The potential and limitations of computed tomography in the assessment of lymph node metastases in the patients with renal cell carcinoma

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Abstract

Introduction and Objectives. This study aims to present performance and limitations of computed tomography (CT) in detecting and characterizing the lymph node involvement in patients with renal cell carcinoma (RCC), in an attempt to support the urologic team in choosing the best surgical approach.
Material and Methods. This is retrospective study conducted on a total of 94 patients (63 men and 31 women, age range 33-79 years, mean age 55.7) that underwent radical nephrectomy associated with extensive lymph node dissection in Center for Uronefrology and Renal Transplantation, Fundeni Clinical Institute, from January 1st 2014 to December 31st 2014 for renal cell carcinoma confirmed on histopathology, that performed preoperative contrast-enhanced CT. CT results were compared with surgical and pathological findings.
Results. Considering the 10 mm size as the normal limit value of the nodal short-axis diameter, we found a suboptimal value of CT specificity (CT specificity = 65.07%) in diagnosing lymph node metastases in patients with renal cell carcinoma Instead, we found a good value of CT sensitivity (CT sensitivity = 80.6%) in the detection of regional lymphatic metastasis of renal cell carcinoma.
Conclusions. CT has a limited value in characterizing the nature of lymph node hyperplasia (tumor versus inflammatory) in patients with renal cell carcinoma, especially in the presence of tumor necrosis, most likely due to the pronounced immune reaction caused by the primary cancer and the presence of necrosis.

Key words: renal cell carcinoma, lymph node metastases, CT

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Introduction

Renal cell carcinoma (RCC) is the main cause of death among urologic cancers, although takes the third place in incidence, following prostate carcinoma and transitional cell carcinoma of the bladder. It is the worst in cancer specific prognosis (more than 40% of the patients with RCC die of the disease), compared to the 20% mortality observed in prostate cancer or bladder carcinoma [1].

Regional lymphatic metastasis is an important prognostic factor for renal carcinoma, the 5-years recurrence-free survival interval without lymph node dissection being null.

The normal lymphatic drainage pattern of the right kidney is into the precaval, retrocaval and interaortocaval nodes, while the left kidney drained to the paraaortic, preaortic and retroaortic nodes.

Renal cell carcinoma may alter normal lymphatic flow in the kidney. 25-38% of renal carcinoma has regional lymph node metastasis of the homolateral renal hilum, para-aortic and paracaval and/or in tumor contralateral lymph nodes, but also retrograde caudally. Metastatic mediastinal lymph nodes may occur due to lymphatic extension through the thoracic duct [2].

A recent analysis suggest that the left kidney tumors had an increased frequency of enlarged lymph nodes in the ipsilateral suprahilar region (18%) compared with the right kidney tumors (1.7%). This difference may be explained by the concentration of lymphatic tissue surrounding the aorta and the relative paucity surrounding paracaval tissue [3].

Lymph node metastases are found incidentally in 14% of the occulted cases of renal carcinomas, diagnosed at autopsy only [4].

Regional lymphatic metastasis represents one of the surgical and pathological criteria of TNM classification.

MDCT is the most used imaging technique for initial staging of renal carcinoma. Its shorter examination time, higher spatial resolution and the possibility of 3D illustration of nodal shape and the relations between nodes and vessels with the advantage of measuring of the shortest axis or the ratio of longitudinal to transverse diameter (L/T ratio) make this imaging technique to have a major role in screening lymph node metastases in renal carcinoma.

Determining lymph node metastases on conventional cross-sectional imaging techniques such as multi detector computed tomography or magnetic resonance imaging depends on two diagnostic criteria: size criteria and criteria of nodal metastases location. Usually, the most common diagnostic criteria for determining lymph node metastases is the size criteria, an increase of nodal short-axis diameter more than 10 mm being considered pathological. MRI recent studies take into consideration the upper limits of 8 mm for round nodes and 10 mm for oval nodes in minimum short-axis diameter [5]. However, preoperatively normal-sized lymph nodes on imaging techniques could be tumor invaded, as demonstrated by the presence of nodal micrometastases on histopathological examination.

Objective

This study aims to present the performance and limitations of computed tomography (CT) in detecting and characterizing the lymph node involvement in patients with renal cell carcinoma (RCC) that received surgical treatment associated with extensive lymph node dissection, in an attempt to better understand the relationship between imaging, intraoperative and histopathological findings of enlarged lymph nodes, and to support the urologic surgeon in choosing the best surgical methods for these patients.

Materials and methods

This retrospective study was performed on a total of 94 patients (63 men and 31 women, age range 33-79 years, mean age 55.7) who underwent radical nephrectomy associated with extensive lymph node dissection in Center for Uronefrology and Renal Transplantation, Fundeni Clinical Institute from January 1st 2014 to December 31st 2014 for renal cell carcinoma confirmed on histopathology, that performed preoperative contrast-enhanced CT. Contrast-enhanced acquisitions were obtained during arterial, nephrographic and urographic phases.

Images obtained on CT scan were assessed for the presence of regional lymphadenopathy, determining the nodal pathology and the local tumor staging.

To express lymph node hyperplasia it was considered the 10 mm size as the normal limit value of the nodal short-axis diameter. Renal hilar, paraaortic and paracaval nodes measuring more than 10 mm in short-axis diameter were considered to be metastatic.

This study excluded patients who did not underwent lymphadenectomy in the surgical treatment of renal cell carcinoma, patients who were evaluated by CT without using a contrast media, patients below the

age of 18 years and also patients lost to clinical follow-up.

CT staging was compared with surgical and pathological staging as the gold standard.

Patients were staged according to the TNM classification (adapted from current version of American Joint Committee on Cancer 2002):

N = regional lymph nodes (hilar, paraaortic or paracaval) [6]
Nx- regional lymph nodes cannot be assessed
N0- no regional lymph node metastasis
N1- metastasis in a single regional lymph node
N2- metastasis in more than one regional lymph node

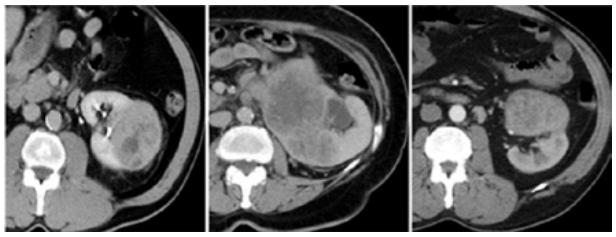
Results

48 patients (51.06%) had RCC on the left side and 46 patients (48.94%) on the right side.

Computed tomography assessment of metastatic involvement of regional lymph nodes (hilar, paraaortic and paracaval) showed the following results: 58 patients (61.70%) were correctly staged, 29 patients (30.86%) were overstaged and 7 patients (7.44%) were understaged.

In 22 of 29 overstaged patients (75.86%) the lymph nodes were larger than 1 cm in short-axis diameter, were called metastatic nodes both on imaging and intraoperative findings, but the histopathological results have characterized these lymph nodes as inflammatory nodes. In the other 7 patients (24.14%) overstaged, CT examination showed the presence of metastases in more than one regional lymph node (stage N2), while the histopathological results confirmed the presence of metastases in a single regional lymph node (stage pN1), the remaining nodes being characterized as inflammatory nodes. 20 of 29 overstaged patients (68.96%) have tumor necrosis according to clinical and histopathological findings.

In 6 of 7 patients (85.71%) with false-negative CT results of lymph node metastases, pathological examinations showed micrometastases in nodes of less than 1 cm in short-axis diameter. 1 patient (14.29%) pN2 stage was understaged N1 on CT scan because the lymph nodes could not be identified independently from the renal tumor.



A *B* *C*

Fig. 1 A. CT appearance of left-sided RCC with a few normal-sized paraaortic lymph nodes. On pathological examinations, these lymph nodes contained metastatic tumors.
B. CT image of large left-sided RCC with enlarged paraaortic lymph nodes. The histopathological examination confirmed the presence of metastases in these lymph nodes.
C. CT appearance of left-sided RCC with one enlarged left paraaortic lymph node. The histopathological examination characterized this lymph node as a reactive node.

We calculated the sensitivity and the specificity of CT in the assessment of lymph node metastases and we found a good value of CT sensitivity (80.6%) in the detection of regional lymphatic metastasis of renal cell carcinoma. Instead, we found a suboptimal value of CT specificity (65.07%) in the characterization of lymph node involvement in these patients.

Discussions

In our study, the quite increased percentage of false-positive CT diagnoses of lymph node metastases is explained by the presence of reactive lymph node hyperplasia. Inflammatory changes of enlarged lymph nodes in patients with renal cell carcinoma are most likely due to an exacerbated immune response in these patients and may be caused by the presence of tumor necrosis.

Furthermore, the false-negative results are explained by the presence of micrometastases in nodes of less than 1 cm in short-axis diameter. Another cause of underestimating the N stage can be found when lymph nodes and the tumor form a conglomerate mass in which the individual elements cannot be distinguished. For this reason one patient was understaged on CT scan in our study.

The results from the current study in conjunction with other studies [7], [8], [9] showed a poor concordance between clinical and imaging N staging (with CT/MRI conventional imaging techniques) and histopathological findings.

The limited value of CT conventional imaging technique achieved in our study in characterization of the type of nodal hyperplasia (reactive / inflammatory changes vs. metastatic involvement) is argued by using

lymph node size as the only diagnostic criteria.

Therefore size criterion is neither a sensitive, and particularly, nor a specific criterion.

New technologies such as the use of lymph tropic properties of ultra-small super paramagnetic nanoparticles iron oxide (USPIO) for contrast-enhanced MRI [10], [11], diffusion-weighted sequences (DW-MRI) [12], [13] and positron emission tomography (PET) might result in a diagnostic improvement by providing information about molecular or physiologic activity, as has already been shown in bladder and prostate cancer [14], [15].

Certainly detection of lymph node metastases requires lymph node dissection. The role of lymphadenectomy in the treatment of patients with renal cell carcinoma is still a subject of debate. An analysis having as starting point the only randomized study addressing the role of regional lymphadenectomy in combination with radical nephrectomy for RCC [16], suggest that if radical nephrectomy is truly indicated, a regional lymphadenectomy in these patients may be beneficial for the following reasons: morbidity is minimal, staging is more accurate and the removal of lymph nodes containing microscopic metastases may be useful to some patients [17].

Conclusions

The sensitivity of preoperative CT is good for detecting nodal hyperplasia in patients with renal cell carcinoma.

CT has a limited value in characterizing the nature of lymph node hyperplasia (tumor versus inflammatory) in patients with renal cell carcinoma, especially in the presence of tumor necrosis, most likely due to the pronounced immune reaction caused by the primary cancer and the presence of necrosis.

The specificity of CT in characterizing lymph node involvement is suboptimal, being reliant exclusively on lymph node size and morphologic characteristics.

Accurate detection of lymph node metastases continues to rely on lymphadenectomy despite continuous improvement of cross-sectional imaging techniques.

„ACKNOWLEDGEMENT: This paper is supported by the Sectoral Operational Programme Human Resources Development (SOP HRD), financed from the European Social Fund and by the Romanian Government under the contract number POSDRU/159/1.5/S/137390".

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