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# Incidence and predisposing factors associated with peri-intubation cardiac arrest: A systematic review and meta-analysis

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**Abstract:**

**OBJECTIVES:** Various studies have delved into its incidence and risk factors, but a comprehensive meta-analysis exploring this life-threatening complication during emergent endotracheal intubation has been lacking. This study quantitatively assesses the global incidence and associated risk factors of peri-intubation cardiac arrest (PICA).

**METHODS:** We conducted a systematic literature search on PubMed, Embase, Web of Science, and Cochrane Library from inception to October 28, 2024. Two independent authors searched, reviewed, and evaluated selected studies. Any peer-reviewed published studies reporting the incidence of PICA among adults ($\geq$18 years) outside of the operating theater were included. Studies reporting incidence within heterogeneous populations or from overlapping groups were excluded. The primary outcome focused on determining the global incidence of PICA, while the secondary outcome addressed associated risk factors. A random-effects model was used to aggregate overall incidence rates. Subgroup analysis and meta-regression were conducted to examine PICA incidence in different locations and with the study's sample size. The publication bias was assessed via Egger's test and visualization of the funnel plot. The risk of bias was evaluated using the Joanna Briggs Institute Critical Appraisal Checklist.

**RESULTS:** Fifteen articles met the inclusion criteria for the meta-analysis. PICA incidence varied from 0.5% to 23.3%. The estimated pooled incidence was 2.7% (95% confidence interval [CI]: 1.9–3.6) across PICA in the emergency department (ED) (2.5%, 95% CI: 1.4–3.7) and outside of the ED (2.9%, 95% CI: 2.2–3.6). Egger's test yielded $P = 0.009$, indicating potential publication bias due to small-study effects, as suggested by the funnel plot. Meta-regression analysis revealed higher incidence in studies with smaller populations. Notably, preintubation hypotension, hypoxemia, and body mass index were found to be the most associated risk factors for PICA. Additionally, there was significant variability in PICA definitions, ranging from immediate to occurrences within 60 min after intubation.

**CONCLUSION:** PICA occurrences during emergent endotracheal intubation reached up to 3%, showing a similar rate both within and outside the ED. While limitations such as heterogeneity and potential bias exist, these findings underscore the imperative for prospective research. Prospective studies are warranted to further delineate this critical aspect of emergent intubation.

**Keywords:**

Cardiac arrest, emergent intubation, incidence, peri-intubation cardiac arrest

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**Box-ED section**

**What is already known on the study topic?**
- Previous studies have shown that peri-intubation cardiac arrest (PICA) is a serious complication of emergent intubation
- However, its exact incidence and risk factors have been inconsistent.

**What is the conflict on the issue? Has it importance for readers?**
- The lack of consensus on PICA's incidence and risk factors hinders effective prevention and management strategies
- This is crucial for healthcare providers to improve patient outcomes.

**How is this study structured?**
- We conducted a systematic review and meta-analysis involving a comprehensive literature search of four databases, data extraction, statistical analysis, and interpretation of the results.

**What does this study tell us?**
- PICA occurred in approximately 3% of emergent intubation cases within and outside the emergency department
- While limitations exist, these findings emphasize the need for further prospective research to understand PICA better and develop effective prevention strategies.

## Introduction

Emergent intubation, a frequently performed procedure in critically ill patients, carries significant mortality and long-term disability risks due to complications such as hypotension, pulmonary aspiration, misplacement in the esophagus or bronchus, and the severe consequence of cardiac arrest.[1-4] Despite its prominence, cardiac arrest during emergent intubation is under-described in existing literature, lacking the attention it warrants.

Various studies have explored the incidence of peri-intubation cardiac arrest (PICA) across diverse healthcare settings without anesthesiologists, including prehospital scenarios, emergency departments (EDs), intensive care units (ICUs), and hospital wards.[4-7] Discrepancies in PICA definitions, ranging from immediate to events within 60 min after intubation, contribute to the reported variability.[6-9] In EDs, documented PICA rates vary widely from 0.5% to 23.3%, while in the ICU or hospital ward, the incidence remains more constrained, ranging from 1.2% to 5.3%.[2,3,6,8,10,11] Importantly, the outcomes of PICA relative to other causes of cardiac arrest remain unclear, necessitating a comprehensive assessment of associated predisposing factors for developing effective mitigation strategies. Previous studies have identified risk factors such as pulmonary edema, preintubation hypotension, hypoxemia, advanced age, shock index (SI), and the frequency of intubation attempts.[10,12-14] However, a definitive meta-analysis encompassing these aspects during emergent endotracheal intubation is notably absent. This study fills that gap by quantitatively evaluating the global incidence, outcomes, and predisposing risk factors associated with PICA, hypothesizing that its findings will underscore the critical importance of this condition and prompt physicians to explore effective strategies for mitigating its consequences during emergent intubation.

## Methods

We prepared this systematic review and meta-analysis based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statements.[15] We prospectively registered the study protocol on the PROSPERO website (Registration ID: CRD42023392729, http://www.crd.york.ac.uk/PROSPERO).

### Search strategy and study selection

We thoroughly searched four databases – PubMed, EMBASE, Web of Science, and Cochrane Collaboration – covering their inception to October 28, 2024. Our search was not restricted to any language. We used a combination of Medical Subject Heading terms, incorporating various spellings and endings, to identify articles relevant to terms such as "intubation," "tracheal intubation," "emergency intubation," "heart arrest," "cardiac arrest," "cardiopulmonary resuscitation," "prevalence," and "incidence." Detailed information on search terms and strategies is available in Supplementary Tables 1, 2 and Figures 1-4. Additionally, we extended our search to include websites, organizations, pertinent reviews, and references to locate additional eligible studies. Unpublished trials registered at ClinicalTrials.gov were also sought using similar search terms. Citations from relevant articles were explored as well. The results extracted from these databases underwent screening to remove duplicate studies, and the remaining studies were integrated into the Rayyan QCRI website.

### Inclusion criteria and outcome of interest

The criteria for inclusion in this study were outlined as follows:

1. Participants and intervention: Any peer-reviewed published interventional or observational study that involved individuals aged 18 years and above who had a cardiac arrest during emergency intubation
2. Outcome measures: Studies were required to assess or report the incidence or prevalence of cardiac arrest during emergency intubation, endotracheal intubation-related cardiac arrest, or PICA.

Patients will be included regardless of the presence of the airway equipment delivered before the cardiac arrest occurs. Exclusion criteria were animal studies, review articles, case reports and case series, editorials, commentaries, and book chapters. Studies will be excluded if they report <five patients. There are no restrictions on gender and ethnicity. Articles will be excluded if they report the incidence (or prevalence) within a heterogeneous (i.e., mixed pediatric and adult patients where outcomes are not specific to the adult population) or overlapping populations.

Two authors (N. M. and W. W.) independently screened study titles and abstracts to identify potentially eligible studies. The authors extracted and independently assessed the full-text articles of the identified studies against the predetermined criteria. Any disparities were resolved through discussion and consensus. The primary outcome of interest was the incidence of PICA. The secondary outcomes included the outcomes after PICA (return of spontaneous circulation [ROSC], survival to hospital discharge, and neurologically intact survival at hospital discharge) and predisposing factors associated with PICA.

### Data extraction and assessment of the study risk of bias

We extracted information from the selected articles using a structured data extraction form. This form encompassed details such as the first author, publication year, study design, study location, enrollment period, study population and setting, the definition of PICA, participants' age, and the incidence of PICA. All the collected data were input into a Microsoft Excel spreadsheet. Two authors (N. M. and W. W.) independently assessed the risk of bias in the included studies, and any disagreements will be resolved by discussion between these authors. The study risk of bias was assessed using the Joanna Briggs Institute Critical Appraisal Checklist.[16]

### Statistical analysis

The extracted database was exported to Stata MP 16 statistical software (StataCorp LLC, College Station, TX, USA) for statistical analysis. An estimate of the pooled incidence of PICA and the corresponding 95% confidence interval (CI) were calculated. The random-effects model was used to adjust for predicted significant heterogeneity among studies. Subgroup analyses were performed based on different locations of PICA. Meta-regression was also conducted to examine the PICA incidence concerning the study's sample size. The publication bias was assessed using Egger's test and visualization of the funnel plot. Heterogeneity among studies was evaluated using the $I^2$ statistics. All tests were two-sided, with $P < 0.05$, considered statistically significant.

## Results

### Characteristics of the included studies and risk of bias evaluation

Figure 1 illustrates the flow diagram representing the study selection process. A total of 1,340 original articles were identified through four electronic databases. A final selection was made, encompassing 15 articles, following meticulous adherence to predefined inclusion criteria. The sample sizes in the selected studies, conducted between 1990 and 2021, ranged from 210 to 15,776, involving data collected from 44,144 patients who underwent emergent tracheal intubation. Among these, 725 were diagnosed with PICA. Table 1 provides a summary of the basic characteristics of the included studies. Participant's ages averaged between 48 and 75. Seven studies were conducted specifically in the ED.[4,8,10,13,14,18,19] Geographically, the studies were predominantly concentrated in the United States (five)[2,4,7,13,20] and South Korea (four),[8,10,17,19] followed by France (two),[5,6] Japan (one),[11] Scotland (one),[18] and Taiwan (one).[14] One was a cohort study conducted in 29 countries globally.[3] Participants surviving from PICA had an average ROSC, survival to hospital discharge, and favorable neurological outcome at hospital discharge of 52.9%–77.6%, 18.0%–58.6%, and 14.3%–55.3%, respectively. Regarding study risk of bias assessment, 11 studies scored 8–9 out of 9, while 4 received 6–7 out of 9.

### The overall incidence of peri-intubation cardiac arrest

The heterogeneity test indicated significant variation among the studies ($I^2 = 96.0\%$, $P < 0.01$), necessitating the application of a random-effects model for analysis. The estimated pooled incidence of PICA was 2.7% (95% CI: 1.9–3.6). The incidence was not different among studies conducted inclusively at the ED (2.5%, 95% CI: 1.4–3.7) and outside of the ED (2.9%, 95% CI: 2.2–3.6). Notably, there was significant variability in PICA definitions, ranging from immediate to occurrences within 60 min after intubation. Figure 2 illustrates the Forest plot showing the incidence of PICA among patients who underwent emergent tracheal intubation. Meta-regression analysis revealed that studies with smaller sample sizes had a higher incidence of PICA [Supplementary Figure 1].

### Predisposing factors associated with peri-intubation cardiac arrest

Nine studies evaluated in this analysis reported at least one predisposing factor associated with PICA.[4-8,10,13,14,17] Preintubation hypotension and hypoxemia were mostly independent factors (four studies), followed by medication use (three studies). Tables 2 and 3 summarize the details of predisposing factors and effect sizes of independent predisposing factors associated with PICA.

**Table 1: Characteristics of included studies**

| First author, year | Study design | Country, study duration | Study population | Setting | PICA definition (min) | Population (*n*), age median (IQR) – years | Incidence of PICA, *n* (%) | Outcomes of PICA | | | Quality score (out of 9) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | ROSC (%) | Survival to hospital discharge (%) | Good neurological outcome at discharge (%) | |
| Russel, 2022[2] | RCT | USA, 2019–2021 | Adult critically ill patients (aged ≥18 years) undergoing tracheal intubation with sedation and positive pressure ventilation | ICU | Within 60 min | 1065, 62 (51–70) | 17 (1.6) | N/A | 58.6 | N/A | 8 |
| Yang, 2022[14] | Retrospective, nested case–control study | Taiwan, 2016–2020 | Adult (aged >18 years) nontraumatic patients admitted to the ED and required emergency oral tracheal intubation | ED | Within 20 min | 5130, 74 | 92 (1.8) | N/A | N/A | N/A | 9 |
| Gil-Jardiné, 2022[6] | Secondary analysis of RCT | France, 2014–2016 | Out-of-hospital adult (aged ≥18 years) patients requiring emergency tracheal intubation | Prehospital | Within 15 min | 1226, 55.9±19* | 35 (2.8) | N/A | N/A | N/A | 8 |
| April, 2021[4] | Multi-center prospective registry study | USA, 2016–2018 | Adult patients requiring emergency intubation | ED | Within 15 min | 15776, 51.5±19.6* | 157 (1.0) | 67.5 | N/A | N/A | 9 |
| Russotto, 2021[3] | Multi-center prospective cohort study | 29 countries, 2018–2019 | Critically ill adults (≥18 years) requiring in-hospital intubation | ICU, ED, wards | Within 30 min | 2964, 63 (49–74) | 93 (3.1) | N/A | N/A | N/A | 9 |
| Park, 2019[17] | Retrospective observational study | South Korea, 2016–2017 | Adults (≥18 years old) who developed cardiac arrest during intubation | General wards | Within 20 min | 362, 58.7±19.1* | 15 (4.1) | 73.3 | 53.3 | 53.3 | 8 |
| De Jong, 2018[5] | Retrospective analysis of multi-center prospective study | France, 2001–2016 | All intubation procedures for adult patients (aged ≥18 years) | ICU | Within 5 min | 1847, 62 (50–73) | 49 (2.7) | 71.4 | 26.5 | N/A | 9 |
| Ono, 2018[11] | Retrospective observational cohort study | Japan, 2007–2017 | Trauma patients who underwent emergency tracheal intubation | Prehospital, ED | Immediate after intubation | 537, 60 | 17 (3.2) | N/A | N/A | N/A | 7 |
| Wardi, 2017[7] | Retrospective case–control study | USA, 2011–2016 | Adults (aged ≥18 years) who required intubation and experienced a cardiac arrest after being discharged from OR | In-patient | Within 20 min | 547, 60.0±16.2* | 29 (5.3) | 72.4 | 48.3 | 31.0 | 8 |
| Ko, 2015[8] | Retrospective cohort study | South Korea, 2007–2011 | Adult patients (≥18 years) who developed cardiac arrest | ED | Within 20 min | 210, 64 (53–73) | 49 (23.3) | 77.6 | 34.7 | 14.3 | 8 |
| Kerslake, 2015[18] | Retrospective cohort study | Scotland, 1999–2011 | All patients who underwent any attempt at tracheal intubation | ED | N/A | 3738, 48 | 30 (0.8) | N/A | N/A | N/A | 6 |
| Kim, 2014[10] | Matched case–control study | South Korea, 2007–2011 | Adult (≥18 years) nontraumatic, critically ill patients who had emergency airway management | ED | Within 10 min | 2403, 64.5±11.3* | 41 (1.7) | 75.6 | 36.6 | 14.6 | 9 |
| Cho, 2013[19] | Retrospective, subgroup analysis of the registry | South Korea, 2006–2012 | All older patients (≥65 years) requiring emergency intubation | ED | N/A | 4891, 75.0±6.8* | 24 (0.5) | N/A | N/A | N/A | 6 |

*Contd...*

**Table 1: Contd...**

| First author, year | Study design | Country, study duration | Study population | Setting | PICA definition (min) | Population (*n*), age median (IQR) – years | Incidence of PICA, *n* (%) | Outcomes of PICA | | | Quality score (out of 9) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | ROSC (%) | Survival to hospital discharge (%) | Good neurological outcome at discharge (%) | |
| Heffner, 2013[13] | Retrospective cohort study | USA, 2007 | Adult patients (≥18 years) who were not in cardiac arrest before intubation | ED | Within 10 min | 410, 48.6±19.1* | 17 (4.1) | 52.9 | 18.0 | N/A | 9 |
| Mort, 2004[20] | Retrospective study | USA, 1990–2002 | Adult patients (≥18 years) who required intubation | Hospital wards | Within 10 min | 3035, 67 | 60 (2.0) | 65.0 | 31.0 | N/A | 6 |

*Reported as mean±SD. ED: Emergency department, ICU: Intensive care unit, IQR: Interquartile range, N/A: Not applicable, OR: Operating room, PICA: Peri-intubation cardiac arrest, RCT: Randomized-controlled trial, ROSC: Return of spontaneous circulation, SD: Standard deviation

## Publication bias

Significant asymmetry was observed upon visually inspecting the funnel plot [Figure 3]. Egger's test yielded $P = 0.009$, indicating potential publication bias.

## Discussion

In our comprehensive analysis, encompassing 44,144 patients undergoing emergent tracheal intubation, the estimated pooled incidence of PICA was 2.7%. This incidence remained consistent between studies conducted exclusively in the ED and those performed outside the ED (2.9% vs. 2.5%). However, substantial heterogeneity arose from varying PICA definitions and sample sizes among the included studies.

Our findings align with prior reports of PICA incidence in emergency intubation settings, ranging from 0.5% to 5.3%.[4,10,14,19] Notably, a retrospective cohort study by Ko *et al*.[8] reported a higher PICA incidence (23%) in a tertiary referral center in Korea, focusing on adult ED patients experiencing cardiac arrest associated with intubation. The methodology, limited sample size, and exclusion of noncardiac arrest patients intubated in the ED could contribute to the observed disparity. Gil-Jardiné *et al*.[6] and Ono *et al*.[11] noted a correlation between PICA incidence in prehospital and inhospital settings, suggesting a potential influence of a physician-on-scene system on intubation quality. However, additional studies are needed to explore PICA incidence in prehospital settings without physician presence.

Our review also found that the patient's hemodynamic status before intubation is a crucial factor influencing the incidence of PICA. Airway manipulation during intubation could activate the sympathetic and parasympathetic nervous systems,[21] posing a risk of cardiac arrest in hemodynamically compromised patients through various pathways. Postintubation hypotension can result from increased intrathoracic pressure, vasodilation, or myocardial depression due to anesthetics.[22] Patients entering the ED with low oxygen levels or blood pressure requiring immediate endotracheal intubation face an elevated risk of rapid deterioration and cardiac arrest during the procedure. Preintubation hypotension and hypoxemia have been documented as significant independent factors in four studies, with medication use highlighted in three studies in our review. Furthermore, the SI showed a notable association, emphasizing the importance of hemodynamic stability assessment before intubation. Heffner *et al*.[13] found that a 0.1 increase in SI before intubation was significantly linked to a 1.2-fold increase in the likelihood of developing cardiac arrest. In addition, a published meta-analysis has revealed a significant

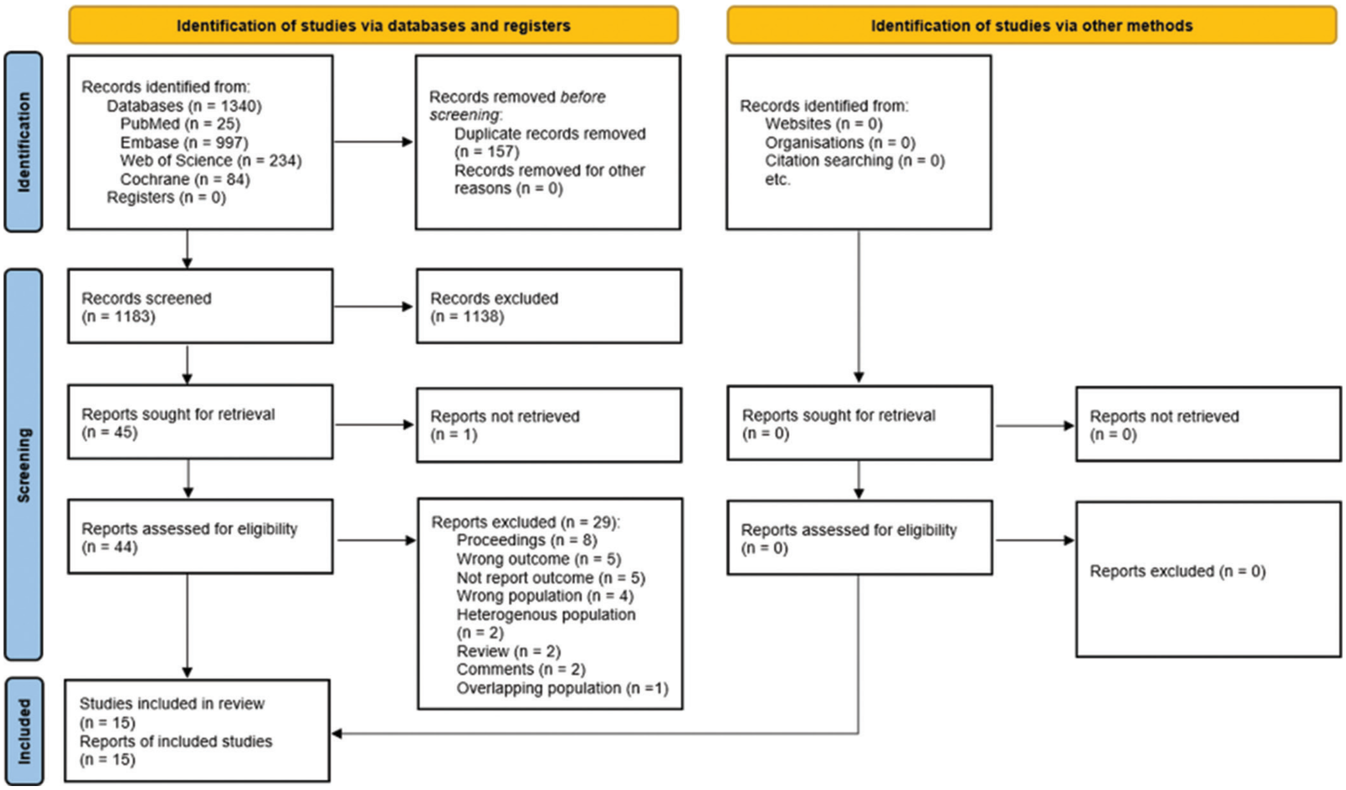


**Figure 1:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement study flow diagram

**Table 2: Predisposing factors associated with peri-intubation cardiac arrest**

| First author, year | Pulmonary edema | Preintubation hypotension | Elevated lactate levels | Age | Hypoxemia | SI | BMI | Medications | GCS $\leq 8$ | Number of attempts |
|---|---|---|---|---|---|---|---|---|---|---|
| Russel, 2022[2] | - | - | - | - | - | - | - | - | - | - |
| Yang, 2022[14] | ✓ | ✓ | ✓ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ |
| Gil-Jardine, 2022[6] | - | ✗ | - | - | ✓ | ✗ | ✓ | ✓ | ✗ | ✗ |
| April, 2021[4] | - | ✓ | - | ✗ | ✓ | - | - | ✗ | - | - |
| Russotto, 2021[3] | - | - | - | - | - | - | - | - | - | - |
| Park, 2019[17] | - | - | - | ✗ | - | ✗ | - | ✓ | - | ✓ |
| De Jong, 2018[5] | ✗ | ✓ | - | ✓ | ✓ | - | ✓ | ✗ | ✗ | - |
| Ono, 2018[11] | - | - | - | - | - | - | - | - | - | - |
| Wardi, 2017[7] | ✗ | ✗ | - | ✗ | ✗ | ✓ | ✗ | ✓ | - | ✗ |
| Ko, 2015[8] | - | ✗ | - | ✗ | ✓ | - | - | ✗ | ✗ | ✗ |
| Kerslake, 2015[18] | - | - | - | - | - | - | - | - | - | - |
| Kim, 2014[10] | - | ✓ | - | ✗ | ✗ | ✗ | - | ✗ | - | ✗ |
| Cho, 2013[19] | - | - | - | - | - | - | - | - | - | - |
| Heffner, 2013[13] | - | ✗ | - | ✗ | ✗ | ✓ | - | ✗ | - | ✗ |
| Mort, 2004[20] | - | - | - | - | - | - | - | - | - | - |
| Total | 1/3 | 4/8 | 1/1 | 1/8 | 4/8 | 2/6 | 2/4 | 3/9 | 0/4 | 1/7 |

✓: Independent risk factor, ✗: No association, -: Not mentioned, BMI: Body mass index, GCS: Glasgow Coma Scale, SI: Shock index

association between preintubation hypotension and PICA, with low between-study heterogeneity.[23] This indicates a high degree of consistency in the findings across the various studies included in the meta-analysis. Positive pressure ventilation applied to patients with preexisting hypotension before intubation could increase intrathoracic pressure, exacerbating shock by reducing venous return, thus decreasing cardiac output and potentially leading to cardiac arrest from a scientific perspective.[24] Therefore, optimizing the preintubation phase through hemodynamic resuscitation in patients with a noncrash airway should reduce PICA.

Moreover, our pooled analysis is consistent with the recently published meta-analysis[23] that hypoxemia

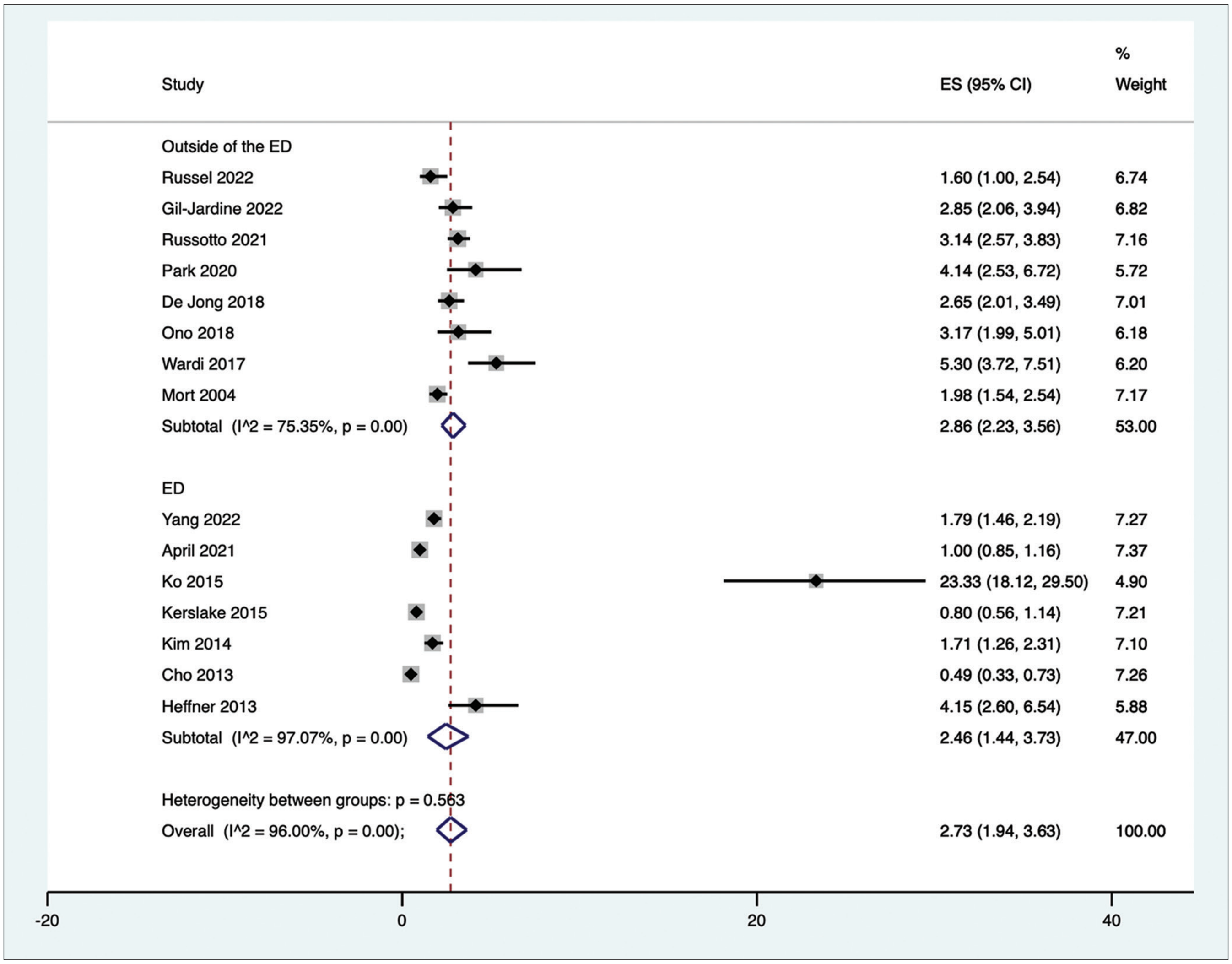


**Figure 2:** Forest plot of the subgroup analysis based on different locations, showing the incidence of peri-intubation cardiac arrest among patients who underwent emergent intubation, with 95% confidence intervals. ED: Emergency department, CI: Confidence interval

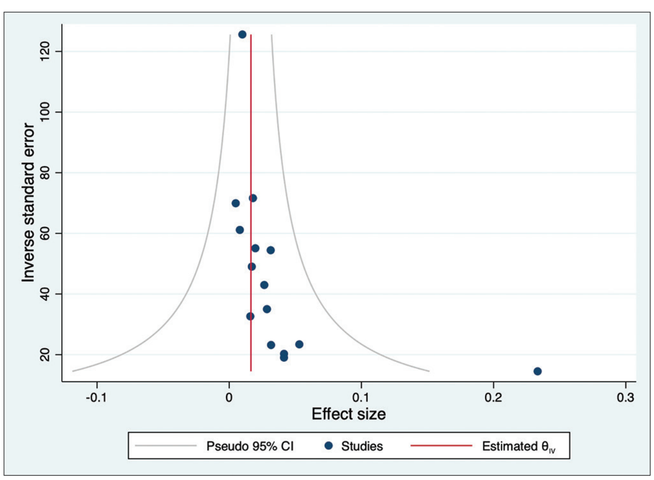


**Figure 3:** Funnel plot showing publication bias of studies on the incidence of peri-intubation cardiac arrest. CI: Confidence interval

before intubation has been recognized as a predisposing factor for PICA. In clinical practice, hypoxemic respiratory failure is a frequent indicator for emergent intubation, and bradycardia and cardiac arrest are considerably more likely when hypoxemia is present.[25,26] Given that the specific method of preoxygenation and oxygen delivery may vary depending on the facility and the intubation setting (such as ED, ICU, or general wards), it is advisable for clinicians to carefully consider these factors and choose the most appropriate method for preoxygenation and oxygen delivery.[27-29]

## Limitations

Some limitations need to be addressed in our study. First, we observed significant variability in the definition of PICA across the included studies. The diverse definitions, ranging from immediate to occurrences within 60 min after intubation, might introduce inconsistency and limit comparability. Second, exploring pooled data from distinct settings, including ED, ICU, and hospital wards, contributes to potential biases and may impact the

**Table 3: Independent predisposing factors for peri-intubation cardiac arrest**

| First author, year | Predisposing factor | OR | 95% CIs |
|---|---|---|---|
| Yang, 2022[14] | Cardiogenic pulmonary edema | 5.92 | 1.04–33.57 |
| | Preintubation SBP <90 mmHg | 5.22 | 1.48–18.34 |
| | 0.11 mol/L increase in lactate | 1.01 | 1.00–1.02 |
| Gil-Jardine, 2022[6] | BMI >30 kg/m$^2$ | 4.85 | 1.82–12.90 |
| | $SpO_2$ before intubation <90% | 3.40 | 1.50–7.60 |
| | Rocuronium (compared to succinylcholine) | 2.47 | 1.08–5.64 |
| April, 2021[4] | Preintubation SBP <100 mmHg | 6.2 | 4.5–8.5 |
| | $SpO_2$ before intubation <90% | 3.1 | 2.0–4.8 |
| Park, 2019[17] | Number of intubation attempts | 3.10 | 1.12–7.86 |
| | NMBA use for RSI | 1.21 | 1.08–3.15 |
| | Use of succinylcholine | 3.45 | 1.20–5.49 |
| | Pre-ETI vasopressor use | 2.69 | 1.15–7.42 |
| De Jong, 2018[5] | Preintubation SBP <90 mmHg | 3.41 | 1.80–6.45 |
| | $SpO_2$ before intubation <80% | 3.99 | 2.10–7.58 |
| | BMI >25 kg/m$^2$ | 2.01 | 1.02–3.95 |
| | Age >75 years old | 2.25 | 1.08–4.68 |
| Wardi, 2017[7] | Intubation around shift change | 4.05 | 1.46–11.19 |
| | Use of succinylcholine | 3.10 | 1.10–8.66 |
| | SI $\geq$1.0 | 2.67 | 1.01–7.10 |
| Kim, 2014[10] | Preintubation SBP $\leq$90 mmHg | 3.67 | 1.58–8.55 |
| Heffner, 2013[13] | 0.1 increase in preintubation SI | 1.16 | 1.00–1.30 |
| | 10 kg increase in weight | 1.37 | 1.10–1.70 |

BMI: Body mass index, ETI: Endotracheal intubation, NMBA: Neuromuscular blocking agent, RSI: Rapid sequence intubation, SBP: Systolic blood pressure, CI: Confidence interval, OR: Odds ratio, SI: Shock index

generalizability of the findings. However, we conducted the subgroup analysis by the location of cardiac arrest (ED and outside of ED) and found no differences in the incidence of PICA. In addition, several unmeasured factors may influence this outcome. In addition to the location of intubation, variables such as the patient's underlying disease severity, the intubator's experience level, the use of specific medications during intubation, and the type of intubation equipment employed could significantly impact the risk of PICA. To gain a more comprehensive understanding of these factors and their potential impact on PICA, future research should incorporate detailed data collection on these variables. Third, the presence of significant asymmetry in the funnel plot, indicating potential publication bias, may affect the overall estimation of PICA incidence. Furthermore, the study period for data collection spans from 1990 to 2021. Changes in clinical practices, medical technology advancements, and emergency care improvements over this extended timeframe may introduce confounding variables that need to be adequately addressed. Finally, most of the studies included were conducted retrospectively and might not represent the actual effect estimate for the incidence of PICA. Therefore, future prospective studies are warranted to address this important but under-recognized condition.

## Conclusion

Our systematic review and meta-analysis highlight the significant risk of PICA in emergent intubation settings. The identified risk factors, including preintubation hemodynamic instability and hypoxemia, underscore the importance of meticulous patient assessment and optimization before intubation. Future prospective studies are warranted to explore the underlying mechanisms of PICA further and to develop evidence-based strategies for its prevention and management.

### Author contribution statement

NM and WW developed the concept and drafted the manuscript. NM and WW performed data acquisition and wrote the manuscript. WW performed data and statistical analyses and revised the manuscript. All authors reviewed and approved the final version of the manuscript.

### Conflicts of interest

None Declared.

### Ethical approval

Not applicable.

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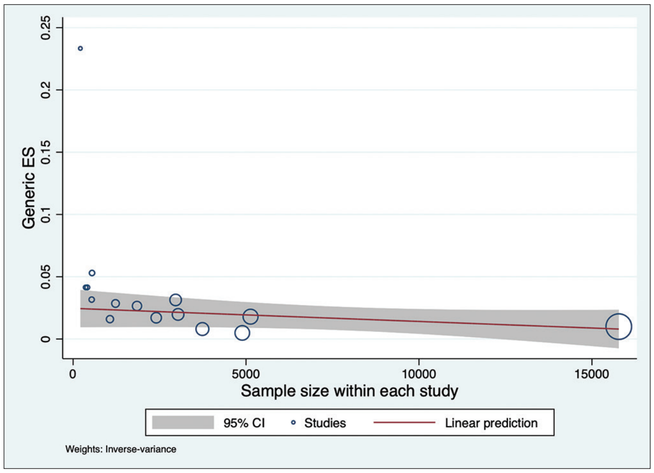
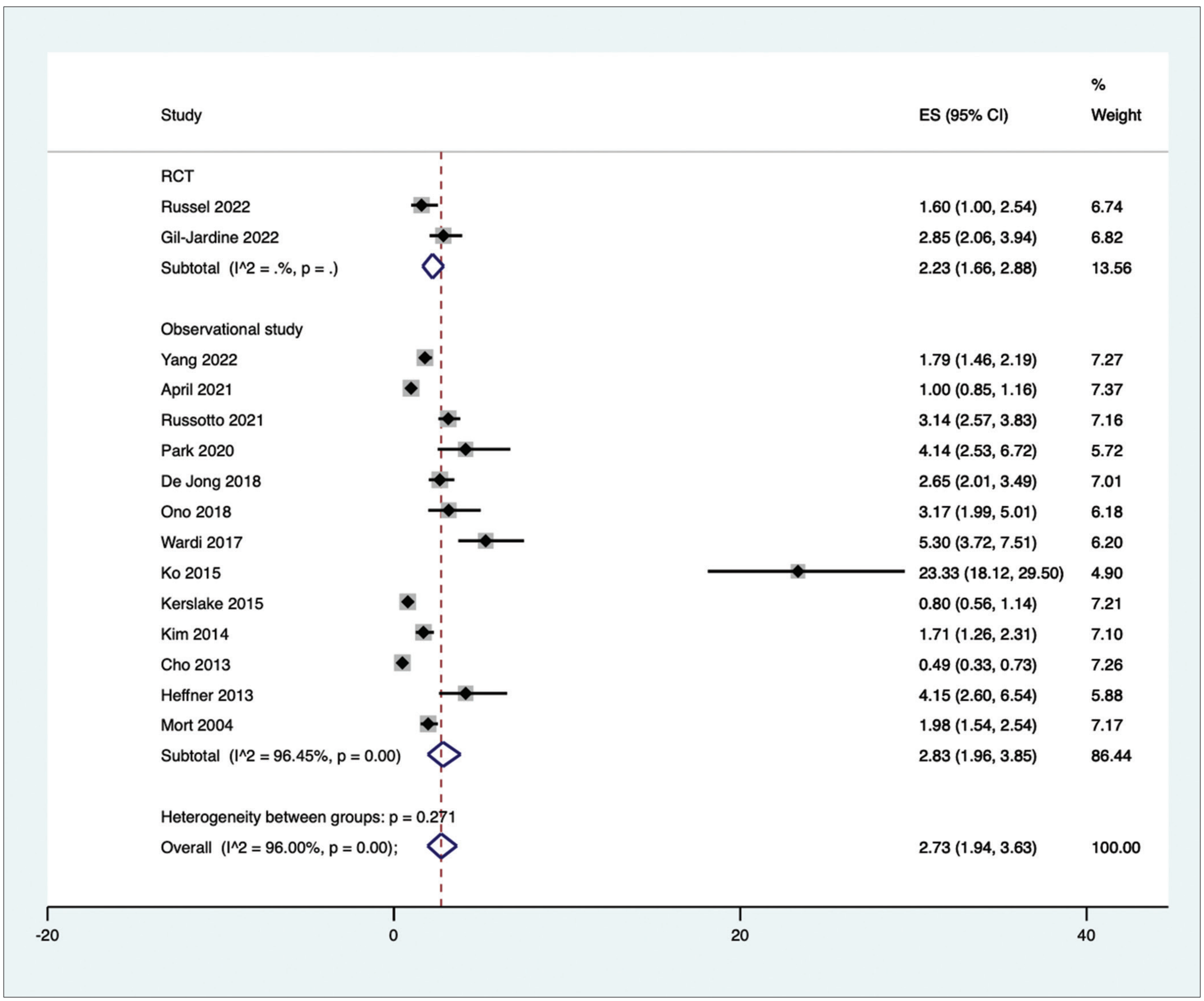
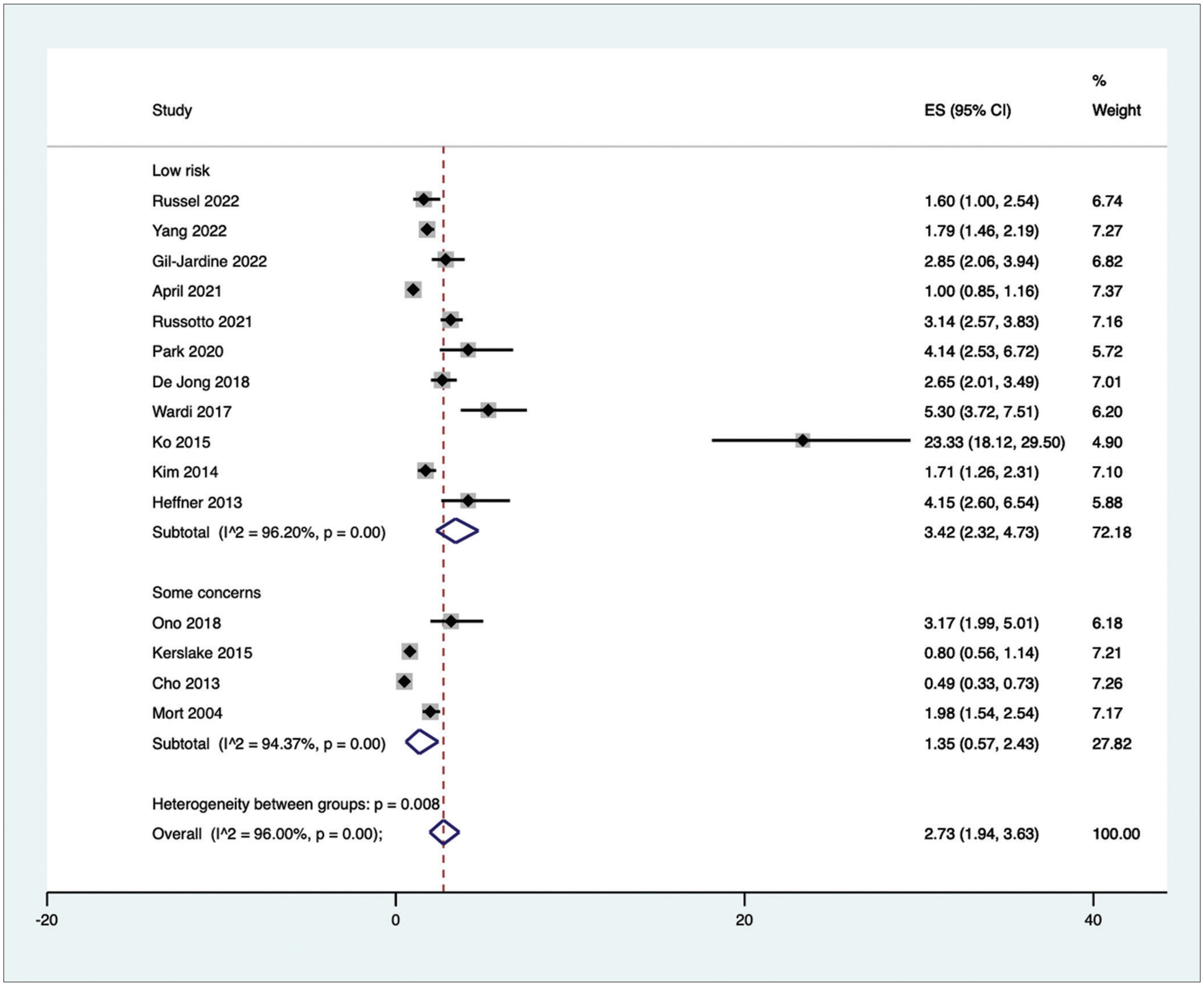


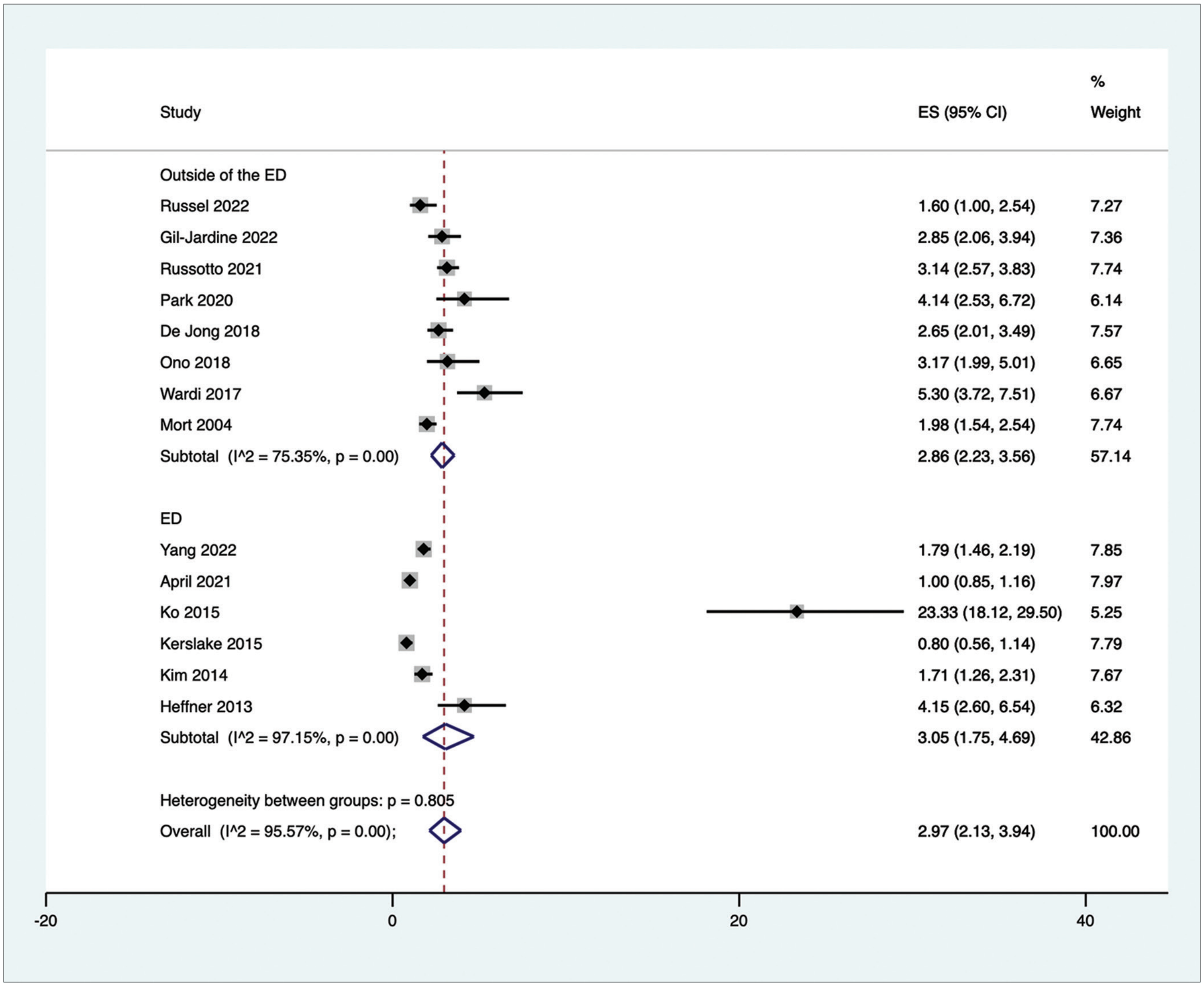

**Supplementary Figure 1:** Meta-regression plot using bubble plots with a linear prediction line. The bubbles are drawn with sizes proportional to the inverse variance of a sample size of individual studies toward the linear prediction. CI: Confidence interval




**Supplementary Figure 2:** Forest plot of the subgroup analysis based on study design, showing the incidence of peri-intubation cardiac arrest among patients who underwent emergent intubation, with 95% confidence intervals. CI: Confidence interval, ES: Effect size, RCT: Randomized-controlled trial




**Supplementary Figure 3:** Forest plot of the subgroup analysis based on study risk of bias, showing the incidence of peri-intubation cardiac arrest among patients who underwent emergent intubation, with 95% confidence intervals. CI: Confidence interval, ES: Effect size




**Supplementary Figure 4:** Forest plot of the subgroup analysis based on different locations, showing the incidence of peri-intubation cardiac arrest among patients who underwent emergent intubation, with 95% confidence intervals. CI: Confidence interval, ES: Effect size, ED: Emergency department

**Supplementary Table 1: Quality assessment using the Joanna Briggs Institute's critical appraisal checklist of included studies**

| Joanna Briggs Institute's critical appraisal checklist | Russel, 2022 | Yang, 2022 | Gil-Jardine, 2022 | April, 2021 | Russotto, 2021 | Park, 2020 | De Jong, 2018 |
|---|---|---|---|---|---|---|---|
| Was the sample frame appropriate to address the target population? | Unclear | Yes | Unclear | Yes | Yes | Yes | Yes |
| Were study participants sampled in an appropriate way? | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Was the sample size adequate? | Yes | Yes | Yes | Yes | Yes | Unclear | Yes |
| Were the study subjects and the setting described in detail? | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Was the data analysis conducted with sufficient coverage of the identified sample? | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Were valid methods used for the identification of the condition? | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Was the condition measured in a standard, reliable way for all participants? | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Was there appropriate statistical analysis? | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Was the response rate adequate, and if not, was the low response rate managed properly? | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Total score (out of 9) | 8 | 9 | 8 | 9 | 9 | 8 | 9 |

| Joanna Briggs Institute's critical appraisal checklist | Ono, 2018 | Wardi, 2017 | Ko, 2015 | Kerslake, 2015 | Kim, 2014 | Cho, 2013 | Heffner, 2013 | Mort, 2004 |
|---|---|---|---|---|---|---|---|---|
| Was the sample frame appropriate to address the target population? | Unclear | Yes | Unclear | Unclear | Yes | Unclear | Yes | Unclear |
| Were study participants sampled in an appropriate way? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Unclear |
| Was the sample size adequate? | Unclear | Unclear | Yes | Yes | Yes | Yes | Yes | Yes |
| Were the study subjects and the setting described in detail? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Was the data analysis conducted with sufficient coverage of the identified sample? | Yes | Yes | Yes | Unclear | Yes | Unclear | Yes | Yes |
| Were valid methods used for the identification of the condition? | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes |
| Was the condition measured in a standard, reliable way for all participants? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Was there appropriate statistical analysis? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Was the response rate adequate, and if not, was the low response rate managed properly? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Total score (out of 9) | 7 | 8 | 8 | 6 | 9 | 6 | 9 | 6 |

**Supplementary Table 2: Electronic search terms**

| Database | |
|---|---|
| **Sources** | **Search terms** |
| PubMed | #1 ((((((((“heart arrest” [MeSH Terms]) OR (“Out-of-Hospital Cardiac Arrest” [MeSH Terms])) OR (cardiac arrest [Title/Abstract])) OR (cardiopulmonary resuscitation [Title/Abstract])) OR (CPR [Title/Abstract])) OR (resuscitation [Title/Abstract])) OR (out-of-hospital cardiac arrest [Title/Abstract])) OR (out-of-hospital [Title/Abstract])) |
| | #2 (“Intubation”[MeSH Terms] OR “Intubation, Intratracheal”[MeSH Terms] OR “Rapid Sequence Induction and Intubation”[MeSH Terms]) |
| | #3 ((“Epidemiology”[MeSH Terms] OR “Incidence”[MeSH Terms]) OR “Prevalence”[MeSH Terms]) OR “Cross-Sectional Studies”[MeSH Terms] |
| | #1 AND #2 AND #3 |
| Embase | #1 (“heart arrest“/exp OR “arrest, heart“ OR “asystole“ OR “asystolia“ OR “asystoly“ OR “cardiac arrest“ OR “circulation arrest“ OR “circulatory arrest“ OR “heart arrest“ OR “heart arrest, induced“ OR “heart asystole“ OR “heart standstill“ OR “induced heart arrest“) |
| | #2 (“intubation“/exp OR “intubation“) |
| | #3 (“prevalence“/exp OR “prevalence“ OR “prevalence study“ OR “incidence“/exp OR “incidence“ OR “incidence rate“ OR “rate, incidence“ OR “cross-sectional study“/exp OR “cross-sectional design“ OR “cross-sectional research“ OR “cross-sectional studies“ OR “cross-sectional study“) |
| | #1 AND #2 AND #3 |
| Web of Science | #1 heart arrest (All) or cardiac arrest (All) or cardiopulmonary resuscitation (All) or CPR (All) or resuscitation (All) OR out-of-hospital (All) or out-of-hospital cardiac arrest (All) or asystole (All) or shockable rhythm (All) |
| | #2 intubation (All) or (TI=(intubation)) |
| | #1 AND #2 |
| Cochrane Collaboration | Intubation AND arrest in Title Abstract Keyword - (Word variations have been searched) |