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MedEst|2026 | Vol.6: e519 | ISSN: 2789-7567 |RNPS: 2524| LETTER TO THE EDITOR

Towards an ethical protocol for tumor lysis syndrome: first steps towards its creation

Hacia un protocolo ético para el síndrome de lisis tumoral: primeros pasos para su confección

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Dear Director:

Tumor lysis syndrome (TLS) represents one of the most critical paradoxes in modern oncology, as it depicts a situation where maximum therapeutic efficacy can, in turn, trigger an iatrogenic and lethal metabolic emergency. This syndrome, characterized by a massive electrolyte imbalance secondary to tumor cell destruction that can lead to multiple organ failure, transcends its mere biochemical definition to delve into a clinical complexity that entails profound ethical dilemmas. (1) For its diagnosis, the criteria described by Cairo and Bishop in 2004 and updated in an expert consensus in 2010 have been used for more than two decades, (2) and these criteria have been adopted to date by all research on the subject. (3)

These criteria establish biochemical parameters: the presence of two or more laboratory abnormalities such as hyperuricemia, hyperkalemia, hyperphosphatemia, and/or hypocalcemia, with variations equal to or greater than 25% from baseline, and clinical parameters such as lethal cardiac arrhythmias occurring between three days before and seven days after cancer treatment. (2,3)

However, despite the widespread recognition and application of these criteria in clinical practice, there is a notable lack of guidelines addressing the ethical management of TLS. The available evidence is limited to describing clinical strategies, leaving a significant gap in the integration of ethical principles into the care of these patients. (1,3,4) Therefore, it is imperative to move beyond viewing TLS as merely a laboratory problem and complement its clinical management with initial guidelines for developing an ethical management protocol.

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According to Correa Rodríguez, [4] a first approach to this problem is provided by case reports that reveal devastating outcomes, where the absence of an ethical perspective exacerbates suffering and demonstrates a profound gap in the quality of care. In turn, the critical analysis of cases and the identification of gaps in ethical knowledge constitute essential starting points for the construction of an ethical framework.

Furthermore, the etiology of the syndrome, more documented in hematological malignancies, is currently showing an increase in solid tumors. [3] It is also observed spontaneously—even as the first manifestation of the disease—or after non-classically cytolytic therapies, such as targeted therapies or immunotherapy. [5,6]

However, the available evidence convincingly illustrates the unpredictability, severity, and consequent ethical dilemmas of TLS. Cases in metastatic lung cancer demonstrate that, even with personalized prophylaxis, TLS can progress spontaneously and fulminantly. [4,7] These trajectories underscore the urgent need for realistic informed consent that communicates the possibility of death from the moment of diagnosis.

Similarly, the immediate integration of palliative care in aggressive diseases is essential to avoid therapeutic obstinacy in the face of rapid deterioration and facilitates decision-making consistent with the prognostic reality. An example of this is patients who survive TLS but die weeks or months later after refusing further therapy or due to cancer progression. [7,8] This shows that early palliative assessment would have helped patients and their families navigate this situation with greater clarity.

The ethical paradox intensifies with new cancer therapies. Cases like the one presented by Asakura et al. [5], involving lung-related strokes induced by promising agents such as pembrolizumab, exemplify the calculated harm of precision oncology and document potentially fatal complications. This calls into question the true nature of cancer remission, where the most effective therapy is also the most dangerous.

The same evidence also finds support in the complications arising from therapeutic management. In the same patient described by Asakura [5], aggressive hydration as a therapeutic approach led to pulmonary edema and required intubation. This is the archetypal case where, after applying all available technical support and the most promising therapies, a palliative care discussion and informed consent are necessary to address all possible complications.

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Consequently, there are also cases where the patient has been stabilized, allowing them to resume scheduled cancer therapy after palliative care. [9] This makes the early integration of palliative care emerge not as a renunciation, but as an essential component for navigating these dilemmas proactively and humanely.

Conversely, its absence is palpable in scenarios of obstinacy, as in the case presented by Kunimoto et al., [10] where a patient with ovarian cancer and SLT culminated in intestinal perforation, forcing a family discussion about unfeasible surgeries versus comfort at a stage of extreme severity. In conclusion, proactive integration at the time of diagnosis of metastatic disease could have facilitated advance discussions about catastrophic scenarios and avoided futile interventions.

Another point to highlight is the complications arising from standard prophylaxis, which raise second-order maleficence dilemmas. An example of this is the use of rasburicase, in which fatal methemoglobinemia has been reported in patients with undiagnosed glucose-6-phosphate dehydrogenase deficiency, or severe anaphylaxis upon first exposure. [1,4]

Furthermore, allopurinol and febuxostat can precipitate obstructive nephropathy due to xanthine crystals. This demonstrates that preventing one harm and inducing another gives rise to reflection on genuine informed consent and the adequate communication of all possible risks. [1]

Therefore, all consent in modern oncology must be developed based on the entirety of the disease trajectory. This allows for a clear explanation of any complication to the patient, however infrequent or improbable it may be. This will empower patients to make an informed decision.

Moving from reflection to collaborative and protocol-driven action with the development of an ethical framework for therapeutic dissemination (TDS) must begin with the recognition of the dilemmas addressed in this letter. Table 1 summarizes the emerging ethical dimensions identified in the analyzed cases, justifying the need for a structured approach.

Table 1. Fundamental Ethical Dimensions

Ethical dimension	Problem identified	Guiding question
Therapeutic paradox	Simultaneous therapeutic efficacy	How do we communicate to patients that the most

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	and iatrogenic harm	effective therapy can also be the most dangerous?
Informed consent	Highly complex scenarios not foreseen in standard consent forms	How do we explain the risks of treatment versus the risks of the disease without creating false expectations?
Limits of life support	Available technology that can prolong suffering	When does life support cease to be beneficial and become therapeutic obstinacy?
Second-order harm	Serious complications arising from prophylaxis itself	Do we inform patients about the risks of medications that are precisely intended to prevent harm?
Justice and equity	Unequal access to prophylaxis, intensive care, and follow-up	Is it ethical for social or geographical context to determine the likelihood of surviving long-term illness?
Early palliative care integration	Exclusive curative approach that delays addressing suffering	Why wait for treatment failure to integrate palliative care if the underlying disease is advanced?

Source: Own elaboration.

Based on this evidence, we propose, in Table 2, a summary of the structure of a protocol based on the ethical components identified, so that oncologists, bioethicists, and clinical teams can develop tools adapted to their contexts. We urge the community to adopt, discuss, and validate frameworks to bridge the gap between ethical and clinical management.

Table 2. Summary of the structure of an ethical management protocol for SLT

Ethical component	Concrete action	Purpose
Risk assessment and communication	- Comprehensive assessment of the psychosocial context and access barriers. - Specific informed consent for SLT that explains its paradoxical nature and the risks of prophylaxis.	To respect autonomy through informed decision-making and contextualize risk.
Stratification and proportional prophylaxis	- Risk classification that combines clinical criteria with contextual factors such as support network and distance to the center. - Shared decision-making regarding	To apply the principles of beneficence and non-maleficence in a proportionate

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	care setting (outpatient/inpatient) based on risk and context.	and fair manner.
Acute management with a quality-of-life perspective	- Active monitoring of symptom burden and patient understanding during the risk phase. - Activation of ethical triggers, such as persistent renal failure or progressive cancer without curative options, to reassess goals.	To prevent therapeutic obstinacy and maintain a focus on quality of life.
Integration of palliative care and follow-up	- Early referral to palliative care for advanced metastatic disease or high risk of serious complications. - Structured follow-up to assess renal sequelae, psychosocial impact, and access barriers encountered.	To ensure a timely transition in care goals and promote justice and systemic learning.

Source: Own elaboration.

BIBLIOGRAPHIC REFERENCES

1. Correa Rodríguez JG. ¿Supervivencia a qué precio? Redefiniendo la calidad de vida en la encrucijada entre el síndrome de lisis tumoral y la terapia curatva. Univ. Méd. Pinareña [Internet]. 2025 [cited 09/02/2026]; 21(1): e1479. Available in: https://revgaleno.sld.cu/index.php/ump/article/view/1479

2. Cairo MS, Coiffier B, Reiter A, Younes A; TLS Expert Panel. Recommendations for the evaluation of risk and prophylaxis of tumour lysis syndrome (TLS) in adults and children with malignant diseases: an expert TLS panel consensus. Br J Haematol. [Internet] 2010 [cited 09/02/2026]; 149(4): 578-586. Available in: https://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2010.08143.x

3. Alqurashi RM, Tamim HH, Alsubhi ZD, Alzahrani AA, Tashkandi E. Tumor Lysis Syndrome in Patients With Solid Tumors: A Systematic Review of Reported Cases. Cureus [Internet]. 2022 [cited 09/02/2026]; 14(10): e30652. Available in: https://pmc.ncbi.nlm.nih.gov/articles/PMC9685209/

4. Correa Rodríguez JG. Los criterios de Cairo-Bishop y la imperativa necesidad de un marco ético para el síndrome de lisis tumoral. EsTuSalud [Internet]. 2026 [cited 09/02/2026]; 8(1): e486. Available in: https://revestusalud.sld.cu/index.php/estusalud/article/view/486.

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5. Asakura T, Shinojima T, Hiruta S, Asakura H. Fatal Tumor Lysis Syndrome Induced by Pembrolizumab in Advanced Renal Pelvis Cancer. IJU Case Rep [Internet]. 2025 [cited 08/02/2026]; 9(1): e70097. Available in: https://pmc.ncbi.nlm.nih.gov/articles/PMC12747779/

6. Kikuchi M, Miyabe R, Matsushima H, et al. Tumor lysis syndrome following letrozole for locally advanced breast cancer: a case report. Surg Case Rep [Internet]. 2024 [cited 09/02/2026]; 10(1): 100. Available in: https://pmc.ncbi.nlm.nih.gov/articles/PMC11043241/

7. Koura S, Parekh V, Parikh AD, Kaur K, Dunn BK. Spontaneous Tumor Lysis Syndrome Secondary to Metastatic Small Cell Lung Cancer. Cureus [Internet]. 2023 [cited 08/02/2026]; 15(2): e34557. Available in: https://pmc.ncbi.nlm.nih.gov/articles/PMC9985463/

8. Mao W, Jiang X, Wang M, et al. Spontaneous tumor lysis syndrome following liver biopsy: a case report and literature review. Front Oncol [Internet]. 2025 [cited 08/02/2026]; 15(1): 1683025. Available in: https://pmc.ncbi.nlm.nih.gov/articles/PMC12646902/

9. Omori S, Shigechi T, Kawaguchi K, Ijichi H, Oki E, Yoshizumi T. Successful Prevention of Tumour Lysis Syndrome in HER2-positive Breast Cancer: Case Report and Literature Review. Anticancer Res [Internet]. 2023 [cited 08/02/2026]; 43(5): 2371-2377. Available in: https://ar.iiarjournals.org/content/43/5/2371.long

10. Kunimoto S, Tashima L, Ito K, Hori K. Advanced ovarian cancer that resulted in death from intestinal perforation following tumor lysis syndrome: A case report. Int J Surg Case Rep [Internet].2022 [cited 08/02/2026]; 98(1): 107518. Available in: https://pmc.ncbi.nlm.nih.gov/articles/PMC9420503/

CONFLICT OF INTEREST

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