Predictors of dobutamine and RBC administration among patients treated with early goal directed therapy in the emergency department

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Study Objectives

To examine the frequency and predictors of dobutamine administration and/or red blood cell (**RBC**) transfusion among septic patients meeting criteria for "advanced" central venous oxygen saturation (**ScvO2**)-guided therapies while undergoing early goal directed therapy (**EGDT**) in the emergency department (**ED**).

Background

EGDT has been shown to reduce mortality as compared to standardized resuscitation by targeting a goal ScvO2 of 70% or greater, in addition to standardized central venous pressure (**CVP**) and mean arterial pressure (**MAP**) targets. However, in contemporary studies and clinical practice, few patients meet indications for "advanced" ScvO2-guided therapies as recommended by the original EGDT protocol, namely the administration of dobutamine and/or transfusion of RBCs if ScvO2 remains less than 70% once CVP and MAP targets have been reached. Additionally, it is unclear how often patients who qualify for these interventions actually receive them.

Methods

Retrospective review of a prospectively collected database of patients with severe sepsis or septic shock treated with EGDT in one of 21 Northern California Kaiser Permanente EDs between March 2010 and September 2012.

Patients who simultaneously achieved both a CVP of 8 mmHg or greater and a MAP of 65 mmHg or greater within the first six hours of EGDT eligibility were screened for inclusion.

Patients were included if they had a ScvO2 measurement of less than 70% within 15 minutes of meeting both CVP and MAP goals, along with either:

1) ScvO2 of less than 70% at the end of the six hour protocol

2) Administration of dobutamine or RBC transfusion

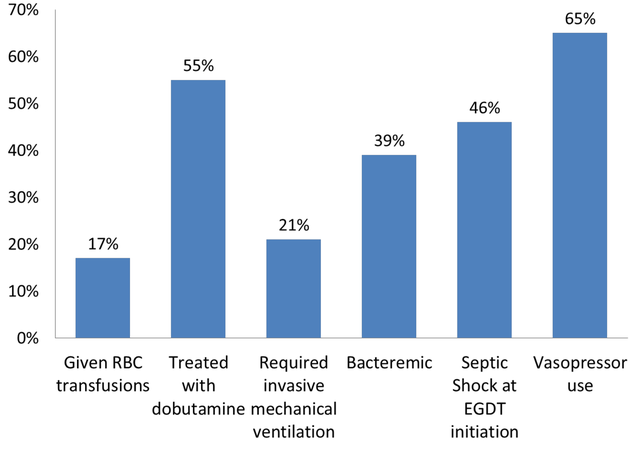

Figure 1: Categorical covariates (n=440)

Variable (unit)	Median	IQR
Age (years)	74	63-83
Initial venous lactate (mmol/L)	4.4	3.0-6.3
Initial ScvO2 (%)	62	54-68
Hemoglobin (g/dL)	11.5	9.2-13.4
Highest CVP (mmHg)	16	13-21
Percent lactate clearance (%)	45	22-63
SAPS 3 (score)	41	35.7-42.9

Table 1: Continuous covariates (n = 440)

Statistical Methods

Categorical variables were compared using chi-square tests or Fisher's exact test. Multiple logistic regression was used to analyze independent predictors of dobutamine and RBC transfusion using the following variables obtained during the first six hours of EGDT eligibility:

Age, initial ScvO2, highest CVP value, initial venous lactate, percent lactate clearance, mechanical ventilation, vasopressor administration, hemoglobin of less than 10 g/dL and an electronic Simplified Acute Physiology Score III (**SAPS 3**) – a modified version of the original SAPS 3 mortality prediction scoring system, derived and validated among Northern California Kaiser Permanente patients.

The goodness-of-fit for regression models was assessed using the Hosmer-Lemeshow test.

Results

2894 patients underwent EGDT during the 31-month study period. 440 (15%) patients met study inclusion criteria. A total of 202/440 (46%) of patients had septic shock at EGDT initiation and 171/440 (39%) had bacteremia. 94/440 (21%) required invasive mechanical ventilation and 278/440 (65%) were given vasopressors in the ED.

Independent predictors of dobutamine administration were:

- **Vasopressor use (AOR 2.9, 95% CI 1.8-4.7)**
- **Hemoglobin of 10 g/dL or greater (AOR 4.8, 95% CI 3.0-7.7)**

Among the 285 patients with hemoglobin of 10 g/dL or greater, 189 (66%) were treated with dobutamine. Only vasopressor administration (AOR 3.5, 95% CI 2.0-6.2) independently predicted dobutamine administration.

Among the 155 patients with a hemoglobin less than 10 g/dL, 74 (48%) were transfused with red blood cells.

Independent predictors of red cell transfusion were:

- **Hemoglobin less than 7 g/dL (AOR 5.5, 95% CI 1.5-19.9)**
- **Dobutamine administration (AOR 0.2, 95% CI 0.1-0.4)**

Conclusions

In this retrospective cohort, patients undergoing EGDT with ScvO2 values less than 70% despite meeting CVP and MAP goals were not consistently treated with dobutamine and/or red cell transfusion. These findings suggest specific barriers to therapy implementation. Of note, lactate clearance, which has been proposed as a surrogate resuscitation endpoint for ScvO2, was not identified as an independent treatment predictor.

Patients were significantly more likely to be treated with dobutamine if they required vasopressor therapy or if they lacked an indication for red blood cell transfusion (i.e. had a hemoglobin of 10 g/dL or greater). The observed association with vasopressor use may indicate greater perceived severity of illness and clinical concern for suboptimal ScvO2 values by treating clinicians.

Among patients eligible for red cell transfusion with a hemoglobin less than 10 g/dL, patients were significantly more likely to be transfused if the hemoglobin was less than 7 g/dL. This likely represents controversy among practicing clinicians regarding the appropriate hemoglobin transfusion threshold in sepsis (10 g/dl vs. 7 g/dl) owing to conflicting data regarding the efficacy of stored blood as means of augmenting tissue oxygen delivery. The negative correlation between dobutamine use and RBC transfusion among patients eligible for both therapies may represent clinician hesitancy to institute multiple advanced ScvO2-guided therapies simultaneously.

These findings potentially represent some ambivalence among clinicians towards specific elements of the published algorithmic EGDT treatment guidelines, namely those addressing subnormal ScvO2 values. Randomized studies addressing the utility of specific therapies would help alleviate or justify this ambivalence.

About CREST Network

The Clinical Research in Emergency Services & Treatments (CREST) Network is a multi-center, collaborative network at Kaiser Permanente that encourages, enables and executes research in Emergency Medicine. **www.kpcrest.net**