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اصول تنظیم قراردادها

پروپوزال نویسی

آموزش مهارت های کاربردی در ندوین و چاب مقاله
Diagnostic Accuracy of Ultrasonography and Radiography in Detection of Pulmonary Contusion; a Systematic Review and Meta-Analysis

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Abstract

Introduction: Ultrasonography is currently being used as one of the diagnostic modalities in various medical emergencies for screening of trauma patients. The diagnostic value of this modality in detection of traumatic chest injuries has been evaluated by several studies but its diagnostic accuracy in diagnosis of pulmonary contusion is a matter of discussion. Therefore, the present study aimed to determine the diagnostic accuracy of ultrasonography and radiography in detection of pulmonary contusion through a systematic review and meta-analysis. Methods: An extended systematic search was performed by two reviewers in databases of Medline, EMBASE, ISI Web of Knowledge, Scopus, Cochrane Library, and ProQuest. They extracted the data and assessed the quality of the studies. After summarization of data into true positive, false positive, true negative, and false negative meta-analysis was carried out via a mixed-effects binary regression model. Further subgroup analysis was performed due to a significant heterogeneity between the studies. Results: 12 studies were included in this meta-analysis (1681 chest trauma patients, 76% male). Pooled sensitivity of ultrasonography in detection of pulmonary contusion was 0.92 (95% CI: 0.81-0.96; I2= 95.81, p<0.001) and its pooled specificity was calculated to be 0.89 (95% CI: 0.85-0.93; I2 = 67.29, p<0.001) while these figures for chest radiography were 0.44 (95% CI: 0.32-0.58; I2= 87.52, p<0.001) and 0.98 (95% CI: 0.88-1.0; I2= 95.22, p<0.001), respectively. Subgroup analysis showed that the sources of heterogeneity between the studies were sampling method, operator, frequency of the transducer, and sample size. Conclusion: Ultrasonography was found to be a better screening tool in detection of pulmonary contusion. Moreover, an ultrasonography performed by a radiologist / intensivist with 1-5MHz probe has a higher diagnostic value in identifying pulmonary contusions.

Key words: Pulmonary contusion; ultrasonography; radiography; diagnostic tests, routine

Introduction:

Pulmonary contusion is a common complication of traumatic thoracic injuries. Reports indicate that 25 to 80% of thoracic traumas are associated with pulmonary contusion (1, 2). Various techniques have been proposed for detection of this lesion including clinical assessment, chest radiography (CXR), arterial blood gas, and computed tomography (CT) scan (3, 4). CXR is the most common diagnostic tool in detection of pulmonary contusion but presence of hemothorax or pneumothorax might complicate the diagnosis (5-7). Moreover, identification of this lesion in CXR is not possible in the first 6 hours after injury (8, 9). CT scan is the most accurate diagnostic tool for pulmonary contusion and can detect the lesion right after the injury (10, 11). Ultrasonography reported to have acceptable sensitivity...
and specificity in detection of pulmonary contusion (11-13). In the last 10 years many studies have evaluated the diagnostic values of ultrasonography and radiography in detection of traumatic thoracic injuries including pulmonary contusion (14-16), but reaching a consensus has been hindered by the vast disagreements on this subject. One of the ways to overcome this problem is conducting a systematic review and meta-analysis (17, 18). In this regard, we aimed to compare the diagnostic values of these two modalities in detection of pulmonary contusion through a meta-analysis of the available literature.

Methods:

Search strategy and selection criteria

Search strategy was based on the keywords related to ultrasonography and chest radiography including “Ultrasound” OR “Chest Film” OR “Chest Radiograph” combined with pulmonary contusion-related terms including “Contusions” OR “Pulmonary Contusion” OR “Lung Contusion”. The systematic search was carried out in databases of Medline (via PubMed), EMBASE, ISI Web of Knowledge, Scopus, Cochrane Library, and ProQuest directed at finding retrospective and prospective original articles. We run a hand search using Google Scholar for extracting further studies. Bibliographies of the related and review articles were scanned in order to find relevant undiscovered studies in our systematic search. The search keywords were extracted from Medical Subject Heading (MeSH) terms and EMTREE.

Review and editorial articles, case reports, letters to editors, poster presentations, and meeting abstracts were excluded from this survey. Application of a reference test other than CT scan and conducting the study on animal samples were also considered as exclusion criteria. Two reviewers (M.Y, P.G) extracted data in true positive (TP), true negative (TN), false positive (FP), and false negative (FN). In cases where these values could not be obtained neither from the article nor by contacting the authors, the survey were excluded from the study.

Figure 1: Flowchart of the study.
### Table 1: Characteristics of included studies

| Study             | No. of Patient (+ / -) | Age (years) | Male (%) | Reference / Index | Transducer / Operator | Sampling       | Weaknesses                                      |
|-------------------|------------------------|-------------|----------|-------------------|-----------------------|-----------------|-----------------------------------------------|
| Lichtenstein 2004 | 184 / 200              | 58±15       | NR       | CT / US, CXR      | 5 MHz / Intensivist   | Consecutive    | ----                                          |
| Soldati 2006 (11) | 37 / 51                | 35 (18-89)  | 72.4     | CT / US, CXR      | 3.5- to 5-MHz / EP    | Consecutive    | The most patients were assessed retrospectively |
| Elmali 2007 (20)  | 39 / 21                | 43 (16-85)  | 80       | CT / CXR          | NA / Radiologist      | Consecutive    | Low sample size                               |
| Traub 2007 (21)   | 44 / 97                | 47 (18-89)  | 75       | CT / CXR          | NA / Radiologist      | Convenience    | Retrospective design                         |
| Rocco 2008 (22)   | 63 / 117               | 42±14       | 66.7     | CT / US, CXR      | 3.5 MHz / Intensivist | Consecutive    | Possibility of selection bias                |
| Xirouchaki 2011 (13) | 54 / 30               | 57±21.5     | 81       | CT / US, CXR      | 5–to 9-MHz / Intensivist | Convenience    | Low sample size                               |
| Hyacinthe 2012 (23) | 147 / 90              | 39 (22-51)  | 82       | CT / US, CXR      | 5-to 2-MHz / EP       | Consecutive    | Possibility of selection bias                |
| Blasińska 2013 (24) | 11 / 49               | NR          | NR       | CT / CXR          | NA / Radiologist      | Consecutive    | Low sample size                               |
| Chardoli 2013 (25) | 11 / 189               | 38 (16-90)  | 84       | CT / CXR          | NA / EP               | Convenience    | Lack of Blinding                              |
| Leblanc 2014 (26) | 38 / 7                 | 36 (15-56)  | 71       | CT / US, CXR      | 5-to 1-MHz / Intensivist | Convenience    | Low sample size                               |
| Helmy 2015 (27)   | 40 / 10                | 39 (18-67)  | 70       | CT / US, CXR      | 5 MHz / Intensivist   | Convenience    | Possibility of selection bias                |
| Vafaei 2015 (12)  | 48 / 104               | 31 (4-67)   | 77.6     | CT / US, CXR      | 3.5-to 7-MHz / EP     | Convenience    | Possibility of selection bias                |

1. (+ / -): (number of patient with contusion / number of patient without contusion); 2. Number are presented as mean ± standard deviation or (range). CT: Computed tomography; CXR: Chest radiography; EP: Emergency physician; NA: Not applicable; NR: Not Reported; US: Ultrasonography.
Data extraction
Two reviewers (M.Y, P.G) independently assessed the titles and abstracts of the articles found in the systematic search. Then the full texts of the potentially relevant articles were evaluated and the data from the studies that met the inclusion criteria were precisely summarized in details. No time or language limitations were established. Quality assessment of the articles was performed according to the guidelines suggested by 14-Item Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool (28). Based on this criteria, all included studies were screened for presence of selection, performance, recording, and reporting biases.

Demographic characteristics of the patients including age, gender, the number of patients with/without pulmonary contusion according to the results of CT scans, characteristics of ultrasound device (transducer, frequency) and its operator, blinding status, and sampling method (consecutive, convenience). Finally, the number of TP, TN, TN, and FN cases were recorded. Disagreements were solved by the third author (M.H). The method proposed by Sistrom and Mergo (29) was used to extract the data presented as charts. Web-based programs were utilized to calculate the number of TP, TN, TN, and FN cases from the articles in which only the sensitivity and specificity were presented.

Statistical analysis
Analysis was done by STATA 11.0 statistical software via “MIDAS” module. Summary receiver operative curves (SROC), sensitivity, specificity, positive likelihood ratio and negative likelihood ratio of ultrasonography and radiography in detection of pulmonary contusion with 95% confidence interval (95% CI) were estimated. In cases where data were presented separately for each hemi-thorax the information were included separately as presented in the original article. Due to the significant heterogeneity between the included studies, mixed effects binary regression model was applied. Heterogeneity was evaluated through calculation of $I^2$ and $\chi^2$ tests and a p value of less than 0.1 along with an $I^2$ greater than 50% were considered as presence of considerable heterogeneity (30).

In order to recognize the sources of heterogeneity, subgroup analysis was performed considering the sampling method (consecutive/ convenience), operator (emergency physician/ other specialists) or the interpreting physician, the ultrasound device’s frequency of the transducer (1-5 MHz/ 5-10 MHz), and sample size (less than 100 patients/ more than 100 patients). In all the analyses, p value of less than 0.05 was considered as statistically significant.

Results:
Study characteristics
Search in the mentioned databases yielded 15 studies that met the inclusion criteria. Further manual search resulted in finding 3 more related surveys. After summarization and quality assessment, 12 studies were included (11-13, 19-27) (Figure 1). A total of 716 patients with pulmonary contusion and 965 subjects without were evaluated. Their age ranged from 4 to 90 years old and male patients comprised 76% of the study population. The summary of included surveys is presented in Table 1. Diagnostic accuracy of ultrasonography and radiography in detection of pulmonary contusion were assessed simultaneously in eight studies (11-13, 19, 22, 23, 26, 27) and the accuracy of radiography was evaluated individually in four surveys (20, 21, 24, 25). Considerable heterogeneity was observed between the studies (P<0.001). No publication bias was observed in evaluation of the diagnostic accuracy of ultrasonography (p = 0.97) and chest radiography (p = 0.15) (Figure 2).

Meta-analysis
- Ultrasonography
Area under the curve of SROC for ultrasonography in pulmonary contusion diagnosis was found to be 0.93 (95% CI: 0.91 - 0.95) (Figure 3-A). Pooled sensitivity of ultrasonography in this regard was 0.92 (95% CI: 0.81 - 0.96; $I^2 = 95.81$, p < 0.001) and its pooled specificity was estimated to be 0.89 (95% CI: 0.85 - 0.93; $I^2 = 67.92$, p < 0.001). Ultrasonography had pooled positive and negative likelihood ratios of 8.94 (95% CI: 5.95 - 93.36; $I^2 = 67.92$, p < 0.001) and 0.09 (95% CI: 0.04 - 0.22; $I^2 = 66.36$, p < 0.001), respectively (Figure 4).

Table 2 demonstrates the results of subgroup analysis. The sensitivity of this modality was lower when consecutive sampling method was used (0.87 vs. 0.97), procedure was performed via an emergency specialist (0.77 vs. 0.95), sample sizes of higher than 100 patients, the sensitivity (0.86 vs. 0.96), and frequencies of ultrasonography probe was higher than 5 MHz (0.86 vs. 0.93).

- Chest Radiography
Data from 12 surveys were included in this part of meta-analysis (11-13, 19-27). Area under the SROC for radiography in detection of pulmonary contusion was 0.72 (95% CI: 0.67 - 0.75) (Figure 3-B). Pooled sensitivity and specificity of this diagnostic tool were 0.44 (95% CI: 0.32 - 0.58; $I^2 = 87.52$, p < 0.001) and 0.98 (95% CI: 0.88 - 1.0; $I^2 = 95.22$, p < 0.001), respectively. Pooled positive and negative likelihood ratios were also calculated to be 19.69 (95% CI: 3.59 - 108.07; $I^2 = 88.75$, p < 0.001) and 0.57 (95% CI: 0.45 - 0.72; $I^2 = 93.13$, p < 0.001), respectively (Figure 5).

Subgroup analysis showed that the sensitivity of radiography is affected by the interpreting physician of the plain film (emergency physician/ other specialists) and sample size (Table 2). According to the results of this analysis, the sensitivity of this imaging modality is higher when the radiographs were interpreted by a radiologist or intensivist (0.49; 95% CI: 0.30-0.68) compared to an
Table 2: Subgroup analysis of diagnostic accuracy for chest radiography and ultrasonography in detection of pulmonary contusion

| Covariate          | No. of studies | Bivariate random-effect model |  |  |  |  |
|--------------------|----------------|--------------------------------|----------------|--------------------------------|
|                    |                | Sensitivity (95% CI) | P  | Specificity (95% CI) | p  | heterogeneity, I² | P* |
| **Ultrasonography**|                |                                |  |                                |    |                      |    |
| Patient enrollment |                |                                |  |                                |    |                      |    |
| Consecutive        | 5              | 0.87 (0.78-0.96)              | 0.16 | 0.90 (0.86-0.95) | <0.001 | 49.0 % | 0.14 |
| Convenience        | 3              | 0.97 (0.94-1.00)              | 0.88 (0.82-0.95) |                                |    |                      |    |
| Operator           |                |                                |  |                                |    |                      |    |
| Emergency physician| 3              | 0.77 (0.62-0.93)              | <0.001 | 0.90 (0.84-0.95) | <0.001 | 68.0 % | 0.04 |
| Other physician    | 5              | 0.95 (0.92-0.99)              | 0.89 (0.84-0.94) |                                |    |                      |    |
| Sample size        |                |                                |  |                                |    |                      |    |
| < 100              | 4              | 0.96 (0.90-1.00)              | 0.38 | 0.94 (0.89-0.99) | <0.001 | 55.0 % | 0.11 |
| ≥ 100              | 4              | 0.86 (0.73-0.99)              | 0.88 (0.84-0.95) |                                |    |                      |    |
| Frequency          |                |                                |  |                                |    |                      |    |
| 1-5 MHz            | 5              | 0.93 (0.87-1.0)               | 0.41 | 0.88 (0.84-0.91) | <0.001 | 58.0 % | 0.09 |
| 5-10 MHz           | 3              | 0.86 (0.65-1.0)               | 0.93 (0.89-0.98) |                                |    |                      |    |
| **Radiography**    |                |                                |  |                                |    |                      |    |
| Patient enrollment |                |                                |  |                                |    |                      |    |
| Consecutive        | 6              | 0.45 (0.26-0.63)              | 0.90 | 0.99 (0.96-1.00) | 0.72 | 0.0 % | 0.61 |
| Convenience        | 6              | 0.44 (0.24-0.63)              | 0.95 (0.85-1.00) |                                |    |                      |    |
| Operator           |                |                                |  |                                |    |                      |    |
| Emergency physician| 6              | 0.40 (0.21-0.58)              | 0.74 | 0.98 (0.94-1.00) | 0.03 | 0.0 % | 0.79 |
| Other physician    | 6              | 0.49 (0.30-0.68)              | 0.97 (0.90-1.00) |                                |    |                      |    |
| Sample size        |                |                                |  |                                |    |                      |    |
| < 100              | 6              | 0.55 (0.38-0.72)              | 0.15 | 0.94 (0.82-1.00) | 0.99 | 36.0 % | 0.21 |
| ≥ 100              | 6              | 0.35 (0.19-0.51)              | 0.99 (0.97-1.00) |                                |    |                      |    |

*, P value < 0.1 was considered as significant for heterogeneity; CI: Confidence interval.
emergency specialist (0.40; 95% CI: 0.21 - 0.58).

Discussion:
The present meta-analysis is the first to assess the diagnostic accuracy of ultrasonography and radiography in detection of pulmonary contusion. The results illustrate a higher sensitivity of ultrasonography compared to radiography (0.92 vs. 0.44) in this regard, whereas the specificity of radiography was slightly higher (0.97 vs. 0.89). Since these two imaging modalities are the first diagnostic tools for assessment of traumatic thoracic injuries, their screening accuracy is of utmost importance. Accordingly, ultrasonography has better screening performance characteristics in detection of pulmonary contusion compared to radiography.

Various studies have pointed out the fact that diagnostic accuracy of ultrasonography is directly dependent on the skills of the operator (14, 15, 31, 32). Findings of the present survey were also congruent with this statement to some extent. The results demonstrated a higher sensitivity of ultrasonography in detection of pulmonary contusion when performed by a radiologist or an intensivist compared to emergency specialists. This might be due to the nature of pulmonary contusion whose diagnostic signs are very challenging to detect. The most important signs of pulmonary contusion identified by ultrasonography include multiple B-lines and an irregularly delineated tissue image which might be a moderately hypo-echoic blurred lesion (16). Furthermore, after observation of these signs, the operator should rule out pneumothorax as well. Therefore, experience plays an important role in pulmonary contusion diagnosis.

Frequency of transducer was another factor affecting the diagnostic accuracy of ultrasonography. Application of transducers with frequencies lower than 5MHz yield greater diagnostic values compared to higher. This finding is also related to the nature of the lesion. Contusion in characterized by parenchymal injuries and accumulation of fluid and blood in the lung tissues (16). These tissues lie in the deepest layers of chest cavity and so the penetrating power of ultrasound wave is more important than the image resolution (which is directly related to the wave’s frequency). Since ultrasound waves with lower frequencies have greater penetrating powers, application of these probes increases the chances of pulmonary contusion diagnosis. Sample size was also found to have an effect on diagnostic values of ultrasonography and radiography in detection of pulmonary contusion. The sensitivity of both these modalities was found to be higher in the studies with sample sizes of less than 100 patients. This might be due to possible selection bias in these studies (33). Selection of patients with severe traumas and so the higher chances of injury identification via imaging would be prominent in these studies. Moreover in some of these surveys, pneumothorax patients had been excluded which might have made the diagnosis easier (27).

Utilization of three strategies has improved the quality of the present meta-analysis. Firstly, comprehensive search in databases to include the maximum number of related surveys and secondly, elimination of publication bias. Thirdly, the effects of heterogeneity between the studies were controlled by subgroup analysis. On the other hand, simultaneous inclusion of retrospective and prospective studies might be considered as a limitation of this study. However, evaluation of outliers on the scatterplot based on standardized predictive random effects revealed that retrospective surveys are not the cause of diversity between the studies. Moreover, due to the observational nature of included studies, precise assessment of causal relationships was impossible.

Conclusion:
The results of present meta-analysis revealed the better screening performance characteristics of chest ultrasonography compared to radiography in detection of pulmonary contusion. It should be mentioned that these characteristics where dependent on operator and characteristics of device.

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Conflict of interest:
None

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Figure 2: Deeks’ funnel plot asymmetry test for assessment of publication bias. P values < 0.05 were considered as significant. Ultrasound (A); Radiography (B). ESS: Effective sample sizes.

Figure 3: Summary receiver operating curves (SROC) with prediction and confidence contours of ultrasonography (A) and chest radiography (B) in detection of pulmonary contusion. AUC: Area under the curve; SENS: Sensitivity; SPEC: Specificity.
Figure 4: Forest plot of screening performance characteristics of chest ultrasonography in detection of pulmonary contusion. Sensitivity and specificity (A); Diagnostic likelihood ratio (DLR) (B). CI: Confidence interval.
**Figure 5:** Forest plot of screening performance characteristics of chest radiography in detection of pulmonary contusion. Sensitivity and specificity (A); Diagnostic likelihood ratio (DLR) (B). CI: Confidence interval.
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اصول تنظیم قرار دادها

پروپوزال نویسی

آموزش مهارت های کاربردی در ندوین و چاپ مقاله