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Original Contribution

Role of inferior vena cava diameter in assessment of volume status: a meta-analysis

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Abstract

Background and Objective: Hypovolemic shock is an important cause of death in the emergency department (ED). We sought to conduct a meta-analysis to quantify existing evidence on sonographic measurement of inferior vena cava (IVC) diameter in assessing of volume status adult ED patients.

Methods: A search of 5 major databases of biomedical publication, EMBASE, Ovid Medline, evidence-based medicine (EBM) Reviews, Scopus, and Web of Knowledge, was performed in first week of March 2011. Studies meeting the following criteria were included: (1) prospectively conducted, (2) measured IVC diameter using ultrasonography, (3) inpatients under spontaneous ventilation, and (4) reported IVC diameter measurement with volume status or shock. Article search, study quality assessment, and data extraction were done independently and in duplicate. Mean difference in IVC diameter was calculated using RevMan version 5.5 (Cochrane collaboration).

Results: A total of 5 studies qualified for study eligibility from 4 different countries, 3 being case-control and 2 before-and-after design, studying 86 cases and 189 controls. Maximal IVC diameter was significantly lower in hypovolemic status compared with euvolemic status; mean difference (95% confidence interval) was 6.3 mm (6.0-6.5 mm). None of the studies blinded interpreters for volume status of participants.

Conclusion: Moderate level of evidence suggests that the IVC diameter is consistently low in hypovolemic status when compared with euvolemic. Further blinded studies are needed before it could be used in the ED with confidence.

1. Introduction

Rapid volume loss is the primary cause of death in conditions such as major trauma, postpartum hemorrhage, and gastrointestinal bleeding [1]. Accurate estimation of volume status in these patients is important to estimate volume repletion and monitor for adverse consequences of fluid overload, especially in patients with multiple comorbidities such as congestive hear failure. There are several modes to assess volume status in these conditions, such as physical examination findings of shock and tissue hypoperfusion, vital signs, tissue perfusion measurement, biochemical markers of metabolism, central venous pressure measurement, and sonographic measurement of inferior vena cava (IVC) diameter [2]. Some of these indicators either have a lag period in appearance due to body's compensatory

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mechanism for initial volume loss or are invasive and time consuming to be used efficiently in time-sensitive settings such as the emergency department (ED). For example, blood pressure could be maintained to normal level with up to 30% of total body water loss, which is significant enough to initiate multiple-organ failure [3]. Serum lactate level is used as surrogate marker of severe tissue hypoperfusion, but its utility in early detection of hemodynamic instability and to guide fluid resuscitation is not yet defined [2].

The IVC is a highly collapsible major vein, and its diameter closely correlates with right side cardiac functions [4]. The IVC diameter has not found to be affected by body's compensatory vasoconstrictor response to volume loss [5]. Hence, it reflects volume status more closely than other parameters based on arterial system such blood pressure, pulse rate, diameter of aorta, and others. Studies in the past have demonstrated utility of IVC diameter in monitoring volume status in patients undergoing hemodialysis and in patients under mechanical ventilation in intensive care units [6,7]. In recent years, sonographic assessment of IVC diameter to assess volume status and guide fluid resuscitation is gaining popularity in the EDs, too. There is no large multicenter study available to accurately define usability of sonographic measurement of IVC diameter and change in IVC diameter during respiratory cycle to estimate volume status in the ED. To consolidate existing evidence, we sought to conduct a meta-analysis of studies conducted in the ED to define role of sonographic assessment of IVC diameter in estimation of volume status in adult population.

2. Methods

This meta-analysis follows the reporting guidelines for Meta-analysis of Observational Studies in Epidemiology and the Preferred Reporting Items for Systematic reviews and Meta-analyses statement [8,9].

2.1. Search

A comprehensive search was performed in the first week of March 2011 of 5 major databases of biomedical publication: EMBASE, Ovid Medline, EBM Reviews, SCOPUS, and Web of Knowledge and was updated in the second week of August 2011. No language restrictions were applied. Search strategy is available as Web-only appendix (Appendix A). To minimize the publication bias, references cited in potentially eligible articles and conferences proceeding of major emergency medicine organizations (Society for Academic Emergency Medicine, American College of Emergency Medicine, and Canadian Association of Emergency Physicians) for the last 2 years were hand searched. Authors of abstract in these meeting were further searched in PubMed for potential full articles.

2.2. Study selection

Studies meeting following criteria were included: (1) prospectively conducted, (2) measured IVC diameter through ultrasonography (USG), (3) in patients under spontaneous ventilation, and (4) reported IVC diameter measurement with volume status or shock. Studies including less than 10 patients (case reports and small case series), mechanically ventilated patients, conducted in setting apart from ED or ED equivalent and studies not based on original studies were excluded. Based on above inclusion and exclusion criteria, study selection was done in 2 phases by 2 reviewers independently (SC and DA). Phase 1 included screening titles and abstracts, and phase 2 included review of full text of potentially eligible studies from phase 1. All the disagreements were resolved by consensus. References of potentially eligible articles were hand searched to minimize publication bias.

2.3. Quality assessment

There is not well-validated and widely accepted checklist for quality assessment of study methodology of observational studies. We have reviewed Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool and Newcastle-Ottawa scale to develop an individualized checklist for current study [10,11]. The individualized checklist for this study covered subject selection, comparability, and measurement of IVC diameter in assessing quality of study methodology (Table 1). Although studies have reported

Table 1 Quality assessment of study methodology

	Akhili	Yanagawa 2005	Yanagawa 2007	Sefidbakhat	Weekes
1. Patients selected in an unbiased fashion (consecutive or random sample)?	Yes	Yes	Yes	Yes	Yes
2. Study sample representative of a wide spectrum of the severity of disease?	Yes	Yes	Yes	Yes	Yes
3. Comparison groups clearly defined?	Yes	Yes	Yes	Yes	Yes
4. IVC diameter assessed without knowledge of the shock or volume status?	No	No	No	No	No
5. Shock status assessed without knowledge of the IVC diameter?	Yes	Yes	Yes	Yes	Yes
6. IVC diameter measured in the same objective way in both groups?	Yes	Yes	Yes	Yes	Yes
7. IVC diameter measurement personnel adequately trained?	Yes	Yes	Yes	Yes	Yes

excellent interrater agreement in USG measurement of IVC diameter among ED physicians, we still believe that level of expertise could influence visual estimation of IVC diameter as its a user-dependent technology [12]. Thus, we decided to include clinician's level of expertise in quality assessment. Responses to each criterion were dichotomized to yes and no/unclear. Allocation of score for each component is controversial, as the components of study methodology do not weight equally. Henceforth, we decided to report components rather reporting a score for each study.

2.4. Quantitative data synthesis

Two investigators (SC and DA) did data extraction from each study in duplicate, independently. Data points with discrepancies between 2 reviewers were resolved by cross-checking the full text together. Main data points extracted from each study were year of publication, study settings and country, number of subjects included, subject selection, characteristics of cases and controls, mean or median IVC diameter amongst cases and controls, and characteristics of IVC measurement (probe used, site of measurement, cycle of respiration, axis of measurement, level of expertise of person measured, etc). Inferior vena cava diameter is altered with volume status and respiration, higher being in expiration compared with inspiration. In addition, the expiration diameter is found to be more valuable in assessing volume status [13]. Hence, in this systematic review, we have collected maximal IVC diameter during expiration, which is at the end of expiration phase of respiration. Weighted mean and weighted mean difference between cases and controls were calculated. Studies where SD for maximal IVC diameter was not reported and 10% of mean value was taken as SD to calculate weighted mean difference. Weighted mean and weighted mean difference between cases and controls were calculated using fixed effect model. Heterogeneity between studies has been addressed using *I*-square statistics. Data synthesis and analysis were done using RevMan version 5.1 (Cochrane Collaboration) for Mac OS X.

3. Results

Fig. 1 demonstrates study selection flow. In phase 1, 2 reviewers had interobserver agreement of 81%, κ (SE) = 0.70. In phase II of study selection, agreement was 95%, κ (SE) = 0.88 (12). A total of 5 studies qualified for study eligibility from 4 countries. Of the included studies, 3 were case control [14-16] in study design, and 2 were before-and-after studies [17,18]. In studies of before-and-after study design, same patients were considered as cases (before volume repletion) and controls (after volume repletion). Overall, 86 cases and 189 controls were studied. Table 2 summarizes characteristics of included studies. Fig. 2 summarizes studies' qualities that were mainly limited for assessment of IVC diameter was not blinded for volume status. All the studies have measured IVC diameter of hepatic segment.

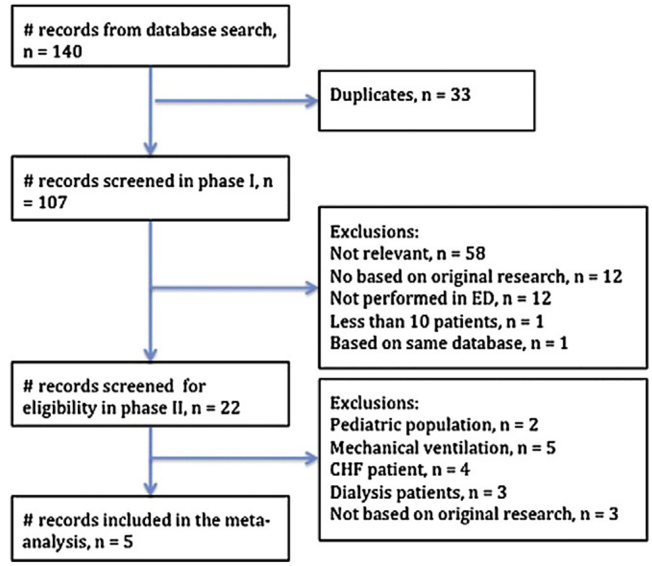

Fig. 1 Flow diagram of study selection.

As shown in Fig. 2, maximal IVC diameter was significantly in shock group when compared with euvolumic controls, mean (95% confidence interval) difference was 6.3 mL (6.0-6.5 mL). On *I*-square statistics, there was significant heterogeneity between studies in IVC diameter, *I*-square = 99%. One of the evident sources of heterogeneity is the difference in size of IVC diameter both in hypovolumic and euvolumic status in different ethnic populations, lower being in Asian population studies by Yanagawa et al [14,17] and higher in white [18].

4. Limitations

Major limitation of this meta-analysis is number of studies. Attempt has been made to include more studies by using liberal inclusion criteria, but there was no increase in number of studies potentially eligible for this systematic review. Another limitation of this meta-analysis is significant heterogeneity among studies that could not be explained. A subgroup analysis based on ethnic group has not been done due to very few numbers of studies being available.

5. Summary of findings

This systematic review included 5 prospectively conducted studies in adult ED population studying change in IVC diameter based on volume status. The maximal IVC diameter during expiration measured in hepatic segment is

Table 2 Characteristics of included studies

Author/country/year of publication	Study design	Age, mean (SD), y	% of male; cases/controls	Subject selection	Exclusion criteria	Control group	IVC measurement
Akhili/Turkey/2010	Case control	Cases: 36 (15) Controls: 36 (11)	54/44	Early stage of hemorrhagic shock (trauma or GI bleed) and had mild level of shock findings according to the classification of the American College of Surgeons	History of cor pulmonale, TR, CHF, renal failure, portal HTN, taking antihypertensives or inotropic agents or an eventual diagnosis of cardiac tamponade and/or pneumothorax	Age- and sex-matched healthy volunteers	• Maximal AP diameter at entrance of hepatic vein into IVC • By 2 ED physicians with trauma radiology training and averaged
Sefidbakht/Iran/2007	Case control	Cases: 32 (7) Controls: 38 (9)	73/79	Hypotensive trauma patients presented within 1.5 h of injury without significant amount of infusion	Cardiopulmonary arrest or unsuitable for USG visualization of IVC due to technical problems (severe obesity, severe gas distension, stab wound at the epigastrium, etc)	Age- and sex-matched normotensive trauma patients	• Maximal AP diameter just below the diaphragm in the hepatic segment • By 2 radiologists
Yanagawa/Japan/2005	Case control	Cases: 53 (6) Controls: 39 (4)	50/76	All trauma patients with shock; shock was defined as systolic BP of <90 mm Hg with clinical manifestations	Cardiopulmonary arrests or unsuitable for USG visualization of the IVC because of obesity, a full stomach, or a stab wound at the epigastrium	Normotensive adult trauma patients	• Maximal AP diameter of retrohepatic segment • By critical care physician independently and values were averaged
Weekes/United States/2011	Before and after	63 (18)	46/46	Presented to ED with hypotension (systolic BP <100; MAP <65) with signs and symptoms of shock and ED physician intended to use fluid challenge	Unstable or absent cardiac rhythm Suspected CHF, inability to obtain adequate quality US images, known pregnancy Significant traumatic condition Inability of the patient to tolerate the positioning for the USG examination or predicted ED stay of <45 min	Cases after 20-min fluid challenge	• Maximal AP diameter at approximately 3 cm caudal to the junction of the right atrium
Yanagawa/Japan/2007	Before and after	41 (5)	69/69	All trauma patients with shock transferred to level 1 trauma center	Admitted during night or BP did not respond to fluid resuscitation	Cases after normalization of BP with fluid resuscitation	• Maximal IVC diameter just below the diaphragm by 2 critical care physicians and averaged

TR indicates tricuspid regurgitation; CHF: congestive heart failure; AP, anteroposterior; BP, blood pressure; MAP, mean arterial pressure; GI, gastrointestinal.

	Cases			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Akilli 2010	14	1.2	28	29	2.4	50	9.6%	−15.00 [−15.80, −14.20]
Sefidbakht 2007	5.6	0.8	11	11.9	2.2	77	13.2%	−6.30 [−6.98, −5.62]
Weekes 2011	15.5	7.3	24	20.7	4.9	24	0.5%	−5.20 [−8.72, −1.68]
Yanagawa 2005	7.7	0.3	10	13.4	0.7	25	55.7%	−5.70 [−6.03, −5.37]
Yanagawa 2007	6.9	0.7	13	10.7	0.7	13	21.1%	−3.80 [−4.34, −3.26]
Total (95% CI)			86			189	100.0%	−6.26 [−6.51, −6.02]

Heterogeneity: $Chi^2 = 550.03$, df = 4 ($P < .00001$); $I^2 = 99\%$
Test for overall effect: Z = 49.64 ($P < .00001$)

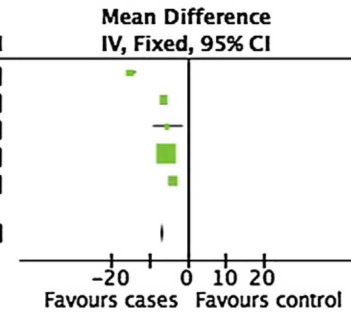

Fig. 2 Weighted mean difference in inferior vena cava diameter.

consistently and significantly lower in hypovolemic status when compared on euvolemic status. Included studies enrolled patients with wide spectrum of disease severity. With increasing popularity of point-of-care sonography, IVC diameter could be a reliable and quick mode of volume status assessment and guide fluid resuscitation in adult population in ED [19].

Collapsibility index of IVC or caval index, which is defined as IVC expiration (IVC inspiration/IVC expiration), can also be measured using bedside USG. The collapsibility index is associated with the volume status. It was found to be significantly higher in patients with volume loss as compared with the control group [18]. This signifies that as circulating blood volume decreases, IVC diameter decreases, furthermore, during the inspiration phase of respiration, and eventually collapses.

Sonographic measurement of IVC diameter is dependent on technology and expertise level of personnel performing and interpreting. Availability of smaller and less expensive ultrasound equipment providing higher quality image have increased its feasibility for bedside use in quick examination and image interpretation. With increasing popularity, more and more clinicians from different specialties are getting well versed with USG. Measurement of IVC diameter had shown excellent interobserver agreement among emergency medicine physicians [12]. There is evidence that IVC diameter measured on computed tomography is diagnostic for shock stage, but it is not favorable in terms of cost, time, and radiation exposure ED [20], whereas bedside USG is fairly inexpensive and devoid of radiation exposure associated with computed tomographic examination. The maximal IVC diameter and rate of change with fluid resuscitation are also found to be prognostic of response to fluid resuscitation in adults with shock [17].

6. External validity of results and future directions

The studies in this systematic review included subjects from academic urban ED or equivalent setting from 4 different countries. Subjects represented wise spectrum of disease severity. Hence, study results have good external validity. Controls in each study were not significantly different from cases apart from volume status, and the IVC is measured in the same way in cases and controls to minimize confounders. Thus, the difference in IVC diameter between cases and controls could be attributed to volume status with great confidence.

7. Conclusion

Meta-analysis of prospective studies reporting sonographic measurement of IVC diameter and its relationship with volume status suggest its potential usability in guiding fluid resuscitation in adult ED population under spontaneous ventilation.

References

[1] Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet 1997;349(9061):1269-76.
[2] Wilson M, Davis DP, Coimbra R. Diagnosis and monitoring of hemorrhagic shock during the initial resuscitation of multiple trauma patients: a review. J Emerg Med 2003;24(4):413-22.
[3] Manning J. Fluid and blood resuscitation in Emergency medicine: a comprehensive study guide. New York: McGraw-Hill; 2004.
[4] Moreno FL, Hagan AD, Holmen JR, et al. Evaluation of size and dynamics of the inferior vena cava as an index of right-sided cardiac function. Am J Cardiol 1984;53(4):579-85.
[5] Nette RW, Ie EH, Vletter WB, et al. Norepinephrine-induced vasoconstriction results in decreased blood volume in dialysis patients. Nephrol Dial Transplant 2006;21(5):1305-11.
[6] Feissel M, Michard F, Faller JP, et al. The respiratory variation in inferior vena cava diameter as a guide to fluid therapy. Intensive Care Med 2004;30(9):1834-7.
[7] Mandelbaum A, Ritz E. Vena cava diameter measurement for estimation of dry weight in haemodialysis patients. Nephrol Dial Transplant 1996;11(Suppl 2):24-7.
[8] Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;283(15):2008-12.
[9] Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009;339:b2535.

[10] Whiting P, Rutjes AW, Reitsma JB, et al. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. BMC Med Res Methodol 2003;3:25.

[11] Wells GA, Brodsky L, O'Connell D, Shea B, Henry D, Mayank S, Tugwell P. An evaluation of the Newcastle Ottawa Scale: an assessment tool for evaluating the quality of non-randomized studies. XI Cochrane Colloquium: Evidence, Health Care & Culture. Volume 26. Barcelona, Spain; 2003.

[12] Fields JM, Lee PA, Jenq KY, et al. The interrater reliability of inferior vena cava ultrasound by bedside clinician sonographers in emergency department patients. Academic Emergency Medicine 2011;18(1): 98-101.

[13] Morishita Y, Ando Y, Ishii E, et al. Comparison of markers of circulating blood volume in hemodialysis patients. Clin Exp Nephrol 2005;9(3):233-7.

[14] Yanagawa Y, Nishi K, Sakamoto T, et al. Early diagnosis of hypovolemic shock by sonographic measurement of inferior vena cava in trauma patients. J Trauma 2005;58(4):825-9.

[15] Sefidbakht S, Assadsangabi R, Abbasi HR, et al. Sonographic measurement of the inferior vena cava as a predictor of shock in trauma patients. Emergency Radiology 2007;14(3):181-5.

[16] Akilli B, Bayir A, Kara F, et al. Inferior vena cava diameter as a marker of early hemorrhagic shock: a comparative study. Ulus Travma Acil Cerrahi Derg 2010;16(2):113-8.

[17] Yanagawa Y, Sakamoto T, Okada Y. Hypovolemic shock evaluated by sonographic measurement of the inferior vena cava during resuscitation in trauma patients. J Trauma Inj Infect Crit Care 2007;63(6):1245-8 [discussion 1248].

[18] Weekes AJ, Tassone HM, Babcock A, et al. Comparison of serial qualitative and quantitative assessments of caval index and left ventricular systolic function during early fluid resuscitation of hypotensive emergency department patients. Acad Emerg Med 2011; 18(9):912-21.

[19] Moore CL, Copel JA. Point-of-care ultrasonography. N Engl J Med 2011;364(8):749-57.

[20] Vu C, Ray C, Vu T, et al. Is IVC size predictive of shock? Am J Roentgenol 2010;194(5):192.

Appendix A. Search Strategy

Ovid Databases

Embase 1988 to 2011 Week 38, Ovid MEDLINE(R) 1996 to September Week 2 2011, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to September 2011, EBM Reviews - ACP Journal Club 1991 to September 2011, EBM Reviews - Database of Abstracts of Reviews of Effects 3rd Quarter 2011, EBM Reviews - Cochrane Central Register of Controlled Trials 3rd Quarter 2011, EBM Reviews - Cochrane Methodology Register 3rd Quarter 2011, EBM Reviews - Health Technology Assessment 3rd Quarter 2011, EBM Reviews - NHS Economic Evaluation Database 3rd Quarter 2011

1 DIAMETER.ab. or DIAMETER.ti. or DIAMETER.kw. n = 260702
2 Inferior Vena cava.ab. or INFERIOR VENA CAVA.ti. or Inferior Vena cava.kw. n = 17424
3 (hypovolumic or hemorrhagic or shock or volume status).ab. or hypovolumic.kw. or hemorrhagic.kw. or volume status.kw. or shock.kw. or hemorrhagic.ti. or volume status.ti. or shock.ti. or hypovolumic.ti. n = 214116
4 #1 AND #2 AND #3, n = 77
5 Remove duplicates from #4, n = 47

SCOPUS:

6 6. (TITLE-ABS-KEY(inferior vena cava)) AND (TITLE-ABS-KEY(diameter)) AND ((TITLE-ABS-KEY(VOLUME status) OR TITLE-ABS-KEY(hemorrhagic) OR TITLE-ABS-KEY(hypovolumic) OR TITLE-ABS-KEY(shock)) AND SUBJAREA(mult OR medi OR nurs OR vete OR dent OR heal) AND PUBYEAR > 1995), n = 56

Web of Science:

7 Title = (Inferior Vena cava) OR Topic = (Inferior Vena cava) Databases = SCI-EXPANDED Timespan = All Years, n = 7776
8 Title = (diameter) OR Topic = (diameter) Databases = SCI-EXPANDED Timespan = All Years, n = 278,096
9 Title = (shock) OR Topic = (shock) OR Title = (hypovolumic) OR Topic = (hypovolumic) OR Title = (hemorrhagic) OR Topic = (hemorrhagic) OR Title = (voolume status) OR Topic = (volume status) Databases = SCI-EXPANDED Timespan = All Years, n = 194,954
10 #7 AND #8 AND #9, n = 64
11 #5 AND #6 AND #10, N = 140
12 Remove duplicate from 11, n = 107