Systematic Review and Meta-Analysis of Effects of Transfusion on Hemodynamic and Oxygenation Variables*

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Objectives: RBC transfusions can increase oxygen availability to the tissues, but studies have provided conflicting results. The objectives of this study were, therefore, to evaluate, using systematic review and meta-analysis, the effects of transfusion on hemodynamic/oxygenation variables in patients without acute bleeding.

Data Sources: PubMed, Scopus, Cochrane Database of Systematic Reviews, and Embase from inception until June 30, 2019.

Study Selection: All articles that reported values of prespecified hemodynamic or oxygenation variables before and after RBC transfusion.

Data Extraction: Publication year, number of patients, number of transfusions and the type of population studied, hemodynamic and oxygenation data (heart rate, cardiac index, mixed venous oxygen saturation or central venous oxygen saturation, oxygen delivery index, oxygen consumption index, oxygen extraction ratio, arteriovenous oxygen difference and arterial blood lactate) before and after transfusion. We performed a meta-analysis for each variable for which there were sufficient data to estimate mean differences. We also performed subgroup analyses comparing septic with nonseptic patients.

Data Synthesis: We retrieved 6,420 studies; 33 met the inclusion criteria, 14 of which were in patients with sepsis. In the meta-analysis, the estimated mean differences and 95% CIs comparing the periods before and after transfusion were −0.0 L/min/m^2 (−0.1 to 0.1 L/min/m^2) ($p = 0.86$) for cardiac index; −1.8 beats/min (−3.7 to 0.1 beats/min) ($p = 0.06$) for heart rate; 96.8 mL/min/m^2 (71.1–122.5 mL/min/m^2) ($p < 0.01$) for oxygen delivery index; 2.9% (2.2–3.5%) ($p < 0.01$) for mixed venous oxygen saturation or central venous oxygen saturation; −3.7% (−4.4% to −3.0%) ($p < 0.01$) for oxygen extraction ratio; and 4.9 mL/min/m^2 (0.9–9.0 mL/min/m^2) ($p = 0.02$) for oxygen consumption index. The estimated mean difference for oxygen consumption index in the patients with sepsis was 8.4 mL/min/m^2 (2.3–14.5 mL/min/m^2; $p = 0.01$).

Conclusions: Transfusion was not associated with a decrease in mean cardiac output or mean heart rate. The increase in mean oxygen delivery following transfusion was associated with an increase in mean oxygen consumption after transfusion, especially in patients with sepsis. (*Crit Care Med* 2020; 48:241–248)

Key Words: blood lactate; cardiac output; hematocrit; intravenous fluids; oxygen delivery; oxygen consumption; sepsis

Almost 70% of acutely ill patients have anemia, which can have multiple causes (1, 2). Compensatory mechanisms to maintain oxygen delivery (Do_2) to the tissues during anemia in normovolemic conditions include an increase in cardiac index (CI) due to increased sympathetic tone, resulting in increased heart rate (HR) and contractility, as well as a reduction in blood viscosity associated with reduced vascular resistance (3, 4). These compensatory processes to maintain stable cellular metabolism are reflected by an increase in oxygen extraction ratio

*See also p. 271.

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Dr. Cavalcante dos Santos helped design the study, performed the literature review, extracted the data, analyzed data, drafted the article, and read and approved the final version. Dr. Orbegozo helped design the study, performed the literature review, extracted the data, revised the article for intellectual content, and read and approved the final version. Drs. Mongkolpun, Galfo, Nan, and Bogossian performed the literature review, extracted the data, revised the article for intellectual content, and read and approved the final version. Dr. Taccone revised the article for intellectual content, read and approved the final version. Dr. Vallet provided data, revised the article for intellectual content, and read and approved the final version. Dr. Creteur revised the article for intellectual content, read and approved the final version. Dr. Vincent helped design the study, helped interpret the data, revised the article for intellectual content, and read and approved the final version.

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(O_2ER) with a reduction in mixed venous oxygen saturation (Svo_2) or central venous oxygen saturation ($Scvo_2$) (3, 5). It is only in severe cases of anemia or when CI is very compromised that Do_2 may fall below a critical level, resulting in a shift of cellular metabolism to anaerobic pathways with an increase in blood lactate levels (5).

The rationale for using RBC transfusions to increase hemoglobin concentration is to relieve cardiac work and, in severe cases, to correct the mismatch between Do_2 and oxygen consumption (Vo_2) (4, 6–8). However, the effects of transfusion on CI may differ depending on the underlying cardiac preload and function; for example, patients with sepsis, who may already have an elevated CI, may have a different response to that of patients without sepsis (9). Surprisingly, the hemodynamic effects of transfusion have not been well studied, and the reported effects on oxygen-derived variables from the limited data available are inconsistent (10–13). The divergent results and the small size of many of the studies make it an ideal area for systematic review and meta-analysis.

We therefore conducted a systematic review to evaluate the effects of RBC transfusion on hemodynamic and oxygenation variables in patients without acute bleeding.

MATERIALS AND METHODS

We searched PubMed, Scopus, the Cochrane Database of Systematic Reviews and Embase from inception until June 30, 2019, to identify studies that reported hemodynamic and oxygenation variables before and after RBC transfusion. The search string is shown in the **Online Supplement** (Supplemental Digital Content 1, http://links.lww.com/CCM/F62). References of included papers were reviewed to identify further studies. In conducting our study, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement (14).

Eligibility Criteria

We considered all published clinical studies that reported the effects of RBC transfusion in patients without acute bleeding, and in which data before and after transfusion were reported for at least one of the following variables: CI or CO, Svo_2 or $Scvo_2$, oxygen delivery (Do_2) index (Do_2I), oxygen consumption (Vo_2) index (Vo_2I), and O_2ER. We included prospective and retrospective clinical trials and observational and interventional studies. We excluded animal studies, studies during pregnancy, those in which the CI was artificially maintained before and after transfusion, as during cardiopulmonary bypass, and those with populations in which the mean patient age was less than 18 years. There was no restriction based on language.

Study Selection

Titles and abstracts of the retrieved references were screened independently by three authors (E.C.d.S., W.M., E.G.B.) to assess eligibility for full-text review. The selected full texts were then screened independently by the same reviewers to ensure they met inclusion criteria. Any disagreements were resolved by a fourth author (J.L.V.).

Data Abstraction and Validity Assessment

From each retrieved article, six authors (E.C.d.S., D.O., W.M., V.G., W.N., E.G.B.) extracted mean or median values before and after transfusion of the following hemodynamic and oxygen variables, whenever available: hemoglobin, HR, CI, pulmonary artery occlusion pressure (PAOP), Svo_2 or $Scvo_2$, Do_2I, Vo_2I, O_2ER, arteriovenous oxygen difference (AVo_2) and arterial blood lactate. When variables were measured at different time intervals, we extracted the values for the timepoints closest to the transfusion. For descriptive purposes, we also extracted the following variables: author, publication year, number of patients, number of transfusion events, transfusion duration, number of RBC units transfused, and the type of population studied (sepsis, acute respiratory failure, postsurgery, and other). When possible, we contacted the authors of the original studies to retrieve missing data. Two authors (E.C.d.S. and E.G.B.) independently assessed the quality of the studies using the Newcastle-Ottawa Scale (comparability questions were not considered because we were not comparing groups, but assessing before-after intervention effects) (15).

Systematic Review and Meta-Analysis

For the systematic review, a detailed description of all included studies is given, reporting whether the means or medians of the prespecified hemodynamic and oxygen variables changed or not after transfusion, according to study population (sepsis, acute respiratory failure, postsurgery, and others).

We performed meta-analyses of mean hemodynamic or oxygenation variables, including only the studies that provided sufficient data to enable estimation of the mean difference and 95% CIs for that variable when comparing the periods before and after RBC transfusion. When the values reported were medians, we used the data to calculate the means. If a study presented data only in different subgroups of patients, each study group was considered separately for meta-analysis purposes. Anticipating a high degree of heterogeneity inherent to the differences between experimental protocols, we used a DerSimonian and Laird random-effects model. Subgroup analyses were performed for septic versus nonseptic patients (studies with mixed groups of patients were excluded from these analyses). We assessed heterogeneity across studies using Cochran's Q test and the I^2 statistic (16).

All analyses were conducted using Comprehensive Meta-Analysis V3 software (Biostat, Englewood, NJ). Statistical significance was considered at an alpha level of 0.05.

RESULTS

From a total of 6,420 studies, 63 were selected for full-text analysis and four added from references of eligible studies. Thirty-four studies were excluded after full-text review (**Fig. 1**). The remaining 33 studies were generally of moderate-to-good quality (**Table S1**, Supplemental Digital Content 1, http://links.lww.com/CCM/F62).

Systematic Review

Five studies reported data separately for different subgroups of patients: two studies in groups with high or normal blood lactate levels (10, 11), one study according to a restrictive or a liberal strategy (transfusion if hemoglobin < 7 or < 9 g/dL) (17), one study according to normal or low gastric intramucosal pH (pHi) (18) and one according to RBC storage time (≤ 19 d or >

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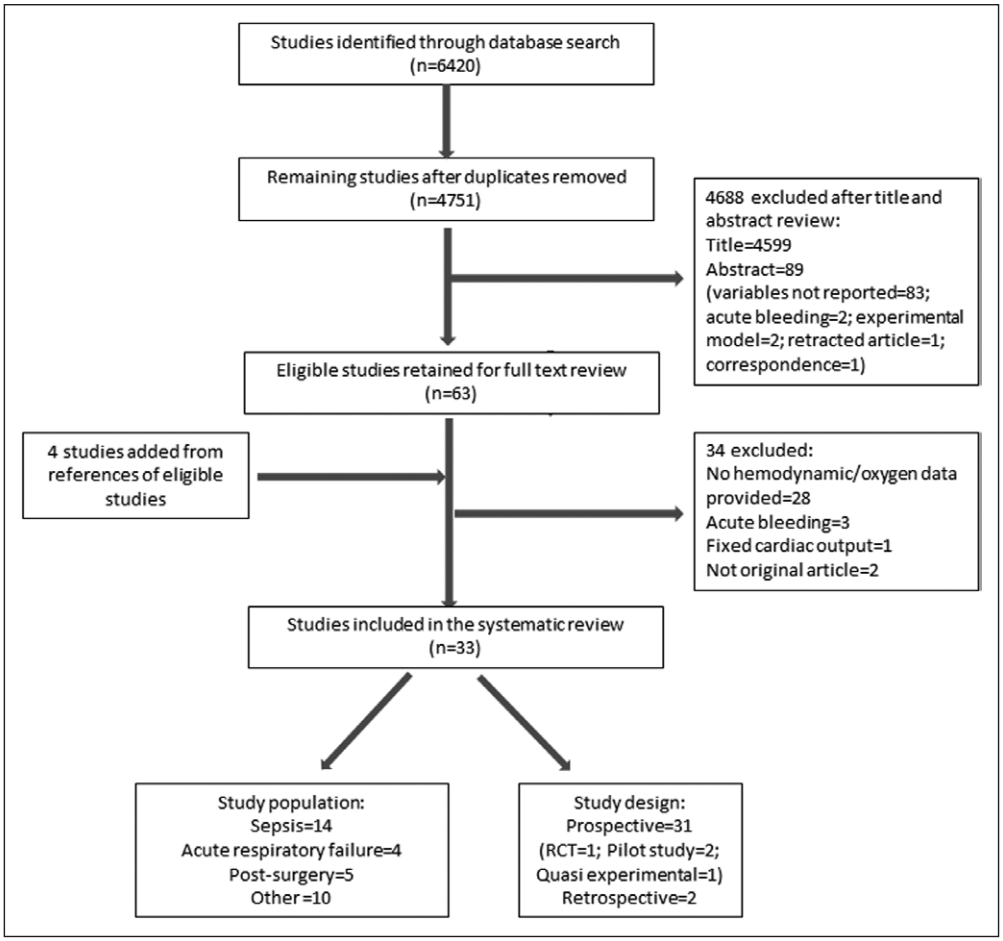

Figure 1. Flow chart showing selection of articles. RCT = randomized controlled trial.

20 d) (19). Therefore, we included 38 groups of patients in the systematic review (**Table 1**; and **Table S2**, Supplemental Digital Content 1, http://links.lww.com/CCM/F62).

Sepsis. Fourteen of the studies (17 study groups, 355 patients) (10, 12, 17, 18, 20–29) were in patients with sepsis (Table 1; and Table S2, Supplemental Digital Content 1, http://links.lww.com/CCM/F62). CI was reported in nine of these studies (11 study groups, 169 patients) and mean or median values did not change significantly after transfusion in any of them. Mean or median hemoglobin increased significantly in the 12 studies (15 study groups, 275 patients) in which it was reported and mean or median Do_2I increased consistently in the eight studies (10 study groups, 150 patients) where it was reported.

Svo_2 or $Scvo_2$ was reported in 10 studies (12 study groups, 265 patients): there was a significant increase in mean or median values after transfusion in three (12, 20, 26) and no significant change in five (21–25). One study reported a significant increase in patients managed using a restrictive transfusion strategy, but no significant change in patients managed using a liberal strategy (17); another reported a significant increase in Svo_2 in patients with low, but not with normal, pHi (18).

O_2ER was reported in six studies (seven study groups, 119 patients): there was a significant decrease in mean or median values after transfusion in four (12, 20, 27, 28), no change in one (23) and one reported a significant decrease in patients with normal blood lactate levels, but not in patients with elevated lactate levels (10).

Vo_2I was reported in eight studies (10 study groups, 150 patients): there was a significant increase in mean or median values after transfusion in one (21), no significant change in six (12, 18, 20, 23, 27, 29) and in one study there was a significant increase in patients with elevated blood lactate levels before transfusion, but not in those with normal lactate levels (10).

Acute Respiratory Failure. Four of the studies (five study groups, 61 patients) were in patients with acute respiratory failure (Table S2, Supplemental Digital Content 1, http://links.lww.com/CCM/F62). CI was provided in three studies (44 patients) and mean or median values did not change after transfusion (11, 30, 31). Do_2I was provided in three studies (46 patients) and mean or median values increased significantly in all (11, 31, 32). Svo_2 was provided in three studies (46 patients): there was a significant increase in mean or median values in two (11, 32) and no significant change in the other one (31).

O_2ER was reported in two studies (29 patients): there was no significant change in mean values in one (31), and one reported a significant decrease in median values in patients with normal lactate levels, but not in those with elevated lactate levels (11).

Vo_2I was reported in all four studies (61 patients); mean values did not change in two (30, 32), increased in one (32), and one study reported a significant increase in patients with elevated lactate levels, but not in patients with normal lactate levels (11).

Postsurgery Populations. Five studies (251 patients) were conducted in postsurgery patients (Table S2, Supplemental Digital Content 1, http://links.lww.com/CCM/F62).

One study was conducted in patients postcardiac surgery (67 patients) (33). Mean CI did not change significantly after transfusion. Mean Do_2I and Svo_2 or $Scvo_2$ increased, mean O_2ER decreased, and mean Vo_2I did not change.

Four of the studies (184 patients) were in mixed populations of surgical patients (34–37). CI was reported in two of the studies (78 patients); mean values increased significantly in one after transfusion (34) but were unchanged in the other (35). Do_2I was reported in two studies (78 patients) and mean values increased in both (34, 35). Svo_2 or $Scvo_2$ was provided in three

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TABLE 1. Summary of Effects of Transfusion on Hemodynamic and Oxygenation Variables in the Systematic Review

Study Population (*n* = Total No. of Study Groups)	Variable (*n* = No. of Study Groups Reporting Variable)				
	Mean or Median Cardiac Index (L/min/m²)	Mean or Median Oxygen Delivery Index (mL/min/m²)	Mean or Median Mixed Venous Oxygen Saturation or Central Venous Oxygen Saturation (%)	Mean or Median Oxygen Extraction Ratio (%)	Mean or Median Oxygen Consumption Index (mL/min/m²)
Sepsis (*n* = 17)	↔ (*n* = 11)	↑ (*n* = 10)	↑ (*n* = 5)	↓ (*n* = 5)	↑ (*n* = 2)
	NR (*n* = 6)	NR (*n* = 7)	↔ (*n* = 7)	↔ (*n* = 2)	↔ (*n* = 8)
			NR (*n* = 5)	NR (*n* = 10)	NR (*n* = 7)
ARF (*n* = 5)	↔ (*n* = 4)	↑ (*n* = 4)	↑ (*n* = 3)	↓ (*n* = 1)	↑ (*n* = 2)
	NR (*n* = 1)	NR (*n* = 1)	↔ (*n* = 1)	↔ (*n* = 2)	↔ (*n* = 3)
			NR (*n* = 1)	NR (*n* = 2)	
Postsurgery (*n* = 5)					
Cardiac surgery (*n* = 1)	↔ (*n* = 1)	↑ (*n* = 1)	↑ (*n* = 1)	↓ (*n* = 1)	↔ (*n* = 1)
General surgery (*n* = 4)	↑ (*n* = 1)	↑ (*n* = 2)	↑ (*n* = 3)	↓ (*n* = 3)	↑ (*n* = 1)
	↔ (*n* = 1)	NR (*n* = 2)	NR (*n* = 1)	NR (*n* = 1)	↔ (*n* = 1)
	NR (*n* = 2)				NR (*n* = 2)
Other (*n* = 11)					
Trauma (*n* = 1)	↓ (*n* = 1)	↔ (*n* = 1)	NR	NR	↔ (*n* = 1)
Neurologic (*n* = 2)	NR (*n* = 2)	NR (*n* = 2)	↑ (*n* = 1)	NR	NR
			↔ (*n* = 1)		
Heterogeneous (*n* = 8)	↓ (*n* = 1)	↑ (*n* = 2)	↑ (*n* = 2)	↓ (*n* = 1)	↔ (*n* = 2)
	↔ (*n* = 3)	NR (*n* = 6)	↔ (*n* = 5)	↔ (*n* = 3)	NR (*n* = 6)
	NR (*n* = 4)		NR (*n* = 1)	NR (*n* = 4)	

(↔) = no statistically significant change before and after RBC transfusion, (↓) = a statistically significant decrease after RBC transfusion, (↑) = a statistically significant increase after RBC transfusion, ARF = acute respiratory failure, NR = not reported.

studies (135 patients) and mean or median values increased in all (35–37). O_2ER was provided in three studies (131 patients) and mean or median values decreased in all (34, 35, 37). Vo_2I was reported in two studies (78 patients): mean values were unchanged in one (35) and increased in the other (34).

Other Populations. In one study in trauma patients (eight patients), mean CI decreased after transfusion; there were no significant changes in mean Do_2I or Vo_2I (38). In two studies in neurologic patients (83 patients), mean $Scvo_2$ increased in one (39) and was unchanged in the other (40). Other variables were not reported.

Seven studies (eight study groups, 703 patients) included heterogeneous patient populations (Table S2, Supplemental Digital Content 1, http://links.lww.com/CCM/F62). CI was reported in four of these studies (97 patients): mean values decreased in one (41) and were unchanged in three (13, 42, 43). Do_2I was reported in two studies (44 patients) and mean or median values increased significantly in both (13, 43). Svo_2 or $Scvo_2$ was reported in six studies (652 patients): mean or median values were unchanged in four (41, 43–45), increased in one (13) and increased in another in patients after transfusion of "old," but not "fresher" blood (19). O_2ER was reported in four studies (121 patients): mean or median values were unchanged in three (42–44) and decreased in one (13). Vo_2I was provided in two studies (44 patients) and mean or median values were unchanged in both (13, 43).

Meta-Analyses

After contacting the authors of two studies, we were able to divide their cohorts into patients with and without sepsis (36, 43) and one study provided individual patient data so that we could separate septic from nonseptic patients (32). Therefore, a total of 41 study groups were included in the meta-analyses (**Tables S3** and **S4**, Supplemental Digital Content 1, http://links.lww.com/CCM/F62): 20 in patients with sepsis (10, 12, 17, 18, 20–29, 32, 36, 43), 10 in patients without sepsis (30–33, 36–40, 43), and 11 in mixed populations (11, 13, 19, 34, 35, 41, 42, 44, 45).

Hemoglobin. The mean hemoglobin increased by 1.6 g/dL after transfusion (39 study groups, 1,343 patients; 95% CI,

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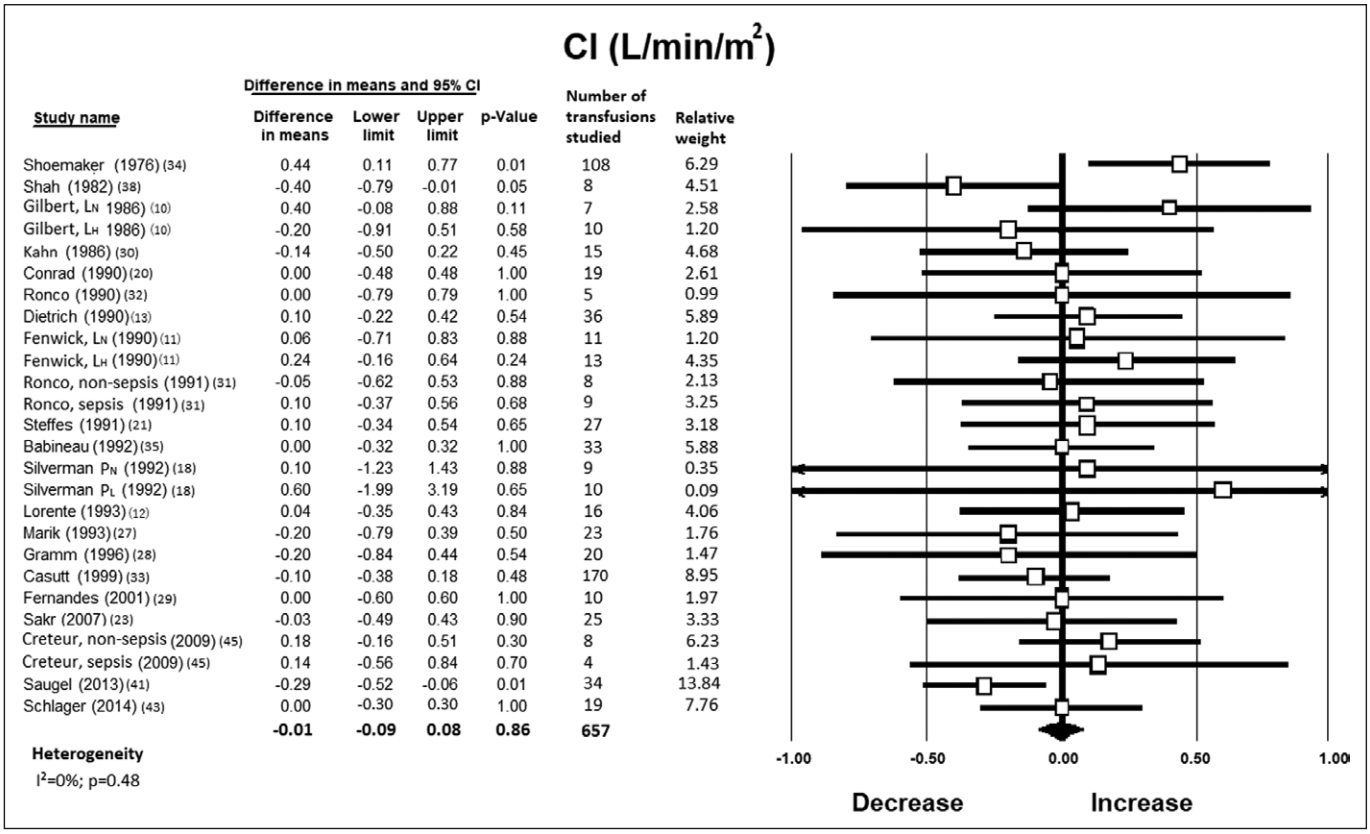

Figure 2. Forest plots for the meta-analysis of changes in mean cardiac index (CI) after RBC transfusion. L_H = subgroup high lactate, L_N = subgroup normal lactate, P_L = subgroup low intramucosal pH, P_N = subgroup normal intramucosal pH.

1.5–1.8, $p < 0.01$; Q = 573.5, degrees of freedom (*df* [Q]) = 38, $p < 0.01$, $I^2 = 93.4\%$; **Fig. S1**, Supplemental Digital Content 1, http://links.lww.com/CCM/F62). Mean hemoglobin increased in patients with and without sepsis (**Table S5**, Supplemental Digital Content 1, http://links.lww.com/CCM/F62).

Hemodynamic Variables. The mean CI did not change after transfusion (26 study groups, 480 patients; mean difference –0.0, 95% CI, –0.1 to 0.1 L/min/m_2, $p = 0.86$; Q = 25.4, *df* (Q) = 25, $p = 0.48$, $I^2 = 0.0\%$; **Fig. 2**). Likewise, mean HR was not affected (24 study groups, 560 patients; mean difference –1.79; 95% CI, –3.7 to 0.1 beats/min, $p = 0.06$; Q = 68.9, *df* (Q) = 23, $p < 0.01$, $I^2 = 66.6\%$; **Fig. S2**, Supplemental Digital Content 1, http://links.lww.com/CCM/F62). These patterns were similar in patients with and without sepsis (Table S5, Supplemental Digital Content 1, http://links.lww.com/CCM/F62).

The mean PAOP increased slightly but consistently by 1.4 mm Hg after transfusion (20 study groups, 340 patients; 95% CI, 0.7–2.1, $p < 0.01$; Q = 52.9, *df* (Q) = 19, $p < 0.01$, $I^2 = 64.1\%$; **Fig. S3**, Supplemental Digital Content 1, http://links.lww.com/CCM/F62). These patterns were similar in patients with and without sepsis (Table S5, Supplemental Digital Content 1, http://links.lww.com/CCM/F62).

Oxygen-Derived Variables and Blood Lactate Levels. After transfusion, mean Do_2I increased by 96.8 mL/min/m^2 (22 study groups, 393 patients; 95% CI, 71.1–122.5, $p < 0.01$; Q = 164.4, *df* (Q) = 21, $p < 0.01$, $I^2 = 87.2\%$; **Fig. S4**, Supplemental Digital Content 1, http://links.lww.com/CCM/F62), mean Svo_2 or $Scvo_2$ increased by 2.9% (32 study groups, 1,228 patients; 95% CI, 2.2–3.5, $p < 0.01$; Q = 84.9, *df* (Q) = 31, $p < 0.01$, $I^2 = 63.5\%$; **Fig. 3**), and mean O_2ER decreased by 3.7% (21 study groups, 484 patients; 95% CI, –4.4 to –3.0, $p < 0.01$; Q = 63.9, *df* (Q) = 20, $p < 0.01$, $I^2 = 68.7\%$; **Fig. S5**, Supplemental Digital Content 1, http://links.lww.com/CCM/F62). These patterns were similar in patients with and without sepsis (Table S5, Supplemental Digital Content 1, http://links.lww.com/CCM/F62).

Mean AVo_2 increased by 0.1 mL/dL after transfusion (11 study groups, 200 patients; 95% CI, 0.0–0.2, $p = 0.03$; Q = 14.6, *df* (Q) = 10, $p = 0.15$, $I^2 = 31.7\%$; **Fig. S6**, Supplemental Digital Content 1, http://links.lww.com/CCM/F62). Mean Vo_2I increased by 4.9 mL/min/m^2 (23 study groups, 408 patients; 95% CI, 0.9–9.0, $p = 0.02$; Q = 82.2, *df* (Q) = 22, $p < 0.01$, $I^2 = 73.3\%$; **Fig. 4**). In the analysis including just studies conducted in patients with and without sepsis, mean AVo_2 increased in non-septic but not in septic patients, and mean Vo_2I increased only in the septic patients (Table S5, Supplemental Digital Content 1, http://links.lww.com/CCM/F62).

Mean blood lactate levels decreased by 0.02 mmol/L after transfusion (22 study groups, 854 patients; 95% CI, –0.04 to 0.00, $p = 0.02$; Q = 11.7, *df* (Q) = 21, $p = 0.95$, $I^2 = 0\%$; **Fig. S7*a***, Supplemental Digital Content 1, http://links.lww.com/CCM/F62). However, this was largely influenced by one small study with a large relative weight; when this study was removed, the difference was no longer significant (–0.05; 95% CI, –0.12 to 0.02; $p = 0.2$; **Fig. S7*b***, Supplemental Digital Content 1, http://links.lww.com/CCM/F62).

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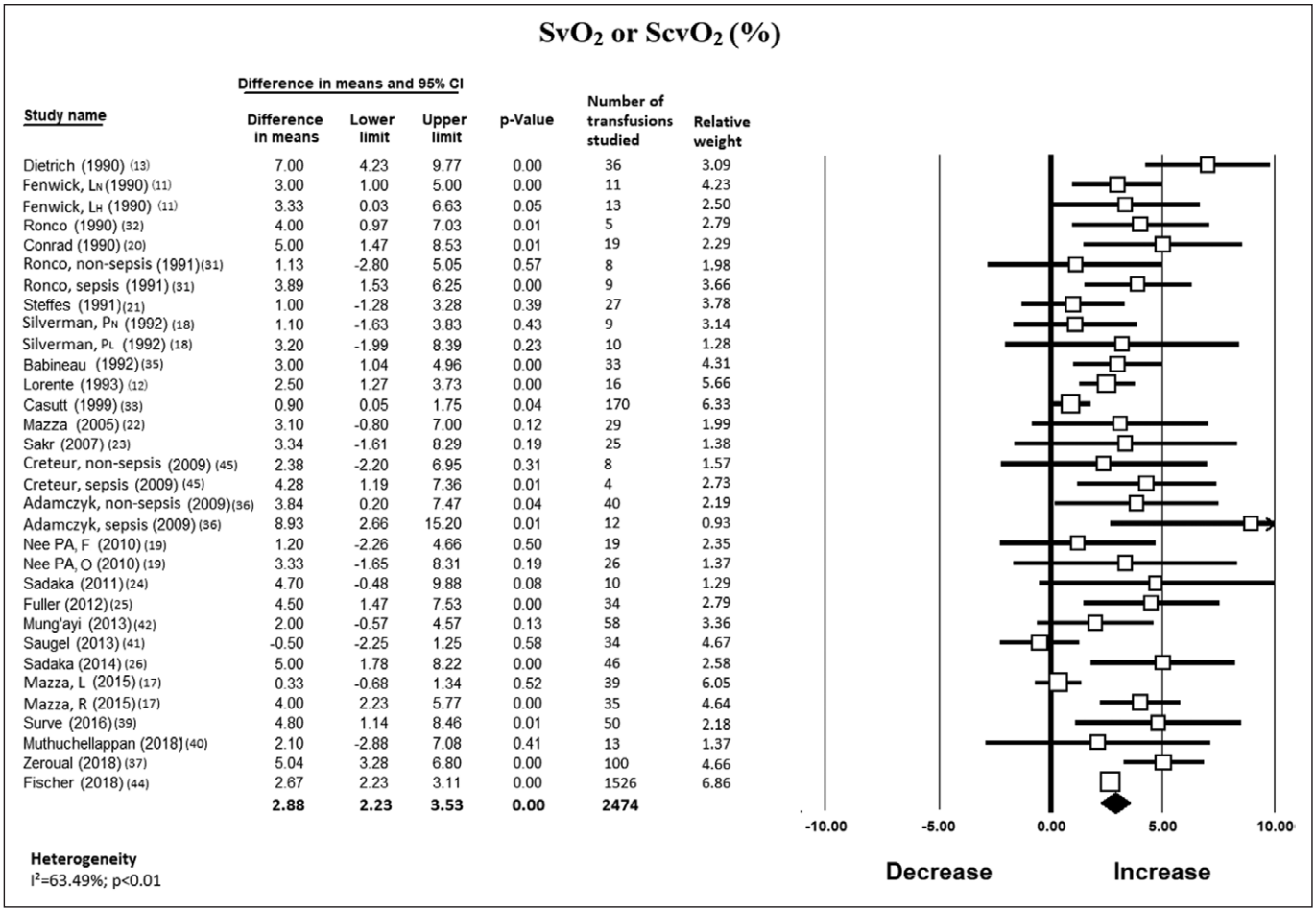

Figure 3. Forest plots for the meta-analysis of changes in mean mixed venous oxygen saturation (Svo_2) or central venous oxygen saturation ($Scvo_2$) after RBC transfusion. F = subgroup fresh RBCs less than or equal to 19 d, L = subgroup liberal strategy, L_H = subgroup high lactate, L_N = subgroup normal lactate, O = subgroup old RBCs greater than or equal to 20 d, P_L = subgroup low intramucosal pH, P_N = subgroup normal intramucosal pH, R = subgroup restrictive strategy.

DISCUSSION

Our main findings are that RBC transfusions in studies of patients without acute bleeding were not consistently associated with a decrease in mean cardiac output or mean HR. The increase in mean Do_2 was associated with an increase in mean Vo_2I, especially in patients with sepsis.

The typical host response associated with normovolemic anemia is an increase in sympathetic tone resulting in increased cardiac output (3, 4, 46). One would anticipate that RBC transfusion would have the opposite effect: the increase in whole blood viscosity combined with increased afterload as well as a reduction in sympathetic tone would result in a decrease in cardiac output and HR (3, 4). In hyperdynamic septic patients, Gramm et al (28) reported that CI did not decrease after RBC transfusion despite a reduction in HR, suggesting an increase in stroke volume. On the other hand, in a prospective study in a heterogeneous ICU population, Saugel et al (41) reported a decrease in CI associated with a decrease in HR, and no change in stroke volume. In our meta-analysis, there was no significant difference in the mean cardiac output or mean HR before and after transfusion. It is possible that a decrease in cardiac stimulation due to reduced adrenergic activity may be compensated by an increase in venous return due to a blood volume effect at least in some patients.

The effects of RBC transfusion on Vo_2I are controversial. Our meta-analysis revealed that RBC transfusions were associated with a significant increase in mean Do_2I and Vo_2I. In the absence of a change in the mean cardiac output or HR in these relatively stable patients, the increase in the mean Do_2I was likely due to an increase in arterial oxygen content. In septic patients, Steffes et al (21) reported an increase in Vo_2I associated with the increase in Do_2I, whereas Gramm et al (28) reported a stable Vo_2 as O_2ER decreased. In our meta-analysis, the increase in mean Vo_2I was observed primarily in patients with sepsis suggesting a possible greater effect of transfusion on tissue oxygenation in these patients. However, the increase in the mean Vo_2 does not necessarily reflect an increase in local tissue oxygenation in all individual patients.

Of note, we did not evaluate effects on microcirculatory variables, but previous studies have not consistently shown an improvement in the microcirculation after RBC transfusion

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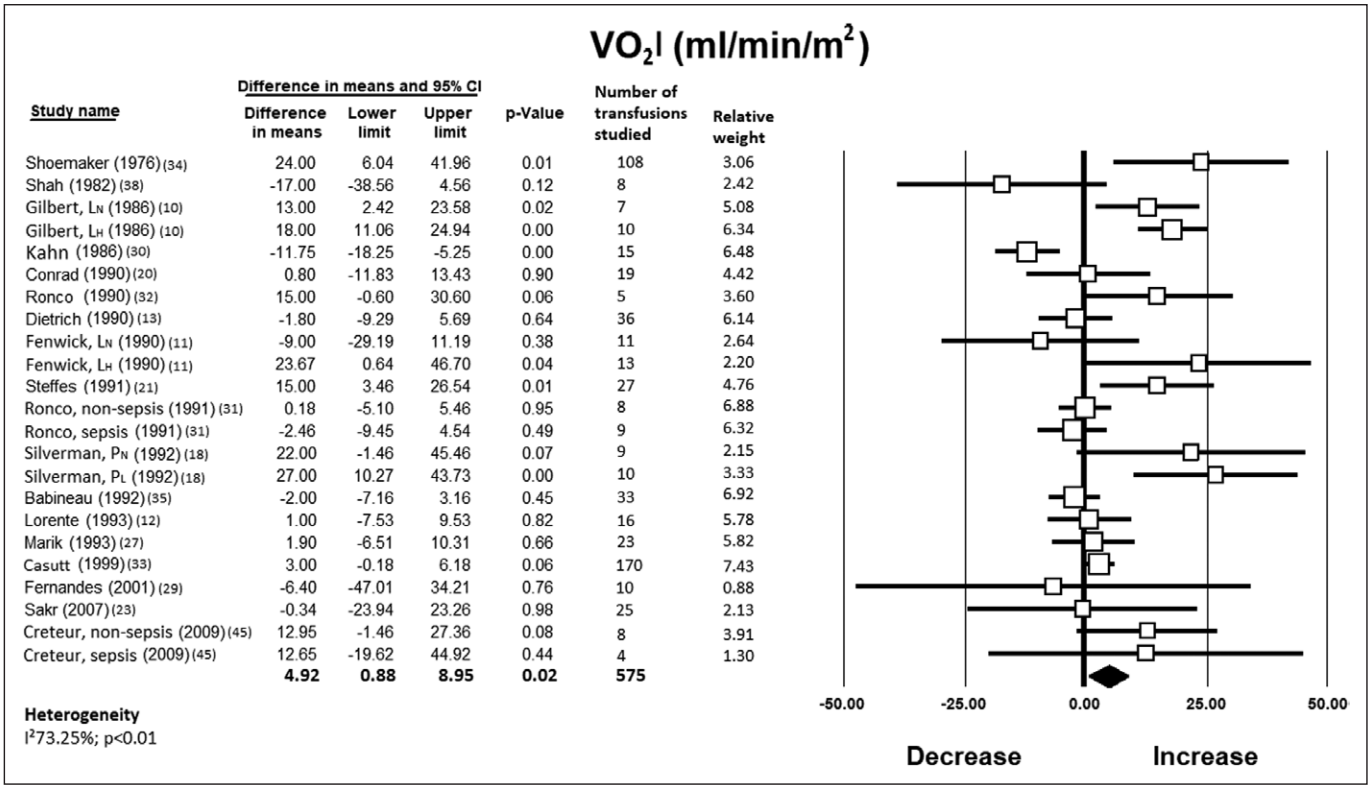

Figure 4. Forest plots for the meta-analysis of changes in mean oxygen consumption index (Vo_2I) after RBC transfusion. L_H = subgroup high lactate, L_N = subgroup normal lactate, P_L = subgroup low intramucosal pH, P_N = subgroup normal intramucosal pH.

(23, 24, 43). Thus, the increase in Vo_2I may reflect improved cellular metabolism rather than oxygenation, although this remains speculative. It is possible that the septic patients may have represented a more unstable population; indeed, some had elevated lactate levels before transfusion, suggesting a greater imbalance between Vo_2I and Do_2I (11). Lactate levels may be expected to decrease as Vo_2I increases, but the changes will be relatively slow (47). Mean blood lactate levels decreased after transfusion in the studies that reported this variable, albeit by a small degree; unfortunately, blood lactate was only reported in a few studies, preventing more detailed analysis. Furthermore, without control groups, it is difficult to separate the effects of transfusions from those of a spontaneous lactate decline over time as a result of global improvement.

Our review has several limitations. First, studies were generally small and observational, with most conducted in single centers. Second, the heterogeneity of studies was large in terms of different populations and study aims, numbers of RBC units transfused, initial hemoglobin concentrations, storage age of transfused blood, use or not of leukoreduced RBCs, the duration and volume of transfusion and the timing of measurements. Third, although most studies specified that included patients did not receive other fluids and there were no changes in ventilator variables, temperature, sedation, and analgesia, vasoactive or inotropic drugs immediately before, during and immediately after transfusion, we cannot ensure this was the case for all patients. As all results are based on mean values across study groups, we therefore cannot exclude the possibility that some patients may be outliers. Fourth, there were insufficient measurements made later after blood transfusion to be able to determine the longer-term effects on Do_2 and Vo_2. We also have no follow-up data so did not consider the effects of transfusion or the benefits of the increase in Vo_2I on outcomes, but this was not the aim of the study.

CONCLUSIONS

Our results highlight some interesting effects of RBC transfusion on mean hemodynamic and oxygenation variables in groups of patients without acute bleeding. First, mean cardiac output and mean HR did not change significantly after transfusion. Second, despite a small but consistent increase in mean Svo_2 or $Scvo_2$, mean Vo_2I increased; this finding was present notably in patients with sepsis, raising the possibility that transfusion may help to reverse the alterations in cellular oxygenation in some patients with sepsis. There is a need for further, larger prospective studies to determine the possible impact of these changes on cellular oxygenation and clinical outcomes and how such information could be used to individualize transfusion decisions.

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