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Review Article

Emergency Department Applications of Inflammatory Markers: A Narrative Review

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Abstract

This is a narrative review of the role and applications of inflammatory markers in emergency departments, emphasizing their significance in rapid and accurate assessment of patients with urgent health concerns. The markers discussed include C-reactive protein (CRP), white blood cell count, erythrocyte sedimentation rate (ESR), procalcitonin, and serum amyloid A (SAA). Each of these markers has certain physiological roles. CRP serves as a crucial acute-phase reactant in response to inflammatory signals, while white blood cell count plays a vital role in immune response. ESR acts as a nonspecific marker of inflammation, with procalcitonin being elevated in bacterial infections, whereas SAA responds to inflammation and infection. These markers have several roles in the emergency departments. CRP plays a key role as an infection marker and is used in monitoring inflammatory conditions and tissue damage. White blood cell count is highlighted for its utility in evaluating various conditions, including infections, inflammations, autoimmune diseases, and sepsis. ESR is a diagnostic tool in emergency settings for assessing and monitoring inflammatory conditions. Procalcitonin's diagnostic specificity for bacterial infections is underscored, aiding in prompt and accurate diagnosis in emergency situations. SAA, as an acute-phase protein, has a role in inflammation and, infection responses, with applications in evaluating infections, monitoring inflammatory diseases, diagnosing and monitoring sepsis, and assessing other inflammation-related conditions. In conclusion, SAA has diverse applications in emergency departments, offering valuable insights into infection detection, monitoring chronic inflammatory diseases, diagnosing sepsis, evaluating inflammation-related conditions, and providing rapid insights in emergency scenarios. The importance of these inflammatory markers in enhancing diagnostic accuracy, guiding treatment decisions, and optimizing patient care in critical situations is emphasized throughout the review.

Keywords

- inflammatory markers
- emergency departments
- immune response
- diagnostic tools
- critical care

Introduction

Emergency departments serve as critical health care units that provide rapid and effective evaluation of patients with urgent health concerns. In this context, inflammatory markers play a crucial role in the assessment of patients, contributing to the swift and accurate delivery of health care services. This review will delve into the role and applications

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of commonly used inflammatory markers in emergency departments.[1]

Inflammatory markers are biological indicators that reveal inflammatory processes occurring in the body. These markers offer valuable insights into how the patient's immune system responds and provide information about potential infections or damage. Among the fundamental inflammatory markers frequently utilized in emergency departments are C-reactive protein (CRP), white blood cell (WBC) count (leukocyte count), erythrocyte sedimentation rate (ESR), procalcitonin (PCT), and serum amyloid A[2,3] (SAA; ►**Fig. 1**). CRP is a plasma protein that rapidly increases in acute inflammatory conditions, serving as a vital indicator, especially in situations such as infections and tissue damage. WBC count assesses the number of WBCs in the body, playing a pivotal role in identifying inflammatory conditions like infections. ESR measures the rate at which red blood cells settle in blood, regarded as an indicator of inflammatory processes.[3,4] PCT is a marker specifically elevated in bacterial infections, providing essential information for diagnosis. SAA is another marker associated with inflammation and tissue damage.[5,6] This review will comprehensively explore the role of these inflammatory markers, their evaluation in different scenarios, and how they guide health care professionals in assessing the overall health and prognosis of patients undergoing inflammatory processes in emergency settings. Accurate assessment of these markers enhances the efficiency of emergency departments by facilitating prompt diagnosis and directing patients to appropriate treatments.

Materials and Methods

This is a narrative, nonsystematic review of the literature. A single major database was searched (PubMed, NIH, United States). The main articles on the subject were retrieved and reviewed by the author. A draft document was produced and was further developed by multilateral discussions. The revised version was reviewed and finalized by the author.

Here, we explore the role of these inflammatory markers, their evaluation in different scenarios, and how they guide health care professionals in assessing the overall health and prognosis of patients undergoing inflammatory processes in emergency settings. Accurate assessment of these markers enhances the efficiency of emergency departments by facilitating prompt diagnosis and directing patients to appropriate treatments.

C-Reactive Protein

CRP is an important acute-phase reactant produced by the liver in response to inflammatory signals within the body. Its physiological role lies in its ability to detect and respond to various forms of tissue damage, infection, or inflammation. In a healthy state, the levels of CRP in the blood are typically low. However, when there is an inflammatory stimulus, such as an injury, infection, or chronic inflammation, the liver increases the production of CRP.[7] CRP plays a crucial role in the immune response by binding to damaged cells and foreign particles, including bacteria and other microorganisms. This binding activates the complement system, a part of

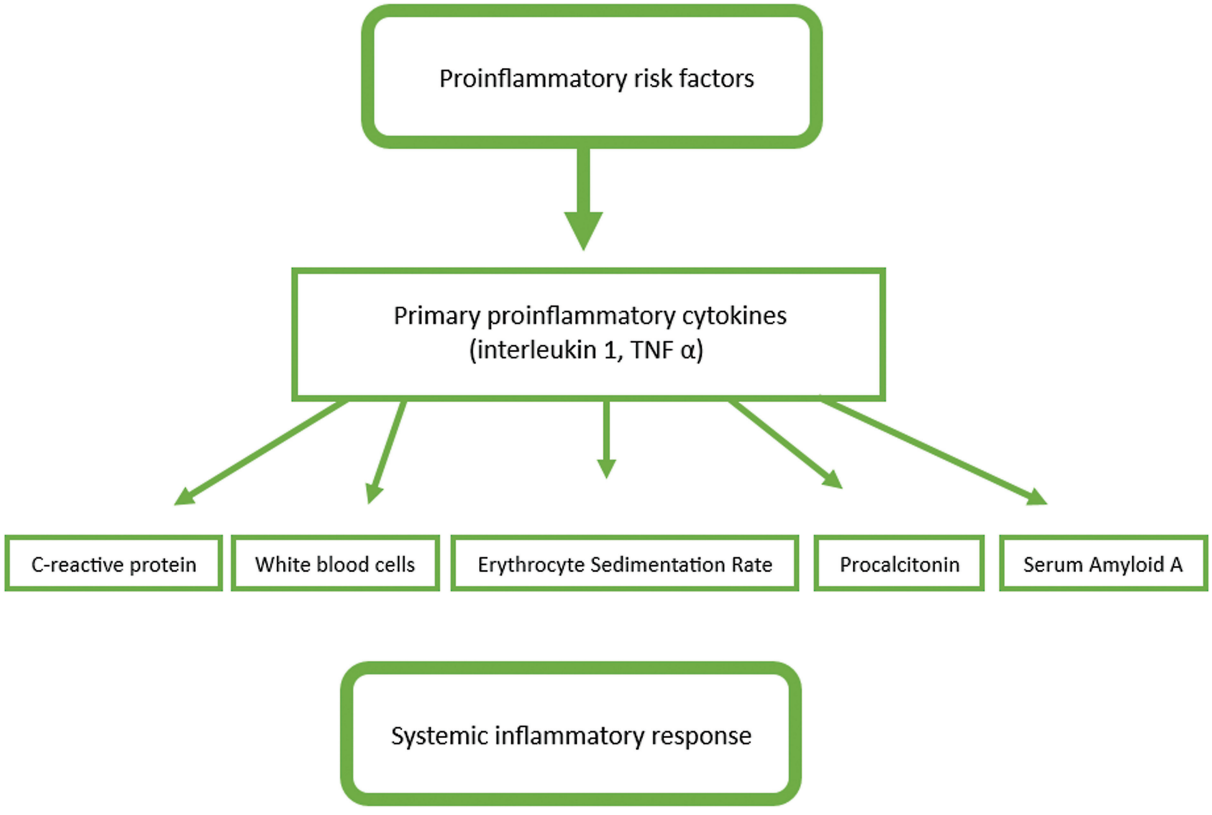

Fig. 1 Inflammatory process. TNF-α, tumor necrosis factor-α.

the immune system responsible for enhancing the body's ability to eliminate pathogens. Additionally, CRP aids in the phagocytosis of these targeted particles, facilitating their removal from the bloodstream.[8] One of the distinctive features of CRP is its rapid response to inflammatory stimuli. Its levels can surge within hours of the onset of inflammation, making it a valuable clinical marker for assessing the presence and intensity of inflammatory processes. Elevated CRP levels in the blood are indicative of an ongoing inflammatory response, providing health care professionals with essential information for diagnosis, monitoring treatment effectiveness, and evaluating the overall health status of an individual.[9,10] In summary, CRP is a key component of the body's acute-phase response, playing a pivotal role in detecting and responding to inflammatory signals. Its physiological functions contribute to the body's defense mechanisms against infections and tissue damage, making it a valuable biomarker in clinical settings.

In emergency departments, CRP can play a crucial role in assessing a patient. Here are some applications of CRP in emergency departments:

- *Infection marker*: CRP levels typically increase during infections. Therefore, when a patient presents to the emergency department with signs of infection, CRP levels can help assess the presence and severity of an infection.
- *Monitoring inflammatory conditions*: chronic inflammatory conditions, such as autoimmune or rheumatic diseases, may require regular monitoring of CRP levels. In such cases, evaluating CRP levels when a patient visits the emergency department can help track the effectiveness of the treatment plan.
- *Monitoring tissue damage and trauma*: CRP can also serve as an indicator of tissue damage or trauma. For instance, in a patient arriving at the emergency department after an accident, CRP levels can assist in assessing the severity of the trauma.
- *Sepsis assessment*: in a patient suspected of sepsis, CRP levels are crucial for evaluating the severity of systemic infection and guiding sepsis management.
- *Monitoring treatment response*: regular monitoring of CRP levels can be employed to assess the effectiveness of initiated treatment. This helps determine improvements or deteriorations in the patient's condition.

The use of CRP in emergency departments may vary depending on the patient's specific condition and symptoms. Therefore, the utilization of CRP should be planned based on a thorough clinical assessment and consideration of the patient's medical history.

White Blood Cell Count

WBCs, also known as leukocytes, are essential components of the immune system and play a vital role in maintaining the body's defense against infections and foreign invaders. The physiology of WBC count involves dynamic regulation and response mechanisms.

WBCs originate from hematopoietic stem cells in the bone marrow and are categorized into different types, including neutrophils, lymphocytes, monocytes, eosinophils, and basophils. Each type has specific functions in the immune response.[11] Neutrophils are the most abundant WBCs and are the first responders to infection. They engulf and destroy bacteria, fungi, and other pathogens through a process called phagocytosis. Lymphocytes, including T cells and B cells, are crucial for adaptive immunity. They recognize and remember specific pathogens, providing long-term immunity.[12–15] Monocytes, upon entering tissues, mature into macrophages, which are effective phagocytes involved in immune regulation and tissue repair. Eosinophils and basophils play roles in allergic reactions and defense against parasites.[16] The regulation of WBC count is tightly controlled to maintain homeostasis. Factors such as cytokines, growth factors, and signaling molecules influence the production, maturation, and circulation of WBCs. In response to infection or inflammation, the body can release additional WBCs to enhance the immune response.[16,17] Abnormalities in WBC count can indicate various health conditions, such as infections, inflammatory diseases, leukemia, or autoimmune disorders. Monitoring WBC count is a valuable diagnostic tool for assessing overall immune health and identifying potential underlying medical issues. Regular blood tests are conducted to measure WBC count and ensure a balanced immune response in the body.[11–17] In the emergency department, WBC measurement is employed to evaluate various conditions, including infections, inflammations, autoimmune diseases, or blood cancers. Elevated WBC levels are often indicative of infection or inflammation. In such cases, health care professionals can assess the severity of the infection and initiate appropriate treatment measures. Conversely, decreased WBC levels may signal a weakened immune system or bone marrow issues. In this scenario, the emergency department team can assess the patient's risk of infection and implement necessary protective measures.

WBC measurement in the emergency department is also instrumental in identifying and monitoring serious conditions such as sepsis. Sepsis is a life-threatening response to an overwhelming infection, and WBC levels aid in evaluating the severity of sepsis.[18] Moreover, WBC analysis provides valuable insights into the patient's overall health and helps guide medical interventions promptly. In cases of high WBC, indicating infection, health care providers can promptly administer antibiotics or other targeted therapies. Conversely, in situations of low WBC, indicating immunosuppression, additional precautions can be taken to safeguard the patient from potential infections.[19] The versatility of WBC measurement extends beyond infectious diseases. It plays a vital role in assessing inflammatory conditions such as arthritis and autoimmune disorders, guiding health care professionals in tailoring treatment plans according to the patient's specific needs.

Erythrocyte Sedimentation Rate

The ESR is a laboratory test that measures the rate at which red blood cells (erythrocytes) settle in a vertical column of blood within a specific time frame. This test is a nonspecific marker of inflammation, providing valuable information

about the presence and severity of inflammatory processes in the body.[20] In physiological terms, when blood is drawn and placed in a vertical tube, the red blood cells gradually settle due to gravitational forces. The rate at which they descend is influenced by various factors, including the concentration of certain proteins in the blood. During inflammation, the concentration of acute-phase proteins, particularly fibrinogen, increases. This elevation in protein levels causes red blood cells to aggregate more easily, resulting in a faster sedimentation rate.[21] The ESR is commonly used in clinical settings to aid in the diagnosis and monitoring of inflammatory conditions such as infections, autoimmune diseases, and certain cancers. Elevated ESR levels may indicate the presence of an inflammatory process, but it does not specify the cause. Therefore, further investigations are typically required to identify the underlying condition.[20] Physicians interpret ESR results alongside other clinical information and diagnostic tests to formulate a comprehensive understanding of the patient's health status. While an elevated ESR is a useful indicator of inflammation, it is essential to consider it in conjunction with other clinical assessments for accurate diagnosis and appropriate management.[22]

In conclusion, ESR is a valuable tool in assessing inflammatory activity within the body. Its physiological basis lies in the altered settling behavior of red blood cells during inflammatory states, providing clinicians with insights into the presence and intensity of inflammation, facilitating timely diagnosis and treatment decisions.

Due to its role as a crucial diagnostic tool, ESR is utilized in emergency departments to assess and monitor inflammatory conditions. In the fast-paced environment of an emergency setting, quick and informative tests are essential for efficient patient care. ESR is particularly valuable in emergencies where inflammatory processes are suspected, but the exact cause is unknown. The test helps health care professionals identify and gauge the severity of conditions such as infections, autoimmune diseases, and inflammatory disorders. Its simplicity and relatively rapid results make it a practical choice for initial assessments in emergency situations.[23]

When a patient presents with symptoms indicative of inflammation, an ESR test can provide rapid insights. Elevated ESR levels suggest the presence of an inflammatory process, prompting further investigations to determine the underlying cause. This aids emergency physicians in making timely and informed decisions about patient management and treatment strategies.[24]

In emergency scenarios, where time is often a critical factor, the ESR can be instrumental in quickly ruling out or confirming the likelihood of inflammatory conditions. This allows health care providers to promptly initiate appropriate interventions, such as administering antibiotics in cases of infection or initiating anti-inflammatory therapies for autoimmune conditions. Moreover, ESR is part of a comprehensive diagnostic approach, complementing other clinical assessments and imaging studies. While it does not pinpoint the specific cause of inflammation, it serves as a valuable initial screening tool. The information obtained from the ESR, along with the patient's clinical presentation, history, and other test results, guides emergency health care professionals toward accurate diagnoses and effective treatment plans.

In conclusion, the use of ESR in emergency departments provides a rapid and valuable means of assessing inflammatory conditions, facilitating timely interventions, and optimizing patient care in critical situations.

Procalcitonin

PCT is a precursor peptide of calcitonin, and its physiological role is primarily associated with calcium metabolism regulation. Produced by parafollicular cells (C cells) of the thyroid gland, PCT normally undergoes conversion to calcitonin, which plays a role in maintaining calcium homeostasis by inhibiting bone resorption. In cases of bacterial infections and sepsis, the body's response to inflammation is heightened, leading to the release of proinflammatory cytokines. Interestingly, PCT production increases significantly in response to bacterial infections but is minimally affected during viral infections or noninfectious inflammatory processes.[25] The physiological function of elevated PCT in bacterial infections is not entirely understood, but it is believed to be part of the body's defense mechanism. Some hypotheses propose that PCT might have antimicrobial properties or modulate the host response to infection. While its precise role in infection is complex, the diagnostic utility of measuring PCT levels lies in its specificity to bacterial infections.[26]

In emergency medicine, where prompt and accurate diagnosis is crucial, measuring PCT levels provides valuable information to health care professionals. Elevated PCT levels suggest a higher likelihood of bacterial infection, guiding clinicians in initiating appropriate antibiotic therapy promptly.[27] The dynamic nature of PCT levels during the course of infection also helps in monitoring the effectiveness of treatment. A decline in PCT levels over time indicates a positive response to therapy, assisting clinicians in adjusting treatment plans as needed.[27,28]

In summary, while PCT's physiological role in infection is not fully elucidated, its diagnostic value lies in its specificity to bacterial infections. In emergency settings, where rapid and precise decisions are paramount, measuring PCT levels aids in the early identification of bacterial infections and facilitates timely and targeted therapeutic interventions.

Serum Amyloid A

SAA is an acute-phase protein that plays a significant role in the body's response to inflammation and infection. Produced primarily by hepatocytes in the liver, SAA levels can increase dramatically in response to various stimuli, including infection, trauma, and inflammatory conditions.[29] Physiologically, SAA is involved in the transportation of cholesterol and its incorporation into high-density lipoproteins (HDL). It contributes to the remodeling of HDL particles, influencing their function in lipid metabolism. In normal conditions, SAA levels are relatively low, but they can rapidly rise in the presence of inflammatory signals. During acute inflammation, such as an infection, trauma, or tissue injury, the liver responds by synthesizing and releasing SAA into the

bloodstream. Elevated levels of SAA can activate immune cells and contribute to the inflammatory cascade, playing a role in the body's defense mechanisms.[29,30] While acute-phase proteins like SAA are essential for the immediate response to challenges, prolonged elevation may be indicative of chronic inflammation and contribute to the pathogenesis of various diseases. Chronically elevated SAA levels have been associated with conditions such as cardiovascular disease, rheumatoid arthritis, and certain cancers. In the context of emergency medicine, measuring SAA levels can provide valuable diagnostic information. Elevated SAA may indicate the presence of an acute inflammatory process, guiding health care professionals in assessing the severity of the condition and determining appropriate interventions.[31]

Therefore, SAA is a critical acute-phase protein involved in the body's response to inflammation. Its physiological role in lipid metabolism and its rapid elevation during inflammatory states make it a valuable marker for assessing acute and chronic inflammatory conditions in emergency medical settings.

SAA holds diverse applications in the emergency department, offering valuable insights into various medical scenarios. Primarily associated with acute inflammatory responses and infections, the measurement and assessment of SAA in emergency settings can lead to several crucial applications. Potential applications of SAA in the emergency department include the following:

- *Evaluation of infections*: SAA serves as a valuable biomarker for the detection of acute inflammatory conditions, particularly infections. Rapid elevation in SAA levels can indicate the presence and severity of an infection.
- *Monitoring inflammatory diseases*: Measurements of SAA can be utilized to monitor the progression of chronic inflammatory diseases, such as rheumatoid arthritis. This aids in assessing the patient's response to treatment.
- *Diagnosis and monitoring of sepsis*: SAA levels are indicative of severe infections, and their measurement is valuable in diagnosing and monitoring conditions like sepsis. Early recognition and prompt initiation of treatment are critical in managing sepsis.
- *Assessment of other inflammation-related conditions*: SAA can be employed to evaluate conditions associated with inflammation, including vasculitis. This provides essential information about the patient's overall inflammatory status.
- *Detection of acute inflammation*: rapid measurement of SAA levels can assess how quickly a patient is mounting an inflammatory response, providing valuable information in emergency scenarios.

In the emergency department, these applications of SAA contribute to a better understanding of patients' conditions, aiding in accurate diagnoses and the development of effective treatment strategies.

New Markers

High mobility group box 1 (HMGB1) is a nuclear protein released during cellular stress or inflammation, contributing to inflammatory processes and tissue damage. Numerous studies have explored HMGB1's potential as an inflammation marker, indicating its significance in diagnosing and monitoring various inflammatory conditions. While promising, further validation studies are crucial to establish its specificity and sensitivity in clinical applications.[32,33]

Neopterin, a byproduct of tetrahydrobiopterin oxidation, is induced by interferon-gamma, released during immune system activation. Its increased production by macrophages makes neopterin a promising biomarker for inflammation, showcasing its potential diagnostic value.[34–37]

SCUBE-1 (signal peptide-CUB-EGF domain-containing protein 1) is a gene that encodes a protein expressed in the vascular system. Circulating levels of SCUBE-1 have been proposed as a marker for conditions like cardiovascular diseases, thromboembolic events, and inflammation-related disorders. Measuring its levels holds promise for evaluating and monitoring clinical conditions, emphasizing its potential as a valuable biomarker.[38–41]

These biomarkers—HMGB1, neopterin, and SCUBE-1—offer potential avenues for assessing inflammatory states and various clinical conditions. While their promise is evident, rigorous validation through further studies is necessary to ascertain their reliability and specificity in diverse clinical applications.

Conclusion

Inflammatory markers play a pivotal role in the efficient evaluation and management of patients in emergency departments. We have highlighted the significance of CRP, WBC, ESR, PCT, and SAA as crucial indicators of inflammatory processes. CRP, as a rapid responder to inflammation, aids in diagnosing and monitoring various conditions, including infections and tissue damage. WBC count provides valuable insights into immune health, guiding the assessment of infections, inflammations, and autoimmune disorders. ESR serves as a nonspecific yet informative marker of inflammation, assisting in the diagnosis and monitoring of various inflammatory conditions. PCT's specificity to bacterial infections makes it a valuable tool in emergency settings for prompt identification and targeted treatment of such infections. SAA, associated with acute-phase responses, offers diverse applications, from evaluating infections to monitoring chronic inflammatory diseases.

In the dynamic and time-sensitive environment of emergency departments, the judicious use of these inflammatory markers enhances the accuracy and speed of diagnoses. These markers aid health care professionals in promptly initiating appropriate treatments, monitoring responses to therapy, and optimizing patient care. As we advance in understanding the intricate roles of these markers, future research may uncover further applications, refining their utility in emergency medicine. The integration of these inflammatory markers into routine emergency assessments contributes to improved patient outcomes and reinforces the pivotal role of inflammation assessment in emergency health care practices.

Author's Contribution

S.Ö. drafted , revised, and finalized the article to fulfill the ICMJE authorship criteria.

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Conflict of Interest

None declared.

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