Prognostic Associations of the Neutrophil-To-Lymphocyte and Platelet-To-Lymphocyte Ratio in Patients Treated with Surgery for Pleural Mesothelioma after Radiotherapy

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Purpose/Objective(s)

Immunity profile have had prognostic implications in some thoracic malignancies. We examine the prognostic significance of neutrophil-to-lymphocyte ratios (NLR) and platelet-to-lymphocyte ratios (PLR) at different time points for patients with malignant pleural mesothelioma (MPM) treated with Surgery for Mesothelioma After Radiation Therapy (SMART)

Materials and Methods

From a prospective study database, we identified all patients with histologically proven MPM treated with Surgery for Mesothelioma After Radiation Therapy (SMART). Complete blood count (CBC) values were collected, and the NLR, PLR immune profiles were calculated at 4 time points: pre-RT (before radiation),), pre-op (after radiation/before surgery), 1m-post-op (30-60 days after surgery) and 3m-post-op (60-180 days after surgery). The endpoints of interest were: overall survival (OS), disease-free survival (DFS), and time to distant recurrence (DR). Each was measured in months starting from the date of starting treatment. OS and DFS were assessed using the Cox Proportional-Hazards Model, and distant recurrence (contralateral chest, pericardium, abdomen, liver, bone or other distant) was compared using the Fine-Gray sub-distribution hazard model to account for competing risks from local/mediastinum recurrence and death.

Patient demographics

	n=123
Age at diagnosis	
Mean (sd)	64.6 (8.9)
Median (Min,Max)	66 (33,82)
Gender	
Female	28 (23)
Male	95 (77)
Preop subtype	
biphasic	29 (24)
epithelial	94 (76)
Side of mesothelioma	
left	37 (30)
right	86 (70)
Stage	
I	6 (5)
II	5 (4)
III	65 (54)
IV	45 (37)
Missing	2
N positive	
0	45 (37)
1	77 (63)
Missing	1

Univariate Overall Survival

	HR(95%CI)	p-value
Age at diagnosis		0.3097
<=65	Reference	
>65	1.2360 (0.8213,1.8603)	
Gender		0.0984
f	Reference	
m	1.5613 (0.9206,2.6481)	
Preop subtype		**0.0040**
biphasic	Reference	
epithelial	0.5029 (0.3150,0.8027)	
A NtoL	1.0324 (0.9580,1.1126)	0.4036
B NtoL	1.0021 (0.9906,1.0138)	0.7218
C NtoL	0.9984 (0.9873,1.0095)	0.7730
D NtoL	**1.0504 (1.0121,1.0900)**	**0.0094**
C-B NtoL	0.9951 (0.9845,1.0057)	0.3615
D-C NtoL	1.0085 (0.9905,1.0270)	0.3567
B-A DC NtoL	1.0050 (0.9866,1.0237)	0.5989
A PtoL	1.0003 (0.9988,1.0019)	0.6762
B PtoL	1.0002 (0.9999,1.0006)	0.2390
C PtoL	1.0000 (0.9996,1.0003)	0.8731
D PtoL	**1.0035 (1.0006,1.0064)**	**0.0181**

Multivariate Overall Survival

	HR(95%CI)	p-value
Preop subtype		**0.0311**
biphasic	Reference	
epithelial	0.5597 (0.3302,0.9487)	
D NtoL	**1.0635 (1.0228,1.1058)**	**0.0020**
D PtoL	**1.0042 (1.0014,1.0071)**	**0.0037**

Results

Between 2008 to 2020, 123 MPM patients were treated on the SMART protocol. Patient demographics were: median age 66 (range: 33-82) years, epithelial histology 94 (76%), biphasic histology 29 (24%). On univariate analysis (UVA) epithelial histology was significantly associated to improved OS hazard ratio (HR) 0.5029 (0.3150-0.8027) P= 0.0040, $NLR_{3m\text{-}post\text{-}op}$ HR 1.0504 (1.0121-1.0900) P= 0.0094 and $PLR_{3m\text{-}post\text{-}op}$ HR 1.0035 (1.0006-1.0064) p-value = 0.0181. On multivariate analysis (MVA) for OS epithelial histology HR 0.5597 (0.3302-0.9487) P=0.0311, $NLR_{3m\text{-}post\text{-}op}$ 1.0635 (1.0228-1.1058) P= 0.0020 and $PLR_{3m\text{-}post\text{-}op}$ 1.0042 (1.0014-1.0071) P=0.0037. On MVA for DFS epithelial histology HR 0.4573 (0.2721-0.7684) P=0.0031 and $NLR_{3m\text{-}post\text{-}op}$ HR 1.0587 (1.0188-1.1002) P=0.0036. On UVA and MVA NtoL and $PLR_{3m\text{-}post\text{-}op}$ were not significantly correlated to DR HR 1.0251 (0.9771,1.0754) P= 0.3100 and HR 0.9997 (0.9992,1.0003) P= 0.3700, respectively. Epithelial histology was significantly associated with DR on UVA HR 0.4459 (0.2657,0.7481) P=0.0022 but not on MVA HR 0.6182 (0.3401,1.1240) P= 0.1100.

Conclusion

In this study, we found that the 3 month post-operative NLR and PLR as well as epithelial histology were significantly associated with DFS and OS but not DR.

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