Wydawnictwo UR 2020
ISSN 2544-1361 (online); ISSN 2544-2406
doi: 10.15584/ejcem.2020.1.8

http://www.ejcem.ur.edu.pl/en/
European Journal of Clinical and Experimental Medicine
Eur J Clin Exp Med 2020; 18 (1): 38–41

REVIEW PAPER

Piotr Przyczyna [1,2(ABDFG)], David Aebisher [3(ABDFG)], Dorota Bartusik-Aebisher [4(ABDFG)], Ewa Kaznowska [1,2(ABDFG)]

Treating kidney cancer – a review

[1] Clinical Department of Pathomorphology, Clinical Hospital No. 1, Rzeszów, Poland
[2] Department of Pathomorphology, Medical College of Rzeszów University, Rzeszów, Poland
[3] Department of Photomedicine and Physical Chemistry, Medical College of Rzeszów University, Rzeszów, Poland
[4] Department of Biochemistry and General Chemistry, Medical College of Rzeszów University, Rzeszów, Poland

ABSTRACT

Introduction. Kidney cancer in the structure of registered cases was in 6th place in men and 8th in women.

Aim. Understanding the molecular biology of renal cell carcinoma has made it possible to produce new diagnostic methods.

Material and methods. This review was performed according to a systematic literature search.

Results. Minimally invasive techniques seem to have a bright future in kidney cancer. However, they still require many clinical trials before they enter the general clinical use.

Conclusion. Photodynamic therapy, thanks to research conducted in kidney cancer, will find application in cancer of other organs.

Keywords. kidney cancer, malignant tumors, MRI

Introduction

The number of malignant tumors in Poland over the last three decades has more than doubled, reaching more than 140.5 thousand cases in 2010, affecting about 70,000 men and 70.5 thousand women.[1] The incidence of malignant tumors in Poland in 2015, in absolute numbers, was 81,659 for men and 81,661 for women. These numbers, in Podkarpacie, were respectively 4,665 and 4,276.[2] The mortality rate for malignant neoplasms in Poland in 2015 totaled in absolute numbers 55,663 men and 44,938 women, and 28,586 in the Podkarpacie region alone for men and 1,904 for women. Kidney cancer in the structure of registered cases was in 6th place in men (3.9%) and 8th in women (2.4%). In Podkarpacie, kidney cancer took one place higher - 5th place in men (5.1%) overtaking stomach cancer, and 7th place in women (3.1%) overtaking cervical cancer.[2] Although the incidence of kidney cancer in men was lower than the average for EU countries, in 2010 the mortality rate was about 25% higher than the average for EU countries (data from 2009).[3] In 2013/14, the percentage of deaths from cancer was about 30 percent. lower than the average for Poland, however, malignant kidney tumors are still a serious epidemiological problem.[4] Almost 90%

Corresponding author: David Aebisher, e-mail: daebisher@ur.edu.pl

Participation of co-authors: A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 24.10.2019 | Accepted: 8.01.2020
Publication date: March 2020

Przyczyna P, Aebisher D, Bartusik-Aebisher D, Kaznowska E. *Treating kidney cancer – a review.* Eur J Clin Exp Med. 2020;18(1):38–41. doi: 10.15584/ejcem.2020.1.8

of malignant kidney tumors are renal cell carcinomas (RCC), while 80% of renal cell carcinomas are clear cell carcinomas (RCCC).[5-6] The most important prognostic factors in 5-year survival are the clinical stage, grade, local stage of the tumor, the status of local lymph nodes and the presence of distant metastases.[7-16]

Material and methods

This article is based on an analysis of articles posted on the PubMed website (https://www.ncbi.nlm.nih.gov/pubmed), books and websites.

Results

Minimally invasive techniques

Percutaneous ablation and cryotherapy were originally intended only for patients with one kidney, patients with multiple tumors, elderly patients, and for those patients who did not qualify for surgery. However, the percentage of these procedures has recently increased in patients with small tumors, most frequently detected incidentally.[17] Eight percent of patients in the US are treated with minimally invasive methods, compared to 1998, when only 4% were treated using these methods.[18] This is possible thanks to the positive opinions of preliminary reports on the control of the cancer process.[19-23]

Operational techniques

Surgical treatment should be divided into two categories:

a) saving operations. The goal of sparing treatment should be optimal regional tumor control, combined with minimizing ischemia, ideally under 30 minutes.[24] Patients with T1a and T1b tumors (i.e. tumors that do not exceed 7 cm in the largest dimension) and the normal function of the other kidney have comparable results to those operated with the radical nephrectomy technique.[25-27] Nevertheless, some patients cannot be operated on with saving techniques due to the unfavorable location of the tumor or local advancement. In the hands of an experienced surgeon, the results obtained using the laparoscopic, laparotomy and robotic methods are comparable.

b) radical nephrectomy. During this operation the kidney, perirenal fat tissue, regional lymph nodes and adrenal glands are removed.[28] This is the preferred technique for tumors growing in the inferior vena cava. However, it leads to an increased risk of chronic kidney disease and increased mortality associated with the cardiovascular system.[29-31]

Sparing therapy is more likely to preserve kidney function, reduce the number of cardiovascular events and reduce mortality therefore, radical treatment should not be used when a saver treatment is possible.[32-33] Studies show that there are no significant differences in the group of lymphadenectomy patients and in the group of patients who did not remove lymph nodes.[34] Lymph nodes are pre-operatively assessed in computed tomography and/or in magnetic resonance imaging as well as intraoperative palpation. Some authors report that CT/MRI may not show the presence of small metastases to regional lymph nodes.[35] Adrenalectomy should only be performed if the adrenal glands appear suspicious in preoperative imaging or when the tumor is located in the upper pole of the kidney near the adrenal glands.[36-37] Metastasomy is performed in patients with diagnosed synchronous metastases or in patients with metachronic metastases in the general good state, which metastases responded to therapy and are removable. This treatment should be considered because complete removal of metastases improves the prognosis.[38]

Systemic treatment

a) chemotherapy

Most kidney cancers develop from proximal tubules. These coils have a high level of expression of the P-glycoproteins responsible for drug resistance. For this reason, chemotherapy is not routinely used. The only exception is the combination of 5-fluorouracil with immunotherapy, but these data need confirmation.[39]

b) immunotherapy

IFN-alpha in randomized studies has demonstrated survival compared to patients with metastatic renal cancer receiving hormone therapy.[40] The combination of biological drugs is of interest to several randomized trials. For now, there is no evidence that combining drugs gives better results than monotherapy.[41]

c) angiogenesis inhibitors

Understanding the molecular biology of renal cell carcinoma has made it possible to produce new drugs. These include two recently-registered drugs in the US and Europe - these drugs target the vascular endothelial growth factor (VEGF) and platelet derived growth factor (PDGF) genes.[42]

Sorafenib is an inhibitor of many kinases that have activity against, inter alia, Raf-1, VEGFR-2, PDGFR. Three months of taking the drug increases the percentage of patients with progression free from 43% to 75% compared to placebo.[43] Sunitinib is an oxindole tyrosine kinase inhibitor (oxindol tyrosine kinase (TK) inhibitor). The median of progression-free survival in patients using sunitinib (11 months) is longer than in those using TNF-alpha (5 months).[44]

Photodynamic therapy

Currently, photodynamic therapy in renal cancer is only used in preclinical studies.[45] The first study in mice 46 reported tumor necrosis to a depth of 3-5mm without any side effects. In 2008, the first studies with photo-

dynamic therapy in in vitro kidney cancer appeared. It turned out that the uptake of marker (hypericin) and apoptosis occurs in almost 100% of cancer cells.[46,47] An additional discovery was the increase in radiosensitivity. In clinical practice, photodynamic therapy is used to assess surgical margins during sparing procedures.[48]

Conclusion

In the last century, the treatment of choice in kidney cancer was nephrectomy. The more the procedure was performed with a wider margin, the better. Currently, thanks to a better understanding of molecular biology and the conduction of numerous studies, we come to the conclusion that saving treatments should not be just an alternative. Radical nephrectomy should be another option, not the first. Particular mention should be made of photodynamic therapy. It seems to be a safe and at the same time extremely effective and easy to carry out therapy. It is to be hoped that patients with renal insufficiency and other complications of nephrectomy will soon be only a fraction of a percent of patients with kidney cancer. Photodynamic therapy, thanks to research conducted in kidney cancer, will find application in cancer of other organs.

Acknowledgments

Dorota Bartusik-Aebisher acknowledges support from the National Center of Science NCN (New drug delivery systems-MRI study, Grant OPUS-13 number 2017/25/B/ST4/02481).

References

1. Epidemiologia. Krajowy Rejestr Nowotworów Web site. http://onkologia.org.pl/k/epidemiologia/
2. Nowotwory złośliwe w Polsce. Krajowy Rejestr Nowotworów Web site. http://onkologia.org.pl/wp-content/uploads/Nowotwory_2015.pdf
3. Nowotwory złośliwe nerki. Krajowy Rejestr Nowotworów Web site. http://onkologia.org.pl/nowotwory-zlosliwe-nerki-c67/#e
4. Raport NIZP-PZH: onkologiczna mapa Polski. Serwis Zdrowie Web site. https://zdrowie.pap.pl/raport/onkologiczna-mapa-polski
5. Moch H, Gasser T, Amin MB, et al. Prognostic utility of the recently recommended histologic classification and revised TNM staging system of renal cell carcinoma: a Swiss experience with 588 tumors. *Cancer.* 2000;89:604–614.
6. Leibovich BC, Lohse CM, Crispen PL, et al. Histological subtype is an independent predictor of outcome for patients with renal cell carcinoma. *J Urol.* 2010;183:1309–1315.
7. Ficarra V, Schips L, Guille F, et al. Multiinstitutional European validation of the 2002 TNM staging system in conventional and papillary localized renal cell carcinoma. *Cancer.* 2005;104:968–974.
8. Frank I, Blute ML, Leibovich BC, et al. Independent validation of the 2002 American Joint Committee on cancer primary tumor classification for renal cell carcinoma using a large, single institution cohort. *J Urol* 2005;173:1889–1892.
9. Zisman A, Pantuck AJ, Chao D, et al. Reevaluation of the 1997 TNM classification for renal cell carcinoma: T1 and T2 cutoff point at 4.5 rather than 7 cm. better correlates with clinical outcome. *J Urol.* 2001;166:54–58.
10. Klatte T, Patard JJ, Goel RH, et al. Prognostic impact of tumor size on pT2 renal cell carcinoma: an international multicenter experience. *J Urol.* 2007;178:35–40; discussion 40.
11. Lam JS, Klatte T, Patard JJ, et al. Prognostic relevance of tumour size in T3a renal cell carcinoma: a multicentre experience. *Eur Urol.* 2007;52:155–162.
12. Minervini A, Lilas L, Minervini R, Selli C. Prognostic value of nuclear grading in patients with intracapsular (pT1-pT2) renal cell carcinoma. Long-term analysis in 213 patients. *Cancer.* 2002;94:2590–2595.
13. Dall'Oglio MF, Antunes AA, Sarkis AS, et al. Microvascular tumour invasion in renal cell carcinoma: the most important prognostic factor. *BJU Int.* 2007;100:552–555.
14. Dall'Oglio MF, Ribeiro-Filho LA, Antunes AA, et al. Microvascular tumor invasion, tumor size and Fuhrman grade: a pathological triad for prognostic evaluation of renal cell carcinoma. *J Urol.* 2007;178:425–428; discussion 428.
15. Lam JS, Shvarts O, Said JW, et al. Clinicopathologic and molecular correlations of necrosis in the primary tumor of patients with renal cell carcinoma. *Cancer.* 2005;103:2517–2525.
16. Sengupta S, Lohse CM, Leibovich BC, et al. Histologic coagulative tumor necrosis as a prognostic indicator of renal cell carcinoma aggressiveness. *Cancer.* 2005;104:511–520.
17. Capitanio U, Montorsi F. Renal cancer. Published Online August 26, 2015.
18. Woldrich JM, Palazzi K, Stroup SP, et al. Trends in the surgical management of localized renal masses: thermal ablation, partial and radical nephrectomy in the USA, 1998–2008. *BJU Int.* 2013; 111:1261–1268.
19. Ljungberg B, Bensalah K, Canfi eld S, et al. EAU guidelines on renal cell carcinoma: 2014 update. *Eur Urol.* 2015; 67:913–924.
20. Hoffmann NE, Bischof JC. The cryobiology of cryosurgical injury. *Urology.* 2002;60 (1):40–49.
21. Katsanos K, Mailli L, Krokidis M, McGrath A, Sabharwal T, Adam A. Systematic review and meta-analysis of thermal ablation versus surgical nephrectomy for small renal tumours. *Cardiovasc Intervent Radiol.* 2014;37:427–437.
22. Kunkle DA, Egleston BL, Uzzo RG. Excise, ablate or observe: the small renal mass dilemma-a meta-analysis and review. *J Urol.* 2008; 179:1227–1233.
23. Motzer RJ, Jonasch E, Agarwal N, et al. Kidney Cancer, Version 3.2015: featured updates to the NCCN guidelines. *J Natl Compr Canc Netw.* 2015;13:151–159.
24. Funahashi Y, Hattori R, Yamamoto T, et al. Ischemic renal damage after nephron-sparing surgery in patients with normal contralateral kidney. *Eur Urol.* 2009;55:209–215.

25. Leibovich BC, Blute ML, Cheville JC, et al. Nephron sparing surgery for appropriately selected renal cell carcinoma between 4 and 7 cm results in outcome similar to radical nephrectomy. *J Urol.* 2004;171:1066–1070.
26. Hollingsworth JM, Miller DC, Dunn RL, et al. Surgical management of low-stage renal cell carcinoma: technology does not supersede biology. *Urology.* 2006;67:1175–1180.
27. Shuch B, Lam JS, Belldegrun AS. Open partial nephrectomy for the treatment of renal cell carcinoma. *Curr Urol Rep.* 2006;7:31–38.
28. Motzer RJ, Jonasch E, Agarwal N, et al. Kidney Cancer, Version 2.2017, NCCN Clinical Practice Guidelines in Oncology. *Journal of the National Comprehensive Cancer Network*. 2017;15(6):804–834.
29. Huang WC, Levey AS, Serio AM, et al. Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. *Lancet Oncol.* 2006;7:735–740.
30. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med.* 2004;351:1296–1305.
31. Thompson RH, Boorjian SA, Lohse CM, et al. Radical nephrectomy for pT1a renal masses may be associated with decreased overall survival compared with partial nephrectomy. *J Urol* 2008;179:468–471.
32. Kim SP, Thompson RH, Boorjian SA, et al. Comparative effectiveness for survival and renal function of partial and radical nephrectomy for localized renal tumors: a systematic review and meta-analysis. *J Urol.* 2012;188:51–57.
33. Weight CJ, Larson BT, Gao T, et al. Elective partial nephrectomy in patients with clinical T1b renal tumors is associated with improved overall survival. *Urology.* 2010;76:631–637.
34. Blom JH, van Poppel H, Marechal JM, et al. Radical nephrectomy with and without lymph-node dissection: final results of European Organization for Research and Treatment of Cancer (EORTC) randomized phase 3 trial 30881. *Eur Urol.* 2009;55:28–34.
35. Capitanio U, Becker F, Blute ML, et al. Lymph node dissection in renal cell carcinoma. *Eur Urol.* 2011;60:1212–1220.
36. Kuczyk M, Munch T, Machtens S, et al. The need for routine adrenalectomy during surgical treatment for renal cell cancer: the Hannover experience. *BJU Int.* 2002;89:517–522.
37. Kuczyk M, Wegener G, Jonas U. The therapeutic value of adrenalectomy in case of solitary metastatic spread originating from primary renal cell cancer. *Eur Urol.* 2005;48:252–257.
38. Ljungberg B. *The role of metastasectomy in renal cell carcinoma in the era of targeted therapy*. *Curr Urol Rep*. 2013;14(1):19-25.
39. Stadler WM, Huo D, George C, et al. Prognostic factors for survival with gemcitabine plus 5-fluorouracil based regi--mens for metastatic renal cancer. *J Urol.* 2003;170:141–1145.
40. Medical Research Council Renal Cancer Collaborators. Interferon-alpha and survival in metastatic renal carcinoma: early results of a randomised controlled trial. *Lancet.* 1999;353:14–27.
41. Negrier S, Escudier B, Lasset C, et al. Recombinant human interleukin-2, recombinant human interferon alfa-2a, or both in metastatic renal-cell carcinoma. Groupe Francaisd'Immunotherapie. *N Engl J Med.* 1998;338:1272–1278.
42. Patard JJ, Rioux-Leclercq N, Fergelot P. Understanding theimportance of smart drugs in renal cell carcinoma. *Eur Urol.* 2006;49:633–643.
43. Escudier B, Eisen T, Stadler WM, et al. TARGET StudyGroup. Sorafenib in advanced clear-cell renal-cell carcinoma. *N Engl J Med.* 2007;356:125–134.
44. Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. *N Engl JMed.* 2007;356:115–124.
45. Bozzini G, Colin P, Betrouni N, et al. Photodynamic therapy in urology: What can we do now and where are we heading; *Elsevier Review*; Available online 22 February 2012
46. Pomer S, Grashev G, Sinn H, Kalble T, Staehler G. Laser induced fluorescence diagnosis and photodynamic therapy of human renal cell carcinoma. *Urologia Internationalis.* 1995;55(4):197-201.
47. Wessels JT, Busse AC, Rave-Frank M. Photosensitizing and radiosensitizing effects of hypericin on human renal carcinoma cells in vitro. *Photochemistry and Photobiology*. 2008;84(1):228-235.
48. Popken G, Wetterauer U, Schultze-Seemann W. Kidney preserving tumour resection in renal cell carcinoma with photodynamic detection by 5-aminolaevulinic acid: preclinical and preliminary clinical results. *BJU International.* 1999;83(6):578-582.