

## Therapeutic thoracentesis symptoms and activity: a qualitative study

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**Word count:** 3467 words

## **Abstract**

**Introduction:** Malignant pleural effusions (MPE) commonly occur in patients with advanced cancer. Drainage of fluid aims to relieve symptoms and improve quality of life.

**Objectives:** To improve our understanding of how therapeutic aspiration affects symptoms and activities in patients with MPE.

**Method:** Patients presenting to the Pleural Clinic at Norfolk and Norwich University Hospital with a confirmed or suspected MPE participated in up to three semi-structured interviews during their diagnostic/therapeutic pathway. Interviews were analysed using framework analysis, by two researchers independently.

**Results:** Sixteen patients participated. Symptoms reported before drainage included breathlessness, cough, chest pain, fatigue and anorexia. Symptoms affected their activities, including walking, bending over and socialisation. Patients described anxiety about the underlying diagnosis and fear of over-reliance on others. Expectations of drainage-outcome varied, with some hoping for a cure and others hoping for any improvement. After drainage, breathlessness, chest pain and cough improved in some patients. They reported feeling and sleeping better, but fatigue and poor appetite remained. Participants were more active after aspiration, but the duration of improvement was a few days only. Despite this, patients still felt the procedure worthwhile.

**Conclusion:** Overall health and respiratory symptoms improved following drainage, but constitutional symptoms did not improve. This may be because constitutional symptoms are caused by the underlying cancer. This study suggests that clinicians should consider a range of symptoms, rather than just breathlessness, in planning outcomes for clinical trials. These results are important to inform patients about the potential benefits and duration of symptom improvement after therapeutic aspiration.

## Introduction

A malignant pleural effusion (MPE) is an accumulation of fluid secondary to cancer in the space between the lung and chest wall (the pleural space). It affects around 40,000 people per year in the UK<sup>1</sup>. MPE indicates advanced, incurable cancer. It can develop in patients with known cancer or be the first presentation of a new diagnosis. It can be due to primary mesothelial cancer (mesothelioma) or spread of cancer from another site. Median survival from diagnosis is around 3 to 12 months<sup>2</sup>. Treatment focuses on palliating symptoms and improving quality of life.

Following detection of a pleural effusion, patients are usually referred to a Pleural Clinic for pleural fluid aspiration to aid diagnosis and treatment. Therapeutic aspiration is drainage of a large volume of pleural fluid to relieve symptoms, usually done as an outpatient over about ten minutes. If fluid and symptoms recur, then a definitive pleural procedure (e.g. chest drain and pleurodesis or indwelling pleural catheter insertion) is performed to provide long term symptom control<sup>1</sup>.

Randomised controlled trials (RCTs) aimed at comparing treatments to improve symptoms in patients with MPEs have focussed on breathlessness, often assessed using a visual analogue scale<sup>3-7</sup>. However, not all patients recruited to these trials were assessed as being breathless at baseline and a significant proportion did not experience improvement in breathlessness following pleural fluid drainage. Trial data also demonstrates that patients experience improvements in chest pain following drainage<sup>3</sup>. These data suggest that we should consider a broader range of symptoms and benefits when considering whether to drain a patient's effusion.

The main aim of this study was to improve our understanding of symptoms in patients with known or suspected MPE undergoing therapeutic aspiration and the impact of aspiration on those symptoms. Further aims were to explore the impact this has on patients' activities, psychosocial aspects and their experience of the procedure itself and whether this varied in significant subcategories (gender or underlying cancer type). The findings will influence design of future RCTs and advice given to patients.

## Methods

Sequential patients were recruited from the Pleural Clinic at the Norfolk and Norwich University Hospital, Norwich, UK between January and April 2019. The study was ethically approved by the Greater Manchester West Research Ethics Committee (IRAS ID: 248840) and undertaken in accordance with Good Clinical Practice guidelines. Patients presenting with a new pleural effusion or referred for therapeutic aspiration were screened for eligibility. Eligibility criteria were: adults with a known or suspected MPE diagnosed on chest radiograph, computer tomography scan or ultrasound; attending for therapeutic aspiration; and able to fulfil all study requirements. Exclusion criteria were: visual impairment; conditions requiring chest drain insertion; known transudative pleural effusion; and effusion thought to be primarily due to cardiac, renal or hepatic impairment.

Patients gave written informed consent and then participated in up to three brief focused semi-structured interviews during their therapeutic (and diagnostic) pathway. The interviews were performed by one of two doctors (CT and RF) who were not otherwise involved in the patient's care. Each interviewer performed all interviews for each individual. Interviews took place in a clinic room adjacent to the procedure room. The first interview was prior to their initial therapeutic aspiration and focussed on symptoms, the impact of those symptoms on activities and expectations of therapeutic aspiration and lasted approximately fifteen minutes. The second interview was conducted approximately seven days later, prior to the follow-up clinic appointment at which patients would be reassessed and receive their results. This focussed on how therapeutic aspiration

had affected their symptoms and activities and their experience of drainage and lasted approximately ten minutes. A third interview was conducted if the participant required a further drainage procedure (unless this was performed at the time of the follow-up appointment). This interview focussed on change in symptoms and activities and, if appropriate, how these had led the patient to seek a further drainage procedure. It lasted five to ten minutes. Relatives also participated in the interviews if they and the patient wanted, and these relatives gave verbal consent for the use of their contributions.

A topic guide was followed to ensure all relevant points were addressed. Interviews were audio-recorded, transcribed verbatim, anonymised and analysed by two researchers independently (CT and RF) using framework analysis<sup>8</sup>. The results were then compared, discussed and collated. Recruitment stopped once data saturation occurred<sup>9</sup>.

## **Results**

Sixteen patients were recruited to the study (Figure 1): 12 men and 4 women. Demographics are summarised in Table 1. All patients completed the first interview, thirteen the second and two the third.

### **Symptoms prior to aspiration**

Patients described a range of symptoms before drainage, included respiratory symptoms, such as breathlessness, cough and chest pain, and constitutional symptoms including anorexia and fatigue. However, no symptoms (including breathlessness) were reported by all patients. Other symptoms included wheezing and change in voice.

*"If the coughing was to stop and go away, I would be back to normal."* (83, male, metastatic carcinoid tumour)

Symptoms were exacerbated by lying flat, leading to difficulty sleeping.

*"The worst is sleeping because... if you lie down, the tendency to cough is augmented quite significantly."* (81, male, lymphoma)

### **Activity prior to aspiration**

Patients described how these symptoms affected their daily life and activities, naming several different activities including housework, gardening and climbing stairs. Several sports were mentioned including golf and hiking. There was wide variation in the range of activities that patients mentioned as making them breathless, from minimal exertion (e.g. on talking) to significant activity (e.g. on running). These were activities that they had previously been able to do without breathlessness.

*"I've been getting breathless with climbing the stairs at home. I used to do a lot of walking and um walking up hill made me breathless and its now walking on a level at a reasonable speed I get breathless too"* (75, male, mesothelioma)

Bending over often exacerbated symptoms such as breathlessness and cough. Patients referred to this in relation to activities.

*"Quite uncomfortable when I bend over. I like to pick my little dog up."* (85, female, metastatic lung cancer)

### **Expectations of therapeutic aspiration**

Some patients had high expectations of therapeutic aspiration and were hoping for a cure or to feel normal again.

*"I'm hoping for miraculously to get me back to where I was... get rid of the breathlessness and coughing and carry on with my life." (75, male, mesothelioma)*

Other patients felt that any improvement would be worthwhile. Some mentioned specific factors that they felt might limit the benefit they gained, such as their age or comorbidities.

*"Anything better than I got at the moment." (69, male, mesothelioma)*

Some patients named specific symptoms they hoped would improve, including breathlessness, cough and fatigue.

*"Well I'm hoping that it will make me less breathless and I also hope it will subdue the cough which it theoretically ought to." (81, male, lymphoma)*

Patients also described activities they hoped to be able to do after drainage. Walking was mentioned as important as it facilitated other activities.

*"Yeah, just get more mobile with my son really. Just get more comfortable and be able to get walking – just, you know, get up the road with my dog." (45, female, metastatic breast cancer)*

Patients described frustration at not being able to do certain activities and the effect of this on their emotional well-being and quality of life.

*"And you can tell by the way I'm talking how my quality of life is. I can barely walk over there. You know, it is a lovely sunny day and I'd like to be out enjoying it." (70, male, metastatic pancreatic cancer)*

### **Psychosocial impact of MPE**

Patients spontaneously described the psychological and social impacts of MPE during the interviews. Several patients mentioned anxiety regarding their underlying diagnosis. This was seen both in patients with known malignant diagnoses and those without.

*"I think cause we're so apprehensive about what it is that we can't really think of anything else can we." (Wife of male participant aged 75, mesothelioma, diagnosis not known at interview)*

Another recurrent theme was lack of motivation, with some patients relating this to low mood or to fatigue.

*"It sucks you down so far that you kind of go "oh, it's ok, it's alright." And you just sit on the loo 'cause you can't be arsed to get off." (70, male, metastatic pancreatic cancer)*

Patients often identified alternative explanations for their symptoms, attributing them to other diagnoses, such as COPD, or to a particular event such as a fall, or to ageing.

*"I had been diagnosed with COPD and I put everything down to that at first you see." (85, female, metastatic lung cancer)*

Patients described how being unwell conflicted with their view of themselves as fit and healthy, sometimes expressing this as a loss.

*"Well I've never been ill before, I can't believe I'm like this. I've been so fit and healthy." (81, female, metastatic breast cancer)*

A common fear among patients was reliance on others and becoming a burden.

*"I don't like her pushing me [in the wheelchair] 'cause she has osteoporosis you know. I don't want to put too much strain on her" (79, male, mesothelioma)*

### **Experience of therapeutic aspiration**

The experience of the procedure itself varied widely. A common (but not universal) complaint was pain. Variation was seen within patients who had more than one therapeutic aspiration, with one participant describing his second procedure as much more painful than his first. One participant felt his pre-procedure warning to expect discomfort rather than pain was inaccurate. However, the procedure was generally considered to be tolerable.

*'Not very pleasant. That did hurt when they pushed in at the end, it did hurt. But you put up with it.'* (81, female, breast cancer)

A common theme among patients was the significance to them of the volume of fluid, with many expressing shock at the volume drained. Some patients expressed their expectations for the procedure in terms of the amount of fluid removed, describing a wish for all the fluid to be drained. Patients who had only had part of their effusion drained were disappointed that residual fluid remained.

*"At first, I was rather shocked cause you drained a litre." (81, male, lymphoma)*

### **Symptoms following aspiration**

Following aspiration, patients generally saw an improvement in respiratory symptoms, such as breathlessness, cough and chest pain.

*"Yeah I was feeling fine after I had it done. Breathing had gone back to normal really" (66, male, mesothelioma)*

Sleep also improved. However, some patients were disappointed and hoped for a greater improvement in symptoms.

*"Well the only dream I had which wasn't entirely fulfilled was that the cough would be quite substantially diminished." (81, male, lymphoma)*

Generally constitutional symptoms such as anorexia and fatigue remained after therapeutic aspiration, even if sleep improved.

*'All I know was getting very tired. I could have a good night's sleep I could and then I could sit in my chair and by half past nine I could be off.'* (79, male, mesothelioma)

Rather than naming specific symptoms, some patients described generally feeling better after therapeutic aspiration.

*"It really felt better and normal again." (45, female, metastatic breast cancer)*

The duration of benefit was generally only a few days and by their second interview, seven days post-procedure, many patients felt their symptoms were back to their pre-procedure baseline. Despite this, patients felt the procedure was worthwhile.

*'What you go through is worthwhile if you come out as good as I think I've come out.'* (83, male, metastatic carcinoid tumour)

### **Activity following aspiration**

Patients were generally more active after drainage. Some used their experience of attending the hospital for their second visit to gauge their activity levels, comparing how easy it had been to walk from their car to the clinic room or whether they had needed to use a wheelchair.

*"We've done enough walking this morning... and I haven't found, like I did say last Monday that I was almost ready to want a stop for 5 minutes."* (83, male, metastatic carcinoid tumour)

However, some patients restricted their activity levels to avoid over-exerting themselves.

*"I don't go out of my way to test whether I'm going to get out of breath or not."* (81, male, lymphoma)

Inability to do certain activities was contextualised by its effect on a participant's social life and identity, such as being unable to benefit from the social aspect of playing golf, or other social activities.

*"I used to lead walks of 5, 6, 7 miles and I got back up to doing about 3 and a half miles and then this breathlessness started and I'm lucky if I can do half a mile now"* (75, male, mesothelioma)

Another restriction on social activities was breathlessness when speaking, which one participant mentioned improved significantly after drainage.

*"I can hold a conversation now with somebody without getting out of breath, so things must have improved which I'm very grateful for."* (83, male, metastatic carcinoid tumour)

### **Post hoc sub-group analyses**

Due to the male predominance of the sample group, sub-group analysis was performed to compare responses of male and female patients. No clear differences were identified between the responses of the male and female patients, with similar themes emerging from each. Sub-group analysis also failed to find any substantial differences in themes or symptoms from patients with mesothelioma, compared to other diagnoses.

Responses from patients with a known diagnosis of active cancer at the point of recruitment did show some differences to those without a known diagnosis. These patients showed more awareness of the palliative intention of the procedure, with one participant specifically mentioning his desire to improve his quality of life.

*"I'm trying to aspire to, for as long as I can, this quality of life that you guys keep talking about."* (70, male, metastatic pancreatic cancer diagnosed before recruitment)

Their confirmed diagnosis was also reflected in their concerns about their underlying diagnosis and potential prognosis. However, the symptoms and limitations in activities they described, and their experience of the procedure itself, were broadly similar to those of other patients.

### **Discussion**

This prospective study is the first to use semi-structured interviews with patients with known or suspected MPE before and after therapeutic aspiration. We found patients experienced a wide variety of symptoms causing significant impairment of activity.

Our results showed that breathlessness, chest pain and cough are common symptoms in patients with MPE prior to aspiration, but no single symptom was universally experienced by all patients. This is in keeping with a previous study reporting symptoms in patients with MPE undergoing thoracoscopy<sup>10</sup>. Of note, none of our patients mentioned sweating, despite a previous study which found one third of patients with mesothelioma experience sweating<sup>11</sup>. Patients were limited in their activities, in keeping with previous work which has demonstrated that patients with MPE are sedentary for much of their time, spending a mean of just 9.5 minutes daily doing moderate or vigorous physical activity in one actigraphy-based study<sup>12</sup>.

Prior to therapeutic aspiration, patient expectations generally fell into two categories, with patients wanting either complete relief of their symptoms or feeling that any improvement would be worthwhile. This is in keeping with our previous work designed to determine the minimal important difference in the visual analogue scale for dyspnoea<sup>13</sup>. Although the interview guide was designed to explore symptoms and activities, patients commonly spontaneously raised psychosocial issues, such as low mood, anxiety and a feeling of over-reliance on other people. This demonstrates the importance of these issues for patients. Low mood and anxiety are common in patients with cancer, including mesothelioma<sup>14</sup>.

In keeping with previous research, breathlessness and chest pain decreased following pleural fluid drainage<sup>3</sup>. Secondary to this, patients often experience an improvement in sleep, increased activity and quality of life<sup>3, 12, 15, 16</sup>. Constitutional symptoms, such as fatigue and anorexia, did not improve following aspiration, probably because they are caused by the underlying cancer rather than the MPE. The duration of symptom relief following therapeutic aspiration was only a few days only, which was a novel finding, but there has been previous data demonstrating that recurrence of symptoms predicts need for further drainage<sup>17</sup>. Activity levels increased, in keeping with previous findings. Although some patients found the procedure painful, overall patients felt it worthwhile.

The strengths of this study include the contemporaneous nature of the data collection in relation to the patients' diagnostic and treatment pathway. We were therefore not reliant on patients' recollection of symptoms and how they changed. Furthermore, the use of the semi-structured interviews allowed the discussion to be led by the patient and include topics they felt significant, particularly the psychosocial impact of MPEs.

A potential limitation of our study is the male predominance of the sample. This may partially reflect the relatively high incidence of mesothelioma in the East of England<sup>18</sup>. Mesothelioma predominantly affects males, due to occupational asbestos exposure e.g. plumbers, builders. However, sub-group analysis demonstrated no key differences in the topics raised in the interviews of male patients compared to female patients or in patients with mesothelioma compared to other diagnoses. Another potential limitation is the small proportion of patients who had a third interview (figure 1). However, analysis of the two third interviews that were conducted did not reveal any new themes or symptoms.

These results have implications for the design of future RCTs aimed at determining optimal treatment of patients with MPEs. Previous RCTs have chosen patient reported outcome measures (PROMs) of breathlessness as the primary outcome measure<sup>3, 6</sup>. However, our results show that not all patients are breathless, and that breathlessness is not the only symptom that improves with

drainage. Future RCTs should study a wider range of symptoms (e.g. chest pain, cough, sleep) to fully explore the benefits of fluid drainage. Our results demonstrated improvement in activity levels following aspiration, but there was a wide variation in the specific activities identified and in the level of exertion required to perform those activities (e.g. propelling a wheelchair versus running). This is an important outcome for patients and may be appropriate to use as an outcome in future RCTs, but the optimal way to assess this has not been identified. Some studies have used the Borg score following standardised activity, but this group of frail patients may be unable to do even low amounts of activity leading to low levels of data completeness<sup>17</sup>. Some PROMs use ability to perform specific activities as a measure of breathlessness e.g. the lung cancer module of the European Organisation for the Research and Treatment of Cancer quality of life questionnaire (EORTC QLQ-LC13) asks about breathlessness at rest, on walking and climbing stairs<sup>19</sup>. Our results show that there are no activities performed by all patients which they identify as being impaired by breathlessness. This means that it is difficult to identify generic activities common to this group of patients that could be used as the basis for a PROM. Actigraphy may be a more appropriate a way of measuring patients' overall physical activity in a research context, rather than questionnaires focusing on specific activities<sup>12</sup>.

This study has implications for the management of individual patients. It demonstrates the need to consider a wide range of symptoms, rather than just breathlessness, when considering who may benefit from fluid drainage. Anxiety and low mood are common, and it may benefit patients if we identify these problems and offer treatment and support during their pathway, as has been used in other cancer pathways<sup>20</sup>. It may be helpful to identify what important activities a patient struggles to perform, and work with them to help them achieve this.

Current guidelines advise that patients with a prognosis of less than 28 days should be managed with therapeutic aspiration only, rather than be offered a definitive procedure<sup>5</sup>. Our data demonstrate that this will not provide lifelong symptom relief, even in this poor prognosis group of patients. Despite this short duration of benefit and the discomfort and inconvenience of undergoing therapeutic aspiration, most patients viewed the procedure as worthwhile. This information should aid patient decision making, an important element of patient centred end of life care<sup>21</sup>.

More information prior to aspiration may enable clinicians to better manage patient expectations. Some patients had unrealistic expectations of the benefits of therapeutic aspiration, e.g. that appetite and energy levels would improve or that it would cure the underlying condition. Patients focused on the volume of fluid drained and expressed disappointment if it was not all drained. Information should include the symptoms which may and may not improve, the reasons for doing the procedure and limitations as to the amount of fluid that can be drained during therapeutic aspiration<sup>5</sup>.

Further research is necessary to determine the frequency of these symptoms in patients with MPEs and in what proportion of patients they improve following fluid drainage. Potentially, this could lead to validation of an existing PROM in this subgroup of patients or development of an MPE specific PROM.

### **Disclosures and Acknowledgements**

The authors have no conflicts of interest to declare.

We would like to thank all the patients who took part in this study.

No funding was required for this study.

AW, NMR, MF and EKM conceived of and designed the study. CT and RLF conducted, transcribed and analysed the interviews. All authors contributed to the paper. EKM is responsible for the overall content of the paper and acts as guarantor.

**Table 1: Summary of participant demographics**

<b>Total</b>	16
<b>Mean age (years) (SD)</b>	69 (17.1)
<b>Sex male: female</b>	12:4
<b>Diagnosis at recruitment</b> known cancer: undiagnosed pleural effusion	3:13
<b>Final diagnosis</b> Mesothelioma Lung cancer Breast cancer Other malignancy Non-malignant Suspected malignancy – declined further investigation	4 1 2 4 4 1
<b>Baseline breathlessness on VASD (n=7)/mean (mm)</b>	57
<b>Size of effusion (mean % opacity on chest radiograph)</b>	29%

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