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Diagnostic

Do we need a change in ED diagnostic strategy for adult acute epiglottitis?

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ABSTRACT

Objectives: To retrospectively evaluate the diagnostic performance of qualitative and quantitative radiographic parameters for diagnosing adult acute epiglottitis, and identify the prevalence and risk factors of false-negative neck radiography-based diagnosis of acute epiglottitis.
Methods: An emergency physician and a radiologist independently reviewed neck radiographs of 91 patients with laryngoscopy-confirmed acute epiglottitis and 91 control subjects between March 2010 and June 2016 for qualitative and quantitative radiographic parameters of acute epiglottitis, and concluded a diagnosis. Receiver operating characteristic (ROC) curves were constructed to assess the diagnostic performance of radiographic parameters, while independent risk factors of false-negative diagnosis were determined by multivariate logistic regression analysis. Inter-observer agreement was also calculated.
Results: All radiographic parameters showed good diagnostic performance with sensitivities and specificities of 33.0–80.2% and 64.8–100%, respectively. Epiglottis width (EW) > 6.3 mm showed the highest diagnostic performance (area under the ROC curve [AUC]: 0.867, sensitivity: 75.8%, specificity: 97.8%). Interobserver agreement for all radiographic parameters was excellent (range: 0.893–0.991). The lateral neck radiography-based false-negative diagnosis rate was 31.9%, and previous oral antibiotic usage was an independent risk factor of false-negative results.
Conclusion: EW > 6.3 mm showed the best diagnostic accuracy, facilitating a neck radiograph-based diagnosis of acute epiglottitis. However, false-negative results on neck radiograph are quite common and previous oral antibiotic usage is a risk factor. Based on the knowledge of the usefulness and risk factors of false-negative results of neck radiography, diagnostic process for acute epiglottitis using neck radiography need to be changed.

1. Introduction

1.1. Background

Acute epiglottitis is a supraglottic inflammatory condition that can cause fatalities due to airway obstruction. Acute epiglottitis in children is marked by an acute onset of high fever, sore throat, and rapid progression of toxicity. Previous studies have reported that 85% of children with epiglottitis were symptomatic for <24 h before presenting to the hospital [1,2]. Conversely, adults with acute epiglottitis typically experience a prodrome, similar to that of upper respiratory infection, over a period of 1–2 days [3]. Patients have a sore throat, dysphagia, dyspnea, hoarseness, and stridor, particularly when in the supine position. Fever may develop only in the later stages of the disease in adult patients [4].

While the incidence of acute epiglottitis in children has markedly decreased as a result of vaccination for *Haemophilus influenzae* type b [2,5,6], the incidence of acute epiglottitis in adults has been reported to be increasing [7-10]. There are approximately 1.9 cases of epiglottitis per 100,000 adults, as compared to 0.5 cases per 100,000 children in the United States [11]. Most adult cases are caused by a broad range of bacteria, viruses, and fungi, although most frequently, no organism can be isolated [10]. Owing to the high mortality rate, accurate and early diagnosis is important [12].

Lateral neck radiographs are low-cost and readily available, and are often used as a screening tool in the emergency department (ED) for suspected acute epiglottitis [13]. Many radiographic features have been reported as useful signs for diagnosing acute epiglottitis in lateral neck radiographs [14-19]. Radiologists and clinicians use different radiographic features for diagnosing acute epiglottitis on lateral neck radiographs, depending on their knowledge. Additionally, we have observed that some patients with normal lateral neck radiographs show acute epiglottitis on neck computed tomography (CT) and/or laryngoscopy.

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We hypothesized that each radiographic parameter in neck radiographs may have different diagnostic performance, and some clinical factors may predispose to a false-negative diagnosis based on neck radiographs. In order to test our hypothesis, we designed a case-control study, owing to the rarity of acute epiglottitis. The primary goal of this study was to evaluate the diagnostic performance of known, measurable radiographic parameters for diagnosing acute epiglottitis in adults. The secondary goal of this study was to evaluate the prevalence and risk factors of false-negative diagnoses of acute epiglottitis based on neck radiographs.

2. Methods

2.1. Study population

Our institutional review board approved this retrospective study and waived the need for informed consent. Using a computerized data retrieval system, we searched the hospital database for patients in our institution who met the following criteria. The inclusion criteria were as follows: 1) adults who visited the ED of our hospital between March 2010 and June 2016, and 2) adults in whom a diagnosis of acute epiglottitis (ICD-9 diagnosis code 464.3) was made by means of laryngoscopy performed by an otolaryngologist. The exclusion criteria were as follows: 1) lack of lateral neck radiographs and 2) poor image quality that could jeopardize accurate measurement. Pediatric patients (<18 years) were not included, because pediatric patients with suspected acute epiglottitis underwent neck radiography with conservative treatment only, rather than CT or laryngoscopy.

According to our institute's routine protocol, as of March 2010, CT in the emergency department and/or laryngoscopy (by an otolaryngologist) were performed for the following patients: 1) adults (≥18 years) with a thumb sign on neck radiographs, performed in order to evaluate the severity or complications of acute epiglottitis, 2) adults with hoarseness or dysphagia, performed to confirm or exclude a diagnosis of acute epiglottitis, even though the thumb sign, on neck radiographs, and tonsillar enlargement, on physical examination, were not seen.

One radiologist (D.H.K.) collected the reports of the laryngoscopy and clinical data. The latter included sex, age, underlying comorbid conditions (hypertension, diabetic mellitus, cardiovascular disease, asthma); the presence of clinical symptoms, such as sore throat, dyspnea, hoarseness, dysphagia; the duration from symptom onset to ED visit, initial vital signs in the ED, including systolic blood pressure, diastolic blood pressure, pulse rate, respiratory rate, and body temperature; laboratory results, including white blood cell (WBC) count, and C-reactive protein (CRP) level; additional radiological examination findings, such as neck CT; and the management provided to the patients.

2.2. Control subjects

Control subjects were recruited using a Picture Archiving and Communication Systems (PACS) (Maro-view 5.4, Infinitt, Seoul, Republic of Korea) to search for adult patients who had undergone neck radiography. Patients were recruited by pairing them as age- and sex-matched controls to acute epiglottitis patients in a 1:1 ratio. The radiologist (D.H.K.) reviewed the demographic data, electronic medical records, and radiology reports of the lateral neck radiographs of the selected control subjects. Patients were included if they met the following criteria: 1) the normal lateral neck radiograph interpreted by a neuroradiologist (H.H.J.), 2) absence of a history of trauma or infection, 3) absence of a history of head and neck malignancy, and 4) absence of a history of neck or cervical spine surgery.

The neck radiographs of the patients and control subjects were blinded, mixed, and placed in a random order, to minimize sequential bias, for review.

2.3. Image acquisition and image analysis

All patients and control subjects in the study underwent standard lateral neck radiography. The radiographs were obtained in the standing position with a 15-degree extension of the neck.

All radiographs were evaluated retrospectively by one board-certificated emergency physician (S.H.L.) and one board-certificated radiologist (S.J.Y.), who were not involved in the selection of patients and control subjects. The two reviewers were unaware of the final clinical diagnoses and the prevalence of acute epiglottitis. The two reviewers independently evaluated the patients' and control subjects' lateral neck radiographs for: 1) the presence or absence of the thumb sign, 2) the presence or absence of the vallecula sign, 3) the aryepiglottic folds width (AEW), the epiglottis width (EW), the hypopharynx width (HW), retropharyngeal space (RPS), and retrotracheal space (RTS) on lateral neck images, and 4) the ratios of the AEW and third cervical vertebral body width (C3W), the EW and C3W, and the HW and C3W (Fig. 1). The definition of the radiographic parameters was based on previous studies [14-17]. All measurements were obtained by using electronic calipers in a PACS and the average values of two reviewers were determined. Additionally, reviewers concluded a diagnosis based on the radiographs as “acute epiglottitis” or “normal”.

2.4. Comparison of the final assessments between radiographs and laryngoscopy

To evaluate risk factor of false-negative diagnosis, the final assessments based on the radiographs and laryngoscopy were compared and divided into “true-positive” and “false-negative” results. In cases of discordance about the concluded diagnosis, one emergency physician and the two reviewers evaluated the causes of the discordance and reached a consensus. If both reviewers concluded “acute epiglottitis” and if it was in accordance with the laryngoscopy report, the case was regarded as “true-positive”. Conversely, if both reviewers' conclusions were “normal”, but laryngoscopic assessment concluded “acute epiglottitis”, the case was regarded as a “false-negative”.

2.5. Statistical analysis

Statistical analyses were performed using MedCalc software (Version 12.3.0, Mariakerke, Belgium). Independent *t*-tests were performed for continuous variables, and Pearson's chi-squared test or Fisher's exact test was used for nominal variables. Assessment of diagnostic performance of each radiographic parameter was analyzed by using receiver operating characteristic (ROC) curves. Inter-observer agreement was assessed by calculating the intraclass correlation coefficient (ICC) or weighted-kappa value. Independent risk factors for false-negative diagnosis were identified using multivariate logistic regression analysis. ICCs and kappa values were defined as follows: 0–0.20, poor agreement; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, good; and 0.81–1.00, excellent. We also generated adjusted odds ratios (ORs) and 95% confidence intervals (CIs) from multivariate analysis. p-Values < 0.05 were considered statistically significant.

3. Results

3.1. Characteristics of patients and control subjects

Ninety-five patients with a diagnosis of acute epiglottitis were recruited. Three patients were excluded as no lateral neck radiographs were available; one patient was excluded because of the poor image quality of the neck radiograph. A total of 91 patients (mean age: 45.0 ± 16.3 years; range: 18–81 years; male:female 49:42) were finally included in the study. Among them, 27 patients also underwent CT. Ultrasound (US) or magnetic resonance (MR) examination was not performed in any of the patients. Of the 91 patients, 84 patients were