

Patient and fluid characteristics associated with non-draining malignant pleural effusion

1 Introduction

- TIME3, a randomised controlled trial of intrapleural urokinase versus placebo for patients with non-draining malignant pleural effusion (MPE), demonstrated that these patients appear to be a distinct subgroup of patients with a poor prognosis (median survival 58 days).
- The aim of this study was to identify patient and fluid characteristics associated with this subgroup, to enable further understanding of why patients with non-draining effusion may have poor prognosis.
- We hypothesized that this group of patients would have worse ECOG performance status at baseline and have a higher incidence of malignancies associated with poor prognosis e.g. lung cancer

2 Methods

- Baseline demographics and pleural fluid (PF) characteristics of patients enrolled in TIME3 were compared to patients enrolled in TIME2, a randomised controlled trial of indwelling pleural catheter versus chest drain and pleurodesis for patients with recurrent MPE.
- Demographic characteristics compared were: age, sex, histological type of cancer, C reactive protein (CRP), number of previous pleural procedures and ECOG performance status (PS). Pleural fluid characteristics compared were: total protein, glucose, cytology (positive or negative), pH, lactate dehydrogenase (LDH) and presence of septations on ultrasound.
- These characteristics were compared using t test for linear variables and chi squared for categorical variables.

3 Results

- The median survival was 58 days (IQR 27-123) in TIME3 versus 187 days (IQR 48-358) in TIME2.
- Patients with non-draining effusions had a significantly higher PF LDH (mean 1900 (SD 3100) versus 660 (SD 840), $p<0.001$) and CRP (mean 117 (SD 80) versus 62 (SD 55), $p<0.001$).
- Patients in TIME3 were on average 4 years older (mean 71 years in TIME3 versus 67 in TIME2, $p=0.01$) and less likely to be cytology positive (24% versus 51%, $p=0.021$).

4 Comparison of characteristics

Variable	TIME2	TIME3	Difference (p)
Number of patients	106	71	-
Mean age (years) (SD)	67 (11)	71 (9.4)	0.013
Male: female (% male)	46:60 (43)	41:30 (58)	0.06
Median time to death (days) (IQR)	187 (48-358)	58 (27-123)	
Type of cancer (%):			
• breast	27 (25)	12 (17)	0.47
• lung	25 (24)	22 (31)	
• mesothelioma	11 (10)	9 (13)	
• other	43 (41)	28 (39)	
ECOG PS 0-2:3-4 (% 0-2)	60:46 (57)	42:29 (59)	0.11
Bloods			
Mean white cell count (SD)	9.8 (5.4)	11.0 (5.4)	0.15
Mean CRP (SD)	62 (55)	117 (80)	<0.001
Pleural fluid characteristics			
• Cytology positive:negative (% positive)	54:48 (51)	17:34 (24)	0.021
• pH (SD)	7.4 (0.24)	7.4 (0.34)	1.0
• Glucose (mmol/L) (SD)	5.4 (2.8)	4.6 (3.6)	0.13
• LDH (U/L) (SD)	660 (840)	1900 (3100)	<0.001
• Total protein (g/dL) (SD)	43 (8.1)	41 (10)	0.18
Septated on ultrasound (yes:no)	Not recorded	59:7	-

5 Discussion

- Patients with non draining MPEs have a higher pleural fluid LDH and CRP than those without. There was a large difference in mortality between groups, but despite this no identifiable differences in baseline ECOG, PS or tumour type, despite these variables being associated with a poor prognosis in unselected cohorts of patients with MPE (Clive, 2014).
- We postulate that survival in MPE may be associated with septations and the intrapleural inflammatory milieu.
- Further study of the association between PF LDH, septations and survival is warranted.

6 References

- Clive, AO et al. Predicting survival in malignant pleural effusion: development and validation of the LENT prognostic score. Thorax. 2014 Dec;69(12), 1098-104
- Davies HE, Mishra EK et al. Effects of an indwelling pleural catheter vs chest tube and talc pleurodesis for relieving dyspnoea in patients with malignant pleural effusion: the TIME2 randomized controlled trial. JAMA 2012 Jun 13; 307(22) 2383-9
- Mishra EK et al. Randomised Controlled Trial of Urokinase versus Placebo for Non-draining Malignant Pleural Effusion. Am J Respir Crit Care Med. 2017 Sep 19 (Epub ahead of print)