

New transpulmonary thermodilution approach to assess hemodynamic changes in patients undergoing open abdominal cytoreductive surgery with hyperthermic intraperitoneal chemotherapy

Myoung Hwa Kim

Yonsei University College of Medicine

Young Chul Yoo

Yonsei University College of Medicine

Sun Joon Bai

Yonsei University College of Medicine

Kang-Young Lee

Yonsei University College of Medicine

Nayeon Kim

Yonsei University College of Medicine

Ki Young Lee (✉ kylee504@yuhs.ac)

Yonsei University Health System <https://orcid.org/0000-0003-4893-3195>

Research article

Keywords: anesthesia, cytoreductive surgery, hemodynamic monitoring, hyperthermic intraperitoneal chemotherapy

Posted Date: October 25th, 2019

DOI: <https://doi.org/10.21203/rs.2.16471/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Purpose The current treatment of peritoneal cancer combines cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC). The present study aimed to use the VolumeView™ system to investigate the intraoperative physiological changes, including extravascular lung water, in patients undergoing cytoreductive surgery with HIPEC.

Methods This prospective, observational study enrolled 21 patients undergoing elective cytoreductive surgery with HIPEC at our hospital between December 2014 and April 2016. In all patients, we applied the VolumeView™ system (Edwards Lifesciences, Irvine, CA). Internal jugular vein and femoral artery accesses were required to monitor hemodynamic parameters. Data were recorded and analyzed before skin incision; 30 min before HIPEC initiation; 30, 60, and 90 min after HIPEC initiation; 30 min after HIPEC completion; and 10 min before surgery completion.

Results During HIPEC, patients showed a rise in body temperature, decrease in the systemic vascular resistance index, and increase in cardiac output. The global end-diastolic volume index was 715.4–809.7, and the extravascular lung water index was 6.9–7.3. Rapid insulin (mean, 6.8 units) was administered because of increased glucose levels, and lactate levels steadily increased during HIPEC. Only 1 patient had acute kidney injury postoperatively, and the mean length of hospital stay was 17 days.

Conclusion Our study demonstrated the intraoperative physiological changes in patients undergoing open cytoreductive abdominal surgery with HIPEC. Advanced hemodynamic monitoring should be considered for better anesthetic management in these patients.

Background

Peritoneal carcinomatosis involves the spread of a tumor over the peritoneal surface secondary to seeding of gynecologic and non-gynecologic tumors in the peritoneum. Its treatment is difficult, and outcome is very poor [1, 2]. Recently, cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) has been known to be the optimal surgical approach for peritoneal cancer, and a significantly enhanced survival rate with this treatment approach has been demonstrated by several studies [3–6]. HIPEC involves the direct administration of highly concentrated anti-cancer agents into the tumor tissue via a glucose carrier solution at high temperature. This stresses the cardiovascular system, resulting in an increase in the heart rate (HR), cardiac index (CI), and oxygen consumption and a decrease in the systemic vascular resistance index (SVRI) [7–9]. Therefore, continuous monitoring of arterial blood pressure and central venous pressure (CVP) is important, and in certain cases, vasopressors and inotropic agents are recommended to maintain the blood pressure [10].

In addition, appropriate fluid management and the maintenance of urinary output are critical, as massive fluid shifts and circulating intravascular volume loss occur frequently during surgery [11–13]. The extensive surgical resection and physicochemical injury, as well as HIPEC procedure, can result in the capillary permeability, tissue damage and systemic complications, with postoperative morbidity and

mortality rates up to 41% and 5%, respectively [14, 15]. However, there is insufficient information available on the anticipated metabolic and physiologic derangement for anesthesiologists in the previous studies. The VolumeView™ system (Edwards Lifesciences, Irvine, CA), which has a novel algorithm for the mathematical calculation of the thermodilution curve [16], has been introduced recently. This system provides more precise information for hemodynamic alteration during major abdominal surgery and assists in the management of fluid supply to high-risk patients with issues between fluid restriction and overloading.

The present study aimed to use the VolumeView™ system to investigate the intraoperative physiological changes, including extravascular lung water, in patients undergoing cytoreductive surgery with HIPEC.

Methods

Patients

This was a prospective, observational, single-center study. Our protocol was approved by the appropriate committee (IRB number: 4–2014–0854). Patients were informed of the study objectives and methods 1 day before the surgery, and written consent was obtained from all patients. Adult patients undergoing elective cytoreductive surgery with HIPEC at our hospital between December 2014 and April 2016, were assessed for eligibility. The exclusion criteria were a sudden change in the surgical plan and the retraction of consent.

Anesthesia

The standard monitoring was applied when patients arrived at the operating room, and it included electrocardiography, pulse oximetry, noninvasive blood pressure monitoring, and capnography. The depth of sedation/ anesthesia was monitored using a bispectral index (BIS) monitor (Aspect A–2000™, Aspect Medical System Inc., Newton, MA). Anesthesia was induced with bolus administration of 1.5–2 mg/kg of propofol and 1–2 µg/kg of remifentanyl. Anesthesia was maintained using 4–7% desflurane with the continuous intravenous (IV) infusion of 0.05–0.2 µg/kg/min of remifentanyl. Rocuronium, which is a neuromuscular relaxing agent, was injected at 0.6 mg/kg to facilitate tracheal intubation. Tracheal intubation was performed in female and male patients using a 6.5-mm and 7.5-mm (internal diameter) tracheal tube, respectively. The cuff pressure of the tracheal tube was maintained at 20–25 cm H₂O throughout the surgery. Mechanical ventilation was applied with a tidal volume of 8 mL/kg of ideal body weight, and the respiratory frequency was adjusted to maintain an end-tidal CO₂ concentration of 35–45 mmHg with an air/oxygen mixture (fraction of inspired oxygen 0.5). BIS scores were maintained in the range of 40 and 60, and the mean arterial pressure was controlled within 20% of the pre-induction value. In all patients, a central venous catheter was inserted for additional venous access and hemodynamic monitoring.

HIPEC procedure

All patients with cytoreductive surgery followed by HIPEC. For HIPEC, the open abdomen technique was employed, allowing operators to manipulate and remove abdominal content or mass. Inflow and outflow tubes were connected to a hyperthermia pump. Preheated 5% glucose peritoneal dialysis solution (1000 mL/min) was circulated through the intraabdominal space. When the target temperature of between 41°C and 42°C was reached, chemotherapeutic agents were added to this heated solution. The duration of HIPEC was scheduled for 90 minutes. And, the perfusate was drained through outflow tube and the abdominal cavity was washed out with 4000 mL of normal saline.

Measurements

A VolumeView™ catheter (Edwards Lifesciences) was inserted into the femoral artery and connected to the EV 1000 monitoring system (Edwards Lifesciences). Thermodilution measurements were conducted in sets of 3 subsequent injections of 15 mL cold saline at least, randomly distributed over the respiratory cycle. All hemodynamic parameters were electronically collected and recorded at 500 Hz internally in the EV 1000 system and downloaded for analysis. Hemodynamic parameters, such as CI, stroke volume index (SVI), SVRI, and stroke volume variation (SVV), were continuously measured using the EV 1000 monitor, and new additional hemodynamic data, such as global end-diastolic volume index (GEDI), extravascular lung water index (ELWI), and pulmonary vascular permeability index (PVPI), were extracted. In addition, we defined the following 7 time points: before skin incision; 30 min before HIPEC; 30, 60, and 90 min after HIPEC initiation; 30 min after HIPEC completion; and 10 min before surgery completion, in order to express the course of the procedure. The results of laboratory and arterial blood gas analysis (ABGA) were also documented.

Fluid resuscitation

The amount of serious loss during surgery was estimated by the investigator and was equally substituted with additional crystalloid infusion. We recorded the detectable amount of blood loss in the suction unit during surgery but did not estimate the blood absorbed in the abdominal compresses. An isotonic HES preparation (Volulyte®, Fresenius Kabi AG, Bad Homburg, Germany) was administered for compensating blood loss. The transfusion of red cell concentrates was considered when the hemoglobin level decreased below 8 g/dL. A continuous infusion of vasopressor was routinely utilized for maintaining the mean arterial pressure at not more than 20% below the baseline value during surgery. All patients received a transurethral urine catheter, and urine output was measured hourly. Diuretics were not used during surgery.

Body temperature control

Body temperature was continuously measured with a thermodilution probe in the VolumeView™ catheter. Patients were warmed with a BairHgger™ upper body airstream blanket (3M GmbH, Neuss, Germany), hot line, and heated circuit during cytoreductive surgery. On the other hand, patients were cooled with a BairHgger™ upper body airstream blanket (3M GmbH) and cold IV fluids for maintaining normal body temperature during HIPEC.

Postoperative data

We collected postoperative patient data, including coagulation profiles (platelet count, prothrombin time, and partial thromboplastin time), serum albumin levels, renal function profiles, respiratory function restoration, bowel movement recovery, complications, and lengths of intensive care unit (ICU) and hospital stays. We elucidated the occurrence of acute kidney injury (AKI) according to the Risk, Injury, Failure, Loss, and End-stage Kidney Disease (ESKD) (RIFLE) criteria. The criteria are based on an elevated serum creatinine level and decreased estimated glomerular filtration rate and urinary output from baseline, and they have been used to define AKI and classify patients according to AKI severity [17]. Bowel movement recovery was evaluated according to the gas passing time, sips of water time, and soft diet time. Postoperative complications included surgical complications, which needed re-operation during hospital stay, and non-surgical complications, which needed conservative care.

Statistical analysis

Descriptive analyses were performed to demonstrate patient characteristics. Continuous variables are presented as mean (standard deviation or range), and categorical variables are reported as number of subjects (percentage). All statistical analyses were performed using SPSS (SPSS version 23.0; IBM Corp., Armonk, NY).

Results

Patient characteristics

Among 31 patients who were scheduled to undergo cytoreductive surgery with HIPEC, 22 patients who provided consent were enrolled between November 2014 and April 2016. Of these 22 patients, 1 was excluded because of a change in the surgical plan. The remaining 21 patients were finally analyzed. Table 1 presents the patient demographic data. Colon cancer was the most common cause of peritoneal cancer in our study population. The other causes included appendix cancers, sigmoid cancers, rectal cancers, and others. The departments of hepatobiliary and pancreas surgery and urologic surgery cooperated for colorectal surgery.

Intraoperative management

Anesthetic duration was nearly 12 hours. For postoperative pain control, 17 patients received IV patient-controlled analgesia (PCA) and the remaining 4 patients received epidural PCA. Fluid was administered with total crystalloid at 6983.3 mL and total colloid at 1177.2 mL. The urine output was maintained at 122 mL/h, and the estimated blood loss (EBL) was 780 mL. To decrease the glucose level, rapid insulin (6.8 IU) was administered intravenously. In almost patients (20/21), vasopressors were used, and phenylephrine was infused in 70% of the patients (Table 2).

Intraoperative hemodynamic, respiratory, and metabolic parameters

Table 3 presents the various intraoperative parameters, including physiological changes. During the HIPEC 90-min period, hyperthermia occurred with a mean overall peak body temperature of 38.0°C. The mean blood pressure decreased up to 76 mmHg and HR increased up to 95 bpm until HIPEC completion. Additionally, the CI increased up to 3.8, SVI increased up to 5.2, and SVV increased up to 11.4 during HIPEC. Their peak levels were not at the same time point. In advanced hemodynamic monitoring, the ELWI, PVPI, and GEDI increased overall during HIPEC and changed significantly over time. The SVRI decreased up to 1326.8, and it remained low until the end of surgery. According to ABGA, the serum lactate level increased by 4 times compared with the initial baseline level, and the serum glucose level increased by 2.5 times compared with the initial level.

Postoperative recovery profile

Regarding postoperative coagulation profiles (Table 4), the platelet count, prothrombin time, and partial thromboplastin time decreased when compared with the preoperative levels. Additionally, the albumin level decreased after surgery. One patient experienced acute deterioration of renal function according to the RIFLE criteria during hospital stay. A total of 9 ICU patients received ventilation, and 6 patients were maintained with vasopressors on ICU arrival. Three cases of postoperative complications, including adhesion, bleeding, and wound dehiscence, needed surgical treatments, while 4 cases of complications, including pancytopenia, pneumonia, and pancreas fistula, needed conservative treatments. The mean length of hospital stay was 18.5 days, and the mean length of ICU stay was 1.4 days. Two patients died within the study period (18 months).

Discussion

In our study, we prospectively described the physiological changes during open abdominal cytoreductive surgery with HIPEC. To the best of our knowledge, the present study is the first trial to examine the cardiopulmonary and intravascular volume status with a new thermodilution measurement approach using the VolumeView™ system in cytoreductive surgery with HIPEC.

A previous systemic review of patients treated with cytoreductive surgery and HIPEC due to pseudomyxoma peritonei reported that the median survival duration ranged from 51 to 156 months and that the 5-year survival rate ranged from 52% to 96% depending on the severity of disease at the time of treatment [18, 19]. Moreover, Verwaal et al. showed that patients with peritoneal carcinomatosis secondary to colorectal cancer treated with cytoreductive surgery and HIPEC demonstrated a significant increase of median survival (22 months) when compared with systemic chemotherapy alone (12 months) [20]. Consequently, cytoreductive surgery with HIPEC is currently identified as the standard method for treating peritoneal carcinomatosis secondary to colorectal cancer and appendiceal neoplasm [8].

Despite constant enhancement in surgical and anesthetic techniques, cytoreductive surgery with HIPEC is necessarily related with disturbances in hemodynamics, coagulation, gas exchange, and nutrition [7, 21]. Consequently, understanding the pathophysiological alterations accompanying with cytoreductive surgery with HIPEC is crucial and helpful for patients undergoing anesthesia. There were 3 studies systemically evaluated additional hemodynamic parameters, such as cardiac output and vascular resistance, assessed using either esophageal Doppler or transpulmonary thermodilution (TPTD) and pulse contour analysis [22, 23]. Although the results of the variation of systemic vascular resistance and cardiac output were not consistent and significant [24], a decrease in the SVRI and an increase in the CI were only measured in patients during the open coliseum technique of HIPEC [24], which is consistent with our results.

Considering the wide extent and duration of surgery, the large amount of fluid shifting, the necessity of vasopressor support, and intraoperative pathophysiologic changes need persistent attention, although they are transient in nature. Intraoperative hemodynamic monitoring is multilateral, and across studies on cytoreductive surgery with HIPEC, the monitoring approaches used include at least an invasive central venous and arterial pressure line, and hourly fluid administration and urine amount assessment [26, 27]. However, the CVP and amount of urine are not accurate indices of fluid responsiveness and only help to detect a patient's intravascular volume status [28–30]. In addition, both pulse pressure variation and SVV, which may exhibit faster responses to sudden changes in volume responsiveness, are calculated using an arterial pressure waveform analysis method. However, some studies have reported clinically unacceptable accuracy for these systems in patients with vasodilation or impaired systolic function during a hypovolemic state [31, 32].

To surmount the shortcoming of existing hemodynamic monitoring, a novel TPTD system has been introduced and employed in clinical practice recently. It has a specific thermistor-tipped arterial catheter, the VolumeViewTM catheter, and the EV 1000 monitoring platform [16]. After injection of cold saline in the superior vena cava, TPTD allows the calculation of cardiac output from a TPTD curve recorded using a thermistor-tipped femoral arterial catheter [33]. Additional physiological data, such as the GEDI and ELWI, can be derived from the dilution curve. Volumetric preload indicators, such as the GEDI [34–36], have been reported to be reliable indicators of cardiac preload and have been successfully implemented in therapeutic strategies that may improve outcomes. The GEDI ranged from 715.4 to 809.7 in the present

study, and this level steadily increased during the HIPEC period because of fluid resuscitation for compensating a decreased SVRI and increased SVV and HR. The ELWI, measured with single indicator dilution, is a reliable measure of pulmonary edema that has been validated against postmortem gravimetric measurement in animals [37–39]. Moreover, ELWI and PVPI may be used as criteria indicating the risk of fluid administration [40]. Especially, $ELWI \geq 10$ mL/kg was defined as pulmonary edema, although no definitive quantitative criteria for ELWI associated with pulmonary edema have been established. A previous human autopsy study reported that the normal ELWI value is approximately 7.4 (SD 3.3) mL/kg, and this value can distinguish between healthy and pathological lungs [41]. Because ELWI ranged from 6.9 to 7.3 (peak value during HIPEC) in our study, the risk of occurrence of intraoperative pulmonary edema related to the cytoreductive surgery with HIPEC was lower more than anticipated.

During HIPEC, the circulation support with inotropes/vasopressors does not have definite recommendations [28]. The common practice in the setting of vasodilation was the use of noradrenaline and methoxamine, and it usually depends on institutional protocols. We almost selected and administered phenylephrine to our patients as a vasopressor because of increased HR and decreased SVRI. As a compensatory mechanism for the fallen SVRI, increased CO up to and HR up to were measured using Vigileo™ during HIPEC, which is consistent with previous reports [42, 43]. Especially, the SVRI remained low not only during HIPEC but also postoperatively. In 6 cases, the vasopressor was maintained when leaving the operating room.

The choice of intraoperative fluid infusion involves balanced infusion therapy to maintain preload, colloid oncotic pressure, end-organ perfusion (urinary output), and electrolyte homeostasis [10]. To prevent hemodynamic imbalance and reductions in end-organ perfusion, the main aim of the anesthesiologist should be adequate fluid replacement and blood loss adjustment and maintenance of euvolemia. Moreover, in surgery with HIPEC, AKI usually occurs because of a decrease in blood pressure and insufficiency of intravascular volume. With just maintenance of normovolemia and adequate urine output, no change in creatinine values occurred during cytoreductive surgery and HIPEC [12, 44], and in our study, only 1 patient experienced AKI. It would be helpful to perform comprehensive evaluation of a patient's intravascular volume status with closed monitoring involving various approaches, including the use of the VolumeView™ system [7].

The severity of metabolic imbalances observed during HIPEC rely on the type of carrier solution and degree of hyperthermia. The carrier solution used in this study was a fluid containing 5% dextrose. Metabolic disturbances occur when both glucose and free water are absorbed into the plasma causing increased temperature and dilutional hyponatremia [1]. In our study, body temperature increased up to 38°C for 2 hours during the HIPEC period. Hyperthermia has been shown to increase metabolic activity, HR, carbon dioxide production, and ultimately oxygen consumption [7]. Additionally, a previous study reported increases in the lactate level of 2 to 4 mmol/L [45]. Although the results of this study also showed elevated glucose and lactic acid levels, the levels of electrolytes, such as sodium, were almost in

the normal range. This result may be associated with closed monitoring and adequate fluid management made possible by the new TPTD system.

After HIPEC, patients are mostly admitted to the ICU for monitoring of organ function, management of postoperative complications, and correction of electrolytes and coagulopathy. Physiological perturbations during the perioperative period affect the duration of ICU stay and may precipitate multisystem organ failure [1]. Although the length of ICU stay (1.4 days) in our study was similar to the length reported in other studies, postoperative complications after surgery were unavoidable in our study. Regarding postoperative outcomes, there are many debates about the ideal postoperative nutrition strategies. According to a retrospective study by Arakelian et al., postoperative ileus is a common problem after surgery [46]. Although there are no prospective studies, most patients were tolerable oral feeding between 7 and 11 days postoperatively. To promote healing and improve intestinal transit, early enteral feeding is well known for both safe and beneficial for patients [47–49]. In our study, the recovery time of bowel movement was about 6 days, and the water and soft diet feeding times were lower than the gas passing time.

Some limitations must be acknowledged. This was a prospective observational study and the number of enrolled patients was relatively low. Consequently, it is slightly unreasonable to generalize the results of our study. In addition, it may be more critical to investigate the course of pathophysiologic changes, including fluid redistribution, after HIPEC surgery compared with intraoperative conditions. However, our findings will be a valuable source of information for further studies that address the anesthetic management of patients who are scheduled to undergo major surgery accompanied with severe hemodynamic changes, such as those associated with HIPEC.

In conclusion, our study demonstrated various physiological changes through the developed hemodynamic monitoring system in patients undergoing open cytoreductive abdominal surgery with HIPEC. Fluid therapy remains one of the most challenging issues for the anesthesia team; therefore, anesthesiologists should constantly explore the most optimal intraoperative anesthetic management approach, including the maintenance of intravascular volume status, in major surgery that is expected to result in acute hemodynamic changes.

List Of Abbreviations

ABGA, arterial blood gas analysis; AKI, acute kidney injury; BIS, bispectral index; CI, cardiac index; CVP, central venous pressure; EBL, estimated blood loss; ELWI, extravascular lung water index; ESKD, end-stage Kidney Disease; GEDI, global end-diastolic volume index; HIPEC, hyperthermic intraperitoneal chemotherapy; HR, hazard ratio; ICU, intensive care unit; IV, intravenous; PCA, patient-controlled analgesia; PVPI, pulmonary vascular permeability index; RIFLE, risk, injury, failure, loss, and end-stage kidney disease; SVI, stroke volume index; SVRI, systemic vascular resistance index; SVV, stroke volume variation; TPTD, transpulmonary thermodilution

Declarations

Ethics approval and consent to participate

All procedures performed were in accordance with the ethical standards of the Hospital Research Ethics Committee and Institutional Review Board of Severance Hospital, Yonsei University Health System (IRB number: 4–2014–0854) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The written consent form was obtained from all patients included in our study.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no conflict of interest.

Funding

The VolumeView™ system (in kind) of this research was supported by the Edwards Lifesciences, Korea.

Authors' contributions

M. H. K. substantial contributed to study design and conduct, data acquisition, data analysis, interpretation of data, manuscript writing and drafting, and substantively revising manuscript. Y. C. Y. substantial contributed to study design and conduct, data analysis, interpretation of data and manuscript writing. S. H. B. substantial contributed to study design and conduct. K. Y. L.2 substantial contributed to study conduct. N. K. substantial contributed to data acquisition. K. Y. L.1 participated as the corresponding author and supervised the overall study, substantial contributed to study design and conduct, data analysis, interpretation of data, manuscript writing and drafting, and substantively revising manuscript

Acknowledgement

Not applicable

References

1. Webb CA, Weyker PD, Moitra VK, Raker RK. An overview of cytoreductive surgery and hyperthermic intraperitoneal chemoperfusion for the anesthesiologist. *Anesth Analg* 2013;116:924-31.

2. Koppe MJ, Boerman OC, Oyen WJ, Bleichrodt RP. Peritoneal carcinomatosis of colorectal origin: Incidence and current treatment strategies. *Ann Surg* 2006;243:212-22.
3. Esquivel J, Lowy AM, Markman M, Chua T, Pelz J, Baratti D, et al. The American Society of Peritoneal Surface Malignancies (ASPSM) multiinstitution evaluation of the peritoneal surface disease severity score (PSDSS) in 1,013 patients with colorectal cancer with peritoneal carcinomatosis. *Ann Surg Oncol* 2014;21:4195-201.
4. Glehen O, Mohamed F, Gilly FN. Peritoneal carcinomatosis from digestive tract cancer: New management by cytoreductive surgery and intraperitoneal chemohyperthermia. *Lancet Oncol* 2004;5:219-28.
5. Glehen O, Gilly FN, Boutitie F, Bereder JM, Quenet F, Sideris L, et al. Toward curative treatment of peritoneal carcinomatosis from nonovarian origin by cytoreductive surgery combined with perioperative intraperitoneal chemotherapy: A multi-institutional study of 1,290 patients. *Cancer* 2010;116:5608-18.
6. Sugarbaker PH. New standard of care for appendiceal epithelial neoplasms and pseudomyxoma peritonei syndrome? *Lancet Oncol* 2006;7:69-76.
7. Schmidt C, Creutzenberg M, Piso P, Hobbhahn J, Bucher M. Peri-operative anaesthetic management of cytoreductive surgery with hyperthermic intraperitoneal chemotherapy. *Anaesthesia* 2008;63:389-95.
8. Colantonio L, Claroni C, Fabrizi L, Marcelli ME, Sofra M, Giannarelli D, et al. A randomized trial of goal directed vs. standard fluid therapy in cytoreductive surgery with hyperthermic intraperitoneal chemotherapy. *J Gastrointest Surg* 2015;19:722-9.
9. Suehiro K, Tanaka K, Mikawa M, Uchihara Y, Matsuyama T, Matsuura T, et al. Improved performance of the fourth-generation flotrac/vigileo system for tracking cardiac output changes. *J Cardiothorac Vasc Anesth* 2015;29:656-62.
10. Brienza N, Giglio MT, Dalfino L. Protocolled resuscitation and the prevention of acute kidney injury. *Curr Opin Crit Care* 2012;18:613-22.
11. Thix CA, Konigsrainer I, Kind R, Wied P, Schroeder TH. Ventricular tachycardia during hyperthermic intraperitoneal chemotherapy. *Anaesthesia* 2009;64:1134-6.
12. Verwaal VJ, van Tinteren H, Ruth SV, Zoetmulder FA. Toxicity of cytoreductive surgery and hyperthermic intra-peritoneal chemotherapy. *J Surg Oncol* 2004;85:61-7.
13. Kusamura S, Baratti D, Younan R, Laterza B, Oliva GD, Costanzo P, et al. Impact of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy on systemic toxicity. *Ann Surg Oncol* 2007;14:2550-8.
14. Gusani NJ, Cho SW, Colovos C, Seo S, Franko J, Richard SD, et al. Aggressive surgical management of peritoneal carcinomatosis with low mortality in a high-volume tertiary cancer center. *Ann Surg Oncol* 2008;15:754-63.
15. Baratti D, Kusamura S, Laterza B, Balestra MR, Deraco M. Early and long-term postoperative management following cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. *World*

J Gastrointest Oncol 2010;2:36-43.

16. Kiefer N, Hofer CK, Marx G, Geisen M, Giraud R, Siegenthaler N, et al. Clinical validation of a new thermodilution system for the assessment of cardiac output and volumetric parameters. *Crit Care* 2012;16:R98.
17. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P; Acute Dialysis Quality Initiative Workgroup. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: The Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care* 2004;8:R204-12.
18. Yan TD, Welch L, Black D, Sugarbaker PH. A systematic review on the efficacy of cytoreductive surgery combined with perioperative intraperitoneal chemotherapy for diffuse malignancy peritoneal mesothelioma. *Ann Oncol* 2007;18:827-34.
19. Mohamed F, Cecil T, Moran B, Sugarbaker P. A new standard of care for the management of peritoneal surface malignancy. *Curr Oncol* 2011;18:e84-96.
20. Verwaal VJ, van Ruth S, de Bree E, van Sloothen GW, van Tinteren H, Boot H, et al. Randomized trial of cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy and palliative surgery in patients with peritoneal carcinomatosis of colorectal cancer. *J Clin Oncol* 2003;21:3737-43.
21. Kim KS, Kim YK, Park SH. The hemodynamic changes during continuous hyperthermic peritoneal perfusion. *Korean J Anesthesiol* 1995;29:88-93.
22. Raue W, Tsilimparis N, Bloch A, Menenakos C, Hartmann J. Volume therapy and cardiocircular function during hyperthermic intraperitoneal chemotherapy. *Eur Surg Res* 2009;43:365-72.
23. Thanigaimani K, Mohamed F, Cecil T, Moran BJ, Bell J. The use of cardiac output monitoring to guide the administration of intravenous fluid during hyperthermic intraperitoneal chemotherapy. *Colorectal Dis* 2013;15:1537-42.
24. Schluermann CN, Hoepfner J, Benk C, Schmidt R, Loop T, Kalbhenn J. Intra-abdominal pressure, cardiac index and vascular resistance during hyperthermic intraperitoneal chemotherapy: A prospective observational study. *Minerva Anesthesiol* 2016;82:160-9.
25. Esquivel J, Angulo F, Bland RK, Stephens AD, Sugarbaker PH. Hemodynamic and cardiac function parameters during heated intraoperative intraperitoneal chemotherapy using the open "coliseum technique". *Ann Surg Oncol* 2000;7:296-300.
26. Michard F. Changes in arterial pressure during mechanical ventilation. *Anesthesiology* 2005;103:419-28; quiz 449-5.
27. Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. *Chest* 2008;134:172-8.
28. Sheshadri DB, Chakravarthy MR. Anaesthetic considerations in the perioperative management of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. *Indian J Surg Oncol* 2016;7:236-43.

29. Kumar A, Anel R, Bunnell E, Habet K, Zanotti S, Marshall S, et al. Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects. *Crit Care Med* 2004;32:691-9.
30. Michard F, Teboul JL. Predicting fluid responsiveness in ICU patients: A critical analysis of the evidence. *Chest* 2002;121:2000-8.
31. Sotomi Y, Iwakura K, Higuchi Y, Abe K, Yoshida J, Masai T, et al. The impact of systemic vascular resistance on the accuracy of the flotrac/vigileo system in the perioperative period of cardiac surgery: A prospective observational comparison study. *J Clin Monit Comput* 2013;27:639-46.
32. Suehiro K, Tanaka K, Funao T, Matsuura T, Mori T, Nishikawa K. Systemic vascular resistance has an impact on the reliability of the vigileo-flotracs system in measuring cardiac output and tracking cardiac output changes. *Br J Anaesth* 2013;111:170-7.
33. Reuter DA, Huang C, Edrich T, Shernan SK, Eltzschig HK. Cardiac output monitoring using indicator-dilution techniques: Basics, limits, and perspectives. *Anesth Analg* 2010;110:799-811.
34. Michard F, Alaya S, Zarka V, Bahloul M, Richard C, Teboul JL. Global end-diastolic volume as an indicator of cardiac preload in patients with septic shock. *Chest* 2003;124:1900-8.
35. Hofer CK, Furrer L, Matter-Ensner S, Maloigne M, Klaghofer R, Genoni M, et al. Volumetric preload measurement by thermodilution: A comparison with transoesophageal echocardiography. *Br J Anaesth* 2005;94:748-55.
36. Sakka SG, Ruhl CC, Pfeiffer UJ, Beale R, McLuckie A, Reinhart K, et al. Assessment of cardiac preload and extravascular lung water by single transpulmonary thermodilution. *Intensive Care Med* 2000;26:180-7.
37. Katzenelson R, Perel A, Berkenstadt H, Preisman S, Kogan S, Sternik L, et al. Accuracy of transpulmonary thermodilution versus gravimetric measurement of extravascular lung water. *Crit Care Med* 2004;32:1550-4.
38. Fernandez-Mondejar E, Castano-Perez J, Rivera-Fernandez R, Colmenero-Ruiz M, Manzano F, Perez-Villares J, et al. Quantification of lung water by transpulmonary thermodilution in normal and edematous lung. *J Crit Care* 2003;18:253-8.
39. Kirov MY, Kuzkov VV, Kuklin VN, Waerhaug K, Bjertnaes LJ. Extravascular lung water assessed by transpulmonary single thermodilution and postmortem gravimetry in sheep. *Crit Care* 2004;8:R451-8.
40. Jozwiak M, Teboul JL, Monnet X. Extravascular lung water in critical care: recent advances and clinical applications. *Ann Intensive Care* 2015;5:
41. Neumann P. Extravascular lung water and intrathoracic blood volume: Double versus single indicator dilution technique. *Intensive Care Med* 1999;25:216-9.
42. Esquivel J, Sticca R, Sugarbaker P, Levine E, Yan TD, Alexander R, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in the management of peritoneal surface malignancies of colonic origin: A consensus statement. Society of Surgical Oncology. *Ann Surg Oncol* 2007;14:128-33.

43. Raspe C, Piso P, Wiesenack C, Bucher M. Anesthetic management in patients undergoing hyperthermic chemotherapy. *Curr Opin Anaesthesiol* 2012;25:348-55.
44. Glehen O, Osinsky D, Cotte E, Kwiatkowski F, Freyer G, Isaac S, et al. Intraperitoneal chemohyperthermia using a closed abdominal procedure and cytoreductive surgery for the treatment of peritoneal carcinomatosis: Morbidity and mortality analysis of 216 consecutive procedures. *Ann Surg Oncol* 2003;10:863-9.
45. De Somer F, Ceelen W, Delanghe J, De Smet D, Vanackere M, Pattyn P, et al. Severe hyponatremia, hyperglycemia, and hyperlactatemia are associated with intraoperative hyperthermic intraperitoneal chemoperfusion with oxaliplatin. *Perit Dial Int* 2008;28:61-6.
46. Arakelian E, Gunningberg L, Larsson J, Norlen K, Mahteme H. Factors influencing early postoperative recovery after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. *Eur J Surg Oncol* 2011;37:897-903.
47. Tsahalina E, Razvi K, Alkatib M, Shaw C, Chun LY, Barton DP. Early enteral feeding following major abdominal surgery for recurrent gynaecological cancer. *J Obstet Gynaecol* 2006;26:457-61.
48. Lewis SJ, Egger M, Sylvester PA, Thomas S. Early enteral feeding versus "nil by mouth" after gastrointestinal surgery: Systematic review and meta-analysis of controlled trials. *BMJ* 2001;323:773-6.
49. Moore-Olufemi SD, Padalecki J, Olufemi SE, Xue H, Oliver DH, Radhakrishnan RS, et al. Intestinal edema: Effect of enteral feeding on motility and gene expression. *J Surg Res* 2009;155:283-92.

Tables

Table 1. Patient characteristics

Characteristic	N = 21
Age (years)	59.0 (11.7)
Sex (n, %)	
Male	13 (61.9)
Female	8 (38.1)
Cancer origin (n, %)	
Colon	6 (28.6)
Appendix	6 (28.6)
Sigmoid	4 (19)
Rectal	4 (19)
Others	1 (4.8)
Height (cm)	162.1 (8.5)
Weight (kg)	54.5 (9.5)
ASA physical status classification (n, %)	
I	9 (42.9)
II	7 (33.3)
III	5 (23.8)
Co-operation (n, %)	
Hepatobiliary and pancreatic surgery	7 (33.3)
Urologic surgery	6 (28.6)
Upper gastrointestinal surgery	4 (19.0)
Gynecologic surgery	3 (14.2)
Vascular surgery	1 (4.7)
Thoracic surgery	1 (4.7)

Data are presented as mean (standard deviation) or number (percentage).

ASA, American Society of Anesthesiologists

Table 2. Intraoperative parameters

Intraoperative parameter	
Surgical time (min)	638.8 (207.8)
Anesthetic time (min)	718.1 (207.8)
Patient-controlled analgesia	
Intravenous	17 (81.0%)
Epidural	4 (19.0%)
Input	
Crystalloid (mL)	6983.3 (4496.4)
Hydroxyethyl starch 6% (mL)	976.2 (460.3)
Packed RBC (mL)	207.1 (378.2, 0-1400)
Fresh-frozen plasma (mL)	71.4 (181.4, 0-600)
Albumin (mL)	109.5 (151.3, 0-500)
Output	
Urine output (mL)	1464.8 (898.0)
Estimated blood loss (mL)	780.0 (928.6, 50-3350)
Rapid insulin (unit)	6.8 (4.3)
Vasopressor	
Ephedrine (n, %)	14/21 (66.7)
Phenylephrine (n, %)	15/21 (71.4)
Norepinephrine (n, %)	2/21 (9.5)

Data are presented as mean (standard deviation, range) or number (percentage).

RBC, red blood cell

Table 3. Intraoperative hemodynamic, respiratory, and metabolic variables

Parameter	T1	T2	T3	T4	T5	T6	T7
BT (°C)	36.3 (0.6)	35.7 (0.9)	36.9 (0.9)	37.7 (0.7)	38.0 (0.7)	37.5 (0.7)	36.8 (0.5)
HR (beats/min)	66.1 (12.3)	77.8 (14.7)	83.6 (14.4)	89.4 (16.6)	94.6 (17.6)	87.9 (17.4)	85.9 (15.1)
MBP (mmHg)	78.4 (11.0)	82.9 (9.9)	77.5 (8.4)	76.4 (6.9)	75.5 (7.0)	78.1 (7.5)	76.9 (7.9)
CVP (mmHg)	7.8 (3.2)	7 (2.8)	8.5 (3.0)	8.7 (3.2)	9.2 (3.4)	8.5 (3.7)	9.0 (3.2)
Hemodynamic parameters							
CI (L/min/m ²)	3.0 (0.7)	3.2 (0.8)	3.3 (0.8)	3.5 (0.8)	3.8 (1.1)	3.5 (1.0)	3.3 (0.8)
SVI (mL/beat/m ²)	43.3 (6.3)	47.2 (9.5)	49.7 (11.0)	50.0 (10.0)	50.2 (10.7)	49.6 (10.1)	46.2 (7.3)
SVV (%)	7.9 (4.2)	10.5 (3.7)	9.6 (4.2)	11.0 (4.7)	10.1 (3.9)	11.4 (6.2)	11.2 (5.1)
SVRI (dyn•s/cm ⁵ /m ²)	2327.1 (351.2)	1615.5 (252.0)	1623.5 (399.1)	1326.8 (434.8)	1362.9 (278.0)	1389.2 (293.4)	1467.4 (351.5)
ELWI (mL/kg)	6.9 (0.6)	6.9 (0.5)	7.1 (0.5)	7.1 (0.4)	7.3 (0.4)	7.1 (0.7)	6.9 (0.4)
PVPI	2.0 (0.4)	2.1 (0.4)	2.4 (0.4)	2.5 (0.5)	2.6 (0.4)	2.4 (0.6)	2.3 (0.4)
GEDI	715.4 (82.1)	745.5 (65.7)	779.5 (49.8)	783.6 (58.8)	808.7 (50.0)	809.7 (76.7)	767.1 (43.6)
ABGA							
PO ₂ (mmHg)	187.7 (30.0)	200.5 (34.4)	202.8 (26.3)	188.4 (28.2)	184.3 (29.1)	187.2 (25.5)	196.1 (21.6)
PCO ₂ (mmHg)	33.4 (4.6)	34.8 (3.7)	34.0 (5.2)	34.2 (4.0)	34.2 (3.4)	33.3 (3.1)	33.1 (3.8)
Hematocrit (%)	11.4 (1.4)	10.7 (1.3)	10.8 (1.1)	10.9 (1.2)	10.7 (1.1)	10.6 (1.1)	11.0 (1.0)
pH	7.44 (0.03)	7.39 (0.04)	7.39 (0.04)	7.39 (0.04)	7.40 (0.04)	7.40 (0.04)	7.40 (0.04)
HCO ₃ (mmol/L)	22.8 (2.2)	21.2 (1.7)	20.6 (2.6)	21.0 (1.7)	21.0 (1.7)	20.5 (1.8)	20.3 (1.7)
Lactate (mmol/L)	0.9 (0.3)	1.5 (0.7)	2.2 (0.9)	2.9 (1.2)	3.3 (1.4)	3.5 (1.6)	3.1 (1.8)
Glucose (mg/dL)	88.5 (31.5)	134.0 (31.4)	185.9 (58.0)	215.2 (44.0)	207.2 (35.3)	189.4 (35.3)	160.1 (26.8)
Sodium (mmol/L)	137.0	136.1	135.5	134.5	135.0	134.9	135.7

Data are presented as mean (standard deviation).

BT, body temperature; HR, heart rate; MBP, mean arterial pressure; CVP, central venous pressure; CI, cardiac index; SVI, stroke volume index; SVV, stroke volume variation; SVRI, systemic vascular resistance index; GEDI, global end-diastolic volume index; ELWI, extravascular lung water index; PVPI, pulmonary vascular permeability index; ABGA, arterial blood gas analysis; PO₂, partial pressure of oxygen; PCO₂, partial pressure of carbon dioxide; Hct, hematocrit; HCO₃, bicarbonate

Table 4. Postoperative recovery profiles

Postoperative parameter	
Coagulation profile	
Preoperative platelet count (/μL)	307,048 (127,403)
Postoperative platelet count (/μL)	238,952 (104,884)
Preoperative PT (INR)	1.02 (0.10), 94.4 (8.4)
Postoperative PT (INR)	1.27 (0.29), 76.0 (14.4)
Preoperative pTT (s)	32.6 (9.0)
Postoperative pTT (s)	34.1 (8.2)
Preoperative albumin (g/dL)	3.9 (0.6)
Postoperative albumin (g/dL)	2.4 (0.6)
Acute kidney injury (n, %)	1 (4.8%)
Respiration	
Extubation in the ICU (n, %)	9 (42.9)
Postoperative extubation (time)	9.9 (26.7, 0-124)
Vasopressor maintenance (n, %)	6 (28.6%)
Bowel movement	
SOW (time)	66.3 (29.7)
GPT (time)	144.8 (115.5)
SDT (time)	129.5 (117.3)
Complications (n, %)	7 (33.3%)
Surgical	3 (14.3%)
Non-surgical	4 (19.0%)
Hospital stay	
ICU admission (n, %)	17/21 (81)
ICU LOS (day)	1.4 (1.3)
POD LOS (day)	18.5 (10.2)
*Mortality (n, %)	2/21 (9.5)

Data are presented as mean (standard deviation, range) or number (percentage).

PT, prothrombin time; INR, international normalized ratio; pTT, partial thromboplastin time; ICU, intensive care unit; SOW, sips of water; GPT, gas passing time; SDT, soft diet time; LOS, length of stay; POD, postoperative day

*Death during the study period

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [STROBEchecklist.docx](#)