

## RESECTION INTERVENTIONS IN THE TREATMENT OF HEPATOCELLULAR CANCER IN A SPECIALIZED SURGERY CENTER

Pelts V.A.<sup>1,2</sup>,  
Tropin V.E.<sup>1</sup>,  
Shatalin V.A.<sup>1</sup>

<sup>1</sup> Kuzbass Clinical Emergency Hospital  
named after M.A. Podgorbunsky  
(Nikolaya Ostrovskogo str. 22, Kemerovo  
650991, Russian Federation)

<sup>2</sup> Kemerovo State Medical University  
(Voroshilova str. 22a, Kemerovo 650056,  
Russian Federation)

Corresponding author:  
**Vladislav A. Pelts,**  
e-mail: vpel\_C@rambler.ru

### ABSTRACT

**Background.** The relevance of the treatment of hepatocellular cancer (HCC) is determined by a significant increase in the incidence rate and its high prevalence among primary malignant hepatic tumors.

**The aim of the study.** To summarize the experience of providing specialized medical care to patients with hepatocellular cancer.

**Methods.** We studied the direct results of treatment of patients with primary hepatic cancer treated at the Kuzbass Regional Hepatological Center for the period from January 2015 to August 2022. The materials for the study were medical records of patients with an established diagnosis of primary hepatic cancer, surgical records, results of pathohistologic examination. The exclusion criterion was diagnosed cholangiocellular carcinoma.

**Results.** During the period from 2015 to 2022, 59 patients with primary hepatic cancer were treated at the Kuzbass Regional Hepatological Center. Among them, hepatocellular cancer was diagnosed in 48 cases, cholangiocellular cancer – in 11 cases; radical surgery was performed in 12 patients with hepatocellular cancer; fatal outcome was noted in 1 (2.1 %) patient, complications in the postoperative period developed in 5 (41.7 %) cases and were ranked as I-3, IIb-1 and IVb-1 according to Clavien – Dindo classification.

**Conclusion.** The degree of risk of severe post-resection hepatic failure should be considered one of the main criteria in choosing a strategy for radical surgical treatment. New surgical approaches (laparoscopic vascular isolation of the portal blood flow, using temporary hemostasis in laparoscopic hepatic resections and the device for its implementation) in resection surgery of primary hepatic cancer can improve the immediate results of treatment.

**Key words:** hepatocellular carcinoma, two-staged hepatic resection, post-resection hepatic failure, methods of hemostasis

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## РЕЗЕКЦИОННЫЕ ВМЕШАТЕЛЬСТВА В ЛЕЧЕНИИ ГЕПАТОЦЕЛЛЮЛЯРНОГО РАКА В СПЕЦИАЛИЗИРОВАННОМ ЦЕНТРЕ ХИРУРГИИ

Пельц В.А.<sup>1,2</sup>,  
Тропин В.Е.<sup>1</sup>,  
Шаталин В.А.<sup>1</sup>

<sup>1</sup> ГАУЗ «Кузбасская клиническая  
больница скорой помощи  
им. М.А. Подгорбунского»  
(650991, г. Кемерово,  
ул. Николая Островского, 22, Россия)

<sup>2</sup> ФГБОУ ВО «Кемеровский  
государственный медицинский  
университет» Минздрава России  
(650056, г. Кемерово,  
ул. Ворошилова, 22а, Россия)

Автор, ответственный за переписку:  
**Пельц Владислав Александрович**,  
e-mail: vpel\_C@rambler.ru

### РЕЗЮМЕ

**Обоснование.** Актуальность вопроса лечения гепатоцеллюлярного рака (ГЦК) определяется значимым приростом показателя заболеваемости им и его высокой частотой встречаемости среди первичных злокачественных опухолей печени.

**Цель исследования.** Обобщение опыта оказания специализированной помощи больным гепатоцеллюлярным раком.

**Методы.** Изучены непосредственные результаты лечения больных первичным раком печени, пролеченных в Кузбасском областном гепатологическом центре (КОГЦ) за период с января 2015 по август 2022 г. Материалами для исследования были медицинские карты больных с установленным диагнозом первичного рака печени, протоколы хирургических вмешательств, результаты патолого-гистологического исследования. Критерий исключения – диагностированный холангиоцеллюлярный рак.

**Результаты.** За период с 2015 по 2022 г. в КОГЦ пролечено 59 пациентов с первичным раком печени, из них гепатоцеллюлярный рак диагностирован в 48 случаях, холангиоцеллюлярный рак – в 11; радикальное хирургическое лечение проведено 12 больным ГЦК; летальный исход отмечен у 1 (2,1 %) пациента, осложнения в послеоперационном периоде развились в 5 (41,7 %) случаях и имели градацию тяжести по Clavien – Dindo I-3, IIb-1, IVb-1.

**Заключение.** Степень риска развития тяжёлой пострезекционной печёночной недостаточности следует считать одним из основных критериев в выборе стратегии радикального хирургического лечения. Новые хирургические подходы (лапароскопическая сосудистая изоляция воротного кровотока, использование способа временного гемостаза при лапароскопических резекциях печени и устройства для его осуществления) в резекционной хирургии первичного рака печени позволяют улучшить непосредственные результаты лечения.

**Ключевые слова:** гепатоцеллюлярный рак, двухэтапная резекция печени, пострезекционная печёночная недостаточность, способы гемостаза

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## INTRODUCTION

Hepatocellular carcinoma (HCC) is a liver disease of tumorigenic nature, the prognosis of which is unfavorable, the five-year survival rate does not exceed 15 % [1, 2]. There is a correlation between the number of viral hepatitis B cases in a population and the incidence of primary hepatic cancer, with rates in Asian and central African countries higher than the global average of 150–500 per 100,000 population [3, 4]. Our country has primary hepatic cancer incidence rates of 4–5 cases per 100,000 population, which is 13th in the structure of cancer morbidity and 11th among causes of death. Every year in Russia more than 6 thousand new cases of primary hepatic cancer are detected, usually at a stage that is not subject to special types of medical care. The number of early (first and second) stages is detected in less than 10 % of cases; approximately 58 % of diagnoses correspond to stage 4 of the disease [5–7]. Morphologic verification with the diagnosis of primary hepatic cancer was performed in only 48.9–56.4 % of cases [6, 7]. Thus, the relevance of the treatment of hepatocellular cancer (HCC) is determined by a significant increase in the incidence rate, its high prevalence among primary malignant hepatic tumors, aggressive course of the disease and low figures of 5-year survival. Late disease diagnosis determines insufficient coverage of this group of patients with specialized treatment [8].

## MATERIAL AND METHODS

To analyze the immediate results of treatment, medical records of patients diagnosed with primary hepatic cancer, protocols of surgical interventions, and the results of pathohistological examination were studied. From 2015 to 2022, 48 patients with HCC were treated at the Kuzbass Regional Hepatological Centre (KRHC). There were 32 males (66.7 %) and 16 females (33.3 %); the mean age was  $59.9 \pm 2.6$  years. HCC was diagnosed by pathohistological examination. Thus, males were predominant among those who suffered from HCC.

All the patients admitted to the KRHC were examined according to the clinical guidelines of the Russian Ministry of Health and the standard of care, which included both “routine” methods of blood examination (Complete Blood Count and Biochemical Blood Test) and special methods, which were considered to be the main ones in diagnostics – an alpha-fetoprotein (AFP) test, radiological methods (abdominal ultrasound, multislice-CT of the abdomen, MRI of the abdomen). Liver fibroelastometry was also performed in all cases. In all patients diagnosed with cirrhosis, the functional class of hepatic function according to Child – Pugh was determined, the MELD model (Model for End-Stage Liver Disease) was investigated, and liver fibroelastometry was performed. Patients with diagnosed liver neoplasms less than 1 cm, unavailable for biopsy under ultrasound control, were subjected to dynamic follow-up with subse-

quent monthly follow-up examinations and ultrasound (U/S); in case of growth, they were subjected to histological verification by a fine needle aspiration (FNA) of the liver under U/S. In all other cases, histological verification was performed by needle biopsy under ultrasound control or by diagnostic laparoscopy. 39 patients underwent FNA of the liver under U/S; 9 patients underwent diagnostic laparoscopy and biopsy.

In the course of diagnostics, we used clarifying methods and rating scales of the patient’s functional state, the state of liver function, studied the correlation of the actual liver volume with the criteria for the application of resection method and transplantation technologies, which allowed us to choose the most rational method of treatment.

HCC patients were staged according to the Barcelona classification of HCC (BCLC, Barcelona – Clinic Liver Cancer), which is the most frequently used classification, taking into account the prevalence of the tumor process, functional state of the liver, objective condition of the patient and the expected effectiveness of treatment. However, BCLC has certain disadvantages associated with difficulties in the allocation of patients to stage B: only transarterial chemoembolization (TACE) is recommended in case of ambiguous criteria and recommended disease management [1].

ECOG status (Eastern Cooperative Oncology Group), assessment of liver function in patients with liver cirrhosis combined with HCC according to the following criteria: Child-Pugh classification, MELD, Milan criteria; TNM (Tumor, Nodus, Metastasis) staging was also performed when planning surgical treatment.

Such approach allowed to differentiate the strategy of surgical treatment according to the degree of possible risk of post-resection hepatic failure development, and where it was estimated as statistically significant, we applied stage surgical treatment, the essence of which consists in the formation of vicarious hypertrophy of the planned liver remnant after resection by reduction of portal blood flow of the resected liver lobe.

As a result of staging according to the Barcelona classification of HCC, the patients were distributed as follows: BCLC 0/A – 8 patients, BCLC B – 7, BCLC C – 32, BCLC D – 1.

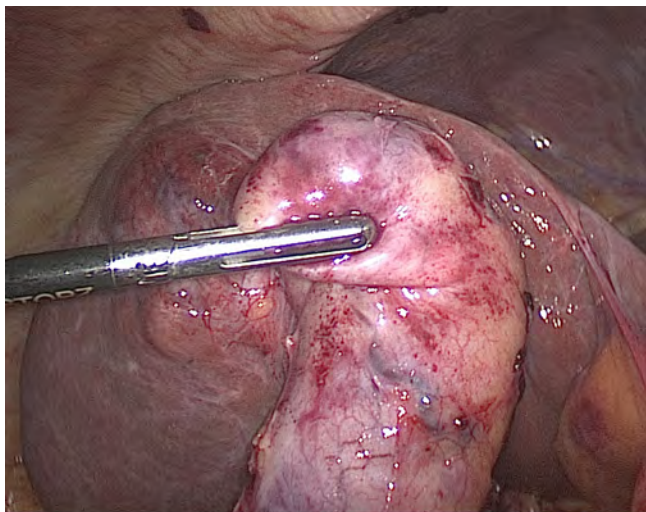
As a result of TNM staging, the patients were distributed as follows: T1bN0M0 – 2 patients, T2N0M0 – 5, T2N1M1 – 2, T2NxM1 – 4, T3N0M0 – 5, T3N1M1 – 16, T4N1M1 – 14.

Liver resections: Atypical (3 liver resections – by laparoscopic method) – 5; anatomical (right-sided hemihepatectomy) – 3; ALLPS (Associated Liver Partition and Portal vein ligation for staged hepatectomy) – 1; laparoscopic vascular isolation of portal vein – 2; staged extended right-sided hemihepatectomy – 2; liver transplantation – 1.

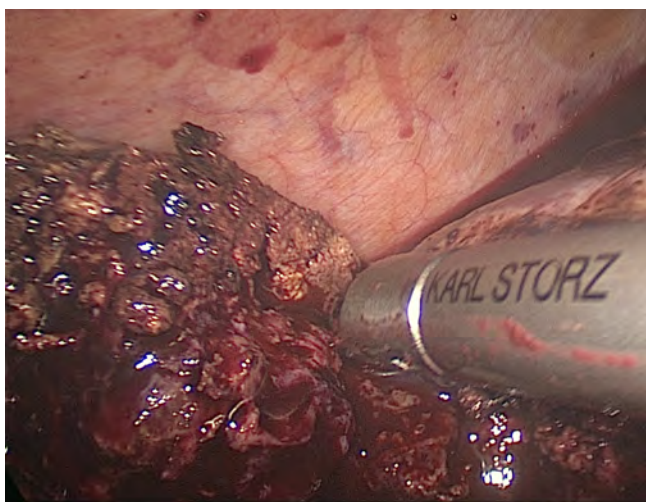
In 3 cases the operation was performed in the volume of atypical liver resection by laparoscopic method, the method of instrumental liver clamping was used for parenchyma separation. Blood loss during surgery



ranged from 50 to 250 ml, with an average of  $150 \pm 58$  ml (Fig. 1–3).



**FIG. 1.**  
*Tumor of the right lobe of the liver with gallbladder invasion*



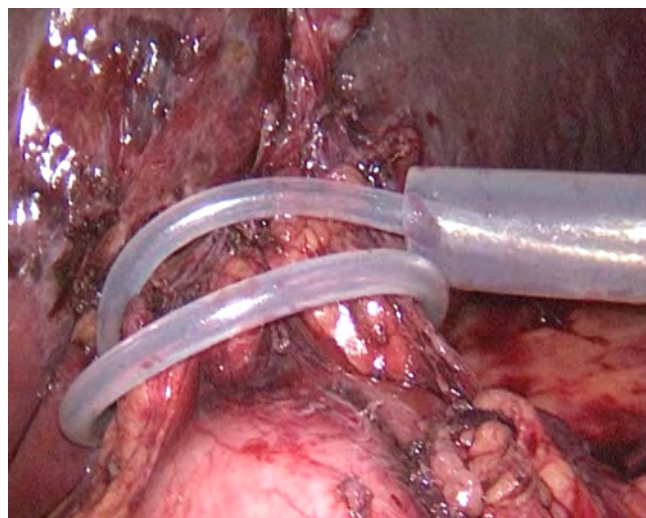
**FIG. 2.**  
*Stage of laparoscopic atypical resection of a liver area with a tumor*



**FIG. 3.**  
*The stage of final hemostasis after laparoscopic atypical liver resection*

During laparoscopic liver resection the ports were inserted in standard points for the resection method; in order to reduce surgical blood loss, we used the method of laparoscopic hemostasis and a device for its implementation (patent for an invention No. 2772189) (Fig. 4), which allowed to minimize blood loss and thus to achieve optimal immediate results of surgical treatment – absence of general and local complications in this group of patients.

In all cases of the resection method, surgical ultrasound was performed during the intervention in order to accurately localize the focal liver lesion, which allowed for precision liver resection.



**FIG. 4.**  
*Device for temporary hemostasis in laparoscopic liver resections*

In 2 cases due to technical impossibility to perform laparoscopic liver resection the intervention was performed through laparotomy access. The liver digitoclasis method was used to separate the parenchyma; blood loss during surgery ranged from 50 to 300 ml, averaging  $175 \pm 125$  ml.

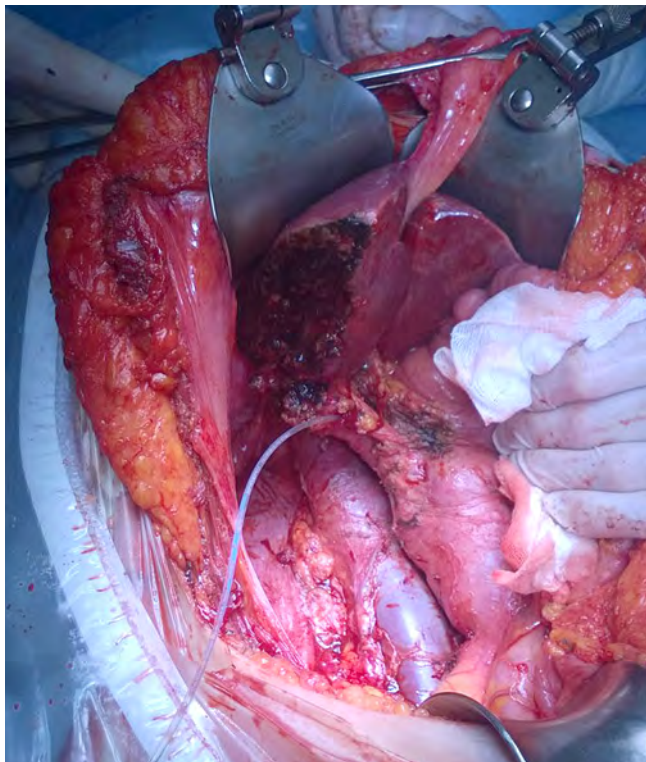
In 3 cases, right-sided hemihepatectomy was performed, when the risk of post-resection hepatic failure in case of extensive liver resections was estimated as minimal; blood loss during surgery ranged from 300 to 1,500 ml, with an average of  $766 \pm 371$  ml (Fig. 5).

The necessary conditions for this were functional class A of concomitant cirrhosis (Child – Pugh) and sufficient volume of liver parenchyma remaining after resection.

In 2 cases radical surgical treatment of HCC was performed by a stage method, the essence of which was the formation of vicarious hypertrophy of the remaining left lobe of the liver by laparoscopic vascular isolation of the portal vein of the liver. Subsequently, after a compensatory pause and formation of vicarious hypertrophy confirmed by CT with liver



volumetry, we performed a radical stage of surgical treatment – extended right-sided hemihepatectomy. Blood loss during surgery ranged from 500 to 1,000 ml, with an average of  $750 \pm 250$  ml (Fig. 6).



**FIG. 5.**  
*The final view of the surgical field after right-sided hemihepatectomy*

The 1<sup>st</sup> stage of liver resection was performed in one of the patients in order to clarify the clinical site for ALLPS technique and early formation of vicarious hypertrophy of the remaining liver stump; subsequently, the development of the Multiple Organ Dysfunction Syndrome (MODS) in the patient and his death from the developed complication were noted. Blood loss during surgery amounted to 500 ml.

In case of impossibility to use the resection method in HCC (invasion of the hepatic vein confluence area), orthotopic liver transplantation was performed in one case, uncomplicated course of the postoperative period was stated, and the patient was discharged on the 12th day of the postoperative period.

## IMMEDIATE RESULTS

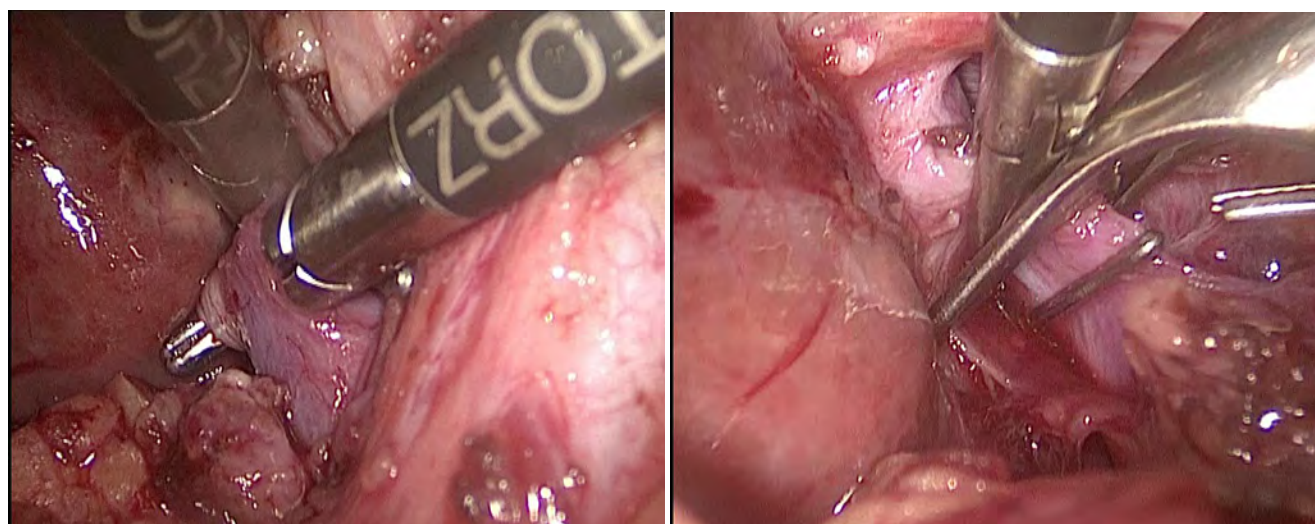
Twelve patients underwent radical surgery. Postoperative mortality was 1 (8.3 %) case and total mortality was 1 (2.1 %) case.

Complications developed in 5 (41.7 %) cases and had Clavien – Dindo I-3, IIIb-1 and IVb-1 grading of severity.

## DISCUSSION

As a result of generalization of the 7-year experience of rendering specialized medical care in the profile section to the patients with hepatocellular cancer it is necessary to state the shortcomings of early disease diagnostics, which is evidenced by a relatively small number of performed radical surgical interventions due to the diagnosis of predominantly advanced forms of the disease in 36 (75 %) cases.

The selection of patients for surgery should be considered problematic due to significant risks of hepatic failure after liver resection, taking into account the fact that HCC



**FIG. 6.**  
*Stages of laparoscopic vascular isolation of portal blood flow in the right hepatic vein*

relatively rarely develops in an intact organ, and more often – on the background of pre-existing cirrhosis. To solve the problem of post-resection hepatic failure, a group of patients with indications for a staged method of surgical treatment should be singled out.

Laparoscopic liver resections with the use of blood-saving techniques, as well as methods of staged surgical treatment, allowing to effectively prevent the development of severe forms of post-resection hepatic failure, should be considered promising in the treatment of HCC.

## CONCLUSION

The degree of risk of severe post-resection hepatic failure should be considered one of the main criteria in choosing a strategy for radical surgical treatment.

A new surgical approach (laparoscopic vascular isolation of portal blood flow) in operations to create vicarious hypertrophy of the group of two-stage surgical treatment in resection surgery of primary hepatic cancer, as well as the use of new methods of precision hemostasis during laparoscopic liver resections (method of temporary hemostasis during laparoscopic liver resections and a device for its implementation) allow to improve the immediate results of treatment of patients by reducing the number of severe forms of post-resection hepatic cancer, as well as the use of new methods of hemostasis during laparoscopic liver resections.

Resection techniques for HCC patients should be performed in a timely manner; laparoscopic liver resections should be considered a priority where possible [9].

Staged surgical treatment of HCC allows to perform extensive liver resections, bypassing the development of severe post-resection hepatic failure [10].

The use of ALPPS in the treatment of HCC is limited by the risks of unfavorable outcomes due to the development of severe postoperative complications [11].

Unsatisfactory results of HCC treatment require improvement of early diagnosis approaches.

### Financing

The study was conducted without sponsorship.

### Ethical review

The study complies with the principles of the Declaration of Helsinki (1964) and has been reviewed by the local ethical committee (meeting minutes No. 132B dated 01.11.2022).

### Conflict of interest

The authors of this article declare the absence of a conflict of interest.

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**Information about the authors**

**Vladislav A. Pelts** – Cand. Sc. (Med.), Head of the Kuzbass Regional Hepatological Centre, Kuzbass Clinical Emergency Hospital named after M.A. Podgorbunsky; Associate Professor at the Department of Advanced-Level Surgery, Kemerovo State Medical University, e-mail: vpel\_c@rambler.ru, <https://orcid.org/0000-0001-8230-6676>

**Valentin E. Tropin** – surgeon at the Kuzbass Regional Hepatological Centre, Kuzbass Clinical Emergency Hospital named after M.A. Podgorbunsky, e-mail: tropinvalentin19rus@mail.ru, <https://orcid.org/0000-0002-1103-7162>

**Vladimir A. Shatalin** – Resident Physician, Surgeon at the Kuzbass Regional Hepatological Centre, Kuzbass Clinical Emergency Hospital named after M.A. Podgorbunsky, e-mail: voff.shatalin@yandex.ru, <https://orcid.org/0000-0002-4968-0460>