GOAL DIRECTED HEMODYNAMIC THERAPY DECREASES POSTOPERATIVE COMPLICATIONS. A MULTICENTER RANDOMIZED CONTROLLED TRIAL. **FEDORA TRIAL**

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MATERIAL AND METHODS

The study is a multi-center randomized controlled clinical trial performed at 5 different medical centres in Spain between 2011 and 2014. The study was performed and reported in accordance with the CONSORT statement.

Study population

Patients eligible for enrolment were 18 yr of age or older scheduled for major surgeries under general anesthesia, including laparoscopic or open abdominal, urology, gynecology and orthopedic procedures. Surgeries fulfilled at least one of the following criteria: the expected duration ≥ 2 hours, estimated blood loss greater than 15% of volaemia, transfusion requirements of at least 2 packed red blood cells. Patients were excluded if they were scheduled for emergency surgery or were classified as American Society of Anesthesiology (ASA) equal or greater than 4.

Study protocol

Intraoperative management

Patients randomized to the control group received a continuous infusion of balanced crystalloid (Ringer lactate) with an infusion rate of 3-5 ml/kg/h in cases of laparoscopic surgery, and 5-7 ml/kg/h in open surgery. They were also allowed to receive colloid solution (HES 6% 130/0.4, Voluven®, Fresenius Kabi, Germany) titrated by heart rate, blood pressure, urine output.

Intervention group patients received intra-venous fluids, vasopressors and inotropes according to a hemodynamic algorithm, as shown in Figure 1. Intraoperative hemodynamic monitoring was conducted by esophageal Doppler (CardioQ, EDM™; Deltex Medical, Inc., Chichester, UK)

Outcomes

The primary outcome was overall postoperative complications. Postoperative predefined complications were recorded for each patient for up to 180 days after surgery.

Secondary outcomes were: Hospital length of stay (defined as the number of days spent in the hospital from the day of surgery to hospital discharge or death), intensive care unit length of stay, reintervention, time to onset of oral tolerance and ambulation, and all cause of mortality at 180 days following surgery.

RESULTS

A total of 450 patients were enrolled and 428 were randomized between 2011 and 2014; 224 patients were allocated to the haemodynamic therapy algorithm, and 226 to standard of care. Twenty patients had to be excluded from the study and/or analysis because of various reasons. Baseline patient characteristics were similar between the groups. The number of complications was significantly lower in the GDHT group when compared with Control group (56 complications vs 198 complications, respectively $p < 0.01$). Similarly the number of patients with complications was lower in the GDHT group 15% vs 27.6% in control group, $p = 0.001$, OR: 0.46 CI 95%: 0.29-0.75 (Relative Risk Reduction 56.4%). hospital length of stay was reduced two days in the GDHT group, there was no significant difference in the number of patients that underwent reintervention (GDHT: 13 patients versus CG: 25 patients), and no differences in mortality were found at 180 days follow-up (GDHT: 10 patients versus CG: 9 patients)

Total Complications	GOAL DIRECTED HEMODYNAMIC THERAPY (n 214)		USUAL CARE (n 214)		OR	CI 95%
	n	%	n	%		
Overall complications	56	17	198	82	0.43	0.29-0.75
Number of patients with complications	32	15	59	27.6		
Stroke	1	0.47	0	0	3.01	0.21-74.4
AKI	5	2.34	21	9.84	0.22	0.08-0.56
ARDS	1	0.47	12	5.6	0.07	0.01-0.61
Anastomotic breakdown	3	1.40	8	3.74	0.36	0.09-1.39
Arrhythmia	2	0.93	7	3.27	0.27	0.05-1.35
Cardiac arrest	0	0	4	1.87	0.98	0.96-1.00
Cardiopulmonary edema	0	0	13	6.07	0.93	0.90-0.97
DVT	0	0	0	0	1	0.01-50.6
Delirium	0	0	4	1.87	0.98	0.96-1.00
Gastrointestinal bleed	0	0	2	1.93	0.19	0.00-4.15
Infection source uncertain	0	0	13	6.07	0.03	0.00-0.58
Blodstream infection	0	0	2	0.93	0.19	0.00-4.15
Myocardial infarction	0	0	1	0.47	0.33	0.01-8.19
MINS	1	0.47	4	1.87	0.24	0.02-2.22
Pneumonia	4	1.87	22	10.28	0.16	0.05-0.49
Paralytic ileus	15	7.01	25	33.18	0.15	0.08-0.27
Postoperative haemorrhage	2	0.93	8	3.74	0.24	0.05-1.58
PE	0	0	0	0	1	0.01-50.6
Surgical site infection superficial	4	1.87	16	7.48	0.23	0.07-0.71
Surgical site infection deep	6	2.84	23	10.75	0.24	0.095-0.60
Surgical site infection organ-space	7	3.27	8	3.74	0.87	0.31-2.44
Urinary tract infection	2	0.93	5	2.34	0.34	0.07-2.05

Overall volumes of intra-venous colloid and crystalloid administered during the intraoperative period were similar (GDHT 985 ml versus usual care 984 ml). Administration of fluids postoperatively was also equivalent in both groups

CONCLUSIONS

The use of EDM guided hemodynamic algorithm reduces postoperative complications and LOS in adult patients undergoing major surgery. However, mortality measured at 180 days was not affected.