CRITICAL CARE

REVIEW

Clinical review: Goal-directed therapy - what is the evidence in surgical patients? The effect on different risk groups

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Abstract

Patients with limited cardiac reserve are less likely to survive and develop more complications following major surgery. By augmenting oxygen delivery index (DO_2I) with a combination of intravenous fluids and inotropes (goal-directed therapy (GDT)), postoperative mortality and morbidity of high-risk patients may be reduced. However, although most studies suggest that GDT may improve outcome in high-risk surgical patients, it is still not widely practiced. We set out to test the hypothesis that GDT results in greatest benefit in terms of mortality and morbidity in patients with the highest risk of mortality and have undertaken a systematic review of the current literature to see if this is correct. We performed a systematic search of Medline, Embase and CENTRAL databases for randomized controlled trials (RCTs) and reviews of GDT in surgical patients. To minimize heterogeneity we excluded studies involving cardiac, trauma, and paediatric surgery. Extremely high risk, high risk and intermediate risks of mortality were defined as >20%, 5 to 20% and <5% mortality rates in the control arms of the trials, respectively. Meta-analyses were performed and Forest plots drawn using RevMan software. Data are presented as odd ratios (OR; 95% confidence intervals (CI), and *P*-values). A total of 32 RCTs including 2,808 patients were reviewed. All studies reported mortality. Five studies (including 300 patients) were excluded from assessment of complication rates as the number of patients with complications was not reported. The mortality benefit of GDT was confined to the extremely high-risk group (OR = 0.20, 95% CI 0.09 to 0.41; $P < 0.0001$). Complication rates were reduced in all subgroups (OR = 0.45, 95% CI 0.34 to 0.60; $P < 0.00001$). The morbidity benefit was greatest amongst patients in the extremely high-risk subgroup (OR = 0.27, 95% CI 0.15 to 0.51; $P < 0.0001$), followed by the intermediate risk subgroup (OR = 0.43, 95% CI 0.27 to 0.67; $P = 0.0002$), and the high-risk subgroup (OR 0.56, 95% CI 0.36 to 0.89; $P = 0.01$). Despite heterogeneity in trial quality and design, we found GDT to be beneficial in all high-risk patients undergoing major surgery. The mortality benefit of GDT was confined to the subgroup of patients at extremely high risk of death. The reduction of complication rates was seen across all subgroups of GDT patients.

Introduction

A significant number of patients who undergo major surgery suffer postoperative complications, many of which may be avoidable [1,2]. The associated health and financial loss is significant, especially considering patients who suffer from postoperative complications suffer long-term morbidity [3]. A significant proportion of patients undergoing surgery suffer from postoperative complications, and identification of this cohort of patients may enable appropriate preventative measures to be taken [4]. Perioperative goal-directed therapy (GDT) aims to match the increased oxygen demand incurred during major surgery, by flow-based haemodynamic monitoring and therapeutic interventions to achieve a predetermined haemodynamic endpoint. When carried out early, in the right patient cohort, and with a clearly defined protocol, GDT has been shown to reduce postoperative mortality and morbidity [5].

Despite this, postoperative GDT is not carried out widely, perhaps due to the lack of evidence for its benefit from large multicenter randomized clinical trials. Scepticism about GDT may exist for a number of reasons: many of the studies performed may be considered outdated; the high mortality rates in some of the studies performed are not representative of current clinical

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practice; and pulmonary artery catheters (PACs) are used in many of the clinical trials but have been largely superseded by less invasive haemodynamic monitors. A recent meta-analysis has demonstrated that although studies prior to 2000 demonstrate a benefit in mortality, studies conducted after 2000 demonstrate a significant reduction in complication rates [5]. Furthermore, the reduction in complication rates is significant regardless of the type of haemodynamic monitor used.

We hypothesized that the benefits of GDT are greater in patients who are at higher risk of mortality. We defined risk by the mortality rate of the study population undergoing major surgery. We conducted this meta-analysis to determine if GDT in high-risk surgical patients undergoing major non-cardiac surgery improves postoperative mortality and morbidity, and if this was affected by the mortality risk among the population studied.

Methods

Eligibility criteria

We reported only randomized controlled trials, that reported morbidity (complications) and mortality as primary or secondary outcomes. GDT was defined as the term encompassing the use of haemodynamic monitoring and therapies aimed at manipulating haemodynamics during the perioperative period to achieve a predetermined haemodynamic endpoint(s). Studies with GDT started pre-emptively in the perioperative period (24 hours before, intraoperative or immediately after surgery) were included. The GDT must have an explicit protocol, defined as detailed step-by-step instructions for the clinician based on patient-specific haemodynamic data obtained from a haemodynamic monitor or surrogates (for example, lactate, oxygen extraction ratio), and predefined interventions carried out by the clinician in an attempt to achieve the goal(s). Interventions included fluid administration alone or fluids and inotropes together. As the use of inotropic agents was aimed at a specific haemodynamic goal(s) and titrated accordingly, fixed dose studies of inotropes were excluded. Only studies involving adult general surgical populations were included, and studies involving cardiac, trauma and paediatric surgery were excluded.

Information sources

A systematic literature search of MEDLINE (via Ovid), EMBASE (via Ovid) and the Cochrane Controlled Clinical trials register (CENTRAL, issue 4 of 2012) was conducted to identify suitable studies. Only articles written in English were considered. Date restrictions were not applied to the CENTRAL and MEDLINE searches. EMBASE was restricted to the years 2009 to 2012 [6]. The last search update was in April 2012.

Search strategy

We included the following search terms: goal-directed therapy, optimization, haemodynamic, goal oriented, goal targeted, cardiac output, cardiac index, oxygen delivery, oxygen consumption, cardiac volume, stroke volume, fluid therapy, fluid loading, fluid administration, optimization, supranormal, lactate and extraction ratio. Search terms were entered into the electronic databases using search strategy methods validated by the Cochrane collaboration (see Box 1 for search strategies used) [7]. In addition to searching electronic databases, previous review articles on the subject were hand-searched for further references.

Methodological quality of included studies

Methodological quality of included studies was assessed using criteria described by Jadad and colleagues [8]. The Jadad scale analyzes methods used for random assignment, blinding and flow of patients in clinical trials. The range of possible scores is 0 (lowest quality) to 5 (highest quality). Studies were not excluded based on Jadad scores.

Analysis of outcomes

Three investigators independently screened both the titles and abstracts to exclude non-pertinent studies. Relevant full text articles were then retrieved and analysed for eligibility against the pre-defined inclusion criteria. Information from selected studies was extracted using a standardized data collection form. Data were collected independently by three different investigators (GA, NA and CC) and discrepancies resolved by a fourth author (MC).

Hospital mortality was reported in all the included articles and was the primary outcome of our study. Morbidity, expressed as number of patients with complications, was the secondary outcome. Mortality risk groups were based on the definition of the high-risk surgical patient by Boyd and Jackson, such that patients whose risk of mortality was 5 to 19% and ≥20% were classified as high-risk and extremely high-risk, respectively [9]. We therefore performed subgroup analyses based on the control group mortality in each study. We created three subgroups based on the mortality rate of the control group. Mortality rates of 0 to 4.9%, 5 to 19.9%, and ≥20% were considered intermediate, high risk, and extremely high risk, respectively. Mortality and complications were analyzed according to the above subgroups. Studies were also analyzed according to the type of monitor used, type of interventions, the therapeutic goals, and the use of 'supranormal' physiological goals.

Statistical analysis

Dichotomous data outcomes were analysed using the Mantel-Haenszel random effects model and results

Box 1. Search strategies

1. MEDLINE database (OVID interface): the Cochrane highly sensitive search strategy was used:

#1. randomized Controlled Trials as Topic/
#2. randomized controlled trial/
#3. random Allocation/
#4. double Blind Method/
#5. single Blind Method/
#6. clinical trial/
#7. controlled clinical trial.pt.
#8. randomized controlled trial.pt.
#9. multicenter study.pt.
#10. clinical trial.pt.
#11. exp Clinical Trials as topic/
#12. or/1-11
#13. (clinical adj trial$).tw.
#14. ((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.
#15. randomly allocated.tw.
#16. (allocated adj2 random$).tw.
#17. or/13-16
#18. 12 or 17
#19. case report.tw.
#20. letter/
#21. historical article/
#22. or/19-21
#23. 18 not 22
#24. exp surgery/
#25. surgery.tw.
#26. surgery.mp.
#27. 24 or 25 or 26
#28. exp goal directed/ or goal directed.tw. or goal directed.mp.
#29. exp goal oriented/ or goal oriented.tw. or goal oriented.mp.
#30. exp goal target/ or goal target.tw. or goal target.mp.
#31. exp cardiac output/ or cardiac output.tw. or cardiac output.mp.
#32. exp cardiac index/ or cardiac index.tw. or cardiac index.mp.
#33. exp oxygen delivery/ or oxygen delivery.tw. or oxygen delivery.mp.
#34. exp oxygen consumption/ or oxygen consumption.tw. or oxygen consumption.mp
#35. exp cardiac volume/ or cardiac volume.tw. or cardiac volume.mp.
#36. exp stroke volume/ or stroke volume.tw. or stroke volume.mp.
#37. exp fluid therapy/ or fluid therapy.tw. or fluid therapy.mp.
#38. exp fluid loading/ or fluid loading.tw. or fluid loading.mp.
#39. exp fluid administration/ or fluid administration.tw. or fluid administration.mp.
#40. exp optimization/ or optimization.tw. or optimization.mp.
#41. exp optimisation/ or optimisation.tw. or optimisation.mp.
#42. exp supranormal/ or supranormal.tw. or supranormal.mp.
#43. exp lactate/ or lactate.tw. or lactate.mp.
#44. exp extraction ratio/ or extraction ratio.tw. or extraction ratio.mp.
#45. #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #0 or #41or #42 or #43 or #44
#46. #23 and #27 and #45

2. Embase (OVID interface): search restricted to the years 2009 to 2012:

#1. Clinical trial/
#2. Randomized controlled trial/
#3. Randomization/
#4. Single blind procedure/
#5. Double blind procedure/
#6. Crossover procedure/
#7. Placebo/
#8. Randomi?ed controlled trial$.tw.
#9. Rct.tw.
#10. Random allocation.tw.
#11. Random allocated.tw
#12. Allocated randomly.tw.
#13. (allocated adj2 random).tw.
#14. Single blind$.tw.
#15. Double blind$.tw.
#16. Placebo$.tw
#17. Prospective study/
#18. Or/1-17
#19. Case study/
#20. Case report.tw.
#21. Abstract report/or letter/
#22. Or/19-21
#23. 18 not 22
#24. surgery
#25. exp surgery/or surgery
#26. surg$
#27. 24 or 25 or 26
#28. exp heart/ or heart.mp.) and output.mp.
#29. exp heart output/ or heart output.mp.
#30. goal directed
#31. goal oriented
#32. goal target
#33. exp heart index/ or heart index.mp.
#34. exp heart stroke volume/ or heart stroke volume.mp.
#35. exp oxygen consumption/ or oxygen consumption.mp.
#36. oxygen delivery.mp.
#37. exp fluid therapy/
#38. fluid administration.mp
#39. fluid loading.mp.
#40. hemodynamic.mp
#41. supranormal.mp.
#42. optimisation.mp.
#43. optimization.mp.
#44. exp lactate/
#45. extraction ratio.mp
#46. #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45
#47. #23 and #27 and #46

3. Cochrane clinical trials database (CENTRAL):

#1. surgery in Trials
#2. surgical* in Trials
#3. surgery* in Trials
#4. #1 OR #2 OR #3
#5. cardiac near output* in trials
#6. cardiac near volume* in Trials
#7. cardiac near index* in Trials
#8. oxygen near delivery* in Trials
#9. oxygen near consumption* in Trials
#10. supranormal* in Trials
#11. stroke near volume* in Trials
#12. fluid near therapy* in Trials
#13. fluid near administration* in Trials
#14. fluid near loading* in Trials
#15. extraction near ratio* in Trials
#16. lactate* in Trials
#17. goal near directed* in Trials *
#18. goal near oriented* in Trials
#19. goal near target* in Trials
#20. Hemodynamic near optimization* in trials
#21. Haemodynamic near optimization * in trials
#22. Optimization* in trials
#23. Optimisation* in trials
#24. #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23
#25. #4 AND#24

presented as an odds ratio (OR) with 95% confidence intervals (CI). The meta-analysis was carried out using review manager ('Revman') for MAC (version 5.1, Cochrane collaboration, Oxford, UK). Statistical heterogeneity was assessed using the I^2 methodology. When an I^2 value of >50% was present heterogeneity and inconsistency were considered significant, and when it was >75% these were considered highly significant [10]. All *P*-values were two-tailed and considered statistically significant if <0.05.

Results

Included trials

The search strategy used in this study produced 12,938 potential titles (Figure 1). After screening of titles and abstracts, 307 references were identified as relevant to perioperative GDT. After further screening of titles and abstracts against our inclusion criteria, 85 references were retrieved for full text analysis. Detailed full text evaluation excluded 13 studies, as they were not randomized controlled trials [11-23]. Analysis of the remaining 72 randomized controlled trials produced the following exclusions: studies focusing on fluid management strategies (that is, liberal versus restrictive) [24-33], use of 'fixed dose' inotropic agents not titrated to a predetermined goal [34-38], cardiac surgery [39-44], trauma [45-52], paediatric surgery [53] and critically ill medical populations [54-62]. A study not using protocols to direct application of GDT was also excluded [63]. The quality of the trials was analysed using the Jadad score. The median Jadad score was 3.

Description of studies

A total of 32 studies were included in the meta-analysis (Table 1) [64-95]. These 32 studies included a total of 2,808 patients, 1,438 in the GDT arm and 1,370 in the control treatment arm. Five studies included patients who were considered extremely high risk, 12 included patients who were high risk, and 15 included patients who were intermediate risk. The intermediate-risk, high-risk, and extremely high-risk mortality subgroups included 1,569, 924, and 315 patients, respectively. There were similar numbers of patients in the GDT and control arms. Twenty studies initiated GDT at start of surgery, whilst the other studies initiated GDT before or immediately after surgery.

Mortality

Three studies did not report any deaths in the control or intervention group. All 32 studies included mortality rates (Figure 2). Although there was an overall benefit on mortality (OR 0.52, 95% CI 0.36 to 0.74; $P = 0.003$), subgroup analyses revealed that mortality benefit was seen only in studies that included extremely high risk patients (OR 0.20, 95% CI 0.09 to 0.41; $P < 0.0001$) but not for the intermediate-risk patients (OR 0.83, 95% CI 0.41 to 1.69; $P = 0.62$). There was a trend towards a reduction in mortality in the high risk group (OR 0.65, 95% CI 0.39 to 1.07; $P = 0.09$; Figure 2). Further subgroup analyses of mortality as an endpoint revealed that mortality was reduced in the studies using a pulmonary artery catheter (OR 0.3, 95% CI 0.15 to 0.60; $P = 0.0007$), fluids and inotropes as opposed to fluids alone (OR 0.41, 95% CI 0.23 to 0.73; $P = 0.002$), cardiac index or oxygen delivery index as a goal (OR 0.36, 95% CI 0.21 to 0.36; $P = 0.0003$), and a supranormal resuscitation target (OR 0.27, 95% CI 0.15 to 0.47; $P < 0.00001$) (Table 2).

Morbidity

Twenty-seven studies (including 2,477 patients) reported the number of patients with postoperative complications. Meta-analysis of these studies revealed an overall significant reduction in complication rates (OR 0.45, 95% CI 0.34 to 0.60; $P < 0.00001$; Figure 3). Consistent with the mortality benefits, the reduction in morbidity was greatest in the extremely high-risk group (OR 0.27, 95% CI 0.15 to 0.51; $P < 0.0001$). However, there was also a significant morbidity benefit in the intermediate risk group (OR 0.43, 95% CI 0.27 to 0.67; $P = 0.0002$) and the high-risk groups (OR 0.56, 95% CI 0.36 to 0.89; $P = 0.01$) (Figure 3). The reduction in the number of patients suffering postoperative complications was seen across all subgroups, apart from studies that did not use the oxygen delivery index (DO_2I; ml/minute/m^2), the cardiac index (CI; ml/minute/m^2), stroke volume (SV; ml), or corrected flow time (FTc) as a goal (OR 0.48, 95% CI 0.22 to 1.04; $P = 0.06$), although this approached statistical significance (Table 3).

Discussion

We believe that GDT in high-risk surgical patients is likely to have the greatest benefit if carried out early, in the right patient cohort and with a clearly defined protocol. We performed this meta-analysis to test the hypothesis that patients with the highest perioperative risk gain the greatest benefits from GDT. Studies without clearly defined GDT protocols and studies that initiated GDT late in the postoperative course were therefore excluded from our meta-analysis. Studies were stratified into different risk groups based on the mortality rate of the control group in the study. Heterogeneity in the year of study, patient demographics, type and urgency of surgery, and health care facilities among the different studies are likely to account for the difference in mortality rates.

A reduction in mortality associated with GDT was seen only in the extremely high-risk group of patients (baseline mortality rate of >20%). A baseline mortality rate of >20%

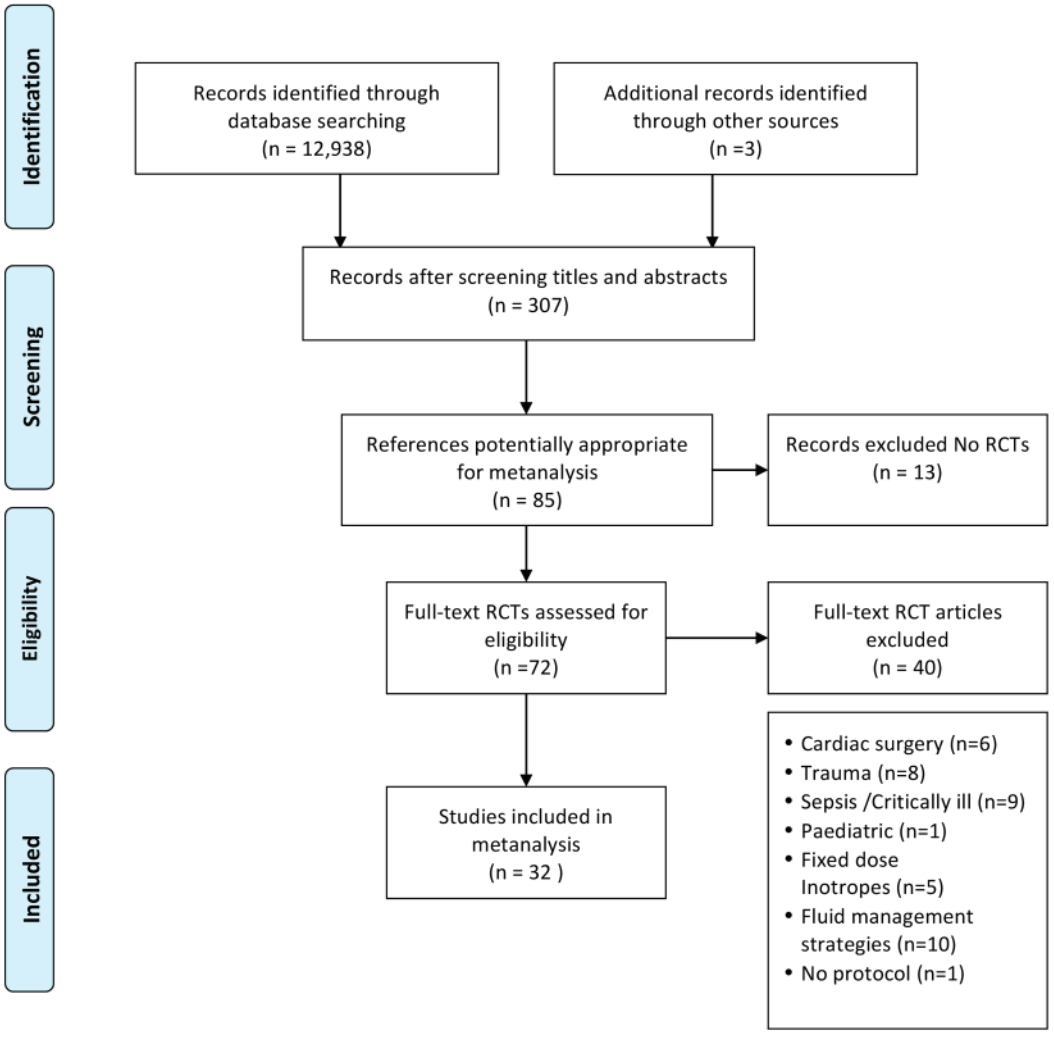

Figure 1. Flow diagram illustrating search strategy. RCT, randomised controlled trial.

is unusual in current practice [4,96]; in this sense it is interesting to note that two of five studies with a baseline mortality rate of >20% were carried out within the past decade. Neither of these studies demonstrated a survival benefit with GDT [80,97]. One of these studies demonstrated a reduction in complication rates [97], whilst the other demonstrated a trend towards a reduction in complication rates [80].

Supranormal physiological targets, targeting DO_2I or CI, the use of inotropes in addition to fluids, and the use of a PAC were also associated with an improvement in survival. As first demonstrated by Shoemaker and colleagues [19], a supranormal physiological target of global oxygen delivery to ameliorate the oxygen deficit incurred during major surgery is associated with a survival benefit. This is likely to explain the other associations with an improvement in morbidity across all risk groups. The combination of fluids and inotropes is more likely to achieve a supranormal physiological target, as opposed to fluids alone. All eight studies using the oesophageal doppler used fluids alone, reflected by the lack of mortality benefit with the use of FTc or SV as a target. The survival benefit associated with the use of PACs is unlikely to be due to the use of the PACs *per se*. The survival benefit associated with PAC use may be explained by a number of factors. These include the ability to measure and therefore achieve supranormal DO_2I, and the use of inotropes in addition to fluids in all studies using a PAC.

The reduction in the number of patients suffering post-operative complications was seen across all subgroups, apart from studies that did not use DO_2I, CI, SV, or FTc as a goal. However, there was a trend towards fewer complications among the GDT cohort in these studies. Goals used by these studies included lactate, pulse pressure variation, plethysmographic variability index,

Table 1. Summary of included studies

Study	Year	Jadad score	Type of surgery	Number of patients GDT group	Number of patients control group	Type of monitor in GDT group	Intervention type	Goals in GDT group	Goals in control group	Mortality GDT (%)	Mortality control (%)	Complications GDT (%)	Complications control (%)
Bender *et al.* [64]	1997	1	Elective vascular/aortic	51	53	PAC	Fluid and inotropes	CI ≥ 2.8 PAWP 8-14 SVR <1100	Standard care	1.96	1.9	13.73	13.21
Benes *et al.* [65]	2010	3	Elective abdominal	60	60	Flotrac	Fluid and inotropes	SVV <10% CI ≥2.5	MAP >65 HR <100 CVP 8-12	1.67	3.3	30	58.33
Berlauk *et al.* [66]	1991	2	Peripheral vascular surgery	68	21	PAC	Fluid and inotropes	CI ≥2.8 PAWP 8-14 SVR <1100	Standard care	1.47	9.5	16.7	42.8
Bonazzi *et al.* [67]	2002	2	Elective vascular	50	50	PAC	Fluid and inotropes	CI >3.0 PAWP 10-18 SVR <1,450 DO_2I >600	Standard care	0	0	4	8
Boyd *et al.* [68]	1993	1	Abdominal/vascular	53	54	PAC	Fluid and inotropes	MAP 80-110 PAWP 12-14 SpO_2 >94% Hb >12 UO >0.5ml/kg/h DO_2I >600	MAP 80-110 PAWP 12-14 SpO_2 >94% Hb >12 UO >0.5ml/kg/h	5.66	22.2	NS	NS
Buettner *et al.* [69]	2008	2	Major abdominal or gynaecological	40	40	PiCCO	Fluids	SPV <10% HCt >23% Normal clotting	Standard care	0	2.5	NS	NS
Cecconi *et al.* [70]	2011	4	Total hip replacement	20	20	Flotrac	Fluid and inotropes	SV change DO_2I >600	Standard care	0	0	80	100
Challand *et al.* [71]	2012	5	Major open/ laparoscopic colorectal	89	90	OD	Fluids	SV change	Standard care	5.62	4.4	33.71	28.89
Conway *et al.* [72]	2002	2	Major bowel resection	29	28	OD	Fluids	FTc >0.35 SV change	Standard care	0	3.6	17.24	32.14
Donati *et al.* [73]	2007	3	Elective major abdominal/aortic	68	67	CVC	Fluids	O_2ER <27% MAP >80 UO >0.5 CVP 8-12 Hb >10	MAP >80 UO >0.5 CVP 8-12 Hb >10	2.94	3	13.24	40.3
Forget *et al.* [74]	2010	2	Major intrabdominal	41	41	Masimo pulsoximeter	Fluids	PVI <13%	Standard care	4.88	0	78.05	100

Continued overleaf

Table 1. Continued

Study	Year	Jadad score	Type of surgery	Number of patients GDT group	Number of patients control group	Type of monitor in GDT group	Intervention type	Goals in GDT group	Goals in control group	Mortality GDT (%)	Mortality control (%)	Complications GDT (%)	Complications control (%)
Gan *et al.* [75]	2002	5	Elective general, urological, gynaecologic	50	50	OD	Fluids	FTc >0.35 SV change	Increase HR >20% baseline sBP <90 or CVP <20% baseline	0	0	42	76
Harten *et al.* [76]	2008	3	Emergency abdominal	14	15	Lidco	Fluids	PPV	Standard care	7.14	13.3	50	26.67
Jhanji *et al.* [77]	2010	3	Major surgery	45	45	LiDCO	Fluids	SV	CVP standard care	11.11	13.3	57.58	66.67
Lobo *et al.* [78]	2000	3	Major surgery	19	18	PAC	Fluid and inotropes	DO_2I >600	Standard care	15.79	50	31.58	66.67
Lobo *et al.* [79]	2006	3	Major surgery	25	25	PAC	Fluid and inotropes	PWP 12-16 MAP 70-110 HCt >30%, SAO_2 >94% UO >0.5 DO_2I >600	PAWP 12-16 MAP 70-110 HCt >30% SaO_2 >94% UO >0.5	8	28	16	52
Lopes *et al.* [80]	2007	2	Major surgery	17	16	IBPplus; Dixtal	Fluids	ΔPP <10%	Standard care	11.76	31.3	41.18	75
Mayer *et al.* [81]	2010	2	Major gastrointestinal surgery	30	30	Flotrac	Fluid and inotropes	CI >2.5 SVV <12%	CVP 8-12 MAP >65 UO >0.5	6.67	6.7	20	50
Noblett *et al.* [82]	2006	5	Colorectal	51	52	OD	Fluids	FTc >0.35 SV change	Standard care	0	1.9	1.96	15.38
Pearse *et al.* [83]	2005	3	Major surgery	62	60	LiDCO	Fluid and inotropes	DO_2I >600	SaO_2 ≥94% Hb >8 Temp >37°C HR <100 or <20 above baseline MAP 60-100 CI ≥2.5	11.29	15	43.55	68.33
Senagore *et al.* [84]	2009	3	Elective lap colorectal	42	22	OD	Fluids	SV response	Standard care	2.38	4.7	NS	NS
Shoemaker *et al.* [85]	1988	2	Major surgery	28	60	PAC	Fluid and inotropes	CI >4.5 VO_2 >170 DO_2I >600	Standard care	3.57	30	28.5	50
Sinclair *et al.* [86]	1997	2	Neck of femur repair	20	20	OD	Fluids	FTc >0.35 SV change	Standard care	5	10	NS	NS

Continued overleaf

Table 1. Continued

Study	Year	Jadad score	Type of surgery	Number of patients GDT group	Number of patients control group	Type of monitor in GDT group	Intervention type	Goals in GDT group	Goals in control group	Mortality GDT (%)	Mortality control (%)	Complications GDT (%)	Complications control (%)
Szakmany *et al.* [87]	2005	3	Major abdominal	20	20	PiCCO	Fluids	ITBV 850-950 ml/m^2	CVP Standard care	9.09	5	NS	NS
Ueno *et al.* [88]	1998	2	Hepatic resection	16	18	PAC	Fluid and inotropes	CI >4.5 VO_2 >170 DO_2I >600	SpO_2 >95% Mean PAOP 11-15 mmHg Hb >10	0	11.1	0	27.78
Valentine *et al.* [89]	1998	3	Aortic	60	60	PAC	Fluid and inotropes	CI >2.8 PAWP 8-15 SVR <1100	Standard care	5	1.7	25	16.67
Van Der linden *et al.* [90]	2010	4	Vascular	40	17	LiDCO + CVC	Fluid and inotropes	CI >2.5	Standard care	7.5	0	10	0
Venn *et al.* [91]	2002	3	Neck of femur repair	30	60	OD	Fluids	FTc >0.35 SV change	Standard care	10	6.9	34.4	72.4
Wakeling *et al.* [92]	2005	3	Colorectal	67	67	OD	Fluids	SV change	Standard care	0	1.5	35.82	56.72
Wenkui *et al.* [93]	2010	3	Elective GI Cancer	109	105	Lactate	Fluids	Lactate <1.6	Standard care	0.92	3.8	22.94	33.3
Wilson *et al.* [94]	1999	4	Major surgery	92	46	PAC	Fluid and inotropes	DO_2I >600	Standard care	3.26	17.4	41.3	60.87
Ziegler *et al.* [95]	1997	2	Vascular	32	40	PAC	Fluid and inotropes	PAOP >12	Standard care	9.38	5	25	27.5

CI, cardiac index (ml/minute/m^2); CVP, central venous pressure (cmH_2O); CVC, central venous catheter; DO_2I, oxygen delivery index (ml/minute/m^2); FTc, corrected flow time; GDT, goal-directed therapy; Hb, haemoglobin (g/dl); Hct, haematocrit (%); HR, heart rate (beats/minute); ITBV, intrathoracic blood volume; VO_2, oxygen consumption (ml/minute); MAP, mean arterial pressure (mmHg); NS, not stated; O_2ER, oxygen extraction ratio (%); OD, oesophageal Doppler; PAC, pulmonary artery catheter; PAOP, pulmonary artery occlusion pressure (mmHg); PAWP, pulmonary artery wedge pressure (mmHg); PP, pulse pressure; PPV, pulse pressure variation; PVI, plethysmographic variability index; SAO_2, aterial oxygen saturation; sBP, systolic blood pressure (mmHg); SpO_2, oxygen saturation (%); SV, stroke volume (ml); SVR, systemic vascular resistance (dynes-s/cm^5); SVV, stroke volume variation (%); UO, urine output (ml/kg/h); VO_2, oxygen consumption (ml/minute).

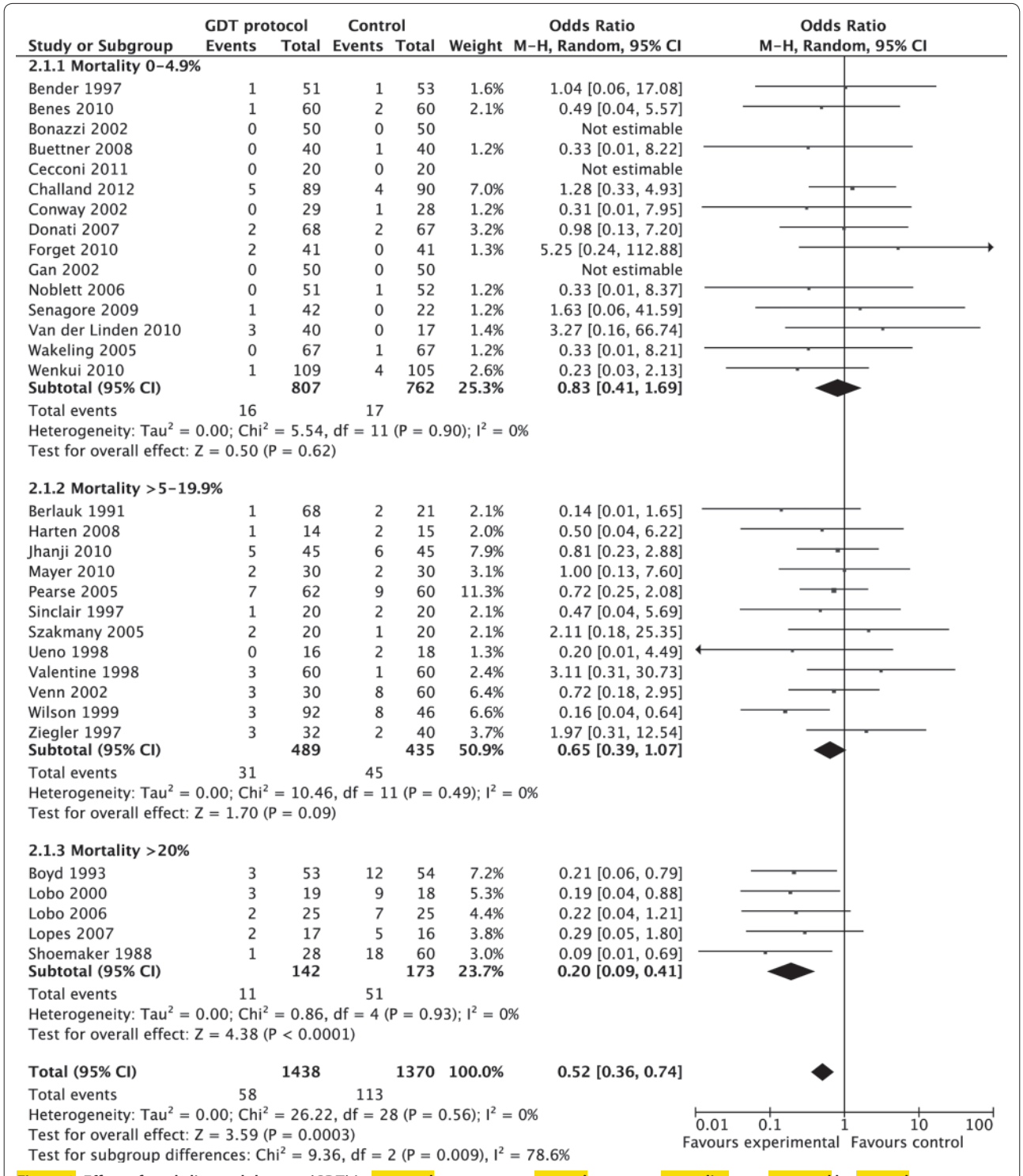

Figure 2. Effect of goal-directed therapy (GDT) in protocol group versus control group on mortality rate, grouped by control group mortality rates. CI, confidence interval; M-H, Mantel-Haenszel.

pulmonary artery occlusion pressure, oxygen extraction ratio, and intrathoracic blood volume [73,74,76,80,87, 93,95]. Consistent with the trends seen with mortality, the reduction in complication rates was most profound in the extremely high-risk group of patients, protocols with supranormal physiological targets, targeting DO_{2I} or CI, and the use of inotropes in addition to fluids. In contrast to the benefits seen in mortality, however, the subgroup

Table 2. Mortality by subgroup analysis

	Number of studies	Number of patients in GDT group	Mortality in GDT group (%)	Number of patients in control group	Mortality in control group (%)	Odds ratio	95% CI	*P*-value
Risk group								
Intermediate risk	15	807	16 (2.0)	762	17 (2.2)	0.83	0.41-1.69	0.62
High risk	12	489	31 (6.3)	435	45 (10.3)	0.65	0.39-1.07	0.09
Extremely high risk	5	142	11 (7.7)	173	51 (29.5)	0.2	0.09-0.41	<0.0001
Fluid/inotropes								
Fluid	16	732	25 (3.4)	738	38 (5.1)	0.72	0.42-1.23	0.23
Fluid + inotrope	16	706	33 (4.7)	632	75 (11.9)	0.41	0.23-0.73	0.002
Goal								
Supranormal	9	365	19 (5.2)	351	65 (18.5)	0.27	0.15-0.47	<0.00001
Normal	23	1073	39 (3.6)	1,019	48 (4.7)	0.80	0.51-1.27	0.35
Target								
CI/DO_2I	15	674	30 (4.5)	592	73 (12.3)	0.36	0.21-0.36	0.0003
FTc/SV	9	423	15 (3.5)	434	23 (5.3)	0.78	0.40-1.52	0.46
Other	8	341	13 (3.8)	344	17 (4.9)	0.78	0.35-1.72	0.54
Type of monitor								
PAC	11	494	20 (4.0)	445	62 (13.9)	0.3	0.15-0.6	0.0007
ODM	8	378	10 (2.6)	389	17 (4.4)	0.77	0.35-1.69	0.51
Other	13	566	28 (4.9)	536	34 (6.3)	0.74	0.43-1.28	0.28

CI, cardiac index (ml/minute/m^2); DO_2I, oxygen delivery index (ml/minute/m^2); FTc, corrected flow time; ODM, oesophageal doppler monitor; PAC, pulmonary artery catheter; SV, stroke volume (ml).

using the 'other cardiac output monitors' had a greater reduction in complication rate than the subgroup using the PAC. This may relate to the complexity and invasive nature of the PAC in comparison to less invasive cardiac output monitors [98-100].

There remains significant heterogeneity in complication rates among postoperative patients in different centres [4,96]. Although differences in patient demographics are not modifiable, optimal management of the high-risk surgical patient during the perioperative phase may improve overall outcomes. Despite a requirement for an increase in healthcare resources to offer early GDT to high-risk surgical patients, reductions in immediate postoperative complications translate to overall benefits in healthcare costs. Any perceived increase in resource allocation results in a lower patient mortality and morbidity, and therefore a financial saving [101]. Furthermore, reduction in immediate postoperative complications has far-reaching effects, with a potential beneficial effect on long-term survival [102].

This meta-analysis includes trials from 1988 to 2011. As surgical techniques, perioperative care, and patient selection have been refined over these years, the overall mortality of patients has reduced. As such, the applicability of historical trials to current day practice may not be valid. This has recently been evaluated in a meta-analysis of 29 perioperative GDT trials carried out between 1995 and 2008 [5]. There was an approximate halving of mortality rates in the control group every decade (29.5%, 13.5%, 7%). Despite a reduction in mortality rate, the morbidity rate remained constant, with approximately a third of patients experiencing postoperative complications. Perioperative GDT should therefore offer a reduction in complication rates in current practice.

We acknowledge that there is an element of subjectivity in our decision to include trials in this meta-analysis. Many studies were conducted in single centres with limited patient numbers, and not all studies conducted were of a high quality design. This is reflected by the median Jadad score of 3. The effect of study quality on outcomes of GDT trials has been analysed in a recent meta-analysis [5]. Most perioperative GDT trials were singe-centre studies, and only a few were conducted in a double-blind manner. In contrast to the lower quality studies, the higher quality studies (defined as a Jadad score of at least 3) did not demonstrate any benefit in mortality reduction. However, the beneficial effect of reduction in perioperative complication rates was evident irrespective of trial quality.

One of the main limitations of this study is the lack of data on the volume and type of fluids given, and the dose of inotropes used due to variation and inconsistencies in

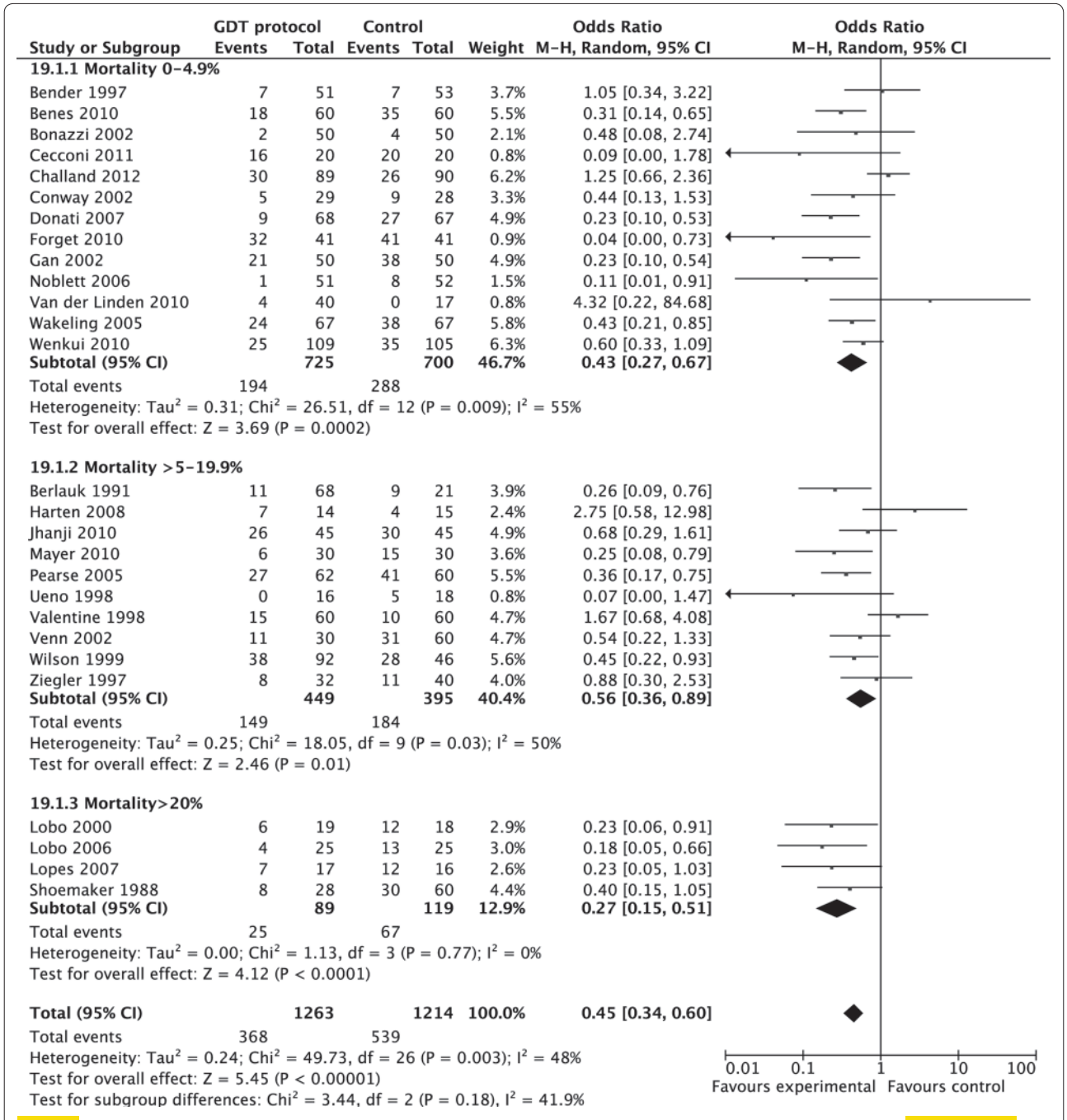

Figure 3. Effect of goal-directed therapy (GDT) in protocol group versus control group on the number of patients with complications, grouped by control group mortality rates. CI, confidence interval; M-H, Mantel-Haenszel.

reporting. However, it must be emphasised that the absolute volume of fluids used *per se* is not as important as the way in which fluid is given. Fluid therapy must be titrated against a patient's response to a fluid challenge, with the use of haemodynamic monitoring [103]. Such 'goal-directed' fluid therapy must also be given at the right time, as GDT is not beneficial after complications have already developed [104,105].

One of the other limitations is missing data on the number of patients with complications, due to variations in reporting of complications in the literature, with some studies reporting the number of complications as opposed to the number of patients with complications. Furthermore, we acknowledge that the definitions and coding of complications are likely to vary between studies. We have analysed data extracted from studies,

Table 3. Complications by subgroup analysis

	Number of studies	Number of patients in GDT group	Patients with complications in GDT group (%)	Number of patients in control group	Patients with complications in control group (%)	Odds ratio	95% CI	*P*-value
Risk group								
Intermediate risk	13	727	194 (26.7)	698	288 (41.3)	0.43	0.27-0.67	0.0002
High risk	10	449	149 (33.2)	395	184 (46.6)	0.56	0.36-0.89	0.01
Extremely high risk	4	89	25 (28.1)	119	67 (56.3)	0.27	0.15-0.51	<0.0001
Fluid/inotropes								
Fluid	12	610	198 (32.5)	636	299 (47.0)	0.47	0.30-0.73	0.0007
Fluid + inotropes	15	653	170 (26.0)	578	240 (41.5)	0.44	0.30-0.64	<0.0001
Goal								
Supranormal	8	312	101 (32.4)	297	153 (51.5)	0.34	0.23-0.51	<0.00001
Normal	19	951	267 (28.1)	917	386 (42.1)	0.51	0.36-0.73	0.0002
Target								
CI/DO2I	14	621	162 (26.1)	538	229 (42.6)	0.41	0.28-0.61	<0.0001
FTc/SV	7	361	118 (32.7)	392	180 (45.9)	0.50	0.30-0.84	0.009
Other	6	281	88 (31.3)	284	130 (45.8)	0.48	0.22-1.04	0.06
Type of monitor								
PAC	10	441	99 (22.4)	391	129 (33.0)	0.49	0.30-0.80	0.005
ODM	6	316	92 (29.1)	347	150 (43.2)	0.46	0.25-0.86	0.01
Other	1!	506	177 (35.0)	476	260 (54.6)	0.41	0.26-0.64	0.0001

CI, cardiac index (ml/minute/m^2); DO_2I, oxygen delivery index (ml/minute/m^2); FTc, corrected flow time; ODM, oesophageal doppler monitor; PAC, pulmonary artery catheter; SV, stroke volume (ml).

rather than data of individual patients. As some of the studies included were carried out several years ago, obtaining data on individual patients would not have been possible. Despite these limitations, the results remain consistent across many subgroups of patients, and are consistent with other recent meta-analyses, supporting our hypothesis [5,106] and the recent EUSOS study which showed a mortality of 4% [107]. The benefit in terms of reduction of complications of GDT in the intermediate risk group may have implications for the majority of the European surgical population.

Conclusion

Despite heterogeneity in trial quality and design, early GDT among high-risk surgical patients has a significant benefit in reducing rates of complications. There is also an associated reduction in mortality among patients at extremely high risk of perioperative death. GDT is of greatest benefit in patients with the highest risk of mortality.

This is part of a series on *Perioperative monitoring*, edited by Dr Andrew Rhodes

Abbreviations

CI, cardiac index (ml/minute/m^2); DO_2I, oxygen delivery index (ml/minute/m^2); FTc, corrected flow time; GDT, goal-directed therapy; PAC, pulmonary artery catheter; SV, stroke volume (ml).

Competing interests

MC: Edwards Lifesciences, LiDCO, Deltex, Applied Physiology, Masimo, Bmeye, Cheetah, Imacor (travel expenses, honoraria, advisory board, unrestricted educational grant, research material). MH: lecture fees from Edwards, Deltex, hutchinson technology and LidCO. AR: honoraria and advisory board for LiDCO. Honoraria for Covidien, Edwards Lifesciences and Cheetah. NA: travel expenses from LiDCO.

Published: 5 March 2013

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doi:10.1186/cc11823
Cite this article as: Cecconi M, *et al.*: Clinical review: Goal-directed therapy - what is the evidence in surgical patients? The effect on different risk groups. *Critical Care* 2013, **17:**209.

Review

Clinical review: How is risk defined in high-risk surgical patient management?

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Published online: 9 February 2005
This article is online at http://ccforum.com/content/9/4/390

Critical Care 2005, **9**:390-396 (DOI 10.1186/cc3057)

Abstract

The definition of risk in surgical patients is a complex and controversial area. Generally risk is poorly understood and depends on past individual and professional perception, and societal norms. In medical use the situation is further complicated by practical considerations of the ease with which risk can be measured; and this seems to have driven much risk assessment work, with a focus on objective measurements of cardiac function. The usefulness of risk assessment and the definition of risk is however in doubt because there are very few studies that have materially altered patient outcome based on information gained by risk assessment. This paper discusses these issues, highlights areas where more research could usefully be performed, and by defining limits for high surgical risk, suggests a practical approach to the assessment of risk using risk assessment tools.

Introduction

What is a high-risk patient? What do we mean by risk? Why do we want to assess risk? How do we want to use this analysis? As intensivists we use risk assessment to identify a highly selected group of patients who are at such high risk of morbidity and mortality that they might benefit from high-dependency unit or intensive care unit (ICU) care perioperatively, and we seek to identify those patients who might benefit from haemodynamic manipulation to improve these outcomes. The intensivist's perception of risk and aims of risk assessment may well differ from that of the patient, carers and other doctors, leading to communication difficulties. The present paper explores risk, the need for risk assessment, perception of risk, and various methods for assessing risk. We also explore some of the problems and misconceptions about risk assessment.

The perception of risk

As a society we do not think rationally about risk. Our ability to risk assess is poor and we seem to be driven by fear and hope as much as by rational evidence. The terms applied to risk are also confusing; it is unlikely that many decision-makers can differentiate the information available from 'relative risk', 'absolute risk' and 'number needed to treat' (see Table 1). There is also little to suggest that the knowledge of risk influences public response – recent examples include the scare over 'mad cow disease' and the MMR vaccine [1] – and there is little research available as to how knowledge of patient risk modifies our behaviour as doctors. Furthermore, there is little evidence of any reduction in morbidity or mortality following the institution offering a risk assessment protocol in the clinical setting [2]. The poor uptake of risk identification strategies and optimisation protocols may be as much to do with our blunted cultural perception of risk as with resource limitations. The patient, their family, the surgeon, the anaesthetist, the intensivist and the hospital administrator are all likely to perceive risk in entirely different ways while labouring under the misapprehension of a common dialogue.

In the context of patient treatment when discussing risk the perspective of the individuals involved will not only receive the risks differently, but will also prioritise and compare the risks in a different way (Table 2). Furthermore, there is confusion between risks when used as a screening tool: it is, for example, probable that most individuals with a poor outcome will not manifest the risk factor, and conversely some individuals with a good outcome will have the risk [3]. The discussion of risk can therefore be fraught with difficulty and in many cases is open to misinterpretation and profound misunderstandings.

Why is risk assessed?

The reason for risk assessment depends on who is making the assessment. Risk assessment is performed both for the individual patient and for a patient cohort. A doctor may assess the individual patient's risk in order to better inform

APACHE = Acute Physiology and Chronic Health Evaluation; ASA = American Society of Anesthesiologists; ICU = intensive care unit; POSSUM = Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity.

Table 1

Different ways to describe 'risk'

Placebo arm ($n = 1000$)	Treatment arm ($n = 1000$)	Relative risk reduction	Absolute risk reduction	Number needed to treat
200	100	50	10	10
20	10	50	1	100
2	1	50	0.1	1000

In this example, a treatment trial involving 2000 patients, 'relative risk reduction' remains the same while 'absolute risk reduction' and 'number needed to treat' show differences in the appreciation of risk as the success of the treatment is modelled to change.

Table 2

Important milestones in the perception of high risk

Patient	Ability to return to work
	Possibility of disability
	Success of operation
Family	Will patient be able to resume role as carer?
	Will patient survive?
Nurse	Infection transmission
	Violence towards self
Surgeon	Likelihood of operative success
	Possibility of operative misadventure
Anaesthetist	Likelihood of surviving 30 days
	Likelihood of surviving the anaesthetic
Intensivist	Likelihood of leaving the intensive care unit
	Prolonged stay on the intensive care unit
Administrator	Outcome poorer than comparative unit
	Care costing more than allocated

the patient and to allow consensual decisions for procedures to be undertaken. Risk assessment might allow consideration of a change in plan to reduce that individual's risk; for example, a more limited operation, modification of the planned anaesthetic technique or perioperative haemodynamic optimisation. In a more complex format, risk is assessed to allow suitable targeting of therapeutic options and decision-making with regard to treatment choices so that a suitable balance of risks, often between the possible side effects and dangers of surgery and the potential success of treatment, can be made. Implicit in risk assessment for the individual is the intention of subsequent action to achieve risk reduction, but as already noted this is often not achievable.

At an institutional level the assessment of risk for a group of patients can be used to target resources, both financially and in terms of personnel and facilities. In this context, risk assessment is no longer targeted towards the individual patient. Similarly, risk assessment can be used as part of a standardisation tool to allow comparison of outcomes between different surgeons or hospitals who are undertaking similar procedures. Risk assessment tools need to be able to account for differences in populations such that one hospital's cohort of patients might be more frail at the outset.

What is a high-risk surgical patient?

In the context of critical care 'high risk' is used to donate the global risk of mortality or morbidity, particularly with regard to organ failure, compared with other groups at lower risk. As regards surgical patients, information provided by the National Confidential Enquiry into Peri-Operative Deaths helps to address the issue of where a baseline for risk might lie [4]. There are between 2.8 million and 3.3 million operations per year in England, Wales and Northern Ireland. The risk of death within 30 days of any operation has been estimated as between 0.7% and 1.7%. The National Confidential Enquiry into Peri-Operative Deaths also provides information that we are not good at estimating surgical risk; surgeons perceived that was increased risk in only 66% of the patients that actually died, which equally means that an increased risk was not identified in 44% of these patients.

From a practical point of view 'high risk' can probably be defined in two different ways: the first is relevant to an individual and suggests that the risk to an individual is higher than for a population; the second compares the risk of the procedure in question with the risk of surgical procedures as a whole. In the first scenario it would be tempting to state that risk is 'high' if the risk for an individual falls above two standard deviations of the risk for the entire population undergoing that type of surgery. This could be described as a statistical approach but we suggest that this is only rarely applicable due to lack of knowledge of baseline risk and also to general misunderstandings of this type of statistical analysis. We suggest that a far more understandable description of high risk would be if the individual's risk of mortality is either $>5\%$ or twice the risk of the population undergoing that procedure. The second description also addresses the second scenario, and we suggest that a high-risk procedure is one with mortality greater than 5%.

Furthermore, we would suggest that surgical patients for whom the probable mortality is greater than 20% should be

Table 3

Control group mortality in four well-known studies that have investigated 'high-risk' surgical patients

Study	Mortality (%)
Shoemaker and colleagues [6]	33
Boyd and colleagues [57]	22.2
Wilson and colleagues [58]	17
Sandham and colleagues [59]	7.7

considered 'extremely high-risk' patients. Studies show that mortality for this cohort can be improved by haemodynamic optimisation and their care should ideally be discussed with ICU preoperatively. We understand that, at least in the United Kingdom, there are limited ICU resources available for this but we should recognise that there is evidence that pre-emptive strategies could reduce the mortality for this group. There is conflicting evidence that intraoperative haemo-dynamic optimisation may modify the outcome for surgical patients with a predicted mortality less than 20%. An improved outcome for this cohort may be seen in reduced hospital bed-days rather than a reduction in mortality, but due to the number of surgical patients even modest reductions in length of stay would have huge resource benefits.

We have made some suggestions of general limits for defining 'high risk'. We fully understand, however, that how 'high risk' is actually defined is influenced by all the personal perceptions and expectations already mentioned, as well as the more pragmatic possibilities of influencing change and costs. It is also interesting to compare the presented definitions with the various studies of 'high risk' surgical patients where different levels of risk have been thought to be appropriate (Table 3).

Risk assessment in surgical patients

There are a number of tests that can be used to preoperatively stratify risk in surgical patients. These can be divided into general tests and scores, and those specific for myocardial problems; specifically, postoperative myocardial infarction and sudden cardiac death. There are various risk assessment scores that aim to identify other morbidity-specific outcomes, such as respiratory failure, wound infection or sepsis, but we have limited ourselves to mortality and cardiac outcomes as these constitute the best known scores and tend to be applicable to wider groups of operative procedures.

General preoperative risk stratification

There are a number of methods by which risk can be assessed preoperatively. These can be related to the type of surgery and the known risks and outcomes of the planned procedures, or they can be related to factors within the patient themselves. Risk factors related to the surgery include the surgical procedure and whether that procedure is undertaken in an elective fashion or as an emergency. A number of databases have demonstrated the higher risk associated with emergency procedures. Risk factors related to the patient can be relatively simple to isolate, such as the patient's age, or can take into account various methods for assessing comorbidity or physiological reserve. The simplest and most widely used method for assessing the comorbidity is the American Society of Anesthesiologists (ASA) grading on a scale of I to IV; this combined with the type of urgency of surgery has been shown to be related to postoperative mortality [5]. Other pragmatic assessments of preoperative comorbidity have been employed by various investigators attempting to identify patients at higher risk of morbidity and mortality following surgery. One method, originally described by Shoemaker and colleagues [6] and adapted by Boyd and colleagues [7], identifies patients by the pre-selected list of criteria presented in Table 4. While these types of preoperative assessment clearly identify patients at much higher risk than those in the general population of patients undergoing surgery, they are open to some subjective interpretation that makes them less robust to use if they are carried outside the original institution.

Table 4

Clinical criteria for high-risk surgical patients used by Shoemaker and colleagues [6] and adapted by Boyd and colleagues [7]

Previous severe cardiorespiratory illness – acute myocardial infarction, chronic obstructive pulmonary disease, or stroke
Late-stage vascular disease involving aorta
Age >70 years with limited physiological reserve in one or more vital organs
Extensive surgery for carcinoma (e.g. oesophagectomy, gastrectomy cystectomy)
Acute abdominal catastrophe with haemodynamic instability (e.g. peritonitis, perforated viscus, pancreatitis)
Acute massive blood loss >8 units
Septicaemia
Positive blood culture or septic focus
Respiratory failure: PaO_2 <8.0 kPa on FIO_2 >0.4 or mechanical ventilation >48 hours
Acute renal failure: urea >20 mmol/l or creatinine >260 mmol/l

The ASA classification of physical status was originally introduced in 1941 as a tool for statistical analysis [8]. It was modified in 1963 when the number of grades was reduced from seven to five [9]. More recently an additional suffix 'E' for emergency operation has been added. A high ASA score is predictive of both increased postoperative complications and mortality after non-cardiac surgery. The ASA classification has relatively robustly stood the test of time, probably

Table 5

American Society of Anaesiologists' status classification: modified from Wolters and colleagues [10]

Class	Description	Mortality (%)
I	Healthy	0.1
II	Mild systemic disease – no functional limitation	0.7
III	Severe systemic disease – definite functional limitation	3.5
IV	Severe systemic disease – constant threat to life	18.3
V	Moribund patient unlikely to survive 24 hours with or without operation	93.3
E	Emergency operation	

because it is simple to calculate without requiring additional resources. It may be surprising that it is predictive, as ASA scoring does not take into account age, weight or the nature of the intended operation. Studies show that there may be significant interoperator variability in ASA scoring. Other more complex scoring systems have greater prognostic accuracy but ASA scoring remains useful [10]. It has began to be used outside operating theatres, such as in helping to assess patients fitness for endoscopy, and it is a useful tool to help non-anaesthetists to consider potential procedural-related risks (see Table 5).

A slightly different approach has been taken by Older and colleagues, who have performed preoperative cardio-pulmonary testing to define an anaerobic threshold in patients in the preoperative period [11,12]. In an initial study of 187 patients, there were 55 patients in whom the anaerobic threshold was $<$11 ml/min/kg; of these, 10 patients died (a mortality rate of 18%). There were 132 patients with an anaerobic threshold $>$11 ml/min/kg, and of these one patient died (mortality rate of 0.8%). If a low anaerobic threshold was associated with preoperative ischaemia on the electro-cardiogram the results were much worse, with eight of 19 patients dying (giving a mortality rate of 42%). When the ischaemia was associated with the higher anaerobic threshold, one patient out of 25 died (a mortality rate of 4%) [11]. This work has been taken further, by describing different treatment paths for the high and low anaerobic threshold groups, and although this is not a randomised trial the results appear to show that greater degrees of intervention in the low anaerobic threshold group reduce mortality [12].

Many of these methods used for assessing risk in the preoperative period are labour intensive and require expensive and specialised equipment; this is particularly so for the assessment of anaerobic threshold. While these efforts may be good at assessing risk, there is a paucity of clinical studies showing how this has changed the management of either individual patients or groups of patients. We hope that soon data will appear showing how preoperative risk assessments have changed individual patient management; for example, how surgical anaesthetic perioperative practice has changed for an individual patient. While this would be a good start and would allow decision-makers to place the techniques for assessing preoperative risk in a decision-making context, we still really require studies to show how preoperative assessments have changed outcomes as part of a clinical trial. The only literature with which we are familiar in this context comes from the work concerning goal-directed therapy, which shows that when risk is assessed based on very simple preoperative scores, and when treatment is targeted to various goals of cardiorespiratory function, both mortality and morbidity are reduced [13].

Preoperative risk stratification for myocardial events

Two cardiac risk indices are well known. The first is the Goldman Index [14], which represents a practical and inexpensive method for identifying cardiac risk [15], but over time may need to be modified to represent the true mortality rate [16]. A second score was developed by Detsky and colleagues [17], and both this score and the Goldman Index are good predictors of perioperative cardiac events with odds ratios of 0.642 (95% confidence interval, 0.588–0.695) for the Goldman index and of 0.601 (95% confidence interval, 0.544–0.657) for the modified Detsky index [18]. Other factors such as comorbidity and intraoperative factors influence outcome, however, and no preoperative system will be completely accurate [19,20].

There are many methods to investigate cardiac function and coronary artery perfusion, and it is hardly surprising that many have been investigated for their ability to stratify risk in surgical patients undergoing non-cardiac surgery [21,22]. It is disappointing that while many of these can clearly identify different risks, there is very little information that outcome is improved by knowing the risk [23–25].

A recent study has confirmed that exercise stress testing can be a useful method of risk stratification. Gauss and colleagues shown that an ST-segment depression of 0.1 mV or more in the exercise electrocardiogram had an odds ratio

of 5.2 (95% confidence interval, 1.5–18.5; $P = 0.01$) of predicting a myocardial infarction or postoperative myocardial cell injury in non-cardiac surgery patients [26]. A combination of clinical variables and exercise electrocardiography improved preoperative risk stratification.

Other studies have used echocardiography [27] and stress echocardiography to risk-stratify surgical patients. But adding echocardiographic information to established predictive models may not alter the sensitivity, specificity or predictive values in a clinically important way [28]. Dobutamine stress echocardiography resulting in hypotension [29], ischaemia [30] or wall motion abnormalities [31,32] can have predictive value for postoperative cardiac events [33–37]. Dipyridamole echocardiography has also been used with good predictive results [38,39]. Furthermore, echocardiography without pharmacological stress can also be a useful screening test [40], and can be used during surgery and can give useful information on cardiac status [41,42].

As has already been discussed there is a paucity of clinical information describing how any of these preoperative risk assessments has either influenced the management of individual patients or of patient groups in the context of a clinical study. One notable exception is a study by Poldermans and colleagues [43]. Patients undergoing major vascular surgery were identified as being of particularly high risk by dobutamine echocardiography and were then randomised to receive perioperative care or standard care plus perioperative β-blockade with bisoprolol. A total of 1351 patients were screened and 112 patients suitable for randomisation were identified. Study results showed that mortality from cardiac causes was significantly reduced in the bisoprolol group [43]. The lack of further clinical data, however, has not prevented professional and learned groups from producing written guidelines for patient management. The American College of Cardiology published guidelines in 1996 on the preoperative assessment of patients having non-cardiac surgery and gave specific indications for the use of blockade in these patients [44]. Although the most recently published version of these guidelines is less didactic [45], they still show how consensus opinion can influence clinical management even though the evidence base is so poor.

Postoperative risk stratification

In the global context of critical care medicine there is a number of scoring systems in general use. Many of these systems are used for severity of illness scoring so that standardised comparisons can be made between patient groups and between ICUs; however, to some extent they can be used to assess risk for patient groups if not for individual patients. Severity of illness scoring systems such as Sepsis-related Organ Failure Assessment and Therapeutic intervention scoring system are widely known, but perhaps the most widely used scoring system is the Acute Physiology and Chronic Health Evaluation (APACHE) scoring system [46]. The APACHE system includes chronic health data concerning the individual patient and physiological data collected during the patients first 24 hours of intensive care treatment. The APACHE system, in common with other general scoring systems, can only be used after an operation, and therefore any risk assessment ability within these scores can only be applied post hoc to groups of patients. In the APACHE system, risk comparisons are frequently undertaken by comparing standardised mortality ratios, and there is some doubt about the standardised mortality ratio to robustly allow comparisons to be made [47].

The scoring system that has been specifically designed for surgical patients is the Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM) score [48]. This is generally accepted to be a good scoring system for routine use [49], and is better than the APACHE system for a general surgical group of patients [50]. But in specific situations such as ruptured abdominal aortic aneurysms POSSUM scoring is not a good predictor of outcome and APACHE scoring is better [51]. POSSUM scoring was also inaccurate in laparoscopic colectomy [52]. Variations of POSSUM scoring have been suggested that may work better in gastrointestinal surgery [53], specifically in oesophageal surgery [54] and vascular surgery [55]. Furthermore, in one study POSSUM scoring has been used as part of a risk stratification analysis to identify patients who might benefit from postsurgical high-dependency care or ICU care [56].

Conclusion

Risk is a term that is understood differently by different individuals depending on expectation and previous experience. There are methods that can be used to assess risk in various patient groups, but these provide population risks and are not directly applicable to individual patients. Frequently the cut off between those patients assessed as being at high risk and those at lower risk depends on the cost and complexity of providing treatment to correct the risk, rather than on the risk itself. It remains extremely disappointing that there is little evidence that any change in patient outcome has been driven by the pre-existing knowledge of risk for that patient. In the future, risk assessment in medical practice, particularly in intensive care medicine where risks of the ultimate negative outcome are so high, will only be advanced by the following: an inclusive debate involving patients, medical staff and other religious, ethical and cultural groups to understand the nature of medical risk and to form priorities in its assessment and management; the development of more accurate methods to assess and predict risk prior to the onset of an index event, which can be directed towards identifying risk for the individual; and the conduct of clinical trials to show that prior knowledge of individual risk can allow treatment and management decisions to be adapted to treat different

patients in different ways with a benefit in patient outcome, however that is to be defined.

In our opinion the two most useful scoring systems in surgical risk assessment remain the ASA score and the clinical criteria as used by Shoemaker/Boyd and colleagues. Both of these assessments are simple to use and do not require additional resources. The purpose of an effective scoring system is to highlight potential high-risk patients for busy hospital practitioners and to act as a focus for generating a multidisciplinary risk/benefit discussion between interested parties.

Competing interests

The author(s) declare that they have no competing interests.

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