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ORIGINAL ARTICLE

The impact of neutrophil-to-lymphocyte, platelet-to-lymphocyte and haemoglobin-to-platelet ratio on localised renal cell carcinoma oncologic outcomes

L'impact du rapport neutrophiles-lymphocytes, plaquettes-lymphocytes et hémoglobine-plaquettes sur les résultats oncologiques du carcinome rénal localisés

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Summary
Introduction. — The neutrophil to lymphocyte ratio (NLR) and the platelet to lymphocyte ratio (PLR) are established markers of systemic inflammation. Moreover, anemia is a known adverse prognostic factor and reduced haemoglobin to platelet ratio (HPR) seems associate to poor outcomes in urothelial cancer. Aim of the current study was to explore the prognostic value of NLR, HPR and PLR in patients harboring localized RCC.

Materials and Methods 184 patients undergoing partial and radical nephrectomy for renal mass in a single hospital were retrospectively analyzed. Uni- and multivariate logistic regressions were performed to assess associations between various risk factors, including NLR, PLR and HPR and locally advanced disease ($\leq$ pT2 vs. $\geq$ pT3) and tumor grade. Kaplan Meier curves and Cox regressions were constructed to assess the association of NLR, PLR and HPR to

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recurrence free survival (RFS), cancer specific survival (CSS) and overall survival (OS). To determine thresholds for variables, we considered the 75th percentile of our distribution of values, which was computed at 3.45 for NLR, 189 for PLR and 0.48 for HPR. A two-sided $P < 0.05$ defined statistical significance.

Results. — Patients with an elevated NLR (> 3.45) were more likely to present with ≥ pT3 stage ($p = 0.046$). RFS was significantly different according to NLR value, with patients having an NLR > 3.45 experiencing significantly worst RFS ($P = 0.019$); similarly, an increased PLR was significantly associated to a reduced RFS ($P = 0.012$). Restricting the Cox regression to patients with locally advanced disease (≥ pT3), NLR was even more associated to recurrence (HR 3.22; 95%CI: 1.06—9.81, $P = 0.039$). Patients exhibiting an NLR > 3.45 ($p = 0.03$) or a PLR > 189 ($P = 0.005$) did have a significantly worse CSS, while a HPR < 0.48 did not predict CSS ($P = 0.12$) on Kaplan Meier curves. Finally, an increased NLR ($P = 0.047$), increased PLR ($P = 0.0006$) and decreased HPR ($P = 0.05$) were all associated to a poor overall survival on univariate analysis. On multivariate analysis, only HPR remained significantly predictive of OS (HR 0.077; 95%CI: 0.02—0.37, $P = 0.001$).

Conclusions. — In this single-center study analyzing non-metastatic RCC, an increased NLR was significantly associated to a reduced RFS, CSS and OS on univariate analyses and to RFS on multivariate analysis. Larger prospective studies are needed to validate our findings.

Level of evidence.— 4.

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Résumé

Introduction. — Le rapport neutrophile/lymphocyte (NLR) et le rapport plaquette/lymphocyte (PLR) sont des marqueurs établis de l'inflammation systémique. L'anémie est un facteur pronostique défavorable connu et une diminution du rapport hémoglobine/plaquettes (HPR) pourrait être associée à un moins bon pronostic dans le cancer rénal. Le but de cette étude était d'explorer la valeur pronostique des NLR, HPR et PLR chez les patients ayant un cancer à cellules rénales localisé.

Matériel et Méthodes. — Un total de 184 patients opérés d'une néphrectomie partielle ou radicale pour une tumeur rénale dans un seul centre hospitalier ont été analysés de manière rétrospective. Des régressions logistiques uni- et multivariées ont été réalisées pour évaluer les associations entre divers facteurs de risque, y compris le NLR, le PLR et le HPR et la maladie localement avancée (≤ pT2 vs ≥ pT3) et le grade tumoral. Les courbes de Kaplan Meier et des régressions de Cox ont été construites pour évaluer l'impact du NLR, du PLR et du HPR sur la survie sans récidive (SSR), la survie spécifique au cancer (SSC) et la survie globale (SG). Les seuils choisis pour les différents marqueurs correspondent au 75e percentiles des distributions : ils ont été calculés à 3,45 pour le NLR, 189 pour le PLR et 0,48 pour le HPR. Un $p < 0,05$ a été considéré comme significatif.

Résultats. — Les patients avec un NLR > 3,45 étaient plus à risque de présenter un stade ≥ pT3 ($p = 0,046$). Un NLR > 3,45 et un PLR > 189 étaient associés avec une SSR diminuée ($p = 0,019$ et $p = 0,012$, respectifs). En limitant la régression de Cox aux patients atteints d'une maladie localement avancée (≥ pT3), le NLR élevé était associé à la récidive (HR 3,22 : IC 95 % : 1,06—9,81, $p = 0,039$). Les patients présentant un NLR > 3,45 ($p = 0,03$) ou un PLR > 189 ($p = 0,0005$) avait une SSC significativement réduite, alors que un HPR < 0,48 n'était pas associé à la SSC sur la curbe de Kaplan-Meier. En fin, un NLR augmenté ($p = 0,047$), un PLR augmenté ($p = 0,0006$) et un HPR réduit ($p = 0,05$) étaient associés à une réduction de SG en analyse univariée. Seulement l'HPR restait significativement prédictive d'une SG réduite en analyse multivariée (HR 0,077 : 95 %CI : 0,02—0,37, $p = 0,001$).

Conclusions. — Dans cette étude monocentrique analysant le RCC non métastatique, une augmentation du NLR était significativement associée à réduction de la SSR, SSC et SG sur des analyses univariées et à SSR sur l'analyse multivariée. De plus amples études prospectives sont nécessaires pour valider nos résultats.

Niveau de preuve.— 4.

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Introduction

Renal cell carcinoma (RCC) is a major health concern in western countries, as incidence is increasing given the upsurge of abdominal imaging exams [1]. In Belgium, incidence has risen from 1352 new case in 2004 to 1688 in 2014, representing an overall 24.85% increase across ten years, respectively +31.6% in men and +14.6% in women [2]. Although abdominal imaging determined a stage shift to earlier diagnosis, 20—30% of patients will still progress to metastatic disease after surgical resection [3]. As such, in the urologic community there is currently great debate on the identification of patients who could potentially benefit from adjuvant therapy in order to reduce the risk of progression. Large trials have reported conflicting results concerning the benefit of adjuvant therapy [4,5], but overall the risks and morbidity of tyrosine kinase inhibitor (TKI) therapy exceed the potential benefit of such therapy in the adjuvant setting [6], and current guidelines do not recommend such adjuvant strategy [7]. We are therefore in desperate need of biomarkers to stratify patients and shed light on those who are at higher risk of relapse, in order direct adjuvant or other aggressive therapies to the right patients and improve recurrence free survival (RFS), cancer specific (CSS) and overall survival (OS).

RCC is a highly immune-sensitive cancer, as is testified the efficacy of checkpoint inhibitors [8]. As such, host systemic inflammation and immune dysregulation has been associated to poor prognosis [9]. The neutrophil to lymphocyte ratio (NLR) and the platelet to lymphocyte ratio (PLR) are established markers of systemic inflammation, which have been introduced to predict surgical outcomes [10]. The NLR is based on the concept that neutrophils represent the inflammatory response, whereas lymphocytes reflect cell-mediated immunity, with consequent modification of cytokine secretion in the tumor microenvironment [11]. Increased NLR is associated to poor oncologic outcomes, as found in various oncologic procedures like hepatocellular, ovarian and colorectal cancer resection [12,13]. Platelet count has also been integrated in ratios in order to express systemic inflammation, with elevated levels (thrombocytosis) associated to an increased degree of inflammatory response. As such, an increased platelet-to lymphocyte ratio (PLR) has been associated to systemic inflammation and worse prognosis [14]. Moreover, anemia is a known adverse prognostic factor in multiple solid tumors; Investigators have found that a reduced haemoglobin to platelet ratio (HPR) (i.e. anemia and thrombocytosis) could be associated to more aggressive disease and poor oncologic outcomes in urothelial bladder cancer [15], while its prognostic value in RCC has not yet been explored. The advantages of NLR, PLR and HPR include the low cost, reproducibility and easy availability. Although studies have suggested that NLR and PLR may be a predictor of disease recurrence and of survival in metastatic RCC patients [16,17], the impact of such index on localized disease remains uncertain. The aim of the current study was to explore the value of NLR, HPR and PLR in patients harboring localized RCC in a single hospital setting, using a prospective database of RCC patients.

Material and Methods

After obtaining institutional review board and ethical committee (No. P2017/135) approval, all patients undergoing partial or radical nephrectomy for renal mass in a single hospital were prospectively included in our registry beginning in January 2008 ($n = 306$). We then retrospectively reviewed our registry and included in the present analysis patients with non-metastatic RCC. Exclusion criteria were: metastatic disease, oncocytoma, chronic inflammatory disease, hematopoietic disease, infection, hyperpyrexia, concomitant tumor other than RCC and immunosuppressive therapy including corticosteroids. After excluding 122 ineligible patients, a total of 184 patients were included in the registry.

The surgical approach (partial vs. radical; minimally-invasive vs. open) was decided according to multidisciplinary approach. Patient characteristics and comorbidities were encoded by a junior urologist in the registry. ASA score was determined by a senior anesthesiologist. Patients were followed with clinical, biochemical and imaging (thoracoabdominal CT) work-up every 3 months for the first two years, semestrial for years 3—5, and then yearly, unless the clinical exam indicated the suspect of recurrent disease.

Statistical analyses

NLR was computed dividing absolute neutrophil count by lymphocyte count, according to the preoperative blood test, which is normally performed one week before surgery. Similarly, PLR was calculated dividing absolute platelet count by lymphocyte count and HPR by diving haemoglobin by platelet count. The difference in distribution of NLR, PLR and HPR values across various RCC histotypes was evaluated via Kruskall-Wallis test. Uni- and multivariate logistic regressions were performed to assess associations between various risk factors, including NLR, PLR and HPR and locally advanced disease ($\leq$ pT2 vs. $\geq$ pT3) and tumor grade. Explored risk factors included age, sex, BMI, hypertension, diabetes, smoking status, NLR, PLR and HPR. NLR, PLR and HPR were explored as continuous (logarithmically transformed given non-parametric distribution) and categoric variables. Various cut-offs have been proposed for the three indices: in the present study, we considered the 75th percentile of our distribution of values, which was computed at > 3.45 for NLR, > 189 for PLR and < 0.48 for HPR.

We then performed Kaplan Meier curves to assess the impact of NLR, PLR and HPR on RFS, CSS and OS. Log-rank test were conducted to explore statistical significance of such curves. Uni- and multivariate Cox regression models were constructed to evaluate risk factors for RFS, CSS and OS. NLR, PLR and HPR were logarithmically transformed for cox regressions given non-parametric distribution. Given the collinearity between pT stage and Nuclear Grade (Spearman's $\rho = 0.38$, $P < 0.001$), and given the higher impact of pT stage on oncologic outcomes [18], multivariate analyses were adjusted to pT stage and age only. A two-sided $P < 0.05$ defined statistical significance. All analyses and graphics were performed using the Stata software version 12.

Table 1 General characteristics of the cohort.

Age (years) Median (IQR)	62 (53–67)
Mean ± SD	60 ± 12
Sex M/F	134 (73%)/50 (27%)
BMI (kg/m^2) Median (IQR)	27.2 (24.1–28.9)
Mean ± SD	27.2 ± 4.4
Smoker	
No	129 (70%)
Yes	55 (30%)
HTA	
No	77 (42%)
Yes	107 (58%)
Diabetes	
No	139 (76%)
Yes	45 (24%)
ASA score	
1	17 (9%)
2	111 (60%)
3	55 (30%)
4	1 (1%)
eGFR (ml/min) Median (IQR)	60 (59–84)
Mean ± SD	63 ± 21
Hb (gr/dl) Median (IQR)	14.1 (13.0–15.2)
Mean ± SD	13.9 ± 1.78
Platelets (×10 3/μl) Median (IQR)	239 (201–285)
Mean ± SD	249 ± 71
Neutrophils (×10 3/μl) Median (IQR)	4.6 (3.6–5.595)
Mean ± SD	4.738 ± 1.645
Lymphocytes (×10 3/μl) Median (IQR)	1.745 (1.390–2.260)
Mean ± SD	1.857 ± 0.746
Neutrophil-lymphocyte ratio (NLR) Median (IQR)	2.48 (1.90–3.46)
Mean ± SD	3.07 ± 2.34
Platelet-lymphocyte ratio (PLR) Median (IQR)	136 (103–189)
Mean ± SD	160.8 ± 127.1
Hb-Platelet ratio (HPR) Median (IQR)	0.59 (0.48–0.71)
Mean ± SD	0.61 ± 0.22

Table 2 Pathologic characteristics of renal tumors.

Surgical approach	
Partial nephrectomy	85 (46%)
Radical nephrectomy	99 (54%)
pT	
pT1a	76 (41%)
pT1b	45 (24%)
pT2	19 (10%)
pT3a	34 (18%)
pT3b	9 (5%)
pT4	1 (1%)
pN	
pNx	174 (95%)
pN0	8 (4%)
pN1/2	2 (1%)
Maximal size Median (IQR)	4.3 (2.5–7)
Mean ± SD	5.1 ± 3.3
Histology	
ccRCC	131 (71%)
TP type I	16 (9%)
TP type II	22 (12%)
Chromophobe	9 (5%)
Non classifiable	6 (3%)
Grade	
I	17 (9%)
II	68 (37%)
III	73 (40%)
IV	20 (11%)
Undetermined	6 (3%)

Results

General characteristics of the cohort are illustrated in Table 1. Pathologic results are visible in Table 2. Of note, 24% of patients presented with locally advanced ≥ pT3 disease. Median NLR value was 2.48 (IQR 1.90–3.45), median PLR was 137 (103–189) and median HPR was 0.59 (0.48–0.71).

Subtypes of RCC did not differ in terms of NLR, PLR or HPR (all $P = 0.17$) (Table 3), while patients harboring Chromophobe RCC appeared to be younger. When analyzing risk factors for an elevated tumor grade (Furhman ≥ 3), only age was a significant predictor (OR 1.04 95%CI 1.02–1.07, $P = 0.002$), while NLR, PLR and HPR were not significantly associated to tumor grade (all $P = 0.22$). Regarding locally advanced disease, patient with an elevated NLR (> 3.45) were more likely to present with ≥ pT3 stage (OR 2,09, 95%CI: 1.01–4.37, $P = 0.046$). In fact, if NLR was ≤ 3.45, 20% of patients harbored locally advanced disease (≥ pT3), while if NLR was > 3.45, this rate increase to 35%. BMI, diabetes, hypertension and smoking status were not significantly associated to pT stage (all $P > 0.05$).

After a median follow-up of 46 months (IQR 18–66), 21 patients experienced a metastatic recurrence. RFS was significantly different according to NLR value, with patients having an NLR > 3.45 experiencing significantly worst RFS (Fig. 1, log rank $P = 0.019$); similarly, an increased PLR was significantly associated to a reduced RFS (Fig. 1, log rank $P = 0.012$). HPR however was not a significant predictor of RFS ($P = 0.11$). On multivariate Cox regression, NLR was a significant predictor of recurrence (HR 2.51; 95%CI: 1.03–6.13 $P = 0.044$). pT stage was significantly associated to RFS (HR 8.59; 95%CI: 3.26–22.6, $P < 0.001$), while neither age, HTA, diabetes nor BMI appeared to predict recurrence (all $P > 0.05$). Moreover, PLR (HR 2.37; 95%CI: 0.92–6.12 $P = 0.07$) and HPR (HR 0.41; 95%CI: 0.11–1.48 $P = 0.18$) were not significant predictor of RFS on multivariate analysis. Restricting the Cox regression to patients with locally advanced disease (≥ pT3), NLR was even more associated to recurrence (HR 3.22; 95%CI: 1.06–9.81, $P = 0.039$), while PLR (HR 2.96; 95%CI: 0.88–9.99, $P = 0.08$) and HPR (HR 0.22; 95%CI: 0.05–1.02, $P = 0.052$) were not associated to recurrence in this subset of patients.

Regarding survival outcomes, we registered 7 cancer-specific deaths and 6 non-cancer specific deaths in the present cohort. No patient with pT1 disease died during follow-up as a consequence of RCC. Patients exhibiting an NLR > 3.45 did have a significantly worse CSS (Fig. 2,

Table 3 Age, NLR, PLR and HPR distribution according to histologic subtype.

	ccRCC ($n=131$)	TP I ($n=16$)	TP II ($n=22$)	Chromophobe($n=9$)	Mixte ($n=6$)	*P*
Age	63 (54–70)	61 (45–69)	61 (57–65)	50 (43–56)	57 (48–61)	0.05
NLR	2.47 (1.97–3.63)	2.89 (2.29–4.68)	2.35 (1.94–2.94)	1.69 (1.62–2.84)	2.87 (1.46–4.59)	0.17
PLR	142 (104–191)	125 (91–191)	132 (89–163)	141 (110–161)	162 (65–248)	0.72
HPR	0.59 (0.48–0.7)	0.66 (0.58–0.75)	0.58 (0.53–0.73)	0.52 (0.48–0.58)	0.68 (0.46–0.81)	0.28

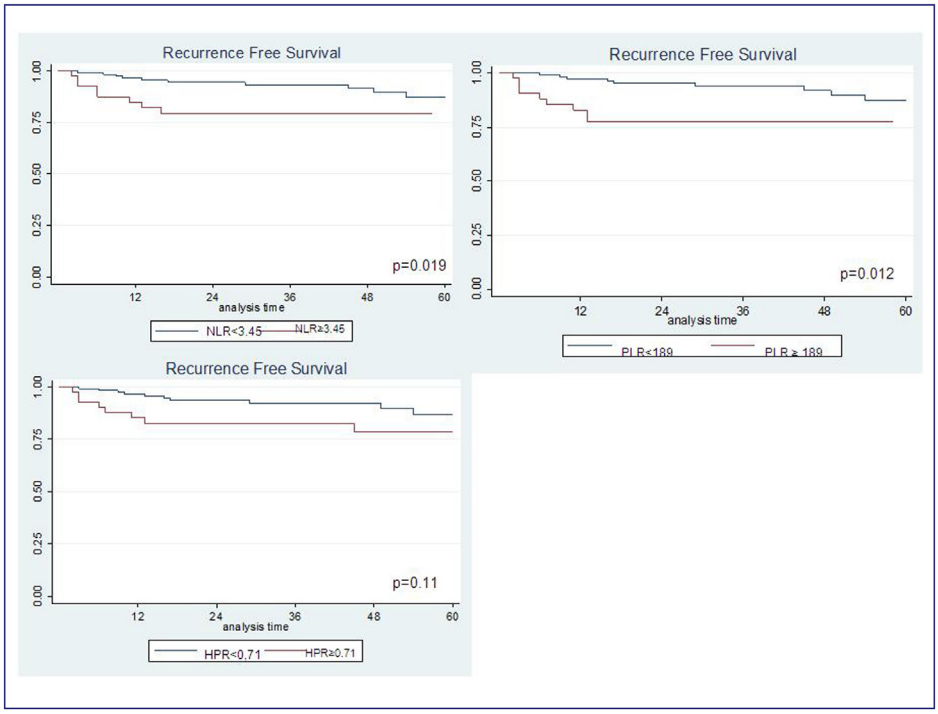

Figure 1. Recurrence free survival according to NLR, PLR and HPR.

Figure 2. Cancer specific survival according to NLR, PLR and HPR.

Log-rank test $P = 0.03$). Moreover, a PLR > 189 was significantly associated to worse CSS (Fig. 2, Log-rank test $P = 0.0005$), while a HPR < 0.48 did not predict cancer specific mortality ($P = 0.12$). On multivariate analyses, NLR (HR 2.57; 95%CI: 0.74—8.99 $P = 0.14$), PLR (HR 4.34; 95%CI: 0.98—19.22 $P = 0.053$) and HPR (HR 0.04; 95%CI: 0.004—1.21, $P = 0.058$) did not predict significantly CSS.

Finally, an increased NLR (Log-rank $P = 0.047$), increased PLR ($P = 0.0006$) and decreased HPR ($P = 0.05$) were all associated to a poor overall survival (Fig. 3). On multivariate analysis, only HPR remained significantly predictive of OS (HR 0.077; 95%CI: 0.02—0.37, $P = 0.001$); NLR ($P = 0.11$) and PLR (0.13) were not significantly associated to OS on multivariate analysis.

Discussion

Inflammation plays a major role on oncogenesis and cancer progression, and this is particularly true for RCC [19]. Multiple inflammatory markers have been explored during the past ten years in RCC, most frequently with conflicting results [20—22]. Moreover, many of the proposed markers are laborious to quantify, or require a tumor specimen to be analyzed. In fact, in order for a marker to enter clinical practice, this must be readily available, easy to measure and possibly of low cost. In this context, the NLR and PLR have been proposed and multiple investigators have presented intriguing finding on the association between this simple biomarker and RCC outcomes [9,23]. Although data on the impact of NLR in the metastatic setting are available [24,25], evidence is still controversial in non-metastatic RCC [26]. In the present study NLR was a significant predictor of RFS in clinically localized RCC, and a significant association was found with CSS and OS on univariate analyses. Moreover, an increased NLR was associated to locally advanced disease (≥pT3). PLR on the other hand was predictive of RFS, CSS and OS on univariate analyses, though these associations did not attain statistical significance on adjusted regressions.

Indeed, these findings are in line with previously reported results, although the cut-off for NLR value varies significantly across studies. Lucca et al, in 430 patients with non-metastatic pT1-3 clear cell RCC, found NLR to be predictive of RFS, even after adjustment to tumor stage, size and grade [27]. Wen et al., with a cut-off of 1.7, which was curiously lower than the mean NLR (2.72 ± 2.25), detected a significant impact of NLR on multivariate analyses both on RFS ($P = 0.019$) and OS ($P = 0.015$) [23]. Keskin et al. retrospectively reviewed 211 patients with RCC of multiple histologies, reporting significantly higher NLR and PLR in non-surving patients at two years follow-up [28]. Finally, in the largest study to date on RCC, Byun et al. explored NLR in a large, multicentric cohort of 1284 patients [9]. Using a cut-off of 3.7, similarly as in the present study, the investigators found a significant association between NLR and RFS, CSS, as well as tumor size, sarcomatoid differentiation and tumor necrosis (all $P < 0.001$). Hu et al. performed a metanalysis evaluating the impact of NLR in a 15 studies, for a total of 3357 patients [11]. Although different studies had different cut-offs, globally an increased NLR predicted significantly RFS (HR 2.18; 95% CI: 1.75 to 2.71; $P < 0.001$) and OS (HR 1.82; 95% CI: 1.51 to 2.19; $P < 0.001$). However, it must be highlighted that other studies yielded contrasting results, in that no statistically significant association was detected between NLR and RFS of non-metastatic RCC [29,30]. The reason for such difference is most probably multifactorial, due to the inherent variability of the NLR and to the different cut-off set in the various studies. Dalpiaz

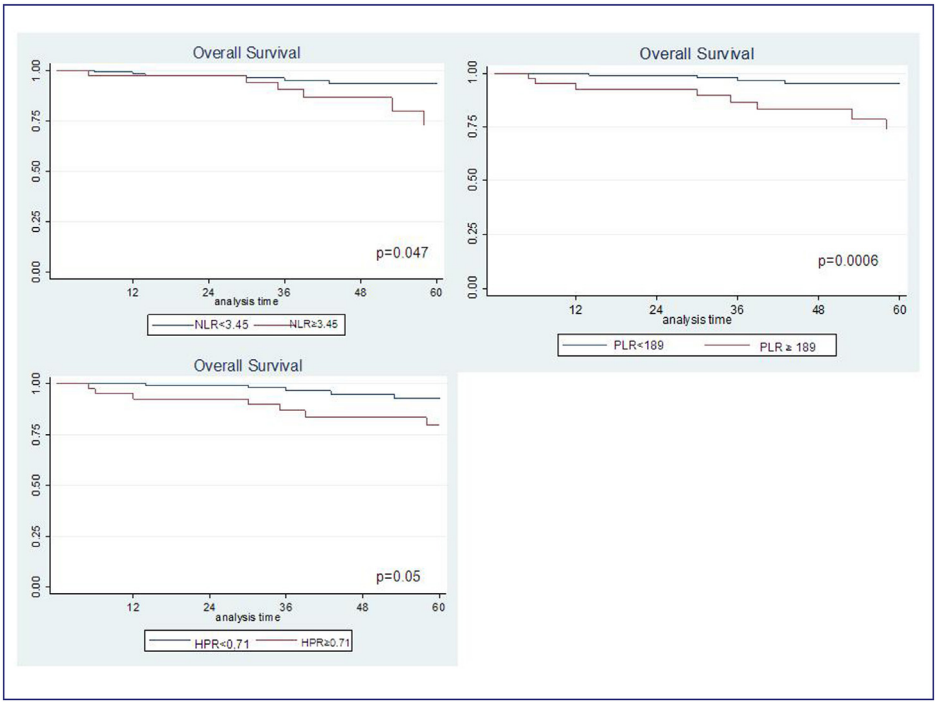

Figure 3. Overall survival according to NLR, PLR and HPR.

et al. reported a retrospective study analyzing the derived NLR index in RCC, which has been proposed to simplify calculation of NLR in large clinical studies [31]. This index is calculated as the absolute neutrophil count divided by the absolute count of leukocytes minus the absolute count of neutrophils [32], and has been shown to be associated to oncologic outcomes in RCC. In their study, the authors confirmed the collinearity of dNLR with standard NLR ($\rho = 0.84$), and the association of dNLR to CSS ($P = 0.037$) and metastatic free survival ($P = 0.041$) on multivariate analysis. NLR was also associated to OS in a study by Hu et al., analyzing 484 patients with surgically resected RCC, and NLR was superior to dNLR, PLR and CRP measurement to predict survival outcomes [14].

HPR is an interesting ratio, which takes into consideration the negative impact of an anemic associated to thrombocytosis. Investigators have evaluated its impact is staging of other tumors, as nasopharyngeal carcinoma [33]. Moreover, in the urologic field, La Croce et al. reported the impact of a reduced HPR in patients with urothelial carcinoma treated by radical cystectomy: in a retrospective study analyzing over 900 patients, a reduced HPR was significantly associated to more aggressive disease, reduced CSS and OS. However, to date, this ratio has not yet been applied to RCC. In the current study we did not find a significant association between HPR and RFS or CSS, although patients in the lower quartile of HPR (< 0.48) did show a significantly reduced OS. Though this finding is limited by the small sample of our study, it is to our knowledge the first to report the impact of such ratio in RCC oncologic outcomes and encourages exploring such value in larger trials.

An area of current great interest in the field of RCC is the field of adjuvant therapy. To date, especially given the results of the ASSURE trial [4], guidelines do not recommend adjuvant TKI adjuvant therapy [7], and advise rather to wait for metastatic disease given the uncertain oncologic benefit and the morbid adverse events which TKIs can determine. As such, the identification of high-risk patients, potential candidates for adjuvant therapy in order to delay recurrence is of uttermost importance. In the present study, NLR was more predictive of recurrence in a subanalysis of patients with $\geq$ pT3 disease. Although barely hypothesis generating, we believe that NLR could be tested, in larger specifically designed trials, as a potential biomarker to guide adjuvant therapy. Multiple studies have confirmed its value in the risk stratification of patients for recurrence after nephrectomy as NLR and PLR reflect the immunitary status of the host. Current treatments for RCC, as TKI and in the future checkpoint-inhibitors, are highly dependent of host immunity: could a serum biomarker as simple as NLR help in selecting high-risk patients, eventually candidates for adjuvant immunotherapy? In the ASSURE trial, even after subanalysis according to tumor prognostic categories, no advantage in RFS was found in patients receiving adjuvant TKI [34], thus it would seem unlikely that NLR could add significant information. Nonetheless, a recent secondary analysis of the S-TRAC study evaluated the impact of NLR on RFS and CSS. Patients treated with adjuvant Sunitinib were more likely to have a reduced NLR at 4 weeks after therapy, with a trend towards improved RFS (HR 0.744, $P = 0.0729$) [35]. Moreover, immunotherapy with checkpoint inhibitors is currently under study in the adjuvant setting. Authors have reported significant modifications of NLR after immunotherapy in metastatic RCC [36], associated to improved outcomes. Indeed, the hypothesis that such inflammatory indices could help predict responders to immunotherapy remains intriguing and should be tested.

Our study presents limitations. First, the sample size is limited, with a likely effect on the lack of statistical power of our multivariate analyses. Second, we did not evaluate NLR after surgery, in order to account for possible variations inherent to the marker itself. Moreover, we do not dispose of standardized evaluation of inflammatory indices in the post-operative phase: indeed, the absence of normalization of these indices should be analyzed and could add potential information to preoperative analysis. Finally, albeit a median follow-up of 46 months, we recorded only 7 cancer specific deaths in the present cohort, thus limiting the strength of CSS and OS analyses.

Conclusions

In this single-center study analyzing non-metastatic RCC, an increased NLR was significantly associated to RFS, CSS and OS on univariate analyses and to RFS on multivariate analysis. PLR predicted RFS and CSS on univariate analyses and HPR was significantly associated to OS. Albeit its limitations, NLR may be of interest in the risk stratification of patients undergoing surgery for RCC. Larger prospective studies are needed to validate our findings.

Acknowledgments

None.

Disclosure of interest

The authors declare that they have no competing interest.

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