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REVIEW ARTICLE

Definitions of hospital-acquired pneumonia in trauma research: a systematic review

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Abstract

Purpose What are reported definitions of HAP in trauma patient research?

Methods A systematic review was performed using the PubMed/MEDLINE database. We included all English, Dutch, and German original research papers in adult trauma patients reporting diagnostic criteria for hospital-acquired pneumonia diagnosis. The risk of bias was assessed using the MINORS criteria.

Results Forty-six out of 5749 non-duplicate studies were included. Forty-seven unique criteria were reported and divided into five categories: clinical, laboratory, microbiological, radiologic, and miscellaneous. Eighteen studies used 33 unique guideline criteria; 28 studies used 36 unique non-guideline criteria.

Conclusion Clinical criteria for diagnosing HAP—both guideline and non-guideline—are widespread with no clear consensus, leading to restrictions in adequately comparing the available literature on HAP in trauma patients. Studies should at least report how a diagnosis was made, but preferably, they would use pre-defined guideline criteria for pneumonia diagnosis in a research setting. Ideally, one internationally accepted set of criteria is used to diagnose hospital-acquired pneumonia.

Level of evidence Level III.

Keywords Hospital-acquired pneumonia · Trauma patient research · Clinical definition · Guideline criteria · Diagnostic criteria · Diagnosis

Abbreviations

ATS	American Thoracic Society
BSAC	British Society for Antimicrobial Chemotherapy
CDC	Centers for Disease Control and Prevention
ECDC	European Center for Disease Prevention and Control
HAP	Hospital-acquired pneumonia
IDSA	Infectious Disease Society of America
SIR	Swedish Intensive Care Registry
VAP	Ventilator-associated pneumonia

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Background

Nosocomial pneumonia is among the most frequent complications in trauma patients and is associated with increased mortality and poor prognosis [1–3]. The incidence of nosocomial pneumonia ranges from 4.3 to 38.3% in the literature, and this wide variety may cast doubt on the individual studies' comparability [4, 5].

Several types of nosocomial pneumonia have been described in the literature [6]. Most guidelines on nosocomial pneumonia create a distinction between hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) [7–9]. Although VAP essentially is a particular

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type of HAP, the etiology is not the same. In VAP, endotracheal intubation enables upper respiratory tract colonization by inserting a foreign body; therefore, the two pneumonia types should not be considered equivalent [10]. Nonetheless, the diagnostic criteria are similar for HAP and VAP in most guidelines, though they differ in the exact duration of mechanical ventilation and the time between mechanical ventilation and pneumonia onset to distinguish VAP from HAP [7–9].

To diagnose hospital-acquired pneumonia, microbiologic diagnostics are superior to clinical symptoms or radiologic examination [10]. Collecting sputum or tracheal secretions has high sensitivity but low specificity, while bronchoalveolar lavage and comparable methods have both high sensitivity and specificity. However, as fluid is introduced into the lungs, bronchoalveolar lavage is generally unsuitable for non-mechanically ventilated patients and is, therefore, mainly used to diagnose VAP [11]. Thus, HAP diagnosis is reliant on clinical criteria.

The combination of varying incidence and diagnostic criteria reliance raises the question of what criteria have been previously used to diagnose HAP in trauma patient research [12, 13]. Potentially, HAP incidence varies because of the use of different diagnostic criteria. Therefore, this systematic review was conducted to create an overview of reported definitions of hospital-acquired pneumonia in trauma research.

Methods

This systematic review was performed according to the Preferred Reporting Items for Systematic research and Meta-Analysis (PRISMA) checklist and registered on PROSPERO (review identification number CRD42022350131) [14].

Search strategy and execution

A literature search was performed in PubMed/MEDLINE. The search syntax was constructed to identify studies that stated a definition for pneumonia (Supplemental Table 1) from initiation to September 2019. The search syntax included the following: the MeSH terms and subheadings "Wounds and Injuries," "Injuries," "Pneumonia," "Incidence," "Prevalence," "Risk Factors," and "Prevention and Control"; keywords derived from the MeSH terms and subheadings; and additional keywords on trauma patients, clinical criteria, definitions, prediction, and prophylaxis. Animal studies were excluded from the syntax.

Review process

The search results were imported into Rayyan for processing [15]. Rayyan is a free online tool that helps researchers conduct systematic reviews. Studies in trauma patients with a reported definition of HAP were included, with no limitations set on the type of trauma. We excluded certain study populations (pediatric, burns, (near-)drowning, non-traumatic fractures, postmortem), other entities of pneumonia or pulmonary complications (solely as an outcome or mixed with HAP), non-original research papers, and studies in a language other than English, Dutch, or German. We assumed that all Intensive Care Unit admitted patients were at risk for VAP unless stated differently. Subsequently, we excluded studies that did not use clinical criteria to diagnose HAP but presented references to these studies separately in Supplemental Table 2.

One reviewer (TK) assessed the in- and exclusion stepwise: first, the patient population; second, the pneumonia outcome; and lastly, other remaining criteria. The same reviewer assessed the methodological quality using the MINORS criteria: a clarification of used criteria can be found in Supplemental Table 3 [16]. The possible score on the MINORS criteria ranges from 0 (lowest) to 24 (highest) for comparative studies. In non-comparative studies, 16 is the highest possible score. Any borderline cases were discussed with a second reviewer (DS) before definitive in-/exclusion or quality scoring.

For each study, the following data were obtained: first author, year of publication, study period, study design, cohort size, and the applied diagnostic criteria. All data extraction was conducted by one reviewer (TK).

Results

The PubMed/MEDLINE database search resulted in 5758 studies. One hundred and sixteen studies were eligible for the qualitative comparison; seventy studies (60%) did not use clinical criteria to diagnose HAP (e.g., medical records or ICD-codes; Supplemental Table 2). The remaining 46 studies were included in the qualitative analysis [12, 17–64]. The study selection process is summarized in the PRISMA flowchart (Fig. 1). The included studies were performed retrospectively (21/46) and prospectively (25/46). Table 1 shows the baseline characteristics of the included studies.

Diagnostic criteria

Forty-eight unique criteria were described in the included studies. We divided the criteria into five main categories: clinical (pulmonary symptoms and vital signs), laboratory (e.g., C-reactive protein, leukocytes), microbiologic (cultures or pathology), radiologic (X-ray or computed tomography), and miscellaneous (prescribed antibiotics and diagnosis in the medical health record). Radiologic criteria were most commonly used in the included studies (45/46) [12,

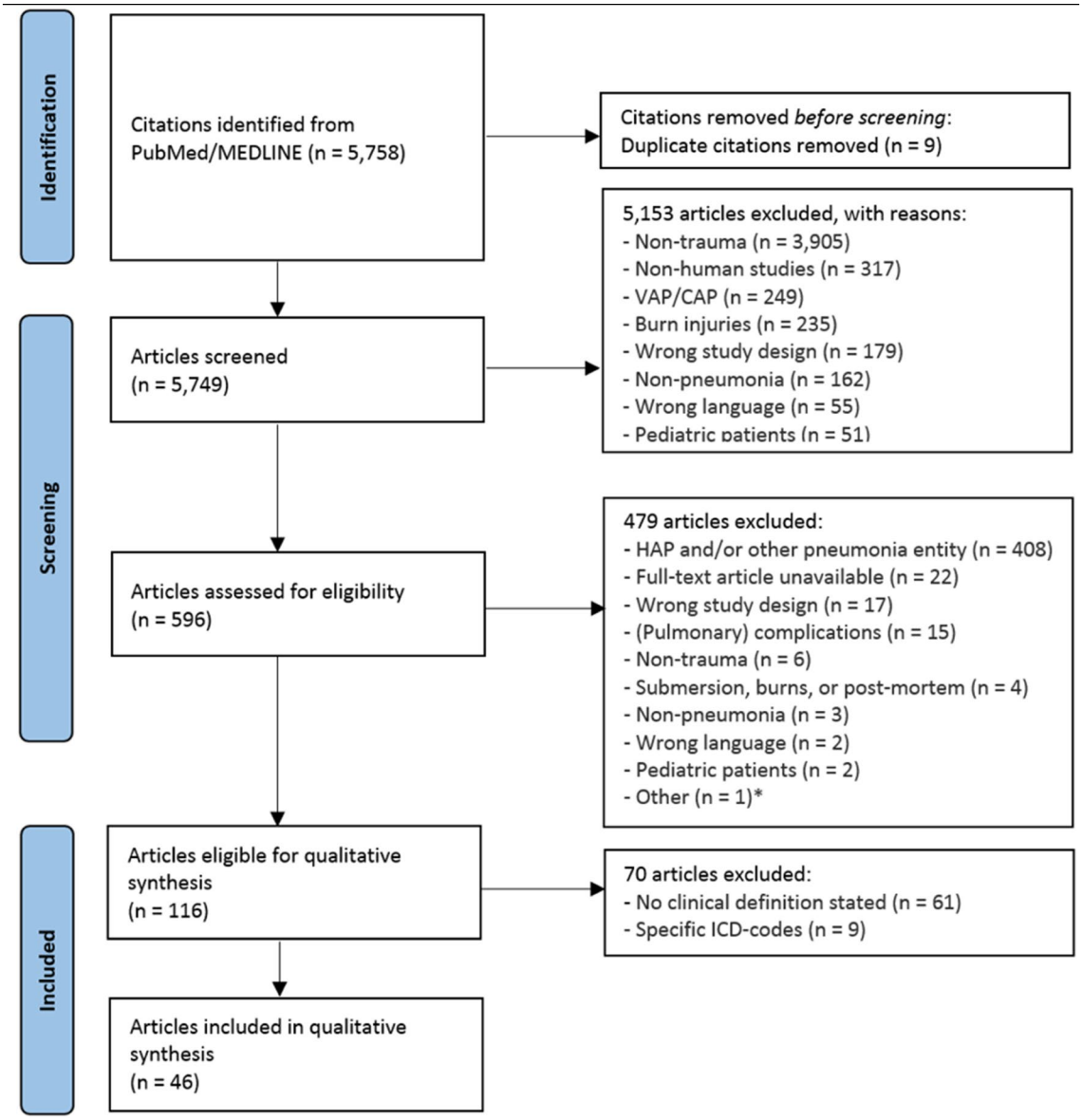


Fig. 1 The PRISMA flow diagram, illustrating the in- and exclusion process of studies on trauma patients with a reporting, clinical definition of HAP

18–63]. Clinical, laboratory, and microbiologic criteria were applied in 72, 28, and 39 percent of the included studies, respectively. Miscellaneous criteria were present in eight studies: four studies with only non-guideline criteria [12, 28, 30, 61] and as an addition to guideline criteria in the other four other studies [26, 27, 45, 48].

Guideline criteria were used to diagnose HAP in 18 out of 46 studies (Table 2). The five guidelines that were used originated from the United States of America or Europe: the Centers for Disease Control and Prevention (CDC), the European Center for Disease Prevention and Control (ECDC), the American Thoracic Society/Infectious Disease Society of America (ATS/IDSA), the Swedish Intensive Care Registry (SIR), and the British Society for Antimicrobial Chemotherapy (BSAC). The CDC criteria were cited in 13 out of 18 studies, whereas the ATS/IDSA, ECDC, SIR, and BSAC guidelines were used in the remaining four studies. Two studies applied the criteria of two different guidelines:

Table 1 Baseline characteristics of included studies

Author	Year	Country	Study period	Design	Cohort size	Study quality[§]
Seok [19]	2019	Korea	2013–2018	Retrospective, observational, single-center study	207	14
Conradsson [20]	2019	South Africa	2013–2014	Prospective, population-based cohort study	139	14
Warren [18]	2019	United States	2014–2016	Quasi-experimental pretest–posttest evaluation plan	417	12
Wutzler [17]	2019	Germany	2010–2014	Retrospective, observational study	1,162	15
Djuric [23]	2018	Serbia	2014–2016	Prospective patient-based, single-center surveillance study	406	20
Guo [22]	2018	China	2010–2016	Randomized double-blind, placebo-controlled clinical trial	204	15
Yadollahi [21]	2018	Iran	2015–2017	Prospective cohort	10,553	11
Denis [24]	2018	Canada	2010–2015	Prospective cohort study	159	16
Folbert [26]	2017	The Netherlands	2011–2013	Naturalistic cohort study	452	14
Yoo [25]	2017	Korea	2010–2014	Prospectively compiled database was used to identify retrospective patients	272	17
Curtis [27]	2016	Australia	2014	Retrospective before-after cohort study	546	21
Ewan [61]	2015	England	2009–2010	Prospective study	90	9*
Yun [28]	2015	United States	2009–2010	Multicenter, observational cohort	423	9*
Kamiya [29]	2015	Japan	2009–2012	Retrospective comparative analysis using an historical cohort control	62	14
Landeen [30]	2014	United States	2005–2011	Retrospective observational study	364	18
Yang [12]	2014	United States	2003–2011	Single-center retrospective cohort study	619	15
Mica [32]	2013	Switzerland	1996–2007	Retrospective study	628	16
Hyllienmark [33]	2013	Sweden	2007–2011	Retrospective cohort study	322	12*
Schirmer-Mikalsen [31]	2013	Norway	2004–2009	Prospective study	133	14
Yeung [34]	2012	United States	2003–2010	Patient control study	162	22
Hakim [35]	2012	Egypt	2008–2011	Randomized, parallel-arm, open-label study	55	7*
Strumwasser [36]	2011	United States	2005–2010	Retrospective study	106	7*
Becher [23]	2011	United States	2008–2009	Retrospective study	116	12
Karunakar [24]	2010	United States	1997–2005	Retrospective review	110	16
Worrall [25]	2010	United States	*Unknown period*	Retrospective analysis	130	10
García-Alvarez [26]	2010	Spain	1998–2001	Prospective study	290	11
Friese [27]	2008	United States	2000–2003	Retrospective, observational cohort analysis	678	13
Schirmer-Mikalsen [28]	2007	Norway	1998–2002	Retrospective study	133	11
Giamberardino [29]	2007	Brazil	2000–2001	Retrospective study	416	9
Bochicchio [31]	2004	United States	1997–1999	Prospective study	182	11
Kamel [32]	2003	United States	1997–1999	Retrospective observational study	131	14
McKinley [33]	2002	United States	*Unknown*	2-year prospective data comparison	117	12
Carson [34]	1999	United States	1983–1993	Retrospective cohort study	9,598	12
Claxton [35]	1998	Canada	1981–1994	Retrospective study	72	14
Bozorgzadeh [36]	1999	United States	*Unknown period*	Prospective, randomized study	300	15
Gonzalez [37]	1998	United States	1992–1995	Double-blind randomized clinical trial	139	15
Allen [38]	1997	United States	*Unknown 4-year period*	Retrospective review	210	8
Morrison [39]	1996	United States	1989–1994	Retrospective cohort study	80	6*
Renz [40]	1995	United States	1988–1991	Prospective case series	254	8*

Table 1 (continued)

Author	Year	Country	Study period	Design	Cohort size	Study quality[§]
Nichols [41]	1994	United States	1988–1992	Double-blind, randomized clinical trial	119	19
Beraldo [42]	1993	Brazil	1989	Review study	664	4*
Rello [43]	1992	Spain	1988–1990	Prospective Study	161	14
Moore [44]	1989	United States	1984–1987	Prospective, randomized study	308	15
Moore [45]	1989	United States	1985–1987	Prospective, randomized study	59	13
LoCurto [46]	1986	United States	1984–1985	Prospective, randomized study	58	13
Grover [47]	1977	United States	*Unknown*	Double-blind prospective study	75	13

[§]The study quality was measured using the MINORS criteria; the potential score ranges from 0 (lowest) to 16 or 24 (highest)

[*]These studies could score a maximum of 16 points

Djuric et al. used the CDC and ECDC guidelines, and Ewan et al. used the ATS and BSAC guidelines [23, 61]. In the studies that used guideline criteria, 33 unique criteria were observed. The remaining 28 out of 46 studies described 37 non-guideline criteria to diagnose HAP (Table 3).

A detailed overview of the used criteria in all included studies was added in Supplemental Table 4.

Methodological quality of included studies

The MINORS score for comparative studies ranged from 9 to 22 on a potential maximum score of 24. For non-comparative studies, the range was 4 to 9 out of 16. The minimum (9 vs. 4) and maximum scores (22 vs. 21) were not considerably different for studies with guideline and non-guideline criteria, respectively (Table 1; Supplemental Table 5).

Discussion

This systematic review provides a general overview of criteria utilized in trauma patient research to diagnose hospital-acquired pneumonia. In only 46 out of 5749 original studies, well-defined criteria were reported, either pre-defined by published guidelines or clear non-guideline criteria. Forty-eight unique criteria were presented and clustered into five categories: clinical, laboratory, microbiological, radiological, and miscellaneous.

In the 28 studies without pre-defined guideline criteria to diagnose HAP, 37 unique criteria were reported. The heterogeneity in the applied criteria can mainly be attributed to the vast diversity in clinical, laboratory, and microbiological thresholds. For example, when considering leukocyte count as an indicator of HAP, up to five different thresholds were reported, describing both an elevated and decreased leukocyte count as indicative of HAP. One could imagine that a lower cut-off point of leukocytosis (e.g., 10×10^9/L versus 13×10^9/L) may lead to a higher estimate of HAP cases in a research population. Similar threshold differences were observed for body temperature, including "fever" or "febrile" as subjective criteria.

Some studies cited established guidelines as a basis for diagnosis, but the authors added new criteria or deleted pre-defined criteria, thus introducing (potential) aggregate bias. For instance, four studies added "medical record documentation" or "start of antibiotic treatment" as a criterion to diagnose pneumonia in addition to guideline criteria [12, 28, 30, 61]. Also, several studies added specific criteria (e.g., hypothermia, worsening gas exchange, leukopenia, and bronchoalveolar lavage) to the ATS/IDSA criteria [12, 22, 34, 61, 64]. Though all are clinically relevant criteria, adjusting pre-defined criteria complicates the comparison of studies that use the same guidelines and increases bias.

Eighteen studies applied existing guideline criteria to diagnose HAP. However, five different guidelines were encountered, leading to a further decrease in uniformity. We encountered a similar variation in body temperature and leukocyte count cut-offs (Table 2) [7–9, 65–67]. However, the number of variations was lower for the pre-defined guideline criteria: three versus five cut-offs for body temperature and leukocytosis. The 2015 ATS/IDSA guideline contained no distinct thresholds for hyperthermia and leukocytosis, resulting in differences between studies that used this guideline (Table 2) [67]. Despite the attempts to generate uniformity in diagnosing HAP by creating and using guideline criteria, the abovementioned differences make it difficult to compare the available literature completely. Only five studies diagnosed HAP based on the exact same criteria.

Guidelines are continuously updated based on new insights and available literature. The earliest CDC guideline dates from 1988, and the most recent from 2018. During these 30 years, the criteria for pneumonia diagnosis have changed substantially. For example, the 1988 CDC criteria for pneumonia diagnosis were clinical, radiologic, or microbiologic, while body temperature was not included as a criterion [68]. However, the 2018 guideline provides

Table 2 Pre-defined guideline criteria used to diagnose hospital-acquired pneumonia in trauma patient research

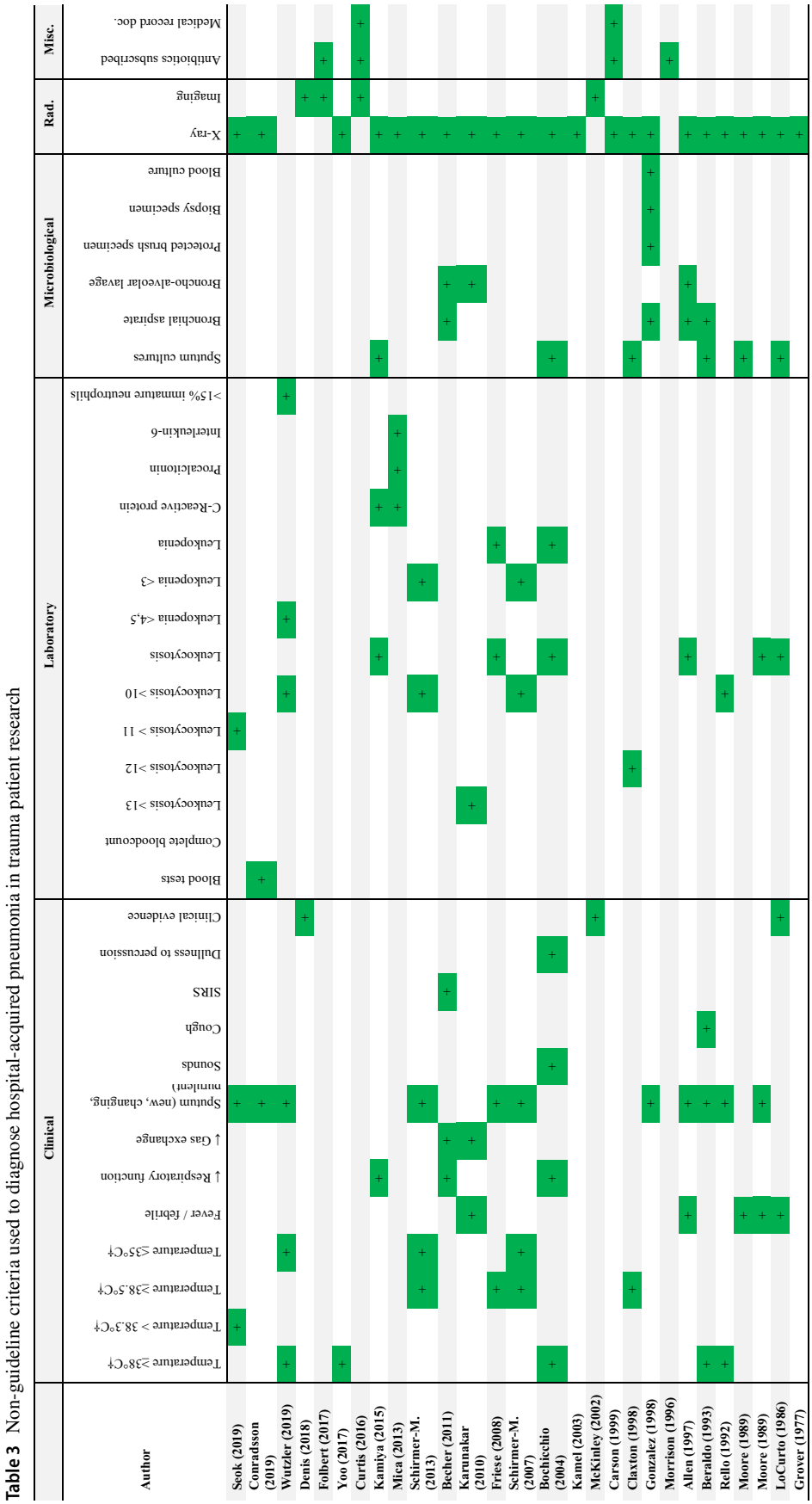
Guideline issued by, Year	Clinical												Laboratory							Microbiological										Rad.		Used by (Author, Year)
	Temperature ≥38°C†	Temperature ≥38.3°C†	Temperature ≥38.5°C†	Dyspnea	Tachypnea	↓ Gas exchange	Sputum (new, changing, or purulent)	Sounds	Cough	Clinical evidence	>70y, altered mental status	Dullness to percussion	Leukocytosis >12	Leukocytosis >10	Leukocytosis	Leukopenia <5	Leukopenia <4	Leukopenia	CRP >100mg/L	Bronchial or tracheal aspirate	Broncho-alveolar ; Corresponding respiratory and blood culture	Protected brush specimen	Biopsy specimen	Blood culture	Pleural fluid	Infection with an uncommon pathogen	Histopathologic evidence	X-ray	Imaging	
CDC, 1988							+	+		+		+								+		+	+	+			+	+		Nichols, 1994 Renz, 1995 Bozorgadeh, 1999
CDC, 1996							+	+				+								+		+		+			+	+		Giamberardino, 2007 García-Alvarez, 2010
CDC, 2004	+			+	+	+	+	+	+		+		+				+			+	+	+		+	+		+	+		Yun, 2015 (+ medical record documentation)
CDC, 2008	+			+	+	+	+	+	+		+		+				+			+	+	+		+	+		+	+		Strumwasser, 2011 Hakim, 2012 Landeen, 2014 (+ medical record documentation)
CDC, 2014	+			+	+	+	+	+	+		+		+				+			+	+	+		+	+		+	+		Djuric, 2018*
CDC, 2017	+			+	+	+	+	+	+		+		+				+			+	+	+		+	+		+	+		Yadollahi, 2018
CDC, 2018: PNU1	+			+	+	+	+	+	+		+		+				+												+	Warren, 2019
ATS(/IDSA), 2005	+					+	+								+			+										+		Worrall, 2010 (+ leukocytosis >12; leukopenia <4) Yeung, 2012 (+ temperature ≤36°C; ↓gas exchange; + clinical evidence) (+ leukocytosis >10; leukopenia <5) (+ medical record documentation) Yang, 2014 (+ ↓gas exchange) (+ leukocytosis >10) (+ broncho-alveolar lavage) (+ medical record documentation) Ewan, 2015* (+ medical record documentation) Guo, 2018 (+ ↓gas exchange) (+ broncho-alveolar lavage)
BSAC, 2008		+				+	+							+			+											+		Ewan, 2015* (+ medical record documentation)
ECDC, 2012	+			+	+	+	+	+	+				+				+			+	+	+		+	+				+	Djuric, 2018*
SIR, *unknown*			+																+			+	+						+	Hyllienmark, 2013

†: ≤ and <, and ≥ and > are used interchangeably in this table when body temperatures are corresponding between studies

*These studies used more than one guideline

Abbreviations: ATS, American Thoracic Society; BSAC, British Center for Antimicrobial Chemotherapy; CDC, Centers for Disease Control and Prevention; CRP, C-reactive protein; ECDC, European Center for Disease Prevention and Control; Rad., radiological; SIR, Swedish Intensive Care Registry; ↓, worsening

Table 3 Non-guideline criteria used to diagnose hospital-acquired pneumonia in trauma patient research



†: ≤ and <, and ≥ and > are used interchangeably in this table when body temperatures are corresponding between studies

Abbreviations: *Misc* miscellaneous, *Rad* radiological, *SIRS* systemic inflammatory response syndrome, ↓ worsening

a more elaborate set of clinical, radiological, microbiological, and laboratory criteria [7]. As a result, it is more difficult to compare older data sets to more recent studies. Full implementation of or compliance with guideline criteria in clinical practice is hardly feasible for two reasons: patient care and study design. Study subjects are patients; therefore, clinical examination and experience remain decisive in starting pneumonia treatment. The authors understand that an inconclusive or negative X-ray should not delay antibiotic treatment, and awaiting a microbial culture is not mandatory or necessary in seriously ill patients. Using guideline criteria for pneumonia diagnosis in retrospective studies might be impracticable. Also, uniform diagnostic criteria for pneumonia are hard to accomplish in database or registry studies. Nonetheless, these limitations should be mentioned when encountered.

Previously, review studies have been issued on lacking definitions in trauma research, such as fracture-related infections and non-unions of long bones [69–71]. To resolve a lack of definition, these review studies provide a basis for a consensus definition. Subsequently, Delphi method studies can be helpful in reaching consensus. Our study displays the wide variety of clinical criteria for HAP diagnosis in trauma research and exhibits how studies ought to be compared with caution. The comparison of results is essential in trauma patient research and for guidelines. Guideline issuers pursue workable and representable guidelines to help clinicians in decision-making. Continuous improvement is established with the results of clinical studies, for which comparability of results is necessary. Our results emphasize this importance. Though our study addressed a scientific problem rather than a clinical one, it can still impact day-to-day practice.

One established definition of HAP would improve the comparability of trauma research; expert consensus could be a solid foundation to start with. Given the complexity of trauma patients, any diagnostic definition should address potential issues and pitfalls to avoid overdiagnosis. Currently, hyperthermia is incorporated in all guidelines, and sputum and dyspnea (with or without worsening gas exchange) in all but one. Leukocytosis, a common marker for infection, is included in all guidelines. Microbiologic information and evidence of infection aid in diagnosis and treatment; the CDC and ECDC describe several types of respiratory cultures. Radiologic evidence of pneumonia—either radiographic or CT imaging—also supports a diagnosis. Expert consensus should incorporate these criteria. Nonetheless, hypo- or hyperthermia, dyspnea, and leukocytosis are also signs of the systemic inflammatory response syndrome, commonly observed in trauma patients and potentially complicating the diagnostic process [72]. Also, posttraumatic fever may have a non-infectious origin, such as neurogenic fever, and trauma is associated with an increased immune response, adding to the need for a dedicated leukocytosis threshold [73, 74]. Lastly, sputum can result from (severe) pulmonary contusion, though unlikely to be purulent [75]. We propose that a decision-making algorithm includes hyperthermia (≥ 38.5 ℃) and leukocytosis ($> 12 \times 10^9$/L) as major criteria, in addition to microbiologic and radiologic evidence. Dyspnea and (purulent) sputum should be considered minor criteria. Our considerations and recommendations serve as a basis for expert consensus.

Some limitations of this study should be considered. Firstly, PubMed/MEDLINE was the only search engine used in this study, which could result in an incomplete overview of applied clinical criteria for HAP diagnosis. However, the wide variety of clinical criteria and the difficult comparison between studies are evident in the current number of included studies. Secondly, our overview of reported diagnostic criteria did not consider the recommended combinations of these criteria. Not doing so resulted in a more comprehensible overview of used criteria and did not diminish the conclusion of this study.

Conclusion

As few studies in trauma patient research report a clear, clinical definition of hospital-acquired pneumonia, results cannot be adequately compared. Moreover, the wide variety of non-guideline criteria and diversity in pre-defined guideline criteria do not facilitate proper comparison. Studies should at least report how a diagnosis was made, but preferably, they would use pre-defined guideline criteria for pneumonia diagnosis in a research setting. Ideally, one internationally accepted set of criteria is used to diagnose hospital-acquired pneumonia.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00068-024-02509-8.

Author contributions TK: Conceptualization, Methodology, Investigation, Visualization, Writing - Original Draft; DS: Conceptualization, Methodology, Investigation, Writing - Original Draft; FH: Conceptualization, Resources, Writing - Review & Editing; KB: Conceptualization, Visualization, Writing - Review & Editing; RH: Conceptualization, Supervision, Writing - Review & Editing; MvB: Conceptualization, Methodology, Supervision, Writing - Review & Editing. All authors have read and agreed to the published version of the manuscript.

Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

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