Original Article

Carotid artery corrected flow time and respiratory variation of blood flow peak velocity for prediction of hypotension after induction of general anesthesia in adult patients undergoing emergency laparotomy for peritonitis: A prospective, observational study

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Abstract

Background and Aims: Doppler waveform analysis of carotid artery has been found to predict fluid responsiveness in patients undergoing elective surgeries. We evaluated the role of carotid artery corrected flow time (FTc) and respiratory variation of blood flow peak velocity (δV_{peak}) in predicting post induction hypotension in patients undergoing emergency laparotomy for peritonitis.
Material and Methods: Adult patients ($n = 60$) with perforation peritonitis undergoing emergency laparotomy under general anesthesia (GA) were recruited in this prospective, observational study. Carotid ultrasonography was performed pre-induction, to determine FTc and δV_{peak}. Post-induction hemodynamic parameters were recorded for 5 minutes. Spearman's rank correlation coefficient was used to determine the relationship between hypotension and carotid artery measurements.
Results: Post-induction hypotension occurred in 48.3% of patients. The carotid artery FTc was significantly lower ($P = 0.008$) in patients who developed post-induction hypotension, but δV_{peak} was statistically similar ($P = 0.62$) in both groups. Spearman's rank correlation coefficient revealed a statistically significant correlation between FTc and systolic blood pressure (SBP) change at one-minute post induction ($r^2 = -0.29$, $P = 0.03$); however statistical significance were not achieved at 2 minutes and 3 minutes ($P = 0.05$ at both time points). Carotid artery FTc had an area under the receiver operating characteristic (AUROC) curve (95% CI) of 0.70 (0.57–0.84) to predict post-induction hypotension and best cutoff value of 344.8 ms with a sensitivity and specificity of 61% and 79%, respectively. Carotid artery δV_{peak} had an AUROC curve (95% CI) of 0.54 (0.39–0.69) to predict post-induction hypotension and best cutoff value of 7.9% with a sensitivity and specificity of 62% and 55%, respectively.
Conclusion: Carotid artery FTc and δV_{peak} are not reasonable predictors of hypotension in patients undergoing emergency laparotomy for perforation peritonitis.

Keywords: Carotid artery corrected flow time, doppler ultrasonography, fluid responsiveness, post-induction hypotension, preload

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Introduction

Blood pressure perturbations during general anesthesia (GA) in adult patients are common, and incidence of intraoperative hypotension depends on the definition used. A review of the hemodynamic records of more than 4000 patients revealed that around 10% of the patients developed severe hypotension after induction of GA.[1] Another observational study reported that incidence of intraoperative hypotension was 36.5% in patients undergoing elective non-cardiac surgery.[2] A fall in blood pressure below the auto-regulation threshold of a particular organ is associated with decreased tissue oxygen delivery. Intraoperative hypotension is thus found to be an independent risk factor for acute myocardial infarction, stroke, acute kidney injury, and prolonged hospital stay.[1,3-7]

Patients undergoing surgery are at a risk of developing hypovolemia due to multiple reasons including preoperative routine fasting and bowel preparation, which increases the risk of intraoperative hypotension.[8] A number of studies evaluated various hemodynamic parameters before induction of GA to identify patients at risk of hypotension. Zhang *et al*.[9] reported that preoperative hypovolemia identified by the inferior vena cava (IVC) collapsibility index and IVC diameter predicts post-induction hypotension. Recently, pupillary diameter and the area of internal jugular vein in Trendelenburg position were found to be predictors of hypotension after induction of GA.[10,11] However, none of the previous studies were conducted in patients undergoing emergency surgeries. In fact, patients undergoing emergency laparotomy following peritonitis carry a high risk of developing hypotension and increased perioperative morbidity and mortality.

Carotid artery corrected flow time (FT_c) and respirophasic variations in the carotid artery blood flow peak velocity ($\eth V_{peak}$) measured using Doppler were found to be predictors of fluid responsiveness in spontaneously breathing patients. They also predicted the risk of hypotension after induction of GA in patients undergoing elective surgery.[12,13] We hypothesize that carotid artery FTc could be a predictor of hypotension after induction of GA in patients undergoing emergency laparotomy for peritonitis.

Material and Methods

After receiving Institutional Ethics Committee approval, Date: 02-11-2018, Ethical approval Number: (IEC-574/02.11.2018) and obtaining informed consent from the participants, 60 patients were recruited in this prospective, observational study. Adult patients (aged between 18 and 65 years) with American Society of Anesthesiologists (ASA) Physical Status (PS) I–III, undergoing emergency laparotomy for proven or clinically suspected peritonitis under GA were recruited. This study was registered in the National Clinical Trial Registry of India (www.ctri.nic.in, CTRI/2019/04/018483). Patients with known peripheral arterial disease or atherosclerosis, pregnancy, BMI >30 kg/m^2, ASA PS IV or higher, history of previous neck surgery, cardiomyopathy, arrhythmias, hemodynamic instability requiring inotropes/vasopressors, or refusal to participate were excluded.

Upon arrival in the preoperative holding area, 3-lead electrocardiography (ECG), pulse oximetry, and non-invasive blood pressure monitoring were commenced. Patients were placed in supine position with nothing kept under their head. Ultrasound measurements of the carotid artery were then obtained 10 minutes prior to the induction of GA. FTc and $\eth V_{peak}$ were measured using carotid ultrasonography, as previously described by Blehar *et al*.[13] and Song *et al*.[14] Both parameters were measured by either of the three investigators (CAK, RT, or ARC) using an ultrasound device (SonositeM-Turbo™ Ultrasound System, SonoSite, Inc. Bothell, WA, USA) with a linear 6–13 MHz transducer. Investigators who collected Doppler data did not have access to the hemodynamic data at the time of induction of GA. All measurements were taken thrice over three consecutive cardiac cycles, and an average was used. FTc was calculated by dividing the flow time by the square root of the cycle time. Maximum and minimum peak systolic velocities were obtained in a single respiratory cycle, and $\eth V_{peak}$ was calculated as follows: (maximum peak velocity − minimum peak velocity)/[(maximum peak velocity + minimum peak velocity)/2] × 100.

In the operating room 3-lead ECG, pulse oximetry, and non-invasive blood pressure measurements were obtained. A 20-G arterial catheter was inserted in the radial artery under local anesthesia, and beat-to beat arterial blood pressure monitoring was instituted. Following this, anesthesia was induced with 2 mcg/kg of intravenous fentanyl and 0.2–0.3 mg/kg of etomidate. Endotracheal intubation with appropriately sized cuffed tube was facilitated by 1.2 mg/kg of intravenous rocuronium. At the time of induction, all patients received around 200–250 ml of crystalloid. Further management was as per the attending anesthesiologist's discretion. A modified rapid sequence induction and intubation was performed in all patients. Heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded for 5 minutes after induction of GA.

Sample size estimation

The sample size was estimated using easyROC v. 1.3, a web-based tool that works on the R- platform.[15] Kim *et al*.[12]

reported in 2018 that the area under the curve (AUC) for 95% confidence interval (CI) was 0.82 for carotid FTc to predict fluid responsiveness in neurosurgical patients. We assumed that FTc might have a lower predictive validity of 0.7 for post-induction hypotension. Based on this result, a sample of 54 patients (considering one-third of all patients would develop hypotension) achieved 80% power and probability of 0.05 for rejecting null hypothesis. Assuming a dropout of 10%, 60 patients were recruited in this study.

Statistical analysis

The lowest SBP and MAP recorded after induction was used to calculate the percentage decrease in SBP and MAP from baseline in each patient. The percentage changes in heart rate (HR) from baseline level, either increase or decrease, were also calculated, and the largest change was used for analysis. Data were presented as median and interquartile range (IQR) for continuous variables and as absolute numbers or percentages for categorical variables. The development of clinically significant hypotension after induction was analyzed with respect to patient characteristics, hemodynamic data, and carotid artery measurements using Mann–Whitney U test or χ^2 test, where appropriate. Spearman's rank correlation coefficient was used to test the relationship between the carotid artery measurements and percentage decrease in MAP from baseline level after induction of GA. Hypotension was defined as a 30% reduction in SBP or 20% reduction in MAP from the baseline or as an absolute SBP <90 mm Hg and MAP <65 mm Hg within 3 minutes after induction of GA.

ROC curve analysis with 95% CI was performed to determine the ability of the two ultrasound-derived parameters, FTc and δV_{peak}, to predict hypotension after induction of GA for all patients. A comparison of the two ROC curves was done using the nonparametric technique described by DeLong *et al.*[16] The optimal cutoff values were identified as the values that maximize the Youden index (sensitivity + specificity − 1).[17]

Results

Of the sixty-eight patients evaluated for inclusion in this study, sixty patients were finally recruited (n = 60) with a median (IQR) age of 40.5 (32–54) years. The proportion (95% CI) of patients who developed hypotension after induction of anesthesia was 48.3% (35.9–60.9). Baseline demographic parameters of the patients are presented in Table 1. Pre-induction SBP, DBP, and MAP were similar in patients who developed hypotension and those who did not ($P = 0.06$, $P = 0.50$, and $P = 0.08$, respectively; Mann–Whitney U test). However, patients who developed hypotension had a significantly higher pre-induction heart rate (median [IQR] 105 [88–118] vs 95 [86–102]; $P = 0.03$). Carotid artery FTc was significantly lower ($P = 0.008$) in patients who developed post-induction hypotension, but δV_{peak} was statistically similar ($P = 0.62$) in both the groups.

Spearman's rank correlation coefficient revealed a statistically significant correlation between carotid artery FTc and change in SBP at 1 minute after induction of anesthesia ($r^2 = -0.29, P = 0.03$); however, statistical significance was not achieved at 2 minutes and 3 minutes ($P = 0.05$ at both the time points). A significant correlation was found between decrease in MAP at 1, 2, and 3 minutes, and carotid artery FTc ($P = 0.02$, $P = 0.04$, and $P = 0.007$, respectively). Scatter plot showing the correlation between decrease in SBP and MAP with carotid artery FTc is provided in Figure 1.

Carotid artery FTc had an area under the receiver operating characteristic (AUROC) curve (95% CI) of 0.70 (0.57–0.84) to predict post-induction hypotension. The best cutoff value of carotid artery FTc was 344.8 ms with a sensitivity and specificity of 61% and 79%, respectively [Figure 2]. Carotid artery δV_{peak} had an AUROC (95% CI) of 0.54 (0.39–0.69) to predict post-induction hypotension and best cutoff value of 7.9% with a sensitivity and specificity

Table 1: Baseline demographic parameters of the patients (Data presented as mean [SD], median [IQR], or proportions)

	All patients (n=60)	Hypotension (n=29)	No hypotension (n=31)	Significance
Age (y)	40.5 (32–54)	42 (32-54)	38 (32-50)	P=0.83
BMI (kg/m²)	23.6 {21.3–24.9)	23.6 (21.2–26)	23.5 (21.3–24.8)	P=0.59
Sex (Male/Female)	37/23	20/9	17/14	P=0.26
ASA PS (I E/II E)	28/32	12/17	16/15	P=0.43
Baseline SBP (mm Hg)	126 (118–130)	128 (122–131)	122 (114–130)	P=0.06
Baseline DBP (mm Hg)	84 (75–91.5)	85 (80–90)	82 (73–93)	P=0.50
Baseline MAP (mm Hg)	93 (87–98.55)	95 (90–98)	90 (85–99)	P=0.08
Baseline Heart Rate (bpm)	97 (88–109.5)	105 (88–118)	95 (86–102)	P=0.03
Carotid FTc (ms)	324.9 (307.2–365.2)	316.3 (304.3–334.9)	352.8 (316.7–379.7)	P=0.008
Peak velocity variation (%)	8 (5.4–13.7)	7.5 (4.5–13.5)	9.4 (5.8–13.9)	P=0.62

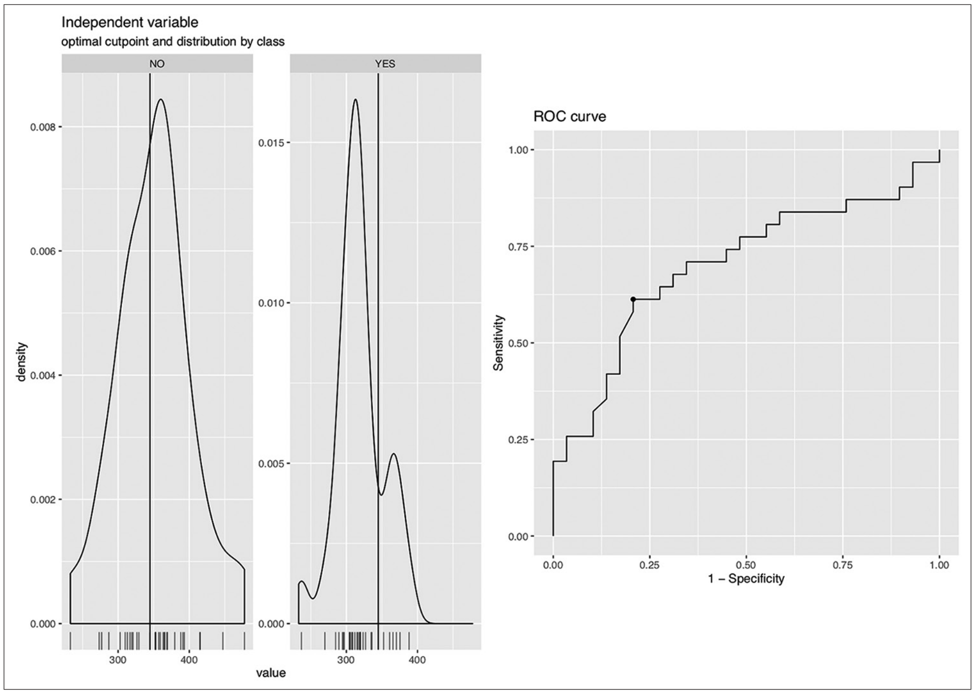

Figure 1: Receiver operating characteristic curve showing sensitivity and specificity of carotid artery corrected flow time to predict post-induction hypotension

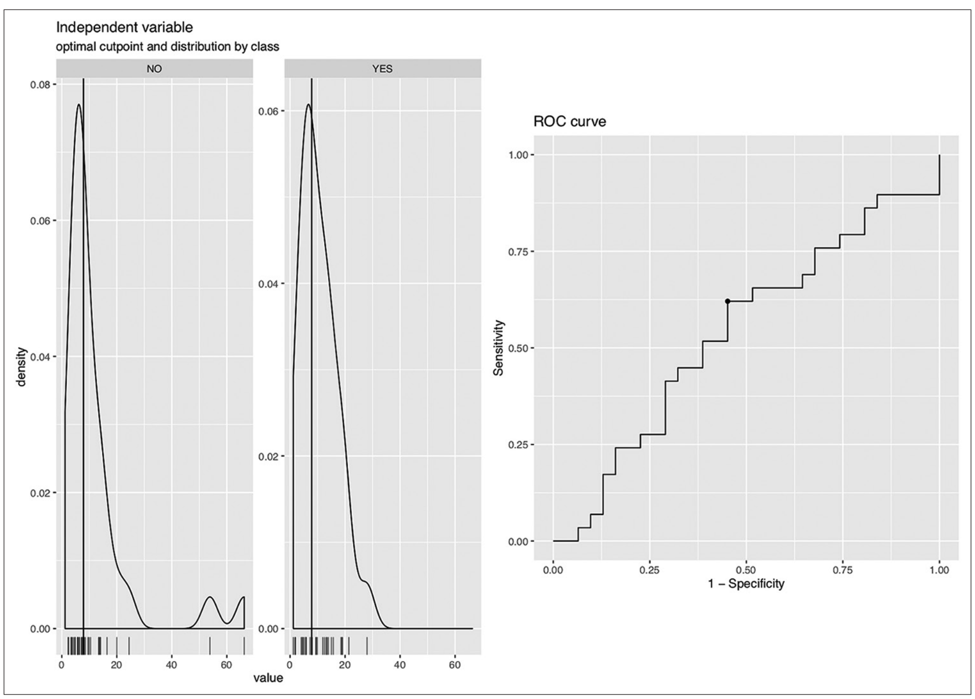

Figure 2: Receiver operating characteristic curve showing sensitivity and specificity of carotid artery peak velocity variation to predict post-induction hypotension

of 62% and 55%, respectively [Figure 3]. However, carotid artery FTc had higher AUROC than ∂V_{peak} for predicting post-induction hypotension ($P = 0.01$).

Discussion

In our study, nearly half of the patients undergoing emergency laparotomy for peritonitis developed post-induction hypotension. We observed that carotid FTc and ∂V_{peak} as assessed by Doppler ultrasonography (USG) did not predict hypotension after induction of GA in patients undergoing emergency laparotomy for peritonitis. And the patients who developed hypotension had a significantly higher heart rate than patients who did not.

Patients undergoing emergency laparotomy have increased risk of developing post-induction hypotension due to the

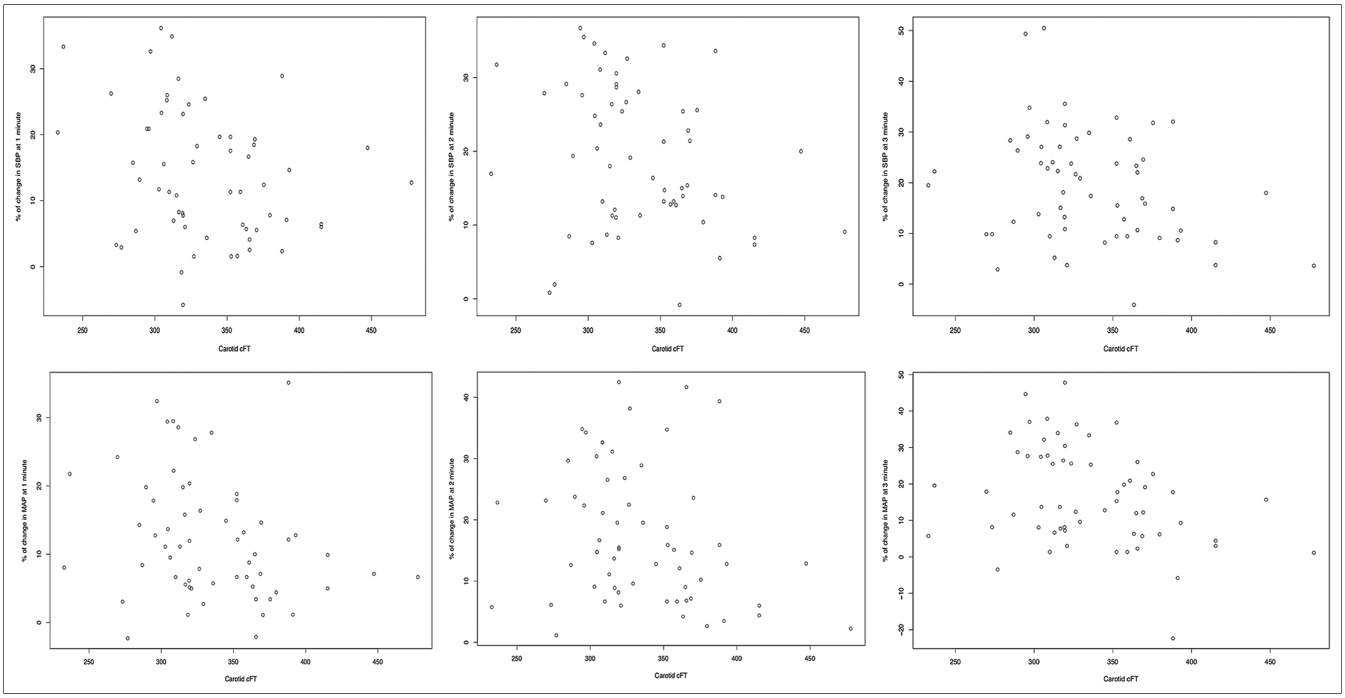

Figure 3: Scatterplot showing correlation between decrease in systolic blood pressure at 1 minute, 2 minute, and 3 minutes (upper panel) and decrease in mean arterial pressure at 1 minute, 2 minute, and 3 minute (lower panel) with carotid artery corrected flow time

vasodilatory effects of the anesthetic agents in the background pre-existing hypovolemia and impaired compensatory response.[9,18,19] Hypotension due to various reasons leading to tissue hypoperfusion increases postoperative morbidity and mortality. Therefore, assessing the intravascular volume status will guide in the administration of adequate fluid to prevent hypotension as the preoperative volume status may vary in different patients.

Recently, several bedside USG modalities for assessing volume status have been introduced.[9-14] Extensive studies were conducted on IVC USG but with conflicting results in spontaneously breathing patients and limited utility in patients with increased right-sided heart pressures.[12,20,21] Certain drawbacks such as diversity of the methods used, lack of evidence-based cutoffs, and technical difficulty in obese patients limited the use of IVC USG.[22] Blehar *et al*.[13] were the pioneers in assessing the intravascular volume status measuring FTc in the carotid artery using USG. As the carotid artery is superficial and easily accessible, FTc can be quickly measured and is not affected by spontaneous breathing.[12,14]

Our study observed that FTc and δV_{peak} did not predict hypotension; this is in contrast to previous studies reported earlier. Blehar *et al*.[13] demonstrated that low FTc indicated volume depletion, and intravenous fluid administration in dehydrated patients resulted in significant increase in FTc. Carotid flow time in spontaneously breathing patients as observed by Kim *et al*.[12] also reported that FTc was predictive of fluid responsiveness. They found that increase in stoke volume index (SVI) after fluid challenge correlated with FTc and δV_{peak} values before fluid challenge and changes in FTc and δV_{peak} caused by fluid challenge.

In patients with peritonitis, there is excessive production of inflammatory mediators and development of systemic inflammation that leads to vasodilatation and increased microcirculatory flow.[23] Our study population consisted of patients with perforation peritonitis with a decreased systemic vascular response due to the presence of a generalized inflammation. It is worth mentioning that FTc is affected by both preload and afterload. A normal FTc may be due to a combination of a low preload and a higher-than-normal afterload. Due to the release of pro-inflammatory mediators and nitric oxide (NO), these patients are found to have a decreased systemic vascular resistance along with a normal or increased cardiac output even though the systolic function is compromised due to poor contractility.[24] The cardiac output is maintained by increasing the heart rate despite the increased left ventricular end-systolic volume and left ventricular end-diastolic volume, which can explain the tachycardia in our study in patients who developed hypotension post induction.[25] Previous studies have been conducted in elective surgeries where carotid artery FTc was found to be a predictor of post-induction hypotension.[26] Our study could not corroborate the same findings probably due to the altered vascular physiology seen in perforation peritonitis patients due to the generalized systemic inflammation. The FTc is affected by ventricular preload, cardiac contractility, and systemic vascular resistance (SVR). Thus, factors affecting preload and afterload would alter the FTc.[27] Apart from this, patients with peritonitis usually have tachypnea and increased respiratory drive, which could have contributed to the lower diagnostic accuracy of carotid artery $\eth V_{peak}$ to predict post-induction hypotension. Previous existing study using carotid Doppler–derived parameters to predict fluid responsiveness have been conducted in patients undergoing elective surgeries. And no study has been carried out in emergency surgeries where the body's normal physiological response may have been altered due to systemic inflammation. The limitation of our study is that it is from a single center, which may reduce the generalizability. Further research with a larger sample size is needed to determine fluid responsiveness in the group of patients undergoing emergency surgeries where excessive fluid administration may be harmful.

Conclusion

FTc and $\eth V_{peak}$ as measured by carotid Doppler test did not significantly predict hypotension in patients undergoing emergency laparotomy for perforation peritonitis. Further randomized, controlled studies are required to assess the intravascular volume status to observe if FTc and $\eth V_{peak}$ can predict hypotension in this group of patients.

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Conflicts of interest

There are no conflicts of interest.

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