. The random effects model, which accounts for variations among the studies, yielded an OR of 1.1108 with a wider 95% CI of 0.9604 to 1.2847. This result was not statistically significant, as evidenced by a z score of 1.42 and a *P* value of .1568. The quantification of heterogeneity revealed a τ^2 of 0.0217, with a CI ranging widely from 0.0077 to 3.5914, and a tau value of 0.1475 (95% CI: 0.0880–1.8951). The heterogeneity test further confirmed the variability with a Q value of 65.80 and a *P* value of less than .0001.

3.11. Analyzing ventilation requirements in pulmonary infection patients

The specific focus of this meta-analysis was on the association between CRP levels and the requirement for ventilation in patients with pulmonary infections (Fig. 14). The high degree of heterogeneity among the studies, indicated by an I^2 value of 92.8%, suggested that the random effects model would be more appropriate. This model accounts for the possibility that different studies are estimating different, yet related, effects. The random effects model produced an OR of 1.8981, with a broader 95% CI of 0.9651 to 3.7331. While this result approached statistical significance, it did not reach conventional levels of significance with a z-score of 1.86 and a *P* value of .0633. The heterogeneity was quantified with a τ^2 value of 0.5287, and tau was calculated to be 0.7271, indicating substantial variability that the fixed effect model would not adequately address. The heterogeneity test confirmed significant variability among the study outcomes (Q = 55.59, degrees of freedom (df) = 4, *P* < .0001).

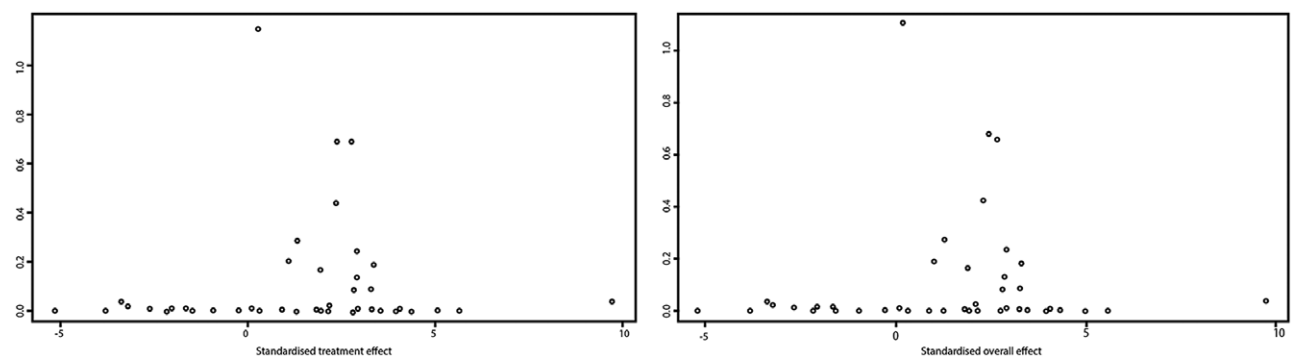

Figure 7. Begg's test for funnel plot asymmetry and Egger's test for funnel plot asymmetry. (A) Begg's test for funnel plot asymmetry in meta-analysis. (B) Egger's Test for funnel plot asymmetry in meta-analysis.

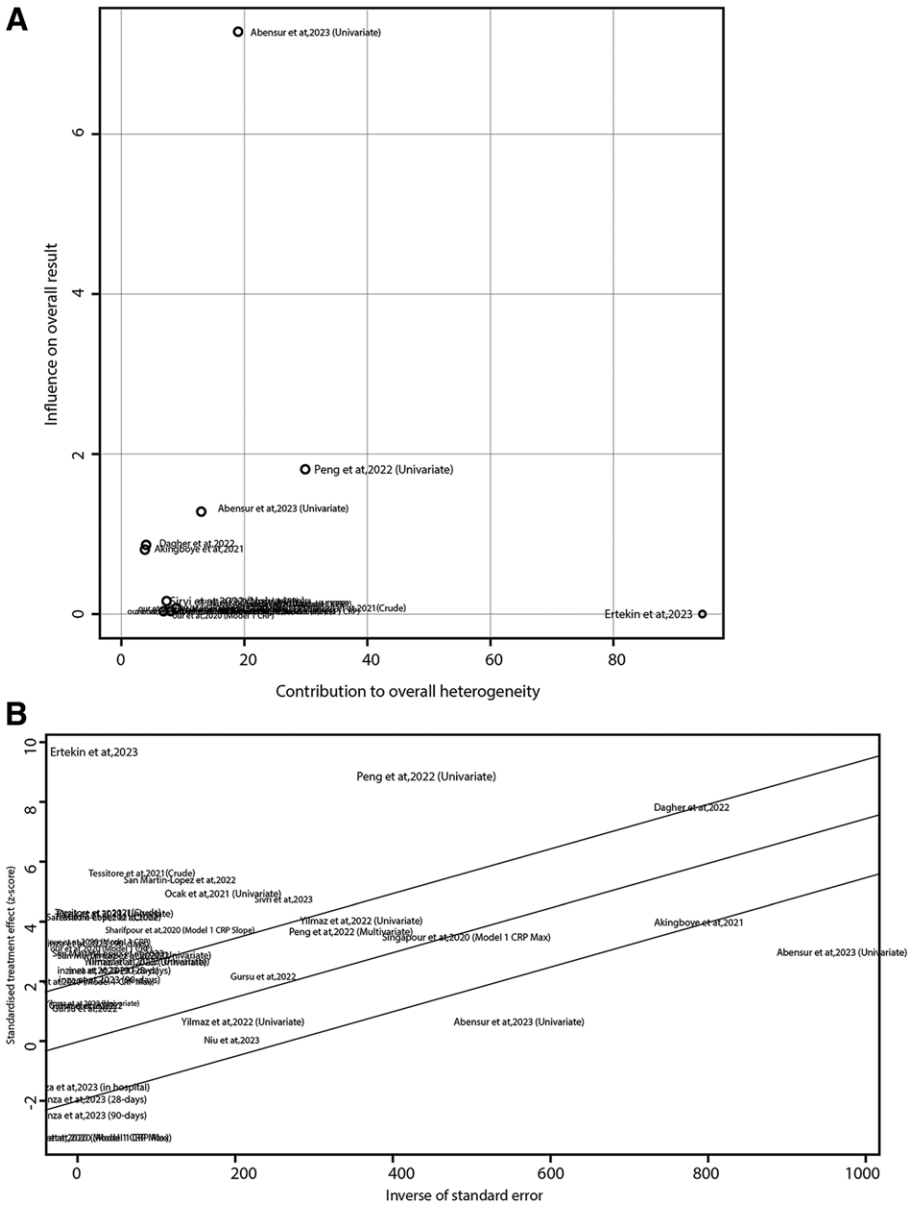

Figure 8. Baujat plot for heterogeneity source identification and Galbraith plot for study influence. (A) Baujat plot for heterogeneity source identification. (B) Galbraith plot for study influence in meta-analysis.

4. Discussion

In the realm of pulmonary infections, the diagnostic utility of CRP levels has been extensively studied, revealing a complex landscape of sensitivity and specificity that underscores its nuanced role in clinical settings. The evidence, drawn from various contexts, highlights CRP's significant yet variable efficacy in identifying lower respiratory tract infections, with reported sensitivities and specificities spanning from as low as 8% to as high as 99%, and from 27% to 95% respectively, as discussed in a systematic review.[51] Particularly noteworthy is the demonstrated high sensitivity (91%) and specificity (93%) of CRP for diagnosing pneumonia in hospitalized patients presenting with acute respiratory symptoms, at a threshold exceeding 48 mg/L, which underscores its potential as a critical biomarker for facilitating timely and accurate treatment interventions.[52] Additionally, CRP has been advocated as a supportive tool in the diagnosis of community-acquired pneumonia, though its precise contribution, beyond serving as an adjunct to clinical judgment, remains less clearly defined.[53] Similarly, in critically ill patient populations, CRP is recognized as a valuable indicator of infection, although specific performance metrics remain undetermined, highlighting a gap in the existing literature.[54] CRP can help clinicians make treatment decisions for lung diseases. however, it is important to consider the unique circumstances of each patient. Clinicians can make the best choice for each patient to improve clinical outcomes by combining CRP levels with other information such as symptoms and medical history.

The ability of CRP and other biomarkers to predict mortality risk in patients with pulmonary disease has been studied. Studies have shown that combining CRP with biomarkers such as white blood cell count can give us better insight into mortality risk. This improved understanding allows for more accurate risk assessments and personalized treatment strategies,[55,56] and interleukins,[57] can provide a more nuanced risk stratification for patients, particularly those with severe infections leading to hospitalization or critical care scenarios. This approach uses multiple biomarkers to accurately predict mortality from lung diseases. Like a traditional approach, it goes beyond using a single biomarker, taking into account multiple immune responses that reflect the severity of the infection. Nevertheless, caution is

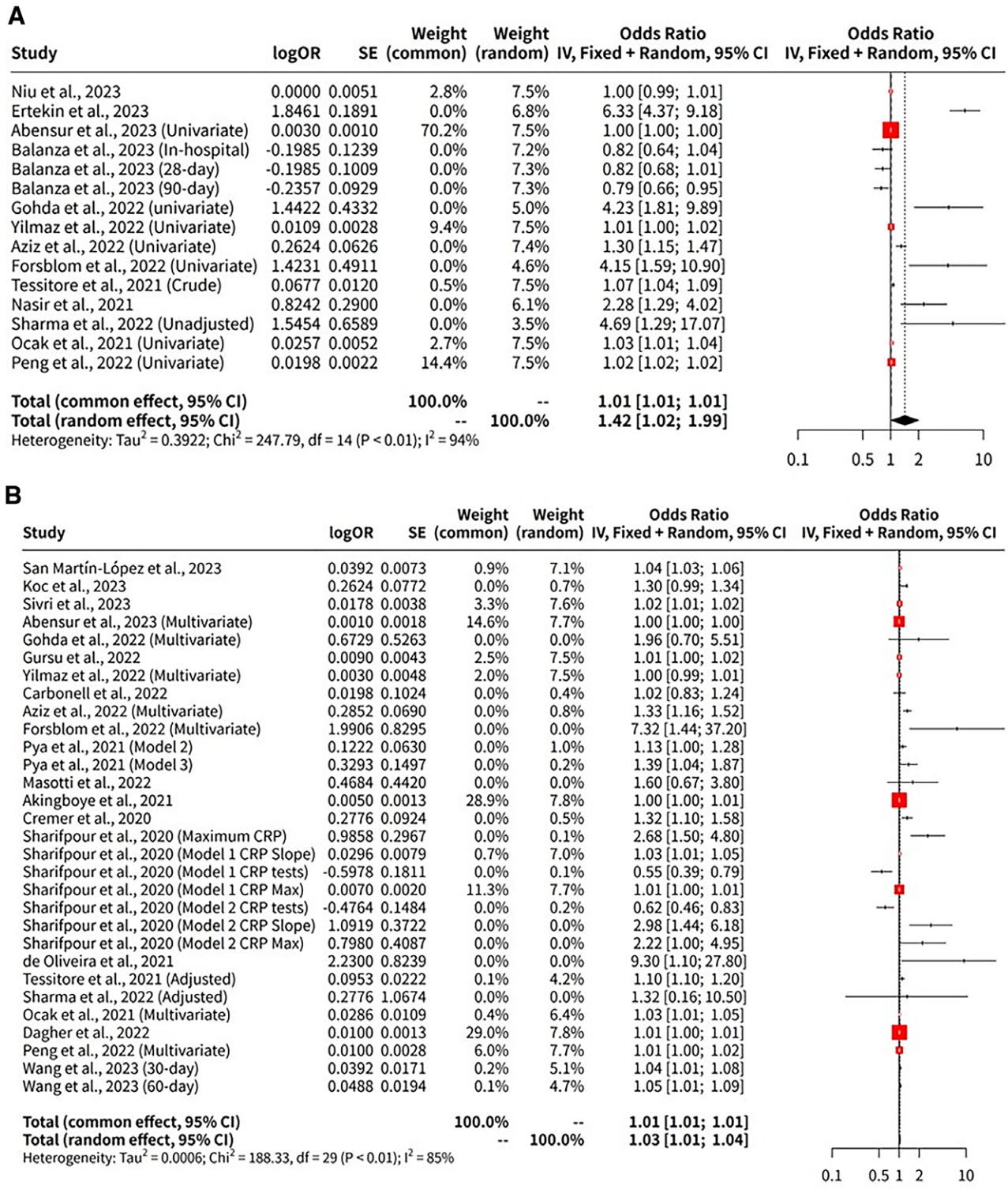

Figure 9. Effects of univariate analysis and multivariate analysis on heterogeneity. (A) Effects of univariate analysis on heterogeneity in meta-analysis. (B) Effects of Multivariate analysis on heterogeneity in meta-analysis.

warranted when using CRP to predict mortality. Although CRP helps detect inflammation and infection, it can also be affected by other factors, such as chronic inflammation. therefore, CRP levels alone may not fully predict the severity or outcome of pneumonia.

Our study investigated the association between CRP levels and mortality risk in people with lung disease. To understand the effect of elevated CRP levels on mortality risk, we used two statistical models, HR and OR. In our study, assuming that all studies were equal, we found a small but significant increase in the risk of death associated with elevated CRP levels in particular, every 1-unit increase in CRP was is associated with a 0.65% increase in the chance of dying from pneumonia. These results suggest that although the increased risk of death with increasing CRP levels is small, it is statistically significant. This subtle difference between HR and OR measures highlights the importance of considering both in assessing the impact of elevated CRP levels on mortality risk.

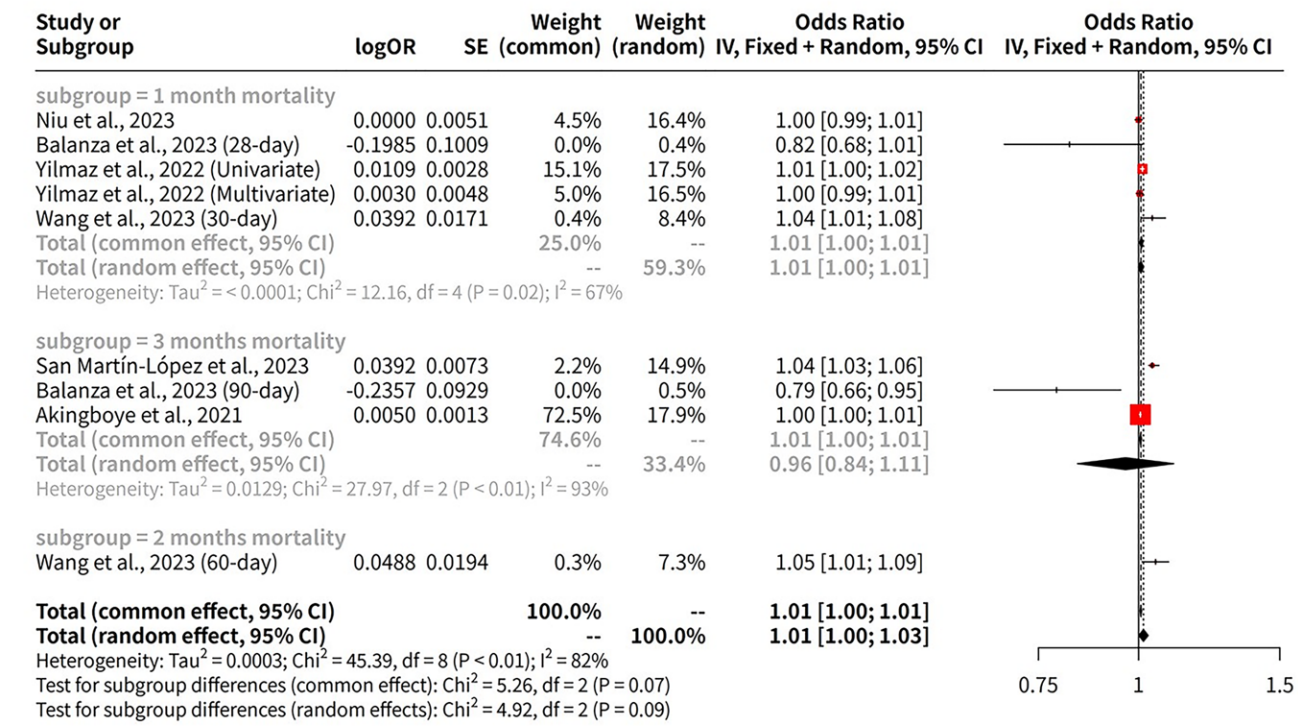

Figure 10. Mortality rates over different follow-up times in pulmonary infection patients.

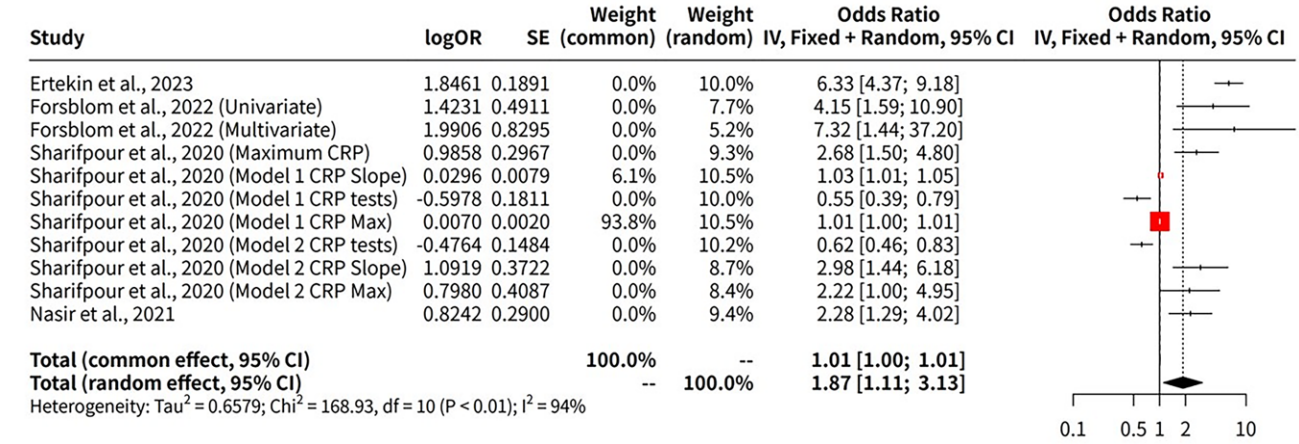

Figure 11. Analysis of CRP levels above 100 mg/L on mortality rates. CRP = C-reactive protein.

The fixed-effects model assumes that all studies have the same effect size, which may not be true in real-world data. The random-effects model accounts for the differences between studies and yields an HR of 1.0488. Although this implies a significantly higher risk than the fixed-effects model, the confidence interval (0.9978–1.1024) and z value (1.87) indicate that this difference is not significant at the standard alpha level of 0.05 This difference emphasizes the importance of considering study variability when interpreting meta-analysis findings.

Furthermore, when analyzing data using OR, the random effects model suggested a more pronounced effect, with an OR of 1.2033, indicating that patients with elevated CRP levels had a 20.33% higher odds of mortality compared to those with lower levels. This result was statistically significant, contrasting with the less definitive HR results, potentially due to the OR's nature of exaggerating effect size, especially in the context of rare outcomes. The significant heterogeneity observed in our meta-analysis, as evidenced by high I^2 values and confirmed by Q tests, justifies the use of random effects models for both HR and OR analyses. This heterogeneity could stem from differences in study populations, definitions of elevated CRP levels, and methods of mortality assessment among the included studies. The presence of publication bias, suggested by asymmetry in funnel plots and supported by significant Egger's and Begg's test results, could also influence the interpretation of both HR and OR results. This indicates a tendency for the publication of studies with positive findings or larger effect sizes, especially in the context of CRP level and mortality risk.

Several included studies involved patient populations with varying degrees of systemic inflammation, which might contribute to the elevated CRP level independently of pulmonary infections. The potential confounding effects of chronic inflammatory conditions, such as rheumatoid arthritis, cardiovascular disease, or diabetes, were acknowledged as limitations in isolating CRP elevations caused specifically by pulmonary infections.

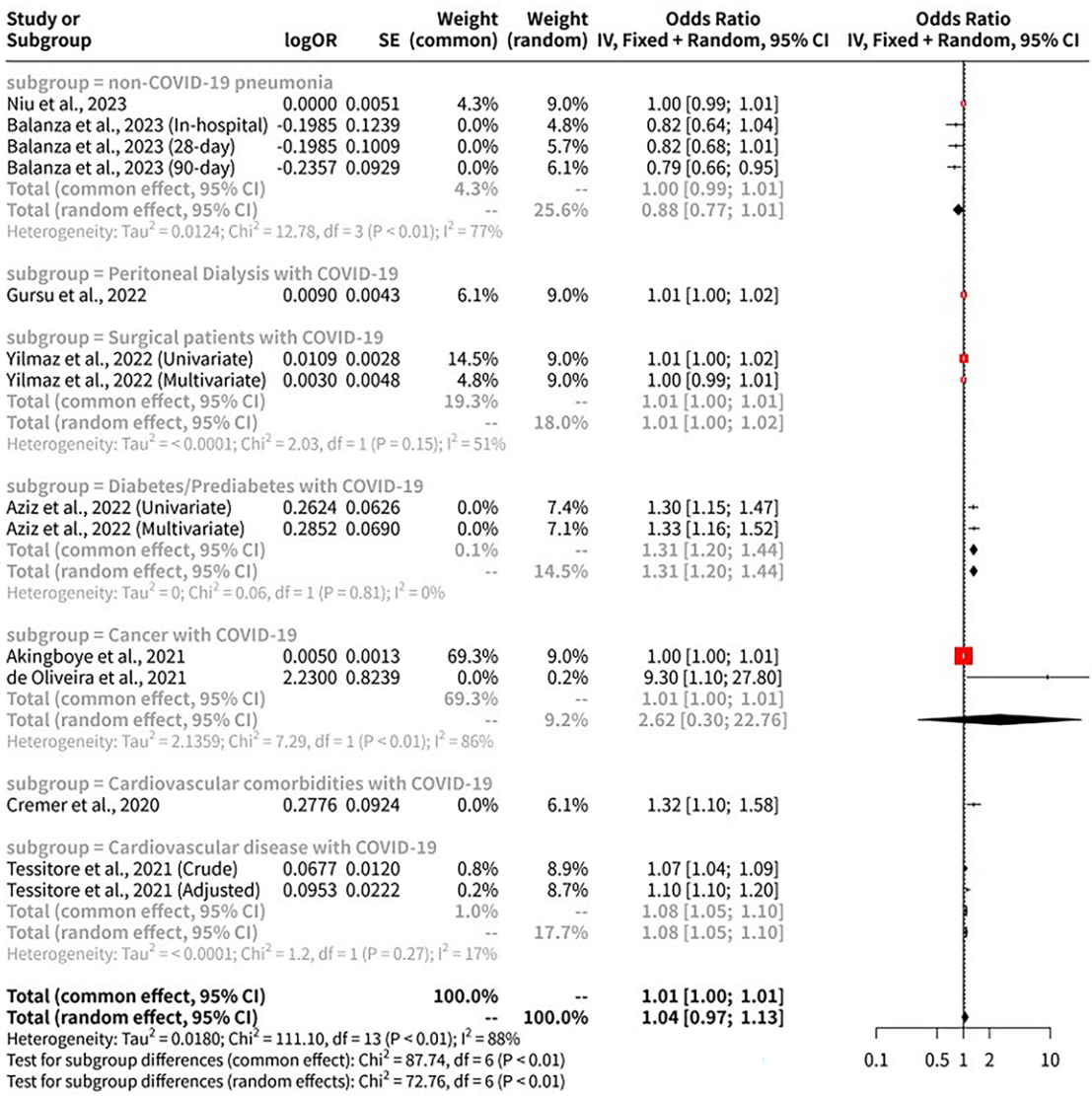

Figure 12. Subgroup analysis by comorbidities in pneumonia patients.

Due to inconsistencies in the reporting of systemic inflammation or coexisting inflammatory diseases across studies, it was infeasible to perform subgroup analysis or meta-regression to separate infection-specific CRP elevations from those arising from chronic conditions. CRP level above 100 mg/L, which was associated with increased mortality in the included studies, may reflect the cumulative effects of both systemic and infection-driven inflammation, emphasizing its role as a general marker of severe illness rather than a disease-specific predictor. Future research should aim to incorporate detailed patient profiles, including markers of chronic inflammation and disease severity, to better differentiate between systemic and infection-related CRP elevations and their respective contributions to mortality risk.

The observed discrepancies between the HR and OR results highlight a critical methodological consideration. OR, often used in case-control studies, can exaggerate effect sizes in contexts with high baseline risks, whereas HR, derived from time-to-event data, accounts for the timing and sequence of events, providing a more nuanced understanding of risks over time. In this analysis, the OR yielded statistically significant results ($P < .0033$), while the HR approached, whereas did not achieve statistical significance under the random effects model ($P = .0608$). This divergence may reflect the inherent differences in these measures, particularly the OR's sensitivity to the distribution of event frequencies and potential overestimation of risk in high-prevalence settings. The random effects model for OR indicated a larger effect size (OR: 1.2033, 95% CI: [1.0635, 1.3614]), contrasting with the HR's narrower range (HR: 1.0488, 95% CI: [0.9978, 1.1024]). Such findings highlight the importance of careful interpretation, particularly in scenarios with substantial heterogeneity or differences in underlying event distributions. Additionally, the significant publication bias observed in the OR analysis (Egger's test: $P < .0001$) might influence the apparent strength of the association. This emphasizes the need to contextualize OR results, especially when heterogeneity and asymmetry are substantial, as indicated by high I^2 and tau² values. Subgroup analysis provided further insights, with the multivariate OR results indicating a smaller and more consistent effect size compared with the univariate results, suggesting that adjustment for confounders mitigates the inflation of effect sizes in OR models.

Additionally, the influence of confounding factors, such as chronic inflammation, autoimmune diseases, and obesity on CRP level warrants consideration. These factors can independently elevate CRP level, potentially obscuring the relationship between CRP level and mortality risk in patients with pulmonary disease. While this analysis accounted for

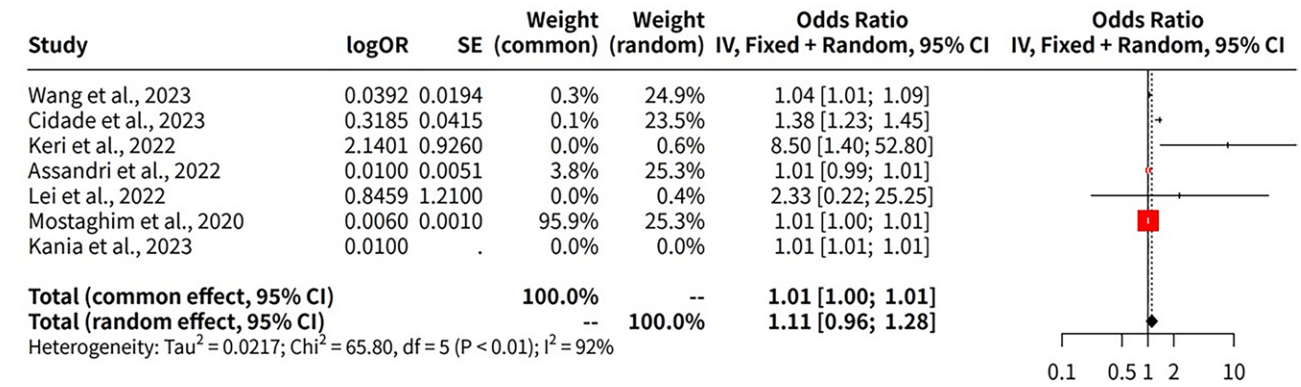

Figure 13. Analysis in meta-analysis on ICU admission with OR value.

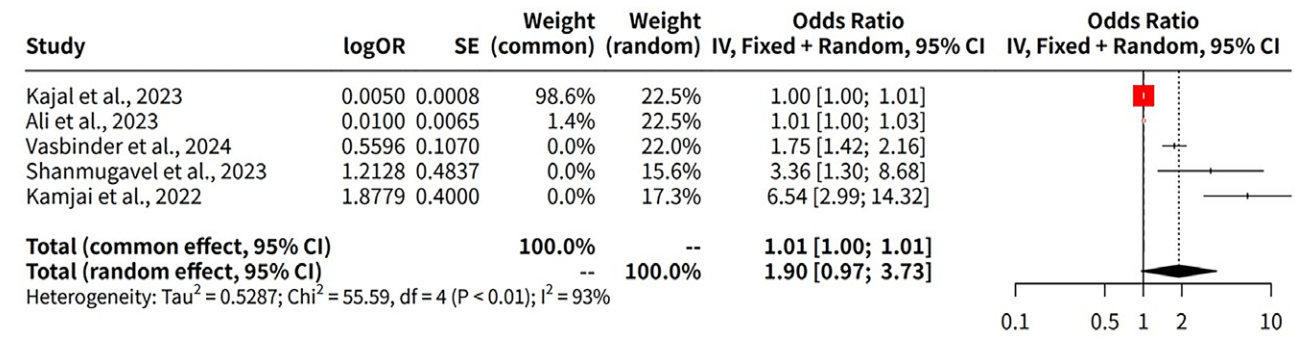

Figure 14. Association between CRP levels and requirement for ventilation. CRP = C-reactive protein.

heterogeneity across studies, the lack of adjustment for these specific factors in the included studies remains a significant limitation. Future research should incorporate multivariable models or stratified analyses to adjust for these variables, enabling a more accurate assessment of CRP's independent predictive value for mortality. Expanding the scope of analyses to include populations with well-documented comorbid conditions can further enhance the reliability of CRP as part of a biomarker applicable for mortality risk stratification. The selection of a > 100 mg/L CRP threshold was guided by its clinical relevance and frequent use in the literature to denote severe inflammatory responses. Future studies will consider analyzing alternative thresholds to capture a broader spectrum of outcomes and refine the understanding of CRP's prognostic value. The inconsistent reporting of CRP measurement methods in the included studies represents a limitation of this meta-analysis. Standardized reporting of CRP assay techniques and other patient-level variables would enable more robust analyses, including meta-regression, to clarify their potential influence on the observed associations. Future meta-analyses should consider incorporating additional study characteristics, such as detailed patient demographics and standardized CRP measurement methods, to enhance the understanding of heterogeneity sources and the robustness of the results.

In the context of this meta-analysis, variability in CRP thresholds and units across studies was acknowledged as a potential source of heterogeneity. While some studies reported CRP in mg/L, others used alternative units or thresholds for defining elevated levels. Efforts were made to account for these discrepancies by standardizing extracted data wherever possible, converting units to mg/L for consistency and recalibrating thresholds based on the most commonly used clinical guidelines. To reduce variability, studies with clearly defined CRP measurement protocols, including reporting units and threshold levels, were prioritized during the study selection process. Studies with ambiguous or inconsistent CRP reporting were excluded to minimize bias introduced by non-standardized measurements. Despite these measures, complete standardization across all studies was not achievable due to limited reporting details in some included studies. This limitation is acknowledged as a potential source of residual heterogeneity and was considered in the interpretation of the findings.

These studies have provided valuable information, but have important limitations. Many studies have not considered other factors that may affect CRP levels, such as ongoing inflammation. This may make the relationship between CRP levels and mortality risk less clear. Furthermore, different levels of CRP are used, making it difficult to compare the results of different studies. Finally, there may be bias in published studies, which means that the results may not provide a complete picture of the relationship between CRP levels and risk of death.

5. Conclusion

Combining CRP with other biomarkers improves the prediction of mortality in patients with pulmonary disease. However, more research is needed to ensure that similar methods are used in different studies, and to confirm findings in different patient groups. Current evidence suggests that CRP can be used as part of a biomarker suite to assess mortality risk in patients with pulmonary disease Although CRP measurement can provide valuable insights, it is important as clinicians consider alongside a thorough clinical assessment to make appropriate decisions. Future research to refine the utility of CRP should focus on addressing limitations, such as assessing the influence of underlying factors on CRP levels, searching for and potentially combining with other biomarkers.

Author contributions

Conceptualization: Hongxun Yuan.
Formal analysis: Li Qiao.

Funding acquisition: Hongxun Yuan.
Methodology: Li Qiao.
Project administration: Hongxun Yuan.
Writing – original draft: Li Qiao.
Writing – review & editing: Hongxun Yuan.

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