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Should We Do Lymphadenectomy in Localised Kidney Cancer?

F. Liedberg

Introduction

Nodal involvement in renal carcinoma is described in 3.3–46 % of patients in the literature [1, 2]. Such a wide range of lymph node metastases depends mainly on selection of patients, but type of cohort investigated, i.e. autopsy series as compared to surgical series and extent of lymphadenectomy performed in surgical series, also have an impact on the prevalence of lymph node metastases. Also the continuous downward stage migration of the disease results in lower rates of lymph node metastases in series published in the modern era. The current lecture will try to answer the question „Should we do lymphadenectomy in localised renal carcinoma", and will expand the answer somewhat beyond the current updated EAU-guidelines from April 2010 and the following statement:

Lymph Node Dissection

An extended or radical lymph node dissection does not appear to improve long-term survival following tumour nephrectomy. Thus, for staging purposes, the lymph node dissection can be limited to the hilar region. In patients with palpable of CT-detected enlarged lymph nodes, resection of the affected lymph nodes should be performed to obtain adequate staging information.

Localised Renal Carcinoma

In the new TNM-classification published 2009 some changes have been made as compared to the 2002 classification. See below:

TNM 2009 Renal cancer
- Primary tumour T
- T1a Tumour ≤ 4 cm
- T1b Tumour > 4 cm but ≤ 7 cm in greatest dimension
- T2a Tumour > 7 cm but ≤ 10 cm in greatest dimension, limited to the kidney (localised disease)
- T2b Tumour > 10 cm, limited to the kidney (localised disease)
- T3a Tumour grossly extends into renal vein or perirenal and/or sinus (peripelvic) fat but not beyond Gerota's fascia
- T3b Tumour grossly extends into vena cava below the diaphragm
- T3c Tumour grossly extends into vena cava above the diaphragm or invades the wall of vena cava
- T4 Tumour grossly invades beyond Gerota's fascia (including contiguous extension into the ipsilateral adrenal gland)

Regional Lymph Nodes N
- N0
- N1 Metastases in single regional lymph node
- N2 Metastases in more than one regional lymph node

Renal Lymphatic Drainage

The lymphatic drainage of the retroperitoneum, and the kidneys in particular, is unpredictable. The initial anatomic description of retroperitoneal lymphatics by Parker [3] indicates a variable pattern, which has been further verified, among others, in an autopsy study by Johnsen [4]. Autopsies of 554 patients with clinically undetected renal carcinoma were identified. Of all patients, 80 had lymph node metastases, with only one out of 4 patients (25 %) with lymph node metastases restricted to the retroperitoneum as compared to lymph node metastasis outside the retroperitoneum. Isolated paracaval or paraaortic lymph node metastases without any other metastatic deposits were identified in only 5 subjects (0.9 % of all 554 patients).

Extent and Technique of Lymphadenectomy

The variability of the lymphatic drainage described above explains the disagreement about the ideal limits of lymph node dissection (LND) in renal carcinoma [5–7]. Limited as compared to extended dissection results in understaging, especially on the right side, were interaortocaval lymph nodes are the primary lymphatic landing area. Frozen section examination (FSE) of intraoperatively detected or preoperatively described enlarged lymph nodes has recently been investigated in 114 patients. Only 32 % of patients with enlarged nodes had lymph node metastases, and when comparing FSE with lymph node status in a regional lymphadenectomy, 89 % sensitivity was reported, indicating that FSE maybe could be used to avoid unnecessary lymphadenectomy in patients with enlarged lymph nodes [8].

Imaging Techniques

In an often cited investigation by Studer, an incidence of only 42 % of histologically positive nodes was noticed in a series with preoperatively enlarged (> 1 cm) nodes on abdominal CT [9]. There is currently no imaging method that can differentiate enlarged inflammatory nodes due to the tumour from metastatic ones. The value of FDG-PET/CT in renal carcinoma is at present not clear. Recently the first description of sentinel node imaging and surgery has been published, showing that the sentinel node concept is feasible also in renal carcinoma [10]. Possible applications of the sentinel node concept and clinical use of the method might be possible in the future.

Lymphadenectomy in:

I. Patients with Localised Disease (T1–T2, N0, M0)

The lack of survival advantage in a randomized trial [11] together with the low incidence of positive nodes (3.3 %) in localised disease substantiates the recommendation to refrain from lymphadenectomy in these patients. The staging role of lymphadenectomy in these patients is also questionable in the abscence of effective adjuvant therapies.

II. Patients with Localised High-risk Disease (T3–T4, N0, M0)

In localised high-risk tumours the value of lymphadenectomy is currently unclear. The randomized EORTC trial 30881 included only 30 % of this patient category, and the study was with such a low incidence of lymph node metastases in this patient category (4 %) underpowered to conclude that survival without lymphadenectomy is equvalent to survival with lymphadenectomy. Risk factors for lymph node metastases such as clinical stage T3–T4, size > 10 cm, Fuhrman-grade III–IV**,** presence of sarcomatoid differentiation and histological necrosis have been identified in a multivariable analysis by Blute et al. [5]. However only tumour size and necrosis can be ascertained prior to surgery, and despite the fact that two or more of those risk factors was associated with a 15-fold higher incidence of regional lymph node metastases, such a stratification is not possible preoperatively with the identified risk factors. Tumour size and symptom classification has been identified in one study, and a nomogram was constructed [12], however the extent of lymphadenectomy was limited and not standardized in the study population. Thus, no firm recommendation can be made for these patients. However one institution states that „in the abscence of any risk factors or incidental suspicious lymphadenopathy, probably any LND beyond the hilar nodes is not justified" due to the low incidence of lymph node metastases [13].

III. Patients with Regional Lymph Node Metastases without Distant Metastases

For patients in this category any evidence-based recommendations can be made. However, from retrospective studies it is a well-known fact that 1–10 % of patients have isolated retroperitoneal lymph node dissemination [4, 6], and that surgical cure is possible [6, 14]. In this patient category the challenge is to identify those patients preoperatively, as the patient might benefit from an extended lymph node dissection in addition to remove enlarged lymph nodes. The limits of such an extended dissection in this group of patients is not known, however the interaortacaval nodes in right-sided tumours is probably of great importance [10]. Of course the extent of dissection is also affected by the patient's age, comorbidities and performance status.

IV. Patients with Lymph Node Metastases and Distant Metastases

If cytoreductive nephrectomy is indicated in such a patient, the lymphadenectomy surgery could include only grossly enlarged nodes. Exstirpating lymph node metastases could possibly improve the effect of systemic therapies [15] as nodal disease shows a poor response to immunotherapy. No firm recommendation can however be made for these patients with regard to lymphadenectomy more than that an extended lymph node dissection is not indicated, as complications due to the lymph node surgery might prolong time to systemic palliative therapies.

Conclusions

In the era of increasing numbers of incidentally detected small renal carcinomas, lymphadenectomy in localised disease is seldom indicated. It is only beneficial in the absence of distant metastases, and under such circumstances possible as an extended dissection, where there might be a narrow therapeutic window for patients with local metastases only. However, there is clearly a lack of proper studies in these patients. The use of frozen section analysis of enlarged lymph nodes might be beneficial. In cytoreductive surgery before systemic therapies, exstirpation of grossly positive nodes could possibly be beneficial as part of the cytoreductive approach**,** but current knowledge is inadequate to give firm recommendations.

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