Anesthetics considerations in peritonitis

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Abstract

Peritonitis remains an illness with a significant mortality rate in surgery. Age, male sex, and the inability to control the source are associated with greater mortality. Anesthesia and perioperative medicine should aim to stop the increase in metabolic debt in the pre-surgical phase and to provide *metabolic steering* during surgery. Early goal directed therapy (EGDT) is still the mandatory cornerstone of management, presented here in several different versions, depending on the monitoring system available in the local clinical environment. The discharge from the operating room to a proper clinical setting must be based on a suitable scoring system, such as APACHE II (*acute physiology and chronic health evaluation*). Clinical surveillance, when the patient is on the ward, has to be governed for a period using a nursing score like the modified early warning score. Antimicrobial therapy, as well as appropriate timing of administration is both important. Analgesia, locoregional whenever possible, is also an important tool for preventing complications, which occur mainly during the postoperative period, and most frequently in the first month.

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Introduction

Peritonitis is an inflammation of the peritoneum that may have multiple causes: exogenous pathogens as well as iatrogenic causes.

It can be classified into *primary* (spontaneous bacterial invasion of the serosa), *secondary* (to intra-abdominal lesions) *tertiary* (due to persistent/recurrent infections in a specific cohort of patients, *i.e.* indwelling device carriers - such as peritoneal dialysis patients, immunodeficient patients, *etc.*)[1] each can be divided further into localized or diffuse, according to the extent of the infection. We will focus on peritonitis of surgical interest - secondary and tertiary - which are the most important in anesthesia practice.

Peritonitis is a major killer in general surgery, with a mortality rate that has dropped from an 80-100% mortality rate in the 1910s to 22-55%[2] in the most recent reports. Mortality from peritonitis is correlated to the severity of the disease: extent, presence of systemic inflammatory response (SIRS)/sepsis (as shown in Table 1[2]), concomitant organ failure, unsuccessful source control, older age, gender.[3]

Source control is sometimes achievable conservatively. In any case, only a limited number of scenarios (*e.g.*, necrotizing pancreatitis and abdominal abscesses in hemodynamically stable patients) are treatable without surgery but with alternative approaches, such as percutaneous drainage.[4]

In all cases, the choice to rush to the operating room (OR) is a decision to be taken as a team - surgeon and anesthesiologist - who should both use a common key to understand the real needs and priorities of the patient.

The aim of this review is to provide the available evidence to anesthesiologists who treat these patients.

Methods of research

A review of the literature was conducted in PubMed using the words *peritonitis anesthesia* and *peritonitis analgesia*, and the search was limited to papers from the last 6 years. 131 articles were retrieved, and 91 of them were excluded due to a lack of strict clinical pertinence (experimental settings, animal models), very restricted populations (*i.e.*, pediatrics), very restricted fields of study (*i.e.*, peritoneal dialysis tube complications, elective surgery). Single Case Report papers and papers written in languages other than English were also excluded.

After that, while the paper was being developed, some other important and highly cited or seminal papers were added to the analysis, to eventually reach a total number of 66 retrieved publications.

Preoperative to-dos

1) *Nutritional support and pre-habilitation* are well known key factors in gastrointestinal (GI) Tract surgery. However, it is not commonly possible to put preoperative strategies focused on minimizing mortality and morbidity in place, since the relative urgency of secondary peritonitis (patients are usually admitted from the Emergency Department, or rapidly deteriorating while on the ward as in-patients). Therefore, in this kind of emergent patient, paying attention to nutrition is meant to prevent forms of secondary peritonitis in GI surgery, rather than to reduce mortality once peritonitis has occurred.[5]

2) In the most emergent setting, the initial assessment of the patient affected by this condition should include collecting the *history* of previous illnesses, a *physical examination* (focusing on cardiovascular, respiratory, renal function assessment).

3) *Blood tests* must also be obtained (WBC, hemoglobin, platelets, bilirubin, BUN, creatinine, electrolytes, ABG, lactates), as well as an ECG and standard CXR.

4) Early *treatment for abdominal pain* is not to be deferred for fear of masking diagnosis, since there is evidence that early treatment neither delays diagnosis, nor masks clinical findings.[6]

5) The anesthesia-related cardiological *Risk* can be assessed at the start of surgery using many tools, varying from the very simple quantitative metabolic equivalent of task (METs, conventionally set to 3.5 ml $O_2 \cdot kg^{-1} \cdot min^{-1}$ per point)[7] revised cardiac risk index (RCRI - online at http://goo.gl/vmqzKo)[8] to the American College of Surgeons National Surgical Quality Improvement Program Surgical Risk Calculator (ACS NSQIP Surgical Risk Calculator - online: http://goo.gl/ewTxGY).[9] ACS-NSQIP is the most up-to-date and effective, although it is quite awkward to obtain in an emergent setting. It retains its ability to stratify morbidity and mortality in the general elective surgical population.

Eventually, only a non-life-threatening situation will allow time for a cardiological referral, if indicated, while the most emergent clinical scenarios must rely on the anesthesiologist only, in order to reduce this specific risk.

The general morbidity and mortality risk assessment is best obtained at the end of surgery. This further stratification can help to make a sound decision with regard to admitting the patient to the ICU in order not to waste a valuable, and expensive, resource.

As stated before, ACS NSQIP can provide general survival information for these patients.

The Portsmouth Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (P-POSSUM - online: http://goo.gl/4uyRCK) is also a well-established score for assessing the risk of GI patients, with the advantage of having been developed based on a cohort of colonic resections scheduled for elective surgery.[9]

6) Once the diagnosis has taken place, empiric *Antibiotic Therapy* must start.

Combinations such as carbapenems + quinolones, antianaerobes + aminoglicosides + 3rd generation cephalosporins/quinolones, clindamicyn + monobactams can be appropriate. Once anti gram- and anti-anaerobes activity is guaranteed, there is no evidence that any one regimen is better than any other, thus confirming that the indication should take place after considering local guidelines (achieved through collaboration between surgeon and anesthesiologist), costs and availability.[10]

As stated, timely access to the OR is of the utmost importance, with a few exceptions, such as necrotizing pancreatitis or source localization in sites that are conveniently approachable by percutaneous drainage. The main indications for surgery are a) to control the infection source b) to prevent abdominal hypertension. The timing should be balanced between surgeon and anesthesiologist, and focuses mainly on the restoration of fluids (early goal directed therapy - EGDT, better if following *advanced* guiding) and the cardiological risk assessment. Patients with more than two comorbidities at Lee index (RCRI class IV) and METs <4 should be evaluated very carefully at this point, delaying OR access if needed.[11]

Intraoperative to-dos

The anesthesiologist should pursue several goals during the operative period. The first should be:

a) the assessment of the correctness of the *antibiotic prophylaxis* and the correct *specimen sampling*. The anesthetist should oversee checking that the appropriate antibiotic has been prescribed and given with the right timing. The patient should leave the OR with a prescribed regimen (around-the-clock/continuous) in order not to miss any administration, if needed.

The second target should be to help obtain, later, in the actual surgical theatre, microbiological sample(s) to tailor the antibiotic therapy to the causative pathogen(s).

b) Before induction the anesthetist should consider a *fluid challenge*, as a drop in systemic vascular resistance, still depressed by SIRS and enhanced by anesthesia drugs, can be catastrophic.

c) The placement of an *arterial line*, possibly before induction, and a *central venous line* placement, is pivotal[12] The latter, particularly, though not so useful for determining fluid responsiveness itself, is meant to obtain a $ScvO_2$ measurement. It is a reliable

Table 1. Clinical Classification of organism's response to infections.

Pathological entity	Definition
Bacteremia	Presence of bacteria in bloodstream
SIRS	Two or more of the following: • Temperature >38°C or <36°C • Heart rate >90 BPM • Ventilatory frequency >20 BPM or $PaCO_2$ <4.3 kPa (33 mmHg) • WBC <4000/mL or >12,000/mL or >10% immature forms
Sepsis	SIRS with clinical evidence of infection
Severe sepsis	Sepsis associated with organ dysfunction, hypotension (SAP <90 mmHg or <40% mmHg from baseline), hypoperfusion abnormalities
Septic shock	Sepsis-induced hypotension despite fluid resuscitation, hypoperfusion abnormalities

Adapted from Levy *et al.*, 2003.[2]

proxy of cardiac output and - if a way to monitor cardiac output is available - is also compulsory for obtaining oxygen delivery (DO_2, DO_2I if indexed per corporeal surface) and oxygen consumption (VO_2, VO_2I if indexed). These measures are required for proper goal-directed therapy.[13] Having placed a central venous line will be also useful for administering inotropes, if required, and for obtaining blood samples.

d) *A urinary catheter* also has to be placed, to measure diuresis hourly.

e) As stated, an *estimation of the cardiac output* (CO, CI if indexed) should be performed during surgery, balancing the invasiveness, economic variables of the working institution and the comorbidities of the patient. The choice can range from an invasive system (pulse contour analysis systems being preferable to the more invasive intracardiac thermodilution catheters) to semi-invasive systems such as esophageal Doppler monitoring - which can provide continuous data during surgery and also after discharge from the OR - to the intermittent use of TEE (trans esophageal echocardiography) to assess cardiac output using left ventricle output tract velocity time integral (LVOT VTI) calculation (http://goo.gl/29oeKr).

Depending on the monitoring system used during the perioperative period, different approaches are proposed. Consider the diagram in Figure 1[14] f a CO/CI system is not present; the one in Figure 2[14] if a continuous CO/CI measurement system is in place; an *intermediate* version of EGDT is proposed if non-continuous measurement of CO/CI is used, as when using LVOT VTI TEE calculation (Figure 3[14]).

Induction

Ileus and delayed gastric emptying are often present in peritonitis, and this fact is a sound risk for inhalation at the very beginning of surgery. Therefore, anesthesia induction should be performed as per full stomach emergency induction. Rapid sequence induction (RSI) and cricoid pressure are performed routinely in our institution even though there's conflicting evidence regarding its real usefulness.[15] Every available device to handle a difficult intubation should be kept close to the theatre. None of the proposed protocols for RSI are free of hemodynamic risk, and due to the very high doses of induction agents needed to achieve a very rapid onset, fleeting arterial oxygen desaturation can also occur. Nonetheless, RSI+cricoid pressure must be considered the mainstay in this kind of setting.[15,16] Fiberoptic awake intubation - a procedure that wastes time - should be reserved only for catastrophic head/neck anatomic situations or for obese patients with an expected difficult bag-mask ventilation and difficult intubation.

Maintenance

The surgery will be short, focusing on the clearance of the septic cause according to the principles of *damage control*, when treatment is delayed after clinical stability is achieved (Table 2).[11]

The intraoperative period has to be considered a moment of *metabolic steering,* as the anesthesiologist continues to put in place measures to shift the balance from a catabolic to an anabolic state, while the surgeon is removing the causes. Optimizing fluids and providing adequate oxygen delivery are the key concepts to equip the patient's organism to fight the illness.[17] The best option is to continuously keep track of perfusion parameters such as diuresis (0.5-0.8 mL/kg/h in adults), lactacidemia, advanced hemodynamic parameters (*i.e.*, CO/CI and systemic vascular resistances), and fluid responsiveness parameters such as stroke volume variation (SVV).

To enforce an EGDT, the classical algorithm contains vasopressors - to correct low resistances states, inotropes - to counterbalance low cardiac output, and transfusion as a last option, if indexed oxygen delivery and indexed oxygen consumption drop below the threshold values (500-600 mL/min/m^2 for DO_2I, 140-160 mL/min/m^2 for VO_2I), provided that the other hemodynamic parameters are fully optimized.[18] We report the formulas to calculate DO_2I, VO_2I and $C_{[a/v]}O_2$:

$$DO_2I = CI * [\text{Arterial Oxygen Content}] * 10 \quad (1)$$

$$VO_2I = CI * [\text{Arterial Oxygen Content}] - [\text{Venous Oxygen Content}] * 10 \quad (2)$$

$$C_{[a/v]}O_2 = 0.0138 * Hb * Sat_{[a/v]}O_2 + 0.0031 * pO_2 \quad (3)$$

When CO measurement is not provided, the oxygen extraction index (O_2EI) can be used as a satisfying estimate of VO_2:

$$O_2EI = (SaO_2 - ScvO_2)/SaO_2 * 100 \quad (4)$$

The relative risk of ileus caused by fluid excess following traditional EGDT can be reduced by using one of the proposed *advanced* versions of it, with the most consistent evidence related to the esophageal Doppler measurement system.[19] Even though recent clinical trials like the POEMAS suggest that perioperative EGDT is not associated with a reduction in complications and overall length of stay (LOS)[20] they were not considered in/for our septic and hemodynamically instable cohort of patients. Their hemodynamic imbalance put them at risk of crossing the threshold between hypovolemia and hypervolemia[21] that is associated with ileus, perforation, and other surgical complications.

Analgesia

Early pain control is not just an ethical task but is also a key factor in minimizing the incidence of prolonged bed rest after surgery, inducing early deambulation and promoting effective coughing. These effects reduce the incidence of respiratory complica-

Table 2. Traditional vs modern approach to abdominal sepsis.

	Traditional approach to septic abdomen	Modern approach to septic abdomen
Pre-operative	Diagnostic delay Operative delay	Urgent CT if appropriate Early ABX and Volume Resuscitation
Intraoperative	Vasopressors Definitive Surgery, long procedure	Damage/source Control Surgery, short procedure
Postoperative (ICU)	Multi organ failure Early death	Ongoing resuscitation

Adapted from Wong *et al.*, 2005[10] and Moore *et al.*, 2011.[63]

tions. All these achievements save days of LOS and prevent the waste of resources.

Establishing a multi-modal analgesia is paramount, with a well-established central role of neuraxial continuous analgesia in patients at risk of prolonged ileus, as well as patients with increased cardiac or respiratory risk.[22,23] Neuraxial block (thoracic epidural) is preferable to other extra-axial blocks such as paravertebral block, tranversus abdominis plane (TAP) block, rectus sheath block and continuous wound infusion, since the first also has a desired positive effect on bowel function and pancreatic microcirculation[24,25] as well as ensuring improved cardiac protection.[26,27] Sepsis is not a contraindication itself, so only serious hemodynamic instability (*i.e.*, septic shock - as is the case for every loco-regional anesthesia maneuver, and most notably neuraxial ones), coagulopathy, and existing anticoagulant therapy should be considered absolute contraindications to this technique.[28] The usual contraindications, such as infection of the entry site of the catheter or patient refusal, should be added to this.

If an epidural catheter is not in place at the start of the surgery (*i.e.*, due to technical difficulties, concomitant contraindicated medications, *etc.*) the other previously mentioned extra-axial loco-regional techniques play their role as rescue therapies.[29-31] These alternatives come with a growing body of evidence regarding the importance of the administration of local anesthetics themselves. Evidence of this has been found even on uncommon routes, such as low dose continuous intravenous perfusion in the perioperative period[32] or nebulized in the peritoneal cavity during laparoscopic

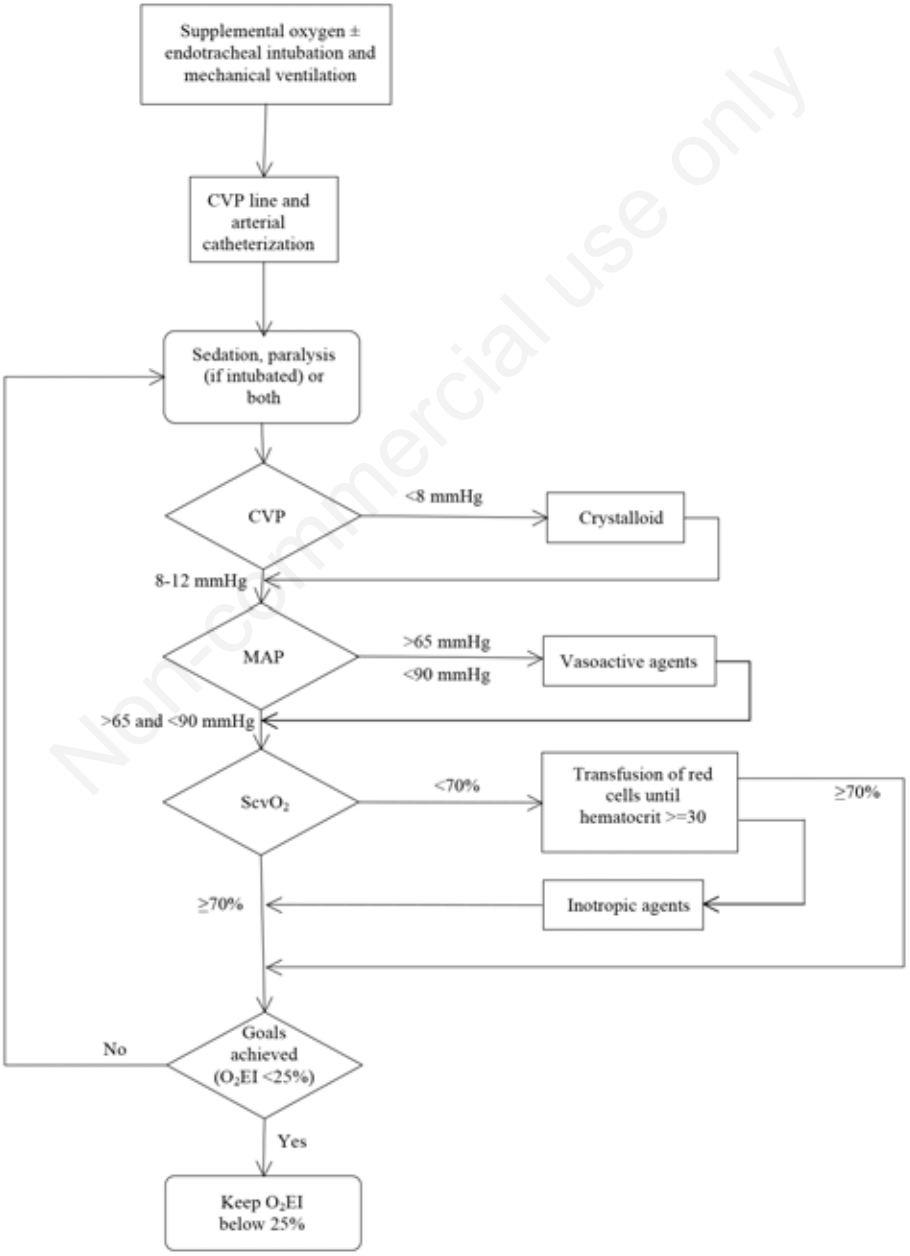

Figure 1. ***Classic*** **early goal directed therapy. Adapted from Rivers *et al.*, 2001[14] with permission.**

surgery.[33,34] Opiates should be administered intravenously as patient-controlled analgesia, the intramuscular route should be avoided, and the oral route should be established as soon as possible.[22,35,36]

Non-steroidal-antinflammatory drugs (NSAID) should also play a role in a complete multimodal framework, when not contraindicated. There is clinical evidence for some molecules: ibuprofen (associated with oxycodone, caffeine or acetaminophen,[37-39] etodolac,[40] ketoprofen and dexketoprofen,[41] lumiracoxib and parecoxib,[42,43] mefenamic acid,[44] naproxen,[45] piroxicam,[46] lornoxicam,[47] acetaminophen (alone or codeine-associated).[48,49] These drugs should be used for a period of time that does not exceed 2-3 days, to avoid renal toxicity in a patient prone to microcirculation distress due to infectious conditions.

Open or closed abdomen?

Every patient with abdominal sepsis should be monitored for intra-abdominal pressure (IAP), since the medical condition itself of intra-abdominal hypertension can be a reason to open the abdomen.

Trans-bladder technique is the standard for IAP measurement. Thus, at the end of surgery a pressure line should be connected,

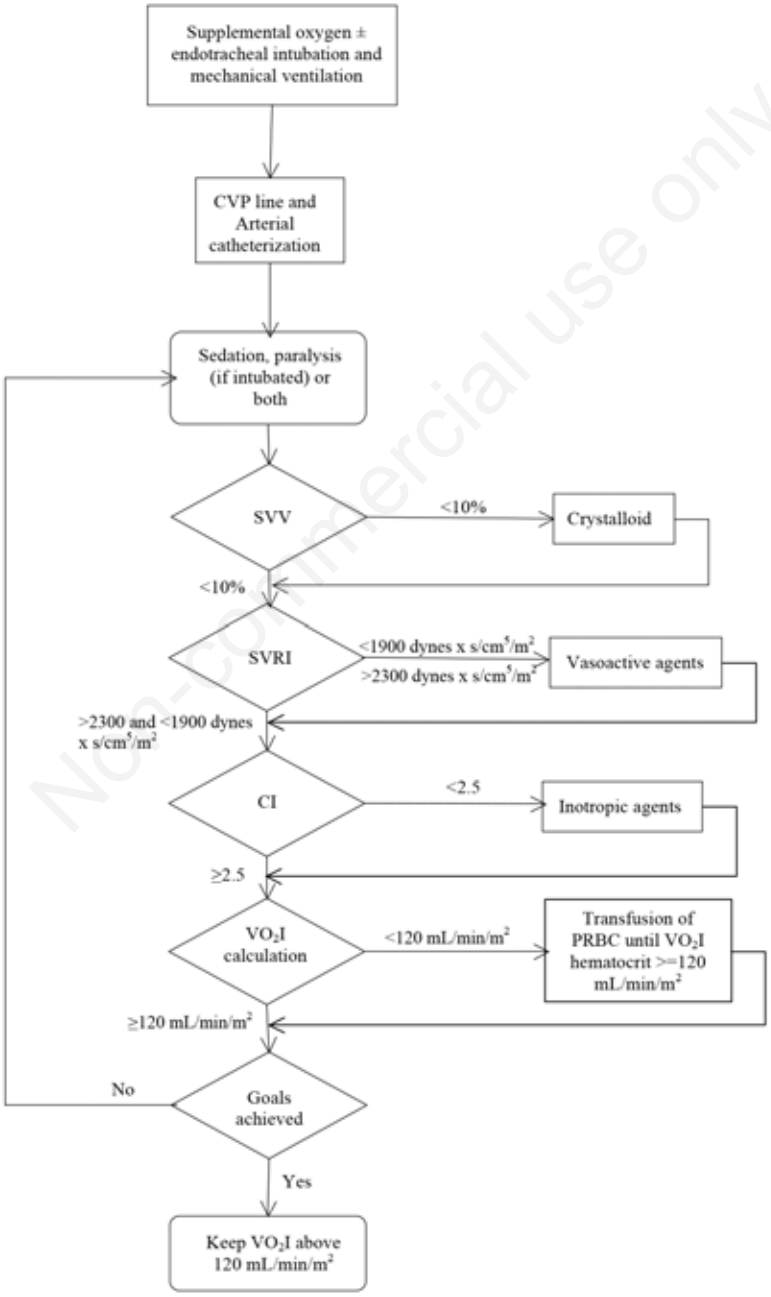

Figure 2. ***Advanced*** **early goal directed therapy. Adapted from Rivers *et al.*, 2001[14] with permission.**

using a sterile technique, to the urinary catheter, or a line for intermittent measurement should be put in place.[50]

Intra-abdominal hypertension (IAH, IAP >12 mmHg) and abdominal compartment syndrome (ACS, IAP >20 mmHg), although the least debatable, is not the only factor in deciding whether or not to start open abdomen treatment (OA). Severe ileus, major contamination, suspected failure to control the source of infection, severe sepsis and massive fluid resuscitation all affect the decisions of the surgical team.[51] The duration of treatment and closure techniques may vary, and considering the high morbidity associated with OA, this decision must be balanced with the environmental characteristics of one's institution.

Airway pressure is not a reliable proxy for direct IAP measurement[50,52] and should not substitute it when deciding whether to start an OA.

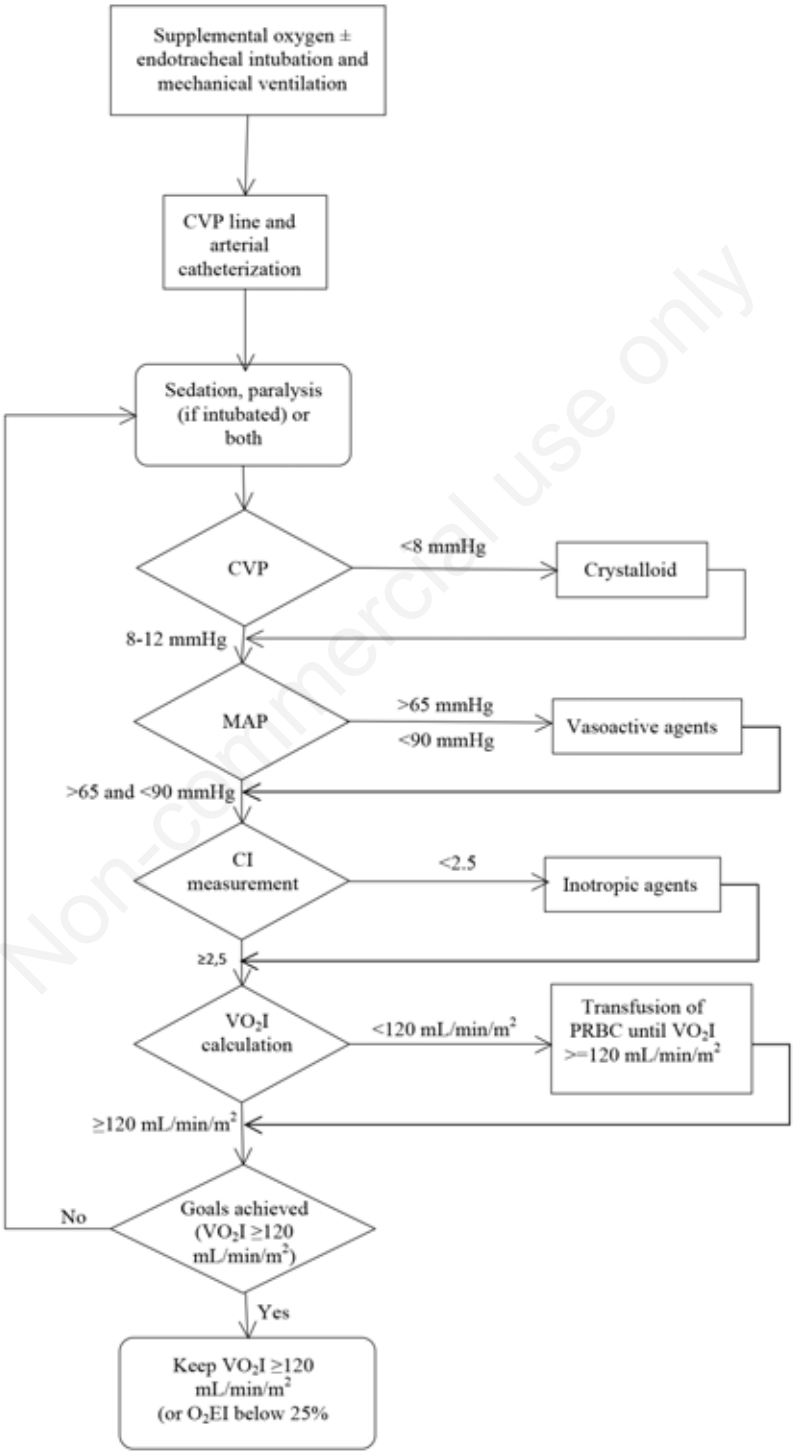

Figure 3. ***Intermediate*** **early goal directed therapy. Adapted from Rivers *et al.*, 2001[14] with permission.**

Postoperative to-dos

The first 30 days after surgery are clouded by the highest mortality risk, with pneumonia and myocardial infarction being the most relevant killers.

Developing local guidelines to prevent and intercept those events early can effectively reduce mortality. High-risk patients undergoing emergent abdominal surgery are often less likely to receive adequate postoperative care than patients undergoing elective abdominal surgery.

The routine use of scoring systems to stratify patient risk and to allocate resources accordingly is a keystone concept. Nonetheless, they are not commonly used.

The Intensive Care Admission APACHE II score (online: http://goo.gl/6IcKPV)[53] is strictly correlated to the mortality risk of the patient admitted to the surgical ICU. It must be calculated using the pre-resuscitation parameters, and not those the emerge after surgery and critical care maneuvers.[17]

The sequential organ failure assessment (SOFA) score (online: http://goo.gl/U7Xyan) is the most valuable tool for continuously assessing the condition of severely ill patients while in the ICU. Its tendency has been shown to relate to mortality in several studies, and it should be utilized every 24 hours in every inpatient.[54-56]

Strict goal directed therapy - at this point handled with punctual CI and filling volume measurement - should be continued for 3 days after admission, with the administration of blood products tailored to that, since it has been shown that patients who had a restrictive RBC had a significantly lower mortality rate[57] too.

Antibiotic therapy should be continued for 7-10 days, and reassessed daily with microbiological data. A further period of antimicrobial therapy should be considered carefully, to avoid microbial resistance.

When to transfer a patient to a monitored bed

A patient eligible for a direct transfer to the surgical ward should have received definitive surgical therapy and should be not hemodynamically impaired at the end of surgery and should not have a significant metabolic debt. Unfortunately, a validated scoring system for the anesthesiologist to forecast this at the very beginning of surgery is not available, considering the extreme variability of intra-surgical possibilities. Notwithstanding, ACS NSQIP can be considered an interesting tool for assessing, together with the surgeon, the perioperative risk at the end of surgery, to predict LOS, and finally to decide whether to discharge the patient to a surgical ward.

Nevertheless, a patient with ongoing inotrope/vasoconstrictor therapy, lactacidemia above 3 mmol/L and/or IAP>12 (IAH) should be sent to the ICU intubated in for weaning and intensive treatment.

Patients with an open abdomen and controlled IAP should be considered for respiratory weaning and subsequent extubation in the OR, with a planned admission to an intensive/sub-intensive care unit or ward if an adequate nurse to patient ratio exists. In fact, although the ideal ratio remains unclear, the settings with the higher nurse to patient ratios have less morbidity and mortality than settings with fewer.[58]

While on the ward, 7-day surveillance for SIRS-sepsis complications with an early warning score assessment (*i.e.*, MEWS:[59,60] http://goo.gl/oVMFLj) should be set. The MEWS value at the time of ICU discharge is also correlated with mortality.[61]

Early rehabilitation and respiratory physiotherapy, early deambulation and the use of postoperative ERAS protocols can be useful for preventing a number of of these uneventful complications.

How to prevent postoperative delirium

Older age, dehydration, and sepsis are risk factors for postoperative delirium, a condition that can cause extubation failure, respiratory failure, more risk of hospital acquired pneumonia, delayed ambulation, overall longer LOS, and trauma.

There are many tools for early diagnosis, the treatment being limited to space/time reorientation, enforcing parental affective pressure, with little evidence to support the efficacy of pharmacological pre-treatment for at-risk patients.[62] An ESA special committee is expected to release a dedicated guideline soon [https://www.esahq.org/about-us/the-esa/committees/guidelines-committee/task-force-on-reduction-of-postoperative-delirium/].

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