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# Current practices in the management of malignant pleural effusions: a survey among members of the European Society of Thoracic Surgeons

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## Abstract

**OBJECTIVES:** Malignant pleural effusion (MPE) commonly complicates advanced malignancy and their exact management is still undefined. We undertook a survey to determine the current practice among members of the European Society of Thoracic Surgeons (ESTS).

**METHODS:** A cross-sectional survey focused on the current practice of management of MPE was developed by the authors. The questions were outlined after a review of the literature and circulated in an Internet-based survey format.

**RESULTS:** Computed tomography (125, 92%) and chest X-ray (106, 78%) are the most common imaging modalities performed in the initial evaluation. Video-assisted thoracoscopic surgery for washout and pleurodesis (93, 68%) was reported as the preferred approach to patients with uncomplicated MPE. Sixty-one (45%) of the responding colleagues routinely use large bore chest tubes for draining malignant effusions. Forty-nine (35%) surgeons would not apply suction to the drainage system, whilst 50 (37%) would use -2 kPa or less. Talc (124, 91%) is the most commonly used sclerosing agent for pleurodesis in the context of malignant pleural effusion. The practice of 76 (56%) of the respondents is not informed by any clinical guidelines, whilst 60 (44%) reported adhering to the 2010 British Thoracic Society Pleural Disease Guideline. Seventy-one (52%) declared that the guidance was in need of updating or revision.

**CONCLUSIONS:** This survey demonstrates the lacking adoption of the existing clinical guidance in this field, as well as the need for more contemporary guidelines for a better-informed practice. The ESTS Working Group on the management of MPE has been established for this purpose.

**Keywords:** Malignant pleural effusion • Survey • ESTS Malignant Pleural Effusion Working Group

## INTRODUCTION

Malignant pleural effusion (MPE) commonly complicates advanced malignancy, posing a high burden of symptomatic disease. The annual incidence of MPE in the United States was estimated at 150 000 cases in year 2000 [1] and is thought to have risen since, despite the absence of robust epidemiological data.

Multiple aetiologies, the various mechanisms that contribute to fluid accumulation, a plethora of treatment options that have yet to be class ranked and a frail patient cohort with a highly abbreviated life expectancy [2] often compound to pose significant management challenges with a significant financial burden [3].

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Currently available clinical guidance was published in 2000 and 2010 by the American Thoracic Society and by the British Thoracic Society respectively [1, 4, 5]. Since then, it has been an expansion in our understanding about this subject and in our pharmacological and interventional armamentarium. A search of the largest clinical trials registry [6] (clinicaltrials.gov) in May 2016 revealed 86 active trials dealing with the topic of MPE at the time of writing this article. Clinical practice is thought to be resultantly highly variable, although no published data previously existed to support this claim.

We will present in this paper the results of a cross-sectional survey of the current practice in the management of MPE amongst members of the European Society of Thoracic Surgeons (ESTS).

## MATERIALS AND METHODS

A cross-sectional survey focused on the current practices of management of MPE was developed by the authors. The questions were outlined after a review of the literature. There was no pilot testing or validation performed for this survey.

A questionnaire (Supplemental material) was designed by the authors and circulated in an internet-based survey format (typeform.com). All members of the ESTS were sent an initial and a single subsequent reminder email 6 weeks later. The responses were collected from consultant thoracic surgical colleagues with a relevant practice and collected in the 75 days between 1 February 2016 and 15 April 2016.

The questionnaire was anonymous. In addition to the demographic data (country of practice, years in independent thoracic surgical practice, volume and frequency of referral of MPE to surgery), 15 questions explored various aspects of the care provided for patients with MPE, including: diagnostic approach, use of bedside ultrasound, intervention, details of chest drainage, details of pleurodesis, the adherence to the current clinical guidance and the question about further development of new guidelines.

Responses were collected in quantitative or multiple-choice question formats (with the option for non-univocal responses), where possible. This was to facilitate completion, increase engagement and allow for meaningful interpretation.

All data were imported into a database and summarized using descriptive statistics. Descriptive data are presented as frequencies (both number and percentages given) or median with interval range (IR). Tests of statistical significance were not performed for individual questions, as the number of possible comparisons is too high to reveal meaningful conclusions. The Relative Standard Error (absolute gauge between the sample survey and the total population) was not calculated.

## RESULTS

Responses were received from 136 non-trainee members, with a median of 12 years of independent thoracic surgical practice (range 0–34 years). Cronbach's alpha was 0.81, implying good reliability of the questionnaire [7]. Due to information regarding the total number of consultant members of the ESTS with a relevant practice not being available, we are unable to calculate a response rate. All submitting respondents had 100% completion rate for relevant questions, by virtue of the design of the electronic questionnaire.

The collected responses reflect the practice across five continents: Europe: 97 (71%), Asia: 17 (13%), North America: 9 (7%), South America: 7 (5%), and Africa: 6 (4%), 43 countries in total (Table 1).

### Pre-selection and volume

Of the responding surgeons, 78 (57%) declared that they get referral mostly about unilateral pleural effusions for workup. The volume of malignant pleural effusions encountered typically in a year of practice ranged between 2 and 200, with a median of 40 cases per surgeon.

### Diagnosis

Computed tomography (125, 92%) and plain postero-anterior chest X-ray (106, 78%) are the most common imaging modalities performed in the initial evaluation of a pleural effusion suspicious for malignancy (Table 2). Notably, only 55 (40%) of the respondents declared using ultrasound guidance for pleural aspiration and drainage.

**Table 1:** Distribution of the collected responses across the five continents

| Country | No. of responses | Relative frequency |
|---|---|---|
| Italy | 13 | 9.6 |
| UK (United Kingdom) | 10 | 7.4 |
| Germany | 9 | 6.6 |
| Greece | 9 | 6.6 |
| Turkey | 9 | 6.6 |
| USA (United States of America) | 8 | 5.9 |
| Spain | 7 | 5.1 |
| France | 6 | 4.4 |
| Romania | 5 | 3.7 |
| Russia | 5 | 3.7 |
| Belgium | 4 | 2.9 |
| Brazil | 4 | 2.9 |
| Austria | 3 | 2.2 |
| Denmark | 3 | 2.2 |
| Portugal | 3 | 2.2 |
| China | 3 | 2.2 |
| Bulgaria | 2 | 1.5 |
| Hungary | 2 | 1.5 |
| Switzerland | 2 | 1.5 |
| Ukraine | 2 | 1.5 |
| Chile | 2 | 1.5 |
| Egypt | 2 | 1.5 |
| Saudi Arabia | 2 | 1.5 |
| South Africa | 2 | 1.5 |
| Armenia | 1 | 0.7 |
| Croatia | 1 | 0.7 |
| Cyprus | 1 | 0.7 |
| Estonia | 1 | 0.7 |
| Georgia | 1 | 0.7 |
| Latvia | 1 | 0.7 |
| Netherlands | 1 | 0.7 |
| Slovenia | 1 | 0.7 |
| Canada | 1 | 0.7 |
| Ecuador | 1 | 0.7 |
| India | 1 | 0.7 |
| Indonesia | 1 | 0.7 |
| Iran | 1 | 0.7 |
| Japan | 1 | 0.7 |
| Jordan | 1 | 0.7 |
| Malaysia | 1 | 0.7 |
| Mozambique | 1 | 0.7 |
| Thailand | 1 | 0.7 |
| Tunisia | 1 | 0.7 |

Cytology and differential cell count (127, 93%) and lactate dehydrogenase (83, 61%) are the most commonly requested laboratory investigations on pleural fluid samples. In cases of non-diagnostic outcomes of cytology despite a high clinical index of suspicion for malignancy, 59 (43%) respondents would not attempt a repeat investigation, while 28 (21%) would do so on more than one further occasion.

## Management strategies

Video-assisted thoracoscopic surgery (VATS) for washout and pleurodesis (93, 68%) was reported as the preferred approach to patients with uncomplicated malignant pleural effusions, whilst VATS pleurectomy-decortication (81, 60%) is the most commonly reported in multiloculated effusions or in the presence of trapped lung (Table 3).

**Table 2:** Surveýs questions and results about the diagnostic of MPE

*Question* 12: Which of the following diagnostic tests would you perform routinely in your evaluation of a pleural effusion suspicious for malignancy?

| | *n* | % |
|---|---|---|
| Computed tomography (CT) | 125 | 92 |
| Postero-anterior chest X-ray | 106 | 78 |
| Pleural aspiration | 96 | 71 |
| Video-assisted thoracoscopic surgery | 76 | 56 |
| Lateral chest X-ray | 60 | 44 |
| Ultrasound | 45 | 33 |
| Positron emission tomography/computed tomography (PET/CT) | 32 | 24 |
| Bronchoscopy | 31 | 23 |
| Serum tumour markers | 24 | 18 |
| Image-guided percutaneous pleural biopsy | 19 | 14 |
| Local anaesthetic thoracoscopy | 16 | 12 |
| Abrams needle pleural biopsy | 12 | 9 |
| Positron emission tomography (PET) | 9 | 7 |
| Magnetic resonance imaging (MRI) | 0 | 0 |

*Question* 14: Which of the following tests would you routinely request on a pleural fluid sample in suspected malignant effusion?

| | *n* | % |
|---|---|---|
| Cytology and differential cell count | 127 | 93 |
| Lactate dehydrogenase (LDH) | 83 | 61 |
| Glucose | 78 | 57 |
| pH | 76 | 56 |
| Protein | 74 | 54 |
| Microscopy and culture | 71 | 52 |
| Gram stain | 56 | 41 |
| Amylase | 23 | 17 |
| Tumour markers | 23 | 17 |
| Haematocrit | 17 | 13 |
| Other | 4 | 3 |
| N-terminal pro-brain natriuretic peptide (NTproBNP) | 3 | 2 |

*Question* 16: Which of the following tumour markers would you routinely test for in potentially malignant pleural fluid?

| | *n* | % |
|---|---|---|
| Carcinoembryonic antigen (CEA) | 77 | 60 |
| CA 125 | 62 | 55 |
| CA 153 | 45 | 40 |
| CYFRA | 28 | 25 |
| Mesothelin | 25 | 22 |
| Other | 23 | 21 |

## Chest drainage

Sixty-one (45%) of the responding colleagues routinely use large bore (24Fr or larger) chest tubes for draining malignant effusions, while 37 (27%) would normally go for small bore (14Fr or smaller) options. The reported median maximal volume of malignant effusion that could be safely drained was 1.500 ml (range 200–5000 ml).

Regarding the suction, 49 (35%) surgeons would not apply suction to the drainage system, while 50 (37%) would employ -2 kPa or less. Only 9 (7%) stated that they would use suction of -7 kPa or more.

## Pleurodesis

Talc (124, 91%) is the most commonly-used sclerosing agent in attempting pleurodesis in the context of MPE. Other used agents are Bleomycin (6, 4%), Tetracycline (4, 3%), Iodine (1, 1%) and Doxycycline (1, 1%). Eighty-six (63%) colleagues routinely advocate patient rotation to promote uniform spread and widespread action of sclerosant in the initial period after instillation.

## Guidelines

The practice of 76 (56%) of the respondents is not informed by any clinical guidelines, while 60 (44%) reported adhering to the 2010 British Thoracic Society Pleural Disease Guidelines [5].

Seventy-one of them declared that the guidance was in need of updating or revision (27–45% among those who currently use some form of clinical guideline and 44–58% among those who do not follow any guideline).

Topics highlighted as needing to be addressed by future guidance included (1) optimal method and frequency of pleural

**Table 3:** Strategy for management of MPE

*Question* 17: Which of the following routinely form part of your management of patients with uncomplicated malignant pleural effusions?

| | *n* | % |
|---|---|---|
| VATS washout and pleurodesis | 93 | 68 |
| Intrapleural sclerosant via intercostal tube (pleurodesis) | 65 | 48 |
| Therapeutic pleural aspiration (single) | 60 | 44 |
| Intercostal tube drainage (single) | 56 | 41 |
| Observation in asymptomatic patients | 50 | 37 |
| Indwelling pleural catheter | 45 | 33 |
| Therapeutic pleural aspiration (repeated) | 32 | 24 |
| Intercostal tube drainage (repeated) | 11 | 8 |
| Pleurectomy | 6 | 4 |
| Thoracotomy for washout and pleurodesis | 3 | 2 |
| Other | 1 | 1 |
| Pleuro-peritoneal shunting | 1 | 1 |

*Question* 22: Which of the following form part of your strategy for managing malignant effusions when multiloculated or in the context of trapped lung?

| | *n* | % |
|---|---|---|
| VATS pleurectomy/decortication | 81 | 60 |
| Indwelling pleural catheter | 59 | 43 |
| Thoracotomy for pleurectomy/decortication | 27 | 20 |
| Intrapleural sclerosant via intercostal tube (pleurodesis) | 24 | 18 |
| Intrapleural fibrinolytics via intercostal tube | 21 | 15 |
| Other | 4 | 3 |

drainage; (2) use of bedside image guidance, (3) indications, timing and sclerosing agent choice in pleurodesis; (4) local and general anaesthetic thoracoscopy and standards for those performing such procedures; and (5) palliative surgical interventions.

## DISCUSSION

MPE is commonly encountered in thoracic surgical practice, although the volume of cases declared by our respondents varied greatly. We further noticed an inherent bias precluding to the participation in our survey of those colleagues with a particular interest in the field.

There is in literature only one previous survey on the management of recurrent MPE [8]. In this survey there were 253 replies with an overall response rate of 56%; nevertheless, the percentage of surgeons was only 60%. The sample reported in the current survey is representative of current surgical practice without survey sampling bias as under-coverage or non-response bias.

While being unable to calculate an accurate response rate for our survey, we note a similar engagement as for similar studies previously performed amongst members of the ESTS (median 150 responses, range 105–235) and published between 2008 and 2015 [9–13]. Furthermore, the authors specifically restricted participation to independent clinicians with a relevant practice to obtain increasingly meaningful results. Despite asking participants to only complete the questionnaire once, we are unable to fully exclude multiple responses without the loss of anonymity. On the contrary, this survey shows a doubled number of cases than the previous report of McAlpine *et al*. [8].

The authors observed that the current guidance was published over five years ago and it is largely composed of recommendations based on moderate (level B) or low (level C) quality evidence [14]. In fact, 10 of 27 (37%) explicit recommendations in the BTS guidance from 2010 are indicated as level C [5]. Notably, the reported practices are only aligned with the guidance in one of the three of the level B recommendations in the BTS 2010 guidelines: the use of Talc for pleurodesis is in fact performed by 91% of responding surgeons. However, only 27% would use small bore chest tubes for pleural drainage, while only 37% do not practice patient rotation after instillation of an intrapleural sclerosant. The relative frequencies are similar for those who state adherence to the guidelines and those who do not.

Questionnaire surveys are open to bias and the variable response rates polled may reflect different approaches. The next step should be to consider whether the result is of any practical significance.

While this report makes no attempt to test current practices in relation to contemporary evidence or outcomes and does not reflect a consensus or best practice statement, it does constitute the first attempt to document expert preference and practice from a large number of thoracic surgeons in a valid and reliable fashion that may serve as a basis for further work in this field.

This survey demonstrates the poor adoption of the existing clinical guidance, as well as the need for more contemporary and updated guidelines for a better-informed practice. The ESTS Working Group on the management of MPE has been established for this purpose.

## SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

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**Conflict of interest**: none declared.

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