Supplement 1. Supplementary materials for the manuscript

In order to respect space limitation in the main manuscript, we present further information on Methods and Results in the electronic supplementary material.

1. Study population

We included low-risk patients (aged 18–70 years, with an American Society of Anesthesiologists physical status of 1–3) undergoing elective thoracolumbar spine surgery with instrumentation (mostly pedicle screws and rods), a laminectomy involving 3 or more levels without instrumentation, or scoliosis surgery. The exclusion criteria comprised renal impairment (creatinine of >2.0 mg/dL or an estimated glomerular filtration rate of <60 mL/min); cardiovascular disease (coronary artery disease, congestive heart failure, or cardiac arrhythmia), a body mass index (BMI) of >30 kg/m^2; complete cord lesion; hemodynamic instability (hypotension or uncontrolled hypertension), and respiratory system compliance (Crs) of <30 mL/cmH$_2$O. We excluded those patients with cardiac arrhythmia, obesity, or a Crs of <30 mL/cmH$_2$O because the pulse-pressure variation (PPV) cut points would be different for those groups.

2. Intervention

In the case of the control group, the attending anesthesiologists administered a fluid therapy in accordance with good clinical practice, with the goal of keeping the mean arterial pressure at ±25% from baseline. The design of the goal-directed therapy (GDT) protocol was based on our review of published studies [1,2]. Patients in the GDT group received the fluid management and vasopressors depicted in Fig. 1. The arterial line was connected to the monitor, and the baseline PPV and Crs in the supine position were measured. If the PPV was <13%, the patient was considered euvolemic and proceeded with the baseline infusion (4 mL/kg/hr). However, if the baseline PPV was >13%, rapid crystalloid infusion was administered until either the PPV reached a value of <13% or 10 mL/kg of fluid had been infused, in order to optimize the patient's condition. The patient was then placed in the prone position and the new PPV (called "acceptable PPV") was measured. We considered an acceptable PPV to be equal to the supine PPV plus the percentage change in the Crs when changing from the supine to the prone position. For example, if there was a 10% decrease in the Crs after the prone position, then the acceptable PPV would be 14.3%.

During the operation, the protocol was as follows. If PPV values were ≤the acceptable PPV, baseline crystalloid infusion alone (4 mL/kg/hr) was continued. When the PPV values were more than the acceptable PPV, a crystalloid bolus of 200 mL in 10 minutes was administered until a PPV value ≤the acceptable PPV (repeatable at a maximum of 10 mL/kg) was reached. If the mean arterial pressure was less than 75% of the baseline, a vasopressor (ephedrine or noradrenaline) was given. Ephedrine (6 mg) was administered to those patients who had a hypotensive episode with a heart rate of less than 100 beats per min (bpm), whereas noradrenaline (4–8 mcg) was used if the heart rate was >100 bpm. For the treatment of blood loss, packed red cells were given if the hematocrit was less than 25%. However, if it was over 25%, 6% hydroxyethyl starch 130/0.4 in 0.9% NaCl (Voluven; Fresenius Kabi France, Sevres, France) was used when the estimated blood loss (EBL) reached 10%–20% of the total blood volume. Alternatively, for EBLs of <10% of the total blood volume, acetated Ringer's solution was administered to 1.5 times the EBL.

3. Outcome measurement

Patients were monitored daily for signs of postoperative complications for a period of 14 days or until their hospital discharge. Renal complications were defined as oliguria (a urine output of <0.5 mL/kg/hr×12 hours) or rising creatinine ×2 (a rise in serum creatinine levels, compared with baseline) [3]. A respiratory complication was defined as a respiratory failure which required ventilatory support [4]. Cardiovascular complications were defined as the number of hypotensive episodes (systolic blood pressure <90 mm Hg, mean arterial pressure <60 mm Hg, a decrease in blood pressure of more than 25% from baseline, or the need for vasopressor therapy), cardiac arrhythmias (atrial fibrillation with rapid ventricular response, high-grade heart block, ventricular arrhythmias, a heart rate of <40 bpm, or any cardiac arrhythmias which needed treat-

eTable 1. Subgroup analysis in patients undergoing ≥4 level of laminectomy with instrumentation and laminectomy with tumor removal

Characteristics	Control (n=14)	GDT (n=15)	*p*-value
Type of surgery			0.742
≥4 level instrumentation	11 (78.6)	11 (73.3)	
Laminectomy with tumor removal	3 (21.4)	4 (26.7)	
Duration of surgery (min)	263 .57±28.79	227.33±23.38	0.334
Blood loss (mL)	625 (250–1,400)	600 (150–900)	0.498
Intraoperative fluid			
Crystalloid (mL)	2150 (1,600–3,700)	2300 (1,000–2,850)	0.348
Colloid (mL)	0 (0–0)	250 (0–500)	0.181
Packed red cells (unit)	0 (0–0)	0 (0–0)	0.301
Urine output (mL/kg/hr)	1.15±0.22	1.21±0.22	0.849
Incidence of intraoperative hypotension	10 (71.4)	8 (53.3)	0.316
Length of hospital stay (day)	9.5 (8–15)	9 (7–11)	0.223
Renal complications	9 (64.3)	10 (66.7)	0.893
Respiratory complications	2 (14.3)	0	0.129
Cardiovascular complication	9 (64.3)	7 (46.7)	0.340
Neurological complication	2 (14.3)	0	0.129
Bowel ileus	10 (71.4)	5 (35.7)	0.058

Values are presented as number (%) or mean±standard deviation, or median (interquartile range).
GDT, goal-directed therapy.

ment), and suspected myocardial infarction (ST elevation or ST depression of more than 1 mm in limb lead monitoring, confirmed by a 12-lead electrocardiogram) [5,6]. Neurological complications were defined as stroke (confirmed by a computed tomography scan), postoperative delirium (diagnosed by mini-mental state examination), and an onset of weakness or numbness [7]. Gastrointestinal complication was defined as bowel ileus (a delay in the passing of stools to after the third postoperative day) [8]. Other complications (such as unplanned critical care admission and unexpected remained intubation) were recorded.

4. Subgroup analysis

We conducted the subgroup analysis including more invasive surgical procedure (laminectomies involving more than 3 levels of instrumentation and laminectomies with tumor removal). Fourteen patients in the control group and 15 patients in GDT group were included. The results still remain robust, except for the postoperative bowel ileus that GDT provided promising result with marginally significant effect (*p*=0.058) (eTable 1).

References

1. Gan TJ, Soppitt A, Maroof M, et al. Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. Anesthesiology 2002;97:820-6.
2. Bacchin MR, Ceria CM, Giannone S, et al. Goal-directed fluid therapy based on stroke volume variation in patients undergoing major spine surgery in the prone position: a cohort study. Spine (Phila Pa 1976) 2016;41:E1131-7.
3. Hoste EA, Clermont G, Kersten A, et al. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. Crit Care 2006;10:R73.
4. Ferreyra G, Long Y, Ranieri VM. Respiratory complications after major surgery. Curr Opin Crit Care 2009;15:342-8.
5. Papazian L, Forel JM, Gacouin A, et al. Neuromuscular blockers in early acute respiratory distress syndrome. N Engl J Med 2010;363:1107-16.
6. London MJ. Cardiovascular problems in noncardiac surgery. Curr Opin Crit Care 2009;15:333-41.

7. Mashour GA, Woodrum DT, Avidan MS. Neurological complications of surgery and anaesthesia. Br J Anaesth 2015;114:194-203.

8. Behm B, Stollman N. Postoperative ileus: etiologies and interventions. Clin Gastroenterol Hepatol 2003;1:71-80.