Pleural effusion in haematological malignancies: an educational position statement

Olivia Walsh[1,2], Arran Patel[3], Najib Rahman[1,2,4] and Graham Collins[3]

[1]Oxford Centre for Respiratory Medicine, Churchill Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, UK. [2]Oxford Pleural Unit, Oxford University Hospitals, Oxford, UK. [3]Oxford Centre for Haematological Medicine, Churchill Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, UK. [4]Oxford NIHR Biomedical Research Centre, Oxford, UK.

Corresponding author: Olivia Walsh (olivia.walsh@ouh.nhs.uk)

Shareable abstract (@ERSpublications)
Pleural effusions in haematological malignancy are common and often complex. This review outlines causes, diagnostic challenges and management strategies, highlighting evidence gaps and areas for future research. https://bit.ly/3KtJB7j

Cite this article as: Walsh O, Patel A, Rahman N, *et al*. Pleural effusion in haematological malignancies: an educational position statement. *Breathe* 2026; 22: 250265 [DOI: 10.1183/20734735.0265-2025].

Received: 20 Aug 2025
Accepted: 24 Nov 2025

Abstract

Pleural effusion is a known complication of haematological malignancies, including lymphomas, leukaemias and multiple myeloma. The true overall incidence of pleural effusion in haematologic disorders is not precisely established, but case series suggest it occurs in roughly 20–48% of patients with these diseases. Among all malignant pleural effusions (MPEs), about 10–16% are attributable to haematologic cancers (especially lymphomas/leukaemias). The development of a pleural effusion in this context poses significant diagnostic challenges, as traditional tests such as pleural fluid cytology or pleural biopsy often have low diagnostic yield. Importantly, the underlying mechanisms of pleural effusion in haematological malignancy are diverse, ranging from direct pleural infiltration and mediastinal nodal obstruction to chylothorax, cardiac dysfunction, and treatment-related complications. These varied aetiologies not only complicate diagnosis but also have direct implications for both immediate and long-term management. Moreover, emerging evidence indicates that the presence of a pleural effusion in patients with haematological malignancies may reflect advanced disease or evolving complications and is often associated with a poorer prognosis. This position statement provides an overview of the prevalence, pathophysiology, diagnostic approach, management strategies, and prognosis of pleural effusions in haematological malignancies, and offers evidence-based recommendations to guide clinical practice.

Introduction

Pleural effusion is a recognised complication of haematological malignancies, including lymphomas, leukaemias and multiple myeloma. Although the precise incidence across all haematological malignancies is uncertain, case series suggest that pleural effusions occur in ∼20–48% of patients during the course of their illness [1]. Among all malignant pleural effusions (MPEs), haematological cancers account for ∼10–16%, with lymphomas and leukaemias being the most frequent contributors [1].

The development of a pleural effusion in this context presents several challenges. The underlying aetiology is heterogeneous, encompassing malignant infiltration, lymphatic obstruction, treatment-related complications, infection and systemic comorbidities. This diversity complicates diagnosis and necessitates a careful, multimodal approach. Traditional diagnostic tests such as pleural fluid cytology or blind pleural biopsy often yield limited sensitivity, while newer tools including flow cytometry and thoracoscopy may provide additional clarity.

Importantly, pleural effusions in haematological malignancies are not benign phenomena. Their occurrence frequently indicates advanced disease, increased tumour burden or treatment-associated complications, and in many cases is associated with poorer prognosis.

This position statement summarises current understanding of the prevalence, mechanisms, diagnostic strategies and management of pleural effusions in haematological malignancy, while highlighting prognostic implications and unmet research needs.

Prevalence and aetiology in haematological malignancies

Pleural effusions are relatively common across haematological malignancies, although frequency and mechanisms vary by disease.

- Lymphomas are the haematological malignancy most often associated with pleural effusions. Effusions are reported in up to 30% of Hodgkin lymphoma and ∼20% of non-Hodgkin lymphoma, particularly those with bulky mediastinal disease [1]. Lymphoma-related effusions form the majority of haematological MPEs. A distinct entity, primary effusion lymphoma, is a rare, aggressive B-cell lymphoma accounting for ∼4% of HIV-associated non-Hodgkin lymphoma, presenting almost exclusively with serous effusions, usually without solid tumour masses.
- Leukaemias make up to ∼21% of haematological malignancy-associated MPEs [2]. In chronic lymphocytic leukaemia (CLL), malignant effusions typically reflect advanced disease or transformation (Richter syndrome). In acute leukaemias, particularly acute lymphoblastic leukaemia, effusions are relatively common, but more often reactive or infection-related than truly malignant. Distinguishing malignant infiltration from para-malignant or reactive causes is critical.
- Multiple myeloma is implicated in ∼13% of haematological malignancy cases presenting with effusions [1]. ∼6% of patients develop a pleural effusion, but <1% represent true myelomatous effusion with plasma cell infiltration [3, 4]. Most effusions in multiple myeloma are secondary to cardiac dysfunction, renal impairment, infection or amyloidosis. Myelomatous effusion is rare, but carries grave prognostic significance.
- Other disorders such as myelodysplastic syndrome, myelofibrosis and thalassaemia rarely cause effusions, and when present they are often benign, related to extramedullary haematopoiesis (EMH) or infection [2].

In children, lymphomas and leukaemias predominate, accounting for 52–81% of malignant effusions in paediatric series [2].

Pathophysiology

The mechanisms underlying pleural effusion in haematological malignancies are diverse, and can be divided into malignant and para-malignant pathways.

- Malignant pleural effusion: in haematological malignancies, MPEs arise from direct pleural infiltration by malignant cells or dissemination *via* lymphatic or haematogenous spread. Cytological or flow cytometric detection of clonal lymphoid or plasma cell populations confirms this process. In non-Hodgkin lymphoma, pleural involvement is reported in 6–15% of cases, while myelomatous effusions remain rare (<1%) [2–4]. Bulky mediastinal disease can also impair pleural lymphatic drainage, further contributing to effusion.
- Para-malignant effusions: not all effusions represent direct tumour involvement. Systemic effects such as infection, heart or renal failure, and treatment-related toxicity may lead to exudative or transudative effusions. Chylothorax is particularly associated with lymphoma, occurring in ∼19% of MPEs, usually due to thoracic duct obstruction [1]. EMH in myelofibrosis or thalassaemia may also cause recurrent exudative effusions.

The majority (80–88%) of haematological malignancy effusions are exudates by Light's criteria, with chylous effusions accounting for 12–20%. True transudates are uncommon and usually reflect concomitant organ dysfunction. Effusions may occur at presentation or, more commonly, during relapse or advanced stages, serving as markers of disease activity.

Diagnostic approach

Accurate diagnosis is essential, both to clarify the underlying cause and to guide appropriate management.

Clinical assessment and imaging

History, examination, and imaging (chest radiography, computed tomography, ultrasound) remain first-line. Ultrasound is particularly useful for detecting septations, guiding safe aspiration, and differentiating free-flowing from loculated effusions, and in skilled hands can demonstrate malignant pleural thickening. Computed tomography may reveal lymphadenopathy, pleural thickening, or pulmonary infiltrates suggesting infection or malignant infiltration.

Thoracentesis and pleural fluid analysis

Initial fluid evaluation should include biochemical studies (protein, lactate dehydrogenase, glucose, pH, triglycerides), cytology, microbiology and cell count. Cytology remains the cornerstone of diagnosis,

although sensitivity is modest: ~60–70% in general MPE and ~46% in haematological malignancies [5]. Immunocytochemistry and flow cytometry significantly increase yield, particularly for lymphoma and leukaemia, by detecting clonal populations even when morphology is equivocal. Triglyceride testing should be performed in all haematological malignancy effusions to exclude chylothorax, as up to 20% are not grossly milky. The detection of malignant cells in exudative or haemorrhagic effusions may reflect passive spillover rather than true pleural infiltration; correlation with imaging or biopsy is essential.

Pleural biopsy and thoracoscopy

When cytology is nondiagnostic, tissue sampling is required. Medical thoracoscopy offers direct visualisation and targeted biopsy, achieving diagnostic rates >90% in suspected malignancy. Although specific haematological malignancy data are limited, its role is endorsed when less invasive tests fail. Image-guided pleural biopsy is an alternative, although yield is lower in diffuse microscopic infiltration as is seen in lymphomas.

Adjunctive investigations

Flow cytometry is particularly valuable in haematological malignancy effusions, enabling detection of minimal residual disease or immunophenotypic aberrancy. In multiple myeloma, electrophoresis of pleural fluid can identify monoclonal proteins. Microbiology is essential, as infection is a common alternative or concurrent cause.

Overall, a multimodal approach (integrating cytology, immunophenotyping, biopsy and imaging) is crucial. Multidisciplinary discussion (respiratory, haematology, pathology) is recommended in complex cases (figure 1).

Management

Management must address both the underlying malignancy and the effusion itself.

- Systemic treatment of the malignancy is paramount. Chemotherapy or targeted therapy often leads to effusion resolution in lymphoma or leukaemia. In multiple myeloma, systemic antimyeloma therapy may improve myelomatous effusions. For some patients, effusion response can serve as a surrogate marker of systemic control. Targeted agents such as dasatinib and less commonly ibrutinib may cause lymphocytic, exudative effusions that mimic malignancy; diagnosis requires exclusion of progression elsewhere and improvement upon drug withdrawal.

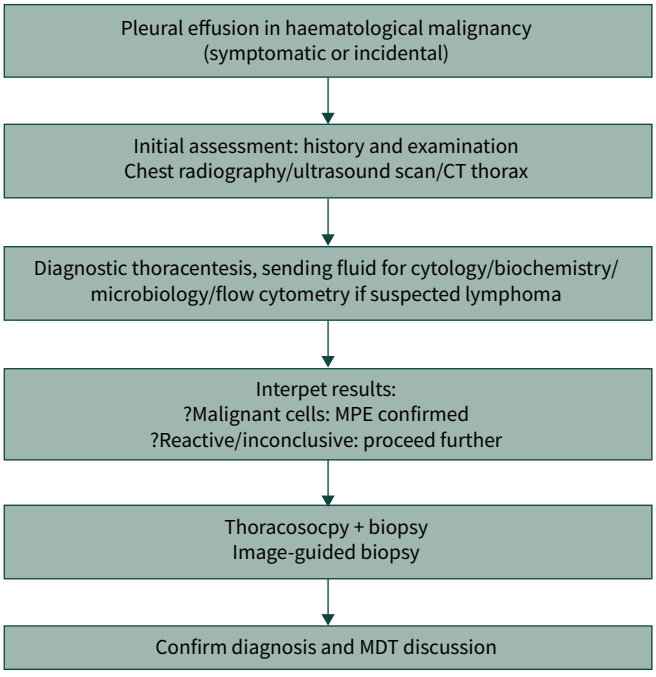

FIGURE 1 Diagnostic approach to pleural effusion in haematological malignancy. CT: computed tomography; MPE: malignant pleural effusion; MDT: multidisciplinary team.

- Symptomatic drainage is frequently required for dyspnoea relief. Thoracentesis provides temporary benefit, but effusions often recur. For recurrent effusions, indwelling pleural catheters (IPCs) and talc pleurodesis are established options. Randomised trials in solid-tumour MPEs show similar efficacy between IPC and talc, and both approaches are extrapolated to haematological malignancies. IPCs are especially useful for trapped lung or patients with limited survival. In immunocompromised patients, including those with haematological malignancies, data from Faiz *et al.* [5] and a 2023 review [6] indicate no evidence of higher IPC-related infection rates compared to solid tumours.
- Intrapleural therapies: fibrinolytics (*e.g.* tissue plasminogen activator) may be considered in septated or loculated effusions, although evidence is limited to small series. Intrapleural rituximab or chemotherapy have been reported anecdotally, but there is a lack of strong evidence. Agents including ibrutinib and venetoclax can increase bleeding risk; procedural timing and haematological parameters should be reviewed. Rare spontaneous pleural haemorrhage has been reported with these drugs.
- Radiotherapy: in select cases such as pleural plasmacytomas, EMH or bulky lymphoma masses, low-dose radiotherapy can reduce tumour burden and facilitate fluid resolution.
- Surgery: procedures such as pleurectomy or pleuroperitoneal shunting are rarely needed, and are reserved for refractory cases.
- Nonmalignant causes: where effusions are para-malignant, management should target the underlying mechanism, for example, antibiotics for infection, diuretics for cardiac dysfunction, and disease-specific therapy for EMH.

Ultimately, management must be individualised, balancing prognosis, performance status and patient preference. Procedures in neutropenic or thrombocytopenic patients require multidisciplinary planning, with transfusion support and careful timing to minimise complications

Prognosis

The prognostic significance of pleural effusions in haematological malignancies varies with disease subtype and context.

- In lymphoma, prognosis depends largely on chemosensitivity. Effusions at diagnosis may not worsen long-term outcomes if remission is achieved. However, refractory or recurrent effusions usually indicate advanced disease and poor survival [7].
- In leukaemia, effusions often represent reactive phenomena, although in CLL or transformed disease they may mark aggressive biology. Prognosis is worse when effusions reflect treatment-refractory disease [8].
- In multiple myeloma, true myelomatous effusion is associated with poor outcomes. A 2022 study [2] reported median survival of ~13 months *versus* 37 months for myeloma with other extramedullary disease [3]. Historically, survival as low as 4–6 months has been reported.
- In paediatric cases, prognosis is more favourable, reflecting the curability of many childhood haematological malignancies [9].

While general MPE prognostic scores such as LENT (pleural fluid lactate dehydrogenase, Eastern Cooperative Oncology Group performance score, neutrophil-to-lymphocyte ratio and tumour type) classify lymphoma and leukaemia as “low risk”, these models were developed in solid tumours and have limited utility in haematological malignancies [1]. No validated haematological malignancy-specific scoring tool exists.

Overall, effusions often signal advanced disease and worse outcomes, although prognosis ultimately reflects the underlying malignancy’s biology and response to treatment [7–9].

Recommendations

- Vigilance: new respiratory symptoms in haematological malignancy patients should prompt evaluation for effusion.
- Diagnostic thoroughness: always perform a full fluid analysis (biochemistry, microbiology, cytology, chylothorax assessment and immunophenotyping). Consider thoracoscopy if nondiagnostic.
- Interdisciplinary management: optimal care requires coordination between respiratory, haematology and pathology teams.
- Systemic therapy first: treat the malignancy promptly (local interventions provide symptom relief, but rarely alter prognosis).
- Tailored supportive management: IPC or pleurodesis should be considered for recurrent effusions. Target specific causes (*e.g.* chylothorax, infection, EMH).
- Prognostic counselling: patients should be counselled sensitively on the implications of effusion, particularly in multiple myeloma or refractory lymphoma.
- Research priority: prospective studies and registries are urgently needed to define incidence, prognostic markers and optimal management strategies in haematological malignancies.

Conclusion

Pleural effusion is a common and clinically significant complication of haematological malignancy. Mechanisms of effusion formation are diverse which requires careful diagnostic workup and knowledge of the potential differential diagnosis; where caused by malignancy, their presence often signals advanced disease and therapeutic challenges. A systematic, multidisciplinary approach is required to establish the underlying cause, relieve symptoms and align effusion management with the treatment of the primary malignancy. Although survival implications vary across disease subtypes, myelomatous effusion and refractory lymphoma effusions remain particularly adverse.

High-quality data remain scarce, and current practice is largely extrapolated from solid tumour MPEs. Dedicated research, ideally through multicentre prospective studies, will be essential to improve prognostication and guide tailored interventions. In the meantime, awareness, vigilance and coordinated management are crucial to optimise outcomes for patients with haematological malignancy-associated pleural effusion.

Conflict of interest: The authors declare that the position statement was written in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. N. Rahman is a current member of the *Breathe* editorial board. O. Walsh, G. Collins and A. Patel do not have any conflicts of interest.

References

1 Das DK. Serous effusions in malignant lymphomas: a review. *Diagn Cytopathol* 2006; 34: 335–347.
2 Gao L, Xu J, Xie W, *et al.* Clinical characteristics and prognosis of multiple myeloma with myelomatous pleural effusion: a retrospective single-center study. *Technol Cancer Res Treat* 2022; 21: 15330338221132370.
3 Ramos AL, Trindade M, Pinto AS, *et al.* Pleural effusion and multiple myeloma – more than meets the eye: a case report. *Mol Clin Oncol* 2021; 15: 238.
4 Aurangabadkar G, Lanjewar A, Jadhav U, *et al.* A case of Hodgkin's lymphoma presenting with pleural effusion. *J Datta Meghe Inst Med Sci Univ* 2021; 16: 773–775.
5 Faiz SA, Pathania P, Song J, *et al.* Indwelling pleural catheters for patients with hematologic malignancies. A 14-year single-center experience. *Ann Am Thorac Soc* 2017; 14: 976–985.
6 Porcel JM, Cordovilla R, Tazi-Mezalek R, *et al*. Efficacy and safety of indwelling catheter for malignant pleural effusions related to timing of cancer therapy: a systematic review. *Arch Bronconeumol* 2023; 59: 566–574.
7 Clive AO, Kahan BC, Hooper CE, *et al.* Predicting survival in malignant pleural effusion: development and validation of the LENT prognostic score. *Thorax* 2014; 69: 1098–1104.
8 Bhatkal SA, Handa A, Lele A, *et al.* Survival in patients with malignant pleural effusion undergoing chemical pleurodesis: a retrospective analysis. *BMC Pulm Med* 2015; 15: 39.
9 Montemayor-Portillo E, Bielsa S, Corral J, *et al.* Efficacy and safety of indwelling pleural catheters for malignant effusion: a systematic review and meta-analysis. *Arch Bronconeumol* 2023; 59: 373–382.