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Development of a guideline on reading CT images of malignant pleural mesothelioma and selection of the reference CT films

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ABSTRACT

Purpose: International experts developed a guideline on reading CT images of malignant pleural mesothelioma for radiologists and physicians. It is intended that it act as a supplement to the current *International Classification of HRCT for Occupational and Environmental Respiratory Diseases*.
Methods: The research literatures on mesothelioma CT features were systematically reviewed. Ten mesothelioma CT features were adopted into the guideline prepared according to experts' opinion. The terminology of mesothelioma CT features and mesothelioma probability were agreed by consensus of experts. The CT reference films for each mesothelioma feature were selected based on agreement by experts from 22 definite mesothelioma cases confirmed pathologically and immunohistochemically. To support the validity of the mesothelioma probability, 4 experts' readings of CT films from 57 cases with or without mesothelioma were analyzed by kappa statistics between the experts; sensitivity and specificity for mesothelioma were also assessed.
Results: The mesothelioma CT Guideline was developed, providing the terminology of CT features and the mesothelioma probability, the judgement of severity, the distribution of mesothelioma, and the revised CT reading sheet including mesothelioma items. The CT reference films with ten mesothelioma typical

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features were selected. The average linearly and quadratically weighted kappa of the agreement on the 4-point scale mesothelioma probability were 0.58 and 0.71, respectively. The average sensitivity and specificity for mesothelioma were 93.2% and 65.6%, respectively.
Conclusion: The evidence-based mesothelioma CT Guideline developed may serve as a good educational tool to facilitate physicians in recognising mesothelioma and improve their proficiency in diagnosis of mesothelioma.

1. Introduction

Malignant pleural mesothelioma (MPM) is an aggressive tumor that develops from the mesothelial cells of the pleura. Although all types of asbestos e.g., white, blue and brown asbestos were widely abandoned in many industrialized countries in the 1980s, the incidence of MPM is still growing in most of these countries [1]. The patients suffering from MPM often present symptoms such as dyspnea, chest pain, cough, and weight loss. The prognosis of MPM is so poor that half of the patients can survive less than one year following the confirmed diagnosis.

MPM is likely to be misdiagnosed as tuberculous pleurisy, and metastatic pleural tumors of lung cancer. Early diagnosis of the mesothelioma is often difficult, and it has usually reached an advanced stage by the time it is accurately diagnosed. Conventional CT is more sensitive and specific than plain chest radiography in the diagnosis of both parenchymal and pleural diseases related to asbestos exposure. CT remains the main imaging modality used in the initial evaluation of patients with suspected MPM. Improvement in the proficiency of reading MPM CT and the early diagnosis for MPM poses challenges to occupational physicians in health surveillance and screening for patients.

The International Classification of HRCT for Occupational and Environmental Respiratory diseases (ICOERD) has been developed for screening, epidemiological and clinical study of respiratory diseases caused by occupational and environmental factors [2]. This classification was partly validated because it could describe and assess the parenchymal and pleural abnormalities of pneumoconiosis on CT images [3,4]. Since asbestos exposure associated MPM has aroused an extensive social concern issue in many countries, experts considered the possibility of developing a guideline for radiologists, chest physicians, general physicians and occupational physicians regarding the reading of MPM CT images that act as a supplement part to the ICOERD.

The current study describes the process of the development of the guideline on reading CT films of MPM (MPM-CT Guideline) and selection of the reference MPM CT films by experts. In order to support the validity of MPM probability, the experts' CT readings were statistically analyzed to assess the agreement in the diagnosis of MPM between experts and also calculated the sensitivity and specificity for MPM over the experts' CT readings.

2. Materials and methods

2.1. Development of the MPM-CT guideline

2.1.1. Literature review for MPM typical CT features

The MPM-CT Guideline was developed based on the systematic search and review of the literatures on MPM CT findings published since 1980 from PubMed database. The MPM CT features were described in different studies [5,6]. Kawashima and Libshitz [7] reported CT findings from MPM in 50 patients included pleural thickening in 46 (92%), interlobar fissure pleural thickening in 43 (86%), and pleural effusions in 37 (74%), contractions of the involved hemithorax in 21 (42%), and focal pleural masses were seen in 4 (8%). Half of these cases demonstrated chest wall invasion.

Okten et al. [8] retrospectively reviewed CT scans of 66 patients, which were performed before any invasive procedure was done. The most common CT findings of these MPM cases were pleural effusion (80.3%), pleural thickening (77.2%), volume contraction (37.9%), involvement of mediastinal pleura (31.8%) and interlobar fissure (28.8%).

From the CT scans of 99 MPM cases, Metintas et al. [9] found that the most common MPM CT features were circumferential lung encasement by multiple nodules (28%); pleural thickening with irregular pleuropulmonary margins (26%); and pleural thickening with superimposed nodules (20%).

Wang et al. [10] reported that the key CT findings suggesting MPM include "unilateral pleural effusion", "nodular pleural thickening", and "interlobar fissure thickening".

Ten features frequently observed in MPM cases were therefore adopted into the current guideline according to experts' expertise: unilateral pleural effusion ("ue"), nodular pleural thickening ("nt"), interlobar fissure thickening ("it"), mediastinal pleural thickening ("mt"), tumoral encasement of lung ("te"), calcified plaque engulfment ("pe"), invasion (iv"), diminished lung ("dl"), contracted hemithorax ("ch") and pleural mass ("pm").

2.1.2. Workshops on defining the terminology

There were two workshops at which the experts discussed the development of the guideline. In the 1st workshop, experts participated in the discussion for developing guideline, and proposed some important MPM CT features to be adopted into the guideline. At the 2nd workshop, the MPM CT features "ch", "dl" "pm" and "others" were added into the guideline according to experts' proposal. The contents of the guideline were reviewed and modified according to experts' suggestion, including the terminology of CT features, MPM probability, judgement, and so on. On the text of the guideline, the "localized" or "diffuse" type were provided for the reader to make a judgement of the MPM type according to its distribution. The MPM severity is to be assessed according to the overall impression of the CT findings as: "mild", "moderate" or "advanced".

The MPM probability was defined as follows: Grade 1: negative; no abnormal findings on CT, or abnormal findings of other diseases; Grade 2: low probability of MPM; Grade 3: moderate probability of MPM; Grade 4: high probability of MPM.

2.2. Selection of MPM CT reference films

2.2.1. Subjects for CT readings

In June 2005, a newspaper article reported that five students suffered from MPM, who had live near the Kubota Plant, a currently closed large asbestos cement pipe factory in Amagasaki City, Hyogo Prefecture, Japan. The factory used crocidolite and chrysotile to produce cement pipes between 1957 and 1975 with an annual average usage of 4670 tons of crocidolite and an annual average of 4600 tons of chrysotile [11]. Many residents supposed that their diseases such as MPM and lung cancer that they experienced might be due to environmental asbestos exposure from the plant. As of April 2007, two of the authors (N.K. and S.K.) investigated medical records including the pathological reports when available,