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Advantages of mesenteric approach to pancreatoduodenectomy for pancreatic head cancer with invasion of great vessels

Mikael G. Abgaryan, Aleksei G. Kotelnikov, Aleksandr N. Polyakov, Ivan G. Avdyukhin, Omar A. Egenov, Henian Sun, Ivan S. Stilidi

N.N. Blokhin National Medical Research Center of Oncology
(Moscow, Russian Federation)

Abstract

Aim – to compare standard and mesenteric approaches to surgical treatment of patients with pancreatic head cancer invading the portal and/or superior mesenteric veins and to evaluate their advantages.

Material and methods. Surgical treatment of 192 patients with pancreatic head cancer with portal and/or superior mesenteric vein invasion was performed. In 43 (22.4%) cases, pancreatoduodenal resection was performed through the mesenteric approach, in the remaining 149 (77.3%) patients, the standard approach to surgical treatment was used.

Results. The median duration of operations with the mesenteric approach was 290 min., with the standard one, 300 min., the median blood loss was 1120 ml and 1800 ml, respectively, $p=0.0002$. No statistically significant differences in the long-term treatment results were found for mesenteric and standard approaches: progression of pancreatic head adenocarcinoma was diagnosed in 48.8% and 49%, respectively; the median overall survival was 24.5 months and 22.3 months; the median progression-free survival was 21.3 months and 22.1 months, respectively. Analysis of long-term treatment results depending

on the type of approach and the degree of radicality of surgical intervention showed that the incidence of local relapse with standard access in non-radically operated patients is significantly higher (40.6% vs 7.7%, $p = 0.001$).

Conclusion. The advantages of the mesenteric approach over the standard approach to surgical treatment of patients with pancreatic head cancer with portal and/or superior mesenteric vein invasion are as follows: 1) it makes it possible to assess the prevalence and operability of the tumor as early as at the beginning of the surgical intervention; 2) it ensures a significantly higher frequency of operations in the R0 volume; 3) it ensures significantly less blood loss during surgery; 4) after circular resection of the main veins it provides more opportunities to perform end-to-end plastic surgery, which reduces the risk of thrombosis due to the formation of only one anastomosis and reduces the time of clamping of the main veins, reducing the risk of liver and intestinal ischemia.

Keywords: mesenteric approach; pancreatic head cancer; pancreatoduodenectomy; portal vein resection; superior mesenteric vein resection.

Conflict of interest: nothing to disclose.

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Information about authors

Mikael G. Abgaryan – Cand. Sci. (Medicine), Senior Researcher, Oncologist of the Department of Abdominal Oncology No. 1 of the N.N. Trapeznikov Research Institute of Clinical Oncology. ORCID: 0000-0001-8893-1894

E-mail: abgaryan.mikael@gmail.com

Aleksei G. Kotelnikov – Dr. Sci. (Medicine), Leading Researcher of the Department of Abdominal Oncology No. 2 (Hepatopancreatobiliary Zone Tumors) of the N.N. Trapeznikov Research Institute of Clinical Oncology. ORCID: 0000-0002-2811-0549

E-mail: kotelnikovag@mail.ru

Aleksandr N. Polyakov – Cand. Sci. (Medicine), Senior Researcher of the Department of Abdominal Oncology No. 2 (Hepatopancreatobiliary Zone Tumors) of the N.N. Trapeznikov Research Institute of Clinical Oncology. ORCID: 0000-0001-5348-5011

E-mail: dr.alexpg@gmail.com

Ivan G. Avdyukhin – oncologist of the Department of Abdominal Oncology No. 1 of the N.N. Trapeznikov Research Institute of Clinical Oncology.

ORCID: 0000-0002-3524-1037

E-mail: ivan.avdyukhin@yandex.ru

Omar A. Egenov – Cand. Sci. (Medicine), Oncologist, Department of the Abdominal Oncology No. 2 (Hepatopancreatobiliary Zone Tumors) of the N.N. Trapeznikov Research Institute of Clinical Oncology.

ORCID: 0000-0002-8681-7905

E-mail: egenov.omar@mail.ru

Henian Sun – oncologist of the Department of Abdominal Oncology No. 1 of the N.N. Trapeznikov Research Institute of Clinical Oncology.

ORCID: 0000-0001-5574-0047

E-mail: sunalaric@gmail.com

Ivan S. Stilidi – Academician of the Russian Academy of Sciences, Dr. Sci. (Medicine), Director.

ORCID: 0000-0002-0493-1166

E-mail: biochimia@yandex.ru

***Corresponding Author**

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Преимущества брыжеечного доступа к панкреатодуоденальной резекции при раке головки поджелудочной железы с инвазией магистральных сосудов

М.Г. Абгарян, А.Г. Котельников, А.Н. Поляков, И.Г. Авдюхин,
О.А. Егенов, Хэнянь Сунь, И.С. Стилиди

ФГБУ «Национальный медицинский исследовательский центр онкологии имени Н.Н. Блохина»
Минздрава России (Москва, Российская Федерация)

Аннотация

Цель – сравнить стандартный и брыжеечный доступы к хирургическому лечению больных раком головки поджелудочной железы, инвазирующим воротную и/или верхнюю брыжеечную вены, и оценить их преимущества.

Материал и методы. Проведено хирургическое лечение 192 больных раком головки поджелудочной железы с инвазией воротной и/или верхней брыжеечной вены. В 43 (22,4%) случаях панкреатодуоденальную резекцию выполнили через брыжеечный доступ, у остальных 149 (77,3%) пациентов использовали стандартный подход к хирургическому лечению.

Результаты. Медиана длительности операций с брыжеечным доступом составила 290 мин., со стандартным – 300 мин., медиана кровопотери – соответственно 1120 мл и 1800 мл, $p=0,0002$. Статистически значимых различий отдаленных результатов лечения при брыжеечном и стандартном доступах не выявлено: прогрессирование аденокарциномы головки поджелудочной железы диагностировано соответственно у 48,8% и 49%, медиана общей выживаемости составила 24,5 мес. и 22,3 мес., медиана выживаемости без прогрессирования – 21,3 мес. и 22,1 мес. соответственно. Анализ отдаленных результатов лечения в зависимости от вида доступа и степени радикальности хирургического вмешательства

показал, что частота развития местного рецидива при стандартном доступе у нерадикально оперированных больных достоверно выше (40,6% vs 7,7%, $p=0,001$).

Заключение. Преимущества брыжеечного доступа перед стандартным подходом к хирургическому лечению больных раком головки поджелудочной железы с инвазией воротной и/или верхней брыжеечной вены заключаются в следующем: 1) дает возможность оценить распространенность и операбельность опухоли уже в начале хирургического вмешательства; 2) обеспечивает достоверно более высокую частоту выполнения операций в объеме R0; 3) обеспечивает достоверно меньшую кровопотерю во время операции; 4) после циркулярной резекции магистральных вен дает больше возможностей выполнить пластику «конец в конец», что снижает риск развития тромбоза за счет формирования только одного анастомоза и уменьшает время пережатия магистральных вен, уменьшая риск ишемии печени и кишечника.

Ключевые слова: брыжеечный доступ; рак головки поджелудочной железы; панкреатодуоденальная резекция; резекция воротной вены; резекция верхней брыжеечной вены.

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Сведения об авторах

Абгарян М.Г. – канд. мед. наук, старший научный сотрудник, врач-онколог отделения абдоминальной онкологии №1 НИИ Клинической онкологии имени академика РАН и РАМН Н.Н. Трапезникова.

ORCID: 0000-0001-8893-1894

E-mail: abgaryan.mikael@gmail.com

Котельников А.Г. – д-р мед. наук, ведущий научный сотрудник отделения абдоминальной онкологии №2 (опухолей гепатопанкреатобилиарной зоны) НИИ Клинической онкологии имени академика РАН и РАМН Н.Н. Трапезникова.

ORCID: 0000-0002-2811-0549

E-mail: kotelnikovag@mail.ru

Поляков А.Н. – канд. мед. наук, старший научный сотрудник отделения абдоминальной онкологии №2 (опухолей гепатопанкреатобилиарной зоны) НИИ Клинической онкологии имени академика РАН и РАМН Н.Н. Трапезникова.

ORCID: 0000-0001-5348-5011

E-mail: dr.alexpr@gmail.com

Авдюхин И.Г. – врач-онколог отделения абдоминальной онкологии №1 НИИ Клинической онкологии имени академика РАН и РАМН Н.Н. Трапезникова.

ORCID: 0000-0002-3524-1037

E-mail: ivan.avdyukhin@yandex.ru

***Егенов Омар Алиевич** – канд. мед. наук, врач-онколог отделения абдоминальной онкологии №2 (опухолей гепатопанкреатобилиарной зоны) НИИ Клинической онкологии имени академика РАН и РАМН Н.Н. Трапезникова.

ORCID: 0000-0002-8681-7905

E-mail: egenov.omar@mail.ru

Сунь Хэнянь – врач-онколог отделения абдоминальной онкологии №1 НИИ Клинической онкологии имени академика РАН и РАМН Н.Н. Трапезникова.

ORCID: 0000-0001-5574-0047

E-mail: sunalaric@gmail.com

Стилиди И.С. – академик РАН, профессор, д-р мед. наук, директор.

ORCID: 0000-0002-0493-1166

E-mail: biokhimia@yandex.ru

***Автор для переписки**

Список сокращений

ПЖ – поджелудочная железа; ПДР – панкреатодуоденальная резекция; ВБВ – верхняя брыжеечная вена; ВВ – воротная вена.

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INTRODUCTION

The literature contains very few reports on the mesenteric approach for surgical treatment of pancreatic head cancer. The first publication on the mesenteric approach to pancreatoduodenal resection appeared as late as in 1993. Japanese surgeons A. Nakao *et al.* suggested the mesenteric approach using the principal rule of oncological surgery as the guide: minimal contact with the tumor prior to its mobilization and vessel ligation [1]. The authors developed an approach through the root of the transverse mesocolon to sequentially expose the branches of the superior mesenteric artery. This provided the possibility of evaluating the resectability of the tumor as early as on the start of the surgical intervention, dissecting the tissue from the side not affected by the tumor, ligate the lower pancreoduodenal artery and other branches of the superior mesenteric artery in the early stages of the surgery, perform lymphadenectomy around the superior mesenteric artery and the superior mesenteric vein (SMV), facilitated the reconstruction of the portal vein in the formation of the end-to-end anastomosis, facilitated decrease of venous congestion in the area of the pancreatic head, minimize the intraoperative blood loss and improve the possibilities of performing the radical resection of the tumor [2, 3]. In 2007, I. Gockel *et al.* [4] reported the use of mesenteric approach

to perform the total resection of the 'mesopancreas'. This anatomic term has been mentioned in the literature only in the recent years similarly to the term 'mesorectum' and the surgery of total mesorectumectomy in colorectal cancer [4]. No final definition of the 'mesopancreas' has been formed to date despite the fact that the Japanese classification of pancreatic cancer [5] contains a detailed description of the anatomy of extrapancreatic neural plexi. In the literature, 'mesopancreas' is in many cases identified as the 'reproportal plate' [6–8], referring to the retroperitoneal adipose tissue located posterior to the pancreas and the portal vein and anterior to the aorta, between the origins of the superior mesenteric artery and the celiac trunk. This is not absolutely true from the anatomical standpoint, since microscopically it is the adipose tissue and the neural plexi of the pancreatic head (PLpH and PLpHI), limited by the visceral arteries and not covered with fascia [9–12]. However, the term 'mesopancreas' is important from the clinical and surgical perspectives, since resection of the entire aforementioned complex of tissues is actually a radical resection [10, 13, 14].

Considering the clinical relevance of this issue and the near absence of studies comparing mesenteric and standard approaches for surgical treatment of pancreatic head cancer, we present the results of our investigation.

■ AIM

To compare standard and mesenteric approaches to surgical treatment of patients with pancreatic head cancer invading the portal and/or superior mesenteric veins and to evaluate their advantages.

■ MATERIAL AND METHODS

This study includes a retrospective analysis of 192 patients' records who had undergone surgical treatment of the pancreatic head invading the portal and/or superior mesenteric veins at the N.N. Blokhin National Medical Research Center of Oncology of the Ministry of Health of Russia in 2002-2023. In 43 (22.4%) cases, pancreatoduodenal resection was performed through the mesenteric approach, in 149 (77.3%) patients, the standard approach to surgical treatment was used. Mesenteric approach was used in 2 (12.5%) of the 16 patients with resection of the portal vein; in 15 (18.1%) of 83 patients with resection of the superior mesenteric vein; in 26 of 93 patients (28%), with resection of both major veins (portal and superior mesenteric veins).

Circular resection of the principal veins was performed in 36 (83.7%) patients using mesenteric approach and 108 (72.5%) patients using standard approach, the median length of resection was 4 cm (from 1.5 to 8 cm) and 3 cm (from 0.5 to 1 cm), respectively, with a statistically significant difference between medians, $p=0.0009$ (Table 1).

The reconstruction of the principal veins in these patients was performed as follows:

1) End-to-end anastomosis in 21 (48.8%) and 76 (51%) patients, median length: 3 cm (from 1.5 to 7 cm) and 2 cm (from 0.5 to 4.5 cm), respectively, with a statistically significant difference between medians, $p=0.007$;

2) Autovenous prosthetic repair in 2 (4.7%) and 4 (2.7%) patients, median length: 4.5 cm (4 and 5 cm) and 3.5 cm (from 2 to 4 cm);

3) Gore-Tex synthetic prosthetic repair in 13 (30.2%) and 28 (18.8%) patients, with credible difference between groups, $p=0.083$. The median lengths were 5 cm and 3 cm, respectively, with a statistically significant difference between medians, $p=0.006$.

Partial wall resection was performed in 7 (16.3%) and 41 (27.5%) patients, with median resection lengths of 2 cm and 1.5 cm, respectively. For reconstruction, a running suture technique was used, with median suture lengths of 2 cm and 1.5 cm for each group.

RESULTS

The histological study identified adenocarcinoma in all 192 patients included in the study. The R0 tumor resection rate, confirmed histologically, was 97.7% ($n=42$) with the mesenteric approach and credibly exceeded this value in the standard approach to surgery: only 78.5% ($n=117$, $p=0.001$). R1 surgeries were performed in 2.3% ($n=1$) patients with mesenteric approach and 19.5% ($n=29$, $p=0.003$) with standard approach; R2 surgeries, in 0% and 2%, respectively. The medians of surgery durations in the mesenteric and standard approaches were near similar, 290 and 300 minutes, respectively; at the same time, the median blood loss in the mesenteric approach is credibly lower, 1120 ml vs. 1800 ml, $p=0.0002$. The blood loss under mesenteric approach varied

from 200 ml to 3200 ml, with the standard approach, from 50 ml to 8500 ml.

We identified no statistically significant differences in the remote outcomes of treatment of patients with pancreatic head cancer with invasion of major veins regardless of the type of surgical approach. Progression of adenocarcinoma of the pancreatic head was diagnosed in 48.8% ($n=21$) patients with mesenteric approach and in 49% ($n=73$) patients with standard approach. The local recurrence rate was 14% ($n=6$) and 14.8% ($n=22$) respectively, the mortality rate was 55.8% ($n=24$) and 56.4% ($n=84$), the median survival rate was 24.5 months and 22.3 months, the median progression-free survival was 21.3 months and 22.1 months. At the moment of the study completion, 41.9% ($n=18$) of patients with mesenteric approach and 42.3% ($n=63$) with standard approach remained alive without evidence of disease; tumor progression was observed in 2.3% ($n=1$) and 1.3% ($n=2$) of patients, respectively/ Deaths occurred due to surgical complications: 9.3% ($n=4$) and 8.7% ($n=13$); or disease progression 46.5% ($n=20$) and 47.7% ($n=71$).

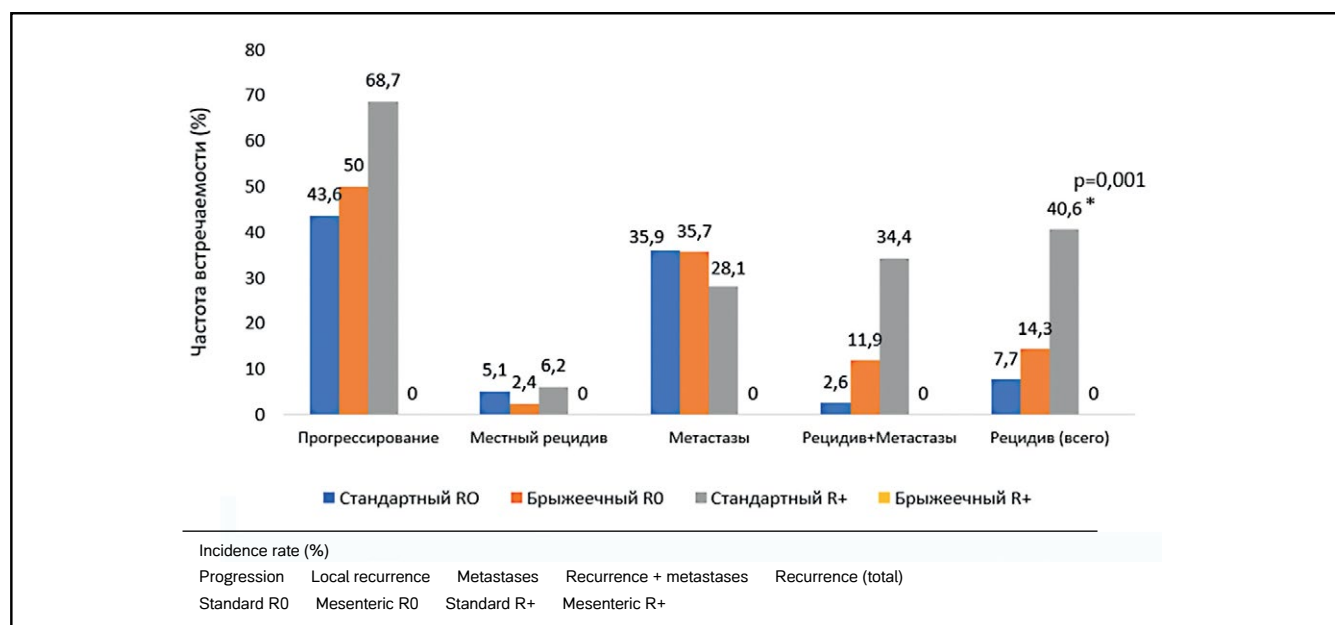
Since we found no statistically significant differences in long-term treatment outcomes based on surgical approach, we evaluated its impact in combination with the degree of radical

Parameter		Approach type			
		Standard (n=149)		Mesenteric (n=43)	
		Abs.	%	Abs.	%
Portal and/or superior mesenteric vein resection type					
Circular	Type	108	72,5	36	83,7
	Length, cm (min-max)	3 [2;5; 4] (0,5-10)		4* [3; 5,8 (1,5-8,0) 0,0009	
Partial wall	Type	41	27,5	7	16,3
	Length, cm (min-max)	1,5 [1; 2] (0,5-3,5)		2 [1,5; 2,5] (0,5-2,5)	
Portal and/or superior mesenteric vein reconstruction type					
Running suture		41	27,5	7	16,3
Median length, cm (min-max)		1,5 [1; 2] (0,5-3,5)		2 [1,5; 2,5] (0,5-2,5)	
End-to-end		76	51,0	21	48,8
Median length, cm (min-max)		2,5 [2; 3,5] (0,5-4,5)		3 [2,5; 5,0] (1,5-7)* 0,007	
Autovenous prosthesis		4	2,7	2	4,7
Median length, cm (min-max)		3,0 [2,5; 3,5] (2-4)		4,5 [4; 5] (4-5)	
Synthetic prosthesis		28	18,8	13	30,2
Median length, cm (min-max)				5 [4; 6] (3-8)* 0,006	
Degree of radicality of the surgery					
R0		117	78,5	42	97,7* 0,001
R1		29	19,5	1	2,3* 0,003
R2		3	2,0	-	-
Медиана длительности операции, мин. (мин-макс)		300 [255; 360] (190-640)		290 [240; 330] (190-460)	
Медиана кровопотери, мл (мин-макс)		1800 [900; 3000] (50,0-8500,0)		1120* [700; 1500] (200,0-3200,0) 0,0002	
**Statistically significant differences as compared to the standard approach, p<0.05					

**Statistically significant differences as compared to the standard approach, $p<0.05$

Table 1. Characteristics of standard and mesenteric approaches to surgical treatment of patients with cancer of the head of the pancreas with invasion of the major veins

Таблица 1. Характеристика стандартного и брыжеечного доступов к хирургическому лечению больных раком головки ПЖ с инвазией магистральных вен



resection (Fig. 1). This approach allowed identification of a credibly more frequent development of local recurrences in non-radically operated patients with standard approach (40.6% vs. 7.7%, $p=0.001$).

DISCUSSION

Considering many years of clinical practice, this comparative study of mesenteric versus standard approaches for pancreatic head cancer with portal vein and/or superior mesenteric vein invasion demonstrates clear advantages of the mesenteric technique. Although the mesenteric approach required higher qualification of the operating surgeon, it gives the opportunity of performing radical surgeries credibly more frequently ($p=0.001$). We were able to perform R0 resection of the tumor invading the major veins in 97.7% patients, whereas similar radical surgeries using the standard approach were possible only in 78.5% patients.

The mesenteric approach also demonstrates a definitive advantage of significantly reduced intraoperative blood loss ($p=0.0002$). In our study, median blood loss in patients with mesenteric approach was 1200 ml, whereas in the standard approach it reached 1800 ml. Maximum individual blood loss in mesenteric approach was 3200 ml, whereas in the standard approach it was 2.6 times higher at 8500 ml. We believe that the reduced blood loss results from the ability provided by the mesenteric approach to assess tumor extent and resectability early in the operation, to ligate vessels feeding the tissues of the operating area, e.g. gastroduodenal and pancreaticoduodenal arteries.

Our analysis of the options of resection and reconstruction of major veins depending on the approach to the operating field showed that the mesenteric approach provides wide opportunities of end-to-end reconstruction of the portal vein and/or superior mesenteric vein without using the prosthetic after circular resection. Formation of only one anastomosis

Figure 1. Types and frequency of progression of pancreatic head cancer with invasion of the major veins depending on access to surgical treatment and the degree of its radicality.

Рисунок 1. Виды и частота прогрессирования рака головки ПЖ с инвазией магистральных вен в зависимости от доступа к хирургическому лечению и степени его радикальности.

significantly reduces the risk of thrombosis development. In the mesenteric approach, we formed the end-to-end anastomosis in the statistically greater resection length ($p=0.007$), which in individual cases reached 7 cm.

We identified no statistically significant effect of the approach on the long-term outcomes of surgical treatment of pancreatic head cancer with invasion into major veins. However, the analysis of long-term outcomes depending on the approach type and degree of radicality of surgery showed a credibly more frequent development of local recurrence in the standard approach in non-radically operated patients (40.6% vs. 7.7%, $p=0.001$). It is to be mentioned that by the end of the study the single non-radically operated patient with mesenteric approach survived without signs of tumor progression for 12 months after the surgery and adjuvant chemotherapy.

CONCLUSION

The advantages of mesenteric approach to surgical treatment of patients with pancreatic head cancer with invasion into portal and/or superior mesenteric vein were identified as follows: 1) possibility of assessing tumor extent and operability early in the procedure, 2) credibly more frequent R0 surgeries performance, 3) credibly reduced intraoperative blood loss, 4) more opportunities of end-to-end major vein reconstruction after the circular resection, which decreases the risk of thrombosis by forming just one anastomosis and reduces the time of compression of major veins, thus lowering the risk of ischemia of the liver and the intestines. ■

ADDITIONAL INFORMATION	ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ
Ethical Approval Statement. The article was performed as part of the dissertation "Angioplasty operations in abdominal oncology" for the degree of Doctor of Medical Sciences. The thesis topic was approved by the Scientific Council of the Scientific Research Institute of Clinical Oncology n.a. Academician of the Russian Academy of Sciences and the Russian Academy of Medical Sciences N.N. Trapeznikov, Blokhin National Research Medical Center of Oncology, Ministry of Health of the Russian Federation.	Этическая экспертиза. Статья выполнена в рамках диссертации «Ангиопластические операции в абдоминальной онкологии» на соискание ученой степени доктора медицинских наук. Тема диссертации утверждена на ученом совете НИИ Клинической онкологии имени академика РАН и РАМН Н.Н. Трапезникова ФГБУ НМИЦ онкологии имени Н.Н. Блохина Минздрава России.
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Conflict of interest. The authors declare that there are no obvious or potential conflicts of interest associated with the content of this article.	Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с содержанием настоящей статьи.
Contribution of individual authors. Abgaryan M.G., Avdyukhin I.G., Egenov O.A., Sun H.: data collection, analysis and interpretation, preparation of the text of the article. Stilidi I.S.: study concept and design. Kotelnikov A.G., Polyakov A.N.: editing of the article. The authors gave their final approval of the manuscript for submission, and agreed to be accountable for all aspects of the work, implying proper study and resolution of issues related to the accuracy or integrity of any part of the work.	Участие авторов. Абгарян М.Г., Авдюхин И.Г., Егенов О.А., Сунь Х. – сбор, анализ и интерпретация данных, подготовка текста статьи. Стилиди И.С. – концепция и дизайн работы. Котельников А.Г., Поляков А.Н. – редактирование текста статьи. Все авторы одобрили финальную версию статьи перед публикацией, выразили согласие нести ответственность за все аспекты работы, подразумевающую надлежащее изучение и решение вопросов, связанных с точностью или добросовестностью любой части работы.

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