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Original Article

Validation of the RAPID score in a Danish population with pleural infection

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ABSTRACT

INTRODUCTION. The incidence of pleural infection, a condition associated with increased mortality, is rising internationally. The RAPID (renal, age, purulence, infection source and dietary factor) score is a prognostic tool designed to stratify patients into risk categories based on five clinical baseline parameters. The aim of the study was to validate the RAPID score as a tool for assessment of prognosis, in the form of mortality, in patients with pleural infection in a Danish setting.

METHODS. This was a retrospective observational cohort study including all patients coded with an International Classification of Diseases, version 10 (ICD-10) code for pleural infection (DJ86 Pyothorax) at a regional University Hospital in a five-year period. Medical records were reviewed retrospectively, RAPID scores were calculated and study participants were stratified into risk groups: low (RAPID scores: 0-2), medium (RAPID scores: 3-4) and high (RAPID scores: 5-7). The primary outcome was three-month mortality. Secondary outcomes were 12-month mortality, length of hospital stay, failure of initial medical treatment and surgical intervention.

RESULTS. Overall mortality at three months was 18.0%. Mortality according to RAPID risk category was as follows: Low risk 2.4% (95% confidence interval (CI): 0.1-12.6), medium risk 17.0% (95% CI: 7.7-30.8) and high risk 39.4% (95% CI 22.9-57.9). Hazard ratios for three-month mortality, with low risk as reference, were 7.5 (95% CI: 0.9-60.1; p = 0.057) for medium risk and 20.6 (95% CI: 2.7-157.6; p = 0.004) for high risk.

CONCLUSION. The findings of this study support the use of the RAPID score as a prognostic tool for assessment of mortality risk in patients with pleural infection in Danish healthcare.

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The incidence of pleural infection is increasing globally and affects nearly 700 Danish patients annually [1]. Pleural infection is associated with increased morbidity and mortality, with 12-month mortality estimated to be 15-20%, a median length of hospital stay of 17 days and 5-22% of patients needing surgical intervention [1-4].

For assessment of prognosis, Rahman and colleagues developed the RAPID-risk prediction score, which remains the only specific outcome prediction tool for pleural infection. The score was derived and validated using the largest prospective multicentre randomised controlled trials to date (MIST-1 and MIST-2) and stratifies patients into three risk groups (low, medium and high) based on baseline blood urea, age, purulence of pleural fluid,

infection source and serum albumin [5]. The PILOT study validated the RAPID score, the largest longitudinal observational study on pleural infection conducted [6]. Several subsequent studies have found an association between RAPID score and three-month mortality, 12-month mortality and length of hospital stay [2, 6, 7].

The RAPID risk-prediction score has been prospectively validated in the UK, the US, Australia and South Africa [3, 6]. However, to our knowledge, the RAPID risk score has yet to be validated for use in a Danish healthcare setting.

This study aimed to validate the RAPID risk-prediction score as a prognostic tool in a Danish healthcare setting by retrospectively reviewing medical records of patients admitted with pleural infection. Prognosis, as measured by mortality, was compared between the three risk groups to investigate differences in three-month mortality. Secondary outcomes were 12-month mortality, length of hospital stay, failure of initial medical treatment and use of surgical intervention.

METHODS

Study design, population and data collection

This was a retrospective observational cohort study. Medical records were collected retrospectively and reviewed for all patients admitted with pleural infection (ICD-10: DJ86 Pyothorax) at the Department of Respiratory Medicine, Odense University Hospital (OUH), Denmark, from 1 January 2017 to 31 December 2021.

The Department of Respiratory Medicine at OUH serves as the primary referral centre for Funen (0.5 million inhabitants) and as a tertiary referral centre for the Region of Southern Denmark (1.22 million inhabitants) in cases of treatment failure at the primary admission centre. In complicated cases, where a need for assistance with chest tube placement (ultrasound-guided or surgical placement) or intrapleural therapy emerges, patients are also referred to the department.

Treatment of pleural infection at all hospitals comprised by this study adheres to the national guideline developed by the Danish Society for Respiratory Medicine and the Danish Society for Cardiothoracic Surgery, which describes initial diagnostics, antibiotics and choice of chest tubes [1].

Eligibility criteria

The inclusion criteria were adult patients (≥ 18 years) with a diagnosis of pleural infection based on international criteria used in previous trials [5].

A clinical history compatible with pleural infection – a pleural collection that was either:

- purulent or

- gram stain/culture positive or

- acidic with a low pH < 7.2 or

- low pleural fluid glucose (in the absence of an accurate pH measurement) or

- septated pleural collection clinically considered most likely secondary to pleural infection.

Ethical approval

In accordance with Danish legislation, ethics committee approval was waived in view of the retrospective design. The study was conducted according to the guidelines of the Declaration of Helsinki, and data permission was approved under the authority of the Region of Southern Denmark on 15 February 2022 (ID 22/8470).

RAPID score

A database was developed containing patient characteristics (including age, gender, comorbidities and primary admission site) and baseline clinical parameters needed for calculation of the RAPID score (**Table 1**). RAPID scores were calculated, and patients were stratified into risk groups (low, medium and high) as in previous studies [5].

TABLE 1 The RAPID risk prediction score, developed by Rahman et al. [5].

Parameter	Score
Renal: urea, mmol/l	
< 5.0	0
5.0-8.0	1
> 8.0	2
Age, yrs	
< 50	0
50-70	1
> 70	2
Purulence of pleural fluid	
Purulent	0
Non-purulent	1
Infection source	
Community-acquired	0
Hospital-acquired	1
Dietary factor: albumin, g/l	
≥ 27.0	0
< 27.0	1
Risk category	
Low	0-2
Medium	3-4
High	5-7

Primary and secondary outcomes

Patient outcomes were compared between the three risk groups. The primary outcome of the study was three-

month mortality. Secondary outcomes included 12-month mortality, length of hospital stay, failure of initial medical treatment and surgical intervention.

Total length of hospital stay was calculated from time of admission to time of discharge. This included time spent at other hospitals before or after being transferred to or from the department. Failure of initial medical treatment was defined as no symptomatic or paraclinical progress (assessed using blood samples and pulmonary ultrasound) within five days of arrival at the department. Surgical intervention included video-assisted thoracic surgery (VATS), thoracotomy and decortication performed during the hospital stay.

Statistical analyses

Statistical analyses were performed using SPSS version 28 (IBM Corporation, New York, USA).

Patient characteristics were reported as mean standard deviation for continuous variables or frequencies and proportions for categorical variables. Between-group differences in comorbidities were analysed using the χ^2 test.

Patients with missing or incomplete RAPID score data were excluded from the study. In case of missing data on patient outcomes, these subjects were excluded from the statistical analysis.

A Shapiro-Wilks test was performed on continuous variables to assess for normal distribution.

Mortality was reported as proportions and corresponding 95% confidence intervals (CI). Between-group differences in mortality were presented using hazard ratios with associated 95% CI. Differences in survival were analysed using Kaplan-Meier plots.

Length of hospital stay was reported as median and interquartile range (IQR), and between-group differences were analysed using the Mann-Whitney-U test.

Failure of initial medical treatment and use of surgical intervention were reported as proportions with corresponding 95% CI.

Trial registration: not relevant.

RESULTS

Study participants

From 2017 to 2021, 162 admissions with the ICD-10 code DJ86 were registered. One was excluded due to coding error, and 39 were excluded due to missing baseline parameters needed to calculate the RAPID score. Among these, blood urea nitrogen had not been measured in 37, and the appearance of the pleural fluid was not described in two. Thus, a total of 122 patients were included in the statistical analysis. Due to missing data, seven patients were excluded from the statistical analysis for 12-month mortality (**Figure 1**).

FIGURE 1 Mortality between the three risk groups over three months (**A**) and 12 months (**B**).

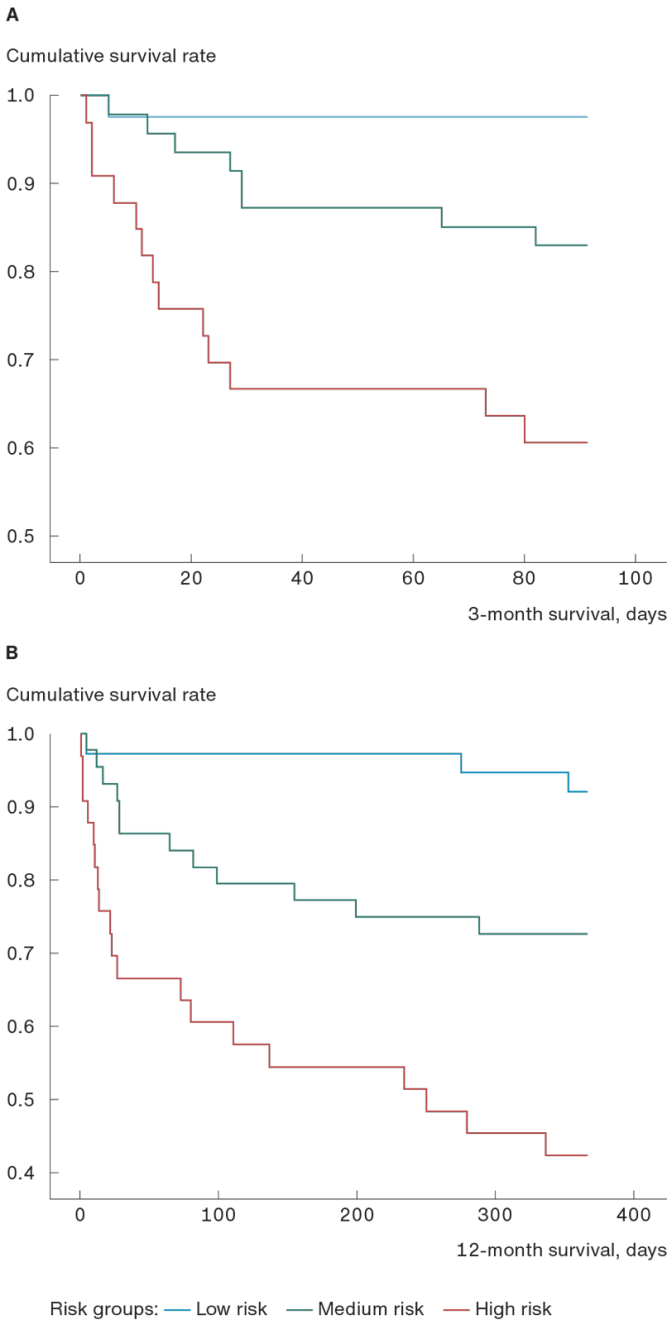

Table 2 presents the baseline characteristics of the study participants. A total of 71/122 (58.2%) of the included study participants had their primary admission at the OUH, whereas 51/122 (41.8%) were transferred from other hospitals in the region.

TABLE 2 Baseline characteristics of 122 study participants with pleural infection.

Variable	Result
Demographic characteristic	
Age, mean ± SD, yrs	68 ± 14
Male sex, n/N (%)	84/122 (68.9)
Source of infection, n/N (%):	
Community-acquired	104/122 (85.2)
Hospital-acquired	18/122 (14.8)
Pleural fluid characteristics	1
Pleural fluid purulence, n/N (%)	50/122 (41)
pH, mean ± SD[a]	6.97 ± 0.28
Loculation, n/N (%)[b]	89/109 (81.7)
Blood, mean ± SD	1
Urea, mmol/l	8.4 ± 8.5
Albumin, g/l	29.7 ± 4.8
Comorbidities, n/N (%)	1
Asthma	10/122 (8.2)
Atrial fibrillation	34/122 (27.9)
COPD	18/122 (14.8)
Cancer:	
Previous	18/122 (14.8)
Current	20/122 (16.4)
Heart disease	28/122 (23)
Hypertension	51/122 (41.8)
Interstitial lung disease	1/122 (0.8)
Previous pleural infection	12/122 (9.8)
Renal disease	20/122 (16.4)
Diabetes mellitus	18/122 (14.8)
Primary admission site, n/N (%)	
Odense University Hospital	71/122 (58.2)
Kolding Hospital	9/122 (7.4)
Vejle Hospital	4/122 (3.3)
Svendborg Hospital	26/122 (21.3)
Soenderborg Hospital	4/122 (3.3)
Aabenraa Hospital	7/122 (6.6)

SD = standard deviation.
a) Data only available for 85/122 study participants.
b) Data only available for 109/122 study participants.

The proportion of patients with at least one comorbidity was 69.0% for the low-risk group, 87.2% for the medium-risk group and 90.9% for the high-risk group. The between-group differences in overall comorbidity were found to be significant (p = 0.025).

Primary outcome

Within three months of admission, 22 out of 122 had died, corresponding to an overall three-month mortality of 18.0%. In the three risk groups, mortality was as follows: low risk (RAPID score: 0-2) 2.4% (95% CI: 0.06-12.6), medium risk (RAPID score: 3-4) 17.0% (95% CI: 7.7-30.8) and high risk (RAPID score: 5-7) 39.4% (95% CI: 22.9-57.9) (**Table 3**) and (Figure 1).

TABLE 3 Primary and secondary outcomes for 122 patients with pleural infection according to baseline RAPID risk category.

	RAPID risk category: score			Statistical comparison			
Outcome	low risk: 0-2 [n = 42]	medium risk: 3-4 [n = 47]	high risk: 5-7 [n = 33]	χ^2, 2 df	Mann-Whitney	HR (95% CI)	p value
Mortality, % (95% CI)							
3-mo. [N_{tot} = 122]	2.38 (0.06-12.57)	17.02 (7.65-30.81)	39.39 (22.91-57.86)	-	-	Medium vs low risk: 7.52 (0.94-60.12)	0.057
						High vs low risk: 20.61 (2.69-157.63)	0.004
12-mo. [N_{tot} = 115]	7.89 (1.66-21.38)	27.27 (14.96-42.79)	57.58 (39.22-74.52)	-	-	Medium vs low risk: 3.9 (1.10-18.81)	0.035
						High vs low risk: 10.65 (3.14-36.06)	< 0.001
Median length of total hospital stay, days, median (IQR) [N_{tot} = 122]	12 (9-17)	19 (12-30)	23 (15-32)	-	Low risk vs medium risk	-	0.002
					Low risk vs high risk		0.001
Failure of initial medical treatment, n (%; 95% CI) [N_{tot} = 122]	2 (4.76; 0.58-16.16)	20 (42.55; 28.26-57.82)	20 (60.61; 42.14-77.09)	5.51	-	-	0.064
Surgical intervention, n (%; 95% CI) [N_{tot} = 122]	1 (2.38; 0.06-12.57)	4 (8.51; 2.37-20.38)	0 (0; 0-10.50)	4.053	-	-	0.132

CI = confidence interval; df = degrees of freedom; HR = hazard ratio; IQR = interquartile range.

Hazard ratios for three-month mortality, with low-risk as the reference group, were 7.5 (95% CI: 0.94-60.1; p = 0.057) for the medium-risk group and 20.6 (95% CI: 2.7-157.6; p = 0.004) for the high-risk group.

Secondary outcomes

Overall mortality at 12 months was 34/115 (29.6%). Mortality in the three risk groups was as follows: Low risk 7.9% (95% CI: 1.7-21.4), medium risk 27.3% (95% CI: 15.0-42.8) and high risk 57.6% (95% CI: 39.2-74.5) (Table 3) and (Figure 1).

Hazard ratios for 12-month mortality, with low risk as the reference group, were 3.9 (95% CI: 1.1-18.8; p = 0.035) for the medium-risk group and 10.7 (95% CI: 3.1-36.1; p < 0.001) for the high-risk group.

Median length of hospital stay was 12 days (IQR: 9-17) for the low-risk group, 19 days (IQR: 12-30) for the medium-risk group, and 23 (IQR: 15-32) for the high-risk group. Between-group comparisons found that the differences in length of hospital stay were significant (p = 0.002 for low versus medium risk, and p = 0.001 for low versus high risk).

A total of 42/122 (34.4%) patients experienced failure of initial medical treatment, defined as no symptomatic or paraclinical progress within five days of being admitted to the department. Failure of initial treatment in the three risk groups was as follows: 4.8% in the low-risk group, 42.6% in the medium-risk group, and 60.6% in the high-risk group (Table 3).

A total of 5/122 patients (6.6%) underwent surgical intervention in the form of VATS, thoracotomy or decortication during their hospital stay, 1/42 (2.4%) in the low-risk group, 4/47 (8.5%) in the medium-risk group, and 0/33 (0.0%) in the high-risk group (Table 3).

The differences in failure of initial medical treatment and surgical intervention between the three risk groups were non-significant (Table 3).

DISCUSSION

This study supports the applicability of the RAPID score in a Danish population, reinforcing its role as a prognostic tool for pleural infection. High-risk patients had significantly increased three- and 12-month mortality, longer hospital stays, and a trend towards a higher initial treatment failure than low-risk patients.

Our findings align with those reported by Corcoran and colleagues in the PILOT study [6]. We found three-month

mortality rates of 2.4%, 17.02% and 39.4% compared with 2.3%, 9.2% and 29.3% for low-, medium- and high-risk groups, respectively.

Mortality rates at 12 months in the three risk groups were 7.9%, 27.3% and 57.6% for the low-, medium- and high-risk groups, respectively. These results are similar to those reported by White and colleagues, who reported 10%, 25% and 55% 12-month mortality [7].

Although it remains unclear why RAPID parameters independently relate to mortality, increased age, blood urea and low serum albumin suggest frailty [5]. Low serum albumin may result from inflammation or poor nutrition [8, 9]. Notably, age and blood urea are also included in the CURB-65 score used to assess the severity of pneumonia [10].

Our data demonstrate a significant difference in length of hospital stay between the three risk groups, suggesting an association between duration of hospitalisation and increasing RAPID score. Patients in the medium-risk and high-risk groups had longer hospital admissions than patients in the low-risk group. These differences may be a result of the patients in the high-risk group being frailer as they exhibited a significantly higher frequency of comorbidities than the low- and medium-risk groups.

Naturally, when interpreting these findings, important limitations should be considered, encompassing a retrospective design with missing variables in more than 20% of patients, and a risk of single-centre bias. Conversely, it should be considered that a risk may exist of overestimating the proportion of patients with high RAPID scores across the entire study population as patients admitted to a peripheral hospital who were successfully alleviated of their pleural infection without the need for transferral to the university hospital were not included in the study.

To our knowledge, this is the first study validating the use of the RAPID risk-prediction score on patients with pleural infection in a Danish healthcare setting. Encouragingly, only one out of 162 patients assessed for study inclusion was erroneously ICD-10 coded, supporting earlier findings that the Danish National Registry of Patients is characterised by a high positive predictive value in regard to pleural empyema [11].

As demonstrated by the results, the RAPID score can successfully stratify patients by increasing mortality risk. Stratifying patients into risk groups at baseline helps clinicians identify patients with an increased risk of adverse outcomes. Beyond informing personalised patient discussions regarding prognosis, early risk stratification may allow clinicians to consider earlier escalation of treatment to intrapleural and/or surgical therapies.

The debate as to whether surgical intervention or combination intrapleural fibrinolytic and enzyme therapy should be used as first-line treatment of pleural infection is the subject of ongoing study [12]. Improved outcomes and reduced risk of conversion and adverse events with VATS have made the treatment more accessible to older patients. Mortality risk predicted by the RAPID score may potentially be of use in the future in informing the benefit-risk balance of proceeding to VATS surgery. Thus, patients in whom the risk of death from untreated pleural infection is greater than their predicted operative mortality may be considered for surgical intervention. Previously, this treatment modality was limited to a select group of young and fit patients. To clarify its full utility, future prospective studies are warranted triaging patient to varying levels of treatment based on baseline RAPID score.

CONCLUSION

The findings in the present study add credence to the robust predictive ability of the RAPID score and support its use as a prognostic tool for assessment of mortality risk in patients with pleural infection in Danish healthcare.

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