Synergistic Hyperthermia in Multimodal Oncology: Balancing Tumour Response with the Preservation of Health-Related Quality of Life.

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Introduction: Oncological hyperthermia (HT), the controlled elevation of tumour temperature to 39–43 °C, serves as a powerful radio- and chemosensitizer. In contemporary oncology, the assessment of health-related quality of life (QoL) has emerged as a vital prognostic indicator and a primary objective for patients, who often prioritize functional independence and symptom control over marginal survival gains. This is particularly relevant given the "discordance gap" frequently observed in advanced cancer, where patients receive aggressive treatments that may not align with their personal values. HT offers a unique biological synergy by inhibiting DNA repair and reoxygenating hypoxic tumour niches while maintaining a "toxicity-neutral" profile.

Objectives: This study aims to synthesize clinical evidence of regional HT in improving locoregional control (LRC) and overall survival (OS) while critically assessing its impact on patient-reported quality of life (QoL) and goal-concordant care (GCC).

Methods: A review of contemporary randomized controlled trials and real-world longitudinal analyses was performed across various tumour entities. Patient-reported outcomes (PROs) were assessed using the EORTC QLQ-C30 instrument to quantify changes in functional scales and symptom burden post-treatment.

Results: Evidence confirms that HT significantly enhances survival; landmark trials reported a 6-year OS of 79% in high-risk soft tissue sarcoma and a 5-year OS of 81.9% in locally advanced cervical cancer. In advanced pancreatic cancer, the addition of modulated electro-hyperthermia (mEHT) prolonged median OS to 20 months compared to 9 months with standard care ($p < 0.001$). Despite this therapeutic escalation, HT maintains a "toxicity-neutral" profile, with no significant increase in systemic adverse events. Longitudinal analyses show that curative-intent HT stabilizes Global Health Status and significantly improves emotional (EF) and social functioning (SF) at 12 months ($p < 0.01$). Palliative cohorts experienced rapid pain relief within 3 months ($p = 0.01$) without compromising physical autonomy.

Conclusions: Hyperthermia facilitates the delivery of goal-concordant care by intensifying local tumour response without the systemic trade-offs characteristic of aggressive multi-agent chemotherapy. By preserving functional independence and cognitive integrity, HT addresses the priorities of many cancer patients who value quality of life alongside survival While quality

assurance protocols are necessary for treatment consistency, the future of the field depends on shifting the focus toward patient-centered outcomes. There is an urgent need to incorporate QoL as a primary endpoint in future prospective studies to fully validate HT as a cornerstone of personalized oncology that respects "what matters most" to the patient.

Keywords: Hyperthermia; Quality of Life; Goal-Concordant Care; Radiosensitization; Patient-Reported Outcomes.