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Surgical liver resection in multimodal therapy of hepatic malignant affections: A 4-year study

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BACKGROUND: *The goal of our study was to evaluate our hitherto 4-year surgical treatment of liver malignancies.*

METHODS: *Our team performed 43 liver resections from 1997 to 2000. Of these, 10 were primary tumours and 33 metastases. The most frequent indication for resection in our sample was for colorectal cancer - in total 27 patients. Metastatic pancreatic cancer or metastases of malignant melanoma account for rarer indications to surgery. We considered CT arterio-portography (CTAP) as the most significant preoperative examination from all available radiological methods.*

RESULTS: *Proper resection of the liver is possible even without special technical equipment. No patient between the ages of 22 - 82 years died in the 30-day postoperative period. Our postoperative morbidity was 18.6%. The most frequent complication was prolonged biliary secretion from drains. In our study, recurrent liver malignancies occurred most frequently - within 6 months from the primary resection.*

CONCLUSION: *Radical resection procedure may be facilitated for the greatest number of patients with primary or metastatic liver malignancies by the cohesive cooperation of a number of specialists.*

KEY WORDS: *Liver Neoplasms; Neoplasm Metastasis; Hepatectomy*

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INTRODUCTION

Primary and secondary malignant diseases of the liver have a poor prognosis and high incidence of recurrences. Surgical liver resection is the only potentially curative treatment option. The aim of the surgeon's participation in multimodal therapy is to ensure radical liver resection for the greatest number of patients.

Largely due to a well-developed colorectal and pancreato-biliary surgical program, an increasing number of patients with primary and mainly secondary metastatic hepatic tumours have been treated in our department. This article reviews and evaluates our 4-year experience with resections of the liver, and attempts to put into context the results and methods of our workplace with others in medical literature.

MATERIALS AND METHODS

Material

From January 1997 to December 2000 our team performed liver resections in a total of 43 patients. The sample consisted of 23 men and 20 women. Ages ranged from 22 - 76 years (median age 59 years) in men and from 29 to 82 years (median age 60 years) in women. The predominant indication for liver resection was metastatic colorectal carcinoma, which was found in 27 patients. Other tumours included were metastases from solitary malignant melanoma in 2 cases, GIT carcinoid in 2 cases, pancreatic carcinoma in 1, and gastric carcinoma also in 1 case. With regards to primary tumours, the incidence of cholangio- and hepatocellular carcinoma (6 patients) was the highest in our population, gallbladder carcinoma was the second (3 patients), and very rarely was the primary Grawitz tumour directly proliferating into the liver (Table 1).

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Table 1. Liver resections from 1997 to 2000: Review of indications for liver resection

Indication	N (%)	
Ca hepato-cholangiocellular	6	(14)
Ca of the Gallbladder	3	(7)
Grawitz tumour	1	(2)
Meta colorectal carcinoma	27	(63)
Meta carcinoid	2	(5)
Meta malignant melanoma	2	(5)
Meta gastric cancer	1	(2)
Meta pancreatic cancer	1	(2)
Total	43	(100)

Solid primary tumour sizes ranged from 35 to 80 mm, excepting gallbladder bed resection in one of the cases of gallbladder carcinoma, where only tumours not exceeding T2 according to TNM classification were indicated for resection.

The diameter of metastases resected ranged from 9 - 110 mm. In total, we resected 54 metastasis in 33 patients. Of all metastases, 24 (44 %) were smaller than 20 mm, 18 (33 %) varied in size from 20 to 50 mm and 12 (22 %) were larger than 50 mm. Solitary metastasis was found in 20 patients (60 %), 2 - 3 metastases in 11 patients (33 %) and more than 3 metastatic areas were detected in 2 patients (6 %) (Tables 2,3).

Table 2. Liver resections from 1997 to 2000: Number of metastases

Number of metastases in resected samples	N (33 patients)
1	20
2-3	11
>3	2

Table 3. Liver resections from 1997 to 2000: Diameter of metastasis

Diameter of metastases (mm)	N (54 metastases)
9 – 20	24
20 – 50	18
> 50	12

Methods

Indications for liver resections are based on standardised examination. During the last 2 years, all patients studied underwent CTAP examination. Among available examinations, CTAP has the best sensitivity for multifocal lesions and is capable of their precise localisation in liver parenchyma in comparison with conventional CT and ultrasonographic examination. In addition to common laboratory tests, relevant onco-markers were monitored. We do not utilise DSA (digital subtraction angiography) of the hepatic blood supply as a standard test of preoperative examination. After CTAP examinations, radiologists could inform us about important atypical findings in blood supply. This requires selective cannulation of the common hepatic artery and the superior mesenteric artery. In patients with cirrhosis, functional assessment of hepatic parenchyma was done by cholescintigraphy. Chemoembolisation of hepatic lesions with lipiodole, either alone or in combination with embolisation of portal venous branches, offers new possibilities for downstaging of lesions that were originally not suitable for resections. The purpose of this approach is to stimulate compensatory parenchymal hypertrophy of the contralateral liver lobe before the more extensive resection is performed. Neoadjuvant or adjuvant chemotherapy is only used as an adjunct medication in clinical studies, and is not considered standard therapy.

Resections are done mostly after a transversal subcostal laparotomy, which is then prolonged behind the medial axis, in combination with a vertical incision starting from the xiphoid process (Mercedes - Benz incision). The technique of resection used is dependent upon available equipment. As argon-beam, harmonic scalpel or CUSA (ultrasound dissector) were not available, we used the digito-clastic technique. Closure of the incised parenchyma was aided by spray-coagulation of the surface with a hemostyptic net attachment. We did not use the method of total vascular liver exclusion. Through careful preparation of the hilus and resections performed anatomically total blood loss was minimised. The extent of surgery depends on the lesion size and localisation. We always utilised a 10 mm zone of safety in performing our resections. Standard drainage of the resected bed is done until secretion is minimal. This prevents the development of fluid collections and their possible infection. After liver resection all patients were followed up at regular intervals and according to standard procedures in cooperation with oncologists, radiologists, pathologists etc.

RESULTS

During the period from 1997 to 2000 our team performed 43 liver resections. We increased the number of resections per year from the original of 4 per annum to 23 resections in 2000. Through this high number of resections we were able to minimise the incidence of postoperative complications otherwise found in workplaces with a lower frequency of such major surgeries (Figure 1).

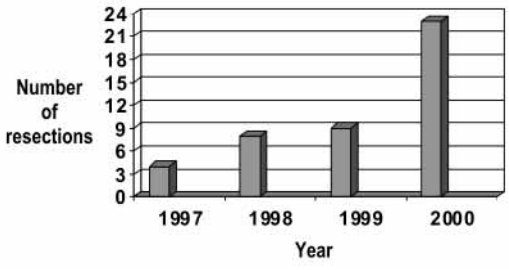

Figure 1. Liver resections from 1997 to 2000: Number of liver resections from 1997 to 2000

The same team of surgeons performed all operations. Operations included all types of resections: extra-anatomical excisions - 6 cases, segmentectomy and bisegmentectomy - 5 cases, hemihep-

atectomy and extended hemihepatectomy - 21 cases (Table 4).

Table 4. Liver resections from 1997 to 2000: Review of performed surgeries

Type of surgery	n	Surgeries for reasons of metastasis
Hemihepatectomia dx. (HHE)	13	11
HHE sin.	4	3
HHE sin. cum seg.V,VIII	1	
HHE dx. cum seg. IV	2	2
HHE dx. cum seg I	1	1
Bisegmentectomia	8	7
Segmentectomia	8	4
Wide excision	6	5
Total	43	33

Bisegmentectomy and larger resections are always anatomical ones, with ligature done of the relevant supply. Our perioperative blood loss usually did not exceed 560 ml, and in more than 30% of patients, blood loss was less than 200 ml. During the peri- and postoperative period following liver resection, transfusion was unnecessary in 48% of patients, and only in one patient 11 transfusion units were required for bleeding in the subsequent surgical revision (Figures 2,3)

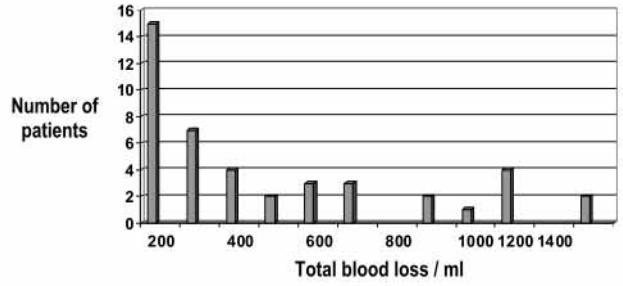

Figure 2. Liver resections from 1997 to 2000: Total peroperative blood loss

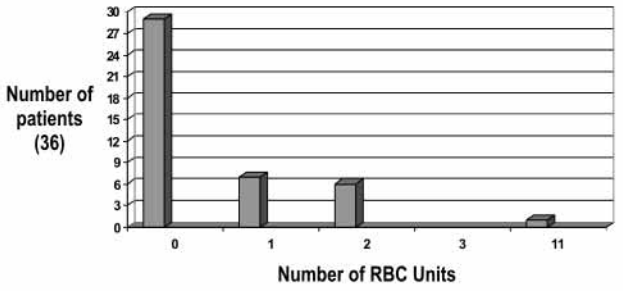

Figure 3. Liver resections from 1997 to 2000: RBC transfusions applied to patients in association with liver malignant lesion resection

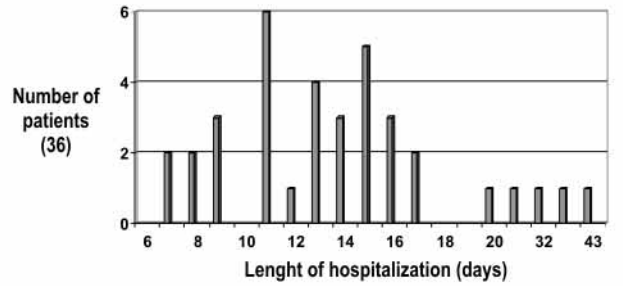

Figure 4. Length of hospitalisation following liver resection, 1997-2000

Total average duration of hospitalisation was 15.1 days, with 91% of patients being hospitalised for less than 17 days (Figure 4).

The implementation of our study on liver resection was later justified not only on the basis of long-term outcomes, but also on the low incidence of postoperative morbidity and mortality. In the 30-day period following resection, none of the patients died. Two patients had to undergo surgical revision; one for surgical bleeding from the wounded liver surface after hemihepatectomy and one in a polymorbid patient for suspected biliary peritonitis, but with a later finding of ascites from generalised decompensation. The most common complication was prolonged biliary secretion (4 patients), which lead to subphrenic abscess in two cases. The abscesses in both cases were treated by CT guided drainage. Surgical intervention was not necessary. During the aforementioned period, no iatrogenic injury to the biliary tract or larger vessels was reported (Table 5).

Table 5. Liver resections from 1997 to 2000: Postoperative morbidity and mortality

Complication type	N	Surgical revision	Mortality
Prolonged biliary secretion – more than 14 days (from which with abscess)	4 (2)	-	0
Pneumothorax	1	-	0
Successive embolism of AP	1	-	0
Haemoperitoneum	1	1	0
Suspecting biliary peritonitis	1	1	0
Total	8 (18.6%)	2 (4.6%)	0 (0%)

Long-term follow-up is still limited by the number of performed surgeries in individual years. Thirty-six patients were followed-up for at least 6 months. Seven of these 36 patients (19%) died from disease dissemination. Recurrence was reported in 17 patients (47%).

Complete remission was noted in 19 (53%) of 36 patients followed up for more than 6 months.

We were able to follow up 25 patients in one year; 15 of these (60 %) were still alive. Greater than two year survival was found in 9 patients, 6 being without signs of recurrence. Only 16 patients were followed up for more than 2 years. Recurrences or dissemination were found most frequently in the interval from 0 to 6 months from primary resection (Figure 5).

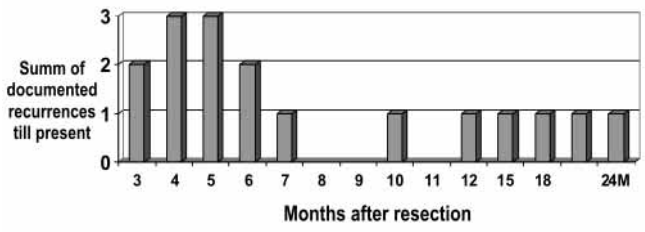

Figure 5. Liver resections from 1997 to 2000: Distribution of number of recurrences with respect to months following resection

In one case, resection of the second liver segment for recurrence of rectal carcinoma metastases was performed 10 months after a right-sided hemihepatectomy. Even before the first resection, this patient underwent chemoembolisation of diffuse metastases of the right liver lobe by the embolisation of the right branch of the portal vein. Further resection of the hypertrophic left liver lobe was then possible.

DISCUSSION

At the very beginning of our study on liver resection, it was necessary to address several concerns. Unequivocal indications for liver resection are primary resectable liver tumours, low differentiated gallbladder cancer, and resectable metastases of colorectal cancer (CRC) (1). However, we indicated resection in other selected cases: solitary metastases of other solid tumours, i.e. malignant melanoma, tumours of the stomach and carcinoid syndrome. One resection of solitary metastasis from pancreatic cancer was also done in a very young male patient with the intention of prolonging the patient's life (2-4). The criteria for indications for attempting resection of metastasis in colorectal carcinoma are:

1) Presumed radical resection R0;

2) Presumed R1 or R2 resection with the possibility of using alternative therapies for the remnant tumour (alcoholisation, chemoembolisation, etc.);

3) Resection of previous unresectable metastasis after successful downstaging.

In addition to multiorgan involvement contraindications to resection are foremost patient morbidity precluding the necessary operation (5).

The most important imaging method in our study, excepting classical CT or ultrasonography, was CTAP. It has a high sensitivity (about 96%) for multifocal lesions, and ensures a low percentage of perioperative non-resectable findings in comparison with those presumed preoperatively (6). In this context, we must mention that perioperative sonography is not available, and the extent of surgery must be fully determined by preoperative examination and perioperative finding upon palpation.

Our surgical team uses a modified "digito-clastic method" with the help of soft forceps following ligature of captured structures by absorbable material for liver dissection. We believe that in comparison with teams using methods such as CUSA, argon-beam, Jet-cutter and others, the number of complications or perioperative blood loss has not been increased (7). We prefer anatomical resections (except for small lesions) to atypical resections, respecting arterial and portal branches (8).

Maintaining a 10 mm macroscopic safety zone, and the minimisation of blood loss are the two prognostic factors which may be influenced mostly by surgeons (9-11). We presume that perioperative mortality of 0% and morbidity of 18% reported in our population fulfilled the qualification for continuing our study (4).

Adjuvant chemotherapy is not suggested as a standard approach after curative liver resections. Due to low or no therapeutic response, adjuvant chemotherapy is not indicated in primary liver lesions or gallbladder lesions. Surgical resection is therefore the only option for curative therapy. For the large part of metastatic CRC the role of adjuvant chemotherapy is not clear in case of metastatic liver disease. More extensive studies were performed, which did not show the benefit of adjuvant chemotherapy after R0 resections (12,4). Continued patient care by oncologists following curative resection of liver metastasis could help to answer this question. On the other hand, the capability of neoadjuvant therapy in terms of transforming non-resectable lesions to resectable ones is undisputed (13).

We could not evaluate long-term outcomes in our 4-year study, because only 16 patients were followed up for more than 24 months. It is significant that 10 out of 17 demonstrated recurrences or disseminations developed within 6 months after radical liver resection. One may question whether the absence of perioperative sonography even with CTAP examination could explain the apparent early dissemination after performed resections on the basis of non-diagnosed multiple or bilateral perioperative lesions (5).

CONCLUSION

Our team performed 43 liver resections during a period of four years; ten were for primary lesions and 33 for metastatic tumours. A precise indication for surgery and established operative procedure performed by the same team are the basis for an acceptable morbidity and mortality. CTAP examination has the highest sensitivity for multifocal and bilateral lesions in comparison with other available examination methods. The use of 10 mm macroscopic safety zone and low perioperative blood loss can influence long-term resection outcome. We also monitored other prognostic factors such as number and size of metastases, levels of onco-markers, etc. Multimodal cooperation of surgeons with mainly oncologists, radiologists and pathologists can ensure optimal standardised care to growing number of patients with malignant liver diseases even in local conditions.

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