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Inferior Vena Cava Collapsibility Index Versus Passive Leg Raise To Assess Fluid Responsiveness in Non-Intubated Septic Patients - A Prospective Observational Study

Anne-Marie Githaiga*, Wangari Waweru-Siika, Mohamed Jeilan, Idris Chikophe, Vitalis Mung'ayi

Department of Anaesthesiology, Aga Khan University Hospital, Nairobi, Kenya

Email address:

dr.githaiga@yahoo.com (Anne-Marie Githaiga)

*Corresponding author

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Abstract: *Background*: Rapid fluid loading at diagnosis of sepsis is part of standard treatment. Predictive tools of fluid responsiveness are required to guide fluid resuscitation. The Passive Leg Raise [PLR] manoeuvre can predict fluid responsiveness in non-intubated patients with sepsis. The Inferior Vena Cava Collapsibility Index [IVCCI] can also be utilised but is not routinely performed. *Aim*: To investigate the correlation between Inferior Vena Cava Collapsibility Index [IVCCI] and a Passive Leg Raise [PLR] manoeuvre for the assessment of fluid responsiveness in non-intubated septic patients in a tertiary referral hospital in Sub-Saharan Africa. *Methodology*: A prospective observational study which recruited non-intubated septic patients who were hypotensive [mean arterial pressure less than 65 mm Hg], requiring fluid resuscitation. Focused Cardiac Ultrasound [FoCUS] was used to measure IVCCI followed immediately by a PLR manoeuvre for comparison. Patients were classified as fluid responders if they had an IVCCI ≥ 50% and/or an increase of 10% in pulse pressure following a PLR. The correlation between IVCCI and PLR on each patient in predicting fluid responsiveness was then assessed. *Results*: 38 patients satisfied the inclusion criteria. McNemar's test yielded a p=0.039 indicating that PLR test and IVCCI are not equivalent in predicting fluid responsiveness in non-intubated septic patients. A Cohen's Kappa of 0.283 signified only a "fair" correlation between the two. An IVCCI cut-off of 30% would have resulted in a near- perfect agreement as evidenced by a Cohen's Kappa value of 0.93. A cut off between 30-40% would give a Cohen' Kappa of 0.81 with a strong level of agreement. *Conclusion*: The PLR test and IVCCI test have a fair correlation and are not identical in predicting fluid responsiveness in non-intubated spontaneously breathing septic patients.

Keywords: Fluid Responsiveness, Passive Leg Raise Manoeuvre, Inferior Vena Cava Collapsibility Index, Focused Cardiac Ultrasound, Sepsis

1. Introduction

The primary goal of fluid resuscitation in sepsis is to increase stroke volume by increasing left ventricular preload therefore improving cardiac output and perfusion. The risk of excessive fluid administration has however been established, with deleterious outcomes recorded in multiple studies [1–6]. Self et al [5] looked at the clinical outcome of liberal versus restrictive fluid management and concluded that the two did not result in a difference in mortality. However, the conservative strategy resulted in more days off mechanical ventilation and reduced ICU-stay in this cohort and did not result in more kidney dysfunction and that excessive fluid administration is associated with increased mortality due to end-organ damage such as pulmonary oedema requiring prolonged mechanical ventilation, cerebral oedema and impaired bowel function. The clinical equipoise lies in the fact that there is little evidence for the exact dosing of the fluid required. Establishing hemodynamic status and volume requirements is complex and making a reliable prediction of

an increase in cardiac output upon fluid administration is difficult yet necessary [7–9]. Fluid responsiveness is the foundation of fluid resuscitation. It is defined as the response of stroke volume to fluid loading and ascertains if a patient would benefit from fluid administration.

Clinical parameters are unreliable for the assessment volume status in septic patients [7–11]. Static and dynamic parameters have instead been investigated to predict fluid responsiveness in these patients, with dynamic parameters exhibiting a higher level of accuracy for this purpose [12].

A Passive Leg Raise manoeuvre is validated to predict fluid responsiveness in the non-intubated patient [8, 12–16]. It however has several challenges such as the requirement of invasive devices to measure a change in cardiac output, and the need for changes in position that may be worsen clinical outcome such as in head injury patients. It is also not useful in patients who are agitated due to movement which can give unreliable results [8, 16].

Focused Cardiac Ultrasound [FoCUS] has become increasingly available to clinicians, enabling a more definite assessment of hemodynamic instability and its likely cause [10, 17–24]. Fluid responsiveness and any underlying cardiac pathology can quickly be determined using FoCUS [24]. The assessment of Inferior Vena Cava Collapsibility Index [IVCCI] using FoCUS has the potential to minimise the challenges faced with a PLR manoeuvre [21, 25, 26].

There is a paucity of data on predicting fluid responsiveness in spontaneously breathing non-intubated septic patients in this setting as prior studies have largely been focused on mechanically ventilated patients.

The main objective of this study was to determine how well the Inferior Vena Cava Collapsibility Index, as measured by FoCUS, predicts fluid responsiveness in non-intubated spontaneously breathing patients with sepsis when compared to the passive leg raise manoeuvre.

2. Methods

Participation was voluntary. The researchers explained purpose of the study and its associated risks and benefits to the participants or their next of kin and consent sought. Ethical approval was obtained from the Institutional Ethics Review Committee [IERC] of the Aga Khan University, Nairobi prior to study initiation- Reference number 2019/IERC/70.

2.1. Study Design

This was a prospective, observational non-randomized study.

2.2. Study Setting and Population

The study was conducted at the Aga Khan University Hospital, Nairobi [AKUHN] Kenya, a 280-bed private hospital. The hospital has an 11-bed Intensive Care Unit [ICU], a 16-bed High Dependency Unit [HDU] and a 6-bed Coronary Care Unit [CCU] that together constitute the AKUHN Critical Care Units. Patients were recruited from the hospital's Accident and Emergency [A&E] Department and Critical Care Units. The target population consisted of non-intubated patients with a diagnosis of sepsis. Patients were identified as having a confirmed focus of infection coupled with hypotension corresponding to a MAP ≤ 65mmHg and a serum lactate ≥2 requiring fluid resuscitation.

2.3. Eligibility Criteria

Patients aged 18 years and above with a diagnosis of sepsis who presented in A&E or within 6 hours of admission to the Critical Care Units with hypotension requiring fluid resuscitation were included. Patients receiving positive pressure ventilation [invasive or non-invasive] were excluded. Any patient with a condition that would result in erroneous results from either tool were excluded. These included pregnant patients, patients with pulmonary artery hypertension, heart failure, active airway obstruction, raised intra-abdominal or intra-cranial pressure and those with unclear FoCUS images. Patients requiring immediate emergency intervention such as cardiopulmonary resuscitation, defibrillation, or electrical cardioversion were also excluded.

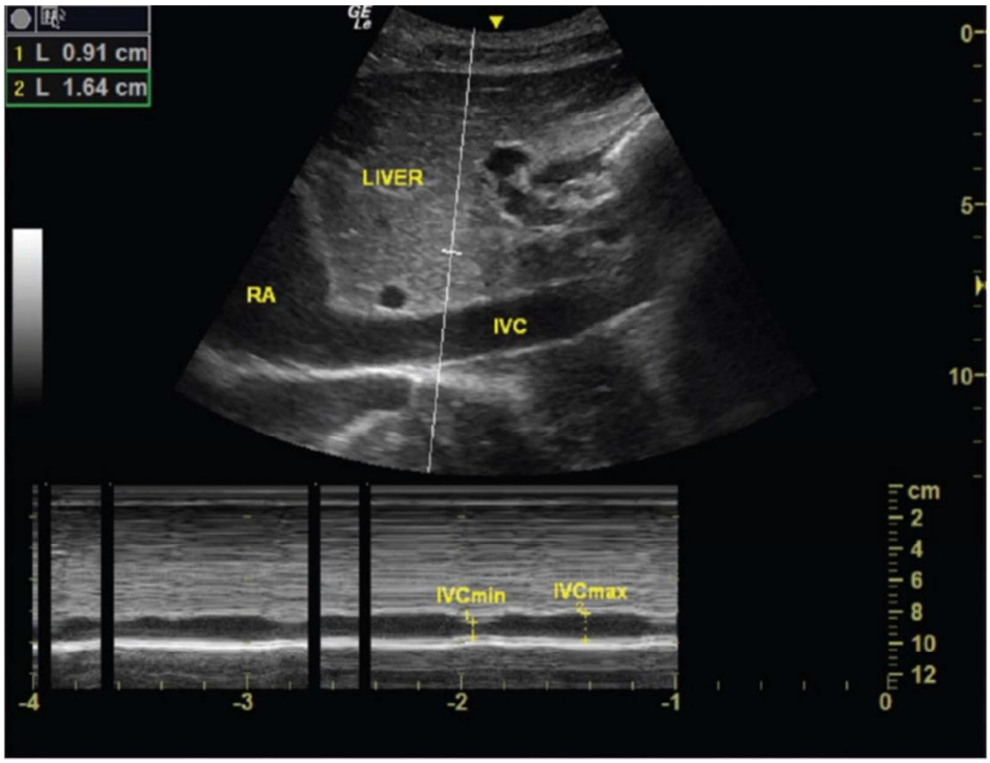
2.4. Sample Size Calculation

McNemar's test was used to calculate the sample size. Parameters were derived from a previous pilot study by Peachy et al [28] which assessed the effect of PLR on IVCCI. This study stated that the power calculation was difficult as no previous work was available to base this upon and an estimated sample size of >30 was sufficient. The discordant pairs i.e., the proportion of patients who are fluid responsive with an IVCCI and those who are non-responsive with a PLR = 45% [0.45], and those who are fluid responsive with a PLR and non-responsive with an IVCCI = 10% [0.1]. This came to a sample size of 33.

2.5. Data Collection

IVCCI measurements - Echocardiographic imaging and measurements were performed using a Phillips Lumify ® handheld ultrasound device with a phased array probe. Location of measurement of the IVC was kept standard for all patients to ensure accuracy. Inferior vena cava collapsibility index [IVCCI] was measured using a subcostal vena cava view. The probe was moved progressively to the right and pointed cranially. The hepatic veins and entrance of the IVC into the right atrium were identified and the IVC diameters was measured 2 cm caudal to the right atrium using M-mode during inspiration and expiration [19–21]. [Figure 1] Inferior vena cava measurements were collected over a 20-second period of respirations using the M-mode cursor, and the IVCCI calculated. IVCCI was calculated as the difference between maximum IVC diameter during expiration and minimum IVC diameter during inspiration divided by the maximum diameter x 100 % i.e.,

$$\frac{[\text{IVC diameter [expiration]} - \text{IVC diameter [inspiration]}]}{\text{IVC diameter [expiration]}} \times 100\ \%$$



RA, Right atrium; IVC, Inferior Vena Cava; IVCmin 1, Minimum IVC diameter on inspiration; IVCmax 2, Maximum IVC diameter on expiration

Figure 1. *Method of Obtaining IVCCI Measurements The hepatic veins and entrance of the IVC into the right atrium were identified and the IVC diameters was measured 2 cm caudal to the right atrium using M-mode during inspiration and expiration. Inferior vena cava measurements were collected over a 20-second period of respirations using the M-mode cursor, and the IVCCI calculated. IVCCI was calculated as the difference between maximum IVC diameter during expiration and minimum IVC diameter during inspiration divided by the maximum diameter.*

An IVCCI of ≥ 50% was used to classify a patient as a potential fluid responder and <50% as a non-responder. All FoCUS assessments were performed by a trained echocardiographer and recorded for later review and validation by the study cardiologist.

Passive Leg Raise Manoeuvre Measurements-IVCCI measurements were followed immediately by a PLR manoeuvre in each patient for comparison. The PLR manoeuvre was performed in three stages:

1) The head was elevated initially at 45 degrees in a semi-recumbent position before obtaining indices at baseline. A non-invasive blood pressure reading was taken in this position, following which pulse pressure was calculated as follows: Pulse pressure = [systolic blood pressure - diastolic blood pressure].
2) The patient was then placed supine and the legs raised to 45 degrees for 60 seconds using position adjustment indicators on the hospital bed. Pulse pressure was recorded after 60 seconds in this position.
3) The patient was then returned to baseline position [head elevated at 45 degrees]. Patients with an increase in pulse pressure of >10% in the supine position were classified as fluid responders and those with <10% as non-responders.

The combination of IVCCI and PLR measurements took less than 5 minutes to perform per patient. The correlation between fluid responders versus non-responders via PLR and IVCCI was then assessed.

2.6. Data Analysis

The data collected were explored using medians [Interquartile Range, IQR] or means and standard deviations [SD] and summarized continuous data e.g., age and weight of the patient. These were first tested for normality assumption using the Shapiro-Wilk test. Means and SD were used if the normality assumptions held and medians and IQR if normality assumptions were not valid. Frequencies with corresponding percentages were used for categorical data e.g., gender. The primary outcome was binary in nature [responder or non-responder] generated from IVCCI and PLR manoeuvre measurements from the same patient. The correlation between these outcomes was tested using McNemar's test to compare paired proportions. A p-value of <0.05 was considered statistically significant. The level of agreement between the two tests was quantified using Kappa statistics where values ≤0 as none to slight, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 as substantial, and 0.81-1.00 as almost perfect agreement. All tests were done using SPSS version 20.

3. Results

This study was conducted at AKUHN between January and March 2020. During this time 1231 patients were admitted in A&E, 328 in HDU and 91 in ICU. Of these 100 patients were

diagnosed to have sepsis. The total number of patients considered for recruitment in A&E, ICU and CCU during this period was 63. 37 of the potential patients were either admitted outside of the recruitment hours or were not captured during convenience sampling. Of these, 7 patients met the diagnosis of sepsis but did not require fluid resuscitation. Another 6 patients required intubation and artificial ventilation and were therefore excluded. A total of 50 patients with a diagnosis of sepsis and hypotension were screened. Emergency medical intervention such as cardioversion and cardiopulmonary resuscitation was indicated in 12 out of these 50 patients hence, they were not recruited. The remaining 38 patients were eligible for inclusion in the study. Five subjects were later excluded as follows: 2 relatives declined to give consent for participation, 2 patients had poor FoCUS images and 1 patient had head injury and the Passive Leg Raise Manoeuvre was therefore contraindicated.

The STROBE [Strengthening the Reporting of Observational Studies] diagram summarizes the flow of the study [Figure 2].

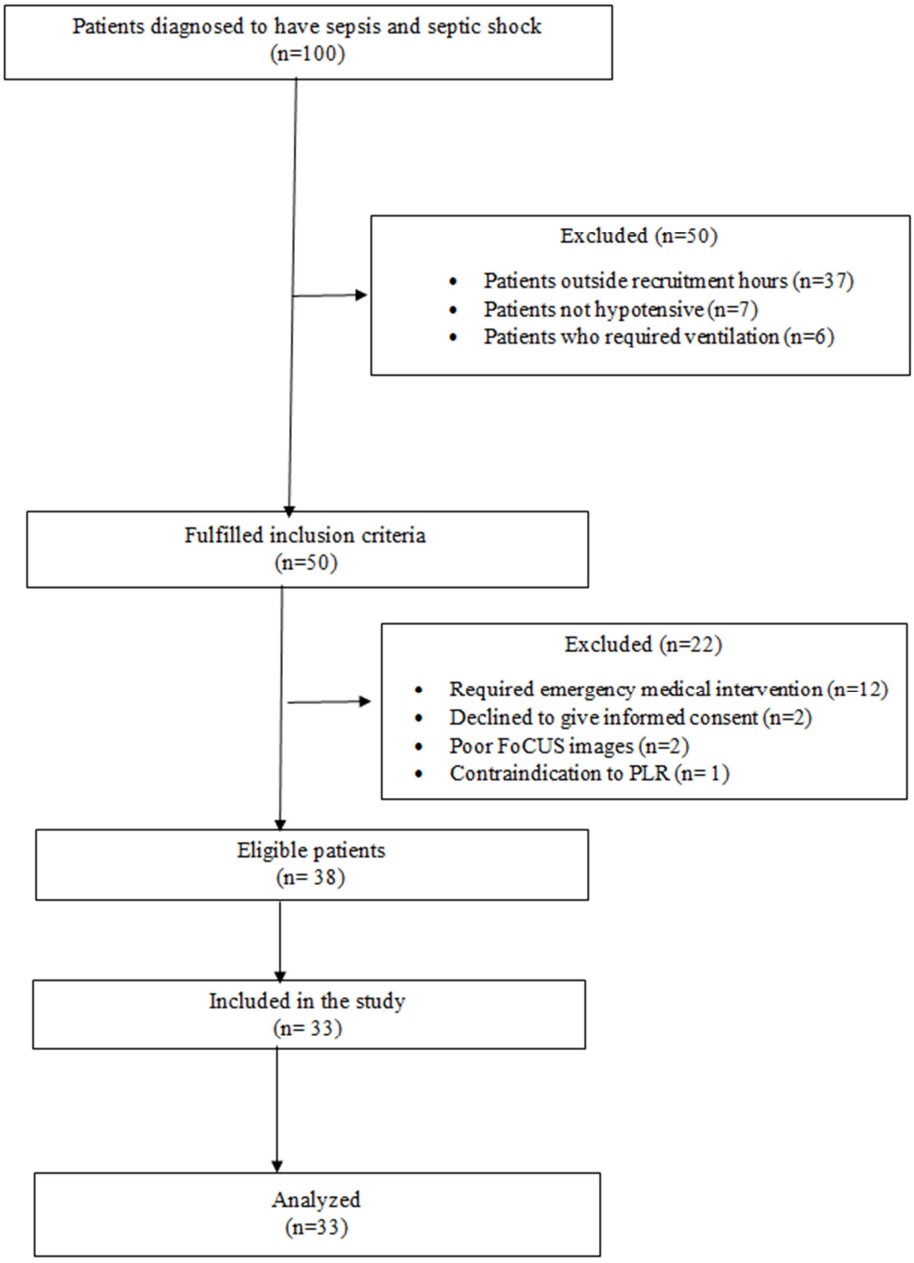


Figure 2. *STROBE flow diagram of patient distribution 1231 patients were admitted in A&E, 328 in HDU and 91 in ICU. Of these 100 patients were diagnosed to have sepsis. The total number of patients considered for recruitment in A&E, ICU and CCU during this period was 63. 37 of the potential patients were either admitted outside of the recruitment hours or were not captured during convenience sampling. Of these, 7 patients met the diagnosis of sepsis but did not require fluid resuscitation. Another 6 patients required intubation and artificial ventilation and were therefore excluded. A total of 50 patients with a diagnosis of sepsis and hypotension were screened. Emergency medical intervention such as cardioversion and cardiopulmonary resuscitation was indicated in 12 out of these 50 patients hence they were not recruited. The remaining 38 patients were eligible for inclusion in the study. Five subjects were later excluded as follows: 2 relatives declined to give consent for participation, 2 patients had poor FoCUS images and 1 patient had head injury and the Passive Leg Raise Manoeuvre was therefore contraindicated.*

In total, 17 [51.5%] of 33 patients were aged 60 years and above, with a mean age of 58.6 years [interquartile range, IQR, 45.5-75.5]. Of these, 19 [57.6%] were male and 14 [42.4%] female. A total of 24 [72.7%] of 33 patients were not on vasopressor support at the time of recruitment. All those on vasopressor support were found in the HDU. The Shapiro-Wilk test was used to determine normality in the distributions of the continuous variables. All data were normally distributed. These baseline characteristics are summarized in table 1.

Table 1. *Baseline Characteristics of study subjects who were diagnosed with sepsis requiring fluid resuscitation. [n=33] Values are mean [SD]. 17 [51.5%] of 33 patients were aged 60 years and above, with a mean age of 58.6 years [IQR, 45.5-75.5]. Of these, 19 [57.6%] were male and 14 [42.4] female. A total of 24 [72.7%] of 33 patients were not on vasopressor support at the time of recruitment.*

Baseline characteristics				
	n	**Mean**	**Standard deviation**	**%**
Gender				
Male	19			57.6
Female	14			42.4
Age				
<60 years	16	58.64	19.89	48.5
≥60 years	17			51.5
Weight				
<70 kg	14	70.94	12.35	42.4
≥70 kg	19			57.6
Vasopressor support				
No	24			72.7
Yes	9			27.3
Department				
ED	3			9.1
HDU	25			75.8
ICU	4			12.1
CCU	1			3

ED, emergency department; HDU, high dependency unit; ICU, intensive care unit; CCU, coronary care unit.

A total of 6 [66.7%] of 9 patients on vasopressor support at the time of recruitment were classified as fluid responsive using the PLR manoeuvre. This is summarized in table 2 below.

Table 2. *A total of 6 [66.7%] of 9 patients on vasopressor support at the time of recruitment were classified as fluid responsive using the PLR manoeuvre.*

Passive leg raise manoeuvre				
		Non-responsive	**Responsive**	**Total**
Vasopressor support	No	6	18	24
	Yes	3	6	9
Total		9	24	33

Each patient therefore underwent a PLR manoeuvre and IVCCI measurements which grouped them into either responders or non-responders. The passive leg raise manoeuvre classified 9 [27.3%] out of 33 patients as non-fluid responsive while 24 [72.7%] were classified as responsive. The Inferior Vena Cava Collapsibility Index classified 16 [48.5%] of 33 patients as potential responders using IVCCI measurements while 17 [51.5%] were classified as non-responders. These are summarized in table 3.

Table 3. *Each patient underwent a PLR manoeuvre and IVCCI measurements which grouped them into either responders or non-responders. The PLR manoeuvre classified 9 [27.3%] as non-fluid responsive and 24 as fluid responsive. The IVCCI classified 16 as responders and 17 as non-responders.*

PLR	Responder	24 (72.7%)
	Non-responder	9 (27.3%)
IVCCI	Responder	16 (48.5%)
	Non-responder	17 (51.5%)

PLR, passive leg raise; IVCCI, inferior vena cava collapsibility index.

McNemar's test to compare paired proportions yielded a p=0.039 signifying a statistically significant difference between the two tests. The Cohen's Kappa level of agreement between the PLR manoeuvre and IVCCI was 0.283, denoting a "fair" level of agreement. This is summarized in table 4 below.

Table 4. *IVCCI and PLR: McNemar's test to compare paired proportions yielded a p=0.039 signifying a statistically significant difference between the two tests. The Cohen's Kappa level of agreement between the two was 0.283, denting a "fair" level of agreement.*

		PLR		Total	McNemar's Test p-value	Cohen's Kappa
		Responder	Non-responder			
IVCCI	Responder	14	2	16		
	Non-responder	10	7	17	0.039	0.283
TOTAL		24	9	33		

PLR, passive leg raise; IVCCI, inferior vena cava collapsibility index.

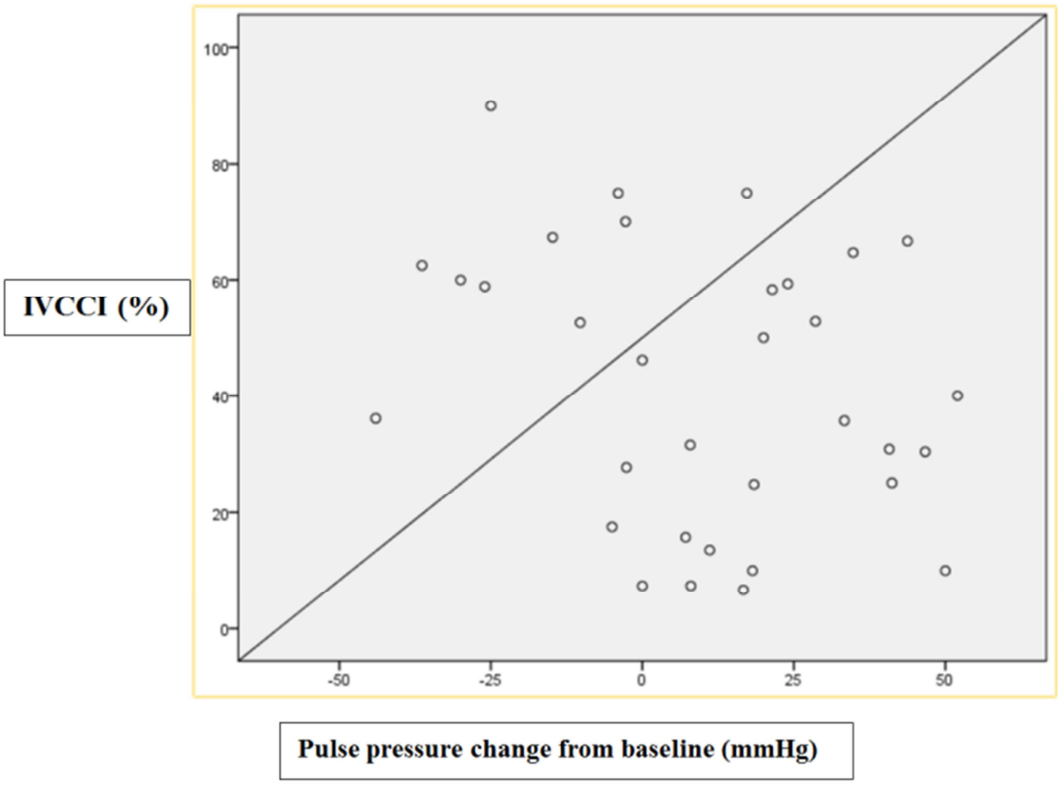
An IVCCI cut-off of 30% would have resulted in 21 fluid responsive patients and thus a better correlation with the PLR manoeuvre method. This lower cut-off would have given a near- perfect agreement with a Cohen's Kappa value of 0.93. An IVCCI cut off between 30-40% would give a Cohen's Kappa of 0.81 with a strong level of agreement. This is summarised in table 5.

Table 5. *IVCCI threshold and level of agreement. An IVCCI cut-off of 30% would have resulted in 21 fluid responsive patients and thus a better correlation with the PLR manoeuvre method. This lower cut off would have given a near-perfect agreement with Cohen's Kappa value of 0.93. An IVCCI cut off between 30-40% would give a Cohen's Kappa of 0.81 with a strong level of agreement.*

IVCCI CUT OFF (%)	COHEN'S KAPPA VALUE	LEVEL OF AGREEMENT
≥ 50	0.28	Fair
30-40	0.81	Strong
30	0.93	Near Perfect

IVCCI, Inferior Vena Cava Collapsibility Index

There is a low positive correlation of the two tests as summarised in Figure 3.



IVCCI, Inferior Vena Cava Collapsibility index

Figure 3. *Scatter plot of IVCCI and PLR. There is a low positive correlation of the two tests.*

4. Discussion

The PLR manoeuvre is validated to assess fluid responsiveness in spontaneously breathing non-intubated patients. It is in addition clinically underutilised due to several contraindications in performing this technique [16]. Inferior vena cava measurements using FoCUS offers a potential solution to this problem as it is easily accessible and does not require the change in position of critically ill

patients. This present study sought to determine if there was a correlation between two dynamic parameters in predicting fluid responsiveness in spontaneously breathing non-intubated septic patients at AKUHN: the PLR manoeuvre and IVCCI measurements.

4.1. Baseline Characteristics

A total of 1650 patients were admitted from the 3 departments during the study period, 100 of whom had a diagnosis of sepsis. Lukoko et al [27] stated that patients with a diagnosis of sepsis and septic shock made up 17.5% of the critical care admissions at AKUHN. However, during our study period only 6% of the patients had sepsis. This study used convenience sampling mainly during working hours and thus screened a total of 63 patients out of the possible 100 subjects. It is possible that the other 37 patients were missed out as they may have presented to the hospital outside working hours. This may have posed a selection bias.

Our study population consisted of 33 non-intubated spontaneously breathing septic patients, the majority of whom were aged 60 years or more, with a mean age of 58.64 years [IQR 45.5-75.5]. This mirrors current data which states that sepsis is more common in patients older than 60 years [29]. Epidemiologic data has shown that the incidence of affected males is 52-65%, in keeping with our finding that the majority of patients in our cohort were male [57.6%] [29].

Most of our patients were recruited from the HDU [n=25, 75.8%]. The higher recruitment from the HDU as opposed to A&E was most likely because spontaneously breathing septic patients are moved quickly to the AKUHN critical care units following initial fluid resuscitation, as per our admission criteria. Those patients, 6 in number, requiring multi-organ support and ventilation were admitted to the ICU, hence were excluded. The 12.1% of patients recruited from the ICU were classified as HDU patients by institutional admission criteria.

Passive leg raise as a predictor of fluid responsiveness.

This study found passive leg raise to be predictive of fluid responsiveness and it was simple to perform. A systematic review by Chaves et al [7] assessed 649 spontaneously breathing patients for fluid responsiveness. Of those, 340 [52%] were found to be fluid responsive. Passive leg raising showed a high accuracy to predict fluid responsiveness in these patients. Similarly, this study found PLR to be predictive of fluid responsiveness in spontaneously breathing patients. However, the technical challenges documented in this systematic review were not experienced in this study. The PLR was contraindicated in only one patient who had raised intracranial pressure. Compared to the IVCCI measurements, this study found that the PLR was easier to perform as it did not require patient cooperation, ability to sustain and hold inspiratory breaths and the slight discomfort of the pressure of the echocardiographic probe.

This study used the PLR as the validated tool for the assessment of fluid responsiveness and standardised its measurement for all patients. The PLR manoeuvre needs to be performed in a standard sequence and results must be interpreted accurately for it to be a reliable predictor of fluid responsiveness. The rate limiting factors for performing PLR include the following: the presence of contraindications to a PLR, the initial patient position and the methods used to interpret the hemodynamic changes to identify fluid response. In this study, the PLR baseline assessment was made in the semi-recumbent position. He et al [30] demonstrated that when PLR is initiated from a semi-recumbent position, it is more accurate than the supine position as there is more displacement of blood from the venous compartment and reduced hip joint stimulation. This study used non-invasive blood pressure measurements to derive changes in pulse pressure associated with the PLR manoeuvre. This may have posed a limitation in accuracy when compared to invasive methods. However, this approach may have eliminated the variation of the invasive blood pressure apparatus transducer position during changes in patient position. There are limited invasive measurement techniques available in our resource-limited setting, thus the change observed in pulse pressure in our cohort is an acceptable compromise, as evidenced by He et al [30]. This study can therefore reliably use the obtained PLR manoeuvre observations to predict fluid responsiveness in non-intubated septic patients. Most of our patients [72.7%] were considered fluid responsive using the PLR manoeuvre. This provided a baseline from which we compared the IVC measurements as a predictor of fluid responsiveness.

4.2. IVCCI as a Predictor of Fluid Responsiveness

Clinically, the perceived limitations of the PLR manoeuvre make it underutilised. This study hypothesized that FoCUS would offer a potential solution to this problem. In a systematic review, Mandeville et al. [24] conclude that FoCUS was a useful non-invasive tool for assessment of septic patients, and transthoracic analysis of IVC diameter changes with respiration provided prediction to fluid responsiveness. This present study however did not find IVCCI measurements to be a predictive of fluid responsiveness in our cohort when compared to PLR manoeuvres. PLR is considered validated as Preau et al quote a sensitivity of 86% and a specificity of 90%. There was therefore a discrepancy in predicting fluid responsiveness using the PLR manoeuvre and IVC measurements on the same patient. We found that the Inferior Vena Cava Collapsibility Index classified only 16 [48.5%] of 33 patients as fluid responders while the PLR identified a much higher proportion at 24 [72.7%] of 33 patients.

Given that the PLR is the validated tool there may be several reasons as to why we did not find similar results with IVC measurements.

IVCCI reflects the decrease in inferior vena cava diameter during inspiration. Although the literature describes cut-off values ranging from 39-50% for IVCCI in terms of response to fluid expansion, the cut-off value of $\geq$ 50% has been most reported. This study utilised a cut-off of $\geq$ 50% to predict a fluid responder. In comparison to other studies using similar techniques as ours, an IVCCI of 25% produced fewer false-negative patients than previously suggested cut-off parameters. Preau et al [21] examined IVCCI in non-

intubated septic patients and reported an IVCCI cut-off of 31%. This is a significantly lower cut-off than our study. It is therefore likely that our IVCCI threshold of 50% did not exclude fluid responsiveness in our population, leading to a significant proportion of false negatives due to this variable range in definition. From our data, a cut-off of 30% would have resulted in 21 fluid responsive patients using IVCCI measurements. This lower cut-off would have given a near-perfect agreement with a Cohen's Kappa value of 0.93. A cut off between 30-40% would give a Cohen' Kappa of 0.81 with a strong level of agreement. Further studies may explore these cut-off values for the IVCCI as we do not have documented normal measures for our study population.

Secondly, we did not have a standardized respiratory pattern for our study subjects. The fluctuating respiratory effort in breathing of these subjects due to the response to sepsis and septic shock may lead to false positives or false negatives [11]. Exaggerated inspiratory effort, producing increased negative intrathoracic pressures may induce IVCCI ≥ 50% in the absence of fluid responsiveness. Shallow breathing on the other hand, with small intrathoracic pressure changes, may suggest the absence of IVCCI <50% even in the presence of fluid responsiveness. This may therefore have affected the results and contributed to the discrepancy between fluid-responsiveness by PLR versus that by IVCCI. Furthermore, if a patient was severely volume contracted, their computed IVCCI may have been narrow and thus may have been falsely classified as a non-responder.

Echocardiographic imaging and measurements were performed using a Phillips Lumify ® handheld ultrasound device, and all measurements were performed by the same specialist echocardiographer. There was therefore no change in level of expertise or quality of equipment for all the study subjects which was kept standard. Any patients in whom clear ultrasound images for FoCUS could not be obtained were excluded. This ensured accurate images and IVC measurements that were standard across the board. The echocardiographer excluded 2 patients who had poor FoCUS images due to truncal obesity and gaseous distension in the peritoneal cavity. The discrepancy between PLR and IVCCI in our results was therefore most likely to be due to patient factors rather than being operator dependent.

Majority [66%] of patients who were classified as non-responsive using a PLR manoeuvre were not on vasopressor support. This meant that primary physicians could have administered more fluid in order to achieve hemodynamic instability which would cause fluid overload and end organ damage., This finding reinforces the importance of using dynamic parameters to assess fluid responsiveness in septic patients prior to fluid administration [7].

4.3. Strengths

FoCUS IVCCI measurements were performed by the same qualified echocardiographer, using the same standard equipment. Any patients in whom clear ultrasound images could not be obtained were excluded. Only 2 out of 33 patients had poor ultrasound images which may signify a high utility of IVCCI in this cohort of patients. This utility points to the fact that it was possible to attain good images for IVCCI measurements in majority of this cohort. Furthermore, a standardised protocol for obtaining PLR manoeuvre measurements was employed. This ensured objectivity in PLR measurements which were therefore accurate and reliable. The fact that only 6% of patients admitted with a diagnosis of sepsis required invasive ventilation justifies the objective of this study: Majority were spontaneously breathing and thus establishing a tool to predict fluid responsiveness in this population that is both validated and easy to apply clinically is crucial.

4.4. Limitations

Firstly, convenience sampling was adopted to recruit patients. As noted, out of the 100 patients who had a diagnosis of sepsis and septic shock in the study period, only 63 encountered the research team. The echocardiographer also excluded any patients in whom images were not obtainable. This may have resulted in a sampling bias. Secondly, researchers and clinicians were not blinded. Therefore, efforts to achieve end-goals of fluid resuscitation may have caused selection bias. Furthermore, a surrogate marker for stroke volume was used to assess fluid responsiveness in PLR manoeuvre. Changes in pulse pressure using non-invasive blood pressure measurements however are not the gold standard. Nevertheless, as this study was purely observational, we could not advocate for invasive methods for research purposes.

Additionally, breathing patterns were not standardized across the study subjects and thus may have contributed to the discrepancy in the two tests. Perhaps documentation on the type of respiratory pattern should be considered in future studies. Lastly, our chosen IVCCI threshold of ≥50% may not have been sufficient to exclude fluid responsiveness in patients who were volume depleted. Extreme volume depletion may cause a narrow IVC diameter that will provide a false negative result to fluid responsiveness.

5. Conclusion

In conclusion, this study showed only fair correlation in the assessment of fluid responsiveness between a PLR manoeuvre and IVCCI in our cohort of spontaneously breathing non-intubated septic shock patients.

The PLR test and IVCCI test are not equivalent in predicting fluid responsiveness in non-intubated spontaneously breathing septic patients in AKUHN. The influence of breathing pattern on IVCCI and our chosen threshold may have influenced our results. Further studies on this topic may explore lower cut-off values of the IVCCI to predict fluid responsiveness, as the measurements used in prior studies are not defined in our study population. Furthermore, a wide range of echocardiographers or physicians trained in FoCUS may be explored to ascertain if similar images and results may be arrived at.

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