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# Impact of PCO2 gap protocol application on early postoperative mortality and organ failure in high risk surgical patients undergoing major abdominal surgeries

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***Abstract*---**Background: high risk surgical patients undergoing major abdominal surgeries still have higher rate of mortality and organ failure rates in the early postoperative period. Objective: We aimed to assess PCO2 gap protocol application in the intraoperative and early post-operative (first 12 hours) on postoperative mortality and organ failure in high risk surgical patients undergoing major abdominal surgeries compared to a classical goal directed therapy protocol (GDT) targeting mean arterial blood pressure (MAP), mixed venous oxygen saturation (SvO2), central venous pressure (CVP), Haematocrite value (Hct) and urine output (UOP). Patients and Methods: Guided by Shoemacker et al score 80 high risk surgical patients undergoing major abdominal surgeries were divided into two groups group A PCO2 gap algorithm was applied intraoperative and 12 h postoperative end point PCO2 gap 2-6mm Hg ,group B goal directed therapy protocol targeting MAP > 65mmHg, CVP between 8-12cmH2O, Haematocrite value more than 30, Svo2 >75% and urine output more than >0.5 ml/kg/hr an applied intraoperative and 12 postoperative


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end point . Postoperative organs dysfuctions were assessed using the Sequential Organ Failure Assessment (SOFA) score recorded daily ICU discharge then every three days till discharge home. Results: GDT group had significantly higher SOFA score on the 1st, 3rd and 6th postoperative days. Post-operative mortality in PCO2 gap (7.5%) protocol group was significantly less than GDT group(25%) P value0.03 and post-operative 3 organ failures 17.5% in PCO2 gap compared to 30% in GDT P value0.06. Conclusion: Application of the PCO2 gap protocol for resuscitation intra operative and 12 hours postoperative had decreased severity of postoperative organ failure and mortality in high risk surgical patients undergoing major abdominal surgeries in comparison with a classic early goal directed therapy.

***Keywords*---**Pco2 gap, goal directed therapy, high risk surgical patients.

## Introduction

Notwithstanding the observable decline in perioperative mortality and morbidity rates in the last decades it remains high in the subgroup of high-risk patients [1]. High risk surgical patients are medically complex and have limited physiologic reserves. The inability to meet increased oxygen (O2) demand with surgical trauma especially in major abdominal surgeries either by an increase in Oxygen supply or by increasing Oxygen extraction can lead to tissue hypoxia[2-3]. Tissue hypoxia due to tissue hypoperfusion is a leading antecedent of postoperative organ failure and mortality following major surgery [4-5].

Early identification of high-risk patients improve surgical decision-making, preoperative optimization, and patient-specific intraoperative and postoperative management which have a positive impact on postoperative outcomes. The Enhanced Recovery After Surgery (ERAS) © protocols are increasingly applied in perioperative services worldwide [6-7]. The application of ERAS protocols has resulted in remarkable benefits to both the patients and hospitals with a shorter length of hospital stay by 30–50%, a similar rate of complication decline, and a significantly reduced re-admissions rate to the hospital [8-9].

Perioperative fluid management is an important element in the success of ERAS protocols. The use of goal-directed fluid therapy (GDT) is becoming a cornerstone protocol for the appropriate perioperative fluid/volume management [10]. commonly used targets mean arterial blood pressure (MAP) more than 65mmHg, central venous pressure between 8-12 cmH2O , Haematocrite value more than 30,mixed venous oxygen saturation ( ScvO2) more than 75% and urine output more than >0.5 ml/kg/hr [11]. Early goal-directed therapy treatment flowchart, Kaiser Permanente Northern California figure 1 was used in this study.

The difference between venous carbon dioxide and arterial carbon dioxide pressure (pCO2 gap) has been represented as a parameter reflecting tissue hypo perfusion in critically ill patients who are under -resuscitated. The pCO2 gap/CavO2 ratio has also been described as an indicator of the respiratory quotient, thus the relationship between Oxygen delivery (DO2) and Oxygen consumption (VO2) [12,13].

Most of the literature delineating pCO2 gap and the pCO2 gap/ CavO2 ratio was taken from studies on animal or intensive care unit (ICU) patients. To date, publications pertaining to the operative setting are sparse[14]. Robin et al concluded that High PCO2 gap values were associated with a higher rate of postoperative complications in high risk surgical patient underwent major abdominal surgeries. No study has assessed the ability of hemodynamic protocols based on the pCO2 gap measurement to decrease postoperative complications[15]. Vallet et al.[12] proposed a protocol to diagnose and treat various types of shocks in septic patients using Svo2-pco2 gap algorithm which was used in this study. The aim of this study was to compare postoperative outcomes between Svo2-pco2 gap algorithm and early goal directed therapy (GDT) in resuscitation of high risk patients who underwent major abdominal surgeries. Both protocols were applied intraoperative and 12 hours postoperative. The main outcomes were post-operative mortality and post-operative organ failures.

**Patients and Methods**

This was single center a prospective randomized trial done between January 2020 and March 2021. After approval from ethical committee of south valley university, Qena, Egypt. Eighty high risk surgical patients scheduled for major abdominal surgeries were included in the research after giving written informed consent from the patients or from the patient's legal representative. The criteria for inclusion are that of Shoemacker et al. criteria summarized in Table 1.

Table (1): Demographic, surgical and intensive care inclusion criteria high-risk criteria Values

| Criteria | Values |
|---|---|
| Demographic criteria | ▪ Age ≥70 yrs<br>▪ ASA class ≥3<br>▪ Severe nutritional problems<br>▪ Previous severe respiratory illness<br>▪ Chronic renal failure<br>▪ Chronic liver failure<br>▪ Ischemic heart disease (infarction or angina)<br>▪ Malignant neoplasia |
| Surgical criteria | ▪ Major abdominal surgery<br>▪ Prolonged surgery ≥8 hrs<br>▪ Urgent surgery<br>▪ Septic surgery<br>▪ Vascular clamping ≥1 hr<br>▪ Surgical procedures<br>▪ Esophagectomy<br>▪ Gastrectomy<br>▪ Small bowel resection<br>▪ Large bowel resection |

| | |
|---|---|
| | ▪ Hepatectomy<br>▪ Pancreatectomy<br>▪ Intraabdominal vascular surgery<br>▪ Other |
| Intensive care criteria | ▪ Shock<br>▪ Acute Respiratory failure<br>▪ Haemorrhage (Hb < 7 g/dL)<br>▪ Acute coronary syndrome |

Data are presented as absolute value (%). Severe nutritional problems: body mass index ≤ 17 kg/m$^2$ or weight loss > 10 % in 6 months. Chronic renal failure: creatinine clearance < 60 ml.min−1.1.73 m−2 or creatinine > 176 µmol.L−1. Chronic liver failure: bilirubin > 78 µmol.L-1 or prothrombin time < 55% or well documented cirrhosis.

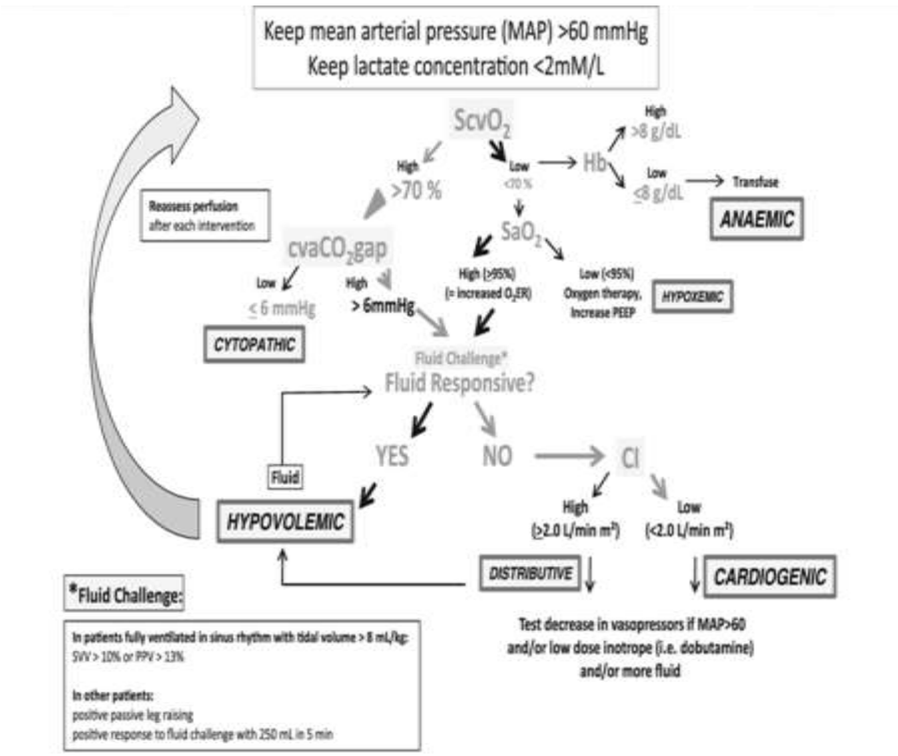


Figure (1): The ScvO2-cvaCO2gap-guided protocol. ScvO2 venous central O2 saturation, cvCO2gap central venous-to-arterial pCO2 difference, SaO2 arterial O2 saturation, CI cardiac index, SVV stroke volume variability, PPV pulse pressure variability [12].

**The participants were randomly divided into two equal groups: Group (A)**

ScvO2-cvaCO2gap-guided protocol (PCO2 gap protocol) figure (1) applied intraoperative and 12 h postoperative end point PCO2 gap aiming to keep pCO2 below 6 mmHg. Readings of Scvo2, PCO2 gap, Hct, SpO2, cardiac index (CI) if needed was taken every 2 hours intra operative and every 4 hours post-operative.

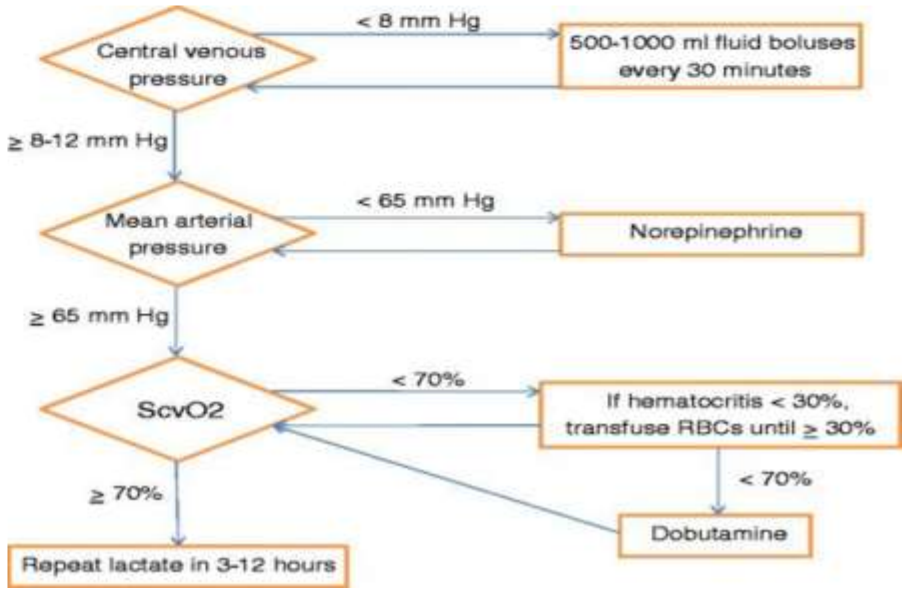


Figure (2): Early goal-directed therapy treatment flowchart, Kaiser Permanente Northern California. Patients are considered for central venous oxygenation saturation (ScvO2)-guided therapies once their central venous and mean arterial pressures have been optimized with fluid and vasopressor therapies as indicated. Patients with ScvO2 values less than 70% are transfused with red blood cells (RBCs) until the hematocrit is 30% or greater, followed by dobutamine administration if ScvO2 remains <70% [16].

Group (B) Early goal-directed therapy treatment flowchart, Kaiser Permanente Northern California figure (2) was applied intraoperative and 12 h postoperative targeting MAP > 65mmHg, CVP between 8-12cmH2O, Hematocrit value more than 30, Svo2 >75% and urine output more than >0.5 ml/kg/hr. Readings of Scvo2, Hct, UOP, CVP and MAP was taken every 2 hours intra operative and every 4 hours post-operative.

All patients were evaluated preoperatively, demographic data (age, sex, weight), type of surgical procedure and base line sequential organ failure (SOFA) score were obtained. General anaesthesia for all patients were carried on according to our local standards. Standard monitoring intraoperative included electrocardiography, noninvasive blood pressure end-tidal CO2 pulse oximetry and urine ouput determinded by insertion of urinary catheter (Foley's catheter). for central venous pressure and mixed venous oxygen saturation monitoring during major surgery, all patients from both groups catheterized by standard three-lumen catheter central line (Certofix trio, B Braun, Germany) in the right internal jagular vein, catheter tip positioned within the superior vena cava, and correct positioning were verified by chest radiograph for arterial sampling arterial catheters (Arteriofix, B Braun, Germany) placed before the beginning of surgery. Premedication, general anaesthesia and reversal of anesthesia for all patients were carried on according to our local standards.

All patients were admitted to the surgical intensive care unit after surgeries finished and was all managed according to their allocated group. Standard postoperative monitoring was include: electrocardiograph (heart rate), noninvasive arterial pressure, pulse oximetry and urine output. organ dysfunctions were assessed daily in the ICU and every 3 days after discharge from ICU using SOFA score. Organs dysfunction are central nervous system dysfunction (coma), heart failure, renal failure, liver failure, respiratory failure and coagulopathy 30 days mortality were noted.

**Statistical analysis**

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (x2) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

**Results**

Mean age of patients with GDT was 56.67 ± 12.35 years and mean body mass index was 27.51 ± 7.56 kg/m$^2$ while mean age of $PCO_2$ group was 51.56 ± 13.67 years with mean body mass index was 27.93 ± 4.11 kg/m$^2$. Majority (80% of GDT group and of $PCO_2$ of enrolled patients was males (Table 2).

Table (2): Baseline data of enrolled patients

| | GDT (n= 40) | $PCO_2$ gap (n= 40) | P value |
|---|---|---|---|
| Age (years) | 58.67 ± 12.35 | 54.56 ± 11.67 | 0.13 |
| Sex<br>Male<br>Female | <br>32 (80%)<br>8 (20%) | <br>30 (75%)<br>10 (25%) | 0.29 |
| BMI (kg/m$^2$) | 26.51 ± 7.56 | 25.93 ± 4.11 | 0.79 |

Data expressed as frequency (percentage), mean (SD). P value was significant if < 0.05. GDT: goal directed therapy; PCO2 gap: venous-arteria carbon dioxide partial pressure gap; BMI: body mass index. Diagnosis and surgical intervention of enrolled patients are summarized at table. Perforated viscus was the major indication for surgery in both groups followed by intestinal obstruction and cholecystitis. Also, the most frequent surgical interventions were exploration and resection& anastomosis (Table 3).

Table (3): Diagnosis and type of surgery of enrolled patients

| | GDT (n= 40) | $PCO_2$ gap (n= 40) | P value |
|---|---|---|---|
| Diagnosis<br>Perforated viscus | <br>22 (52.5%) | <br>16 (40%) | 0.24 |

| | | | |
|---|---|---|---|
| Intestinal obstruction | 4 (10%) | 5 (12.5%) | |
| Gall bladder perforation | 2(5%) | 3 (7.5%) | |
| Diverticulitis | 4 (10%) | 4 (10%) | |
| Fecal fistula | 4 (10%) | 3 (7.5%) | |
| Duodenal stenosis | 0 | 3 (7.5%) | |
| Fournier gangrene | 2 (5%) | 0 | |
| Irreducible hernia | 1 (2.5%) | 1 (2.55%) | |
| MVO | 1 (2.5%) | 1(2.5%) | |
| Obstructive jaundice | 0 | 2 (5%) | |
| Diaphragmatic rupture | 0 | 2 (5%) | |
| Surgery | | | 0.16 |
| Exploration | 25 (62.5%) | 24 (60%) | |
| Resection& anastomosis | 9 (22.5%) | 4 (10%) | |
| Cholecystectomy | 0 | 5 (12.5%) | |
| Intestinal repair | 2 (10%) | 2 (5%) | |
| CBD exploration | 0 | 2 (5%) | |
| Choledochojejunostomy | 0 | 3 (7.5%) | |
| Debridement | 2 (5%) | 0 | |
| Gastrojejunostomy | 1 (2.5%) | 0 | |
| Ileocecal resection | 1 (2.5%) | 0 | |

Data expressed as frequency (percentage). P value was significant if < 0.05. GDT: goal directed therapy; $PCO_2$: carbon dioxide; MVO: mesenteric vascular occlusion; CBD: common bile duct.

**Risk factors among enrolled groups**

Old age of the patient was the most frequent reported risk factor among both groups (50% of GDT and 55% of the $PCO_2$ group) followed by urgent surgery (40% of GDT and 50% of the $PCO_2$ group) and peritonitis (40% of GDT and 20% of the $PCO_2$ group). Other reported risk factors (Table 4).

Table (4): Risk factors among enrolled groups

| | GDT (n= 40) | $PCO_2$ gap (n= 40) | P value |
|---|---|---|---|
| Old age | 19 (47.5%) | 21 (52.5%) | 0.57 |
| Urgent surgery | 18 (45%) | 20 (50%) | 0.52 |
| Peritonitis | 16 (40%) | 10 (25%) | 0.15 |
| Sepsis | 11 (27.5%) | 6 (15%) | 0.19 |
| Chronic kidney disease | 6 (15%) | 2 (5%) | 0.13 |
| Diabetes mellitus | 4 (10%) | 3 (7.5%) | 0.65 |
| Malignant neoplasm | 3 (7.5%) | 4 (10%) | 0.65 |
| Anaemia | 6(15%) | 4(10%) | 0.50 |
| Malnourished | 5 (12.5%) | 3 (7.5%) | 0.70 |

Data expressed as frequency (percentage). P value was significant if < 0.05. Both groups had insignificant differences as regard SOFA score at baseline, and 9$^{th}$ day and 12$^{th}$ day postoperatively but GDT group had significantly higher SOFA score postoperatively (3.01 ± 1.09 vs. 1.75 ± 0.45; P< 0.001), at 3$^{rd}$ (3.62 ± 1.10 vs. 2.11

± 0.65; P= 0.01) and 6th (4.17 ± 2.11 vs. 1.75 ± 1.01; P= 0.02) postoperative days (Table 5, Figure 3).

Table (5): SOFA score among enrolled groups at different time

| | GDT (n= 40) | $PCO_2$ gap (n= 40) | P value |
|---|---|---|---|
| Baseline SOFA | 2.81 ± 1.22 | 2.25 ± 1.09 | 0.33 |
| 1st day postop SOFA | 3.01 ± 1.09 | 1.75 ± 0.45 | < 0.001 |
| 3rd day SOFA | 3.62 ± 1.10 | 2.11 ± 0.65 | 0.01 |
| 6th day SOFA | 4.17 ± 2.11 | 1.75 ± 1.01 | 0.02 |
| 9th day SOFA | 4.27 ± 1.76 | 2.29 ± 1.65 | 0.53 |
| 12th day SOFA | 6.28 ± 1.21 | 4.60 ± 2.01 | 0.30 |

Data expressed as frequency (percentage), mean (SD). P value was significant if < 0.05. GDT: goal directed therapy; $PCO_2$: carbon dioxide; SOFA: Sequential Organ Failure Assessment.

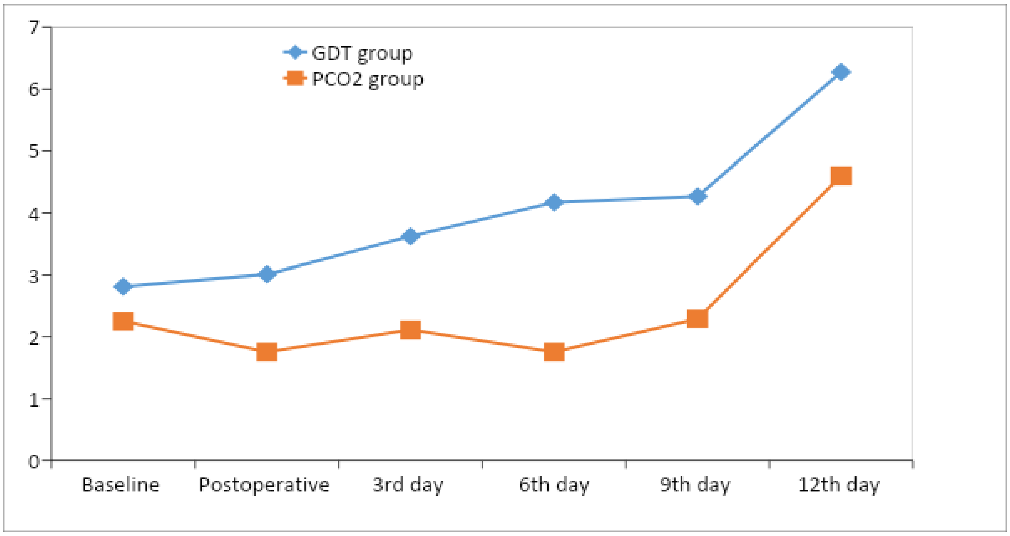

Figure (3): Mean SOFA score among enrolled groups

It was found that frequency of different organ failure was insignificantly higher among patients with GDT in comparison to those with $PCO_2$ gap. Mortality occurred in 10 (25%) patients of GDT group while only three patients were died in the PCO2 group (Table 6).

Table (6): Outcome among enrolled groups

| Variable | GDT (n=40) | Pco2 (n=40) | P value |
|---|---|---|---|
| CNS failure(Glagow coma scale <10) | 8(20%) | 3(7.5%) | 0.10 |
| Respiratory failure | 10(25%) | 7(17.5%) | 0.40 |
| Cardiovascular failure | 11(27.5%) | 5(12.5%) | 0.090 |
| Liver failure | 6(15%) | 3(7.5%) | 0.30 |

| | | | |
|---|---|---|---|
| Renal failure | 12(30%) | 6(15%) | 0.10 |
| Coagulopathy | 9(22.5%) | 5(12.5%) | 0.20 |
| Patients with MOFS | 12(30%) | 7 (17.5%) | 0.06 |
| Organ failures free patients | 28(70%) | 33(82.5%) | 0.188 |
| Mortality | 10 (25%) | 3 (7.5%) | 0.03 |

Data expressed as frequency (percentage). P value was significant if < 0.05. GDT: goal directed therapy; $PCO_2$: carbon dioxide ,MOFS multi organ failure syndrome

**Discussion**

Impaired tissue oxygenation in critically ill patients may be due to multiple factors could progressively lead to adverse outcomes such as organ dysfunction, organ failure, prolonged stay in Intensive Care Unit (ICU) and in hospital and increased mortality. Early detection of tissue hypoxia and maintenance of adequate tissue oxygenation are considered the key elements in the care of critically ill patients. Optimization of hemodynamics and improvement of both metabolic status and tissue oxygenation are primarily addressed via "goal-directed" therapies [1].

Unfortunately, the adequacy of tissue perfusion remains difficult to assess. A broad use of monitoring tools and parameters has been reported to help clinicians in resuscitation of critically ill patients, but their non-specificity to tissue hypoxia exploited the need for additional markers to be investigated. The difference between venous carbon dioxide and arterial carbon dioxide pressure (pCO2 gap) has been described as a parameter reflecting tissue hypo perfusion in critically ill patients who are insufficiently resuscitated. The pCO2 gap/CavO2 ratio has also been introduced as an indicator of the respiratory quotient, thus the relationship between DO2 and VO2 [2].

Most of the knowledge about the pCO2 gap and the pCO2 gap/ CavO2 ratio has come from studies in the literature on animal models or Intensive Care Unit (ICU) patients. To date, publications pertaining to the operative setting are sparse, specifically the ability of hemodynamic protocols based on the pCO2 gap measurement to decrease postoperative adverse outcomes including ICU days and length of hospital stay LOS [6].

Despite advances in anesthetic techniques and monitoring, the outcomes in certain high-risk groups remain very high. Goal directed therapy (GDT) was introduced with the aim of improving the outcomes in this group. Surgery imposes a stress response that increases oxygen demands. Studies have shown that an inability to increase the supply to the tissues is associated with poorer outcomes after surgery. Improving the cardiac output (CO) and oxygen delivery (DO2) to meet the tissue demands under stress has been the principle underlying GDT. The targets have been achieved by various monitoring techniques such as the pulmonary artery catheter, oesophageal Dopplerand pulse contour analysis systems (LidCO Plus™, PiCCO™, Flotrac-Vigileo™) [5].

The main aim of this study was to compare between goal directed therapy and PCO2 gap algorithm application on outcomes of high-risk patients undergoing major abdominal surgery. This prospective randomized trial was conducted. This study included 80 high risk surgical patients scheduled for major abdominal and vascular surgery and admitted to the ICU of South Valley University Hospital, Qena, Egypt. The duration of the study eanged from 6-12 months.

**The main results of this study were as following**

Mean age of patients with GDT was 56.67 ± 12.35 years and mean body mass index was 27.51 ± 7.56 kg/m2 while mean age of PCO2 group was 51.56 ± 13.67 years with mean body mass index was 27.93 ± 4.11 kg/m2. Majority (80% of GDT group and of PCO2of enrolled patients was males. There was no statistically significant difference between both groups as regard age, sex & BMI. Our results were in agreement with study of Sayed[4], as they reported that there was no statistically significant difference between both groups as regard age, sex & BMI. The mean age of patients with GDT was 56.67 ± 12.35 years and means body mass index was 27.51 ± 7.56 kg/m2 while mean age of PCO2 group was 51.56 ± 13.67 years with mean body mass index was 27.93 ± 4.11 kg/m2. Majority (80% of GDT group and of PCO2 of enrolled patients were males.

Also, Hussin et al. [7], revealed that there was no statistically significant difference between the groups regarding demographic data (age, sex, height, and weight). Worldwide, there are over 312 million surgical procedures performed annually. While many of these patients fall into a low-risk group, it has been previously estimated that up to 10% of patients can be classified as a high surgical risk. Those patients in the high-risk group account for 80% of post-operative mortality[8].

The present study showed that as regard diagnosis and surgical intervention of enrolled patients; Perforated viscus was the major indication for surgery in both groups followed by intestinal obstruction and cholecystitis. Also, the most frequent surgical interventions were exploration and resection& anastomosis. Old age of the patient was the most frequent reported risk factor among both groups (50% of GDT and 55% of the PCO2 group) followed by urgent surgery (40% of GDT and 50% of the PCO2 group) and peritonitis (40% of GFT and 20% of the PCO2 group) with no statistically significant difference between the studied groups.

Our results were supported by study of Robin et al. [6], as they reported that major abdominal surgery (71%) was the most common surgical intervention for their enrolled patients. Similarly, Sayed[4], demonstrated that the most frequent surgical interventions were exploration and resection and anastomosis. Furthermore, Mayer et al. [5], revealed that both groups were comparable with respect to co-morbidities and the type of surgery. The current study showed that as regard intraoperative data among enrolled groups: both groups had insignificant differences as regard intraoperative crystalloid administration (6.11 ± 2.98 vs. 5.76 ± 2.34 (l); P= 0.83) and operative time (4.43 ± 1.01 vs. 4.32 ± 1.22 (hour); P= 0.10). Only six patients in GDT group received intraoperative colloid (0.75 ± 0.35 (l)). Plasma and packed RBCs transfusion showed no differences between both groups. None patient in both groups required intraoperative inotropes or vasopressors.

In accordance with our results, study of Kumar et al. [9], as they reported that the duration of surgery was comparable between groups A and B (4.62 ± 1.47h and 4.46 ± 1.38h) respectively. In the study in our hands, there was no statistically significant difference between both groups as regard vital signs. There was no statistically significant difference between both groups as regard mean value of base deficit between two groups in the intraoperative and 12 hs after ICU admission period. Our results were supported by study of Hussin et al. [7], as they reported that there were no statistically significant changes between both groups in the mean arterial blood pressure, heart rate, central venous pressure, and serum lactate values at 24 hours after admission.

GDT aims to meet the patient's increased oxygen demand incurred in the perioperative period, by targeted intervention, guided by haemodynamic monitoring. Increased perioperative oxygen delivery, with reduced oxygen debt in survivors compared to non-survivors was first observed by Shoemaker et al. in the 1980s. Shoemaker et al. thus hypothesized that targeting supranormal physiological parameters in the perioperative setting would therefore decrease morbidity and mortality. They described targets of a cardiac output >4.5 $L/min/m^2$, and an oxygen delivery >600 ml/min/m2. The management of perioperative fluid administration is a different entity to fluid management in the setting of a patient presenting acutely unwell, for example with sepsis. This difference is explained by the different processes occurring at the cellular level in the two conditions and the different reasons and goals of fluid therapy[10].

Perioperative GDT describes fluid administration, with the aim of optimizing a patient's cardiac function and ultimately oxygen delivery. It is used for a time limited period, both during and after a surgical intervention. Many of the patients given fluids postoperatively, as part of GDT, may have a heart rate and blood pressure within the normal range. The fluid is given with the aim of increasing preload and therefore stroke volume and cardiac output to potentially supranormal targets. GDT is conducted for a set time period postoperatively. This is in contrast to patients presenting with sepsis, where the time course may not initially be predictable and fluids and vasopressors may be required to ensure adequate end organ perfusion[11].

The inability to meet an increase in oxygen (O2) demand with surgical trauma either by an increase in O2 delivery or an increase in O2 extraction can lead to tissue hypoxia. Several markers of impaired tissue oxygenation have been explored to help identify patients at increased risk of complications. Postoperative organ failure has been shown to be associated with reduced central venous O2 saturation (ScvO2), which explores the balance of O2 delivery and tissue O2 consumption. However, there is evidence that O2-derived variables are poorly correlated with anaerobic metabolism. Indeed, both normal and high values (that is, ≥75%) for ScvO2 do not preclude the presence of tissue hypoxia in case of impaired O2 extraction capabilities, which may therefore limit the usefulness of ScvO2 monitoring. In contrast, it has also been shown that strategies aimed at reducing high serum lactate levels, as a warning signal of a persistent tissue hypoxia at ICU admission, could reduce length of stay and mortality. However, a rise in lactate level may be delayed compared with markers of tissue oxygenation adequacy, such as oxygen extraction, and could be not sensitive enough to reflect tissue hypoperfusion[12].

Previous relatively small studies have proposed central venous-to-arterial carbon dioxide gradient (PCO2 gap), a global index of tissue perfusion, as a useful measurement to characterize the insufficient flow state in spite of apparently normal macro-circulatory parameters. Tissue partial pressure of carbon dioxide (PCO2) reflects metabolic alterations due to inadequate perfusion in actively metabolized tissues. The PCO2 gap, which has been shown to be inversely related to cardiac output (CO), is considered as a marker of the ability of the venous blood flow to remove the CO2 excess produced in tissues. Thus, an impaired tissue perfusion during a reduced blood flow is the main determinant of a rise of the PCO2 gap[13].

Our results showed that both groups had insignificant differences as regard SOFA score at baseline, and 9th day and 12th day postoperatively but GDT group had significantly higher SOFA score postoperatively (3.01 ± 1.09 vs. 1.75 ± 0.45; P< 0.001), at 3rd (3.62 ± 1.10 vs. 2.11 ± 0.65; P= 0.01) and 6 th (4.17 ± 2.11 vs. 1.75 ± 1.01; P= 0.02) postoperative days. It was found that frequency of different organ failure was insignificantly higher among patients with GDT in comparison to those with PCO2 gap. Mortality occurred in 10 (25%) patients of GDT group while only three patients were died in the other group..

In the study of Robin et al. [6] supported these results through prospective single-center observational study in a 1-year period, which included 150 high risk surgical patient's total. They observed that a high PCO2 gap (≥ 6 mmHg) was associated with more organ failure and longer duration of mechanical ventilation Also, Abdalazeem et al. [14], conducted a study on 100 adult patients diagnosed with severe sepsis or septic shock and were divided in two groups according to ΔPCO2. The high ΔPCO2 group was associated with higher incidence of complication and organ failure than normal ΔPCO2 group.

Although these studies have demonstrated that targeting PCO2 in management of critically ill patients has an impact on lowering morbidity with hemodynamic stability, the results of a study conducted by Guinot et al. [15], in 2017 came in disagreement with the above findings. They ran the study on 393 patients who undergone cardiac surgery with Cardio Pulmonary Bypass (CPB) and their results did not support an association between PCO2 gap and postoperative outcomes (morbidity, mortality, SOFA scores, ICU length of stay). This contradiction could be explained by the change in physiopathology of the cardiac surgical population included in Guinot study. Most relevant publications have highlighted the significant impact of CO on PCO2 gap that the PCO2 gaps represent an indicator for CO meeting the global metabolic demand, i.e. Elimination of CO2 produced by peripheral tissues. The impact of CPB on CO2 production and acid-base balance could change the balance between partial CO2 tension and CO2 content by changing metabolic conditions, blood flow, body temperature, and alveolar ventilation[17].

The conflict between results could well suggest that it may be not sufficient to direct resuscitation towards PCO2 gap only. The use of PCO2 gap in conjunction with ScvO2 has also been investigated and has been shown to predict the patient's outcome better than using ScvO2 alone [18]. In a Study by Vallée et al.[19], it was suggested that ICU resuscitated patients, targeting only ScvO2 may not be sufficient to guide therapy. They proposed that even if the target value of 70% ScvO2 is met, a P (cv-a) CO2 more than 6 mmHg could be a useful marker for inadequately resuscitated patients.

Furthermore, Portran et al. [20], designed an original pilot study for patients who had undergone standard cardiac surgery to investigate the value of ΔPCO2 as aprognostic tool and comparing that with an existing algorithm that involves targeting values of ΔPCO2, ERO2 and lactate. High ΔPCO2 (≥6 mmHg) was observed on ICU admission and on POD1 tat also failed to predict prolonged duration of stay in ICU. However, a significant increase in both ICU and hospital LOS was noted in the group of patients who were managed by the algorithm. The association between POD1 values of ΔPCO2, and POD1 variations for ΔPCO2 and ERO2 or lactate were inconclusive or absent at best, suggesting that an approach combining the ICU admission values of ΔPCO2, ERO2 and lactate could predict outcomes regarding ICU and hospital stays more effectively than ΔPCO2 alone. Recent studies published in 2019 proposed that ratio of PCO2 gap to the arterial-venous oxygen content difference also may be useful as a target for resuscitation they concluded that Pcv-aCO2/Ca-vO2 is an important predictor of postoperative major organ morbidity and mortality in patients undergoing cardiac surgery[21].

In Sayed[4], study, they opted for drawing samples from central venous catheter rather than PAC. Results may be different if PAC was used, but choice was in favor of feasibility and partly because PAC is not routinely used in management of high-risk patients in our ICU. Finally, PCo2 gap and the conventional markers in GDT (serum lactate, mixed venous oxygen saturation) all have different physiological kinetics and taking all these physiological differences into account may alter results but also it would be very difficult. Part of their choice of methodology was to provide practitioners with feasible simple bedside tool that according to our findings may lead to avoid longer ICU and hospital stays.

This wide difference in findings regarding correlation of PCo2 with worse outcomes cannot be solely attributed to the applied protocols of resuscitation but also should factor in the progress of the disease itself and type of patient which clearly differ in the previously mentioned studies. Indeed, all these results are derived from research point of view, however they could be seen as first step to use a CO2 gap to guide resuscitation therapy in daily practice. While keeping mind the feasibility e of use and the range of possibilities of CO2 gaps that supports introducing it as a tool in daily ICU practice (Suryasa et al., 2022).

**Conclusion**

Application of the ScvO2-cvaCO2gap-guided protocol (pco2 gap) for resuscitation intra operative and 12 hours postoperative had decreased the postoperative organ failure in high risk surgical patients undergoing major abdominal surgeries in comparison with a classic early goal directed therapy , pco2 protocols also showed lower adverse outcomes and mortality rate than GDT protocol our results still needs confirmation by consequent larger sample trials and may be devising a protocol that could incorporate pco2 values along with other parameters, and not as a sole target for resuscitation, to better reflect changes during resuscitation of critically ill patients.

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