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A Predictive Model for Tumor Lysis Syndrome in Acute Myelogenous Leukemia.

Anthony R. Mato, MD,[1,*] Brett E. Riccio, MD,[2,*] Li Qin, PhD,[3,*] Daniel Heitjan, PhD,[1,*] Alison Loren, MD,[1] Martin Carroll, MD,[1] David Porter, MD,[1] Donald Tsai, MD,[1] Edward Stadtmauer, MD,[1] Sasha Perl, MD,[1] Alan Gewirtz, MD,[1] Sunita Nasta, MD,[1] Stephen Schuster, MD,[1] Steven Goldstein, MD,[1] Selina M. Luger, MD[1]

[1]Hematologic Malignancies Program, University of Pennsylvania, Philadelphia, PA, USA

[2]FHCRC, Seattle, WA, USA

[3]Medicine, Beth Israel Deaconess, Boston, MA, USA

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Abstract

Tumor lysis syndrome (TLS) is defined by the metabolic derangements of hyperuricemia, hyperphosphatemia, hypocalcemia, and hyperkalemia in the setting of rapid tumor destruction. In acute myelogenous leukemia (AML), TLS management and prophylaxis is largely based on data derived from the non-AML patient population. To characterize the association between AML and TLS, a retrospective cohort analysis was conducted to estimate TLS incidence and identify TLS predictive factors. At our institution, all AML patients routinely receive allopurinol and intravenous fluids for TLS prophylaxis during induction chemotherapy. An understanding of the incidence and risks of TLS may allow us to tailor our treatments and avoid unnecessary toxicities. To estimate TLS incidence during induction we examined Cr, PO_4, K, and uric acid in 194 AML patients aged 18–86 undergoing induction chemotherapies between 1998 and 2003. Nineteen patients (9.8% 95% CI 5.2% – 15%) developed TLS within 8 days of initiation of therapy as defined by either (i) doubling of baseline serum creatinine in association with hyperphosphatemia (PO_4 > 5 mg/dL), hyperuricemia (UA > 7 mg/dl), or hyperkalemia (K >5 mmol/L) in 6 patients or (ii) a stable Cr with elevations in two of the above electrolytes in 13 patients. We examined several parameters hypothesized in the literature to be TLS predictors. In univariate analysis, elevated pre-chemotherapy values for uric acid (UA) (p=.0003), Cr (p=.0025), LDH (p=.0001), WBC (p =.0058) male sex (p =.0064), and CMML (p=.0292) were significant. In multivariate analysis, pre-chemotherapy

LDH (p=0.01, OR 3.01, 95% CI 1.5–6.2) and UA (p =0.01, OR 2.00, 95% CI 1.4–2.8) remained significant TLS predictors. We then performed a second logistic regression using re-coded versions of LDH and UA based on the quantiles of the initial pre-chemotherapy values. Based on the odds ratios for LDH and UA we constructed a scoring algorithm by assigning weights to these predictors in a 1:2 ratio. Entitled The Penn Predictive Score of Tumor Lysis Syndrome (PPS-TLS), the score is defined as follows: LDH score = 2 if LDH ≥ 2416 mg/dL, 1 if LDH ≥ 721 mg/dL and LDH < 2416 mg/dL, or 0 if LDH < 721 mg/dL, UA score = 4 if UA ≥ 5.2 mg/dL, 2 if UA ≥ 2.8 mg/dL and UA < 5.2 mg/dL, or 0 if UA < 2.8 mg/dL. (Normal range for LDH and UA 313 to 618 mg/dL and 3.0–7.5 mg/dL respectively). The total score is the summation of the pre-chemotherapy LDH and UA scores for the subject. The median PPS-TLS score for our patients with TLS is 5 (Range 3–6). Table 1 describes the sensitivity, specificity, and positive likelihood ratio (LR +) for each PPS-TLS score The PPS-TLS represents, to our knowledge, the first predictive model for TLS in AML. This analysis may lay the groundwork for the development of the first evidence-based guidelines for TLS monitoring and management in AML. We are currently designing a study to assess the external validity of this predictive model.

Table 1: Sensitivity, Specificity and LR for PPS-TLS Scores

Score	**0**	**1**	**2**	**3**	**4**	**5**	**6**
Sensitivity	1	1	1	1	0.89	0.63	0.42
Specificity	0	0.08	0.21	0.40	0.67	0.85	0.96
LR+	1.0	1.1	1.26	1.67	2.7	4.2	10.5

Author notes

Corresponding author