

# THE ESTIMATION OF LIVER SURGERY RESULTS IN COLORECTAL METASTASES IN THE PRIVOLZHISKY DISTRICT MEDICAL CENTER OF FEDERAL MEDICO-BIOLOGIC AGENCY OF RUSSIA (NIZHNY NOVGOROD) ACCORDING TO INTERNATIONAL REGISTER LIVERMETSURVEY

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There have been analyzed the results of surgical treatment of 128 patients with metastases of colorectal cancer in the liver operated in the Privolzhsky District Medical Center of Federal Medico-Biologic Agency of Russia (Nizhny Novgorod). There has been carried out the comparative assessment of the results processed by means of international register LiverMetSurvey ([www.livermetsurvey.org](http://www.livermetsurvey.org)) with collective data of the project published. All main aspects were compared. Age, primary tumour localization, the number, size and localization of hepatic metastases, the presence of associated pathologies, as well as the volume of surgeries performed in the compared groups had differences representing the work of Regional Hepatology Centre. The main difference was in postoperative survival of such patients: according to International register, two-year survival amounts to 76%, and in our centre — 57%. The obtained results of the analysis show the approaches to the treatment of this difficult group of patients in the Privolzhsky district medical center correspond to the international protocol.

**Key words:** colorectal liver metastases, liver surgery, International register LiverMetSurvey ([www.livermetsurvey.org](http://www.livermetsurvey.org)).

According to autopsies 20–70% of oncological patients have metastases in the liver [1, 2]. They amount about 95% among all tumoral lesions of the organ. The share of metastatic lesion of the liver in colorectal cancer [3–5] is particularly high: the number of cases of such liver lesions exceeds 20–30 times the frequency of primary cancer of the liver. Therefore the considerable number of published studies on liver surgery is devoted to metastatic colorectal cancer [6–10].

The colorectal cancer (CRC) within the structure of malignant tumors ranks fourth after the cancer of the lung, mammary gland and prostate. Nevertheless, as to the lethality is concerned, this neoplasm ranks the second after the cancer of the lung [11]. Annually about 850 000 new cases of CRC are being diagnosed in the world and 500 000 persons [12] die. In Europe annually about 380 000 new cases of CRC are diagnosed, and about 200 000 people die

[13]. In Russia it is annually diagnosed more than 50 000 of new cases of CRC [14]. According to American Cancer Society (2007), in the USA annually about 150 000 cases of CRC are revealed. Synchronous metastases in the liver have been defined in 15–27% of patients with newly diagnosed CRC. In the remote period in 30–40% of patients after primary tumor resection, metachronous metastases in the liver develop [15, 16], in most patients the metastases being localized only in the liver [17, 18].

The application of various modern medical techniques in the form of system chemotherapy, embolization and combined chemoembolization of hepatic artery or portal vein, as well as various ways of local destruction of hepatic metastases to a certain degree improve the quality of life and prolong longevity of these patients. Nevertheless, there is no alternative to radical surgical treatment of metastatic CRC of the liver until now [19–22]. Thus, in recent years

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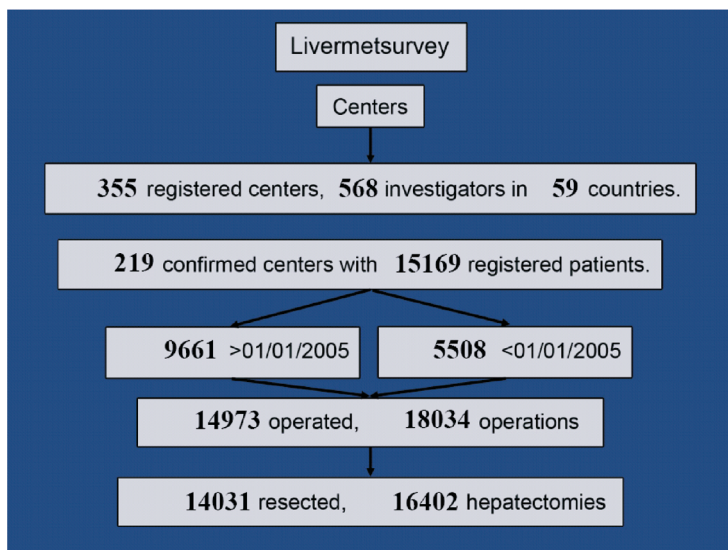


Fig. 1. The generalized information of the International register LiverMetSurvey (www.livermetsurvey.org).

The original work of the hepatologic center is the results of surgical treatment of patients with colorectal liver metastases as the most frequent cause of malignant focal liver lesions. According to numerous publications, the postoperative lethality in focal malignant diseases of the liver amounts about 5–8%, but careful selection of patients and observation of modern perioperative reports can reduce lethality to zero values [25]. The use of criteria for selection of patients when planning an operative intervention in hepatic colorectal metastases was stated to enable to reach five years' survival rate in 60% of cases [26, 27].

Large amounts of information on the results of surgical treatment of metastatic lesions of the liver in CRC are published by the International register LiverMetSurvey (www.livermetsurvey.org) under the supervision of Professor Rene Adam (Paris). In the register the data of 59 specialized hepatologic centers from various countries (Fig. 1) is united.

taking into account the prognostic factors, the liver resection in colorectal metastases is included in treatment standards [23, 24].

Russia is presented by 13 establishments. Thus, the Privolzhsky district medical center (Nizhny Novgorod, Russia) has participated in the project since 2007 and is registered in the list of the centers by number 127 (Fig. 2).

List of the LiverMetSurvey centers

Country	City	Institution	Main investigator	First inclusion	Last inclusion	Operated patients	Resected patients
<b>Portugal</b>						<b>1069</b>	<b>988</b>
<b>registered centers</b>							
Romania	Bucharest	Center Of General Surgery And Liver Transplantation, Fundeni Clinical Institute	Irinel Popescu	03/07/2006	29/01/2010	159	155
	Cluj-Napoca	Clinique Chirurgicale No.3, Cluj	Liviu Vlad	03/11/2006	31/03/2010	48	47
<b>Romania</b>						<b>207</b>	<b>202</b>
<b>registered centers</b>							
Russia	Kirov	Kirov Center Of Liver Surgery	Vladimir M. Rusinov	-	-	-	-
	Krasnodar	Private Hospital 21 Century Clinic	Andrey Yankin	13/08/2010	16/05/2011	14	14
	Moscow	A.V.Vishnevsky Institute Of Surgery	Mikhail Efanov	16/12/2010	29/06/2011	123	122
	Moscow	City Hospital	Igor Kuznetsov	-	-	-	-
	Moscow	Hospital # 77	Sergey Mikhailov	-	-	-	-
	Moscow	Medical And Rehabilitation Center	Nikolay Ermakov	-	-	-	-
	Moscow	National Reserch Center Of Surgery	Oleg Skipenko	24/06/2006	30/12/2010	239	219
	Moscow	State Research Center Of Coloproctology,	Andrew Lavrinenko	-	-	-	-
	Moscow	The Central Clinical Hospital #1 Of The Llc Rzd (Russian Railways), Hpb-Surgical Dept.	Alexey Severtsev	-	-	-	-
	Nizhny Novgorod	Privolzhsky Federal Medical Center	Vladimir Zagainov	06/12/2007	30/06/2011	128	126
	Rostov-On-The Don	Rostov Research Oncology Institute	Alexander Shaposhnikov	14/06/2009	16/06/2010	4	-
	Surgut	Surgery Technology Center	Vladimir Darvin	-	-	-	-
	Ufa	Republican Centre Surgical Gepatology	Radmir Rakhimov	-	-	-	-
<b>Russia</b>						<b>508</b>	<b>481</b>

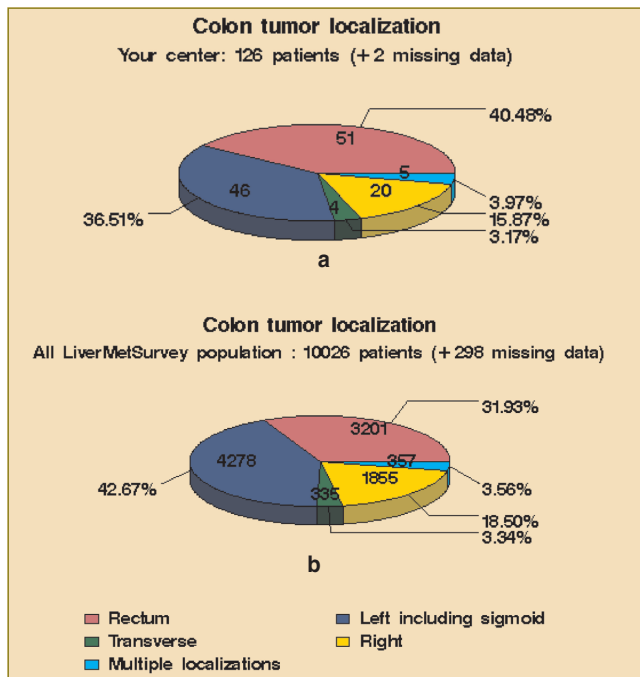
Fig. 2. The comparative analysis of the hepatologic centers activity in Russia registered in International register LiverMetSurvey (www.livermetsurvey.org)

**The research objective** is to carry out the profound analysis and the international audit of own results of surgical treatment of the colorectal metastatic lesions of the liver and compare them with those published by International register LiverMetSurvey ([www.livermetsurvey.org](http://www.livermetsurvey.org)).

**Materials and Methods.** The results of various operative interventions on the liver with CRC metastases performed in our center on 128 patients were analyzed. Among the operated there were 75 women (58.6%) and 53 men (41.4%) at the age of 32–80 years (middle age —  $62.3 \pm 1.5$  yrs). In the last two years the basic growth of the number of operations on hepatic metastases in CRC was due to the increase of the number of patients operated for bilobate metastatic lesions of the liver [28].

Until now in the literature there are still differences in the classifications reflecting the volume of surgeries on the liver performed. It causes problems when carrying out the comparative analysis of the results of surgical treatment of hepatic tumors. In 2000 the Committee of the International Association of Hepatologists in Brisbane (Australia) has adopted the universal anatomic and surgical classification using the division of the liver into three sections: a lobe (hemiliver), section, sector (section) and a segment (segment). Depending on the liver part to be removed the following terms are used: hemihepatectomy, sectionectomy (sectorectomy) and segmentectomy [29]. To unify the results of surgical treatment we used this classification. Liver resection has always been carried out in its anatomic variant, and in 103 cases (80.4%) large and extremely large resections have been made performing the following operative interventions: right portal hemihepatectomy — 54 patients (42.1%), broadened right hemihepatectomy — 32 (25%), left portal hemihepatectomy — 10 (8.3%), broadened left hemihepatectomy — 3 (2.7%), right sectorectomy (VI and VII segments removal) — 7 (5.4%), mesohepatectomy (removal of the IV, V and VIII segments) — 4 (3.1%), left sectorectomy (II and III segments removal) — 3 (2.3%), segmentectomy — 15 (11.7%). In 61 patients (47.6%) the resection of certain organs, tissues or large vessels involved in tumoral process was performed simultaneously with the intervention on the liver. In 17 cases the diaphragm resection was made, in 3 cases the right adrenal gland was removed, in 17 — intestines fragments. 8 patients underwent the resection of inferior cava or portal veins with variants of their reconstruction. The resection and reconstruction of extrahepatic bile ducts was carried out in 5 cases. One patient also had pancreaticoduodenal resection due to the involvement of the duodenal and the head of pancreas into tumor process. In other 13 cases various variants of partial removal of other organs and tissues were performed. The preliminary treatment of the vascular and secretory legs to a segment or a sector was always carried out in performing the segmental liver resections. Lymphadenectomy from hepatoduodenal ligament was an obligatory component.

**Results and Discussion.** First of all the indexes of primary CRC localization (Fig. 3) were compared. In our center the tumor was more frequently localized in the rectum — in 40.5% of cases and according to the International register data — in 31.9%. There are also



**Fig. 3.** Primary tumor localization — the source of metastases in the liver: a — the data of our center; b — the data of the International register

minor differences in terms of tumor location in the left parts: according to our observations — 36.5%, and in the register — 42.6%. Nevertheless, the neoplasm total location in the left parts and the rectum has appeared to be almost identical: in our center — 77.3%, in the register — 74.5%. Therefore, the patients with primary localization of the CRC in the left parts and the rectum most frequently run the risk of metastatic lesions of the liver. This group of patients requires special attention at initial examination as well as careful dispensary supervision after primary tumor removal for early detection of possible metachronous metastases.

The age of operated patients varies from 30 till 83 years (middle age  $62.3 \pm 1.5$  year). More often the operation was carried out on patients aging from 50 till 70 years (Fig. 4). Nevertheless, the age peak was between 50 and 60 years (middle age — 56 years). The patients in the comparable group were more frequently operated at the age of 50–80 years, thus their peak age is 60–70 years. Therefore, the age group was 10 years older compared to our patients. The discrepancy can be explained by more skeptical attitude of out-patient departments to surgical treatment of hepatic metastases of CRC in patients of elderly age. According to our supervisions women (58.6%) were operated more frequently and in compared group the number of female patients was 35.3%. The difference may probably be explained by shorter longevity of men in the Russian Federation (<http://www.rg.ru/2011/11/02/trud.htm>).

*With regard to synchronous metastases*, we have operated 45% patients and in the compared group — 55%, thus, some discrepancy of performed operations can be seen. Revealing synchronous metastases in CRC is often considered to be an advanced case. Especially it concerns the cases of metastases detection during emergent

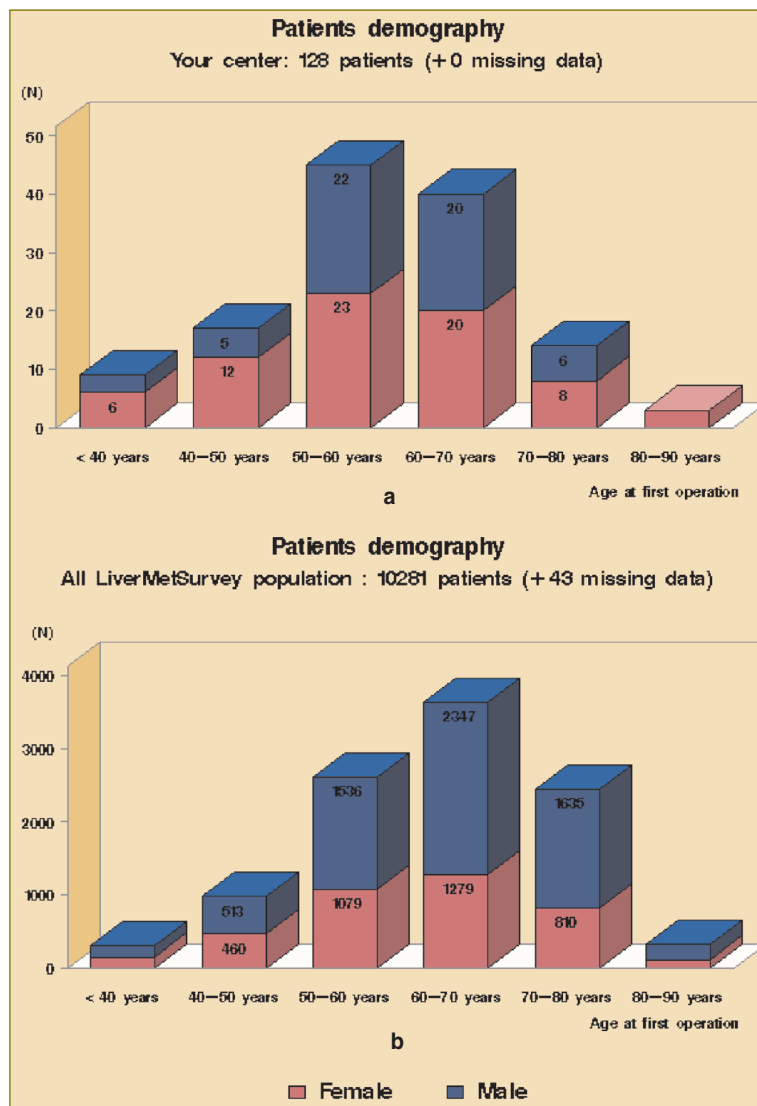


Fig. 4. Age and sex in compared groups of patients: a — the data of our center; b — the data of the International register

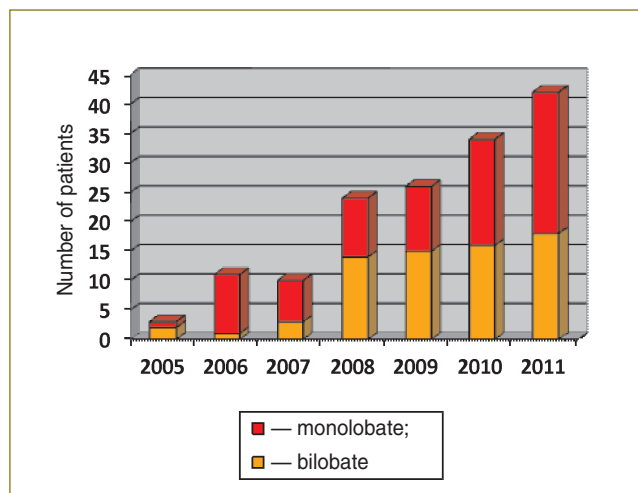


Fig. 5. The dynamics of the number of operative interventions in monolobate and bilobate metastases of CRC in the Privolzhsky district medical center

operations for tumoral large bowel obstruction. It shows once more the necessity of giving information on modern opportunities of surgery to all doctors attending this difficult group of patients. Nevertheless, it should be noted that according to statistical researches metachronous colorectal hepatic metastases are diagnosed at the average of 40% of patients and synchronous — in 15–27% of cases [15, 16, 18].

The minimal differences in compared groups are seen in the number of patients operated for bilobate and monolobate metastases of CRC. According to our data, in monolobate metastatic lesions of the liver 40.3% of patients were operated, while in compared group — 36.7%, and 59.7% and 64.3% of patients, correspondingly, were operated for bilobate innidiation. The steady increase in the number of operated patients with bilobate hepatic metastases of CRC is the general tendency of medical care improvement of the most difficult group of patients. We are annually increasing the number of interventions in bilobate metastases of CRC using the auxiliary technologies aiming at the increase of resectability (Fig. 5).

The comparative study of survival functions of patients with mono- and bilobate metastatic lesion of the liver in CRC has showed no differences in these groups.

The indexes of the number of metastases in the liver in compared groups are almost identical (Fig. 6). And the patients with the solitary metastases prevail in both groups. However, the metastases of the maximum size (more than 3 cm) occur much more often in our patients. In the compared group the patients with metastases less than 3 cm prevail. It should be emphasized that the patients with metastases of 10 cm and more prevail absolutely in our studies, while in compared group there are only single instances

of patients with similar metastases. This untoward situation in our work can be explained by the defects of prophylactic medical examination, late medical aid appealability and low patients compliance.

As for the accompanying pathology is concerns (13.89%) the data of our group does not differ from those of the general register (14.42%).

Additional special technologies are used to increase respectability in more than a quarter of patients (26%), while in the compared group — only in 22.62%.

There are no significant differences in the use of auxiliary technologies in the compared groups (Fig. 7). Nevertheless, mainly we use the device we have developed for local tumors destruction (thermoablation), the tumors being exposed to super-high frequency energy (the patent of the Russian Federation No. 2368406). The developed technique meets the basic requirements for the methods of local destruction: the border of tissue destruction exceeds 1 cm from the tumor edge, by analogy with “open” radical (R0) surgery; the destruction mechanism does not have even

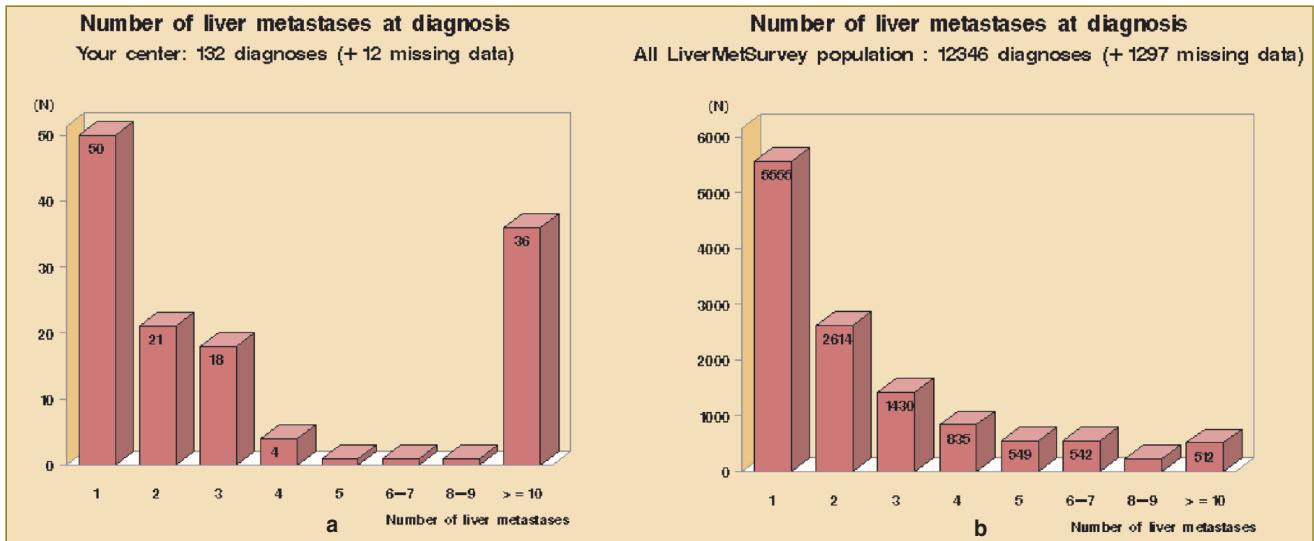


Fig. 6. The quantity and sizes of metastases in compared groups: a — the data of our center; b — the data of the International register

minimum system toxic effect on organism on the principle of the local coagulation necrosis. The advantages of thermoablation by means of super-high frequencies over the known techniques of radiothermoablation are due to short exposure time and programmed spatial characteristics of a destruction zone. The suggested technique is easy to use, especially during operative intervention combined with liver resection. The complications related to its application are not found [1].

Almost identical approach to the use of double-step tactics of surgical treatment of metastases (See Fig. 7) is noted. As it has been mentioned above, 52 patients (48.14%) with bilobate multiple metastatic lesions of the liver have been operated. 32 of them had one-stage operation: the maximum possible anatomic extensive resection of the liver. One-stage operation can be performed on patients with good functional reserves of the liver without marked accompanying pathology. The bandage or embolization by hepaspheres of the right branch of the portal vein was carried out to stimulate the compensatory hyperplasia of the left hepatic lobe prior to the broadened resection of the right hepatic lobe. Then in about four weeks the broadened right hemihepatectomy was performed. The use of this tactics made it possible to carry out prevention of hepatic insufficiency.

The main part of the patients (80.4%) had “extensive hepatic resections”. In these conditions the portal or broadened hemihepatectomies with removal of three and more segments were performed. And sparing hepatic resections were carried out only in 19.6% of patients. In the compared group large hepatic resections were performed in 53.6% of cases and sparing ones — in 46.48%. This

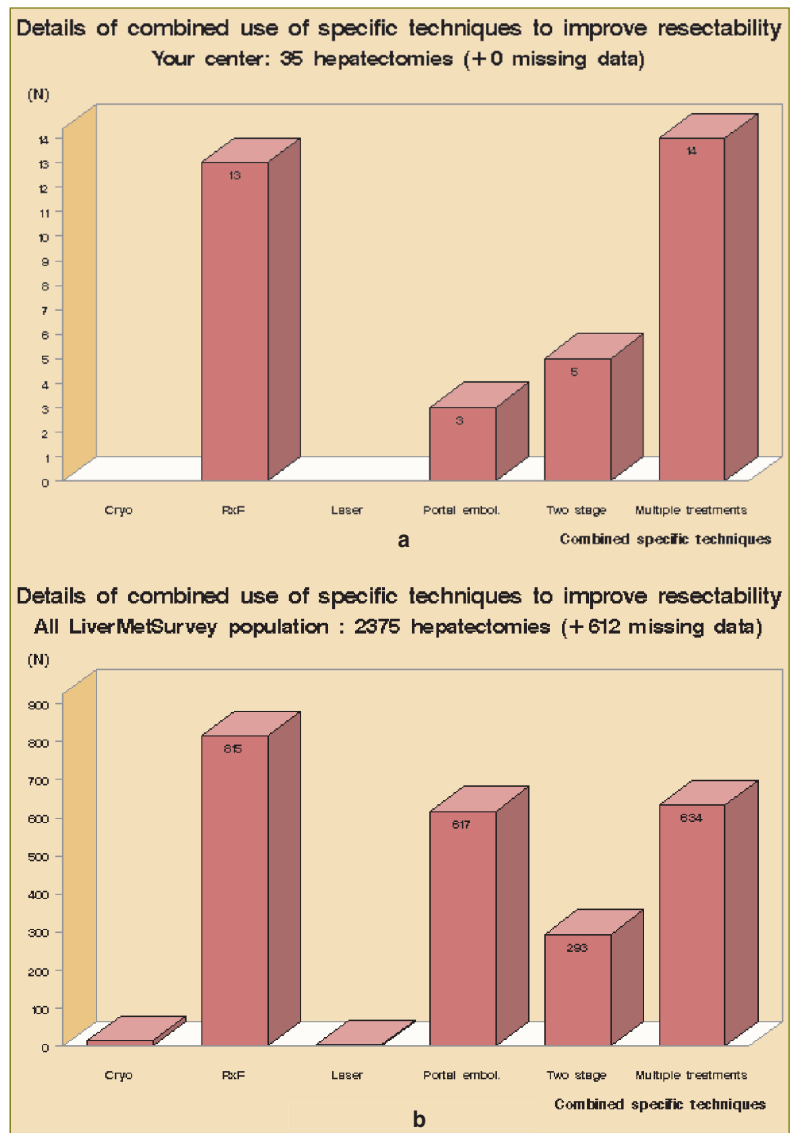
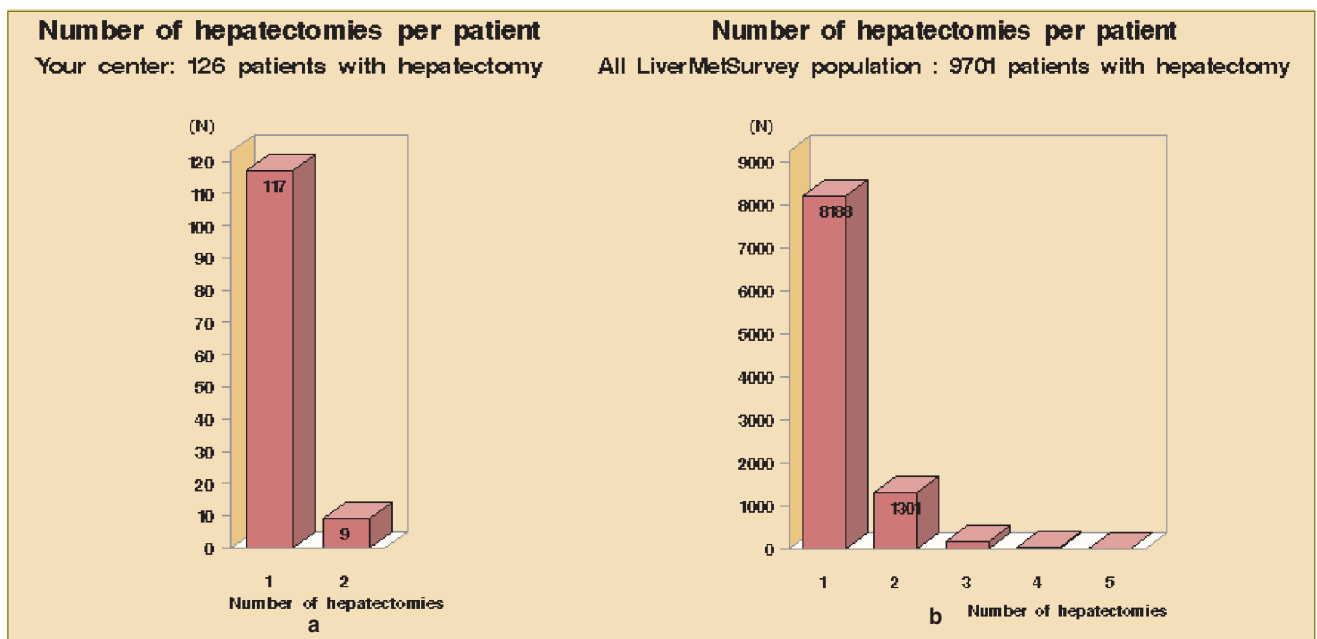


Fig. 7. Type of applied auxiliary technologies: a — the data of our center; b — the data of the International register

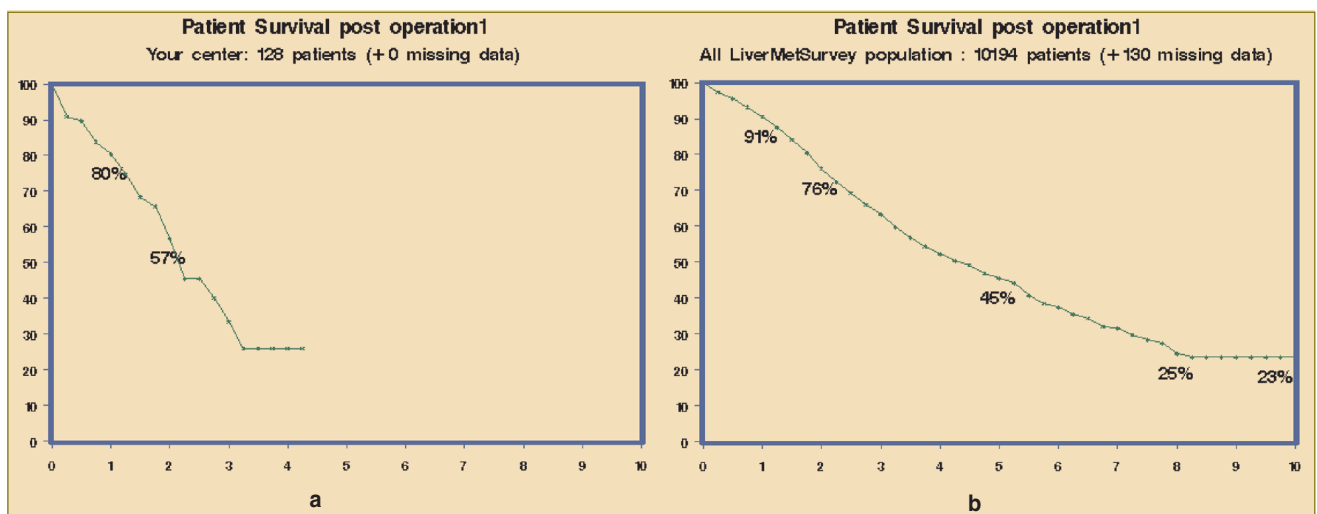
is explained first of all by extensive prevalence of tumoral process in our patients requiring R0-resection.

An obvious difference in the number of repeated operations for CRC metastases in the liver (Fig. 8) is seen. The international register covers almost ten years' period of supervision of patients, while our follow-up period does not exceed four years. Till 2008 we have carried out only individual operations in hepatic metastases of CRC, therefore, the basic part of operative interventions was performed within the last four years (2008-2011). Over the given period 9 patients were re-operated for the recurrence of the disease. In the course of time these indexes will approach the international ones. It should be noted that numerous operative interventions (up to 5) in persistent recurrences give evidence of surgery priority in complex treatment of CRC hepatic metastases.

The two-year survival rate of the patients operated in our center amounts 57 %, and in the International register — 76% (Fig. 9). These significant differences can be explained by various factors. First of all, tumoral process in the patients operated in our center was more extensive and they have to undergo more extended surgeries. Besides, originally we performed some operations on patients with initially doubtful operability. And adjuvant the chemotherapy was insufficient during this period. The general postoperative lethality was 8.3%. Hepatic insufficiency remains the most common and serious complication that occurs in 20.4% of patients with various severity level. An effective method of hepatic failure treatment that is not corrected by drug therapy is Continuous Veno-Venous Hemodiafiltration (CVVH). The perfection of the perioperative proceeding of patients has essentially improved the direct results of



**Fig. 8.** The number of repeated operations in metastases recurrence: *a* — the data of our center; *b* — the data of the International register



**Fig. 9.** The remote results (survival rate) of the operated patients: *a* — the data of our center; *b* — the data of the International register

treatment. Intraoperative bleedings which occur quite often during the last years were treated using the devices of intraoperative blood return (Sell-Saver-5, CATS, Haemonetics, USA). Recently, the experience gained and perfection of operation techniques have enabled to reduce considerably the frequency of this complication. It should be noted that in 2009-2010 59 hepatic resections for colorectal metastases were performed, one patient (1.7%) died. We expect the life span of the patients operated in our center to increase by overcoming negative factors and increasing observation period. When carrying out the next analysis of life expectancy of the operated patients using Kaplan-Mayer's method there was registered the increase in the median of survival of our patients from 22.8 to 31 months that will be demonstrated in the next audit of the International register.

**Conclusion.** The comparative estimation of our own results of surgical treatment of the colorectal metastatic lesions of the liver in Privolzhsky district medical center of FMBA of Russia (Nizhny Novgorod) and the published data of International register LiverMetSurvey ([www.livermetsurvey.org](http://www.livermetsurvey.org)) has shown the approaches to treatment of this difficult group of patients in our Center to correspond to the international report. The accumulated experience and increase in the number of operations will enable to overcome some remaining differences that will be shown in the next publication of the results in the International register.

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