Review

A Systematic Review of the Prognostic Role of Hematologic Scoring Systems in Patients With Renal Cell Carcinoma Undergoing Nephrectomy With Curative Intent

Nathan Grimes,[1] Matthew Tyson,[2] Cathal Hannan,[3] Colin Mulholland[2]

Abstract

The objective is to evaluate the prognostic benefit of the Glasgow Prognostic Score (GPS), neutrophil–lymphocyte ratio (NLR), platelet–lymphocyte ratio (PLR), and Prognostic Nutrition Index (PNI) in patients with localized renal cell carcinoma undergoing nephrectomy with curative intent. Embase and MEDLINE databases were searched for all publications before April 2015. Duplicates were excluded, and inclusion/exclusion criteria were applied to all abstracts; of those remaining, full articles were obtained and inclusion/exclusion criteria were again applied, and the remaining articles were included and critically appraised. Eight articles were included in this review. Three articles were included for GPS. Outcomes included recurrence-free survival, cancer-specific survival (CSS), and overall survival (OS). All articles demonstrated better prognosis associated with a lower GPS on multivariate analysis: 1-year recurrence-free survival hazard ratio (HR), 7.0 ($P = .001$); CSS HR, 6.7 to 8.6 ($P < .001$); and OS HR 4.2 ($P < .001$). Four articles were included for NLR. All articles demonstrated elevated NLR to be associated with a poorer prognosis. Two articles demonstrated elevated NLR to be associated with a lower progression-free survival. One article demonstrated elevated NLR to be associated with a lower CSS (HR, 1.02, $P = .009$), and 2 articles demonstrated elevated NLR to be associated with a lower OS (HR, 1.02-1.6). No articles were included for PLR, and only 1 article was identified for PNI. There may be a role for modified GPS and NLR in patients with renal cell carcinoma undergoing nephrectomy with curative intent. Evidence for PLR and PNI is minimal.

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Introduction

Each year in the United Kingdom, there are more than 10,000 new renal cancers diagnosed, and the incidence has more than doubled over the past 35 years.[1] Renal cell carcinoma (RCC) is the most common renal malignancy and accounts for approximately 85% of renal tumors.[2] At the time of presentation, approximately 70% patients will have localized disease amenable to nephrectomy[3]; however, 20% to 40% of these patients will subsequently develop metastatic disease.[4-6]

[1]Department of Urology, Belfast City Hospital, Belfast, Northern Ireland
[2]Department of Urology, Altnagelvin Area Hospital, Derry, Northern Ireland
[3]School of Medicine, Queen's University Belfast, Belfast, Northern Ireland

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Address for correspondence: Nathan Grimes, MRCS, Department of Urology, Belfast City Hospital, Belfast, Northern Ireland BT9 7AB
E-mail contact: nggrimes@doctors.net.uk

After nephrectomy for localized disease, patients will be followed up with radiologic investigations to diagnose localized recurrence or subsequent metastatic disease. Several follow-up regimens have been described[7]; however, there is currently no consensus as to the optimum surveillance timing, and the British Association of Urological Surgeons guidelines recommend that frequency of follow-up should be individualized to each patient depending on risk of recurrence.[8]

The systemic inflammatory response in patients with malignancy plays a role in disease progression and tumor biology itself. Several hematologic scoring systems based on systemic inflammatory response to malignancy have been developed to predict prognosis in patients with cancer. These are based on basic hematologic investigations that can be performed preoperatively and have been shown to be of prognostic value in a range of malignancies.[9-11]

The Glasgow Prognostic Score (GPS) is calculated with a combination of the patient's C-reactive protein (CRP) concentration and serum albumin concentration. Patients with a nonelevated CRP (≤10 mg/L)

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and normal serum albumin (≥ 35 g/L) have a score of 0. The presence of an elevated CRP (> 10 mg/L) or hypoalbuminemia (< 35 g/L) scores 1, and the presence of both elevated CRP and hypoalbuminemia scores 2. The modified Glasgow Prognostic Score (mGPS) is similar, but differs in that an isolated hypoalbuminemia with a nonelevated CRP does not result in a score of 1.[9] Similar to the GPS, the Prognostic Nutrition Index (PNI) is based on a combination of inflammatory response (measured with lymphocyte count) and nutritional status (measured with serum albumin concentration). It is calculated with the formula "10 × serum albumin concentration (g/dL) + 0.005 × lymphocyte count (count/μL)."[12]

Several studies have demonstrated prognostic scoring systems to predict prognosis in patients with RCC, but the majority of these have focused on patients with metastatic disease.[2,13-15] Their role in localized RCC is less clear. If there was a prognostic value of these hematologic scoring systems, they may have a role in postoperative follow-up in patients undergoing nephrectomy with curative intent.

The aim of this review is to evaluate the prognostic benefit of the GPS, mGPS, neutrophil–lymphocyte ratio (NLR), platelet–lymphocyte ratio (PLR), and PNI in patients with localized RCC undergoing nephrectomy with curative intent.

Materials and Methods

Database searches were performed on MEDLINE and Embase on April 18, 2015, and all articles published before this date were considered for inclusion in this review. Search terms used were "exp carcinoma, renal cell," "Glasgow prognostic score OR modified Glasgow prognostic score OR GPS OR mGPS," "prognostic nutrition index OR Onodera's prognostic nutrition index OR PNI," "platelet lymphocyte ratio OR PLR," and "neutrophil lymphocyte ratio OR NLR."

Abstracts were retrieved for all identified citations and reviewed independently by 2 authors. Abstracts that did not meet inclusion/exclusion criteria were excluded. For the remaining abstracts, full articles were obtained and again reviewed independently by 2 authors applying inclusion/exclusion criteria. Where discrepancies arose between the 2 authors regarding inclusion or exclusion of an article, an agreement was made after a joint discussion. All included articles were then critically appraised using the Critical Appraisal Skills Programme tool.[16]

Inclusion Criteria

- Articles publishing outcome data for patients with resectable RCC
- Articles publishing original data (ie, not review articles)
- English language

Exclusion Criteria

- Abstracts published from conference proceedings
- Articles including only patients with unresectable disease
- Articles including patients undergoing cytoreductive therapy for advanced disease
- Articles including malignancies other than RCC

The primary outcome to be assessed was survival after resection in different cohorts according to their prognostic scores. Secondary outcome assessed was the time from resection to the diagnosis of locally recurrent or metastatic disease.

Results

The results of database searches are summarized in Table 1. The initial database search identified 85 articles. Figure 1 shows how inclusion and exclusion criteria were applied to these. Eight articles were included for review; 3 included data on GPS,[17-19] 4 included data on NLR,[20-23] and 1 included data on PNI.[24] There were no articles identified that presented data on PLR for patients undergoing resection with curative intent. Articles included in this review are summarized in Tables 2 and 3.

Patient Demographics

Eight studies were included in this review representing a total of 3132 patients; 59.5% to 71.9% were male, and the median age was 60 to 65 years. Three articles collected data prospectively,[17-19] 1 article collected data retrospectively,[21] 2 articles retrospectively reviewed a prospectively maintained database,[20,24] and 2 articles did not state how data were collected.[22,23] Patient follow-up postoperatively was generally good, with median follow-up ranging from 16 months to more than 9 years. Three studies had a median follow-up greater than 5 years.[17,18,23]

Glasgow Prognostic Score

Three articles including 377 patients and data on mGPS met inclusion criteria.[17-19] All 3 studies included only patients with

Table 1 Search Strategy (No Filters) and Results From Searching Embase and MEDLINE Databases

	Search Strategy	MEDLINE[a]	Embase[b]
1	Exp carcinoma, renal cell/	23,738	48,686
2	GPS	173	364
3	mGPS	63	131
4	GPS	14,460	22,186
5	mGPS	136	242
6	2 or 3 or 4 or 5	14,611	22,445
7	PNI	13	29
8	Onodera's PNI	1	4
9	PNI	614	1129
10	7 or 8 or 9	624	1140
11	Platelet lymphocyte ratio	45	180
12	PLR	579	1065
13	11 or 12	591	1103
14	Neutrophil lymphocyte ratio	290	991
15	NLR	1238	2496
16	14 or 15	1365	2872
17	1 and 6	7	13
18	1 and 10	0	5
19	1 and 13	2	4
20	1 and 16	14	40

Abbreviations: GPS = Glasgow Prognostic Score; mGPS = modified Glasgow Prognostic Score; NLR = neutrophil–lymphocyte ratio; PLR = platelet–lymphocyte ratio; PNI = Prognostic Nutrition Index.
[a]Database: Ovid MEDLINE(R) <1946 to 18.04.15>.
[b]Database: Embase <1974 to 18.04.15>.