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## Article

# Value of Carotid Corrected Flow Time (FTc) or Changes Value of FTc Could Be More Useful in Predicting Fluid Responsiveness Undergoing Robot-Assisted Gynecologic Surgery

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**Abstract:** This prospective study aimed to evaluate the ability of point-of-care Doppler ultrasound measurements of carotid-corrected flow time and changes in corrected carotid flow time (FTc) induced by volume expansion to predict fluid responsiveness in patients undergoing robot-assisted gynecological surgery in a modified head-down lithotomy position. FTc was measured using Doppler images of the common carotid artery before and after volume expansion. The stroke volume index at each time point was recorded using the MostCare instrument. Fluid responsiveness was defined as a stroke volume index  $\geq 10\%$  increase after volume expansion. Half (50%) of the 52 patients responded positively. The areas under the receiver operating characteristic curves measured to predict fluid responsiveness for the corrected carotid flow time and changes in the FTc were 0.82 [95% confidence interval: 0.705–0.937;  $P < 0.0001$ ] and 0.67 (95% confidence interval: 0.520–0.815;  $P < 0.05$ ), respectively. The optimal cut-off value for the FTc and the change in FTc were 356.5 ms and 19.5 ms, respectively. FTc is a more reliable predictor of fluid responsiveness than FTc induced by volume expansion in gynecological patients undergoing robot-assisted laparoscopic surgery in the modified head-down lithotomy position.

**Keywords:** Doppler ultrasound; corrected time flow; fluid responsiveness; robotics

## 1. Introduction

Fluid management during anesthesia is necessary to control vascular tone, maintain the circulating volume, and improve cardiac output. Hypovolemia and hypervolemia can increase perioperative complications, including pulmonary edema, electrolytes, hemodilution coagulopathy, tissue hypoperfusion, and acid-base derangements. Optimizing perioperative fluid treatment often improves postoperative outcomes, reduces perioperative complications, and shortens hospitalization [1,2]. Therefore, assessing volume status and responsiveness is essential for fluid management in patients undergoing surgery and with critical illnesses.

The earliest static indices (central venous and pulmonary arterial wedge pressure) used clinically could not accurately assess volume status [3,4]. Dynamic indices (stroke volume variation and pulse pressure variation) are derived from cardiopulmonary interactions during mechanical ventilation and may guide fluid management. Although functional hemodynamic parameters have been shown to reliably predict fluid responsiveness, factors such as pulmonary compliance, cardiac function, and mechanical ventilation may limit their broad clinical application [5,6]. The ideal hemodynamic monitoring technique should be less invasive, continuously dynamic, simple to operate, and less expensive. Due to their noninvasive nature and easy access, bedside ultrasound

techniques have gained widespread application and are commonly used for fluid management in perioperative and critical care units. In addition, carotid corrected flow time (FTc) measured in the common carotid artery is considered a reliable method for predicting fluid reactivity [7–9]. Previous studies have found that  $\Delta$ FTc induced by the recruitment maneuver or the passive leg raise test could effectively identify “fluid responsive” patients with increased stroke volume after adequate fluid resuscitation [10,11].

The main aim of our study was to assess the ability of point-of-care FTc and  $\Delta$ FTc induced by volume expansion to predict the responsiveness of fluid in patients undergoing robot-assisted gynecological surgery in a modified head-down lithotomy position.

## 2. Materials and Methods

### 2.1. Study Population

The study protocol was approved by the Institutional Review Board of Chongqing University Cancer Hospital (approval number: CZLS2021041-A) and registered in the Chinese Clinical Trial Register (ChiCTR2200060573). Written informed consent was obtained from all the patients. This prospective study included 52 American Society of Anesthesiologists (ASA) class I–III patients scheduled to undergo robot-assisted gynecological surgery in a modified head-down lithotomy position. Exclusion criteria were body mass index  $>30$  or  $<15$  kg/m<sup>2</sup>, arrhythmia, decreased cardiac function (moderate or severe valve regurgitation, left ventricular ejection fraction  $< 50$  %, right ventricular dysfunction), a history of carotid artery stenosis of 50%, chronic obstructive pulmonary disease, chronic kidney disease, pregnancy, or unwillingness to participate in the study.

### 2.2. Anesthesia technique

The patients were placed supine in the operating room and underwent standard monitoring, including electrocardiography, heart rate (HR), pulse oxygen saturation, and noninvasive blood pressure. Anesthesia induction using propofol (2–3 mg/kg), sufentanil (0.3–0.5  $\mu$ g/kg), midazolam (1–2 mg), and tracheal intubation was facilitated with rocuronium (0.8 mg/kg). Intraoperative anesthesia was maintained with continuous infusion of propofol (1.5–3 mg/kg/h), remifentanyl (0.02–0.2  $\mu$ g/kg/min), and sevoflurane (1.5–2.5 vol%). Neuromuscular blockade was maintained by rocuronium (0.15 mg/kg) administered at 30–40 minute intervals. The radial artery was catheterized after the induction of anesthesia. The tidal volume was set at 6 mL/kg of predicted body weight in volume-controlled mechanical ventilation mode using a WATO EX-65 anesthesia machine (Mindray Medical Systems, Shenzhen, China), and the positive end-expiratory pressure was set at 5 cmH<sub>2</sub>O. An end-tidal carbon dioxide concentration of 35–45 mmHg was maintained by controlling the ventilation frequency parameters. Pneumoperitoneum was achieved by continuous carbon dioxide inflation while maintaining an intra-abdominal pressure of 12 mmHg. During the study procedure, all patients were placed in the modified head-down lithotomy position, and intraoperative maintenance fluids were administered with Ringer’s solution at a rate of 4 mL/kg/h.

### 2.3. Hemodynamic monitoring

Following arterial insertion, the arterial pressure signal was simultaneously transmitted to the operating room IntelliVue MP40 monitor (Philips Medizin Systeme Boblingen GmbH, Boeblingen, Germany) and the MostCare device (Vygon, Vytech, Padova, Italy) using a Y-cable. The patient was positioned for surgery, and the arterial signal was calibrated to zero. MostCare, a multiparameter hemodynamic monitoring tool, utilizes pressure recording analysis methods to estimate cardiac output without requiring calibration. By analyzing the arterial waveform signal sampled at a high rate of 1000 Hz, MostCare accurately identifies the dicrotic notch’s position and calculates the area under the arterial pressure waveform and systemic vascular impedance to determine the stroke volume [12,13]. Notably, the square-wave test was performed to ensure the normalcy of the arterial waveform after connecting the monitor, effectively excluding any under-or-overdamping of the pressure signal [14].

## 2.4. Study procedures

The study protocol was conducted at least 45 min after the intra-abdominal pressure was maintained at 12 mmHg while the patient was hemodynamically stable (i.e., the change in mean arterial pressure and heart rate was less than 10% over 5 minutes). Vasoactive medications were not administered during the study period. Upon program initiation, baseline hemodynamic variables (HR, mean arterial pressure [MAP], PPV, and stroke volume index [SVI]) were obtained, and carotid FTc was measured ( $T_0$ ). Subsequently, a 250 mL infusion of Ringer's solution was administered for 10 min. Hemodynamic variables were re-recorded 5 min after fluid expansion ( $T_1$ ) completion. FTc was calculated as follows:  $\Delta FTc = FT_{CT1} - FT_{CT0}$ . Fluid responsiveness was defined as an SVI increase of  $\geq 10\%$  after fluid administration [11].

## 2.5. Carotid ultrasonography

The ultrasonic parameters were measured using a portable ultrasound device (Mindray Medical Systems, Shenzhen, China). The following scanning protocol acquired images of the common carotid artery: (1) a high-frequency line array transducer was placed transversely at the lower border of the thyroid cartilage, ensuring the common carotid artery was centered on the screen; (2) the long axis B-mode image of the common carotid artery was obtained with the probe marker pointing towards the patient's head; (3) the sample volume was placed at the center of the arterial vessel, and the cursor angle was adjusted parallel to the direction of blood flow, with an insonation angle of  $\leq 60^\circ$ , approximately 2 cm proximal to the carotid bifurcation; (4) a satisfactory spectrum is displayed and frozen by adjusting the optimal sampling volume and angle, then measurement was performed by the caliper function on the machine. Flow time (FT) was measured from the beginning of the systolic upstroke to the dicrotic notch. HR was obtained by measuring the interval between the beginning of two consecutive Doppler flow upstrokes. The average of three consecutive cycles was recorded once stability was achieved and the quality reached an acceptable level (Figure 1). FTc was calculated using the Wodey formula:  $FTc = FT + [1.29 \times (HR - 60)]$  [15].

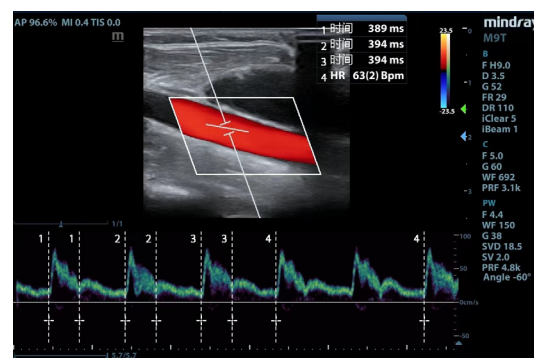


Figure 1. Carotid Doppler waveform.

## 2.6. Sample size calculation and statistical analysis

PASS ver.15.0 (IBM Corp, Armonk, NY, USA) was used to calculate the sample size. A previous study reported that the area under the curve (AUC) was 0.82 for the descending aorta FTc to predict fluid responsiveness. We hypothesized that the carotid FTc might have a low predictive capacity of 0.75. [9] We compared this value with the null hypothesis (AUC = 0.50, ratio of sample sizes in the negative/positive groups = 1) and generated a sample size of 50 patients (type I error = 0.05, power = 0.90). With an expected dropout rate of 10%, 55 patients were included.

Normality was tested for all quantitative data using the Kolmogorov-Smirnov test. Data are presented as the mean (standard deviation), median (interquartile range), and absolute numbers or percentages (%). Continuous variables of patient characteristics were compared between responders and non-responders using an independent-sample t-test or Mann-Whitney U test and the chi-square test for categorical data. Hemodynamic parameters before and after volume expansion (VE) were

assessed using the paired t-test or Wilcoxon signed-rank sum test. In contrast, between-group comparisons were performed using the t-test or Mann–Whitney U test.

Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive ability of FTc and FTc, and the AUC values were compared using the DeLong method [16]. The optimal cut-off value was determined using the maximum Youden index (sensitivity + specificity - 1) [17]. We applied a gray-zone approach to describe an inconclusive range, considering threshold values corresponding to a sensitivity and specificity of 90% [18]. Pearson correlation coefficient was used to investigate the association between carotid ultrasound variables and percentage changes in SVI after VE.

Statistical analyses were performed using the MedCalc ver. 20.1.0 (MedCalc Software, Ostend, Belgium), GraphPad Prism ver. 9.4.0 (GraphPad Software, San Diego, CA, USA), and SPSS ver. 27.0 (IBM Corp, Armonk, NY, USA). A P value <0.05 was regarded as statistically significant.

3. Results

Of the 59 initially screened patients, 55 were enrolled in the study. Three patients were excluded due to high airway pressure (n = 1), severe hypotension (n = 1), or unexpected cardiac arrhythmia (n = 1). Ultimately 52 patients were included in this study.

The final analysis divided the responders and non-responders in half (Figure 2). The demographics of the participants are shown in Table 1. There were no significant differences in patient characteristics between responders and non-responders.

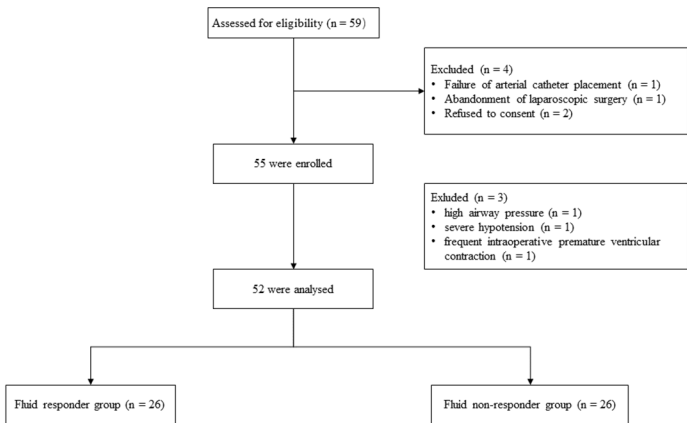


Figure 2. Flow chart of the number of patients enrolled in the study and included in the analyses.

Table 1. Patient characteristics.

| Variables                       | Overall<br>(n=52) | Responder<br>(n=26) | Non-Responders<br>(n=26) | P-Value |
|---------------------------------|-------------------|---------------------|--------------------------|---------|
| Age, year                       | 50.9±10.9         | 51.4±10.1           | 50.5±11.8                | 0.773a  |
| BMI, kg/m2                      | 23.6±3.2          | 23.6±3.6            | 23.7±2.8                 | 0.966a  |
| ASA physical status<br>(II/III) | 43,9              | 22,4                | 21,5                     | 1b      |
| Diagnosis, n (%)                |                   |                     |                          | 0.637c  |
| Vaginal cancer                  | 6(11.5)           | 4(15.4)             | 2(7.7)                   |         |
| Cervical Cancer                 | 28(53.8)          | 14(53.8)            | 14(53.8)                 |         |
| Endometrial cancer              | 18(34.6)          | 8(30.8)             | 10(38.5)                 |         |
| Comorbidities, n (%)            |                   |                     |                          | 0.206c  |
| Hypertension                    | 5(9.6)            | 1(3.8)              | 4(13.8)                  |         |

| Others                                                                                                                                                                                                            | 5(9.6) | 4(13.8) | 1(3.8) |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|---------|--------|
| BMI Body mass index, ASA American Society of Anesthesiologists physical status. a Independent t-test, b Mann–Whitney U c chi-square test. Data are presented as mean (standard deviation), number of patients (%) |        |         |        |

The hemodynamic, ventilatory, and ultrasound parameters before and after VE are presented in Table 2. Higher MAP was observed in non-responders than responders at each time point, but there was no difference before and after rehydration. The baseline PPV, SVI, and FTc were comparable between the two groups, and PPV significantly decreased in both groups after VE, whereas FTc significantly increased. In contrast, SVI after VE showed significant changes only in the responders.

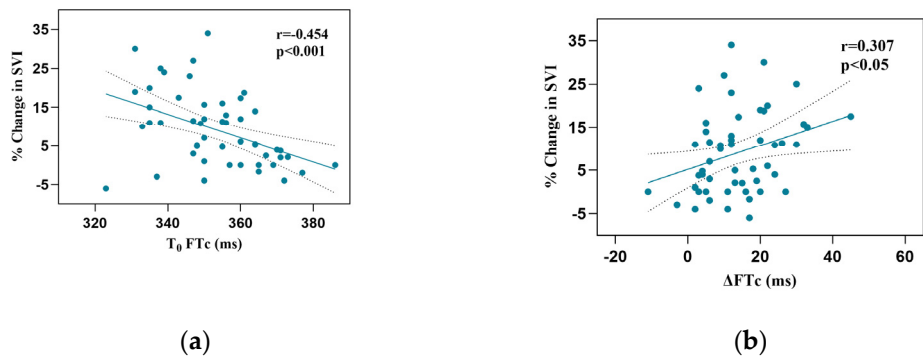
**Table 2.** The hemodynamic, ventilatory, and ultrasound parameter characteristics before and after volume expansion.

|                             | T0            | T1            | P (T0 VS T1) |
|-----------------------------|---------------|---------------|--------------|
| HR (beats/min)              |               |               |              |
| R                           | 68.7±9.5      | 66.9±7.8      | 0.016        |
| NR                          | 65.6±8.3      | 68.3±7.3      | 0.002        |
| Map (mm Hg)                 |               |               |              |
| R                           | 75.6±6.7 *    | 75.5±6.4 *    | 0.689        |
| NR                          | 80.3±8.4      | 80.4±8.5      | 0.889        |
| Pplat (cm H <sub>2</sub> O) |               |               |              |
| R                           | 20.9±3.3      | 21.4±3.1      | 0.004        |
| NR                          | 20.6±2.8      | 21.0±2.7      | 0.009        |
| VT (ml)                     |               |               |              |
| R                           | 319.1±31.4    | 318.2±32.9    | 0.697        |
| NR                          | 323.5±24.2    | 323.1±23.3    | 0.777        |
| Crs (ml/cmH <sub>2</sub> O) |               |               |              |
| R                           | 17.0±4.1      | 16.6±3.8      | 0.11         |
| NR                          | 17.8±3.2      | 17.2±2.8      | 0.013        |
| PPV (%)                     |               |               |              |
| R                           | 7.0(4.8-9.0)* | 6.0(4.8-6.3)* | 0.014        |
| NR                          | 5.0(4.0-7.0)  | 4.0(3.8-5.3)  | 0.003        |
| SVI (ml/min <sup>2</sup> )  |               |               |              |
| R                           | 41.4±9.8*     | 46.5±10.1     | <0.001       |
| NR                          | 48.2±6.3      | 48.2±7.1      | 0.932        |
| FTc (ms)                    |               |               |              |
| R                           | 347.3±11.4*   | 364.5±11.8*   | <0.001       |
| NR                          | 362.7±15.1    | 373.1±17.2    | <0.001       |

HR Heart rate, MAP Mean arterial pressure, Pplat Plateau pressure, VT Tidal volume, Crs Respiratory compliance, PPV Pulse pressure variation, SVI Stroke volume index, FTc Carotid corrected flow time, R Responder, NR Non-Responders. Data are mean ± standard deviation or median (interquartile range). \* P < 0.05 comparison between responders and non-responders at each time point.

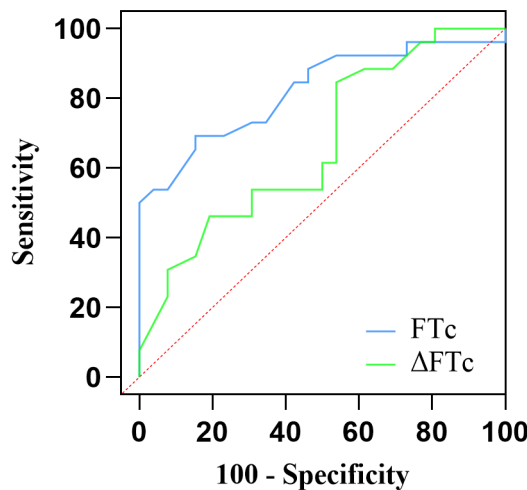
Responder patients had a more significant increase in FTc after VE than non-responders (17.2±10.9 vs 10.4±9.0 ms, P < 0.05). Baseline FTc and FTc correlated with the percentage change in

SVI after VE ( $r = -0.454$ , 95% confidence interval [CI]:  $-0.647$ – $-0.207$ ,  $P < 0.001$ ;  $r = 0.307$ , 95% CI: $0.371$ – $0.535$ ],  $P < 0.05$ , respectively; Figure 3).



**Figure 3.** Relationship between F/Tc,  $\Delta$ F/Tc, and SVI. (a) Relationship between F/Tc and SVI; (b) Relationship between  $\Delta$ F/Tc and SVI.

AUC values of F/Tc were 0.82 (95% CI: $0.705$ – $0.937$ ;  $P < 0.0001$ ), showing excellent predictive capability for fluid responsiveness. The optimal cut-off value of F/Tc was 356.5 ms, with a sensitivity of 69.2% and a specificity of 84.6%. In contrast, the ability of  $\Delta$ F/Tc to predict fluid responsiveness with an AUC of 0.67 (95% CI: $0.520$ – $0.815$ ;  $P < 0.05$ ) indicates a lower accuracy. The optimal cutoff value of  $\Delta$ F/Tc was 19.5 ms, with a sensitivity of 84.6% and specificity of 46.2%. However, the predictive accuracy for fluid responsiveness was not significantly different between the F/Tc and  $\Delta$ F/Tc groups ( $P = 0.12$ ). The gray zone for F/Tc (347.1–359.9 ms) contained 14 patients (27 %). The grey zone for  $\Delta$ F/Tc (4.7–22.2 ms) contained 33 (63%) patients (Table 3, Figure 4).



**Figure 4.** Comparison of the receiver operating characteristic curves for the prediction of fluid responsiveness.

**Table 3.** Diagnostic ability of different parameters to predict fluid responsiveness.

| AUC<br>(95%CI) | P-Value | Cut of<br>value | Sensitivity<br>(95%CI) | Specificity<br>(95%CI) | Grey zone | Patients in<br>grey zone<br>(%) |
|----------------|---------|-----------------|------------------------|------------------------|-----------|---------------------------------|
|                |         |                 |                        |                        |           |                                 |

|      |                    |         |          |                  |                  |                |    |
|------|--------------------|---------|----------|------------------|------------------|----------------|----|
| FTc  | 0.82 (0.705–0.937) | <0.0001 | 356.5 ms | 69.2 (50.0–83.5) | 84.6 (66.5–93.9) | 347.1–359.9 ms | 27 |
| ΔFTc | 0.67 (0.520–0.815) | <0.05   | 19.5 ms  | 84.6 (66.5–93.9) | 46.2 (28.8–64.5) | 4.7–22.2 ms    | 63 |

FTc Carotid corrected flow time, ΔFTc Changes in the corrected carotid flow time, AUC Area under the receiver operating characteristic curve, CI Confidence interval.

4. Discussion

Among gynecologic patients undergoing robot-assisted laparoscopic surgery in a modified head-down laparotomy position, the results of our study suggest that the carotid FTc assessed using Doppler ultrasound is an excellent predictor of fluid responsiveness. Although ΔFTc induced by VE also could predict fluid responsiveness, it showed only moderate predictive capability. Our results also showed that 63% of patients were in the gray zone of FTc, compared to 27% of patients in the gray zone of FTc, which is significantly lower. The grey zone was defined as the area where responders and non-responders were not well separated.

Perioperative fluid management is directly related to patient survival, and volume assessment is essential for guiding the individualization and accuracy of intraoperative fluid therapy. Monitoring has evolved from being static to dynamic. In recent years, researchers have focused on developing noninvasive techniques with significant accuracy and precision, thus avoiding the complications of invasive monitoring and analyzing the response to fluid therapy [3–6,19]. Since then, portable ultrasound has been widely recommended for volume status assessment in critical care, emergency, and perioperative patients because of its convenient, non-invasive, easy-to-acquire, and reproducible characteristics.

Recent studies have increasingly identified a statistically significant correlation between changes in FTc and intravascular volume status [7,8,20]. Accordingly, as intravascular volume decreases, FTc tends to decrease as well. In contrast, volume-deficient patients experience an increase in FTc following volume infusion. Patients with advanced renal failure had significantly lower FTc values after hemodialysis, and there was a statistically significant negative correlation between the volume of fluid excreted during hemodialysis and changes in FTc [8]. Mackenzie et al. found that FTC decreases after acute blood loss and that passive leg raising restores FTc to predicted levels in acute hypovolemia [20]. Assessing the correlation between changes in volume status and changes in carotid FTc, Blehar et al. reported that dehydrated patients receiving fluid resuscitation showed an increase in carotid FTc from a mean of 299 ms before injection to a mean of 340 ms after injection. Moreover, the carotid FTc responded more significantly to changes in intravascular volume than to negligible changes in HR and MAP [7]. Similarly, our results showed an increase in FTc in both groups of patients after fluid injection, a more pronounced increase in responders, and no significant changes in HR or blood pressure.

A growing body of evidence highlights the significance of ultrasound measurement of carotid FTc in volume management. Kim et al. confirmed that FTc could accurately predict volume responsiveness in spontaneously breathing patients with an AUC of 0.84. [9] Jung et al. considered carotid FTc as a reliable predictor to assess fluid responsiveness in patients with low tidal volume mechanical ventilation; a systematic review analysis revealed that the diagnostic characteristics of FTc varied, with sensitivity ranging from 60% to 73%, specificity from 82% to 92%, and an optimal cutoff of the area under the receiver operating characteristic (AUROC) from 0.7526 to 0.8819 [21]. The higher optimal cutoff value of 356.5 ms obtained in our study may be based on the patient’s positioning, potentially increasing venous return and affecting the FTc measurement.

However, the absolute value of FTc alone as a static indicator has limitations as it depends on left ventricular preload, cardiac inotropy, and systemic vascular resistance [22]. Based on the above findings, researchers hypothesized that changes in FTc can be considered an indicator of fluid reactivity. Jalil et al. first attempted to determine whether passive leg raising induced increase in FTc

can be used to predict fluid responsiveness in critically ill patients with a cardiac output monitor, ultimately concluding that an increase of  $\geq 24.6\%$  in the FTc in response to passive leg raising is a reasonable predictor of fluid responsiveness [23]. In patients with early undifferentiated shock, Barjaktarevic et al. demonstrated through prospective experiments that not only changes in FTc evoked by a passive leg raising operation can determine fluid responsiveness but also a threshold of 7 ms as FTc to define fluid responsiveness with a specificity of 96% and sensitivity of 68% [11]. While passive leg raising is a straightforward method to evaluate fluid responsiveness, its implementation during surgery is challenging. Consequently, alternative interventions are necessary. Therefore, the following experiment directly illustrated that the percentage change in FTc induced by the recruitment maneuver used to predict fluid responsiveness in supine patients under general anesthesia is feasible [10]. Our study data gave a higher absolute value for change in FTc with a cutoff value of 19.5ms (sensitivity of 84.6% and specificity of 46.2%). Regardless of whether the threshold for a change in FTc with a fluid challenge varied from 7 ms to 30 ms or a 25% relative change, possible reasons for this difference include the following: first, our study object was in a head-down position, which would have increased venous return and cardiac preload; second, the hemodynamic effects of pneumoperitoneum were complex; and finally, we identified responders and non-responders by additional fluid supplementation [24,25]. Therefore, it is easy to note that  $\Delta$ FTc increases significantly in patients who respond to fluids after intravenous infusion or passive leg raising.

This study has several limitations. We didn't utilize the gold standard for monitoring fluid responsiveness, replacing it with a less invasive continuous hemodynamic monitor. Although the MostCare monitor showed good agreement with echocardiographic measurements, potential errors may be unavoidable under the dual effects of pneumoperitoneum and head-down position. The impact of cerebrovascular tension on the common carotid artery cannot be excluded entirely, and brain autoregulatory mechanisms and blood carbon dioxide levels correlate with the former. Finally, the results cannot be generalized to other patients because of the specificity of the type of disease and the surgical approach, such as facial and cerebral surgery or open surgery.

## 5. Conclusions

The carotid FTc measured using Doppler ultrasound is a reasonable predictor of the modified head-down lithotomy position. This extensive gray zone may limit the clinical replication of FTc. We will continue to conduct additional clinical trials and offer additional reference points for perioperative volume management.

**Author Contributions:** Conceptualization, XX.T and HL.L; methodology, JQ.L; software, Q.C; validation, TJ.Y, and HL.L; formal analysis, XX.T; investigation, JQ.L; resources, Q.C; data curation, TJ.Y; writing—original draft preparation, XX.T, JQ.L; writing—review and editing, TJ.Y, HL.L; supervision, HL.L; funding acquisition, JQ.L, Q.C.

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**Institutional Review Board Statement:** The study protocol was approved by the Institutional Review Board of Chongqing University Cancer Hospital (approval number: CZLS2021041-A).

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

**Data Availability Statement:** The data analyzed and preserved during the current study are available from the corresponding author upon reasonable request via e-mail.

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**Conflicts of Interest:** None

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