Minerva Anestesiologica 2019 May;85(5):514-21
DOI: 10.23736/S0375-9393.18.13041-0

ORIGINAL ARTICLE

Size and shape of the inferior vena cava before and after a fluid challenge: a pilot study

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ABSTRACT

BACKGROUND: Recent meta-analyses failed to support the reliability of ultrasound assessment of the inferior vena cava (IVC) to predict fluid responsiveness. However, the techniques utilized were heterogeneous. We hypothesized that the variability of the elliptic section and caliber of the IVC along its course may influence ultrasound evaluation. Therefore, we investigated IVC size and shape at four levels, before and after a fluid challenge.
METHODS: Twenty mechanically-ventilated adult patients who received a fluid challenge after cardiac surgery were enrolled. They were regarded as responders if the cardiac index increased more than 15%. Before and after the fluid challenge, IVC anteroposterior (AP) and lateral (LA) diameters, the flat ratio, and the distensibility index were assessed by ultrasound just above the iliac veins, at the confluence of the renal veins, before the confluence of the hepatic veins (where blood flow velocity was also measured), and after it.
RESULTS: At all levels, IVC section was elliptical, so that IVC diameters varied between a minimum and a maximum according to the measurement angle. Such interval increased in correspondence of the renal veins, where IVC section was more eccentric. The distensibility index was higher when assessed on AP diameters. After the fluid challenge, non-responders showed a diffuse increase of AP diameters, whereas responders showed an increase of blood velocity before the confluence of the hepatic veins.
CONCLUSIONS: The elliptic section should be considered when assessing IVC size. AP diameters are shorter and more affected by the respiratory cycle. After a fluid challenge, an increase of blood velocity associated with unchanged AP diameters may suggest fluid responsiveness.

(*Cite this article as:* Biasucci DG, Cina A, Calabrese M, Antoniucci ME, Cavaliere C, Bevilacqua F, *et al.* Size and shape of the inferior vena cava before and after a fluid challenge: a pilot study. Minerva Anestesiol 2019;85:514-21. DOI: 10.23736/S0375-9393.18.13041-0)

KEY WORDS: Vena cava, inferior; Resuscitation; Critical care; Cardiac Surgical Procedures; Hypovolemia; Ultrasonography.

Fluid therapy is crucial in the perioperative period in order to maintain a normal blood volume.[1] Too restrictive policies may cause hypovolemia and impair patients' hemodynamics by decreasing cardiac preload,[2] whereas liberal ones have been associated to an increased rate of complications and a longer length of stay in hospitals.[3, 4] In medium and high risk patients, the assessment of stroke volume (SV) variations and fluid responsiveness has been suggested to optimize fluid administration.[5] Fluid responsiveness has been defined as an increase in SV by 10-15% after a fluid challenge (250-500 cc).[6] A recent meta-analysis concluded that fluid responsiveness applied to goal-directed therapy in critically-ill patients "appears to be associated with reduced mortality, ICU length of stay, and duration of mechanical ventilation."[7]

Literature suggests that fluid challenges accomplished for acute circulatory failure may turn out to be negative in about 50% of cases.[8] Since the size and collapsibility of the inferior vena cava (IVC) has been utilized to estimate central venous pressure,[9, 10] it may be of value to anticipate the results of fluid challenge or decide whether to perform it or not.[11] Barbier *et al.* found that in septic patients a threshold of 18% in the IVC distensibility index (calculated as the difference in inspiratory and expiratory diameters divided by the expiratory diameter and converted to percentage) allows discriminating fluid responders;[12] successively, Feissel *et al.* reported a threshold of 12% with positive and negative predictive values of 93% and 92%.[13] Those findings were only partly confirmed by later studies. Recent reviews and meta-analyses concluded that the assessment of IVC diameter may be useful to guide fluid therapy,[14-16] but its value to predict central venous pressure is uncertain.[17, 18] Furthermore, "variations in IVC diameters has a limited ability to predict fluid responsiveness" and a negative test does not rule it out.[14, 15]

IVC evaluation has been performed with static and dynamic parameters assessed by ultrasound and by CT-imaging on different parts of the vein.[19-28] Static parameters are the diameter and the ratio between minor and major axes of IVC elliptical section (flat ratio), while dynamic ones are the collapsibility and distensibility indices, respectively during spontaneous breathing and mechanical ventilation. Measurements are usually performed on the thoracic tract, just after the confluence of the hepatic veins, or on the abdominal tract, before the hepatic veins or in correspondence of the renal veins.

In order to test whether IVC evaluation may be affected by the technique utilized, we investigated the size, the degree of eccentricity, and the distensibility of IVC section at four levels before and after a fluid challenge.

Materials and methods

Study design and setting

This is a preliminary, single-center, prospective, observational, cohort study which was conducted in a cardiac surgical intensive care unit (CS-ICU) of a University Hospital over a period of six months.

Patients

After obtaining the local Ethic Committee approval, twenty adult patients who had undergone cardiac surgical procedures and gave their informed consent were enrolled. The criteria of inclusion were the presence of an arterial catheter and of a pulmonary artery catheter (both routinely positioned before surgery according to the internal protocol) and the decision of the attending physician to perform a fluid challenge (eventually followed by a fluid expansion) during the first three postoperative hours. Such decision was based on the presence of clinical signs of inadequate hemodynamics or tissue hypoperfusion (heart rate >100 min^{-1}, systolic blood pressure <90 mmHg, cardiac index <2.2 L/min/m^2, urine output <0.5 ml/kg/h, plasma lactates >2 mmmol/L). Criteria of exclusion were: age <18 years-old, Body Mass Index (BMI) >30 kg/m^2, clinically significant tricuspid insufficiency and/or right heart failure, suspected sepsis, bleeding from surgical drainages >150 mL/h, allergy to starch, more than 1000 mL of hydroxyethyl starches already administered during the previous 24 hours.

Methods

After their arrival in the CS-ICU, patients were connected to a mechanical ventilator using flow-controlled, volume-cycled mode and sedated with propofol (1-2 mg/kg/h) and remifentanil (1-2 mcg/kg/h) to a Ramsey sedation score of 5 (a sluggish response to a light glabellar tap). The study protocol included two sets of measures, before and after the fluid challenge.

Before the challenge, hemodynamic parameters were registered and the sonographic evaluation of IVC diameters was performed with the bed in a 30° semi recumbent position. Then the bed was moved to a supine neutral position to assess the intra-abdominal pressure (IAP), which was measured three minutes later, and then repositioned in the 30° semi recumbent position. The fluid challenge was performed by injecting a solution of hydroxyethyl starches, 6-9 mL/kg, in 30 minutes. At the end, hemodynamic measurements and sonographic assessment were repeated.

Cardiac output was measured with the method of thermodilution; the averaged result of three measurements was registered provided that differences between them were less than 10%. Cardiac Index (CI) was obtained by dividing cardiac output by body surface area. Patients in whom CI increased by ≥15% after the fluid challenge were classified as fluid responders. IAP was assessed after instilling 25 mL of saline into the bladder. The symphysis pubis was used as the reference line.

The sonographic evaluation of IVC was carried out by an expert radiologist with an Esaote MyLab Five ultrasound device equipped with a convex phased-array transducer (3.5-5 MHz). AP and LA diameters were measured at the end of inspiration and at the end of expiration at four levels by anterior and lateral axial scans: 1) 1 cm above the confluence of common iliac veins; 2) immediately below the confluence of the right renal vein; 3) 1 cm before the confluence of the hepatic veins; and 4) 1 cm after the confluence of the hepatic veins. At level 3, maximum and mean blood flow velocity (FV) was also assessed using the Pulsed wave Doppler module with an insonation angle <60°. At each level, we calculated: 1) the flat ratio, *i.e.* the ratio between AP and LA diameters; and 2) the distensibility index, *i.e.* the variation of IVC diameter during the respiratory cycle divided by the minimum value and converted to percentage, which was assessed on both AP and LA diameters.

Statistical analysis

Continuous variables were reported as means (SD) or medians (range) according to the type of distribution. Data were analyzed with ANOVA for repeated measures; *post-hoc* analysis was performed with the Student-Newman-Keuls (SNK) Test. A P value of less than 0.05 was considered to indicate statistical significance.

Based on the findings of a previously published study,[29] we designed our study to have an 80% power to detect a 20% difference in percentage collapse of the IVC between measurement locations, alpha was set at 0.05. The decision to use a 20% difference was based on the fact that several authors have published discriminatory breakpoints near this value. Our calculated sample size was 17 patients. We planned to enroll 20 patients, which would allow 15% data loss from eventually inadequate IVC visualization. Furthermore, being it a pilot study, a power analysis, even if not necessary for the meaning of the study itself, should theoretically require at least 20 patients.

The program Statistica version 10 (Statsoft, USA) was utilized.

Results

Twenty consecutive patients were enrolled in the study (16 males and four females, aged 63.1 [10.8], BMI 27.3 [3.4]). They underwent myocardial revascularization (N.=11), myocardial revascularization plus aortic valve replacement (N.=3), aortic valve replacement (N.=2), aortic valve repair (N.=1), mitral valve repair (N.=1), aortic and mitral valve replacement (N.=1), interventricular septum defect and tricuspid valve repair (N.=1). Twelve patients out of 20 (60%) presented a positive loading test. Abdominal pressure was 10.3 (3.3) mmHg.

Table I reports hemodynamic parameters. After the loading test, the values of all but HR increased. Baseline values did not differ between responders and non-responders, apart from CI ones, which were lower in responders (SNK test: P=0.016). That difference disappeared after the fluid challenge, because CI increased significantly only in responders (ANOVA: interaction between GROUP and TEST: P<0.001).

Table II and Figure 1, 2 show IVC diameters before and after the fluid challenge in responders and non-responders. Baseline values confirmed that the vein had an elliptic section over its entire course (AP diameters were significantly shorter than LA ones). Both diameters increased along the course of the vein, but patterns were different. AP diameter had a steep increase from level 2 to 3 (renal veins - hepatic veins), which was present both in responders and non-responders (P=0.0001 and P=0.0003, respectively). LA di-

TABLE I.—*Hemodynamics before and after a loading test with 6-9 mL/kg of colloids given in 30 minutes, in responders (in whom CI increased more than 15%) and non-responders. Values are reported as means (SD). ANOVA for repeated measures was utilized to test differences between responders and non-responders (GROUP), and before and after the loading test (LOAD).*

	HR	MAP	MPAP	CVP	PCWP	CI	CI Δ (%)
Responders (N.=12)							
Baseline	94 (10)	73 (7)	20 (5)	9 (3)	11 (5)	2.0 (0.4)	36 (18)
After loading test	92 (8)	81 (9)	22 (7)	11 (3)	13 (4)	2.6 (0.3)	
Non-responders (N.=8)							
Baseline	93 (14)	70(12)	19 (2)	9 (3)	9 (2)	2.6 (0.3)	2 (8)
After loading test	91 (11)	77(8)	23 (5)	12 (4)	13 (4)	2.7 (0.4)	
ANOVA							
GROUP	0.2839	0.5612	0.7221	0.9348	0.4435	0.1517	
LOAD	0.1535	0.0006	0.0429	0.0004	0.0073	0.0000	
INTERACTION	0.8937	0.3206	0.5416	0,1100	0.4205	0.0000	

HR: heart rate (b/min); MAP: mean arterial pressure (mmHg); MPAP: mean pulmonary artery pressure (mmHg); CVP: central venous pressure (mmHg); PCWP: pulmonary capillary wedge pressure (mmHg); CI: cardiac index (L/min/m²); CI Δ: CI increase (%).

TABLE II.—*IVC diameters before and after a fluid challenge (FC) with 6-9 mL/Kg of colloids given in 30 minutes, in responders (in whom CI increased more than 15%) and non-responders. Values are means (SD) expressed in mm. P values are referred to* post-hoc *comparisons performed with SNK-test.*

	Inferior Vena Cava diameters before and after a fluid challenge at the 4 different levels							
	1 Iliac veins		2 Renal veins		3 Before hepatic veins		4 After hepatic veins	
	AP	LA	AP	LA	AP	LA	AP	LA
A	11.5 (2.4)	21.0 (3.0)	10.0 (2.7)	21.6 (3.7)	12.6 (3.4)	20.4 (3.1)	14.3 (4.6)	23.7 (3.0)
B	13.8 (3.1)	22.1 (3.0)	12.3 (3.7)	24.2 (3.9)	15.8 (4.2)	22.5 (3.6)	15.9 (4.8)	25.5 (1.9)
A *vs.* B P	0.8724	0.8605	0.7220	0.6990	0.1579	0.1880	0.2718	0.6467
C	11.1 (2.2)	21.3 (3.6)	10.9 (2.6)	25.4 (4.9)	16.1 (4.8)	26.3 (4.3)	16.4 (3.4)	27.1 (5.2)
A *vs.* C P	0.8728	0.9150	0.7089	0.6592	0.7815	0.4092	0.8997	0.7434
D	13.3 (2.3)	23.6 (3.0)	14.0 (1.8)	25.8 (4.0)	19.4 (4.6)	27.8 (6.8)	19.8 (4.2)	27.8 (5.3)
C *vs.* D P	0.0097	0.0030	0.0002	0.8170	0.0001	0.0840	0.0001	0.3164

IVC: inferior vena cava; AP: anteroposterior diameter; LA: lateral diameter; CI: cardiac index; A: before fluid challenge in responders; B: after fluid challenge in responders; C: before fluid challenge in non-responders; D: after fluid challenge in non-responders.

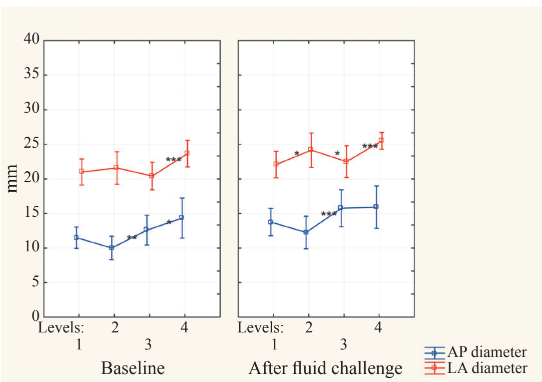

Figure 1.—Trends of IVC diameters in responders. Levels: 1: confluence of iliac veins; 2: confluence of renal veins; 3: 1 cm before the confluence of hepatic veins; 4: 1 cm after the confluence of hepatic veins.
Post-hoc comparisons (SNK test) between adjacent levels: *P<0.05; **P<0.001; ***P<0.001.

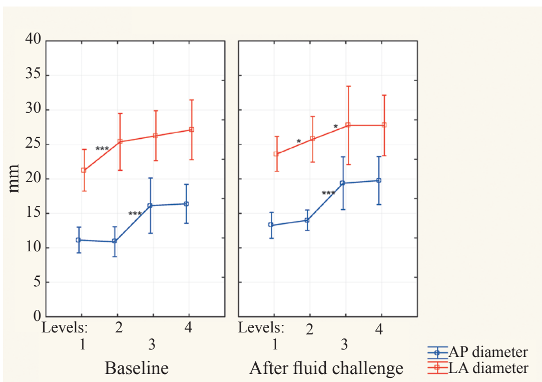

Figure 2.—Trends of IVC diameters in non-responders. Levels: 1: confluence of iliac veins; 2: confluence of renal veins; 3: 1 cm before the confluence of hepatic veins; 4: 1 cm after the confluence of hepatic veins.
Post-hoc comparisons (SNK test) between adjacent levels: *P<0.05; ***P<0.001.

ameter increased markedly from level 1 to 2 in non-responders (P=0.0002), and from level 3 to 4 in responders (P=0.0002). After the fluid challenge, IVC diameters increased (ANOVA: P=0.0030); however, post-hoc comparisons reached statistical significance only in non-responders, in whom AP diameter increased at all levels (Table II).

Table III reports the values of the flat ratio, which expresses the degree of eccentricity of IVC elliptical section: the higher the ratio, the more the section was close to a circle. Baseline values showed a minimum at level 2 (renal veins) and a maximum at levels 3 and 4 (just before and after hepatic veins); that trend was common to responders and non-responders. After the fluid challenge, R increased significantly at levels 2 in responders and 2,3, and 4 in non-responders.

Table IV reports the values of the distensibility index. The index was higher when assessed on AP diameters than on LA ones (P=0.0000) and did not change significantly after the loading test, nor was different between responders and non-responders.

Finally, we found IVC peak and mean blood FV values assessed at level 3 (1 cm before hepatic veins) to be affected by the fluid status and to differ between responders and non-responders

TABLE III.—*Flat ratios (ratios between AP and LA diameters) before and after a fluid challenge (FC) with 6-9 mL/Kg of colloids given in 30 minutes, in responders (in whom CI increased more than 15%) and non-responders. Values are means (SD) and are expressed in percentages. P values are referred to* post-hoc *comparisons performed with SNK-test.*

	Ratios between AP and LA IVC diameters before and after a fluid challenge at different levels			
	1 Iliac veins	2 Renal veins	3 Before hepatic veins	4 After hepatic veins
A	55.6 (14.2)	46.8 (11.8)	62.2 (14.9)	60.9 (18.2)
B	63.6 (18.5)	51.1 (14.1)	70.3 (15.2)	62.4 (19.1)
A *vs.* B P	0.1714	0.1680	0.0482	0.8712
C	52.6 (7.4)	43.2 (8.3)	60.8 (11.8)	60.7 (9.2)
A *vs.* C P	0.8995	0.6094	0.9782	0.9994
D	57.0 (13.1)	54.8 (5.4)	70.7(10.7)	71.7 (12.3)
C *vs.* D P	0.4711	0.0033	0.0310	0.0163

IVC: inferior vena cava; AP: anteroposterior diameter; LA: lateral diameter; CI: Cardiac Index; A: before fluid challenge in responders; B: after fluid challenge in responders; C: before fluid challenge in non-responders; D: after fluid challenge in non-responders.

TABLE IV.—*The distensibility index (100 x (inspiratory diameter – expiratory diameter)/expiratory diameter) before and after a fluid challenge (FC) with 6-9 mL/Kg of colloids given in 30 minutes, in responders (in whom CI increased more than 15%) and non-responders. Values are percentages expressed as medians (1st quartile; 3rd quartile). ANOVA: comparison between AP and LA diameters: P=0.0000*

	Distensibility index before and after a fluid challenge at different levels							
	1 Iliac veins		2 Renal veins		3 Before hepatic veins		4 After hepatic veins	
	AP	LA	AP	LA	AP	LA	AP	LA
A	14.3 (1.9; 18.8)	4.9 (1.1; 9.6)	17.7 (10.4; 6.7)	4.8 (3.6; 9.1)	11.9 (0.0; 23.8)	2.4 (0.0; 6.3)	8.1 (0.0; 15.0)	0.0 (-2.7; 4.5)
B	10.9 (0.0; 20.0)	6.1 (0.0; 10.4)	11.1 (1.5; 24.1)	1.8 (0.0; 6.0)	6.3 (0.0; 10.3)	4.2 (0.0; 9.4)	5.6 (1.2; 20.6)	4.1 (0.0; 7.4)
A *vs.* B P	0.9066	0.9982	0.3121	0.9961	0.8685	0.9946	0.9815	0.9289
C	9.1 (2.1; 12.8)	4.4 (-3.4; 5.2)	15.0 (8.8; 23.8)	0.0 (-3.0; 6.9)	11.3 (1.0; 16.8)	4.0 (-1.3; 4.5)	9.8 (7.1; 15.7)	1.5 (-3.0; 3.9)
A *vs.* C P	0.9742	0.9995	0.4801	0.9974	0.9954	0.9973	0.9904	0.9963
D	8.6 (1.7; 26.7)	1.9 (-2.8; 4.5)	7.2 (1.7; 14.5)	5.7 (1.0; 8.7)	5.7 (4.2; 7.5)	4.6 (0.0; 8.3)	9.7 (6.0; 13.7)	3.9 (0.6; 9.9)
C *vs.* D P	0.9499	0.9777	0.2401	0.9972	0.9024	0.9217	0.9616	0.9847

IVC: inferior vena cava; AP: anteroposterior diameter; LA: lateral diameter; CI: cardiac index; A: before fluid challenge in responders; B: after fluid challenge in responders; C: before fluid challenge in non-responders; D: after fluid challenge in non-responders.

after a fluid challenge. Baseline mean and peak blood FV were found to be higher in responders than in non-responders (peak FV difference between responders and non-responders 12.4 cm/s, P=0.012). After fluid challenge, mean and peak FV were found to significantly increase in responders compared to non-responders: peak FV difference before and after fluid challenge in responders 11.5 cm/s *vs.* 1.8 cm/s in non-responders with P=0.018; mean FV difference before and after fluid challenge in responders 7.3 cm/s *vs.* 0.1 cm/s in non-responders with P=0.043.

Discussion

Based on our data, the static and dynamic parameters commonly measured with ultrasound to assess IVC size and shape are affected by the tract of the vein taken into account and by the measurement angle. IVC section is elliptical, so that diameter measurements may vary between a maximum and a minimum; this interval varies along the course of the vein since the section is flatter at the confluence of the renal veins. The distensibility index, which measures the effects of the respiratory cycle on IVC diameters, is higher when assessed on the abdominal course of the vein and when AP diameter is considered rather than LA one. In our study, the fluid challenge caused an increase of IVC size, which involved the AP diameter more than LA one, so that the section of the vein became less eccentric.

In our study, neither the static indices, nor the dynamic ones discriminated responders from non-responders before the test. Interestingly, in the present study, we found that the changes of IVC size and blood FV observed after loading test presented different patterns in responders and non responders. The former showed small changes of IVC diameters, but a significant increase of blood velocity within the vein; that finding may indicate that blood flow to the heart increased without an increase of the intravenous pressure. Conversely, non-responders showed an increase of AP diameters and a consequent decrease of IVC eccentricity, while blood velocity did not change. That pattern may suggest that after the loading test the pressure inside the vein increased. Hypothetically, ultrasound monitoring of IVC diameters and FV may be added to hemodynamic changes to decide whether the response to a loading test indicates fluid responsiveness or not.

To assess fluid responsiveness, IVC ultrasound is usually performed after the confluence of the hepatic veins from the sub-xiphoid view,[20, 30] unless technical difficulties. Alternatively, the assessment is performed on the tract before the confluence of the hepatic veins from the right midaxillary line.[31, 32] Whatever technique is utilized, the parameters considered are static (diameters, degree of eccentricity) and dynamic (distensibility and collapsibility indices). CT imaging of the IVC has also been utilized to predict fluid responsiveness.[22, 23, 25-27] and measures were commonly performed at the confluence of the renal veins, where the degree of eccentricity of IVC section is greater. Measurements at that level were initially proposed also for ultrasound assessment.[19] Our data suggest that Irregularities of IVC shape may affect those techniques differently.

In the supine position, abdominal viscera compress IVC against the vertebral column. The elliptical section of the vein is more or less eccentric in relation to the pressure inside the vessel, the intra-abdominal pressure, and the characteristics of the wall.[25] Our data show that the degree of eccentricity is lower after the confluence with the hepatic veins just 1-2 cm before the junction with the right atrium. On the other hand, the ratio between minor and major axes (flat ratio)[32] or viceversa (flatness index)[24] may reflect fluid responsiveness at the confluence of the renal veins where, according to our data, IVC section is characterized by the greatest degree of eccentricity.

Collapsibility and distensibility indices are the dynamic parameters utilized respectively in spontaneously-breathing and mechanically-ventilated patients to evaluate fluid responsiveness. They are usually assessed in different portion of the IVC course: just after the confluence with hepatic veins or few centimeters before. In spontaneously-breathing patients, the two methods agree,[30] but measurements performed after hepatic veins confluence may underestimate IVC collapsibility.[32] Our data show that in mechanically-ventilated patients, variations in the size of the vein during the respiratory cycle mainly concern the AP diameter. Consequently, the distensibility index may vary according to which diameter is taken into account. In spontaneously-breathing patients, the concordance between measurements performed by the two windows improves when the flat ratio decreases,[30] suggesting that the degree of eccentricity of IVC section affects the measurements of the dynamic parameters.

Fluid responsiveness assessed by a loading test remains a gold-standard for guiding fluid therapy in critically-ill patients.[5, 33, 34] In this study, the results of the fluid challenge were not anticipated by ultrasound since baseline values of IVC static and dynamic measurements did not differ between responders and non-responders. Since it is a pilot study, the low number of patients enrolled may explain why ultrasound parameters did not differ between responders and non-responders. However, some results of this study allow to advance some hypotheses to be verified in future larger trials. The comparison between the size of the IVC at his origin and at the confluence of renal veins pointed out a potentially useful difference between responders and non-responders. In non-responders, LA diameters at the level of renal veins was 20% larger than at the confluence of the iliac veins. This increase of caliber was probably caused by the flow of blood from the kidneys; in responders, its absence may indicate a hypovolemic state.

Limitations of the study

The major limitation of the present study may be represented by the fact that this is only a pilot study which, nonetheless, may play an important role in planning future larger trials needed to confirm these results.

Conclusions

In conclusion, the elliptical section of the IVC and the different degrees of eccentricity along its course influence the static and dynamic parameters used for the evaluation with ultrasound. Some Authors underlined the need for standardization of the technique of measurement; according to our data, the process should also take into account the differences between AP and LA diameters and their different behavior during the respiratory cycle. Our data also suggest that an increase of FV within the IVC after a fluid challenge may represent a sign of fluid responsiveness, contrary to an increase of AP diameters. Further studies are needed to confirm such difference.

What is known

- Variation of IVC AP diameter is a well known non-invasive marker of intravascular volume status, correlating its percentage collapse to CVP.
- There has been a lack of standardization across investigations and measurements at different sites along IVC course may significantly differ.

What is new

- The elliptical section of the IVC and the different degrees of eccentricity along its course influence the static and dynamic parameters used for the evaluation with ultrasound.
- The more reliable site for IVC measurement is at the confluence of the renal veins.
- Increased blood velocity within the IVC after a fluid challenge may represent a sign of fluid responsiveness, contrary to an increase of AP diameters.

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Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions.—Daniele G. Biasucci: protocol elaboration, manuscript editing; Alessandro Cina: ultrasound measurements, manuscript editing; Carlo Cavaliere: statistical analysis; Marial Calabrese: data collection; Maria E. Antoniucci: data collection; Francesca Bevilacqua: data collection; Franco Cavaliere: protocol elaboration, manuscript editing.

Comment in: Guarracino F, Bertini P. Dynamic indices of preload and fluid responsiveness: some certainty in the midst of the uncertain. Minerva Anestesiol 2019;85:460-1. DOI: 10.23736/S0375-9393.19.13590-0

Article first published online: November 22, 2018. - Manuscript accepted: November 5, 2018. - Manuscript revised: September 25, 2018. - Manuscript received: May 23, 2018.