Journal of Clinical Monitoring and Computing (2019) 33:365–371
https://doi.org/10.1007/s10877-018-0190-8

ORIGINAL RESEARCH

Outcome impact of hemodynamic and depth of anesthesia monitoring during major cancer surgery: a before–after study

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Received: 11 June 2018 / Accepted: 30 July 2018 / Published online: 3 August 2018

Abstract
Hemodynamic and depth of anesthesia (DOA) monitoring are used in many high-risk surgical patients without well-defined indications and objectives. We implemented monitoring guidelines to rationalize hemodynamic and anesthesia management during major cancer surgery. In early 2014, we developed guidelines with specific targets (Mean arterial pressure > 65 mmHg, stroke volume variation < 12%, cardiac index > 2.5 l min^{-1} m^{-2}, central venous oxygen saturation > 70%, 40 < bispectral index < 60) for open abdominal cancer surgeries > 2 h. Pre-, intra-, and post-operative data were collected from our electronic medical record database and compared before (March–August 2013) and after (March–August 2014) guideline implementation. A total of 596 patients were studied, 313 before (Before group) and 283 after (After group) guideline implementation. The two groups were comparable for age, ASA score, physiological P-POSSUM score, and surgery duration, but the operative P-POSSUM score was higher in the after group (20 vs. 18, p = 0.009). The use of cardiac output, central venous oxygen saturation and DOA monitoring increased from 40 to 61%, 20 to 29%, and 60 to 88%, respectively (all p-values < 0.05). Intraoperative fluid volumes decreased (16.0 vs. 14.5 ml kg^{-1} h^{-1}, p = 0.002), whereas the use of inotropes increased (6 vs. 11%, p = 0.022). Postoperative delirium (16 vs. 8%, p = 0.005), urinary tract infections (6 vs. 2%, p = 0.012) and median hospital length of stay (9.6 vs. 8.8 days, p = 0.032) decreased. In patients undergoing major open abdominal surgery for cancer, despite an increase in surgical risk, the implementation of guidelines with predefined targets for hemodynamic and DOA monitoring was associated with a significant improvement in postoperative outcome.

Keywords Consciousness monitors · Hemodynamic monitoring · Perioperative care · Postoperative complications

1 Introduction

Patients undergoing high-risk surgery are likely candidates for postoperative complications. In the large International Surgical Outcome Study [1], the postoperative morbidity rate, or proportion of patients who developed at least one complication, was 27% after major surgery, and 50% in patients who were admitted to a critical care unit as routine immediately after surgery. Postoperative complications affect both short and long-term outcomes [2] and are responsible for a dramatic increase in hospital length of stay and costs [3]. Hemodynamic monitoring has been proposed to preserve organ perfusion during high-risk surgery, and to decrease postoperative morbidity [4, 5]. Multicenter randomized controlled trials have yielded conflicting results [6–9], but recent meta-analyses suggest a clinical benefit when working within well-defined hemodynamic targets [9–11]. The Society of Anesthesiology of São Paulo State (SAESP) now recommends hemodynamic optimization for patients undergoing major surgery [12]. Monitoring depth of anesthesia (DOA) has been proposed to rationalize the use of anesthetic drugs, and several studies suggest it may be useful to decrease postoperative delirium [13–15].

A large portion of patients undergo lengthy, high-risk surgical procedures at AC Camargo Cancer Center, São Paulo, Brazil. Before 2014, DOA and hemodynamic monitoring were used at the discretion of the anesthetist, and without

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any specific recommendations. Given the body of evidence accumulating on the potential benefits of intraoperative monitoring, we developed monitoring guidelines for adult cancer patients undergoing major abdominal surgery in our institution. The evidence supporting the use of DOA and hemodynamic monitoring is mainly based on controlled trials done in highly selected patients [10, 11, 16] and may not be extrapolated to the uncontrolled conditions of our daily practice. Therefore, we designed this study to assess the impact of our newly created guidelines on postoperative outcome in real-life conditions.

2 Methods

The study protocol was approved by the Ethics and Research Committee of the hospital (#2.334.350) on 18 October 2017. Guidelines were developed for hemodynamic and DOA monitoring. Minimally invasive cardiac output monitoring (FloTrac, Edwards Lifesciences, Irvine, CA), central venous oxygen saturation monitoring (PreSep, Edwards Lifesciences), and DOA monitoring (BIS, Covidien, Boulder, CO) were recommended for all adult patients undergoing abdominal cancer surgery expected to last more than 2 h. The following hemodynamic targets were recommended: mean arterial pressure (MAP) > 65 mmHg, stroke volume variation (SVV) < 12% (pending tidal volume is > 7 ml kg^{-1} ideal body weight), cardiac index > 2.5 L min^{-1} m^{-2}, and central venous oxygen saturation ($ScvO_2$) > 70%. The recommendation for DOA was to maintain the bispectral index (BIS) between 40 and 60. Guidelines were developed by our monitoring committee and several internal meetings were organized between September and November 2013 to inform anesthetists and nurses working in our operating theatres. Anesthetists had the freedom to adapt targets to individual needs and clinical scenario, and there was no specific recommendation regarding the type and dosage of fluids and drugs to achieve the targets.

Pre-, intra-, and post-operative data were collected retrospectively from our electronic medical record database (MV electronic patient record, Recife, Brazil) and compared before (Before group, from March to August 2013) and after (After group, from March to August 2014) guidelines were implemented. Adult patients who underwent open abdominal surgery lasting more than 2 h were included consecutively. We studied the same 6-months period in 2013 and 2014 (March–August) to avoid potential seasonality differences in patient case mix. Before surgery, we assessed age, sex, physical status by the American Society of Anesthesiologists (ASA score), Porthmouth Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (P-POSSUM). During surgery, we assessed the duration of the procedure, the type and amount of fluid, vasoactive and inotropic drugs administered. After surgery, we extracted 19 potential postoperative complications from our electronic database. They were entered in the database at the time of hospitalization, with the criteria commonly used in our institution (listed in the supplementary material), including the Confusion Assessment Method (CAM) [17, 18] score for postoperative delirium. The postoperative morbidity rate was defined as the proportion of patients who developed at least one postoperative complications before hospital discharge. The ICU admission rate, the ICU and postoperative hospital length of stay, and the in-hospital mortality rate were extracted as well from the database.

All statistical analyses were performed using the statistical package IBM SPSS version 22 (IBM, Armonk, NY, USA). Variables that were normally distributed were compared using Student's t-test for independent measurements; the data were presented as means and standard deviations. The variables that presented non-parametric distribution were compared using the Mann–Whitney test; the data were presented as medians and interquartile ranges. Categorigal variables were compared using the chi-square or Fisher exact test; the data were presentes as counts (%). A logistic regression model was constructed to further investigate the association between group assignment and the postoperative morbidity rate using type of surgery and P-POSSUM score as covariates. Statistically significance was set at p-value < 5%.

3 Results

A total of 596 patients were studied, 313 before (Before group) and 283 after (After group) guideline implementation. Before surgery, the two groups were comparable in terms of age, ASA score, physiological P-POSSUM score, and duration of surgery (Table 1). Surgical procedures were the same in both groups, with the exception of colorectal surgery that was more common in the Before group (Table 1). The operative POSSUM score was slightly but significantly higher in the After than in the Before group (Table 1).

After guideline implementation, the use of cardiac output, $ScvO_2$ and DOA monitoring significantly increased from 40 to 61% (+53% relative increase), 20 to 29% (+45% relative increase), and 60 to 88% (+47% relative increase), respectively (Table 2). Intraoperative total fluid volume and colloid volumes decreased. Less patients received colloids whereas more patients received inotropes (Table 2). The rate of postoperative delirium (16 vs. 8%, p = 0.005) and urinary tract infection (6 vs. 2%, p = 0.012) decreased. We observed a 12% relative decrease in postoperative morbidity which did not reach statistical significance (Table 3). However, after adjustment for the type of surgery and operative POSSUM

Table 1 Main characteristics of the study population

	Before group $n=313$	After group $n=283$	p
Age (years)	60 (49; 68)	59 (48; 68)	0.310
Female, *n* (%)	169 (53.9)	166 (58.6)	0.282
Weight (kg), median (Q1–Q3)	70 (60; 83)	70 (61; 82)	0.943
ASA physical status, *n* (%)			0.126
I	27 (8.6)	20 (7.1)	
II	195 (62.3)	171 (60.4)	
III	76 (24.2)	86 (30.4)	
IV	15 (4.8)	6 (2.1)	
P-POSSUM			
Physiological	15 (13; 18)	14 (12.25; 18)	0.150
Operative	18 (14; 22)	20 (16; 23)	**0.009**
Surgical procedure, *n* (%)			
Colo-rectal	111 (35.5)	76 (26.8)	**0.029**
Liver resection	22 (7.0)	31 (10.9)	0.124
Cystectomy	12 (3.8)	8 (2.8)	0.649
Gastric or pancreatic	45 (14.4)	33 (11.7)	0.389
Emergency laparotomy	48 (15.3)	41 (15.5)	0.861
Cytoreductive surgery	29 (9.3)	39 (13.8)	0.109
Other	46 (14.7)	55 (19.4)	0.152
Surgery duration (min)	290 (205; 442)	285 (210; 400)	0.749

Bold results achieved statistical significance

Data are presented as count (%) or median (Q1–Q3)

P-POSSUM Portsmouth Physiological and Operative Severity Score for the enumeration of Mortality and morbidity, *ASA* American Society of Anesthesiologists

score, the logistic regression model showed that guideline implementation was independently associated with postoperative morbidity (Table 4). The median postoperative hospital length of stay was longer in the Before group (Table 5).

4 Discussion

In patients undergoing major open abdominal surgery for cancer, despite an increase in surgical risk, the implementation of guidelines for hemodynamic and DOA monitoring was associated with a significant decrease in urinary tract infection, postoperative delirium and hospital length of stay. Thus, our findings suggest that simple initiatives, such as the development and implementation of monitoring guidelines, may have a significant impact on postoperative outcome.

Previous studies [13, 14] have shown that DOA monitoring may be associated with a decrease in anesthetic exposure, a faster neurological recovery, and a decrease in postoperative delirium. The use of DOA monitoring significantly increased after the implementation of our guidelines, which may explain the observed decrease in postoperative delirium. The use of hemodynamic monitoring also increased from the Before to the After group. We are not aware of any clinical study demonstrating an impact of hemodynamic optimization on neurological complications. However, we cannot exclude that a better cerebral perfusion may have played a role as well in the reduction of postoperative delirium. Several studies suggest that improved tissue perfusion may explain an association between reduced infectious complications and hemodynamic optimization [19]. Our findings are

Table 2 Intraoperative characteristics

	Before group	After group	p
Total fluid volume (ml kg h^{-1}), median	16.0 (12.1; 20.0)	14.5 (10.7; 18.3)	**0.002**
Crystalloid volume (ml kg h^{-1}), median	13.8 (10.6; 18.3)	13.5 (10.1; 16.8)	0.071
Colloid use, n (%)	236 (75)	152 (54)	**< 0.001**
Colloid volume (ml kg h^{-1}), median	1.6 (0.2; 2.7)	0.5 (0; 1.9)	**< 0.001**
PRBC transfusion, n (%)	95 (30.4)	64 (24.4)	0.103
FFP transfusion, n (%)	28 (8.9)	17 (6.0)	0.179
Dobutamine use, n (%)	19 (6.1)	32 (11.3)	**0.022**
Noradrenaline use, n (%)	31 (9.9)	28 (9.9)	0.997
Monitoring, n (%)			
CO and SVV	124 (39.9)	172 (60.8)	**< 0.001**
CVP	112 (35.9)	88 (31.1)	0.226
$ScvO_2$	61 (19.5)	81 (28.6)	**0.009**
Depth of anesthesia	188 (60.1)	248 (87.5)	**< 0.001**

Bold results achieved statistical significance

Data are presented as count (%) or median (Q1–Q3)

CO cardiac output, *CVP* central venous pressure, *FFP* fresh frozen plasma, *PPV* pulse pressure variation, *PRBC* packed red blood cell, *$ScvO_2$* central venous oxygen saturation

Table 3 Postoperative complications

	Before group	After group	*p*
Morbidity rate, n (%)	144 (46.2)	115 (40.6)	0.175
Superficial wound infection, n (%)	21 (6.7)	20 (7.1)	0.863
Deep wound infection, n (%)	19 (6.1)	16 (5.6)	0.829
Organ-space wound infection, n (%)	34 (10.9)	31 (11.0)	0.971
Urinary tract infection, n (%)	18 (5.8)	5 (1.8)	**0.012**
Anastomotic leakage, n (%)	12 (3.8)	9 (3.2)	0.666
Pneumonia, n (%)	22 (7.0)	12 (4.2)	0.143
Prolonged mechanical ventilation (> 48 h), n (%)	18 (5.8)	9 (3.2)	0.132
Acute respiratory distress syndrome, n (%)	5 (1.6)	0 (0)	0.063
Reintubation, n (%)	17 (5.4)	9 (3.2)	0.179
Acute kidney injury, n (%)	42 (13.4)	36 (12.7)	0.801
Renal replacement therapy, n (%)	8 (2.6)	9 (3.2)	0.642
Deep venous thrombosis, n (%)	4 (1.3)	0	0.126
Pulmonary embolism, n (%)	1 (0.3)	1 (0.4)	1.000
Myocardial infarction, n (%)	3 (1.0)	3 (1.1)	1.000
Stroke, n (%)	0 (0)	1 (0.4)	0.293
Delirium, n (%)	49 (15.7)	23 (8.1)	**0.005**
PRBC transfusion, n (%)	48 (15.3)	38 (13.4)	0.508
Reoperation, n (%)	38 (12.1)	26 (9.2)	0.245
Hemodynamic instability, n (%)	39 (12.6)	36 (12.7)	0.959

Bold results achieved statistical significance

Data are presented as count, n (%)

PRBC packed red blood cell

Table 4 Logistic regression model assessing guidelines implementation as a risk factor for morbidity rate adjusted for surgical P-POSSUM and type of surgery

	OR	95% CI OR	*p*
P-POSSUM (operative)	1.081	1.04–1.12	< **0.001**
After group	0.670	0.46–0.97	**0.038**
Type of surgery (colo-rectal)	0.906	0.61–1.36	0.633

Bold results achieved statistical significance

95% CI 95% confidence interval, *P-POSSUM* Portsmouth Physiological and Operative Severity Score for the enumeration of Mortality and morbidity, *OR* odds ratio

Table 5 Postoperative length of stay and mortality

	Before group	After group	*p*
ICU admission, n (%)	244 (78.0)	222 (78.4)	0.885
ICU LOS (days)	2.7 (1.7–3.7)	2.0 (1.7–3.6)	0.105
Hospital LOS (days)	9.6 (6.5–17.3)	8.8 (5.7–14.2)	**0.032**
Hospital mortality, n (%)	28 (8.9)	23 (8.1)	0.721

Bold results achieved statistical significance

Data are presented as count (%) or median (Q1–Q3)

ICU intensive care unit, *LOS* length of stay

in line with the results of a meta-analysis of 26 randomized controlled trials reporting a significant reduction in urinary tract infections with hemodynamic optimization in patients undergoing major surgery [19].

The 12% reduction in overall postoperative morbidity did not reach statistical significance and was lower than reduction rates reported in recent meta-analyses of randomized controlled trials investigating the effects of hemodynamic optimization [9–11]. This may first be explained by the fact that patients from the After group had a higher surgical P-POSSUM score. Indeed, the logistic regression model showed that the implementation of our guidelines was independently associated with postoperative morbidity. Second, our study was a real-life evaluation, not a randomized controlled trial. Our recommendations led to a significant increase in DOA and hemodynamic monitoring (relative increase around 50%). However, some patients in the Before group were monitored. And in the After group, not all patients benefitted from the new monitoring strategy (Table 2).

Adoption of monitoring intervention varied. Depth of Anesthesia monitoring was adopted in most patients (88%), cardiac output monitoring was adopted in less than two-thirds (61%) of our patients, and $ScvO_2$ monitoring in less than one-third (29%). Although we did not survey our

clinical team, one can speculate such a behavior was related, at least in part, to the respective invasiveness and ease of use of monitoring techniques. Suboptimal adoption of recommendations is a common finding in quality improvement programs. In the UK, Kuper et al. [20] implemented hemodynamic optimization in patients undergoing major abdominal surgery. The adoption rate was already 20% before and increased to only 65% after the implementation of hemodynamic guidelines. Despite this non-optimal implementation rate, like in our study, they reported a significant decrease in hospital length of stay. In line with these findings, another and more recent before-after comparison reported a significant decrease in hospital length of stay after the adoption of hemodynamic optimization increased from 7 to 61% [21].

We recommended more frequent use of monitoring tools, and to using them differently, with specific physiologic targets. For instance, fluid was recommended only when SVV was > 12%. Therefore, one may speculate that continuous monitoring of SVV helped to prevent unjustified fluid boluses in non-responder patients. This may explain why the proportion of patients who received colloids and the total volume of fluid administered during surgery were lower in the After group. Similarly, inotropes were recommended when cardiac index was $< 2.5\ l\ min^{-1}\ m^{-2}$. Continuous monitoring of cardiac output enabled the detection of low flow states that otherwise may have remained undetected. This is likely the reason why more patients received dobutamine in the After group.

Both groups received around 15 ml kg h^{-1} of fluid (crystalloid and colloids) during the surgical procedure, which can be considered as a liberal strategy [22, 23]. This may be explained by several factors, including a fluid maintenance rate around 6 ml kg h^{-1}, the volume replacement for clear liquid fasting periods of > 8 h (current practice in our institution), as well as surgical blood loss. One quarter of our patients received red blood cells, but we were unable to quantify blood loss due to lack of recorded totals in our database. Of note, the After group received significantly, but only slightly less fluid than the Before group. A recent meta-analysis [11] studied the impact of goal directed fluid strategies on fluid management. It showed that such strategies often have no significant impact on the total volume of fluid received by surgical populations. It suggested that the outcome benefits of goal directed fluid strategies are related to the fact that some patients receive more fluid, whereas, other patients receive less, depending on fluid responsiveness and individual needs. Timing of fluid administration has also been advocated to explain differences in postoperative outcome despite comparable intraoperative fluid volumes [6].

Our study has limitations. It is a before–after comparison and the lack of randomization explains that the two groups were not perfectly matched for surgical procedures, resulting in an operative P-POSSUM score higher in the After group. This may only favor the Before group and could not explain the observed outcome benefits in the After group. We did a logistic regression analysis showing that guidelines implementation was an independent predictor of postoperative morbidity. However, because our study was not a randomized controlled trial, we cannot claim causality between guidelines implementation and improvement in postoperative outcome. Also, because the use of hemodynamic and DOA monitoring increased at the same time, we cannot assess their respective influence on the results. Our goal was to investigate the association between monitoring and outcome in real life conditions, outside the strict conditions of controlled trials [24]. This approach has been used in several studies including some with significant impact on quality of surgical and critical care [25, 26]. Randomized controlled trials are valuable to demonstrate causality, but their findings are not always reproducible in the uncontrolled conditions of our daily practice [24, 27, 28]. Our study design had the advantage to eliminate the learning effect that inevitably contaminates control groups in non-blinded randomized controlled trials. Additionally, the decision to perform a before–after comparison was based on the prior utilization of both DOA and hemodynamic monitoring in some of our patients. Therefore, it would have been questionable from a practical and ethical standpoint to create an artificial control group where DOA and hemodynamic monitoring would have not been allowed. We did not ask clinicians to follow a strict therapeutic protocol but simply to consider recommendations developed by our monitoring committee. We believe our results may have been different if we had used a strict protocolized strategy and tracking tools or target screens to optimize compliance [29]. We acknowledge that the hemodynamic variables we decided to monitor (MAP, CI, SVV and $ScvO_2$), as well as the recommended physiologic targets, are debatable. Indeed, simpler strategies based on pulse pressure variation [30] or stroke volume monitoring [31] have been shown to be useful to improve postoperative outcome. Using personalized targets might also be more appropriate than using the same physiologic objectives for all [32, 33]. Finally, monitoring equipment has a cost, which may be a barrier to wide-spread clinical adoption. In the fair estimation of the return on investment, the potential savings associated with a reduction in postoperative complications and length of stay must be considered [34, 35]. Unfortunately, we did not have access to cost information so that we were unable to assess the impact of our recommendations on hospital finances.

5 Conclusion

In patients undergoing major open abdominal surgery for cancer, despite an increase in surgical risk, the implementation of guidelines with predefined targets for hemodynamic and DOA monitoring was associated with a significant improvement in postoperative outcome.

Acknowledgements We thank Desiree Chappell, Louisville, KY, for English editing.

Author contributions All authors participated in the study design and in the interpretation of data. MFL and LAM were involved in data collection and data analysis. MFL and FM drafted the manuscript, and all authors contributed to and approved the final version.

Compliance with ethical standards

Conflict of interest MFL, LAM and DBG have no conflict of interest to declare. AYC is the president of Fundação para Segurança do Paciente, a non-profit organization to improve patient safety. EHGJ is a member of the speakers' bureau for Edwards Lifesciences. FM is the managing director of MiCo, a Swiss consulting firm specialized in medical e-nnovations.

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