Inferior vena cava diameter as a predicting factor for hypotension after induction of general anesthesia in elderly patients

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Research article

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Abstract

Background: To evaluate the use of inferior vena cava diameter (IVCD) to predict post-induction of general anesthesia (IGA) hypotension in older patients. Methods: Part I involved 60 older patients undergoing general anesthesia for surgery (group T). We determined the optimal cutoff value (OCV) of the most sensitive index (MSI) (the collapsibility index (IVCci), distensibility index, or respiratory variation rate) that best predicted post-IGA hypotension in older adult patients. Part II involved 66 older adult patients who underwent general anesthesia for surgery. In accordance with the MSI determined in part I, patients were divided into group B (MSI ≥ OCV, n=42) and group S (MSI < OCV, n=24).

Methods

Our study was approved by the Ethics Committee of Fuyang District First People's Hospital, and followed the principles of the Helsinki Declaration. Written informed consents were obtained from patients. The study was a two-part prospective, clinical trial. We obtained the IVCci threshold for patients with post-IGA hypotension due to lack of blood volume in Part I. We increased the liquid infusion step for elderly patients with hypovolemic blood to verify the effect of hypovolemic state before induction on the post-IGA hypotension incidence in elderly patients in Part II.
patients with hypovolemic blood to verify the effect of hypovolemic state before induction on the post-IGA hypotension incidence in elderly patients in Part II. Informed consent was obtained from the patients or their families.

The subjects were older adult patients (n=126) who underwent general anesthesia for surgery between March 2017 and June 2017 in the Department of Anesthesia, Fuyang District First People's Hospital, Hangzhou. We included female or male patients aged 65-94 years with an American Society of Anesthesiologists grade of I-III. Exclusion criteria were: mental disorder, obesity, severe peripheral vascular disease, thoracic disease, pleural effusion/increased intrapleural pressure, heart valve disease, unstable angina, cardiac dysfunction, presence of valvular pathologies and presence of cardiac dysfunction autonomous nervous system disorder, pacemaker/cardioverter, hypertension, respiratory distress, pulmonary hypertension (the diagnosis of these diseases was made by echocardiography or by medical history), patients who used drugs that affect the cardiovascular system, potentially difficult airway, abdominal effusion/increased intra-abdominal pressure, uncooperative patients, and unsuccessful ultrasonographic scanning of the IVC. Patients were preoperatively fasted for 12 h, with fluid deprivation for 4 h.

**Part I (group T).** An intravenous trocar was preoperatively placed in 60 older adult patients who underwent general anesthesia for surgery between March 2017 and April 2017 in the preparation room, followed by intravenous infusion of compound sodium chloride at 10 ml/kg/h. After entering the operation room, patients were sedated with intravenous midazolam (0.01 mg/kg, Jiangsu Enhua Pharmaceutical Co., Ltd., China). A nasal catheter was used to deliver oxygen at 2 L/min. Local anesthesia was applied to enable catheterization of the radial artery. The ambient temperature in the operation room was maintained at 25°C. Before IGA, the following measurements were taken: electrocardiographic monitoring, systolic BP, diastolic BP, mean arterial pressure (MAP), heart rate (HR), and bispectral index. Patients were placed in supine position for 5 min to stabilize their hemodynamics. An ultrasound machine (Sonosite, Inc., Bothell, WA, USA) with a 3.5 MHz probe (L25x, 3.5 MHz; SonoSite) was used to locate the posterior hepatic IVC vertically along the right costal margin. The internal IVC diameter (IVCD) was measured at a position 2 cm from the entrance to the right atrium. Ultrasound images were synchronized. The maximum and minimum ICVD (IVCmax and IVCmin) were measured at end inspiration and end expiration, respectively. Measurements were performed in triplicate, and the mean was used to calculate the IVC collapsibility index (IVCci = (IVCmax - IVCmin)/IVCmax×100%), the IVC distensibility index (IVCd = (IVCmax - IVCmin)/IVCmin × 100%), and the IVC respiratory variation rate (IVCrv = (IVCmax - IVCmin)/[0.5 × (IVCmax + IVCmin)] × 100%). All IVCD measurements were performed by one physician (T.W.) who was fully trained and experienced in echocardiography. Systolic BP, diastolic BP, and MAP were then measured every 20 s for a total of three times just before IGA. Mean BPs were calculated and used as baseline BP values. Five minutes after IVCD measurements were performed, IGA was initiated via intravenous administration of sufentanil (0.5 µg/kg, Yichang Renfu Pharmaceutical Co., Ltd., China) for 60 s, propofol (1.8 mg/kg, Beijing Fresenius-Kabi Pharmaceutical Co., Ltd., China) at a rate of 40 ml/10 s, and cisatracurium besilate (0.2 mg/kg, Shanghai Dongying Pharmaceutical Co., Ltd., China).
Mask ventilation was provided following jaw thrust with tidal volume at 8-10 ml/kg, respiratory rate at 18–20 breaths/min, and end-tidal carbon dioxide partial pressure at 34–45 mmHg (1 mmHg = 0.133 kPa). Bispectral index was maintained at 40–60. Tracheal intubation was performed 5 min after IGA to enable mechanical ventilation.

**Part II.** An intravenous trocar was placed in 66 patients who underwent general anesthesia for surgery between May 2017 and June 2017 in the preparation room, followed by intravenous infusion of compound sodium chloride at 10 ml/kg/h. The operation room ambient temperature, hemodynamic monitoring, midazolam sedation, and IVCD measurements were performed as described in part I. IVCD measurements were used to calculate the most sensitive index (MSI). The optimal cutoff value (OCV) of the MSI from part I was used to divide the patients in part II into two groups: group B (MSI ≥ OCV), and group S (MSI < OCV). Prior to IGA, group B were administered an intravenous bolus of compound sodium chloride (8 ml/kg) over a period of 30 min to maintain sufficient body fluid volume. Group S were administered an intravenous infusion of compound sodium chloride injection at 10 ml/kg/h for 30 min for volumetric maintenance. IGA was started after 30 min of infusion in both groups. IGA was performed as described in part I. Sevoflurane (1–2%) was used to maintain anesthesia after tracheal intubation. We recorded the pre- and post-infusion MAP and HR of both groups, and the lowest MAP and HR in the period between IGA and surgery commencement.

Those who did not have hypotension were observed for at least 10 min between IGA and surgery commencement. Hypotension was defined as a MAP decrease of ≥ 20% from baseline, and bradycardia was defined as a HR of < 40 beats/min. If hypotension occurred, phenylephrine (50 µg, Shanghai Hefeng Pharmaceutical Co., Ltd., China) was administered intravenously. If bradycardia occurred, atropine 0.5 mg was administered intravenously. These two medications were re-administered as necessary until MAP was ≥ 20% of the baseline value and HR was ≥ 40 beats/min. The number of patients who received phenylephrine and/or atropine was recorded during IGA.

**Statistical analysis.**

Quantitative values were expressed as the mean ± SD. The paired-sample t-test was used to compare paired samples. Comparisons between groups were carried out with the independent sample t-test, and correlation analysis was carried out using Pearson’s coefficient. The receiver operating characteristic (ROC) curve of the observed results was generated, and the area under the ROC curve was calculated. One-way analysis of variance (ANOVA) was used for multi-group comparisons, followed by Bonferroni’s correction. Replicate measurements were analyzed using ANOVA, and numerical data were analyzed using the chi-squared test, with p<0.05 considered statistically significant. The statistical analysis was performed with SPSS 22.0 (SPSS Inc., Chicago, IL, USA).

**Results**

The characteristics of the patients included in part I did not significantly differ from those in part II [Table 1].
Part I. General information. There were 12 patients excluded; the reasons for exclusion were unsuccessful ultrasonographic scanning of the IVC (n=11), and unexpected difficult intubation (n=1). Hence, the data from 48 patients were analyzed (Tables 1 and 2). Phenylephrine (50 μg) was administered to 43 of 48 (89.6%) patients due to hypotension during IGA. No patient was administered atropine due to bradycardia.

Patients without post-IGA hypotension had significantly increased $IVC_{\text{max}}$ ($p<0.05$) and $IVC_{\text{min}}$ ($p<0.05$), and decreased $IVC_{\text{ci}}$ ($p<0.05$) and $IVC_{\text{rvr}}$ ($p<0.05$), compared with those with post-IGA hypotension (Table 2).

Regarding the effect of $IVC_{\text{ci}}, IVC_{\text{di}},$ and $IVC_{\text{rvr}}$ on the prediction of post-IGA hypotension, the ROC curves of all three variables were 0.935 (95% confidence interval: 0.853–1.0; Fig. 1). When $IVC_{\text{ci}}, IVC_{\text{di}},$ and $IVC_{\text{rvr}}$ were all optimized to be 37%, 62.5%, and 47.5%, respectively, the sensitivity was 81.1% and the specificity was 87.3%.

As the part I results showed that pre-anesthesia $IVC_{\text{ci}}, IVC_{\text{di}},$ and $IVC_{\text{rvr}}$ were equally valuable in predicting post-IGA hypotension in older adult patients, we reviewed the literature and found that only $IVC_{\text{ci}}$ was reportedly able to predict post-IGA hypotension. Therefore, the optimal cutoff value of $IVC_{\text{ci}}$ of 37% was used to group the patients for infusion in the second part of the study.

Part II. There were 16 patients excluded, the reasons were unsuccessful ultrasonographic scanning of the IVC (n=14), and other reasons (n=2). Hence, the data from 50 patients were analyzed. In group B, 24 of 33 (72.7%) patients were administered phenylephrine (50 μg) for hypotension during IGA, while 9 did not have hypotension during IGA. In group S, 15 of 17 (88.2%) patients were administered phenylephrine (50 μg) due to hypotension during IGA, while 2 did not have hypotension during IGA. No patient was administered atropine due to bradycardia.

MAP and HR did not significantly change after infusion in either group. In both groups, post-IGA MAP and HR were significantly decreased compared with the corresponding values before and after infusion ($p<0.05$, Table 3).

Discussion

Older adult patients experience increased vascular stiffness, and a decline in baroreceptor function and reflex regulation capabilities\(^1\). During IGA, older adult patients have lower tolerance to intravenous anesthetic drugs. These drugs directly inhibit the portion of the central nervous system relevant to the cardiovascular system or the cardiovascular system itself, lower the stroke volume and peripheral blood vessel resistance, and rapidly lower BP\(^3\). Hence, older adult patients are particularly susceptible to rapid BP decrease during the IGA. BP and HR can markedly decrease in older adult patients\(^15\)–\(^16\). Propofol and sufentanil lower BP, mainly through the direct relaxation of vascular smooth muscle and/or decrease of sympathetic nerve excitation via the central nervous system. Sufentanil lowers HR mainly through vagal
nerve stimulation via the central nervous system, while propofol does not have prominent effects on HR\textsuperscript{3,17}. Cisatracurium besilate at clinical doses has little effect on the cardiovascular system\textsuperscript{18}. When propofol and sufentanil are combined, the effects on hemodynamics are synergistic or additive. However, in general, propofol is the major drug that causes the post-IGA lowering of BP in older adult patients. Additional factors leading to post-IGA hypotension include the pathological factors of disease, and preoperative preparations (including fasting, fluid deprivation, and enema) that cause relative or absolute insufficiency in fluid volume status.

There are many methods used to predict post-IGA hypotension, including cardiac index, stroke volume index, post-induction stroke volume variation, HR variability\textsuperscript{19-20}, and perfusion variation index\textsuperscript{1}. The IVC\textsubscript{ci} can reportedly predict the occurrence of post-IGA hypotension in a relatively accurate way\textsuperscript{13}. However, the subjects in these previous studies were not older patients. In the present study involving older adults, a pre-IGA infusion of compound sodium chloride was administered to confirm that the incidence of post-IGA hypotension in older adult patients was reduced. The main arteries of older patients are stiff and/or the small ones have high resistance\textsuperscript{14}, and therefore the insufficient fluid volume status is not always detected. Furthermore, reoperative nervousness and low ambient temperature can easily cause stress and subsequently increase BP. Thus, more prominent hypotension can occur after IGA. To reduce the effects of these stressful factors, we kept the operation room quiet and instructed the patients to breathe gently; patients were also administered low dose midazolam after entering the operation room, and the operation room ambient temperature was maintained at 25°C.

In part I, the IVC\textsubscript{ci,dir} and IVC\textsubscript{rvr} were calculated using different formulae; however, although the calculation methods differed, all three factors represented the fluid volume status of a specific patient at a specific timepoint and specific location, and therefore they all had the same area under the ROC curve. Previous studies have indicated that the IVC\textsubscript{ci} can be used to predict post-IGA hypotension\textsuperscript{13}. Therefore, IVC\textsubscript{ci} was selected for the grouping in part II. IVC ultrasound examination can predict fluid volume responses in patients on mechanical ventilation\textsuperscript{21}. Although it is hard to control the respiration rate and tidal volume in patients with spontaneous respiration, and the cardiopulmonary interactions were different in those patients compared with the patients on mechanical ventilation, the IVCD could still similarly predict the post-IGA hypotension to some degree in those with spontaneous respiration\textsuperscript{10,13}.

Hypotension is partially dependent on fluid volume. Therefore, the insufficient fluid volume resulting from preoperative fasting and fluid deprivation causes even greater blood vessel resistance and increases the patients’ needs for fluid and fluid volume responses. Those patients with insufficient fluid volume had an accompanying higher IVC\textsubscript{ci} and small IVCD, and were more likely to have post-IGA hypotension. Therefore, higher IVC\textsubscript{ci} and smaller IVCD were associated with a higher risk of developing post-IGA hypotension.

Blood volume supplementation is the most fundamental method for preventing post-IGA hypotension. The present study found that pre-IGA administration of crystal salt solution effectively lowered the incidence of post-IGA hypotension in older adult patients. However, such infusion did not prevent post-IGA
hypotension in all older adult patients, indicating that fluid volume increase before IGA could only complement the relative relaxation effects of IGA to a certain degree and correct the resultant blood volume insufficiency. The time period between entering the operation room and IGA initiation is very short, and fluid supplementation takes time, which is usually not possible in clinical practice before IGA. During part II, intravenous infusion of compound sodium chloride significantly lowered the incidence of post-IGA hypotension, indicating that pre-IGA infusion and the resultant rapid fluid volume increase were effective. However, a large volume of infusion within a short period might cause acute heart failure in older adult patients. Therefore, we tried to prolong the fluid supplementation duration (30 min), and administered 0.05 mg/kg intravenous midazolam to minimize an increase in BP related to nervousness.

In part II, the pre-IGA intravenous fluid bolus was 8 ml/kg, which was within the safe range of preoperative baseline body fluid volume. After rapid infusion of a certain amount of crystal salt solution, the blood volume expansion rate increased. Such a rapid increase in the effective circulating blood volume led to the pressure increase of the pulmonary circulation, which further resulted in the activation of pulmonary artery baroreceptors. In response to this baroreceptor activation, the systemic arterial BP decreases. Hence, there was no increase in BP after infusion. All these results showed that older age was not a critically problematic factor when rapid body fluid volume expansion was performed. Older patients who are in good health without cardiopulmonary disease could adequately tolerate the infusion procedures. Therefore, the methods used in our study prevented overexpansion of fluid volume, consistent with previous reports.

The present study had some limitations. First, there was a relatively high incidence of post-IGA hypotension, which was related to the dosage of induction drugs. Second, individual patients respond differently to surgical trauma, and so the data collection was ended before surgery commencement. Third, only IVC<sub>ci</sub> was used for infusion grouping. The potential use of the other IVC indices needs further investigation. Fourth, the baseline BP of older adult patients was taken after the patients had entered the operation room and before IGA was initiated. Thus, the measured BP was higher than the actual BP, which might explain the relatively high incidence of hypotension. Fifth, the sample size was small and may not be representative of the general population. The present findings need to be confirmed in a multi-center study with large sample size.

Conclusions

Pre-IGA IVCD has value in predicting post-IGA hypotension in older adult patients.

Abbreviations

IGA: induction of general anesthesia, IVC: inferior vena cava, IVCD: inferior vena cava diameter, OCV: optimal cutoff value, MSI: most sensitive index, IVC<sub>ci</sub>: collapsibility index, IVC<sub>max</sub> and IVC<sub>min</sub>: maximum and minimum ICVD. IVC<sub>ci</sub>: IVC collapsibility index, IVC<sub>di</sub>: IVC distensibility index, IVC<sub>rv</sub>: IVC respiratory variation rate, MAP: mean artery pressure, HR: heart rate.
Declarations

Ethics approval and consent to participate: Yes.
Consent to publish: Yes.
Availability of data and materials: The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests: None.

Funding: no

Authors’ Contributions

T.L designed this trial and edited the manuscript; G.C collected and interpreted data. All approved the final version of the manuscript.

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### Tables

**Table 1.** Characteristics of the patients.

| Index                        | group B        | group S        | P value |
|------------------------------|----------------|----------------|---------|
| Age (year)                   | 76.7±10        | 75.4±9         | 0.498   |
| BMI (kg/m^2)                 | 22.8±2.1       | 22.3±2.3       | 0.087   |
| Gender (M/F)                 | 26/22          | 24/26          | 0.585   |
| ASA (I/II)                   | 44/4           | 48/2           | 0.326   |
| Duration of surgery (min)    | 92.8±23.6      | 86.5±21.8      | 0.241   |

Data are expressed as mean±standard deviation or number. BMI-Body Mass index, ASA-American Society of Anesthesiologists

**Table 2.** Compares the pre-IGA hemodynamic results and pre-IGA IVC ultrasound images according to whether or not post-IGA hypotension was developed.
| Variable       | Developed hypotension (n=43) | No developed hypotension (n=5) | P-value |
|----------------|------------------------------|-------------------------------|---------|
| MAP, mmHg      | 105.5±12.6                   | 110.0±19.7                    | 0.560   |
| HR, beats/min  | 80.2±10.0                    | 73.7±8.5                      | 0.277   |
| IVC_{max}, cm  | 1.60±0.22                    | 1.91±0.03                     | 0.021   |
| IVC_{min}, cm  | 0.93±0.17                    | 1.31±0.21                     | 0.011   |
| IVC_{ci} (%)   | 40.9±8.2                     | 32.1±9.8                      | 0.045   |
| IVC_{di} (%)   | 74.1±22.3                    | 48.2±20.3                     | 0.055   |
| IVC_{rvr} (%)  | 52.9±12.6                    | 38.3±14.3                     | 0.048   |

Data are expressed as mean± standard deviation. IGA-induction of anesthesia, IVC-inferior vena cava, MAP-mean blood pressure, HR-heart rate, IVC_{max}-maximum diameter of the IVC, IVC_{min}-minimum diameter of the IVC, IVC_{ci}-collapsibility index of the IVC, IVC_{di}-distensibility index of the IVC, IVC_{rvr}-respiratory variation rate of the IVC

**Table 3**- Comparisons of the MAP, HR before infusion, after infusion and after induction of general anesthesia

| Index                          | Group B       | Group S       | P-value |
|-------------------------------|---------------|---------------|---------|
| Pre-infusion MAP (mmHg)       | 110.3±9.4     | 109.3±10.8    | 0.818   |
| Post-infusion MAP (mmHg)      | 111.0±7.9     | 109.1±10.1    | 0.994   |
| Post-IGA MAP (mmHg)           | 82.5±7.2<sup>ab</sup> | 80.2±7.7<sup>ab</sup> | 0.685   |
| Pre-infusion HR (beat/min)    | 76.3±10.2     | 77.4±12.4     | 0.280   |
| Post-infusion HR (beat/min)   | 73.1±7.9      | 64.2±12.1<sup>ab</sup> | 0.153   |
| Post-IGA HR (beat/min)        | 61.5±8.3<sup>ab</sup> |               | 0.512   |
\( aP < 0.05 \) compared with pre-infusion blood pressure and heart rate, \( bP < 0.05 \) compared with post-infusion blood pressure and heart rate, Pre-infusion MAP, HR-mean artery pressure and heart rate before infusion, Post-infusion MAP, HR-mean artery pressure and heart rate after infusion, Post-IGA MAP, HR-mean artery pressure and heart rate after induction of general anesthesia.

**Figures**
Figure 1

Receiver operating characteristic curves showing the ability of the preoperative collapsibility index, distensibility index and respiratory variation rate of the inferior vena cava to predict hypotension after induction of general anesthesia.