

Time to next procedure in patients with malignant pleural effusion undergoing aspiration: derivation and initial validation of the RED score

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The Clinical Question

Are there patient characteristics that can predict time to next pleural procedure in the setting of known or suspected malignant pleural effusion (MPE) undergoing therapeutic aspiration?



Take Home Message

The respiratory rate (R), effusion depth on ultrasound (E), and dyspnea measured using the visual analogue scale (D) are predictive of time to next procedure in those presenting with malignant pleural effusion (MPE) requiring thoracentesis.

Background

Breathlessness from MPE is the most common symptom relieved by fluid drainage, usually managed with initial aspiration and more definitive management on subsequent procedures as stated by the British Thoracic Society guidelines.

Volume drained and pleural fluid analysis (TP, pH, LDH, and cholesterol) have been described as predictors of time to next procedure for pleural effusion, but are only obtainable after drainage. Effusion size on chest x-ray is a proven predictor of time to next pleural procedure.

The authors of this study decided to use ultrasound, rather than chest X-ray, as a potential predictor for next pleural procedure. RR and breathlessness have not been assessed in prior studies.

Current Practice:

- No existing standardized pathway to predict when a patient might need repeat thoracentesis
- Follow up imaging is often pursued after 4-6 weeks (outpatient) or more routinely (inpatient)
- Return precautions are often given



Study design

Study design:

- Prospective Observational Cohort Study. No randomization, blinding, or control groups
- N: 241
- Study groups: derivation cohort (n = 180), two RED score validation cohorts (n = 31, n = 57)
- Settings: 10 UK Hospitals, either inpatient or outpatient setting
- Enrollment and Treatment period: Between November 2021 and June 2023

Follow-Up:

Post-Discharge Day 7	Post-Discharge 30 Days & 3 Months
In-person	In-person or by telephone
Completed Quality of Life Assessment (EQ-5D 5L)	Completed Quality of Life Assessment (EQ-5D 5L)
Chest X-ray	Treatments (including repeat drainage) recorded
Thoracic Ultrasound	Mortality Recorded
7-day VASD Diary	Established Final Diagnosis

Primary outcome:

Time to next procedure, categorized as fast (1-13 days) and not fast (14+ days or none)

Secondary Outcome(s):

Time to next procedure for slow (>42 days) or not slow (<42 days) groups

Intervention(s):

No interventions in this study.



Population

Inclusion criteria:

>18 years old, pleural effusion diagnosed on US or CT scan requiring therapeutic aspiration, known/suspected malignancy as cause of effusion

Exclusion criteria:

known pleural infection, known transudative effusions thought primarily due to cardiac, renal, or hepatic impairment, and current pregnancy or breast feeding

Baseline characteristics:

	Derivation Cohort	First Validation Cohort	Second Validation Cohort
# of Participants	180	31	57
Age (years), mean (SD)	71.6 (12.5)	72.4 (10.1)	69.9 (13.5)
% Female	52.2	41.9	63
% Inpatient	20	16.1	26
Previous ipsilateral drainage (% yes)	20	19.4	19.3
ECOG performance status (0:1:2:3:4)	0: 25 (13.9%) 1: 67 (37.2%) 2: 56 (31.1%) 3: 31 (17.2%) 4: 1 (0.6%)	11:15:4:1:0	5:26:11:14:1
O2 Sat on RA (%), mean (SD)	95.5 (2.2)	95.3 (2.7)	95.4 (3.0)
RR, mean (SD)	18.5 (3.4)	18.8 (2.7)	20.0 (5.3)
Pre-procedure Effusion Depth (cm), mean (SD)	11.6 (3.2)	12.6 (3.2)	12.6 (4.3)
Pre-procedure Effusion Height (cm), mean (SD)	15.5 (6.1)	18.0 (4.8)	-
Pre-procedure US Septation (% yes)	5.6	12.9	-
Neutrophils : Lymphocytes, mean (SD)	6.9 (6.9)	5.8 (3.4)	-
Baseline Breathlessness Score (VASD), mean (SD)	6.9 (2.3)	5.3 (3.1)	6.0 (2.9)



Outcomes

Primary outcomes

- RR, effusion depth on US, and baseline VASD were independent predictors of time to next procedure for fast vs not-fast differentiation
- A predictive model was created to predict fast vs not-fast repeat pleural procedure; no significant difference was seen between observed and predicted outcomes when this model was applied
 - Equation created/applied: $\text{Log-odds} = -4.52 + 1.03(\text{RR} > 22) + 0.22(\text{VASD}) + 0.21(\text{effusion depth})$

Secondary outcomes looking at biomechanical performance

- Effusion depth on US and baseline VASD were independent predictors of time to next procedure for slow vs not slow differentiation
- A predictive model was created to predict slow vs not slow repeat pleural procedure; no significant difference was seen between observed and predicted outcomes when this model was applied
 - Equation created/applied: $\text{Log-odds} = 3.4 - 0.24(\text{VASD}) - 0.26(\text{effusion depth})$

Adverse events

Not recorded.

RED Score Calculation:

1. Obtain the following values: RR (breaths/min), effusion depth (visceral to parietal pleura, cm), dyspnea (using VASD)
2. First, add effusion depth + VASD score
3. Add 5 points if $\text{RR} > 22$

High RED Score (> 21): likely to need another ipsilateral therapeutic pleural procedure within 2 weeks

Medium RED Score (<21): likely to need another ipsilateral therapeutic pleural procedure within 2-6 weeks

Low RED Score (< 14): unlikely to need another ipsilateral therapeutic pleural procedure within 6 weeks

High RED score was significant for the following compared to medium or low RED scores:

- Greater volume drained (high vs medium: mean difference $321 \pm 77\text{mL}$, $p < 0.001$; high vs low: mean difference $588 \pm 124\text{mL}$, $p < 0.001$)
- Greater post-drainage effusion depth (high vs medium: mean difference $3.5 \pm 0.84\text{cm}$, $p < 0.001$; high vs low: mean difference $5.4 \pm 1.3\text{ cm}$, $p < 0.001$)
- Greater decrease in VASD (high versus medium, mean difference $1.4 \pm 0.40\text{cm}$, $p = 0.002$; high versus low, mean difference $3.1 \pm 0.65\text{ cm}$, $p < 0.001$)
- Greater subsequent pleural procedures (high vs medium: adjusted $p = 0.041$; high vs low: adjusted $p = 0.003$)
- More likely to have admission due to breathlessness due to effusion (13/54 patients compared with 14/122, $p = 0.032$)

Medium RED score was significant for the following compared to low RED score:

- Greater decrease in VASD (mean difference $1.7 \pm 0.61\text{ cm}$, $p = 0.018$)

Original primary outcome was size of effusion on chest x-ray 7 days after therapeutic drainage; however, this was found to be unreliable, so they changed the primary outcome to the current primary outcome.

The two validation cohorts were small.

Their RED score needs external validation and to be tested against existing scores using pleural fluid and other markers.

The study only aims to define when they might undergo repeat thoracentesis.

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Suggested Reading

1. Mishra EK, Clark A, Laskawiec-Szkonter M, et al. Trial protocol: Reaccumulation rate of pleural effusions after therapeutic aspiration: an observational cohort study to determine baseline factors associated with rate of pleural fluid reaccumulation following therapeutic aspiration in patients with malignant pleural effusion attending a pleural clinic (REPEAT). *NIHR Open Res.* 2023;3:5.
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3. Fjaellegaard K, Petersen JK, Rasmussen DB, et al. Prediction of time to next therapeutic thoracentesis and identification of risk factors of rapid pleural fluid recurrence: a prospective observational study. *Respiration.* 2023;102:333-40.
4. Addala D, Sundaralingam A, Bedawi E, et al. Patient experiences of malignant pleural effusion management: a qualitative study. In: *British Thoracic Society Winter Meeting 2022*; 2022 Nov 23–25; London, UK. Programme and Abstracts.

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