

**Ph.D Thesis**

**RESULTS WITH ANTERIOR HEMIHEPATECTOMY AND MESOHEPATECTOMY  
WITHOUT HILAR DISSECTION IN TREATMENT OF LIVER TUMOUROUS DISEASES**

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## **Introduction**

It is difficult to estimate the frequency of focal liver diseases, especially considering the asymptomatic nature of various forms, in the average population. Benign and malignant liver disorders occur in 1% of the population as a post mortem discovery. Due to different reasons though, the ratio of recognised cases in different places of the world, therefore the need for surgical solutions is expected to increase based on recorded data in related publications . Many factors can contribute to this:

Imaging methods, that are becoming more and more accessible in the civilised world, such as ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) that can detect liver lesion in about 5% of symptom free cases could increase detection ratio. Presumably, the widespread use of oral anticoncipient and anabolic steroid use also contributes to the more frequent formation of symptom free focals, which, according to data in recorded publications, increases the likelihood of liver cell adenoma and focal nodular hyperplasia formation. According to our experience, not only the number of endemic parasitic liver cysts is increasing in Mediterranean countries of the continent as an inevitable consequence of globalisation and international migration, but also the number of liver cirrhosis and the induced hepatocellular cancer (HCC) cases caused by hepatitis type B and C, which is quite frequent in the Far East. Hepatitis B virus, sustained for decades, can increase the risk of HCC by about 100 times, while the risk induced by toxic, chronic liver defects increases by about 10 times. About 2-60% HCC can also be found in cirrhotic liver. Domestically, the most common cause of primary liver cancer is alcoholic liver disease as an endemic. Among focal liver diseases malignant, solid tumors represent a much larger proportion. We can expect the occurrence of metastasis in about 50% of malignant diseases. Excluding primary liver cancer, all tumours can result in liver metastasis, but most frequently the gastrointestinal tumours can spread to the liver from the area of the hepatic portal vein. According to worldwide data more than half all malignant tumours are of gastrointestinal origin and about 60-70% of all liver metastasis originate from colorectal carcinoma. Domestically, colon cancer is ranked at 2-3 in mortality statistics.

Based on these data, it is expected that the number of focal liver diseases will increase all over the world and a surgical alternative will arise more frequently in exceptional cases, primarily because the majority of benign liver diseases and all forms of primary or secondary cancers are

only curable with surgical methods according to our current knowledge.

Performing liver resection surgeries were basically made possible by three main factors:

- information about the functional anatomy of the liver
- development of methods suitable for removing benign or malignant centers
- global, rapid development of narcosis and postoperative intensive therapy.

Risk associated with surgery has significantly decreased over the past three decades with the rapid development of surgical techniques and intensive therapeutical methods and as a result surgical mortality rates were reduced from about 20-25% to 5%. International liver surgery has developed an arsenal of such surgical solutions from almost zero, that makes it possible to safely remove liver tissues of almost any size, even in multiple steps. Those surgical objectives that should be maximally considered during liver resection also became clearly defined, and characterise the work of individual liver surgical centers:

- 1 reduction of blood loss during operations
- 2 sustaining a tumour free safety zone in case of malignant diseases
- 3 keeping the necrotic zone beside the resection surface at a minimal level
- 4 averting bile leakage and abscess following the surgery
- 5 reducing time of surgical hypoxia
- 6 keeping functionally satisfactory residual liver parenchyma with the completion of surgery.

The so-called „finger fracture” parenchyma dissection technique published by Thon That Tung in 1965 was gradually replaced by the UH or water-jet surgery in liver surgery centers all over the world. The use of ultrasound dissector (cavitron ultrasonic surgical aspirator-CUSA) according to data recorded in related literature possesses significant advantages compared to the „finger fracture” method:

- 1 less blood loss during surgery, therefore less need for transfusion, which is beneficial for long term survival
- 2 smaller postoperative morbidity ratio
- 3 less early postoperative mortality
- 4 the tumour free edge is larger and can be kept safe during surgeries
- 5 the serum bilirubin level is lower following these surgeries, which refers to lower

degree of liver cell necrosis.

Based on knowledge regarding functional anatomy and segmental anatomy of the liver, liver resection with CUSA dissector has become a standard method. Prior to these, preliminary dissection and definitive attendance of liver hilus structure was only justified when performing *hemihepatectomies (HH)*.

The most common form of expanded liver resection is HH on the right side, which often complemented the removal of the Liver segment IV. The method itself is widely standardised. During the surgery, the liver ligaments are cut for the total mobilisation of the right segment, separate the liver from the vena cava, dissecting the liver hilus, then tying them off on the affected side. Then the assistant removes the sick liver part, after that the dissection and tying off of hepatic vein is performed. The actual dissection is only performed then.

One serious drawback of this method is that the liver has to be pulled strongly and rotated for resection during the maneuver and as a result the hepatic vein and inferior vena cava could crack. This could cause significant blood loss. Beyond this, in case of extremely large tumours, the scope of view significantly narrows down between the luxated liver lobe and rib angle both for the surgeon and for the assistant, so it is often really difficult to correctly address blood vessels entering the vena cava and reducing bleeding during the dissection. The rotated liver lobe can reduce the reflux of blood from the inferior v. cava towards the heart, which can have a depressive effect on the circulation. According to related literature, the intraoperative hypotonia is a risk factor, though indirectly, in per- and postoperative mortality and tumour recidivation. Tumour cell formation due to liver compression, or in case of an infected bile, the intravascular spreading of bacteria and the possibility of tumour/bacterium formation could increase, while the liver tumour could also crack during the manipulation, further increasing the possibility of blood loss and spreading of tumours. Additional disadvantage of traditional HH is that blood vessels supplying the left side of the liver are under compression during the operation, which can lead to the functional failure of the remaining liver parenchyma due to the long time of ischaemia.

The technical development of liver resection methods (CUSA, Water-Jet, Harmonic Scalpel) to prevent the disadvantages mentioned above provided an opportunity to perform a so-called „*anterior*/without mobilisation" for resection/*hemihepatectomy (AHH)*, without the mobilisation of the liver, which was first introduced by Ozawa in 1992.

The method of AHH significantly differs from conventional/traditional hepatectomies,

since the resection of the sick liver does not require mobilisation and removal in the early stages of the operation, and the tumorous part of the liver is left untouched and the ligation of hepatica branch and the portal vein branch is performed. The separation of parenchyma starts on the convex surface of the liver and advances towards the v. cava, following the Cantlie line most commonly on the border of the two lobes of the liver. The v. hepatica that drains the affected liver lobe is addressed along with the bile channel of the affected side.

Then, the liver ligaments of the sick liver lobe are cut and the tumorous specimen is placed in front of the abdominal wall. The advantages of the AHH technique are primarily apparent in the elimination of technical difficulties experienced during traditionally performed HHs, the peroperative morbidity data and the significant improvement of late survival results. The advantages of the method according to surgical teams frequently applying the AHH technique are the following:

- 6 the intraoperative blood loss can be less due to the elimination of v. cava és a v. hepatica iatrogenic injuries
- 7 the available surgical area is not narrowed with the removal of the liver, in fact the supply of retrohepatic blood vessels leading to the v. cava is safe all along
- 8 the blood supply of the intact part of the liver is not damaged when the sick part is removed
- 9 the method does not influence blood supply to the v. cava significantly during the surgery therefore no serious circulation depression has to be taken into consideration
- 10 lower chance of tumour rupture and intravascular tumour, or spread of bacteria
- 11 the abovementioned collectively result in lower peroperative morbidity, mortality and longer expected illness free survival
- 12 moreover, this surgical method also provides an opportunity for the safe removal of tumours in the lobus caudatus previously regarded as incurable.

Temporary liver function disorders occur in 0-70% of the operated cases, following the expanded liver resection, according to literary data. However, liver failure is a feared fulminant, in cases a complication with fatal results, which especially has to be taken into consideration due to the high ratio of parenchyma loss especially following the right lobe resection of the cirrhotic liver. Therefore, it is important to give a preliminary estimate of the planned resection along with the degree of cirrhosis and the capacity of functional reserve. The comparison of these two

parameters determines whether the resection can be performed without special preconditional treatments for the surgeon. Determining fatal liver failure is partly based on the judgement of the surgeon and can partly be estimated with preoperative tests. According to literary data about 20-25% residual parenchyma is required in case of functionally intact liver, or in case of cirrhosis about 40% remaining liver tissue is necessary following resection to avoid fatal liver failure when applying preoperative chemotherapy.

Consequently, methods offering organ sparing solutions appeared in liver surgery as an obvious effort. The so-called *mesohepatectomia (MH)*, which provided an opportunity to avoid the resection of the entire right or left lobe of the liver in case of tumours located in the middle segments (IVa, IVb, V, VIII) of the liver developed as a possible method of parenchyma sparing. The MH is possible due to the anatomical location of the biliovascular structure, because the blood vessels supplying the lateral liver segments run relatively close to the bile channels and the lower surface of the liver, therefore there is a possibility to isolate central segments of blood vessels and bile channels during the surgery, without damaging the bile drainage and blood supply of lateral segments. MH as a surgical technique can be connected to Wu C. C. and his associates and was first published in 1993 as a surgical method for addressing tumours of central liver segments. The operations were performed after preliminary meticulous preparation of liver hilus and addressing the blood vessels (in cases intraparenchymal) of the central liver segments. In spite of this, surgical blood loss (2450 ml) and the length of the surgery (7.9 hours) was significant. Scudamore and associates reported of surgical results with much lower transfusion requirements (914 ml) in 2000, but the length of surgery still remained similar with their technique as in the case of expanded liver resections (238 minutes vs. 304 minutes).

Although, the indication of the MH is not totally clarified due to the relatively low number of cases published in related literature, the advantages and disadvantages of surgeries performed this way are distinct based on the experiences of the authors.

Unequivocal advantages when performing MH are:

- 13 resectability ratio of centrally located liver tumours can increase due to the applied technique
- 14 the residual parenchyma mass is significantly larger following the resection, therefore the postoperative morbidity is lower and liver failure can be avoided
- 15 postoperative liver and bilirubin deviations are settled earlier than following expanded

extended resections

16 long term illness free survival is better, than with traditionally performed HH.

However, we can also consider more serious technical disadvantages when performing MH based on recorded literary data:

17 hilus dissection requires more precision, therefore significantly increases the length of surgery

18 more significant blood loss has to be taken into consideration during surgery

19 the blood supply of lateral segments and bile drainage could easily become damaged when performing MH, making expanded liver resection necessary.

20 increased likelihood of bile leakage due to the dual surface of parenchyma-resection.

We began our liver surgical activities considering the abovementioned in 1992. Our institute had the opportunity to carry out significant technical developments in 1996 and we obtained a CUSA dissector and Ultracision device. Observing the excellent surgical results achieved with these devices recorded in related literature, we thought that we will not only apply them in daily practice when performing conventional hemihepatectomies, but will also introduce the *anterior hemihepatectomy* and *mesohepatectomy* procedure at our clinic.

We expected an improvement in the resectability ratio of liver tumours with the introduction of both methods. Naturally, the introduction of new devices and the two new surgical methods could only be implemented with increased caution. We decided during „practice” that we will not generate such any situations, that could result in an irrevocable operative situation and puts the patient in danger. The definitive liver hilus biliovascular ligation performed in the early stages of the surgery of both AHH and MH surgeries as published in the original literary publications could generate such a scenario.

We decided to *keep the integrity of liver hilus during the surgeries* when performing both the AHHs and later the MHs due to the initial uncertainty of our preoperative and intraoperative diagnostics and the number of inherent pitfalls in the technical details of the new surgery types. The then accessible literary data did not refer to cases when the actual removal of the liver tumour is not possible due to surgical techniques or anaesthetic reasons and this only becomes apparent at the end of the parenchyma dissection contributing greatly to the modification of the technique and raising question about the destiny of definitive devascularised sick liver lobe from



the hilus. Can its circulation be restored without a permanent damage to the liver, or can the surgery be stopped in such cases without a fatal outcome?

My examinations were aimed at proving the practical applicability and safe nature of *anterior hemihepatectomy* and *mesohepatectomy* surgery technique modification, and in order to do so, I examined and compared the surgical and postoperative results of liver resections performed with this method with perioperative results of *traditional hemihepatectomies* performed in the same timeframe in a retrospective manner.

## Objectives

Our current work was aimed at answering the following questions:

1. Does the lack of definitive attendance prior to parenchyma dissection have an effect on the length of the surgery when performing *anterior hemihepatectomy* on the liver hilus?
2. How does our method influence blood requirements when performing *anterior hemihepatectomy*? Can such advantages of *anterior hemihepatectomy*, known from related literature, be preserved with the application of this method compared to traditionally performed resection?
3. Does the surgical technique applied during *anterior hemihepatectomy* influence perioperative morbidity, mortality and length of hospitalisation?
4. Can the more favorable late survival data be preserved with our method of applied *anterior technique* compared to traditionally performed hemihepatectomies?
5. How does the lack of blood vessel preparation of central liver segments and definitive attendance influence the length of surgery during *mesohepatectomies* compared to traditionally performed *hemihepatectomies* and how does this compare to the length of surgery known from related literature?
6. Do blood requirements increase with our technique of *mesohepatectomies* and how does surgical blood loss data compare with the data previously published in literature?

7. Can the favourable postoperative morbidity data and the favourable length of hospitalisation recorded in related literature be preserved when performing mesohepatectomies with our resection technique?

## **Patients and methods**

We treated patients in 1346 cases with diffuse or focal liver diseases between 1<sup>st</sup> July, 1992 and 1<sup>st</sup> July, 2006. Resection type surgery was performed in 455 cases in this patient group. The resection expanded to 3 or more liver segments in 191 cases. Pericystectomy or fenestration was performed on 50 patients. Surgical biopsy during laparoscopic or open surgery was performed in 188 cases.

The surgical indication was malignant in 253 cases, and benign in 202 cases with patients who underwent resection. Primary liver cancer occurred in 54, metastasis in 199 cases in the abovementioned patient group. During the resection of benign mutations 42 focalis nodularis hyperplasia, 47 cavernosus haemangioma, 14 hepatocellularis adenoma, 66 parasites, or simplex cysts or 33 other benign tumours were removed.

We compared the surgical data of HHs (n=67) between 1<sup>st</sup> July, 1992 and 1<sup>st</sup> May, 2005 with the data of AHHs (n=52) between 1<sup>st</sup> July 1996 and 1<sup>st</sup> May, 2005 as well as the results of MHs (n=21) performed between 1<sup>st</sup> January and 1<sup>st</sup> July 2006 with the perioperative data of HHs (n=23) performed during the same period. The comparison of surgical data was made retrospectively.

### **Patients**

There was no difference regarding the distribution of age and gender ( $p=0.513$  and  $p=0.778$ ) of the patient group who underwent AHH and the jointly examined HHs. The average size of tumours was (AHH:  $11.6 \pm 4.9$ , HH :  $10 \pm 4.8$  cm), which did not differ significantly from each other ( $p=0.265$ ). In 11 cases primary liver cancer was the surgical indication for AHH, metastasis of colon cancer in 28 cases, metastasis of solid tumours in other organs in six cases and benign mutation in seven cases. Resection on the left was performed in 10 cases. The resection was carried out due to primary liver cancer in 12 cases, metastasis of colon tumour in 38 cases, metastasis of other organs in five cases and benign mutation in 12 cases when performing HH.

Primary tumour can be expected in all cases as a condition of indicated liver resection due to metastasis, or the resection of R0 previously performed and the exclusion of metastasis affecting other organs. We detected a small degree of peritoneal tumour spread affecting the

region of diaphragm and the infiltration of diaphragm in the case of AHH with four patients and in three instances in the case of HH.

We also performed diaphragm resection for these patients. The final histology also proved cirrhosis in six cases after HH was performed.

There was no significant difference ( $p=0.863$ ) regarding the age distribution of patients who underwent MH and HH between 1<sup>st</sup> January, 2001 and 1<sup>st</sup> July, 2006. The average size of tumours was (MH:  $10\pm 4.2$ , HH :  $14.2\pm 4.6$  cm), which proved to be a significant difference in favour of the HH group ( $p=0.021$ ). The surgical indication was liver cancer in three cases for MH, gall bladder cancer in two cases, metastasis of colon tumour in 10 cases, metastasis of other solid tumour in one case and benign mutation in five cases. Resection was performed in connection with HH in six primary liver cancer cases, in nine cases of colon tumour metastasis, in three cases of other solid tumour metastasis and in five cases of benign mutation. We detected that the tumour affected the diaphragm in three-three cases for both surgery types. We performed the partial resection of the diaphragm in these cases, the diaphragm could be reconstructed with direct suture, requiring a net implant. The final histology indicated cirrhosis regarding one patient when performing MH and two patients with HH.

### **Preoperative test**

Identical testing protocols were carried out for all surgery types prior to the planned liver surgery to determine the degree of resection, the involvement of blood vessel structures, and the remaining liver capacity, which included abdominal ultrasound, CT, liver angiography, liver enzyme, serum bilirubin, hemostasis test, ICG test, hepatitis B and C antibodies test, alpha-phetoprotein, carcinoembryonic antigen test, and ELISA test in when suspecting parasitic liver cyst, and when colon tumour metastasis was possible it also included CA19-9 and C125 tests. We did not routinely perform preoperative arterial chemoembolisation and/or selective v. portae branch embolisation, but we had to resort to such preconditioning in order to reduce tumour size and to achieve the hypertrophy of the intact side prior to AHH in eight and in four cases prior to HH. The embolization of the arterial or selective porta branch was not performed in the examined patient groups regarding MHs.

### **Anaesthetic considerations**

Surgical procedures, beside general anaesthetics and intensive therapy, included

monitoring arterial and central venous pressure, during which we kept central venous pressure at around five water cm in order to avoid reflux from the hepatic vein, however we did not apply positive pressure ventilation. On the day of the surgery we applied cephalosporin antibiotic prophylaxis, which was cefoperazone 2 gr (Cefobid), or cefotaxime 1 gr (Cefalekol). Depending on the actual blood loss, we gave the patient crsytalloid, plasma expander or blood group identical or selected blood. Surgery was not performed in extracorporeal circulation in the examined patient groups. All patients were given low molecule weight heparin formulas for thromboprophylaxis.

### **Surgical technique**

During the surgeries laparotomy was performed with bilateral subcostal, upper-arched transverse incision applying a retractor in case of HH, AHH as well as the MH technique. We did not perform a thoraco-abdominal exploration. Following the laparotomy and ruling out diffuse carcinosis in order to determine operability and to select the method of surgery, we felt tumour and if it was required with the help of intraoperative UH we clarified its relation to the loculum, hilus, the liver veins and vena cava. If the tumour was ruptured or felt soft, mouldering and therefore threatening with rupture, widely infiltrated the loculum or based on its location made vein preparation difficult, then we performed AHH on the affected side. Otherwise, we performed traditional HH, which we also expanded to the IV. liver segment if it was required. MH was performed in case of those central liver tumours, when the one cm resection safety zone made it possible to ensure good venous drainage as well as blood and bile drainage of lateral liver segments from the liver hilus.

The steps of the traditionally performed HH were the following: we performed the total mobilisation of the right or left side of the liver lobe by cutting the ligaments. We searched for the biliovascular structure then we dissected and tied them off. We did not dissect the infra- and superhepatic section of the v. cava in advance, somewhat differing from recommendations made in related literature. We did not apply total vascular exclusion during these surgeries. We lifted the sick liver out of its bed after addressing the hilus, then we usually addressed, depending on the surgical situation, the affected v. hepatica side. We then marked the resection border by dissecting the Glisson capsule, also using an intraoperative UH if necessary. In case of or when suspecting a malignant tumour, we kept a one cm safety zone in most cases (51 cases) resecting the affected liver side by using a CUSA UH knife considering the Couinaud-type segmental

borders. We also used a Baron/Pringle maneuver in the first phase of the HHs in 30 cases to reduce blood loss. We did not apply such pressure with latter HH surgeries.

We applied the original technical descriptions with the following adjustments when performing AHH: we cut the a lig. falciforme hepatis in all cases after determining operability mentioned before, then carefully lifting the upper surface of the liver we prepared the right and left branch of the v. portae and the a. hepatica, but did not tie them off permanently in the beginning of the surgery, but „en masse” held the blood vessels supplying the sick liver down for a short period of time, until the border of the two halves of the liver stood out. Generally, this helped to determine the place of resection, but in uncertain cases we also applied intraoperative UH to determine the place of the resection. Baron/Pringle pressure was only applied in the first 10 cases of AHH. The average pressure time was  $44.2 \pm 3.6$  minutes, which did not differ significantly from the compression time ( $p=0.322$ ) applied during HHs. The blood and bile drainage was free throughout in the following surgeries. We used an intraoperative UH with this method as well to keep the safety zone when it was necessary. We did not dissect the infra- and suprahepatic section of the v. cava, similarly to traditionally performed HHs. We began the resection without lifting the liver on the convex surface of the liver, progressing towards the v. cava, carefully pulling apart the two liver halves. We explored the retrohepatic v. cava and the v. hepatica supplying the sick liver half with gradual pulling and dissection, as well as the other accessory blood vessels in this location, then tied them off. It was only then when we tied off the biliovascular structures in the hilus supplying the affected liver half. We lifted the sick liver half out of the abdominal cavity after cutting the side ligaments in the final phase of the surgery. We also performed the resection of individual segments on two occasions regarding an AHH on the left side. All AHHs were performed with CUSA dissector.

The steps of the MH are almost identical with our method established during AHHs: we cut through the lig. falciforme hepatis in all cases after determining operability as mentioned above, then bimanually sensing the area between the vv. Hepaticae, we determined whether retrohepatic cava section is infiltrated by tumour. Then we carefully lifted the lower surface of the liver and prepared the right and left branch of the v. portae and the a. hepatica, but did not dissect them to the primary branches of the porta leading to the individual central segments thus

differing from the technique introduced in the literature. This way the parenchyma located at the lower surface of the liver remained intact in all cases. In this phase of the surgery we checked if the biliovascular condition of lateral segments was intact prior to the actual resection. If they proved to be intact, then we dissected the Glisson capsule according to dual resection line using an electrical knife, then we cut the parenchyma towards the cava from the convex surface of the liver using a CUSA dissector according to the method applied with AHH. We did not apply a hilus pressure either continuously or intermittently during the MHs, thus differing from literary data. We also omitted all forms of portal compression with HHs compared with the surgical results of MHs.

We coagulated the smaller bleeding blood vessels in the early stages of the surgeries with all forms of liver resection, using non-absorbing sutures or clips for the larger ones. We did not use a suturing device during the surgeries. We coagulated the resection surfaces with argon plasma in all surgery types and placed formulas saturated with thrombogenic agents on the surface then covered them with omentums. We fixated the remaining liver half to the abdominal wall in all cases, following the hemihepatectomy or the previous ligament to prevent blood supply disorders and consequent hypoxia originating from possible twisting. After performing MHs we sutured the remaining right and left lateral segments with absorbing sutures. We drained the surgical area after all resections.

### **Postoperative treatment**

During the evaluation of surgical results we observed intraoperative, early (<30 days), late (>30 days) complications. Cholestatic and necrosis indicating liver enzymes / alkaline phosphatase (AP), gamma glutamyl transpeptidase (GGT) and glutamine acid-oxalacidum-transaminas (GOT) and according to newer terminology aspartate-aminotransferase (AST), lactate-dehydrogenase (LDH), glutamate pyruvate transaminase (GPT), or according to newer terminology alamin-aminotransferase (ALT)/, total and direct bilirubin, hemostatic factors (INR, APTI, PI, TI) were checked on the 1. 3. 5. and 7. postoperative day, or on different days too if it was required. Patients were examined again every three then every 6 months. Patients were monitored for an average of 32 months. 32 of our patients received systematic chemotherapy following traditionally performed HHs, according to Mayo, then in the last two years according to deGramont protocoll. Eight patients did not agree to undergo offered chemotherapy. 1 patient

did not receive adjuvant chemotherapy due to a serious accompanying illness. We did not receive such data about 14 of our patients

13 patients received systematic chemotherapy from those who were operated due to malignant illness following AHH according to the protocol mentioned above. Three patients did not agree to undergo adjuvant chemotherapy. The Oncology Team of our University did not recommend the adjuvant treatment due to the stage of the accompanying illness and/or histology of the liver tumour for 19 patients. We do not possess reliable data about 10 of our patients regarding chemotherapy.

Six patients received adjuvant chemotherapy following MHMH. Two patients did not accept the offered treatment, the Oncology Team did not recommend the postoperative treatment for five patients and we do not possess reliable data regarding three patients.

### **Statistical analysis**

We used Independent Samples T-test and Analysis of Variance-t (ANOVA) to compare results, cumulative survival was calculated by using Kaplan – Meier, and Log-rank test. Results were calculated with SPSS 9.0 software. Significance level was determined at  $p \leq 0.05$ .



## Results

We did not lose any patients in the early postoperative phase following the application of AHH technique. Two patients died during conventionally performed HHs, due to anaphylaxia and coagulopathy caused by parasitosis. The surgeries were considered curative in all cases.

Complications were experienced with 20 patients following AHH. Icterus ceased spontaneously in 18 cases, we settled the severe hypovolemia by restoring water balance, the subcutaneous seroma was eliminated by changing the dressing. Complication arose with 23 patients following HH, we had to reoperate one patient twice due to bleeding. We lost this patient due to coagulopathy in the early postoperative phase. Fatal anaphylactic reaction occurred during the resection of large echinococcus cyst during the surgery with one patient. Bile leakage (4 cases) ceased after performing HH as a result of drainage left on the surgical area and no interventional radiological actions or reoperations were performed. The abscess detected under the diaphragm was curable with UH controlled percutan punctio and drainage.

Surgical time did not differ significantly ( $174.5 \pm 42.8$  vs.  $175.7 \pm 62.3$  minutes,  $p=0,954$ ) and the average length of nursing ( $20.4 \pm 13.5$  vs.  $18.3 \pm 6.9$  day,  $p=0,602$ ) did not differ significantly in the case of AHH and the traditionally performed HHs.

Blood requirement was significantly less when performing AHH ( $1.6 \pm 2.1$  E), than with traditionally performed HHs ( $4 \pm 4.8$  E,  $p=0,04$ ). We were able to perform AHHs in 22 cases, and HH in 18 cases without using blood products.

Excluding the data of surgeries due to benign mutations (AHH-7 patients, HH-12 patients), we did not find significant difference between the two groups regarding survival ( $p=0,386$ ). Average survival was  $11.7 \pm 7.9$  months among the deceased (25 patients) following AHH,  $30.5 \pm 18.3$  months have passed since the surgery for those who are still alive (20 patients). Average survival (excluding patients lost due to DIC in the early postop. phase) was  $15.6 \pm 15$  months among the deceased (31 patients) following traditionally performed HH due to malignant illness,  $33.8 \pm 30.5$  months have passed since the surgery for those who are still alive (23 patients).

We did not lose any patients in the early postoperative following MH. One patient died due to significant blood loss and consequent DIC. We had to reoperate this patient twice due to bleeding. The surgeries were considered curative in all cases.

We experienced complications with three patients following MH. In one case the bile leakage was sorted out with drainage left on the surgical area. The consecutive pleuritis and feverish condition of the other patient got well as a result of treatment with antibiotics. The fever of the third patient was eliminated with antibiotic treatment.

We experienced complications with six patients regarding HHs performed in this timeframe. The detected bile leakages stopped as a result of lasting drainage of the surgical area, as result no endoscopic intervention was needed. We detected fluid accumulation on the surgical area following a total three HHs, which proved to be biloma in two cases and abscess below the diaphragm in one case. All of them were eliminated with UH controlled puncture and drainage.

We detected significant differences between the two groups when comparing the length of surgeries:  $123.4 \pm 47.8$  minutes with MH, and  $169.2 \pm 48.4$  minutes ( $p=0.006$ ) with HH.

There was no significant difference among the surgical blood requirements of individual groups:  $3.2 \pm 2.7E$  during MH,  $3.9 \pm 4.5E$  ( $p=0.236$ ) during HH. Some of the surgeries were performed without blood- or blood product both in the case of MH (6 cases), and in the case of HH (6 cases).

Length of hospitalisation did not differ significantly in the case of given surgical groups:  $13.8 \pm 12.6$  days when performing MH,  $19.9 \pm 8.2$  days ( $p=0.316$ ) when performing HH.

We detected significantly lower variances on all examined days when we routinely checked liver enzymes indicating cholestasis and necrosis on the 1., 3., 5., and 7. days in the early postoperative phase compared to normal values following MH, but the degree of variance in the MH and HH groups only proved to be significant on the 7. postoperative day in favour of MHs ( $p<0.001$ ). On the same days when we checked serum bilirubin results, the variances proved to be significantly better every day compared to the normal values, excluding the first day, after performing MH than in the case of HHs ( $p=0.037$ ,  $p=0.038$ ,  $p<0.041$ ).

## **Discussion**

Primarily due to the remarkable development of surgical techniques (CUSA, Water-Jet, UH, cell saver, extracorporeal circulation) in liver surgical centers in the past two decades the mortality of expanded liver resection was reduced to 3-5% from 20-25%. In itself however, the development of the surgical technique could not have had such remarkable results, if it were not supported by the rapid technological developments in related professions (pathophysiology, hepatology, radiology, anaesthesia, intensive therapy, pathology...). New insights into the functional anatomy of the liver, clarification regarding the nomenclature of liver functional anatomy, estimating surgical bearing capacity based on evidences, different types of surgical methods for removing liver tumours, peroperative intensive treatment and multimodal treatment of malignant liver tumours in teams collectively led to a reduced operative risk for patients suffering from benign liver illness, and the prospects and life quality of patients with primary or secondary malignant liver tumours significantly improved.

In the past two decades, the objectives and expectations within the circles of liver surgery were clearly defined which have to be taken into consideration to a maximum extent when performing liver resection surgeries and provide an opportunity for comparing the data and results of individual surgical teams. The parameters below regarding resection liver surgeries can also qualify the results of individual liver surgical centers:

- 21 reduction of perioperative blood requirement and required blood supply, the degree of which also has an unfavourable effect on expected tumour free survival as well as on the parameters of morbidity/mortality
- 22 the resection and surgical hypoxia time, which also influences postoperative morbidity
- 23 keeping a tumour free safety zone in case of malignant illness, which is a prognostical factor of recidive tumours and expected tumour free survival
- 24 maintaining the necrotic zone at a minimal level beside the resection surface, which can reduce postoperative morbidity by preventing the increase of enzymes and bilirubin levels indicating necrosis following the surgery, bile leakage and abscess
- 25 saving functionally sufficient residual liver parenchyma after the surgery, which can ensure avoiding a fulminant liver failure.

It appears that professional opinion is also based on the abovementioned parameters when comparing the new, annually introduced liver resection equipment and modifications in the

surgical techniques.

An entirely new chapter began in the course of the liver surgical activity of our clinic which began 1992, when the opportunity arose in 1996 to use a CUSA then an Ultracision equipment. Supported by the favourable early experiences published in related literature, but being cautious of surprises caused by modern technique, we carefully integrated the new technical elements into our daily liver surgical activities. Considering the reliability of existing imaging tests and being beware of unusual elements used in connection with AHH, we decided to avoid irrevocable surgical situations (such as: de facto attendance of liver hilus to be resected) during „practice”. This concept was greatly influenced by the fact that literary data provided then and published since did not refer to actions to be taken in surgeries when following the parenchyma dissection, contrary to pre- and perioperative findings, the total and final removal of liver tumour can not be performed due to surgical technique or anaesthetic reasons. What should be done to the sick liver half definitive devascularised from the hilus? Does it have to be restored or can its circulation be restored without permanent damage to the remaining liver, or can the surgery be abdicated in such cases without fatal outcome?

Our surgical team was motivated by the doubts and questions mentioned above when we began performing AHHs in 2001 and MHs in 1996 with such technical modifications, which preserved the integrity of the liver hilus during the expanded liver resection. We did not change the introduced methods over the years due to the early and good results of the thus performed AHHs and MHs. We find it an obvious advantage regarding the applied AHH technique, beside the achieved results, that the method provides an opportunity to safely perform a surgery even in unexpected cases arising at the end of the operation.

The hepatectomies, technically based on the so-called „finger fracture” parenchyma dissection method published by Thon That Tung in 1965, which was accompanied by significant blood loss and complications, were replaced by UH or water jet liver resection methods, which had lower blood requirements and significantly better postoperative morbidity and mortality parameters. The liver resection in anatomical units, including the most commonly performed hemihepatectomy on the right side, became a conventional but by far standardized surgical solution.

Many disadvantages and pitfalls of this method became known, which originate from the

technique of the method and the lifting, pulling and rotation of sick liver side in front of the ribs. The most important disadvantages are the following: lifting and rotation of tumorous liver half narrows down the surgical area, making the correct care for bleeding difficult, the pressure of v. cava can result in hypotension and cardio depression, the compression of the left liver side can result in its hypoxial damage, tumour and/or bacteria embolus or anaphylactogenic substances from the rotated liver half can infiltrate the circulation, the direct power inflicted can result in the cracking of the rotated liver half resulting direct tumorous spreading and serious bleeding. These technical disadvantages can directly or indirectly, but significantly worsen perioperative morbidity, mortality and can effect the long-term tumour free survival according to literary data. At the same time, the main problem with these surgeries is still the significant blood loss, which, beyond the possible iatrogenic damage of vv. hepaticae és a v. cava, originates from deeper resection levels.

The occasional significant blood requirements based on literary data, can significantly worsen perioperative morbidity and long term survival. We have also lost a patient due to polytransfusion and consequent coagulopathy applied during traditionally performed HHs. Many surgical teams recommend the tying off the affected biliovascular structures of the liver following the preparation of the liver hilus prior to actual parenchyma dissection to reduce the blood loss when performing traditional HHs. Even so, the venous reflux originating from the v. hepatica can result in serious blood loss during surgeries, if, as it is recommended by Makuuchi, the v. hepatica is not cared for as early as possible following the lifting of the right liver half. Tying off, in case of traditionally performed right side HHs, results in significant reduction in blood loss during such surgeries, according to observations.

Observing the disadvantages of traditionally performed hepatectomies, it was recognised and published by Ozawa, that the so-called anterior liver resection method in 1992, which almost totally eliminated the disadvantages of traditional HHs and put the surgical treatment of such tumours into a fundamentally new light, which due to their size and location and the possibility of tumour rupture made it impossible to prepare and address the v. hepatica in the early stages of HHs because of possible tumour rupture. This method, due to its nature, could not have been established without the previously mentioned rapid developments in surgical techniques (CUSA, Water-Jet, Ultracision).

The possibility of a serious venous reflux from the intact vv. hepaticae can always be

expected when performing AHH, since during the application of the anterior technique, the retrohepatic blood vessels and v. hepatica supplying the sick liver half can only be addressed after the actual dissection, in fact there is no real opportunity to reduce serious bleeding with temporary compression due to the lack of mobilisation of the affected liver half. Because of this, Hohenberger and associates regard this surgical technique more demanding in blood requirements and only perform it on the basis of strict indications.

It seems from the parameters of blood loss, that the liver mobilisation method, published by Belghiti and further developed by Suzuki, which provides easier access to bleeding from deeper levels can improve the parameters of blood loss when performing AHH. It seems though that irrespectively of the Belghiti's technical suggestion, blood loss is significantly lower or can be kept at a similar level by the appropriate use of Water-Jet or CUSA UH dissector when performing AHH than compared traditional hemihepatectomies, based on the experiences of surgical teams with a higher number of cases. Our own experiences and results also support the recorded data of Lai and his associates, according to which the blood loss parameters similar to HHs experienced during the early period of AHH introduction and practice, significantly reduce in favour of the AHH technique.

We did not use the technique recommended by Belghiti és Suzuki in connection with the AHHs we performed, but we still managed to keep blood requirements at a significantly lower level with the applied modifications of the original AHH technique compared to the surgical blood loss data of HHs. This is even more interesting considering that according to our preferred and introduced AHH method, the hilus is not addressed definitively in the early phase of the surgery, but the biliovascular structures supplying the sick liver half are only tied off permanently in the final phase of the dissection. This way, the afferent circulation of the liver remains intact all throughout during the resection, therefore it can seem logical that this could result a significant blood loss. This can be prevented by paying increased attention during preparation and reducing blood loss when performing resection. This could however result in a significantly longer surgery, worsening postoperative morbidity data, also accompanied by a longer application of hilus pressure. Based on our results, our surgical team managed to develop a harmonic AHH technique that does not require hilus compression in most cases, where the intact blood supply of the liver hilus all throughout the resection did not increase the length of the surgery significantly.

Critically observing the blood requirement data of our surgeries we cannot disregard the

fact that iatrogenic v. hepatica, or cava cracking responsible for the greatest degree of blood loss did not occur in the examined patient group, but final histology proved the presence of cirrhosis in six patients. We think that this could have contributed to the formation of the significant difference.

It is important to mention that in synchrony with the practice of AHH technique that many surgical teams with a large number of cases share the opinion that applying pressure on the hilus can be avoided or can be reduced to a minimum during these surgeries. Our own experiences support this therefore we performed most of our surgeries (AHH-42 patients, HH-37 patients) without a total or a partial Baron/Pringle maneuver.

Naturally, the method we introduced still ensures the possibility of a better blood supply in the retrohepatic blood vessels, since even with a larger sized tumour the surgical space between the ribs and the liver is not narrowed down when performing AHH, which is compulsively accompanies the rotation and lifting of the tumorous liver when performing conventional HH.

This surgical technique also allows the safe resection of the lobus caudatus. We performed lobus caudatus resection twice in connection with our AHH method. These patients recovered without complications.

In accordance with previous literary observation, we noticed the same ratio of peroperative complications (AHH: 20/52, HH: 23/67) when applying the two different techniques, which healed without reintervention in the case of AHH. We could cure complications that developed in connection with HH with conservative therapy and interventional radiological methods. According to our experiences the fact that we drained the surgical area following all performed resections, contrary to a number of literary recommendations, greatly contributed to this.

During the examined HHs, we had to reoperate a patient twice due to bleeding and unfortunately we lost this patient in the early postoperative phase due to coagulopathy induced by polytransfusion. The other anaphylactic fatality that occurred when performing HH, raised the question of preferring the AHH technique during surgeries for extended liver resections due to large, parasite cysts with thin walls in order to achieve lower pressure on the cyst. Overall, we

also detected more favourable mortality data similarly to recorded literature when following our AHH technique. The significantly lower blood requirements, the more favourable length of the surgery, in correlation with literary data, resulted in more favourable morbidity results when performing the preferred AHHs. Accordingly, no significant differences were found between the two surgical groups regarding the length of the hospitalisation in accordance with this.

The large size of tumours, which in itself is a bad prognosis, can significantly make traditional HH more difficult, at the same time the mobilisation of the liver half can easily lead to tumour rupture, or it can promote the rupture or the splitting off of the tumour, further worsening the prospects of the patients. In case of large, fragile tumours the anterior technique is more beneficial by all means, because it ensures a better illness free survival according to literary data. Iatrogen, visible tumour rupture did not occur in any of the examined groups in connection with our surgeries but we detected local peritoneal spread in connection with performing AH in four cases and in three cases when performing HH as well as tumorous propagation affecting the diaphragm, which were removed during surgeries. The performed liver resections and resection of the affected part of the diaphragm did not increase tumour free interval in our cases either, but similarly to data in published literature, improved the life quality of patients. At the same time, contrary to published data in related literature, the ratio of advanced tumour stages in relation to performing AHH can be a reason for the unfavourable survival results experienced with our patients. We think, that considering the abovementioned, the lower survival rate of our patients is not the consequence of AHH modifications in the AHH technique but rather that of the large volumes and advanced stage of tumours.

A basic requirement during expanded liver surgeries beside significant reduction of blood loss is the minimisation of hypoxia time, preservation of parenchyma possessing sufficient functional reserve when finishing completing the surgery as well as establishing a tumour- and necrosis free safety zon, which is a prognostic factor of tumour recidivity and postoperative morbidity.

The method, first called mesohepatectomy (MH) by Wu C.C. and his associates in 1993, primarily meets the requirements of parenchyma sparing, which was used for removing the tumours from the central segments of the liver (IVa, IVb, V, VIII), sparing the lateral segments of the liver halves during the resection. They reported of significant surgical times (7.9 hours) and blood loss parameters (2450 ml) experienced during their surgeries. This could be due to many



factors, which should primarily be searched for in the reported surgical techniques:

- 26 we believe that it lengthens surgery time, that in their cases beyond the often time-consuming preliminary liver hilus dissection, due to the large size of the tumour, they meticulously searched for and addressed the biliovascular structures of the central liver segments.
- 27 this is complemented by a dual resection parenchyma surface that forms during MH, which is also time consuming to address correctly.

In 2000 Scudamore and associates have reported of a significantly more favourable MH in blood requirements (914 ml) and surgery time (238 minutes). Their surgical team applied a total or partial portal pressure in half of the cases to reduce blood loss when performing selective hilus dissection. They also found lower morbidity in case of MH than in the case of HHs, which is explained by the prior setting of liver function values due to larger residual liver parenchyma. This early remission advantage could also be ensured in those cases, when the surgical hypoxia time was longer during these resections in the examined patient group. At the same time, surgical time could still be regarded significant with their technique.

We decided that we are going to attempt to leave the afferent blood vessel/bile supply intact instead of the hilus dissection in connection with MHs as well, based on the favourable early experiences tested and introduced during AHHs. We expected saving time of intraparenchymal dissection often performed in the liver hilus from the method. We also had to take the possible increase of blood requirement into consideration, since the liver also receives blood from the afferent side during the MHs performed with this technique. However, based on the favourable experiences recorded in related literature regarding portal pressure and taking our own favourable experiences regarding AHHs into consideration, we decided not perform a Baron/Pringle maneuver during either MHs or the HHs performed during the same period.

We found significant differences among the lengths of surgeries regarding MHs performed with this technique in favour of MHs (MH: 123.4 ±47.8 minutes, HH: 169.2±48.4 minutes) between the 2001 and 2006 period . We assume that this unexpected good result could have been influenced by the precise but at the same time relatively fast paced surgical technique developed during AHHs along with the lower rate of cirrhosis (MH: one patient, HH: two

patients) compared to recorded literature.

At the same time, the technique we applied resulted in significantly more favourable surgical lengths during MHs than the data previously recorded in related literature.

We did not find a difference regarding blood requirements compared to traditionally performed HHs, which is in accordance with previously published data. Contrary to our expectations, abandoning the meticulous dissection of liver hilus and biliovascular ligatura from the beginning of the surgery, did not lead to an increased blood requirement, in addition, we could achieve more favourable blood requirement data with this method compared to related findings of other surgical teams.

We could perform six MHs without the use of blood products with the increased surgical routine.

At the same time, performing MH could also be a more difficult task technically, due to the parenchyma dissection that requires more precision. If we did not perform this with sufficient caution, then the blood supply and bile drainage of lateral segments could be damaged, making us resort to hepatectomy and consequently losing the long term benefits of this surgery type. No such complication occurred during our surgeries, which was largely due to preoperative imaging tests as well the help provided by our radiologists in intraoperative UH. The dual resection liver surface, originating from the essence of MH, could at the same time increase the possibility bile leakage and early bleeding when performing this type of surgery. Previously to this, we coagulated the lateral liver halves with argon plasma then we suture them together in our daily practice following the MHs. The surgical area is always drained similarly to other liver surgeries. Significant bile leakage occurred with one of the three postoperative complications experienced with MHs, but this ceased as a result routine drainage applied on surgical area. No radiological intervention, bile drainage or reoperation was required.

The favourable effect of MH, which is primarily due to the lack of hypoxia time originating from the essence of our introduced technique, was detectable in the normalisation of liver function enzymes and bilirubin serum settling. The normalisation of enzymes indicating cholestatic and necrosis occurred earlier following MH. The difference in enzyme level was significantly lower on every examined day compared to the normal values following MH. We found significant difference on the 7. postoperative day between the two groups in favour of MH. Increase inserum bilirubin level following MH and HH compared to normal levels was

significantly lower following MH on every examined day excluding the first day than during HHs. It is not surprising, based on the abovementioned data that the length of hospitalization did not differ significantly in the individual groups. This data are in accordance with the published favourable postoperative results following MHs.

The late survival data cannot really be compared, due to the shortness of the time that has passed since performing MH, but all patients who were operated with this technique, are still alive, their average tumour free intervals are 20.7 months. In connection with the complex oncological treatment of these patient groups, the Chinese publication about Chen and associates deserves much attention, where the results of artery or portal embolization prior to MHs based on 246 operated patients are published. They used preconditioning embolization prior to 89 MHs and could achieve significantly better tumour free survival with the applied method. Based on the abovementioned data it can be assumed that this method could be easily combined with our MH method lacking hilus dissection, as in this case the preliminary artery embolization or selective v. porta embolization cannot interfere the preparation of liver hilus. Maybe this could also promote the long term tumour free prospects of our patients following MHs.

## Summary

The results, achievements and new findings of our work are summarised as follows:

The modification of the dissection method of the liver hilus introduced in anterior hemihepatectomy (AHH) and mesohepatectomy (MH) surgeries is suitable for the resection of large and centrally located liver tumours, because

1. The method introduced in connection with **anterior hemihepatectomia** did not raise the time of surgery significantly compared to traditionally performed hemihepatectomies (HH).
2. We proved that we could not only maintain favourable indicators regarding the use of blood in the course of **anterior hemihepatectomies** recorded in related publications, but could achieve significantly more favourable blood use results with this method compared to traditionally performed **hemihepatectomies**.
3. The perioperative morbidity of the modified liver resection method applied in the course of **anterior hemihepatectomy** was similarly favourable to that of traditional **hemihepatectomies**, while mortality data were unequivocally better when performing **anterior type surgeries**. We proved that the introduced method did not lengthen hospitalization significantly.
4. The late survival results did not differ significantly in the case of the modified **anterior** technique compared to conventionally performed **hemihepatectomies**.
5. We proved that with our method of mesohepatectomies, the length of surgery can be significantly shortened, compared to traditionally performed **hemihepatectomies** and the length of the surgery is significantly shorter than the previously recorded data.
6. We proved that the introduced **mesohepatectomy** surgical procedure does not increase blood requirements in patients compared to traditionally performed **hemihepatectomies** and our results were significantly better than in previously published papers.
7. We proved that our modification of **mesohepatectomies** ensures similarly good postoperative morbidity data as the MH technique described in literature while preserving the advantages regarding the favourable length of hospitalization.

## Scientometrics

### Publications supporting the Ph.D thesis:

1. **Takács I**, Varga G., Hallay J., Szappanos M., Sáy P.: Fokális májbetegség miatt végzett reszekciók eredményei. *Magy. Seb.* 52, 21-25 (1999).
2. P. Tóth, **I. Takács**, L. Kerekes, P. Sáy: Chirurgische Behandlung der intraabdominellen Blutung bei Peliose der Leber. *Chirurg* 73, 83-85 (2002). **IF: 0.848**
3. **Takács I.**, Vágvölgyi A., Pósn J., Hallay J.: A primer és szekunder májdaganatok sebészi kezelése. Surgical treatment for primary and secondary tumours of the liver. *Magy. Seb.* 55, 243-249 (2002).
4. **Takács I.**, Furka A., Boland M.G., Pósn J., Vágvölgyi A., Kotán R., Hallay J., Sáy P.: Anterior approach for liver resection in the treatment of large liver tumors. *Chir. Gastroenterol.* 21, 371-375 (2005). **IF: 0.128**
5. **Takács I.**, Furka A., Boland M.G., Pósn J., Vágvölgyi A., Kotán R., Hallay J., Sáy P.: Anterior májreszekció, mint a nagyméretű májtumorok ellátására alkalmas műtéti módszer. Anterior approach for liver resection in the cases of the treatment of large liver tumors. *Magy. Seb.* 59, 362-368 (2006).
6. **Takács I.**, Furka A., Kovács G., Árkosy P., Szentkereszty Zs., Vágvölgyi A., Pósn J., Sáy P.: Mesohepatectomy without hilar dissection in the treatment of malignant focal liver diseases. *Hepatogastroenterology* 54, 201-205 (2007). **IF: 0.904**

**Impact factor: 1.88**

### Publications in other subjects:

1. Kovács I., Sz. Kiss S., **Takács I.**: Malignus nyelőcső szűkületek palliációja. *Magy. Seb.* 47, 79-85 (1994).
2. **Takács I.**, Sz. Kiss S., †Kiss S., Varga I.: Bronchiectasia miatt végzett tüdőrezekcióink eredménye. *Med. Thor.* 48, 343-347 (1995).
3. †Kiss S., **Takács I.**, Kerekes L.: Gyermekkori mellkassérülések ellátásával szerzett tapasztalataink. In: Dr. Ács G.: *Aktuális kérdések a gyermektraumatológiában.* 152-154

(1995).

4. Bóni J., Incze D., Nábrádi Z., **Takács I.**, Péterffy Á.: Tüdőtuberculosis miatt 1986-1995. között operált betegek adatainak elemzése. Med. Thor. 49, 121-126 (1996).
5. † Kiss S., **Takács I.**, Sz. Kiss S., Nábrádi Z., Incze D., Bóni J.: A veleszületett rekeszsérv miatt operált betegek adatainak elemzése. Med. Thor. 49, 297-303 (1996).
6. G. Varga, **I. Takács**, Z. Csiki, P. Tóth, M. Péter, P. Sáy: Postoperative chemoembolism treatment of primary and metastatic malignant hepatic tumours. Acta Chir. Hung. 36, 370-372 (1997).
7. Sz. Kiss S., Szerafin T., Tóth J., Kollár S., **Takács I.**: Hörgőcsonek védelem a costomediastinalis zsírszövet felhasználásával. Magy. Seb. 51, 199-202 (1998).
8. András Cs. Szűcs F. Zs., Csiki Z., Gál I., **Takács I.**, Sáy P., Péter M.: Primer és szekunder májdaganatos betegek lipiodolos kemoembolizációval végzett helyi kezelésének klinikai értékelése. Orv. Hetil. 32, 1773-1779 (2000).
9. Cs. András, Z. Csiki, I. Gál, **I. Takács**, L. Antal, Gy. Szegedi: Retrospective Evaluation of 5-fluorouracil-interferon  $\alpha$  Treatment of Advanced Colorectal Cancer Patients. Pathol. Oncol. Res. 6, 175-178 (2000).
10. Szentkereszty Zs., Vágvolgyi A., Kollár S., **Takács I.**, Sáy P.: Nem parazitás eredetű máj- és lép ciszták laparoscopos fenestrációja. Laparoscopic fenestration of non parasitic cysts of the liver and spleen. Endoscopia 3, 21-23 (2000).
11. A. Nagy, L. Kozma, I. Kiss, I. Ember, **I. Takács**, J. Hajdu, Nadir Er Farid: Copy number of cancer genes predict tumour grade and survival of pancreatic cancer patients. Anticancer Res. 21, 1321-1326 (2001). Impact factor: 1.416
12. **Takács I.**, Vágvolgyi A., Sasi Szabó L., Sáy P.: A laparoscoppal végzett májresekciónak kezdeti tapasztalatai. Our experiences in laparoscopic liver resections. Endoscopia 4, 9-12 (2001).
13. Csáky G., **Takács I.**, Veres L., Boland M.G.: Benignus, göbös strumák minimálisan lebenyeltávolítással végzett műtéteinek korai eredményei Early results following extensive surgery for benign nodular goiter (Minimum lobectomy). Magy. Seb. 55, 268-271 (2002).
14. Vágvolgyi A., **Takács I.**, Árkosy P., Péter M., Sáy P.: Near total hepatectomy in two steps for surgical treatment of liver metastasis of colorectal tumour. Hepatogastroenterology 50, 2176-2178 (2003). Impact factor: 0.837

15. **Takács I.**, Pákozdi A., Szekanecz Z., Vágvolgyi A., Dezső B., Dévényi K., Sály P.: Májresectio ritka parazitás fertőzés miatt. Visceralis típusú larva migrans szindróma. (Liver resection due to a rare parasitical infection. Visceral larval migrans syndrome). Orv. Hetil. 145. 25, 1333-1336 (2004).
16. **Takács I.**, Szerafin T., Kotán R., Kovács J., Sály P.: Intraoperatíven diagnosztizált parazitás májciszta laparoszópos reszekciója Harmonic Scalpel segítségével. Laparoscopic resection of intraoperative diagnosed parasitic cyst of the liver with the use of Harmonic Scalpel. Magy. Seb. 57, 219-223 (2004).
17. Kerekes L., **Takács I.**, Kollár S., Veres L., Sály P., Sz.Kiss S.: Változások a tüdő echinococcus cysta sebészi kezelésében. Changes in surgical therapy of pulmonary hydatid cysts. Magy. Seb. 57, 358-362 (2004).
18. Hallay J., Micskei Cs., Fülesdi B., Kovács G., Szentkereszty Zs., **Takács I.**, Árkosy P., Sipka S., Sály P.: FREKA TRELUMINA szonda alkalmazása pancreatoduodenectomiát követően. Use of tube FREKA TRELUMINA tube after pancreatoduodenectomy. Magy. Seb. 58, 402-405 (2005).
19. Sasi Szabó L., **Takács I.**, Árkosy P., Sály P., Szentkereszty Zs.: Laparoscopic treatment of non parasitic hepatic cysts. Surg. Endosc. 20 (4), 595-597 (2006). Impact factor: 1,962
20. Szentkereszty Zs., Pósn J., Pető K., Sály P., Boros M., **Takács I.**, Sz.Kiss S.: Sternoclavicularis ízület fertőzésének sebészi kezelése. Surgical management of sternoclavicular joint infections. Magy.Seb. 2007. 60: 514-517.

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