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Review article

The prognostic value of the neutrophil-lymphocyte ratio in renal oncology: A review

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Abstract

Background: The neutrophil-lymphocyte ratio (NLR) is a biological marker of inflammation with a significant prognostic value in the field of oncology.

Aim: In this review, we discuss the prognostic value of the NLR in renal cell carcinoma (RCC).

Material and Method: We conducted a literature review of the PubMed database in August 2016. Initial research identified 31 publications. Following full-text screening, 15 studies were finally included: 7 studies concerning metastatic or locally advanced renal cancer, 6 studies dealing with localized renal cancer, 2 articles evaluating the NLR in renal cancer whatever the status of the disease (metastatic or localized).

Results: For localized RCC, an NLR o 3 was predictive of a reduced risk of recurrence (hazard ratio ¼ 1.63 [1.15, 2.29]). The prognostic value of the NLR was stronger for metastatic or locally advanced RCC. An NLR o 3 predicted increased overall survival (hazard ratio ¼ 1.55 [1.36, 1.76]), progression-free survivals (hazard ratio ¼ 3.19 [2.23, 4.57]), and a response to systemic treatment.

Conclusion: In current practice, the NLR is a simple and inexpensive prognostic factor with potential improvement in the prognostic performance of nomograms used in renal oncology.

Keywords: Inflammation; Kidney neoplasms; Neutrophil-lymphocyte ratio; Nomograms; Prognosis

1. Introduction

The neutrophil-lymphocyte ratio (NLR) is a marker of inflammation and an independent prognostic factor for many cancers [1]. For such cancers, the NLR has been identified as a poor prognostic factor of overall survival, disease-specific survival, and free-progression survival for metastatic cancer [1]. For colorectal cancer, Walsh et al. [2] reported in 2005 that an NLR > 5 on diagnosis was an independent prognostic factor of decreased overall survival and specific survival. For small cell lung cancer, an NLR > 4 on diagnosis was associated with a poor performance status, a locally advanced disease, and a poor response to systemic treatment [3]. The prognostic value of the NLR was also confirmed for gastric, liver, and ovarian cancer [4–6].

The NLR could also be of prognostic value for urological cancers [7,8]. To date, the prognostic systems validated for renal cell carcinoma (RCC), such as the UCLA Integrated Staging System score for localized RCC and the Memorial Sloan Kettering Cancer Center (MSKCC) score modified by Heng for metastatic RCC, have taken into account a combination of clinical criteria (Eastern Cooperative Oncology Group or Karnofsky), biological criteria (LDH, calcium, hemoglobin, and neutrophils), histological criteria (Fuhrman), and imaging parameters (tumor size) but excluded the NLR [9,10].

The aim of this study was to conduct a review of the literature to evaluate the prognostic effect of the NLR in

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RCC and to compare the relevance of this single biological ratio with multifactorial nomograms.

2. Materials and methods

2.1. Search strategy and eligibility criteria

We conducted a literature review of the PubMed database in August 2016. The search algorithm was "Kidney Neoplasms" [MeSH] AND "neutrophil-lymphocyte ratio" (all fields). Studies evaluating the prognostic value of the NLR in kidney cancer were included. We excluded references dealing with cancers other than RCC. The language restriction was limited to articles in French and English. We excluded case reports, editorials, conference abstracts, and reviews. A first screening of the articles was performed with the titles and the abstracts. A second screening was performed with the full texts to definitively include/exclude the studies for this review.

2.2. Extraction and analysis of data

In the included studies, we took into account the following data: the type and level of evidence of the study, the number of patients, patient age on diagnosis, the NLR and the time of its dosage (NLR pretreatment vs. posttreatment), the initial staging of the RCC (localized vs. metastatic), the type of treatment, and the oncological outcomes. The primary end point was the overall survival for metastatic disease and the recurrence-free survival for localized disease. Secondary outcomes were specific survival and the progression-free survival. A synthesis of the data was performed with Review Manager 5.2 software (Informatics and Knowledge Management Department, Cochrane, London, UK).

3. Results

3.1. Search results

The PRISMA diagram of the literature search is presented in Fig. 1. The initial research identified 31 publications. Twenty-five references matched the inclusion criteria. Following full-text screening, 16 studies were included. One study was excluded owing to a lack of data. We finally included 15 studies: 7 studies concerning metastatic or locally advanced renal cancer and 6 studies dealing with localized renal cancer. Two articles evaluated the NLR in renal cancer whatever the status of the disease (metastatic or localized). The characteristics of the included studies are summarized in Table 1.

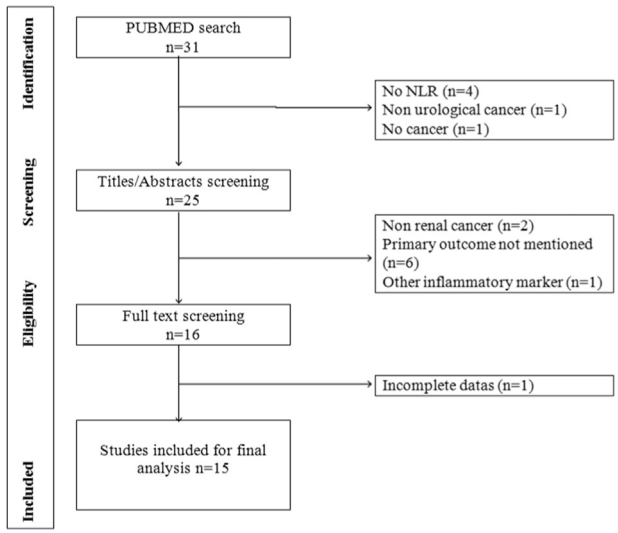

Fig. 1. PRISMA flow diagram.

3.2. NLR and localized renal cancer

In the 6 studies dealing with localized renal cancer, a high NLR on diagnosis was significantly associated with an increased risk of recurrence compared with a low NLR (hazard ratio = 1.63 [1.15–2.29]). The NLR was not significant for overall survival (Fig. 2A and B).

Pretreatment NLR was determined from a preoperative blood test. The threshold of NLR among the 6 aforementioned studies ranged from 2.7 to 5. All of the patients had surgical treatment with total or partial nephrectomy. Mean follow-up ranged from 3.3 to 9.3 years.

The NLR was an independent prognostic factor for recurrence in 3 studies. A high NLR was associated with a risk of recurrence ranging from 1.17 to 3.12 (1 excluded) in multivariate analysis.

The postnephrectomy NLR was evaluated in 1 study and was associated with an increased risk of recurrence (Table 2).

For Grivas et al. [11] and de Martino et al. [12], an NLR superior to 2.7 was a predictive factor of a metastatic lymph node disease on the final histology ($P = 0.04$). In multivariate analysis, a preoperative NLR superior to 2.7 was a prognostic factor for recurrence but not for overall survival.

Ohno et al. [13] analyzed the kinetics of the NLR at different timelines: before nephrectomy, after nephrectomy, and on recurrence. In their study, which included 250 nephrectomies for localized conventional cell renal carcinoma, 10-year recurrence-free survival was significantly higher for patients with an NLR inferior to 2.7 on diagnosis (64.4% vs. 83.7%, $P = 0.0004$). The patients who had a high NLR before nephrectomy and who normalized the NLR after nephrectomy were at greater risk of recurrence: disease-free survival at 10 years 52% vs. 83.5% ($P = 0.0487$). For these patients, recurrence corresponded to a re-increase in the NLR of more than 2.7 ($P = 0.009$) [13].