



“PORTAL VENOUS DOPPLER CONGESTIVE INDEX: A PROMISING TOOL FOR EARLY DETECTION OF CAPILLARY LEAK SYNDROME IN SEPSIS PATIENTS”

Radiology

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ABSTRACT

Aims: The study aimed to investigate the predictive value of the Portal Venous Doppler Congestive Index in identifying Capillary Leak Syndrome (CLS) risk in sepsis patients, with a focus on enhancing early recognition and intervention strategies. **Patients and Methods:** A prospective cohort study was conducted at J.J.M. Medical College, Davanagere, Karnataka, involving 80 sepsis patients meeting specific inclusion criteria. Patients underwent imaging procedures, including ultrasonography and portal venous Doppler examination, with data meticulously collected using a structured proforma. **Results:** Among the patients, Capillary Leak Syndrome (CLS) was identified in 62 out of 80 cases, with ultrasonographic findings revealing common features such as gall bladder wall thickening, ascites, pleural effusion, splenomegaly, and increased portal venous diameter. Comparison of portal venous parameters between CLS-positive and CLS-negative patients showed significant differences in portal vein diameter, flow velocity, cross-sectional area, and Congestive Index. **Conclusion:** The study underscores the significance of the Portal Venous Doppler Congestive Index in early CLS detection among sepsis patients. The index demonstrates high sensitivity and specificity, offering a valuable tool for timely and personalized therapeutic interventions to improve patient outcomes and reduce mortality rates associated with septic shock.

KEYWORDS

Capillary leak syndrome (CLS), Portal vein doppler, Congestive index, Sepsis

INTRODUCTION

Capillary leak syndrome (CLS) poses a significant challenge in the care of sepsis patients, often resulting in increased morbidity and mortality rates. Timely identification of CLS is paramount for effective intervention and improved patient outcomes^[1,2]. In this context, the Portal Venous Doppler Congestive Index emerges as a promising tool with the potential to revolutionize the detection of CLS in sepsis patients.

Despite advancements in diagnosis and management, septic shock continues to exhibit a mortality rate as high as 30%–40%, contributing to millions of deaths globally each year. Early intravenous fluid (IVF) resuscitation, a fundamental aspect of septic shock treatment, aims to restore intravascular volume and enhance cardiac output to optimize end-organ perfusion^[1]. However, the endothelial dysfunction characteristic of sepsis leads to fluid extravasation into tissues. Excessive fluid administration can result in interstitial edema and iatrogenic organ damage, underscoring the critical need for improved physiological markers to tailor hemodynamic resuscitation to individual patient needs^[1,2].

Real-time assessment of venous congestion in multiple organs using Doppler ultrasonography at the bedside offers a valuable approach. By evaluating venous congestion through measurements or flows in the inferior vena cava (IVC), hepatic vein (HV), portal vein (PV), and intrarenal veins (IRV), clinicians can gain insights into hepatic hemodynamics and vascular congestion^[1,7]. The Congestive Index derived from Portal Venous Doppler serves as a quantitative indicator of portal venous flow disturbances, reflecting hepatic congestion and vascular permeability changes characteristic of CLS^[3-8].

This study aims to explore the predictive value of the Portal Venous Doppler Congestive Index in identifying CLS risk in sepsis patients, enhancing early recognition and intervention strategies. By potentially serving as a sensitive and specific indicator of impending CLS, this tool has the capacity to empower healthcare providers to initiate targeted therapies promptly, potentially improving patient outcomes and alleviating the burden of this complex complication in sepsis management^[8].

Pathophysiology

Endothelial Dysfunction in CLS is characterized by heightened endothelial hyperpermeability, resulting in fluid shifts and intravascular hypovolemia. This dysfunction extends to the vasculature of the portal vein, potentially modifying portal venous

flow dynamics^[2,5].

The Inflammatory Response triggered by sepsis initiates endothelial activation and the release of proinflammatory mediators, disrupting vascular endothelial integrity systemically and within the portal vein^[2,5]. The Dysregulation of the angiotensin-Tie2 pathway, central to CLS pathophysiology, may impact portal venous flow by altering angiotensin levels and Tie2 receptor activation, affecting vascular permeability and contributing to portal vein congestion^[5].

Glycocalyx Dysfunction, characterized by glycocalyx shedding in CLS-related endothelial dysfunction, compromises the barrier function of the vascular endothelium, including that of the portal vein, potentially influencing portal venous flow dynamics and contributing to congestion^[6]. Fluid Dynamics, encompassing fluid shifts and overload in CLS, can influence vascular congestion, including in the portal vein, with changes in the Portal Venous Doppler Congestive Index reflecting the hemodynamic status of sepsis patients^[4-8].

MATERIALS AND METHODS

The prospective study was conducted at the Department of Radiodiagnosis, J.J.M Medical College, Davanagere, Karnataka, focusing on patients with sepsis. It employed a prospective cohort design and included patients exhibiting fever along with clinical symptoms and signs of sepsis, supported by laboratory evidence of elevated C-reactive protein (CRP) levels and leukocytosis/leukopenia. The study spanned from March 2022 to November 2023, covering a 20-month period with a sample size of 80 patients. The sampling technique used was convenience sampling.

Inclusion Criteria:

Patients with fever presenting symptoms like low blood pressure, rapid heart rate, rapid breathing, confusion, decreased urine output, extreme fatigue, and laboratory findings showing elevated CRP and leukocytosis/leukopenia.

Exclusion Criteria:

- Patients with chronic liver disease or tumors.
- Individuals with known hypoalbuminemia.
- Patients with a known history of hypotension.
- Individuals with known portal vein or splanchnic vessel thrombosis.
- Patients who decline to consent to participate in the study.

Method Of Collection Of Data

The data collection methodology for the study involved the utilization

of a structured pre-prepared case proforma to document patient details, clinical history, and serological status of individuals meeting the inclusion criteria. The data collection process included initial imaging through ultrasonography, followed by portal venous Doppler examination, with all findings meticulously recorded.

Methodology

The study commenced post obtaining clearance from the institutional ethical committee, with all enrolled cases undergoing imaging procedures after securing written consent. Abdominal and chest wall ultrasonography was conducted in real-time using grey scale and color Doppler modes with a 3.5-5 MHz convex curvilinear probe on a GE Voluson E6 machine upon admission. Patients were typically scanned after 4-6 hours of fasting in a supine or left decubitus position. A general assessment of the liver was performed to exclude chronic liver pathologies. Various sonographic features like gall bladder wall edema, thickness, ascites, pleural effusion, and splenomegaly were evaluated. The statistical analysis was conducted to evaluate the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of Portal venous Doppler in predicting the development of capillary leak syndrome in sepsis patients.

Portal Doppler Study:

The portal vein was assessed either subcostally or intercostally for grey scale measurements of diameter and cross-sectional area. Color and spectral Doppler assessments were conducted to evaluate flow velocity, direction, and calculate the Congestive Index using the formula:

Cross-sectional area (cm^2)

Portal venous velocity (cm/sec)

Ultrasonographic features and Doppler findings were subsequently correlated with clinical outcomes and laboratory results.

Representative Cases:

Case-1:

The 56-year-old male patient arrived with a history of high-grade fever persisting for three days, accompanied by generalized weakness and hypotension. Laboratory tests revealed leucocytosis, with a total leukocyte count of 16230cells/cu.mm and elevated CRP of 286mg/L. Additionally, a portal venous Doppler was conducted upon admission [Figure 1 & 2].

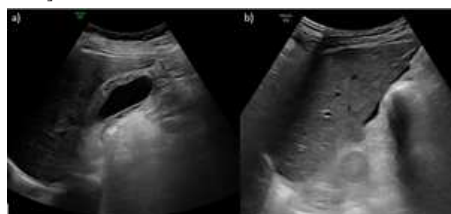


Figure 1: a) Grey scale USG Right subcostal oblique approach showed oedematous increased GB wall thickness. b) USG Abdomen showed minimal fluid collection in hepatorenal pouch.

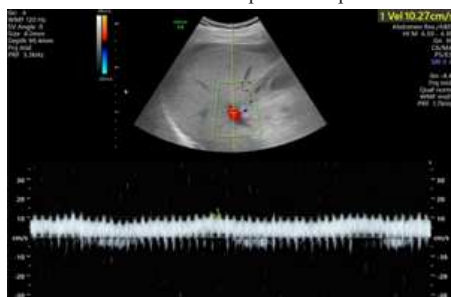


Figure 2: The spectral color Doppler image showed normal color uptake with a normal hepatopetal flow pattern and normal respiratory variation, but with a reduced flow velocity of 10.2 cm/sec. The portal vein diameter measured 14 mm, indicating dilation.

Upon subsequent examination, the individual presented with CLS, and laboratory tests revealed elevated levels of hemoglobin and hematocrit.

Case-2:

The 67-year-old female patient with uncontrolled diabetes arrived with a history of high-grade fever persisting for six days, accompanied by

generalized weakness, burning micturition and pain abdomen. Laboratory tests revealed leucocytosis, with a total leukocyte count of 18520cells/cu.mm, elevated CRP of 319mg/L and HbA1c of 9.5. Additionally, a portal venous Doppler was conducted upon admission [Figure-3 & 4].

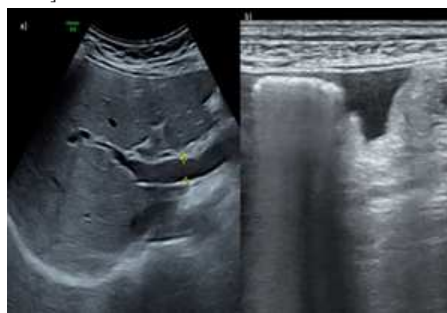


Figure 3: a) Grey scale USG Right subcostal oblique approach showed dilated portal vein of 14.5 mm in maximum caliber. b) USG Abdomen showed minimal fluid in inter-bowel region.

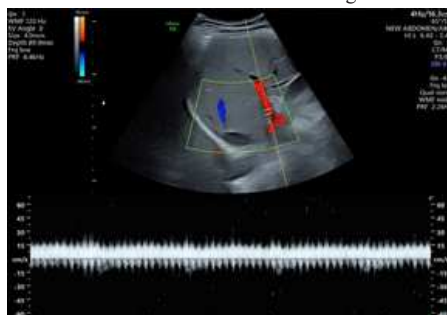


Figure 4: The spectral color Doppler image showed normal color uptake with a normal hepatopetal flow pattern and normal respiratory variation, but with a reduced flow velocity of 11.6 cm/sec. The portal vein diameter measured 14.5 mm, indicating dilation.

RESULTS

There is no sex distribution, with the condition common in the elderly age group (55-70years). CLS was found in 62 out of 80 patients, representing 77.5% of the total cases. The majority of CLS cases were observed in patients aged between 55-70 years, with 53 patients falling within this age range, accounting for 66.2% of the CLS cases.

The Ultrasonographic findings revealed the following distribution among the patients [Table-1]:

- Oedematous gall bladder wall-thickening were observed in 52 cases, constituting 65% of the total patients.
- Ascites was present in 44 cases, representing 55% of the patients.
- Bilateral pleural effusion was identified in 17 cases, making up 21.25% of the patients.
- Splenomegaly was detected in 33 cases, representing 41.25% of the patients.
- Increased portal venous diameter (>13mm) was found in 59 cases, representing 73.75% of the patients.

Table 1: Ultrasonographic findings among sepsis patients

Features	No. of cases	Percentage
Gall bladder wall edema	52	65%
Ascites	44	55%
Bilateral pleural effusion	17	21.25%
Splenomegaly	33	41.25%
Increased portal venous diameter (>13mm)	59	73.75%

In patients with CLS, the mean portal vein diameter was 14.8 mm, with a portal vein flow velocity of 15.7 cm/sec and a cross-sectional area (CSA) of 1.53 cm^2 . Conversely, CLS-negative patients had a smaller portal vein diameter of 9.4 mm, with a higher flow velocity of 28.8 cm/sec and a smaller CSA of 1.05 cm^2 [Table-2].

Table 2: Comparison of Portal Venous Parameters between CLS-Positive and CLS-Negative Patients

Mean value	CLS positive patients	CLS negative patients
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Portal vein diameter	14.8 mm	9.4 mm
PSV of portal vein	15.7 cm/sec	28.8 cm/sec
CSA of portal vein	1.53 cm ²	1.05cm ²
Congestive Index	0.097	0.036

The average congestive index was 0.097 among CLS-positive patients and 0.036 among CLS-negative patients. Portal vein peak systolic velocity (PSV) exhibited higher sensitivity and significance. The congestion index demonstrated the highest specificity. Sensitivity was 95.16%, specificity was 100%, PPV was 100%, NPV was 85.71%, and diagnostic accuracy was 96.25%. The study indicates that combining ultrasonography with portal vein Doppler significantly increases sensitivity and positive predictive value (PPV) in predicting the development of CLS in sepsis patients.

DISCUSSION

The use of the Portal Venous Doppler Congestive Index shows promise in detecting Capillary Leak Syndrome early in sepsis patients. This index provides a way to measure disruptions in portal venous flow, which can indicate hepatic congestion and changes in blood vessel permeability linked with CLS. Despite improvements in diagnosis and treatment, septic shock still leads to high mortality rates of 30%–40%, causing millions of deaths globally each year. Prompt intravenous fluid resuscitation is crucial in managing septic shock, aiming to restore fluid volume and improve heart function for better organ blood flow.^[3,4] During sepsis, endothelial dysfunction causes fluid to leak into tissues, highlighting the need for better markers to guide fluid treatment based on individual patient needs. Doppler ultrasound allows doctors to assess venous congestion in real-time across different organs, giving important information about liver blood flow and congestion. The Portal Venous Doppler Congestive Index could help healthcare providers start targeted treatments quickly, improving early detection and treatment of CLS in sepsis patients.^[2-9]

By using the sensitivity and specificity of portal venous Doppler measurements, including diameter, CSA, velocity, and the Congestive Index, healthcare providers can significantly improve diagnostic accuracy. Combining ultrasound with portal venous Doppler can increase sensitivity and PPV, leading to earlier treatment and better outcomes. This combination of technology and clinical expertise is a step forward in personalized medicine for critically ill patients, potentially reducing the harm caused by septic shock and its complications.

CONCLUSION:

The study highlights the crucial role of the Portal Venous Doppler Congestive Index in early detecting Capillary Leak Syndrome among sepsis patients. Results emphasize the importance of timely CLS identification for improving outcomes and reducing septic shock mortality rates. Utilizing this index to assess venous congestion and hepatic hemodynamics can aid in predicting CLS risk early, facilitating tailored interventions.

In conclusion, the study affirms the index's sensitivity and specificity in identifying impending CLS, offering clinicians a valuable tool for initiating timely and personalized therapeutic interventions. This innovative approach has the potential to transform sepsis management by enhancing early recognition and intervention strategies, thereby improving patient care and outcomes in the realm of sepsis-related complications.

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