

Editorial comments to paper published in this issue on pgs. 152–155

## The article "Radical or simple nephrectomy in localized renal cell carcinoma: what is a choice?"

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In their paper, Professor A. Shulyak and Doctor O. Banyra discuss and compare the long-term outcomes of radical and simple nephrectomy as an option for surgical treatment of localized kidney tumors (renal cell carcinoma). The authors characterized overall survival and cancer-specific survival rates in both groups. Analysis revealed that these types of procedures did not affect the evaluated parameters as overall survival and cancer-specific survival rates in both groups did not differ statistically. Because lymphadenectomy is the fundamental difference between simple and radical nephrectomy, the authors call its value in the treatment of localized RCC into question in light of the above-mentioned results.

Thorough review of medical literature concerning the significance of extended lymphadenectomy accompanying nephrectomy reveals divergent (pro- and contra) opinions fluctuating between extremes. The role of that procedure in the treatment algorithm of kidney carcinoma sparks a debate and still remains controversial. There is no consensus regarding its aims, benefits, or disadvantages. Different authors prove their distinct points of view on primary regional node removal. Thus finally, the role of lymphadenectomy remains undefined.

Renal cell carcinoma accounts for almost 90% of primary renal cancers. Nephrectomy remains the standard treatment for renal cell carcinoma both localized and metastatic. In the former case, the procedure is performed with curative intention but in the latter as an important adjunct to drug treatments or novel complementary multimodality therapies.

The original description of radical nephrectomy was given by Robson in 1969, which recommended ipsilateral adrenalectomy and extended removal of lymphatic tissue adjoining large vessels up to the aortic bifurcation. Because the survival rate was affected by the presence of nodal metastases and the fate of patients who developed metastases at the time of first presentation was irrevocably fatal, common sense ordered at least regional lymphadenectomy as a curative procedure. This concept was supported by observations that by following the oncologic rules, removal of metastatic (or presumably micrometastatic) nodes improved prognosis in some other cancers leaving a given patient free of residual disease.

Nevertheless, the issue has complicated itself since the late 80's. With the advent of extensive implementation of USG and CT examination, a large number of kidney tumors were diagnosed incidentally in an early, localized stage (organ confined). In the first half of the last century only 7% of kidney tumors had been detected incidentally, but by the end of the 20<sup>th</sup> century this number reached up to 60% [1, 2]. The incidence of nodal involvement fell from 30% in the eighties to 3% nowadays [1, 3]. The incidence of nodal metastases is strongly related to T stage and grade: 5.2% to 13.2% in T1-2 and 23.4% to 36% in T3-4 stages. A similar correlation was observed with reference to tumor grade [1, 2]. Unfortunately, the percentage of nodal metastases in locally advanced and/or metastatic cases still remains very high (46% and 62%, respectively) [3]. Thorough statistical analyses of benefits of extended lymph nodes dissection questioned its positive influence on patients' survival. As has been presented, only 5% of patients will benefit from lymph-

adenectomy, but, contrary, others published valid data in favor of that procedure [3].

More recent multivariate analyses revealed that nodal involvement increased the disease-specific mortality by a factor of nearly eight. Furthermore, refraining from lymphadenectomy in node-involved cases increased disease-related death rate 3-fold [1, 2]. The National Cancer Institute study on metastatic patients after radical nephrectomy revealed an 8.5-month median survival in patients with nodal involvement and 15-month median survival without nodal changes [4]. Such results were confirmed elsewhere [5].

Contemporary imaging procedures allow disclosing even subtle nodal pathologies, but not all enlarged lymph nodes are metastatic. As has been presented, preoperatively suspected bulked nodes are microscopically positive in only 40% of cases [1, 6]. Due to the low rate of nodal pathology in localized RCC (up to 3%), lymphadenectomy is not recommended in patients without evidence of distant metastases and/or nodal involvement [1, 2, 6].

Taking all of above into account, lymphadenectomy is justified only in cases with suspected adenopathies or/and with nodal metastases or/and with distant metastases as organ metastases are commonly associated with node involvement [1, 6]. When lymphadenectomy is being considered the number of excised nodes is of crucial importance [6]. Because the accuracy of histopathological assessment correlates with the number of resected nodes, at least 13 nodes should be excised [6].

Does removal of all involved lymph nodes during radical nephrectomy really improve patient survival?

This almost Hamletic question still remains unanswered while the collected data remains ambiguous [1, 3]. Several published single-institution reports and clinical trials were disappointing and did not reveal any benefits of nodal dissection [2, 3, 7]. On the contrary, some other analyses found survival benefits of extended lymphadenectomy for low-stage patients as compared with patients without nodal dissection [3]. Of great interest is the most recent study published in the *Journal of Urology* in May 2011 [8]. Authors focused on the relationship between the number of removed lymph nodes and patient survival. The study went through databases of 9,586 RCC patients, among them 1,265 had nodal metastases. During follow-up (median 3.5 years) 25% died of RCC (20% of node-negative v. 58% of node-positive patients). Five-years disease-specific survival in the node-negative group was 80%, but in the node positive group reached only 36%. What's more, in the latter group the number of metastatic nodes inversely correlated with survival. But, probability of disease-specific survival increased with total number of removed nodes (49% for 15 nodes compared to 39% for only 5 nodes removed). The most recent paper harmonizes with the data published before [6]. Lymphadenectomy had no effect on survival of patients with negative nodes [8].

The foregoing considerations exemplify that medicine leaves very little room for decisive statements. Early papers recommended radical transperitoneal nephrectomy with extended lymphadenectomy in each RCC case. The subsequent disappointing results put "surgical trends" toward simple lumbar nephrectomy. Nowadays,

surgical oncology unites both trends trying to implement extended lymphadenectomy only for cases at high risk of nodal metastases. Now, it remains to work out reliable predictive nomograms determining patients who can benefit from extended procedures. Decision on type of nephrectomy with or without extended lymph nodes dissection should take into account several factors as patient age and performance status, risk of nodal or/and distant metastases, tumor size, and the possible use of adjuvant combined therapies with multikinase inhibitors or other innovative therapies currently under evaluation.

In addition, it was presented that transperitoneal access seems to be safer than the classic lumbar one used for simple nephrectomy [3]. Mortality of patients after radical nephrectomy is significantly lower than the mortality rate after the simple procedure (0.9% vs. 2.3%), which is probably due to much better visualization of large vessels [3]. The EORTC study on patients with organ-confined tumors randomized into radical nephrectomy and simple nephrectomy subgroups revealed no statistical differences in intra- and post-operative complications and outcomes at least.

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