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# EMERGENCY GENERAL SURGERY IN COVID-19 PATIENTS: A META-ANALYSIS

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#### ABSTRACT

**Background.** The Coronavirus disease of 2019 (COVID-19) pandemic has significantly disrupted healthcare systems, including the management of emergency general surgery. Although the pandemic has officially ended, the new variants are continuously emerging, underscoring to need to standardize the management protocols of emergency general surgery in COVID-19 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 Intensive Care Unit admissions.

**Methods.** A systematic search was conducted using PubMed, Embase, Cochrane Library, Scopus, and Web of Science databases, 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 I² 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 with 95% Confidence Interval (95% CI) of 2.4263, 3.7184, and risk ratio of 2.8333 (95% CI: 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 intensive care unit 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 Or-

ganization in March 2020 [Lescure FX et al., 2020; Machhi J et al., 2020; Tadesse S, Muluye W, 2020; Brown WA et al., 2021]. Most COVID-19 patients developed mild-moderate upper respiratory tract symptoms (fever, cough & fatigue) [Huang C et al.,

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2020; Rodriguez-Morales AJ et al., 2020; Brown WA et al., 2021]. 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 [Machhi J et al., 2020; Stawicki SP et al., 2020; Brown WA et al., 2021].

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 [Abate et al., 2020]. Emergency general surgery 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 [Abate et al., 2020; Collaborative Covids, 2020; Doglietto F et al., 2020; Brown WA et al., 2021]. These findings underscore 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.

## **MATERIAL AND 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 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (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," "Intensive Care Unit 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 Polymerase Chain Reaction (PCR) testing or clinical evaluation. Randomized controlled trials, 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 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 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 I2 statistic (low heterogeneity: I2 < 30%, moderate heterogeneity: I<sup>2</sup> 30%-60%, high heterogeneity: I<sup>2</sup> > 60%). Publication bias assessed with funnel plot giving visual inspection for symmetry, as well as by linear regression analysis as an alternative to Egger's Test.

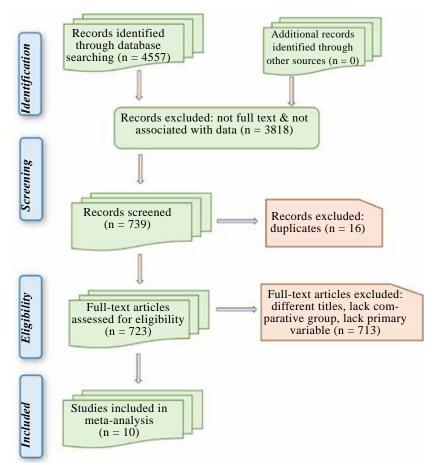


Figure 1: PRISMA Flow Diagram.

TABLE 1. Study characteristics (In all sources Comparison/control group Present.)

First Author	Country	Year	TS
Fallani et al. (2021	Italy	2021	
Fernández-Martínez et al., 2021	Spain	2021	EGS
Chan et al., 2022	UK	2022	EGS
Gebran et al.,2022	UK	2022	EGS
Lund et al., 2021	USA	2021	EGS
McGuinness, Harmston 2021	NZ	2021	EGS
Tarim et al., 2021	Turkey	2021	EGS
Sá et al., 2021	Portugal	2021	UES
Martínez Caballero et al, 2021	Spain	2021	AC
Willms AG et al., 2020	Germany	2021	AU
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**Note:** TS - Type of surgery, NZ-New Zealand, UK-United Kingdom, EGS - Emergency General Surgery, UES - Urgent/Emergency Surgery, AC-Acute Cholecystitis, AA-Acute Appendicitis

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, with additional contributions from one case-control study [Fernández-Martínez M et al., 2021].

Table 1. Summary of study characteristics, including first author's name, country, year of publication, type of surgery performed, and the presence or absence of a comparative/control group.

Table 2. Summary of patient demographics variables, including total number of patients, age, sex.

Outcome Variables: Table 3. Summary of patient mortality and

Demographic variables of patients according to literature sources taking into mechanical ventilation, and account the area of residence

	To	tal	Age (year)		Gender (M/F)		
First Author	Covid	Non-	Covid	Non-covid	Covid	Non-	
		covid				covid	
Fallani et al.	149	183	49 (26.5-70),	44 [24-61]	94/55	97/86	
Fernández-Martínez et al.	27	126	$57.5 \pm 21 \text{ (total)}$	-	91/62 (total)		
Chan et al.	223	422	48.6 (Mean)	48.5	114/109	191/231	
Gebran et al.	344	701	17-70 (total)	-	220/124	406/295	
Lund et al.	229	279	59.3, (Mean)	56.7	102/127	121/158	
McGuinness, Harmston	627	650	57 (Median)	57	327/300	314/336	
Tarim et al.	132	195	50, (Median)	53	74/58	82/113	
Sá et al.	457	643	67, (Median)	63	261/196	368/275	
Martínez Caballero et al.	257	215	69 (52-80)	68 (50-80)	146/111	118/97	
			(Median)				
Willms et al.	888	1027	36 ± 20 (Mean)	35±19	468/420	510/517	

TABLE 3. Outcome variables of patients according to literature sources taking into account the area of residence

First Author	Mortality Rates		Morbidity Rates		Mechanical Ventilation		ICU Admission	
	Covid	Non- covid	Covid	Non- covid	Covid	Non- covid	Covid	Non- covid
Fallani et al.	6%	4.9%	35.6%	18%	ns		ns	
Fernández-Martínez et al.	18.5%	7%	85.7%	26.7%	66%	0	36%	14%
Chan et al.	5.8%	2.4%	5.6%	4.8%	ns		8.5%	7.1%
Gebran et al.	40.1%	2.9%	72.7%	0	23.9%	0	ns	
Lund et al.	5%	4%	25%	29%	ns		ns	
McGuinness, Harmston	4%	3%	ns		ns		ns	
Tarim et al.	3%	3.1%	7%	1.5%	ns		ns	
Sá et al.	11.40%	5.9%	ns	ns	ns		ns	
Martínez Caballero et al.	11.9%	3.2%	100%	26%	ns		ns	
Willms et al.	0.1%	0.2%	14.3%	13.3%	ns		4.5%	3.9%

Effect size measures calculated from mortality rates

	Effect Size	Odds	Odds Ratio,	Risk	Risk Ratio,
First Author	(Cohen's d)	Ratio	95% CI	Ratio	95% CI
Fallani et al.	0.684	1.239	0.478, 3.211	1.225	0.497, 3.014
Fernández-Martínez et al.	1.666	3.016	0.919, 9.896	2.643	0.957, 7.289
Chan et al.	1.383	2.504	1.08, 5.794	2.417	1.079, 5.412
Gebran et al.	12.384	22.415	13.718, 36.626	13.828	8.840, 21.630
Lund et al.	0.698	1.263	0.543, 2.937	1.25	0.559, 2.798
McGuinness, Harmston	0.744	1.347	0.738, 2.460	1.333	0.745, 2.385
Tarim et al.	0.534	0.967	0.267, 3.501	0.968	0.278, 3.37
Sá et al.	1.134	2.052	1.326, 3.176	1.932	1.294, 2.885
Martínez Caballero et al	2.257	4.086	1.23, 13.618	3.719	1.234, 11.210
Willms et al.	0.276	0.500	0.041, 6.037	0.5	0.042, 6.016

TABLE 2. morbidity rates, need for ICU admission rates.

> Overall, COVID-19 group patients demonstrated significantly higher mortality having odds ratio of 3.0036 (95% CI: 2.4263, 3.7184) and risk ratio of 2.8333 (95% Cl: 2.3127, 3.4712). Table 3 presents the individual odds ratio and risk ratio of these 10 studies.

Table 4 summarizes the effect sizes calculated from mortality rates in both the COVID-19 and non-CO-VID-19 groups. Similarly, the odds of experiencing postoperative complications were significantly higher among COVID-19 patients, as shown in Table 2, 3. Only two studies reported the use of mechanical ventilation due to pulmonary complications associated with COVID-19, while three studies mentioned ICU admissions.

The meta-analysis has yielded an estimated effect size of approximately TABLE 4. 2.35 with a standard error of 1.29. The heterogeneity statistics indicate a very high level of variability among the studies (I<sup>2</sup> = 99.86%), suggesting that the results may not be consistent across the included studies. The forest plot (fig. 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 inter-

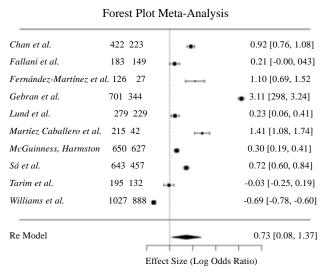


Figure 2. Forest plot & effect size of meta-analysis

vals (CI) for mortality between COVID-19 and non-COVID-19 patients across included studies. The dashed line represents the null effect (odds ratio = 1). The effect size (fig. 2) displays the effect sizes (Cohen's d) for each study, along with confidence intervals.

Visual inspection of the funnel plot (fig. 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. The results of the linear regression analysis, which serves as an alternative to Egger's Test, indicate that the intercept is approximately 2.966, and the coefficient for the standard error (SE) is -7.864. The p-value for the SE coefficient is 0.751, which suggests that there is no significant relationship between the effect sizes and their standard errors, indicating a lack of evidence for publication bias.

### **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 CO-VID-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 or even in managing

emergency general surgery in COVID-19 patients in non-pandemic period.

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 was reported in a few studies; however, this is within the principles of surgery [Ciarleglio FA et al., 2021; Lazzati A et al., 2021; Singh C et al., 2021]. 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 [Willms AG et al., 2020]. There were NOM failure as well, leading to operative intervention, again according to the surgical principles [Martínez Caballero J et al., 2021].

The meta-analysis revealed a markedly higher postoperative mortality rate in COVID-19 patients, as reported in several other studies [Doglietto F et al., 2020; Ciarleglio FA et al., 2021; Lazzati A et al., 2021; Singh C et al., 2021; Aloyan K et al., 2021; Carrier FM et al., 2021; Prasad NK et al., 2021; Alelyani RH et al., 2022; Pratha AR et al., 2023]. This aligns with prior reports suggesting that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection exacerbates perioperative risks due to factors such as hyperinflammatory states, coagulopathies, and pulmonary compromise [Saleh SK et al., 2020; Yuki K et al., 2020; Luca M et al., 2021; Aloyan K et al., 2021; Pratha AR et al., 2023; Cascella M et al., 2024]. The disproportionate impact on older adults and those with comorbidities underscores the need for heightened vigilance

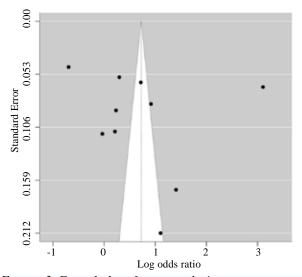


FIGURE 3. Funnel plot of meta-analysis

in these patients. Hypertension, diabetes, Chronic Obstructive Pulmonary Disease, cardiovascular disease, cerebrovascular disease and chronic renal disease were reported as major risk factors for serious events in these patients [Nandy K et al., 2020; Wang B et al., 2020; Ciarleglio FA et al., 2021; Singh C et al., 2021; Luca M et al., 2021; Prasad NK et al., 2021]. COVID-19 patients experienced a higher rate of postoperative complications, particularly respiratory complications [Doglietto F et al., 2020; Aloyan K et al., 2021]. 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 [Kavanagh BP, 2007; Hedenstierna G, Edmark L, 2010; Alazawi W et al., 2016; Ball L et al., 2018; Scholten R et al., 2019; Duggan M, Gerstein NS et al., 2020; Rieder M et al., 2020]. 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 [Prasad NK et al., 2021; Alelyani RH et al., 2022; Pratha AR et al., 2023]. 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 [Prasad NK et al., 2021]. 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 en-

sure adequate resource planning during pandemics to accommodate the surgical burden [Lazzati A et al., 2021; Carrier FM et al., 2021]. 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 (I² = 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.
- Exploration of long-term outcomes, including quality of life and functional recovery in CO-VID-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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