# EVALUATION OF CHANGES IN MEAN ARTERIAL PRESSURE AND PULSE PRESSURE FOLLOWING PASSIVE LEG RISING TEST AS INDEX AND PREDICTOR OF FLUID RESPONSIVENESS IN SEPTIC SHOCK PATIENTS

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**Abstract:** Reduced oxygen supply, excessive oxygen consumption, or insufficient oxygen utilization1 causes cellular and tissue hypoxia, which is characterized as shock. Hypoperfusion, for whatever reason, causes cells to malfunction due to insufficient oxygen and substrate supply. Initial resuscitation in shock patients involves administering fluids to raise preload and, by extension, cardiac output. It is crucial to avoid fluid overload and hypovolemia while treating shock patients. Pulmonary edema, increased intraabdominal pressure, and increased intracranial pressure are complications that may occur or worsen if fluids are given to a patient who is not responding. Therefore, before trying volume expansion, it is crucial to identify possible fluid responders. Researchers in this study assessed the efficacy of the passive leg raising test in assessing fluid responsiveness in patients with septic shock by measuring changes in mean arterial pressure and pulse pressure.

***Keywords:*** *Septic Shock, Septic Shock, Fluid Resuscitation, Mean Arterial Pressure, Pulse Pressure, Passive Leg Rising Test, Dysfunction*

## Introduction

The intravascular volume expansion (VE) technique is an important component of the hemodynamic therapy for critically ill patients who are suffering from hypoperfusion. In the early stages of sepsis, the administration of fluids and other early resuscitation techniques have the potential to save lives. [1,2] As a consequence of ventricular edema (VE), patients who have either right or left ventricular failure may have a deterioration in microvascular perfusion and oxygen delivery, in addition to peripheral and pulmonary puffiness. [3,4]

ISSN:0975 -3583,0976-2833 VOL 11, ISSUE 09, 2020

A patient who is insensitive to preload may have an exacerbation of pulmonary edema, respiratory failure, extended mechanical ventilation time, and the development of intra-abdominal hypertension as a consequence of a high venous ejection fraction (VE). [5,6] Through a technique known as passive leg raising (PLR), which includes bringing venous blood from the legs into the intrathoracic compartment, it is possible to induce an increase in the volume of blood in the intrathoracic space as well as an increase in the preload on the heart. [7,8] The purpose of the present experiment was to determine whether or whether the measurement of SVI, in conjunction with measuring PLR, could be used to predict the hemodynamic response to VE.[9,10]

Fluid therapy is often administered to severely sick individuals experiencing shock as a primary treatment option. Several studies including a recent meta-analysis have shown that the PLR test is a valid approach for detecting preload response. When doing a PLR, five criteria must be considered, say Monnet and Teboul. [11] To begin, rather than beginning in the supine position, PLR should begin in the semi-recumbent. Secondly, measuring blood pressure is insufficient for evaluating the PLR effects; direct monitoring of cardiac output is required. [12] Thirdly, as the effects of PLR may disappear within 1 minute, the method used to evaluate cardiac output during PLR needs to be sensitive enough to identify temporary alterations. The fourth point is that cardiac output has to be monitored before, during, and after PLR. [13,14] This is to ensure that it recovers to baseline when the patient is returned to the semi-recumbent posture. Fifthly, adrenergic stimulation may be triggered by pain, cough, discomfort, or waking, leading to an incorrect interpretation of changes in cardiac output. As an additional sixth rule, it is important to rule out any potential confounding factors or underlying conditions that could affect the PLR. These include conditions like elevated intrathoracic pressure, cardiac tamponade, right ventricular infarction or failure, and intra-abdominal hypertension (IAH), which is defined as an IAP greater than 12 mmHg. [15,16]

A certain amount of blood from the lower extremities and abdominal compartment is used to imitate a fluid challenge and boost preload in PLR. A PLR often involves the "autotransfusion" of around 300 mL of blood into the central circulation from the legs and mesenteric splanchnic pool. One advantage it has over other options is that further fluids won't be added if the patient isn't responding to them, unlike with a fluid bolus or challenge. In fact, venous return and mean systemic filling pressure (Pmsf) are both increased by a PLR in the presence of preload responsiveness. A false negative PLR test may be caused by IAH, according to a publication in the August edition of Critical Care Medicine by Beurton and colleagues. [17]

## Review of literature

**Taccheri (2021) [18]**In patients with low Vt who were mechanically ventilated while totally sedated, demonstrated that changes in PPV generated by PLR correctly followed preload dependence. Nonetheless, the inclusion of 30 patients in this single-center trial was insufficient, and preload responsiveness was defined as increases in CI of 10% or more due to PLR, rather than changes in CI due to volume expansion. Furthermore, individuals with spontaneous breathing activity reduce the accuracy of PLR-induced changes in PPV.

ISSN:0975 -3583,0976-2833 VOL 11, ISSUE 09, 2020

**Hans-Peter Wiedemann (2022) [19]** Patients in critical care who are experiencing tissue hypoperfusion typically need fluid infusion to optimize their hemodynamics. Volume expansion aims to increase preload, which in turn improves cardiac index (CI) and oxygen supply. Fluid overload, on the other hand, may cause pulmonary and peripheral edema, which in turn increases mortality, intensive care unit length of stay, and other complications.

**Significance of the study**

This work is important because it may lead to better ways of treating septic shock, an illness that is fatal. A non-invasive and easily applicable method to guide fluid resuscitation in these patients is offered by this research, which examines the assessment of changes in mean arterial pressure (MAP) or pulse pressure (PP) after the passive leg raising (PLR) test as indicators of fluid responsiveness. When it comes to septic shock, this is especially important since enhancing hemodynamic stability and improving outcomes for patients depend on quick and correct evaluation of fluid status. If this study's results hold up, they might help reduce septic shock-related morbidity and mortality by creating more targeted fluid management regimens. The work furthers our knowledge of hemodynamic surveillance in critically sick patients by illuminating the value of MAP and PP fluctuations post-PLR; this, in turn, improves clinical practice & patient care in intensive care units.

**Statement of the Problem**

In order to guide fluid management methods and optimize hemodynamic stability, it is necessary to precisely assess fluid responsiveness in septic shock patients. Current techniques for measuring fluid responsiveness, however, could be too intrusive, expensive, or otherwise unworkable in certain medical contexts. Thus, it is necessary to investigate the potential of non-invasive hemodynamic markers, including changes in MAP and PP after the passive leg raising (PLR) test, to predict the responsiveness of fluid in septic shock. The purpose of this research is to fill this knowledge a vacuum by investigating the relationship between post-PLR changes in MAP and PP and fluid responsiveness; ultimately, we hope that this will provide doctors with a useful tool for directing fluid resuscitation in patients with septic shock.

**Research methodology**

T.S. Misra Medical College and Hospital in Lucknow, India, namely its Medical Intensive Care Unit, served as the setting for this research.From March 2021 until May 2022, the recruiting process lasted for fourteen months. Medical critical care unit patients hospitalized during recruiting.

- **Recruitment**

All patients were recruited after being informed about the research and its procedure, since this was an observational prospective study. In situations when the patient was under the influence of drugs or was in a coma, their next of kin or legal guardian's consent was requested.

- **Datacollection**

While the primary investigator was present in the mental health intensive care unit (MHDU), we enrolled all consecutive patients admitted to the medical or high dependency unit who were in need of a hydration bolus and who fulfilled the inclusion and exclusion criteria. In order to collect this data, we made use of data abstraction forms.

ISSN:0975 -3583,0976-2833 VOL 11, ISSUE 09, 2020

- **Inclusion criteria**

1. Hypoperfusion-symptomatic patients include those who have low blood pressure, high lactate levels, reduced urine output, or chilly extremities.
2. The treating intensivist should determine whether these patients need a hydration challenge. Hemodynamic patterns, volume responsiveness tests, or clinical assessment may all inform this choice.
3. Patients must be at least 18 years old.

- **ExclusionCriteria**
  1. Patients who are hesitant to take part
  2. Abdominal pressure that is more than 15 mm Hg
  3. The time of pregnancy
  4. Arrhythmias absent of rare ventricular ectopics
  5. Surgery on the spine, lower extremities, or pelvis, as well as lower limb fractures, are all reasons to avoid passive leg raises.
  6. before legs amputated above or below the knee
  7. A weak thoracic echo window prevents the interrogation of the left ventricular outflow tract.
  8. The measurement should be between 27 and 35 centimeters in the middle of the upper arm.
- **Statistical methods**

We used Epidata version 3.1 for data input. The SPSS program (version 14) was used to compute descriptive statistics. The research by Lakhal *et al*.35 served as the basis for the calculation of the sample size. Instead of using 48% sensitivity and 91% specificity, which were used in the previous research, we decided to calculate the sample size with a suitable sensitivity of 70 to 80% after Lakhal *et al*.'s comprehensive review of the ROC studies. The sensitivity range of 70-80% was determined using 70 observations for the responder group and 70 observations for the non-respondent group. A 95% confidence interval and 10% margin of error were also included.

**Results**

During the duration of this research, a grand total of 20,027 patients were admitted to the medical critical care unit. Only 176 observations (representing 69 individuals) were retained for the final analysis, out of a total of 214 observations (78 patients). There were 38 observations (9 patients) that were not included because some of the data was missing.

**Patient Demographics**

**Table1:** Table of Demographics

| | |
|---|---|
| Age (Mean ± SD) (years) | 46±16 |
| Male/Female (n) | 33/36 |
| Male : Female ratio | 0.9:1 |
| BMI (Mean ± SD) kg/m2 | 24.75±3.74 |
| MUAC (Mean ± SD)(cm) | 28.6±2.25 |

The average age of our sample group was 46 years old, which is younger than the typical demographic profile of patients admitted to intensive care units. Researchers used a gender ratio of 0.9:1 due to an equal number of male and female participants. The average BMI of the people who took part in the research was 24.75 kg/m2.The majority of patients had healthy body mass indices,

ISSN:0975 -3583,0976-2833 VOL 11, ISSUE 09, 2020

according to the results. The mid-arm measurement was 28.6 cm in total. Arterial lactate levels of 3.46 mmol/L were typical among patients experiencing shock. Prior to treatment, around 66% of patients had elevated arterial lactate concentrations.

With an average SAPS II score of 65 upon admission, the mortality rate was close to 78%. Nearly 50% of patients were admitted to the emergency room.Not only that, but we discovered that the vast majority of our patients (78%) were actually referred to us by other medical facilities.After hypotension (18.8% of instances), oliguria (49.3% of cases), and elevated lactate concentration (31.9% of cases), fluid bolus delivery was most commonly induced by these other symptoms.

In terms of hemodynamic instability, 85% of patients admitted to the critical care unit were found to be suffering from septic shock. According to our findings, hypovolemic shock is the most serious type of shock, followed by anaphylactic shock and cardiogenic shock.

Acute pulmonary embolism due to obstructive shock occurred once. Early on, inotropes were unnecessary for around a third of patients. More than three inotropes were required by 6% of the 66% who required them to maintain stable blood pressure.

Nearly 37% of patients were using a single inotrope, while 23% were using two. The research population included 7 patients who had cardiac arrests upon arrival. Approximately 16% of patients arrived at the hospital without any co-morbidities. Among the remaining 84%, diabetes mellitus was the leading risk factor, accounting for 23.8% of all cases.Nearly 14% of patients also had hypertension, making it the second most prevalent co-morbidity.

Using immunosuppressive drugs was the third most prevalent risk factor, at around 17%, followed by having a present malignancy at 11.5%. This is somewhat surprising.The majority of the chronic organ damage found in this investigation was chronic liver disease. Patients undergoing non-invasive and mechanical ventilation have their ventilator settings analyzed below.

**Table2:** Ventilation parameters for neonates (n=11/69)

| **Variable** | **FiO2(%)** | **P/Fratio** | **TidalVolume(ml)** | **PEEP(cm ofH2O)** | **Pressuresupport(PS)** |
|---|---|---|---|---|---|
| Median | 28 | 265 | 320 | 8 | 8 |
| Minimum | 24 | 220 | 300 | 6 | 8 |
| Maximum | 60 | 320 | 400 | 10 | 15 |

According to the data in the table, out of eleven patients who underwent non-invasive ventilation (NIV), the average FiO2 was 28% and the P/F ratio was 265. The average pressure support and maximum end inspiratory pressure were both 8 cm of water.

ISSN:0975 -3583,0976-2833 VOL 11, ISSUE 09, 2020

**Table3:** Technical Details of Ventilation (n=58/69)

| Variable | FiO2(%) | P/Fratio | Tidal Volume(ml) | PEEP(cmof H2O) | PS |
|---|---|---|---|---|---|
| Median | 60 | 259 | 300 | 10 | 15 |
| Minimum | 30 | 146 | 300 | 5 | 8 |
| Maximum | 90 | 389 | 480 | 15 | 20 |

The majority of patients obviously needed mechanical breathing, as can be seen from up above. The average tidal volume that was given:

**Responders** – this includes all observations where the change in stroke volume variance was at least 15%.

**Non responders**- those instances in which the reduction in stroke volume was less than 15% Following the strobe diagram, we can see that out of 36 patients, 106 had responder variants and 33 had non-responder variants.

**Table4:** Identification Needed for Respondents and Non-Responders

| Responder Status | N | Median |
|---|---|---|
| Yes | 36 | 1 |
| No | 33 | 1 |

Using inotropes was similarly prevalent in both groups, as seen in the preceding table.A non-significant p-value of 0.262 was determined using the Mann Whitney test.

**Table5:** The Responder and Non-Responder Arms' Mid-Upper Arm Circumference.

| Mid Upper Arm Circumference (Mean ± Sd) (CM) | Responder | Non responder |
|---|---|---|
| | 28.47±2.28 | 28.76 ±2.23 |

There was no statistically significant difference (p =0.603) between the two groups in the independent t test.

**Table6:** Concentration of arterial lactate in the responding and non-responsing arms

| Arterial Lactate Concentration (Mean ± SD) (mmol/L) | Responder | Non responder |
|---|---|---|
| | 3.9±1.9 | 2.9±2.3 |

An study of independent t-tests between the two groups revealed no statistically significant difference (p=0.077).

**6.2 SepticShock**

**Table7:** Septic shock patients that either react or do not are categorized as a breakup.

| | | Responder | Non responder |
|---|---|---|---|
| Septic Shock(n) | Yes | 29(80.6%) | 30(90.9%) |
| | No | 7(19.4%) | 3(9.1%) |

The negligible p-value of 0.380 obtained from the chi-square test

ISSN:0975 -3583,0976-2833 VOL 11, ISSUE 09, 2020

**Primary Outcome**

Before we could use echocardiography to assess fluid loading, we wanted to know how sensitive and specific the change in mean arterial pressure was, as it corresponds to a 15% increase in stroke volume. We also looked for PP changes in connection to the 15% increase in stroke volume shown by echocardiographic assessments of fluid loading. To that end, we have compiled a table showing the study's variables' baseline hemodynamic parameters.

**Table8:** Hemodynamic Characteristics of the Research Sample

| **Responder** | | | | | **Nonresponder** | | | |
|---|---|---|---|---|---|---|---|---|
| **Vari able s** | **Base** | **Post plr** | **Pre bolus** | **Post bolus** | **Base** | **Post plr** | **Pre bolus** | **Post bolus** |
| MAP mm hg | 77±8 | 79±10.9 | 77±8.6 | 83±9.5 | 76±10.6 | 77±9.8 | 77±7.8 | 79±8.8 |
| PP mm Hg | 38±14.4 | 41±15.5 (a) | 38±14.8 | 42±16.2 | 41±12.0 4 | 42±14.4 | 42±13.76 | 42±14.1 |

With the aforementioned hemodynamic parameter, we have access to all of the data collected during the research. Based on the data presented, it is evident that the only parameters for which PLR showed a statistically significant difference were heart rate, pulse pressure, and systolic blood pressure.

**6.4 Roc Curve for Mean Arterial Pressure**

Making the ROC curve included comparing the percentage change in mean arterial pressure to the gold standard, which is defined as an increase in stroke volume of >= 15% on fluid loading. After assessing the ROC curve for mean arterial pressure, a 0.64 area under the curve was determined, which included a standard error of 0.042. A MAP change of 3.0% was linked to a sensitivity of 50% and specificity of 82.9%, as we found.

**Table9:** MAP 2X2TABLE

| | **Responder** | **Non responder** | **Total** |
|---|---|---|---|
| Map change >= 3% | 53 | 12 | 65 |
| Map change <3% | 53 | 58 | 111 |
| Total | 106 | 70 | 176 |

We have adjusted our readings to have a reduced sensitivity while yet maintaining a high degree of specificity. This will allow us to make a significant difference in the proportion of patients whose mean arterial pressure can be managed at the bedside. At greater sensitivity levels, the ROC curve was in agreement with the null hypothesis; therefore we couldn't choose a more sensitive threshold.

**Roc Curve for Pulse Pressure Change**

**Table10:** Pulse Pressure2x2Table

| | **Responder** | **Non responder** | **Total** |
|---|---|---|---|
| Pp change >= 5% | 51 | 17 | 68 |
| Pp change <5% | 55 | 53 | 108 |
| Total | 106 | 70 | 176 |

ISSN:0975 -3583,0976-2833 VOL 11, ISSUE 09, 2020

The Area under the curve was greater for pulse pressure ROC tracing than for MAP (0.668 vs. 0.640). We find that with a pulse pressure cutoff of 5%, our sensitivity for predicting fluid responsiveness is 48% and our specificity is 75%, according to the ROC curve evaluation.

**Comparison of Mean Arterial Pressure Change with Subgroup Analysis of Respondent Observations**

The prediction of fluid responsiveness by MAP change was not as good as expected.Given this, we had considered other variables that may have caused this bad reading, or confounding factors. All 106 respondent observations were split into two categories by us. There were two groups: one where the MAP predicted fluid responsiveness and the other where it did not.

Group 1 had 53 observations and group 2 had 53 observations due to the 50% sensitivity of the MAP. Based on the factors provided below, we have split the analysis:

**Table11:** Respondents experiencing a spike in sepsis

| Test | Septic shock (responderObservations) |
|---|---|
| MAP+ | 36 /54 |
| MAP- | 47 / 54 |

An important p-value of 0.01 was determined using the Chi-square test. The MAP negative group had a much larger patient population.Septic shock patients may have less accurate NIBP readings due to their vasodilatory status.

1) Modes of Ventilation and Types

**Table12:** Gold Standard and Test Breakup by Ventilation Mode

| Test | Ventilation(n) | | | | Total |
|---|---|---|---|---|---|
| | NIV | SPONT | SIMV | PSIMV | |
| MAP+ | 2 | 5 | 42 | 4 | 53 |
| MAP- | 4 | 5 | 44 | 0 | 53 |

A chi-square test comparing the two groups yielded a non-significant P value of 0.19. It seems that the accuracy of NIBP was unaffected by the ventilation modes.

**Table13:** Interrupting Inotrope Use in Response

| Test | Inotrope(n) | | | | Total |
|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | |
| MAP+ | 12 | 23 | 13 | 5 | 53 |
| MAP- | 19 | 22 | 11 | 1 | 53 |

The chi-square test yielded a non-significant P value of 0.25 across all categories.

**Table14:** Concentration of lactate in the response standard.

| Test | Lactateconc>2.5 |
|---|---|
| MAP+ | 41/53 |
| MAP- | 39/53 |

ISSN:0975 -3583,0976-2833 VOL 11, ISSUE 09, 2020

When comparing the two groups, the p-value was >0.05, indicating that there was no statistically significant difference.

**Discussion**

The most reliable way to assess fluid responsiveness in ICU patients is using invasive blood pressure monitoring, which measures the change in pulse pressure in response to PLR.It correctly differentiated between responders and non-responders and tracked the changes made. The results of non-invasive blood pressure monitoring were what we had anticipated. It is essential to get a non-invasive blood pressure measurement during the first hour following cardiopulmonary resuscitation since it is often the only choice. In addition, this would have been useful in cases when resources are limited and portable echocardiograms or artery transducers aren't easily available at the bedside.

Concerning volume responsiveness during PLR, the provided research had enough power to determine if NIBP data might substitute invasive artery measurements. References 22 and 23 the sample size had met its initial objective. [24] The sample also accurately represented the demographics often seen in India's medical ICUs. We have also thought about the possible reasons behind NIBP's poor research performance. Prior studies have shown that variables including cuff placement, arterial flexibility, vasomotor tone changes, and pressure on surrounding tissues, arm size, and arrhythmia are the primary causes of potential differences between invasive and non-invasive blood pressure measures. (27, 28) The algorithms used to calculate blood pressure also vary throughout manufacturers.

Attempts were made to address some of the previously noted issues by eliminating patients with arrhythmia, keeping the cuff placement constant (arm), and not include patients who exceeded the cuff restrictions set by the manufacturer. [31] in Each patient in the medical critical care unit was likewise given the same Phillips MP50 equipment, which helped us achieve our aim of removing algorithm-induced bias. References (32, 33) vasomotor tone and the pressure provided to the arteries by the surrounding structures were among the areas that were neglected. at the 34th page Strong inotropic support was necessary for 67% of our patients during their stay, which causes peripheral vasoconstriction and makes reading computations more difficult. There is an increase in surrounding subcutaneous edema after prolonged ICU stays; this puts pressure on arteries and makes reading difficult. [35]

**Conclusion**

A non-invasive technique called passive leg raise (PLR) was shown to have a sensitivity of 50% and a specificity of 82.9%. Both sensitivity and specificity were shown to be related with a 3% MAP threshold. The passive leg lift non-invasive pulse pressure change (PP) method has a sensitivity of 48% and a specificity of 75%. This is related to the 5% PP threshold.

ISSN:0975 -3583,0976-2833 VOL 11, ISSUE 09, 2020

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