Conservative management of occult pneumothorax in mechanically ventilated patients: A systematic review and meta-analysis

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BACKGROUND: The aim of this systematic review was to investigate the safety and effectiveness of conservative management versus prophylactic intercostal catheter (ICC) insertion for the management of occult pneumothoraces in mechanically ventilated patients.

METHODS: PubMed, Embase, CINAHL, Web of Science, Cochrane Central, and other trial registries were searched. Eligible studies were critically appraised using standardized instruments. Meta-analysis was performed with mixed-methods logistic regression where appropriate and sensitivity analyses were performed with alternative statistical methods (Stata™ 15 or RevMan 5.3) or summarized in narrative. Randomized controlled trials (RCTs) and cohort studies were analyzed separately.

RESULTS: Twelve studies with a total of 354 participants were included; three RCTs (178 participants) and nine cohort studies (176 participants). The majority of the included studies, particularly the cohort studies, were well conducted. Two of the RCTs were rated as low quality. Statistically significant differences were observed in the RCT analysis: ICC insertion (any reason) (odds ratio, 2.86; 95% confidence interval, 1.26–6.43, 2 RCTs) in favor of prophylactic ICC; ICC complications (odds ratio, 0.12; 95% confidence interval, 0.02–0.62, 2 RCTs) in favor of conservative management. Nonstatistically significant differences were observed for progression of pneumothorax, ICC insertion (progression to simple pneumothorax), and ICC insertion (nonpneumothorax reasons). Results of analyses showed high imprecision (wide confidence limits). Conservative management showed a low rate of tension pneumothorax (2.8%). Complications were higher in the ICC group (19.5% vs. 5.8%).

CONCLUSION: Available evidence suggests that conservative management is safe for the management of occult pneumothoraces in mechanically ventilated patients, especially when undergoing short-term (<4 days) ventilation. We recommend that patients undergoing mechanical ventilation for a procedure alone and patients suspected to be ventilated less than 4 days can be conservatively managed. (*J Trauma Acute Care Surg.* 2021;91: 1025–1040. Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Systematic review and meta-analysis, level III.

KEY WORDS: Occult pneumothorax; mechanical ventilation; conservative management; intercostal catheter.

Occult pneumothorax is air within the pleural cavity that is diagnosed with a computed tomography (CT) scan which has not been suspected on the basis of preceding clinical examination or chest X-ray.[1–3] The overall incidence of occult pneumothorax in trauma patients is reported to be around 5%;[1,2] however, not all trauma patients receive a CT scan.

Computed tomography imaging for trauma is being utilized more frequently[4] and is increasingly safer, with faster scan times, higher resolution, thinner slices, and lower radiation doses delivered.[5,6] Consequently, diagnosis of occult pneumothorax is also more common.

Although occult pneumothoraces were first identified over 30 years ago, there is no consensus on the best management strategy; especially so with patients receiving mechanical ventilation. The principal source of trauma education internationally (the Advanced Trauma Life Support course) recommends that a patient with a known pneumothorax should not undergo general anesthesia or receive mechanical ventilation without having an intercostal catheter (ICC).[7] However, in selected circumstances (i.e., subclinical/occult pneumothorax), there is provision to opt for careful observation of the patient.[7] These guidelines highlight the risk of tension pneumothorax while receiving mechanical ventilation;[7] however, placement of an ICC does not remove the risk of tension pneumothorax, because of the risk of malpositioning, blocking, or kinking, and may actually delay the diagnosis of a tension pneumothorax because of the assumption that the pneumothorax has been effectively treated.[8] Intercostal catheter insertion also produces pain and has a high complication rate—reported at approximately 20%.[9] Inconsistencies in practice are confirmed by a survey completed in the United Kingdom, revealing disagreement between medical specialties that commonly manage this group of patients, with prophylactic placement of an ICC varying from 28% to 100%.[10]

Previous reviews that have addressed this topic included few studies and variable results for and against conservative management.[11,12] Neither of these previous reviews investigated mechanically ventilated patients specifically, nor provided a combined estimate of effect; however, they do highlight the ongoing inconsistencies of how best to manage occult pneumothoraces. Workplace experience has shown inconsistent practice in the management of occult traumatic pneumothoraces in mechanically ventilated patients and no clear rationale for the choice of management from one patient to another. The lack of consistent clinical practice can potentially lead to adverse outcomes for patients and potentially unnecessary interventions.

To investigate the management of occult pneumothorax in mechanically ventilated patients, a systematic review was performed to answer the following question: In the mechanically ventilated patient, is conservative management safe and effective for traumatic occult pneumothorax when compared with insertion of a prophylactic ICC?

METHODS

This review was conducted in accordance with an *a priori* protocol[13] and the methodology of JBI.[14] It has been reported according to the Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) guidelines,[15] and this review was prospectively registered on the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42019132958).

Study Identification and Eligibility

A comprehensive search was conducted on June 17, 2019. PubMed, EMBASE, CINAHL (EBSCO), Web of Science, and

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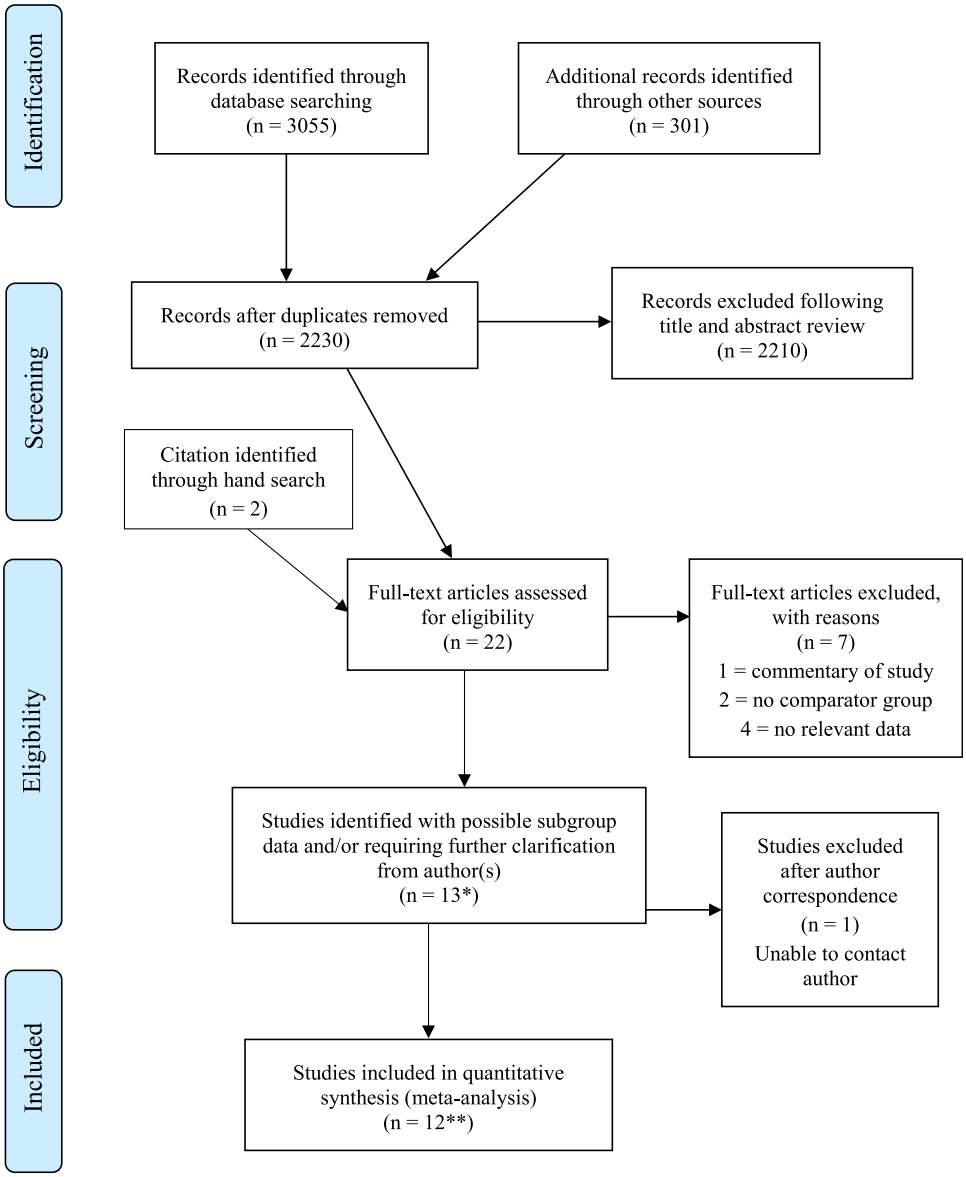
Cochrane Central Register of Controlled Trials were searched with no limitation on publication date or language. The search for unpublished studies included Clinicaltrials.gov, International Clinical Trials Registry, and the Australian and New Zealand Clinical Trials Registry. The search strategy is available in the supplemental data, http://links.lww.com/TA/C38). The reference lists of all included studies were screened for additional studies.

The review considered studies that included stable patients of any age, diagnosed with a traumatic (blunt or penetrating) occult pneumothorax on thoracoabdominal CT scan, who received mechanical ventilation. Eligible studies evaluated conservative management for occult pneumothorax compared with prophylactic ICC insertion. Occult hemopneumothoraces were excluded from the review. To fully inform both efficacy and adverse effects of treatment, randomized controlled trials (RCTs) and comparative prospective and retrospective cohort studies were considered for inclusion.

Studies reporting one or more of the following outcomes were considered: progression of pneumothorax, ICC insertion for any reason, incidence of tension pneumothorax, incidence of pneumonia/empyema, all-cause mortality, ICC insertion (tension pneumothorax), ICC insertion (progression to simple pneumothorax), ICC insertion (nonpneumothorax reasons), length of stay (LoS) in hospital and intensive care, duration of mechanical ventilation, duration of ICC, hemodynamic instability, pain, and analgesia requirements.



* *13 studies/15 publications*
**12 studies/14 publications

Figure 1. PRISMA diagram.

TABLE 1. Characteristics of Included Studies

Study	Setting/context	Participant characteristics	Participants	Stated outcomes	Description of main results/author's conclusion	Comments
Ball et al. 2005[36]	Study design: Retrospective cohort study Country: Canada Site: Level I trauma center, single center Period: June 2002 to July 2003	Inclusion criteria: All trauma patients with ISS >12, who had CT scan showing occult PTX Age: All ages Insertion technique: Blunt dissection with 28 or 32F ICC Trauma type: Blunt and penetrating CT scanner: chest/abdomen/pelvis or abdomen/pelvis, LightSpeed QZ/I-plus scanner with 5 mm slices	Total: 49 patients with occult PTX ICC group: 23 Conservative Mx group: 26 Ventilated subgroup: ICC group: 13 Conservative Mx group: 4	ICC placement ICU and hospital LoS Ventilation days Size of chest tube Chest tube complications Pulmonary complications	No serious complications resulted from conservative Mx; however, two patients in the conservative Mx group required an ICC for progression of PTX. 22% of patients with ICCs had tube-related complications or required repositioning. Authors concluded that due to ICC insertion often having adverse consequences, rethinking an algorithmic policy of prophylactic thoracostomy is crucial.	Ventilated subgroup: In the conservative Mx group there was one patient requiring ICC insertion for progression of PTX. In the ICC group there were 3 complications (one malpositioning and two vascular injuries).
Brasel et al. 1999[45]	Study design: RCT Country: United States Site: Multicenter (two centers) Period: January 1995 to December 1997	Inclusion criteria: All blunt trauma patients with occult PTX seen on abdominal CT Age: Over 18 years Insertion technique: 36F blunt dissection Trauma type: Blunt only CT scanner: CT scanner: abdominal, General Electric HiSpeed Advantage 10 mm slices Ventilation settings: TV 8–10 mL/kg Peak pressure limits 30–35 mm Hg	Total: 39 patients with 44 occult PTX ICC group: 18 Conservative Mx group: 21 Ventilated subgroup: ICC group: 9 Conservative Mx group: 9	Respiratory distress PTX progression Pneumonia Retained hemothorax Placement of ICC LoS Ventilator days	No difference in overall complication rate. No patient had respiratory distress related to the occult PTX or required emergent ICC placement. 20% of patients conservatively managed required chest tube placement. Authors concluded that conservative Mx is safe regardless of the need for mechanical ventilation.	Ventilated subgroup: 2 PTX progression occurred in conservative Mx group (requiring ICC placement) and 3 patients in ICC group (not requiring further ICC). No tension PTX in either group. Reason for ventilation: 3 patients in each group had ventilation for procedure only. 6 in each arm ventilated for greater or equal to 1 d.

Clements et al. 2021[37,38,40]	Study design: RCT Country: Canada Site: multicenter, regional trauma centers Period: October 2006 to February 2020	Inclusion criteria: Patients with occult PTX identified on CT Age: Over 18 years Insertion technique: Blunt dissection or Seldinger technique Trauma type: Blunt and penetrating CT scanner: Any site, model not specified	Total: ICC group: 64 Conservative Mx group: 69	Primary outcome: Composite variable denoting respiratory distress (defined as acute change from a "stable" baseline clinical state that required the urgent placement of an ICC, an acute increase by 0.2 FiO_2, requirement for pharmacological paralysis to improve ventilator synchrony, requirement for manual bag-mask ventilation or prone ventilation, or documentation of an adverse respiratory event in the medical record) "Failure" of observation was considered the need for formal pleural drainage. Secondary outcomes were divided into respiratory related (requirement for ICC, tracheostomy, ICC dwell time, ventilator associated pneumonia or acute respiratory distress syndrome) or global (death, ventilator days, ICU and hospital LoS) Drainage complications	23% ICC complication of which 73% had suboptimal ICC positioning. Risk of respiratory distress was similar between two groups. Failure of observation was rare (6%) for patients just ventilated for an operative procedure. There was a significant difference in the failure rates of patients ventilated for less than 4 d when compared with 4 or more days (17.6% vs. 41.3%) Authors have recommended that patients predicted to require more than short term PPV should receive an ICC by the most experienced clinicians or interventional radiologists in order to potentially avoid the all too common ICC complications that are frequently encountered in modern health care.	ICC insertion was required in 18 patients in conservative Mx group (2 tension PTX, 5 progression to simple PTX, 11 for non–PTX-related reasons) and in 10 patients in ICC group (4 for progression to simple PTX, 6 for non–PTX-related reasons). Mortality was 4 in the conservative Mx group and 6 in the ICC group. ICC complications occurred 15 times in ICC group (13 malpositioning). Incidence of pneumonia/empyema was 17 in observed group and 9 in ICC group.
Collins et al. 1992[35]	Study design: Retrospective cohort study Country: United States Site: Level 1 trauma center (University of California Irvine Medical Centre) Period: not specified	Inclusion criteria: Trauma patients undergoing CT scanning of abdomen and pelvis within 1 hour of arrival showing occult PTX Age: Not specified Insertion technique: "Standard fashion" Trauma type: Blunt only CT scanner: Abdomen/pelvis, model not specified	Total: 26 patients with 27 occult PTX ICC group: 13 Conservative Mx group: 14 Ventilated subgroup: ICC group: 6 Conservative Mx group: 7	Hospital and ICU LoS ICC dwell time Complications Mortality	Identified 2 significant complications of ICC insertion (intercostal artery laceration and self-removal). Conservative Mx produced 2 complications (one delayed PTX and one delayed hemothorax with possible delayed PTX), both resolved with placement of ICC. No patient developed tension PTX. 2 patients died, both considered unrelated to ICC or occult PTX.	Ventilated subgroup: There was one patient in each group requiring ICC placement (ICC group: progression of PTX due to self-removal of ICC, conservative Mx group: non–PTX-related reasons). 1 patient in each group died.

Continued next page

TABLE 1. *(Continued)*

Study	Setting/context	Participant characteristics	Participants	Stated outcomes	Description of main results/author's conclusion	Comments
Enderson et al. 1993[46]	Study design: RCT Country: United States Site: single center, University of Tennessee Medical Centre Period: October 1990 to May 1992	Inclusion criteria: Trauma patients undergoing abdominal CT showing occult PTX Age: "Adult" Insertion technique: Blunt dissection 36F Trauma type: Blunt and penetrating CT scanner: Abdominal scans, model not specified	Total: 40 occult PTX ICC group: 19 Conservative Mx group: 21 Ventilated subgroup: ICC group: 12 Conservative Mx group: 15	Major complications: Progression of PTX Empyema Pneumonia Minor complications: Atelectasis Hospital and ICU LoS	9 patients had complications in conservative Mx group (8 progression of PTX including 3 tension PTX, 1 pneumonia, 1 empyema, 3 atelectasis) and 8 patients in ICC group (1 pneumonia, 8 atelectasis). All progression of PTX happened to patients receiving mechanical ventilation. Results suggested that patients with occult PTX requiring mechanical ventilation are at significant risk for progression of their PTX and development of tension PTX. Therefore, ICC should be used in all patients with occult PTX requiring mechanical ventilation.	Ventilated subgroup: In conservative Mx group 8 patients had progression of PTX requiring ICC placement (including 3 tension PTX), 1 developed empyema following insertion of an ICC for progression of PTX. Reason for ventilation: All 15 in conservative Mx group and 10 out of 12 in the ICC group had an operation. However not stated if ventilation was required preoperation/postoperation.
Fulton & Bratu 2015[18]	Study design: Retrospective cohort study Country: Canada Site: single center, Stollery Children's hospital Period: January 2001 to December 2011	Inclusion criteria: Mechanically ventilated, ISS score >12 and a diagnosis of PTX (presence of occult PTX determined with chart review) Age: 0–17 years Insertion technique: Unspecified Trauma type: Blunt and penetrating to be included (however all patients had blunt) CT scanner: Abdomen +/− thorax, unspecified model	Total: ICC group: 0 Conservative Mx group: 19 (15 children)	Placement of ICC Progression of PTX Complications	All patients were successfully managed without the need for ICC. Results suggest that occult PTX in pediatrics can be managed without ICC.	There was no progression of PTX and no ICC insertions required in the conservative Mx group. Reason for ventilation: 6 of 19 patients had less than 24 hours ventilated.

Holmes et al. 2001[47]	Study design: prospective cohort study Country: United States Site: Single center, Level 1 trauma center Period: over 28-month period	Inclusion criteria: Blunt trauma patients undergoing abdominal CT Age: younger than 16 years Insertion technique: Unspecified Trauma type: Blunt only CT scanner: Abdominal scans, either 4th generation Toshiba-900 (5 mm slices) or helical CTi by General Electric (3 mm if <10 kg, 5 mm if 10–50 kg, 7 mm if >50 kg)	Total: 12 occult PTX (11 patients) ICC group: 1 Conservative Mx group: 11 Ventilated subgroup: ICC group: 1 Conservative Mx group: 2	Respiratory compromise Hemodynamic compromise ICC placement	Incidence of occult PTX in pediatric blunt trauma is low. ICC is infrequently required for occult PTX. Further RCT required.	Ventilated subgroup: No patient in either group had respiratory or hemodynamic compromise or need for ICC placement.
Lee et al. 2010[20]	Study design: Retrospective cohort study Country: Hong Kong Site: Prince of Wales Hospital, Shatin (university teaching hospital) Period: January 2006 to December 2007	Inclusion criteria: Severely injured patients with blunt chest trauma undergoing thoracic CT found to have occult PTX Age: All ages Insertion technique: Not specified Trauma type: Blunt only CT scanner: Thoracic CT, unspecified model	Total: 44 occult PTX (36 patients) ICC group: 8 Conservative Mx group: 36 Ventilated subgroup: ICC group: 8 Conservative Mx group: 8	Nature and number of complications Mortality	Patients that received mechanical ventilation in the trauma room were more severely injured (ISS 48 vs. 33) than those that received mechanical ventilation in the operating room. All those patients who were ventilated in trauma room received an ICC. No complications associated with conservative Mx. Since ICC is not without complication it may be possible to extend the concept of conservative Mx to those who received ventilation in trauma room within this study.	Ventilated subgroup: There were no complications or mortality in the conservative Mx group. In the ICC group there was 1 major complication (empyema) and 3 minor complications (persistent intercostal neuralgia and wound infection).

Continued next page

TABLE 1. *(Continued)*

Study	Setting/context	Participant characteristics	Participants	Stated outcomes	Description of main results/author's conclusion	Comments
Llaquet Bayo et al. 2016[21]	Study design: retrospective cohort study Country: Spain Site: single center, Level 2 teaching hospital Period: March 2006 to December 2013	Inclusion criteria: Multiple trauma patients diagnosed with occult PTX and admitted to critical care section of hospital Age: older than 16 years Insertion technique: Not specified Trauma type: Blunt and penetrating CT scanner: Thoracic and abdominal, model not specified	Total: 126 occult PTX ICC group: 53 Conservative Mx group: 73 Ventilated subgroup: ICC group: 26 Conservative Mx group: 16	Success rate of conservative management (considered failed if ICC required) Tension PTX rate Hospital and ICU LoS Mortality Drainage complications (poor positioning, loss, infection or bleeding	11% (8/73) failure of conservative Mx, 19% (3/16) in ventilated subgroup. 8 cases required ICC insertion: 5 for hemothorax, 3 for progression of PTX. 1 was prophylactical placed presurgery. 3 patients presented complications associated with the drainage (2 inserted into subcutaneous tissue; 1 lost position). Concluded that treatment of choice for occult PTX is clinical observation including in mechanically ventilated patients.	Ventilated subgroup: In the conservative Mx group 3 patients required ICC placement (1 for progression of PTX, 2 for non–PTX-related reasons). Mortality was 3 in conservative Mx group and 8 in ICC group. 2 complications of ICC in ventilated patients.
Notrica et al. 2012[22]	Study design: prospective cohort study Country: United States Site: multicenter, 16 institutions Period: 2008–2009	Inclusion criteria: Patients with traumatic occult PTX Age: younger than 18 years Insertion technique: At the discretion of attending surgeon Trauma type: Blunt and penetrating CT scanner: Unspecified site and model Ventilation settings: Average Tidal volume, 7.2 ± 1.1 mL/kg; average peak inspiratory pressure, 19.7 ± 5.2 mm Hg	Total: 52 occult PTX (51 patients) ICC group: 3 Conservative Mx group: 49 Ventilated subgroup: ICC group: 1 Conservative Mx group: 8	Placement of ICC Hospital and ICU LoS Ventilator days Indication for ICC Mortality Complications Average tidal volume and peak inspiratory pressure also measured	Only 2% (1/49) failed conservative Mx. 2 PTX progressed in size in conservative Mx group, only one required ICC. Authors concluded that this demonstrated safety of conservative Mx of occult PTX less than 16.5 mm. The physical discomfort, potential morbidity and risk of complications of ICC must now be compared with the relative safety of conservative Mx.	Ventilated subgroup: Neither group had progression of PTX nor need for ICC insertion. Reason for ventilation: 4 patients in conservative Mx group and 1 in ICC group underwent an operation.
Wilson et al. 2009[23]	Study design: retrospective cohort study Country: Canada Site: Multicenter, Used Nova Scotia Trauma Registry, Period: October 1994 to March 2003	Inclusion criteria: Blunt trauma patients with ISS >12 and PTX diagnosis (occult PTX was identified through review of imaging) Age: All ages Insertion technique: Not specified Trauma type: Blunt only CT scanner: Site or model not specified	Total: 68 occult PTX ICC group: 35 Conservative Mx group: 33 Ventilated subgroup: ICC group: 29 Conservative Mx group: 16	Hospital LoS Mortality Intervention and time to intervention (ICC placement and its relation to mechanical ventilation)	There were no instances of PTX progression or tension PTX in the observation group. LoS was longer in ICC group (10 vs. 7 d, $p = 0.01$), mortality similar. Conclusion from authors: conservative Mx may be safe.	Ventilated subgroup: No progression of PTX or tension PTX in either group. Reason for ventilation: In conservative Mx group, 16 patients had an operation. 10 of these received ventilation only for the operation.

Zhang et al. 2016[3]	Study design: retrospective cohort study Country: Singapore Site: single center, Tan Tock Seng Hospital Period: January 2009 to December 2012	Inclusion criteria: Patients in trauma database with an CT scan visualizing the thorax partially or fully showing occult PTX. Age: All ages Insertion technique: Not specified Trauma type: Blunt only CT scanner: 64 slice multidetector CT, any CT visualizing the thorax	Total: 83 occult PTX ICC group: 35 Conservative Mx group: 48 Ventilated subgroup: ICC group: 7 Conservative Mx group: 5	Hospital LoS Subsequent requirement for ICC Expanding PTX Wound infection Pleural effusion Empyema Mortality	Increased hospital LoS for ICC group (13 vs. 5.5 d, $p = 0.008$). No difference in mortality. 4/48 conservatively Mx patients had progression of PTX requiring ICC. ICC group 7/35 had complications and 3/35 had progression of PTX. Patients who had ICC were nearly 10 times more likely to have a complication (OR, 9.92). Authors advocated for conservative Mx in light of inherent ICC complications.	Ventilated subgroup: In the conservative Mx group, 1 patient required ICC placement for progression of PTX.

PTX, pneumothorax; Mx, management; ICC, intercostal catheter; MV, mechanical ventilation; TV, tidal volume.

Following the search, all records were collated and uploaded into Endnote X8.2 (Clarivate Analytics, Philadelphia, PA)[16] and duplicates removed. Titles and abstracts were then screened twice by one reviewer (J.A.S.) to determine eligibility. Potentially relevant studies were retrieved in full and their citation details imported into the JBI SUMARI software (JBI, Adelaide, Australia).[17] The full texts of selected citations were assessed in detail against the inclusion criteria by one reviewer (J.A.S.), and uncertainties that arose during inclusion were resolved through discussion with a second and third reviewer (P.S., E.A.).

Assessment of Methodological Quality and Data Extraction

Eligible studies were critically appraised by two independent reviewers (J.A.S., A.V.) using standardized critical appraisal instruments from JBI for experimental studies and comparable cohort studies.[14] Any discrepancies were resolved through discussion between the reviewers (J.A.S., A.V.). Appraisal criteria were specific to study design, therefore direct comparison between the studies designs was not possible. Randomized controlled trials were deemed higher quality evidence because of the nature of their study design.

Data were extracted from studies included in the review using a modified standardized data extraction tool.[14] The data extracted included specific details about the population (age, sex, and Injury Severity Score [ISS]), study methods, the intervention and comparator, and outcomes of significance to the review objective. Authors of the nine articles[3,18–25] published within the last 10 years were contacted to request missing or additional data and to clarify any details regarding study conduct.

Data Analysis

To account for sparse data, the presence of zero values, and group imbalances that were observed for the majority of outcomes, a mixed-methods logistic regression model was selected for the primary analysis. Logistic regression has been shown to perform well with rare events and also with group imbalance and does not require continuity correction,[26–31] and the mixed-methods model accounts for heterogeneity between studies while using a one stage approach.[29,32] Logistic regression was performed using Stata™ V15 (Stata Corp LLC, College Station, TX).[33] The impact of the chosen model on the effect size estimate was also explored using sensitivity analyses.[31] Models used for sensitivity analyses included Mantel-Haenszel (M-H) random effects model and Peto odds ratio (POR) for RCT data, and M-H fixed-effects model and POR for data extracted from included cohort studies.[26–28] Sensitivity analyses were performed using RevMan V5.3 (Copenhagen: The Nordic Cochrane Centre, Cochrane).[34]

Effect sizes were expressed as odds ratios and their 95% confidence intervals. Meta-analysis of experimental and observational data was completed separately for each outcome. In all analyses, raw event counts were used as adjusted estimates were not provided. Impact of sample size and event counts, that is, studies that appeared to have a marked influence in terms of their contribution to the overall effect in any analysis, were explored using sensitivity analysis. Any study that did not have complete data for a given outcome was not included in the meta-analysis

TABLE 2. Assessment of Methodological Quality Using JBI Critical Appraisal Tools[14]

Included studies	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Total
RCTs:														
Brasel et al.[45]	U	U	Y	N	N	U	N	Y	Y	U	U	Y	Y	5
Enderson et al.[46]	Y	Y	N	N	N	U	U	Y	Y	U	U	Y	Y	6
Clements et al.[37,38,40]	Y	Y	Y	N	N	U	Y	Y	Y	Y	Y	Y	Y	10
Total Y score (%)	66.6	66.6	66.6	0.0	0.0	0.0	33.3	100	100	33.3	33.3	100	100	
Cohort studies:														
Ball et al.[36]	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	Y			10
Collins et al.[35]	N	Y	Y	U	U	Y	U	U	Y	U	Y			5
Fulton & Bratu[18]	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	U			9
Holmes et al.[47]	Y	Y	Y	U	U	Y	Y	Y	Y	N	Y			8
Lee et al.[20]	Y	Y	Y	Y	U	Y	U	U	U	U	Y			6
Llaquet Bayo et al.[21]	Y	Y	Y	Y	U	Y	Y	Y	Y	Y	Y			10
Notrica et al.[22]	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y			10
Wilson et al.[23]	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	Y			10
Zhang et al.[3]	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y			10
Total Y score (%)	66.6	100	100	77.7	55.5	100	77.7	77.7	88.8	33.3	88.8			

Studies are rated as Yes (Y), No (N) or Unclear (U) for each question. An 'unclear' rating indicates that the relevant details could not be found in the articles and the data could not be ascertained (either due to the author being uncontactable or unable to provide additional information, or the article having been published over 10 years ago). Randomized controlled trials and cohort studies are reported separately.

Appraisal criteria for RCTs:

(1)Was true randomization used for assignment of participants to treatment groups? (2)Was allocation to treatment groups concealed? (3)Were treatment groups similar at baseline? (4)Were participants blind to treatment assignment? (5)Were those delivering treatment blind to treatment assignment?(6)Were outcome assessors blind to treatment assignment?(7)Were treatment groups treated identically other than the intervention of interest? (8)Was follow up completed and if not, were differences between groups in terms of their follow up adequately described and analyzed? (9)Were participants analyzed in the groups to which they were randomized? (10)Were outcomes measured in the same way for treatment groups? (11)Were outcomes measured in a reliable way? (12)Was appropriate statistical analysis used? (13)Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial)?

Appraisal criteria for cohort studies:

(1)Were the two groups similar and recruited from the same population? (2)Were the exposures measured similarly to assign people to both exposed and unexposed groups? (3)Was the exposure measured in a valid and reliable way? (4)Were confounding factors identified? (5)Were strategies to deal with confounding factors stated? (6)Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)? (7)Were the outcomes measured in a valid and reliable way? (8)Was the follow up time reported and sufficient to be long enough for outcome to occur? (9)Was the follow up complete, and if not, were reasons to los to follow up described and explored? (10)Were strategies to address incomplete follow up utilized? (11)Was appropriate statistical analysis used?

for that outcome; rather, the available study results were considered and included in a narrative summary, where appropriate.

RESULTS

Search and Study Selection

Searches of databases and trial registries returned a total of 3,356 records; following removal of duplicates, the titles and abstracts of the remaining 2,230 unique records were screened (Fig. 1). Following exclusion of 2,210 records, 20 were eligible for retrieval and review. Two further articles[35,36] of interest were identified from the reference lists of full text articles. Overall, 22 full text articles were assessed for eligibility. One of the articles[37] described a pilot of a later published study[38] and a further article described an interim analysis[19] of the same study.[38] Where appropriate, data from these articles[19,37] have been amalgamated with the later report[38] and treated as one study. Seven[24,39–44] articles were excluded following full-text review (Fig. 1). One further article,[25] which did not include occult pneumothorax as a subcategory among their published data, was excluded following unsuccessful attempts to contact the authors. Overall, 12 studies were included (14 articles), comprising three RCTs and nine cohort studies (two prospective and seven retrospective), with a total of 354 participants (178 in the RCTs and 176 in the cohort studies) (see Fig. 1).

Characteristics of Included Studies

Characteristics of the included studies are reported in Table 1. Of the included studies, one RCT[38] recruited only mechanically ventilated patients, while two[45,46] recruited patients regardless of their mechanical ventilation status. One cohort study[18] included only mechanically ventilated patients, the remaining eight[3,20–23,35,36,47] included patients receiving mechanical ventilation and patients who were breathing without mechanical support.

The three RCTs[38,45,46] included adult patients only. Three[18,22,47] of the nine cohort studies included only pediatric patients, one[21] included patients older than 16 years, and the remaining[3,20,23,35,36] included all ages. Two RCTs were conducted in the United States[45,46] and one in Canada.[38] Three cohort studies were conducted in Canada[18,23,36] and the United States,[22,35,47] and one in Hong Kong,[20] Singapore,[3] and Spain,[21] respectively.

Methodological Quality of Included Studies

In two of the included RCTs[38,46] it was clear that appropriate randomization and allocation concealment was used. Two trials[38,45] had similar treatment groups. Because of the nature of the intervention, none of the trials could blind either patient or clinician, however it was unclear if assessors were blinded to treatment allocation. Treatment groups were treated identically other than the intervention of interest in one trial,[38]

TABLE 3. Results of Logistic Regression Analyses and Statistical Model Sensitivity Analyses (M-H and POR meta-analyses) Comparing Conservative Management of Occult Pneumothoraces with ICC Insertion

Outcomes	No. Studies	LR OR, Effect Size (95% CI)	M-H OR, Effect Size (95% CI)	POR, Effect Size (95% CI)
Progression of PTX				
RCTs	3	2.18 (0.86–5.50)	2.00 (0.33–12.15)	2.11 (0.89–4.99)
Cohort studies	6	2.58 (0.39–17.09)	1.54 (0.31–7.56)	1.69 (0.21–13.49)
ICC insertion (any reason)				
RCTs	2	2.86 (1.26–6.43)	5.05 (0.37–68.45)	2.73 (1.30–5.72)
Cohort studies	6	1.78 (0.45–7.04)	1.74 (0.45–6.7)	1.77 (0.45–7.01)
ICC insertion (progression to simple PTX)				
RCTs	3	2.94 (0.90–9.59)	2.70 (0.58–12.55)	2.66 (0.95–7.46)
Cohort studies	6	3.7 (0.29–47.8)	2.11 (0.42–10.64)	3.57 (0.32–39.54)
ICC insertion (non-PTX reason)				
RCTs	2	1.77 (0.61–5.10)	**	**
Cohort studies	6	1.72 (0.31–9.5)	1.71 (0.37–7.83)	1.71 (0.31–9.55)
ICC complications				
RCTs	2	0.12 (0.02–0.62)	**	**
Cohort studies	5	†	1.25 (0.22–7.12)	0.30 (0.02–4.0)
Incidence of pneumonia/empyema				
RCTs	1	1.92 (0.79–4.70)*		
Cohort studies	3	0.7 (0.19–2.5)	0.73 (0.21–2.47)	0.7 (0.21–2.47)
Mortality (all cause)				
RCTs	1	0.58 (0.15–2.14)*		
Cohort studies	3	0.36 (0.1–1.27)	0.4 (0.12–1.31)	0.41 (0.13–1.24)

*Calculated odds ratio only as meta-analysis not possible.
**Two stage meta-analysis unable to be performed due to double arm zero event count in one RCT.
†Logistic regression meta-analysis unable to be performed due to zero events in conservative management group of all included cohort studies.
‡Two stage meta-analysis unable to be performed due to double arm zero event count in one RCT, calculated odds ratio and 95% CI are presented for remaining RCT.
Visual representation of these results are presented in Figure S1, http://links.lww.com/TA/C38 for RCTs and Figure S2, http://links.lww.com/TA/C38 for cohort studies.
Individual M-H and POR meta-analyses forest plots can be found in supplemental data (see Figs. S2-S11, http://links.lww.com/TA/C38).
LR, logistic regression; OR, odds ratio; CI, confidence interval.

it was unclear in Enderson et al.,[46] and in Brasel et al.,[45] the conservative management group had signs posted indicating participants had an undrained pneumothorax. Follow-up was complete, and all participants were analyzed in their allocated groups. Two trials[45,46] did not indicate how they measured progression of pneumothorax. Appropriate statistical analysis was completed, and appropriate study design was used in all RCTs. Two RCTs[45,46] were rated as low quality because of the incomplete information provided in their methods, including absence of a Consolidated Standards of Reporting Trials (CONSORT) diagram, which could not be clarified with the authors because of the time that had elapsed since publication (see Table 2).

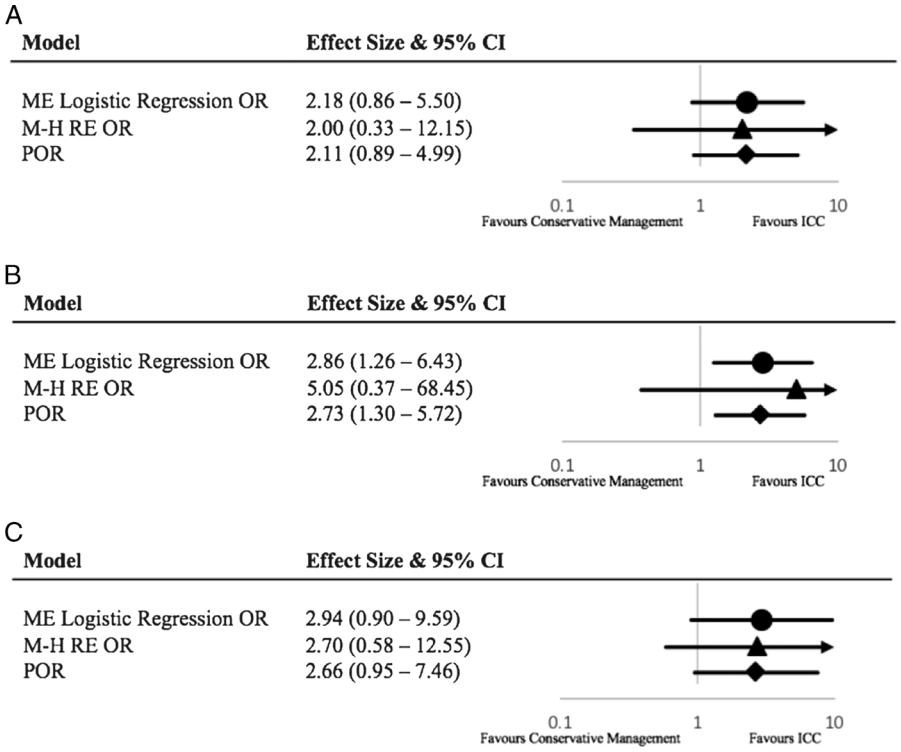
Considering the included cohort studies (see Table 2), six[20–23,36,47] had similar populations, and all nine measured the exposure in a consistent way. Confounding factors were identified in seven studies,[3,18,20–23,36] with five studies[3,18,22,23,36] explaining how they dealt with these confounding factors. However, no study adjusted effect estimates for the stated confounding factors. Participants in all the studies were free of the outcome at the beginning of the study. Outcomes were measured in a reliable way, and follow-up times were stated in seven studies,[3,18,21–23,36,47] while eight[3,18,21–23,35,36,47] stated their follow-up rates. Three studies[3,18,21] stated how loss to follow-up was addressed. Appropriate statistical methods were used in eight studies.[3,20–23,35,36,47] Overall, five[3,21–23,36] of the nine cohort studies rated well for methodological quality (See Table 2).

Progression of Pneumothorax and ICC Insertion

There was a statistically significant difference favoring ICC insertion for the outcome of ICC insertion for any reason (informed by two RCTs, including high-quality trial). There was also a nonstatistically significant trend toward ICC insertion for progression of pneumothorax (informed by all three RCTs, including low and high qualities) (see Table 3; Fig. 2). Logistic regression analysis of the cohort studies shows similar, although nonstatistically significant results in these two outcomes (see Table 3; Fig. S1, http://links.lww.com/TA/C38).

The trial by Enderson et al.[46] contributes to both of these outcomes, with higher incidence reported than the other RCTs. Exploring the impact of this study via sensitivity analyses shows the effect estimate for progression of pneumothorax in the RCT logistic regression analysis and the calculated logistic regression OR from the remaining RCT[38] in ICC insertion (any reason) substantially decreasing (see Table 4).

There was a trend toward the ICC group for the outcomes of ICC insertion for progression to simple pneumothorax and nonpneumothorax reasons for analysis of both RCTs and cohort studies (Table 3). The impact of the study by Enderson et al.[46] was also explored in the outcome of ICC insertion (progression



CI – confidence interval, ME – mixed effects, M-H – Mantel-Haenszel, RE – random effects, POR – Peto odds ratio, OR – odds ratio

***A** – progression of pneumothorax: three RCTs*
***B** – ICC insertion (any reason): two RCTs*
***C** – ICC insertion (progression to simple pneumothorax): three RCTs*

Figure 2. Visual representation of calculated effect estimates from logistic regression meta-analysis and statistical model sensitivity meta-analyses of included RCTs.

to simple pneumothorax), where the sensitivity analysis shows a significant reduction in the effect estimate (see Table 4). Sensitivity analyses changing the statistical model of choice for these outcomes align with the findings of the primary analyses (see Table 3).

Complications, Mortality, LoS, and Other Outcomes

The incidence of tension pneumothorax was low in both the conservative management and ICC groups. Five instances were reported (2.8%) in the conservative management group, all in the included RCTs.[19,46] Three of these five cases were reported by Enderson et al.[46] There was one incident of tension pneumothorax (0.5%) in the ICC group, reported in a cohort study.[21] All tension pneumothoraces required placement of an ICC.

In the RCTs and cohort studies combined, overall ICC complications occurred in 19.5% of patients in the ICC group and in 5.8% of patients conservatively managed when an ICC was

TABLE 4. Sensitivity Analyses Exploring the Impact of Enderson et al.[46]

Outcomes	No. Studies	LR OR, Effect Size (95% CI)	M-H OR, Effect Size (95% CI)
Progression of PTX			
RCTs	3	2.18 (0.86–5.50)	2.00 (0.33–12.15)
Without Enderson et al.[46]	2	1.05 (0.38–2.94)	01.08 (0.38–3.06)
ICC insertion (any reason)			
RCTs	2	2.86 (1.26–6.43)	5.05 (0.37–68.45)
Without Enderson et al.[46]	1	1.84 (0.77–4.35)*	
ICC insertion (progression to simple PTX)			
RCTs	3	2.94 (0.90–9.59)	2.70 (0.58–12.55)
Without Enderson et al.[46]	2	1.67 (0.47–5.97)	1.52 (0.44–5.32)

*Calculated odds ratio only as meta-analysis not possible.
Individual M-H and POR meta-analyses forest plots are presented in supplemental data (see Figs. S2, S4 and S8, http://links.lww.com/TA/C38).

required to be inserted; this was statistically significant in the RCT analysis (Table 3). Considering the cohort studies that informed ICC complications, there were a small number of patients and no incidents in the conservative management group, therefore, logistic regression could not be performed; M-H and POR meta-analyses showed marked variation in results because of the small numbers and continuity correction for the M-H analysis (Table 3). A breakdown of the ICC complications that occurred can be found in the supplementary data (Table S1, http://links.lww.com/TA/C38). Of the 13 malpositioning complications, 11 required a replacement ICC; subjecting the patient to a second procedure.

There was no statistically significant difference in the incidence of pneumonia/empyema; however, there were contradictory effect estimates between the RCT and cohort study data (see Table 3).

For the outcome of all-cause mortality, the cohort study primary analysis shows a trend towards conservative management. The calculated logistic regression odds ratio from the one RCT[38] that reported mortality data supports the cohort study primary analysis (see Table 3).

Randomized controlled trial[38] data showed no difference in intensive care unit (ICU) or hospital LoS; however, the data from two cohort studies[21,35] suggested that the conservative management group had a shorter ICU and hospital LoS, with the difference between groups being more pronounced in the ICU LoS (Supplemental data: Table S2 and S3, http://links.lww.com/TA/C38). There is no difference in the reported duration of mechanical ventilation between the two groups, reported in two RCTs[38,45] (Supplemental data: Table S4, http://links.lww.com/TA/C38). Hemodynamic instability was reported in only one cohort study,[21] with no difference between the groups. In the conservative management group of Clements et al.,[38] there were four instances of hemodynamic instability; two were due to tension pneumothoraces, one from a splenic laceration, and a further that was unexplained. Duration of ICC dwell was recorded in only the ICC group of two studies[35,38] (Supplemental data: Table S5, http://links.lww.com/TA/C38), the duration of dwell for ICCs inserted in the conservative management group wasn't recorded in any of the included studies. Pain and analgesia requirements were not reported in any of the included studies.

DISCUSSION

The results of this systematic review suggest that conservative management is safe, with 76% of patients avoiding an invasive procedure; also, the low incidence of tension pneumothoraces and the statistically significant lower rate of ICC complications when an ICC is required to be inserted appear to reinforce the safety of conservative management. Interestingly, the study by Clements et al[38] showed a significantly lower "failure" of conservative management (defined as the need for ICC insertion) in patients requiring short term ventilation (less than 4 days), and this is lower again if ventilated for a procedure only.

Prophylactic ICC insertion is more effective in reducing the need for an ICC to be inserted for any reason; further there is a trend toward prophylactic ICC insertion for the outcomes of progression of pneumothorax, ICC insertion (progression to simple pneumothorax) and ICC insertion (nonpneumothorax reasons).

Despite the limits of the evidence in this review (small sample sizes, variable study quality, and imprecision in many of the results), and given the noninvasive nature of conservative management, the low incidence of tension pneumothorax, the highly monitored environment in which mechanically ventilated patients are cared for, and the evident harms associated with ICC insertion; the available evidence demonstrates that conservative management is safe and appropriate, especially in patients undergoing short-term ventilation. The risk-benefit of ICC insertion appears to shift for patients requiring long-term (>4 days) mechanical ventilation, although the sample size is small.

The outcomes of progression of pneumothorax, ICC insertion for any reason, and ICC insertion for progression to simple pneumothorax in the RCT analysis were heavily skewed in favor of the ICC group by the study by Enderson et al.,[46] which reported a much higher incidence of progression of pneumothorax than the other two RCTs.[38,45] The reason for this higher incidence is unclear from the information provided, however it can be speculated that the common ventilator settings of the time may have contributed to it. Prior to the seminal ARMA study from the Acute Respiratory Distress Syndrome Network (ARDSNet),[48] tidal volumes of 10–12 ml/kg were common, with concomitant high airway pressures. Since then, a shift towards the routine use of lower tidal volumes (6–8 ml/kg) has been accepted,[49–52] which results in lower airway pressures. Since it is thought to be the trans-pulmonary pressure gradient that is responsible for the progression of pneumothorax, lower pressures intuitively result in a reduced incidence of progression. Unfortunately, tidal volumes were not reported in the study by Enderson et al.[46] Sensitivity analyses performed to explore the influence of this study[46] suggested that the risk of progression of pneumothorax and ICC insertion (progression to simple pneumothorax) were decreased compared with the primary analyses. The use of a bag-valve-mask for transport to/from ICU may pose a similar problem with the inability to control tidal volumes often leading to high volumes being provided.[53] The short duration of use may not cause a problem; however, the alternative would be a transport ventilator.

For some outcomes, there were noticeable differences between effect estimates from RCTs and cohort studies; these included contradictory results in the incidence of pneumonia/empyema and decreased LoS in both hospital and ICU in the conservative management group in the cohort studies. This may be because of the differences in how confounding factors were handled between study designs. It is likely that in the cohort studies, more severely injured patients would be preferentially chosen to receive an ICC if they had an occult pneumothorax. This potential bias would explain the higher incidence of pneumonia/empyema and longer time in ICU/hospital for the ICC group in the cohort studies. The only objective evidence to support the acuity of included patients was the ISS, however there was no significant difference in the baseline characteristics of the cohort studies.

When comparing the safety of the two management strategies, the major concerns with conservative management are progression of pneumothorax, tension pneumothorax, and need for ICC insertion. Progression of pneumothorax occurred in less than one in nine patients. Since Enderson et al.[46] in 1993, there have been three tension pneumothoraces reported, two in ICC group, and one in conservative management group. It is important to note that the insertion of an ICC does not completely

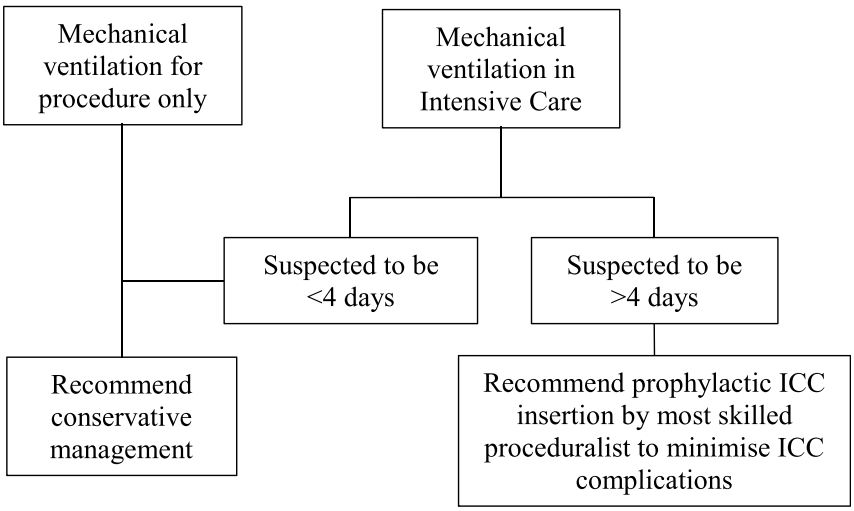


Figure 3. Recommended treatment algorithm.

negate the risk of tension pneumothorax. 76% of patients in the conservative management group did not require ICC insertion.

As an invasive procedure ICC insertion is not without risks. The total incidence of ICC complication in this analysis was 16.7% (19.5% in the ICC group), in keeping with previously published literature.[9,54–58] The incidence was higher in the ICC group; possible explanations for this include suboptimal conditions in urgent ICC insertion and easier insertion following pneumothorax progression. When an ICC is inserted for progression of pneumothorax or hemothorax in patients managed conservatively, there is often time to ensure optimal conditions and positioning are used (except in the case of a tension pneumothorax). In the case of insertion of an ICC for pneumothorax, placement of a large-bore ICC will be easier after it has progressed, as there will be more space within the pleural cavity; this also allows for insertion of a pigtail drain via the Seldinger technique.

There is growing evidence to support the use of pigtail drains for traumatic chest injuries. An RCT[59] reported significantly lower pain scores in patients who received a pigtail drain versus a large-bore ICC on the day of insertion and over the days after insertion. The same authors also investigated the effectiveness of pigtail catheters for drainage of pneumothoraces, with comparable efficacy to wide bore ICCs.[60] The comparable efficacy was confirmed by two meta-analyses.[61,62] One study[38] reported the method used for ICC insertion in the conservative management group, with pigtail drain used in five of 18 and the remaining 13 receiving a surgical ICC. It would be interesting to ascertain whether the use of a pigtail catheters for progression of pneumothorax improves outcomes.

Limitations inherent to this systematic review include small sample sizes and sparse data, which led to high imprecision (wide confidence intervals) for the majority of outcomes and low certainty of the findings from this review as a consequence. The screening process was, for the most part, performed by one reviewer, which increases the risk of omitting relevant articles. Care was taken at all stages to ensure there were no errors of omission. There is also likely to be available data that were not included in this systematic review because of the inability to access it. All but two[18,38] of the included studies included ventilated patients as a subset of the total study participants, these studies, for the most part, did not report the outcomes for ventilated patients separately, hence these data were lost to this systematic review.[22,23,36,46,47] Some data were clarified with the authors; however, many of the studies were conducted over 10 years ago, and the data are no longer available, and some authors did not respond to correspondence. In addition, two cohort studies[3,23] did not report complete data for the ICC group, especially for the ventilated subgroup. Because of this, data from these two studies could not be included in any analyses.

Compared with the previous 'mini-reviews',[11,12] this review included a higher number of patients within the RCTs and cohort studies, and more outcomes were assessed. This provides a more complete picture of the benefits, harms, and adverse effects of both management strategies. The results of this review are in keeping with the findings of previous reviews, however the more explicit methods used, and the larger evidence pool increase the certainty in our findings. Ideally, further large multicenter RCTs are required too fully address this question as the evidence is still limited in this review. There have, however, been difficulties in performing these with the largest RCT recruiting only 133 patients over a 14-year period, with the trial eventually being terminated early because of the stated protocol violations and study fatigue.[38]

CONCLUSION

More evidence is required to fully inform the effectiveness of conservative management for occult pneumothoraces in mechanically ventilated patients. However, the evidence we have to date suggests that conservative management is a safe alternative to prophylactic ICC insertion for the initial management of occult pneumothoraces in mechanically ventilated patients, provided that the patients are in a highly monitored environment, the treating clinicians are aware that the patient has an occult pneumothorax and that there is appropriate staff available to recognize and treat tension pneumothorax if it occurs. If admission is to a facility that lacks the immediate availability of

appropriately trained critical care staff, consideration should be given to referral and transfer or early prophylactic ICC insertion. To promote consistency in practice, clear guidelines should be created, aligning which patients can be conservatively managed and how progression of pneumothorax is to be monitored. We would recommend that patients undergoing mechanical ventilation for a procedure alone and those patients thought to be unlikely to require ventilation beyond 4 days can be safely managed conservatively. If a patient is suspected to required prolonged ventilation (i.e., traumatic brain injury, severely injured multitrauma) then insertion of a prophylactic ICC by an experienced proceduralist (to reduce the risk of ICC complications) is recommended (see Fig. 3).

AUTHORSHIP

J.A.S., E.A., P.S. participated in the study design. J.A.S. participated in the literature search, data collection, and analysis. J.A.S., E.A., P.S. participated in the data interpretation. J.A.S. participated in the writing of the article. E.A., P.S. participated in the critical revision.

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DISCLOSURE

The authors declare no funding or conflicts of interest.

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