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Imaging the Critically Ill

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Guiding Clinical Care Using Pancreatic Stone Protein

The role of point-of-care testing in the early identification and management of sepsis, the need for better sepsis markers to identify sepsis, an overview of the Pancreatic Stone Protein (PSP) and clinical evidence highlighting its effectiveness as a biomarker.

Pancreatic Stone Protein

Infections are a leading cause of morbidity and mortality among critically ill patients. The early detection of severe infections is essential to improve patient outcomes. To date, none of the biomarkers that have been investigated have proven to be effective in detecting life-threatening infections quickly and accurately. Despite this lack of effectiveness and sub-optimal performance, C-reactive protein (CRP) and procalcitonin (PCT) are widely used within the clinical setting.

Pancreatic stone protein (PSP) is a new biomarker that has been evaluated in numerous studies and different clinical settings, including emergency rooms and ICUs. PSP is a C-type lectin-binding protein from a family of proteins involved in inflammatory processes during infection and sepsis. Several clinical studies have shown the effectiveness of PSP in diagnosing infection, characterising its severity and predicting patient outcomes.

PSP and Sepsis

One of the most common reasons for admission to ICUs is sepsis. Sepsis is associated with significant morbidity and mortality, and its incidence continues to increase. However, the clinical recognition and assessment of sepsis can be challenging as its symptoms are highly variable and non-specific. Also, when treating sepsis patients, clinicians often face the dilemma of minimising unnecessary antibiotic prescriptions while ensuring timely administration to save lives. Biomarkers can play an important role in helping clinicians make timely and accurate treatment decisions.

There is no doubt that the early recognition and management of sepsis improves patient outcomes. Biomarkers like PSP can help in identifying early signs of infection and sepsis. If not recognised and managed early, sepsis can become life-threatening with septic shock and multiple organ failure (Pugin et al. 2021).

PSP has been studied in several patient cohorts, including critically ill, post-cardiac surgery, and severe burn patients.

> **PSP shows high diagnostic accuracy in differentiating sepsis from non-infectious systemic inflammatory response syndrome**

In particular, burn victims are in a state of hyperinflammation that can often camouflage septic events. This can delay diagnosis and targeted treatment in such patients and increase the risk of poor outcomes. There is a need to facilitate sepsis detection to help prevent further deterioration of the patients' condition (Klein et al. 2021).

Study findings showcase some unique features of PSP. It can discriminate septic events from non-septic ones in patients with high inflammatory stress levels. PSP levels significantly increase in the blood up to 72h before the manifestation of sepsis. Hence, close monitoring of PSP levels can help identify patients at high-risk of developing sepsis. Compared to other routine inflammatory biomarkers, PSP demonstrates a significant interaction between time and presence of sepsis, thus enabling clinicians to discriminate between patients who are septic compared to those who exhibit a non-septic course (Klein et al. 2021).

PSP is a promising biomarker for sepsis as it increases before clinically proven sepsis and shows a high level of robustness towards sterile inflammatory stimuli such as trauma or repetitive surgeries. During an infection, the pancreas rapidly releases high levels of PSP into the bloodstream, which results in two immunological pathways: direct aggregation and immobilisation of bacteria and binding and subsequent activation of neutrophil granulocytes. A study by Keel et al. (2009) showed that PSP is upregulated in blood after trauma, and these levels are related to the severity of infection. PSP also binds to and activates neutrophils. Polytrauma patients admitted to the ICU with increased PSP levels one day after admission are more likely to develop sepsis, compared to those whose PSP levels remain low or have a moderate increase. Serial measurements of PSP can help clinicians assess the risk of developing post-traumatic sepsis. Hence, PSP is an acute-phase protein and could be an effective marker for post-traumatic complications. Using the PSP biomarker on the abioSCOPE® enables Point-of-Care (POC) diagnostics for clinicians in the ICU and those in the emergency department.

Levels of pro-inflammatory markers are significantly altered due to trauma or surgery and present a major problem to clinicians as it can interfere with the clinical identification of infection. While this is

true for all established markers, including C-reactive protein (CRP) and Procalcitonin (PCT), the robustness of PSP blood levels is an important criterion for a sepsis biomarker. PSP levels are not impacted by initial debridement and subsequent burn trauma-related surgeries. This highlights the specificity of PSP for infectious and septic events in burn patients (Klein et al. 2020). PSP has also shown the highest diagnostic accuracy among the tested biomarkers in differentiating sepsis from non-infectious systemic inflammatory response syndrome (SIRS) (Llewelyn et al. 2013).

A systematic review and meta-analysis aiming to determine the performance of PSP in diagnosing infection among hospitalised patients confirmed that PSP was able to detect infection and had high sensitivity and specificity. PSP performed better than both CRP and PCT. However, the combination of PSP and CRP further enhanced its diagnostic accuracy (Prazak et al. 2021).

Conclusion

The lack of a gold standard test to diagnose sepsis in critically ill patients and the often non-specific features of the entity sepsis highlight the need for a biomarker that could predict worsening clinical status, identify severe disease earlier, improve prognosis, have high diagnostic accuracy, be specific and sensitive to disease and quick and easy to implement and assess. Current clinical data on PSP emphasise its advantages for the early identification of sepsis. PSP is an effective biomarker with a short half-life. It also has high accuracy, predictive value, high sensitivity and specificity, and the PSP test is easy to perform at the POC. Serial measurements of PSP can facilitate patient management, guide antibiotic therapy, help reduce antibiotic resistance, and have the added advantage of POC technology at the bedside.

Key Points

- Pancreatic Stone Protein (PSP) is a promising biomarker for sepsis.
- Levels of PSP demonstrate a steep rise before clinically visible and/or proven sepsis.
- PSP is able to detect infection and sepsis in conditions of high inflammation, including trauma, peritonitis, infections, and burns.
- PSP can also be an effective tool for identifying patients at the highest risk of prolonged hospitalisation, more severe illness and need for intensive treatment.
- Rapid and easy evaluation of PSP is enabled thanks to the POC technology (abioSCOPE®), facilitating timely and accurate clinical decision making.

Disclaimer

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