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Can vena cava ultrasound-guided volume repletion prevent general induced hypotension in elderly patients? A mini-fluid challenge

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Abstract

Background: Hypotension is often occurring after induction of general anesthesia (IGA) and can cause organ hypoperfusion and ischemia which associated with adverse outcomes in patients having both cardiac and non-cardiac surgery. Elderly patients are particularly more vulnerable and at increased risk to the depressant effect of anesthetic drugs. So, recognition and prevention of such event are of clinical importance. This study recruited patients aged above 60 years, with ASA physical status classification I-II-III who were scheduled for surgery under general anesthesia with the aim to assess the effectiveness of preoperative IVC ultrasonography in predicting hypotension which develops following IGA and its association with the volume status in elderly patients receiving general anesthesia, through measurements of the maximum inferior vena cava diameter (dIVCmax), minimum inferior vena cava diameter (dIVCmin), inferior vena cava collapsibility index (IVC-CI), and basal and post-induction mean arterial pressure (MAP).

Results: Thirty-nine (44.3%) of the 88 patients developed hypotension after IGA, and it was significantly more in patients who did not receive preoperative fluid (p = 0.045). The cut-off for dIVCmax was found as 16.250 mm with the ROC analysis. Specificity and sensitivity for the cut-off value of 16.250 mm were calculated as 61.2% and 76.9%, respectively. The cut-off for IVC-CI was found as 33.600% with the ROC analysis. Specificity and sensitivity for the cut-off value of 33.600% were calculated as 68.7% and 87.2%, respectively.

Conclusions: IVC ultrasonography may be helpful in the prediction of preoperative hypovolemia in elderly patients in the form of high IVC-CI and low dIVCmax. The incidence of hypotension was lower in patients who received fluid infusion before IGA.

Keywords: General anesthesia, Hypotension, Inferior vena cava, ROC analysis, Ultrasound

Background

One of the common complication after induction of general anesthesia (IGA) is hypotension which mostly occurs between IGA and surgical stimulation (Reich et al., 2005). There are many predisposing factors that can lead to hypotension during anesthesia. Some of the anesthetic drugs can lead to myocardial depression or vascular dilatation and hence can cause hypotension. One very important factor is the volume status of the patient. The patients coming for surgery can be hypovolemic for multiple reasons. Also, the patient's age is described as a significant predictor of hypotension after IGA (Reich et al., 2005). The elderly patients have decreased tolerance to intravenous anesthetic drugs because these drugs inhibit the cardiovascular system to cause dilatation of blood vessels and lower blood pressure (BP) rapidly (Vuyk et al., 2015). Several studies have

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explained the effect of hypotension on various organ systems and their functioning; it can present as myocardial injury, stroke, or acute kidney injury in patients undergoing general (Bijker et al., 2012) and cardiac (Walsh et al., 2013) surgeries. Therefore, it is essential to avoid or minimize hypotension during IGA. Assessing the volume status accurately is not simple. Many invasive techniques (e.g., pulmonary arterial catheter, PiCCO®, and Vigileo®) are available for evaluation of volume status among other elements of hemodynamic parameters, but their wide application is not a reasonable option due to financial restrictions and relatively high complications (Vincent et al., 2015)

The utility of noninvasive ultrasound assessment by anesthesiologists is a widespread and competent aid in the safe anesthesia application. Assessment of inferior vena cava (IVC) diameters is one of the measurements that can be applied to predict hypotension and evaluate the volume status of the patient (Zhang & Critchley, 2016). The maximum and minimum diameters of the IVC (IVCmax and IVCmin, respectively) are measured to calculate the collapsibility index of IVC (IVC-CI) using the formula, IVC-CI = (IVCmax–IVCmin)/IVCmax. Evidence recommends that the diameter of IVC is a dependable indicator of intravascular volume and respiratory variation is valuable in anticipating response to fluids. A higher collapsibility index indicates a decreased volume status commonly with a small IVC diameter (Seif et al., 2012).

In this study, we aimed to evaluate the effectiveness of preoperative IVC ultrasonography (IVC diameters/ IVC-CI) in predicting hypotension, which develops following anesthesia induction, and in determining hypovolemia occurring in elderly patients.

Methods

After getting the approval of the Research Ethics Committee (REC) Board and registration of the trial retrospectively at the Pan African Clinical Trials Registry, this prospective randomized controlled study was conducted at Benha university surgical hospital between August 2020 and March 2021. The study was conducted on 88 consenting patients aged more than 60 years, with the American Society of Anesthesiologists (ASA) physical status classes I, II, and III, who required general anesthesia (induction with propofol) followed by endotracheal intubation. Exclusion criteria included patients with cardiac morbidities (unstable angina, tight valvular lesions, and impaired contractility with ejection fraction < 40%) and patients with uncontrolled hypertension, uncompensated respiratory disease (generalized wheezes, defective functional capacity, peripheral O2 saturation < 90% on room air), high intraabdominal pressure (intraabdominal mass pressing IVC), anticipated difficult airway, and emergency surgery.

Patients were allocated into two groups: group A in which patients did not receive intravenous (IV) fluid before IGA and group B in which patients received IV infusion of compound sodium chloride at a rate of 10 ml/kg/h over 30 min before IGA. Randomization of the patients was obtained through a computer-generated program.

Patients were preoperatively fasted for at least 8 h and fluid deprivation for 4 h. Upon arrival to the preparation room, an IV cannula was inserted for patients in group B, followed by an IV infusion of compound sodium chloride solution at a rate of 10 ml/kg/h for 30 min. In the operating room, standard monitors (ECG, noninvasive blood pressure monitor, and pulse oximetry) were applied, an IV line was secured, and pre-medications (ondansetron 4 mg and ranitidine 50 mg) were delivered. Intravenous midazolam (0.01 mg/kg) was given to sedate the patients, and a nasal catheter was applied to deliver oxygen at 2 l/min.

IVC ultrasonography measurements were done before general anesthesia in a supine position and during spontaneous breathing. Basal maximum and minimum IVC diameters were measured over a single respiratory cycle using built-in software. The collapsibility index (CI) was calculated using the following formula: IVC-CI = ((IVCmax − IVCmin)/IVCmax) × 100.

Description of the technique

IVC ultrasonography measurements were conducted using a curved transducer which was set to abdominal mode (1–5 MHz; General Electric; GE, “LOGIQ P5” ultrasound machine). The IVC was visualized using a paramedian long-axis view via a subcostal approach according to the methodology described by the American Society of Echocardiography. Initially, a two-dimensional image of the IVC as it joins the right atrium was acquired. To distinguish the aorta from IVC, a pulse wave Doppler was used. Alternation in the diameter of IVC with normal regular breathing was measured distal to the right atrium by 2–3 cm using M-mode imaging. Expirium (dIVCmax) and inspirium (dIVCmin) were measured at least 3 times, and IVC collapsibility index (IVC-CI) was calculated using special formula as mentioned earlier. An IVC collapsibility of more than 50% was considered as a sign of hypovolemia. Data of the patient were excluded if there was a difference of more than 0.2 cm in measurements of dIVCmax between any 2 images.

Induction of standard routine general anesthesia was achieved using fentanyl (1mcg/kg) and propofol (1–2 mg/kg) which were titrated till there was a loss of response to verbal command; then, atracurium (0.5 mg/kg) was given for muscle relaxation. The endotracheal tube was placed after 3 min of mask ventilation. Patients who experienced difficult airway intubation were excluded from the study because of too much stimulation. Maintaining of anesthesia was done by isoflurane (1–1.5%) and atracurium 10 mg increments every 20 min. Solution of ringer lactate was infused at a rate of 2 ml/kg/h. Data collected were MAP and heart rate (HR) at baseline, followed by 3 min (after induction), 6 min (after intubation), and 10 min (before surgical incision), respectively.

Hypotension in the period after IGA was defined by a more than 30% drop in MAP from the baseline reading or MAP lower than 60 mmHg. Any episode of prolonged (i.e., duration more than or equal to 2 min) or severe (MAP less than 55 mmHg) hypotension was managed by incremental 5-mg doses of ephedrine. For significant bradycardia (HR less than 50 beats/min), atropine (0.3 mg) was used.

The primary outcome in our study was to assess the predictive ability of pre-induction IVC measurements in predicting significant hypotension after IGA. The following data were recorded as secondary outcomes: maximum and minimum IVC diameters measured 10 min before administration of general anesthesia, as well as the IVC-CI that was calculated using a special formula. MAP and HR were measured at 3-min intervals beginning from the baseline preoperative reading till skin incision. Demographic data include gender, age, ASA physical status, body mass index (BMI), history of hypertension, duration of fasting, administration of vasopressors, and the dose of propofol used for induction.

Statistical analysis

Data were analyzed by using SPSS version 25 (IBM, Armonk, NY, USA). Quantitative parametric data were presented as mean ± SD and were analyzed by unpaired

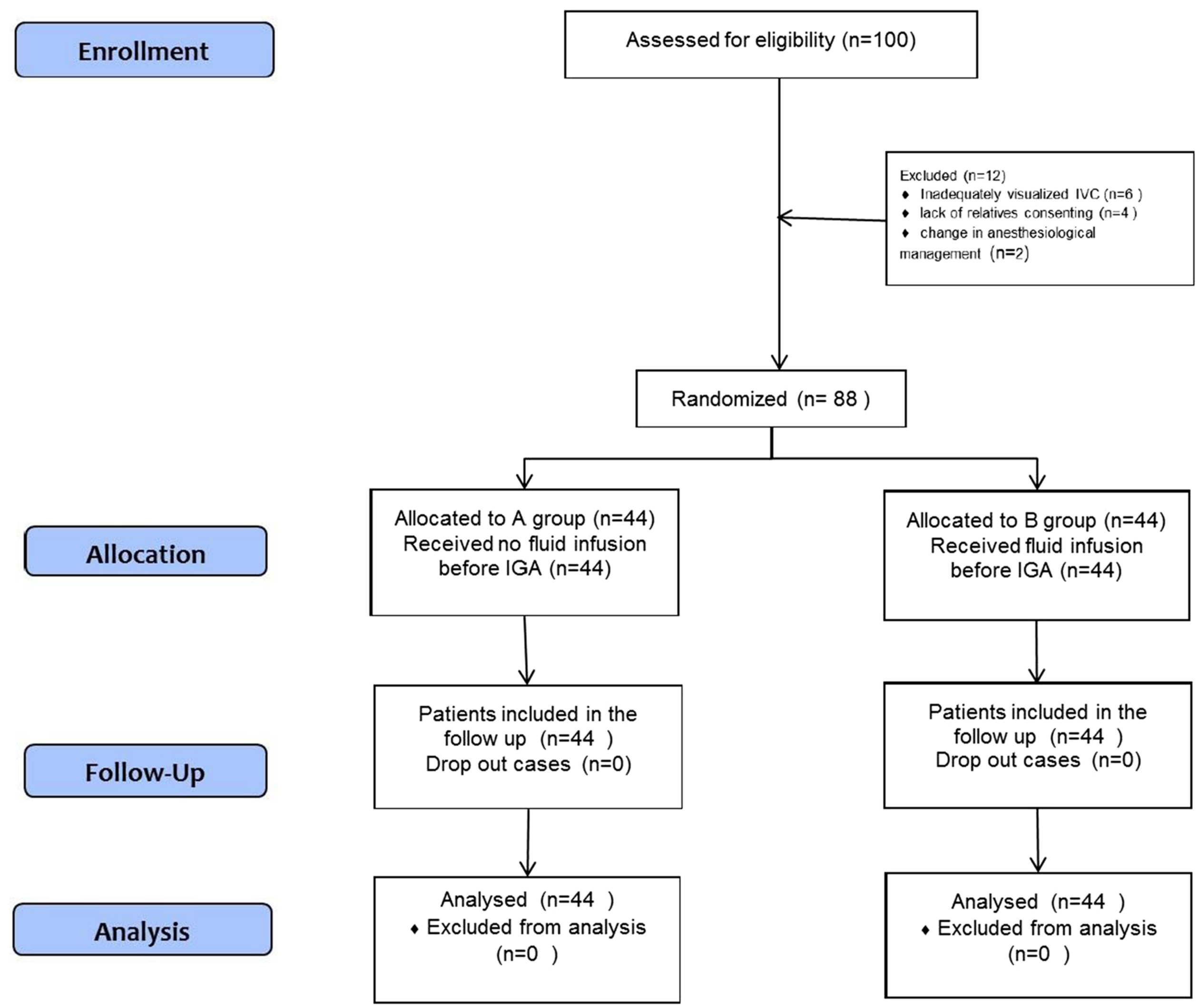

Fig. 1 CONSORT flow chart of the study groups

Table 1 Comparison of demographic characteristics between the two study groups

Characteristics	**Group A (*n* = 44)**		**Group B (*n* = 44)**		***p*-value**
Age (years)	66.47 ± 4.97		62.93 ± 13.24		0.1
Gender	M	F	M	F	0.39
	25	19	21	23	
BMI (kg/cm2)	26.70 ± 4.56		25.97 ± 3.80		0.41
ASA (I/II/III)	(6/16/22)		(5/18/21)		0.89
Dose of propofol (mg)	142.04 ± 17.33		139.77 ± 14.18		0.51
Fasting duration (hours)	8.23 ± 0.94		8.59 ± 1.18		0.11
History of hypertension	No	Yes	No	Yes	0.51
	21	23	18	26	

t-test. Qualitative data were presented as numbers and percentage and were analyzed by the chi-square test. The predictive ability of the group in correct prediction of hypotension was measured with the calculation of the receiver operating characteristic (ROC) and the area under the curve (AUC). *p*-value < 0.05 was considered statistically significant.

The sample size was estimated according to a previous study done by Şevki et al. (Şevki et al., 2019), and the change in post-induction MAP was the variable of interest. Assuming that there is a reduction in MAP by 30% in group A, using a power of at least 80%, the two-sided α error is 5% level and the calculated effect size was 0.615. A sample size of 43 patients per group was obtained by G*Power software version 3.1.9.4 (Universitat Keil, Germany). Fifty patients were enrolled per group to avoid the effect of dropout.

Results

The total number of patients recruited in this study was 100. We excluded 12 previously eligible patients because of inadequate visualization of IVC (6 cases), an absence of relatives' consenting (4 cases), and a change in anesthesia management plan (2 cases). Finally, 88 patients who meet the inclusion criteria were enrolled in the study and equally distributed between both groups (Fig. 1). No significant differences were found in sex distribution, age, BMI, ASA physical status, history of hypertension, and fasting duration between both groups (Table 1). An induction dose by propofol was 142.04 ± 17.33 in group A and 139.77 ± 14.18 in group B which was statistically comparable between the two groups ($p = 0.51$).

Post-induction MAP was significantly lower in group A (72.68 ± 13.92) compared to group B (78.68 ± 13.78) with *p*-value 0.045 (Table 2) (Fig. 2). Also, post-induction HR showed a significant increase in group A (83.23 ± 11.61) compared to group B (78.1 ± 8.93) with *p*-value 0.023 (Table 3).

The number of patients, who developed significant hypotension after IGA, was 39 patients (44.3%) who were divided into 25 patients in group A (56.8%) and 14 patients in group B (31.8%). Out of these 39 patients, 14 patients developed a MAP < 60 mmHg after 3 min of induction with propofol and 11 patients received vasopressor as a rescue measure (Table 4).

IVC values (dIVCmax/dIVCmin/IVC-CI) were markedly lower in group A than in group B, and this difference was statistically significant ($p < 0.01$) (Table 5).

Whether dIVCmax and IVC-CI have a diagnostic value in detecting hypotension was studied with the ROC curve analysis. In the ROC analysis, it was found that the maximum diameter and collapsibility index of IVC have diagnostic value in detecting the occurrence of hypotension. *AUC* was found as 0.799, 95% *CI* 0.706–0.892 ($p < 0.001$). The optimal cut-off value for dIVCmax was found as 16.250 mm with the ROC analysis. Specificity and sensitivity for the cut-off value of 16.250 mm were calculated as 61.2% and 76.9%, respectively (Fig. 3). *AUC* was found as 0.833, 95% CI 0.749–0.916 ($p < 0.001$). The cut-off for IVC-CI was found as 33.600% with the ROC analysis. Specificity and sensitivity for the

Table 2 Comparison of MAP values at basal and after anesthesia induction between the two study groups

	Group A (*n* = 44)	**Group B (*n* = 44)**	***p*-value**
MAP pre-induction (mmHg)	102.38 ± 11.045	104.13 ± 11.35	0.46
MAP post-induction (mmHg)	72.68 ± 13.92	78.68 ± 13.78	0.045
MAP post-intubation (mmHg)	78.81 ± 11.09	80.5 ± 9.97	0.45
MAP pre-surgical incision (mmHg)	76.88 ± 14.85	77.79 ± 12.67	0.75

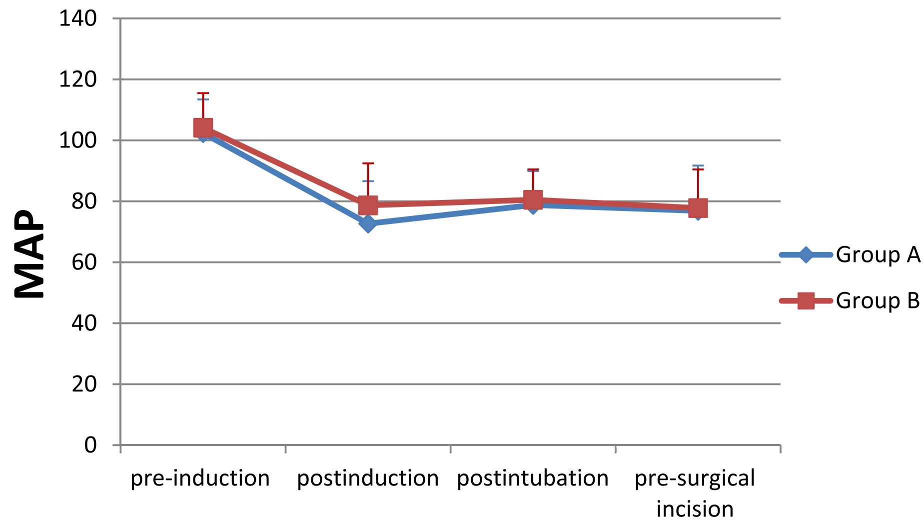

Fig. 2 Comparison of basal and post-induction MAP between the two study groups

cut-off value of 33.600% were calculated as 68.7% and 87.2%, respectively (Fig. 4).

Discussion

Various physiological changes occur related to aging in all organ systems, including increased vascular stiffness and decreased baroreceptor function and reflex regulation abilities (Frederick & Ronald, 2015). During IGA, elderly patients experienced lower tolerance to IV anesthetic drugs. These drugs inhibit the cardiovascular system itself or the part of the central nervous system responsible for the cardiovascular system which leads to a decrease in the peripheral blood vessel resistance and stroke volume (Vuyk et al., 2015). Hence, elderly patients are specifically susceptible to a rapid decline in BP and HR during IGA (Isitemiz et al., 2014).

Ultrasonography of IVC in order to guide the evaluation of intravascular volume status is a noninvasive and easy-to-apply hemodynamic monitoring method which is being growingly used in recent years. Given the value of detecting the preoperative volume status, it may be beneficial in guiding the treatment of critically ill patients (Dipti et al., 2012).

Table 3 Comparison of HR values at basal and after anesthesia induction between the two study groups

	Group A (*n* = 44)	Group B (*n* = 44)	*p*-value
HR pre-induction (beat\min)	80.25 ± 11.22	78.38 ± 10.78	0.42
HR post-induction (beat\min)	83.23 ± 11.61	78.1 ± 8.93	0.023
HR post-intubation (beat\min)	81.79 ± 10.94	79.11 ± 10.39	0.24
HR pre-surgical incision (beat\min)	80.54 ± 9.079	79.47 ± 10.1	0.6

In our study, we observed that evaluation of the patients with IVC ultrasonography before IGA was predictive in predicting post-induction hypotension. IVC-CI was more predictive than dICVmax. In IVC screening, the optimal cut-off values for predicting hypotension were found as 33% for IVC-CI and 1.6 cm for dIVCmax with specificity and sensitivity of 68.7% and 87.2% for IVC-CI and 61.2% and 76.9% for dIVCmax, respectively. Similar results were reported by Sevki et al. who studied the predictive value of IVC ultrasonography in patients exposed to mechanical bowel preparation before gastrointestinal surgery. They reported cut-off values for dIVCmax and IVC-CI as 15.750 mm and 32.746% respectively with the ROC analysis (Şevki et al., 2019). Another study was carried out by Wu and Guocan who measured the IVC diameters in elderly patients undergoing GA with or without administration of preoperative fluid infusion. It demonstrated close results to our study with an IVC-CI cut-off value of 37%. It also reported that patients without post-induction hypotension had significantly increased IVCmax and decreased IVC-CI compared with those with post-induction hypotension. However, these data are still unpublished (Wu & Yu, 2019).

Table 4 Comparison of hypotensive rates after induction between the two study groups

	Group A (*n* = 44)	Group B (*n* = 44)	*p*-value
Hypotension after induction (%)	25 (56.8%)	14 (31.8%)	0.01
MBP < 60 (mmHg)	10 (22.7%)	4 (9.1%)	0.08
MBP drop percentage (mmHg)	29.2 ± 9.38	24.3 ± 10.22	0.023
Patients received vasopressors	7 (15.9%)	4 (9.1%)	0.33

Table 5 Comparison of IVC measurement values between the two study groups

	Group A (*n* = 44)	Group B (*n* = 44)	*p*-value
dIVCmax (mm)	14.87 ± 1.88	17.05 ± 1.85	< 0.001
dIVCmin (mm)	9.01 ± 2.02	11.75 ± 1.74	< 0.001
IVC-CI (%)	40.10 ± 7.35	31.44 ± 4.69	< 0.001

Zhang et al. found the cut-off values of IVC measurements before general anesthesia induction in predicting post-induction hypotension as 43% for IVC-CI and 1.8 cm for dIVCmax and demonstrated that IVC-CI was more predictive than dIVCmax (Zhang & Critchley, 2016). These values were confirmed by a more recent study published by Purushothaman et al., who reported the same values as Zhang et al. (Purushothaman et al., 2020). The guidelines by the American Echocardiography Society instruct the use of the diameter and collapsibility index of IVC in the evaluation of volume status. IVC-CI > 50% in dehydration patients indicates a CVP < 8 mm Hg (Nagdev et al., 2010). Muller et al. found that a collapsibility index > 40% predicted response to fluid therapy, in their study with patients in the intensive care unit (Muller et al., 2012). Airapetian et al. showed that only inspiration variation of IVC ≥42% could correctly predict an increase in CO after fluid infusion (Airapetian et al., 2015).

In our study, the IVC-CI cut-off value was lower than the previous literatures. Even normovolemic elderly patients are still susceptible to develop hypotension after IGA due to additional factors, including the pathological diseases and the physiological changes related to this age as mentioned before, explaining this low value.

In contrast, Szabo et al. study reported moderate performance results of IVC-CI in predicting post-induction hypotension with high specificity but low sensitivity at a 50% cut-off value (Szabó et al., 2019).

In elderly patients, post-induction hypotension can be more prominent than expected due to increased stiffness of the main and small arteries that offer high resistance so the deficient fluid volume status is not always detected. Furthermore, preoperative anxiety and low ambient temperature can cause stress and subsequently elevate BP (Frederick & Ronald, 2015). In our study, IV infusion of crystal salt solution was administered before IGA to affirm that the incidence of post-induction hypotension in elderly patients related mainly to hypovolemia. This cope with our results regarding the maximum diameter of IVC that was significantly lower ($p < 0.001$) and the

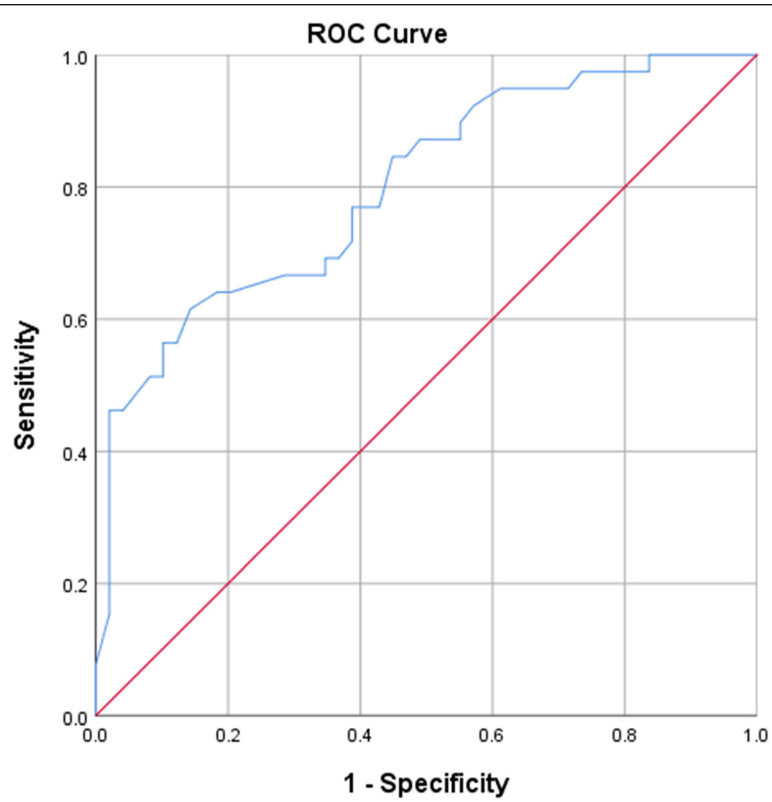

Fig. 3 ROC curve showing the ability of preoperative maximum diameter of IVC to predict hypotension after IGA

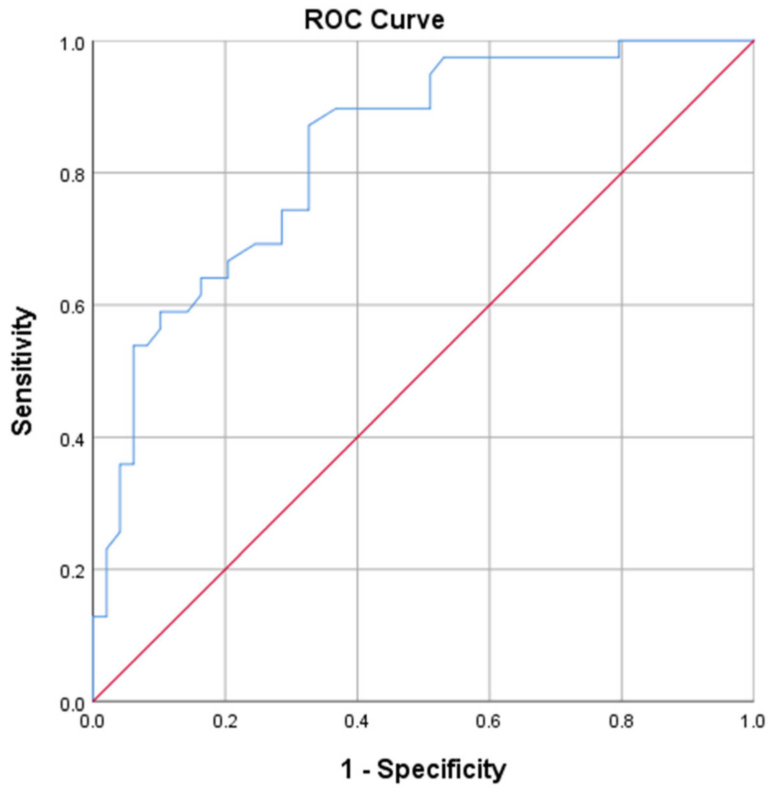

Fig. 4 ROC curve showing the ability of preoperative collapsibility index of IVC to predict hypotension after IGA

collapsibility index that was significantly higher ($p < 0.001$) in patients who did not receive fluid before IGA (group A). Also, post-induction MAP was significantly lower in group A ($p = 0.045$). We believe that the most important factor triggering hypotension was the intravascular volume status of patients because there was no significant difference in patients' ages, gender, ASA physical status, BMI, fasting hours, or the dose of propofol. There are several studies that support our findings regarding the effect of volume state on post-induction BP (Zhang & Critchley, 2016; Şevki et al., 2019; Wu & Yu, 2019). Other studies assumed that hemodynamic fluctuations intraoperatively and at the anesthetic induction period were not related to hypovolemia (Kaydu & Gokcek, 2018; Jacob et al., 2008).

This study has several limitations. Since spontaneous breathing was replaced by positive pressure ventilation, we could not measure post-induction IVC-CI. Doses of propofol were variable among the patients; such variability might be developed from titration of propofol rather than administration with standard monitoring such as entropy/bispectral index monitoring (BIS). Finally, a larger population should be included in the study in order to obtain more powerful findings.

Conclusion

Results of this study indicate that elderly patients undergoing general anesthesia are under an increased risk for hypotension, because of decreased intravascular volume, which not always can be detected. Screening of those patients in the preoperative period with IVC ultrasonography will be guiding in determining the increased risk of hypotension due to hypovolemia, and taking the necessary measures.

Abbreviations

IGA: Induction of general anesthesia; IVC: Inferior vena cava; dIVCmax: Maximum inferior vena cava diameter; dIVCmin: Minimum inferior vena cava diameter; IVC-CI: Inferior vena cava collapsibility index; MAP: Mean arterial pressure; ASA: The American Society of Anesthesiologists; IV: Intravenous; HR: Heart rate; BP: Blood pressure; BMI: Body mass index; ROC: Receiver operating characteristic; AUC: Area under the curve

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Authors' contributions

SR: proof of concept, design, data collection, drafting the manuscript, and critical revision of the manuscript. EW: ultrasound measurements, data collection, data analysis, and interpretation. Both authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and analyzed during this study are available from the corresponding author for 6 months after approval for publication.

Declarations

Ethics approval and consent to participate
Approval by the Research Ethics Committee (REC) Board of Faculty of Medicine, Benha University, was at August 2020 with study number RC8.7.2020 and the trial was registered at the Pan African Clinical Trials Registry (PACTR202011919392248), and written informed consent was obtained from all subjects participating in the trial.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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