A meta-analysis of the diagnostic accuracy of chest ultrasound for the diagnosis of occult penetrating cardiac injuries in hemodynamically stable patients with penetrating thoracic trauma

Ramiro Manzano-Nunez, MD, Alexandra Gomez, MD, David Espitia, MD, Melibea Sierra-Ruiz, MD, Jessica Gonzalez, MD, Jose G. Rodriguez-Narvaez, MD, Andrea C. Castillo, MD, Alejandro Gonzalez, MD, Jose Orjuela, MD, Viviana Orozco-Martin, MD, Felipe Bernal, MD, Felipe Giron, MD, MSc, Angela C. Rios, MD, Paola Carranza, MD, Adolfo Gonzalez-Hadad, MD, Herney A. García-Perdomo, MD, MSc, PhD, *and* **Alberto F. García, MD, MSc**, *Cali, Colombia*

BACKGROUND: We performed a systematic review (SR) and meta-analysis (MA) to determine the diagnostic accuracy of chest ultrasound (US) compared with a pericardial window (PW) for the diagnosis of occult penetrating cardiac injuries in hemodynamically stable patients with penetrating thoracic trauma.

METHODS: A literature search in five databases identified relevant articles for inclusion in this SR and MA. Studies were eligible if they evaluated the diagnostic accuracy of chest US, compared with a PW, for the diagnosis of occult penetrating cardiac injuries in hemodynamically stable patients presenting with penetrating thoracic trauma. Two investigators independently assessed articles for inclusion and exclusion criteria and selected studies for final analysis. Methodological quality was evaluated using Quality Assessment of Diagnostic Accuracy Studies-2. We performed a MA of binary diagnostic test accuracy within the bivariate mixed-effects logistic regression modeling framework.

RESULTS: We included five studies in our SR and MA. These studies included a total of 556 trauma patients. The MA found that, compared with PW, the US was 79% sensitive and 92% specific for detecting occult penetrating cardiac injuries in hemodynamically stable patients. The presence of a concomitant left hemothorax was frequent in patients with false-negative results.

CONCLUSION: This SR and MA found that, compared with PW, US was 79% sensitive and 92% specific for detecting occult penetrating cardiac injuries in hemodynamically stable patients with penetrating thoracic trauma. Caution interpretation of pericardial US results is suggested in the presence of left hemothorax. In these cases, a second diagnostic test should be performed. (*J Trauma Acute Care Surg.* 2021;90: 388–395.

LEVEL OF EVIDENCE: Systematic Review and Meta-analysis, level II.

KEY WORDS: Heart injuries; occult cardiac injuries; ultrasonography; diagnostic imaging; meta-analysis.

The approach to penetrating thoracic injuries has evolved over the last half century.[1,2] Previously, a patient with a suspected penetrating cardiac injury was usually taken to an immediate operation: thoracotomy or sternotomy. In 1977, Arom et al.[3] published the first known descriptions of the surgical technique to perform a pericardial window (PW). From that moment on, the trauma algorithm for penetrating cardiac injuries was modified. Years later, an effort to improve the diagnostic approach to penetrating cardiac injuries via ultrasound (US) was developed.[4,5]

In 1992, Tso et al.[6] informed the use of ultrasonography in patients with blunt abdominal trauma for the first time. Surgeons began to use US in the diagnosis of injuries to other organs, which led to an increasing interest in implementing US in the initial assessment and management of the injured patient. However, it was not until 1999 when Rozycki and colleagues[5] published their seminal study on the accuracy of emergency US for the evaluation of hemopericardium that this technology became widely accepted and introduced into trauma management algorithms.

Since then, there was a rapid development of US in the field of trauma and emergency surgery. However, this shift of paradigm was driven by evidence from studies where some participants underwent one reference standard test and others had a different reference standard test.[4,5] This fact led to varying accuracy of disease confirmation within and across studies. Therefore, comprising the validity of the diagnostic accuracy metrics presented.

Because accurate and consistent confirmation of disease is crucial in diagnostic accuracy studies, it is paramount that all patients who received the index test must also receive the same reference standard. To our knowledge, two contemporary studies that assessed the diagnostic accuracy of US for detecting

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From the Méderi Hospital Universitario Mayor (R.M.-N., D.E., J.G., J.G.R.-N., A.C.C., A.G., J.O., V.O.-M., F.B., F.G.); Escuela de Medicina y Ciencias de la Salud (R.M.-N., D.E., J.G., J.G.R.-N., A.C.C., A.G., J.O., V.O.-M., F.B., F.G.), Universidad del Rosario, Bogotá, DC; Fundacion Valle del Lili, Clinical Research Center (A.G., M.S.-R.), Cali; Hospital Occidente de Kennedy (A.C.R., P.C.), Bogotá, DC; Sección de Urología, Departamento de Cirugía, (A.G.-H., H.A.G.-P.), Universidad del Valle; and Department of Surgery (A.F.G.), Fundación Valle del Lili, Cali, Colombia.

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Address for reprints: Ramiro Manzano-Nunez, MD, Méderi Hospital Universitario Mayor, Department of Surgery, Escuela de Medicina y Ciencias de la Salud, Universidad del Rosario, Bogotá DC, Colombia; email: ramiro.manzano@fvl.org.co; ramiro.manzano@correounivalle.edu.co.

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occult penetrating cardiac injuries used the same types of index and reference standards, meaning that US was subsequently compared with a PW to obtain diagnostic accuracy metrics.[7,8] However, there are no systematic searches looking for additional studies on the same matter. To address this knowledge gap, we performed a systematic review and meta-analysis to determine the diagnostic accuracy of chest US compared with a PW for the diagnosis of occult penetrating cardiac injuries in hemodynamically stable patients with penetrating thoracic trauma.

METHODS

We performed this systematic review according to the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy and in compliance with the suggestions of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations.[9]

Following our main objective, we framed a diagnostic question specifying the types of participants, types of index tests and reference standards, and the types of outcomes as follows: *Participants:* hemodynamically stable trauma patients victims of penetrating thoracic injuries; *Index test*: ultrasonography performed during the initial evaluation in the emergency department; *Reference standard*: PW; *Outcomes:* sensitivity, specificity and likelihood ratios for the diagnosis of occult penetrating cardiac injuries. Therefore, this systematic review answered the following diagnostic question:

1. What is the diagnostic accuracy of chest US, compared with a PW, for the diagnosis of occult penetrating cardiac injuries in hemodynamically stable patients presenting with penetrating thoracic trauma?

Eligibility Criteria

Type of Studies

We expected that patients analyzed in each study underwent a PW after the initial US performed in the emergency department. Therefore, we restricted our inclusion criteria to prospective observational studies and randomized controlled trials (if any) because the only way to compare US with PW is through prospective studies. We included studies published from inception to August 2020; there were no language restrictions.

Participants

The participants were adult patients with penetrating thoracic trauma and possible cardiac injuries, who were hemodynamically stable at the moment of admission and underwent an initial evaluation using US to rule out occult penetrating cardiac injuries.

Index Test and Target Condition

The index test was the US/US. The target condition was "occult cardiac injury," defined as injuries to the myocardium caused by a penetrating wound.

Reference Standards

The reference standard was a PW by any means (i.e., subxiphoid PW, thoracoscopic PW, PW by laparoscopy). Because PW is widely accepted as the criterion standard for diagnosing occult penetrating cardiac injuries, we did not admit another reference standard.

Outcomes

The outcomes of interest were sensitivity, specificity, and likelihood ratios for the diagnosis of occult penetrating cardiac injuries.

Exclusion Criteria

We excluded studies assessing the diagnostic accuracy of chest US compared with other tests/measures. For example, studies comparing chest US versus the patient's condition. We also excluded studies lacking data to calculate sensitivity and specificity.

Electronic Search Strategy

We outlined a systematic search strategy of the available literature following expert recommendations.[10] The literature search was performed from inception to August 2020 in MEDLINE (through Ovid); EMBASE (through Scopus), and the Cochrane Controlled Trials Register Center. We also searched in Google, conferences, clinical trials databases and thesis databases in order to saturate information. Full electronic search strategies are described in the **Supplementary File 1,** http://links.lww.com/TA/B834.

Study Selection and Data Collection

The initial step in the selection process for this systematic review was performed blindly and independently based on the title and abstract. To this end, two authors independently reviewed the titles and abstracts identified in the searches. Articles that appeared relevant for the topic of this review were retrieved as full texts. Two investigators read the full-text articles and selected the studies to be included in this systematic review based on the inclusion and exclusion criteria previously described. A third reviewer resolved disagreements on articles' eligibility.

We extracted the data, as reported in the included studies. We designed a data collection form in which we collected the following information from the included studies: authors, year of publication, study design, region of origin, number of patients, type of injuries, relevant demographic and clinical characteristics, interventions performed, and data about the diagnostic accuracy of chest US for our objective of interest.

Risk of Bias

We evaluated each included study with the Quality Assessment of Diagnostic Accuracy Studies-2 tool, which considers the risk of bias and applicability ratings.

Synthesis of Results (Meta-Analysis)

The numbers of true positives, false positives, false negatives, and true negatives were extracted from each study and imported into a 2×2 table to determine the operative characteristics with their respective 95% confidence interval.

We performed a meta-analysis of binary diagnostic test accuracy within the bivariate mixed-effects logistic regression modeling framework.[11] The pooled performance estimates were reported in forest plots of the estimated sensitivity and specificity of the included studies with a 95% confidence interval. We show the graphical summaries of the fitted model in a plot that included the v, the summary operating point, a 95% confidence region for this point, and a 95% prediction region for a forecast

of the true sensitivity and specificity in a future study. The heterogeneity was assessed with the I^2 test, considering the interpretation that values of 25%, 50%, and 75% correspond to low, medium, and high levels of heterogeneity, respectively.

Positive and negative predictive values were calculated based on a prior probability of the disease's prevalence (p). Predictive values were obtained by integrating their corresponding conditional (on p) versions with respect to a prior distribution for p, which was set from 0.25 to 0.75.

We performed all statistical analyses in Stata statistical software v.14 (Stata Corp, College Station, TX).

RESULTS

We identified a total of 986 articles from the database searching. After screening for title and abstract and excluding duplicates, 13 documents were considered eligible for full-text review. We finally included five studies that fulfilled our inclusion criteria.[7,8,12–14] Figure 1 shows the PRISMA diagram for the selection of the studies.

Characteristics of Included Studies

Studies included in this systematic review were published between 1990 and 2020. All of them were prospective cohorts that evaluated the diagnostic accuracy of US, compared to a PW, for the diagnosis of occult penetrating cardiac wounds in hemodynamically stable trauma patients with penetrating thoracic injuries. Of the five included studies, four included patients from Colombia (n = 2)[7,14] and United Stated (n = 2),[12,13] and one included patients from South Africa.[8] The five reports answered a diagnostic question with similar types of patients, identical types of index tests and reference standards, and the same types of outcomes.

Characteristics of Participants

Table 1 presents an overview of the patients' characteristics. There were 556 participants with a sample size ranging from 65 to 172 patients (median, 105; interquartile range, 73–141). All patients were victims of penetrating thoracic trauma and were hemodynamically stable on admission. All studies reported a thoracic area of particular interest that corresponded to an area between the midclavicular lines, below the clavicles and above the costal margin.

As shown in Table 1, most patients were male, and a higher proportion were victims of penetrating stab wounds. Complications were minimal and included cases of post-operative wound infection and coagulated hemothorax. Mortality was 0% (n = 0) in four of the five reports.

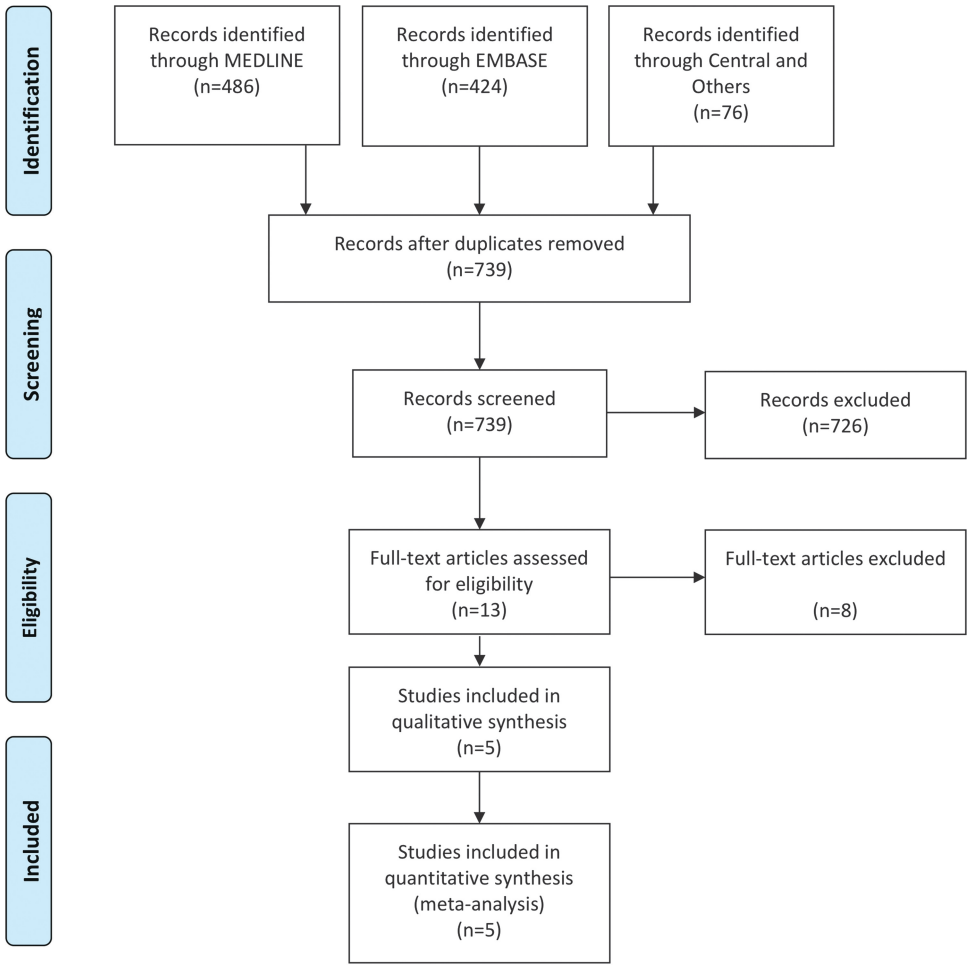

Figure 1. PRISMA diagram.

TABLE 1. Characteristics of the Patients From the Studies Included in the Systematic Review

Author/ Year	Type of Study	Inclusion Criteria	Country/City	N, Total	Age	Sex Female, n (%)	GS/ SW	ISS	Hemothorax, n (%)	H Left, n (%)	Pneumopericardium, n (%)	Complications	Mortality, n (%)
Jimenez 1990	Prospective cohort	Patients with penetrating chest wounds and stable vital signs	EEUU/Chicago	n = 73	NR	NR	NR	NR	NR	NR	NR	2 minor wound infections. 1 case of streptococcal pericarditis	n = 0 (0%)
Dan 1995	Prospective cohort	All patients had penetrating thoracic trauma with cardiac proximity and were hemodynamically stable at the time of US	EEUU/Dallas	n = 105	Median age: 28.6 years	N = 12 (11%)	41/64	NR	n = 47 (44,8%)	NR	NR	"No significant morbidity"	n = 0 (0%)
Nicol 2015	Prospective cohort	All stable patients with penetrating chest wounds with no indication for emergency surgery	South Africa/ Cape town	n = 172	Range 11–75, median age 26 years	N = 4 (4%)	6/166	NR	n = 12 (7%)	n = 11 (6%)	N = 6 (4%)	NR	NR
Piamonte 2012	Prospective cohort	All hemodynamically stable trauma patients with penetrating injuries to the precordium	Colombia/ Bucaramanga	n = 65	Median = 26 (IQR, 21–37)	n = 18 (21%)	7/77.	NR	n = 0	n = 0	NR	NR	n = 0 (0%)
Gonzalez 2020	Prospective cohort	All patients with penetrating injuries to the precordial area and hemodynamically stable	Colombia/Cali	n = 141	Median = 27	N = 4 (3%)	38/103	12 (10–18)	n = 6 (4%)	n = 6 (4%)	NR	1 coagulated hemothorax	n = 0 (0%)

NR, not reported; GS, gunshot; SW, stab wound; ISS, Injury Severity Score; H left, left hemothorax; IQR, interquartile range.

TABLE 2. Data to Populate 2 × 2 Contingency Tables and Pooled Performance Estimates Derived From the Meta-Analysis

	Jimenez 1990	Dan 1995	Piamonte 2012	Nicol 2015	Gonzalez 2020
True positives	9	5	1	117	23
False positives	2	7	0	35	8
False negatives	1	4	0	18	6
True negatives	62	89	64	2	104
Pooled sensitivity (95% CI)			79% (67–88)		
Pooled specificity (95% CI)			92% (41–99)		
Pooled (+)LR (95% CI)			9.5 (0.8–114.3)		
Pooled (−)LR (95% CI)			0.22 (0.14–0.37)		
Diagnostic OR (95% CI)			42 (3–568)		

OR, odds ratio; 95% CI, 95% confidence interval.

US Procedure Characteristics

As shown in Table S1 (available in the Supplementary File 1, http://links.lww.com/TA/B834), the probes used in each study were comparable; however, there were differences in probes fabrication dates, which means differences in technological improvements and image quality between studies. For example, Jimenez's study was published in 1990; in contrast, Gonzalez's study was published in 2020.

The specialty of physicians performing the US was reported in all studies (Table S1). In three of the five articles, the US was performed by an attending surgeon. In one article, the US was performed by a resident of surgery and then repeated by a cardiology fellow. In the remaining article, the US was performed either by a trained radiology resident or a radiology specialist.

Risk of Bias Assessment

All included studies were prospective, performed the US before the surgical procedure, used the same reference standard and included all patients in the analysis. Therefore, there was a low risk of bias regarding patient selection, index test, reference standard, and flow and timing. Also, there were no applicability concerns (Fig. S1 in the Supplementary File, http://links.lww.com/TA/B834).

Quantitative Synthesis (Meta-Analysis)

Table 2 and Figure 2 present the pooled diagnostic accuracy measures of chest US, compared with a PW, for the diagnosis of occult penetrating cardiac injuries. The meta-analysis showed that the sensitivity of chest US was 79%, and the specificity was 92%. The heterogeneity for these pooled performance estimates was high (sensitivity, I^2 = 98.8%; specificity, I^2 = 98.8%). Figure 3 shows the summary curve from the Hierarchical Summary Receiver Operating Characteristic (HSROC) model. Positive and negative predictive values were calculated in 89% and 80%, respectively (Fig. S2 in the supplementary file, http://links.lww.com/TA/B834).

Analysis of False-Negative Results

There were 29 (29/566, 5.1%) patients with a false negative result on US examination. One of these patients was from the study by Jimenez et al.,[12] four from the study by Meyer et al.,[13] and 18 and 6 from Nicol et al.[8] and Gonzalez et al.'s reports,[7] respectively. These patients often presented with hemothorax, which was managed with intercostal drains. In the study by Gonzalez

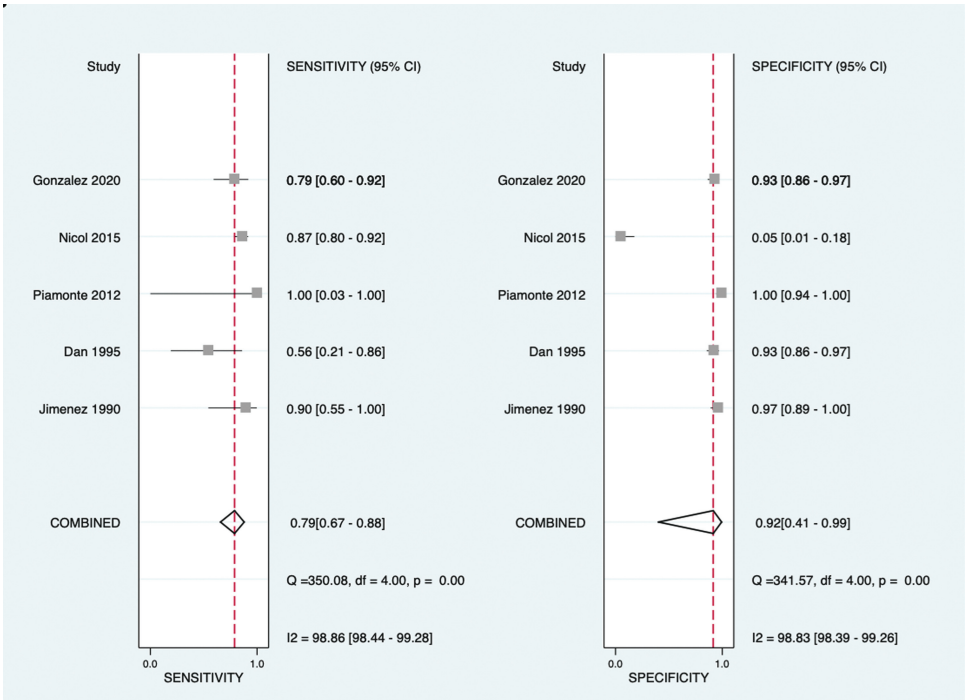

Figure 2. Forrest plot for sensitivity and specificity.

et al.,[7] all patients (n = 6) with a false-negative US result had a concomitant left-sided hemothorax. Similarly, Nicol and colleagues[12] reported that 11 of the 18 patients with false-negative results had a left-sided hemothorax. In six of these 18 patients, a pneumopericardium was detected, but no fluid was seen on the initial US examination. In the same study, one patient with two negative US examinations was discharged home to be readmitted with a delayed symptomatic pericardial effusion.

One study reported the surgical interventions performed in patients with false-negative US results.[7] In this study, all false-negative patients (n = 6) were found to have minor pericardial wounds with neither full-thickness injury to the myocardium nor active bleeding (American Association for the Surgery of Trauma (AAST) grade II heart injuries: penetrating tangential myocardial wounds not extending to the endocardium). These patient's injuries were copiously irrigated with normal saline solution and did not require cardiac repair.

DISCUSSION

After pooling data from five prospective studies, including 556 trauma patients, we found that, compared to PW, US was 79% sensitive and 92% specific for detecting occult penetrating cardiac injuries in hemodynamically stable patients. This study is, to our knowledge, the first comprehensive meta-analysis on this matter. We recommend using US as a diagnostic tool during the initial evaluation of hemodynamically stable patients with penetrating thoracic trauma who are likely to have occult penetrating cardiac injuries.

We advise caution in making decisions based on a negative US result among patients who present with concomitant left hemothorax. Also, because most patients analyzed in this review were victims of stab wounds, we encourage prudence in extrapolating these results to the whole spectrum of patients' victims of gunshot injuries to the chest. These kinds of injuries transfer more kinetic energy to the tissue causing more damage and worse injuries, even in patients who initially present with stable vital signs.

In this study, the pooled sensitivity and specificity were 79% and 92%, respectively. In 1999, Rozycki and colleagues[5] published an influential report showing that US was 100% sensitive and 97% specific for the determination of hemopericardium in patients with penetrating thoracic trauma. These findings were paramount for expanding US use in the trauma bay for the initial approach to the injured patient. However, in their study, not all the patients who received the index test (US) went on to have the reference standard (PW), thus introducing varying accuracy of disease confirmation, which could affect the estimated accuracy. In contrast, we pooled data from five studies using the same types of index test (US) and reference standard (US) and where this latter standard was the best test at diagnosing hemopericardium. Therefore, we consider our findings to be much more accurate than those previously reported. Moreover, because the diagnostic accuracy measures calculated in this study are the result of a meta-analysis, they may provide a more precise estimate of such measures than any individual study contributing to the pooled analysis.

International trauma guidelines state that ultrasonography can be used to document pneumothorax/hemothorax if the operator is trained to do so.[15,16] Ultrasonography is an accepted tool to assess for pericardial fluid rapidly; however, in the presence of hemothorax, a negative study result does not rule out a cardiac injury.[7,8] First, a concurrent laceration in the pericardial sac may allow blood from a cardiac wound to decompress into the adjacent thoracic cavity. Second, in the presence of a concurrent hemothorax, it may be not easy to visualize the pericardium and accurately assess whether the fluid is intrapericardial or extrapericardial. Both situations may increase the likelihood of false-negative reports.[17] Indeed, the analysis of patients with US false-negative results reported in the included studies noted that a significant proportion of them had a concurrent left hemothorax. Meyer et al.[13] focused on the problem of false-negative studies among hemodynamically stable patients with thoracic trauma undergoing chest US to detect occult penetrating cardiac injuries. To this end, they performed a subgroup analysis of patients with penetrating thoracic trauma without associated hemothorax. In this subgroup of patients, no false-negative results were registered, and the US showed accuracy parameters mirroring those of PW. They also found the accuracy parameters of US to be poor if only patients with hemothorax were analyzed.

The clinical significance of US accuracy parameters should be interpreted in the light of patient outcomes. The major concern with a false-negative US interpretation, especially in the presence of left hemothorax, is the potential for missed cardiac injuries, which can lead to readmissions, reoperations, and death.[18–20] Therefore, as major trauma associations have advised it,[15] we recommend that patients with penetrating thoracic trauma and negative US results for hemopericardium; yet with left

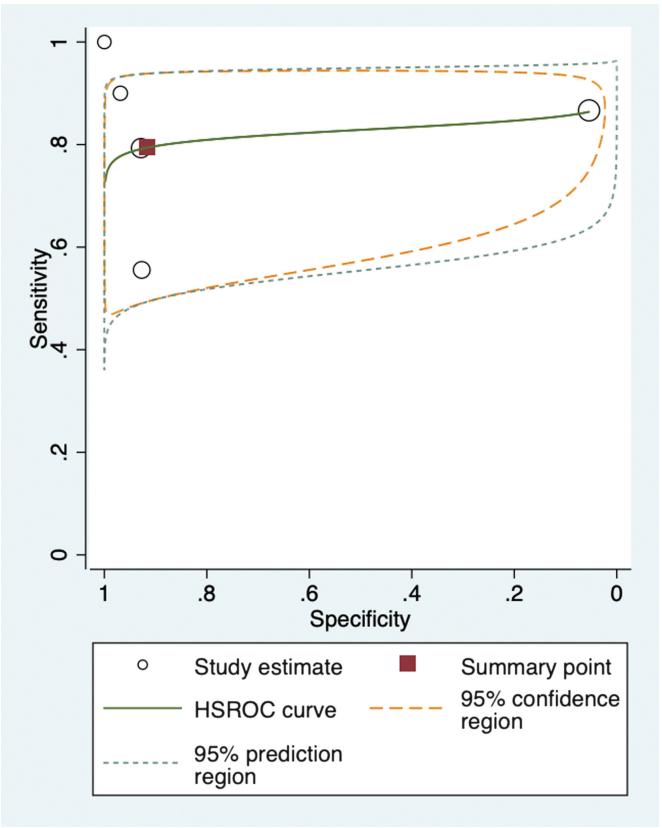

Figure 3. Summary receiver operating characteristic (SROC) curve with confidence regions.

hemothorax undergo a second diagnostic test: either a computed tomography scan,[8] a PW,[7] or video-assisted thoracoscopy surgery[15] to rule out an occult penetrating cardiac injury. Another option is to repeat the US if the diagnosis is in doubt; however, we recommend to move on to computed tomography scan or PW as these tests can be done promptly without the downside associated with the loss of time that comes when repeating US, which in turn, may have a negative impact in patient outcomes if a cardiac injury is present.

The choice of the second diagnostic test would depend on injury topography and the resources available at each hospital. On the other hand, to develop a full picture of the US's role in detecting occult penetrating cardiac injuries, additional studies will be needed that explore a pathway for the diagnosis of this kind of injury among patients with multicavity wounds.

In one of the included studies, the patients with a false-negative result on US examination did not require surgical interventions for cardiac injury repair; instead, at the moment of PW, the pericardial sac was copiously irrigated with normal saline solution until verification that bleeding had ceased, and neither sternotomy nor thoracotomy was performed.[7] This raises the question of whether all hemodynamically stable patients with a positive PW would require a thoracic incision for cardiac injury repair or if the use of PW with drainage is sufficient to treat hemopericardium in this patient population. To date, some case series[21,22] and a randomized controlled clinical trial[23] have shown that using a PW and drainage as the sole treatment for traumatic hemopericardium in hemodynamically stable patients with penetrating chest injuries is not only feasible but also safe and effective because it did not increase mortality and is related to shorter ICU and hospital stay.

Limitations

The main limitation of this systematic review and meta-analysis is the high heterogeneity found in the pooled statistical analysis, which theoretically could affect the validity of the summary estimates presented. Nevertheless, the studies analyzed in this review were highly comparable in design, index and reference tests, and patient population, meaning that the levels of clinical and methodological heterogeneity were probably very low. To the latter, added is the fact that previous simulation studies have shown that determining levels of heterogeneity (I^2) is of little value at the extremes of heterogeneity,[24] such as in our case. Thus, we consider the pooled estimates presented in this report to be reliable and accurate.

This study has additional limitations. First, it is unfortunate that the study did not include a subgroup analysis controlling by US providers; however, subgroup analyses were limited by the number of studies available for creating the subgroups and undertaking a robust analysis. Second, the gap in time between publications reveals a gap in technological improvements and image quality. Most recent publications were performed with modern US machines containing technology that allows for more precise and reliable results. The latter could introduce misclassification bias to the analyses performed. Third, further selection bias could be introduced as the studies analyzed in this review were more likely to include cases not representing the whole spectrum of occult cardiac injuries presentation because of the exclusion of patients with thoracoabdominal wounds with which deep inspiration can become truly thoracic and increase the likelihood of intrathoracic injury.

CONCLUSION

This systematic review and meta-analysis found that, compared with PW, US was 79% sensitive and 92% specific for detecting occult penetrating cardiac injuries in hemodynamically stable patients with penetrating thoracic trauma. Caution interpretation of pericardial US results is suggested in the presence of left hemothorax. In these cases, a second diagnostic test should be performed.

AUTHORSHIP

Only authors who made substantive intellectual contributions were listed as authors. R.M.N. conceived the idea. H.A.G.P. performed the literature search and the risk of bias evaluation. A.G., D.E., A.M., A.C.C., J.G., J.G.R.N., and M.S. selected the articles and extracted the data from them R.M.N., and H.A.G.P. performed the statistical analysis. A.F.G., V.O.M., P.C., A.C.R., F.G., F.B., and J.O. provided critical revisions to the article. All authors contributed writing assistance and performed several reviews of the document. All authors approved the final version for submission. R.M.N. supervised all the processes.

DISCLOSURE

The authors declare no funding or conflicts of interest.

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