ORIGINAL

Diagnostic and Prognostic Role of Delta Neutrophil Index (DNI), With Emphasis on Gastrointestinal Disorders

Función diagnóstica y pronóstica del índice de neutrófilos delta (DNI), con énfasis en los trastornos gastrointestinales

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Abstract

Background: A brand-new biomarker for diagnosis and prognosis for a variety of inflammatory or infectious conditions is the delta neutrophil index (DNI). DNI is a laboratory index that is determined by dividing the total number of peripheral blood neutrophils by the number of immature granulocytes. However, there are few studies that have examined the potential use of DNI as a prognostic biomarker in gastrointestinal disorders and their associated infections. The purpose of this study was to explore the role of delta neutrophil index (DNI) as a biomarker to determine the prognosis of infectious conditions, especially in gastrointestinal diseases.
Methods: The research is a bibliographic review. To review the articles, from the databases PubMed, Science Direct, Scopus, Google Scholar, etc., and based on the inclusion criteria, case reports, cohorts and numerous clinical studies used in a period of mostly 4 years (2019-2023) were selected. The final sample used in this review included 120 articles.
Results and conclusion: The results showed that DNI may be considered as a primary and reliable biomarker for diagnosis, prognosis, initial triage, surgical outcomes, various infections, as well as predicting the severity of pediatric and gynecological conditions and cardiopulmonary or gastrointestinal disorders and etc.

Keywords: Delta Neutrophil Index (DNI), Prognosis, Infectious Conditions, Gastrointestinal Disorders.

Resumen

Antecedentes: El índice delta de neutrófilos (DNI) es un nuevo biomarcador para el diagnóstico y el pronóstico de diversas enfermedades inflamatorias o infecciosas. El DNI es un índice de laboratorio que se determina dividiendo el número total de neutrófilos de sangre periférica por el número de granulocitos inmaduros. Sin embargo, hay pocos estudios que hayan examinado el uso potencial del DNI como biomarcador pronóstico en los trastornos gastrointestinales y sus infecciones asociadas. El propósito de este estudio fue explorar el papel del índice delta de neutrófilos (DNI) como biomarcador para determinar el pronóstico de afecciones infecciosas, especialmente en enfermedades gastrointestinales.
Métodos: La investigación es una revisión bibliográfica. Para la revisión de los artículos, a partir de las bases de datos PubMed, Science Direct, Scopus, Google Scholar, etc, y en base a los criterios de inclusión, se seleccionaron informes de casos, cohortes y numerosos estudios clínicos utilizados en un periodo mayoritariamente de 4 años (2019-2023). La muestra final utilizada en esta revisión incluyó 120 artículos.
Resultados y conclusiones: Los resultados mostraron que el DNI puede considerarse como un biomarcador primario y confiable para el diagnóstico, pronóstico, triaje inicial, resultados quirúrgicos, diversas infecciones, así como para predecir la gravedad de afecciones pediátricas y ginecológicas y trastornos cardiopulmonares o gastrointestinales y etc.

Palabras clave: Índice de neutrófilos delta (DNI), pronóstico, afecciones infecciosas, trastornos gastrointestinales.

Introduction

Excessive production of cytokines and chemokines in the early stages of infection or inflammation limits the migration of neutrophils to the target organ, and therefore fewer mature neutrophils enter the blood circulation to compensate for the lack of active neutrophils. This modification process is referred to as "left shift". By using the DNI index, which actually indicates the ratio of immature granulocytes to the total number of neutrophils, myeloperoxidase channels and nuclear lobularity can be indirectly measured. This technique makes it possible to predict the prognosis in various infectious or inflammatory conditions, and in this way, the number of immature granulocytes in the blood circulation can be shown . This is how DNI is a biomarker that indicates the number of immature neutrophils in the peripheral circulation and is calculated by subtracting the fraction of mature polymorphonuclear leukocytes from the total cells that react to myeloperoxidase[1].

A change in the DNI index occurs before a change in the number of neutrophils or white blood cells. In inflammatory and infectious conditions, this change is primarily the result of the formation of immature granulocytes, which differentiate into granular leukocytes[2]. Various reports have confirmed the role of DNI as an important indicator in determining the prognosis of infection or inflammation[3].

The diagnostic ability of the combined use of DNI and procalcitonin may improve the prediction of sepsis severity and survival[4,5]. showed also that DNI against ESR, CRP and procalcitonin was significantly associated with predicting sepsis and septic shock.

The findings of Park et al. (2020) also showed that the area under the curve (AUC) for peak DNI 24 hours after admission to the emergency department for predicting the development of sepsis was significantly superior to other parameters such as CRP, ESR, procalcitonin and WBC count (**Figure 1**).

Kim et al. on emergency department admissions also showed that comparing ROC curves for predicting acute kidney injury (AKI) the area under the ROC (AUROC) for DNI was significantly higher and more effective than other markers such as CRP, WBC, and neutrophil levels. The AUROC also showed that Time-12 was significantly more reliable than procalcitonin for DNI as well. In addition, the value of DNI during admission to the emergency department was not significantly lower than the values of lactate and procalcitonin, and at Time-12, the value of DNI was not lower than lactate (**Figure 2**). Totally, by comparing C-statistics regarding DNI levels and other markers, this index was superior to CRP, WBC, procalcitonin, and neutrophils in predicting 30-day mortality at Time-12. In predicting 30-day mortality, DNI levels at Time-12 were similar to lactate[2].

This study aimed to investigate the role of delta neutrophil index (DNI) as a biomarker to determine the prognosis of infectious conditions in the context of various diseases, especially in gastrointestinal diseases.

Methods

We searched PubMed, Science Direct, MEDLINE, EMBASE, and other reliable medical indexing websites to identify studies evaluating DNI as a predictive or prognostic factor in infectious conditions, particularly for gastrointestinal diseases.

Figure 1: ROC curves for the predictability of DNI and inflammatory biomarkers at 24 hours after emergency department (ED) admission to predict sepsis in acutely poisoned patients[5].
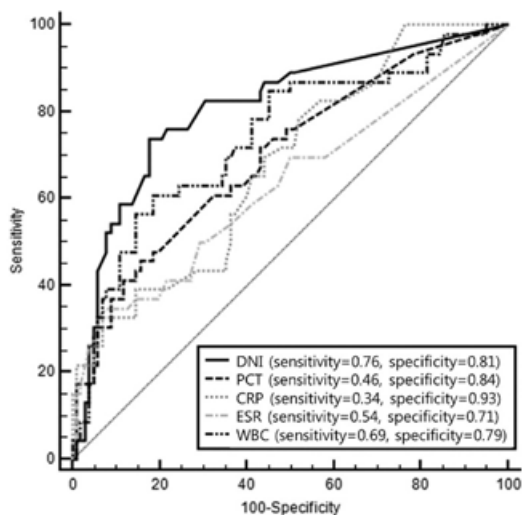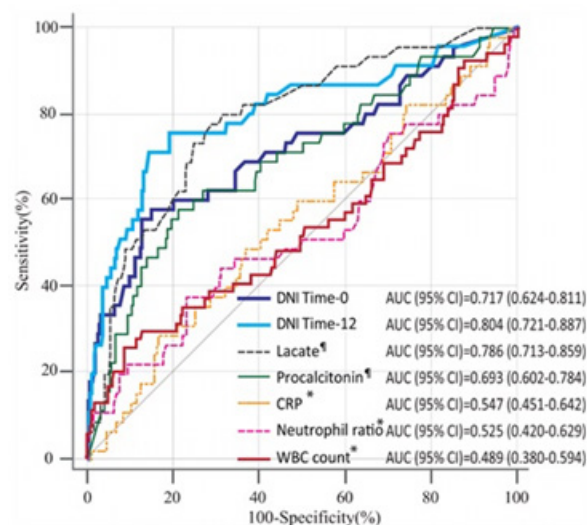
Figure 2: Comparative area under the curve (AUC) for DNI to predict the development of severe acute kidney injury (AKI)[2].

DNI and Non-Gastrointestinal Disorders

Evaluations have shown that increased DNI levels can be a predictive marker in determining the prognosis of chronic obstructive pulmonary disease (COPD)[6]. An increase in DNI level can be considered as a prognostic marker in cases of cardiac arrest[7].

A systematic review shows that, in general, DNI can play an important diagnostic role in patients with infectious diseases and be used more widely. The DNI index is now a new biomarker that It can be used in diagnosing and determining the prognosis of death in patients with infections, it has been confirmed. Also, it has been determined that high levels of DNI, together with C-reactive protein (CRP), the absolute neutrophil count (ANC), absolute lymphocyte count (ALC), platelet count, are predictive factors for the diagnosis of Multisystem Inflammatory Syndrome in Children (MIS-C)[8].

DNI can also be used as a new biomarker to differentiate bacterial infections from candidemia in patients with systemic inflammatory response syndrome (SIRS). Predicting the severity of sepsis and determining the prognosis of 14-day mortality in patients with candidemia is also possible by determining DNI levels[9].

Since the septic status of patients admitted to the emergency department is an important factor for predicting their prognosis and mortality, suitable biomarkers that indicate its severity are of particular importance. Several studies have used the DNI value in evaluating patients with sepsis and bacteremia have been reported[10].

Hence, along with other inflammatory markers such as WBC, CRP and procalcitonin, DNI can also be considered as a diagnostic tool to predict mortality in patients with sepsis, disseminated intravascular coagulation (DIC) and bacteremia[11]. On the other hand, high DNI values can be used to quickly diagnose the severity of sepsis, predict acute kidney injury (AKI) and subsequent 30-day mortality, as well as design treatment strategies. DNI can be also considered as an independent factor of mortality in septic acute kidney injury patients with continuous renal replacement therapy (CRRT)[12].

One study used cluster analysis to determine strong predictors of sepsis that could screen potentially overlooked patients with possible sepsis (eg, sepsis patients without elevated WBC count). The results have shown that although WBC is considered a well-known parameter for sepsis, it had little relationship with sepsis status in elderly clusters. Instead, neutrophil-to-lymphocyte ratio (NLR) and DNI were strong predictors in all subjects[13].

Although delta neutrophil index (DNI) is a marker that has been reported to predict the diagnosis, prognosis, and severity of bacteremia and sepsis, the results of a study of febrile pediatric patients in the emergency department

(ED) suggest that DNI in the absence Bacteremia will not be useful in differentiating bacterial infection without bacteremia (BIWB) from viral infections[14].

In cases of severe infection or inflammation in patients with chronic rhinosinusitis (CRS), evaluation of DNI levels reflects the severity of the disease. Therefore, DNI values may be a useful predictor to determine the need for surgical intervention in these patients[15].

The DNI value as an indicator of infection can be useful in predicting acute pyelonephritis (APN) in patients with urinary tract infection (UTI) suffering from ureteral stones. DNI can be checked together with a complete blood count and the result can be obtained quickly and without incurring additional costs. Hence, Careful management should be considered if DNI levels are >1.3% in patients admitted to the emergency department or outpatient urology clinic for ureteral stones with suspected APN[16].

There is little study on the role of determination of delta neutrophil index (DNI) levels in determining the severity of multiple organ dysfunction (MODS) and short-term mortality. A study investigated the use of automatically calculated DNI as a marker in the prognostic assessment of severity in trauma patients admitted to the intensive care unit (ICU). The results indicated that DNI is useful for rapid and simple estimation of the severity of traumatic injury using an analyzer. Automated hematology is convenient, with no additional cost or time[17].

An interesting association has also been shown between DNI levels and gestational diabetes as a novel inflammatory marker. In such a way that this biomarker is more in women with gestational diabetes than in women with normal pregnancy[18]. Several studies also have reported that DNI levels are increased in certain pathological conditions such as preeclampsia[19].

Postpartum hemorrhage (PPH) is one of the most dangerous complications related to maternal mortality. It is difficult to accurately estimate the amount of bleeding by sight. Using delta neutrophil index (DNI) as a predictive biomarker can also be useful in this regard. The results showed that the relationship between DNI levels and shock index (SI) can be routinely measured in the emergency department (ED) and used as a suitable tool to classify the initial risk level in patients with primary PPH[20].

DNI and Gastrointestinal Disorders

The increase in DNI values can be related to the occurrence of mortality in acute upper gastrointestinal bleeding (UGIB) conditions. It can also help to differentiate between perforated and non-perforated appendicitis[21].

Since predicting severe acute pancreatitis (SAP) in the early stages of clinical evidence is very important to reduce complications and mortality, delta neutrophil index

Figure 3: Receiver operating characteristic curve for predicting severe acute pancreatitis. The model was adjusted for age, sex, diabetes mellitus, hypertension, liver cirrhosis, smoking status, gallstones, and alcohol[2].

Figure 4: ROC curve of complicated acute cholecystitis: IGC: Immature granulocyte count; DNI: delta neutrophil index; WBC: White blood cell; CAR: CRP-to-albumin ratio; ROC: Receiver operating characteristics (Ünsal, 2022).
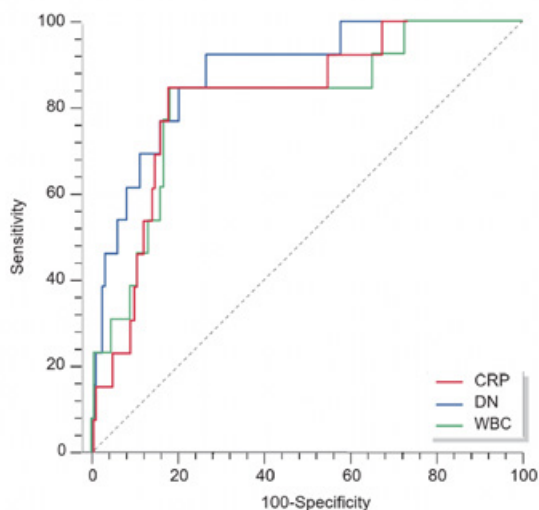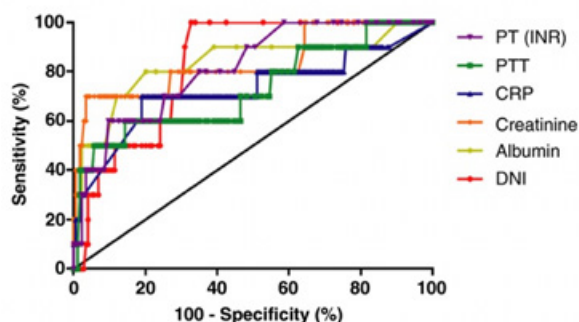
Figure 5: Comparison of the curves related to different serological markers compared to neutrophil delta index in relation to 30-day mortality patients who need urgent abdominal surgery[24].
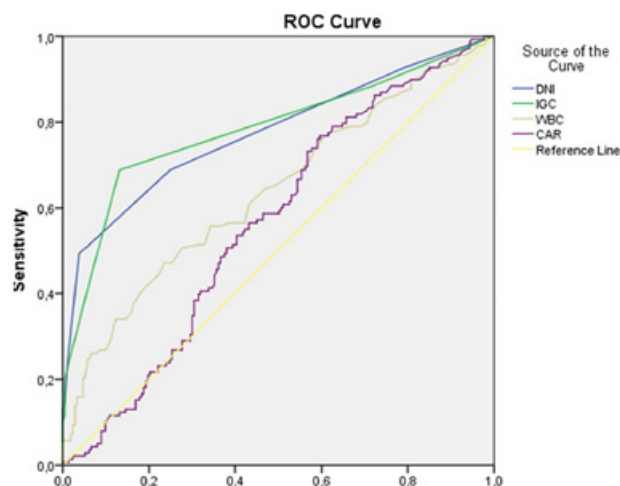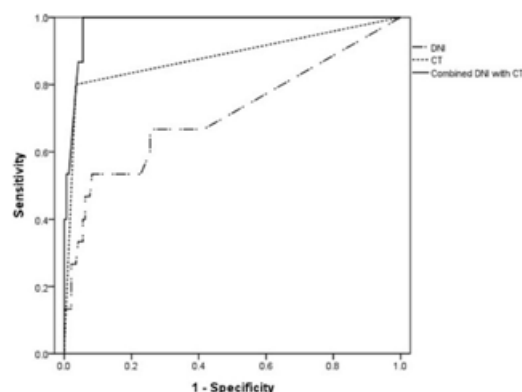
Figure 6: The cumulative efficiency of combined use of DNI and CT and index for the diagnosis of intestinal strangulation in the emergency department (ED)27.

(DNI) is used to diagnose infection and inflammation. However, few studies have evaluated the usefulness of DNI as a predictor of disease progression to severe acute pancreatitis (SAP) (**Figure 3**).

The DNI measured in the emergency department (ED) is a potentially useful auxiliary marker for predicting SAP. This review suggests that intensive care should be considered for patients with severe acute pancreatitis, with a DNI value greater than 1.8% when presenting to the ED[2].

Esophagectomy is a complex and invasive procedure and shows a high incidence of complications. Hence, early detection of complications is important. The results have shown that the evaluation of DNI levels after esophagectomy can be useful as an early predictive biomarker of postoperative complications[22].

Gallbladder disorders, including complicated cholecystitis, can be associated with increased mortality and complications. A study aimed at evaluating the predictive value of the number of immature granulocytes and delta neutrophil index (DNI) showed that IG count and DNI level determination are two new and valuable parameters for the early diagnosis of complicated acute cholecystitis[23].

In patients with acute peritonitis, DNI values can predict 30-day mortality. The results showed that high DNI values can indicate high severity and more disappointing prognosis in acute abdomen. The use of DNI can be also considered as an efficient predictive marker in determining the prognosis of patients who need urgent abdominal surgery. The high levels of DNI can be considered as an efficient predictive marker in determining the prognosis of patients who need urgent abdominal surgery. **Figure 4** compares the functions of PT, PTT, CRP, creatinine, albumin, and DNI with respect to 30-day mortality in such patients. In patients with more underlying diseases, the practical value of DNI as a prognostic indicator for Intra-abdominal infection (IAI) was more valuable. In trauma

patients who have undergone abdominal surgery, delta neutrophil index (DNI) can be a predictor of complications and mortality during emergency surgical interventions[24].

Regarding the prediction for emergency surgical intervention in acute diverticulitis, it can be useful to evaluate DNI levels along with CT. The treatment protocol recommends that if DNI values are more than 0.7% and CT complications suggest the possibility of acute diverticulitis, immediate surgical intervention may be needed[25].

The results show that in mesenteric ischemia, determining the number of immature granulocytes and DNI may be used to evaluate intestinal necrosis. Interpretation of the results of these indices are more reliable than conventional parameters such as WBC, CRP and LDH[26].

Early detection of intestinal strangulation in the emergency department (ED) showed that the initial DNI levels in the strangulation group (SG) were significantly higher than the non-strangulation group (NSG). Initial assessment of DNI along with CT can be an additional useful parameter to improve the diagnostic accuracy of strangulated mechanical bowel obstruction in the emergency department (**Figure 5**)[27].

The results of using delta neutrophil index (DNI) to determine the prognosis of 30-day mortality in patients with spontaneous bacterial peritonitis (SBP) due to advanced cirrhosis were completely satisfactory[28].

Conclusion

This narrative review study showed that DNI is a simple but efficient test that can be quantitatively measured in routine complete blood counts. In diseases such as sepsis, meningitis, pediatric diseases and conditions, urinary infections, some cardiovascular disorders, gynecological conditions, and especially the gastrointestinal system disorders. it has a diagnostic value and can even be a very important biomarker in determining prognosis. Considering the sensitivity, specificity, and area under the curve (AUC), the evaluation of DNI levels can be used to predict severity, surgical outcomes, or mortality, and as a triage tool during the initial admission to the emergency department in patients with gastrointestinal diseases[29].

Finally, a meta-analysis of patients with infectious diseases has shown that the evaluation of DNI levels can serve as a reliable parameter and a potentially useful diagnostic and prognostic tool in the diagnosis of infection and prediction of mortality[30].

As a result, the measurement of DNI levels can also be considered a reliable early biomarker for triage as well as prediction of severity, results of surgical procedures, and mortality rate in gastrointestinal diseases.

Conflicts of Interest
None

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