*Original Article*

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# Stroke volume variation and pleth variability index to predict fluid responsiveness during resection of primary retroperitoneal tumors in Hans Chinese

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**Summary** **Respiration variation in arterial pulse pressure (ΔPP) and pulse oximetry plethysmographic waveform amplitude (ΔPOP) are accurate predictors of fluid responsiveness in mechanically ventilated patients. We hypothesized that stroke volume variation (SVV) and pleth variability index (PVI) can predict fluid responsiveness in mechanically ventilated patients during major surgical procedures in Hans Chinese. This prospective study consisted of fifty-five Hans Chinese patients undergoing resection of primary retroperitoneal tumors (PRPT). During the surgical procedures, hemodynamic data [central venous pressure (CVP), cardiac index (CI), stroke volume index (SVI), SVV, and PVI] were recorded before and after volume expansion (VE) (8 ml•kg$^{-1}$ of 6% hydroxyethyl starch 130/0.4). Fluid responsiveness was defined as an increase in SVI ≥ 10% after VE. Four patients were excluded from analysis for arrhythmia or obvious hemorrhage during VE. Baseline SVV correlated well with baseline PVI, and the changes in SVV was correlated with the changes in PVI ($p < 0.01$) after VE. There were significant increases of CI, SVI and decreases of SVV, PVI in responder (Rs) after VE. ROC results showed that the areas for SVV, PVI were significantly higher than the areas for CI, MAP, CVP, PI ($p < 0.05$). The best threshold values to predict fluid responsiveness were more than 12.5% for SVV and more than 13.5% for PVI in the real surgical setting. The baseline value of SVV, and PVI correlated significantly with volume-induced changes in SVI ($p < 0.01$). Both SVV and PVI could be used to predict intraoperative fluid responsiveness during resection of PRPT in Hans Chinese.**

***Keywords:*** Pulse oximeter, *i.v.* fluids, intraoperative monitoring

## 1. Introduction

Goal-directed intraoperative fluid administration has been shown to reduce postoperative morbidity and shorten hospital stay following abdominal surgery (*1*). Primary retroperitoneal tumors (PRPT) are a rare but diverse group of neoplasms that arise within the retroperitoneal space. Surgical resection is difficult because of close proximity of vital organs and adjacent vascularities. Sufficient blood and intravascular fluids should be prepared according to the size and localization of tumor, so intraoperative transfusion management is particularly important. During resection of PRPT, patients with preexistent cardiac disease or poor myocardial function are exposed to the risk of pulmonary and peripheral edema. Preload assessment is therefore crucial to guide fluid therapy and to prevent excessive fluid loading during resection of PRPT. Static indicators, such as central venous pressure (CVP), and pulmonary capillary wedge pressure (PCWP) have been shown to be poor predictors of fluid responsiveness (*2*). Dynamic indicators of cardiac preload, based on respiratory variations of arterial pulse pressure (ΔPP) and pulse oximetry plethysmographic (ΔPOP) changes have been shown to be sensitive to changes in preload and can predict hemodynamic response to volume expansion in mechanically ventilated patients during perioperative periods (*3-7*).

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A recent Vigileo™/FloTrac™ system (Edwards Lifescience, Irvine, CA, USA) allows for continuous monitoring of cardiac output (CO) based on pulse contour analysis and of respiratory variations in stroke volume (SVV) based on analysis of systemic arterial pressure wave. A few studies performed in the post-anaesthesia, pre-surgery time window (*8*,*9*) or postoperatively (*10*,*11*) have shown controversial results. Another new device (Masimo Radical™ 7 system, Masimo Co., Irvine, CA, USA) can automatically display perfusion index (PI) and calculate the pleth variability index (PVI), which is a new algorithm that automatically calculates ΔPOP. But the ability of PVI to predict fluid responsiveness was evaluated in mechanically ventilated patients preoperatively (*12-14*) or after passive leg rising in spontaneously breathing volunteers (*15*). Whether these two indices can be used for intraoperative fluid responsiveness predictions and fluid optimization in patients undergoing major surgical procedures still has to be demonstrated, and the optimal threshold value of these indices in the surgical setting still has to be determined.

The aim of this study was to test the ability of SVV and PVI to predict intraoperative fluid responsiveness in mechanically ventilated patients during resection of PRPT in Hans Chinese and to compare them with other indicators in this surgical setting.

## 2. Materials and Methods

### 2.1. *Patients characteristics*

This prospective study was approved by institutional review board of General Hospital of PLA. All patients gave informed consent. Between September 2009 and May 2011, there were a total of 55 patients undergoing resection of PRPT that received intraoperative infusion with colloids. All patients were diagnosed preoperatively by ultrasonography, computerized tomograph (CT) and/or magnetic resonance imaging (MRI), or digital subtraction angiography (DSA). Exclusion criteria were: patients younger than 18 years, arrhythmias and intracardiac shunts. Among the final 51 eligible patients, 9 had hypertension and 4 had diabetes, which were treated medically to keep preoperative blood pressure below 140/90 mmHg and fasting plasma glucose under 8 mM. All patients were kept supine during the operation. Histologic types of the 51 cases of retroperitoneal tumors consisted of 18 liposarcoma, 6 lipoma, 11 leiomyosarcoma, 9 nuerofibroma, 4 neurilemmoma, and 3 teratoma cases. The tumors ranged in size from 7 cm to 34 cm in their long axis, and the average diameter was 16.8 cm.

### 2.2. *Anaesthesia methods*

Anaesthesia was induced with *i.v.* bolus administration of fentanil (3 μg/kg), and 2 min later propofol (1.5-2 mg/kg). Orotracheal intubation was facilitated with rocuronium (0.6-0.9 mg/kg). After induction of anaesthesia, a two lumen, 7.0-French central venous catheter (Arrow International Inc.) was inserted in the right internal jugular vein. A radial artery catheter (REFRA-04220, Arrow international Inc.,USA) was inserted in the radial artery. Pressure transducers were placed on the midaxillary line and fixed to the operation table in order to keep the transducer at atrial level during the study protocol. All transducers were zeroed to atmospheric pressure. Anaesthesia was maintained with target controlled infusion (TCI) of propofol (2-4 μg/mL) and continuous infusion of remifentanil (0.3-0.8 $\mu g \cdot kg^{-1} \cdot min^{-1}$) with bispectral index (BIS, Aspect 1000™, Aspect Medical Systems Inc., Natick, MA, USA) kept between 40 and 50. All patients were ventilated in a volume-controlled mode with a tidal volume of 8-10 mL/kg body weight and an inspiratory/expiratory ratio of 0.5. The ventilatory frequency (10-12 cycles) was set to maintain an end-tidal $P_{CO2}$ range of 3.8-4.7 kPa. Positive end-expiratory pressure was set at 0 cm $H_2O$.

### 2.3. *Data recording and analysis*

A dedicated transducer (FloTrac™, Edwards Lifesciences) was connected to the radial arterial line on one side and to the Vigileo™ System (Edwards Lifesciences) on the other side. The system enables the continuous monitoring of SV, SVI, CO, CI and SVV without calibration. The Vigileo (Software version 1.14) analyzes the pressure waveform 100 times per second (100 Hz), and performs its calculations on the most recent 20 s data (*10*,*16*). SVI obtained with this device was recorded and used to discriminate responder and non-responder patients after VE. SVV was calculated as the variation of beat-to-beat SV from the mean value during the most recent 20 sec data and was displayed continuously.

Masimo Radical™ 7 monitor: A pulse oximeter probe (LNOP® Adt, Masimo Co., Irvine, Canada) was placed on the index finger and wrapped with black paper to minimize light interference. The probe was connected to a Masimo Radical 7 monitor with PVI software (version 7.0.3.3). PVI is an automatic measure of the dynamic change in PI that occurs during a complete respiratory cycle. PVI calculation measures changes in PI over a time interval sufficient to include one or more complete respiratory cycles and was displayed continuously (*14*). At each step of the study protocol, the following were recorded simultaneously: heart rate (HR), systolic arterial pressure, mean arterial pressure (MAP), diastolic arterial pressure, and end-expiratory CVP.

### 2.4. *Experiment protocol*

Intraoperative infusion with 8 $mL \cdot kg^{-1}$ of 6% hydroxyethyl starch were started when MAP dropped

more than 20% from preoperative values, and completed between 20 to 30 min. Hemodynamic measurements were performed before, and within 30 sec after volume expansion without stimulation, in order to limit changes in vasomotor tone that may have affected PVI value (*14*). During the volume expansion, ventilator settings were kept consistent. If obvious hemorrhage (volume > 100 mL) or arrhythmias happened, the infusion protocol would be terminated and patient would be treated accordingly.

2.5. *Statistical analysis*

All data are presented as mean ± S.D. Distribution normality was assessed using the Kolmogorov-Smirnov test. Changes in hemodynamic measures induced by volume expansion were assessed using one-way analysis of variance. Patients were divided into two groups according to the percent increase in SVI after intravascular volume expansion: responders (Rs) were defined as patients demonstrating an increase in SVI ≥ 10% after intravascular volume expansion and non-responders (NRs) as patients whose SVI changed < 10%. Receiver operating characteristic (ROC) curves were generated for SVV, PVI, SVI, CI, CVP, MAP, and PI varying the discriminating threshold of each and areas under the ROC curves were calculated. The areas of ROC curves were compared according to the method described by Hanley and McNeil (*17*). Threshold values for each parameter were determined by considering values that yielded the greatest sensitivity and specificity. Pearson's test was used to test correlation. A *p*-value less than 0.05 was considered as statistically significant. All statistical analysis was performed using statistical software (Statview 5.01, SAS Institute, Cary, NC, and SPSS 15.0, SPSS, Chicago, IL, USA).

## 3. Results

3.1. *Patients selection*

Fifty-five patients were initially included, four patients were excluded from analysis for arrhythmia (three patients: two had ventricular premature contraction, one had atrial fibrillation) or obvious hemorrhage during the protocol (one patient; bleeding > 100 mL during volume loads). Fifty-one patients consisted of 26 males and 25 females between 19 and 69-year-old (mean age, 48.7 ± 13.4 year).

3.2. *Changes in hemodynamic variables after volume expansion*

Hemodynamic measurements in Rs and NRs at baseline and after VE are given in Table 1. After VE, no significant changes were found in NRs, while in Rs, there were significant changes of CI (from 2.9 ± 0.5 to 3.3 ± 0.7 $L \cdot min^{-1} \cdot m^{-2}$; $p = 0.009$), SVI (39.1 ± 8.1 to 46.8 ± 10.3 $mL/m^2$; $p = 0.008$). At the same time we observed significant decreases in both SVV (from 18.4 ± 5.8% to 8.7 ± 3.7%; $p = 0.004$) and PVI (from 19.5 ± 6.6% to 12.0 ± 5.0%; $p = 0.002$) in Rs. Before VE, SVV and PVI were significantly higher in Rs than in NRs, but there was no difference in CI, SVI, CVP, MAP and PI at baseline (Table 1). We found a significant correlation between SVV and PVI at baseline ($r = 0.727$, $p = 0.0001$).The change in SVV after VE was correlated with the change in PVI after VE ($r = 0.693$, $p = 0.002$) (Figure 1).

3.3. *Dynamic indices and static indices to predict fluid responsiveness*

Thirty-one patients were Rs (ΔSVI ≥ 10%) and 20 were NRs. The areas under the ROC curve, showing the ability of the hemodynamic parameters to discriminate between Rs and NRs, are shown in Table 2. The areas for SVV, PVI were significantly higher than the areas for SVI, CI, MAP, CVP and PI ($p < 0.05$). An SVV threshold of > 12.5% discriminated Rs with a sensitivity of 87.9% and a specificity of 83.3%. A PVI threshold of > 13.5% discriminated Rs with a sensitivity of 77.4% and a specificity of 80.0%. There was no significant difference between the areas under the ROC curve for SVV and PVI.

3.4. *Dynamic indices and static indices to quantify response to intravascular volume expansion*

There were no significant correlations between baseline values of MAP, CVP and CI and the percent change in SVI (ΔSVI) after fluid expansion (respectively, $r = -0.284$, $p = 0.054$; $r = -0.220$, $p = 0.121$; $r = -0.241$, $p=0.090$). In contrast, the baseline value of SVV and PVI correlated significantly with the change in SVI induced by fluid expansion (respectively, $r = 0.446$, $p = 0.001$; $r = 0.362$, $p = 0.009$), which indicated that the higher SVV and PVI at baseline, the higher ΔSVI (Figure 2).

## 4. Discussion

This study demonstrates that SVV measured by the Vigileo™ System and PVI measured by the Masimo™ Radical 7 monitor can be used to predict the effects of volume expansion during the resection of RPRT in Hans Chinese.

The results showed that 31 patients were Rs (ΔSVI ≥ 10%) and 20 were NRs. This may be related to inclusion criteria of patients who needed colloid infusions. This study compared the relationship between SVV and PVI intraoperatively, which showed that SVV has a good agreement with PVI. This finding is in agreement with previous studies (*7*,*18*), which compared ΔPOP and ΔPP in mechanically ventilated patients under general

**Table 1. Hemodynamic variables before and after volume expansion in fluid responders and fluid non-responders**

| | Fluid non-responders ($n$ = 20) | | | Fluid responders ($n$ = 31) | | | |
|---|---|---|---|---|---|---|---|
| | Baseline | Volume expansion | P1 | Baseline | P2 | Volume expansion | P3 |
| HR (beats $min^{-1}$) | 69.7 (17.7) | 71.2 (15.7) | 0.752 | 68.9 (14.6) | 0.520 | 72.7 (14.5) | 0.797 |
| MAP (mmHg) | 73.1 (12.7) | 81.5 (18.9) | 0.649 | 66.0 (10.5) | 0.060 | 76.1 (15.2) | 0.185 |
| CVP (mmHg) | 9.4 (5.0) | 11.3 (5.3) | 0.680 | 7.8 (3.4) | 0.126 | 9.8 (3.6) | 0.717 |
| CI (liter $min^{-1}$• $m^{-2}$) | 3.3 (0.8) | 3.5 (0.9) | 0.809 | 2.9 (0.5) | 0.190 | 3.3 (0.7) | 0.009 |
| SVI ( mL•$m^{-2}$) | 46.7 (7.8) | 50.2 (8.6) | 0.837 | 39.1 (8.1) | 0.091 | 46.8 (10.3) | 0.008 |
| SVV (%) | 11.2 (3.7) | 6.3 (3.2) | 0.126 | 18.4 (5.8) | 0.001 | 8.7 (3.7) | 0.004 |
| PVI (%) | 11.3 (6.2) | 8.7 (3.8) | 0.618 | 19.5 (6.6) | 0.001 | 12.0 (5.0) | 0.002 |
| PI (%) | 3.9 (2.5) | 3.6 (2.4) | 0.922 | 3.3 (1.8) | 0.166 | 3.3 (1.6) | 0.643 |

Data are mean (S.D.). HR, heart rate; MAP, mean arterial pressure; CVP, central venous pressure; CI, cardiac index; SVI, stroke volume index; SVV, stroke volume variation; PVI, pleth variability index; PI, perfusion index. P1, volume expansion value *vs.* baseline value in non-responders; P2, baseline value in responders *vs.* baseline value in non-responders; P3, volume expansion value *vs.* baseline value in responders.

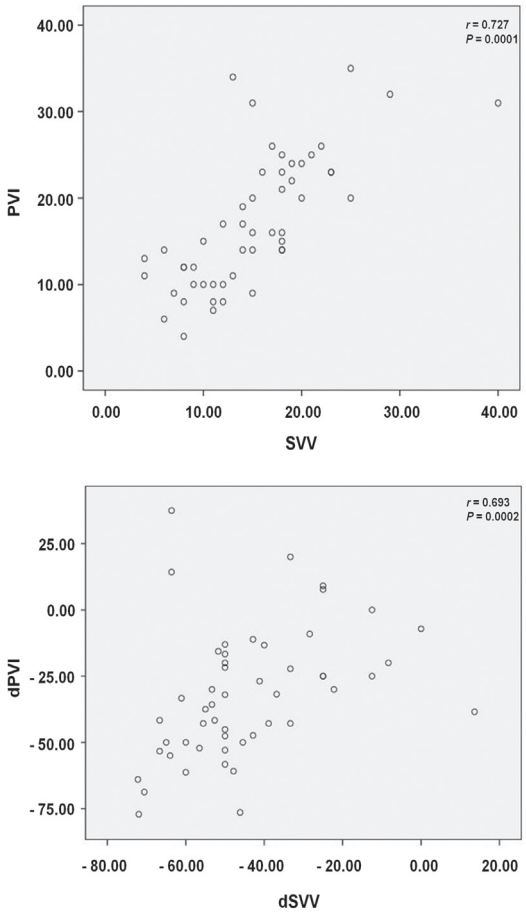


**Figure 1. Relationships between baseline values of SVV and PVI (*upper*), and between percent changes in SVV and PVI after volume expansion (*lower*).**

anaesthesia preoperatively. All of these studies proved that ΔPOP is closely related to ΔPP perioperatively, and is sensitive to changes in ventricular preload (*19*).

SVV obtained with the Vigileo™ system showed its efficacy of predicting responsiveness to fluid loading under general anesthesia in stable conditions (*8-10*). Conversely, one study found that SVV was unable to predict fluid responsiveness after cardiac surgery (*11*). Thus, further studies are required to address this controversy. In this study, the ability of SVV-Vigileo™ to predict responsiveness to fluid loading was assessed during surgical procedures. ROC curves demonstrated that SVV, PVI could predict fluid responsiveness to colloids, and more efficiently than CI, CVP, and MAP, which is in agreement with increasing evidence that static preload indicators are not suited for functional hemodynamic monitoring (*20*). The results showed that SVV > 12.5% discriminated Rs with a sensitivity of 87.9% and a specificity of 83.3% during major surgery. Monitoring of hemodynamic variables such as SV/SVI and CO/CI are regarded to be more reliable measures for assessing the adequacy of volume replacement therapy than simple pressure monitoring (*21*). If SVI were low and SVV, and PVI were high, it may be more accurate to make a diagnosis of hypovolemia, and may help for fluid optimization in complicated surgery procedure settings.

Respiratory variation in the ΔPOP waveform amplitude has been studied in mechanically ventilated patients (*18*,*22*). Pleth variability index (PVI) (Masimo Co., Irvine, Canada) is a novel algorithm allowing for automated and continuous monitoring of ΔPOP (*7*). Some studies had extended PVI assessment to the perioperative period, and their results showed that there was a significant correlation between PVI before volume expansion and change in CI/SVI after volume expansion (*9*,*14*). But Broch *et al.* showed that PVI was not able to predict fluid responsiveness with sufficient accuracy, and the accuracy of PVI to predict fluid responsiveness was improved on analyzing patients with higher PI values (*25*). These studies were performed under stable hemodynamic conditions, right after induction of general anaesthesia and before main surgical procedures. Whether this index can be used for intraoperative fluid responsiveness predictions still has to be demonstrated. To our knowledge, this is the first paper to observe the relationships between PVI and fluid response during surgical procedures. Our results showed a significant positive linear correlation between PVI at baseline and percent changes in SVI (ΔSVI) induced by intravascular volume expansion. ROC curves results also showed that PVI has predictive

**Table 2. Areas under the ROC curves and cutoff values of various hemodynamic parameters for prediction of fluid responsiveness**

| | Optimal threshold value | Sensitivity (%) | Specificity (%) | AUC (95% CI) | *p*-value |
|---|---|---|---|---|---|
| SVV | 12.5% | 87.9 | 83.3 | 0.862 (0.761-0.963) | 0.001 |
| PVI | 13.5% | 77.4 | 80.0 | 0.785 (0.651-0.920) | 0.002 |
| SVI | 43.5 mL•m$^{-2}$ | 83.3 | 91.0 | 0.726 (0.577-0.875) | 0.057 |
| CI | 2.85 liter min$^{-1}$• m$^{-2}$ | 72.2 | 75.8 | 0.651 (0.488-0.813) | 0.071 |
| CVP | 7.5 mmHg | 61.1 | 63.6 | 0.606 (0.447-0.779) | 0.203 |
| MAP | 67.5 mmHg | 66.7 | 69.7 | 0.686 (0.517-0.776) | 0.059 |
| PI | 3.49% | 61.1 | 66.7 | 0.647 (0.485-0.808) | 0.079 |

AUC (95% CI), area under ROC curve (95% CI); SVV, stroke volume variations; PVI, pleth variability index; SVI, stroke volume index; CI, cardiac index; CVP, central venous pressure; MAP, mean arterial pressure; PI, perfusion index. *p*-value, comparison with AUC = 0.5.

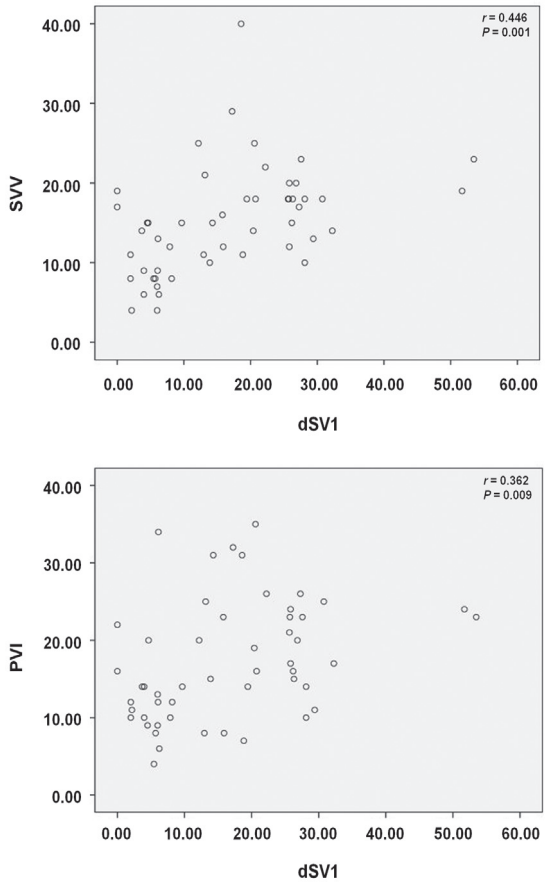


**Figure 2. Relatiships between SVV (*upper*) and PVI (*lower*) before volume expansion and percent increase in stroke volume index after VE.**

value for fluid responsiveness intraoperatively. So, monitoring fluid responsiveness using a non-invasive device may help for fluid optimization in the operating room, especially in some patients who do not need invasive artery monitoring.

In the surgical setting, whether some surgical stress factors, such as nociceptive stimulation, intraoperative bleeding and fluid loss have influenced PVI are still unknown. PI depends on vasomotor tone and sympathetic tone, which may affect the pulsatile absorption component (*23*). Keller *et al.* found that PVI was a weak predictor of fluid responsiveness in a spontaneously breathing volunteer (*15*). It appears that PVI is not yet able to distinguish between changes in PI induced by respiration from changes induced by any other phenomenon. Cannesson *et al.* proved that PVI was more stable in mechanical ventilated patients under general anaesthesia preoperatively (*14*). This may be related to a decrease in sympathetic tone related to general anaesthesia and vasomotor tone does not impact PVI (*12*,*13*). The accuracy of PVI to predict fluid responsiveness was improved on analyzing patients with higher PI values (*25*). If a patient's finger is inaccessible for monitoring purposes, or during states of low peripheral perfusion, the plethysmographic dynamic index can be used in the forehead or ear (*26*). Our results showed that SVV and PVI could predict fluid responsiveness during major abdominal surgery in complicated dynamic conditions, which proved that surgical stress factors did not affect SVV and PVI's clinical value as a predictor of fluid responsiveness. In this study, the areas under the ROC curve for SVV (0.862) and PVI (0.785) are less than Zimmermann's results (*9*), in which the areas of ROC curves for SVV and PVI were 0.993 and 0.973 respectively. But both SVV and PVI achieved statistical significance in this real surgical setting. Our results of the best threshold values to predict fluid responsiveness were more than 12.5% for SVV and more than 13.5% for PVI during the surgical setting, compared with Zimmermann's results of 11% for SVV and 9.5% for PVI. So, during the surgical procedure, many intraoperative factors such as nociceptive stimulation, intraoperative occult bleeding and fluid loss can easily affect SVV and PVI's readings, but our results showed that both of them were still good indicators of intraoperative fluid responsiveness, and the threshold values derived from this study maybe more instructional in guiding fluid expansion during major surgical procedures.

In conclusion, the baseline value of SVV, PVI correlated significantly with volume-induced changes in SVI, SVV have good agreement with PVI during resection of PRPT in Hans Chinese. Both of them could predict fluid responsiveness in a complicated surgical setting.

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