Correlation Between Internal Jugular Vein Collapsibility Index and Mean Arterial Pressure in Assessing the Response of Fluid Resuscitation in Critically Ill Patients

Critical Care and Shock, Vol. 26 No. 3, Juni 2023

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Dr. Bambang Pujo Semedi, dr., SpAn-TI., Subsp. TI(K)., Subsp. An.Ped(K)

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SUBMISSION

11 MARET 2023

Manuscript submission Bambang Pujo Semedi

Bambang Pujo Semedi <bambang-p-s@fk.unair.ac.id> Sat, Mar 11, 2023 at 9:38 AM
To: "critcareshock@gmail.com" <critcareshock@gmail.com>

Dear Dr Simon Nanlohy, MD
Editor-in-Chief
Critical Care and Shock

I am please to informed you that we would like to submit our manuskrip entitled "Correlation Between Internal Jugular Vein Collapsibility Index and Mean Arterial Pressure in Assessing The Response of Fluid Resuscitation In Critically-Ill Patients" to be considered for publication by critical Care and Shock.

Hereby I attached the documents as follows :

1. Cover Letter
2. Tittle Page
3. Main Body Text
4. Table & Figure

We believe that the manuscript is appropriate for the publication because it contains new data regarding the practice of internal vein jugular collapsibility index in resources constrained setting

Thank you very much for the consideration

Looking forward to hearing from you soon

Kindly regards,

Bambang Pujo Semedi, MD

Consultant Anestesiologist and Intensivist

The Head of Department of Anaesthesiology and Reanimation

Faculty of Medicine, Universitas Airlangga

Dr Soetomo General Academic Hospital, Surabaya, Indonesia.

Critical Care and Shock BPS 11 maret 2023 FINAL.docx
1750K

CORRESPONDING AUTHOR CHANGED

13-15 MARET 2023

Bambang Pujo Semedi <bambang-p-s@fk.unair.ac.id>

Manuscript submission Bambang Pujo Semedi

Critical Care and Shock <critcareshock@gmail.com> Mon, Mar 13, 2023 at 11:47 PM
To: Bambang Pujo Semedi <bambang-p-s@fk.unair.ac.id>

Dear Bambang,

Thank you for your email and the article intended to be published in Critical Care and Shock.
We saw that the corresponding author is not you. FYI, it is our policy to only communicate with the corresponding author. It is to make sure that our readers can communicate with him/her easily somedays. Therefore, we want to suggest that you change the corresponding author to you or ask Prof. Rehatta to email us. After this issue is clear, then we will accept the article to be published in the June 2023 issue.
Thank you for your kind understanding. We look forward to hearing from you soon.

Best regards,
Simon
[Quoted text hidden]

Manuscript submission Bambang Pujo Semedi

Bambang Pujo Semedi <bambang-p-s@fk.unair.ac.id> Tue, Mar 14, 2023 at 6:24 AM
To: Critical Care and Shock <critcareshock@gmail.com>

Dear dr Simon.

There is no problem with the corresponding author. We are always in active contact with her easily.

Thank you for your information

Best regards
Bambang Pujo Semedi
[Quoted text hidden]

Manuscript submission Bambang Pujo Semedi

Critical Care and Shock <critcareshock@gmail.com> Tue, Mar 14, 2023 at 12:04 PM
To: Bambang Pujo Semedi <bambang-p-s@fk.unair.ac.id>

Dear Bambang,

Thank you for your immediate response. We assume that you would like to change the corresponding author name from you to her. Are we right?

Simon
[Quoted text hidden]

Manuscript submission Bambang Pujo Semedi

Bambang Pujo Semedi <bambang-p-s@fk.unair.ac.id> Tue, Mar 14, 2023 at 12:06 PM
To: Critical Care and Shock <critcareshock@gmail.com>

Yes, that is correct.
[Quoted text hidden]

Bambang Pujo Semedi <bambang-p-s@fk.unair.ac.id>

Manuscript submission Bambang Pujo Semedi

Critical Care and Shock <critcareshock@gmail.com> Tue, Mar 14, 2023 at 12:10 PM
To: Bambang Pujo Semedi <bambang-p-s@fk.unair.ac.id>

Ok, no problem. We will reply her email.
Thank you for the confirmation.

Best wishes,
Simon
[Quoted text hidden]

Nancy Margarita Rehatta <rita@fk.unair.ac.id>

Manuscript Bambang Pujo Semedi

EXECUTIVE DIRECTOR <rita@fk.unair.ac.id> 14 March 2023 at 06:37
Reply-To: dir_chen16@yahoo.com.tw
To: "critcareshock@gmail.com" <critcareshock@gmail.com>, Bambang Semedi <bpsemedi@gmail.com>

Dear Dr Simon Nanlohy,MD
Editor-in-Chief
Critical Care and Shock

I am pleased to informed you that we would like to submit our manuscript entitled "Correlation between internal jugular vein collapsibility index and mean arterial pressure in assessing the response of fluid resuscitation in critically ill patients" to be considered for publication by Critical Care and Shock. I will always in active contact with you easily.

Best regards,
Prof Rita

INFORMATION OF ARTICLE PROCESSING CHARGE TERMS

15 MARET 2023

Nancy Margarita Rehatta <rita@fk.unair.ac.id>

Manuscript Bambang Pujo Semedi

Critical Care and Shock <critcareshock@gmail.com> 15 March 2023 at 00:16
To: rita@fk.unair.ac.id

Dear Professor Rehatta,

It is our pleasure to receiving your article. We have accepted it to be published in the June 2023 issue.
Please be informed that there is a publication fee of USD 600.00. If you agree with those terms, we will send you the invoice.
Thank you for your kind attention, and looking forward to hearing from you.

Best regards,
Simon
[Quoted text hidden]

INVOICE RECEIVED

15 MARET 2023

Nancy Margarita Rehatta <rita@fk.unair.ac.id>

Manuscript Bambang Pujo Semedi

EXECUTIVE DIRECTOR <rita@fk.unair.ac.id> 15 March 2023 at 04:16
Reply-To: dir_chen16@yahoo.com.tw
To: Critical Care and Shock <critcareshock@gmail.com>

Dear Dr Simon

We agree with those terms.
Thank you for your information.

Best regards,
Prof Rita
[Quoted text hidden]

Nancy Margarita Rehatta <rita@fk.unair.ac.id>

Invoice from Critical Care and Shock Journal (002/CCS/III/2023)

1 message

Critical Care and Shock Journal <service@intl.paypal.com> 15 March 2023 at 12:00
Reply-To: Critical Care and Shock Journal <critcareshock@gmail.com>
To: "rita@fk. unair. ac. id" <rita@fk.unair.ac.id>

Dear rita@fk.unair.ac.id,

You've received an invoice.

Critical Care and Shock Journal sent you an invoice for $600,00 USD

Minimum due:

Due date: 25 March 2023

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Seller note to customer

Since you are the author from Indonesia, you may pay this publication fee using our PayPal account or transfer the money directly to our account below: Name: Simon Nanlohy Bank: Sinarmas Account number: 0047684757 Amount: Rp 9,180,000 Thank you.

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15 MARET 2023

Nancy Margarita Rehatta <rita@fk.unair.ac.id>

Manuscript Bambang Pujo Semedi

EXECUTIVE DIRECTOR <rita@fk.unair.ac.id> 15 March 2023 at 12:59
Reply-To: dir_chen16@yahoo.com.tw
To: Critical Care and Shock <critcareshock@gmail.com>, Bambang Semedi <bpsemedi@gmail.com>

Dear Dr Simon

Thank you for your invoice. This is our payment.

Best reards
Prof Rita

[Quoted text hidden]

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Penerima

SIMON NANLOHY

Bank Sinarmas - 0047684757

Detail Transaksi

Nominal Transfer	**Rp 9.180.000**
Metode Transfer	BI Fast
Tujuan Transaksi	Lainnya
Biaya Transaksi	**Rp 2.500**
Total Transaksi	**Rp 9.182.500**

Rekening Sumber

ARINA SETYANINGTYAS

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Keterangan Transaksi

publication fee BPS RITA 002ccs3

Nancy Margarita Rehatta <rita@fk.unair.ac.id>

Manuscript Bambang Pujo Semedi

Critical Care and Shock <critcareshock@gmail.com> 15 March 2023 at 13:11
To: rita@fk.unair.ac.id

Dear Professor,

Thank you for the payment.
We will contact you later with the galley proof of your article or if we have any questions regarding your article.

Best regards,
Simon
[Quoted text hidden]

LETTER OF ACCEPTANCE REQUESTED

15 MARET 2023

Nancy Margarita Rehatta <rita@fk.unair.ac.id>

Manuscript Bambang Pujo Semedi

EXECUTIVE DIRECTOR <rita@fk.unair.ac.id> 15 March 2023 at 17:21
Reply-To: dir_chen16@yahoo.com.tw
To: Critical Care and Shock <critcareshock@gmail.com>

Dear Dr Simon
Thank you very much.
May we get the letter of acceptance of the journal officially?

Best regards
Prof Rita

[Quoted text hidden]

LETTER OF ACCEPTANCE RECEIVED

18 MARET 2023

Nancy Margarita Rehatta <rita@fk.unair.ac.id>

Manuscript Bambang Pujo Semedi

Critical Care and Shock <critcareshock@gmail.com> 18 March 2023 at 03:01
To: rita@fk.unair.ac.id

---------- Forwarded message ---------
From: **Critical Care and Shock** <critcareshock@gmail.com>
Date: Sat, Mar 18, 2023, 2:30 AM
Subject: Re: Manuscript Bambang Pujo Semedi
To: <dir_chen16@yahoo.com.tw>

Dear Professor,

Please find attached the Acceptance Letter you requested.
Thank you.

Best wishes,
Simon
[Quoted text hidden]

Nancy Margarita Rehatta, 002.CCS.III.2023.pdf
88K

Critical Care&Shock

Editor-in-Chief: Prof. Joseph Varon, MD, FACP, FCCP, FCCM

Jl. Tawakal Raya No. 21, Jakarta 11440, Indonesia
Contact name: Simon Nanlohy
Email: critcareshock@gmail.com
Web: https://criticalcareshock.com/

Acceptance letter

18 March 2023

Professor Nancy Margarita Rehatta,
Department of Anesthesiology and Reanimation, Dr. Soetomo General Academic Hospital, Faculty of Medicine, Universitas Airlangga, Surabaya 60132, Indonesia

Dear Professor,

Thank you for submitting your article intended to be published in Critical Care and Shock Journal (ISSN: 14107767). Our reviewers have reviewed it, and we are glad to let you know that we have accepted it. The detailed data of your article are as follows:

1. Title: "Correlation between internal jugular vein collapsibility index and mean arterial pressure in assessing the response of fluid resuscitation in critically ill patients"
2. Author(s): Bambang Pujo Semedi, Nancy Margarita Rehatta, Jusak Nugraha, Soetjipto, Ronald Melviano, Arie Utariani.
3. Corresponding author and affiliation: Professor Nancy Margarita Rehatta. Department of Anesthesiology and Reanimation, Dr. Soetomo General Academic Hospital, Faculty of Medicine, Universitas Airlangga, Surabaya 60132, Indonesia.
4. Time of publication: June 2023.

Best regards,

Simon Nanlohy, MD

REVIEW 1

17 APRIL 2023

Nancy Margarita Rehatta <rita@fk.unair.ac.id>

Manuscript Bambang Pujo Semedi

Critical Care and Shock <critcareshock@gmail.com> 17 April 2023 at 18:07
To: rita@fk.unair.ac.id

Dear Professor,

When did you cite Ref 12?

Simon
[Quoted text hidden]

MANUSCRIPT REVISED 1

17 APRIL 2023

Nancy Margarita Rehatta <rita@fk.unair.ac.id>

Manuscript Bambang Pujo Semedi

EXECUTIVE DIRECTOR <rita@fk.unair.ac.id> 17 April 2023 at 19:18
Reply-To: dir_chen16@yahoo.com.tw
To: Critical Care and Shock <critcareshock@gmail.com>

Dear Dr Simon.

This is our manuscript that we have revised. Thank you for your correction.

Best Regards,

Prof Rita
[Quoted text hidden]

Critical Care and Shock BPS 17 april 2023 revision.docx
1754K

To,

The Editor

Sub: Submission of Manuscript for publication

Dear Sir,

We intend to publish an article entitled **"Correlation Between Internal Jugular Vein Collapsibility Index And Mean Arterial Pressure In Assessing The Response Of Fluid Resuscitation In Critically-Ill Patients "** in your esteemed journal as an Original Article.

On behalf of all the contributors I will act and guarantor and will correspond with the journal from this point onward.

Prior publication : none

Support : none

Conflicts of interest : none

Permissions : none

We hereby transfer, assign, or otherwise convey all copyright ownership, including any and all rights incidental thereto, exclusively to the journal, in the event that such work is published by the journal.

We would like to suggest following referees for the article.

Thanking you,

Your's sincerely,

Corresponding contributor

Prof Dr. Nancy Margarita Rehatta, dr, Sp.An.KIC.KNA

Department of Anesthesiology and Reanimation, Faculty of Medicine, University Airlangga, Dr. Soetomo General Academic Hospital, Surabaya 60132, East Java Indonesia Telp +62315020251

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Manuscript Title: Correlation Between Internal Jugular Vein Collapsibility Index And Mean Arterial Pressure In Assessing The Response Of Fluid Resuscitation In Critically-Ill Patients

I/we certify that I/we have participated sufficiently in the intellectual content, conception and design of this work or the analysis and interpretation of the data (when applicable), as well as the writing of the manuscript, to take public responsibility for it and have agreed to have my/our name listed as a contributor. I/we believe the manuscript represents valid work. Each author confirms they meet the criteria for authorship as established by the ICMJE. Neither this manuscript nor one with substantially similar content under my/our authorship has been published or is being considered for publication elsewhere, except as described in the covering letter. I/we certify that all the data collected during the study is presented in this manuscript and no data from the study has been or will be published separately. I/we attest that, if requested by the editors, I/we will provide the data/information or will cooperate fully in obtaining and providing the data/information on which the manuscript is based, for examination by the editors or their assignees. Financial interests, direct or indirect, that exist or may be perceived to exist for individual contributors in connection with the content of this paper have been disclosed in the cover letter. Sources of outside support of the project are named in the cover letter.

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All persons who have made substantial contributions to the work reported in the manuscript, but who are not contributors, are named in the Acknowledgment and have given me/us their written permission to be named. If I/we do not include an Acknowledgment that means I/we have not received substantial contributions from non-contributors and no contributor has been omitted.

Name	**Signature**	**Date signed**
1 Bambang Pujo Semedi, MD Anesthesiology Consultant & Intensivist		March 9, 2023
2. Prof Dr. Nancy Margarita Rehatta, MD Anesthesiology Consultant & Intensivist		March 10,2023
3. Prof. Dr. Jusak Nugraha, MD Consultant Clinical Pathologist		March 10, 2023
4. Prof Soetjipto, MD, MS, PhD		March 10,2023
5. Ronald Melviano, MD Anesthesiologist		March 9, 2023
6. Dr Arie Utariani, MD Pediatric Anesthesiology Consultant		March 9,2023

Type of article: Original

Title of the article: **Correlation Between Internal Jugular Vein Collapsibility Index And Mean Arterial Pressure In Assessing The Response Of Fluid Resuscitation In Critically-Ill Patients** Authors

Bambang Pujo Semedi, MD

Doctoral Program of Medical Science, Faculty of Medicine, Universitas Airlangga, Surabaya, East Java, Indonesia

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1. Prof Dr. Nancy Margarita Rehatta, MD
   Department of Anesthesiology and Reanimation, Dr. Soetomo General Academic Hospital, Faculty of Medicine, University Airlangga, Surabaya 60132, East Java Indonesia Telp +62315020251
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3. Prof Soetjipto, MD, MS, Ph.D
   Department of Medical Biochemistry, Faculty of Medicine, Airlangga University, Surabaya, Indonesia, Indonesia
4. Ronald Melviano, MD
   Anesthesiologist
   Samuel Kristian Lerik Regional Public Hospital, Kupang, East Nusa Tenggara, Indonesia.

5. Dr Arie Utariani, MD

Pediatric Anesthesiologist Consultant

Department of Anesthesiology and Reanimation, Dr. Soetomo General

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Indonesia Telp +62315020251

Affiliations

Doctoral Program of Medical Science, Faculty of Medicine, Universitas

Airlangga, Surabaya, East Java, Indonesia

(Running title)

Address (including email) of the corresponding author

Prof Dr. Nancy Margarita Rehatta, MD

Department of Anesthesiology and Reanimation, Faculty of Medicine, University

Airlangga, Dr. Soetomo General Academic Hospital, Surabaya 60132, East Java

Indonesia Telp +62315020251

Email : rita@fk.unair.ac.id

Total number of pages: 13

Total number of photographs: 2

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for the text: 2562

Source(s) of support: no

Presentation at a meeting: no

Conflicting Interest (If present, give more details): no

Contribution Details (to be ticked marked as applicable):

	Bambang Pujo Semedi	Nancy Margarita Rehatta	Jusak Nugraha	Soetjipto	Ronald Melviano	Arie Utariani
Concepts	✓	✓	✓	✓	✓	✓
Design	✓	✓	✓	✓	✓	✓
Definition of intellectual content	✓	✓	✓	✓	✓	✓
Literature search	✓	--	--	--	✓	✓
Clinical studies	✓	--	--	--	✓	✓
Experimental studies	✓	--	--	--	✓	✓
Data acquisition	✓	--	--	--	✓	✓
Data analysis	✓	--	--	--	✓	✓
Statistical analysis	✓	--	--	--	✓	✓
Manuscript preparation	✓	--	--	--	✓	✓
Manuscript editing	✓	--	--	--	--	--
Manuscript review	✓	--	--	--	--	--

Title of the article: **Correlation Between Internal Jugular Vein Collapsibility Index And Mean Arterial Pressure In Assessing The Response Of Fluid Resuscitation In Critically-Ill Patients**

Abstract:

Background: Response to resuscitative fluid administration is often difficult to assess clinically, especially in critically-ill patients, and therefore it is necessary to use tools to evaluate the response. One of the modalities that can be used is ultrasonography to measure the internal jugular vein collapsibility index (IJVCI) during the respiration cycle

Aim: To evaluate the correlation between IJVCI and mean arterial pressure (MAP) in assessing response to resuscitative fluid administration in critically-ill patients.

Patients and Methods: This is an experimental study with pre-post test groups, assessing the response to resuscitative fluid administration in critically-ill patients.

Results: A total of 28 subjects aged 18–65 years old were included in the inclusion criteria of this study. The average age of subjects was 50.18 years. Twenty-one subjects responded to to the administration of 500 mL RL crystalloid fluid within 30 minutes based on the internal jugular vein collapsibility index. Subjects were observed into two periods, the pre-test and post-test periods. There was a significant difference in the IJVCI before and after 500 mL of RL between two groups ($p<0.05$). As a predictor of IJVCI associated with increased MAP at the cut-off value of 44.40 with a sensitivity of 76.9% and a specificity of 80%. This study showed that IJVCI has a negative correlation with increased MAP ($p<0.05$).

Conclusions :The measurement of the internal jugular vein collapsibility index can be used to assess the response to resuscitative fluid administration in critically-ill patients.

Keywords: IJVCI, MAP, critically-ill patients.

Introduction:

Assessment of intravascular volume status and hypovolemia in critically-ill patients in the ICU or resuscitation room is often an issue, especially if only relying on physical examination and vital signs. The use of portable echocardiography to measure the inferior vena cava collapsibility index (IVC) during the respiration cycle can predict the assessment of cardiac output (CO) but has limitations in terms of lack of equipment availability, ultrasound expertise, and difficulty in identifying the inferior vena cava.[1,2] Critical illness is defined as a disease process that causes instability of the body's physiology, which can lead to failure of bodily functions or death in a short period of time. System disorders that cause death most quickly are generally disorders of the neurological, cardiovascular, and respiratory systems. [3]

Accurate assessment of intravascular volume status for treating severe hypovolemia or shock is very challenging but has a very important role in critical illness. It is important to avoid administering fluids that can increase morbidity and mortality, and therefore assessing fluid response in critically-ill patients precisely and accurately is very important.[2]

Studies have shown that the response to fluid administration can be defined as a 15% increase in stroke volume (SV), cardiac output (CO), or mean arterial pressure (MAP) after administration of 500 mL of fluid. Mean arterial pressure (MAP) is defined as the average arterial pressure in one cardiac cycle, systolic and diastolic. Cardiac output and systemic vascular resistance affect MAP.[1,4] Imaging techniques using ultrasonography have reported that the internal jugular vein collapsibility index (IJVCI) indicative of hypovolemic conditions is <39%.[5, 6, 7, 8, 9, 10, 11, 12] The Sequential Organ Failure Assessment (SOFA) score is a scoring system to

determine the extent of organ failure in an individual. The score is based on six different values, each representing respiratory, cardiovascular, liver, coagulation, renal, and nervous system parameters The greater the score, the higher the mortality rate.[13] Other studies recommended the use of shock index (SI). Shock index (SI), is the ratio of the ratio of heart rate (HR) to systolic blood pressure (SBP). [14]

This prospective study was conducted to evaluate the correlation between IJVCI and mean arterial pressure (MAP) in assessing response to resuscitative fluid administration in critically-ill patients.

Subjects and Methods:

This is an experimental study with pre-post test groups in critically-ill patients. Assessment of the response to resuscitative fluid administration uses mean arterial pressure >15%, which is associated with the internal jugular vein collapsibility index. The study was conducted in the intensive care unit (ICU) of Dr. Soetomo General Academic Hospital Surabaya from April 2016 to May 2016. The subjects were patients between the ages of 18–65 years old, breathing spontaneously or fully controlled by mechanical ventilation, approved by the family to participate in the study with a signed consent form, and an internal jugular vein collapsibility index of >40%. The subjects did not have spinal cord injury, cardiac arrhythmia, irregular breathing pattern, and hemorrhage.

Criteria for critical illness: an illness with impairment of one or more vital functions (respiratory, cardiovascular, neurological) that if not treated immediately will be life-threatening in a short period of time.

Response to fluid administration:

Internal jugular vein collapsibility index: A comparative measurement of the internal jugular vein diameter during inspiration and expiration using ultrasonography with a linear transducer of 7–10 MHz.

Fluid challenge: A procedure of administering a limited amount of fluid within a predetermined time to assess the response to volume addition. In this study, 500 mL of Ringer's lactate solution was administered within 30 minutes.

Response to fluid administration: The presence of change in hemodynamic status following a fluid challenge is determined by measuring mean arterial pressure. If the MAP is >15%, the patient is considered responsive to fluid administration.

Research Flow

a. Patients with critical illness who met the inclusion criteria had their internal jugular vein collapsibility index measured using ultrasonography with a linear transducer of 7-10 MHz.
b. Performed fluid challenge by administering 500 mL of Ringer's lactate solution within 30 minutes.
c. Measurement of internal jugular vein collapsibility index using ultrasonography with a linear transducer of 7-10 MHz by a standardized researcher.

Data Collection

Data collection includes the name, age, sex, vital signs, primary diagnosis, SOFA score and internal jugular vein collapsibility index measurement.

Data Analysis

The study data were collected from the two periods prior to and following treatment, and are then analyzed using SPSS for Windows 20.0 software (IBM, Armonk, NY,

USA). Numerical data were tested for normality with Shapiro Wilk, where data with normal distribution were presented in terms of mean and standard deviation (SD), and data with non-normal distribution were given in median and minimum, and maximum range values. The two means which were normally distributed were analyzed using the T-test, and the paired t test analyzed those that were pre test and post test groups. Correlation between variables was carried out by bivariate analysis; data that were normally distributed were analyzed using Pearson's correlation, while abnormal data were analyzed using Spearman's correlation. The Receiver Operating Character (ROC) curve was used to find the optimal cut-off value and calculate the sensitivity and specificity for examining IJVCI and MAP. A p-value of less than 0.05 ($P < 0.05$) is considered a statistically significant difference.

Results:

Subject Characteristics

The study was conducted on 28 subjects aged 18–65 years old who suffered from critical illness, observed into two periods, the pre-test and post-test groups. The average age of patients with critical illness was 50.18 years. The average body weight of this study group was 55.29 kg. The mean SOFA score of this study group was 6.61 and the mean shock index was 2.1. (Table 1)..Meanwhile, the data for sex obtained from the results of statistical frequency tests identified 17 males and 11 females .

Based on Table 2, there were 24 patients with mechanical ventilation control and 4 with spontaneous breathing, in accordance to the inclusion criteria.

Difference In Hemodynamic Status Prior To And After 500 ml Rl Administration

To assess the response to fluid administration in critically-ill patients, MAP, and heart rate before and after 500 mL RL crystalloid solution administration within 30 minutes were compared.

There was a significant difference in MAP and heart rate values before and after the administration of 500 mL RL crystalloid solution within 30 minutes ($p<0.05$) (Table 3).

Difference In Internal Jugular Vein Collapsibility Index Prior To And After 500 ml RL Administration

Based on Table 4, the McNemar statistical test showed that there was a significant difference in the internal jugular vein collapsibility index before and after 500 mL of RL crystalloid fluid administration. Despite 7 subjects that were found to have no change in the internal jugular vein collapsibility index, 21 subjects had a decreased internal jugular collapsibility index.

The receiver operating characteristic (ROC) curve analysis was used to calculate the cut-off value, sensitivity, and specificity of IJVCI as predictors of responses in increasing of mean arterial pressure. Youden's index with the highest sum of sensitivity and specificity was used to determine the optimal cut-off value for differentiation. Based on ROC curve, IJVCI showed AUC 0.764 (95%CI [0.572-0.956]; p=0.018) [Figure 1]. Correlation analysis has been carried out with Spearman correlation to analyze the association of IJVCI and the increasing of MAP. It was found a significant that the IJVCI was negatively correlated with an increase in MAP ($r^2 = 0.510$; $p = 0.000$; Figure 2).

Discussion

The general concept of fluid challenge administration to quickly observe a response to fluids following a very limited amount of fluid administration, and there are 4 important elements that must be considered before conducting the technique[3]:

(a) Type of fluid. Either crystalloid or colloid can be used, as we already know about the advantages and benefits of each. In this case, neither is superior than the other, but the important thing to know is when to give and the reason for choosing that particular fluid. In this study, we used the 500 mL RL crystalloid fluid within 30 minutes with the expectation that the fluid we administered within that time period can still remain intravascular before entering the interstitial tissues, although in theory colloid fluids last longer in the intravascular but with side effects that may be greater than the administration of crystalloid fluids.

(b) The rate of fluid administration. A previous study by Muller L, Toumi M, et al. in 2011 conducted a fluid challenge technique using 100 ml crystalloid in the first 1 minute followed by 400 ml within 14 minutes, and found that it was safe to do so with a significant response and no significant side effects [15];

(c) Response assessment. The most important parameters to consider are clinical conditions that describe hemodynamic improvements such as blood pressure, MAP, and heart rate. The results of this study showed a significant difference ($p < 0.05$) in the comparative clinical parameters prior to and after 500 mL RL crystalloid fluid administration.

(d) Complications. Pulmonary edema due to congestive heart failure is the most serious complication of fluid administration. Assessment of the response to fluids using the internal jugular vein collapsibility index is influenced by cardiopulmonary

interactions, where the most influential factors are the intrathoracic pressure during respiration and venous return to the right atrium. Hyperinflation can cause the heart to be pushed into the cardiac fossa in addition to an increased intrathoracic pressure, and an increased pressure in the right atrium can also disrupt venous blood flow to the right atrium leading to a distention of the internal jugular vein. Response to fluid administration will be difficult to assess in patients with these problems, and 7 of the 28 study participants did not experience changes in the internal jugular vein collapsibility index prior to and after the administration of 500 mL RL crystalloid fluid within 30 minutes.

Assessment of volume status using the internal jugular vein collapsibility index has previously been performed by Keith Killu, Victor Coba et al. in 2010, which reported that an internal jugular vein collapsibility index of >39% is indicative of hypovolemia, and conversely that of <39% is indicative of normovolemia, with $p=0.001$ ($p < 0.05$).[5] In our study, we found that an internal jugular vein collapsibility index of 44.40 is the optimal cut-off value for differentiation normovolemia or hypovolemia. This suggests that the collapsibility index can be used to assess volume status.

The efficacy of evaluating the fluid administration response by using the internal jugular vein collapsibility index in the 28 subjects resulted in 21 subjects showed a response, with a change in collapsibility index following administration of 500 mL RL crystalloid fluid within 30 minutes, with a p value = 0.00^{a} ($p < 0.05$). This shows that there is a significant difference, which means that the internal jugular vein collapsibility index is effective for assessing fluid response.

Limitations

The sample selection of this study was not completely homogeneous, so in order to achieve good homogeneity, it is necessary to have similar disease types to assess the response to fluids. This study has not yet compared the effectiveness of assessing the response to fluid using the internal jugular vein collapsibility index with other modalities such as CVP and IVC, CI, and therefore further research needs to be conducted to assess the factors that affect the internal jugular vein collapsibility index. Discrepancies in response between the subjects may be due to other factors such as high intrathoracic pressure, cardiac contractility problems, or other causes. The presence of these factors can make the fluid response difficult to assess.

Conclusion

The internal jugular vein collapsibility index is effectively used to assess the response to resuscitative fluid administration in critically-ill patients aged 18–65 years old. There is a significant difference in the internal jugular vein collapsibility index prior to and after administration of 500 mL RL crystalloid fluid within 30 minutes. No significant side effects were onserved in the administration of 500 mL RL fluid within 30 minutes.

Approval from research ethics committee

This research has obtained approval from the Research Ethics Committee of Dr. Soetomo General Hospital Surabaya with the following number 447/ Panke.KKE/VI/2016.

Acknowledgement:

We thank all teacher, the resident, nursing staff, laboratory staff in Soetomo Hospital, Medical Science, Faculty of Medicine, Universitas Airlangga involved

in patient management and data collection, without whose hard work and dedication the study would not have been possible.

Abbreviations:

CO : Cardiac output

CI : Cardiac Index

CVP : Centrak venous pressure

IJVCI : Index Jugular Vascular Collapsibility Index

IVC : Inferior vena cava

MAP : Mean Arterial Pressure

RL : Ringer Lactate

ROC : receiver operating characteristic

SD : Standard deviation

SOFA : Sequential Organ Failure Assessment

SI : Shock Index

SV : Stroke volume

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Tables:

Table 1. Subject Characteristics

Characteristics	n	Mean	±SD
Age	28	50.18	17.304
Weight	28	55.29	10.484
SOFA	28	6.6071	2.16606
Shock Index	28	1.215	0.26
Initial MAP	28	62.6321	7.47856
Initial HR	28	111.1071	17.51050
RR	28	18.7500	3.53422
Final MAP	28	73.0929	7.41375
Final HR	28	105.4643	15.62638

Table 2. Frequency of respiratory assistance

Respiratory assistance	Frequency	Percentage (%)	Cumulative percentage (%)
Ventilator-controlled	24	85.7	85.7
Spontaneous breathing	4	14.3	100.0
Total	28	100.0	

Table 3. Comparison between Pre-test and Post Test Groups

Variables	**Pre-Test Groups**	**Post Test Goups**	**p value**
MAP, mean ± SD (mmHg)	62.63 ± 7.48	73.09 ± 7.4	0.000*
Heart rate, mean ± SD	111.11±17.51	105.46 ±15.62	0.000*
Sistolik Presure mean ± SD (mmHg)	89.71 ± 8.04	100.86 ± 9.59	0.000*
Shock Index	1.25 ± 0.26	1.05 ± 0.19	0.000*

[1]Paired T-test; *statistically significant ($p < 0.05$)

Table 4. The efficacy of internal jugular vein collapsibility index in evaluating fluid responsiveness

Initial IJV CI	Final IJV CI		N	Sig
	Low (<40%)	High (>40%)		
Low (<40%)	0	0		
High (>40%)	21	7	28	0.00[a]

Note: McNemar statistical test, *significant difference with p <0.05

Figure Legends

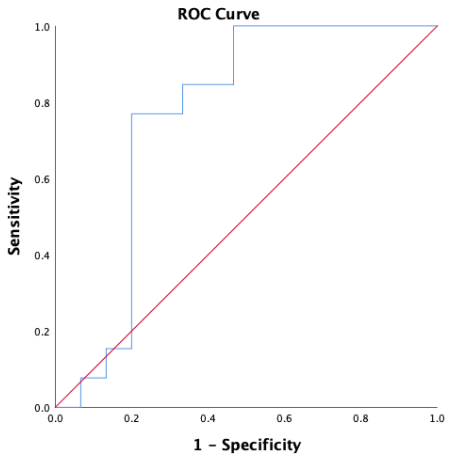

Figure 1. ROC curve of IJVCI towards the increasing of MAP

(the cutoff value with the increasing of MAP was 44.40 with sensitivity of 76.9% and specificity of 80%)

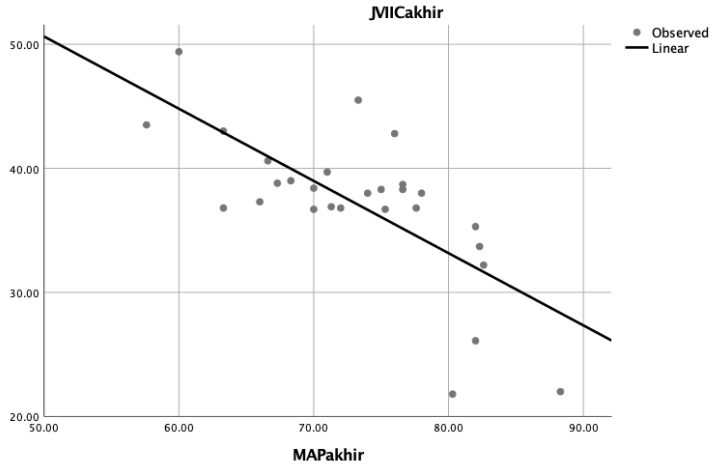

Figure 2. The correlation between IJVCI and MAP (p 0.000)

REVIEW 2

10 MEI 2023

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Manuscript Bambang Pujo Semedi

Critical Care and Shock <critcareshock@gmail.com> 10 May 2023 at 00:45
To: rita@fk.unair.ac.id

Dear Professor,

Please find attached your article with some comments/requests in it that need your response ASAP.
Thank you.

Best wishes,
Simon
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To,

The Editor

Sub: Submission of Manuscript for publication

Dear Sir,

We intend to publish an article entitled **"Correlation Between Internal Jugular Vein Collapsibility Index And Mean Arterial Pressure In Assessing The Response Of Fluid Resuscitation In Critically-Ill Patients "** in your esteemed journal as an Original Article.

On behalf of all the contributors I will act and guarantor and will correspond with the journal from this point onward.

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We would like to suggest following referees for the article.

Thanking you,

Your's sincerely,

Corresponding contributor

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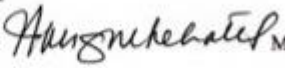
2. Prof Dr. Nancy Margarita Rehatta, MD Anesthesiology Consultant & Intensivist		March 10,2023
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4. Prof Soetjipto, MD, MS, PhD		March 10,2023
5. Ronald Melviano, MD Anesthesiologist		March 9, 2023
6. Dr Arie Utariani, MD Pediatric Anesthesiology Consultant		March 9,2023

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	Bambang Pujo Semedi	Nancy Margarita Rehatta	Jusak Nugraha	Soetjipto	Ronald Melviano	Arie Utariani
Concepts	✓	✓	✓	✓	✓	✓
Design	✓	✓	✓	✓	✓	✓
Definition of intellectual content	✓	✓	✓	✓	✓	✓
Literature search	✓	--	--	--	✓	✓
Clinical studies	✓	--	--	--	✓	✓
Experimental studies	✓	--	--	--	✓	✓
Data acquisition	✓	--	--	--	✓	✓
Data analysis	✓	--	--	--	✓	✓
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Manuscript preparation	✓	--	--	--	✓	✓
Manuscript editing	✓	--	--	--	--	--
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Abstract Page

Title of the article: **Correlation Between Internal Jugular Vein Collapsibility Index And Mean Arterial Pressure In Assessing The Response Of Fluid Resuscitation In Critically-Ill Patients**

Abstract:

Background: Response to resuscitative fluid administration is often difficult to assess clinically, especially in critically-ill patients, and therefore it is necessary to use tools to evaluate the response. One of the modalities that can be used is ultrasonography to measure the internal jugular vein collapsibility index (IJVCI) during the respiration cycle

Aim: To evaluate the correlation between IJVCI and mean arterial pressure (MAP) in assessing response to resuscitative fluid administration in critically-ill patients.

Patients and Methods: This is an experimental study with pre-post test groups, assessing the response to resuscitative fluid administration in critically-ill patients.

Results: A total of 28 subjects aged 18–65 years old were included in the inclusion criteria of this study. The average age of subjects was 50.18 years. Twenty-one subjects responded to to the administration of 500 mL RL crystalloid fluid within 30 minutes based on the internal jugular vein collapsibility index. Subjects were observed into two periods, the pre-test and post-test periods. There was a significant difference in the IJVCI before and after 500 mL of RL between two groups ($p<0.05$). As a predictor of IJVCI associated with increased MAP at the cut-off value of 44.40 with a sensitivity of 76.9% and a specificity of 80%. This study showed that IJVCI has a negative correlation with increased MAP ($p<0.05$).

Conclusions :The measurement of the internal jugular vein collapsibility index can be used to assess the response to resuscitative fluid administration in critically-ill patients.

Keywords: IJVCI, MAP, critically-ill patients.

Commented [DK1]: Approximately 250 words

Introduction:

Assessment of intravascular volume status and hypovolemia in critically-ill patients in the ICU or resuscitation room is often an issue, especially if only relying on physical examination and vital signs. The use of portable echocardiography to measure the inferior vena cava collapsibility index (IVC) during the respiration cycle can predict the assessment of cardiac output (CO) but has limitations in terms of lack of equipment availability, ultrasound expertise, and difficulty in identifying the inferior vena cava.[1,2] Critical illness is defined as a disease process that causes instability of the body's physiology, which can lead to failure of bodily functions or death in a short period of time. System disorders that cause death most quickly are generally disorders of the neurological, cardiovascular, and respiratory systems. [3]

Accurate assessment of intravascular volume status for treating severe hypovolemia or shock is very challenging but has a very important role in critical illness. It is important to avoid administering fluids that can increase morbidity and mortality, and therefore assessing fluid response in critically-ill patients precisely and accurately is very important.[2]

Studies have shown that the response to fluid administration can be defined as a 15% increase in stroke volume (SV), cardiac output (CO), or mean arterial pressure (MAP) after administration of 500 mL of fluid. Mean arterial pressure (MAP) is defined as the average arterial pressure in one cardiac cycle, systolic and diastolic. Cardiac output and systemic vascular resistance affect MAP.[1,4] Imaging techniques using ultrasonography have reported that the internal jugular vein collapsibility index (IJVCI) indicative of hypovolemic conditions is <39%.[5, 6, 7, 8, 9, 10, 11, 12] The Sequential Organ Failure Assessment (SOFA) score is a scoring system to

determine the extent of organ failure in an individual. The score is based on six different values, each representing respiratory, cardiovascular, liver, coagulation, renal, and nervous system parameters The greater the score, the higher the mortality rate.[13] Other studies recommended the use of shock index (SI). Shock index (SI), is the ratio of the ratio of heart rate (HR) to systolic blood pressure (SBP). [14]

This prospective study was conducted to evaluate the correlation between IJVCI and mean arterial pressure (MAP) in assessing response to resuscitative fluid administration in critically-ill patients.

Subjects and Methods:

This is an experimental study with pre-post test groups in critically-ill patients. Assessment of the response to resuscitative fluid administration uses mean arterial pressure >15%, which is associated with the internal jugular vein collapsibility index. The study was conducted in the intensive care unit (ICU) of Dr. Soetomo General Academic Hospital Surabaya from April 2016 to May 2016. The subjects were patients between the ages of 18–65 years old, breathing spontaneously or fully controlled by mechanical ventilation, approved by the family to participate in the study with a signed consent form, and an internal jugular vein collapsibility index of >40%. The subjects did not have spinal cord injury, cardiac arrhythmia, irregular breathing pattern, and hemorrhage.

Criteria for critical illness: an illness with impairment of one or more vital functions (respiratory, cardiovascular, neurological) that if not treated immediately will be life-threatening in a short period of time.

Response to fluid administration:

Internal jugular vein collapsibility index: A comparative measurement of the internal jugular vein diameter during inspiration and expiration using ultrasonography with a linear transducer of 7–10 MHz.

Fluid challenge: A procedure of administering a limited amount of fluid within a predetermined time to assess the response to volume addition. In this study, 500 mL of Ringer's lactate solution was administered within 30 minutes.

Response to fluid administration: The presence of change in hemodynamic status following a fluid challenge is determined by measuring mean arterial pressure. If the MAP is >15%, the patient is considered responsive to fluid administration.

Research Flow

a. Patients with critical illness who met the inclusion criteria had their internal jugular vein collapsibility index measured using ultrasonography with a linear transducer of 7-10 MHz.
b. Performed fluid challenge by administering 500 mL of Ringer's lactate solution within 30 minutes.
c. Measurement of internal jugular vein collapsibility index using ultrasonography with a linear transducer of 7-10 MHz by a standardized researcher.

Data Collection

Data collection includes the name, age, sex, vital signs, primary diagnosis, SOFA score and internal jugular vein collapsibility index measurement.

Data Analysis

The study data were collected from the two periods prior to and following treatment, and are then analyzed using SPSS for Windows 20.0 software (IBM, Armonk, NY,

USA). Numerical data were tested for normality with Shapiro Wilk, where data with normal distribution were presented in terms of mean and standard deviation (SD), and data with non-normal distribution were given in median and minimum, and maximum range values. The two means which were normally distributed were analyzed using the T-test, and the paired t test analyzed those that were pre test and post test groups. Correlation between variables was carried out by bivariate analysis; data that were normally distributed were analyzed using Pearson's correlation, while abnormal data were analyzed using Spearman's correlation. The Receiver Operating Character (ROC) curve was used to find the optimal cut-off value and calculate the sensitivity and specificity for examining IJVCI and MAP. A p-value of less than 0.05 ($P < 0.05$) is considered a statistically significant difference.

Results:

Subject Characteristics

The study was conducted on 28 subjects aged 18–65 years old who suffered from critical illness, observed into two periods, the pre-test and post-test groups. The average age of patients with critical illness was 50.18 years. The average body weight of this study group was 55.29 kg. The mean SOFA score of this study group was 6.61 and the mean shock index was 2.1. (Table 1)..Meanwhile, the data for sex obtained from the results of statistical frequency tests identified 17 males and 11 females .

Based on Table 2, there were 24 patients with mechanical ventilation control and 4 with spontaneous breathing, in accordance to the inclusion criteria.

Difference In Hemodynamic Status Prior To And After 500 ml Rl Administration

To assess the response to fluid administration in critically-ill patients, MAP, and heart rate before and after 500 mL RL crystalloid solution administration within 30 minutes were compared.

There was a significant difference in MAP and heart rate values before and after the administration of 500 mL RL crystalloid solution within 30 minutes ($p<0.05$) (Table 3).

Difference In Internal Jugular Vein Collapsibility Index Prior To And After 500 ml RL Administration

Based on Table 4, the McNemar statistical test showed that there was a significant difference in the internal jugular vein collapsibility index before and after 500 mL of RL crystalloid fluid administration. Despite 7 subjects that were found to have no change in the internal jugular vein collapsibility index, 21 subjects had a decreased internal jugular collapsibility index.

The receiver operating characteristic (ROC) curve analysis was used to calculate the cut-off value, sensitivity, and specificity of IJVCI as predictors of responses in increasing of mean arterial pressure. Youden's index with the highest sum of sensitivity and specificity was used to determine the optimal cut-off value for differentiation. Based on ROC curve, IJVCI showed AUC 0.764 (95%CI [0.572-0.956]; p=0.018) [Figure 1]. Correlation analysis has been carried out with Spearman correlation to analyze the association of IJVCI and the increasing of MAP. It was found a significant that the IJVCI was negatively correlated with an increase in MAP ($r^2 = 0.510$; $p = 0.000$; Figure 2).

Discussion

The general concept of fluid challenge administration to quickly observe a response to fluids following a very limited amount of fluid administration, and there are 4 important elements that must be considered before conducting the technique[3]:

(a) Type of fluid. Either crystalloid or colloid can be used, as we already know about the advantages and benefits of each. In this case, neither is superior than the other, but the important thing to know is when to give and the reason for choosing that particular fluid. In this study, we used the 500 mL RL crystalloid fluid within 30 minutes with the expectation that the fluid we administered within that time period can still remain intravascular before entering the interstitial tissues, although in theory colloid fluids last longer in the intravascular but with side effects that may be greater than the administration of crystalloid fluids.

(b) The rate of fluid administration. A previous study by Muller L, Toumi M, et al. in 2011 conducted a fluid challenge technique using 100 ml crystalloid in the first 1 minute followed by 400 ml within 14 minutes, and found that it was safe to do so with a significant response and no significant side effects [15];

(c) Response assessment. The most important parameters to consider are clinical conditions that describe hemodynamic improvements such as blood pressure, MAP, and heart rate. The results of this study showed a significant difference ($p < 0.05$) in the comparative clinical parameters prior to and after 500 mL RL crystalloid fluid administration.

(d) Complications. Pulmonary edema due to congestive heart failure is the most serious complication of fluid administration. Assessment of the response to fluids using the internal jugular vein collapsibility index is influenced by cardiopulmonary

interactions, where the most influential factors are the intrathoracic pressure during respiration and venous return to the right atrium. Hyperinflation can cause the heart to be pushed into the cardiac fossa in addition to an increased intrathoracic pressure, and an increased pressure in the right atrium can also disrupt venous blood flow to the right atrium leading to a distention of the internal jugular vein. Response to fluid administration will be difficult to assess in patients with these problems, and 7 of the 28 study participants did not experience changes in the internal jugular vein collapsibility index prior to and after the administration of 500 mL RL crystalloid fluid within 30 minutes.

Assessment of volume status using the internal jugular vein collapsibility index has previously been performed by Keith Killu, Victor Coba et al. in 2010, which reported that an internal jugular vein collapsibility index of >39% is indicative of hypovolemia, and conversely that of <39% is indicative of normovolemia, with p=0.001 ($p < 0.05$).[5] In our study, we found that an internal jugular vein collapsibility index of 44.40 is the optimal cut-off value for differentiation normovolemia or hypovolemia. This suggests that the collapsibility index can be used to assess volume status.

The efficacy of evaluating the fluid administration response by using the internal jugular vein collapsibility index in the 28 subjects resulted in 21 subjects showed a response, with a change in collapsibility index following administration of 500 mL RL crystalloid fluid within 30 minutes, with a p value = 0.00[a] ($p < 0.05$). This shows that there is a significant difference, which means that the internal jugular vein collapsibility index is effective for assessing fluid response.

Commented [SN2]: What did you mean by this superscript a?

Limitations

The sample selection of this study was not completely homogeneous, so in order to achieve good homogeneity, it is necessary to have similar disease types to assess the response to fluids. This study has not yet compared the effectiveness of assessing the response to fluid using the internal jugular vein collapsibility index with other modalities such as CVP and IVC, CI, and therefore further research needs to be conducted to assess the factors that affect the internal jugular vein collapsibility index. Discrepancies in response between the subjects may be due to other factors such as high intrathoracic pressure, cardiac contractility problems, or other causes. The presence of these factors can make the fluid response difficult to assess.

Commented [SN3]: Did you mean inferior vena cava collapsibility index?

Conclusion

The internal jugular vein collapsibility index is effectively used to assess the response to resuscitative fluid administration in critically-ill patients aged 18–65 years old. There is a significant difference in the internal jugular vein collapsibility index prior to and after administration of 500 mL RL crystalloid fluid within 30 minutes. No significant side effects were onserved in the administration of 500 mL RL fluid within 30 minutes.

Approval from research ethics committee

This research has obtained approval from the Research Ethics Committee of Dr. Soetomo General Hospital Surabaya with the following number 447/ Panke.KKE/VI/2016.

Acknowledgement:

We thank all teacher, the resident, nursing staff, laboratory staff in Soetomo Hospital, Medical Science, Faculty of Medicine, Universitas Airlangga involved

in patient management and data collection, without whose hard work and dedication the study would not have been possible.

Abbreviations:

CO : Cardiac output

CI : Cardiac Index

CVP : Centrak venous pressure

IJVCI : Index Jugular Vascular Collapsibility Index

IVC : Inferior vena cava

MAP : Mean Arterial Pressure

RL : Ringer Lactate

ROC : receiver operating characteristic

SD : Standard deviation

SOFA : Sequential Organ Failure Assessment

SI : Shock Index

SV : Stroke volume

Tables:

Table 1. Subject Characteristics

Characteristics	n	Mean	±SD
Age	28	50.18	17.304
Weight	28	55.29	10.484
SOFA	28	6.6071	2.16606
Shock Index	28	1.215	0.26
Initial MAP	28	62.6321	7.47856
Initial HR	28	111.1071	17.51050
RR	28	18.7500	3.53422
Final MAP	28	73.0929	7.41375
Final HR	28	105.4643	15.62638

Commented [SN4]: Please give the unit for all the parameters.

Table 2. Frequency of respiratory assistance

Respiratory assistance	Frequency	Percentage (%)	Cumulative percentage (%)
Ventilator-controlled	24	85.7	85.7
Spontaneous breathing	4	14.3	100.0
Total	28	100.0	

Commented [SN5]: Did you mean this was n (number of the subjects)?

Table 3. Comparison between Pre-test and Post Test Groups

Variables	Pre-Test Groups	Post Test Goups	p value
MAP, mean ± SD (mmHg)	62.63 ± 7.48	73.09 ± 7.4	0.000*
Heart rate, mean ± SD	111.11±17.51	105.46 ±15.62	0.000*
Sistolik Presure mean ± SD (mmHg)	89.71 ± 8.04	100.86 ± 9.59	0.000*
Shock Index	1.25 ± 0.26	1.05 ± 0.19	0.000*

[1]Paired T-test; *statistically significant ($p < 0.05$)

Commented [SN6]: Which part of the table does this description (1) want to describe?

Table 4. The efficacy of internal jugular vein collapsibility index in evaluating fluid responsiveness

Initial IJV CI	Final IJV CI		N	Sig
	Low (<40%)	High (>40%)		
Low (<40%)	0	0		
High (>40%)	21	7	28	0.00[a]

Note: McNemar statistical test, *significant difference with $p < 0.05$

Figure Legends

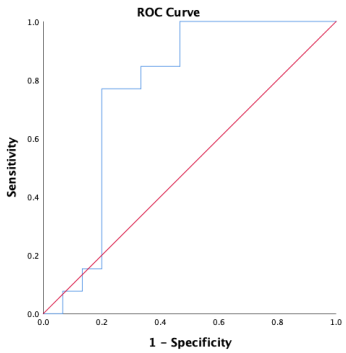
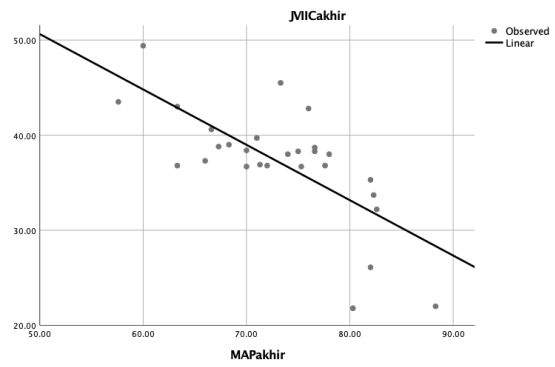


Figure 1. ROC curve of IJVCI towards the increasing of MAP

(the cutoff value with the increasing of MAP was 44.40 with sensitivity of 76.9% and specificity of 80%)



Commented [SN7]: Please use English in your Figure.

Figure 2. The correlation between IJVCI and MAP (p 0.000)

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10 MEI 2023

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Manuscript Bambang Pujo Semedi

EXECUTIVE DIRECTOR <rita@fk.unair.ac.id> 10 May 2023 at 05:26
Reply-To: dir_chen16@yahoo.com.tw
To: Critical Care and Shock <critcareshock@gmail.com>

Dear Dr Simon
This is our manuscript that we have revised. Thank you for your corrections.

Best Regards
Prof Rita
[Quoted text hidden]

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To,

The Editor

Sub: Submission of Manuscript for publication

Dear Sir,

We intend to publish an article entitled **"Correlation Between Internal Jugular Vein Collapsibility Index And Mean Arterial Pressure In Assessing The Response Of Fluid Resuscitation In Critically-Ill Patients "** in your esteemed journal as an Original Article.

On behalf of all the contributors I will act and guarantor and will correspond with the journal from this point onward.

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Thanking you,

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Corresponding contributor

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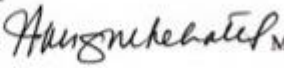
2. Prof Dr. Nancy Margarita Rehatta, MD Anesthesiology Consultant & Intensivist		March 10,2023
3. Prof. Dr. Jusak Nugraha, MD Consultant Clinical Pathologist		March 10, 2023
4. Prof Soetjipto, MD, MS, PhD		March 10,2023
5. Ronald Melviano, MD Anesthesiologist		March 9, 2023
6. Dr Arie Utariani, MD Pediatric Anesthesiology Consultant		March 9,2023

Type of article: Original

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	Bambang Pujo Semedi	Nancy Margarita Rehatta	Jusak Nugraha	Soetjipto	Ronald Melviano	Arie Utariani
Concepts	✓	✓	✓	✓	✓	✓
Design	✓	✓	✓	✓	✓	✓
Definition of intellectual content	✓	✓	✓	✓	✓	✓
Literature search	✓	--	--	--	✓	✓
Clinical studies	✓	--	--	--	✓	✓
Experimental studies	✓	--	--	--	✓	✓
Data acquisition	✓	--	--	--	✓	✓
Data analysis	✓	--	--	--	✓	✓
Statistical analysis	✓	--	--	--	✓	✓
Manuscript preparation	✓	--	--	--	✓	✓
Manuscript editing	✓	--	--	--	--	--
Manuscript review	✓	--	--	--	--	--

Abstract Page

Title of the article: **Correlation Between Internal Jugular Vein Collapsibility Index And Mean Arterial Pressure In Assessing The Response Of Fluid Resuscitation In Critically-Ill Patients**

Abstract:

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Background: Response to resuscitative fluid administration is often difficult to assess clinically, especially in critically-ill patients, and therefore it is necessary to use tools to evaluate the response. One of the modalities that can be used is ultrasonography to measure the internal jugular vein collapsibility index (IJVCI) during the respiration cycle

Aim: To evaluate the correlation between IJVCI and mean arterial pressure (MAP) in assessing response to resuscitative fluid administration in critically-ill patients.

Patients and Methods: This is an experimental study with pre-post test groups, assessing the response to resuscitative fluid administration in critically-ill patients.

Results: A total of 28 subjects aged 18–65 years old were included in the inclusion criteria of this study. The average age of subjects was 50.18 years. Twenty-one subjects responded to to the administration of 500 mL RL crystalloid fluid within 30 minutes based on the internal jugular vein collapsibility index. Subjects were observed into two periods, the pre-test and post-test periods. There was a significant difference in the IJVCI before and after 500 mL of RL between two groups ($p<0.05$). As a predictor of IJVCI associated with increased MAP at the cut-off value of 44.40 with a sensitivity of 76.9% and a specificity of 80%. This study showed that IJVCI has a negative correlation with increased MAP ($p<0.05$).

Conclusions :The measurement of the internal jugular vein collapsibility index can be used to assess the response to resuscitative fluid administration in critically-ill patients.

Keywords: IJVCI, MAP, critically-ill patients.

Introduction:

Assessment of intravascular volume status and hypovolemia in critically-ill patients in the ICU or resuscitation room is often an issue, especially if only relying on physical examination and vital signs. The use of portable echocardiography to measure the inferior vena cava collapsibility index (IVC) during the respiration cycle can predict the assessment of cardiac output (CO) but has limitations in terms of lack of equipment availability, ultrasound expertise, and difficulty in identifying the inferior vena cava.[1,2] Critical illness is defined as a disease process that causes instability of the body's physiology, which can lead to failure of bodily functions or death in a short period of time. System disorders that cause death most quickly are generally disorders of the neurological, cardiovascular, and respiratory systems. [3]

Accurate assessment of intravascular volume status for treating severe hypovolemia or shock is very challenging but has a very important role in critical illness. It is important to avoid administering fluids that can increase morbidity and mortality, and therefore assessing fluid response in critically-ill patients precisely and accurately is very important.[2]

Studies have shown that the response to fluid administration can be defined as a 15% increase in stroke volume (SV), cardiac output (CO), or mean arterial pressure (MAP) after administration of 500 mL of fluid. Mean arterial pressure (MAP) is defined as the average arterial pressure in one cardiac cycle, systolic and diastolic. Cardiac output and systemic vascular resistance affect MAP.[1,4] Imaging techniques using ultrasonography have reported that the internal jugular vein collapsibility index (IJVCI) indicative of hypovolemic conditions is <39%.[5, 6, 7, 8, 9, 10, 11, 12] The Sequential Organ Failure Assessment (SOFA) score is a scoring system to

determine the extent of organ failure in an individual. The score is based on six different values, each representing respiratory, cardiovascular, liver, coagulation, renal, and nervous system parameters The greater the score, the higher the mortality rate.[13] Other studies recommended the use of shock index (SI). Shock index (SI), is the ratio of the ratio of heart rate (HR) to systolic blood pressure (SBP). [14]

This prospective study was conducted to evaluate the correlation between IJVCI and mean arterial pressure (MAP) in assessing response to resuscitative fluid administration in critically-ill patients.

Subjects and Methods:

This is an experimental study with pre-post test groups in critically-ill patients. Assessment of the response to resuscitative fluid administration uses mean arterial pressure >15%, which is associated with the internal jugular vein collapsibility index. The study was conducted in the intensive care unit (ICU) of Dr. Soetomo General Academic Hospital Surabaya from April 2016 to May 2016. The subjects were patients between the ages of 18–65 years old, breathing spontaneously or fully controlled by mechanical ventilation, approved by the family to participate in the study with a signed consent form, and an internal jugular vein collapsibility index of >40%. The subjects did not have spinal cord injury, cardiac arrhythmia, irregular breathing pattern, and hemorrhage.

Criteria for critical illness: an illness with impairment of one or more vital functions (respiratory, cardiovascular, neurological) that if not treated immediately will be life-threatening in a short period of time.

Response to fluid administration:

Internal jugular vein collapsibility index: A comparative measurement of the internal jugular vein diameter during inspiration and expiration using ultrasonography with a linear transducer of 7–10 MHz.

Fluid challenge: A procedure of administering a limited amount of fluid within a predetermined time to assess the response to volume addition. In this study, 500 mL of Ringer's lactate solution was administered within 30 minutes.

Response to fluid administration: The presence of change in hemodynamic status following a fluid challenge is determined by measuring mean arterial pressure. If the MAP is >15%, the patient is considered responsive to fluid administration.

Research Flow

a. Patients with critical illness who met the inclusion criteria had their internal jugular vein collapsibility index measured using ultrasonography with a linear transducer of 7-10 MHz.
b. Performed fluid challenge by administering 500 mL of Ringer's lactate solution within 30 minutes.
c. Measurement of internal jugular vein collapsibility index using ultrasonography with a linear transducer of 7-10 MHz by a standardized researcher.

Data Collection

Data collection includes the name, age, sex, vital signs, primary diagnosis, SOFA score and internal jugular vein collapsibility index measurement.

Data Analysis

The study data were collected from the two periods prior to and following treatment, and are then analyzed using SPSS for Windows 20.0 software (IBM, Armonk, NY,

USA). Numerical data were tested for normality with Shapiro Wilk, where data with normal distribution were presented in terms of mean and standard deviation (SD), and data with non-normal distribution were given in median and minimum, and maximum range values. The two means which were normally distributed were analyzed using the T-test, and the paired t test analyzed those that were pre test and post test groups. Correlation between variables was carried out by bivariate analysis; data that were normally distributed were analyzed using Pearson's correlation, while abnormal data were analyzed using Spearman's correlation. The Receiver Operating Character (ROC) curve was used to find the optimal cut-off value and calculate the sensitivity and specificity for examining IJVCI and MAP. A p-value of less than 0.05 ($P < 0.05$) is considered a statistically significant difference.

Results:

Subject Characteristics

The study was conducted on 28 subjects aged 18–65 years old who suffered from critical illness, observed into two periods, the pre-test and post-test groups. The average age of patients with critical illness was 50.18 years. The average body weight of this study group was 55.29 kg. The mean SOFA score of this study group was 6.61 and the mean shock index was 2.1. (Table 1)..Meanwhile, the data for sex obtained from the results of statistical frequency tests identified 17 males and 11 females .

Based on Table 2, there were 24 patients with mechanical ventilation control and 4 with spontaneous breathing, in accordance to the inclusion criteria.

Difference In Hemodynamic Status Prior To And After 500 ml Rl Administration

To assess the response to fluid administration in critically-ill patients, MAP, and heart rate before and after 500 mL RL crystalloid solution administration within 30 minutes were compared.

There was a significant difference in MAP and heart rate values before and after the administration of 500 mL RL crystalloid solution within 30 minutes ($p<0.05$) (Table 3).

Difference In Internal Jugular Vein Collapsibility Index Prior To And After 500 ml RL Administration

Based on Table 4, the McNemar statistical test showed that there was a significant difference in the internal jugular vein collapsibility index before and after 500 mL of RL crystalloid fluid administration. Despite 7 subjects that were found to have no change in the internal jugular vein collapsibility index, 21 subjects had a decreased internal jugular collapsibility index.

The receiver operating characteristic (ROC) curve analysis was used to calculate the cut-off value, sensitivity, and specificity of IJVCI as predictors of responses in increasing of mean arterial pressure. Youden's index with the highest sum of sensitivity and specificity was used to determine the optimal cut-off value for differentiation. Based on ROC curve, IJVCI showed AUC 0.764 (95%CI [0.572-0.956]; p=0.018) [Figure 1]. Correlation analysis has been carried out with Spearman correlation to analyze the association of IJVCI and the increasing of MAP. It was found a significant that the IJVCI was negatively correlated with an increase in MAP ($r^2 = 0.510$; $p = 0.000$; Figure 2).

Discussion

The general concept of fluid challenge administration to quickly observe a response to fluids following a very limited amount of fluid administration, and there are 4 important elements that must be considered before conducting the technique[3]:

(a) Type of fluid. Either crystalloid or colloid can be used, as we already know about the advantages and benefits of each. In this case, neither is superior than the other, but the important thing to know is when to give and the reason for choosing that particular fluid. In this study, we used the 500 mL RL crystalloid fluid within 30 minutes with the expectation that the fluid we administered within that time period can still remain intravascular before entering the interstitial tissues, although in theory colloid fluids last longer in the intravascular but with side effects that may be greater than the administration of crystalloid fluids.

(b) The rate of fluid administration. A previous study by Muller L, Toumi M, et al. in 2011 conducted a fluid challenge technique using 100 ml crystalloid in the first 1 minute followed by 400 ml within 14 minutes, and found that it was safe to do so with a significant response and no significant side effects [15];

(c) Response assessment. The most important parameters to consider are clinical conditions that describe hemodynamic improvements such as blood pressure, MAP, and heart rate. The results of this study showed a significant difference ($p < 0.05$) in the comparative clinical parameters prior to and after 500 mL RL crystalloid fluid administration.

(d) Complications. Pulmonary edema due to congestive heart failure is the most serious complication of fluid administration. Assessment of the response to fluids using the internal jugular vein collapsibility index is influenced by cardiopulmonary

interactions, where the most influential factors are the intrathoracic pressure during respiration and venous return to the right atrium. Hyperinflation can cause the heart to be pushed into the cardiac fossa in addition to an increased intrathoracic pressure, and an increased pressure in the right atrium can also disrupt venous blood flow to the right atrium leading to a distention of the internal jugular vein. Response to fluid administration will be difficult to assess in patients with these problems, and 7 of the 28 study participants did not experience changes in the internal jugular vein collapsibility index prior to and after the administration of 500 mL RL crystalloid fluid within 30 minutes.

Assessment of volume status using the internal jugular vein collapsibility index has previously been performed by Keith Killu, Victor Coba et al. in 2010, which reported that an internal jugular vein collapsibility index of >39% is indicative of hypovolemia, and conversely that of <39% is indicative of normovolemia, with p=0.001 ($p < 0.05$).[5] In our study, we found that an internal jugular vein collapsibility index of 44.40 is the optimal cut-off value for differentiation normovolemia or hypovolemia. This suggests that the collapsibility index can be used to assess volume status.

The efficacy of evaluating the fluid administration response by using the internal jugular vein collapsibility index in the 28 subjects resulted in 21 subjects showed a response, with a change in collapsibility index following administration of 500 mL RL crystalloid fluid within 30 minutes, with a p value = 0.00 ($p < 0.05$). This shows that there is a significant difference, which means that the internal jugular vein collapsibility index is effective for assessing fluid response.

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Commented [HM4R3]: *Thank you for this kind correction. The superscript used in the sentence in our manuscript has been removed*

Limitations

The sample selection of this study was not completely homogeneous, so in order to achieve good homogeneity, it is necessary to have similar disease types to assess the response to fluids. This study has not yet compared the effectiveness of assessing the response to fluid using the internal jugular vein collapsibility index with other modalities such as CVP and Inferior vein cava collapsibility(IVC), CI, and therefore further research needs to be conducted to assess the factors that affect the internal jugular vein collapsibility index. Discrepancies in response between the subjects may be due to other factors such as high intrathoracic pressure, cardiac contractility problems, or other causes. The presence of these factors can make the fluid response difficult to assess.

Commented [SN5]: Did you mean inferior vena cava collapsibility index?

Commented [HM6R5]: Thank you for this correction. It has been corrected

Conclusion

The internal jugular vein collapsibility index is effectively used to assess the response to resuscitative fluid administration in critically-ill patients aged 18–65 years old. There is a significant difference in the internal jugular vein collapsibility index prior to and after administration of 500 mL RL crystalloid fluid within 30 minutes. No significant side effects were onserved in the administration of 500 mL RL fluid within 30 minutes.

Approval from research ethics committee

This research has obtained approval from the Research Ethics Committee of Dr. Soetomo General Hospital Surabaya with the following number 447/ Panke.KKE/VI/2016.

Acknowledgement:

We thank all teacher, the resident, nursing staff, laboratory staff in Soetomo Hospital, Medical Science, Faculty of Medicine, Universitas Airlangga involved

in patient management and data collection, without whose hard work and dedication the study would not have been possible.

Abbreviations:

CO : Cardiac output

CI : Cardiac Index

CVP : Central venous pressure

IJVCI : Index Jugular Vascular Collapsibility Index

IVC : Inferior vena cava

MAP : Mean Arterial Pressure

RL : Ringer Lactate

ROC : receiver operating characteristic

SD : Standard deviation

SOFA : Sequential Organ Failure Assessment

SI : Shock Index

SV : Stroke volume

Tables:

Table 1. Subject Characteristics

Characteristics	n	Mean	±SD
Age, *years*	28	50.18	17.30
Weight, *kg*	28	55.29	10.48
SOFA score, *n*	28	6.61	2.17
Shock Index score, *n*	28	1.22	0.26
Initial MAP, *mmHg*	28	62.63	7.48
Initial HR, *per minute*	28	111.11	17.51
RR, *per minute*	28	18.75	3.53
Final MAP, *mmHg*	28	73.09	7.41
Final HR, *per minute*	28	105.46	15.63

Commented [SN7]: Please give the unit for all the parameters.

Commented [HM8R7]: Thank you for the correction. It has been corrected.

Table 2. Frequency of respiratory assistance

.	Number of the subjects (n)	Percentage (%)
Ventilator-controlled	24	85.7
Spontaneous breathing	4	14.3
Total	28	100.0

Commented [SN9]: Did you mean this was n (number of the subjects)?

Commented [HM10R9]: Thank you for the correction. It has been corrected

Table 3. Comparison between Pre-test and Post Test Groups

Variables	**Pre-Test Groups**	**Post Test Goups**	**p value**
MAP, mean ± SD (mmHg)	62.63 ± 7.48	73.09 ± 7.4	0.000[1]*
Heart rate, mean ± SD	111.11 ± 17.51	105.46 ±15.62	0.000[1]*
Sistolik Presure mean ± SD (mmHg)	89.71 ± 8.04	100.86 ± 9.59	0.000[1]*
Shock Index score (n)	1.25 ± 0.26	1.05 ± 0.19	0.000[1]*

[1]Paired T-test; *statistically significant ($p < 0.05$)

Commented [SN11]: Which part of the table does this description (1) want to describe?

Commented [HM12R11]: Thank you for the kind correction. The less things add up.

Table 4.The efficacy of internal jugular vein collapsibility index in evaluating fluid responsiveness

Initial IJVCI	Final IJVCI		N	Sig
	Low (<40%)	High (>40%)		
Low (<40%)	0	0	28	0.000[a*]
High (>40%)	21	7		

Note: [a] McNemar statistical test, *significant difference with $p < 0.050$

Figure Legends

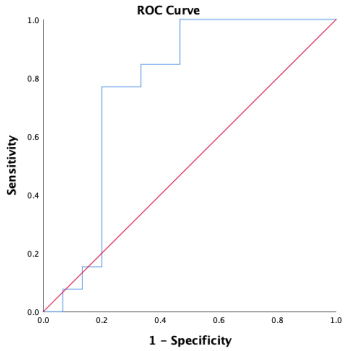

Figure 1. ROC curve of IJVCI towards the increasing of MAP. The cut-off value with the increasing of MAP was 44.40 with sensitivity of 76.9% and specificity of 80%.

Commented [HM14R13]: Thank you for the kind correction. It has been corrected.

Commented [SN13]: Please use English in your Figure.

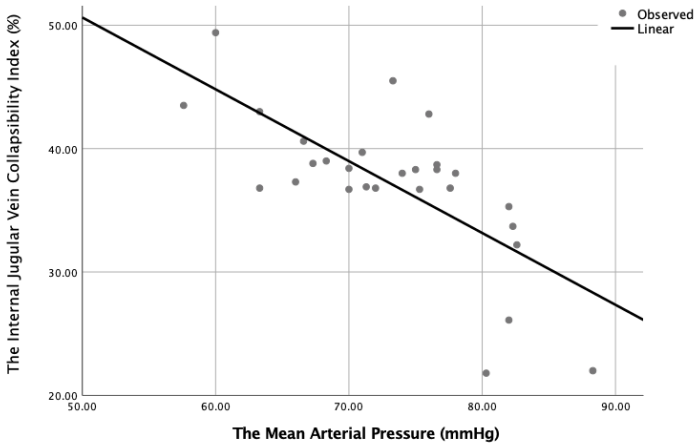

Figure 2. The correlation between IJVCI and MAP (p 0.000) after 500 ml Rl Administration

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Correlation between internal jugular vein collapsibility index and mean arterial pressure in assessing the response of fluid resuscitation in critically ill patients.pdf
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Correlation between internal jugular vein collapsibility index and mean arterial pressure in assessing the response of fluid resuscitation in critically ill patients

Bambang Pujo Semedi[1], Nancy Margarita Rehatta[2], Jusak Nugraha[3], Soetjipto[4], Ronald Melviano[5], Arie Utariani[2]

Abstract

***Background*: Response to resuscitative fluid administration is often difficult to assess clinically, especially in critically ill patients, and therefore it is necessary to use tools to evaluate the response. One of the modalities that can be used is ultrasonography to measure the internal jugular vein collapsibility index (IJVCI) during the respiration cycle.**

***Aim*: To evaluate the correlation between IJVCI and mean arterial pressure (MAP) in assessing response to resuscitative fluid administration in critically ill patients.**

***Patients and methods*: This is an experimental study with pre-post test groups, assessing the response to resuscitative fluid administration in critically ill patients.**

***Results*: A total of 28 subjects aged 18-65 years old were included in the inclusion criteria of this study. The average age of subjects was 50.18 years. Twenty-one subjects responded to the administration of 500 ml Ringer's lactate (RL) crystalloid fluid within 30 minutes based on the IJVCI. Subjects were observed in two periods, the pre-test and post-test periods. There was a significant difference in the IJVCI before and after 500 ml of RL between the two groups ($p<0.05$). As a predictor of IJVCI associated with increased MAP at the cut-off value of 44.40 with a sensitivity of 76.9% and a specificity of 80%. This study showed that IJVCI had a negative correlation with increased MAP ($p<0.05$).**

***Conclusions*: The measurement of the IJVCI can be used to assess the response to resuscitative fluid administration in critically ill patients.**

Key words: IJVCI, MAP, critically ill patients.

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Introduction

Assessment of intravascular volume status and hypovolemia in critically ill patients in the intensive care unit (ICU) or resuscitation room is often an issue, especially if only relying on physical examination and vital signs. The use of portable echocardiography to measure the inferior vena cava (IVC) collapsibility index during the respiration cycle can predict the assessment of cardiac output (CO) but has limitations in terms of lack of equipment availability, ultrasound expertise, and difficulty in identifying the inferior vena cava. (1,2) Critical illness is defined as a disease process that causes instability of the body's physiology, which can lead to failure of body functions or death in a short period of time. System disorders that cause death most quickly are generally disorders of the neurological, cardiovascular, and respiratory systems. (3)

Accurate assessment of intravascular volume status for treating severe hypovolemia or shock is very challenging but has a very important role in critical illness. It is important to avoid administering fluids that can increase morbidity and mortality, and therefore assessing fluid response in critically ill patients precisely and accurately is very important. (2)

Studies have shown that the response to fluid administration can be defined as a 15% increase in stroke volume (SV), CO, or mean arterial pressure (MAP) after the administration of 500 ml of fluid. MAP is defined as the average arterial pressure in one cardiac cycle, systolic and diastolic. Cardiac output and systemic vascular resistance affect MAP. (1,4) Imaging techniques using ultrasonography have reported that the internal jugular vein collapsibility index (IJVCI) indicative of hypovolemic conditions <39%. (5-12) The Sequential Organ Failure Assessment (SOFA) score is a scoring system to determine the extent of organ failure in an individual. The score is based on six different values, each representing respiratory, cardiovascular, liver, coagulation, renal, and nervous system parameters The greater the score, the higher the mortality rate. (13) Other studies recommended the use of shock index (SI). SI is the ratio of heart rate (HR) to systolic blood pressure (SBP). (14)

This prospective study was conducted to evaluate the correlation between IJVCI and mean arterial pressure (MAP) in assessing response to resuscitative fluid administration in critically ill patients.

Subjects and methods

This was an experimental study with pre-post-test groups in critically ill patients. Assessment of the response to resuscitative fluid administration used mean arterial pressure >15%, which was associated with the IJVCI. The study was conducted in the ICU of Dr. Soetomo General Academic Hospital Surabaya from April 2016 to May 2016. The subjects were patients between the ages of 18-65 years old, breathing spontaneously or fully controlled by mechanical ventilation, approved by the family to participate in the study with a signed consent form, and an IJVCI of >40%. The subjects did not have spinal cord injury, cardiac arrhythmia, irregular breathing patterns, and hemorrhage.

Criteria for critical illness: An illness with impairment of one or more vital functions (respiratory, cardiovascular, neurological) that, if not treated immediately, will be life-threatening in a short period of time.

IJVCI: A comparative measurement of the internal jugular vein diameter during inspiration and expiration using ultrasonography with a linear transducer of 7-10 MHz.

Fluid challenge: A procedure of administering a limited amount of fluid within a predetermined time to assess the response to volume addition. In this study, 500 ml of RL solution was administered within 30 minutes.

Response to fluid administration: The presence of change in hemodynamic status following a fluid challenge that was determined by measuring mean arterial pressure. If the MAP increase was >15%, the patient was considered responsive to fluid administration.

Research flow

a. Patients with critical illness who met the inclusion criteria had their IJVCI measured using ultrasonography with a linear transducer of 7-10 MHz.
b. Performed fluid challenge by administering 500 ml of RL solution within 30 minutes.
c. Measurement of IJVCI using ultrasonography with a linear transducer of 7-10 MHz by a standardized researcher.

Data collection

Data collection included the name, age, sex, vital signs, primary diagnosis, SOFA score, and IJVCI measurement.

Data analysis

The study data were collected from the two periods prior to and following treatment and were then analyzed using SPSS for Windows 20.0 software (IBM, Armonk, NY, USA). Numerical data were tested for normality with Shapiro Wilk, where data with normal distribution were presented in terms of mean and standard deviation (SD), and data with non-normal distribution were given in median and minimum, and maximum range values. The two means, which were normally distributed, were analyzed using the t-test, and the paired t-test analyzed those that were pre-test and post-test groups. Correlation between variables was carried out by bivariate analysis; data that were normally distributed were analyzed using Pearson's correlation, while abnormal data were analyzed using Spearman's correlation. The receiver operating character (ROC) curve was used to find the optimal cut-off value and calculate the sensitivity and specificity for examining IJVCI and MAP. A p-value of less than 0.05 ($p<0.05$) was considered a statistically significant difference.

Results

Subject characteristics

The study was conducted on 28 subjects aged 18-65 years old who suffered from critical illness, observed in two periods: the pre-test and post-test. The average age of patients with critical illness was 50.18 years. The average body weight of this study group was 55.29 kg. The mean SOFA score of this study group was 6.61, and the mean shock index was 2.1. (**Table 1**). Meanwhile, the data for sex obtained from the results of statistical frequency tests identified 17 males and 11 females.

Based on **Table 2**, there were 24 patients with mechanical ventilation control and 4 with spontaneous breathing, in accordance with the inclusion criteria.

The difference in hemodynamic status prior to and after 500 ml RL administration

To assess the response of fluid administration in critically ill patients, MAP and heart rate before and after 500 ml RL crystalloid solution administration within 30 minutes were compared.

There was a significant difference in MAP and heart rate values before and after the administration of 500 ml RL crystalloid solution within 30 minutes ($p<0.05$) (**Table 3**).

The difference in IJVCI prior to and after 500 ml RL administration

Based on **Table 4**, the McNemar statistical test showed that there was a significant difference in the IJVCI before and after 500 ml of RL crystalloid fluid administration. Despite 7 subjects that were found to have no change in the IJVCI, 21 subjects had a decreased IJVCI.

The ROC curve analysis was used to calculate the cut-off value, sensitivity, and specificity of IJVCI as predictors of response in increasing of MAP. Youden's index, with the highest sum of sensitivity and specificity, was used to determine the optimal cut-off value for differentiation. Based on the ROC curve, IJVCI showed an area under the curve 0.764 (95%CI [0.572-0.956]; p=0.018) (**Figure 1**). Correlation analysis has been carried out with Spearman correlation to analyze the association of IJVCI and the increase of MAP. It was found significant that the IJVCI was negatively correlated with an increase in MAP ($r^2=0.510$; p=0.000) (**Figure 2**).

Discussion

The general concept of fluid challenge administration is to quickly observe a response to a very limited amount of fluid administration, and there are 4 important elements that must be considered before conducting the technique: (3)

1. Type of fluid. Either crystalloid or colloid can be used, as we already know about the advantages and benefits of each. In this case, neither was superior to the other, but the important thing to know was when to give and the reason for choosing that particular fluid. In this study, we used 500 ml RL crystalloid fluid within 30 minutes with the expectation that the fluid we administered within that time period could still remain intravascular before entering the interstitial tissues, although in theory, colloid fluids last longer in the intravascular but with side effects that may be greater than the administration of crystalloid fluids.
2. The rate of fluid administration. A previous study by Muller L, Toumi M, et al. in 2011 conducted a fluid challenge technique using 100 ml crystalloid in the first 1 minute, followed by 400 ml within 14 minutes, and found that it was safe to do so with a significant response and no significant side effects. (15)
3. Response assessment. The most important parameters to consider are clinical conditions that describe hemodynamic improvements, such as blood pressure, MAP, and heart rate. The results of this study showed a significant difference ($p<0.05$) in the comparative clinical parameters prior to and after 500 ml RL crystalloid fluid administration.
4. Complications. Pulmonary edema due to congestive heart failure is the most serious complication of fluid administration. Assessment of the response to fluids using the IJVCI is influenced by cardiopulmonary interactions, where the most influential factors are the intrathoracic pressure during respiration and venous return to the right atrium. Hyperinflation can cause the heart to be pushed into the cardiac fossa in addition to increased intrathoracic pressure, and increased pressure in the right atrium can also disrupt venous blood flow to the right atrium leading to a distension of the internal jugular vein. Response to fluid administration will be difficult to assess in patients with these problems, and 7 of the 28 study participants did not experience changes in the IJVCI prior to and after the administration of 500 ml RL crystalloid fluid within 30 minutes.

Assessment of volume status using the IJVCI was previously performed by Keith Killu, Victor Coba, et al. in 2010, which reported that an IJVCI of >39% was indicative of hypovolemia, and conversely, that

of <39% was indicative of normovolemia, with p=0.001 (p<0.05). (5) In our study, we found that an IJVCI of 44.40 was the optimal cut-off value for differentiation normovolemia or hypovolemia. This suggested that the collapsibility index can be used to assess volume status.

The efficacy of evaluating the fluid administration response by using the IJVCI in the 28 subjects resulted in 21 subjects showing a response, with a change in collapsibility index following administration of 500 ml RL crystalloid fluid within 30 minutes, with a p-value=0.00 (p<0.05). This showed that there was a significant difference, which meant that the IJVCI was effective for assessing fluid response.

Limitations

The sample selection of this study was not completely homogeneous, so in order to achieve good homogeneity, it is necessary to have similar disease types to assess the response to fluids. This study has not yet compared the effectiveness of assessing the response to fluid using the IJVCI with other modalities such as central venous pressure, inferior vena cava collapsibility, and cardiac index, and therefore further research needs to be conducted to assess the factors that affect the IJVCI. Discrepancies in response between the subjects may be due to other factors such as high intrathoracic pressure, cardiac contractility problems, or other causes. The presence of these factors can make the fluid response difficult to assess.

Conclusion

The IJVCI was effectively used to assess the response to resuscitative fluid administration in critically ill patients aged 18-65 years old. There was a significant difference in the IJVCI prior to and after administration of 500 ml RL crystalloid fluid within 30 minutes. No significant side effects were observed in the administration of 500 ml RL fluid within 30 minutes.

Approval from the research ethics committee

This research has obtained approval from the Research Ethics Committee of Dr. Soetomo General Hospital Surabaya, with number 447/Panke.KKE/VI/2016.

Acknowledgment

We thank all teachers, residents, nursing staff, and laboratory staff in Soetomo Hospital, Medical Science, Faculty of Medicine, Universitas Airlangga, that involved in patient management and data collection, without whose hard work and dedication the study would not have been possible.

Table 1. Subject characteristics

Characteristics	n	Mean	SD
Age (year)	28	50.18	17.304
Weight (kg)	28	55.29	10.484
SOFA	28	6.6071	2.16606
Shock index	28	1.215	0.26
Initial MAP (mmHg)	28	62.6321	7.47856
Initial HR (per minute)	28	111.1071	17.51050
RR (per minute)	28	18.7500	3.53422
Final MAP (mmHg)	28	73.0929	7.41375
Final HR (per minute)	28	105.4643	15.62638

Legend: SOFA=Sequential Organ Failure Assessment; MAP=mean arterial pressure; HR=heart rate; RR=respiration rate; SD=standar deviation.

Table 2. Frequency of respiratory assistance

Respiratory assistance	Number of the subjects (n)	Percentage (%)
Ventilatory controlled	24	85.7
Spontaneous breathing	4	14.3
Total	28	100.0

Table 3. Comparison between pre-test and post-test groups

Variables	Pre-test group	Post-test group	p-value
MAP (mmHg)	62.63±7.48	73.09±7.4	0.000[1*]
Heart rate (beat per minute)	111.11±17.51	105.46±15.62	0.000[1*]
Systolic pressure (mmHg)	89.71±8.04	100.86±9.59	0.000[1*]
Shock index	1.25±0.26	1.05±0.19	0.000[1*]

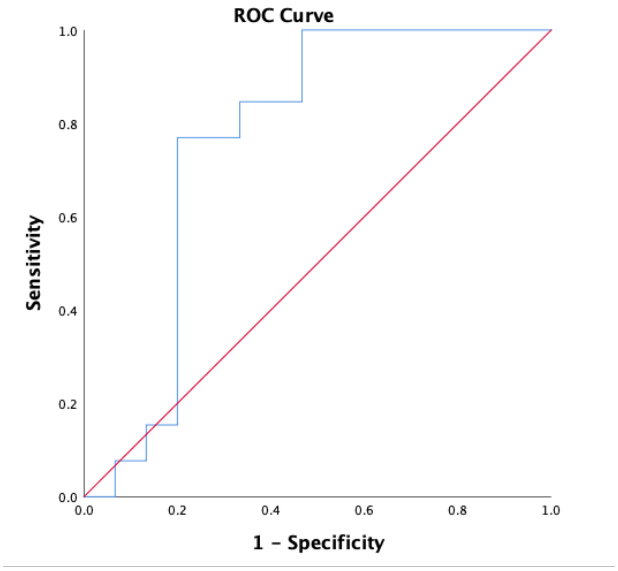
Legend: MAP=mean arterial pressure; SD=standard deviation. All values are mean±SD unless otherwise stated. [1]Paired t-test; [*]statistically significant ($p<0.05$).

Table 4. Efficacy of the IJVCI in evaluating fluid responsiveness

Initial IJVCI	Final IJVCI		n	p-value
	Low (<40%)	High (>40%)		
Low (<40%)	0	0		
High (>40%)	21	7	28	0.00[*]

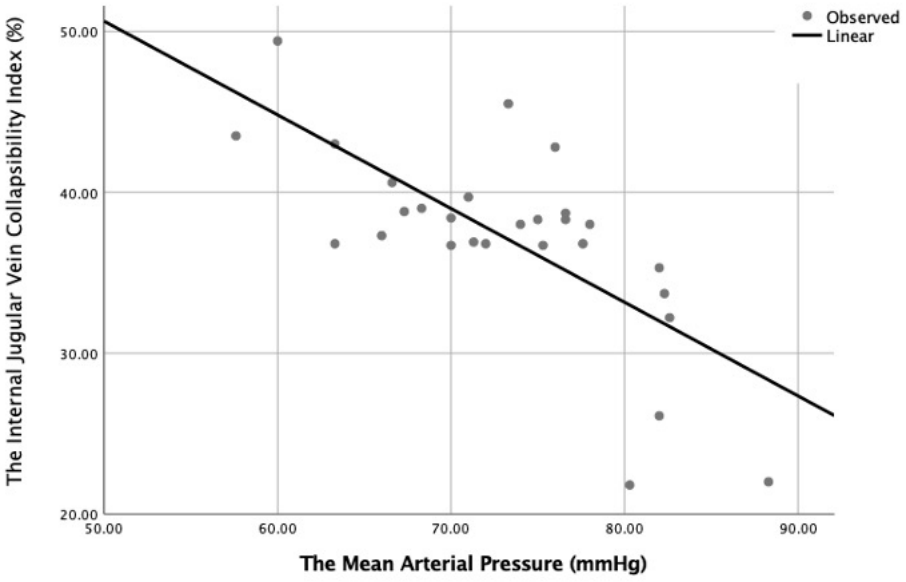
Legend: IJVCI=internal jugular vein collapsibility index.
This test used McNemar statistical test. [*]Significant difference with $p<0.05$.

Figure 1. ROC curve of IJVCI towards the increasing of MAP



Legend: ROC=receiver operating characteristic; IJVCI=internal jugular vein collapsibility index; MAP=mean arterial pressure. The cut-off value with the increasing of MAP was 44.40 with a sensitivity of 76.9% and specificity of 80%.

Figure 2. The correlation between IJVCI and MAP (p 0.000)



Legend: IJVCI=internal jugular vein collapsibility index; MAP=mean arterial pressure.

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