Hepatic Resection for Primary and Metastatic Liver Tumors

PRİMER VE METASTATİK KARACİĞER TÜMÖRLERİ İÇİN GERÇEKLEŞTİRİLEN KARACİĞER REZEKSİYONLARI

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Abstract

Objective: Surgical resection is the standard treatment for malignant liver tumors and selected benign lesions. Results of hepatic resection greatly improved in the last two decades and currently are associated with low morbidity and mortality rates. We analyzed hepatic resections for primary and metastatic liver tumors in our hospital.

Material and Methods: Thirty-eight patients underwent hepatic resection for primary and secondary liver tumors between January 1998 and June 2004. We evaluated patients' characteristics, indications for resections, complications, morbidity and mortality.

Results: Twenty-six percent of patients were operated for primary and 74% for metastatic liver tumors. One patient with cholangiocellular carcinoma who had been treated with left hepatectomy developed recurrence on month 14. Operative mortality developed in one patient who had undergone right hepatectomy for metastasis from adenocarcinoma of the caecum. Mean follow-up period was 34 months. Five (13.5%) patients died during this period.

Conclusion: Hepatic resection offers a long-term survival and potential cure for patients with malignant primary or secondary liver tumors. There has been a gradual increase in the number of hepatic resections for primary and secondary liver tumors with low morbidity and mortality rates.

Key Words: Liver; liver neoplasms

Özet

Amaç: Karaciğer rezeksiyonları uygun malign ve bazı benign tümörler için standart tedavi yöntemidir. Karaciğer rezeksiyonlarından özellikle son 20 yılda giderek daha iyi sonuçlar elde edilmeye başlanmış, morbidite ve mortalite oranları da giderek düşmüştür. Bu yazıda hastanemizde primer ve metastatik tümörler için gerçekleştirdiğimiz karaciğer rezeksiyonları değerlendirilmiştir

Gereç ve Yöntemler: Ocak 1998 ile Haziran 2004 tarihleri arasında 38 hastaya primer veya sekonder karaciğer tümörü nedeni ile rezeksiyon gerçekleştirildi. Bu hastaların özellikleri, rezeksiyon indikasyonları, morbidite ve mortaliteleri değerlendirilmiştir.

Bulgular: Hastaların %26'sı primer, %74'ü metastatik tümör nedeni ile ameliyat edildi. Sol hepatektomi yapılan kolanjiosellüler karsinomlu bir hastada takibinin 14. ayında rekürrens gelişti. Operatif mortalite, çekum adenokarsinomunun metastazı nedeni ile sağ hepatektomi yapılan bir hastada gerçekleşti. Ortalama takip süresi 34 ay olup bu süre içerisindeki mortalite 5 (%13.5)'tir.

Sonuç: Karaciğer rezeksiyonları ile primer ve sekonder malign karaciğer tümörlerinde uzun süreli yaşam ve potansiyel kür elde edilebilmektedir. Karaciğer tümörleri için yapılan rezeksiyonlar düşük morbidite ve mortalite oranları ile giderek artan sayılarda gerçekleştirilmektedir.

Anahtar Kelimeler: Karaciğer; karaciğer tümörü

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Hepatic resection was more common performed in the 1950s.[1] Results of hepatic resections have greatly improved with advances in surgical techniques, increasing understanding of the anatomy, and better perioperative care.[2,3] Surgical resection is the standard treatment for malignant liver tumors and selected benign lesions.[4] Surgery for malignant liver disease, either for primary or metastatic liver tumors, improves survival but appropriate patient selection is important.[2,5] New treatment modalities, including portal vein embolization, perioperative chemotherapy, and local destruction with cryotherapy or radiofrequency ablation, may help to increase the number of patients suitable for surgical resection of their

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tumors, and may prolong survival in case of nonresectability.[6] Currently liver resection may be performed with low mortality (less than 5 percent, 0 percent for selected indications) and morbidity (less than 20 percent) rates.[3,7] Parallel to this, the indications for liver resection were extended, such as, repeated liver resection for recurrent colorectal metastases and hepatocellular carcinoma, and extended hepatectomy for hilar bile duct carcinoma and living donor liver transplantation.[1]

We analyzed hepatic resections performed for primary and metastatic malignant liver tumors in our hospital.

Material and Methods

Thirty-eight patients were operated for primary and secondary liver tumor between January 1998 and June 2004 at the Department of General Surgery, Fatih University Hospital. Patients who were operated for benign liver lesions or who underwent radiofrequency ablation were not included.

In addition to routine blood chemistry (including ALT, AST, ALP, total and direct bilirubin, albumin, prothrombin time), ultrasonography and computed tomography were routinely performed to determine the lesions and their relations. Magnetic resonance imaging was reserved for selected cases. The primary tumor and extra hepatic metastases were investigated in patients who had metastatic liver tumor.

The liver was mobilized by dividing the falciform ligament and dissecting its attachment to the posterior diaphragm, the triangular ligament or both. Intra-operative ultrasonography (used for all patients after 2000) helped to detect lesions that were not identified preoperatively and to identify the anatomy, the relations of the tumor with vascular structures and main bile ducts, resection borders, and parenchymal transsection planes. Pringle maneuver was performed for inflow occlusion during resection. Occlusion time of less then 30 minutes was anticipated. Liver resections without any inflow occlusion were also performed in patients with small and conveniently resectable tumors. Resection borders were marked with electrocautery by incising the capsule and 0.5 cm depth of the liver parenchyme. "Finger fracture" and "crushing clamp" methods were used during dissections. While small vascular structures and bile ducts were clipped during dissections, large ones were tied with silk suture. Great care was taken to leave at least 1 cm of safety margin unless the lesion had a location very close to major vascular structures. Safety margins were left in all patients. During surgery, transfusion was not done unless the amount of bleeding exceeded 1500 mL. A tube drain was placed along the cut surface.

When both extra-hepatic disease and liver metastases were considered safely resectable extrahepatic disease was handled first. Liver resections were performed after primary tumor resections.

Complications and deaths occurring after admission to hospital or within one month were considered perioperative.

Patients were followed-up every 3 months in the first year after liver resection, every 6 months in the second year, and then yearly. Medical reports of the patients were evaluated.

Results

Mean age of the 38 patients was 55.4 (31-73) years. Eighteen patients were males (47%) and 20 were females (53%). Ten (26%) patients were operated for primary and 28 (74%) for metastatic liver tumors. Mean hospitalization time was 5.9 (4-12) days. All patients were class A according to Child-Pugh classification. Details of patients who were operated for primary tumor are listed in Table 1 and for metastatic tumor in Table 2.

One patient who had hepatocellular carcinoma was operated after tumor shrinkage with embolization.

One patient with cholangiocellular carcinoma who had left hepatectomy had recurrence on the 14th month. She had no other problem after segment V resection.

One patient developed mechanical obstruction due to early adhesions on postoperative day 17. She recovered well without any other problem after adhesiolysis.

Table 1. Details of the patients operated for primary liver tumor.

Number of patients	10
Mean age of patients (years)	50 (33-60)
Female/Male	7/3
Number of patients with HBs Ag (+)	3
Mean diameter of tumors (min-max) (centimeters)	5.5 (1-8)
Mean operation time (minutes)	150 (90-240)
Number of patients who had blood transfusion	3 (3.1 units mean (0-5 units))
Mean hospitalization time (min-max) (days)	5.5 (4-9)
Morbidity	Wound infection in one patient
Mortality	0
Indications	Number of patients
Hepatocellular carcinoma	5
Cholangiocellular carcinoma	1
Adenocarcinoma	2
Malign hemangioendothelioma	1
Sarcomatoid carcinoma	1

Types of resections used are summarized in Table 3.

One patient had wedge resection of the right lung simultaneously due to concurrent lung metastasis. This patient had undergone anterior resection for carcinoma of the rectum in another hospital. One underwent splenectomy due to metastasis of serous cystadenocarcinoma of ovaries. Three had partial resection of the small intestine because of invasion. One patient had cholecystectomy because of direct invasion to the gall bladder.

Operative mortality developed in one patient (2.6%) who underwent right hepatectomy (almost 70% of the liver was resected) due to metastasis from adenocarcinoma of the caecum. She died on postoperative day 17 because of hepatic and renal failure.

Mean follow-up period was 34 months. Five (13.5%) patients died during this period.

Discussion

Liver resection is the only treatment that offers the prospect of long term survival and potential cure to patients with malignant primary or secondary liver tumor.[4] Improvements in surgical techniques, preoperative workup, anaesthesiologic management, and perioperative care have reduced the morbidity and mortality rates of hepatic resections.[8-10] There has been a gradual increase in the

Table 2. Details of the patients operated for metastatic liver tumor.

Number of patients	28
Mean age of patients (min-max) (years)	62 (33-73)
Female/Male	14/14
Mean hospitalization time (days)	6.1 (4-12)
Location of the primary tumor	Number of patients
Rectum	10
Colon	8
Ovary	3
Adrenal Cortex	2
Stomach	2
Gall Bladder	2
Unknown Primary	1
Liver resection	Number of patients
Synchronous with primary tumor	16
Secondary resections	12
Number of patients who had transfusion	10 (2.3 units mean (0-4 units))
Mean recurrence time (months)	13 (3-48)
Morbidity	Number of Patients
Wound infection	1
Pleural effusion	1
Mechanical obstruction	1
Mortality	1

Table 3. Types of resections.

Type of resection	Number of patients (%)
Hepatectomy	9 (23.7%)
Right	3
Left	6
Segmentectomy	22 (57.9%)
1 Segment	9
2 Segments	10
3 Segments	2
4 Segments	1
Non-anatomic resections	7 (18.4%)

number of liver resections performed worldwide in the last two decades.[1,10] The aim is to resect the liver with minimal bleeding, leaving adequate functional liver.[2]

Hepatic resection is the treatment of choice for primary liver tumors.[3,5,11] It is important to elucidate a surgical strategy for the selection and counseling of patients based on long-term prognosis after hepatectomy.[3,11] Hepatocellular carcinoma represents one of the most common tumors worldwide. Liver resection still remains the treatment of choice, offering the chance for cure and providing a long-term tumor-free survival.[3,10] The possibilities for surgical resection have undergone significant changes recently because of improved surgical and anesthesiological techniques and better pre- and postoperative care. Curative treatment of hepatocellular carcinoma mainly depends on early diagnosis.[3] Large tumor size is one of the most established risk factor for recurrence of hepatocellular carcinoma.[11] Survival and recurrence rates in small hepatocellular carcinomas (diameter ≤3 cm) are better than in large hepatocellular carcinomas (diameter >3 cm). Age greater than 60 years is an independent risk factor for recurrence. Albumin level <3.5 g/dL, multiple tumors and cirrhosis are risk factors for poor survival.[3,11] Repeat hepatic resection is accepted as the best treatment modality for recurrent intra-hepatic hepatocellular carcinoma. Patients with small hepatocellular carcinomas, young age (<60 years) and good hepatic functional reserve without cirrhosis are good candidates.[11]

Twenty-six percent of our patients were operated for primary liver tumor and 50% of these patients had hepatocellular carcinoma. All of our patients were 60 years or younger. Mean diameter of tumors was 5.5 cm and all resections were performed with a low morbidity rate.

Colorectal carcinoma is the third most common malignancy in Western countries, and its incidence is increasing.[8,12] Approximately one third of patients with colorectal cancer develop liver metastases during the course of the disease.[8,13-16] Unlike many other types of cancers, the presence of liver metastases of colorectal cancer does not preclude curative treatment.[6,16] Synchronous liver metastasis (liver metastases occurring within 12 months of the colon primary) represents 13-25% of newly diagnosed colorectal cancer.[7,12,14] The natural course of unresected colorectal hepatic metastases has a median survival time of less than one year.[6,8] Liver resection is the only effective therapeutic approach offering long-term survival and even cures in pa tients with colorectal liver metastases.[5-7,16-23] Liver metastasis represents the major determinant of outcome following a curative colorectal resection.[17] There is a significant difference in survival between patients undergoing curative and noncurative surgery. Five-year survival rates of 20-51% were reported after curative resection of liver metastases.[2,7,8,13,14,16,17,20,21,24,25] Five-year survival rate for noncurative resection is under 5%.[13] In the presence of extra-hepatic and particularly multifocal metastases, curative resection is not possible in almost 90% of cases. The prognosis of such cases is poor.[16] Repeated hepatectomy for colorectal recurrence is increasingly performed.[15,22] Several prognostic factors were evaluated to define their effect on long-term survival. They are lymph node metastases at the hepatic hilum or mesentery, patients age 65 years or older, extensive liver involvement (25 percent or more), underlying comorbidity of cardiovascular disease, poorly differentiated primary tumor, large number (more than four) and size (more than 5 cm) of hepatic metastases, symptomatic liver metastasis, the presence of satellite nodules, primary colorectal tumor with concurrent liver metastases, positive resection margins, multiple sites of metastasis, intestinal obstruction, advanced stage of the primary colorectal tumor, preoperative CEA level ≥500 ng/mL, LDH level ≥350 U/L, high postoperative CEA values and hemoglobin level <10 mg/dL.[6-8,13,17,20,22] Although four and more metastatic lesions were commonly considered an exclusion criterion in patient selection, a number of recent studies have failed to support this. All patients with technically respectable lesions should be considered for resection.[17]

Although a staged operative approach is recommended by some authors, similar surgical outcome was reported after simultaneous and delayed

hepatic resections.[7] Simultaneous resection of the primary tumor and colorectal liver metastases did not increase mortality and morbidity rates compared with delayed resection.[7,9,12] Moreover, the combination of major hepatectomy and colorectal tumor resection is not associated with increased morbidity. There is no significant difference in 5 year survival rates after simultaneous and delayed resection. Besides, simultaneous resection is better for patients from a psychological point of view, because they feel more comfortable knowing that all the tumor tissue has been removed in a one-stage procedure.[7]

The surgical indications for liver metastases of colorectal cancer were expanded to include all technically resectable metastases numbering 4 or more.[23]

The decision and the extent of surgical resection for liver metastases are based on the patient's condition, extent of the disease, and liver function. The goal of oncological surgery for liver metastases is to remove all the metastatic sites with free margins of at least 1 cm.[6]

Almost 10% of liver metastases are neuroendocrine in origin.[24,25] Hepatic metastases occur in more than half of patients with neuroendocrine tumors. Despite newer chemotherapeutic and immunologic agents, surgical therapy remains the most efficient approach to metastatic disease and offers the longest-lasting benefits.[25] However, as 90% of the metastases of these tumors are multifocal, surgery for liver metastases may be performed in only a small percentage of patients.[18,24] Even surgical debulking of the hepatic disease was shown to improve survival. In any patient for whom it seems possible to resect all gross disease, resection should be undertaken if the operative risk is acceptable, irrespective of tumor type, origin, or clinical presentation. When complete resection is not feasible, current recommendations dictate that the removal of at least 90% of the disease allows adequate palliation for the disease.[25]

In noncolorectal, nonneuroendocrine liver metastases, the role and efficacy of surgery is much less defined. Less than 2-5% of the patients with these malignancies might be potential candidates for liver resection, as most patients suffer from extra-hepatic spread when they develop liver involvement. The tumors of the genitourinary organs may provide satisfactory long-term results. On the contrary, results of liver resection for metastasis of cutaneous melanoma and gastric or pancreatic adenocarcinoma are dismal. Patients with soft tissue sarcoma, breast cancers, and uveal melanoma liver metastases, may sometimes benefit from liver resection with log-term survivals.[18] Liver metastases may be the only sign of breast cancer. Liver metastases develop in approximately half of women with metastatic breast cancer. Hepatectomy for liver metastases of breast cancer may be a useful treatment when associated with prolonged systemic treatment.[18,26] Hepatic resection for ovarian cancer metastases is feasible and perioperative morbidity and mortality rates are acceptable.[27] Distant metastases of gastric cancer are sometimes present in the liver. Complete surgical resection of the primary tumor and liver metastases appears to be the only method of cure in this disease. Five-year survival rate after curative resection for liver metastases of gastric cancer ranges from 0-34%. The number of liver metastases is a significant prognostic factor for survival after hepatectomy in patients with metastasis of primary gastric cancer. Concurrent liver metastases of gastric cancer is not a contraindication for attempts of curative resective therapy because there is no significant difference in survival between synchronous and metachronous liver resection.[23]

We performed synchronous liver resection with primary tumor in 43% of patients with metastatic liver tumor. Synchronous resections were performed with low morbidity rates. Sixty-four percent of our patients who had metastatic liver tumor were colorectal in origin.

Advances in radiodiagnostic technology significantly enhanced preoperative evaluation of the patients. Multiphased helical computed tomography became more accurate. Magnetic resonance imaging revolutionized liver imaging. Percutaneous sonography, digital substruction angiography and computed tomography with angioportography

are other methods for patient evaluation.[3,14] Positron emission tomography scan may also become a useful tool in the future, but needs further evaluation.[14] Laparoscopy and laparoscopic ultrasonography could be helpful in some cases either to avoid unnecessary laparotomy or to adapt abdominal incision to the extent of resection.[6,16]

During the past two decades, intra-operative ultrasonography was demonstrated to be of utmost importance for accurately staging liver tumors and was shown to have a considerable impact on decision making regarding liver surgery for metastatic and primary hepatic malignancies.[5] Intra-operative ultrasonography gives a precise mapping of anatomical relations of the tumors with the main intraparanchymatous vascular pedicles and helps select the type of resection.[6]

We have been routinely using intra-operative ultrasonography during hepatic resections since 2000.

Complications of liver resections include perihepatic fluid collection or abscess 5-10%, bile leak 3%, liver failure 1-5%, hemorrhage 1-2%, wound infection 1-3%, intraabdominal sepsis 1-3%, pleural effusion 2-5%, pneumonia 2-5%, deep vein thrombosis/pulmonary embolism 1-2%, and cardiac failure/myocardial infarction 1%.[6,10]

Our series had a complication rate of 10.6%. Wound infection was present in two (5.6%) cases, pleural effusion in one (2.6%) and ileus in one (2.6%) patient.

Liver failure is one of the most dreadful complications of liver resection, and this concern is more profound in patients with liver cirrhosis because hepatectomy results in removal of functional liver tissue from an organ that already has marginal function.[1] Operative mortality developed in one patient who developed liver failure after resection of 70% of her liver.

In conclusion, hepatic resections for primary and secondary liver tumors are performed with low morbidity and mortality rates because of early diagnosis, improved surgical techniques and postoperative care.

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