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Emergency General Surgery in COVID-19 Patients, a Meta-Analysis

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Keywords: COVID-19; Corona virus; Emergency general surgery; Appendicitis; Acute cholecystitis; Pandemic

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Article

Emergency General Surgery in COVID-19 Patients, a Meta-Analysis

Running title: Emergency surgery in COVID-19.

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Abstract: Background: The COVID-19 pandemic has significantly disrupted healthcare systems, including the management of emergency general surgery. Even though the pandemic ended, the new variants are continuously emerging, making it necessary to standardized the management protocols of emergency general surgery in COVID patients. **Objective:** This meta-analysis aims to evaluate the outcomes of emergency general surgery in COVID-19 patients compared to non-COVID-19 patients, focusing on mortality, postoperative complications, mechanical ventilation, and ICU admissions. **Methods:** A systematic search of PubMed, Embase, Cochrane Library, Scopus, and Web of Science databases was conducted, including studies published between December 2019 and the present. Observational studies, cohort studies, case-control studies, and randomized controlled trials reporting outcomes of emergency general surgery in adult patients with and without COVID-19 were included. A random-effects meta-analysis model was employed, and heterogeneity was assessed using the I^2 statistic. Publication bias was evaluated using funnel plot. **Results:** The analysis included 10 studies encompassing 7559 patients (3118 COVID19 group, 4441 non-COVID19 group). COVID-19 group patients demonstrated significantly higher mortality having odds ratio (OR) of 3.0036 (95% CI: 2.4263, 3.7184) and risk ratio (RR) of 2.8333 (95% Cl: 2.3127, 3.4712). **Conclusion:** Emergency general surgery in COVID-19 patients is associated with worse outcomes, including increased mortality, higher complication rates, and increased ICU admissions. These findings highlight the need for tailored perioperative strategies for COVID patients to mitigate risks.

Keywords: COVID-19; corona virus; emergency general surgery; appendicitis; acute cholecystitis; pandemic

Introduction

The emergence of COVID-19 has imposed unprecedented challenges on global healthcare systems. First reported from Wuhan, China, in December 2019, it spread rapidly around the world and a global pandemic was declared by World Health Organization in March 2020 [1–4]. Most COVID-19 patients developed mild-moderate upper respiratory tract symptoms (fever, cough & fatigue) [1,5,6]. However, in about 8-15% of patients it progresses to a more severe illness with respiratory failure, acute respiratory distress syndrome, multiple organ failure and death [1,3,7].

With its rapid spread and high morbidity and mortality rates, the pandemic has strained resources, disrupted routine medical care, and led to significant delays or modifications in the delivery of surgical services [8]. Emergency general surgery (EGS) represents a critical component of healthcare, often involving life-threatening conditions such as appendicitis, bowel obstruction, or perforation, which demand immediate intervention. The intersection of COVID-19 and EGS has introduced unique clinical complexities, including concerns about viral transmission, altered patient physiology, and resource limitations.

Early reports suggest that COVID-19 patients undergoing surgery face a higher risk of adverse outcomes, including elevated mortality and complication rates [1,8–10]. These findings underscore

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the need for a comprehensive understanding of the pandemic's impact on surgical practice to inform clinical decision-making and resource allocation during future crises. Although, the pandemic is ended, but its new variants are emerging. This makes it necessary to formulate a strategy of managing these patients in emergency surgical conditions, both pathological emergencies and traumatic emergencies.

This meta-analysis aims to evaluate the outcomes of emergency general surgery in COVID-19 patients, comparing them to non-COVID-19 patients. By synthesizing data from available studies, this analysis seeks to provide evidence-based insights into the perioperative risks and challenges associated with managing these patients.

Methods

This section outlines the systematic approach undertaken for the meta-analysis to ensure the inclusion of robust, high-quality studies. The methodology adheres to PRISMA guidelines and focuses on rigorously evaluating outcomes of emergency general surgery in COVID-19 patients.

A comprehensive literature search was conducted across five databases: PubMed, Embase, Cochrane Library, Scopus, and Web of Science. The search spanned publications from December 2019, when COVID-19 was first identified, to the present. Both MeSH terms and free-text keywords were used to ensure broad coverage of relevant studies. Key search terms included:

- COVID-19-related terms: *"COVID-19," "SARS-CoV-2," "coronavirus infection"*
- Surgical terms: *"emergency surgery," "urgent surgery," "general surgery"*
- Outcome measures: *"mortality," "complications," "postoperative outcomes," "ICU admission," "mechanical ventilation"*

The search was limited to English-language publications involving human subjects. Any paper without associated data, like abstracts, editorials and opinions, were excluded. The inclusion criteria were all adult patients (≥18 years) admitted with the diagnosis of emergency general surgery condition, whether undergoing emergency general surgery or managing conservatively, during pandemic with or without confirmed COVID-19 diagnosis via PCR testing or clinical evaluation. Randomized controlled trials (RCTs), cohort studies, case-control studies, or case series with comparative groups (COVID-19 positive vs. COVID-19 negative patients) were selected.

The exclusion criteria were studies involving elective surgeries, non-surgical interventions, or pediatric patients (<18 years), non-comparative studies, reviews, commentaries, and abstracts without associated data, and duplicate studies across different databases.

The screening process adhered to a standardized protocol. Two independent reviewers screened all titles and abstracts against the inclusion/exclusion criteria. Disagreements were resolved through consensus or consultation with a third reviewer. Studies passing the initial screening underwent full-text review to confirm eligibility. A PRISMA flowchart was created to visually represent the screening and selection process.

Data were extracted independently by two reviewers using a standardized extraction template, and discrepancies were resolved by a third reviewer. It includes study characteristics (authors, year of publication, country, study design, sample size), patient demographics (age, gender, comorbidities), surgical details (non-operative management or type of surgery performed). The primary outcome variable is 30-day mortality rate, whereas secondary variables are morbidity, mechanical ventilation and ICU admissions, along with the patients' demography.

Risk of bias was assessed using the Newcastle-Ottawa Scale (NOS) for observational studies. Statistical analysis was performed using R packages for pooled analyses, forest plot generation, and bias evaluations with funnel plot generation. Dichotomous outcomes ie Odds ratios (OR) and risk ratio, with 95% confidence intervals (CIs) were calculated for the primary outcome. A random-effects model was employed due to the anticipated heterogeneity of included studies. Heterogeneity assessment made with I^2 statistic (low heterogeneity: $I^2 < 30\%$, moderate heterogeneity: I^2 30%-60%, high heterogeneity: $I^2 > 60\%$). Publication bias assessed with funnel plot giving visual inspection for symmetry.

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This methodical approach ensures a comprehensive evaluation of emergency general surgery outcomes in COVID-19 patients, laying a foundation for robust clinical insights.

Results

Study Selection and Characteristics

A total of 10 studies were included in the meta-analysis, comprising 7559 patients (3118 COVID-19 group and 4441 non-COVID-19). The PRISMA flow diagram outlines the study selection process (Figure 1). The included studies spanned 8 countries and were published between [2021–2023]. The majority were cohort studies (studies 2-10), with additional contributions from one case-control study (Fernandez et al.).

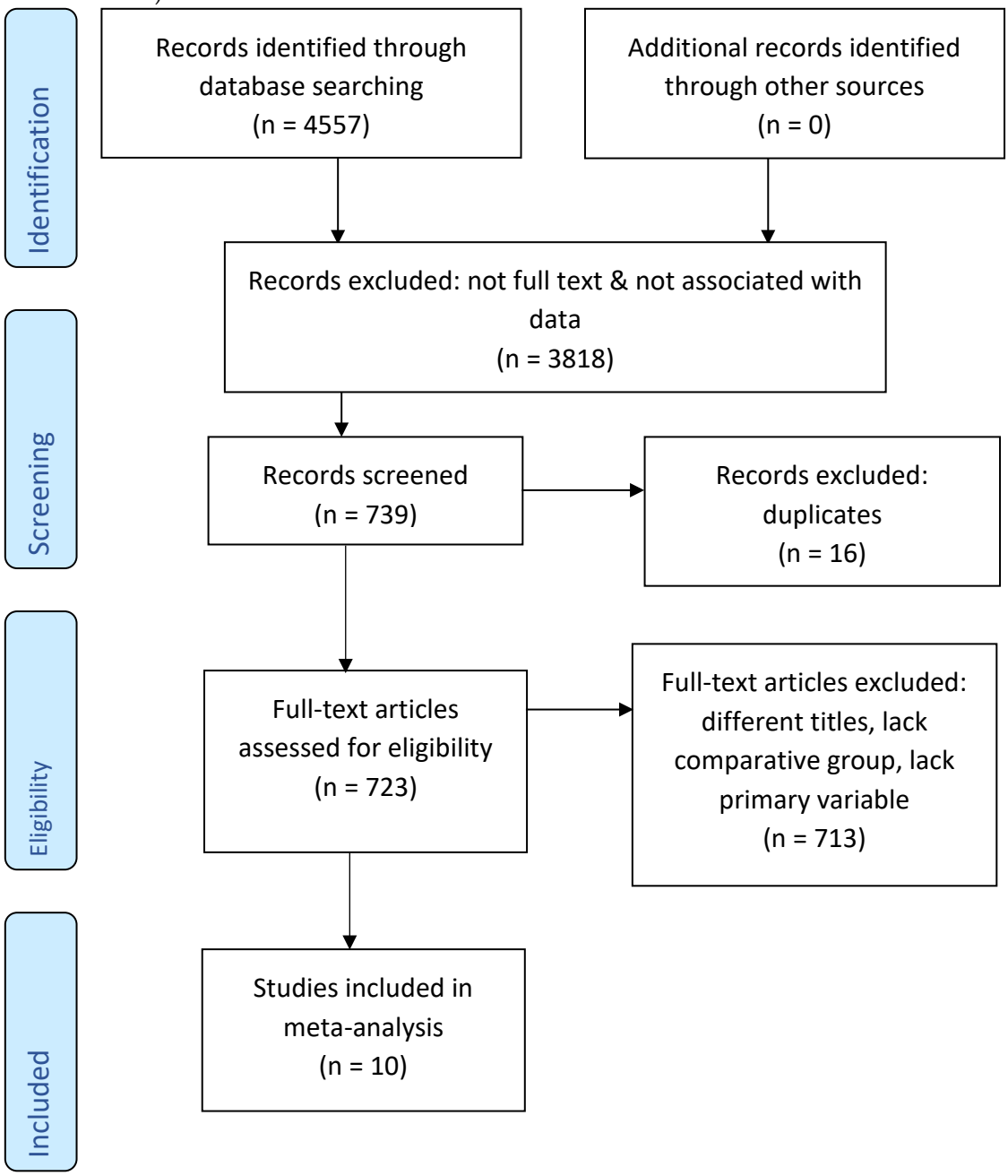

Figure 1. PRISMA Flow Diagram.

Table 1 summarizes the characteristics of the included studies, including first author's name, Country, study year, types of surgeries, and presence/absence of comparative/control group. Table 2

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summarizes the demographics and outcome variables, including total number of patients, age, sex, mortality rate, morbidity rate, mechanical ventilation and ICU admission.

Table 1. Study characteristics.

First Author	Country	Year	Type of Surgery	Comparative/ Control Group
Fernández et al. [11].	Spain	2021	Emergency General Surgery	Present
Andreia et al. [12].	Portugal	2021	Urgent/Emergency Surgery	Present
Sarah et al. [13].	USA	2023	Emergency General Surgery	Present
Matthew et al. [14].	New Zealand	2021	Emergency General Surgery	Present
COVIDSurg Collaborative [15]	UK	2022	Emergency General Surgery	Present
Chan et al. [16].	UK	2023	Emergency General Surgery	Present
Ismail et al. [17].	Turkey	2021	Emergency General Surgery	Present
Arnulf et al. [18].	Germany	2021	Acute Appendicitis	Present
Guido et al. [19].	Italy	2021	Emergency Abdominal Surgery	Present
Javier et al. [20].	Spain	2021	Acute Cholecystitis	Present

Table 2. Demographics and Outcome variables.

First Author	Total patients Covid vs. Non-covid	Patients' Age (year) Covid vs. Non-covid	Gender M:F Covid vs. Non-covid	Mortality Rates Covid vs. Non-covid	Morbidity Rates Covid vs. Non-covid	Mechanical Ventilation Covid vs. Non-covid	ICU Admission Covid vs. Non-covid
Fernández et al.	27, 126	57.5 ± 21 (total)	91:62 (total)	18.5%, 7%	85.7%, 26.7%	66%, 0	36%, 14%
Andreia et al.	457, 643	67, 63 (Median)	261:196, 368:275	11.40%, 5.9%	Not specified	Not specified	Not specified
Sarah et al.	229, 279	59.3, 56.7 (Mean)	102:127, 121:158	5%, 4%	25%, 29%	Not specified	Not specified
Matthew et al.	627, 650	57, 57 (Median)	327:300, 314:336	4%, 3%	Not specified	Not specified	Not specified
COVIDSurg Collaborative	344, 701	17-70 (total)	220:124, 406:295)	40.1%, 2.9%	72.7%, 0	23.9%, 0	Not specified
Chan et al.	223, 422	48.6, 48.5 (Mean)	114:109, 191:231	5.8%, 2.4%	5.6%, 4.8%	Not specified	8.5%, 7.1%
Ismail et al.	132, 195	50, 53 (Median)	74:58, 82:113	3%, 3.1%	7%, 1.5%	Not specified	Not specified
Arnulf et al.	888, 1027	36 ± 20, 35 ± 19 (Mean)	468:420, 510:517	0.1%, 0.2%	14.3%, 13.3%	Not specified	4.5%, 3.9%
Guido et al.	149, 183	49 (26.5-70), 44 [24–61]	94:55, 97:86	6%, 4.9%	35.6%, 18%	Not specified	Not specified
Javier et al.	257, 215	69 (52-80), 68	146:111, 118:97	11.9%, 3.2%	100%, 26%	Not specified	Not specified

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	(50-80) (Median)	

Outcomes Variables

Overall, COVID-19 group patients demonstrated significantly higher mortality having odds ratio (OR) of 3.0036 (95% CI: 2.4263, 3.7184) and risk ratio (RR) of 2.8333 (95% Cl: 2.3127, 3.4712). Table 2 shows the individual OR and RR of these 10 studies.

Table 3 summarizes the effect size calculated from mortality rates in 2 groups. Similarly, the odds of experiencing complications were markedly increased in COVID-19 patients (Table 2). Only 2 studies mentioned the use of mechanical ventilation due to pulmonary complications from COVID19, whereas 3 studies mentioned about ICU admissions.

Table 3. Effect size measures.

First Author	Effect Size (Cohen's d)	Odds Ratio (OR)	95% CI	Risk Ratio (RR)	95% CI
Fernández et al.	1.666187845	3.0158	0.9191, 9.8958	2.6429	0.957, 7.2894
Andreia et al.	1.133756906	2.0521	1.3258, 3.1763	1.9322	1.2942, 2.8847
Sarah et al.	0.697900552	1.2632	0.5433, 2.9366	1.25	0.5585, 2.7979
Matthew et al.	0.744309392	1.3472	0.7377, 2.4602	1.3333	0.7454, 2.3849
COVIDSurg Collaborative	12.3839779	22.415	13.718, 36.6256	13.8276	8.8398, 21.6296
Chan et al.	1.383370166	2.5039	1.082, 5.7941	2.4167	1.0792, 5.4119
Ismail et al.	0.534088398	0.9667	0.267, 3.5008	0.9677	0.2779, 3.37
Arnulf et al.	0.275966851	0.4995	0.0414, 6.0297	0.5	0.0416, 6.0162
Guido et al.	0.68441989	1.2388	0.4778, 3.2118	1.2245	0.4975, 3.014
Javier et al.	2.257458564	4.086	1.226, 13.6181	3.7188	1.2336, 11.2104

The meta-analysis has yielded an estimated effect size of approximately 2.35 with a standard error of 1.29. The heterogeneity statistics indicate a very high level of variability among the studies ($I^2 = 99.86\%$), suggesting that the results may not be consistent across the included studies. The forest plot (Figure 2) illustrates the individual effect sizes for each study along with the overall effect size. It illustrates the pooled odds ratios (OR) and 95% confidence intervals (CI) for mortality between COVID-19 and non-COVID-19 patients across included studies. The dashed line represents the null effect (OR = 1).

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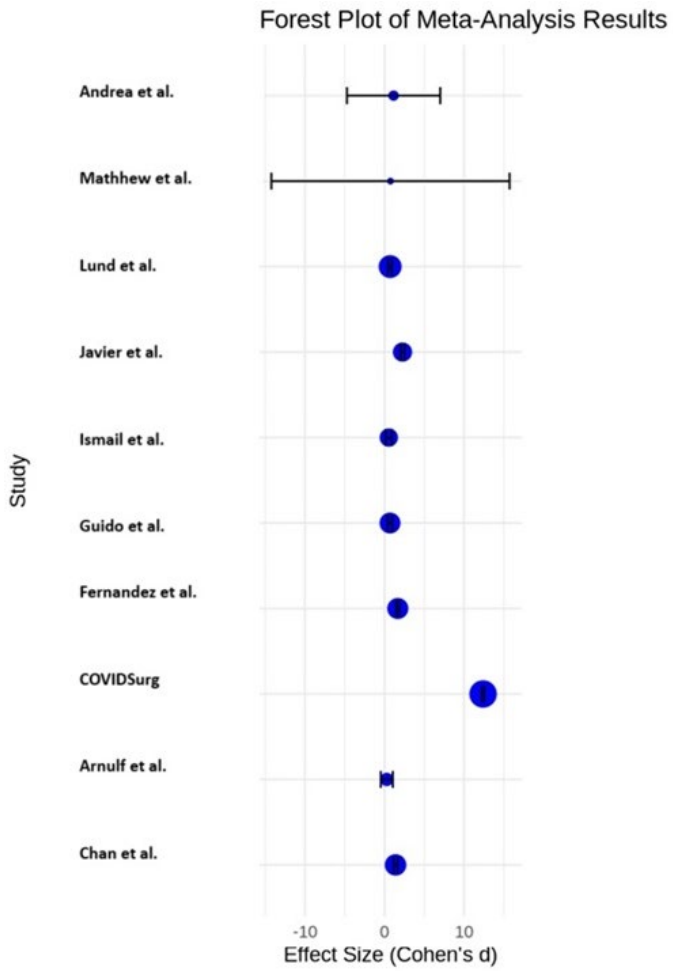

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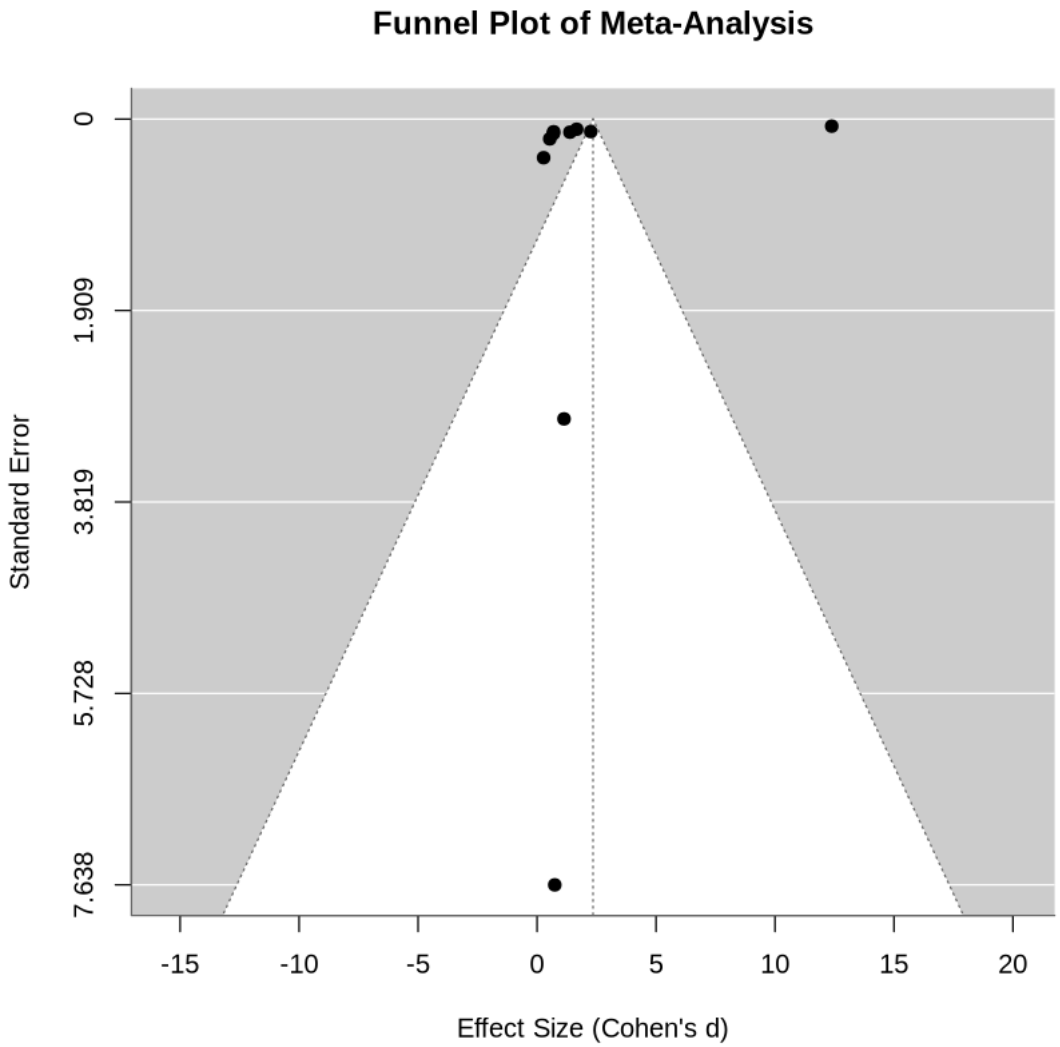

Visual inspection of the funnel plot (Figure 3) for mortality outcomes indicated asymmetry, suggesting potential publication bias. It clearly indicates the effect size (Cohen's d) on the x-axis and the standard error on the y-axis, making it easier to interpret the results. Further, Table 4 shows the descriptive aspects of publication bias.

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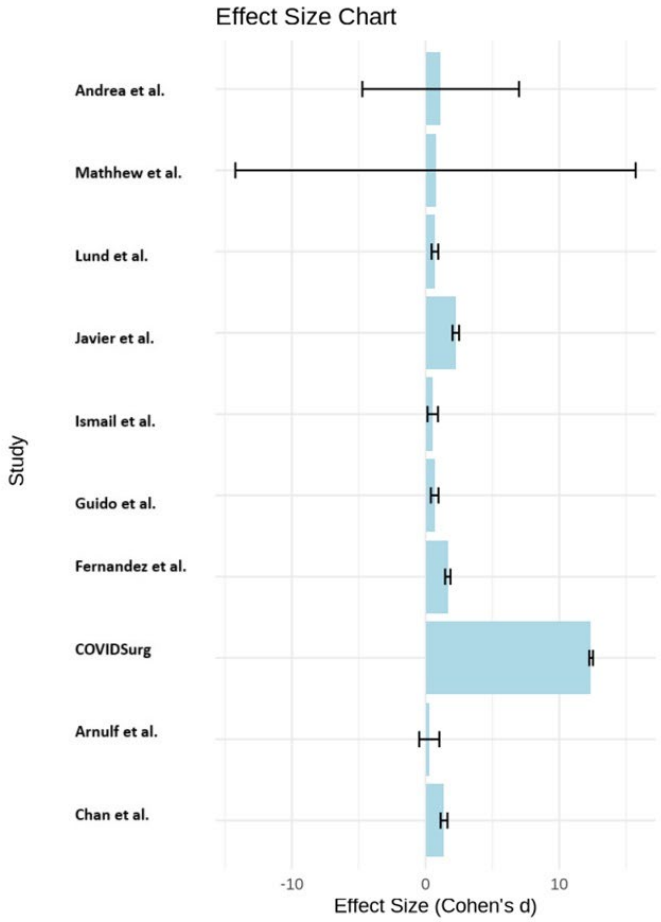

The effect size chart (Figure 4) displays the effect sizes (Cohen's d) for each study, along with error bars representing the confidence intervals.

Table 4. Study bias.

Study No.	Selection Bias	Reporting Bias	Confounding Bias	Measurement Bias	Generalizability Bias	Information Bias
1	Yes	No	Yes	No	Yes	No
2	No	Yes	No	Yes	No	Yes
3	Yes	Yes	No	No	Yes	No
4	No	No	Yes	Yes	No	Yes
5	Yes	No	Yes	No	Yes	No
6	No	Yes	No	Yes	No	Yes
7	Yes	No	Yes	No	Yes	No
8	No	Yes	No	Yes	No	Yes
9	Yes	No	Yes	No	Yes	No
10	No	Yes	No	Yes	No	Yes

Discussion

The COVID-19 pandemic has profoundly impacted healthcare systems globally, necessitating a reevaluation of surgical practices, especially in emergency settings. This meta-analysis, synthesizing data from 10 studies, provides compelling evidence that emergency general surgery in COVID-19 patients is associated with significantly worse outcomes compared to non-COVID-19 patients. These findings highlight the critical need for tailored strategies to optimize surgical care in the context of a pandemic.

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The findings in these studies differ, which may be due to variations in public health interventions, pandemic severity, and healthcare resources across regions. Non-Operative Management (NOM) was reported in a few studies; however, this is within the principles of surgery [21–23]. NOM may have contributed to managing patient loads effectively during the pandemic, and at the same time minimizing the risk of virus spread via the operating room [18]. There were NOM failure as well, leading to operative intervention, again according to the surgical principles [20].

The meta-analysis revealed a markedly higher postoperative mortality rate in COVID-19 patients, as reported in several other studies [21–29]. This aligns with prior reports suggesting that SARS-CoV-2 infection exacerbates perioperative risks due to factors such as hyperinflammatory states, coagulopathies, and pulmonary compromise [24,29–33]. The disproportionate impact on older adults and those with comorbidities underscores the need for heightened vigilance in these patients. Hypertension, diabetes, COPD, cardiovascular disease, cerebrovascular disease and chronic renal disease were reported as major risk factors for serious events in these patients [21,23,28,30,34,35]. COVID-19 patients experienced a higher rate of postoperative complications, particularly respiratory complications [26,29]. The underlying pathophysiological mechanisms, including viral pneumonia, cytokine storm, and altered immune responses, likely contribute to this increased risk. Surgery may exacerbate these mechanisms by adding pro-inflammatory state, as well as causing additional strains on cardiorespiratory systems [36–42]. Notably, abdominal surgeries were associated with a greater complication burden, potentially due to the interplay between intra-abdominal infections and systemic inflammation. The mean hospital stay for COVID-19 patients was significantly longer [24,27,28]. This finding reflects the complexity of managing postoperative recovery in the presence of SARS-CoV-2 infection, compounded by the need for extended monitoring and isolation protocols. The odds of ICU admissions and mechanical ventilation were significantly higher among COVID-19 patients [28]. This likely results from a combination of COVID-19-related respiratory failure, heightened perioperative complications, and resource-intensive postoperative care requirements.

The findings of this meta-analysis have several clinical implications. Surgical decision-making in COVID-19 patients should incorporate a comprehensive risk assessment, prioritizing non-surgical management where feasible or deferring procedures in stable cases until viral clearance. Given the increased need for ICU admissions and prolonged hospital stays, healthcare systems must ensure adequate resource planning during pandemics to accommodate the surgical burden [22,25]. Enhanced infection prevention measures, including preoperative testing and strict intraoperative protocols, are essential to minimize nosocomial transmission and optimize patient outcomes.

Strengths

- Comprehensive and rigorous methodology adhering to PRISMA guidelines.
- Inclusion of diverse study designs across multiple geographical regions, enhancing generalizability.
- Robust statistical analyses to ensure result reliability.

Limitations

- Markedly high heterogeneity (I^2 = 99.86%), likely reflecting variations in healthcare infrastructure, patient populations, and surgical practices.
- Potential publication bias, as suggested by funnel plot asymmetry.
- Limited availability of high-quality randomized controlled trials, with most data derived from observational studies.

Future Directions

- Prospective, multicenter studies to validate these findings and elucidate underlying mechanisms.
- Development of perioperative protocols tailored to COVID-19 patients, emphasizing preoperative optimization and postoperative care.

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- Exploration of long-term outcomes, including quality of life and functional recovery in COVID-19 surgical patients.

Conclusion

This meta-analysis demonstrates that emergency general surgery in COVID-19 patients is associated with significantly higher mortality, complication rates, and healthcare resource utilization. These findings highlight the critical need for tailored perioperative strategies to mitigate risks and improve outcomes. As the world continues to grapple with COVID-19 variants, these insights are invaluable in shaping resilient and adaptive surgical practices.

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Conflict of interest: None.

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