

STRATIFY: Staging by Thoracoscopy in radically treatable Lung Cancer with Minimal Pleural Effusion

AIMS

Lung cancer that is found early can often be treated with the aim of curing it, for example with surgery or radiotherapy. This is called ‘radical’ treatment. Unfortunately, the cancer often comes back afterwards. One possible reason is that it had already spread in a way that was too small to be seen on scans. Doctors call this ‘occult’ (hidden) spread.

Some patients have a very small amount of fluid between the lung and the chest wall when their lung cancer is diagnosed. This is called a minimal pleural effusion (Mini-PE). Their cancer is more likely to come back. Earlier studies, which looked back at patients’ medical records, estimated that 70-80% of patients with a Mini-PE have hidden cancer spread to the lining of the lung. This is known as occult pleural metastases (OPM).

Thoracoscopy is a keyhole procedure in which a doctor passes a thin camera through a small cut between the ribs to look at the lining of the lung and take samples. It is the best test when there is a lot of fluid, but it is not routinely used in patients with a Mini-PE to work out how far their cancer has spread (called ‘staging’). STRATIFY used thoracoscopy to find out how common OPM really is in patients with a Mini-PE whose lung cancer otherwise appears curable. It also tested, for the first time, whether thoracoscopy is practical and safe in these patients.

KEY FINDINGS

- Thoracoscopy found hidden cancer spread to the lining of the lung (OPM) in only **4 of the 27 patients (14%).**
- Fewer patients took part than planned (27 instead of 50), so this figure is not exact: the true figure is likely to lie somewhere between about 4% and 34% (the '95% confidence interval' was 4.2-33.7%). Even so, this is much lower than the 70-80% estimated by earlier studies.
- Thoracoscopy was practical to carry out and safe, and its results directly changed the treatment plan for 8 of the 27 patients (30%).

WHAT DID THE STUDY INVOLVE?

STRATIFY took place between January 2020 and May 2024 in 7 UK hospitals with specialist 'pleural' teams, who treat conditions affecting the lining of the lung. We aimed to recruit 50 patients. All patients who took part had thoracoscopy, and we recorded what was found.

Our main aim was to measure how many patients had OPM. We also wanted to find out whether thoracoscopy could be carried out successfully, whether it was safe, and whether its results changed patients' treatment plans.

Patients could take part if they were aged 16 or over, agreed to take part after being given full information, and had: lung cancer (suspected or confirmed) that had not spread to other parts of the body (stages 1 to 3); a Mini-PE; a good enough level of fitness to be up and about for more than half of the day (known as 'Performance Status 0-2'); and the option of radical treatment if no OPM was found. Patients could not take part if their cancer had already spread elsewhere, or if there was a medical reason why thoracoscopy would not be safe for them.

Thoracoscopy was done in one of two ways. Local Anaesthetic Thoracoscopy (LAT) is done with the patient awake, using an injection to numb the area and often a sedative. Video-Assisted Thoracoscopic Surgery (VATS) is done in an operating theatre under a general anaesthetic. An ultrasound scan was always done before LAT to check that the procedure could go ahead. All

patients had thoracoscopy about a week after joining the study, and the results were sent to their lung cancer team to help plan treatment.

Samples of the fluid were stored for laboratory tests. These tests look for fragments of tumour DNA (called cell-free tumour DNA, or cfDNA) and patterns of proteins (called 'proteomics') in the fluid, to see whether they could predict which patients have OPM.

Patients were involved throughout the study. This included contributing to the funding application (as a co-applicant), the study design and the written information given to participants, and sitting as a full member of the group that managed the study.

WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

Recruitment was interrupted by COVID-19, and we then had to adapt to changes in NHS lung cancer services. Many patients with a Mini-PE also turned out to be too unwell for radical treatment, or to have cancer that had already spread elsewhere. In total, 37 patients were assessed and 27 took part (54% of the 50 planned). Their average age was 69 years.

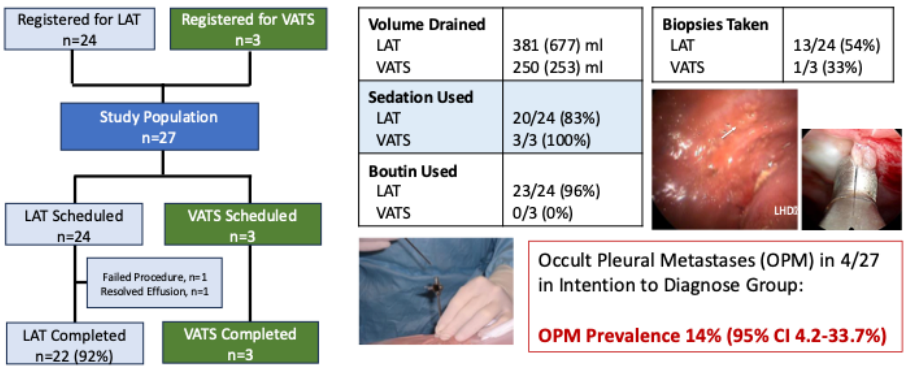


Figure 1. What happened to the 27 patients who took part, and what thoracoscopy found. The diagram, tables and photographs are explained in the text below.

The diagram on the left of Figure 1 shows that 24 patients were booked for LAT and 3 for VATS. Thoracoscopy was completed in 25 of the 27 patients (93%). In the other two patients, the procedure could not be completed in one, and the fluid had cleared up by itself in the other. The tables show how much fluid was drained, and how often a sedative, a special blunt needle for entering the chest (a 'Boutin' needle) and tissue samples (biopsies) were used. The amounts of fluid drained were small, confirming that these were Mini-PEs. The photographs show the procedure being carried out and views inside the chest through the camera.

OPM was found in only 4 of the 27 patients (14%). This figure is based on everyone who joined the study, including the two patients whose thoracoscopy was not completed (called the 'Intention to Diagnose Group' in Figure 1). Because the study was smaller than planned, the true figure could lie anywhere between about 4% and 34% (shown in Figure 1 as '95% CI 4.2-33.7%'). Even at the top of this range, it is much lower than the 70-80% estimated by earlier studies.

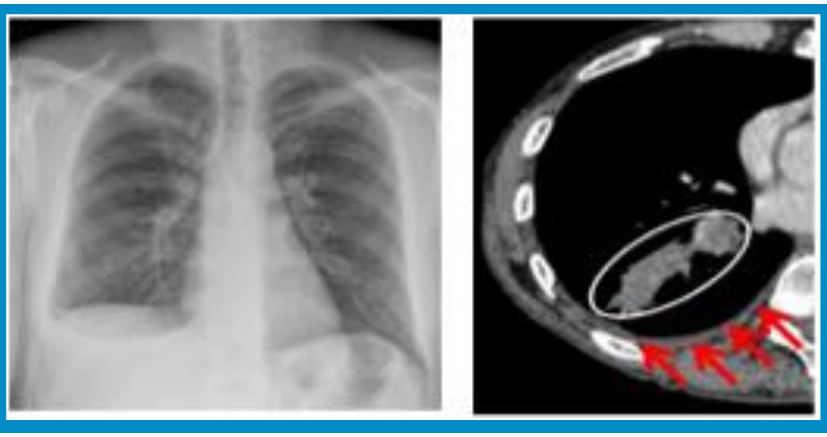
Thoracoscopy was safe: no serious complications (known as Serious Adverse Events) were reported. The results changed the stage of the cancer, which describes how far it has spread, in 5 of the 27 participants (19%). The results changed the lung cancer treatment plan in 8 of the 27 participants (30%). Thoracoscopy was therefore practical, safe and useful in helping lung cancer teams to stage the cancer accurately and choose the most suitable treatment. The laboratory tests on the stored fluid samples (cfDNA and proteomics) are still under way.

WHAT IMPACT COULD THE FINDINGS HAVE?

STRATIFY suggests that hidden cancer spread to the lining of the lung is much less common than previously thought in patients who have a Mini-PE when an otherwise curable lung cancer is diagnosed (Figure 2 shows a typical example). Although the study was smaller than planned, even the highest likely figure (about one in three patients) is well below earlier estimates. Having a Mini-PE should therefore not, by itself, put lung cancer teams off offering radical treatment.

For patients, thoracoscopy gives a clearer picture of how far the cancer has spread before treatment starts, so that each patient can be offered the treatment that suits them best. Patients without hidden spread need not miss out on treatment that could cure them. Patients with hidden spread can avoid major treatment that is unlikely to cure them, and be offered other treatments instead. Because the procedure was practical and safe in this study, our results support its use in hospitals with the right expertise, particularly when the result (OPM present or not) would change the treatment plan.

Figure 2. Scans typical of STRATIFY participants. The chest X-ray (left) shows a Mini-PE on the patient's right side. The CT scan (right) shows the fluid (red arrows) next to an early-stage lung cancer (white oval).



HOW WILL THE OUTCOMES BE DISSEMINATED?

The study results, including the laboratory tests on stored fluid samples (cfDNA and proteomics), will be published in a peer-reviewed scientific journal. This report does not include longer-term results, such as whether changing treatment plans helped patients to live longer. A larger study is now needed to confirm that our findings apply to patients more widely, to look at these longer-term results and to check any promising findings from the laboratory tests.

CONCLUSION

Thoracoscopy to look for hidden cancer spread is practical, safe and useful, because it gives lung cancer teams more accurate information on which to base treatment decisions. It should be considered for patients who have a Mini-PE and a lung cancer that otherwise appears curable.

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