Turk J Anaesth Reanim 2013; 41: 191-4 DOI: 10.5152/TJAR.2013.1630

Invited Review / Davetli Derleme

# Can we Improve Outcome in High Risk Surgery?

## Yüksek Riskli Cerrahide Sonucu İyileştirebilir miyiz?

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Abstract / Özet

Despite the small number of high-risk surgical patients in comparison to all surgical patients, they account for the largest proportion of overall perioperative mortality. Goal directed hemodynamic support may result in a lower incidence of complications and reduced length of hospital stay in these patients. Beyond the standard monitoring of circulation, such as blood pressure and heart rate, further parameters and procedures such as pulse pressure/stroke volume variation-, stroke volume/cardiac index-, and central venous oxygen saturation-guided resuscitation may improve the outcome of high-risk surgical patients. The aim of this review is to focus on the results of animal and clinical studies investigating the usefulness of these indices in the context of goal-directed perioperative support.

**Key Words:** High-risk surgery, goal directed therapy, pulse pressure variation, central venous oxygen saturation, stroke volume, improved outcome

Yüksek riskli cerrahi hastaları tüm cerrahi hastalarına kıyasla az sayıda olmalarına rağmen, tüm perioperatif mortalitenin en büyük kısmından sorumludurlar. Bu hastalarda hedefe yönelik hemodinamik destek daha düşük bir komplikasyon insidansına ve hastanede yatış süresinde azalmaya neden olabilir. Kan basıncı ve kalp hızı gibi dolaşımın standart takibi ötesinde nabız basıncı/atım hacmi varyasyonu-, atım hacmi/kalp indeksi ve santral venöz oksijen satürasyonu-güdümlü resüsitasyon gibi daha ileri parametreler ve uygulamalar yüksek riskli cerrahi hastalarda sonucu iyileştirebilir. Bu derlemenin amacı hedefe yönelik perioperatif destek bağlamında bu endekslerin yararlılığını araştıran hayvan çalışmalarının ve klinik çalışmaların sonuçlarına odaklanmaktır.

**Anahtar Kelimeler:** Yüksek riskli cerrahi, hedefe yönelik terapi, nabız basıncı varyasyonu, santral venöz oksijen satürasyonu, atım hacmi, sonucun iyileştirilmesi

## Introduction

Major surgery is associated with a significant risk of morbidity and mortality in the peri-, and postoperative period, especially in older patients and in cases of severe coexisting diseases. There are an estimated 234 million surgical operations every year worldwide (1). Following implementations of safety standards, the outcome after anaesthesia improved, and although an estimation of perioperative complications and postoperative morbidity is difficult, it has been suggested this may occur in between 3 and 17% of cases (2, 3). Based on an international 7 day cohort study conducted in 28 countries in Europe, the overall mortality was higher than expected in 2011: 4% following major surgery (4). Cohort studies conducted in the nineties were able to detect some preoperative factors, e.g. serum albumin level and the American Society of Anaesthesia class of emergency operation influenced the postoperative mortality and morbidity (5, 6). It is also known that postoperative complications, including renal failure, myocardial infarction and pulmonary embolism also affect the 30-day mortality and long-term survival of patients undergoing major surgery (7).

### Hypovolemia and Outcome

During the nineties, several studies have revealed that intraoperative hypovolemia can be responsible for postoperative complications and organ failure, while optimization of perioperative hemodynamics may result in improved outcome (8-10). However, excessive fluid administration during surgical procedures may also lead to more frequent postoperative complications, so restrictive fluid therapy, meaning significant reduction in crystalloid load, may improve the outcome after major elective gastrointestinal surgery (11-13). On the other hand, fluid restriction may cause hypovolemia and consequently oxygen debt, which can be monitored by reduced central venous oxygen saturation ($ScvO_2$) (14).

It follows simple logic and has also been shown by clinical studies, that early goal directed therapy (GDT) may improve the outcome of critically ill patients (15). In the past decade, several studies have been conducted that have assessed the influence of GDT on organ function, complications and outcome in high-risk surgical patients. These studies suggested that GDT resulted in a lower incidence of complications and reduced length of hospital stay compared to standard management protocols (16, 17). Using heart rate (HR), mean arterial pressure (MAP) and central venous pressure (CVP) only to assess hemodynamic status may be misleading as there is no association between cardiac output and blood pressure, and there is also evidence that filling pressures may be inadequate for predicting fluid responsiveness (18-20). However, invasive arterial and central venous pressure (CVP) monitoring are the most common tools in high risk surgical patients, and are applied in more than 80% of cases worldwide (21).

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Received / Geliş Tarihi : 01.11.2013
Accepted / Kabul Tarihi : 12.11.2013

These approaches are adequate for most patients undergoing surgical procedures, but might not meet the needs of the small number of patients at high risk of complications and death. A retrospective study in the United Kingdom identified a high-risk population of 12.5% regarding all surgical procedures, which accounted for 83.8% of overall mortality and represented a prolonged hospital stay (22). To optimize perioperative the hemodynamic status of this high-risk population, the most frequent parameters that have been used next to standard parameters are cardiac output (CO) and/or oxygen delivery ($DO_2$). To measure CO the use of intermittent thermodilution by the pulmonary artery catheter (PAC) has decreased in surgical patients over the past decades. This decrease is mostly related to the fact that the PAC is highly invasive and has several associated risks. On the other hand, there is growing evidence suggesting that this invasive procedure does not reduce mortality (23).

A less invasive method for assessing and maintaining CO is oesophageal Doppler guided fluid therapy, which can improve hemodynamic parameters and may reduce critical care admissions postoperatively (24). The use of oesophageal Doppler in multiple-trauma patients is associated with a decrease of blood lactate level, a lower incidence of infectious complications, and a reduced duration of intensive care unit (ICU) and hospital stay (25). Oesophageal Doppler guided fluid management in colorectal resection was associated with a 1.5-day median reduction in postoperative hospital stay, faster gut function recovery and significantly less gastrointestinal and overall morbidity (26). Intraoperative intravascular volume loading to optimal stroke volume (SV) guided by oesophageal Doppler during proximal femoral fracture repair resulted in a more rapid postoperative recovery and a significantly reduced hospital stay (10).

In two recent animal experiments, we compared cardiac output and stroke volume guided hemorrhage and fluid resuscitation on porcine. After baseline measurements, animals were bled until the cardiac index (CI) or stroke volume index (SVI) dropped by 50%, after which animals were resuscitated over 60 minutes until baseline CI and SVI values were reached. In the CI-group, stroke volume, global end diastolic volume, central venous oxygen saturation remained significantly lower, while stroke volume variation, central venous-to-arterial carbon dioxide difference ($dCO_2$) remained significantly higher by the end of resuscitation as compared to baseline, indicating that fluid resuscitation might have been inadequate and the normalization of CI was mainly due to the persistently elevated heart rate, rather than restoration of the circulating blood volume. On the contrary, in the SVI group, by the end of resuscitation, stroke volume variation, $ScvO_2$, $dCO_2$ improved significantly or returned to their baseline values by the end of the experiment. In conclusion, in these experiments the SVI-based algorithm resulted in better hemodynamic and oxygenation indices as compared to the CI-based approach (27).

Beyond SV and stroke volume variation (SVV), pulse pressure variation (PPV) measurement is commonly used in clinical practice. PPV monitoring is not associated with additional costs or complications other than arterial catheterization, and intra-arterial blood pressure monitoring is common practice in most patients undergoing high-risk surgery. The variation in arterial pulse pressure induced by mechanical ventilation is known to be a very accurate predictor of fluid responsiveness, and the optimal threshold value is around 12% (28-31). It has been demonstrated that the PPV was comparable with the SVV (32). Monitoring and minimizing PPV (≤10%) by volume loading during high-risk surgery improved postoperative outcome and decreased the length of hospital stay (33, 34). However, it is important to mention that all of these studies were conducted in patients without significant cardiac arrhythmias.

**Assessing and Treating Hypovolemia Induced Oxygen Debt**

The most often used parameters to assess the relationship between oxygen supply and consumption are mixed venous saturation ($SvO_2$) and $ScvO_2$. Although $SvO_2$ is regarded as the most accurate indicator of the balance between global oxygen delivery and consumption, there is good evidence that $ScvO_2$ may serve as an easily obtainable and reliable alternative to manage therapy in critical ill patients (15, 35). Continuous monitoring of the $ScvO_2$ is also possible with a device based on fiberoptic technology via a standard central venous catheter, and values measured by this approach showed good correlation with laboratory values (36).

It has been shown that, following major surgery, reductions in $ScvO_2$ are independently associated with post-operative complications. The optimal cut-off value of $ScvO_2$ for prediction of complications was found to be 64.4% in the early post-operative period (37). Another study which compared pre- and postoperative $ScvO_2$ in patients undergoing major abdominal surgery determined this value to be 73% (38). Also there are data showing that keeping the oxygen extraction ratio, calculated from arterial and central venous oxygen saturation, below 27% resulted in less postoperative organ dysfunction and reduced hospital stay of high-risk surgical patients (16). However, early GDT including the maintenance of $ScvO_2$ higher than 70% in moderate and high risk cardiac surgical patients was found to be inconclusive regarding benefits (39). In a recent observational study in surgical patients, even higher levels of $ScvO_2$ have been reported (84.7±8.3%) (40).

In contrast to these data, in a randomised study conducted by our workgroup, we found higher levels of $ScvO_2$ during the intraoperative period (81.7±7.8%). The aim of this study was to assess the role of $ScvO_2$ as a therapeutic goal of hemodynamic optimization during major abdominal surgery. Our results suggest that $ScvO_2$ of 70% as target should not be used in anaesthetised and mechanically ventilated patients undergoing major surgery: patients received less fluid and had higher lactate levels postoperatively in the group guided by $ScvO_2$ compared to CVP guided patients (41). In a recent, ongoing study we used higher level of $ScvO_2$ as a threshold for fluid therapy: the target level of $ScvO_2$ is 75% and a decrease in $ScvO_2$>3% is also considered as a sign of intraoperative hypovolemia. According to the

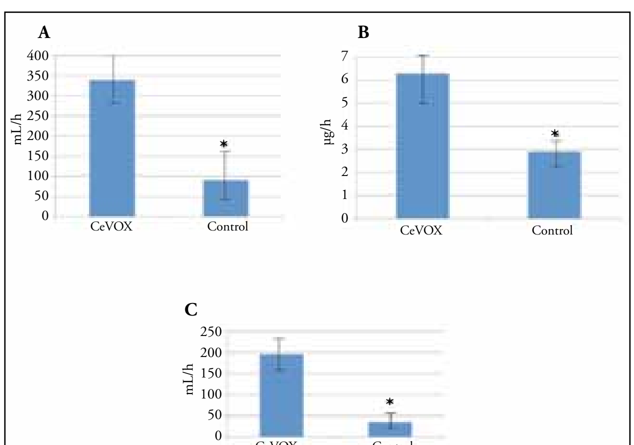


Figure 1. Effects of $ScvO_2$-assisted vs. conventional intraoperative hemodynamic support (42)

A) Colloid; B) Norepinephrine; C) Urine output. Data are presented as median and interquartile range, statistical analysis was performed by Mann-Whitney U test; *, p<0.05

results of our pilot study (n=24), the amount of colloid infusion and norepinephrine received by the $ScvO_2$ group were higher compared to the CVP group, and intraoperative diuresis was also significantly better in the $ScvO_2$-group (Figure 1) (42).

## Summary

There is increasing evidence that advanced hemodynamic monitoring, even using minimaly invasive tools (PPV, $ScvO_2$) to assess hemodynamics and guide volume therapy of high-risk surgical patients intraoperatively, can improve the outcome. There are several factors affecting the "optimal target value" of these indices, and it may be the trend rather than the absolute value which should be taken into account as therapeutic guidance. However, there is not and there will never be, one single parameter with a set value, which one should treat or follow as the target. Therefore, multimodal, individualized care is required to reduce perioperative morbidity and mortality.

**Conflict of Interest**
No conflict of interest was declared by the authors.

**Peer-review:** Invited.

**Author Contributions**
A.M. took part in data collection, processing, analysis and interpretation; Z.M. took part in data analysis, interpretation and as primary investigator.

**Çıkar Çatışması**
Yazarlar herhangi bir çıkar çatışması bildirmemişlerdir.

**Hakem değerlendirmesi:** Davetli.

**Yazar Katkıları**
Çalışmada A.M. veri toplanması, işlemesi, analizi ve yorumu görevlerini; Z.M. ise birincil araştırmacı olarak veri analizi ve yorumlanması görevlerini üstlenmiştir.

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