



# SYSTEMIC IMMUNE RESPONSE AFTER RADIOFREQUENCY AND CRYOABLATION OF LOCALIZED RENAL CELL CARCINOMA



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Thermal ablation techniques can elicit an immune response. The aim of this work is to evaluate the systemic immune response after radiofrequency (RFA) and cryoablation (CRA) of localized renal cell carcinoma (RCC).

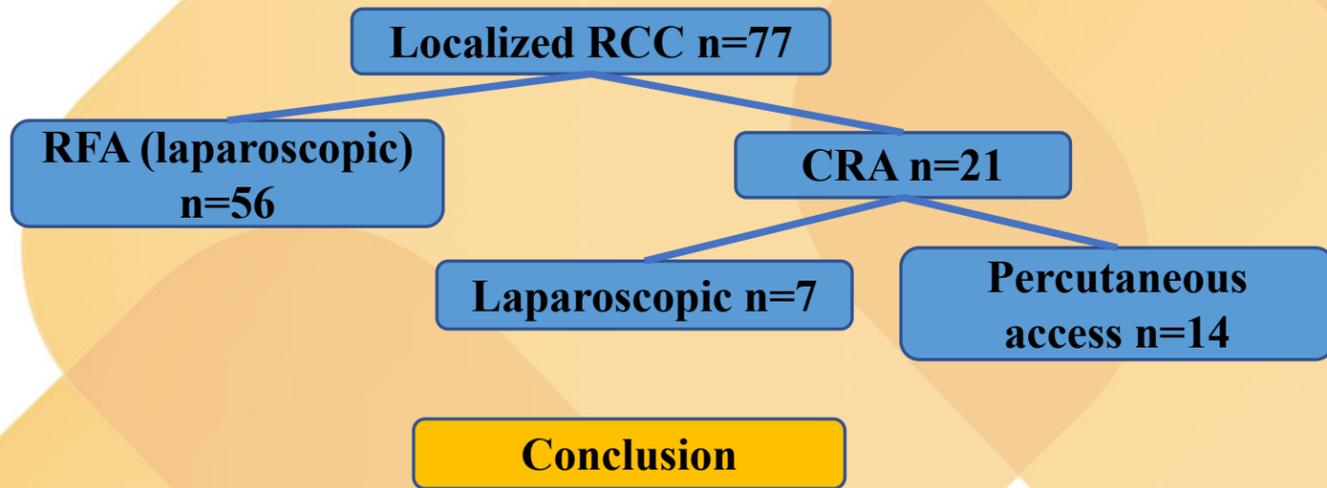
## Materials & Methods

## Results

77 patients were enrolled in this study between 2011 and December 2018 in NMRC of oncology: 56 cases of RFA (laparoscopic) and 21 CRA (7 laparoscopic and 14 percutaneous access). RFA was performed by the standard method on a RITA 1500x device (AngioDynamics, U.S.), with «star burst» probe. CRA performed on the Medical Cryotherapy System (MCS, Russia) with nitrogen pressure of 3 Br, cryoprobes (D=1.5 mm) were introduced into a kidney tumor from three points under CT or ultrasound-control. The tumor was frozen up to -180°C in two cycles with continuous thermometry. The composition of immunocompetent peripheral blood cells (sample volume 5 ml) was evaluated with multicolor flow cytometry (FACS Calibur device, USA): before surgery, on the 1-t, 7-th and 30-th day after.

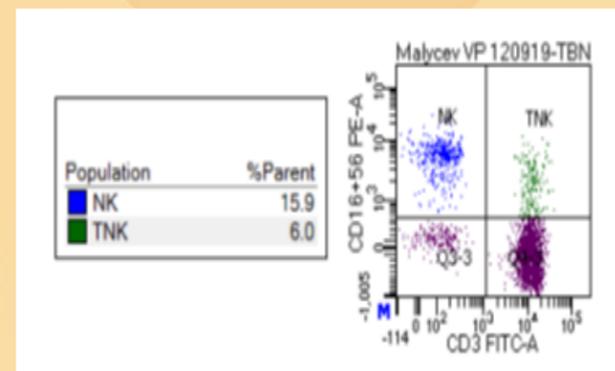
The average age was  $62.3 \pm 11.1$  (36-85) years. All patients underwent a fine-needle biopsy before ablation: in RFA 39 (69.6%) patients had RCC (clear-cell 94.8%, chromophobic 2.6%, papillary 2.6%). The average size of tumor was  $3.34 \pm 0.46$  cm and 97.4 % cases were staged as cT1aN0M0. In second group 16 patients had RCC and 15 were staged as cT1aN0M0. The average tumor size was  $2.6 \pm 2.78$  cm. In each group 3 cases of Clavien-I were revealed, in CRA 1 case of spontaneous pneumothorax (Clavien-III). The median follow-up in the RFA group was 51 months; 5-year disease-free survival was 89.4%. All patients CRA- group were operated in 2018 (the median of observation was not achieved), all are alive, no relapse was detected. The immune status before surgery did not reveal significant deviations from the reference ( $p = 0.18$ ). In the postoperative period in RFA group, the value of CD3-CD19 + (B-lymphocytes), CD3-CD16 + 56 + (NK-cells), CD4 + CD25brightCD127low (T -regulatory lymphocytes) did not change significantly ( $p > 0.05$ ). At the same time, there was a statistically ( $p = 0.016$ ) increased value of CD3 + CD19- (T-lymphocytes) by 30 days of observation from  $1.18 \pm 0.3 \times 10^9/l$  up to  $1.9 \pm 0.3 \times 10^9/l$  due value T-helpers, activated T-helpers) and cytotoxic T- lymphocytes ( $p=0.003$ ). Immunoregulatory index (IRI) increased from  $1,66 \pm 0,6 \times 10^9/l$  to  $2,95 \pm 0,15 \times 10^9/l$  on 30-th day.

The immune response of CRA was similar to the response RFA. On the 7th day and 30th after, most indicators acquired positive dynamics, an increase in the number of T-helpers and T-cytotoxic lymphocytes was noted. However, the growth of T-helpers and T-cytotoxic lymphocytes was more symmetrical, which did not lead to an increase in IRI (CD4<sup>+</sup>/CD8<sup>+</sup>). The level of NK cells also showed an upward trend, but without significant differences ( $p = 0.087$ ). IRI was decreased from  $2.4 \pm 0.81 \times 10^9/L$  to  $2.1 \pm 0.09 \times 10^9/L$  without further rising.



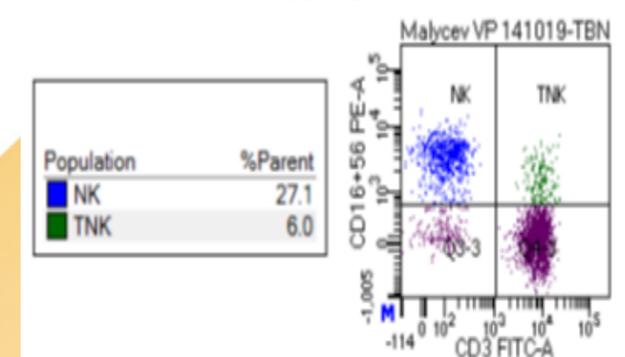
This IRI behavior indicates a more pronounced activation of cytotoxic lymphocytes compared with the response to RFA, which may indirectly indicate a higher immunostimulating potential of CRA.

Before CRA



Results		Norma	
15,9	%	8-17	%
0,31	*10 <sup>9</sup> /L	0.12 -0.37	*10 <sup>9</sup> /L

After CRA



Results		Norma	
27,1	%	8-17	%
0,68	*10 <sup>9</sup> /L	0.12 -0.37	*10 <sup>9</sup> /L