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Research article

Clinical implication of radiographic scores in acute Middle East respiratory syndrome coronavirus pneumonia: Report from a single tertiary-referral center of South Korea

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ABSTRACT

The aim of this study is to determine the earliest cutoff of radiographic score as a potential prognostic indicator of fatal outcomes in patients with acute Middle East respiratory syndrome coronavirus (MERS-CoV) pneumonia. The institutional review board approved this retrospective study. Serial chest radiographies (CXRs) were obtained from viral exposure until death or discharge in 35 patients with laboratory confirmed MERS-CoV infection. Radiographic scores were calculated by multiplying a four-point scale of involved lung area and three-point scale of abnormal opacification, in each of the six lung zones. Receiver operating characteristics (ROC) analyses were performed to identify optimal day and radiographic score for the prediction of respiratory distress, and univariate and multivariate logistic regression analyses were performed to assess significant predictive factors for intubation or tracheostomy. Among 35 patients (22 men, 13 women; median age: 48 years), 25 demonstrated abnormal opacity on CXR (MERS pneumonia), whereas no abnormality was detected in 10 patients (MERS upper respiratory tract infection). Seven patients required ventilator support (intubation group) and three of them eventually expired. The average incubation period was 5.4 days (standard deviation, ± 2.8; range, 2–11). Patients in the intubation group had a higher incidence of diffuse lung involvement, higher radiographic scores, and fibrosing sequela on follow up study compared with those in the non-intubation group. However, patients' age and comorbidity did not differ significantly between the two groups. The ROC analysis revealed an area under curve of 0.726 for the radiographic score on day 10 with an optimal cutoff score of 10 for prediction of intubation, with a sensitivity of 71% and specificity of 67%. Our study suggest that MERS patients with radiographic score > 10 on day 10 from viral exposure require aggressive therapy with careful surveillance and follow-up evaluation.

1. Introduction

Middle East respiratory syndrome (MERS) is an acute viral respiratory disease, caused by a novel virus called MERS coronavirus (MERS-CoV) [1,2]. Since the first reported case of MERS in Saudi Arabia in 2012, 1888 laboratory-confirmed cases of infection with MERS-CoV, resulting in 670 deaths across 27 countries, have been reported to the World Health Organization [3]. The first case of MERS in Korea reported on May 20, 2015, was that of an individual who had developed the disease after traveling to the Middle East countries. Subsequently, this case led to the largest transmission cluster of MERS outside the Arabian Peninsula, resulting in 186 confirmed MERS cases in Korea [4]. Among these 186 cases, 36 were treated in our institution.

Imaging plays a crucial role in making a diagnosis and monitoring disease progress, and chest radiography (CXR) remains the most commonly used imaging modality. Because MERS can be transmitted

Abbreviations: MERS, Middle East respiratory syndrome; CoV, coronavirus; CXR, chest radiography; CT, computed tomography; ER, emergency room; ROC, receiver operating characteristic; URI, upper respiratory tract infection; AUC, area under the ROC curve

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through direct or indirect exposure to MERS-CoV, infection control in health care facilities is a critical issue [5–9]. Patients diagnosed with MERS should be moved to an institutional isolation care unit and personal protective equipment is mandatory for health care workers who handle these patients. Thus, CXR would play a pivotal role in the evaluation of patients with several infectious diseases, including MERS, because it is rapid and easily accessible, compared with computed tomography (CT). Indeed, we relied on the findings of sequential CXR while managing the 36 patients with MERS-CoV infection in clinical practice. However, there is still limited information about the prognostic implication of CXR findings in patients with MERS. Thus, the aim of this study was two-fold. First, we were to describe the serial radiographic characteristics of MERS-CoV pneumonia by analyzing radiographic scores. Second, we tried to identify the earliest cutoff value of radiographic score, which can be considered as a potential prognostic indicator of fatal outcomes in patients with MERS-CoV pneumonia.

2. Materials and methods

The institutional review board approved the study (IRB 2015-07-195), and informed consent was waived for the use of patients' medical and imaging data.

2.1. Study population and exposure

On May 27, 2015, a 35-year-old Korean man visited the emergency room (ER) of our institution with fever, productive cough, and dyspnea. After 2 days (May 29), he reported that he had met another patient with MERS approximately 10 days ago, at a different hospital. The patient was immediately transferred to an isolation care unit. The MERS-CoV infection was confirmed by a sputum assay on May 30. During his stay in the ER, numerous individuals were in contact with him directly or indirectly. Individuals with a possibility of exposure to this virus were quarantined and laboratory tests were conducted if symptoms were noted during the observational period. Consequently, 81 cases of MERS-CoV infection resulting from the exposure at the ER were confirmed, resulting in a total of 90 cases of MERS-CoV infection diagnosed at our institution [8]. Among the 90 patients, 36 were hospitalized in the isolation care unit of our institution. One patient with underlying stage-four lymphoma was not included in this study, as this condition could adversely affect the prognosis. Thus, 35 patients with laboratory-confirmed MERS were included.

We identified the exact time of exposure, symptom onset, and laboratory-diagnosis of MERS in every patient. In addition, all data, including age, sex, premorbid conditions, symptoms, laboratory findings, clinical course and survival outcome were collected from patient electronic medical records. The patients were then subdivided into two groups: patients who required intubation or tracheostomy (intubation group) and those who recovered without respiratory distress (non-intubation group).

2.2. Diagnosis of MERS-CoV infection

All of the diagnoses had been confirmed with real-time reverse-transcription polymerase chain reaction analysis of lower respiratory tract specimens, including sputum and endotracheal aspirates [10]. To be included in the study, at least two repeated diagnostic tests should have been conducted within 48-hour-intervals to arrive at a definitive diagnosis.

2.3. Image acquisition

All the patients who were hospitalized had undergone serial CXR. Posterior-anterior CXR scans were obtained with a digital radiography system (Revolution XQi ADS_28.4, GE Medical Systems, Milwaukee, WI, USA) and by adopting 70–120 kVp, 2–3 mA s and 180 cm source to image distance. Portable digital radiography (MobileDaRt Evolution, Shimadzu, Kyoto, Japan) at bedside with anteroposterior projection was performed for patients who could not stand or move (by adopting 65–75 kV, 1.8–3.2 mA s, 100 cm source to image distance). The images were then interfaced directly to a picture archiving and communication system (Centricity 3.0; GE Healthcare, Mt. Prospect, IL, USA), which displayed all image data on two monitors (1536 × 2048 matrix, 10-bit viewable gray scale, and 450 cd per square meter).

2.4. Image analysis

Two chest radiologists assessed the CXRs (with 5 and 22 years of experience in chest imaging interpretation, respectively). They were blinded to patient information or disease progress, except for the knowledge that these were cases of MERS-CoV infection.

The extent of involvement on CXR was assessed independently for each of the 3 zones: upper (above the carina), middle (upper half of the craniocaudal distance of the remaining lung), and lower (lower half of the craniocaudal distance of the remaining lung) lung zones. The parenchymal abnormality on CXR was graded on a 3-point scale: 1, normal attenuation; 2, ground-glass attenuation; and 3, consolidation. The ground-glass opacity was defined as an area of hazy increased lung opacity, within which margins of pulmonary vessels may be indistinct [11]. Consolidation appears as a homogeneous increase in pulmonary parenchymal attenuation that obscures the margins of vessels and airway walls [11]. Each lung zone, with a total of six lung zones, was then graded based on the following scale (according to the area of the lung affected): 0 if normal, 1 if less than 25% of abnormality, 2 if 25–50% abnormality, 3 if 50–75% abnormality, and 4 if > 75% abnormality was noted. The four-point scale of the lung involvement was then multiplied by the 3-point scale of parenchymal abnormality in each lung zone, resulting in points ranging from 0 to 12 [12,13]. Points from all zones were added to arrive at a final total cumulative score, with values ranging from 0 to 72 (Fig. 1).

Presence of pleural effusion, laterality (unilateral vs. bilateral) of the lesions and that of fibrosing sequelae on serial CXR were also recorded. In terms of anatomic location, the distribution of parenchymal abnormalities was classified as central, peripheral, or mixed. The outer half of the lung was defined as peripheral, while the inner half was defined as central.

2.5. Statistical analysis

Statistical analysis was executed using SAS Version 9.4 (SAS Institute Inc, Cary, NC, USA). Differences in the clinico-radiological characteristics of the patients who were eventually intubated (intubation group) and those who were not (non-intubation group) were assessed using the Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables. Receiver operating characteristic (ROC) curve was plotted to select the appropriate cutoff value of radiographic score from day 5 to 18 to assess maximum sensitivity and specificity for fatal outcome. Univariate and multivariate logistic regression analyses were used to assess significant predictive factors for intubation. When everyday radiographic score was not available, a 3-day moving average of radiographic scores was applied. Interobserver agreements for radiographic scores were determined with intraclass correlation coefficients. $p < 0.05$ was considered to indicate a significant difference.

3. Results

3.1. Demographics and clinical characteristics

Detailed patient characteristics are shown in Table 1. Among 35 patients (22 men, 13 women; median age, 48 years) with laboratory confirmed MERS-CoV infection, 10 did not have any radiographic