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## Occlusion of the vein adjacent to colorectal cancer liver metastasis as a way to increase the radicality of percutaneous radiofrequency thermal ablation

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### ABSTRACT

**Objective.** To evaluate the effectiveness of preoperative coagulation of the vein adjacent to a tumor nodule in sonographically-guided percutaneous radiofrequency thermal ablation of perivascular liver metastases of colorectal cancer.

**Materials and methods.** To address the issue, we compared the results of sonographically-guided percutaneous radiofrequency thermal ablation of perivascular liver metastases of colorectal cancer in 27 patients (aged 60.5 (58; 68) years) without prior coagulation of the adjacent vein (control group) and 26 patients (62.0 (60; 74)) with prior coagulation of the adjacent vein (experimental group).

**Results.** Lower incidence of residual tumor in the ablation area in the patients with prior coagulation of the adjacent vein (14.3 % vs. 29 % of the patients in the control group) and a higher relapse-free survival of such patients (65.2 % vs. 53.6 % and 55.6 % vs. 33.3 %) were reported as compared to the group without prior coagulation of the adjacent vein (after 6 and 12 months, respectively).

**Conclusion.** Preoperative coagulation of the vein adjacent to colorectal cancer liver metastasis allows reducing the effect of heat removal from the RFA zone, thereby contributing to higher radicality of the treatment and resulting both in a lower incidence of residual tumor in the ablation zone and a higher relapse-free survival of patients, notably without significant concomitant changes in the affected part of the liver (segment atrophy).

**Keywords:** radiofrequency thermoablation, liver metastases, coagulation, local thermal exposure, ultrasound, computed tomography.

**Author contributions.** Murashko K.L.; Yurkovskiy A.M.: concept and design of the study, collection of materials and creation of a base of samples; collection of experimental evidence; statistical data processing, editing, discussion of data, review of publications related to the topic of the article, approval of the manuscript for publication.

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## Окклюзия вены, прилежащей к метастазу колоректального рака в печени, как способ повышения радикальности чрескожной радиочастотной термоабляции

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### РЕЗЮМЕ

**Цель исследования.** Оценить эффективность предварительной коагуляции вены, прилежащей к опухолевому узлу, при сонографически контролируемой чрескожной радиочастотной термоабляции периваскулярных метастазов колоректального рака в печени.

**Материалы и методы.** Для решения поставленной задачи проведено сопоставление результатов сонографически контролируемой чрескожной радиочастотной термоабляции периваскулярных метас-

тазов колоректального рака в печени 27 пациентов (возраст — 60,5 (58; 68) года) без предварительной коагуляции прилежащей вены (группа контроля) и 26 пациентов (62,0 (60; 74)) с предварительной коагуляцией прилежащей вены (опытная группа).

**Результаты.** Выявлена меньшая инцидентность остаточной опухоли в зоне абляции у пациентов с предварительной коагуляцией прилежащей вены (14,3 % против 29,0 % у пациентов группы контроля) и большая безрецидивная выживаемость пациентов (65,2 % против 53,6 % и 55,6 % против 33,3 %) в сравнении с группой без предварительной коагуляции прилежащей вены (через 6 и 12 месяцев соответственно).

**Заключение.** Предварительная коагуляция вены, прилежащей к метастазу колоректального рака в печени, позволяет уменьшить эффект теплоотведения из зоны РЧА, тем самым обеспечивая большую радикальность воздействия и, соответственно, меньшую инцидентность остаточной опухоли в зоне абляции, а также большую безрецидивную выживаемость пациентов, причем без существенных сопутствующих изменений печени (атрофии сегмента) в зоне воздействия.

**Ключевые слова:** радиочастотная термоабляция, метастазы печени, коагуляция, локальное тепловое воздействие, ультразвуковое исследование, компьютерная томография.

**Вклад авторов.** Мурашко К.Л., Юрковский А.М.: концепция и дизайн исследования, сбор материалов и создание базы образцов, получение экспериментальных данных, статистическая обработка данных, редактирование, обсуждение данных, обзор публикаций по теме статьи, утверждение рукописи для публикации.

**Конфликт интересов.** Авторы заявляют об отсутствии конфликта интересов.

**Источники финансирования.** Исследование выполнено без спонсорской поддержки.

**Для цитирования:** Мурашко КЛ, Юрковский АМ. Окклюзия вены, прилежащей к метастазу колоректального рака в печени, как способ повышения радикальности чрескожной радиочастотной термоабляции *Проблемы здоровья и экологии*. 2021;18(3):57–63. DOI: <https://doi.org/10.51523/2708-6011.2021-18-3-7>

## Introduction

Primary tumor in the hepatic portal system is the most common cause of liver metastases [1]. Furthermore, those liver metastases can either have pronounced vascularization (in 67 % of the cases) or, alternatively, they can be adjacent to a large vessel [9, 10]. Either case can result in reduced radicality of the management of metastases during radiofrequency ablation (RFA) due to the heat removal effect [2–5]. The latter generally manifests when the size of a vessel (vein) is 3 mm or more [10]. Moreover, such an effect entails a high risk of residual tumor cell persistence in the transition zone due to the heat removal from the RFA zone by the vessel adjacent to the tumor. This dictates the need for vein occlusion (if its diameter is 3 mm or more) before performing RFA of the metastatic lesion [14]. Especially considering that neither segment atrophy, nor systemic inflammatory responses, nor hepatic impairment is observed during occlusion of such veins [14].

In certain cases, malignant liver tumors can stimulate pronounced vascularization, or they can be located in close proximity to large blood vessels. Either case necessitates prior chemoembolization of tumor-supplying vessels in order to minimize heat removal and increase

the radicality of exposure during radiofrequency ablation (RFA) [2–4]. Nevertheless, the use of the given method turned out to cause certain problems in patients with heart failure (if the left ventricular ejection fraction is less than 50 %), with renal impairment (if creatinine level exceeds 177 mmol/L), and in some other medical conditions [5–8]. Needless to say that in such a situation there emerged a need to search for a different way to avoid the heat removal effect.

## Objective

To evaluate the effectiveness of preoperative coagulation of the vein adjacent to a tumor nodule in sonographically-guided percutaneous radiofrequency thermal ablation of perivascular liver metastases of colorectal cancer.

## Materials and methods

We analyzed the results of sonographically-guided percutaneous radiofrequency thermal ablation procedure in 53 patients with liver metastases of colorectal cancer, who had been receiving radiofrequency ablation (RFA) therapy at “Gomel Regional Clinical Oncological Dispensary” from 2014 through 2020. The locoregional treatment was preceded by the image-guided radiotherapy including ultrasound

examination of all the patients and CT angiography (CTA). The diagnosis was morphologically verified using a sonographically-guided trepanobiopsy.

A total of 53 patients underwent percutaneous radiofrequency thermalablation of liver malignancies (25 male patients and 28 female patients), the average age was  $63.6 \pm 10.6$  years. The patients were divided into two groups: a total of 27 patients (50.9 %) without prior coagulation of the adjacent vein (the adjacent vein diameter  $-3.0 \pm 1.7$  mm) were included in the control group, and 27 patients (49.1 %) with prior coagulation of the adjacent vein (the adjacent vein diameter  $-3.0 \pm 1.9$  mm) were included in the experimental group.

Both the control and experimental groups were comparable in terms of the age of the patients (60.5 (58.0; 68.0) years/62.0 (60.1; 74.0) years ( $p = 0.4$ )) and clinical particulars.

The main characteristics of metastatic lesions were evaluated in both the groups along with the length of inpatient stay, types of complications, biochemical blood test results (liver enzymes), the extent of fibrosis, depth of necrosis, median relapse-free periods, and survival rates.

Liver metastases were visualized using the mid-range ultrasound scanner AlokaProsound Alpha 6 with a convex electronic sensor operating in the frequency range from 3.5 to 5 MHz. The evaluation of the blood vessels was carried out by Colour Doppler Imaging (CDI).

A disposable pickup electrode of the Cool-tip™ system (length — 15–25 cm, applied part — 2.0–3.0 cm) and a generator were used for the radiofrequency ablation procedure. The disposable pickup electrode was directed to the target area with a direct puncture of the adjacent blood vessel under ultrasound guidance. Further, the vessel was “sealed” in the “coagulation” mode until the blood flow was no longer visualized (in the CDI mode). Then the electrode was placed in the center of the metastasis to perform tumor ablation (the time of exposure of each lesion —  $14.0 \pm 2.2$  min) with further extraction of the electrode in the “coagulation” mode. In the event when the area of necrosis did not cover the tumor together with a 10-mm zone of the adjacent tissue after single exposure, another application was performed. Postoperative complications were assessed using the five-grade modified Clavien-Dindo classification system [15–20].

The statistical analysis of the obtained results was carried out using the software environment R version 3.2 (R Foundation for

Statistical Computing, Vienna, Austria) and MedCalc 15.6.1 (trial version).

The Shapiro–Wilk test was used to verify that the variables were normally distributed. If the distribution of quantitative values was different from normal, then the results were grouped into 25<sup>th</sup> percentile and 75<sup>th</sup> percentile, while in the event of normal distribution, the results were given as the mean and standard deviation of the mean ( $M \pm SD$ ). The Mann-Whitney U-test and two-tailed Fisher’s exact test were used to compare two independent samples. The results were regarded statistically significant if the  $p$ -value was below 0.05. The Spearman’s rank correlation coefficient ( $r$ ) was used to evaluate the strength of a monotonic relationship between connected variables. A relapse-free survival rate was estimated using the Kaplan-Meier survival analysis.

## Results and discussion

Solitary metastases were reported in 42 (79.2 %) patients, 2 lesions were observed in 8 (15.1 %) patients, and 3 lesions—in 3 (5.7 %) patients (characteristics of the metastases in the control and experimental groups are presented in detail in Table 1).

As it can be seen from Table 1, no statistically significant differences were found between the groups.

As it can be seen from Table 2, no statistically significant differences were reported between the control and experimental groups in terms of the biochemical test results. Meanwhile, hyperenzymemia in both the groups was transient (a gradual decrease in the concentration of enzymes was observed after day 3). As for bilirubin, its concentration was found to be within the normal range in all the patients. Figure 1 visually features the changes in the specified biochemical parameters.

According to the early postoperative follow-up results, mild complications were reported both in the control and experimental groups, and they were generally complex (the complications included mostly vagal reactions combined with a pain syndrome lasting up to 6 hours). Moreover, one case of liver abscess (grade IIIA according to the Clavien–Dindo classification) was reported in each group in the early postoperative period. The above-mentioned information is presented in detail in Table 3.

Table 1. Comparative characteristics of the metastases in the control and experimental groups

Comparative characteristics	Control group (n = 27)	Experimental group (n = 26)	p
f	14 (52 %)	14 (54 %)	0.8
m	13 (48 %)	12 (46 %)	
TNM (T) stage			
2	5 (18 %)	2 (8 %)	0.1
3	8 (30 %)	4 (15 %)	
4	14 (52 %)	20 (77 %)	
Number of liver metastases			
1	20 (74 %)	22 (85 %)	0.1
2	6 (22 %)	3 (12 %)	
3	1 (4 %)	1 (3 %)	
Synchronous metastases			
f	22 (81 %)	20 (77 %)	0.7
m	5 (19 %)	6 (23 %)	
Metachronous metastases			
f	5 (19 %)	6 (23 %)	0.7
m	22 (81 %)	20 (77 %)	
Size of metastases	23.5 mm (20.5; 30.0)	29.0 mm (25; 36)	0.3
Localization of metastases (liver segment)	6 (4; 7)	6 (5; 7)	0.4
Diameter of the adjacent vein	< 3.0 mm	3.5mm(3,2; 3,8)	
Histology, differentiation grade (G)			
G 2	19 (70 %)	18 (69 %)	1.0
G 3	8 (30 %)	8 (31 %)	

Table 2. Comparative characteristics of the biochemical blood test results in the control and experimental groups

Biochemical parameters	Control group	Experimental group	p
Albumin g/L before RFA	42.0 (39.9; 44.2)	41 (38.9; 43.0)	0.3
Albumin g/L, 1 day after RFA	40.5 (36.8; 44.0)	38.6 (35.0; 43.0)	0.3
Albumin g/L, 3 days after RFA	41.1 (36.0; 43.9)	40.0(34.4; 42.3)	0.2
AST U/L before RFA	25.4 (20.9; 32.6)	22.6 (20.1; 29.1)	0.3
AST, 1 day after RFA	198.0 (162.0; 291.0)	214.0 (171.0; 250.0)	0.9
AST, 3 days after RFA	120.0 (95.0; 180.0)	150.0 (116.0; 186.0)	0.3
AST U/L, 3 months after RFA	27.3 (22.5; 35.3)	25.2 (20.3; 35.6)	0.4
ALT U/L before RFA	23.6 (16.4; 31.0)	21.0 (13.5; 23.7)	0.4
ALT, 1 day after RFA	142.0 (108.0; 212.0)	205.0 (132.0; 227.0)	0.2
ALT, 3 days after RFA	92.0 (66.0; 143.0)	122.0 (99.0; 162.0)	0.2
ALT, 3 months after RFA	23.5 (19.0; 29.4)	23.5 (17.7; 35.1)	0.9
Total bilirubin $\mu$ mol/L before RFA	14.1 (10.0; 16.0)	11.8 (8.7; 15.1)	0.2
Bilirubin, 3 days after RFA	13.5 (10.1; 17.5)	11.9 (8.9; 16.3)	0.3

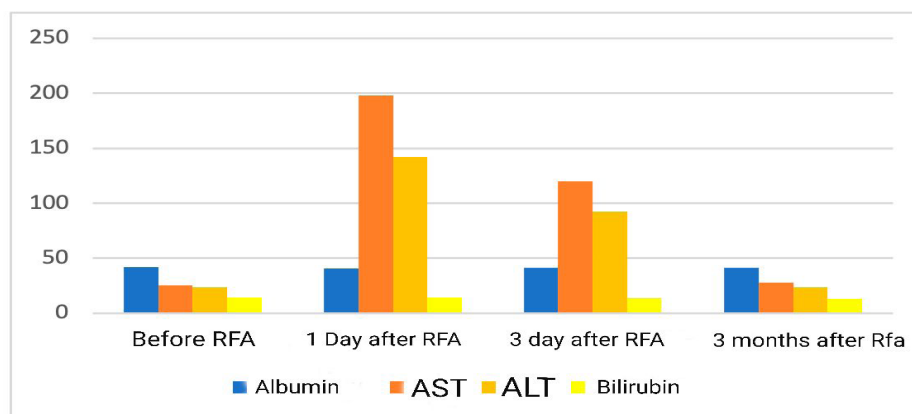


Figure 1. Changes in the concentrations of albumin, ALT, AST and bilirubin in the postoperative period in the control group

Table 3. Incidence of complications and length of in-patient stay after RFA in the control and experimental groups

Comparative characteristics	Control group (n = 27)	Experimental group (n = 26)	p
No complications	18 (67 %)	14 (54 %)	0.4
Grade I-II complications according to the Clavien-Dindo classification	8 (29 %)	11 (42 %)	
Grade III (A, B) complications according to the Clavien-Dindo classification	1 (4 %)	1 (4 %)	1.0
Number of inpatient days	4 (3; 5)	4 (4; 5)	0.9

As it can be seen from Table 3, no statistically significant differences were reported between the control and experimental groups in terms of the incidence of complications and length of in-patient stay.

Considering that no statistically significant differences were reported for most of the above specified evaluation criteria, except, perhaps, for

the diameters of perivascular and nonvascular neoplasms, which were about 29mm (16; 17) and 23.5 mm (18;19) respectively, the X-ray catamnesis of the patients in the control and experimental groups over a 12-month period (CTA follow-up was carried out 1, 3, 6 and 12 months after ablation) is of particular interest (the results are presented in Table 4).

Table 4. Characteristics of post-ablation changes in the liver parenchyma

Post-ablation changes	Control group (n = 27)	Experimental group (n = 26)	p
Extent of fibrosis in the ablation zone (cm <sup>3</sup> ) after 1 day	34.4 (24.5; 70.80)	33.5 (20.6; 82.4)	0.6
Extent of fibrosis in the ablation zone (cm <sup>3</sup> ) after 3 months	24.4 (17.2; 53.1)	24.4 (17.1; 65.5)	0.9
Extent of fibrosis in the ablation zone (cm <sup>3</sup> ) after 6 months	20.6 (17.1; 48.0)	20.6 (14.1; 57.9)	0.8

As it can be seen from Table 4, no statistically significant differences were reported between the groups in terms of the extent of post-ablation fibrosis in the postoperative period. This means that preoperative coagulation of the vein adjacent to the metastasis does not result in a decrease (“contraction”) of the liver segment in the affected area even though it enhances the treatment radicality. The latter can account both for

the reduced incidence of the residual tumor cells in the ablation zone in the patients of the experimental group (14.3 % vs. 29.0 % in the patients of the control group,  $p = 0.043, \chi^2$ ), and a greater relapse-free survival rate of the patients after 6 and 12 months (65.2 % vs. 53.6 % ( $p = 0.4, \chi^2$ ) and 55.6 % vs. 33.3 % ( $p = 0.042, \chi^2$ )) as compared to the control group (Figure 2).

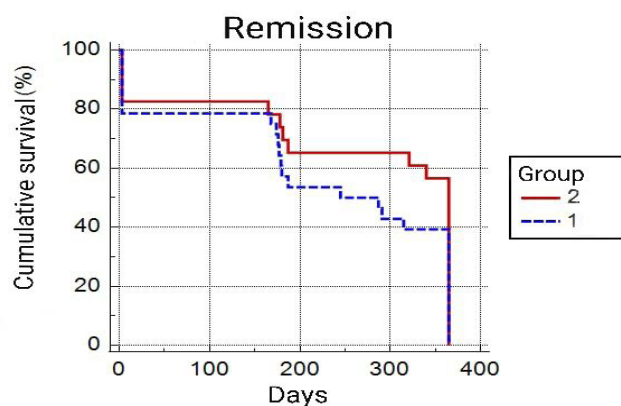


Figure 2. Cumulative relapse-free survival of the patients of the control and experimental groups

## Conclusion

Preoperative coagulation of the vein adjacent to colorectal cancer liver metastasis allows to reduce the effect of heat removal from the RFA zone, thus, contributing to higher radicality of the treatment and resulting both in a decreased incidence of residual disease in the ablation zone and an increased relapse-free

survival of patients, importantly without major associated changes in the affected part of the liver (segment atrophy).

The suggested method does not require any additional financial or technical investments and does not result in prolonged hospitalization.

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