

ASSESSMENT OF FLUID RESPONSIVENESS IN PATIENTS WITH ACUTE CIRCULATORY FAILURE USING ECHOCARDIOGRAPHY

By

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ABSTRACT

Background: Predicting fluid responsiveness, the response of stroke volume (SV) to fluid loading, is a relatively novel concept that aims to optimize circulation, and as such organ perfusion, while avoiding futile and potentially deleterious fluid administrations in critically ill patients. Dynamic parameters have shown to be superior in predicting the response to fluid loading compared with static cardiac filling pressures. Passive leg raising (PLR) as a means to alter biventricular preload in combination with subsequent measurement of the change in stroke volume can provide a fast and accurate way to guide fluid management in a broad population of critically ill patients.

Objective: To assess the fluid responsiveness in patients with acute circulatory failure using left ventricular outflow variation by 2D echocardiography and inferior vena cava diameter.

Patients and Methods: After departmental ethics committee approval and patient consents were obtained, 40 patients included in this work with shock not on mechanical ventilation who were admitted to Critical Care unit of Internal Medicine Department in Al-Hussein Hospital, Al-Azhar University, and The study was carried out during the period from April 2019 to August 2020, 30 patients were responder, and 10 patients were not responder. All patients were subjected to complete history taking, complete physical examination including: arterial blood pressure with mean arterial pressure (MAP) calculation, heart rate (HR), respiratory rate (RR), body temperature (°C). Laboratory investigations included complete blood count (CBC), liver function tests, renal function tests and arterial blood gases (ABGs). In addition, echocardiographic assessment was performed, the left ventricular outflow tract velocity time integral (LVOT) VTI was recorded classically by pulsed wave doppler across LVOT on a 5-chamber apical view, maximum and minimum inferior vena caval DVC values over a single respiratory cycle were measured before and after (PLR).

Results: In the two groups (responder and not responder), 18 (45%) were males and 22 (55%) were females. 22 (55%), 20 (50%), 13 (32.5%), 17 (42.5%), 9(22.5%) were patients with diabetic (DM), hypertensive (HTN), chronic kidney disease (CKD), smoking and on vasoactive drugs respectively, There was no significant difference between the two groups as regard hemodynamic data on admission including temperature, respiratory rate, and pulse rate, There were significant differences between the two groups as regard hemoglobin (Hb), alanine transaminase (ALT), aspartate transaminase (AST) on admission.

By echocardiographic parameters, change of velocity time integral ΔVTI % showed significant difference between the two groups with the areas under the curve 0.800, at the cutoff value 3.409. The sensitivity was 90.0, specificity was 70.0, PPV 90.0%, and NPV 70.0% in predict the response.

Conclusion: Careful management of volume status and fluid administration is an important determinant of outcomes of the critically ill patients. The change in stroke volume displayed predicted fluid responsiveness

in shocked not mechanically ventilated patients with an acceptable sensitivity and specificity than IVC collapsibility Index.

Key words: Fluid responsiveness, VTI, passive leg raising, endoscopic technique, interlaminar approach, lumbar discectomy, minimally invasive.

INTRODUCTION

Fluid resuscitation remains the cornerstone of treatment for patients with acute circulatory failure. Inappropriate administration of fluids has deleterious effects, including volume overload, systemic and pulmonary edema, and limitation of oxygen diffusion to tissues, thereby leading to increased tissue hypoxia (*Hu et al., 2013* and *Pinsky, 2015*).

One method routinely used to evaluate intravascular volume in hypotensive patients uses hemodynamic response to a fluid challenge can be monitored clinically by heart rate, blood pressure, pulse pressure, and urine output or by invasive monitoring with the measurements of the right atrial pressure (RAP), pulmonary artery occlusion pressure (PpAO), and cardiac output (*Mackenzie and Noble, 2014*).

Hemodynamic parameters, such as pleth variability index and stroke volume variation, may better predict fluid responsiveness. However, the measurement of these parameters requires invasive procedures and special monitoring equipment, limiting their clinical application (*Pinsky, 2015*).

Studies have shown that some parameters may be related to volume status. The traditional static parameters, such as intrathoracic blood volume index, pulmonary wedge pressure, pulse pressure variation, and central venous pressure,

have been proved not to be related to patient's a volume status (*Hu et al., 2013*). At same time with the spread of critical care echocardiography, several echocardiographic indices of fluid responsiveness have been proposed in spontaneous and mechanically ventilated patients (*Bentzer et al., 2016*).

The present work aimed to assess the fluid responsiveness in patients with acute circulatory failure using left ventricular outflow variation by 2D echocardiography and inferior vena cava diameter.

PATIENTS AND METHODS

This prospective observational investigation study was conducted on 40 adult patients divided into two groups

- Responders group (R): 30 shocked patients with SV post PLR test $\geq 10\%$.
- Non-responders group (NR): 10 shocked patients with SV post PLR test $< 10\%$.

Patients were admitted to the Critical Care unit of Internal Medicine Department in Al-Hussein Hospital, Al-Azhar University with the diagnosis of shock. Approval of the medical ethics committee of Al-Azhar Faculty of Medicine had been taken. An informed consent from patient or patients' next of kin had been taken before enrollment to the study.

The study was carried out during the period from April 2019 to August 2020.

Inclusion criteria: Age between (18-70) years old, spontaneously breathing patients, and patients diagnosed to have acute circulatory failure.

Exclusion criteria: Incarceration, pregnancy, amputation or severe lower limb ischemia, and contraindication to a passive leg raise (PLR) maneuver (e.g. elevated intracranial pressure, tamponade, acute aortic dissection), resuscitation for more than 48 h.

- All patients included in the study were subjected on admission to complete history taking, complete physical examination including arterial blood pressure with mean arterial pressure (MAP) calculation, heart rate (HR), respiratory rate (RR), and body temperature (°C).
- Laboratory investigations: Complete blood count (CBC), serum creatinine (Cr) (mg/dl), total bilirubin and arterial blood gases (ABGs),
- Echocardiographic assessment was performed: The left ventricular outflow tract (LVOT) VTI was recorded, The IVC was visualized and IVC collapsibility index was calculated from the following formula:
- A standard passive leg rising test was done by placing a patient in a semi-recumbent position for three minutes, then laying the patient supine with the

$$\frac{IVC_{\text{expiratorydiameter}} - IVC_{\text{inspiratorydiameter}}}{IVC_{\text{expiratorydiameter}}} \times 100$$

legs elevated to 45 degrees for three minutes and measuring stroke volume (SV), velocity time integral of left ventricular outflow tract (VTI (LVOT)), inferior vena caval (IVC) collapsibility index, and cardiac output before and immediately (1–3 minutes) following the PLR maneuver (Bendjelid and Romand, 2003).

- Statistical analysis of data by IBM computer using statistical package for the social sciences (SPSS) version 20: unpaired (Independent) t-test to compare quantitative variables between groups and if not normally distributed sample we used Mann-Whitney U. Agreement of the predictive with the responsiveness was expressed in sensitivity, specificity, positive predictive value, negative predictive value and accuracy. Receiver operating characteristic curve (ROC) was plotted to analyze a recommended cutoff, significance test results are quoted as two-tailed probabilities. Significance of the obtained results was judged at the 5% level.

RESULTS

There was a significant relationship between fluid responsiveness and Hb, ALT, AST as p values were 0.001, 0.006, and 0.007 respectively, while no

significant relationship between fluid responsiveness, and other laboratory parameters or present clinical data (Tables 1 and 2).

Table (1): Relation between Clinical and lab Parameters and fluid responsiveness (Mean \pm S.D)

Clinical and Lab. Parameters \ Groups	Responder group. "n=30"	Non responder group. "n=10"	P
Age (years)	59.6333 \pm 11.08426	50.6667 \pm 5.83730	0.913
mean BP (mm/Hg)	52.5000 \pm 10.40143	103.9000 \pm 24.42426	0.601
Pulse (beat/mint)	99.3000 \pm 18.61062	37.2200 \pm 0.12293	0.535
Temp. (°C)	37.4000 \pm 0.34039	28.3000 \pm 3.52924	0.112
R.R (cycle/mint)	30.7667 \pm 3.68298	6.6000 \pm 10.29779	0.072
PH	7.2957 \pm 0.12249	7.2970 \pm 0.12320	0.976
SVC SO2 (%)	0.6307 \pm 0.14729	12.3100 \pm 2.41682	0.574
Hb (g/dL)	9.2767 \pm 2.16073	15.0100 \pm 9.07995	0.001

Table (2): Relation between Clinical and lab Parameters and fluid responsiveness (Mean \pm S.D)

Clinical and Lab. Parameters \ Groups	Responder group. "n=30"	Non responder group. "n=10"	If not normally Distributed	
			Mann-Whitney U	Asymp. Sig. (2-tailed)
TLC (*10 ³ /μl)	15.4967 \pm 11.99340	15.0100 \pm 9.07995	149.000	0.975
ALT (U/C)	30.0200 \pm 25.26306	405.000 \pm 719.07255	77.500	0.024
AST (U/C)	69.6667 \pm 86.63532	524.600 \pm 890.05233	94.000	0.080
S.CR (mg/dL)	3.4880 \pm 2.71850	2.8100 \pm 2.03822	135.500	0.650
UREA (mg/dL)	132.7733 \pm 64.54376	123.6400 \pm 70.36028	132.000	0.574
CVP (cm/H2O)	4.2667 \pm 3.86793	6.6000 \pm 10.29779	127.500	0.477
HCO3 (mmol/L).	18.1433 \pm 5.69807	19.0600 \pm 4.49820	137.500	0.696
LACTATE (mmol/L)	2.9600 \pm 1.39101	2.8400 \pm 2.88798	105.000	0.159

There was a significant relationship between fluid responsiveness from one

hand and Δ VTI % on other hand as p value 0.001 (**Table 3**).

Table (3): Relation between echocardiographic parameters and fluid responsiveness (Mean \pm S.D)

Echocardiographic parameters	Responder group. "n=30"	Non responder group. "n=10"	If not normally distributed	
			Mann-Whitney U	Asymp. Sig. (2-tailed)
Pre-VTI (cm)	20.37 \pm 6.67	20.14 \pm 7.30	150	1.000
Post-VTI (cm)	22.84 \pm 7.02	19.56 \pm 8.93	107.500	0.184
Δ VTI (%)	13.62 \pm 12.63 %	3.59 \pm 16.23 %	60.000	0.005*
Pre-IVC Exp. Diameter (mm)	18.31 \pm 4.90	20.51 \pm 6.42	119.000	0.333
Pre-IVC Insp. Diameter (mm)	11.52 \pm 5.33	14.25 \pm 7.66	113.500	0.254
Post-IVC Exp. Diameter (mm)	19.84 \pm 5.90	20.60 \pm 5.32	140.500	0.767
Post-IVC Insp. Diameter (mm)	12.62 \pm 6.31	12.86 \pm 5.62	138.500	0.719
Pre IVCCI (mm)	39.04 \pm 15.98	34.66 \pm 19.76	112.000	0.235
Post IVCCI (mm)	38.43 \pm 18.34	38.58 \pm 21.47	143.000	0.827
Pre SV (ml)	60.56 \pm 27.20	68.09 \pm 33.59	126.000	0.453
Post SV (ml)	92.06 \pm 59.02	62.55 \pm 36.37	98.000	0.104

As regards Δ VTI % (percent of change between Pre VTI and Post VTI), the areas under the curve were done, and the cut of

point which can differentiate perfectly between responder and non-responders (Table 4 and Fig. 1).

Table (4): Sensitivity and specificity for Δ VTI %

Δ VTI % cut of point	Sensitivity	Specificity	+PV	-PV
>3.409090909	90.00	70.00	90.0	70.0

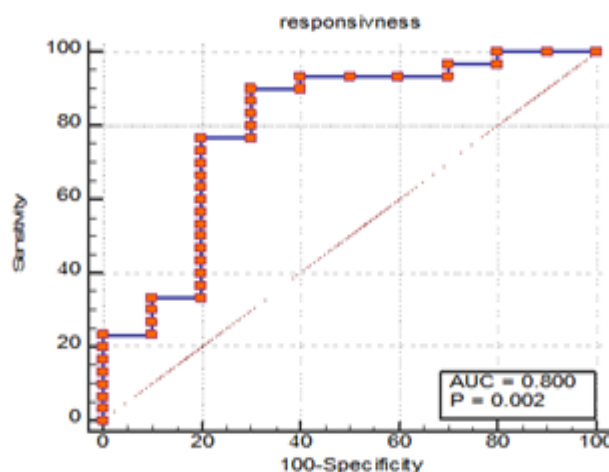


Figure (1): Area under the ROC curve (AUC) for Δ VTI %**DISCUSSION**

Forty spontaneous breathing shocked patients were studied, 45% males and 55% females. 55%, 50%, 32.5%, 42.5%, 22.5% were patients with DM, HTN, CKD, smoking and on vasoactive drugs respectively.

After PLR test there were significant difference change in LVOT (cm), LVOT DIAM (mm) and SV with p values 0.002, 0.000, and 0.001 respectively, while no significant change in IVC DIST. (mm), IVC.COLLAB (mm), COLLAB Index with p values 0.073, 0.445, and 0.805 respectively.

Marik et al. (2013) defined fluid responsiveness an increase of stroke volume of 10-15% after the patient receives 500 ml of crystalloid over 10-15 minutes SV used to define patients as fluid responder if SV increase by 10% after PLR. So, we have 75%, 25% patient fluid responder and fluid non responder respectively.

As regard the age, there was no significant difference between the two groups (59.63 ± 11.08 VS. 59.20 ± 9.67 years). Also, there was no significant difference between responders and non-responders as regards sex in the two groups. In agreement with *Muller et al. (2012)*, there was no significant difference between the two groups with P value 0.58.

The mean arterial blood pressure showed no significant difference between the responder and non-responder patient. This result was in agreement with *Monnet et al. (2011)* and *Pierrakos et al. (2012)* who showed that the fluid-induced changes in cardiac output are not reflected

at all by the fluid-induced changes in mean arterial pressure (MAP).

In this study, the SVC SO₂ showed no significant difference between the responder and non-responder patients. These results were in agreement with *Oliveira-Costa et al. (2012)*, show that the fluid-induced changes in cardiac output are not reflected at all by the fluid-induced changes SVC SO₂.

CVP showed no significant difference between the responder and non-responder patients. This result was in agreement with *Marik et al. (2013)* who conducted a systematic analysis of 24 studies. Five studies compared CVP with measured circulating blood volume, while the other 19 determined the relationship between CVP (and / or change in CVP) and change in cardiac performance following fluid the poor value of CVP in predicting fluid responsiveness could not be emphasized more. Accordingly, authors recommended that CVP should not be used to make clinical decisions regarding fluid management challenge (*Oliveira-Costa et al., 2012*). The laboratory data in this study showed a insignificant difference in Hb level, ALT and AST between responder patients and non-responder, while the other laboratory data show no significant difference. This result was in agreement with (*Cherpanath et al., 2016*).

VTI at base line and after PLRt showed no significant difference but change of VTI was significantly higher in responders than non-responders with $p < 0.001$. The change of VTI showed area under the curve 0.800, at the cut off value 3.409. The sensitivity was 90.0, specificity

was 70.0, PPV 90.0%, and NPV 70.0% in predict the responder.

Brun et al. (2012) assessed the usefulness of change of VTI to predict fluid responsiveness in critically ill patients. His study examined patients with SP developed oliguria and spontaneously breathing. VTI after 500cc PLRt showed AUC 0.93 with sensitivity, specificity, PPV and NPV of 75%, 100%, 100% and 79% respectively. In comparison to our results which showed a best cut off value of 3.409 with AUC 0.800 ($p < 0.001$) with sensitivity, specificity, PPV, NPV was 90%, 70%, 90%, 70% respectively.

In this study, there was no significant difference between the responder and non-responder patients regarding the inferior vena cava expiratory and inspiratory diameters (IVC Exp & IVC Insp) in both group's pre and post Passive Leg Rising tests (PLRt). No statistical significant relation between IVCCI pre and post PLRt Pre (IVCCI).

Muller et al. (2012) showed that cIVC cannot predict fluid responsiveness in spontaneously breathing patients with ACF. His study examined patients spontaneously breathing with acute circulatory failure, and showed AUC of the ROC curve for cIVC was 0.77, with sensitivity, specificity was 70%, 80% respectively. The best cutoff value was 40%. This due to that cIVC was a dynamic preload index. In contrast with findings reported in mechanically ventilated septic patients, dynamic parameters have been shown to be ineffective to predict fluid responsiveness in spontaneous breathing patients (*Summers et al., 2013*).

Spontaneous ventilation implies a very wide range of breathing patterns. In patients with spontaneous ventilation, respiratory variations are highly variable from one cycle to another in a given patient and between different patients. Then, influence of breathing pattern on cIVC is also variable. These results indirectly confirm that spontaneous breathing is a natural limit for the use of a dynamic parameter; cIVC may be influenced by the magnitude of respiratory movements, especially in the case of dyspnea, a typical feature in patients with circulatory failure and/or shock. The wide range of breathing patterns observed in spontaneously breathing critically ill patients is probably confusing. *Kimura et al. (2011)* showed that breathing manner significantly affects cIVC in spontaneously breathing volunteers.

CONCLUSION

Careful management of volume status and fluid administration is an important determinant of outcomes of the critically ill patients. The change in SV displayed predicted fluid responsiveness in shocked not mechanically ventilated patients with an acceptable sensitivity and specificity than IVC collapsibility Index.

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تقييم الاستجابة للسوائل في مرضي فشل الدورة الدموية الحاد باستخدام الموجات فوق الصوتية علي القلب

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خلفية البحث: يعتبر التنبؤ بالإستجابة للسوائل وإستجابة حجم النفضة لإعطاء المحاليل مبدأ جديداً إلي حد ما، حيث أنه يهدف إلي تحسين الدورة الدموية وإرواء الأعضاء أيضاً، بينما يتجنب إعطاء المحاليل الضار وغير المجدي بين مرضي الحالات الحرجة. وقد أظهرت المعلومات الديناميكية أفضلية في التنبؤ بالإستجابة للسوائل مقارنة بالضغوطات الساكنة الناتجة عن امتلاء القلب. ويمكن أن يمدنا إختبار رفع الطرفين السفليين بدون مجهود كوسيلة لتغيير مقدار تحميل البطينيين بالإضافة إلي تسجيل قياسات التغير في حجم النفضة لاحقاً بطريقة سريعة ودقيقة في قيادة عملية التحكم في إعطاء المحاليل لمرضي الحالات الحرجة.

الهدف من البحث: تقييم الإستجابة للسوائل في مرضي فشل الدورة الدموية الحاد بإستخدام الموجات فوق الصوتية علي القلب عن طريق حساب سرعة الوقت التكاملي لمجرى تدفق البطين الأيسر وقطر الوريد الأجوف السفلي.

المرضي وطرق البحث: أجريت هذه الدراسة علي 40 مريضاً يعانون من فشل الدورة الدموية الحاد والذين يتنفسون بدون جهاز تنفس صناعي بعد أخذ الموافقة منهم، وتم تقسيمهم إلي مجموعتين إعتياداً علي مقدار التغير في حجم النفضة بعد إختبار رفع الطرفين السفليين بدون مجهود:

- **المجموعة الاولى (مستجيب):** تشتمل هذه المجموعة علي ٣٠ مريض يعانون من فشل الدورة الدموية الحاد وزاد عندهم مقدار التغير في حجم النفضة بأكثر من أو يساوي ١٠ %.

- **المجموعة الثانية (غير مستجيب):** تشتمل هذه المجموعة على ١٠ مرضي يعانون من فشل الدورة الدموية الحاد وزاد عندهم مقدار التغير في حجم النفضة بأقل من ١٠ %.

وقد تم عمل الآتي لكل المرضى: أخذ التاريخ المرضي الكامل وفحص إكلينيكي شامل وإختبارات معملية مثل صورة دم كاملة ووظائف الكبد ووظائف الكلى وغازات بالدم وموجات صوتية على القلب لقياس سرعة الوقت التكاملي لمجرى تدفق البطين الأيسر، وقياس قطر فتحة الشريان الأبهر، وأكبر وأصغر قطر للوريد الأجوف السفلي خلال دورة تنفسيه كاملة قبل وبعد إختبار رفع الطرفين السفليين بدون مجهود وتم حساب معدل طي الوريد الأجوف السفلي عن طريق حساب الفرق بين أكبر وأصغر قطر للوريد الأجوف السفلي خلال دورة تنفسيه واحده مقسوما علي أكبر قطر ويكتب نسبة مئوية وحساب حجم النفضة عن طريق قياس سرعة الوقت التكاملي لمجرى تدفق البطين الأيسر، وقياس قطر فتحة الشريان الأبهر وتحليل النتائج إحصائياً.

نتائج البحث:

- عدم وجود فارق ذو دلالة إحصائية بين المجموعتين بالنسبة للسن والجنس.
- عدم وجود فارق ذو دلالة إحصائية بين مرضي البول السكري وإرتفاع ضغط الدم الشرياني ومرض الفشل الكلوي المزمن بين المجموعتين.
- عدم وجود فارق ذو دلالة إحصائية بين المجموعتين بالنسبة للعلامات الحيوية وتشمل درجة حرارة الجسم وعدد نبضات القلب وعدد معدل التنفس.
- عدم وجود فارق ذو دلالة إحصائية بين المجموعتين بالنسبة للإختبارات المعملية ما عدا نسبة الهيموجلوبين وإنزيمات الكبد.
- وجود فارق ذو دلالة إحصائية بين المجموعتين بالنسبة للتغير في سرعة الوقت التكاملي لمجرى تدفق البطين الأيسر قبل وبعد إختبار رفع الطرفين السفليين بدون مجهود حيث وجد أنه عند قيمة (٤٠٩,٣) يمكن ان تتوقع الإستجابة للسوائل بحساسية ٩٠ % وخصوصية ٧٠ %.

- لا يوجد فارق إحصائي بين المجموعتين بالنسبة للتغير في القطر الأكبر أو الأصغر للوريد الأجوف السفلي قبل وبعد اختبار رفع الطرفين السفليين بدون مجهود، ولا يوجد فارق إحصائي بين المجموعتين بالنسبة لمعدل طي الوريد الأجوف السفلي.

الاستنتاج: يعتبر التحكم الدقيق في حجم الدورة الدموية وإعطاء السوائل هو محدد مهم في عدد الحالات المتحسنة بين مرضي الحالات الحرجة كما أن التغير في حجم النفضة أثبت القدرة علي التنبؤ بالإستجابة للمحالييل في مرضي فشل الدورة الدموية الحاد والذين يتنفسون بدون جهاز تنفس صناعي بحساسية وخصوصية مقبولة أكثر من معدل طي الوريد الأجوف السفلي.