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Is Surgical Treatment of Liver Hemangiomas Effective for Pain Relief?

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Rezumat

Este tratamentul chirurgical o metodă eficientă de ameliorare a durerii la pacienții cu hemangiom hepatic?

Scop: Tratamentul tradițional al hemangioamelor hepatice este cel chirurgical. La momentul actual se pune însă problema dacă managementul chirurgical al hemangioamelor aduce beneficii suficiente pacienților. În cadrul acestui studiu am evaluat eficacitatea chirurgiei la pacienții cu hemangiom hepatic.
Metode: Patruzeci și doi de pacienți supuși intervenției chirurgicale pentru hemangiom hepatic au fost evaluați retrospectiv și intervievați.
Rezultate: Populația studiată a inclus 36 de femei și 6 bărbați, cu vârste cuprinse între 26 și 65 de ani (vârsta medie 47,8±8,7 ani). Durata medie de internare a fost de 6 zile (limite 3 - 59 zile). Intervalul mediu de timp trecut de la momentul operației a fost de 50 de luni (limite 0-120 luni). S-a remarcat o scădere semnificativă statistic a estimării cantitative și calitative a durerii pe scala durerii ($p<0.05$). Postoperator, durerea nu a încetat la 10 pacienți (ulcer peptic necesitând tratament medical la 4 pacienți, colelitiază la 4 pacienți și nefrolitiază la 2 pacienți).
Concluzii: Pacienții cu hemangioame cavernoase hepatice necesitând tratament chirurgical prezintă beneficii semnificative în ceea ce privește ameliorarea durerii postoperator. Absența ameliorării durerii după operație la anumiți pacienți poate fi datorată unor comorbidități.

Cuvinte cheie: ficat, hemangiom cavernos, chirurgie, estimarea durerii

Abstract

Background: Traditional treatment for liver hemangiomas is surgery. Currently, it is controversial whether hemangioma surgeries are sufficiently beneficial for the patients. In this study, we evaluated the effectiveness of surgery in patients with liver hemangiomas.
Methods: Forty-two patients who underwent surgical operations for hepatic hemangiomas were retrospectively evaluated and interviewed.
Results: Study population included 36 female and 6 male patients whose ages ranged between 26 and 65 years (mean age, 47.8±8.7 years). Their mean duration of hospitalization was 6 days (range, 3–59 days). The median time since surgery was 50 months (range 0-120 months). There was a statistically significant decrease in numerical rating and adjective rating pain scale scores ($p<0.05$). Postoperatively, pain did not cease in 10 patients (peptic ulcers requiring medical treatment in four patients, cholelithiasis in four patients, and nephrolithiasis in two patients).
Conclusion: Patients with cavernous hemangiomas of the liver who require surgical treatment have significant benefits in terms of pain relief following surgery. The lack of pain relief after the surgery in some patients may be related to concomitant medical problems other than the hemangioma.

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Key words: liver, cavernous hemangioma, surgery, pain measurement

Introduction

Hemangiomas are the most frequently seen tumors of the liver, accounting for 3%–20% of liver tumors (1). They are diagnosed incidentally or noticed on autopsy. A study performed by Ochsner and Halpert with 2400 autopsies showed that hemangiomas are encountered in 2% of liver biopsies (2). They are mostly detected in patients between 30–50 years of age. Hemangiomas with a diameter larger than 4 cm are named "giant hemangiomas." They are multifocal in 20% of patients, and are frequently localised in right lobe of the liver (3,4). Liver function tests are frequently within normal limits in patients with giant hemangiomas, except for those who have diffuse liver disease. Natural behaviors of hemangiomas are not known (5). Cavernous hemangioms do not show any progression during follow-up (6). Traditional treatments for liver hemangiomas consist of surgical approaches, however alternative treatment methods can also be applied. Treatment might be ineffective on the long term (7). Although the indications for the treatment of hemangiomas are not clear, surgical treatment might be necessary when they are symptomatic.

In this study, we evaluated the effectiveness of surgery in patients with liver hemangiomas, particularly in terms of pain relief.

Material and Method

Study design and patients

This study was performed using retrospective examinations of patients who underwent surgery for liver hemangiomas in the Department of General Surgery, Hacettepe University School of Medicine between 2000 and 2010. The study was approved by Institutional Review Board approval, and informed consent was waived for the retrospective design of the study. The study was conducted in accordance with the ethical guidelines of the Helsinki Declaration.

Study data

The patients' files were reviewed by a physician for demographic and clinical characteristics of patients. All patients were reached via telephone call to discuss their status after the surgery, with a median postoperative time of 50 months (range 0-120 months).

The biochemical evaluation involved preoperative and postoperative liver function tests. Alanin aminotrasferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and gamma-glutamyl transpeptidase (GGT) levels were determined.

Radiological interventions included abdominal ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI). Pathologic evaluations were performed postoperatively.

Pain measurement

The Numerical Rating Scale (NRS) and Adjective Rating Scale (ARS) were used to determine pain intensities. The NRS scale rates the pain level between 1 to 10, and the ARS scale is numbered between 1 to 6 (*Fig. 1*).

Statistical analysis

Statistical analyses were performed with the Statistical Package for Social Sciences (SPSS) 15.0 software (Chicago, IL, USA). Study data were summarized with descriptive statistics (mean, standard deviation, frequency, percentage, etc.). The Wilcoxon test was used to compare the liver function tests and pre- and postoperative pain scale scores. Statistical significance was accepted at $p < 0.05$.

Results

Study patients and preoperative diagnosis

This study included 42 patients who underwent surgery for liver hemangiomas. There were 36 female and 6 male patients. Mean patient age was 47 years (26-65 years). The mean hospitalization duration was 6 days (range, 3–59 days). Patients were recalled for a control visit following a median of 50 months duration (range, 0-120 months) after the surgery.

Indications for surgery were compression (n=5), mass growth (n=5), pain (n=28), and masses detected incidentally that included giant cavernous hemangiomas (n=4).

To provide a definitive diagnosis, preoperative abdominal US imaging was performed in 25 patients, CT in 30 patients, and MRI in 9 patients.

Surgical technique and postoperative complications

Right hepatic lobectomy (n=11), left hepatic lobectomy (n=6), left lateral segmentectomy (n=4), enucleation (n=20),

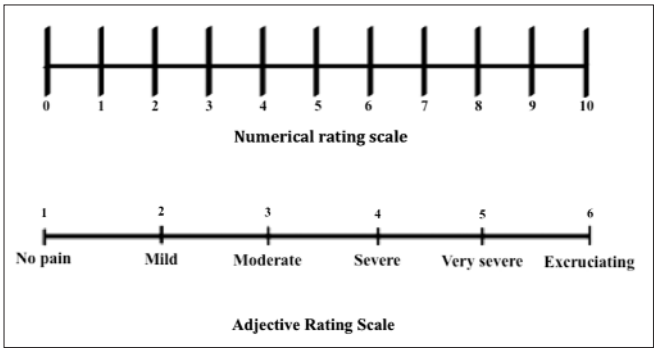

Figure 1. *Numerical and Adjective Rating Scales*

and biopsy only (n=1) were the surgical techniques performed (*Table 1*). The mean diameter of the specimen was 92 mm (range, 45–190 mm). Fifteen patients required transfusions during or after the surgical procedure. There were surgical complication in the postoperative period in three patients, myocardial infarctions in one patient, pneumonia in two patients, wound infections in eight patients, and pleural effusion in two patients (*Table 1*). No patient underwent re-operation due to postoperative bleeding.

Pre- and postoperative pain

There was a dramatic decrease in pain complaints afterv surgery on study control visit (median, 50 months; range 0-120 months postoperatively) ($p < 0.05$, Wilcoxon test), based on both ARS and NRS scales (*Fig. 2*). Further evaluations of the patients who suffered from ongoing pain after the surgery revealed peptic ulcers requiring medical treatment in four patients, cholelithiasis in four patients, and nephrolithiasis in two patients. The patients with cholelithiasis were treated surgically, and patients with nephrolithiasis received additional medical treatment.

Pre- and postoperative liver function tests

On comparison of pre- and postoperative liver function tests, it was found that median preoperative ALT (18.5 IU/L; range, 7-205 IU/L) and AST (20 IU/L; range, 1-219 IU/L) levels significantly increased at postoperation (median ALT, 96 IU/L; range, 12-372 IU/L and median AST, 70.5 IU/L; range, 17-374 IU/L; $p < 0.001$ for both, Wilcoxon test), but there was no significant change in median GGT (19.5 vs. 28.5 IU/L, pre- and postoperative, respectively; $p=0.067$, Wilcoxon test) and ALP values (83.5 vs. 88 IU/L, pre- and postoperative, respectively; $p=0.067$, Wilcoxon test) with surgery.

Discussion

Improved radiological techniques have made the recognition of benign solid liver tumors easier. Differentiation of benign and malignant lesions is based on clinical history and radiological imaging.

Benign non-cystic liver lesions are adenomas, focal nodular hyperplasia, hemangiomas, chronic abscesses, or inflammatory pseudotumors (8-10). Many of these lesions are visualized when radiological imaging is performed for other reasons, especially during laparotomies.

Cavernous hemangioma is the most frequently seen benign mass of the liver, accounting for 3%–20% of such benign masses (11). In females, their prevalence is three times more common compared to males. The age range of subjects in which liver is typically examined is between 30 and 50 years (11). In our study, we examined patients aged between 26–65 years with a male to female ratio of 1/6, similar to the literature.

Surgery seems to be the most adequate and effective treatment method for the management of hemangiomas. Morbidity and mortality rates are low in experienced centers. Resection of hepatic hemangiomas was first performed in 1898 by Herman Pfannenstiel (12). The main surgical techniques for treating hemangiomas are enucleation, liver resection, transplantation, and extracorporeal liver resection. Liver transplantation should be considered for some limited conditions, such as Kasabach-Merritt syndrome or acute rupture of the liver.

Yoon et al. reported that US, CT, and MRI are diagnos-

Table 1. *Surgical techniques and postoperative complications (n=42)*

	n (%)
Surgical techniques	
Right hepatectomy	11 (26.1%)
Left hepatectomy	6 (14.2%)
Left lateral segmentectomy	4 (9.5%)
Enucleation 20 (47.6%)	
Cholecystectomy	24 (42%)
Biopsy 1 (2.3%)	
Complications	
Transfusion need	15 (35%)
Pneumothorax	2 (4.6%)
Myocardial infarction	1 (2.3%)
Wound site infection	8 (19%)
Pleural effusion	2 (4.6%)
Pneumonia	3 (6.9%)

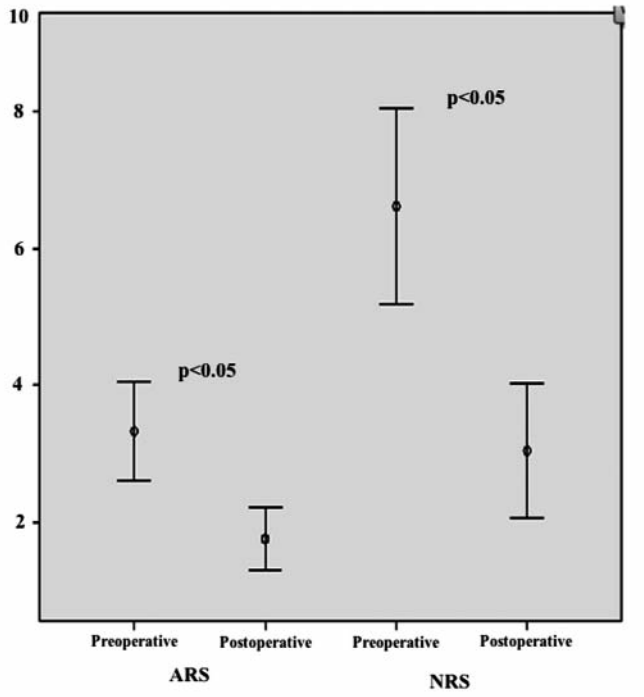

Figure 2. *Preoperative and postoperative Adjective Rating Scale (ARS) and Numerical Rating Scale (NRS) scores of patients. Data on the graph represent median scores with standard deviations as vertical lines. Comparisons were performed with Wilcoxon test ($p<0.05$)*

tic for 57%, 73%, and 84% of patients with hemangiomas, respectively (13). The patients in our study were evaluated with US, CT, and MRI techniques. Needle biopsy was applied in none of the patients. US imaging was coherent in 78.2% of patients. CT imaging was diagnostic in 96.7% of patients, and MRI was sufficient to show lesions in all of the patients. It has been reported in the literature that an increase in the size of the mass fascilitates their diagnosis using radiological procedures (13). In our study, the mean size of the hemangiomas was 92 mm, which is higher than typical sizes reported in the literature.

Our study is more relevant for radiology than other studies. Bismuth stated that, 'When we talk to our patients about lesions in their livers, they may experience anxiety, depending on the lesion' (14). Clinicians should carefully consider symptoms such as abdominal pain, which easily interfere with other medical problems as we showed in our study. However, we found no significant correlation between the severity of pain and the size of cavernous hemangiomas. Hemangiomas usually become symptomatic when they grow beyond 4 cm. Liver function tests and tumor markers are mostly normal at this point (3). Larger lesions may either be asymptomatic or cause symptoms such as pain or compression of the neighbouring organs. Pain is caused by the tension in the Glisson capsule and infarction, thrombosis, or inflammation of the hemangioma.

The most common indications for treatment in symptomatic patients include pain, mass growth, risk of malignancy, local compression, and rupture (15). Pain was reported to be an indication for treatment in 60%, 58% and 78% of patients in studies reported from The Netherlands, United Kingdom and Turkey, respectively (16-18). In our study, the indications for surgery were pain (n=28), mass size (n=5), and signs of compression (n=5).

We performed enucleation in 20 patients, right hepatectomies in 11 patients, left hepatectomies in six patients, and left lateral segmentectomies in four patients. During such surgeries, the patients were evaluated for the presence of cholangiocellular carcinomas. If the presence of these carcinomas was definitively established with frozen section evaluated revealing carcinoma, the surgical procedure was immediately terminated. Our findings suggest that we perform enucleation safely similar to literature (19). We preferred enucleation technique for the following reasons: 1) dissection between healthy liver parenchyma and hemangioma is easier and intraoperative bleeding is less with enucleation, 2) since biliary ducts are not included in the dissection, postoperative biliary leakage is less common with enucleation, 3) loss of healthy liver parenchyma is minimum with enucleation, and 4) recurrence is theoretically expected to be rarer after enuleation.

It is still controversial whether hemangioma surgeries are sufficiently beneficial for the patients. Therefore, studies are still being performed to evaluate postoperative effects and surgical indications. For example, Farges et al. examined 87 patients diagnosed with cavernous hemangioma who complained of pain. After a detailed evaluation, 47 were found to have other pathologies that caused the abdominal pain (20). On the other hand, in this study, seven patients who underwent resection had similar complaints after surgery, suggesting that the pain was not related to the hemangioma. Özden et al. reported that 24 patients who had surgery for cavernous hemangioma (out of 33 patients) no longer complained of pain after their surgeries (18) In our study, preoperative and postoperative pain was measured using the ARS and NRS scales, and we found a significant decrease after the surgery. The patients without any improvement in their symptoms were diagnosed with comorbid nephrolithiasis, cholelithiasis, and peptic ulcer disease.

The main limitation of the study is wide range of postoperative assessment time of study patients (0-120 months). This is due to the retrospective nature of the study including patients operated over a 10-year period. However, in spite of this large range of postoperative assessment time, it is clinically relevant if the patients have no or reduced pain even many years after surgery since these patients had complained for years before the surgery.

Conclusion

In conclusion, the present study demonstrates that patients who undergo surgeries for pain caused by hemangiomas receive significant benefits in terms of pain relief following surgery. The lack of pain relief after the surgery in some patients may be related to concomitant medical problems other than the hemangioma. Therefore, in patients with cavernous hemangiomas of the liver who require surgical treatments, additional comorbidities that may also cause pain should be carefully evaluated.

Conflicts of interest and source of funding

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