

# Good results of surgery for renal cell carcinoma depend on early diagnosis.

## The need for an extensive screening program



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### Good results of surgery for renal cell carcinoma depend on early diagnosis. The needs for an extensive screening program

**AIM:** *The aim of our study was to assess the value of several prognostic factors for patients with clear cell renal carcinoma without distant metastases (M0) who underwent surgery in our Department from 1980 to 2010.*

**MATERIAL OF STUDY:** *We analyzed 131 consecutive patients with clear cell renal carcinoma who had nephrectomy and extended lymph node dissection from 1980 to 2010 were reviewed. Free from cancer survivals were correlated to several prognostic factors including preoperative blood cell count, tumour cellular differentiation and stage of the disease.*

**RESULTS:** *In our study we confirmed the importance of the stage of the tumour, in particular of the T, as prognostic factor. Survival was strictly correlated to the stage of the disease: 10 year cancer free survival was 100% in patients with T1, 83% in patients with T2 N0 and 34% for patients with T3N0. No improvement of results was noted in the last years, due to unchanged proportion of early diagnosis.*

**DISCUSSION:** *Long term survival after surgery for clear cell renal carcinoma depends mainly on the histology type of the tumour and on the stage of the disease. Renal carcinoma does not respond to radio and standard chemotherapy and surgery represents the only effective cure.*

**CONCLUSION:** *Surgery at earlier stages is essential to improve results in patients with renal carcinoma. Earlier diagnosis at the present time is the best possibility to improve results, with the need for extensive use of screening ultrasound test.*

**KEY WORDS:** Lymph node dissection in renal carcinoma, Renal carcinoma, Results of surgery for renal carcinoma

### Introduction

Long term survival after surgery for clear cell renal carcinoma depends mainly on the histology type of the tumour and on the stage of the disease<sup>1,2</sup>. Theoretically,

the diffuse use of abdominal ultrasound and CT scan in recent times in patients with vague abdominal symptoms should have brought to an earlier detection of renal cell carcinoma and eventually to better result after surgery.

The aim of our study was to assess the value of several prognostic factors for patients with clear cell renal carcinoma without distant metastases (M0) who underwent surgery in our Department from 1980 to 2010.

In our study we confirmed the importance of the stage of the tumour, in particular of the T, as prognostic factor. Particular attention was paid to the correlation between extension of the tumour (TNM 2010 classification)<sup>3</sup> and long term survival and to any eventual improvement in early detection of patients with renal cell carcinoma in the period 2000-2010 in comparison to the period 1980-1999.

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## Material and Methods

### Study Design

All patients who underwent radical nephrectomy for clear cell renal carcinoma without evidence of distant metastases (MO) in our Department were retrospectively evaluated for possible inclusion into the study. Overall 131 consecutive patients were included into the study.

### Preoperative study

All patients had complete blood testing, abdominal ultrasound and CT scan.

Function of the opposite kidney was assessed by scintigraphy in selected cases. Forty per cent of the patients were asymptomatic and the cancer was detected by ultrasound or CT scan performed for non specific reasons. This trend was similar in patients who were operated from 1980 to 1999 (78 patients) and in those who had surgery from 2000 to 2010 (53 patients).

### Surgery

Surgery consisted on radical nephrectomy with extended lymph node dissection. Through a midline incision the kidney and adrenal gland were removed, including the Gerota fascia and the perirenal fat. Lymph node dissection was carried out from the ipsilateral diaphragmatic crus down to the iliac bifurcation, including the retrocaval lymph nodes for right kidney tumours. Selected patients with not well functioning opposite kidney underwent partial nephrectomy, but they are not included into the analysis.

### Follow-up

Patients were followed in the clinic every six months. Abdominal ultrasound and CT scan were performed at least every year for the first three years. Thereafter every two years. Follow up ranged from 24 months to 25 years (mean 6 years). Ten patients were lost at follow-up.

### Statistical analysis

Kaplan Meier curves were used to define survival. Only deaths related to cancer diffusion were included into mortality. If a patient died from causes other than from renal cancer he/she was considered excluded from follow up at the time of death. Being a long follow up half of the deaths were related to non renal cancer causes. Comparisons between survival curves were obtained by Log rank test. Multiple regression analysis was used to assess the independent value of each analysed risk factor.

## Results

### Clinical Characteristics of the patients

Out of the 131 patients there were 80 men and 51 females. Age ranged from 16 to 84 years (mean 48 years). Associated morbidities were present in 51% of the

patients, including coronary heart disease in 45 patients (34%), chronic obstructive pulmonary disease in 25 patients (19%), arterial hypertension in 55 patients (42%).

### Staging of the disease

Eight patients had stage I disease, 63 stage II, 45 stage III, and 15 stage IV disease (Table I). There was not significant difference in the prevalence of patients with stage I and stage II disease in the two time periods analysed (1980-1999 versus 2000-2012). None of the 8 patients with T1 disease had lymph node involvement; only 7 out of 70 patients with T2, and 7 out of the 50 with T3 cancer. Overall lymph node involvement was present in 21 out 131 patients (16%).

Tumour grading for cell differentiation showed that 54 patients (41%) had well differentiated tumours (G1), 46 (35%) moderately differentiated (G2) and 30 (23%) poorly differentiated. In one patient no record could be found about tumour differentiation.

### Postoperative complications

There was no case of postoperative mortality. Fifteen patients suffered of major complications including myocardial infarction, transient renal failure and deep vein thrombosis.

### Survival

Among the different risk factors analysed (age, sex, blood cell count, TNM staging, grade of cellular differentiation) only stage of the disease and grade of cell differ-

TABLE I - TNM staging in 131 patients

Staging	N° of patients (%)
Stage I (T1N0M0)	8 (6,1)
Stage II (T2N0M0)	63 (48,1)
Stage III	45 (34,4)
T2N1M0	3
T3N0M0	35
T3N1M0	7
Stage IV	15 (11,4)
T2N2M0	4
T3N2M0	4
T4 N0M0	4
T4N1M0	3

TABLE II - T stage in 131 patients

	1980-1999 78 patients (%)	2000-2010 53 patients (%)	P Value
T1	4 (5,1%)	4 (7,5%)	NS
T2	40 (51,3%)	30 (56,7%)	NS
T3-T4	34 (43,6%)	19 (35,8%)	NS

entiation (G) had statistical significance for survival. But when we used multiple regression analysis only the T of the tumour had independent statistical value. Free from cancer recurrence survival was 100% at 10 years for patients with T1 (similar between patients with T1a and T1b cancer), 83% for patients with T2 (similar between those T2a and T2b) and 34% for those with T3. There was no survivor in patients with T4 at 5 years. ( $p < 0.05$  between T1 and T2;  $p < 0.01$  between patients with T1 and T2 and those with T3 and T4).

There was no difference in survival between patients operated from 1980 to 1999 and those operated from 2000 to 2010, mainly because the T distribution in the two groups of patients was similar (Table II). There was only a slight decrease of patients with t3 t4 who had surgery in the 2000-2010 period.

## Discussion

Renal carcinoma does not respond to radio and standard chemotherapy and surgery represents the only effective cure<sup>4-7</sup>. There are many hypotheses that lead to an immunologic etiology for renal carcinoma<sup>8</sup>. This is confirmed by the fact that lymph nodes are involved in a minority of the patients (16% in our series). There is the possibility that the immunologic system in these patients is in some way defective. This hypothesis is confirmed indirectly by the fact that many patients have lymphopenia which represents a risk factor for shorter survival and that the development of cancer in other organs is frequent<sup>2</sup>. We performed an extended lymph node dissection in all patients and probably our approach has been excessively aggressive considering that none of the patients with T1 and only 7 patients with T2 had lymph node involvement. The hypothesis that clear cell renal carcinoma can have an immunologic origin brings to the need to focalise our efforts in new immunologic therapies, which have shown, at least initially, some promising effects<sup>9-12</sup>.

## Conclusion

In our study we confirmed the importance of the stage of the tumour, in particular of the T, as prognostic factor. This brings to the importance of early diagnosis of patients with renal carcinoma as probably the most effective way to improve survival. One could expect an increased number of early diagnoses and consequently of T1 patients who undergo surgery, for the extensive use of abdominal ultrasound and CT scan in recent times. This did not happen in our experience: the number of patients with T1 was similar between the two time periods analysed 1980-1999 versus 2000.2010, and the survival curves were not very dissimilar between the two time periods. Thus, if we want better survivals for

patients with renal carcinoma two aspects should be improved: earlier diagnosis with well organized mass screening using abdominal ultrasound in patients older than 40 year and more efficient immunotherapy after surgery.

## Riassunto

Lo scopo del lavoro è di valutare i fattori prognostici correlati a pazienti sottoposti a chirurgia per tumori renali a cellule chiare, senza metastasi a distanza (M0).

Abbiamo analizzato 131 pazienti consecutivi, giunti nel nostro Dipartimento in un periodo compreso tra il 1980 ed il 2010 e affetti da carcinoma a cellule chiare. Tali pazienti sono stati sottoposti ad intervento chirurgico di nefrectomia con dissezione linfonodale estesa. La sopravvivenza libera da malattia è stata correlata a vari fattori prognostici che comprendono il valore emocromocitometrico preoperatorio, la differenziazione cellulare del tumore e lo stage della malattia.

La sopravvivenza è strettamente correlata allo staging del tumore: i pazienti con tumori T1 hanno una sopravvivenza a 10 anni pari al 100%, pazienti con staging T2, N0 hanno una sopravvivenza a 10 anni dell'83% e pazienti con staging T3, N0 hanno una sopravvivenza a 10 anni del 34%. La sopravvivenza a distanza dopo chirurgia dipende dal tipo istologico della neoplasia e dallo staging della malattia. La chirurgia negli stadi iniziali è essenziale per migliorare i risultati. La diagnosi precoce, ad oggi è la migliore soluzione per migliorare i risultati.

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