Maximizing oxygen delivery in critically ill patients: a methodologic appraisal of the evidence

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Authors' objectives
To systematically review the effect of interventions designed to achieve supraphysiological values of cardiac index, oxygen delivery and oxygen consumption in critically-ill patients.

Searching
MEDLINE was searched from 1980 to 1994 using the following keywords: 'oxygen consumption', 'hemodynamics' or 'dobutamine'; exploded terms 'intensive care', 'intensive care units' or 'critical care'. Additional material was obtained by examining reference lists of all available articles, primary studies, and the authors' files, and by contacting the authors of primary studies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included.

Specific interventions included in the review
Fluid and pharmacological therapy administered to maximise cardiac index, oxygen delivery and oxygen consumption. The pharmacological therapies included were inotropes and dopexamine.

Participants included in the review
Adults in intensive care units (ICUs) were included.

Outcomes assessed in the review
Mortality rate reported at 28 or 30 days after discharge from the ICU or hospital, or at 14 days, and also the length of stay in the ICU.

How were decisions on the relevance of primary studies made?
All the primary studies were retrieved and independently reviewed in terms of the inclusion criteria: study design, participants, intervention and outcomes.

Assessment of study quality
The methodological quality of the primary studies was evaluated using a scoring system, which assessed randomisation, blinding, analysis, patient selection, comparability of groups at baseline, extent of follow-up, treatment protocol, cointerventions and crossovers. Two assessors independently assigned points to the studies according to how well they met each of the validity criteria.

Data extraction
The data were extracted in duplicate, and any disagreements were resolved by consensus. The primary investigators were contacted to provide any missing information.

Methods of synthesis
How were the studies combined?
The studies were combined using a random-effects model to estimate the common relative risk (RR) of mortality. To estimate the effect that the intervention had on length of stay, a common effect size was estimated across all studies.
How were differences between studies investigated?
A post-hoc subgroup analysis was undertaken to compare the common RRs for studies in which the therapy was initiated pre-operatively, with the common RR of the remaining studies.

Results of the review
Seven RCTs (1,016 patients) were included.

The difference in mortality rate of the treated patients was not significantly different from the controls: RR 0.86 (95% confidence interval, CI: 0.62, 1.20). The average length of ICU stay was slightly shorter for the experimental group than the control group: mean difference -2.5 days (95% CI: -4.8, -0.1). Significant heterogeneity was found.

In the subgroup analysis, there was a significant difference in the combined RRs of the 2 RCTs in which the supraphysiological therapy was initiated pre-operatively, and the remaining RCTs: combined RRs were 0.2 (95% CI: 0.07, 0.55) and 0.98 (95%CI: 0.79, 1.22), respectively.

Authors' conclusions
Interventions designed to achieve supraphysiological goals of cardiac index, oxygen delivery and oxygen consumption did not significantly reduce mortality rates in all critically-ill patients. However, there may be a benefit in those patients in which the therapy is initiated pre-operatively. Methodological limitations weaken the inferences that can be drawn from these studies, and preclude any evidence-based clinical recommendations.

CRD commentary
A fairly limited search was carried out; it is unclear whether there were any restrictions on publication language. The authors emphasise the poor methodological quality of the included studies.

Implications of the review for practice and research
Future research should focus on identifying subgroups of patients who do not self-generate supranormal cardiac index, oxygen delivery or oxygen consumption, and to evaluate whether pharmacological treatment can alter their prognosis. The exact dose and timing of the pharmacological agents needs to be clarified. The dobutamine test may deserve further validation in identifying those patients who lack the cardiorespiratory reserve necessary to meet increased tissue oxygen demands. Future studies in the field should be large, rigorous, employ true randomisation, minimise bias due to cointervention, and analyse on an intention to treat basis. Pre-operative ICU admission of high-risk surgical patients for treatment with dopexamine or dobutamine warrants investigation, ideally with a formal economic evaluation as part of the trial.

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