The role of lymphadenectomy in patients with renal cell carcinoma with isolatedpositive lymph nodes: a retrospective study

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Abstract

Background: several retrospective studies have sugested a proportion of patients with positive lymph node benefits from lymph node dissection (LND) at the time of radical nephrectomy (RN) for renal cell carcinoma (RCC).
Objective: Our aim was to report de clinical and histological features of patients with isolated positive lymph nodes who underwent LND at the time of nephrectomies and the impact of LND on survival rate.
Materials and methods: A retrospective study was carried out on all patients with histopathologicaly confirmed renal cell carcinoma with isolated positive lymph nodes metastases between january 2005 and december 2007. Positive lymph nodes were confirmed in 39 patients (10,3% of all nepherectomies asociated with LND).We excluded 18 pacients with sistemic metastases (pulmonary,bone etc) .We evaluated a group of 21 patients withpositive lymph nodes (with no evidence of systemic metastases) who underwent extended lymph node dissection (from ipsilateral great vessels ,from the crus of the diaphragm to bifurcation of ipsilateral great vessel +/- interaorticocaval region) at the time of RN.All patients were preoperatively evaluated with history, clinical examination, blood samples, abdominal ultrasound , helical abdominal CT scan , chest X-Ray (thoracic CT). All the specimens were assesed by the same pathologist.Follow–up consisted of history, physical examination ,helical abdominal CT scan, chest X-Ray (thoracic CT). We calculated overall survival rate at 3 years.
Results: Preoperative CT scan revealed false-negative results in4 cases (19%)(size of lymph node less than 1 cm).Out of 21 patients, 11 (52,3 %) had clear cell hystology, 5 (23%) papillary, 4 (19%) cromophobe RCC, 5 had sarcomatoid features (23%).Massive tumour necrosis was discovered in 17 cases(80%). Over 80% of pacients have staged T3 and T4 (TNM system) (median tumour size was 9,5 cm); 19 patients(90%) have Fuhrman nuclear grade III and IV. Lymph node size ranges between 0,3 cm and 4,5 cm.We have 8 cancer-free patients at 3 years (38 % and 2,1 % of all LND associated with RN performed in that period). No patient having sarcomatoid component or nuclear grade 4 survived.These pacients have less than 4 lymph node metastases (3 patients with single positive lymph node – size 2 cm, 2,5 cm and respectively 2,8 cm; 2patients had 2 positive lymph nodes - maximum size 0,3 cm, 3 patiens with 3 nodal metastases - maximum size 0,6 cm). Median survival was 23 months.This study is limited by its retrospective feature.
Conclusions: Renal cell carcinoma with isolated positive lymph nodes are agresive cancers with high Fuhrmann nuclear grade, large tumor size. Prognostic is poor.Some benefit may have those with less than 4 isolated positive lymph nodes.

Key words: renal cell carcinoma, extended lymph node dissection, isolated positive lymph node , radical nephrectomy, survival rate

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Introduction

Lymphadenectomy in renal cell carcinoma undoaubtelly improves de accuracy of staging and provides better information prognostic. Survival advantage of LND is controversial.Patients with lymph node metastases have a poor prognostic. Patients with isolated lymph node involvement without systemic metastasis exist and surely have a chance for cure with extensive primary surgery. This paper presents the results of 21 lymph node dissections during radical nephrectomies performed for renal cell carcinomas with isolated positive lymph nodes between January 2005 and December 2007 in our center.

Materials and methods

During 2005 and 2007 about 500 renal tumors in different stages were operated in our Department .We performed lymph node dissection in 376 of cases (75% of all operated patients). Lymph node involvement was pahologically confirmed in 39 cases (10,3 %). We studied a group of 21 patients who underwent extended lymph nodes dissections (from ipsilateral great vessel, from the crus of the diaphragm to the bifurcation of ipsilateral great vessel +/- interaorticocaval region) during radical nephrectomies (transperitoneal) for isolated positive lymph nodes in renal cell carcinomas.

We excluded 18 patients (7 patients with systemic metastases- pulmonary,mediastinum, bone, adrenal etc, 1 patient have unresectable massive preaortic lymph node metastase, 10 patients - limited peripedicular lymph node dissection) .

All the patients were preoperatively evaluated in the standard manner including history, physical examination, blood and urine samples, abdominal ultrasound, helical abdominal CT, chest X-ray (thoracic CT). Clinical stage was assigned by the operative surgeon according to the TNM system.

Staff pahologists of our institution with expertise in genitourinary pathology examined all specimens according to institutional protocols. Lymph node dissections were examined grossly, and all lymphoid tissue was submitted for histological examination. In 2 cases we had frozen sections. We have noted histological features (type, nuclear grade, number, location and diameter of nodes, coagulative tumour necrosis, venous involvement, capsular involvement), tumour size, age, sex.

The follow-up was performed according to institutional protocols and consisted of history, physical examination ,blood samples, helical abdominal CT scan, chest X-Ray (thoracic CT). These informations were obtained from medical register. When patients died, cause of death was determined by the treating physicians, chart review corroborated by death certificate or by death certificate alone. All of patients identified as having died had progressive, widelly disseminated and highly sumptomatic metastases at the time of death. Perioperative mortality (within 30 days of surgery) was censored. Follow-up period ranged between 34 months and 55 months, with a median follow-up of 36 months .

We calculated overall survival rate at 3 years.

Results

Themedian patient age was 59.2 years (range 25.2-71.3). At the time of LND during radical nephrectomy 17 patients (66%) were younger than 60 years, 3 patients were between 60. 1 and 70 yr old and 1 patient was older than 70 yr. A total number of 17 patients (80%) have locally advanced tumors >=T3 (13 patients –T3, 4 patients - T4). One patient had T1b stage and 3 patients had T2 stage.

Out of 21 patients, 11 (52,3 %) had clear cell hystology, 5 (23%) papillary, 4 (19%) cromophobe RCC, 5 patients had sarcomatoid features (23%). Sex ratio was 1,6:1, male to female. Median tumour size was 9,5 cm (range 4,5 cm and 15 cm). More than 80% of patients has tumour bigger than 9,5 cm.

Most patients had higher nuclear grade (10 patients Fuhrman grade IV, 9 patients have Fuhrman grade III). No one had grade I.

Massivetumour necrosis was found in 17 cases (80%). Venous involvement was asociated in 4 cases of isolated positive lymph node .

Number of lymph nodes dissected ranged between 1 and more than 20. Maximum lymph node size was 4,5 cm. 13 patients (61%) had more than 4 lymph nodes affected.

Helical abdominal CT asessed lymph node involvement in 17 cases (81%). This imagistic tool missed 4 cases preoperatively (19%) (histological specimens revealed maximum node length of 0,8 cm).

Overall survival rate al 3 years was 38 %.(8 patients). This represents 2,6 % of all lymph node dissected patients during radical nephrectomy. Histology was: 4 patients had clear cell , 1 papillary, 3 cromophobe RCC. 6 patients had nuclear grade III and two patients had Fuhrman grade II. These pacients have

less than 4 lymph node metastases (3 patients with single positive lymph node – size 2 cm, 2,5 cm and respectively 2,8 cm; 2patients had 2 positive lymph nodes - maximum size 0,3 cm, 3 patiens with 3 positive lymph nodes - maximum size 0,6 cm). Period of follow-up ranged between 34 months and 58 months. Median survival was 23 months.

This study is limited by its retrospective feature and by limited number.

Discussion

Lymph node involvement has long been recognized as a dire prognostic sign, as it is associated with 5 - years and 10-years survival rates of 5% to 30% and 0% to 5%, respectively (Bassil et al.,1985). LND undoubtedly improves the accuracy of staging and provides better prognostic information; however, much debate surrounds the impact of LND on progression-free and overall survival in patients with RCC. Accordind to the results of this study, a few patients are lymph node positive (10,3 % of all lymph node disected patients and 7,8 % of all operated patients). Following the EORTC study, we realize that one needs to do 100 lymph node dissections to bring a possible benefit to only three patients; according to the results of this paper, we did performed more than 300 lymph node dissections to bring a certain benefit for 8 patients; however, omitting this lymph node dissection in all patients would be a missed opportunity. Association between pathologic features of the primary renal tumors (such as nuclear grade, sarcomatoid component, tumor size, stage and presence of tumor necrosis) and the risk of regional positive lymph nodes remains a controversial subject. The results of this paper are limited by its retrospective feature and by limited number of patients.

Conclusions

Renal cell carcinoma with isolated nodal metastases are agressive cancers with high nuclear grade, large tumor size. Prognostic is poor.Some benefit may have those with less than 4 lypmh node metastases and microscopic invasion.

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Rezumat

Introducere Locul limfodisecţieiconsecutivă nefrectomiei radicale în cancerele renale parenchimatoase rămane controversat. Cu siguranţă, această manevră creşte acurateţea diagnosticului şi aduce informaţii prognostice importante. Avantajul acestei metode în supravieţuirea acestor pacienti este controversat. Prognosticul acestora rămane rezervat. Pacienţii cu adenopatii izolate, fără metastaze sistemice sunt şi, cu siguranţă, intervenţia chirurgicală le poate asigura supravieţuirea. Această lucrare prezinta un studiu retrospectiv din clinica noastră pe 21 de pacienţi diagnosticaţi cu cancere renale parenchimatoase şi adenopatii izolate cărora li s-a practicat limfodisectie extensiva în cadrul nefrectomiei radicale în perioada 2005-2007.

Pacienţi şi metodă Între 2005 şi 2007 în clinica noastră au fost operaţi 500 de pacienţi cu tumori renale în diferite stadii. În cadrul nefrectomiei, la 376 de pacienti s-a practicat limfodisecţie. La 39 dintre aceştia, ganglionii disecaţi au fost confirmaţi histopatologic. Am exclus 18 pacienti cu adenopatii pozitive (pacienţi aflaţi în stadiul metastatic, adenopatie masivă preaortică nerezecabilă, pacienţi cu limfodisecţie limitată peripedicular etc). Am studiat un lot de 21 de pacienţi cărora le-am practicat limfodisecţie extensivă (de la diafragmă pană la bifurcaţia aortei şi în regiunea interaorticocavă) în cadrul nefrectomiei radicale. Pacienţii au fost evaluaţi preoperator în maniera clinicii şi a inclus computer tomografie abdominală cu s.c., radiografie pulmonară. Clasificarea clinică a fost făcută de către chirurgul urolog operator în concordanţă cu clasificarea TNM. Anatomopatologii au examinat piesa de nefrectomie şi ţesuturile limfatice prelevate. Informaţiile au fost centralizate din registrul serviciului de anatomopatologie şi din fişele de observaţie clinică. Am calculat rata de supravieţuire globală la 3 ani.

Rezultate Tomografia computerizată a avut o sensibilitatate de 81% în diagnosticul extensiei adenopatice. Subtipurile histopatologice decelate au fost: 11 cazuri – carcinomul convenţional cu celule clare, 6 tipul papilar, 4 cromofob, 5 dintre pacienţi având proporţii variate de fibre sarcomatoide. 90% dintre pacienţi au avut grade nucleare crescute (Fuhrman 3 şi 4). În 80% dintre cazurile studiate s-a observat asocierea cu necroza tumorală, diametrul mediu al tumorilor studiate fiind de 9,5 cm. Supravieţuirea la 5 ani a fost de 19 % (4 pacienţi). Niciunul dintre supravieţuitori nu a avut gradul nuclear 4 şi nici componenta sarcomatoidă. Toţi cei 4 pacienti aflaţi în viaţă la 3 ani au avut sub 4 ganglioni disecaţi şi confirmaţi histopatologic.

Concluzii Pacienţii cu cancere renale şi adenopatii izolate sunt cancere agresive, de dimensiuni mari, şi cu grade nucleare crescute. Prognosticul acestor pacienţi este rezervat. Limfodosecţia extensivă poate asigura supravieţuirea la pacienţii cu invazie microscopică şi cu număr limitat de ganglioni (sub 4).

Cuvinte cheie: carcinom renal, limfodisecţie, nefrectomie radicală