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## Resection for Colorectal Liver Metastases

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### 1. Introduction

Colorectal cancer is the third most frequent cancer in the Western world. About half of the patients develop synchronous or metachronous metastases. The liver is the most common site of such metastases and thus hepatic metastatic disease is a significant socio-medical problem. If it is not treated, the median patient survival is only some months. Surgical resection is the treatment of choice for patients with isolated colorectal liver metastases when feasible. For patients with four or fewer isolated hepatic lesions, five year relapse-free survival rates range from 24 to 58 percent and ten year survival rates vary between 17 and 33 percent. There is a convincing socio-epidemiological evidence of the dramatic unfavourable influence on population wealth of untimely diagnosis and inadequate treatment of the patients with advanced and metastatic colorectal cancer worldwide (Hata et al., 2010; Kostov & Kobakov, 2006a; Stillwell et al., 2011; Tsoulfas et al., 2011).

### 2. Purposes of the study

The purposes of the present paper are to define the variety of liver resections as an important component of the modern treatment of colorectal liver metastases, to describe their operative techniques and postoperative results, to illustrate some peculiar resection patterns from our own patients' contingent and, based on our own experience with the complex preoperative diagnostic algorithm and the individualized indications and contraindications for surgery and multimodal therapy, to outline the advantages of different types of hepatic resections in properly selected cases with colorectal liver metastases as manifested by improved patient's quality of life and survival.

### 3. Material

Patients' contingent included a total of 158 patients who have undergone liver resections for colorectal liver metastases in the Department of Surgery, Naval Hospital of Varna and in the Division of Surgery, Marko Markov Interregional Dispensary and Hospital of Oncological Diseases of Varna, Bulgaria, during a 10-year period (January 1, 2000 - December 31, 2010). Results concerning 108 patients dynamically followed-up for at least one year after the operation were illustrated in this comprehensive retrospective study. Demographic characteristics, preoperative clinical, laboratory and functional diagnosis of the patients,

types of surgical interventions and conservative therapy as well as metastatic tumour localization, volume, number and staging were systematized. Only some of our data could be presented in the present paper.

Number and mean age of male and female patients can be seen on Table 1.

Gender	Patients		Mean age	
	n	%	years	range
Males	68	63	58	36-81
Females	40	37	54	32-79
Total	108	100	59	32-81

Table 1. Patients’ distribution according to gender and mean age

4. Methods

The algorithm for contemporary diagnostic evaluation comprised total colonoscopy, conventional chest radiography, conventional blood tests, serum levels of some tumour markers such as carcinoembryonic antigen (CEA), carbohydrate antigen CA 19.9 and carbohydrate antigen CA 242, abdominal preoperative and intraoperative ultrasonography (for estimation of the type and volume of liver resection), intraoperative cholangiography (for pre- and postoperative bile drainage evaluation in remnant hepatic parenchyma), methylene-blue injection through the portal vein (for assessment of afferent and efferent blood flow in remnant hepatic parenchyma), contrast-enhanced and spiral computed abdominal tomography, MRI in case of contradictory computer tomographic data and histopathology of enlarged hilar lymph nodes. The volume of the liver resection was determined not only by the number, size and localization of the metastases but also by the degree of compensatory hypertrophy of the intact hepatic volume.

The presentation of all the types of surgical interventions included the following:

- i. types of surgical access, liver mobilization, hilar dissection, and hepatic-vein control,
- ii. operative approaches, and
- iii. operative volumes.

Patients’ distribution according to the volume of liver resection is demonstrated on Table 2.

During the last 8 years, a total of 14 patients underwent repeated liver resections. A third resection was done in three of these patients, and a fourth resection was done in two of these patients.

Table 3 indicates the consecutive number and volume of primary and repeated liver resections.

Some essential parameters of colorectal liver metastases in these repeated resections of different consecutive number are summarized on Table 4.

Additionally, multimodal treatment of all the patients with colorectal liver metastases included a variety of chemotherapeutic protocols as aneoadjuvant and/or adjuvant chemotherapy along with radiofrequent ablation, portal vein embolization, and two-stage resection of bilobar colorectal liver metastases (Kostov & Kobakov, 2006). The effect of neoadjuvant chemotherapy was assessed according to the Response Evaluation Criteria in Solid Tumours (Eisenhauer et al., 2009).

Volume of resection	Type of resection	n=108
Monosegmentectomy n=22 (20%)	Sg1	3
	Sg2	2
	Sg3	3
	Sg4	5
	Sg5	2
	Sg6	3
	Sg7	2
	Sg8	2
Bisegmentectomy n=24 (22%)	Sg6,7	4
	Sg5,8	3
	Sg2,3	4
	Sg5,6	3
	Sg4b,5	2
	Sg1,4	2
	Sg7,8	2
	Sg4a,8	2
	Sg3,4b	1
	Sg4 + parts of Sg 1,2,3,5	1
Multisegmentectomy n=62 (57%)	Sg4,5,8	3
	Sg1,4,5,8	2
	Sg1,4b,5,6	1
	Sg5,6,7	1
	Sg3,5,6,7	1
	Sg3,4b,5	2
	Sg4 + part of Sg2,3 + metastasectomy of Sg8	1
	Sg4b,6,7	1
	Sg6,7,8	1
	Sg3+ parts of Sg4,6,8	1
	Left hemihepatectomy (Sg2,3,4±1)	13
	Right hemihepatectomy (Sg5,6,7,8±1)	32
	Right trisectionectomy (Sg1,4,5,6,7,8)	2
	Left trisectionectomy (Sg1,2,3,4,5,8)	1

Table 2. Type and volume of liver resections

Number of resection	Number of patients	Volume of resection					
		One Sg	Two Sg	Three Sg	Trisection-ectomy	Hemihepat-ectomy	Wedge resection
First	14	2	6	2	2	2	-
Second	14	-	-	-	-	-	14
Third	3	-	-	-	-	-	3
Fourth	2	-	-	-	-	-	2

Table 3. Consecutive number and volume of resections

Parameter	First resection	Second resection	Third resection	Fourth resection
CEA > 200 ng/mL	9	9	3	2
CEA ≤ 200 ng/mL	5	5	-	-
synchronous	5	-	-	-
metachronous	9	14	3	2
after < 12 months	6	-	-	-
after ≥ 12 months	8	-	-	-
total number				
One	2	8	2	-
two-three	7	6	1	-
≥ three	5	-	-	2
unilobar	8	12	3	2
bilobar	6	2	-	-
diameter < 20 mm	2	7	2	-
diameter of 20-50 mm	8	5	1	1
diameter ≥ 50 mm	4	1	-	1
nodes in <i>lig. hepato-duodenale</i>	-	-	-	2
positive margins	-	-	-	2
negative margins	14	14	3	-
MSKCC-CRS				
0-2 factors	8	8	1	-
3-5 factors	6	6	2	2

Table 4. Characteristics of colorectal liver metastases in repeated liver resections

One- and three-year survival data were retrospectively recorded up to December, 2010. Memorial Sloan-Kettering Cancer Center Clinical Risk Score (MSKCC-CRS) was used to evaluate the postoperative prognosis of the patients (Arru et al., 2008).

Kaplan-Meier estimates outlined differences with Kaplan-Meier curves. Comparisons of sex and age between segmentectomy and major hepatectomy patients applied chi-square and *t*-test. The *t*-test compared mean blood loss, diameter of colorectal liver metastases, duration of surgery, length of hospital stay, and resection margins. The postoperative complications were compared by means of Fisher's exact test. Patients' homogeneity was comparatively assessed by means of the log rank and Wilcoxon tests.

## 5. Operative techniques of liver resections

### 5.1 Types of surgical access

The following types of surgical access for liver mobilization, hilar dissection, and hepatic-vein control can be used (Kostov & Kobakov, 2010):

Upper medial laparotomy with transversal enlargement to the right until 9<sup>th</sup> intercostal space along with Makuushi incision is most commonly performed to access right or left hemiliver while Mercedes-Benz incision is suitable to access both left and right hemilivers.

Complete liver mobilization passes through five stages: i) interruption of *lig. teres hepatis* between two ligatures, ii) cutting of *lig. falciforme hepatis* up to the subdiaphragmatic part of *vena cava inferior*, iii) search for an accessory left hepatic artery as a branch of *a. gastrica sinistra* when cutting *lig. hepatogastricum*, iv) cutting to the left of both *lig. triangulare sinistrum* and *lig. coronarium hepatis* to left hepatic vein trunk and v) cutting to the right of both *lig. triangulare dextrum* and *lig. coronarium hepatis* to right hepatic vein trunk.

Hilar dissection aims at dividing the vessels designed for the left and right hemiliver that enables the application of hemi-Pringle maneuver. Right hepatic vein extrahepatic part can be reached by interruption of Makuushi ligament. Right hepatic vein is lifted on rubber holder (Fig. 1).

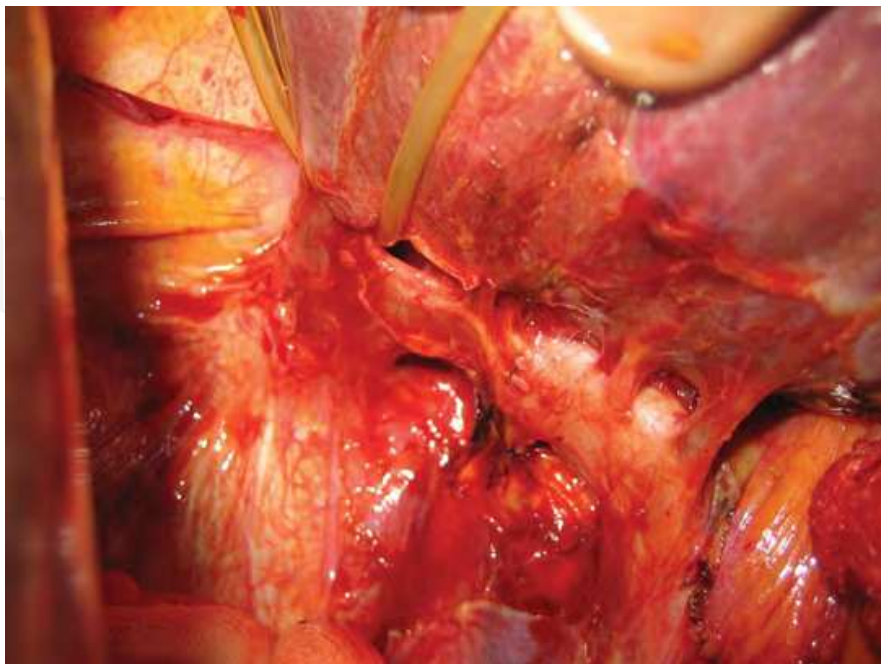


Fig. 1. Right hepatic vein mobilization and short retrohepatic veins



Usually, both left and middle hepatic veins present with a common trunk as their bifurcation is intraparenchymally located (Fig. 2).

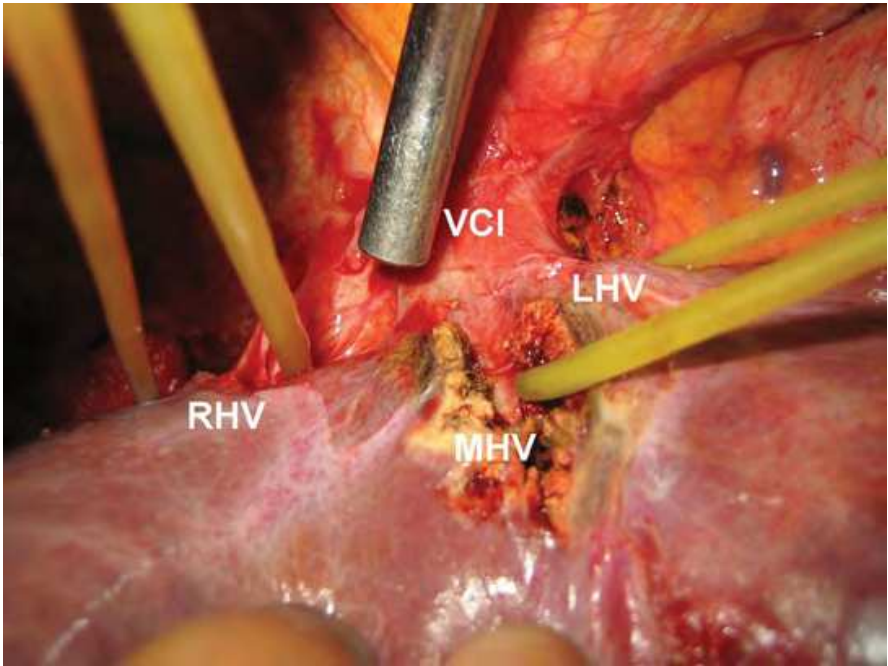


Fig. 2. Extrahepatic mobilization of three hepatic veins enables a complete vascular exclusion of the liver and preserves blood flow through *vena cava inferior*

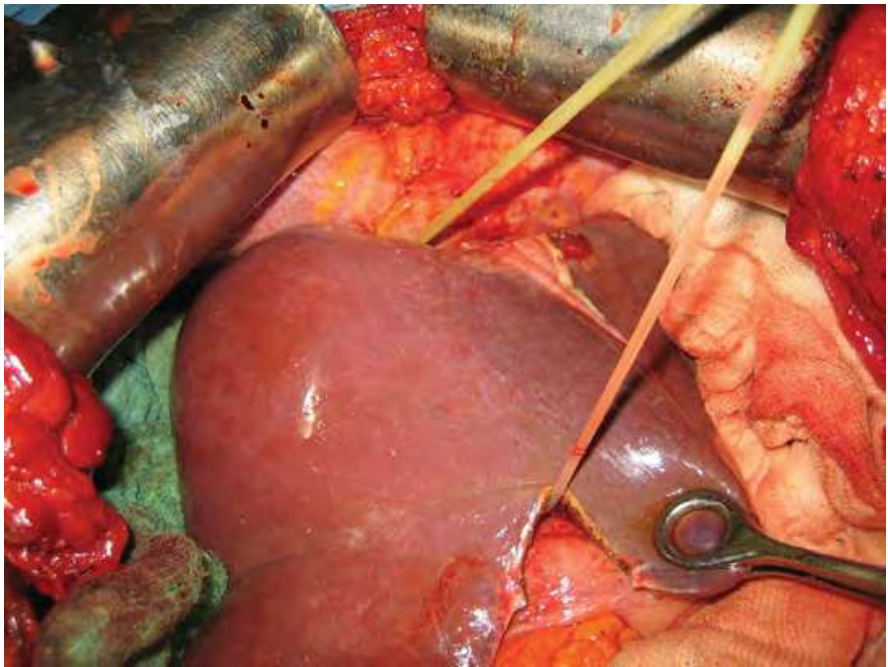


Fig. 3. Single 'hanging'-maneuver

Clamping the three hepatic veins enables a complete vascular exclusion with blood flow preservation through *vena cava inferior*. With single 'hanging'-maneuver, a rubber tape passes cranially between the right and middle hepatic veins but caudally - between hilar vessels for the right and left hemiliver (Fig. 3).

This method is applied in right/left hemihepatectomy or right segmentectomy. With double 'hanging'-maneuver, a second rubber tape is additionally used which passes cranially between the middle and left hepatic veins but caudally - between hilar vessels for the right and left hemiliver (Fig. 4). This method is applied in mesohepatectomy or proximal segmentectomy. With complete vascular exclusion and blood flow interruption through *vena cava inferior* the latter is clamped over the three hepatic veins and over the inflow of renal veins. For that purpose, *vena cava inferior* is mobilized at two sites - below the diaphragm and over the inflow of renal veins ( Fig. 5). Right suprarenal vein is obligatorily interrupted.

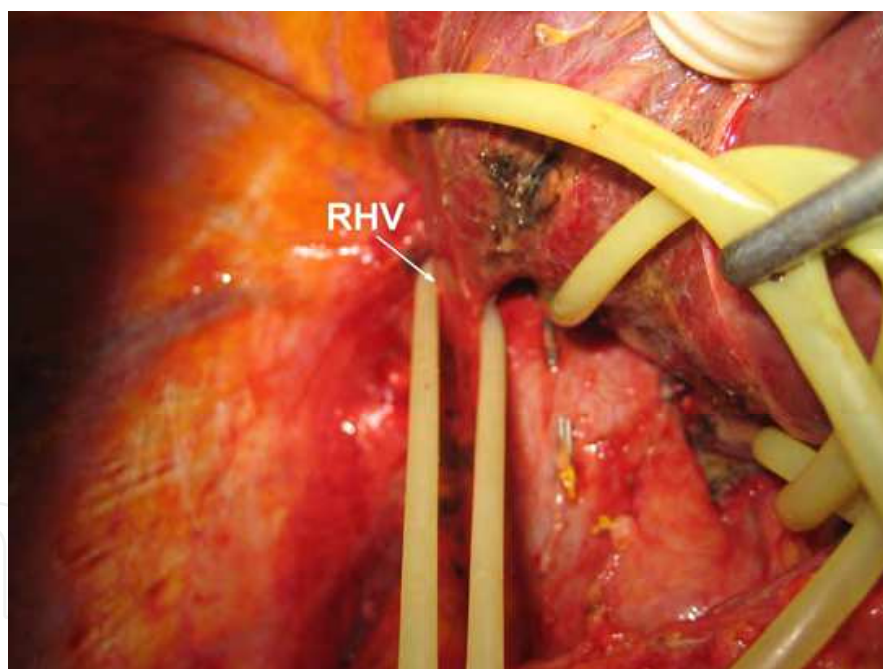


Fig. 4. Double 'hanging'-maneuver



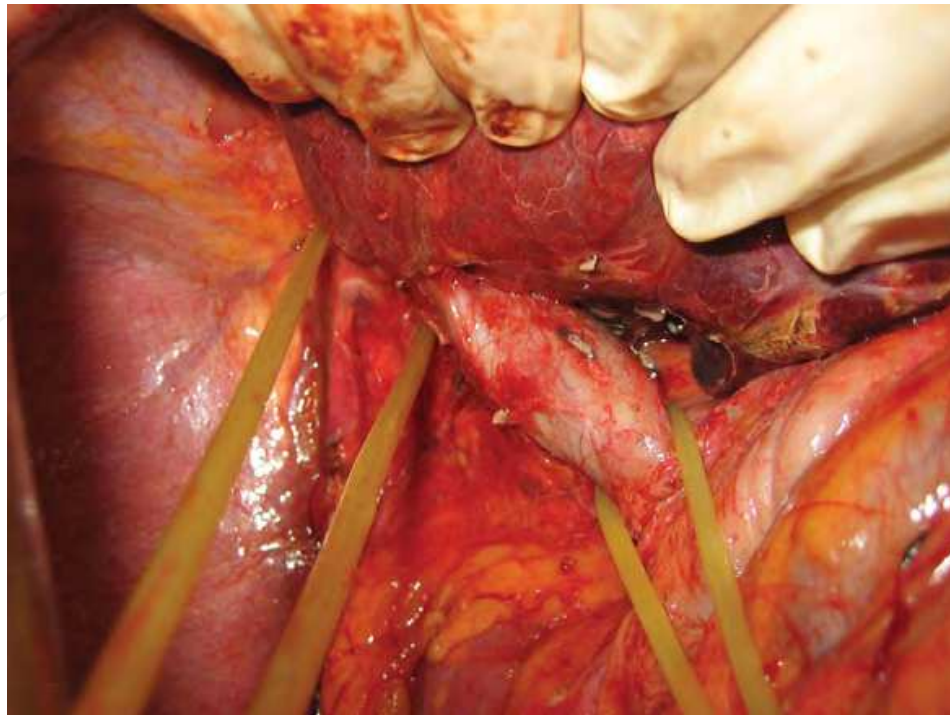


Fig. 5. Preparation for complete vascular exclusion and blood flow interruption through vena cava inferior. Cranial rubber tape passes circularly over the three hepatic veins but the caudal one does over renal veins. Right suprarenal vein is interrupted

## 5.2 Operative approaches

The following operative approaches can be made use of (Kostov & Kobakov, 2010):

- i. extrahepatic approach to the hepatic inflow pedicles for ligation of a portal triad to the Sg 1 and 4, right anterior section, right posterior section, left hemiliver and right hemiliver,
- ii. intrahepatic anterior approach to the hepatic inflow pedicles for ligation of a portal triad to an individual Sg (2, 3, 5, 6, 7 and 8),
- iii. intrahepatic posterior approach to the hepatic pedicles by using Glissonian sheaths, and
- iv. combined extrahepatic and intrahepatic approaches for ligation of a portal triad were used in some bisegmentectomies, right trisectionectomies, and left trisectionectomies.

## 5.3 Operative volumes

According to the localization and expansion of the pathologic process, one of the following operative volumes should be selected by liver surgeons (Kostov & Kobakov, 2010):

### 5.3.1 Segmentectomies

Stages of the following monosegmentectomies - segmentectomy 1 (Sg 1), Sg 2, Sg 3, Sg 4, Sg 5, Sg 6, Sg 7, Sg 8, and wedge resection:

Segmentectomy 1 passes through five stages: i) devascularization of *proc. caudatus*, ii) devascularization of Spiegel's lobe, iii) interruption of short retrohepatic veins which enter directly *vena cava inferior*, iv) mobilization of right, middle and left hepatic veins and v) parenchymal transection at the borderline between Sg1 and Sg4. Resection to the right ends at the borderline to Sg7.

The extrahepatic approach requires interruption of the afferent and efferent blood supply to the hepatic part outside the liver which is subject to removal. Among monosegmentectomies, only Sg1 devascularization can be entirely done through such an approach. With isolated segmentectomy 1, the line of parenchymal transection passing behind the three hepatic veins is of interest (Fig. 6 through Fig. 8).

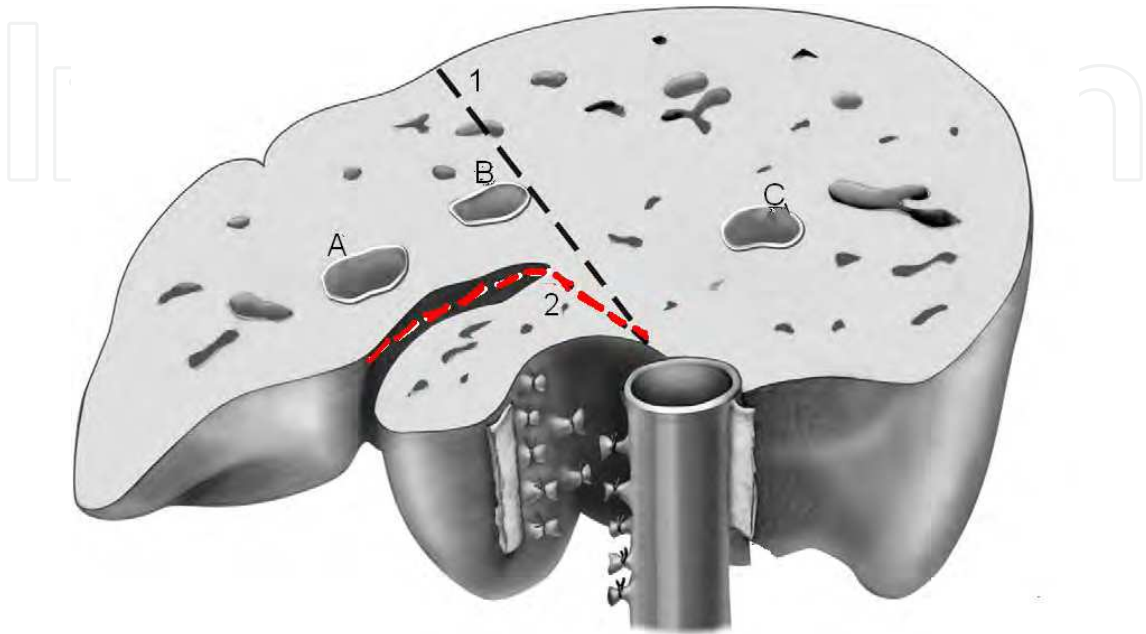


Fig. 6. Line of parenchymal transection (2) when removing Sg 1. Line of dividing the liver into left and right hemiliver (1); left (A), middle (B), and right veins (Liau et al., 2004)

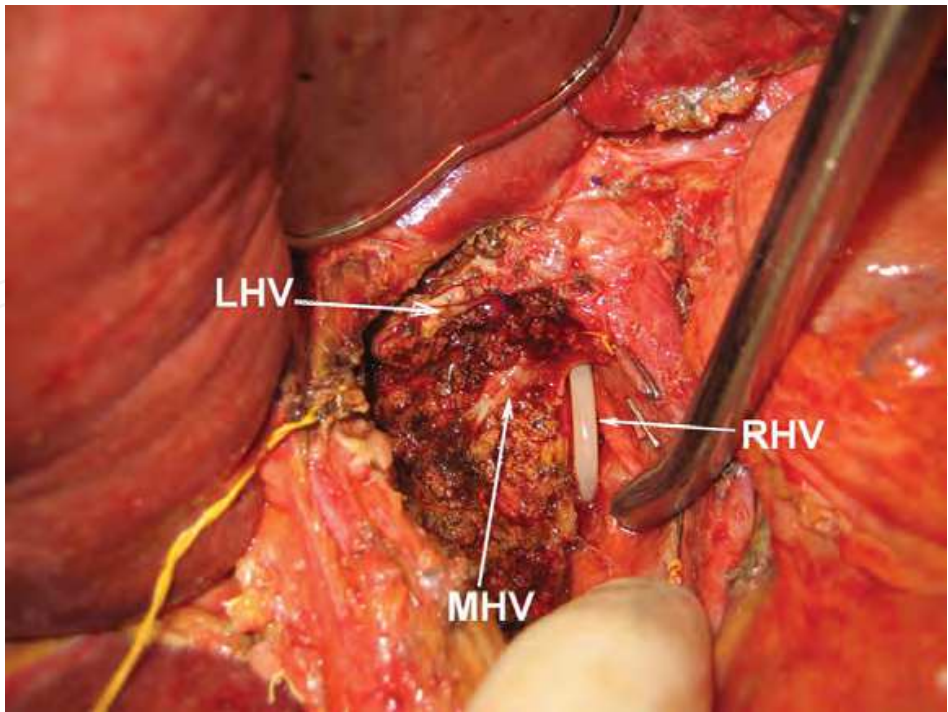


Fig. 7. Removed Sg1 - view from the left. LHV - left hepatic vein; MHV - middle hepatic vein; RHV- right hepatic vein



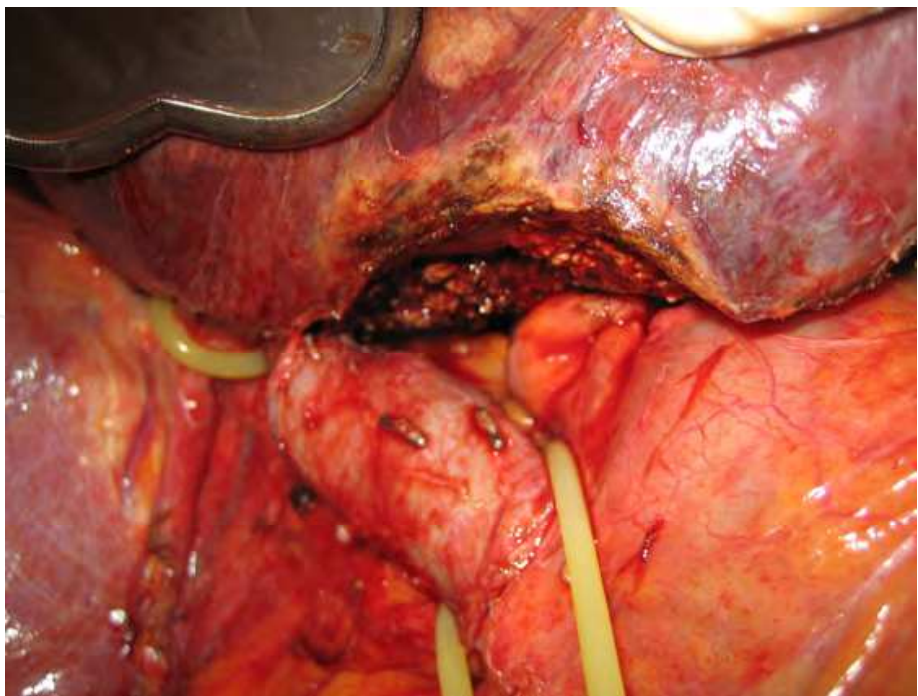


Fig. 8. Removed Sg1 - view from the right.

Both segmentectomy 2 and segmentectomy 3 pass through three stages each: i) definition of borderlines of Sg2 and Sg3 ii) parenchymal transection with intraparenchymal interruption of portal triad vessels for Sg2 and Sg3 (Fig. 9) and iii) interruption of branches of left hepatic vein for Sg2 and Sg3 through anterior intrahepatic access (Fig. 10).

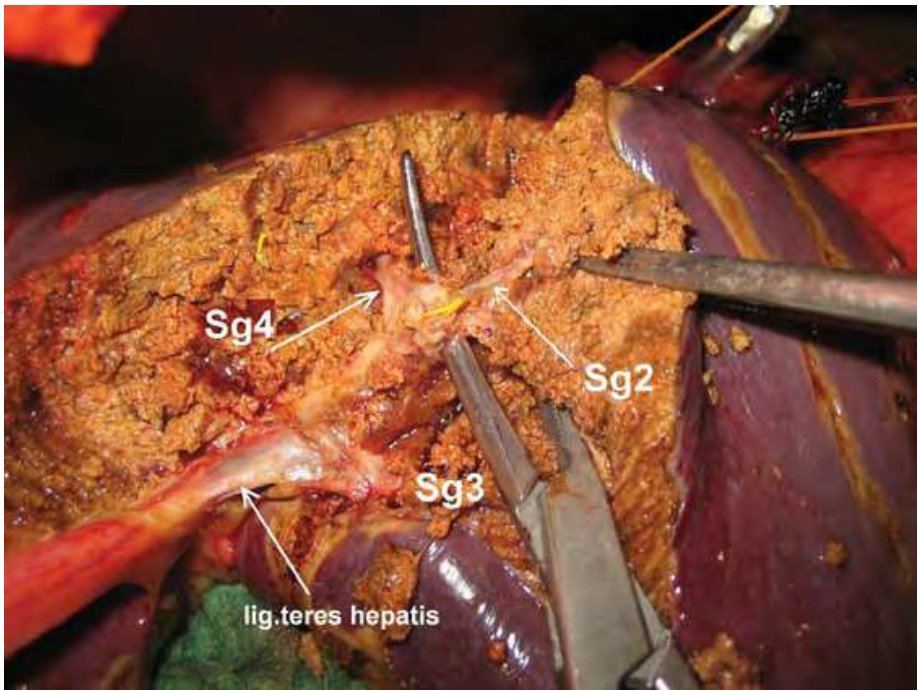


Fig. 9. Sites for interruption of portal triad vessels for Sg2 and Sg3

Segmentectomy 4 passes through five stages: i) extrahepatic interruption of the artery for *lobus quadratus* which, normally, is left hepatic artery branch, ii) ligation of some ascendent

portal veins through extrahepatic access, iii) interruption of descendent portal veins during parenchymal transection along *lig. falciforme hepatis* (Fig. 11), iv) opening and interruption of bile ducts for Sg4 in Rex recessus and v) parenchymal transection along Rex-Cantlie line as middle hepatic vein can be either interrupted, or preserved.



Fig. 10. Anterior intrahepatic access to left hepatic vein

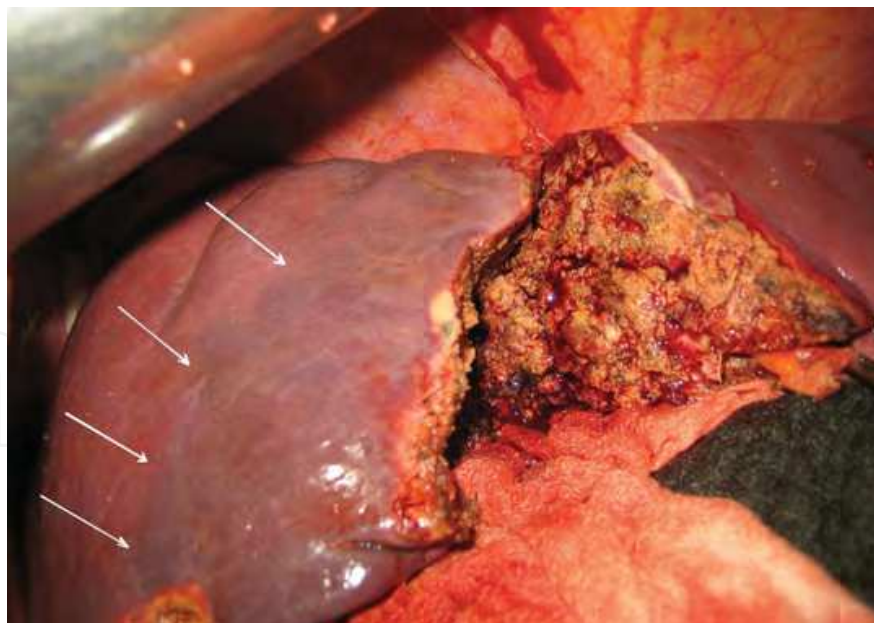


Fig. 11. Ischaemic demarcation of Sg4

Segmentectomy 5 passes through three stages: i) definition of resection borderlines of Sg5. Clamping the vessels for Sg5,8 causes their ischaemic demarcation and visualizes the left and right resection borderlines. The complete Sg5 volume is visualized after injection into segmental portal vein of 5 mL of methylene blue under echographic control, ii) parenchymal



transection along Rex-Cantlie line with intraparenchymal interruption of the vessels for Sg5 and middle hepatic vein preservation. Sg5 devascularization induces ischaemic demarcation of its borderlines and iii) parenchymal transection at the borderline with Sg8 and Sg6. Resection line should pass over Ganz furrow in which the vessels for Sg6 are located.

Segmentectomy 6 passes through three stages: i) definition of resection borderlines of Sg6. Clamping the artery and portal vein for Sg6,7 causes their ischaemic demarcation and visualizes the borderline to Sg5,8. The resection borderlines are visualized after injection into portal vein for Sg6,7 or into segmental portal vein for Sg6 of 5 mL of methylene blue under echographic control (Fig. 12). (ii) parenchymal transection at the borderline between Sg5 and Sg6 with consecutive interruption of the vein and portal triad for Sg6. Sg6 ischaemia allows visualization of its borderline to Sg7 and iii) parenchymal transection along this borderline.

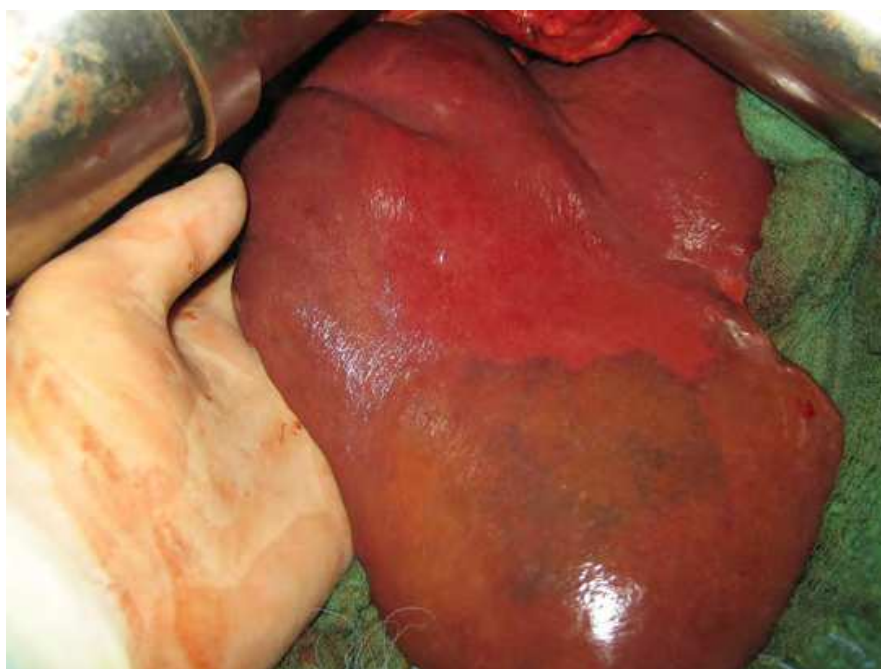


Fig. 12. Sg6 resection borderlines after methylene-blue injection into segmental PV under echographic control

Segmentectomy 7 passes through three stages: i) definition of resection borderlines of Sg7. Clamping the artery and portal vein for Sg6,7 causes their ischaemic demarcation and visualizes the borderline to Sg5,8. The resection borderlines are visualized after injection into portal vein for Sg6,7 or into segmental portal vein for Sg7 of 5 mL of methylene blue under echographic control. Right hepatic vein mobilization prevents bleeding during resection, (ii) parenchymal transection at the borderline between Sg7 and Sg8 with consecutive interruption of right hepatic vein right branch and portal triad vessels for Sg7. Sg7 ischaemic demarcation visualizes its borderline to Sg6 and iii) parenchymal transection along this borderline.

Segmentectomy 8 can be performed through indirect and direct access.

Indirect access - segmentectomy 8 passes through three stages: i) definition of resection borderlines of Sg8. Clamping the artery and vein for Sg5,8 causes their ischaemic demarcation. Right hepatic vein mobilization prevents bleeding during resection, (ii) parenchymal transection along Rex-Cantlie line with intraparenchymal interruption of the



vessels for Sg5 and middle hepatic vein preservation as portal triad vessels for Sg8 is caudally identified and interrupted. Parenchymal transection continues cranially to the borderline with middle hepatic vein where the vein for Sg8 is interrupted. Sg8 devascularization visualizes its borderlines with Sg7 and Sg5 and iii) parenchymal transection along these borderlines in order to preserve right hepatic vein.

Direct access consists in immediate intervention on Sg8. Parenchymal transection passes through three stages: i) definition of resection borderlines of Sg8 visualized after injection into PV for Sg8 of 5 mL of methylene blue under echographic control (Fig. 13). Clamping the artery and vein for Sg5,8 causes ischaemic demarcation of left and right resection borderlines. Right hepatic vein is clamped, if necessary, ii) parenchymal transection at the borderline between Sg4a and Sg8 as, caudally, the vein draining blood from Sg8 into middle hepatic vein and segmental portal triad vessels are consecutively interrupted. Sg8 demarcation visualizes its borderlines with Sg5 and Sg7 and iii) parenchymal transection along these borderlines and obligatory preservation of right hepatic vein.

Wedge resection consists in removal of some part of a given liver segment only.

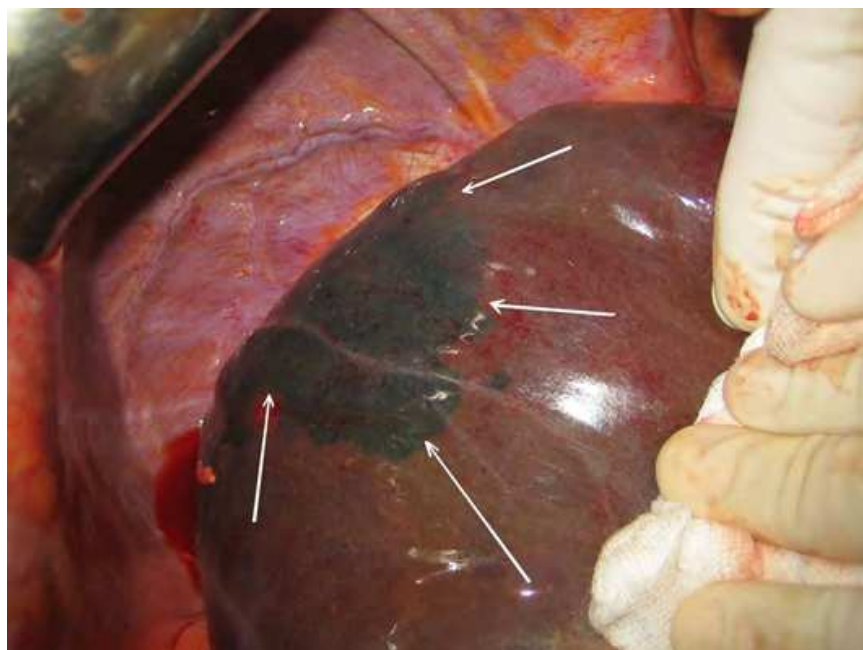


Fig. 13. Borderlines of Sg8 visualized after injection into PV for Sg8 of methylene blue under echographic control

### 5.3.2 Bisegmentectomies

Stages of the following bisegmentectomies - bisegmentectomy 2,3; 6,7; 5,8; 3,4b; 1,4; 4b,5; 5,6; 7,8, and 4a,8:

Bisegmentectomy 2,3 passes through three stages: i) mobilization of left hemiliver through consecutive interruption of *lig. triangulare sinistrum* and *lig. coronarium hepatis sinistrum*, ii) parenchymal transection along the left edge of *lig. falciforme hepatis* and caudal interruption of portal triad vessels for Sg2,3 and iii) left hepatic vein interruption either through extrahepatic access, or through anterior intrahepatic access at the end of parenchymal transection.

Bisegmentectomy 6,7 passes through four stages: i) mobilization of right hemiliver through interruption of *lig. triangulare dextrum* and *lig. coronarium hepatis dextrum*. Extrahepatic

portion of right hepatic vein is liberated and lifted on a rubber tape, ii) definition of resection borderline after interruption of the artery and portal vein for Sg6,7 or by injection of 5 mL of methylene blue into portal vein for Sg6,7, iii) parenchymal transection at the borderline between Sg6,7 and Sg5,8. Caudally, both the vein for Sg6 draining blood into right hepatic vein anterior branch and portal triad vessels for Sg6,7 under it are interrupted and iv) at the end of parenchymal transection, right hepatic vein posterior branch draining blood from Sg7 is interrupted as its anterior branch is preserved.

Bisegmentectomy 5,8 passes through four stages: i) mobilization of right hemiliver through interruption of lig. triangulare dextrum and lig. coronarium hepatis dextrum. Extrahepatic portion of right hepatic vein is liberated and lifted on a rubber tape, ii) definition of resection borderlines of Sg5,8. Extrahepatic interruption of the artery (Fig. 14) and portal vein (Fig. 15) for Sg5,8 causes their ischaemic demarcation (Fig. 16). Sg 5,8 visualization after injection of 5 mL of methylene blue into portal vein for Sg5,8, iii) parenchymal transection at the borderline to lobus quadratus through consecutive interruption of the vein for Sg5 draining blood into middle hepatic vein, of the portal triad vessels for Sg5,8 and the vein draining blood from Sg8 into middle hepatic vein. Sg5,8 devascularization results in ischaemic demarcation line at the borderline to Sg6,7 and iv) parenchymal transection along this borderline includes interruption of the vein draining blood from Sg5 into right hepatic vein as both middle and right hepatic veins are obligatorily preserved.

Bisegmentectomy 3,4b passes through three stages: i) definition of resection borderlines by means of intraoperative echography. To the left, parenchymal transection passes along left hepatic vein but to the right it does along Rex-Cantlie line. Both left and middle hepatic veins are preserved, ii) parenchymal transection along *lig. falciforme hepatis* reaching caudally to the vessels for left segments. Only portal triad vessels for Sg3 and bile ducts for Sg4b are interrupted. Sg3 ischaemia causes demarcation of its borderline to Sg2 along which parenchymal transection is performed and iii) parenchymal transection along Rex-Cantlie line at the borderline between Sg4b and Sg5.

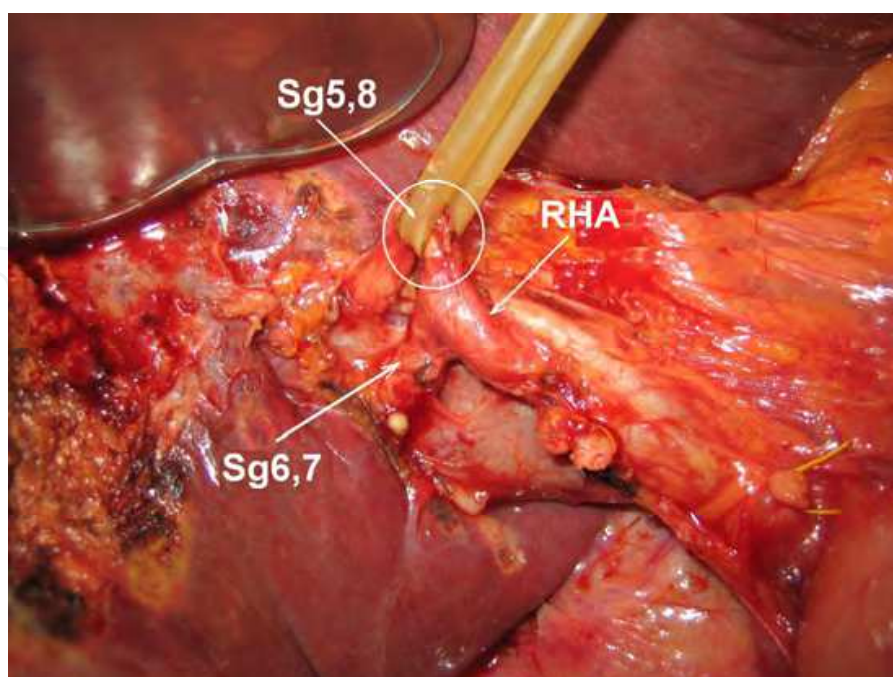


Fig. 14. Mobilization and preparation for interruption of the artery for Sg5,8. RHA - right hepatic artery

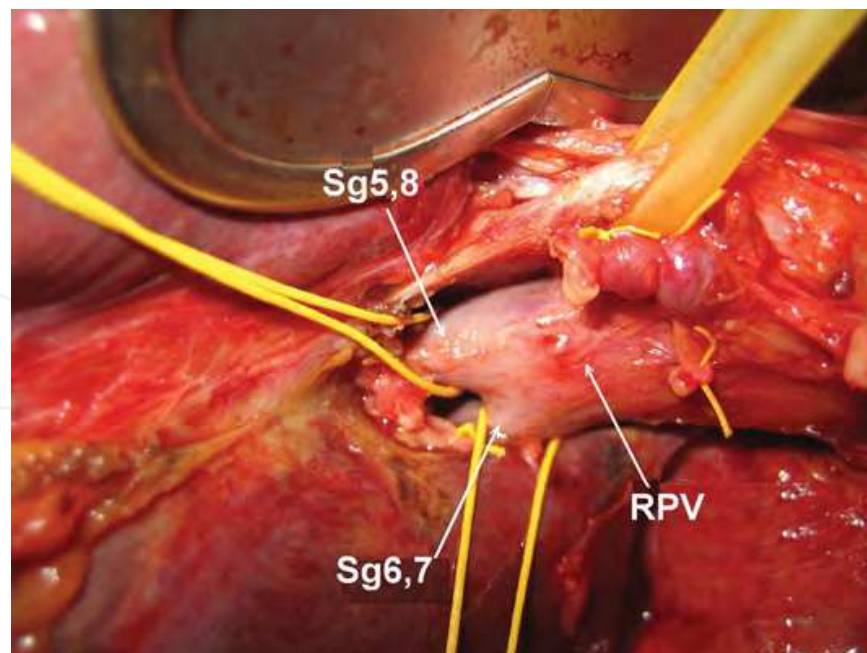


Fig. 15. Mobilization and preparation for interruption of portal vein for Sg5,8. RPV - right portal vein

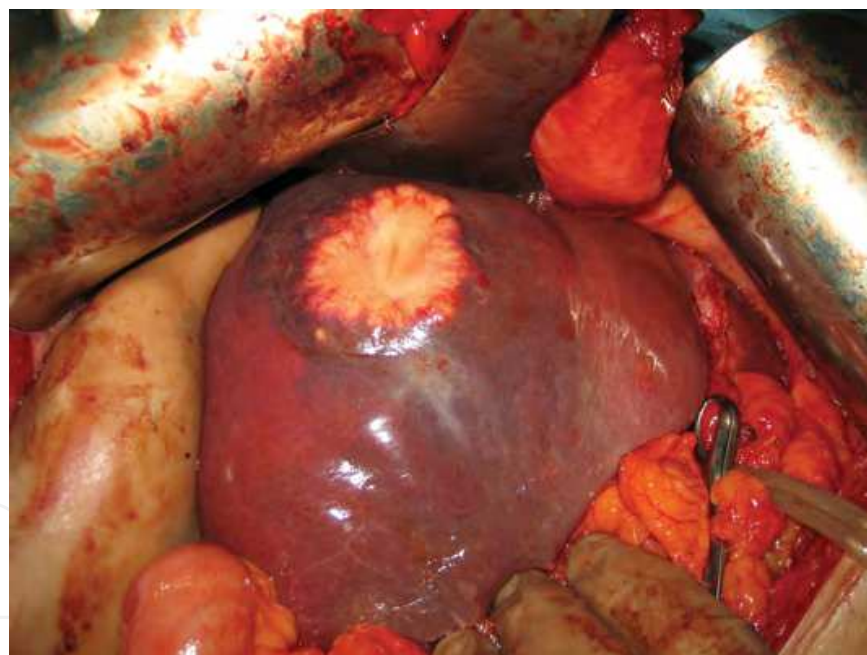


Fig. 16. Ischaemic demarcation of Sg5,8 after their devascularization

Bisegmentectomy 1,4 passes through five stages: i) mobilization of left and right hemiliver and definition of Sg4 resection borderlines. To the left, parenchymal transection passes along *lig. falciforme hepatis* but to the right it follows middle hepatic vein course as defined by means of intraoperative echography, ii) Sg4 devascularization by consecutive interruption of the artery and ascendant portal veins for Sg4 through extrahepatic access, iii) parenchymal transection along *lig. falciforme hepatis* and, caudally, interruption of descendent portal veins for Sg4. After interruption of portal veins for *lobus quadratus*, Rex recessus is reached where the bile duct for Sg4 is identified and interrupted, iv) Sg1



devascularization through extrahepatic access and v) parenchymal transection along Rex-Cantlie line. Cranially, middle hepatic vein is interrupted, if necessary. After bisegmentectomy 1,4, a large parenchymal defect is formed at which bottom the retrohepatic portion of *vena cava inferior* is visible.

Bisegmentectomy 4b,5 passes through four stages: i) definition of resection borderlines. To the left, parenchymal transection passes along *lig. falciforme hepatis* but to the right it does along Rex-Cantlie line. Hilar dissection with division of vessels for right and left hemiliver enables selective clamping the artery and portal vein for Sg2-8, if necessary, ii) parenchymal transection along *lig. falciforme hepatis* as the artery for Sg4 is provisorily clamped as well as ascendant portal veins and bile duct for Sg4b are interrupted, iii) parenchymal transection in a transversal plane at the borderline between Sg4b and Sg5, on the one hand, and between Sg4a and Sg8, on the other hand. Resection line is defined by means of intraoperative echography. Consecutively, distal portion of middle hepatic vein and portal triad vessels for Sg5 are interrupted and iv) Sg5 ischaemia results in demarcation line at the borderline to Sg6 along which parenchymal transection is performed. Caudally, the vein draining blood from Sg5 into right hepatic vein anterior branch is interrupted and portal triad vessels for Sg6-8 are obligatorily preserved.

Bisegmentectomy 5,6 passes through three stages: i) hilar dissection and isolation of the vessels for right hemiliver. Their clamping visualizes the parenchymal transection line between Sg5 and Sg6. Resection borderlines in bisegmentectomy 5,6 are defined by means of intraoperative echography, too, ii) parenchymal transection at the borderline between Sg4 and Sg5 and interruption of the vein draining blood from Sg5 into middle hepatic vein. Caudally, isolation of portal triad vessels for right hemiliver and consecutive interruption of blood supply for Sg5,6. Their ischaemia results in demarcation of their borderline to Sg7,8 and iii) parenchymal transection along this borderline. Caudally, right hepatic vein anterior branch draining blood from Sg5,6 is interrupted and portal triad vessels for Sg7,8 are obligatorily preserved.

Bisegmentectomy 7,8 is possible only in the presence of inferior right hepatic vein draining blood from Sg6. Bisegmentectomy 7,8 passes through four stages: i) mobilization of right hemiliver through interruption of *lig. triangulare dextrum* and *lig. coronarium hepatis dextrum*. Right hemiliver is luxated to the left and the retrohepatic portion of *vena cava inferior* is liberated. Identification of inferior right hepatic vein enables technical performance of bisegmentectomy 7,8, ii) definition of resection borderlines. Hilar clamping the vessels for right hemiliver results in ischaemic demarcation line at the borderline between Sg5,8 and Sg4. Parenchymal transection along this line between Sg8 and Sg4. 'Hanging'-maneuver facilitates hepatic resection. Resection borderline between proximal (Sg7,8) and transversal (Sg5,6) segments is defined by means of intraoperative echography, iii) parenchymal transection along resection borderlines with Sg7,8 devascularization starting at the borderline between Sg6 and Sg7. Initially, right hepatic vein anterior branch is identified and interrupted. Then, in a transversal plane, portal triad vessels for Sg7,8 are reached and interrupted and iv) parenchymal transection in a sagittal plane at the borderline between Sg8 and Sg4. Caudally, the vein draining blood from Sg8 into middle hepatic vein is ligated. Finally, right hepatic vein branch is interrupted.

Bisegmentectomy 4a,8 passes through four stages: i) mobilization of right hemiliver through interruption of *lig. triangulare dextrum* and *lig. coronarium hepatis dextrum*. Right hemiliver is luxated to the left and then right hepatic vein branch is extrahepatically mobilized, ii) definition of resection borderlines. Hilar dissection enables the isolation of the artery and portal vein for Sg5,8. Their clamping visualizes the borderline between Sg8 and Sg6, on the

one hand, and between left and right hemiliver, on the other hand. Transversal resection borderline between Sg8 and Sg5 is established by means of intraoperative echography while the left borderline passes along *lig. falciforme hepatis*, iii) parenchymal transection along Rex-Cantlie line and consecutive interruption of the veins draining blood from Sg5,8 into middle hepatic vein and portal triad vessels for Sg8. Sg8 devascularization results in ischaemic demarcation line at the borderline to Sg5 and iv) parenchymal transection along this line continuing in a sagittal plane between Sg7 and Sg8 and reaching cranially up to the borderline between the right and the middle hepatic vein. Next follows parenchymal transection along *lig. falciforme hepatis* in order to liberate Sg4a ending, cranially, at the borderline between the left and the middle hepatic vein. Finally, both Sg8 and Sg4a are entirely mobilized around middle hepatic vein which is interrupted at its basis.

### 5.3.3 Multisegmentectomies

- i. Stages of the following multisegmentectomies - mesohepatectomy with preservation of Sg1; mesohepatectomy together with Sg1; resection of Sg4b,5,6 and Spiegel's lobe; resection of Sg3,4b,5; resection of Sg3,5-7; resection of parts of Sg3,4b,5,6,8; resection of Sg4b,6,7, and resection of Sg6-8:

Mesohepatectomy (Sg4,5,8) consists in removal of three segments both of which (Sg5 and Sg8) belong anatomically to the right hemiliver while Sg4 belongs to the left hemiliver. This operation is applied in centrally located liver metastases enabling R0 (Fig. 17). Mesohepatectomy with preservation of Sg1 passes through six stages: i) mobilization of left and right hemiliver as double 'hanging'-maneuver lifting on a holder of the right and left hepatic veins facilitates hepatic resection, ii) definition of right resection borderline by consecutive interruption of the artery and portal vein for Sg5,8 (Fig. 18). Parenchymal transection visualizes right resection borderline between Sg5,8 and Sg6,7, iii) interruption of the artery and ascendant portal veins for Sg4 through extrahepatic access. To the left, resection line passes along *lig. falciforme hepatis*. Sg4,5,8 devascularization enables mesohepatectomy at minimal blood loss, iv) parenchymal transection along *lig. falciforme*

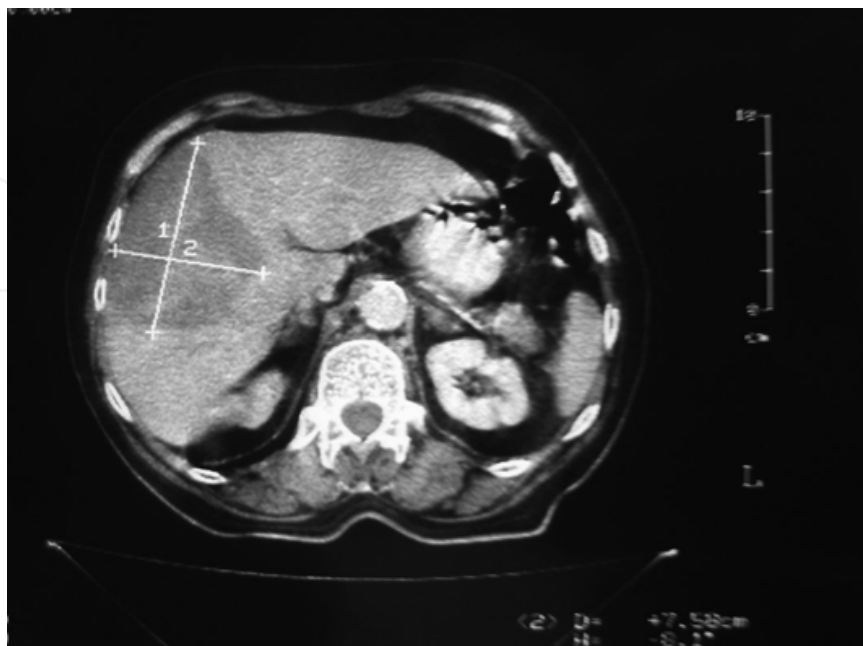


Fig. 17. CT image of liver metastasis in Sg4,5,8



*hepatis* ending at the borderline between the middle and the left hepatic vein. Consecutive interruption of descendent portal veins, the bile duct for Sg4 and the vein draining blood from *lobus quadratus* in left hepatic vein, v) parenchymal transection at the borderline between Sg5,8 and Sg6,7 and consecutive interruption of the vein draining blood from Sg5 into right hepatic vein anterior branch and portal triad vessels for Sg5,8. To the right, parenchymal transection ends at the borderline between the right and the middle hepatic vein and vi) interruption of middle hepatic vein around which these already liberated Sg5,8 and Sg4 are located (Fig. 19). Residual liver volume after removal of Sg4,5,8 is shown on Fig. 20.

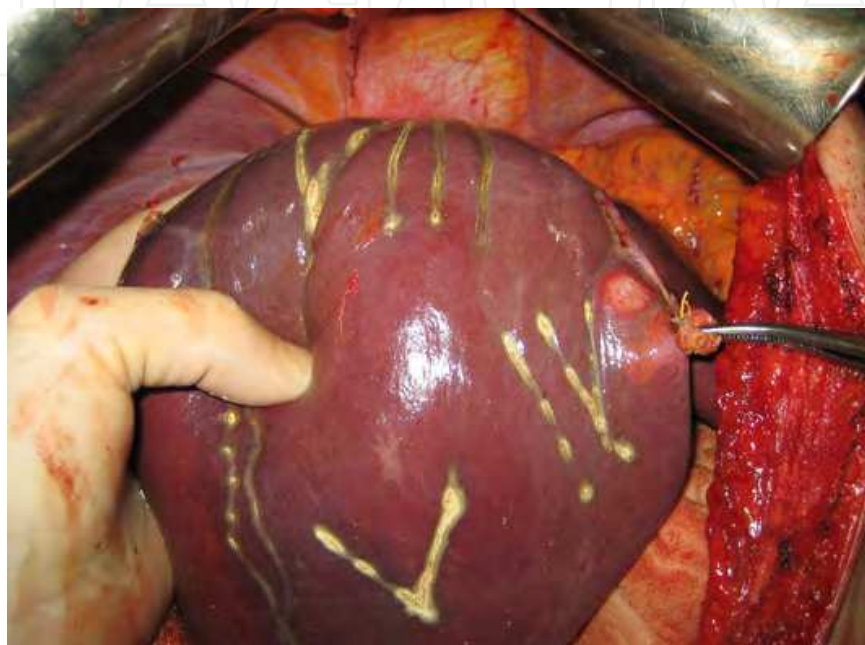


Fig. 18. Liver resection volume in mesohepatectomy (Sg4,5,8)

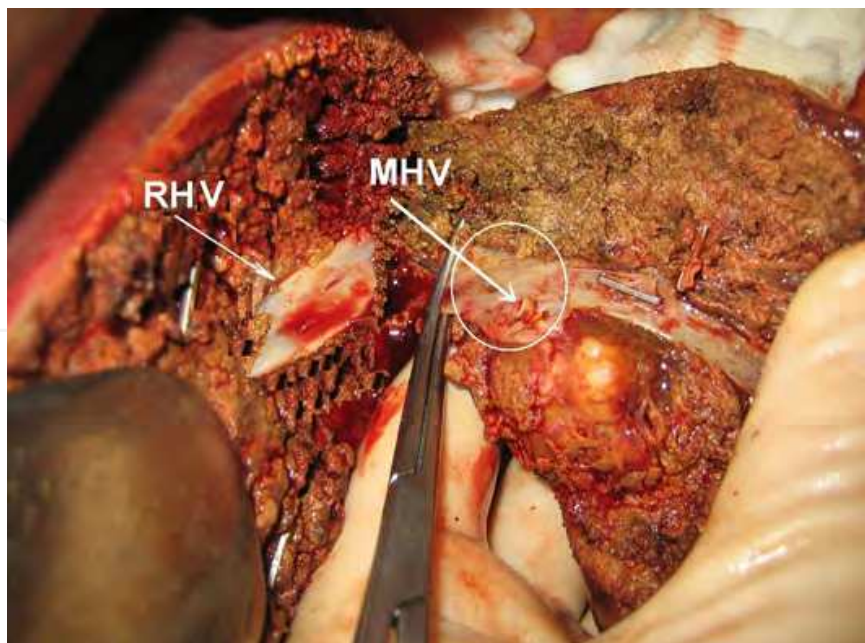


Fig. 19. The site for interruption of the middle hepatic vein is indicated by a circle. MHV - middle hepatic vein; RHV - right hepatic vein

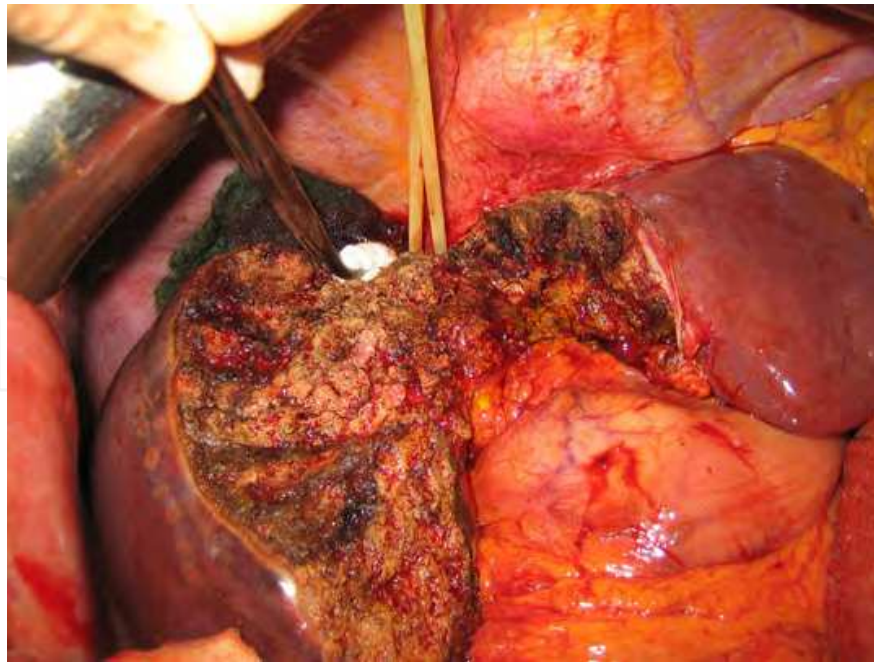


Fig. 20. Residual liver volume after mesohepatectomy (Sg4,5,8)

Mesohepatectomy with segmentectomy 1 is indicated in tumours of central location and passes through seven stages already described in detail in single segmentectomy chapters: i) mobilization of left and right hemiliver by means of double 'hanging'-maneuver, ii) Sg5,8 devascularization through extrahepatic access, iii) Sg4 devascularization through extrahepatic access for the artery and ascendant portal veins, iv) Sg1 devascularization with liberation of the retrohepatic part of *vena cava inferior*, v) parenchymal transection along *lig. falciforme hepatis* ending at the borderline between the middle and the left hepatic vein. Caudally, identification and interruption of descendent portal veins for Sg4 enabling the opening of Rex recessus. Interruption of bile ducts for Sg4 located in Rex recessus, vi) parenchymal transection at the borderline between Sg5,8 and Sg6,7 and vii) middle hepatic vein interruption at the end of parenchymal transection and obligatory intraoperative cholangiography after resection of Sg1,4,5,8 for control of bile drainage from the remnant liver parenchyma.

Resection of Sg4b,5,6 and Spiegel's lobe combines the already described stages in resections of Sg1,4-6. Portal triad vessels for Sg7,8 are obligatorily preserved.

Resection of Sg3,4b,5 combines the already described stages in resections of Sg3,4b,5. Portal triad vessels for Sg6,8 are obligatorily preserved.

Resection of Sg3,5-7 combines the already described stages in resections of Sg3,5-7. Portal triad vessels for Sg8 are obligatorily preserved.

Resection of parts of Sg3,4b,5,6,8 combines the already described stages in resections of Sg3,4b,5,6,8.

Resection of Sg4b,6,7 combines the already described stages in resections of Sg4b,6,7.

Resection of Sg6-8 combines the already described stages in resections of Sg6-8. Portal triad vessels for Sg5 are obligatorily preserved.

ii. Stages of the following hemihepatectomies - left hemihepatectomy (Sg2-4), and right hemihepatectomy (Sg5-8):

Left hemihepatectomy passes through three stages: i) mobilization of left hemiliver through consecutive interruption of *lig. triangulare dextrum* and *lig. coronarium hepatis sinistrum*. Devascularization of left hemiliver with ligation of left hepatic artery and portal vein left branch. If possible, left hepatic duct is liberated without its interruption. Extrahepatically, the trunk of the left and the middle hepatic vein is mobilized enabling the application of 'hanging'-maneuver, ii) parenchymal transection along the ischaemic demarcation line between left and right hemiliver. Resection borderline is defined after injection of 10 mL of methylene blue through portal vein left branch and iii) finally, consecutive interruption of left hepatic duct and left hepatic vein-middle hepatic vein branch. Middle hepatic vein is preserved, if indicated.

Right hemihepatectomy passes through three stages: i) mobilization of right hemiliver through consecutive interruption of *lig. triangulare dextrum* and *lig. coronarium hepatis dextrum*, ii) interruption of the right hepatic and the portal vein right branch. If possible, right hepatic duct is liberated without its interruption. Right hepatic vein mobilization by means of 'hanging'-maneuver facilitates liver resection. Right hemiliver devascularization results in ischaemic demarcation line at the borderline to left hemiliver, and iii) parenchymal transection at the borderline between left and right hemiliver and consecutive ligation of the veins draining blood from Sg5,8 into middle hepatic vein. Finally, interruption of right hepatic duct and right hepatic vein as well as of middle hepatic vein, if indicated.

iii. Stages of the following trisectionectomies - left trisectionectomy (Sg2-5,8), and right trisectionectomy (Sg4-8):

Left trisectionectomy is used in tumours affecting left hemiliver and Sg5,8. No preoperative embolization of portal vein left branch is needed as preserved Sg7 and Sg 6 amount to 30-35% of standard liver volume. Left trisectionectomy passes through five stages: i) mobilization of left hemiliver through consecutive interruption of *lig. triangulare sinistrum* and *lig. coronarium hepatis sinistrum*. 'Hanging'-maneuver application facilitates resection, ii) devascularization of left hemiliver with ligation of left hepatic artery and portal vein left branch, iii) Sg5,8 devascularization through extrahepatic access. Sg5,8 ischaemia causes demarcation line at the borderline to Sg6,7 along which parenchymal transection is performed, iv) consecutive interruption of the vein draining blood from Sg5 into middle hepatic vein and intraparenchymal portal triad vessels for Sg5,8. Parenchymal transection ends at the borderline between the right and the middle hepatic vein. Right hepatic vein is lifted on a rubber holder in order to prevent its injury and v) finally, the trunk of the middle and the left hepatic vein is interrupted. Portal triad vessels for Sg6,7 are obligatorily preserved.

Right trisectionectomy is used in tumours affecting right hemiliver and Sg4. In most cases, preoperative embolization of portal vein right branch is needed in order to achieve hypertrophy of the left hemiliver and, in particular, of Sg2 and Sg3. Right trisectionectomy passes through five stages: i) mobilization of right hemiliver through consecutive interruption of *lig. triangulare dextrum* and *lig. coronarium hepatis dextrum* and short retrohepatic veins; ii) devascularization of right hemiliver with ligation of the right and middle hepatic arteries and the right branch of the portal vein (Fig. 21); iii) devascularization of *lobus quadratus* by means of interruption of the artery and ascendent portal veins for Sg4 through extrahepatic access (Fig. 22).



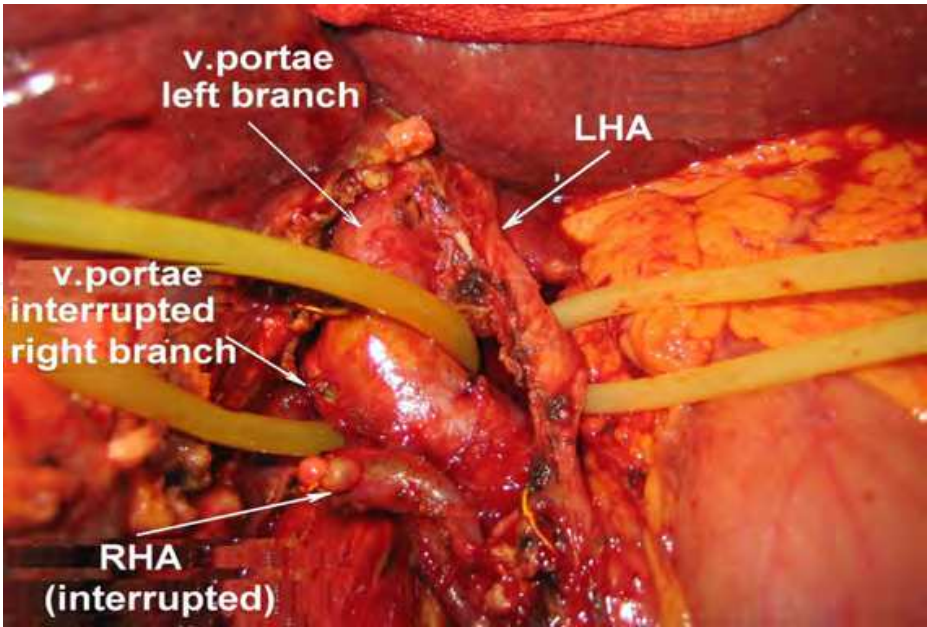


Fig. 21. Right and middle hepatic arteries as well as portal vein right branch are interrupted. LHA – left hepatic artery; RHA - right hepatic artery

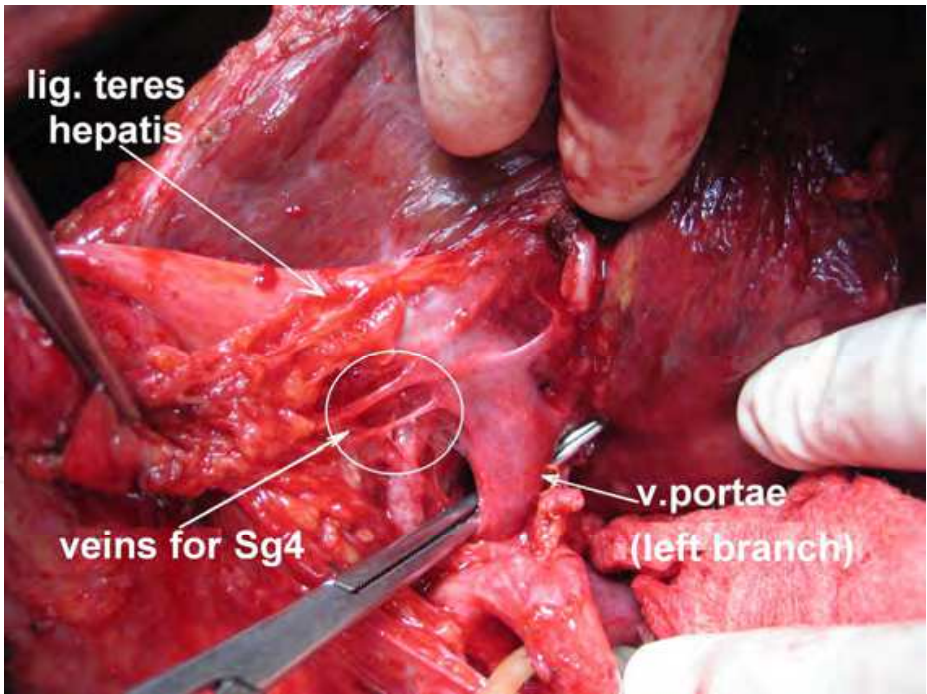


Fig. 22. Sites for interruption of the veins for Sg4 through a combined access.

The interruption of the right hepatic duct is presented on Fig. 23. A preserved left hepatic vein (single ‘hanging’-maneuver) is indicated on Fig. 24, iv) parenchymal transection along *lig. falciforme hepatis* and consecutive interruption of descendent portal veins for Sg 4. Entering *Rex recessus* with interruption of the bile ducts for Sg4 (Fig. 25), and v) cranial ligation of the middle and the right hepatic veins (Fig. 26).

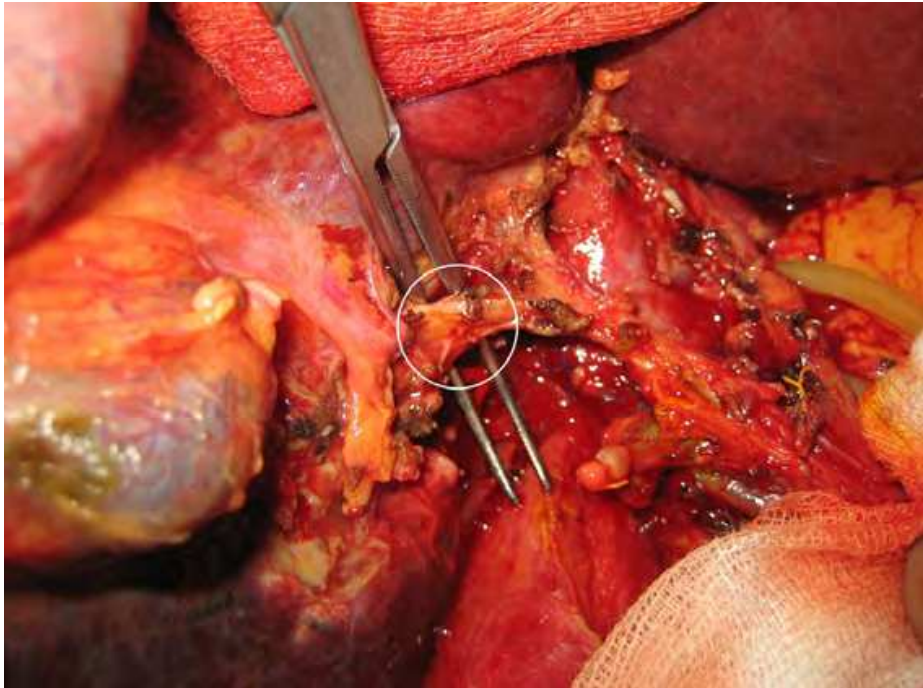


Fig. 23. Interruption of right hepatic duct

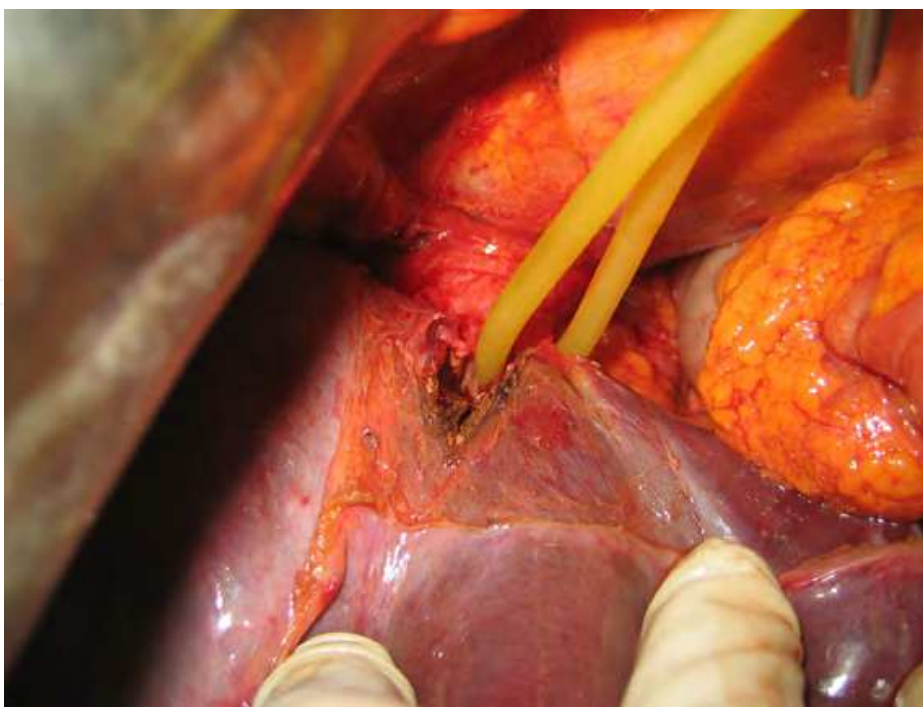


Fig. 24. Preservation of the left hepatic vein through a single 'hanging'-maneuver



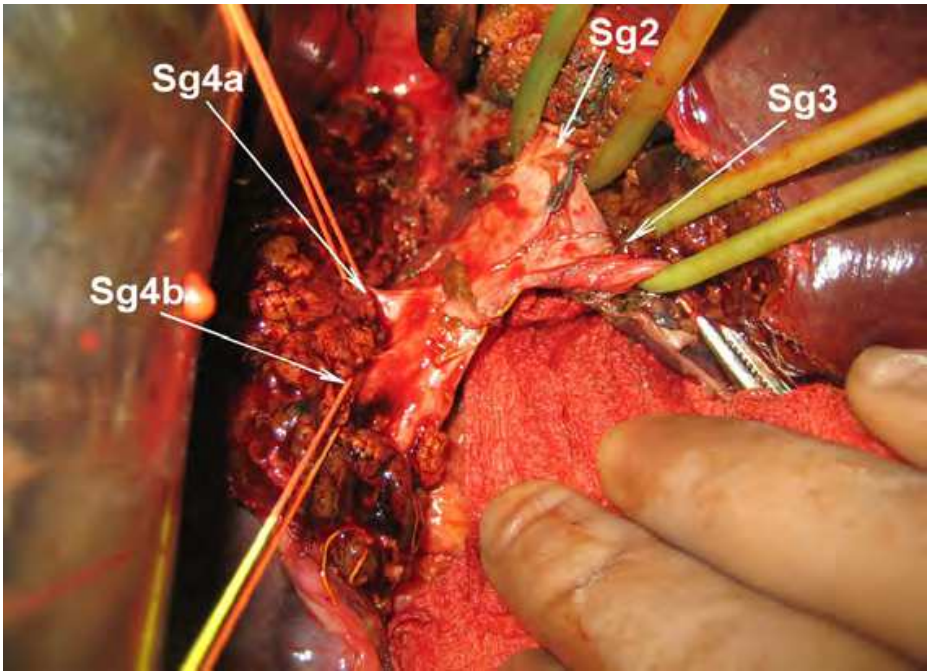


Fig. 25. Entering Rex *recessus* with interruption of the bile ducts for Sg4

In case of damaged blood supply to common hepatic duct, these vessels should be removed with subsequent biliodigestive anastomosis between left hepatic duct and intestinal loop isolated after Roux. Fig. 27 shows residual liver volume following right trisectionectomy.

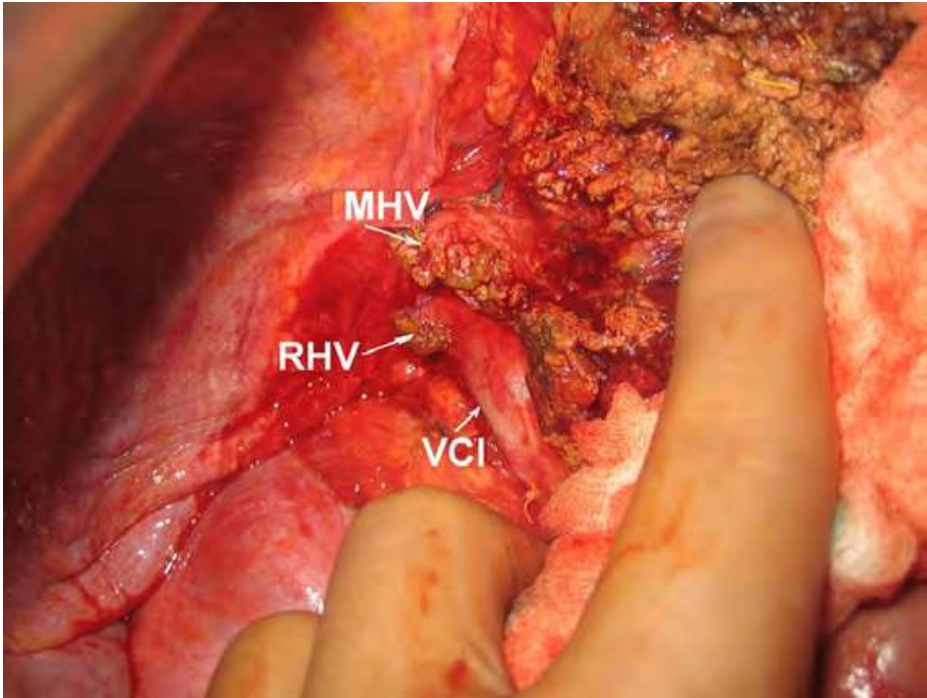


Fig. 26. Interruption of the middle and the right hepatic veins. MHV – middle hepatic vein; RHV – right hepatic vein, VCI - *vena cava inferior*

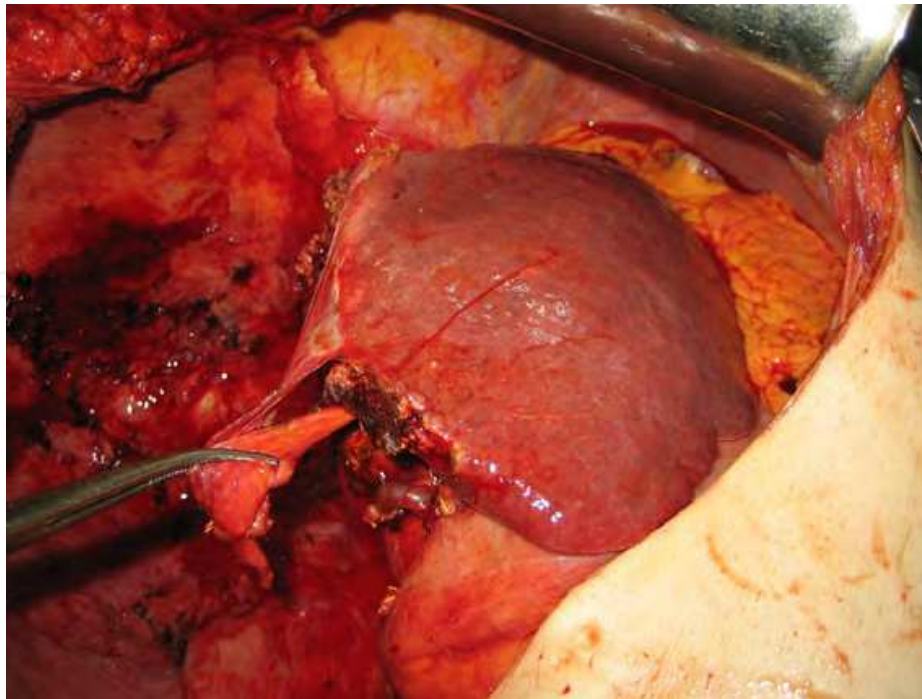


Fig. 27. Residual liver volume after right trisectionectomy

## 6. Results

The results concerning various clinical and laboratory characteristics of the patients having undergone different types of segmentectomies and major liver resections were comparatively demonstrated. The main attention was paid to the following basic parameters: number, diameter, and localization of colorectal liver metastases; postoperative mortality rate; complications; blood loss and required blood transfusions; operative duration; length of hospital stay; resection margins, one-, two and three-year disease-free and overall survival rates.

Some of them are shown in the present paper.

Postoperative complications following monosegmentectomies and bisegmentectomies, on the one hand, and multisegmentectomies, on the other hand, are comparatively presented on Table 5.

It is evident that, as a whole, liver damage caused by the surgical intervention itself occurs statistically significantly more commonly in the patients who have undergone multisegmentectomies.

Some surgical characteristics of monosegmentectomies and bisegmentectomies, on the one hand, and multisegmentectomies, on the other hand, are comparatively presented on Table 6.

Obviously, several surgical patterns of undoubted medical and socio-economic importance such as total blood loss, necessity of blood transfusions and of application of Pringle-maneuver are statistically significantly more unfavourable in the patients who have undergone multisegmentectomies.

Besides, these patients require statistically significantly more often the performance of repeated surgical interventions on the occasion of colorectal liver metastases than those who have undergone mono- or bisegmentectomies.

Complications	Number of removed segments		p
	one or two	≥ three	
number and percentage of patients with complications			
37 (34%)	11 (10%)	26 (24%)	0.092
surgical liver damage	8 (7.4%)	19 (18%)	0.009
hemorrhage	2 (1.8%)	4 (3.7%)	
liver failure	2 (1.8%)	14 (13%)	
bilirrhangia from an opened bile duct	3 (2.7%)	9 (8.3%)	
extrahepatic biliary tree necrosis	-	1 (1%)	
purulent perihepatic collection	2 (1.8%)	4 (3.7%)	
cholangitis	2 (1.8%)	3 (2.7%)	
mechanical jaundice	-	2 (1.8%)	
peritonitis	-	2 (1.8%)	
ascites	2 (1.8%)	14 (13%)	
respiratory tract damage	6 (5.5%)	11 (10%)	0.034
pneumothorax	2 (1.8%)	2 (1.8%)	
pulmonary thromboembolism	-	1 (1%)	
respiratory failure	2 (1.8%)	9 (8.3%)	
pleural effusion > 200 mL	4 (3.7%)	9 (8.3%)	
other complications	3 (2.7%)	8 (7.4%)	0.060
drug-resistant renal failure	2 (1.8%)	7 (6.5%)	
drug-resistant heart failure	2 (1.8%)	7 (6.5%)	
sepsis	2 (1.8%)	8 (7.4%)	
deep vein thrombosis	1 (1%)	1 (1%)	
complications of general nature	8 (7.4%)	15 (13.8%)	0.014
operative wound suppuration	8 (7.4%)	12 (11%)	
operative wound dehiscence	3 (2.7%)	6 (5.5%)	
postoperative herniation	8 (7.4%)	15 (13.8%)	

Table 5. Complications after liver resections

Parameters	Number of removed segments		p
	one or two	≥ three	
positive resection area	2 (1.8%)	4 (3.7%)	0.299
duration of surgery (min)	224±19	211±21	0.368
total blood loss (mL)	480±52	682±48	< 0.001
necessity of haemotransfusion (patients)	16 (14.8%)	45 (41.6%)	< 0.001
necessity of Pringle-maneuver (patients)	20 (18.5%)	52 (48.1%)	< 0.001
stay in reanimation ward (days)	2±1.2	1.5±0.5	0.459
hospital stay (days)	14.7±1.4	13.5±1.6	0.269
repeated operation	2 (1.8%)	9 (8.3%)	< 0.001

Table 6. Surgical patterns of patients with liver resections

Three-year patients’ survival assessed by means of the variables of 22 prognostic criteria is presented on Table 7.

Variables of prognostic criteria	n	%	p
Males	32	47	0.582
females	21	53	
age < 65 years	41	51	0.743
age ≥ 65 years	12	43	
T2-T3 category	32	52	0.944
T4 category	21	46	0.934
G1-G2 tumour differentiation	35	50	0.677
G3 tumour differentiation	18	47	
negative lymph nodes during colorectal cancer surgery	33	53	0.877
positive lymph nodes during colorectal cancer surgery	20	43	
colonic primary tumour	38	51	0.983
rectal primary tumour	15	45	
CEA ≤ 200 ng/mL	42	71	< 0.001
CEA > 200 ng/mL	11	26	
synchronous metastases	13	59	0.834
metachronous metastases	40	50	
after < 12 months	35	51	0.221
after ≥ 12 months	18	46	
diameter < 50 mm	42	49	0.712
diameter ≥ 50 mm	11	50	
≤ 3 metastases	48	55	< 0.001
> 3 metastases	5	30	
unilobar metastases	41	48	0.069
bilobar metastases	12	52	
positive resection areas	-	-	< 0.001
negative resection areas	53	52	
positive lymph nodes in <i>lig. hepatogastroduodenale</i>	1	6	< 0.001
negative lymph nodes in <i>lig. hepatogastroduodenale</i>	52	60	
resection distance ≥ 10 mm	42	52	0.700
resection distance of 5-10 mm	5	56	0.790
resection distance ≤ 5 mm	6	50	< 0.001
monosegmentectomy and bisegmentectomy	29	66	
multisegmentectomy	24	41	0.644
blood loss > 500 mL	29	48	
blood loss ≤ 500 mL	24	51	0.736
application of Pringle-maneuver	34	47	
no application of Pringle-maneuver	19	52	0.743
postoperative complications	29	46	
no postoperative complications	24	53	< 0.001
0-2 factors of MSKCC-CRS	41	64	
3-5 factors of MSKCC-CRS	12	27	< 0.001
extrahepatic dissemination	2	25	
no extrahepatic dissemination	51	54	0.628
neoadjuvant chemotherapy	13	52	
no neoadjuvant chemotherapy	40	48	

Table 7. Prognostic criteria for three-year survival



We identify a small number of prognostic criteria which could be considered statistically significant in the patients with colorectal liver metastases. Here belong the increased levels of CEA, the higher number of colorectal liver metastases (more than three), the negative resection areas, the presence of negative lymph nodes in *lig. hepatogastroduodenale*, the implementation of multisegmentectomy as a less sparing surgical intervention, the presence of at least 3 factors of MSKCC-CRS and the absence of extrahepatic dissemination of the pathological process.

Thus our investigations should be enlarged in future in order to more comprehensively explain the dynamic interactions between the single risk factors for the relatively poor prognosis of this contingent of patients.

## 7. Discussion

Our own results demonstrate the substantial advantages of segmental resection for colorectal liver metastases over major liver resection (Kobakov & Kostov, 2006; Kostov & Kobakov, 2006b; Kostov & Kobakov, 2009). They are the following: conservation of a sufficient liver volume, achievement of lower perioperative morbidity and mortality rates as well as warranting the similar disease-free and overall survival rates. Liver conservation is essential in normal and damaged liver. It reduces the risk of postoperative liver insufficiency from a small liver remnant and in the patients at advanced age or with cirrhosis.

The following prognostic factors exert a statistically significant effect on short- and long-term survival rates after liver resections for colorectal liver metastases: CEA level, presence of metastatic nodes along *lig. hepatoduodenale*, number of metastases, extension of liver resection, resection volume, number of prognostic factors according to MSKCC, and extrahepatic dissemination of primary colorectal cancer.

The following therapeutic strategy should be recommended: i) liver resection for resectable colorectal metastases (at stages IVA and IVB); ii) neoadjuvant chemotherapy for primarily non-resectable colorectal metastases (at stage IVC) when downstaging is feasible to allow radical surgery, and iii) only chemotherapy for colorectal metastases in stage IVD patients.

Recent literature data convincingly indicate the uninterrupted progress in the interdisciplinary field of oncologic liver surgery. Along with original investigations, a lot of review papers, meta-analyses, multicentre reports and randomized controlled trials are currently published by authors from all over the world.

In this respect, multimodal therapy deserves a special attention. It increases the number of resections and improves long-term survival rate (currently more than 40% at 5 years) (Neumann et al., 2010). Advances in staging, surgical technique, perioperative care and systemic chemotherapy contribute to improvement in oncologic outcomes of stage IV colorectal cancer patients (Abdalla, 2011). The limits of resection expand to include cases with more, larger and bilateral colorectal liver metastases as 5-year overall survival exceeds 50% following resection. Tailored, patient-centered treatment includes a variety of liver resections, liver volumetry, and portal vein embolization for preoperative enhancement of the volume and function of the planned future remnant liver (Abdalla, 2011).

Multimodality approach of laparoscopic liver resection is feasible and safe in selected patients. It is associated with a low complications rate (Isoniemi et al., 2011, Lai et al., 2011). Intraoperative ablation extends the limits of hepatectomy in the patients not amenable to complete resection (Brown et al., 2011; Govindarajan et al., 2011; Hammill et al., 2011;



Hompes et al., 2011). Portal vein embolization, radiofrequency ablation, two-stage hepatectomy, conversion therapy and reverse treatment strategy along with hepatectomy are used in the presence of extrahepatic disease (Coimbra et al. 2011; Narita et al., 2011, Tsim et al., 2011). Resection of advanced colorectal liver metastases after a second-line chemotherapy regimen is safe and promising in certain cases. The addition of neoadjuvant chemotherapy should, however, be cost-effective.

Positron emission tomography/computed tomography have a higher accuracy for detection of extra-hepatic and colorectal liver metastases than computed tomography alone (Patel et al., 2011). In patients treated with neoadjuvant chemotherapy, magnetic resonance imaging measurements of steatosis show the highest correlation coefficient and the best diagnostic accuracy, as compared to computed tomography ones (Marsman et al., 2011). Intraoperative ultrasound and preoperative imaging significantly increase the diagnostic accuracy of patients undergoing liver resection for colorectal liver metastases (Lordan et al., 2011).

Metachronous resections have a better outcome than synchronous. Iterative resection is very encouraging and justifies an aggressive surgical approach (Tonelli et al., 2010). Simultaneous resection is safe and efficient in the treatment of patients with synchronous colorectal liver metastases while avoiding a second major operation (Chen et al., 2011). In patients with bilobar synchronous colorectal liver metastases who are candidates for two-stage hepatectomy, combined resection of the primary tumour and first-stage hepatectomy reduces the number of procedures, optimizes chemotherapy administration and may improve outcome (Karoui et al., 2010). The two-stage strategy for colorectal liver metastases can be performed with acceptable morbidity and mortality. The second stage is not feasible in 20-25% of patients. Patients completing the two-stage approach may have long-term survival comparable to those treated with a planned single-stage hepatectomy (Tsai et al., 2010). Concomitant extrahepatic disease in a patient with colorectal liver metastases should not be a contraindication to their resection.

As there is no significant difference in morbidity, mortality, recurrence rate, or survival in anatomical and nonanatomical liver resections, the latter can be used as a save procedure to preserve liver parenchyma (Lalmahomed et al., 2011). The Pringle maneuver does not seem to affect the survival of patients with liver metastases (Ferrero et al., 2010). Ultrasound-guided finger compression of sectional portal pedicle feeding the right posterior section is a feasible, safe, and effective method for performing anatomical right posterior sectionectomy (Torzilli et al., 2011).

Prognostic factors and score systems occupy an important place in oncologic liver surgery (de Haas et al., 2011; Peng et al., 2011; Pulitanò et al., 2011). Although twelve prognostic scoring systems have been identified from 1996 to 2009, there is no 'ideal' system for the clinical management of patients with colorectal liver metastases (Gomez et al., 2010). A predicted positive surgical margin (R1 resection) is not any absolute contraindication to surgery for aggressive or advanced colorectal liver metastases (Tanaka et al., 2011). Liver resection has superior long-term survival which is, however, significantly reduced by the occurrence of post-surgical complications (Schepers et al., 2010). Superior overall health-related quality of life merits an aggressive surgical approach and intensive follow-up to detect recurrence early (Wiering et al., 2011).

## 8. Conclusion

Based on our own results and reliable scientific evidence available worldwide up-to-date, it can be concluded that the patient presenting with colorectal liver metastases deserves a

timely and individualized diagnostic and complex therapeutic approach by an interdisciplinary physician's team. Medical staff's behaviour should be maximally sparing, when possible.

New advances in image diagnostic modalities such as positron emission tomography/computer-aided tomography, steadily improved surgical and microsurgical techniques such as laparoscopic resections along with emerging opportunities for cost-effective chemotherapy and multimodal management promise better perspectives in this field of permanently rising social significance.

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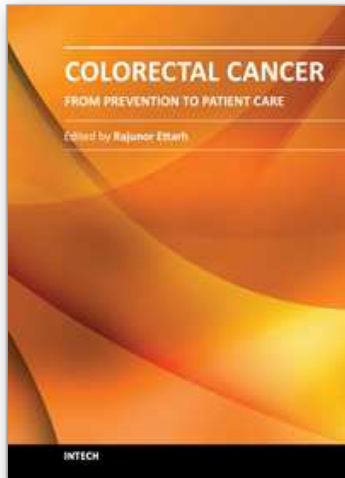
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## **Colorectal Cancer - From Prevention to Patient Care**

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The projections for future growth in the number of new patients with colorectal cancer in most parts of the world remain unfavorable. When we consider the substantial morbidity and mortality that accompanies the disease, the acute need for improvements and better solutions in patient care becomes evident. This volume, organized in five sections, represents a synopsis of the significant efforts from scientists, clinicians and investigators towards finding improvements in different patient care aspects including nutrition, diagnostic approaches, treatment strategies with the addition of some novel therapeutic approaches, and prevention. For scientists involved in investigations that explore fundamental cellular events in colorectal cancer, this volume provides a framework for translational integration of cell biological and clinical information. Clinicians as well as other healthcare professionals involved in patient management for colorectal cancer will find this volume useful.

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