**Supplemental Digital Content**

**Liberal Versus Restrictive Transfusion Strategy in Critically Ill Oncologic Patients: The TRICOP Randomized Controlled Trial**

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**INDEX**

**SUPPLEMENTAL METHODS page 2**

Definition of septic shock

Exclusion criteria

Definition of pragmatic study

Data collection details

Acute myocardial infarction definition

**SUPPLEMENTAL RESULTS page 4**

Multivariate model results for mortality

Protocol deviations

**SUPPLEMENTAL METHODS**

**Definition of septic shock**

Septic shock was diagnosed in the presence of a suspected or verified focus of infection, complicated by cardiovascular dysfunction, characterized by hypotension (arterial mean pressure < 65 mmHg) despite fluid therapy therefore requiring vasopressor therapy.

**Exclusion criteria due to a too high expected mortality or transfusion rate**: do-not-resuscitate orders, hematological malignancy, end-stage renal disease requiring renal replacement therapy, Karnofsky score less than 50 - Karnofsky Performance Scale Index allows patients to be classified according to their functional impairment -, platelet count < 50,000 per mm3, prothrombin time > 14.8 s, anticoagulation therapy, uncontrolled bleeding, or estimated life expectancy < 24 hours.

This was a **pragmatic** study and, with the exception of the RBC transfusion strategy, the treatment given to the patients during the hospital stay, including antibiotics and resuscitation therapy, was performed by the attending physician according to international guidelines and local protocols.

**Data collection**

A team of three investigators collected baseline demographic and cancer characteristics, physical status performance, chemotherapy, comorbidities, and the Charlson co-morbidity index (ref A and B). Diagnosis at ICU admission, source of sepsis, positive cultures, Simplified Acute Physiology Score 3 (SAPS 3) and Sepsis-related Organ Failure Assessment score (SOFA) were recorded as well with both scores using the worst value within the first 24 ICU hours.

Ref A Schag CC, Heinrich RL, Ganz PA: Karnofsky performance status revisited: reliability, validity, and guidelines. J Clin Oncol 1984; 2:187-193

Ref B Charlson ME, Pompei P, Ales KL, MacKenzie CR: A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987; 40:373-383

**Acute myocardial infarction** was defined as an increase or decrease in cardiac troponin I, with at least one value above the 99th percentile of the upper reference limit, electrocardiographic changes or image-based evidence of new loss of viable myocardial).

**SUPPLEMENTAL RESULTS**

In the **multivariate model**, we identified predictors of 28-day mortality (hepatic dysfunction, respiratory dysfunction, platelet transfusion, SAPS3 score, and baseline serum creatinine > 1.5 mg/dL), 60-day mortality (SOFA score, hepatic dysfunction, and baseline serum creatinine > 1.5 mg/dL), and 90-day mortality (SOFA score, hepatic dysfunction, and restrictive transfusion strategy).

**Supplemental Table.** Multivariate Cox proportional hazards model for independent predictors of 28, 60 and 90-day mortality. Only significant variables have been reported

|  |  |  |
| --- | --- | --- |
| **Variable** | **Adjusted HR (95% CI)** | **P value** |
| **28-day mortality** |  |  |
| Hepatic dysfunction | 3.12 (1.59 - 6.13) | 0.001 |
| Respiratory dysfunction | 1.68 (1.19 - 2.37) | 0.003 |
| Platelet transfusion | 1.89 (1.13 - 3.14) | 0.015 |
| SAPS3 | 1.01 (1.01 - 1.02) | 0.021 |
| Baseline serum creatinine > 1.5 mg/dL | 3.24 (1.02 - 10.32) | 0.047 |
| **60-day mortality** |  |  |
| SOFA score | 1.08 (1.04 - 1.12) | <0.001 |
| Hepatic dysfunction | 2.17 (1.15 - 4.1) | 0.016 |
| Baseline serum creatinine > 1.5 mg/dL | 3.4 (1.08 - 10.75) | 0.037 |
| **90-day mortality** |  |  |
| SOFA score | 1.07 (1.03 - 1.11) | <0.001 |
| Hepatic dysfunction | 2.36 (1.25 - 4.45) | 0.008 |
| Strategy (Restrictive) | 1.39 (1.03 - 1.87) | 0.030 |

Abbreviations: CI = confidence interval; SAPS 3 = Simplified Acute Physiology Score 3; SOFA = Sepsis-related Organ Failure Assessment score

Few **protocol deviations** were noted: 3% of patients in the liberal group were not given RBC transfusion on the same day when the hemoglobin threshold was reached, while 5% of patients in the restrictive group received RBC transfusion for refractory shock when the hemoglobin concentration was above the threshold.