J HK Coll Radiol. 2008;11:72-75

ORIGINAL ARTICLE

Thoracocentesis for Potential Malignancy: Does Volume Matter?

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ABSTRACT

Objective: *To determine whether the volume of fluid aspirated during ultrasound-guided thoracocentesis influences the histological diagnosis.*

Methods: *Fifty patients with unilateral pleural effusion of unknown cause, in whom malignancy needed to be excluded, were enrolled in this prospective study. Patients had unresolved effusion despite adequate antibiotic therapy, effusion without signs of sepsis or heart failure, or effusion in conjunction with a clinical history suggestive of malignancy (smoking, cough, weight loss, or haemoptysis). Pleural effusions were detected on the basis of clinical examination and plain film chest radiography, and were confirmed by ultrasound. All patients underwent ultrasound-guided thoracocentesis using a 21 G spinal needle and 2 samples of pleural fluid were obtained — a 10-mL aliquot followed by a 50-mL volume sample. The fluid samples were evaluated separately for malignant cells.*

Results: *Forty seven procedures yielded 2 sufficient volume amounts for analysis. Of the 47 patients included for analysis, 7 had malignancy. The diagnosis of malignancy was separately made on both sample volumes for all 7 patients. The cytological subtype was identical in both samples. There was statistically significant agreement between the 2 volumes for all patients ($p < 0.0001$). No complications were encountered.*

Conclusion: *Aspiration of 50 mL of pleural fluid did not confer any advantage over 10 mL of pleural fluid traditionally used for the diagnosis of malignant pleural effusion.*

Key Words: *Biopsy, fine-needle, Neoplasms, Pleural effusion, malignant*

INTRODUCTION

Pleural effusion is a frequently encountered clinical problem that requires thorough evaluation. Thoracocentesis is performed for pleural effusions for 2 main indications: diagnostic and therapeutic.[1] Therapeutic treatment is typically performed to relieve dyspnoea or to drain infected fluid. Ultrasound guidance is increasingly being used to obtain fluid from the pleural space, particularly when the effusion is small.[2] Thoracocentesis is a relatively safe procedure when performed carefully by experienced operators. The use of radiological guidance, in particular ultrasound guidance, has improved the safety of this procedure.[2] Ultrasound also has the advantage of dynamic assessment of the effusion and can be used to exclude other possible causes of chest radiographic opacification such as pleural thickening and consolidation. In addition, ultrasound can exclude conditions masquerading as pleural effusion such as that seen with an elevated hemidiaphragm or consolidation.

Estimates of the sensitivity of thoracocentesis for the diagnosis of malignant cells vary from 40% to 87%.[1] The precise volume of fluid that should be aspirated is not well defined.[3] Traditionally, a sample volume of 10 mL is aspirated, but there are no guidelines to suggest whether a larger aspirate would be more useful.The complication rate, although low, increases when larger volumes of fluid are aspirated. In situations in which the sample is negative for malignant cells and there is a high index of clinical suspicion for malignancy, the procedure is often repeated and a larger volume of fluid is taken. However, this is an empirical decision, with no scientific basis. At the Department of Radiology, Adelaide and Meath Hospital, Dublin, Ireland, 50-mL

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Submitted: 18 February 2008; Accepted: 2 April 2008.

samples are increasingly requested with the intention of increasing the sensitivity of the diagnosis. This study was performed to determine whether the volume of fluid aspirated during ultrasound-guided thoracocentesis influenced the histological diagnosis.

METHODS

This was a prospective study performed over a 2-year period. Fifty patients (35 men and 15 women; mean age, 62.4 years) were recruited. Ethical approval was obtained and consent was obtained from all patients. Patients with a unilateral pleural effusion in whom malignancy was suspected were enrolled. Inclusion criteria were clinical suspicion that the pleural effusion was related to malignancy (unresolving effusion despite adequate antibiotic therapy), effusion without signs of sepsis or heart failure, or effusion in conjunction with a clinical history suggestive of malignancy (smoking, cough, weight loss, or haemoptysis). A diagnosis of a pleural effusion was based on clinical examination and chest radiographs, and was confirmed by ultrasound for all patients. Exclusion criteria were bilateral effusions (as these were likely to be related to transudates resulting from conditions such as cardiac failure), clinical lung infection in the presence of pyrexia and increased white cell count, and bleeding disorders (international normalising ratio >1.4; platelet count, 50 x 10^9/L).

All patients underwent ultrasound-guided thoracocentesis using a 21 G needle by 1 of 2 operators experienced in ultrasound-guided procedures. The procedure was performed using an aseptic technique under local anaesthetic with 1% lignocaine 10 mL. Ultrasound examination identified the optimum site of needle puncture. Two samples of fluid were taken through the same needle tract. The first sample was a 10-mL aliquot and the second sample was a 50-mL aliquot. The 2 samples were sent to the pathology department and analysed separately for the presence of malignant cells by 2 experienced cytopathologists.

The results were entered into a Microsoft Excel database spreadsheet for comparison and analysis. No patients had any complications following the procedure.

RESULTS

Of the 50 procedures, 47 yielded sufficient samples for analysis. It was not possible to obtain the full 50-mL sample for 3 patients, for whom 20 mL, 35 mL, and 40 mL were obtained. These 3 patients were excluded from the study leaving 47 patients in the final cohort.

Seven patients had malignant cells identified in their sample, as follows: adenocarcinoma (n = 3), non-small cell lung carcinoma (n = 3), and mesothelioma (n = 1). No malignancy was detected in 40 patients. The correct diagnosis of malignancy was made in both samples for all 7 patients, and the correct cytological subtype was noted in both sets of fluid.

Statistical analysis was performed to evaluate whether there was a statistically significant coefficient of agreement between the 2 aliquots (10 mL and 50 mL), and there was 100% agreement between the 2 samples ($p < 0.0001$; agreement, 100%; expected agreement, 74.65%; κ, 1.000; standard error, 0.1459; Z, 6.86).

DISCUSSION

Pleural effusions develop as a result of both local and systemic diseases. The aetiology can be infectious, malignant, or related to renal, cardiac, or hepatic disease. Clinical and radiographic features may help to differentiate the aetiology. Sometimes no specific cause can be identified. The gold standard for analysing pleural fluid is thoracocentesis. Thoracocentesis was first described by Bowditch in 1852 but, despite 150 years of experience, little has been written about the technique.[4] Thoracocentesis is indicated for patients with pleural effusion of unknown cause. For patients with congestive cardiac failure causing effusion, thoracocentesis is indicated when diuresis has failed to relieve the effusion or if the effusion is unilateral.[1] For patients with cardiac failure, the effusion is usually a transudate. Differentiation between a transudate and an exudate can be made by analysing the protein and lactate dehydrogenase levels in the effusion sample and the patient's serum (Light's criteria).[5] Usually, pleural fluid undergoes biochemical, cytological, and microbiological analysis. However, in this study, only the cytological component of the effusion was analysed.

Cytological analysis is sensitive and highly specific for malignant pleural effusions, with accuracy rates ranging from 40% to 87%.[1] Negative cytology in conjunction with a high clinical suspicion of malignancy poses a diagnostic dilemma. Repeat sampling with a larger volume has been proposed by some authors and others have suggested that multiple specimens taken at different times may also be helpful.[6] Garcia et al retrospectively analysed the cytology of multiple fluid specimens of 250 patients.[7] These authors found an added benefit in having 2 fluid specimens, but did not find any added benefit from more than 2 specimens. However,

this study did not address the volume sensitivity of separate specimens.

Guidelines advise that no more than 1000 mL to 1500 mL should be removed at one time, to prevent hypotension or pulmonary oedema.[8] There are few data regarding the minimum fluid volume required for diagnosis. Various studies have used different volumes of aspirated fluid, ranging from 10 mL to 250 mL.[9-11] Leff et al suggested that samples of <250 mL contained too few malignant cells to make a diagnosis.[11] However, most authors have not found this to be the case. In this study, the diagnosis of malignancy was made with confidence, even with 10 mL of fluid. Sallach et al addressed the question of required volume in their study of 374 samples of 6 mL to 2800 mL from patients with confirmed pleural malignancy.[3] This study compared volumes in 4 quartiles of increasing size and found that the diagnosis was not dependent on the volume of fluid aspirated. However, all patients were known to have malignancy in the study by Sallach et al,[3] whereas the diagnosis was unknown or suspected in this study.

The pathological subtype of the tumour has been found to influence the likelihood of yielding a positive thoracocentesis, with pleural adenocarcinoma, breast carcinoma, and non-Hodgkin lymphoma being more likely to result in positive cytology than squamous cell carcinoma or sarcoma.[10,11-14] Processing techniques can also impact on the diagnostic yield with multiple different methods recommended, for example, use of paraffin-embedded cell blocks or smears.[15] The American College of Physicians advise aspiration of 50 mL to 100 mL,[9] but this guideline is not specific for the investigation of malignant pleural effusions and refers to fluid aspiration undergoing microbiological and biochemical evaluation, as well as cytological evaluation. Data from 2 studies show that traditional 10 mL aspirations will yield a positive diagnosis in 56% to 57% of patients.[10,16]

At the Adelaide and Meath Hospital, it has been routine to obtain 10-mL samples for cytological evaluation. However, theoretically, it seems possible that larger samples would reveal a higher yield of positive cytology, and this issue was addressed in this study. The disadvantage of larger samples is that there is a higher risk of complications with increasing aspiration volumes.[8,17] This study has shown that there was no added benefit to obtaining 50-mL samples over the traditional 10-mL sample.

This study had some limitations. The sample volumes were limited to 10 mL and 50 mL, and it may have been useful to have had fluid volumes up to 1000 mL. However, many of the pleural effusions were small and such volumes would not be obtainable from all patients. A 21 G needle, which limits the amount of fluid that can be aspirated, was used for all patients. There was a relatively low rate of malignancy (7 of 47 patients). A higher percentage of positive results would have been preferable. Finally, patients with negative results were not followed up to see whether they developed evidence of malignancy. While this would have created interesting data on the sensitivity of aspiration samples, it was not the purpose of this study and has already been addressed in several other studies.

This study prospectively analysed whether there was any benefit in obtaining 50-mL samples as opposed to the traditional 10-mL samples from patients presenting with a pleural effusion and the possibility of malignancy. There was no added benefit to obtaining a larger sample. This study suggests that a 10-mL sample is adequate for assessment of malignant pleural effusion.

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