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Evidence Synthesis of Outcomes of Extracorporeal Membrane Oxygenation for Life-Threatening Asthma Exacerbations

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To the Editor:

Patients with life-threatening asthma exacerbations who fail to improve on receiving standard and adjunctive therapies (eg, bronchodilators, glucocorticoids, magnesium, anesthetic/inhalational agents) are sometimes considered for extracorporeal membrane oxygenation (ECMO) as salvage therapy.[1] However, reports describing ECMO initiation in patients with life-threatening asthma have varied in both the types of outcomes reported and their estimates. We synthesized the body of evidence, using meta-analyses to estimate the outcomes of adults with life-threatening asthma exacerbations who undergo ECMO.

Methods

We performed a pragmatic evidence synthesis with a meta-analysis.[2,3] This consisted of searching Medline, using the search terms of "(asthma*[Title/abstract]) AND (extracorporeal[Title/abstract])." The search results were screened by title and abstract. Potentially relevant articles underwent full-text review by one investigator (B. H. S.). *A priori* study selection criteria included the enrollment of adults with life-threatening asthma, performance of ECMO, and measurement of at least one of the following outcomes: inpatient mortality rate, weaning from ECMO, ICU length of stay, or complications. Case reports, studies with pediatric patients, and studies of extracorporeal CO_2 removal were excluded. We extracted proportions and SEs for mortality rate, weaning success rate, infection rate, and hemorrhage rate. We extracted means and SEs for ICU length of stay, hospital length of stay, and duration of mechanical ventilation. We calculated SEs when they were not reported. Weighted estimates were calculated by the generic inverse variance method in random effects model (ie, the DerSimonian and Laird method). Heterogeneity (defined as an I^2 statistic > 50%) was managed in a stepwise fashion as planned *a priori*:

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Author contributions: B. H. S. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, conceptualized the study, collected the data, performed the formal analysis, and wrote the manuscript. A. C. L. contributed to analysis design, reviewed and made critical edits to the manuscript. K. C. L. contributed analysis tools, designed the analysis, reviewed and made critical edits to the manuscript.

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None declared.

(1) the input data were confirmed, (2) studies were removed from the meta-analysis one at a time to identify which studies contributed to the heterogeneity, and (3) the responsible studies were compared with the other studies, and characteristics that might have contributed to the differing results were sought. If a reason for the differing results was identified and determined to render the aggregated results unreliable, the outlying studies were excluded.[4]

Results

The search identified 80 articles, from which the full text of six articles was reviewed. Five studies met inclusion criteria and were selected (Table 1).[1,5–9] The studies ranged in size from 10 to 272 patients (total, 449 patients). The in-hospital mortality rate estimated from all five studies was 8% (95% CI, 2%–14%). Inspection of heterogeneity revealed that the smallest studies gave outlying results (studies with only 10 and 16 patients had no deaths). Therefore, we excluded the outlying studies, which yielded an estimated in-hospital mortality rate of 16% (95% CI, 12%–20%) (n = 423 patients) (Fig 1). The weaning (from ECMO) success rate was 93% (95% CI, 81%–105%) (n = 288 patients) and the mean ICU length of stay was 10.18 days (95% CI, 8.18–12.18 days) (n = 137 patients).

Complications reported in these studies included hemorrhage and infection. Hemorrhage had an estimated frequency of 18% (95% CI, 2%–34%) when all studies that examined hemorrhage were included, which increased to 24% (95% CI, 9%–39%) (n = 423 patients) after an outlying study was excluded. Infection frequency was estimated to be 9% (95% CI, −3% to 20%) (n = 423 patients).

Discussion

We conducted an evidence synthesis and meta-analysis to estimate mortality, ECMO weaning success rate, ICU length of stay, and complication rates among patients with near-fatal asthma who received ECMO. We found that in patients receiving ECMO for life-threatening asthma, the hospital mortality rate was low, and most patients were successfully weaned off ECMO.

Our results suggest the in-hospital mortality rate for patients with near-fatal asthma who received ECMO is significantly lower than that among patients who receive ECMO for ARDS, with mortality rates ranging from 34% to 54.4% in the ARDS population.[10,11] Length of stay in the ICU was shorter for patients with near-fatal asthma (10.18 days compared with 29.7 days).[10] In contrast to patients with ARDS, most patients with near-fatal asthma exacerbations are successfully weaned off ECMO and survive to discharge.

The efficacy of ECMO for near-fatal asthma remains unclear without randomized, controlled trials comparing ECMO with standard care without ECMO in patients with near-fatal asthma. The observational study by Zakrajsek et al[5] is encouraging, having found that the mortality rate was lower among those who received ECMO compared with those who did not receive ECMO in near-fatal asthma; however, the effects of ECMO on other outcomes remain difficult to determine.

The main benefit of our study is that our meta-analysis provides a larger pool of patients with near-fatal asthma who received ECMO from which to draw conclusions about the effects of ECMO than any one study alone. Our results may provide clinicians with additional information when assessing whether ECMO would be appropriate for patients with near-fatal asthma.

Our meta-analysis has limitations. Without control groups in the studies, our results do not indicate whether ECMO is superior to standard care without ECMO. The complication categories are broad, and there is no stratification of severity of the complication. Our statistical method, generic inverse variance, places high weight on studies with a small SE, which favors large studies and studies with a small proportion of events. A consequence of the latter is that even small studies may be disproportionately weighted if events are rare, with potentially misleading results. Two studies used the Extracorporeal Life Support Organization Registry with overlapping time periods, and another study used an administrative database that also shares overlap with patients from the Extracorporeal Life Support Organization Registry; this limitation biases the results in favor of the registry. Our meta-analysis examined only inpatient outcomes; future work is needed to examine outcomes after hospital discharge. Finally, we did a pragmatic evidence synthesis rather than a full systematic review; this, in theory, risks missing relevant studies. We were reassured that this is unlikely, however, because a recent review article that performed a systematic literature search did not identify any additional studies.[9]

Our meta-analysis showed that most patients given ECMO for near-fatal asthma can be weaned off ECMO and survive. It provides information on the course, complications, and success rate for patients receiving ECMO for near-fatal asthma. Further study is needed to determine the ideal candidates for ECMO for near-fatal asthma and whether there is any mortality and morbidity benefit to using ECMO for near-fatal asthma compared with not using ECMO. There also may exist subsets of patients who are more or less likely to undergo successful weaning or who may experience complications from ECMO.

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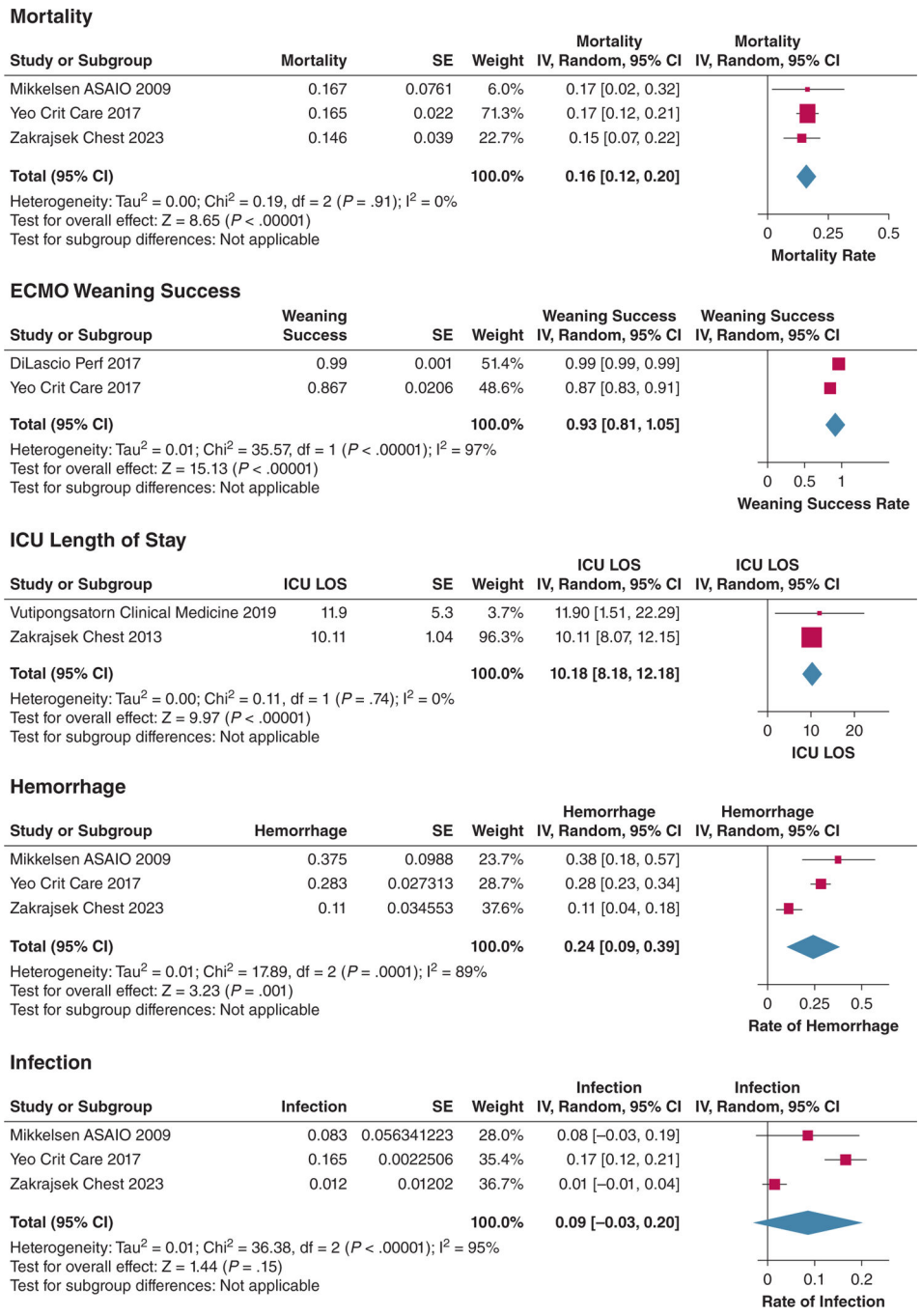

Figure 1 –.

Extracorporeal membrane oxygenation for life-threatening asthma: forest plots. ASAIO = American Society for Artificial Internal Organs; Crit Care = Critical Care; ECMO = extracorporeal membrane oxygenation; IV = inverse variance; LOS = length of stay; Perf = Perfusion.

TABLE 1]

Study Characteristics

Study/Year	No. of Patients	Population	Outcomes Reported
Zakrajsek et al[5]/2023	127	Retrospective, epidemiologic, observational cohort study using a national, administrative data set from 2010 to 2020	Mortality ICU LOS Hemorrhage Infection
Vutipongsatorn et al[6]/2019	10	Single center	Mortality ICU LOS
Yeo et al[1]/2017	272	Extracorporeal Life Support Organization (ELSO) Registry between March 1992 and March 2016	Mortality ECMO weaning Success rate Hemorrhage Infection
Di Lascio et al[7]/2017	16	Single center	Mortality ECMO weaning Success rate Hemorrhage
Mikkelsen et al[8]/2009	24	ELSO Registry from January 1986 to September 2006	Mortality Hemorrhage Infection

ECMO = extracorporeal membrane oxygenation; LOS = length of stay.