ULTRASOUND MEASUREMENT OF THE INFERIOR VENA CAVA DIAMETER TO EVALUATE VOLUME STATUS IN PATIENTS REQUIRING FLUID RESUSCITATION AT EMERGENCY DEPARTMENT, MUHIMBILI NATIONAL HOSPITAL.

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By

Hendry Robert Sawe

A dissertation submitted in (partial) Fulfillment of the Requirements for the Degree of Master of Medicine (Emergency Medicine) of Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled ***Ultrasound measurement of the inferior vena cava diameter to evaluate volume status in patients requiring fluid resuscitation at Emergency Department, Muhimbili National Hospital,*** in (Partial) fulfillment of the requirements for the degree of Master of Medicine (Emergency Medicine) of Muhimbili University of Health and Allied Sciences.

Dr Teri Reynolds

(Supervisor)

Date: _____

Prof V. Mwafongo

(Head of department and Co-Supervisor)

Date: _____

DECLARATION
AND
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I, **Hendry Robert Sawe**, declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.

Signature……. Date……..

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First, I would like to thank almighty God for countless blessings in my life.

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Last but not least, I would like to extend many thanks to my family and work colleagues for their kindly support. I also would like to thank the patients who volunteered for this study; without them, this dissertation would not have been possible.

DEDICATION

To my parents, Mr & Mrs R. Sawe, who have always felt proud and supported me to be a good doctor, from a family of accountants.

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LIST OF ABBREVIATIONS

MNH	-	Muhimbili National Hospital
MUHAS	-	Muhimbili University of Health and Allied Sciences
WHO	-	World Health Organization
KCMC	-	Kilimanjaro Christian Medical Centre
CVP	-	Central Venous Pressure
IVC	-	Inferior Vena Cava
IVCdmin	-	Minimum Inferior vena cava diameter
IVCdmax	-	Maximum Inferior vena cava diameter
LMIC	-	Low and middle income countries
USA	-	United States of America
USS	-	Ultrasound
ED	-	Emergency department
EMD	-	Emergency Medicine Department
ICU	-	Intensive care unit
MOI	-	Muhimbili Orthopedic Institute

Glossary

Emergency department: a medical treatment facility within a hospital or other primary health care center especially equipped and staffed for management of acutely ill patients presenting without prior appointment, either on their own, referred, or by means of ambulances**.**

Caval Index (CI): an ultrasound measurement of the collapsibility of inferior venacava, to estimate the intravascular volume status.

Mean arterial pressure (MAP): the average arterial blood pressure of an individual during a single cardiac cycle, considered to be the perfusion pressure seen by organs in the body.

Central venous pressure (CVP): the venous pressure as measured at the right atrium by means of a catheter introduced through the median cubital vein to the superior vena cava. A CVP of 8mm Hg is considered to be the target for patients requiring volume resuscitation. Hypotensive patients with CVP < 8mm Hg are considered to be in need of further volume resuscitation prior to the use of vasopressors.

Inferior vena cava (IVC): a large vein formed by the union of the two common iliac veins that receives deoxygenated blood from the lower limbs and the pelvic and abdominal viscera and empties into the right atrium of the heart.

ABSTRACT

Background: Hypotension in the emergency department is an independent predictor of in-hospital mortality. Monitoring fluid responsiveness is key for better prognosis of critically ill patients with hypotension and/or shock. Central venous pressure (CVP) is currently used as a standard measure of volume status, but monitoring of CVP is expensive, invasive, has complications and there is evidence in recent literature that CVP is ureliable predictor of volume status. Beside ultrasound of the inferior vena cava (IVC) has been proposed as a safe, non-invasive, and potentially more reliable, measure of volume status. It is not known whether bedside ultrasound measurement of volume status will predict fluid responsiveness with more clinically relevant parameters.

Aim of the study: To determine if ultrasound measurement of IVC diameter can predict fluid responsiveness in patients requiring fluid resuscitation at Emergency Medicine Department, MNH.

Methods: Prospective observational study of adult patients presenting at EMD-MNH with hypovolemia and requiring fluid resuscitation. A structured physician data sheet was used to record serial vital signs, measured IVC during initial fluid bolus, and the treating clinician's impression of patient volume status and suspected cause of hypotension. Subjects were stratified by presenting Caval Index (CI) and clinical estimation of volume status. A T-test was used to compare the mean change in mean arterial pressure (MAP) per unit volume.

Results: A total of 364 patients were enrolled, 52.2% male and 48.8% female, the average age of (36.8 ±10.7) years and (35.9 ±14.0)years respectively. 48.6% patients had a CI <50% and 51.4% patients had a CI ≥ 50%. Patients in a group with CI ≥ 50% had a 2.8 ($p<0.0001$) fold greater fluid responsiveness than patients with CI<50%. Caval Index (CI) was lower and volume responsiveness higher in patients who clinicians rated as moderate and severely dehydrated as compared with those rated mild, though there was a substantial overlap of CI and fluid responsiveness values in these clinical categories.

Conclusion and recommendation: Ultrasound measurement of the inferior vena cava diameter can predict fluid responsiveness in patients requiring intravenous fluids and may be useful to identify patients who will benefit from early and aggressive volume resuscitation.

Ultrasound of the IVC is more effective for this purpose than clinical estimation of volume status. We recommend a feasibility study to assess if bedside ultrasound can be used consistently by a range of clinical providers as an adjunct tool to guide fluid resuscitation.

1: INTRODUCTION AND LITERATURE REVIEW

Hypotension in the emergency department has been shown to be an independent predictor of in-hospital mortality and, if untreated, can progress to shock, a medical emergency defined as inadequate tissue perfusion (1–5). Hypotension can result from hypovolemia, impaired vascular tone, or poor cardiac function, and, in the emergent setting, is associated with high mortality (6). Early recognition and early intervention are vital to prevent progression of hypotension to shock and complete cardiovascular collapse. However, while fluid resuscitation is the mainstay of treatment for hypotension and is essential in patients with hypovolemia or poor vascular tone, excessive volume resuscitation may be harmful in patients whose hypotension results from poor cardiac output (7).

The ability to assess volume status accurately and to identify which hypotensive patients will benefit from volume resuscitation is crucial to management. Unfortunately, clinical examination has been shown to be inconsistent as a means of evaluating volume status (8,9), and there are drawbacks to the use of central venous pressure (CVP), which is widely used as a standard measure of volume status in patients receiving fluid resuscitation. CVP measurement requires expensive monitoring equipment and is not readily available in most low and middle income countries (10). In addition, it requires placement of a central venous catheter, which may be associated with complications in up to 15% of patients (11–13).

Beyond the cost and complications associated with CVP monitoring, the reliability of CVP as a surrogate for intravascular volume is variable (14–16). A recent high-quality meta-analysis concluded that Central venous pressure (CVP) should not be used to make clinical decisions regarding fluid management (17).

The Central venous pressure (CVP), usually describes the pressure of blood in the thoracic vena cava, near the right atrium of the heart. It reflects the "preload": the amount of blood returning to the heart and volume available to pump into the arterial system. Preload is a major determinant of right ventricular end diastolic volume (18). CVP is often used as a surrogate for preload, and attempts have been made to use CVP to predict fluid-responsiveness (19).

However, CVP depends on a myriad of factors, including venous tone and intrathoracic pressure, along with right heart function and myocardial compliance, and may not accurately reflect intravascular volume status.

The inferior vena cava (IVC) is a very compliant vessel whose size varies with changes in intravascular pressure. Consequently, the IVC collapses with inspiration due to the negative pressure created by chest expansion, as the increasing and decreasing intrathoracic pressures cause blood to be pumped in and out of the IVC (20). As these inspiratory and expiratory values are reversed in patients on positive-pressure ventilation, we will use the terms maximum and minimum diameter rather than inspiratory and expiratory.

Since the size and shape of the IVC depends on the circulating blood volume, sonographic evaluation of the IVC provides a non-invasive measure of volume status (21,22).

Although there is no universally-accepted cutoff, in healthy individuals, minimum IVC diameter occurs on inspiration and ranges from 0 to 14mm, and maximum diameter occurs with expiration and ranges from 15 to 20mm at rest. Because these values vary with individial anatomy, relative changes in IVC diameter are more useful indicators of volume status than single measurements.

The IVC collapsibility or Caval Index (CI), defined as (IVCd max– IVCd min)/

IVCd max (23) has been used as a marker of volume status in patients. The closer the Caval Index is to 0% or to 100%, the higher the likelihood that patient is volume over loaded or depleted, respectively (24). Prior studies have shown that a Caval Index of 50% roughly correlates with a CVP of 8mm Hg (the usual cutoff for considering a patient to be hypovolemic) and suggest that a CI of ≥ 50% indicates intravascular hypovolemia (23).

Various studies on the use of bedside ultrasound at Emergency Department have shown that ultrasound assessment of IVC dimensions can be performed by operators with limited echocardiographic experience in a busy outpatient department using handheld ultrasound devices (25,26).

In 2011, Fields et al showed that emergency physicians' ultrasound measurements of IVC diameter have a high degree of inter-rater reliability, and IVC percentage collapse by visual estimation or based on caliper measurements have lower but still moderate to good reliability (27).

Weekes et al showed that serial visual estimations of the respiratory variation of IVC diameter and left ventricular function (LVF) agreed with bedside measurements of Caval Index and LVF during early fluid challenges to symptomatic hypotensive ED patients (28). Nagdev et al, showed that bedside measurements of Caval Index could be a useful noninvasive tool to determine central venous pressure during the initial evaluation of the ED patient (23). The ratio of IVC to aortic diameters, as measured by bedside US, has been shown to be a marginally accurate measurement of acute weight loss in children with hypovolemia and dehydration from gastroenteritis (22).

In areas where resources are limited and transfer may be required for definitive care, bedside ultrasound can have an even greater impact by facilitating critical early diagnosis and initial resuscitation (29). In many areas of sub-Saharan Africa, bedside

ultrasound may be the only economically viable and sustainable modality of imaging (30). Studies done in Rwanda and Liberia, have shown that, introduction and training of bedside ultrasound in hospitals and other health centers is both feasible, economically sustainable and it has higher impact in changing diagnosis in up to 60% of cases (25,31–33).

2: PROBLEM STATEMENT

Intravenous fluids administration remains the cornerstone of the management of patients with hypovolemia and/or shock, with recent data showing improved patient outcomes with the use of early goal directed volume resuscitation in critically ill patients (21,34,35).

Accurate prediction of patient response to fluid challenge is crucial to a positive clinical outcome with fluid resuscitation (36–38). Both under and over resuscitation with fluid may cause poor clinical outcome (7,39). Under-resuscitation may cause tissue hypoperfusion and result in worsening organ dysfunction. Over-resuscitation may result in poor oxygen delivery to tissues and organs, leading to poor patient outcome.

Fluid administration and dosing during resuscitation of hypovolemic patients has largely been empirical, based on clinical examination or, in a high resource centre, by monitoring of central venous pressure (CVP) (19,38).

However, clinical examination may not provide a reliable estimate of volume status, and monitoring of central venous pressure (CVP) is expensive, invasive, requires highly trained staff and has itself been shown to be unreliable as a surrogate for volume status (15,17,40).

In prior studies, bedside ultrasound measurement of the IVC diameter has been shown to correlate to some extent with CVP and other indicators of volume status, but it remains to be seen whether bedside ultrasound of the IVC diameter will correlate with the more clinically relevant parameter of fluid-responsiveness.

3: RATIONALE

The use of bedside IVC ultrasound in the emergency department has a potential to stratify patients who are critically ill and likely to respond to aggressive fluid therapy and can facilitate early intervention to reduce morbidity and mortality. This is particularly important to caring for critically ill patients in our resource-limited settings.

Current recommendations for early goal-directed therapy include aggressive fluid resuscitation to achieve desired heart rates and blood pressure, which has emerged as mainstay of treatment in hypovolemia and shock (35).

We hope that this study will help explain if bedside ultrasound measurement of IVC diameter can identify patients who may benefit from aggressive volume resuscitation and can predict which patients may be put at risk by fluid administration. If ultrasound measurement of IVC diameter proves accurate, this accessible modality may be an alternative to CVP monitoring and, thus, may allow the development of a feasible, affordable and non-invasive goal-directed algorithm for the resuscitation of septic and hypotensive patients in resource limited settings such as Muhimbili National Hospital and across Tanzania.

4: STUDY HYPOTHESES

4.1: First Hypothesis

We expect that patients with baseline Caval Index of greater than or equal to 50% will have a greater rise in mean arterialpressure for a given volume of fluid infused than those with baseline Caval Index of less than 50%.

- Null hypothesis: There is no difference in mean arterial pressure change per unit volume among patients with baseline Caval Index of greater than or equal to 50% compared to those with baseline Caval Index of less than 50%
- Alternative Hypothesis: There is a difference in mean arterial pressure change among patients with baseline Caval Index of greater than or equal to 50% compared to those with baseline Caval Index of less than 50%

4.2: Second Hypotheses

We expect that clinical estimation of volume status by physicians based on clinical examination will be consistent with the estimation of volume status by bedside ultrasound measurement of the IVC.

- Null hypothesis: IVC measurements are not consistent with provider estimation of hydration status based on physical exam.
- Alternative hypothesis: IVC measurements are consistent with provider estimation of hydration status based on physical exam.

5: OBJECTIVES

5.1: Broad Objective

To determine if ultrasound measurement of IVC diameter can predict fluid responsiveness in patients requiring fluid resuscitation at Emergency Medicine Department, MNH

5.2: Specific Objectives

1. To compare the mean arterial blood pressure response to fluid rescucitation in patients with a baseline caval indices greater than or equal to 50% compared to those with a baseline Caval Index of less 50%.
2. To evaluate incremental response to volume infusion by documenting the Caval Index and mean arterial blood pressure measurements after every 500ml of intravenous crystalloid infused.
3. To determine the relationship between bedside ultrasound measurement of Caval Index and the physician's impression of the patient's baseline volume status, rated as mild, moderate or severe volume depletion.

6: STUDY METHODOLOGY

6.1: Study design

This was a prospective observational study of convenience sample of adult patients presenting to the Emergency Medicine Department of Muhimbili National Hospital from 12 May 2012 to 2 October 2012, time periods during which research personnel was available to enroll and evaluate the patients.

6.1.1: Target Population

Adult patients presenting to an acute care setting and requiring intravenous fluid resuscitation.

6.1.2: Accessible Population

Adult patients presenting to the Emergency Department of Muhimbili National Hospital requiring intravenous fluid resuscitation.

6.1.3: Study population

Convinience sample of adult patients clinically judged by treating physician to require intravenous fluid resuscitation, were eligible for enrollment, during time periods when research personnel was available to enroll and evaluate at Emergency Department in MNH.

Exclusion criteria:

- All the participants in whom volume resuscitation was begun prior to notification of research personnel.
- All the participants with known malformation of the heart and/or liver were not recruited.
- Patients in whom the IVC cannot be visualized.

6.2: Study setting

The study was conducted in the Emergency Medicine Department (EMD) of Muhimbili National Hospital (MNH) in Dar es Salaam, Tanzania. The first of its

kind in Tanzania, the EMD was established in 2010 via a public-private partnership between the Ministry of Health and Social Welfare and Abbott Fund Tanzania.

MNH is the largest tertiary care center in Tanzania and the EMD is the clinical training site for the only emergency medicine residency program in the country.

The department serves a high acuity patient population from within Dar es Salaam and receives referral patients from throughout the country. Of the 36000 patients seen each year, only 20% are discharged home from the emergency department. The top disease categories in all patients are trauma, infectious disease and mental health. In patients under 18, infectious disease are the most common; in adults, trauma is the most common (41).

6.3 Study protocol

6.3.1: Sample size

The primary data analysis will be based on a comparison of two means between groups defined by the Caval Index cut-off value of 50%. A study by Weekes et al, suggested that a difference of the mean systolic blood pressure after intravenous fluid infusion between the patients having a Caval Index of more than 50% and those having a Caval Index less or equal to 50% was 21.4mmHg(SD= 12.9) and 35.3mmHg(SD=22.8) respectively. The patient ratio for Caval Index in this study was 1.4 (indices less than or equal to 50% to indicesgreater than 50%) (28).

From the above information, the sample size for this study is calculated from the formula for (42).

$$(z_{1-\alpha/2} + z_{1-\beta})^2 \left\{ \frac{s_0^2}{n_0} + \frac{s_1^2}{n_1} \right\} = (\mu_1 - \mu_0)^2$$

Were

μ_1= mean systolic blood pressure change in patients with Caval Index >50% = (21.4mmHg)

μ_0= mean systolic blood pressure change in patients with Caval Index ≤50 %= (35.3mmHg)

s_1= standard deviation in patients with Caval Index >50% = (22.8mmHg)

s_0= (estimated) standard deviation in patients with Caval Index ≤50%=12.9mmHg)

n_1 = sample size in a group of patients with Caval Index > 50% =10

n_0= sample size in a group of patients with Caval Index ≤ 50%= 14

z_x= point on standard normal distribution with area to the left = x;

α= type I error rate; =0.05

β = type II error rate=1.28 (90% power)

With 0.05 α-level and 90% power. $Z_{1-\alpha/2}=Z_{0.975}$ =1.96 and $Z_{1-\beta}=Z_{0.90}$ = 1.28

Thus, the **minimum** necessary sample size is estimated to be 81.

6.3.2: Approach to subjects

The researcher, when available in the Emergency Department, actively looked for eligible patients or was contacted by the clinician or nurse on duty upon arrival of an eligible patient. The researcher explained the study to the patient or his/her surrogate and obtained consent.

After enrollment of patient in the study, the researcher asked the treating clinician to grade the patient's volume depletion as mild, moderate or severe based on the history and physical examination. The same clinician was then asked what he/she believed to be the main cause of volume depletion and elements of physical examination that caused him/her to give fluid to the patient.

6.3.3: Ultrasound measuments

All measurements were performed by using the M-Turbo ultrasound (SonoSite, Inc.Bothell, Washington USA). The ultrasound was available in the Department of Emergency Medicine and was being used as part of usual clinical care.

The researcher received specific didactic and practical training in the use of bedside ultrasound for IVC measurement. He has succesfuly completed the training program requirement for basic emergency ultrasound and has been working with bedside ultrasound in his clinical duties for over two years.

All study measurements (still image, video clip and m-mode) were recorded on the ultrasound machine and reviewed by an ultrasound fellowship-trained faculty member for accuracy of image acqusition and measurement technique.

With patients lying in supine position, the maximum and minimum inferior vena cava diameter (across the respiratory cycle), were measured 2 to 3 cm from the right atrial border in a long-axis/subxiphoid view.

All patients underwent ultrasound measurements before the initiation of intraveous fluid infusion and after each 500ml of fluid administered for the duration of the initial bolus; measurements were taken after each 500ml up to, but not beyond, two liters.

The volume infused was determined by the treating clinician. The researcher recorded serial vital sign measurements at the same intervals.

6.3.4: Data sheet

A structured physician data sheet was used to record basic anonymous patient demographic information including age and sex, clinician's impressions, and serial measurements of the IVC diameter and vital signs.

6.4: Data analysis

Data collected from the handwritten data sheets were typed into an Excel spreadsheet (Microsoft Corporation, Redmond, WA, USA) and used to calculate the mean arterial pressure and Caval Index.

The data from Excel spread sheets was then imported into SAS Software, version 9.3 (SAS Institute Inc, Cary, NC, USA). Procedure, frequency and univariate functions were performed to check for any outliers and clean the dataset.

Patient descriptive characteristics are reported, including means, medians, and standard deviations. The Caval Index(CI) was categorized into a bivariate (greater than 50% and less or equal to 50%) variable and used when stratifying the patient's change in mean arterial pressure(MAP) per unit volume of fluid infused. The Caval Index(CI) was further assessed by stratifying patients based on the physician clinical assessment of volume depletion.

T-test was used to compare the Caval Index (CI) within the groups.

6.5: Ethics

This study was conducted after obtaining an approval from the Institutional Review Board and the committee on human research of the Muhimbili University of Health and Allied Sciences (MUHAS). Informed consent was obtained from patients or patient proxy before any measurement was done. All data were collected and held by the researcher with no patient identifiers in any process. Data was stored in locked cabinets and encrypted computers.

7: RESULTS

7.1: Descriptive characteristics of the study population

We enrolled 364 patients from 12 May to 2 October 2012. Of these, 190 (52.2%) were males and 174 (48.8%) were females, with an average age of 36.8 years (SD ±10.7 years) and 35.9 years (SD ±13.9 years) respectively. Similar to Muhimbili National Hospital, Emergency Medicine Department patient population data, male patients comprised the majority of the study population. More than half of the patients enrolled in the study were adults aged below 40 years, similar to MNH-EMD patient population (see table 7.1).

Table 7.1: Descriptive characteristics of the study population.

Gender	**Study population** **N=364**	**Muhimbili National Hospital EMD population** **N=58,887***	**Average age of study population**
Male (%)	190 (52.2%)	60.5%	19-67 yrs Mean (36.8 ±10.7 SD)
Female (%)	174 (48.8%)	39.0%	18-89 yrs Mean (35.89±14.0 SD)
***0.5% of the MNH-EMD Population had unknown gender (not recorded)			

Age distribution	**Number studied** **N = 364 (%)**
18-19	16 (4.4%)
20-29	50(13.8%)
30-39	138(37.9%)
40-49	94(25.8%)
50-59	33(9.0%)
60-69	21(5.7%)
70-79	11(3.1%)
80+	1(0.3%)

7.2: Average patient baseline values

The average mean arterial pressure (MAP) of patients on presentation was 66.8mmHg (SD ±10.3mmHg).The mean Caval Index at presentation was 47.7% (SD ±19.3%), and the average bolus given was 1050mls (SD ± 135mls) of intravenous crystalloids (see table 7.2).

Table 7.2: Average patient baseline values

Study population baseline variables	**Mean(±SD)**
Average baseline MAP of study population	66.8 mmHg (SD ±10.3 mmHg)
Average baseline Caval Index(CI) of study population	47.7% (SD ±19.3%)
Average IV fluid bolus given to study population	1050 mls (SD ± 135 mls)

7.3: Indications for volume resuscitation

The indications for volume resuscitation of patients as stated by the clinicians (free text response) included haemorrhage 195 (53.6%), sepsis 61 (16.8%), vomiting 51 (14.0%), poor oral intake 39 (10.7%), and diarrhoea 18 (4.9%) (See table 7.3).

The physical examination findings suggestive of hypovolemia as stated by the clinicians (free text response) included hypotension 154 (42.3%), tachycardia 110 (30.2%), dry mucous membranes 90 (24.7%), and decreased skin turgor 13 (3.6%).

Table 7.3: Indications for volume resuscitation

Clinicians' stated causes of volume depletion	**Frequency N=364**	**Percentage (%)**
Diarrhoea	18	4.9%
Haemorrhage	195	53.6%
Poor oral intake	39	10.7%
Sepsis	61	16.8%
Vomiting	51	14.0%
Physical examination suggestive of hypovolemia	**Frequency N=364**	**Percentage (%)**
Tachycardia	110	30.2%
Decreased skin turgor	13	3.6%
Dry mucous membrane	90	24.7%
Hypotension	151	41.5%

7.4: Clinicians' estimation of patient volume status

Clinicians estimated 146 (40.1%) patients to be mildly dehydrated, 88(24.2%) patients to be moderately dehydrated and 130 (35.7%) patients to be severely dehydrated (see table 7.4).

Overall, the Caval Index (CI) was lower and volume responsiveness higher in patients who clinicians rated as moderate and severely dehydrated as compared with those rated mild. However, there was too much overlap of Caval Index (CI) and fluid responsiveness values in these clinical categories for clinical estimation to be a useful means of directing volume resuscitation.

Table 7.4: Clinicians' estimation of patient volume status

Physicians' assessment	**Percentage (N=364)**	**Baseline Caval Index**		**Change in MAP per unit volume of fluid**	
		Median (%)	**Range (%)**	**Median (mmHg/L)**	**Range (mmHg/L)**
Mild	40.1%	30	9-80	4	(-24) - 33
Moderate	24.2%	53	6-83	6	0 - 29
Severe	35.7%	62	22-95	12	(-10) - 28

7.5: The relationship between Caval Index measurements and fluid responsiveness.

Patients enrolled in the study were divided into two groups, those with Caval Index less than fifty percent (CI< 50%) and those with Caval Index greater or equal to fifty percent (CI ≥ 50%)

There were 177(48.6%) patients in group with the CI <50% and 187(51.4%) patients in group with the CI ≥ 50%.

The patients in a group with CI ≥ 50% had a 2.8 fold (p<0.0001) greater fluid responsiveness than patients with Caval Index <50% (see table 7.5).

Table 7.5: The relationship between Caval Index measurements and fluid responsiveness.

Baseline caval index (CI) **(N=364)**		**Change in MAP per unit volume of fluid (mmHg/L)** **mean (± SD)**	**Confidence Interval** **95% CI**	**p-value** **CI<50 to CI≥50**
Caval Index less than 50% (CI<50)	48.6%	4.0 (± 5.6)	3.6-5.1	<0.0001
Caval Index greater or equal to 50% (CI≥50)	51.4%	11.3 (± 6.3)	10.8-12.1	

7.6: Change in MAP per unit volume of fluid

Within each group (those with CI ≥ 50% and those with CI<50), patients who received only 500ml of intravenous fluid had a similar change in mean arterial pressure per unit volume as patients who received more than 500 ml (See Table 7.6).

Table 7.6: Change in MAP per unit volume of fluid

Baseline Caval Index (CI) **(N=364)**		**Mean change in MAP per interval unit volume of fluid (mmHg/L)**				**Overall Change in MAP per unit volume of fluid (mmHg/L)** **mean (± SD)**
		500ml Mean (± SD)	**1000ml Mean (±SD)**	**1500ml Mean (± SD)**	**2000ml Mean (± SD)**	
Caval Index less than 50% (CI<50)	N=177	(N=83) 4.0 (±6.9)	(N=64) 6.2 (±4.2)	(N=26) 5.2 (±4.0)	(N=4) 5.5 (±2.2)	4 (± 5.6)
Caval Index greater or equal to 50% (CI≥50)	N=187	(N=10) 10.7±7.8	(N=111) 13.1±7.0	(N=37) 10.0±4.8	(N=29) 10.0±3.2	11.3 (± 6.3)

8: DISCUSSION

During resuscitation of critically ill patients who require intravenous fluid, it is important to predict which patients will have a blood pressure increase in response to volume expansion and which may be at risk of harmful volume overload. Prediction of fluid responsiveness is crucial, as this will guide intervention aimed at increasing the overall cardiac output, tissue perfusion and oxygen delivery (43,44).

This prospective observational study in a resource-constrained setting sought to evaluate the use of ultrasound measurement of IVC diameter in predicting fluid responsiveness in patients requiring fluid resuscitation.

The demographic data of the study participants is similar to that of the Muhimbili National Hospital Emergency Medicine Department overall patient population, with the majority being adult males under 40 years of age. This study population age is consistent with the general Tanzanian population, with over half of the population within the age group of 15-64 years according to the recent Tanzania demographics and health survey report (45).

Haemorrhage was the indication for volume resuscitation in over half of the study patients. Majority of the patients who received fluid had a physical examination finding of hypotension and the baseline mean arterial pressure of the study population was 66.8 mmHg.

The results of our study suggests that a Caval Index of greater than or equal fifty percent (CI $\geq$ 50%) is predictive of greater fluid responsiveness to initial bolus of 500ml to 2000ml than a Caval Index of less than fifty percent (CI<50%), with patients in (CI $\geq$50% category) having a change in mean arterial pressure of 11 mmHg compared to (CI<50% category) who had a mean arterial pressure change of

4 mmHg. Previous literature suggest that, a change in mean arterial pressure of greater or equal to 10 mmHg is considered clinically significant, were as a change of 5 mmHg is considered not clinically significant (46–48).

Central venous pressure (CVP) historically has been used to make decisions regarding the administration of intravenous fluids (19,49,50). Despite the fact that CVP is widely used, however, its ability to predict and guide fluid responsiveness has been brought into question. A recent meta-analysis of 24 different studies looking at the ability of CVP to predict fluid responsiveness revealed a very poor relationship between CVP and blood volume as well as the inability of CVP to predict fluid responsiveness across a wide spectrum of clinical conditions (17).

The results of our study suggest that bedside ultrasound may be a very useful tool for rapidly stratifying those patients whose hypotension is likely be responsive to initial fluid bolus. Since hypotension in the emergency department has been shown to be an independent predictor of in-hospital mortality (1,51), early identification, stratification and intervention is essential to improve outcomes (34).

Different studies published in the critical care literature have described a range of implications of Caval Index measurements (20,28,52–54). To our knowledge, this is the first physiological study to report on the relationship between serial measurements of Caval Index and dynamic change in mean arterial pressure per unit volume in patients requiring fluid resuscitation.

A range of clinical signs and symptoms have been proposed in articles and authoritative text books of emergency care (55–57), as appropriate indicators and predictors of volume depleted status. However, a recent meta-analysis of 13 studies on the accuracy of signs, symptoms, and laboratory tests for detecting dehydration

revealed that while some signs and symptoms of dehydration performed better than others, no variable, including physicians' determination of the general appearance of the patients, had adequate sensitivity, specificity and reliability to identify dehydration (8). Similar to previous literature, our results suggest that clinical examination may not provide a reliable enough estimate of volume status. The physician estimation of volume status revealed that despite a trend towards increase in the Caval Index in the patients rated as moderately to severely volume depleted by clinicians, there was substantial overlap in the groups, limiting the utility of clinical estimation to predict volume responsiveness. Also, due to the lack of definitive gold standard criteria for estimation of dehydration status, and the fact that Caval index have mainly been used as a binary measurement (23), we did not calculate the sensitivity and specificity of clinician assessment of degree of dehydration, but instead we have reported on the binary caval index and the change in mean arterial pressure per unit volume for each group of the caval index.

In this study, we found that patients had similar changes in the mean arterial pressure per unit volume, regardless of the amount of intravenous fluid administered for the initial bolus. Our analysis shows that patients were substantially under resuscitated, with only 4 patients in (CI < 50 category) receiving the recommended initial bolus of 2000 mls, Overall more than half of the patients in this study in all categories received between half a liter to one liter as an initial bolus, this may have affected the effect observed change in mean arterial pressure within each group. The negative change in mean arterial pressure per unit volume within each categories was observed in a group of dying patients.

Guidelines and literature used in high-resource setting for fluid resuscitation in hypovolemic patients recommend that patients receive a minimum initial administration of 20ml/kg of crystalloid as a fluid challenge with subsequent fluid challenges every 30 minutes for refractory hypotension within the first 6 hours (34,58,59). This is particularly important since aggressive fluid resuscitation in hypotensive patients has been shown to reduce mortality in patients with sepsis and hypovolemia both in developed and developing world settings (60).

The findings of our study suggests that majority of the patients who are judged by clinicians to be hypovolemic and hence requiring fluid resuscitation did not come close to reaching the target of the recommended initial bolus of intravenous crystalloids in hypotensive patients. Overall, the mean volume of the initial intravenous fluid resuscitation was progressively higher inpatients categorized by treating physician as being severely volume depleted as compared to those categorized as moderate or mild. These findings are similar to the observational study by Jacob et al done in Uganda in a group of severely septic patients; the median resuscitation volume was approximately one-half liter, with more ill-appearing patients more likely to receive early fluid resuscitation (61).

9: LIMITATIONS

1. Our study was designed to evaluate the relationship between a diagnostic test and a physiologic parameter and does not establish the feasibility of use of bedside ultrasound in clinical practice in a resource limited settings.
2. The utilization of bedside ultrasound by a researcher who had dedicated training in ultrasound and was supervised by fellowship trained reviewer may limit the generalisability of the results to other settings.
3. Our convenience sampling method was required by limited investigator availability and the time-sensitive, labour-intensive nature of our study protocol. This sample may not be an accurate representation of the overall Emergency Department population, though we have not identified any source of systematic bias in our samplings.

10: CONCLUSIONS

Ultrasound measurement of the inferior vena cava diameter can predict fluid responsiveness in patients requiring intravenous fluids and may be useful to identify patients who will benefit from early and aggressive volume resuscitation.

The ability of clinicians to estimate with precision the exact degree of volume depletion in patients by using history and physical examination alone is unreliable.

Overall, the amount of intravenous fluid prescribed by clinicians to patients requiring fluid resuscitation in our setting was less than the usual recommended initial bolus.

11: RECOMMENDATIONS

The following recommendations are made based on the research findings.

1. We recommend a feasibility study to evaluate whether ultrasound assessment of volume status can be used consistently by range of clinical providers with basic ultrasound training in the acute care centers.
2. We also recommend that emergency departments should begin to integrate bedside ultrasound assessment of patient volume status as a tool to guide fluid resuscitation.
3. Emergency departments should conduct in-service training for clinicians and other providers, as well as develop clinical protocols for fluid resuscitation.

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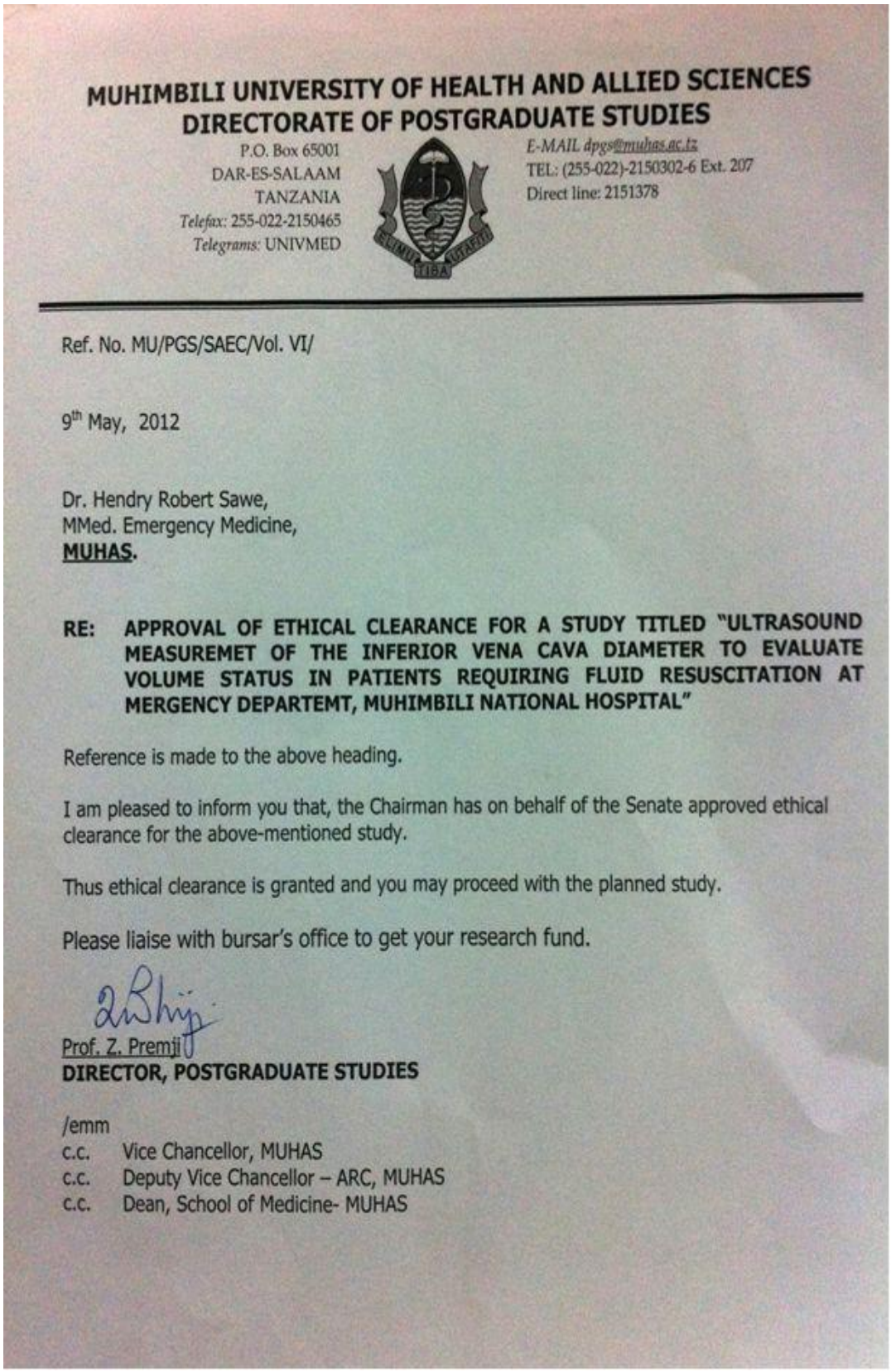
APPENDICES

Appendix A: Ethics clearance letter



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Ref. No. MU/PGS/SAEC/Vol. VI/

9th May, 2012

Dr. Hendry Robert Sawe,
MMed. Emergency Medicine,
MUHAS.

RE: APPROVAL OF ETHICAL CLEARANCE FOR A STUDY TITLED "ULTRASOUND MEASUREMET OF THE INFERIOR VENA CAVA DIAMETER TO EVALUATE VOLUME STATUS IN PATIENTS REQUIRING FLUID RESUSCITATION AT MERGENCY DEPARTEMT, MUHIMBILI NATIONAL HOSPITAL"

Reference is made to the above heading.

I am pleased to inform you that, the Chairman has on behalf of the Senate approved ethical clearance for the above-mentioned study.

Thus ethical clearance is granted and you may proceed with the planned study.

Please liaise with bursar's office to get your research fund.

Prof. Z. Premji
DIRECTOR, POSTGRADUATE STUDIES

/emm
c.c. Vice Chancellor, MUHAS
c.c. Deputy Vice Chancellor – ARC, MUHAS
c.c. Dean, School of Medicine- MUHAS

Appendix B: Consent form English version

TITLE OF THE STUDY:

ULTRASOUND MEASUREMENT OF THE INFERIOR VENA CAVA TO EVALUATE VOLUME STATUS IN PATIENTS REQUIRING FLUID RESUSCITATION AT EMERGENCY DEPARTMENT, MUHIMBILI NATIONAL HOSPITAL

My name is Dr. Hendry Robert Sawe, a final year resident in the department of Emergency Medicine at Muhimbili University of Health and Allied Sciences (MUHAS).

I am conducting a study with the above title as part of my study program.

Aim of the study:

This study aims to determine whether ultrasound measurement of IVC diameter correlates with physician clinical assessment of volume status and how IVC predicts fluid responsiveness in patients requiring fluid resuscitation at Emergency Medical Department, Muhimbili National Hospital.

Participation in this study:

Adult patients presenting to the Emergency Department of the Muhimbili National Hospital with signs of dehydration, hypotension and/or shock clinically judged by attending physician(s) to require intravenous fluid resuscitation will be requested in the enrolment into the study. Patient him/herself or the next of kin if the patient has altered mental status can give a written consent as to be enrolled into the study.
The study involves serial ultrasound measurements of the IVC diameter during resuscitation, and simultaneous serial blood pressure measurements will be recorded as fluid is being administered. All patients will undergo measurements after each 500ml of fluid administered for the duration of the initial bolus. The standard bolus of 2 liters will likely be used in most patients, but where clinicans choose to use a different volume bolus, measurements will be taken after each 500ml, up to, but not beyond, 2 liters.

If you decide not to participate in this study, you/your patient care will not be affected in any way and he/she/you will still receive appropriate care, as any other patient in the department.

Risks:

Physical risks are not anticipated in association with participation in this study as ultrasound is a painless, non-irradiating, non-invasive imaging tool already in use at the bedside in the MNH-ED.

Resuscitation of patients will proceed according to physician protocol and will not be impacted by research considerations. However any reported subject discomfort will be immediately addressed and mitigated.

Benefits:

If you agree to participate in this study, you or your patient will benefit in monitoring of IVC Diameter during fluid resuscitation. The results from this study will be used for building up EMD protocol in monitoring fluid resuscitated patients.

Confidentiality:

All data collected will be treated with strict confidence and stored in locked cabinets and on encrypted computers and will not be revealed to anybody outside the research team.

Cost:

You will not be required to make any payments to participate in this study and no payment will be made to you.

For further information, questions or queries, you can contact:

1. The Principal Investigator,
   Dr. Hendry R. Sawe,
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2. Prof. Victor Mwafongo,
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4. Prof. M. Aboud,
   Director of Research and Publications,
   MUHAS.
   Tel No: +255 22 2150302-6.

I, _____, have read/been told of the contents of this form and have understood its meaning. I agree to participate in this study.

OR

I,_____,
husband/wife/father/mother/_____ have read/been told of the contents of this form and have understood its meaning. I agree to enroll _____ (patient's name in full) in this study

Signature of patient/Next of kin_____
Signature of Researcher _____
Date _____

Appendix C: Consent form English version

FOMU YA RIDHAA YA KUSHIRIKI KATIKA UTAFITI

Jina langu ni Dr. Hendry R Sawe, mwanafunzi wa udaktari bingwa wa wagonjwa wa dharura na mahututi (Emergency Medicine) katika chuo kikuu cha afya na sayansi shirikishi Muhimbili (MUHAS). Ninafanya utafiti kuangalia endapo upimaji wakipenyo cha mshipa unaorudisha damu kwenye moyo kutumia ultasaundi unaitikia vipi wingi au uchache wa kiwango cha maji mgonjwa anayowekewa kupitia dripu wakati wa kuokoa maisha kwa wagonjwa wanaofika idara ya dharura na wagonjwa mahatuti katika hospitali ya Taifa, Muhimbili, Dar es Salaam.

Madhumuni ya utafiti:

Ninafanya utafiti kuangalia endapo upimaji wakipenyo cha mshipa unaorudisha damu kwenye moyo kutumia ultasaundi unaitikia vipi wingi au uchache wa kiwango cha maji mgonjwa anayowekewa kupitia dripu wakati wa kuokoa maisha kwa wagonjwa wanaofika idara ya dharura na wagonjwa mahatuti katika hospitali ya Taifa, Muhimbili, Dar es Salaam.

Ushirikikatikautafiti:

Wagonjwa wenye dalili za kupungukiwa maji mwilini (kwa mtizamo wadakitari anayewahudumia) watakaofika katika idara ya wagonjwa mahututi na dharura Hospitalini Muhimbili wataombwa kushiriki katika utafit ihuu.

Mgonjwa au mbadala wamgonjwa (kama kwa mgonjwa hayupo kwenye akili yake timamu) ataidhinisha kwa maandishi ili mgonjwa apate matibabu wakati yupo ndani ya utafiti.

Utafiti unahusisha upimaji wa mshipa mkubwa unaorudisha damu kwenye moyo, kwa kutumia mashine ya ultrasaundi. Kila mgonjwa atapimwa kipenyo cha mshipa huo kila baada ya kuwekewa dripu ya maji kiasi cha mililita 500 mpaka millilita 2000. Ni uamuzi wa dakitari anayemuona mgonjwa, juu ya kiasi gani cha maji mgonjwa atawekewa.

Kama ukiamua kutoshiriki katika utafiti huu, wewe au mgonjwa wako ataendelea kupata huduma ya kawaida hapo idarani na hataathirika kwa njia yeyote.

Hatari:

Hatutarajii kuwepo na athari/hatari yeyote itokanayo naushiri kikatika utafiti huu, kwa sababu mashine ya ultrasound haiumizi, haitoimionzi haratishi na mpaka sasa inatumika katika kitengo chetu cha wagonjwa wa dharura na mahututi.

Pia matibabu yako/ya mgonjwa wako hayatatokana na ushawishi wa utafiti huu, bali yataendelea kulingana na matakwa ya dakitari wako.

Hali yeyote mbaya au ya kumsumbua mgonjwa itakayotokana na utafitihuu, itashugulikiwa maramoja na ipasavyo.

Faida za utafiti:

Kwa kushiriki katika utafiti huu, wewe au mgonjwa wako atapata faida ya kufanyiwa kipimo hichi cha ultrasoundi kuangalia mshipa huu wa damu wakati matibabu yakiendelea. Pia matokeo ya utafiti huu yatatuwezesha kuandaad ondoo za kutibu wagonjwa wanaohitaji kuwekewa maji katika siku za mbeleni.

Usiri:

Taarifa zote zitakazokusanywa katika utafiti huu zitakuwasiri, hivyo ushiriki wako hautajulikana na mtu. Taarifa hizi zitajulikana kwenye timu ya watafititu.

Malipo:

Kwa kushiriki kwenye utafitihuu, hautalipwa wala hautalipa chochote.

Ukiwa nas wali au tatizo lolote, unawezakuwasiliana nawafuatao:

1. Mtafiti Mkuu,
   Dr. Hendry R.Sawe,
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   MUHAS
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4. Prof. M. Aboud,
   Director of Research and Publications,
   MUHAS.
   Simu: +255 22 2150302-6.

Mimi, _____, nimesoma/ nimesomewa maelezo yote yaliyomo kwenye fomu hii nanimeelewa.

AU

Mimi, _____, mume/mke/baba/mama/_____ nimesoma/nimesomewa maelezo yote yaliyomo kwenye fomu hii na nimeelewa. Nakubali mgonjwa wangu ashiriki katika utafiti huu.

Sahihi y amzazi/mbadala _____
Sahihi ya Mtafiti _____
Tarehe _____

Appendix D: Data sheet **IVC no:_____**

Data sheet

PLEASE ANSWER THIS QUESTION PRIOR TO ULTRASOUND EVALUATION:
Based on the history and physical so far, this patient's volume depletion is (circle one only):

MILD MODERATE SEVERE

What is the MAIN CAUSE of this patient's volume depletion (hemorrhage, vomiting, diarrhea, sepsis, etc)?

_____

What elements of physical exam or history cause you to give fluid in this patient (hypotension, tachycardia, decreased skin turgor, dry mucous membranes, etc.)?

_____

PATIENT INFORMATION (DO NOT INCLUDE ANY PATIENT IDENTIFIERS ON THIS FORM):
AGE: _____ SEX: M F INTUBATED? Y N

MEASUREMENTS during volume resuscitation
*IVC diameter to be measured at 2-3cm from R atrial border.
*Report blood pressure and heart rate taken simultaneously with ultrasound measurements.
*If less than 2 L given, leave blank spaces where volume not applicable. If more than 2L given, complete data sheet only for first 2L

At initiation of bolus:
IVC diameter (on expiration, in mm) _____ BP (SBP/DBP)
IVC diameter (on inspiration, in mm) _____ HR_____
At 500cc:
IVC diameter (on expiration, in mm) _____ BP (SBP/DBP)
IVC diameter (on inspiration, in mm) _____ HR_____
At 1000cc:
IVC diameter (on expiration, in mm) _____ BP (SBP/DBP) _
IVC diameter (on inspiration, in mm) _____ HR_____
At 1500cc:
IVC diameter (on expiration, in mm) _____ BP (SBP/DBP)
IVC diameter (on inspiration, in mm) _____ HR_____
At 2000cc:
IVC diameter (on expiration, in mm) _____ BP (SBP/DBP) _
IVC diameter (on inspiration, in mm) _____ HR_____