Tumor Lysis Syndrome Risk Analysis in a US Community Oncology Setting: A Retrospective Observational Study in Integra Connect Network

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Background

The risk of developing Tumor Lysis Syndrome (TLS) is widely recognized in highly proliferative cancers. Clinicians have adopted the "Howard Criteria" in evaluating clinical characteristics that lead to a higher propensity to develop TLS following chemotherapy. However, no real-world data has been published that quantifies TLS risk factors by cancer type.

The objective of this retrospective electronic health record study is to quantify risk factors that are correlated with a patient's probability to develop TLS during their cancer treatment.

Methodology

Data collection was performed within the Integra Connect database comprised of 17 community oncology network accounts and over 1,900 providers in the US.

Included were all patients ≥18 years of age with a TLS ICD-10-CM diagnosis code E88.3 between January 1, 2017 and September 30, 2020. Patients were excluded if they had a TLS diagnosis without evidence of anti-neoplastic treatment data. To remove bias, patients were excluded who received rasburicase on a prophylactic/preventive basis.

Among patients with a TLS diagnosis, clinical lab values were collected prior to the dates of TLS diagnosis and anti-neoplastic therapy.

A multivariate risk regression analysis was performed to evaluate TLS risk by disease site, by baseline characteristics, and by lab values. The risk analysis compared TLS patients diagnosed with CLL, DLBCL, CML, LGBCL, TCL, MM, and MCL to patients in the database with those cancers who did not develop TLS.

Study Population:

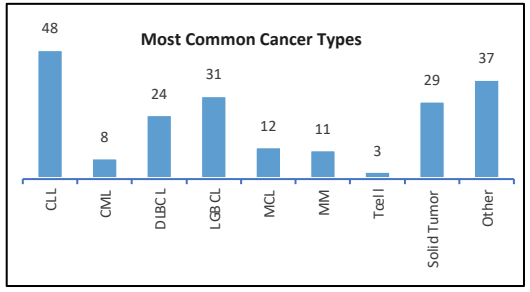
From the Integra Database, a total of 44,106 patient records were identified with a diagnosis of CLL, DLBCL, CML, LGBCL, TCL, MM, or MCL. Of the 44,106 patient records, 2,183 records were excluded from the analyses due to concomitant treatment with rasburicase.

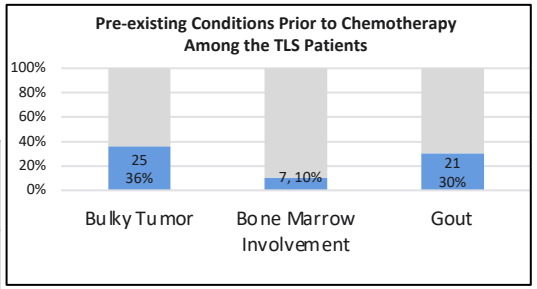
Out of the 41,923 remaining patients, a total of 816 patient records were identified with a diagnosis of TLS and were selected for evaluation. These patient records were compared against the baseline population to calculate the TLS relative risk ratio.

Cancer Type	Total Patient Count	Patients Received Rasburicase	Total Study Population	Study Population with TLS
CLL	9,198	539	8,659	216
DLBCL	7,092	541	6,551	161
CML	2,420	63	2,357	51
LGBCL	13,397	705	12,692	243
T-Cell	584	32	552	22
MM	10,234	185	10,049	87
MCL	1,181	118	1,063	36
Totals	**44,106**	**2,183**	**41,923**	**816**

Medical chart abstraction was conducted in 69 of the 816 TLS patients based on the availability of comprehensive clinical and laboratory medical record.

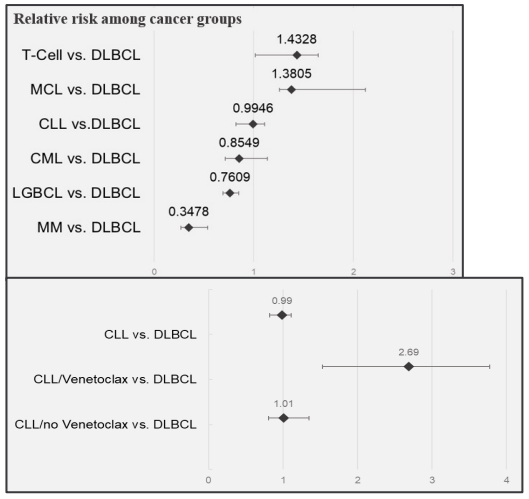
- CLL, LGBCL, and DLBCL have the largest number of patient records with a diagnosis of TLS, although a relatively large proportion of patients were being treated for solid tumors. The analysis identified that developing TLS remains a risk even in patients with solid tumor malignancies which consisted of 29% of patients from abstraction.
- Most of the TLS patients received rituximab, CHOP, or venetoclax in their anti-cancer therapies.
- Bulky tumors (a tumor mass ≥10cm on one side or ≥ 5cm on both sides of the diaphragm) were recorded in 36% (n=25) of the patient records, gout in 30% (n=21), and bone marrow involvement in 10% (n=7).





Results – Relative Risk in Cancer Groups

- The risk of developing TLS in Diffuse Large B-Cell Lymphoma (DLBCL) is widely recognized, thus DLBCL was used as the baseline comparator of TLS risk ratios amongst the cancer types of the TLS patients.
- T-Cell Lymphoma (TCL) and Mantle Cell Lymphoma (MCL) both demonstrated higher relative risk ratios at 1.43 and 1.38, respectively.
- Chronic Lymphocytic Leukemia (CLL) with Venetoclax anti-neoplastic therapy was also highly correlated with the development of TLS with a risk ratio of 2.69.



Results – Relative Risk of Contributing Factors

386 patient records had sufficient laboratory data available for further detailed assessments. Laboratory data was reviewed to confirm the TLS diagnosis. Ultimately, 203 patient records had a confirmed TLS diagnosis and adequate laboratory assessments for additional study.

Multivariate regression analysis indicated that quantified TLS risk factors varied amongst tumor types.

- DLBCL – patients with an ECOG score of 3 developed TLS at a risk ratio of 2.06. Elevated uric acid and calcium were also correlated with an increased risk at 2.12 and 2.07, respectively.
- CLL – both low and high white blood cell counts are most closely associated with TLS; risk ratio of 1.93 and 3.18 respectively.
- The most common risk factor in addition to disease type was elevated LDH levels, with 46% (94) of patients having an LDH level between 280 – 560mg/dL and 18% (37) having LDH greater than 560mg/dL.

Risk Factor		DLBCL	CLL	LGBCL	CML	TCL	MCL	MM
	Reference:							
OCM Status								
OCM Status ‡	Non-OCM	—	2.23	1.5	2.67	—	—	1.72
ECOG Status at Baseline								
ECOG = 3	ECOG =1	2.06	2.03	1.86	—	—	—	—
WBC Value§								
WBC <2		—	3.18	3.44	—	—	—	2.71
WBC [26,50]	WBC	—	—	2.44	—	—	—	
WBC [51,100]	[2,25]	—	—	—	—	10.7	—	4.66
WBC >100		—	1.93	4.34	—	24.9	6.95	—
LDH Value§								
LDH [0,139]	LDH [140-280]	0.99	—	—	—	—	—	—
LDH [281-560]		—	1.9	2.7	—	—	—	2.78
LDH >560		—	2.03	3.31	—	—	—	5.41
Uric Acid§								
UA >=8	UA<8	2.12	—	—	—	—	—	—
Calcium§								
Calcium <7	Calcium [8.5-10]	—	—	2.91	—	5.88	4.33	3.68
Calcium >10		2.07	—	—	—	—	—	—

Conclusions and Limitations

This study has identified risk factors unique to each disease site with a measurable impact on TLS risk that can be identified and potentially mitigated through preventive management and intervention. TLS risk is more evident in hematological malignancies but also in solid tumor malignancies.

Limitations: Retrospective EHR study; confounding and bias may exist due to recording errors.

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