Radiogenomics of Renal Cell Carcinoma: Our Clinical Experience

*Yu.O. MYTSYK, Y.B. BORYS, V.E. DOSENKO, I.V. DATZ, Y.P. DIYCHUK,
V.V. KOWALSKYY, S.M. PASICHNYK, V.M. MATSKEVYCH
Danylo Halytskyi Lviv National Medical University, Lviv, Ukraine*

E-mail: mytsyk.yulian@i.ua

Renal cell carcinoma (RCC) is relatively common pathology that is found roughly in 3 % of all cases of malignant neoplasia in adults and approximately in 90 % of malignant tumors arising because of a kidney [10]. Associations

between imaging features and genomic landscape of RCC have been recently investigated in order to characterize better tumor, diagnosing more precisely, staging and establishing more accurate prognosis comparing to classic histopathologic approach. Such integration of imaging and molecular biomarkers has led to novel concept of “radiogenomics” or “radiogenetics” [4, 5, 7]. A great number of investigators have assessed a role of certain microRNAs (miR) in context of RCC radiogenomics, however the quantity of such works is quite small [3, 4, 9].

In our previous work we have already described usefulness of expression of miR-15a measured in urine during RCC diagnostics [1]. Moreover, high miR-15a expression values have been significantly associated with poor survival rates in patients with RCC [2].

The purpose. The goal of the study is investigation of associations between cross-sectional imaging features of RCC and urine expression levels of miR-15a.

Materials and methods. Conducting of the research has been approved by Ethical Committee of Danylo Halytsky Lviv National Medical University, Ukraine (protocol № 5, 05.25.2015), and has been carried out in accordance with ethical standards formulated in the Declaration of Helsinki 1975. Our study has been conducted at Urology Department of this institution and at General and Molecular Pathophysiology Department of Bogomoletz Institute of Physiology of National Academy of Sciences of Ukraine during 2015-2017 years.

52 adult patients with RCC according to clinical and imaging data have been engaged in the study. The size of the tumors have ranged from 2,08 to 12,7 sm and average size of $7,01 \pm 2,08$ cm. Percutaneous kidney biopsy or previous kidney tumor treatment has been performed in all patients. In all patients' multiphase CT or MRI imaging with contrast enhancement has been performed prior to surgical treatment using standard abdominal protocols [6]. In all cases urine collecting and miR-15a expression measuring has been performed according to earlier described method, using quantitative polymerase chain reaction [1]. Associations between miR-15a expression and such RCC imaging features as necrosis, renal vein invasion, presence of intratumoral calcifications, definition of tumor margin and architecture, presence of collecting system invasion, intratumoral hypervascularity, homogeneous or nodular tumor enhancement pattern on nephrographic phase images have been assessed. All patients have been treated surgically with following pathologic analysis.

Microsoft Excel 2016 and SPSS v.22 software packages have been used for the statistical data processing.

Results and discussion. RCC cases have been classified concordantly to 7th edition of AJCC cancer staging manual: T1aN0M0 ($n = 13$, 25,0 %), T1bN0M0 ($n = 15$, 28,85 %), T2aN0M0 ($n = 12$, 23,08 %), T2bN0M0 ($n = 5$, 9,62 %), T3aN0M0 ($n = 4$, 7,69 %), T3aN1M0 ($n = 3$, 5,77 %). Based on pathologic analysis all RCCs have been classified according to histologic subtypes – clear cell RCC ($n = 22$), papillary RCC ($n = 16$), chromophobe RCC ($n = 14$). Simplified two-tiered Fuhrman grading system has been used, in which grades I and II (low grade, $n = 12$) and grades III and IV (high grade, $n = 10$) have been combined for the clear cell RCC grading.

As a result of our investigation we have found significant evidences of associations between miR-15a expression levels and RCC imaging features. The expression values of miR-15a in urine of patients with RCC have varied from 91,35 to 5,52 relative fluorescence units (RFU), average has been $-54,58 \pm 37,76$ RFU. High expression levels of miR-15a (> 25 RFU) in patients with RCC have been common in presence of such tumor imaging features as necrosis ($p < 0,05$), ill-defined margins of the lesion ($p < 0,05$) and intratumoral hypervascularity ($p < 0,01$). Lower miR-15a expression levels (< 25 RFU) have been associated with imaging evidence of renal vein ($p < 0,05$) and collecting system ($p < 0,05$) invasion, nodular tumor enhancement pattern on nephrographic phase images ($p < 0,05$) and multicystic tumor architecture ($p < 0,05$). However, there has

not been significant association between miR-15a expression and presence of intratumoral calcifications on cross-sectional images ($p > 0,05$). The mean values of miR-15a expression for each of RCC imaging characteristics as well their frequency are presented on figure 1.

Conclusions. Radiogenomic analysis may provide valuable information for predicting of miR-15a expression levels in urine of patients with RCC. In clinical conditions under which there is no possibility to perform genetic assay, imaging features of RCC can be used as surrogates of miR-15a expression to perform prognostication of disease biologic behavior.

Figure 1. Associations between RCC imaging features and mean miR-15 expression levels in urine

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RESEARCH ARTICLES

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Danylo Halytskyi Lviv National Medical University, Department of Urology

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The purpose. The goal of the study is investigation of the associations between cross-sectional imaging features of RCC and urine expression levels of miR-15a.

Materials and methods. 52 adult patients with RCC according to clinical and imaging data have been engaged into study. In all patients' multiphase CT or MRI imaging with contrast enhancement has been performed prior to surgical treatment using standard abdominal protocols. Urine collecting and miR-15a expression measuring has been performed using quantitative polymerase chain reaction. Associations between miR-15a expression and such RCC imaging features as necrosis, renal vein invasion, presence of intratumoral calcifications, definition of tumor margin and architecture, presence of collecting system invasion, intratumoral hypervascularity, homogeneous or nodular tumor enhancement pattern on nephrographic phase images have been assessed. All patients have been treated surgically with the following pathologic analysis.

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Conclusions. Radiogenomic analysis may provide valuable information for predicting of miR-15a expression levels in urine of patients with RCC. In clinical conditions under which there is no possibility to perform genetic assay, imaging features of RCC can be used as surrogates of miR-15a expression to perform prognostication of disease biologic behavior.

Key words: renal cell carcinoma, radiogenomics, microRNA, imaging, biomarker.