

# Short-Time Low PEEP Challenge and Mini-Fluid Challenge to Evaluate Fluid Responsiveness in the Operating Room

## Ekspiryum Sonu Pozitif Basınç (PEEP) Uygulamasının Oluşturduğu Hemodinamik Değişimlerin ve Mini Sıvı Yükleme Testinin Sıvı Yanıtlılığını Öngörme Etkinliklerinin Değerlendirilmesi

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### ABSTRACT

**Objectives:** We aimed to assess the abilities of short-time low positive end-expiratory pressure challenge (SLPC) and mini-fluid challenge (MFC) to predict fluid responsiveness with the uncalibrated arterial waveform analysis device in the operating room.

**Methods:** Stroke volume index (SVI), pulse pressure variation (PPV), and stroke volume variation (SVV) were recorded before SLPC (T1) at the end of the 30 s of SLPC (T2), 3 min after SLPC (T3), 1 min after MFC with the infusion of 100 mL of crystalloid (T4), and 3 min after fluid loading was completed with additional 400 mL of crystalloid (T5). Patients whose SVI increased more than 15% after the fluid loading were defined as responders. Along with PPV and SVV, percentage changes in SVI due to SLPC and MFC were evaluated by the area under the receiver operating characteristics curve (ROCAUC) for predicting fluid responsiveness.

**Results:** Thirty patients completed the study. Fourteen (47%) of them were responders. ROCAUC values of SLPC, MFC, PPV, and SVV were 0.92 (95% CI: 0.76–0.99), 0.94 (95% CI: 0.79–0.99), 0.68 (95% CI: 0.49–0.84), and 0.51 (95% CI: 0.32–0.70), respectively. ROCAUC values of SLPC and MFC were comparable ( $p=0.73$ ), and they were both statistically significantly higher than those of SVV and PPV. The best cutoff values of SVI percentage change to predict fluid responsiveness were 5.1% and 6.7% for SLPC and MFC, respectively.

**Conclusion:** SVI percentage change during SLPC and after MFC can predict fluid responsiveness better than PPV and SVV in the operating room.

**Keywords:** Fluid therapy, intraoperative monitoring, positive pressure respiration, stroke volume

### ÖZ

**Amaç:** Bu çalışmada, ameliyathanede kalibre edilmemiş arteriyel dalga formu analiz cihazı ile sıvı yanıtlılığını tahmin etmek için kısa süreli düşük pozitif ekspirasyon sonu basınç (PEEP) uygulaması (SLPC) ve mini sıvı yükleme testinin (MFC) etkinliklerinin değerlendirilmesi amaçlanmıştır.

**Yöntem:** Atım hacim indeksi (SVI), nabız basıncı varyasyonu (PPV) ve atım hacmi varyasyonu (SVV), SLPC'den önce (T1), SLPC'nin 30. saniyesinde (T2), SLPC'den üç dakika sonra (T3), 100 mL kristalloid infüzyonu ile MFC'den bir dakika sonra (T4) ve ilave 400 mL kristalloid ile sıvı yüklemesi tamamlandıktan üç dakika sonra (T5) kaydedildi. Sıvı yüklemesinden sonra SVI %15'ten fazla artan hastalar yanıt verenler olarak tanımlandı. PPV ve SVV ile birlikte, SVI'daki SLPC ve MFC'den kaynaklanan yüzde değişiklikleri, sıvı yanıtlılığını tahmin etmek için alıcı işletim karakteristiği eğrisi (ROCAUC) altındaki alan tarafından değerlendirildi.

**Bulgular:** Çalışmayı 30 hasta tamamladı. Bunların 14'ü (%47) yanıtlıydı. SLPC, MFC, PPV ve SVV için ROCAUC değerleri sırasıyla 0,92 (%95 GA: 0,76-0,99), 0,94 (%95 GA: 0,79-0,99), 0,68 (%95 GA: 0,49-0,84) ve 0,51 (%95 GA: 0,32-0,70) idi. % GA: 0,49-0,84) ve 0,51 (%95 GA: 0,32-0,70). SLPC ve MFC'nin ROCAUC değerleri karşılaştırılabilir (p:0,73) ve her ikisi de SVV ve PPV'ninkinden istatistiksel olarak anlamlı derecede yüksekti. Sıvı yanıtlılığını tahmin etmek için SVI yüzde değişiminin en iyi eşik değerleri, SLPC ve MFC için sırasıyla %5,1 ve %6,7 idi.

**Sonuç:** SLPC sırasında ve MFC'den sonra SVI yüzde değişimi, ameliyathanede sıvı yanıtını PPV ve SVV'den daha iyi tahmin edebilir.

**Anahtar sözcükler:** İntraoperatif monitörizasyon, sıvı tedavisi, atım hacmi, pozitif basınçlı ventilasyon

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## Introduction

During the intraoperative period, maintaining normovolemia and determining fluid responsiveness for that purpose are main concerns for anesthesiologists. While hypovolemia and low cardiac output are well-known reasons for organ failure, iatrogenic hypervolemia could result in tissue edema and endothelial glycocalyx damage.<sup>[1-3]</sup> Thus, optimizing fluid therapy plays a key part in reducing morbidity and mortality.<sup>[4,5]</sup> In this context, dynamic variables derived from cardiopulmonary interactions as pulse pressure variation (PPV) and stroke volume variation (SVV) have gained the interest of clinicians. Indeed, these indices are shown to predict fluid responsiveness with great specificity and sensitivity.<sup>[6]</sup> However, there are some limitations to these indices such as arrhythmia, static respiratory system compliance (Cr<sub>s</sub>) below 35 mL cmH<sub>2</sub>O<sup>-1</sup>, and tidal volume (TV) below 8 mL kg<sup>-1</sup> of the ideal body weight (IBW).<sup>[7]</sup> Functional hemodynamic tests (i.e., mini-fluid challenge (MFC), end-expiratory occlusion test, passive leg raise test, and short-time low positive end-expiratory pressure [PEEP] challenge [SLPC]) have been developed for those scenarios when SVV and PPV are not applicable.<sup>[8,9]</sup> Of the mentioned tests, PEEP SLPC and MFC have been separately validated in surgical patients in terms of predicting fluid responsiveness in the operating room.<sup>[9,10]</sup> However, these two methods have not been evaluated in the same patient group.

Evaluating fluid response necessitates the measurement of stroke volume. For that purpose, arterial waveform analysis is used frequently. Although there are different methodologies for processing the waveform, their common characteristic is the need for a conversion factor to convert the data from arterial waveform to stroke volume.<sup>[11]</sup> According to the method used for calculating conversion factor, devices can be divided into three groups. Externally calibrated devices use a different cardiac index measurement method (i.e., transpulmonary thermodilution) for calculation. Internally calibrated devices use demographic data (i.e., age, height, and weight) to match the patient with a pre-defined coefficient from its internal library. In addition to that, various arterial waveform features are used as skewness and kurtosis.<sup>[11,12]</sup> There is also a unique device without the need for calibration. This device uses a novel method named Pressure Recording Analytical Method (PRAM) to evaluate arterial waveform and uses this data for the calculation of arterial impedance as the conversion factor.<sup>[13]</sup> While calibrated devices have been widely used for evaluating different fluid responsiveness methods, studies with the uncalibrated device are limited. To the best of our knowledge, there is no study performed with such a device to evaluate the use of SLPC in the operating room.

In line with these points, the present study aimed to assess the abilities of SLPC and MFC to predict fluid responsive-

ness with the uncalibrated arterial waveform analysis device in a surgical patient group ventilated with <8 mL kg<sup>-1</sup> IBW TV s, in the operating room.

## Methods

### Study Design and Patient Selection

This was a single-center observational study of consecutive patients planned to undergo major abdominal surgery between November 2021 and January 2022. All patients included in this study were followed up with invasive blood pressure monitoring through an arterial catheter placed in the radial artery. Patients with the following conditions were excluded: Body mass index (BMI) >35 kg m<sup>-2</sup>, pre-operative arrhythmia, left ventricle ejection fraction <50%, Cr<sub>s</sub> <35 mL cmH<sub>2</sub>O<sup>-1</sup>, valvular heart disease, and ASA score >3. Ethical approval was obtained from the Clinical Research Ethics Committee of Başakşehir Çam and Sakura City Hospital (2021.07.150) and written informed consent was obtained from all patients.

### Anesthesia Management

Patients' peripheral oxygen saturation, heart rate (HR, by five-channel electrocardiography), non-invasive blood pressure, and patient state index (PSI, Masimo Inc., Irvine, CA) were monitored following arrival at the operating room. Anesthesia was induced with 1% propofol to achieve PSI <50 along with 1 mcg kg<sup>-1</sup> fentanyl and 0.6 mg kg<sup>-1</sup> rocuronium bromide. For the maintenance of anesthesia, remifentanyl (0.05–0.3 mcg kg<sup>-1</sup> min<sup>-1</sup>) infusion and propofol infusion (50–300 mcg kg<sup>-1</sup> min<sup>-1</sup>) were used aiming PSI values between 25 and 50. Mechanical ventilation included volume controlled ventilation (Hamilton-C1 ventilator, Hamilton medical, Bonaduz, Switzerland) with a TV <8 mL kg<sup>-1</sup> IBW at a rate of 12–15 min<sup>-1</sup>, an I/E ratio of 1/2 in 40% oxygen and air with a PEEP of 5–7 cmH<sub>2</sub>O. IBW was calculated using Robinson's formula.<sup>[14]</sup>

### Respiratory and Hemodynamic Monitoring

Cr<sub>s</sub> values were automatically calculated by the ventilator after inspiratory and expiratory hold maneuvers were performed.

After the induction of anesthesia, the left radial artery was catheterized following a normal Allen's test. A 20 gauge 8 cm arterial catheter (Vygon, Padova, Italy) was used dedicated for radial artery catheterization and arterial waveform analysis through MostCare monitor (Vygon, Padova, Italy) and attached to the pressure transducer of this device. MostCare monitor uses PRAM for calculating several variables along with stroke volume index (SVI), SVV, and PPV. Unlike other arterial waveform analysis devices, MostCare monitor does not need an external or internal calibration since PRAM allows arterial impedance calculation through arterial waveform analysis.<sup>[13]</sup>

## Protocol

We recorded the hemodynamic and ventilatory parameters at five time points (T1–T5). The first measurement was performed after confirming hemodynamic stability (defined as mean arterial pressure (MAP) change <10% for 3 min) following tracheal intubation. Subsequently, we applied additional 5 cmH<sub>2</sub>O PEEP to patients for 30 s (SLPC). Before PEEP lowering, T2 measurement was performed. During the protocol, patients with MAP <60 mmHg for more than 60 s were excluded and intervened with fluids and/or vasopressors. T3 measurement was performed 3 min after PEEP was decreased to its initial value and was recorded as the second baseline. Thereafter, 100 mL isotonic saline was infused over 1 min (MFC). One minute after MFC was completed, T4 measurement was performed. Finally, T5 measurement was performed 3 min after additional 400 mL of isotonic saline was infused within 10 min to complete 500 mL of fluid loading. Patients whose SVI showed an increase more than 15% after fluid loading were classified as responders. The following parameters were also calculated:

- Percentage change in SVI due to SLPC, SLPC- $\Delta$ SVI%:  $([SVI-T1-SVI-T2]/SVI-T1) \times 100$
- Percentage change in SVI due to MFC, MFC- $\Delta$ SVI%:  $([SVI-T4-SVI-T3]/SVI-T3) \times 100$
- Percentage change in SVI due to fluid loading, FL- $\Delta$ SVI%:  $([SVI-T5-SVI-T3]/SVI-T3) \times 100$ .

## Statistical Analysis

The sample size was calculated by assuming that the area under the receiver operating characteristics curve (ROCAUC) was >0.80 (tested against a value of 0.50) for at least one of the methods used and ratio of the fluid responder cases was over 33%. Accordingly, at least 30 patients were required (type I error of 5% and type II error of 20%).

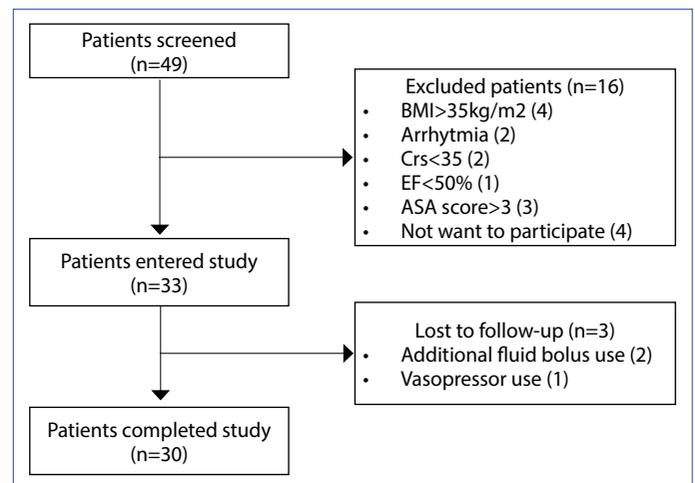
The distribution of interval data was evaluated by Shapiro–Wilk test. Normally distributed data are presented as mean  $\pm$  standard deviation, and non-normally distributed data are presented as median (25<sup>th</sup>–75<sup>th</sup> percentile). Categorical data are presented as frequency. Hemodynamic parameters of responders and non-responders were compared with the Mann–Whitney U-test while repeated measurements within the groups were compared with the Wilcoxon test. The relationships between SLPC- $\Delta$ SVI% and FL- $\Delta$ SVI% and between MFC- $\Delta$ SVI% and FL- $\Delta$ SVI% were evaluated with linear correlation analysis. Receiver operating characteristics curves (ROCs) were created for SLPC- $\Delta$ SVI%, MFC- $\Delta$ SVI%, SVV, and PPV to evaluate their ability to predict fluid responsiveness. ROCAUCs of these variables were compared with the approach defined by DeLong et al.<sup>[15]</sup> Since the reliability of MostCare depends on the quality of the arterial waveform, the presence of dicrotic notch was assured in all patients and the square test was used. Cutoff values for the methods and

their sensitivity and specificity values were calculated using the Youden index (sensitivity + specificity – 1). Statistical significance was set up at  $p < 0.05$ . Statistical analyses were performed using SPSS for Windows, version 21.0 (SPSS Inc., Chicago, IL, USA) or MedCalc, version 16.1 (MedCalc Software Ltd., Ostend, Belgium), as appropriate.

## Results

### Patients' Characteristics and Hemodynamic Data

Thirty-three patients entered study and three of them were excluded due to the need for fluid bolus or vasopressors during the intervention period. Thirty patients completed the study (Fig. 1). Patients' characteristics are shown in Table 1. Fourteen patients (47%) were responders and 16 patients (53%) were non-responders to fluid loading. HR, MAP, SVI, PPV, and SVV values of patients during T1, T2, T3, T4, and T5 measurement times are shown in Table 2.



**Figure 1.** Study flow chart.

BMI: body mass index; Crs: static respiratory system compliance; EF: ejection fraction.

**Table 1.** Characteristics of patients

Variables (n=30)	
Gender (m/f)	18/12
Age (years)	54.3 $\pm$ 12.6
BMI (kg m <sup>-2</sup> )	25.8 $\pm$ 3.1
IBW (kg)	61.3 $\pm$ 7.3
Tidal volume (mL)	445 $\pm$ 48
Driving pressure (cmH <sub>2</sub> O)	10.4 $\pm$ 2.2
Plateau pressure (cmH <sub>2</sub> O)	14.9 $\pm$ 2.1
Tidal volume (mL kg <sup>-1</sup> of IBW)	7.3 $\pm$ 0.4
Static compliance (mL cmH <sub>2</sub> O <sup>-1</sup> )	45.6 $\pm$ 11.9

Values are expressed as mean  $\pm$  SD, or number. m: Male; f: Female; BMI: Body mass index; IBW: Ideal body weight.

**Table 2.** Hemodynamic variables at baseline, after 100 mL fluid loading, and after 500 mL fluid loading

	Baseline (T1)	SLPC (T2)	P1	Baseline2 (T3)	After 100 mL fluid (T4)	P2	After 500 mL fluid (T5)	P3
HR (beat min <sup>-1</sup> )								
Responders	71 (64–85)	73 (64–84)	0.78	70 (63–86)	71 (61–85)	0.29	65 (61–84)	0.04
Non-responders	70 (63–78)	68 (65–81)	0.72	69 (63–79)	68 (61–78)	0.008	69 (64–73)	0.28
P intergroup	0.69	0.48		0.76	0.57		0.53	
MAP (mmHg)								
Responders	69 (63–78)	66 (61–79)	0.47	68 (65–79)	76 (64–87)	0.04	82 (68–97)	0.002
Non-responders	74 (63–82)	75 (59–81)	0.24	71 (66–79)	74 (61–83)	0.55	77 (70–93)	0.003
P intergroup	0.52	0.80		0.52	0.55		0.63	
SVI (mL m <sup>-2</sup> )								
Responders	33 (24–39)	31 (21–35)	0.001	33 (23–38)	37 (26–42)	0.001	42 (33–46)	0.001
Non-responders	35 (32–40)	34 (30–39)	0.001	35 (32–39)	36 (33–40)	0.001	38 (34–43)	0.001
P intergroup	0.21	0.06		0.24	0.65		0.39	
PPV (%)								
Responders	11 (8–14)	14.5 (11–16)	0.001	11.5 (8–14)	7.5 (6–10)	0.001	5.5 (4–7)	0.001
Non-responders	9 (6–10)	11 (9–15)	0.001	9 (7–12)	7 (5–9)	0.007	5 (3–7)	0.001
P intergroup	0.06	0.13		0.09	0.41		0.85	
SVV (%)								
Responders	7 (6–8)	10 (8–11)	0.001	7.5 (6–8)	7 (4–7)	0.04	4 (3–5)	0.001
Non-responders	6 (5–10)	11 (6–15)	0.005	6 (5–10)	5 (3–8)	0.046	4 (3–6)	0.009
P intergroup	0.93	0.57		0.62	0.88		0.40	

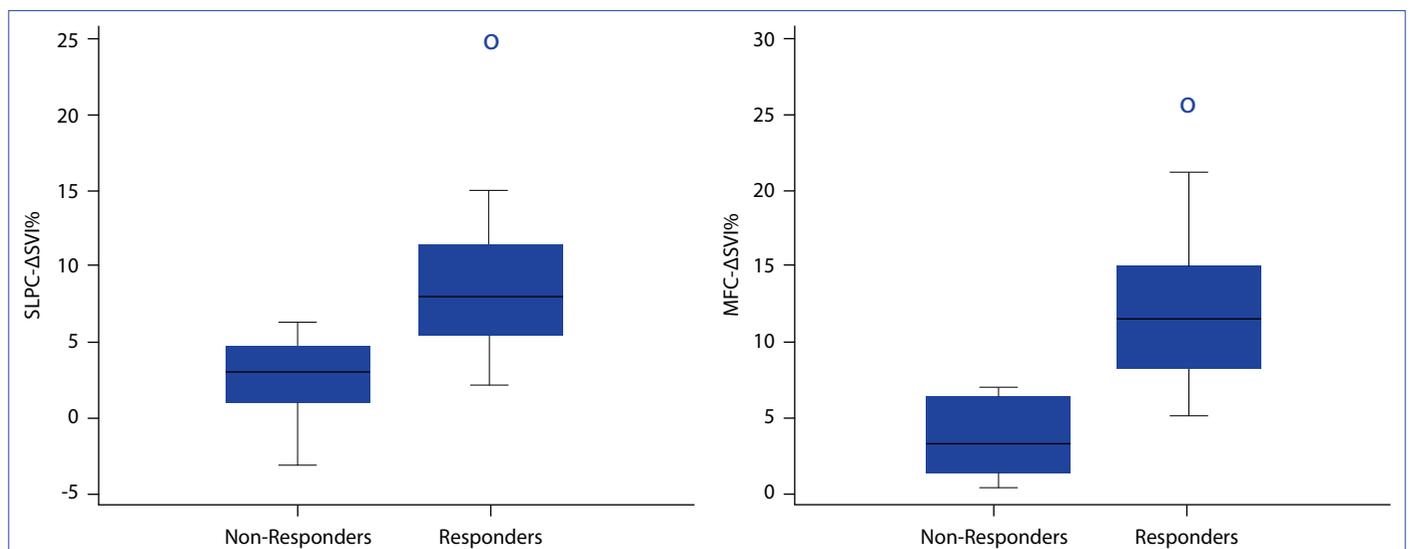
Values are expressed as median (25<sup>th</sup>–75<sup>th</sup> percentile). P1: Comparison between T1 and T2 with Wilcoxon test. P2: Comparison between T3 and T4 with Wilcoxon test. P3: Comparison between T3 and T5 with Wilcoxon test. P intergroup: Comparison between responders and non-responders with Mann-Whitney U-test. HR: Heart rate, MAP: Mean arterial pressure, SVI: Stroke volume index, PPV: Pulse pressure variation, SVV: Stroke volume variation.

### Change in SVI during SLPC and After MFC in Responders and Non-Responders

A higher percentage change in SVI was observed among responders during SLPC ( $p < 0.001$ ). SLPC- $\Delta$ SVI% values were 8.2 (5.5–11.7) and 3.1 (0.6–4.9) in responders and

non-responders, respectively (Fig. 2a).

A higher percentage change in SVI was observed among responders after MFC ( $p < 0.001$ ). MFC- $\Delta$ SVI% values were 11.3 (7.8–15.4) and 2.9 (0.6–6.2) in responders and non-responders, respectively (Fig. 2b).



**Figure 2.** (a) Percentage change in stroke volume index due to short time low PEEP challenge (SLPC- $\Delta$ SVI%) in non-responders and responders ( $p < 0.001$ ). (b) Percentage change in stroke volume index due to mini fluid challenge (MFC- $\Delta$ SVI%) in non-responders and responders ( $p < 0.001$ ). Data are expressed as median, interquartile range and minimum-maximum.

### Change in SVI after FL in Responders and Non-responders and Correlation with SLPC- $\Delta$ SVI% and MFC- $\Delta$ SVI%

A higher percentage change in SVI was observed among responders after FL ( $p < 0.001$ ). FL- $\Delta$ SVI% values were 23.5 (17.3–35.3) and 6.7 (3–10) in responders and non-responders, respectively.

There was a good correlation between SLPC- $\Delta$ SVI% and FL- $\Delta$ SVI% as well as between MFC- $\Delta$ SVI% and FL- $\Delta$ SVI% ( $r$ : 0.54  $p = 0.002$  and  $r$ : 0.53  $p = 0.003$ , respectively.).

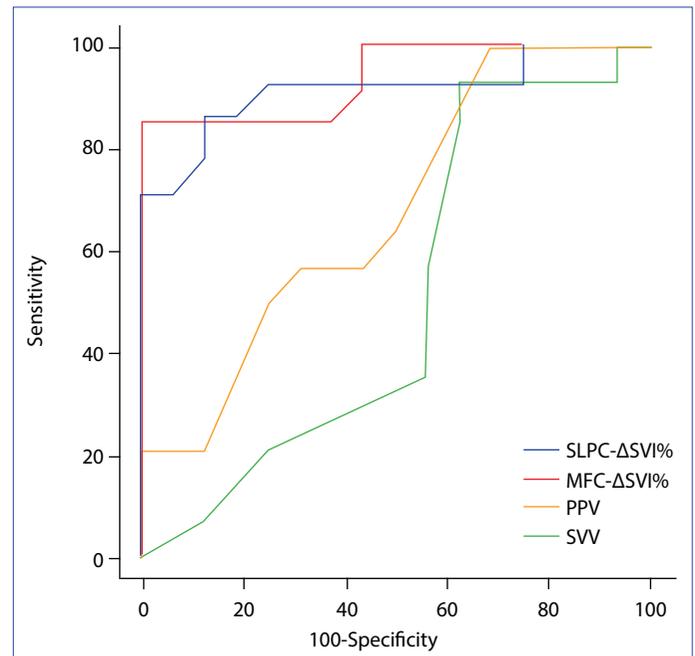
### Predicting Fluid Responsiveness

ROC curves were created to determine the abilities of SLPC- $\Delta$ SVI%, MFC- $\Delta$ SVI%, PPV, and SVV to predict fluid responsiveness. ROC-AUCs of SLPC- $\Delta$ SVI% and MFC- $\Delta$ SVI% (0.92; 95% CI: 0.76–0.99 and 0.94; 95% CI: 0.79–0.99, respectively) were statistically significantly higher than those of PPV and SVV (0.68; 95% CI: 0.49–0.84 and 0.51; 95% CI: 0.32–0.70, respectively) (Fig. 3). There was no statistically significant difference between the ROC-AUCs of SLPC- $\Delta$ SVI% and MFC- $\Delta$ SVI% ( $p = 0.73$ ). Best cutoff values and diagnostic performances of the variables are shown in Table 3.

### Discussion

The main results of this study showed that MFC and SLPC could predict fluid responsiveness with high sensitivity and specificity, and better than SVV and PPV in patients ventilated with  $< 8 \text{ mL kg}^{-1} \text{ IBW TV}$ , in the operating room. ROC-AUC values of MFC and SLPC were comparable.

Our study reproduced the evidence regarding impaired ability of SVV and PPV in patients undergoing low TV ventilation.<sup>[9,16]</sup> TVs below  $8 \text{ mL kg}^{-1} \text{ IBW}$  are shown to be incapable of effectively transmitting respiratory pressure changes to the cardiovascular system.<sup>[17,18]</sup> Since this strategy is strongly recommended as a part of protective ventilation, it has necessitated the need for inventing functional hemodynamic tests (FHTs).<sup>[19]</sup> As previously mentioned, there are four FHTs defined in the literature. Of them, passive leg raise test and end-expiratory occlusion test are not perfect-



**Figure 3.** Receiver operating characteristics curves generated for SLPC- $\Delta$ SVI%, MFC- $\Delta$ SVI%, PPV and SVV for showing their ability to predict fluid responsiveness.  $\alpha$ : Comparison of ROC-AUCs of SLPC- $\Delta$ SVI% and PPV ( $p = 0.047$ ).  $\beta$ : Comparison of ROC-AUCs of SLPC- $\Delta$ SVI% and SVV ( $p = 0.001$ ).  $\gamma$ : Comparison of ROC-AUCs of MFC- $\Delta$ SVI% and PPV ( $p = 0.027$ ).  $\delta$ : Comparison of ROC-AUCs of MFC- $\Delta$ SVI% and SVV ( $p < 0.001$ ). SLPC- $\Delta$ SVI%: percentage change in stroke volume index due to short time low PEEP challenge. MFC- $\Delta$ SVI%: percentage change in stroke volume index due to mini fluid challenge. PPV: pulse pressure variation. SVV: stroke volume variation.

ly suitable for use in the operating room as the first one requires leg raise maneuver and the second one is based on the application of end-expiratory occlusion maneuver that is not available in all anesthesia work stations.<sup>[16,20]</sup>

Short-time low PEEP challenge induces a temporary decrease in venous return that results in the reduction in stroke volume.<sup>[9]</sup> When the patient is on the steep part of the Frank-Starling curve, a change in preload status results in a more significant reduction in stroke volume. Accordingly, in the study in which SLPC was defined for the 1<sup>st</sup> time, Ali et al.<sup>[9]</sup> found that a 14.2% reduction in SVI due to

**Table 3.** Best cutoff values and diagnostic performances of the variables

Variable	Best cutoff value (%)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
SLPC- $\Delta$ SVI%	>5.13	86	87	85	88
MFC- $\Delta$ SVI%	>6.7	86	100	100	89
PPV	>7	100	31	56	100
SVV	>9	93	38	57	86

Best cutoff values were determined using Youden index ( $J = \text{sensitivity} + \text{specificity} - 1$ ). SLPC- $\Delta$ SVI%: Percentage change in stroke volume index due to short time low PEEP challenge. MFC- $\Delta$ SVI%: Percentage change in stroke volume index due to mini-fluid challenge. PPV: Pulse pressure variation. SVV: Stroke volume variation.

SLPC could predict fluid responsiveness with a ROCAUC of 94.4% in patients planned to undergo neurosurgery. In the present study, although ROC-AUC of SLPC- $\Delta$ SVI% is in line with the previous result, the best cutoff value was found to be 5.1%. This difference could be explained in two ways. First, the mean Crs value of the previous patient group was 59 mL cmH<sub>2</sub>O<sup>-1</sup> while it is 45.6 mL cmH<sub>2</sub>O<sup>-1</sup> in the present study. This might have affected the cutoff value as lower Crs values are related with reduced transmission of airway pressure to the cardiovascular system. In accordance with this, in another study performed in intensive care patients whose mean Crs value was 48.7 mL cmH<sub>2</sub>O<sup>-1</sup>, best cutoff value for SLPC- $\Delta$ SVI% was found to be 7.5% with a ROCAUC of 0.95.<sup>[21]</sup> Second, unlike the present study, the arterial waveform analysis device used in the aforementioned studies was one of the internally calibrated devices (FloTrac; Edwards Lifesciences, Irvine, CA, USA).

FloTrac system calculates stroke volume using the standard deviation of the pulse pressure around the MAP as it is linearly related to stroke volume. For the calculation of the standard deviation, data points are sampled at 100 Hz for 20 s. Both systolic and diastolic parts of the arterial wave are used. A conversion factor is also used to convert the measurements to stroke volume. This factor is recalculated every minute by processing patient's demographic data, and the skewness and kurtosis of arterial waveform.<sup>[11,12]</sup> On the other hand, MostCare analyzes the arterial pressure wave with a sampling rate of 1000 Hz. This rate allows detecting the points of instability profile which is a result of forward and backward forces in the arterial system. As a result of this process, arterial impedance is determined for every single waveform, and along with the systolic area, it is used for calculation of stroke volume.<sup>[13]</sup> It is not unexpected that these methodological differences between devices might lead to different results. In a study performed by Smorenberg et al.,<sup>[22]</sup> it was shown that the predictive ability of a method could vary depending on the device used to measure stroke volume.

Short-time low PEEP challenge is superior to MFC in terms of fluid balance since MFC requires an infusion of 100 mL fluid each time.<sup>[23]</sup> However, MFC has the advantage of being the only FHT that does not rely on cardiopulmonary interactions. Therefore, this method can be used not only in patients ventilated with low TVs but also in patients with other scenarios that interrupt cardiopulmonary interactions. Since MFC was defined by Muller et al.<sup>[10]</sup> in 2011, the remarkable predictive ability of this method has been confirmed in patients with spontaneous ventilation, low Crs and high BMI, and in patients ventilated with <8 mL kg<sup>-1</sup> TVs.<sup>[10,16,24,25]</sup> A recent meta-analysis has evaluated seven MFC studies that included 368 fluid challenges in 324

patients and found a pooled ROCAUC of 0.91 with a cutoff value of 5%.<sup>[26]</sup> These results are in line with the ones in the present study.

Recently, there has been an ongoing debate regarding the methodology used in the MFC studies. Vistisen et al.<sup>[27]</sup> claimed that using the same baseline for both predictor and outcome variables might overestimate the accuracy of MFC as these variables are mathematically dependent. As a solution, they suggest obtaining two sets of measurements after MFC with an appropriate time window. In this way, the first sets of measurements can be used to evaluate the response to MFC and the second can serve as the new baseline for fluid challenge. However, we chose to adhere to the conventional method. Thus, we had the opportunity to compare our results with those in the previous studies.

The present study has several limitations. First, all measurements were performed before the surgery started. Therefore, these results cannot be applied to laparotomy procedures directly. Second, we used 3 min of time window between SLPC and MFC, and 1 min between MFC and fluid loading to guarantee the return to the steady state. In addition, we did not measure a new baseline after MFC and before fluid loading as it is in the standard MFC method. Different time windows and methodologies might lead to different results. Third, the reliability of MostCare depends on the quality of the arterial waveform. Therefore, we utilized square test and assured the presence of dicrotic notch in all patients. Fourth, we used TVs <8 mL kg<sup>-1</sup> IBW and PEEP values between 5–7 cmH<sub>2</sub>O. Different TV and PEEP settings may affect the ROCAUC and cutoff values of SLPC. Fifth, patients with Crs <35 mL cmH<sub>2</sub>O<sup>-1</sup> were excluded from the study. Therefore, the ability of SLPC in that patient group cannot be extrapolated from the present study's data.

Percentage changes in SVI after SLPC and MFC could predict fluid responsiveness better than either SVV or PPV in patients with low TV ventilation in the operating room. Classification accuracies of MFC and SLPC are comparable. Therefore, SLPC is a good alternative to MFC as it contributes more to fluid balance.

#### Disclosures

**Ethics Committee Approval:** The study was approved by The Başakşehir Çam and Sakura City Hospital Ethics Committee (Date: 13/07/2021, No: 2021.07.150).

**Informed Consent:** Written informed consent was obtained from all patients.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

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