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REVIEW

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What type of monitoring has been shown to improve outcomes in acutely ill patients?

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Abstract *Objective:* Lack of evidence that some monitoring systems can improve outcomes has raised doubts about their use in the intensive care unit (ICU). The objective of this study was to determine which monitoring techniques have been shown to improve outcomes in ICU patients. *Design:* Comprehensive literature review. *Methods:* We conducted a highly sensitive search, up to June 2006, in the Cochrane Central Register of Controlled Trials (CENTRAL) and MedLine, for prospective, randomized controlled trials (RCTs) conducted in adult patients in the ICU and the operating room (major surgical procedures) and focusing on the impact of monitoring on outcome. *Measurements and results:* Of 4,175 potential articles, 67 evaluated the impact of monitoring in acutely ill adult patients. There were 40 studies related to hemodynamic monitoring, 17 to respiratory monitoring, and 10 to neurological monitoring. Seven studies were classified in two different categories. Positive non-mortality outcomes were observed in 17 of 40 hemodynamic studies, 11 of 17 respiratory, and in all 10 neurological studies. Mortality was evaluated in 31 hemodynamic studies, but a beneficial impact was demonstrated in only 10. For respiratory monitoring, 7 studies evaluated mortality, but only 3 of them showed an improved outcome. We found no neurological monitoring studies that assessed mortality. *Conclusion:* There is no broad evidence that any form of monitoring improves outcomes in the ICU and most commonly used devices have not been evaluated by RCT. This review puts into perspective the recent negative studies on the use of the pulmonary artery catheter in the acutely ill.

Introduction

Monitoring techniques in the intensive care unit (ICU) are primarily used to identify disease patterns and titrate therapies. Understanding of pathophysiological processes may help limit disease progression and promote recovery, so early detection of physiological alterations to guide therapeutic interventions should improve outcomes; however, doubts have been raised about the utility of some monitoring systems, e.g., the pulmonary artery catheter (PAC) [1–3], in the ICU.

In evidence-based medicine, the randomized controlled trial (RCT) represents the ideal study design to validate an intervention; however, demonstration of utility of a monitoring system may be difficult and few monitoring systems have been evaluated by RCT. We performed a systematic review of the literature for RCTs that have evaluated the impact of monitoring systems on outcomes in critically ill patients and in perioperative patients undergoing major procedures.

Methods

We conducted a comprehensive search for all publications of prospective RCTs that focused on the impact of moni-

toring systems in adult critically ill patients and adult perioperative patients undergoing major procedures. A highly sensitive search strategy was carried out in the Cochrane Central Register of Controlled Trials (CENTRAL) and in MedLine using the approach shown in the electronic supplement. Eligibility assessment and data abstraction were performed independently in an unblinded standardized manner by two reviewers (G.A.O and R.L.C). Interrater reliability between the abstractors for RCT selection was evaluated using the κ statistic. Discrepancies about classification and outcome evaluation were resolved by author consensus.

A study was selected when it compared a monitored group of patients with a non-monitored control group or when the health-care team was unaware of monitoring measurements and so was unable to use them to guide therapy. We defined outcome in general, including morbidity and mortality, optimization of therapeutic strategies, complications, costs, and quality of life. We excluded animal and laboratory studies, non-randomized trials, reviews, letters, meta-analyses, guidelines or commentaries, trials comparing monitoring methods without a non-monitored control group, trials evaluating the impact of medicaments or therapies on measurements obtained by a monitoring system, and pediatric studies.

Selected studies were separated into those evaluating hemodynamic (or tissue perfusion), respiratory, neurological, or metabolic variables and, according to the results obtained for each of their outcome objectives, were classified as positive, neutral, or detrimental. Additionally, we classified studies evaluating mortality as primary or secondary outcome studies.

Results

Study selection

A total of 4175 articles were identified and 67 were included (Fig. 1). Interobserver agreement for selection and final classification of the studies was high: κ statistic 0.90. Seven studies [4–10], which assessed two monitoring devices in the same protocol, were enrolled in two different categories.

Hemodynamic and perfusion monitoring (Fig. 2)

Arterial pressure

No RCTs evaluating the impact of arterial pressure monitoring on outcomes when used in the ICU or operating room were identified (Table 1).

Central venous pressure

Two RCTs evaluated the impact of CVP monitoring on outcome in the ICU [8, 11]. One RCT compared conventional intraoperative fluid management with transesophageal Doppler or CVP monitoring to optimize intraoperative fluid therapy in patients with hip fracture [8]. Although in the conventional group a catheter was placed and CVP recorded by the investigator, the clinician was unaware of these measurements and so unable to use them to guide therapy. Patients in the CVP and transesophageal Doppler groups had a significantly higher intraoperative fluid balance; however, there were no differences in mortality or morbidity ($p = 0.24$), although fluid administration guided by CVP monitoring shortened the time before patients were fit for discharge. In the other RCT, fluid challenge targeted at keeping the CVP > 5 mmHg during renal transplant surgery resulted in a greater frequency of onset of graft function within the first three postoperative days than in a control group without CVP monitoring [11].

Pulmonary artery catheter

Sixteen studies assessed a possible influence of the PAC on ICU outcomes: seven in patients undergoing cardiac or major peripheral vascular surgery [6, 9–16]; three in high-risk surgical patients [4, 10, 17]; three in mixed-ICU populations [1, 18, 19]; two in patients with acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) [3, 20]; and one in patients with congestive cardiac failure [2]. Of 15 studies evaluating mortality as a primary or secondary outcome when a PAC was placed [1, 2–4, 6, 9, 10, 12–15, 17–20], nine used predefined hemodynamic targets [2–4, 9, 10, 14–17]; of these, only two [4, 17] demonstrated a positive effect on mortality. Mortality outcomes were not improved in studies that did not include a hemodynamic goal protocol.

In high-risk surgical patients, Shoemaker et al. [4] demonstrated lower mortality when a PAC-protocol group was compared with a PAC control group (4 vs. 33%, $p < 0.01$), as well as with a CVP+PAC-control group (4 vs. 28%, $p < 0.02$). In this study, the PAC was inserted early (preoperatively) and the PAC protocol established before the development of organ dysfunction. There were no differences in mortality between a CVP group and the PAC control group. Complications, duration of mechanical ventilation, as well as ICU and hospital stays, were less in the PAC-protocol group when compared with the CVP+PAC control group. Again in high-risk surgical patients, Sandham et al. [10] reported no significant differences in hospital mortality among groups managed with or without a PAC (7.8 vs. 7.7%) despite having a PAC-directed protocol. Pearson et al. [6] showed no significant differences in morbidity or mortality, but

increased costs, in patients undergoing cardiac surgery when compared with management with a CVP catheter, but no predefined hemodynamic targets were established.

Studies on PAC monitoring in patients undergoing abdominal aortic surgery [12, 13] did not show improved complication rates, duration of intensive care, postoperative hospital stay, or mortality, but no preoperative optimization was conducted and predefined hemodynamic goals were not established. In a study by Joyce et al. [13], all the serious postoperative cardiac complications occurred in patients with impaired left ventricular function, independent of PAC use.

Preoperative hemodynamic optimization with a PAC has been evaluated in four RCTs in patients undergoing major vascular surgery [9, 14–16] and one in patients with proximal hip-fracture repair [17]. Two of these RCTs demonstrated a positive impact on ICU outcomes [14, 17]. Berlauk et al. [14] showed fewer intra- and postoperative adverse events, less early graft thrombosis, and lower mortality rates than in the control group. Likewise, Shultz et al. [17] showed a lower mortality rate in patients undergoing surgical repair of proximal hip fracture. In contrast, three RCTs [9, 15, 16] showed no improvement in morbidity, intraoperative events, ICU stay, hospital stay, or mortality when preoperative optimization was guided by a PAC.

In ALI/ARDS, Richard et al. [20] found no differences in morbidity or mortality in patients randomized to PAC

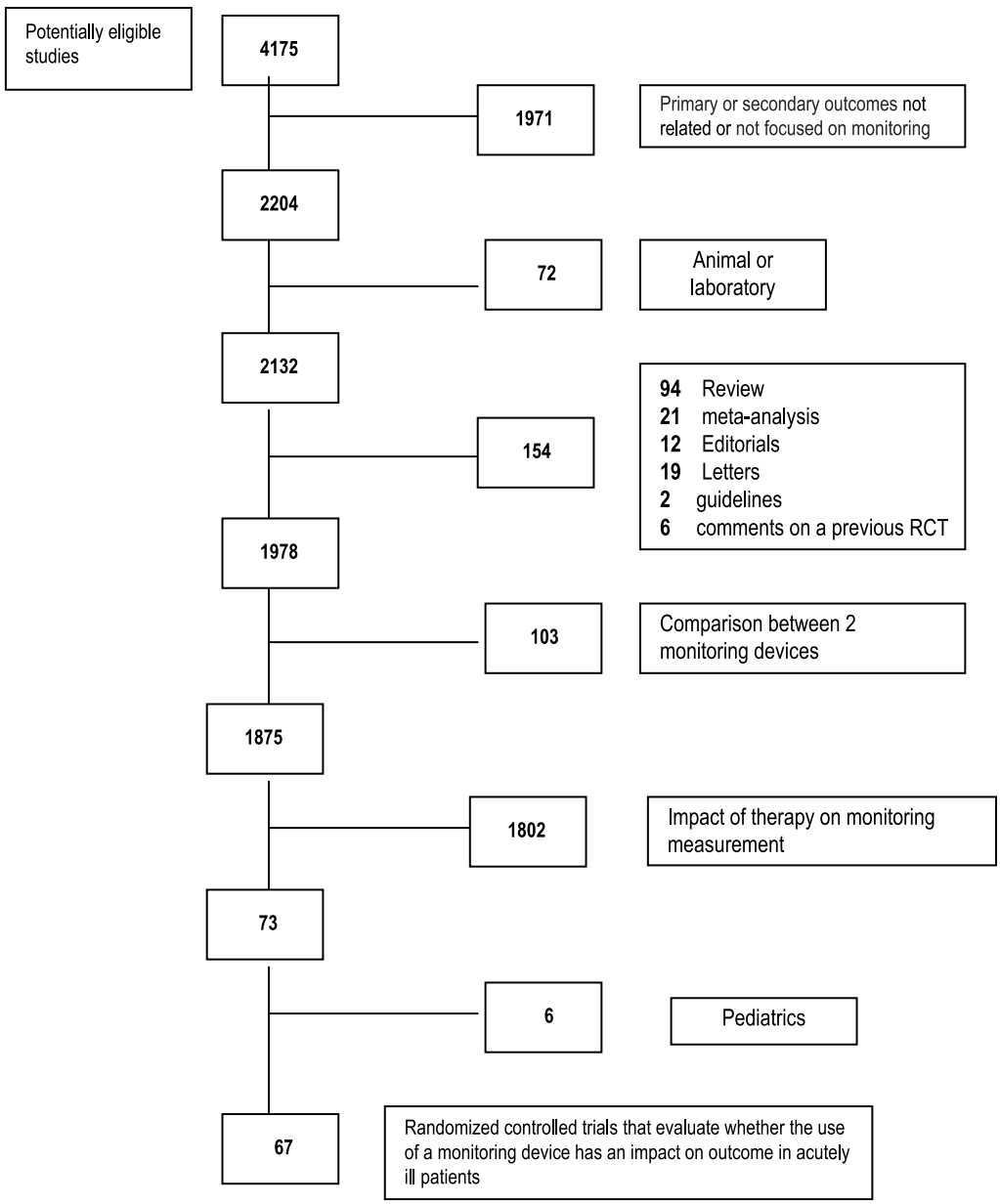

Fig. 1 Study selection process

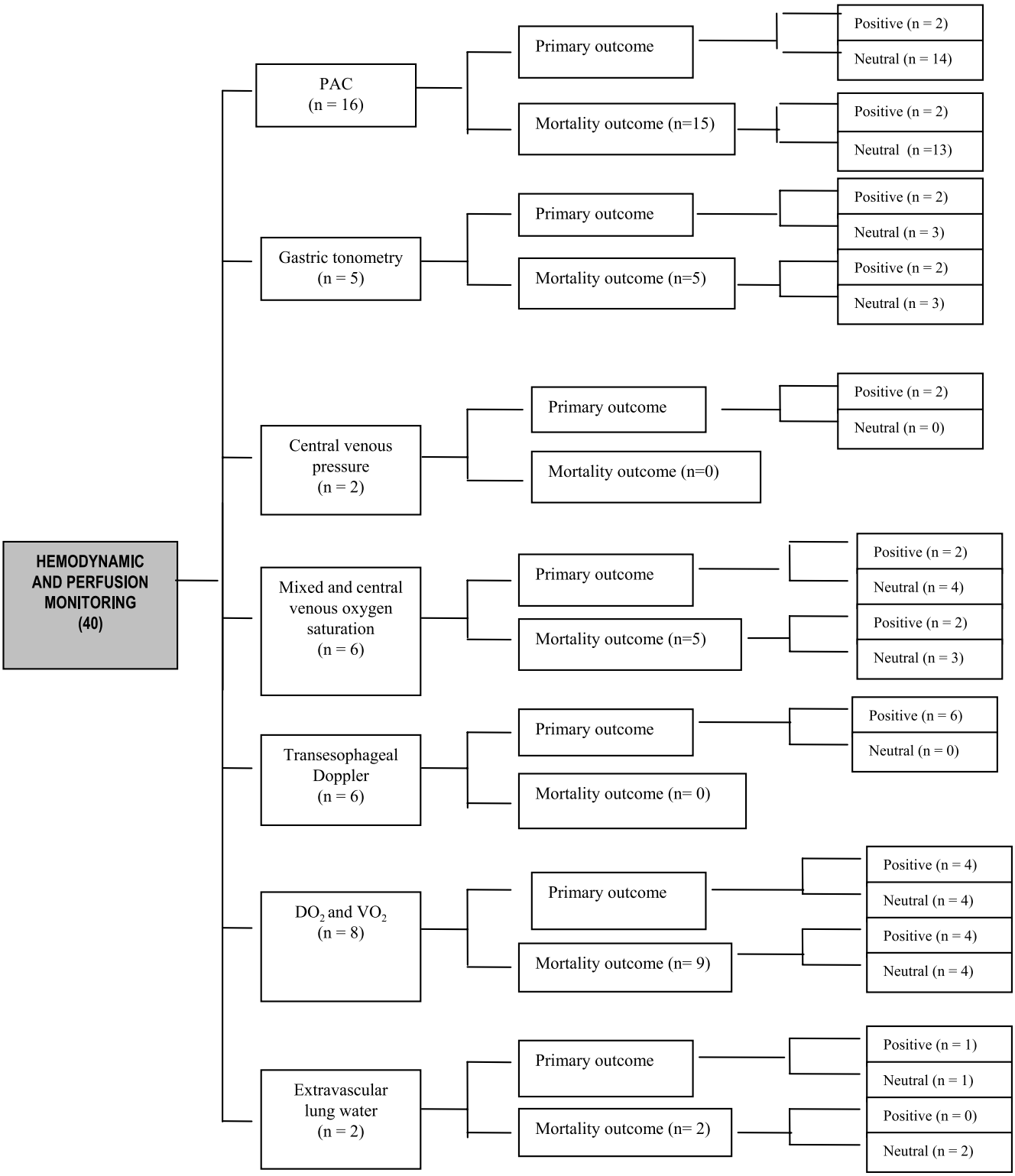

Fig. 2 Summary of outcomes in randomized controlled trials (RCTs) on hemodynamic and perfusion monitoring

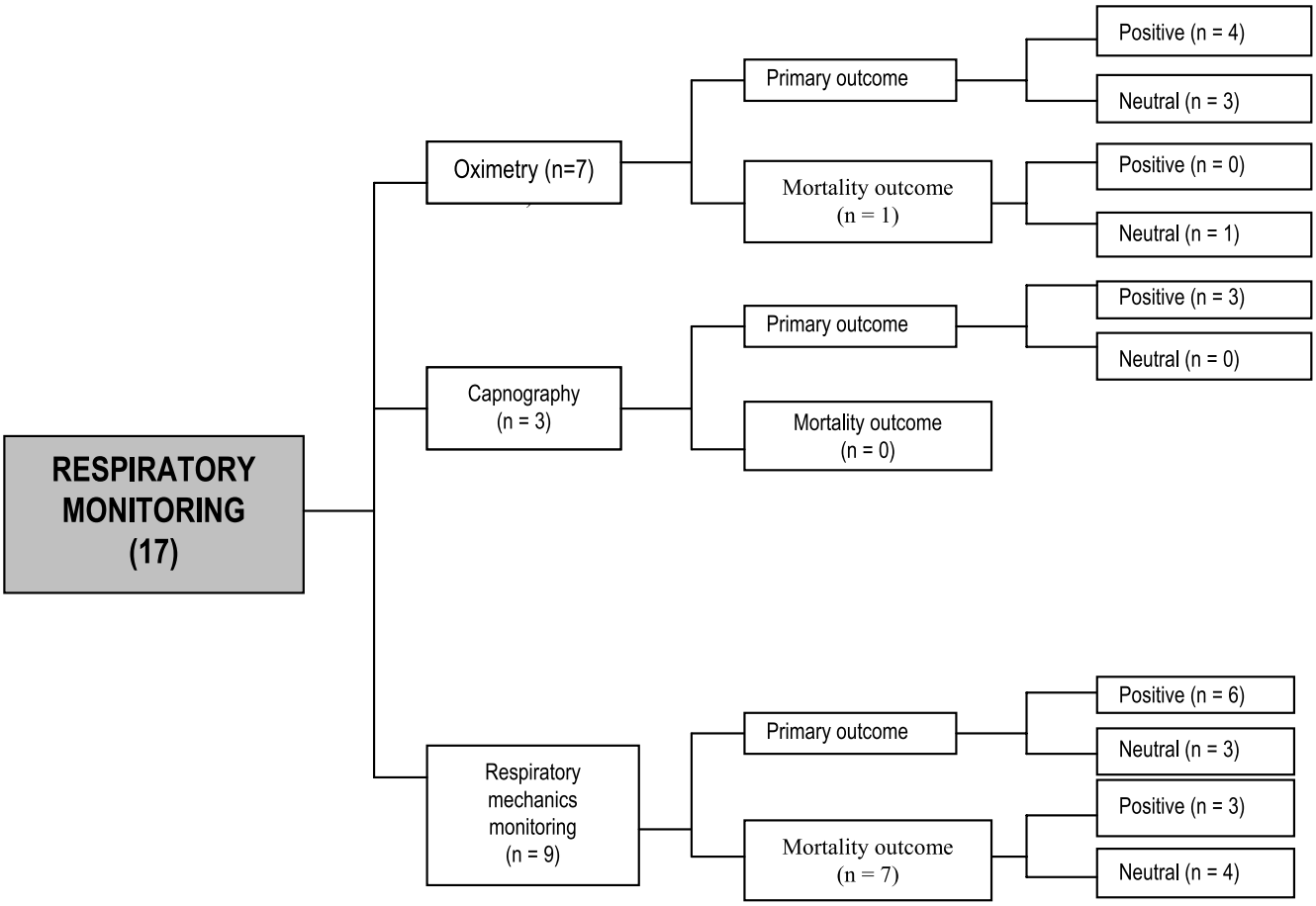

Fig. 3 Summary of outcomes in RCTs on respiratory monitoring

or no PAC. The ARDS Network recently reported similar mortality and organ function measures in patients with ALI managed by PAC-guided compared with CVP-guided therapy, but higher complication rates [3]. In a mixed ICU population, Rhodes et al. [19] also found similar mortality rates, organ dysfunction, and ICU or hospital stays, in patients managed with or without a PAC. Likewise, Harvey et al. [1] found no significant differences in hospital mortality or length of ICU and hospital stays in patients managed with or without a PAC in a mixed ICU population. In these studies, no predefined hemodynamic goals were proposed in the PAC groups.

In patients with severe symptomatic and recurrent heart failure [2], use of a PAC did not significantly affect days alive and out-of-hospital in the first 6 months, mortality, number of days hospitalization, or quality of life.

Extravascular lung water

Eisenberg et al. [21] evaluated the impact of extravascular lung water (EVLW) monitoring to guide therapy in a mixed ICU population. In the routine management group, EVLW was measured, but results were unknown to the primary care physicians, while the protocol group used an EVLW-guided algorithm. In-hospital mortality was not significantly lower in the protocol group (54 vs. 65%). The ICU mortality was similar in all hemodynamic subsets, except for patients with an initially elevated EVLW and pulmonary artery occlusion pressure (PAOP) < 18 mmHg, where the protocol group had lower mortality rates.

Mitchell et al. [22] showed a significant decrease in ventilator days and ICU stay in critically ill patients managed with EVLW monitoring; however, differences in ICU (35 vs. 47%) and hospital (56 vs. 65%) mortality rates did not reach statistical significance.

Transesophageal echocardiography and esophageal Doppler

Six RCTs evaluated the impact of transesophageal echocardiography (TEE) or esophageal Doppler in surgical patients: two [8, 23] in patients undergoing proximal

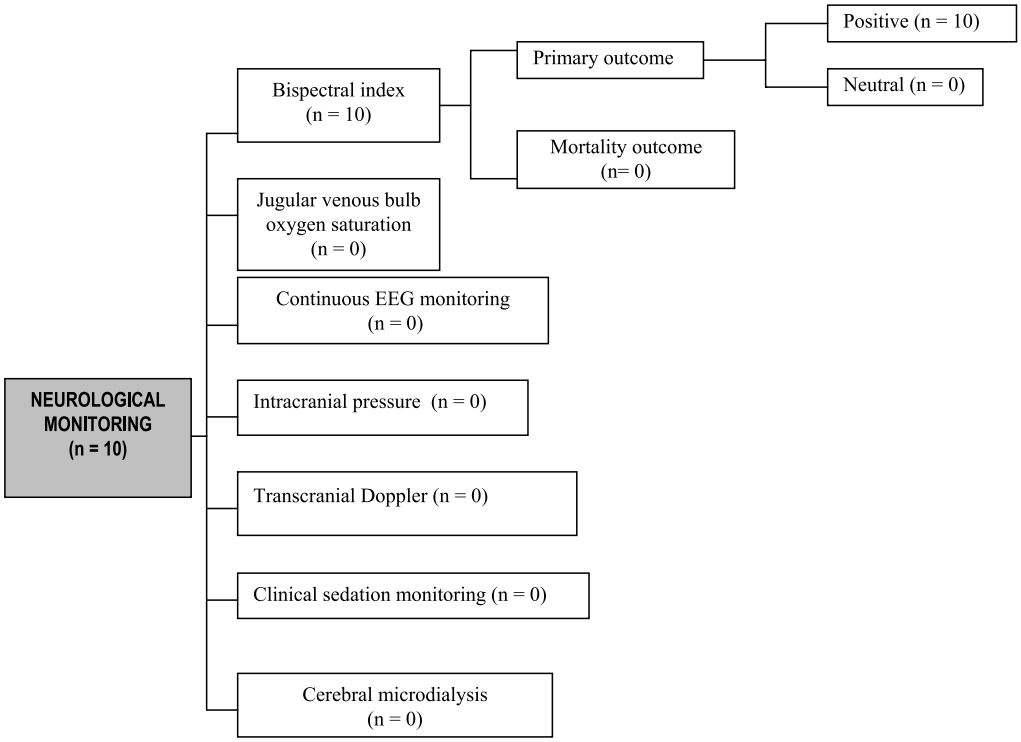

Fig. 4 Summary of outcomes in RCTs on neurological monitoring

femoral fracture repair; two in patients undergoing colon surgery [24, 25]; one in patients undergoing major surgery [26]; and one in patients undergoing cardiac surgery [27]. All the studies used a protocol guided by TEE/esophageal Doppler to optimize fluid loading. A reduction in postoperative complications was reported in all the studies, with a significant reduction in in-hospital length of stay in four studies [8, 23, 26, 27]. None of the studies evaluated mortality.

Gastric tonometry

Although a number of observational studies have demonstrated that intramucosal pH (pHi) is a good indicator of morbidity [28, 29] and mortality [30], we found only five RCTs that assessed the influence of gastric tonometry on outcomes [31, 32–35]. Gutierrez et al. [31] studied 260 medical, postoperative, and trauma patients admitted to the ICU. Patients were randomized to a gastric tonometry-guided protocol or conventional treatment in which pHi values were recorded but not reported to the health-care team. In patients admitted with a low pHi, survival was similar (37 vs. 36%), whereas for those admitted with a normal pHi, it was significantly greater in the protocol than in the control group (58 vs. 42%, $p < 0.01$). Ivatury et al. [32] evaluated optimization of therapy in post-resuscitated trauma patients using a pHi-guided protocol: normalization of pHi in the first 24 h was associated with greater survival compared with the control group; however, in another RCT including trauma patients [35], resuscitation guided by gastric tonometry did not produce significant differences in mortality rates, ventilator days, organ dysfunction, or length of stay.

In a study by Pargger et al. [33], patients were randomized to pHi-guided therapy or control (pHi was registered but treating physicians were blinded to pHi values) after elective repair of infrarenal abdominal aneurysm. Low pHi values (< 7.32) and their persistence were predictors of major complications, but treatment aimed at correcting low pHi values did not improve postoperative outcomes. In resuscitated acutely ill adult patients admitted to the ICU, Gomersall et al. [34] showed no clinically or statistically significant differences in ICU or hospital survival, organ function, or duration of stay in an intent-to-treat analysis for patients randomized to pHi-guided therapy (pHi measurements were obtained in the control group, but not used to guide treatment).

Mixed (SvO_2) and central ($ScvO_2$) venous oxygen saturation

Only six studies have evaluated the impact of these monitoring variables on outcomes [6, 36–40].

Jastremski et al. [36] analyzed the impact and cost-effectiveness of SvO_2 monitoring in medical ICU patients. There was no difference in the number of ICU days,

Table 1 Randomized controlled studies of hemodynamic and perfusion monitoring techniques. *ARDS*, acute respiratory distress syndrome; *CI*, cardiac index; *CVP*, central venous pressure; *EVLW*, extravascular lung water; *ICU*, intensive care unit; *IQ*, interquartile; *LOS*, length of stay; *NA*, not applicable; *PAC*, pulmonary artery catheter; *PAOP*, pulmonary artery occlusion pressure; *SD*, standard deviation; *SOFA*, sequential organ failure assessment; *SVR*, systemic vascular resistance

Reference	No. of centers	No. of patients	Groups (*n*)	Setting/ population	End points	Preoperative optimization	Predefined hemodynamic targets	Impact on non-mortality outcomes	Impact on mortality outcomes
Pulmonary artery catheter									
[17]	1	70	Group 1: no PAC (35); group 2: PAC (35)	ICU/hip fracture surgical repair	ICU mortality; postoperative morbidity	Yes	Yes	Neutral: postoperative morbidity; group 1: 11%; group 2: 10%	Positive: group 1: 29%; group 2: 2.9%
[4]	1	88	Group 1: no PAC (30); group 2: PAC with normal goals (30); group 3: PAC with supranormal goals (28)	ICU/high-risk surgical patients	ICU mortality; hospital, ICU and ventilator days	Yes	Group 2: CI: 2.8–3.5 l/min m^{-2}; DO_2: 400–550 ml/min m^{-2}; VO_2: 120–140 ml/min m^{-2}; group 3: CI > 4.5; DO_2:> 600 ml/min m^{-2}; VO_2: > 170 ml/min m^{-2}	Positive: ICU days, mean (SD): group 1: 11.5 (1.7); group 2: 15.8 (3.1); group 3: 10.2 (1.6)[a] Ventilator days, mean (SD): group 1: 4.6 (1.4); group 2: 9.4 (3.4); group 3: 2.3 (0.5)[a]	Positive: group 1: 23%; group 2: 33%; group 3: 4%[a]
[6]	1	226	Group 1: no PAC (28); group 2: PAC conventional (86); group 3: PAC + SvO2 (66); group 4: reassigned to PAC (33); group 5: reassigned to PAC + SvO2 (13)	ICU/ cardiac surgery	Morbidity, hospital cost, and mortality	No	No	Neutral: cost of care: group 1 < group 2 < group3 ICU stay: no significant differences	Neutral: deaths (*n*): groups 1, 2, and 5: 0; group 3: 1; group 4: 1
[12]	1	102	Group 1: no PAC (53); group 2: PAC (49)	ICU/ abdominal aortic reconst-ructive surgery	Duration of intensive care, hospital stay, hospital cost, and mortality rates	No	No	Neutral: ICU days, mean (SD): 2.1 (1.0) vs. 2.7 (2.6)[b] Hospital days, mean (SD): 9.4 (6.8) vs. 10.2 (8.4)[c]	Neutral: deaths (*n*): group 1: 1; group 2: 0
[13]	1	40	Group 1: no PAC (19); group 2: PAC (21)	ICU/ elective abdominal aortic surgery	Postoperative renal function, ventilatory complications, hospital and ICU stay, and mortality	No	No	Neutral: no differences between groups	Neutral: deaths (*n*): group 1: 1; group 2: 0
[14]	1	89	Group 1: PAC 12 h pre-surgery (45); group 2: PAC 3 h pre-surgery (23); group 3: no PAC (21)	ICU/limb-salvage arterial surgery	Intraoperative complicat-ions, postoperative card-iac morbidity, early graft thrombosis and mortality	Yes	Groups 1 and 2: PAOP < 15 mmHg;	Positive[d]: intra-operative complications: 17.8 vs. 13 vs. 42.9%[d] ICU days, mean (SD): group 1: 19.4 (11.6); group 2: 18.0 (12.0); group 3: 15.4 (7.5) Early graft thrombosis: group 1: 2.2%; group 2: 4.3%; group 3: 9.5%[d]	Neutral: deaths (*n*): group 1: 1; group 2: 0; group 3: 2[e]

[a] $p < 0.01$ PAC-protocol vs. PAC-control group; $p < 0.02$ PAC-protocol with CVP plus PAC-control groups; [b] $p = 0.13$; [c] $p = 0.60$; [d] positive when considering graft thrombosis ($p < 0.05$) and intraoperative complications ($p < 0.05$), no significant difference in ICU stay; [e] groups 1 and 2 vs. group 3: $p = 0.08$

Table 1 Continued

Reference	No. of centers	No. of patients	Groups (*n*)	Setting/ population	End points	Preoperative optimization	Predefined hemodynamic targets	Impact on non-mortality outcomes	Impact on mortality outcomes
[18]	2	33	Group 1: no PAC (17); group 2: PAC (16)	ICU/mixed critically ill patients	Physiological status, ICU stay; and mortality	NA	No	Neutral: hospital days, mean: group 1: 8.1; group 2: 10.3	Neutral: deaths (*n*): group 1: 10; group 2: 9
[15]	1	104	Group 1: PAC (51); group 2: no PAC or PAC when clinically necessary (53)	ICU/ elective vascular surgery	ICU and hospital stay; and mortality	Yes	Group 2: PAOP < 14 mmHg; CI > 2.8 l/min m^{-2}; SVR < 1,100 dyn s/cm^5	Neutral: ICU days, mean (SD): group 1: 2.7 (0.2); group 2: 2.6 (0.5) Hospital days: group 1: 12.5 (1.4); group 2: 12.0 (1.3)	Neutral: deaths (*n*): group 1: 0; group 2: 0
[16]	1	120	Group 1: no PAC (60); group 2: PAC (60)	ICU/ aortic surgery	Pre- and postoperative complications, duration of mechanical ventilation, hospital and ICU stay	Yes	Group 2: PAOP < 15 mmHg; CI > 2.8 l/min/m^{-2}; SVR < 1,000 dyn s/cm^5	Neutral: postoperative events: group 1: 25%; group 2: 17% Mechanical ventilation time, hours (SD): group 1: 6 (1); group 2: 35 (19) ICU days, mean (SD): group 1: 7 (1); group 2: 8 (1) Hospital days, mean (SD): group 1: 13 (2); group 2: 13 (2)	–
[9]	1	100	Group 1: no PAC (50); group 2: PAC (50)	ICU/ infrarenal abdominal aortic aneurysm repair	Cardiovascular morbidity, postoperative renal failure, hospital stay, and hospital mortality	Yes	Group 2: PAOP < 18 mmHg; CI > 3.0 l/min m^{-2}; SVR < 1,450 dyn s/cm^5; DO_2 > 600 ml/min m^2	Neutral: arrhythmia, congestive failure and renal failure: no differences between groups Hospital days, median (IQ range): group 1: 12 (9–16); group 2: 11 (8–15)	Neutral: deaths (*n*): group 1: 0; group 2: 0
[19]	1	201	Group 1: no PAC (106); group 2: PAC (95)	ICU/mixed critically ill patients	Primary end point: 28-day mortality and morbidity; secondary end points: ICU and hospital LOS, and organ dysfunction	No	No	Neutral: median SOFA score, renal failure, ARDS: no differences between groups ICU days, median (IQ range): group 1: 5 (2–12); group 2: 4 (2–10) Hospital days, median (IQ range): group 1: 13 (5–32); group 2: 14 (3–32)	Neutral: deaths, *n* (%): group 1: 46 (47.9); group 2: 50 (47.6)[f]

[f] $p > 0.99$

Table 1 Continued

Reference	No. of centers	No. of patients	Groups (*n*)	Setting/population	End points	Preoperative optimization	Predefined hemodynamic targets	Impact on non-mortality outcomes	Impact on mortality outcomes
[20]	36	676	Group 1: no PAC (341); group 2: PAC (335)	ICU/shock mainly of septic origin, ARDS or both	Primary end point: 28-day mortality; secondary end points: 14- and 90-day mortality; organ system failure, renal support, vasoactive agent-free days; ICU and hospital stay and ventilator-free days	NA	No	Neutral: ICU days, mean (SD): group 1: 11.6 (10.1); group 2: 11.9 (10.0) Hospital days, mean (SD): group 1: 14 (11.6); group 2: 14.4 (11.3) Free days of ventilation: group 1: 5.2 (8.5); group 2: 5.0 (8.5) Free days of renal support, vasoactive agents, or organ failure: no differences between groups	Neutral: 28-day mortality, *n* (%): group 1: 208 (61); group 2: 199 (59)[g]
[10]	19	1,994	Group 1: no PAC (997); group 2: PAC (997)	ICU/high-risk surgical patients	Primary end point: hospital mortality; secondary end points: 6- and 12-month mortality; and morbidity	No	Group 2: PAOP < 18 mmHg; CI > 3.5 l/min m^{-2}; SVR < 1,450 dyn s/cm^5; MAP > 70 mmHg; heart rate < 120/min; DO_2 > 600 ml/min m^{-2}; hematocrit, 27%	Neutral: hospital days, median (IQ range): group 1: 10 (7–15); group 2: 10 (7–15); myocardial infarction, congestive heart failure, arrhythmias, sepsis related to catheters, renal or hepatic insufficiency: no difference between groups	Neutral: in-hospital mortality, *n* (%): group 1: 77 (7.7); group 2: 78 (7.8)[h]; no differences in 6- and 12-month mortality
[1]	65	1,041	Group 1: no PAC (522); group 2: PAC (519)	ICU/mixed critically ill patients	Primary end point: hospital mortality; secondary end points: 28-day and ICU mortality. ICU and hospital LOS	No	No	Neutral: ICU days, median (IQ range): group 1: 12.1 (6.2–22.3); group 2: 11.0 (5.7–21.0) Hospital days, median (IQ range): group 1: 34 (23–61); group 2: 40 (21–70)	Neutral: in-hospital mortality, *n* (%): group 1: 333 (66); group 2: 346 (68)[i]; no differences in 28-day and ICU mortality
[2]	26	433	Group 1: no PAC (218); group 2: PAC (215)	ICU/NYHA IV heart failure patients	Primary end point: days alive out of hospital during 6 months following randomization; secondary end points: exercise tolerance, natriuretic peptides, and quality of life	NA	Group 2: PAOP < 15 mmHg; right atrial pressure < 8 mmHg	Neutral: no difference between groups	Neutral: days alive out of hospital: group 1: 133; group 2: 135

[g] $p = 0.67$; [h] $p = 0.93$; [i] $p = 0.39$

Table 1 Continued

Reference	No. of centers	No. of patients	Groups (*n*)	Setting/ population	End points	Preoperative optimization	Predefined hemodynamic targets	Impact on non-mortality outcomes	Impact on mortality outcomes
[3]	42	1,000	Group 1: no PAC (487); group 2: PAC (513)	ICU/ patients with established acute lung injury	Primary end point: 60-day mortality; secondary end point: organ failure			Neutral: ventilator-free days at day 28, mean (SD): group 1: 13.5 (0.5); group 2: 13.2 (0.5) Organ failure: no difference between groups	Neutral: 60-day mortality: group 1: 26.3%; group 2: 27.4%
DO_2 and VO_2									
[4]	1	88	Group 1: no PAC (30); group 2: PAC with normal goals (30); group 3: PAC with supranormal goals (28)	ICU/high-risk surgical patients	ICU mortality; hospital, ICU, and ventilator days	Yes	Group 2: CI: 2.8–3.5 l/min m^{-2}; DO_2: 400–550 ml/min m^{-2}; VO_2: 120–140 ml/min m^{-2}; group 3: CI > 4.5 l/min/m^{-2}; DO_2: > 600 ml/min/m^{-2}; VO_2: > 170 ml/min m^{-2}	Positive	Positive
[41]	1	107	Group control: standard perioperative care (54); group protocol: increased DO_2 (53)	ICU/high-risk surgical patients	28-day mortality; complications; ICU and hospital LOS	Yes	Both groups (pre-surgery): MAP 80–110 mmHg; PAOP 12–14 mmHg; SaO_2 > 94%; Hg > 12 g/dl; urine output > 0.5 ml/kg h^{-1}; group 2: additionally, DO_2 > 600 ml/min m^{-2}	Positive[j]	Positive
[42]	1	125	Group control: standard care (50); group protocol: supranormal values of DO_2, VO_2 and CI (65)	ICU/ severe trauma patients	Hospital mortality; organ failures, hospital and ICU LOS; ventilator days	No	Group protocol: DO_2I > 670 ml/min m^{-2}; VO_2I > 166 ml/min m^{-2}; CI > 4.5 l/min/m^{-2} within 24 h admission	Positive	Positive
[44]	1	58	Group 1: supranormal DO_2 and VO_2 (27); group 2: standard care (32)	ICU/mixed critically ill patients	Incidence of organ failure and ICU mortality	No	Group 1: DO_2I > 600 ml/min m^{-2}; VO_2I > 150 ml/min m^{-2}; group 2: blinded to values	Neutral	Neutral
[43]	1	138	Control group: standard care (46); epinephrine group (46); dopexamine group (46)	ICU/major elective surgery	Hospital mortality and morbidity	Yes (4 h before surgery)	Groups 2: and 3: DO_2 > 600 ml/min m^{-2}	Positive	Positive
[9]	1	100	Group 1: control (50); group 2: supranormal DO_2 (50)	ICU/infrarenal abdominal aortic aneurysm repair	Cardiovascular morbidity, postoperative renal failure, hospital stay and hospital mortality	Yes	Group 2: PAOP < 18 mmHg; CI > 3.0 l/min/m^{-2}; SVR < 1,450 dyn s/cm^5; DO_2 > 600 ml/min m^{-2}	Neutral	Neutral

[j] Significant reduction in complications ($p = 0.008$), but no differences in ICU and hospital LOS

Table 1 Continued

Reference	No. of centers	No. of patients	Groups (*n*)	Setting/population	End points	Preoperative optimization	Predefined hemodynamic targets	Impact on non-mortality outcomes	Impact on mortality outcomes
[10]	19	1,994	Group 1: control (997); group 2: supranormal DO_2 (997)	ICU/high-risk surgical patients	Primary end point: hospital mortality; secondary end points: 6- and 12-month mortality; and morbidity	No	Group 2: PAOP < 18 mmHg; CI > 3.5 l/min m^{-2}; SVR < 1,450 dyn s cm/^{5}; MAP > 70 mmHg; heart rate < 120/min; DO_2 > 600 ml/min m^{-2}; hematocrit, 27%	Neutral	Neutral
Mixed and central oxygen venous saturation (SvO_2–$ScvO_2$)									
[36]	1	99	Group 1: conventional PAC (49); group 2: PAC with continuous SvO_2 monitoring (50)	ICU/mixed critically ill patients	ICU LOS, catheter complications and catheter days, and ICU mortality	No	No	Neutral	Neutral
[6]	1	226	Group 1: no PAC (28); group 2: PAC conventional (86); group 3: PAC + SvO2 (66); group 4: reassigned to PAC (33); group 5: reassigned to PAC + SvO2 (13)	ICU/cardiac surgery	Morbidity, hospital cost and mortality	No	No	Neutral	Neutral
[37]	56	762	Control group (252); cardiac index group (253); SvO_2 group (257)	ICU/mixed critically ill patients	ICU and 6-month mortality; morbidity	No	Control: standard care; cardiac index group: CI 2.5–3.5 l/min/m^{-2}; SvO_2 group: SvO_2 > 70%	Neutral	Neutral
[38]	1	72	Control group (40); treatment group (32)	ICU/elective peripheral vascular surgery	Perioperative cardiac complications	Yes	Treatment group: Hg > 10 g/dl; PAOP > 12 mmHg; SvO_2 > 65%	Neutral	–
[39]	1	403	Control group: standard care (197); protocol group (196)	ICU/elective cardiac surgical patients	Hospital and ICU stay, and morbidity (organ dysfunction; post-hoc analysis of ICU mortality	No	Protocol group: SvO_2 > 70%; lactate < 2.0 mmol/l	Positive	Positive
[40]	1	263	Standard therapy; early goal-directed therapy	Emergency room/severe sepsis and septic shock	In-hospital mortality; resuscitation end points, organ dysfunction, administered treatments, and resource consumption	NA	Early goal-directed therapy: CVP > 8–12 mmHg; MAP > 65 mmHg; urine output > 0.5 ml/kg h^{-1}; SvO_2 > 70%	Positive	Positive
Gastric tonometry									
[31]	9	260	Control group (125); protocol group (135)	ICU/mixed critically ill patients	ICU mortality	NA	Protocol group: pHi-guided therapy	Positive	Positive[k]

[k] pHi-guided therapy improved survival in patients whose pHi on admission to ICU was normal

Table 1 Continued

Reference	No. of centers	No. of patients	Groups (*n*)	Setting/ population	End points	Preoperative optimization	Predefined hemodynamic targets	Impact on non-mortality outcomes	Impact on mortality outcomes
[32]	1	57	Group 1: pHi normalization (30); group 2: PAC (27)	ICU/major trauma patients	ICU mortality; multiple organ dysfunction	NA	Group 1: pHi-guided therapy	Positive	Positive[1]
[33]	1	55	Group 1: pHi-guided therapy; group 2: control	ICU/ elective repair of infrarenal abdominal aortic aneurysms	Complications, time of ventilation, fluid and vasoactive drug treatment, treatment with vasoactive drugs, ICU and hospital LOS; hospital mortality	No	Group 1: pHi-guided therapy if pHi < 7.32	Neutral	Neutral
[34]	1	210	Control group; intervention group	ICU	ICU, hospital and 30-day mortality; ICU and hospital LOS		Intervention group: additional treatment to patients with persistent pHi < 7.35	Neutral	Neutral
[35]		151	Group 1: conventional care; group 2: pHi-guided therapy; group 3: additional therapies to optimize splanchnic perfusion	ICU/ severe trauma patients	Mortality rates, organ dysfunction, ventilator days, or length of stay	No	Group 2: pHi-guided therapy	Neutral	Neutral
Central venous pressure									
[11]	1	61	Group A: CVP was not read (30); group B: CVP-read (30); guided therapy (31)	Operating room/intraoperative fluid management during renal transplantation	Graft function in early postoperative period	No	Group B: CVP > 5 mmHg	Positive	–
[8]	1	90	Group 1: conventional care (29); group 2: CVP-guided (31); group 3: Doppler-guided (30)	Operating room/intraoperative fluid management of hip fracture	Time to medical fitness to discharge, hospital stay, and morbidity	No	Group 2: fluid management CVP guided	Positive	–
Esophageal Doppler-transesophageal ecocardiography									
[27]	1	60	Group control: standard care (30); group protocol: fluid management Doppler guided	Operating room/ elective cardiac surgery	Gut mucosal perfusion; ICU and hospital LOS	No	Group protocol: fluid management Doppler guided	Positive	–
[23]	1	40	Control group: conventional intraoperative fluid management; protocol group: fluid management Doppler guided	Operating room/ repair of proximal hip fracture	Time declared medically fit for hospital discharge, duration of hospital stay, hemodynamic changes	No	Protocol group: Doppler ultrasonography used to maintain maximal stroke volume	Positive	

[1] Time for pHi optimization was significantly longer in non-survivors. Multiple organ dysfunction was higher in patients who did not have pHi optimized within 24 h

Table 1 Continued

Reference	No. of centers	No. of patients	Groups (*n*)	Setting/ population	End points	Preoperative optimization	Predefined hemodynamic targets	Impact on non-mortality outcomes	Impact on mortality outcomes
[8]	1	90	Group 1: conventional care (29); group 2: CVP-guided (31); group 3: Doppler guided (30)	Operating room/repair of hip fracture	Time to medical fitness to discharge, hospital stay and morbidity	No	Group 3: fluid management Doppler guided	Positive	–
[26]	1	100	Control group (50); protocol group (50)	Operating room/major surgery	Length of hospital stay and postoperative complications	No	Protocol group: fluid management Doppler guided	Positive	–
[24]	1	75	Control group; Doppler group	Operating room/bowel surgery	Hemodynamic parameters, morbidity and hospital stay	No	Doppler group: fluid management Doppler guided	Positive	–
[25]	1	128	Control group (67); Doppler group (67)	Operating room/major bowel surgery	Hemodynamic parameters and hospital stay	No	Doppler group: fluid management Doppler guided	Positive	–
Extravascular lung water									
[21]	1	47	Group 1: protocol group 2: routine management (23)	ICU/mixed critically ill patients	Oxygenation, renal failure, and mortality	No	Group 1: EVLW guided protocol	Neutral	Neutral
[22]	1	101	Group 1: PAC; group 2: EVLW	ICU/mixed critically ill patients	Time of mechanical ventilation, length of ICU stay and mortality	No	Group 2: EVLW guided protocol	Positive	Neutral

decrease in potentially adverse hemodynamic events, or survival between the groups, although the authors still considered that SvO_2 measurement could have a reasonable cost-effectiveness ratio. In a mixed population of critically ill patients, Gattinoni et al. [37] showed no differences in morbidity or mortality when comparing a normal SvO_2 or supranormal cardiac index (CI) with a normal CI control group.

Three studies evaluated SvO_2 monitoring in cardiac and vascular surgery patients [6, 38, 39]. Preoperative optimization of cardiovascular function using a target $SvO_2 > 65\%$ did not reduce intra- or postoperative complications in patients undergoing elective peripheral vascular surgery [38]. Pearson et al. [6] found no significant differences in length of ICU stay, morbidity, or mortality among patients monitored by conventional PAC, SvO_2 – PAC, or CVP; however, Polonen et al. [39] reported a reduction in hospital stay and postsurgical morbidity in cardiac surgery patients randomized to SvO_2 and lactate monitoring in the first 8 postoperative hours. A post-hoc analysis showed improved survival at 6-months and 1-year after randomization in patients who achieved the target SvO_2 and lactate values.

In an RCT evaluating early goal-directed therapy in the treatment of severe sepsis and septic shock, Rivers et al. [40] observed that patients randomized to a protocol group who received treatment guided by $ScvO_2$, in addition to other variables, had less in-hospital mortality than a control group (30.5 vs. 46.5%; $p < 0.009$) and major improvements in organ function.

Oxygen delivery (DO_2) and consumption (VO_2)

We identified eight studies on DO_2 and VO_2 monitoring in ICU patients in which, for the control group, treating physicians were blinded to measurements or the measurements were not used to guide some form of therapy. Four studies in high-risk surgical and severe trauma patients [4, 41–43] showed that a deliberate perioperative increase in CI, DO_2, and VO_2 reduced mortality and complications; however, two studies in mixed ICU populations [44, 45] and another in high-risk surgical patients [10] showed no improvement in organ failure or mortality rates.

Other perfusion monitoring

We identified no RCT that evaluated the influence of other hemodynamic or perfusion monitoring techniques, including hepatic venous oxygen saturation, abdominal pressure monitoring, near-infrared spectroscopy, and mucosal laser Doppler flowmetry, on outcomes.

Respiratory monitoring (Fig. 3)

Pulse oximetry

We identified seven RCTs that evaluated outcomes with pulse oximetry: four in the operating or postoperative room [46–49], two in the ICU [5, 7], and one on a specialized, postsurgical hospital floor [50] (Table 2).

Several studies indicated that pulse oximetry could help to detect hypoxemic events [46, 47]. Moller et al. [48] demonstrated no significant differences in late cognitive dysfunction when perioperative monitoring with pulse oximetry was employed. A large RCT evaluating pulse oximetry in 20,802 surgical patients [49] reported no differences in cardiovascular, neurological, or infectious complications, or in-hospital deaths. Niehoff et al. [5] showed the potential utility of pulse oximetry and capnography in postoperative weaning from mechanical ventilation in a subset of only 24 post-cardiac surgery patients. Finally, Ochroch et al. [50] demonstrated that continuous pulse oximetry did not prevent readmissions to the ICU when cardiac and thoracic postoperative patients were monitored in a specialized postsurgical care floor.

Capnography

We identified three studies of capnography monitoring [5, 7, 51], including two also dealing with pulse oximetry monitoring [5, 7]. In the third study in this group, Helm et al. [51] used capnography to monitor ventilation in prehospital trauma victims, and found a higher proportion of patients who were "normoventilated" at hospital admission in the monitor group than in the monitor-blind group (63 vs. 20%, $p < 0.001$), but final in-hospital outcomes were not reported.

Respiratory mechanics

A number of studies showed that respiratory mechanics monitoring can guide ventilator adjustments as part of protective ventilation strategies in acute respiratory failure [52–56]. Amato et al. demonstrated that a protective ventilation strategy adjusting the positive end-expiratory pressure (PEEP) to above the lower inflection point (LIP) of the static pressure-volume curve and maintaining end-expiratory plateau pressure and peak-inspiratory pressures below 20 and 40 cmH_2O, respectively, improved lung function in patients with ARDS [52], increased the chance of early weaning, and reduced mortality [54]. The control groups in these two studies did not consider airway pressure vigilance.

Ranieri et al. [55] reported a decreased inflammatory response in patients undergoing a protective ventilation strategy using tidal volumes of 5–8 ml/kg and PEEP adjusted above the LIP of the static pressure-volume curve. Recently, Villar et al. [56] showed a reduction in ICU mortality (53 vs. 32%), in-hospital mortality (55 vs. 34%), and ventilator-free days at day 28 (6 vs. 11) with a strategy using low-tidal volume and PEEP adjusted according to the LIP of the static pressure-volume curve.

Other studies did not show a significant difference in mortality rates associated with limited airway pressures [57–59]. An ARDS network study [60] showed that the reduction in mortality rates in patients with ARDS was related to a limitation in tidal volumes more than plateau pressures, questioning the importance of the monitoring of airway pressures.

Neurological monitoring (Fig. 4)

Intracranial pressure

We identified no RCT evaluating the effects of intracranial pressure (ICP) monitoring on outcomes in acutely ill patients.

Depth of anesthesia and continuous electroencephalogram

No RCTs evaluating the impact of continuous depth of anesthesia and continuous electroencephalogram (EEG) monitoring devices on outcomes in the ICU were identified.

Ten studies evaluated the effects of bispectral index (BIS) monitoring during major surgical procedures, including one in patients undergoing abdominal surgery [61], two in mixed major and minor procedures [62, 63], three in cardiac surgery [64–66], two in major surgery [67, 68], one in neurosurgery [69], and one in the emergency department [70] (Table 3). All these studies showed a reduction in anesthetic recovery times and in adverse effects of the anesthetic agent.

Other neurological monitoring

We found no RCTs assessing the effects of jugular venous bulb saturation, transcranial Doppler, near-infrared spectroscopy, or cerebral microdialysis.

Metabolic monitoring

We identified no RCTs that assessed the impact of indirect calorimetry in the ICU.

Table 2 Randomized controlled studies of respiratory monitoring techniques. *ARDS*, acute respiratory distress syndrome; *ICU*, intensive care unit; *LOS*, length of stay; *PEEP*, positive end-expiratory pressure

Reference	No. of centers	No. of patients	Groups (*n*)	Setting/ population	End points	Monitoring variable	Impact on non-mortality outcomes	Impact on mortality outcomes
Oximetry								
[5]	1	24	Control group (12); experimental group (12)[a]	ICU/cardiac surgical patients	Usefulness of pulse oximetry and capnometry during mechanical ventilation weaning	Pulse oximetry and end-tidal CO_2	Positive	–
[46]	2	200	Group 1: pulse oximetry data "available" (100); group 2: pulse oximetry data "unavailable" (100)	Operating room/ mixed surgical procedures[h]	Incidence and severity of hypoxemia in operating room and anesthesia recovery room	Group 2: pulse oximetry available data	Positive	–
[47]	1	35	Group 1: pulse oximetry data "available" (20); group 2: pulse oximetry data "unavailable" to health-care team (15)	ICU/cardiac surgical patients	Detection of clinical unapparent desaturation episodes and necessity of blood gas analysis	Group 2: pulse oximetry available data	Positive	–
[48]	2	736	Group 1: pulse oximetry monitoring (358); group 2: without pulse oximetry monitoring (378)	Operating room/ mixed anesthetized patients[i]	Postoperative cognitive dysfunction	Group 1: pulse oximetry	Neutral	–
[49]	5	20,802	Group 1: oximetry group (10,312); group 2: control group (10,490)	Operating room/ mixed anesthetized patients[i]	Frequency of unanticipated perioperative events, changes in patient care, and the rate of postoperative complications	Group 1: pulse oximetry	Neutral	Neutral
[7]	1	48	Group 1: pulse oximetry and end-tidal CO_2 (24); group 2: control group (24)	Critically ill ventilated patients during inter- and intrahospital transportation	To detect potentially life-threatening problems in ventilated patients	Pulse oximetry and end-tidal CO_2	Positive	–
[50]	1	1,219	Group 1: oximetry group (589); group 2: control group (630)	Specialized post-cardiothoracic surgery care floor	Rate of transfer to an ICU	Continuous pulse oximetry	Neutral	–
Capnography								
[5]	1	24	Control group (12); experimental group (12)[a]	ICU/cardiac surgical patients	Usefulness of pulse oximetry and capnometry during mechanical ventilation weaning	Pulse oximetry and end-tidal CO_2	Positive	–
[7]	1	48	Group 1: pulse oximetry and end-tidal CO_2 (24); group 2: control group (24)	Critically ill ventilated patients during inter- and intrahospital transportation	To detect potentially life-threatening problems in ventilated patients	Pulse oximetry and end-tidal CO_2	Positive	–
[51]	1	97	Monitor group (57); monitor-blind group (40)	Prehospital; major trauma patients	Prehospital tight control of ventilation	End-tidal CO_2	Positive	–

[a] Control group: monitoring with blood arterial gases; experimental group: monitoring with capnometry and pulse oximetry;
[h] 60% of major procedures in both groups;
[i] 65% of patients were ASA-I risk in both groups;
[j] Conventional ventilation: tidal volume (V_t) = 12 ml/kg, minimum PEEP guided by FIO_2 and hemodynamics and normal $PaCO_2$ levels. Protective ventilation: tidal volume < 6 ml/kg, PEEP above the lower inflection point of the static pressure-volume curve, peak pressures < 40 cmH_2O, permissive hypercapnia and stepwise utilization of pressure-limited modes;
[k] Protective ventilation involved PEEP above the lower inflection point on the static pressure-volume curve, a tidal volume < 6 ml/kg, driving pressures of < 20 cm of water above the PEEP value, permissive hypercapnia, and preferential use of pressure-limited ventilatory modes

Table 2 Continued

Reference	No. of centers	No. of patients	Groups (*n*)	Setting/ population	End points	Monitoring variable	Impact on non-mortality outcomes	Impact on mortality outcomes
Ventilatory mechanics								
[52]	1	28	Conventional ventilation (13); protective ventilation strategy (15)[j]	ICU/ARDS	PaO_2/FiO_2 ratio, compliance, weaning rate, and mortality	Static pressure-volume curveand airway peak pressures	Positive	Neutral
[53]	1	71	Conventional ventilation (23); protective ventilation strategy (25)[j]	ICU/ARDS	Hemodynamic parameters and ventilatory variables	Static pressure-volume curve	Positive	–
[54]	2	53	Conventional ventilation (24); protective ventilation strategy (29)[k]	ICU/ARDS	Primary end point: 28-day mortality; secondary end points: survival to hospital discharge, occurrence of clinically detectable barotrauma, and weaning rate	Static pressure-volume curve, plateau and, airway peak pressures	Positive	Positive
[57]	8	120	Control group (60); limited-ventilation group (60)[b]	ICU/ARDS	Primary outcome: in-hospital mortality. Secondary outcomes: barotraumas; multiple organ dysfunction score; individual organ dysfunction; duration of mechanical ventilation; ICU and hospital LOS	Peak inspiratory pressure	Neutral	Neutral
[58]	25	116	Standard treatment group (58); pressure-limitation group (58)[c]	ICU/ARDS	Primary end point: 60-day mortality. Secondary end points: pneumothorax; multiorgan dysfunction; length of mechanical ventilation and ICU LOS	End-inspiratory plateau pressure	Neutral	Neutral
[55]	2	44	Control group (19); protocol group (18)[d]	ICU/ARDS	Pulmonary and systemic cytokine levels	Static pressure-volume curve	Positive	–
[59]	4	52	Traditional tidal volume patients; small tidal volume patients[e]	ICU/ARDS	Hospital mortality, requirements for PEEP or FiO_2, requirements for vasopressors, sedatives or neuromuscular blocking agents, and ventilator-free days	End-inspiratory plateau pressure	Neutral	Neutral
[60]	10	861	Traditional tidal volume; low tidal volume[f]	ICU/ARDS	Primary outcome: hospital mortality. Secondary outcomes: ventilator-free days; days without organ or system failure; barotraumas and IL-6 concentrations	End-inspiratory plateau pressure	Positive	Positive
[56]	8	103	Control group; high PEEP and low tidal volume group[g]	ICU/persistent ARDS	Primary end point: ICU mortality. Secondary end points: ventilator-free days; pulmonary; complications (barotrauma); extrapulmonary organ failures and hospital mortality	Static pressure-volume curve	Positive	Positive

[b] Control group: peak inspiratory pressure could be as high as 50 cm of water and tidal volume was maintained at 10–15 ml per kilogram. Limited ventilation: peak pressure limited to no more than 30 cmH_2O and tidal volumes < 8 ml/kg. PEEP between 5 and 20 cmH_2O to maintain adequate PaO_2;
[c] Standard treatment: assist-control ventilation, Vt of 10 ml/kg or above (up to 15), $PaCO_2$ between 38 and 42 mmHg. Pressure-limitation group: assist-control ventilation, Vt titrated to maintain the end-inspiratory plateau pressure at or below 25 cmH_2O; Tidal volume was maintained at less than 10 ml/kg but not lower than 6 ml/kg or 300 ml, irrespective of the plateau pressure;
[d] Control group: volume-control ventilation, tidal volume titrated to obtain normal $PaCO_2$, PEEP titrated according SaO_2; protocol group: tidal volume was set to obtain a plateau pressure less than upper inflection point of static pressure-volume curve and PEEP 2–3 cmH_2O above the lower inflection point of static pressure-volume curve;
[e] Traditional tidal-volume patients: tidal volume 10–12 ml/kg ideal body weight, reduced if inspiratory plateau pressure was > 55 cm H_2O; small tidal volume patients: tidal volume 5–8 ml/kg ideal body weight, to keep plateau pressure < 30 cmH_2O;
[f] Traditional tidal-volume group: volume assist control, tidal volume 12 ml/kg, plateau pressure ≤ 50, PEEP algorithm to determine oxygenation goals. Low tidal volume group: assist control, Vt 6 ml/kg, plateau pressure ≤ 30, PEEP algorithm to determined oxygenation goals;
[g] Control group: tidal volume was 9–11 ml/kg of predicted body weight (PBW) and PEEP > 5 cmH_2O. In the Pflex/LTV group, tidal volume was 5–8 ml/kg PBW and PEEP was set on day 1 at Pflex + 2 cmH_2O. In both groups, FiO_2 was set to maintain arterial oxygen saturation > 90% and PaO_2 70–100 mmHg, and respiratory rate was adjusted to maintain $PaCO_2$ between 35 and 50 mmHg.

Table 3 Randomized controlled studies of neurological monitoring techniques. *ED*, Emergency department; *BIS*, bispectral index

Reference	No. of centers	No. of patients	groups	Setting/ population	End points	Impact on non-mortality outcomes
[62]	1	80	BIS vs. no BIS	Operating room/mixed surgical procedures[a]	Anesthetic recovery times and anesthetic consumption	Positive
[67]	1	40	BIS vs. no BIS	Operating room/major gynecological surgery	Need for analgesia during surgery under total intravenous anesthesia	Positive
[61]	1	90	BIS vs. no BIS	Operating room/major abdominal surgery	Management of drugs and recovery after anesthesia	Positive
[64]	1	30	BIS vs. no BIS	Operating room/cardiac surgery	Titration of anesthetic drugs	Positive
[68]	Multi-center	2,463	BIS vs. no BIS	Operating room/mixed surgical population including major surgery[b]	Need for anesthetics and the incidence of awareness	Positive
[65]	1	40	BIS vs. no BIS	Operating room/coronary arterial bypass surgery	Reduction of propofol infusion rates	Positive
[66]	1	121	BIS vs. no BIS	Operating room/cardiac surgery with cardiopulmonary bypass	Impact of BIS in anesthetic decision making	Positive
[63]	1	2,463	BIS vs. no BIS	Operating room/mixed surgical procedures: high risk of awareness	Recovery anesthetic times	Positive
[70]	1	105	BIS vs. no BIS	Emergency department/acutely ill patients requiring sedation	BIS during procedural sedation in the ED	Positive
[69]	1	50	BIS vs. no BIS	Operating room/patients undergoing craniotomy	Recovery from anesthesia and altering drug administration	Positive

[a] Complexity of surgical procedures unclear;
[b] 70% of ASA III and IV in both groups

Discussion

Therapy based only on bedside clinical observations is often subjective, sometimes inadequate, and potentially harmful [71]. A wide range of clinical and technological tools allows multiple variables to be assessed at the bedside in an invasive or non-invasive, continuous, or intermittent manner. As monitoring of important physiological variables can guide a number of therapeutic interventions, one could anticipate a strong body of evidence demonstrating that monitoring improves outcomes; however, our literature review illustrates that few RCTs document a positive impact of any monitoring system on outcome.

Multiple limitations can prevent the accurate study of the impact of monitoring on outcomes. Firstly, the need for the monitoring system may be so obvious that it has never been tested, or to test it would be considered unethical. This is true for direct information about so-called vital signs. An RCT on electrocardiogram monitoring in patients with acute myocardial infarction, or on arterial pressure monitoring in shock states, would not be acceptable. Sometimes, also, the benefit/risk profile of a monitoring system may clearly be very good, e.g., for pulse oximetry monitoring; however, it is interesting that even very large RCTs with pulse oximetry could not show significant differences in late cognitive dysfunction, morbidity, or mortality rates [48, 49]. In addition, monitoring devices may never have been subjected to an RCT because they evaluate variables considered to be a sound basis for therapeutic interventions. ICP monitoring is a good example of this. ICP monitoring has not been subjected to an RCT evaluating its impact on outcomes; however, the prognostic value of ICP monitoring has been clearly established [72, 73]. Some observational cohort studies in patients with severe head trauma have demonstrated favorable effects of aggressive ICP-guided treatment on mortality when compared with historic controls [72, 74] or with patients managed in hospitals that did not use this type of monitoring [75]. ICP monitoring has been shown to reveal episodes of intracranial hypertension in severe head trauma patients without tomographic signs of intracranial hypertension [73]. Likewise, observational studies have suggested that monitoring of jugular bulb oxygen saturation (SjO_2) could enable early identification of transitory episodes of cerebral ischemia which would otherwise go undetected and untreated [76, 77] resulting in poorer neurological outcomes [78]. On the other hand, one could apply the same rationale to the PAC as the monitored cardiovascular variables have prognostic value, are less accessible by other techniques, and can be influenced by therapy.

Secondly, the extreme heterogeneity of the populations studied and the multiple therapeutic interventions that may be used can create excessive noise and limit study interpretation.

Thirdly, the way in which the monitoring system is used, and the accuracy with which monitoring data are collected and interpreted, can influence the final results. Monitoring systems cannot improve outcomes per se. The impact of a monitoring system will depend on its correct usage. There may also be significant variability in the in-

terpretation of measured variables by physicians, perhaps particularly true for the PAC [79]. It is difficult to differentiate between poor technology and good technology used poorly. On some occasions, the frontier between a direct monitoring benefit and the benefit of a monitoring-guided therapy is difficult to determine. This is the case in some studies using CI, DO_2, and VO_2 as resuscitation end points in critically ill patients [80–86]. All these studies used a "supranormal" hemodynamic target in the protocol group, whereas the control groups were treated to achieve lesser hemodynamic goals; hence, these studies were not included in our review, although other studies on "supranormal" hemodynamic targets, which included a control group that received standard treatment (when the clinician was unaware of monitoring measurements or when no effort was made to correct the measures obtained through the monitoring device), were included [37, 41–45].

The benefits of monitoring can also be influenced by the timing of the interventions used to correct the altered measurements. Early goal-directed therapy guided by $ScvO_2$ in the first 6 h after admission to an emergency department may improve mortality in severe sepsis and septic shock [40], but restoring SvO_2 in critically ill patients may not show the same benefit when this is achieved later in the course of disease [37]. Likewise, increasing DO_2 to supranormal levels may improve outcome in the early perioperative period [14, 17, 38, 39] but not later [37]; however, in these conditions, the question can be raised as to whether the clinical benefit may have been the result of more attentive and more aggressive therapy, with or without monitoring systems.

The safety and utility of invasive hemodynamic monitoring devices, including the PAC, have been debated for years. The PAC debate was highlighted in 1996 when the results of a prospective cohort study [87] suggested an increased 30-day mortality, greater intensity of care, and longer ICU stays in patients managed with a PAC. A recent European study, using the same methodology (based on a propensity score), could not reproduce these observations [88]. RCTs have not shown increased mortality or morbidity in patients managed with a PAC, except for one study that showed an increase in adverse in-hospital events attributable to higher rates of PAC infection [2]. The lack of demonstrated benefit with the use of PACs could be due to the lack of standardized therapeutic protocols for managing patients in the PAC groups. The same may or may not apply to other monitoring studies.

This literature review has its limitations. Firstly, monitoring is difficult to define; in particular, the distinction between monitoring and diagnostic techniques is often blurred. In addition, monitoring systems may not always reliably measure what they are supposed to. Secondly, one cannot define a homogenous patient population or setting where the monitoring system was assessed. As it is sometimes difficult to establish a distinction between the operating room and the ICU, we extended our review to patients undergoing major procedures, even though the data obtained may not apply fully to critically ill patients in the ICU; for example, data obtained by esophageal Doppler during major surgery [8, 23–26] may not be applicable to guiding fluid challenge in the ICU. Thirdly, due to the range of monitoring systems studied and the limited number and small size of available studies in several groups, we did not perform a meta-analysis, but results of meta-analyses for several individual monitoring systems, e.g., the PAC [89], have recently been published.

Conclusion

In conclusion, although it is often argued that monitoring systems should be subjected to objective evaluation, the value of conducting an RCT to demonstrate an impact of monitoring systems on outcomes may be questioned. Our literature review revealed that monitoring systems have not been well evaluated in RCTs, and that, of the few studies available, most have not yielded positive results. The literature search also revealed somewhat puzzling results, including the lack of evidence supporting the use of pulse oximetry, a widely accepted technique, but some evidence supporting the use of gastric tonometry, a technique which has not really stood the test of time. Finally, the PAC has been subjected to more evaluation than any other monitoring technique in acutely ill patients.

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