

South Russian Journal of Cancer. 2023. Vol. 4, No. 4. P. 32-43 https://doi.org/10.37748/2686-9039-2023-4-4-4 https://elibrary.ru/hetxqy ORIGINAL ARTICLE



MAGNETIC RESONANCE IMAGING RELEVANCE IN DIAGNOSIS AND PROGNOSIS OF EARLY POSTOPERATIVE PERIOD FOLLOWING PANCREATIC CANCER SURGICAL TREATMENT

E. N. Kolesnikov, D. Ya. Iozefi, O. I. Kit, A. Yu. Maksimov™

National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
☑ rnioi@list.ru

ABSTRACT

Purpose of the study. Improvement of the prognostic outcomes for the pancreatic fistula development in surgical treatment for pancreatic cancer by implementation of new diagnostic algorithms for magnetic resonance imaging (MRI) assessment of supposed pancreatic stump.

Materials and methods. We performed a retrospective analysis of MRI results of 1136 patients from the medical data base of National Medical Research Centre for Oncology for 2009–2020. An original scanning technique, trans- and cross-pancreatic imaging and MR spectroscopy of the pancreas in patients with pancreatic cancer, was developed and applied. Preoperative examinations were compared retrospectively: a standard MRI protocol without anatomical orientation of the series; MRI protocol using the developed technology.

Results. 717 patients were diagnosed with advanced pancreatic cancer. Lymph nodes were affected in 302 patients among 419 patients with radical surgeries. All cases were confirmed morphologically. In the group of 419 patients with pancreatic resections, based on the analysis of morphological and clinical data and preoperative MRI data, we developed an original preoperative scale for assessing the risk of pancreatic fistula development and compared its accuracy with other intraoperative scales, FRS and modified FRS. Lactate and lipid complex were selected from a wide range of metabolites. The surgical protocols and results of histological examination of the surgical material were used to prove the accuracy of the study. The overall accuracy of the technique in predicting fistula development was 97.5 %. New visual predictors ("domino" and "white on white" symptoms) based on MRI data were used to improve the scale accuracy.

Conclusion. The developed method of using a modified scale for risk assessment of pancreatic fistula development allows predicting the onset of early postoperative complications already at the preoperative stage. When comparing the calculated risks of pancreatic fistula according to the developed scale with the results by the known scales (FRS and modified FRS), statistical analysis showed a significant difference for the better when compared with FRS (p = 0.0477), and a tendency when compared with modified FRS (p = 0.0544).

Keywords: pancreatic cancer, MRI, MRI assessment, tumor tissue, supposed pancreatic stump

For citation: Kolesnikov E. N., lozefi D. Ya., Kit O. I., Maksimov A. Yu. Magnetic resonance imaging relevance in diagnosis and prognosis of early postoperative period following pancreatic cancer surgical treatment. South Russian Journal of Cancer. 2023; 4(4): 32-43. https://doi.org/10.37748/2686-9039-2023-4-4-4, https://elibrary.ru/hetxqy

For correspondence: Aleksey Yu. Maksimov – Dr. Sci. (Med.), professor, deputy CEO for advanced scientific research, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation.

Address: 63 14 line str., Rostov-on-Don 344037, Russian Federation

E-mail: rnioi@list.ru

ORCID: https://orcid.org/0000-0002-9471-3903

SPIN: 7322-5589, AuthorID: 710705 Scopus Author ID: 56579049500

Compliance with ethical standards: The research was carried out according to the ethical principles, set forth by World Medical Association Declaration of Helsinki, 1964, ed. 2013. The study was approved by the Biomedical Ethics Committee at the National Medical Research Center for Oncology (extract from the protocol of the meeting No. 118 dated 03/11/2019). Informed consent was obtained from all participants of the study.

Funding: this study was funded by a state assignment, registry number 122032300207-0.

Conflict of interest: the authors declare that there are no obvious and potential conflicts of interest associated with the publication of this article.

The article was submitted 07.08.2023; approved after reviewing 06.10.2023; accepted for publication 09.12.2023.

© Kolesnikov E. N., lozefi D. Ya., Kit O. I., Maksimov A. Yu., 2023

Южно-Российский онкологический журнал. 2023. Т. 4, № 4. С. 32-43 https://doi.org/10.37748/2686-9039-2023-4-4-4 https://elibrary.ru/hetxqy 3.1.6. Онкология, лучевая терапия **ОРИГИНАЛЬНАЯ СТАТЬЯ**

ЗНАЧЕНИЕ МАГНИТНО-РЕЗОНАНСНОЙ ТОМОГРАФИИ В ДИАГНОСТИКЕ И ПРОГНОЗЕ ТЕЧЕНИЯ РАННЕГО ПОСЛЕОПЕРАЦИОННОГО ПЕРИОДА ПРИ ХИРУРГИЧЕСКОМ ЛЕЧЕНИИ БОЛЬНЫХ РАКОМ ПОДЖЕЛУДОЧНОЙ ЖЕЛЕЗЫ

Е. Н. Колесников, Д. Я. Иозефи, О. И. Кит, А. Ю. Максимов⊠

НМИЦ онкологии, г. Ростов-на-Дону, Российская Федерация ⊠ rnioi@list.ru

РЕЗЮМЕ

Цель исследования. Совершенствование результатов прогнозирования развития панкреатической фистулы при оперативном лечении рака поджелудочной железы путем внедрения новых диагностических алгоритмов магнитно-резонансной томографии (MPT)-оценки предполагаемой ее культи.

Материал и методы. Проведен ретроспективный анализ результатов МРТ-исследований 1136 пациентов из базы данных медицинской информации ФГБУ «НМИЦ онкологии» Минздрава России за 2009–2020 гг. Разработана и применена оригинальная методика сканирования – транс- и кросспанкреатическая визуализация и методика МР-спектроскопии у пациентов раком поджелудочной железы. Выполнено ретроспективное сравнение предоперационных исследований: стандартный протокол МРТ без анатомического ориентирования серий; протокол МРТ с применением разработанной технологии.

Результаты. Генерализованный рак поджелудочной железы был у 717 пациентов. Поражение лимфатических узлов – у 302 больных среди 419 радикально оперированных. Все случаи были подтверждены морфологических. В группе 419 пациентов, перенесших резекцию ПЖ, на основании анализа морфологических и клинических данных, а также данных предоперационного МРТ мы разработали оригинальную предоперационную шкалу оценки риска развития панкреатического свища, которую сравнили по точности с интраоперационными шкалами: шкалой риска развития панкреатической фистулы (FRS) и модифицированной FRS. Из широкого спектра метаболитов выбраны лактат и липидный комплекс. Для доказательства точности исследования мы использовали протоколы операций и результаты гистологических исследований операционного материала. Общая точность методики в возможности предсказать развитие свища – 97,5 %. Для повышения точности разработанной шкалы использовались новые визуальные предикторы (симптом «домино» и «белое на белом»), основанные на данных МРТ.

Заключение. Разработанный метод использования модифицированной шкалы риска развития панкреатической фистулы позволяет уже на дооперационном этапе предсказать развитие ранних послеоперационных осложнений. При сравнении рассчитанных рисков развития панкреатической фистулы по разработанной шкале с результатами их оценки по известным шкалам (FRS и модифицированной FRS) статистический анализ показал достоверное отличие в лучшую сторону при сравнении с FRS (p = 0,0477), и тенденцию – при сравнении с модифицированной FRS (p = 0,0477).

Ключевые слова: рак поджелудочной железы, MPT-исследование, MPT-оценка, опухолевая ткань, предполагаемая культя поджелудочной железы

Для цитирования: Колесников Е. Н., Иозефи Д. Я., Кит О. И., Максимов А. Ю. Значение магнитно-резонансной томографии в диагностике и прогнозе течения раннего послеоперационного периода при хирургическом лечении рака поджелудочной железы. Южно-Российский онкологический журнал. 2023; 4(4): 32-43. https://doi.org/10.37748/2686-9039-2023-4-4-4, https://elibrary.ru/hetxqy

Для корреспонденции: Максимов Алексей Юрьевич – д.м.н., профессор, заместитель генерального директора по ПНР, ФГБУ «НМИЦ онкологии» Минздрава России, г. Ростов-на-Дону, Российская Федерация.

Адрес: 344037, Российская Федерация, г. Ростов-на-Дону, ул. 14-я линия, д. 63

E-mail: rnioi@list.ru

ORCID: https://orcid.org/0000-0002-9471-3903

SPIN: 7322-5589, AuthorID: 710705 Scopus Author ID: 56579049500

Соблюдение этических стандартов: в работе соблюдались этические принципы, предъявляемые Хельсинкской декларацией Всемирной медицинской ассоциации (World Medical Association Declaration of Helsinki, 1964, ред. 2013). Исследование одобрено Комитетом по биомедицинской этике при ФГБУ «НМИЦ онкологии» Минздрава России (выписка из протокола заседания № 10 от 11.03.2019 г.). Информированное согласие получено от всех участников исследования.

Финансирование: финансирование за счет госзадания: регистрационный № 122032300207-0.

Конфликт интересов: все авторы заявляют об отсутствии явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Статья поступила в редакцию 07.08.2023; одобрена после рецензирования 06.10.2023; принята к публикации 09.12.2023.

INTRODUCTION

The incidence of malignant neoplasms in Russia has been growing for decades, in 2021, oncological diseases were diagnosed in more than 580,415 thousand residents. The "rough" indicator of pancreatic cancer incidence in Russia in 2021 was at the level of 13.1 per 100,000 population, the increase in this indicator since 2011 was 31.08 %, while mortality per 100,000 population was 13.7, with an increase of this indicator by 26.01 % over 10 years [1].

Diagnosis of pancreatic cancer is playing an increasingly important role, allowing you to quickly respond to the extent of the spread of the tumor and choose a reasonable therapeutic strategy for patients. Various imaging methods, such as computed tomography – CT [2; 3], magnetic resonance imaging – MRI [4], endoscopic ultrasound [5] and positron emission computed tomography – PET [6] are becoming increasingly important and are widely used for the diagnosis of pancreatic cancer.

MRI can potentially be a sufficient method for assessing pancreatic fibrosis, which is confirmed by histological studies [4; 7] and is extremely important when planning surgical treatment. Thus, the inclusion of MRI results in a set of techniques that determine the risks of the course of the postoperative period in patients after radical resections of the pancreas is an urgent task.

The surgical method remains the leading one in the treatment of resectable pancreatic tumors [8]. We analyzed the literature sources concerning the calculation of the risk of postoperative complications, especially pancreatic fistulas (PF) after pancreatic resections [9–14]. For example, D. S. Gorin (2022) [15] focused on the following main risk factors: the nature of the tumor lesion, CT signs of "soft" pancreas (accumulation coefficient greater than 1); intraoperative visual and palpatory assessment; the proportion of functioning acinar structures during urgent histological examination of the pancreatic section and the features of its angioarchitectonics.

The scales known to date allow predicting the risk of pancreatic fistula only in the early postoperative period. At the same time, if the risk of developing a fistula could be judged at the preoperative stage, the patient in this case would receive sufficient individualized preoperative preparation.

Purpose of the study was to improve the results of predicting the development of pancreatic fistula in the surgical treatment of pancreatic cancer by introducing new diagnostic algorithms for MRI evaluation of its presumed stump.

MATERIALS AND METHODS

A retrospective analysis of the results of MRI studies of 1136 patients from the database of medical information of the National Medical Research Centre for Oncology, was carried out in the period from 01/01/2009 to 12/31/2020. MRI was performed both at the National Medical Research Centre for Oncology (78.6 %, 893 cases), and on the basis of other medical institutions. It was counted as one case when performing both a biopsy and an operation on a patient.

We considered pancreatic fistula to be the drainage of the discharge from 3 days after surgery, in which amylase was increased by 3 times relative to blood amylase. In the study group of 419 patients who underwent radical surgery for pancreatic cancer, pancreatic fistulas developed in 102 patients (24.3 % of cases).

Taking into account the complex anatomical structure of the pancreas and the spatial location of the organ, we have developed an original scanning technique called trans- and cross-pancreatic imaging.

We performed magnetic resonance examination of abdominal organs in T2 sequences to position the pancreas and determine the direction of the pancreatic and common bile ducts. The peculiarity of the protocol was that we used a technique involving a trans and cross-pancreatic T2-weighted sequence, sections of which were laid through the pancreas parallel and perpendicular to the location of the Virsung duct (Fig. 1).

To obtain an optimal image of the pancreas and the Virsung duct, an oblique T2-weighted image with TE in the range of 80-90, TR 9400-9500 was used, the resolution of the matrix was not lower than 320×192 , while the thickness of the slice should be 3-4 mm, and the distance between the slices was set to 0 mm. The function of starting data collection at coinciding phases of respiration or holding the breath on exhalation was used, the number of slices was sufficient to visualize the main array of pancreatic parenchyma. A T2-weighted image of the pancreas with the main pancreatic (Virsung) duct was obtained.

Then an isovoxel diffusion weight imaginc (DWI) with b 0 s/mm² and b 1000 s/mm² was diagonally laid in the same way parallel to the Virsung duct. Then, by mathematical summation of polychrome diffusion-weighted images with monochrome T2 images, a FU-SION image of the pancreas was obtained at the tomograph workstation using DWI sequence images and a transpancreatic T2 sequence.

The localization of the pancreatic tumor, which often violates the patency of the Virsung duct with its suprastenotic expansion caudal to the tumor, the expansion of small ducts, the condition of the alleged pancreatic stump, was determined.

In the concept of "the alleged stump of the pancreas" we put the following. After determining the position of the tumor in the pancreas, we focused on the mesenteric portal trunk. When the tumor was located proximally to the right of it, we analyzed the distal parts of the gland to the left of it (tail and body) as a supposed stump. When the tumor was located distally to the left of the mesenteric-portal trunk as a supposed stump, we analyzed the distal parts of the gland to the right of it (the head of the pancreas).

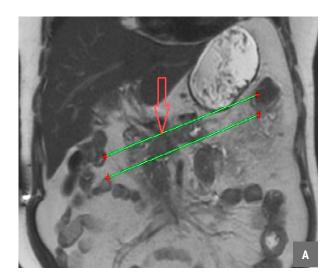
The domino criterion was used as an additional criterion for the diagnosis of pancreatic cancer and evaluation of its alleged stump. We first developed this criterion for the differential diagnosis of pancreatic tumors, and then, with a retrospective analysis of images, we began to observe it in the perifocal zone. The visualization pattern represents small rounded

hyperintensive in T2 multiple areas of dilated collateral pancreatic ducts against the background of an isointensive tumor in conditions of obstruction of the Virsung duct. The ductal system of the pancreas includes small lobular ducts flowing into the main and additional ducts, hyperintensive in T2, hypointensive in T1 due to the liquid component in their lumen. The domino pattern introduced by us is found, according to our data, in 92 % of cases of adenocarcinomas in the head of the pancreas.

Pancreatic MR spectroscopy technique

Lactate and lipid complex were selected from a wide range of metabolites available for determination under conditions of a magnetic field strength of 1.5 T during preliminary research work. We evaluated both the tumor tissue and the presumed pancreatic stump.

The procedure was carried out as follows: after laying the patient in the supine position on the abdominal coil of the diagnostic table of the tomograph, marking (localizer) and calibration series were carried out. T2-weighted series in three planes crossing the pancreas were performed, and axial T1FS LAVA and DWI (b = 0, b = 1000) and T1 double gradient echo in phase and antiphase (dual gradient echo in-phase/out-of-phase) allowing to evaluate its anatomy. In the RadiAnt software package, the area of the most pronounced changes was identified (in normal glands, indicators for the head or body of



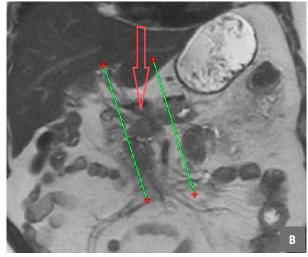


Fig. 1. A – the direction of the slices when planning axial transpancreatic series parallel to the axis of the Virsung duct. The red arrow points to the tumor, the green lines are the boundaries of the most important visualization area. B – the direction of the slices when planning cross-pancreatic series is perpendicular to the course of the Virsung duct. The red arrow points to the tumor, the green lines are the boundaries of the most important visualization area.

the organ were studied). This area was outlined with an oval or round border, the structural heterogeneity coefficient (HC) was calculated as the ratio of the standard deviation value (stdO or SD) to the average signal intensity (SI), according to the formula: HC = stdO/SI. The amount of lipids in the dual echo is measured. The lipid content was quantified using the Dixon method. The sequence of double gradient echo in phase and antiphase (dual gradient echo inphase/out-of-phase) was used for evaluation. The indicators of the signal intensity from the pancreatic parenchyma and spleen in the corresponding zones in the images in phase (SIP) and antiphase (SOP) were used and subsequent calculations using the Dixon formula: Fat fraction = (SIP-SOP)/2*(SIP), where SIP is the ratio of the pancreatic signal to the spleen signal in the images in phase; SOP-the ratio of the pancreatic signal to the spleen signal in the images in the opposite phase.

Also, for a better diagnosis of the prevalence of the tumor process, proton single-pixel spectroscopy of the same area of changes suspected of cancer was performed. The data was transmitted to a computer with an installed program for processing spectra. The values of the spectrum peaks were determined in the Tarquin program and the value of the lactate signal was measured in atomic units a.u. The value of the accountable diffusion coefficient (ADC) was measured by DWI.

To assess the statistical reliability of the results, criteria were used to assess the significance of differences in outcomes depending on the impact of the inclusion factor of the studied developed techniques: Chi-square criterion, Fisher's exact criterion (two-sided).

STUDY RESULTS AND DISCUSSION

Generalized PC was found in 717 patients, among whom 3 had bone metastases. Lymph node lesion was diagnosed in 302 patients among 419 radically operated. All cases were confirmed morphologically.

According to our study, operations for tumors of the pancreatic head prevailed over corporocaudal resections 254 vs. 165, while biopsies were performed more often for pancreatic body cancer than for the head (386 vs. 287). Moderate differentiation of tumors prevailed in most histological findings.

In our sample, the most patients were from 50 to 79 years old, and among them from 60 to 69 years old -471 patients (41.46 %).

In the analyzed group, men 295 (25.97 %) were more likely to suffer from pancreatic head cancer than women 246 (21.65 %). When the tumor is localized in the body of the pancreas, women are more often 265 (23.32 %) than men 232 (20.43 %). When the tumor was localized in the tail of the gland, women (71; 6.25 %) significantly prevailed over men (27; 2.37 %) (χ^2 =18.94; p < 0.00001).

The patients were distributed according to the TNM classification (8th edition), the IV stage of the process prevailed in our study – 585 (51.5 %), the results are shown in Table 1.

A retrospective comparison of preoperative studies was performed to study the diagnostic value of the anatomically oriented series technique: a standard MRI protocol without anatomical orientation of the series (205 cases from 2009 to 2014 inclusive); an MRI protocol using the above technology (from 2014 to 2020 inclusive 214 cases). To prove the accuracy of the study, we used the protocols of

Table 1. Distribution of the PC patients according to the TNM classification (n = 1136)					
TNM	Stage	Patients' number	Patients' share		
T2N0M0	IB	25	2.20		
T3N0M0	IIA	92	8.1		
T1-3N1M0	IIB	128	11.26		
T1-3N2M0	III	174	15.32		
T4NanyM0	III	132	11.62		
TanyNanyM1	IV	585	51.50		

operations and the results of histological studies of the surgical material.

The overall accuracy of the technique for diagnosing the prevalence of pancreatic cancer using anatomically oriented series, which was compared with standard methods, intraoperative picture and the results of postoperative morphological examination, reaches 97.5%, p < 0.005.

Subsequently, we applied the developed technique on 205 operated patients, whom we had previously examined using the standard method. Thanks to the proposed method, 20 additional episodes of perineural extrapancreatic invasion were evaluated and described in detail, the nature and degree of contact of the tumor with the main vessels were clarified. Statistical analysis confirms the advantages of the method. The reliability of the advantages of the high accuracy of the method is confirmed by the low sum of false-positive and false-negative results when using anatomically oriented series compared with standard methods in relation to the local prevalence of the tumor. The exact Fisher criterion (two-sided) is 0.03169.

The study of the diagnostic value of determining the degree of local tumor spread by MR spectroscopy, performed by retrospectively comparing preoperative studies using the standard MRI protocol (205 cases from 2009 to 2014 inclusive) and the MRI protocol using the MRI technology developed by us (from 2014 to 2020 inclusive 214 cases) showed an overall accuracy of 98.75 %.

The method of adding MR spectroscopy demonstrates high accuracy in assessing the tumor, surpassing the standard scanning protocol in terms of the main indicators of diagnostic significance (tumor size, vascular and perineural invasion, retropancreatic spread) – overall accuracy, sensitivity and specificity, which is confirmed statistically (Fisher criterion; p = 0.00917).

The method of metabolically oriented visualization, determination of the proportion of lipids by chemical shift and lactate peak during spectroscopy requires the presence of a solid bulk formation with a homogeneous structure without cavities of decay, necrosis, sinters with a total size of at least 20 × 20 × 20 mm due to the peculiarities of MR spectroscopy.

In a standard MRI examination of the pancreas, isointensive tissue with a smoothed lobular structure was visualized in 28 patients, which did not allow

unambiguously indicating the presence of a tumor in the pancreas. The calculated diffusion coefficient ADC was in the range of 0.0013–0.0021 mm²/s. With MR spectroscopy, Lac values in the range of 850 a.u. indicate active processes of anaerobic glycolysis. According to the measured coefficients of signal intensity and heterogeneity in T2 SI 750; SD 141.4; HC 0.185, according to T1FS SI 611; SD 61.8 HC 0.101. The proportion of lipids according to the Dixon method was in the range of 1.61–1.72 %, which is significantly less than in normal parenchyma and inflammatory changes. Thus, the patients were diagnosed with pancreatic cancer, which was subsequently confirmed by morphological examination of preoperative punctures and the removed tumor.

The technique also made it possible to differentiate formations located outside the tumor in the area of the alleged stump of the gland. Below is an example when a small tumor of the head of the pancreas (14 mm in diameter) and an indistinct formation in its body was diagnosed, which was initially perceived as a metastasis or a second tumor. However, according to the measured signal intensity and heterogeneity coefficients SI T2 445; SD 81; HC 0.182; SI T1FS 674 SD 57 HC 0.084, the proportion of lipids according to the Dixon method is 22.2 %, increased, which is not typical for tumor pathology. With a spectroscopy of Lac 0.0000 a. u. (Fig. 2).

The mentioned above changes were regarded by us as pancreatic steatosis without significant expansion of the Virsung duct, which was confirmed during subsequent surgical treatment during intraoperative revision and ultrasound.

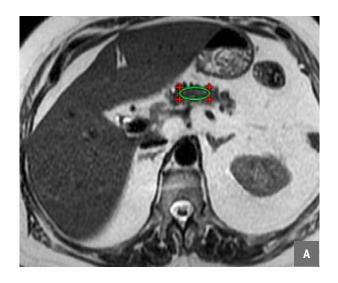
While working on the spectra of pancreatic tissue metabolites in various conditions, we made an interesting observation. The "lipid complex" of Lip 13a peaks at 1.25–1.28 ppm is due to the presence of glycerol and triacyl glyceride analogues. With adenocarcinoma, the average value of this peak reaches 6.9 a.u., with pancreatitis 4.4 a.u. in a normal gland 1.4 a.u.

Literature sources devoted to their significance for the diagnosis of pancreatic adenocarcinoma have not been found at present, however, experience with neuro-oncological spectra demonstrates the presence of this peak in the spectra of cerebral metastases similar to those obtained in the studies of V. Sawlani, M. D. Patel, N. Davies (2020) [16], performed on a magnetic resonance tomograph with

magnetic field intensity fields of 3T. These changes were used by us to study the condition of the perifocal zone of the tumor and the planned stump of the pancreas. To choose surgical tactics already at the preoperative stage, it is necessary to have a judgment about the "tissue density" of the pancreas. Life-threatening complications with pancreatoduodenal resections (pancreatitis of the stump, bleeding, failure of anastomosis sutures) develop just with an "unchanged" gland. Their prevention should be carried out both preoperatively and intraoperatively [11; 17].

Based on the diagnostic techniques we have developed, we have identified a number of new signs,

the determination of which during the assessment of the alleged pancreatic stump in both pancreato-duodenal and distal resections allows us to assume a possible intraoperative situation at the preoperative stage that will affect surgical tactics: the location of the pancreatic duct depending on the resection zone, the nature of drainage of the duct (external or internal), the probability of eruption of the stitches being applied. In order to determine their actual meaning, we compared the data obtained with morphological micro-preparations of the perifocal zone of the tumor and intraoperative macroscopic description of the stump, which we performed together with the surgical team (Table 2).



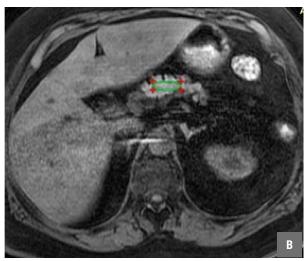


Fig. 2. A – the marker in T2 marks the area of heterogeneity measurement and the voxel placement area for MR spectroscopy; B – the marker in T2fatsat marks the area of heterogeneity measurement and the voxel placement area for MR spectroscopy.

(n = 419)	g parameters for various c	onditions of the pancreatic stump in	trie studied patients	
	Pancreatic stump			
Indicator	Intact tissue (n = 114)	Inflammatory and dystrophic alterations (n = 127)	Fibrous and indurative alterations (n = 178)	
Signal intensity in T2	654.71 ± 6.7	690.29 ± 9.8	640.52 ± 8.6	
HC value T2	0.0744 ± 0.005	0.1117 ± 0.003	0.0653 ± 0.004	
Signal intensity in T1FS	1282.27 ± 10.3	461.40 ± 12.8	1476.11 ± 7.4	
The value of HC inT1FS	0.0792 ± 0.003	0.2234 ± 0.04	0.0543 ± 0.005	
Diffusion (SD/ADC mm2/s)	0.00035/0.0015	0.0004/0.0018	0.00027/0.00011	
The proportion of lipids, %	11.22	16.47	8.12	
Lactate, a.u.	0	0.1	0	

Signs of fibrous indurative changes in the putative stump of the pancreas.

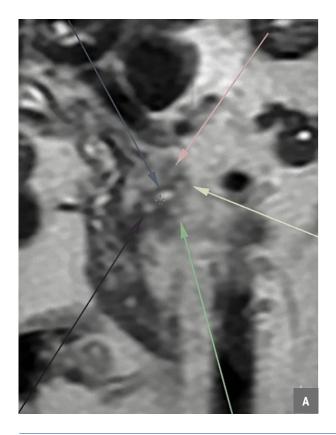
Most often. we considered the signs of fibrous indurative changes in the supposed pancreatic stump at the preoperative stage to be positive, since the pancreatic anastomosis formed during the operation was reliable (due to the absence of thread eruption). One of the most characteristic manifestations of fibrosis and induration was the presence of a domino symptom. In cases where the MRI picture fit into the symptom complex of induration, surgeons applied pancreatic anastamoses on the "lost" drainage. Most often, the operator confidently detected an enlarged pancreatic duct, information about the location of which was also obtained during an MRI examination. The duct was sewn into the lumen of the small intestine. The regions of heterogeneous signal were determined in the supposed stump of the pancreas (arrows are marked in Figure 3A). Microscopic examination determines the enlarged pancreatic duct, cystically altered small ducts against the background of fibrosis in the pancreatic tissue (Fig. 3B).

MRI-picture of inflammatory and dystrophic changes in the supposed stump of the pancreas

послеоперационного периода при хирургическом лечении рака поджелудочной железы

This symptom complex was characterized by the presence of blurred contours of the alleged pancreatic stump, swelling, inflammatory changes, or the inability to determine its boundaries from the underlying adipose tissue, when visually, when describing an MRI study, the area of interest was perceived by us as "white on white". The "white on white" symptom was more characteristic of dystrophic changes, when the pancreatic tissue itself was replaced by fat cells (Fig. 4).

Later, during the joint intaoperative evaluation with surgeons, we encountered a loose, inflamed gland. The possibility of determining the pancreatic duct in the stump was difficult, which led to the need to form an anastomosis either with the entire section of the gland (23 cases), or when installing drainage into the duct by performing external drainage through the enterostome. These cases were accompanied by the greatest number of complications (38 %). Extremely unfavorable were cases when, during the MRI examination in the preoperative period, the contours



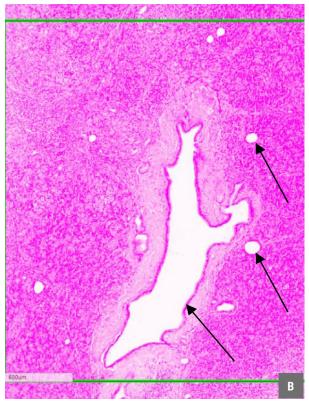


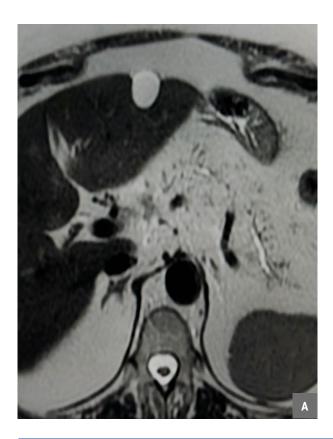
Fig. 3. The "domino" symptom in the perifocal zone of the tumor. In the pancreatic tissue outside the tumor, areas of fibrous tissue with cystic duct expansion are determined. H&E Staining, × 200.

of the gland were not determined, and intraoperative surgeons characterized its density as "soft" during the revision of the pancreas.

Development of a scale for calculating the risk of pancreatic fistula following a radical resections of the pancreas based on MRI data.

In 2013, based on a multicenter study led by M. Callery and including the results of treatment of 445 patients who underwent pancreato-deodunal resections (PDR), a 10-point prognostic scale for the occurrence of postoperative pancreatic fistula (Fistula Risk Score) was developed and adopted [11]. Risk factors on this scale were the soft texture of the gland, pathomorphological data - ampullary or duodenal cancer, neuroendocrine neoplasia, cystic tumors; pancreatic duct diameter less than 5 mm, intraoperative blood loss more than 400 ml. In 2017, the risk scale was modified by American pancreatologists: the texture of the gland and the diameter of the pancreatic duct remained, and gender, body mass index and bilirubin level were added [17]. All the scales described above can only be used intraoperatively. However, prevention of postoperative pancreatitis of the stump of the gland and pancreatic fistula should begin in the preoperative period.

When using known scales, risk stratification is possible only intraoperatively, which does not allow the use of preoperative methods for the prevention of fistula formation. This also applies to the appointment of synthetic analogues of somatostatin in the preoperative period, the duration of preoperative preparation. The scale developed by us, including MRI criteria, allows us to predict the course of the postoperative period at the preoperative stage. The MRI-symptom complexes proposed by us (fibrous indurative changes in the pancreatic stump, unchanged pancreatic tissue, inflammatory and dystrophic changes in the pancreatic stump) have a clear morphological confirmation. During the preoperative period, repeated MRI examination is possible to objectify the effectiveness of therapeutic preparation (reduction of the picture of inflammation) and its effect on the structure of the alleged pancreatic stump (Table 3). The scale does not require statistical calculations, which makes



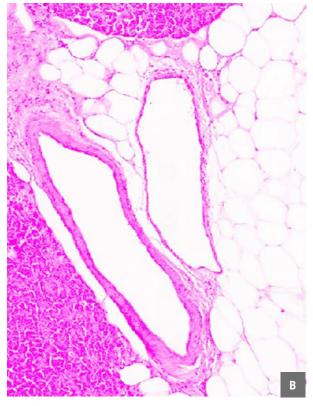


Fig. 4. The "white on white" symptom. There is an almost complete absence of the contours of the pancreas, the tissue of which seems to merge with the surrounding adipose tissue. H&E Staining, × 200.

it available for use. The experience of using such scales shows that their popularity among practitioners is due to the lack of complex mathematical calculations, and the results obtained are understandable.

To predict the possible development of pancreatic fistula retrospectively, we applied 3 risk scales for each patient. At the same time, in the case of calculation on the FRS scale, prognosis mismatch occurred in 52 patients (12.41 %), on the modified FRS scale – in 45 (10.74 %), and on the MRI risk assessment scale – in 48 (11.45 %) patients. In the future, we analyzed each specific case of forecast mismatch. When using the FRS scale, fistulas did not develop in 15 (3.58 %) patients, although they were predicted, in 37 (8.83 %) they developed, although

they were not predicted; with modified FRS - 13 (3.1 %) and 32 (7.66 %), respectively. In the case of using MRI for prediction, 31 (7.4 %) patients did not develop fistulas, although they were predicted, 17 (4.06 %) developed fistulas, but were not predicted. Since we were more interested in the sensitivity of the calculation in favor of predicting a severe complication, analyzing the above figures, the risk calculation turned out to be more accurate when using MRI readings: with the first two scales, the discrepancy was 37 (8.83 %) and 32 (7.64 %), with the third – 17 (4.06 %). Further statistical analysis showed a significant difference (criterion χ^2) when comparing the first (FRS) and third (MRI) scales (p = 0.0477), and a trend when comparing the second (modified FRS) and third (MRI) scales (p = 0.0544).

Table 3. Modified risk scale for the development of pancreatic fistula according to the results of preoperative studies					
Risk factor					
Sex	male	2			
	female	0			
Body Mass Index, kg/m²	< 25	0			
	≥ 25	1			
Total bilirubin, mcMol/L	< 20	0			
	≥ 20	1			
Pancreatic duct diameter identified with the use of MRI, mm	< 3	4			
	3-6	3			
	≥ 6	0			
The texture of the parenchyma of the gland, determined by MRI	Pancreatic stump fibrous and indurative alterations	0			
	Intact pancreatic tissue	1			
	Inflammatory and dystrophic alterations in the pancreatic stump	2			
Risk, summary of poins	minimal	0-2			
	low	3-6			
	intermediate	7-8			
	high	9-10			

Kolesnikov E. N., lozefi D. Ya., Kit O. I., Maksimov A. Yu. ✓ / Magnetic resonance imaging relevance in diagnosis and prognosis of early postoperative period following pancreatic cancer surgical treatment

CONCLUSION

The scale developed by us with the help of additional MRI criteria based on a clearer description of the perifocal zone of the tumor and the entire

pancreatic tissue can be used for the subsequent selection of surgical treatment methods, which generally reduces the number of surgical complications by reducing the number of pancreatic fistulas.

References

- 1. The state of oncological care to the population of Russia in 2021. Edited by A.D. Kaprin, V. V. Starinsky, A. O. Shakhzadova. Moscow: P. A. Herzen MNIOI Branch of the National Medical Research Radiological Center, 2022, 239 p. (In Russ.).
- 2. Tamburrino D, Partelli S, Crippa S, Manzoni A, Maurizi A, Falconi M. Selection criteria in resectable pancreatic cancer: a biological and morphological approach. World J Gastroenterol. 2014 Aug 28;20(32):11210–11215. https://doi.org/10.3748/wjg.v20.i32.11210
- 3. Schima W, Böhm G, Rösch CS, Klaus A, Függer R, Kopf H. Mass-forming pancreatitis versus pancreatic ductal adenocarcinoma: CT and MR imaging for differentiation. Cancer Imaging. 2020 Jul 23;20(1):52. https://doi.org/10.1186/s40644-020-00324-z
- 4. Zhu X, Lu N, Zhou Y, Xuan S, Zhang J, Giampieri F, et al. Targeting Pancreatic Cancer Cells with Peptide-Functionalized Polymeric Magnetic Nanoparticles. Int J Mol Sci. 2019 Jun 19;20(12):2988. https://doi.org/10.3390/ijms20122988
- Hijioka S, Hara K, Mizuno N, Imaoka H, Bhatia V, Mekky MA, et al. Diagnostic performance and factors influencing the accuracy of EUS-FNA of pancreatic neuroendocrine neoplasms. J Gastroenterol. 2016 Sep;51(9):923–930. https://doi.org/10.1007/s00535-016-1164-6
- 6. Wilson JM, Mukherjee S, Brunner TB, Partridge M, Hawkins MA. Correlation of 18F-Fluorodeoxyglucose Positron Emission Tomography Parameters with Patterns of Disease Progression in Locally Advanced Pancreatic Cancer after Definitive Chemoradiotherapy. Clin Oncol (R Coll Radiol). 2017 Jun;29(6):370–377. https://doi.org/10.1016/j.clon.2017.01.038
- Bieliuniene E, Frøkjær JB, Pockevicius A, Kemesiene J, Lukosevicius S, Basevicius A, et al. Magnetic Resonance Imaging as a Valid Noninvasive Tool for the Assessment of Pancreatic Fibrosis. Pancreas. 2019 Jan;48(1):85–93. https://doi.org/10.1097/MPA.000000000001206
- 8. Baichorov ME. Prevention of complications after laparoscopic pancreatoduodenal resection. Dissertation. Moscow, 2021. (In Russ.).
- 9. Gorin DS, Kriger AG, Galkin GV, Kalinin DV, Glotov AV, Kaldarov AR, et al. Predicting of pancreatic fistula after pancreatoduodenectomy. Pirogov Russian Journal of Surgery. 2020;(7):61–67. (In Russ.). https://doi.org/10.17116/hirurgia202007161, FDN: OURZWR
- 10. Kovalenko ZA, Efanov MG. Scoring systems to predict pancreatic fistula after Whipple procedure. Pirogov Russian Journal of Surgery. 2021;(7):71–76. (In Russ.). https://doi.org/10.17116/hirurgia202107171, EDN: ZRAZZQ
- 11. Callery MP, Pratt WB, Kent TS, Chaikof EL, Vollmer CM. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. J Am Coll Surg. 2013 Jan;216(1):1–14. https://doi.org/10.1016/j.jamcollsurg.2012.09.002
- 12. Miller BC, Christein JD, Behrman SW, Drebin JA, Pratt WB, Callery MP, et al. A multi-institutional external validation of the fistula risk score for pancreatoduodenectomy. J Gastrointest Surg. 2014 Jan;18(1):172–179. https://doi.org/10.1007/s11605-013-2337-8
- 13. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. Surgery. 2017 Mar;161(3):584–591. https://doi.org/10.1016/j.surg.2016.11.014
- Mungroop TH, van Rijssen LB, van Klaveren D, Smits FJ, van Woerden V, Linnemann RJ, et al. Alternative Fistula Risk Score for Pancreatoduodenectomy (a-FRS): Design and International External Validation. Ann Surg. 2019 May;269(5):937–943. https://doi.org/10.1097/SLA.00000000000002620
- 15. Gorin DS. Specific complications in surgery of pancreatic tumors. Dissertation. Moscow. Moscow, 2022. (In Russ.).
- 16. Sawlani V, Patel MD, Davies N, Flintham R, Wesolowski R, Ughratdar I, et al. Multiparametric MRI: practical approach and pictorial review of a useful tool in the evaluation of brain tumours and tumour-like lesions. Insights Imaging. 2020 Jul 17;11(1):84. https://doi.org/10.1186/s13244-020-00888-1

Колесников Е. Н., Иозефи Д. Я., Кит О. И., Максимов А. Ю.[™] / Значение магнитно-резонансной томографии в диагностике и прогнозе течения раннего послеоперационного периода при хирургическом лечении рака поджелудочной железы

17. Kantor O, Talamonti MS, Pitt HA, Vollmer CM, Riall TS, Hall BL, et al. Using the NSQIP Pancreatic Demonstration Project to Derive a Modified Fistula Risk Score for Preoperative Risk Stratification in Patients Undergoing Pancreaticoduodenectomy. J Am Coll Surg. 2017 May;224(5):816–825. https://doi.org/10.1016/j.jamcollsurg.2017.01.054

Information about authors:

Evgenii N. Kolesnikov – Dr. Sci. (Med.), associate professor, head of the department of abdominal oncology No. 1, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation. ORCID: https://orcid.org/0000-0001-9749-709X, SPIN: 8434-6494, AuthorID: 347457, Scopus Author ID: 57190297598

Dmitriy Ya. lozefi – head of department of magnetic resonance imaging, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation. ORCID: https://orcid.org/0000-0001-5519-1113, SPIN: 9650-8237, AuthorID: 799176

Oleg I. Kit – RAS academician, Dr. Sci. (Med.), professor, CEO, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation. ORCID: https://orcid.org/0000-0003-3061-6108, SPIN: 1728-0329, AuthorID: 343182, ResearcherID: U-2241-2017, Scopus Author ID: 55994103100

Aleksei Yu. Maksimov 🖾 – Dr. Sci. (Med.), professor, deputy director general for advanced scientific research, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation. ORCID: https://orcid.org/0000-0002-1397-837X, SPIN: 7322-5589, AuthorID: 710705, Scopus Author ID: 56579049500

Contribution of the authors:

Kolesnikov E. N. – scientific guidance, material collection and processing; lozefi D. Ya. – material collection and processing, draft writing; Kit O. I. – study concept, conclusions;

Maksimov A. Yu. - material processing, text revision and scientific editing.