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# Location of Hemangioma is an Individual Risk Factor for Massive Bleeding in Laparoscopic Hepatectomy

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## ABSTRACT

**Background and Objectives:** The scope of laparoscopic surgery has expanded to encompass hepatic resections, specifically hepatic hemangioma. The most serious intraoperative complication is bleeding, often requiring laparotomy. Because risk factors associated with such massive blood loss have not been well evaluated, the intent of this retrospective study was to analyze these risk factors associated with laparoscopic resection of hepatic hemangiomas.

**Methods:** From June 1, 2011 to January 31, 2021, 140 consecutive patients underwent laparoscopic surgery for hepatic hemangioma in our hospital. According to quantity of intraoperative blood loss, they were divided into massive ($\geq$ 800 ml) and minor blood loss ($<$ 800 ml) groups. Perioperative data were analyzed by univariate and multivariate analyses with logistic regression to identify the risk factors for potential massive blood loss during laparoscopic resection.

**Results:** There were 24 and 116 patients in the massive and minor blood loss groups, respectively. Of four risk factors significantly associated with massive blood loss by univariate logistic regression analysis (location of hemangioma in the liver, postcaval or hepatic venous compression, hilar compression, and body mass index exceeding 28) the multifactorial logistic model identified only location in the liver of the hemangioma as statistically ($P = 0.012$) associated with intraoperative massive blood loss.

**Conclusions:** Location of the hepatic hemangioma was the single statistically significant risk factor for massive blood loss during laparoscopic surgery for hepatic hemangioma. Of particular importance, location in Couinaud liver segments I, IVa, VII, and VIII necessitates precautions to mitigate the risk of massive blood loss.

**Key Words:** Laparoscopy, Hepatic hemangioma, Blood Loss, Surgical.

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## INTRODUCTION

Hepatic hemangioma (HH) is the most common benign liver tumor with an incidence by autopsy of 0.4% to 7.3%, but is estimated to affect 3%–20% of the general population.[1, 2] HH is often found by radiological imaging and is usually asymptomatic. Treatment should be considered for patients with abdominal symptoms caused by HH such as abdominal pain or distention, tumor rupture, intratumoral bleeding, Kasabach-Merritt syndrome, and compression of adjacent organs or vessels.[3,4] Surgery is the most effective and widely accepted treatment for these symptomatic HH patients.[5] Rapid progress has continued in the technology and instrumentation[6] of laparoscopic surgery, which is mirrored by increasing acceptance by patients with HH,[7] even giant HH (defined here at $>$10 cm in diameter),[8, 9] to undergo surgical resection with this technique. Nevertheless, certain obstacles remain problematic specifically relating to laparoscopic surgery for HH,[7] the most common and critical of which is potentially severe intraoperative bleeding that often results in conversion to laparotomy. Because the critical risk factors that portend massive blood loss during laparoscopic surgery in HH patients have not been fully evaluated, we conducted the present study to determine potential risk factors of massive blood loss during laparoscopic surgery for hepatic hemangioma. Especially valuable are risk factors that could be identified pre-operatively.

## METHODS

This was a retrospective study comprised of 140 consecutive HH patients who underwent laparoscopic surgery from June 1, 2011 to January 31, 2021 in our hospital. All HH patients were diagnosed primarily by their radiological imaging manifestations, such as abdominal ultrasonography, enhanced abdominal ultrasonography, computerized tomography, enhanced computerized tomography, and magnetic resonance imaging. All HH were histologically confirmed. The surgical indications included symptoms such as abdominal pain or distention caused by HH, or compression of adjacent organs. All the cases were scheduled. One surgeon with extensive experience in laparoscopic hepatobiliary surgery performed all operations. As a sudden hemorrhage over 800 ml will cause hemodynamic instability and uncompensated hemorrhage shock,[10] we set the cutoff value of intraoperative blood loss volume at 800 ml to divide the HH patients into two groups: the massive blood loss (≥ 800 ml) group and the minor blood loss (< 800 ml) group. The perioperative data of the two groups were compared and analyzed, including age, gender, body mass index (BMI) (less than or ≥ 28), prior abdominal surgery, American Society of Anesthesiologists (ASA) risk grading (less than or ≥ 2), liver cirrhosis, diabetes mellitus, hypertension, cardiovascular disease, pulmonary disease, history of smoking, alcohol intaking, the diameter of HH (less than or ≥ 15cm), specific location (Couinaud liver segments I, IVa, VII, and VIII) of the HH, number of hemangiomas (single or multiple), number of involved liver segments (greater than or ≤ 2), hepatic hilar compression, and postcaval or hepatic vein compression. We initially conducted a univariate analysis with logistic regression to identify significant single risk factors for massive blood loss during laparoscopic HH resection, then multivariate logistic regression analysis was performed to discern the key risk factors. Informed consent to collect medical information was obtained from all patients. Data collection and analysis followed the ethical standards of the Declaration of Helsinki. The protocol of this study was approved by the Institutional Ethical Review Board of China-Japan Friendship Hospital.

## SURGICAL PROCEDURES

Under satisfactory general endotracheal anesthesia, patients were positioned in the Trendelenburg position and legs separated. The operating table could be tilted 15° to 45° to the right or left as needed. For hemangiomas located in the posterior right lobe of the liver, the operative table was tilted 45°, the patient's right arm raised and fixed to the head frame, and the right shoulder raised to facilitate mobility of the liver. The surgeon was positioned on the side opposite the HH, the first assistant was across the table from the surgeon, and the second assistant who held the mirror stood between the patient's legs or on the same side as the surgeon.

A standard periumbilical incision was made, and a needle was used to access the peritoneal cavity. A pneumoperitoneum was established with the pressure maintained at 12–14 mm Hg throughout the operation. Trocars were placed according to the location of the HH, and a 30° laparoscope was used. Routine, sequential exploration of the abdominal cavity was carried out to determine the size, number, location, and boundaries of the liver hemangioma. Laparoscopic ultrasound was used to disclose the relationship between the hemangioma and intrahepatic ducts and vessels when necessary. Optimal visualization was based on the principle that the main operative cannula site should be located close to the hepatic dissection site, and the auxiliary cannula sites and laparoscopic camera be located at angles with the operative cannula to facilitate the operation. Either the three-hole or four-hole technique was utilized for a left lateral lobectomy, whereas the five-hole method was used for either a left or right hepatectomy.

The surgical strategies of hemangioma enucleation or anatomic hepatectomy were selected according to the size and location of the liver hemangioma. When possible, enucleation was the preferred technique for most HH cases. Anatomic hepatectomy was typically used for HH that occupied most of certain liver segments. For example, HHs located in the left lateral lobe of the liver (segments II, III) or left half of the liver (segment II, III, IV), a correspondingly left lateral lobectomy or left hepatectomy were performed. Hepatic dissection utilized an ultrasonic knife to incise the liver parenchyma along the pre-resection line from shallow to deep, front to back, to the surface of the Glisson sheath. An Endo-GIA autosuture universal stapler or ECHELON FLEX™ Articulating Endoscopic Linear Cutter was used to transect and close the intrahepatic ducts in the parenchyma of the liver, and Hem-o-lok® clips or absorbable clips are used to control the bile ducts and vessels. When HH enucleation was performed, the liver was first mobilized according to the location of the hemangioma, and then the liver tissue was incised from shallow to deep with an ultrasonic knife following the boundary between hepatic hemangioma and normal liver tissue. Finding the boundary of the hemangioma was the key to enucleation surgery. As the dissection progressed, Hem-o-lok® clips or absorbable clips are used to individually clip the bile ducts then transected with the ultrasonic knife. Special care was taken to avoid entering the parenchyma of the hemangioma to avoid uncontrollable bleeding. Prior to the liver transection phase of the operation, a hilar occlusion band was positioned to encompass the portal triad, and intermittent portal and hepatic arterial blood flow could be occluded if necessary. For patients whose resections were expected to be more difficult and at higher risk of bleeding, autologous blood reinfusion devices were used during the operation.

Following specimen removal, the liver transection surface was irrigated with normal saline then carefully inspected for bleeding or biliary leakage. The bleeding site could be compressed with hemostatic gauze or sutured to stop bleeding. Biliary leakage was sutured with vascular sutures. Finally, the excised hemangioma was placed into a specimen bag, the main cannula site was appropriately expanded, and the specimen was extracted. Drains were routinely placed, and each incision was closed with deep sutures and the skin with glue.

## DATA COLLECTION

Demographic, angiographic, and procedural data were collected from hospital charts or databases.

## STATISTICAL ANALYSIS

Continuous variables are expressed as means ± standard deviation and the t test is used to compare the groups. Categorical data were presented as a percentage or an absolute number. Comparisons were made using the $\chi 2$ test or Fisher's exact test for categorical data and using the Mann–Whitney U test for nonparametric continuous data; $P < .05$ was considered statistically significant. Single-factor logistic regression was used to screen the influencing factors first, and the level of variable selection was set at $\alpha = 0.1$, so variables with $P < 0.1$ in single-factor logistic regression analysis were included in the multifactor logistic regression. In multivariate analysis, $P < .05$ was considered significant, and all tests were two-sided tests. All statistical analyses were performed with the IBM SPSS statistical package, version 21.0 (IBM Corp., Armonk, NY, USA).

## RESULTS

Of the 140 HH patients in the study, 24 patients were enrolled in the massive blood loss (≥ 800 ml) group, and 116 patients in the minor blood loss (< 800 ml) group. No differences were observed in age, gender, BMI, prior abdominal surgery, ASA risk grading, liver cirrhosis, diabetes mellitus, hypertension, cardiovascular disease, pulmonary disease, history of smoking or alcohol intake between the two groups ($P > .05$). Additionally, there were no significant differences in the diameter, number, or involved segments of the hemangiomas between the two groups ($P > .05$). The specific location of the HHs (Couinaud I, IVa, VII, and VIII liver segments) was significantly greater in the massive blood loss group than the minor blood loss group (79.2% vs 28.4%, $P < .001$). The postcaval or hepatic venous compression rate (66.7% vs 23.3%, $P = .048$) and the hepatic hilar compression rate (20.8% vs 6.9%, $P < .001$) were also higher in the massive blood loss group than the minor blood loss group (**Table 1**). Of the 140 HH patients, 128 patients accepted pure laparoscopic surgery, while the other 12 patients were converted to laparotomy. The conversion rate is 8.6%, and the indication for conversion includes bleeding (6/12), adhesions (4/12), and poor access (2/12).

## DISCUSSION

Surgical resection is widely accepted as the most effective treatment for hepatic hemangioma in patients with clinically significant symptoms or complications. Only in the most recent 10–15 years has the laparoscopic approach to liver resection been applied to HH, parallel with the continued evolution of surgical expertise and improved instrumentation. Clear advantages to laparoscopic surgical resection have been recognized.[7,8] However, intraoperative bleeding remains the most serious associated complication, often requiring conversion to laparotomy. There is limited knowledge regarding the risk factors associated with massive blood loss during laparoscopic surgery for HH. Therefore, this was the subject of the present study, ideally to help surgeons evaluate the safety and feasibility of the laparoscopic approach and mitigate the risk of serious intraoperative hemorrhage. Analysis of our data demonstrated that the single most important risk factor for massive blood loss associated with laparoscopic surgery for HH was the specific, posterior, less accessible locations in the liver.

Several factors have deterred the implementation and posed increased difficulty for laparoscopic resection of HHs, including the location within the liver or in the hilum, its diameter, involvement of multiple liver segments, or compression of large vessels. One study[9] developed an operation difficulty score to identify the high-difficulty surgical group. The score mainly included distance from large vessels, involved segments, tumor diameter and location, and the presence of cirrhosis. Not surprisingly, they found that the quantity of bleeding in the high difficulty group was significantly greater than

**Table 1.**
Demographical Data and Hemangioma Characteristics of the Patients

| Variables | Massive Blood Loss Group (n = 24) | Minor Blood Loss Group (n = 116) | P Value |
|---|---|---|---|
| Demographics | | | |
| Age (y, Mean ± SD) | 43.5 ± 8.7 | 45.5 ± 9.6 | 0.345 |
| Gender (%) | | | 0.738 |
| Male | 7 (29.2) | 30 (25.9) | |
| Female | 17 (70.8) | 86 (74.1) | |
| BMI (kg/m$^2$) | | | 0.078 |
| < 28 | 19 (79.2%) | 106 (91.4%) | |
| ≥ 28 | 5 (20.8%) | 10 (8.6%) | |
| Abdominal surgery history | 5/24 (20.8%) | 35/116 (30.2%) | 0.357 |
| ASA grading | | | 0.557 |
| < 2 | 18 (75%) | 80 (69%) | |
| ≥ 2 | 6 (25%) | 36 (31%) | |
| Liver cirrhosis | — | 3 (2.6%) | - |
| Diabetes mellitus | 1 (4.2%) | 9 (7.8%) | 0.852 |
| Hypertension | 2 (8.3%) | 14 (12.1%) | 0.864 |
| Cardiovascular disease | — | 3 (2.6%) | - |
| Pulmonary disease | — | 4 (3.4%) | - |
| Smoking | 2 (8.3%) | 14 (12.1%) | 0.864 |
| Alcohol | — | 13 (11.2%) | - |
| Characteristic of Hemangiomas | | | |
| Diameter (cm) | | | 0.344 |
| < 15 | 22 (91.7%) | 111 (95.7%) | |
| ≥ 15 | 2 (8.3%) | 5 (4.3%) | |
| Location | | | < 0.001 |
| Other segments | 5 (20.8%) | 83 (71.6%) | |
| I, IVa, VII, VIII | 19 (79.2%) | 33 (28.4%) | |
| Number | | | |
| Single | 18 (75%) | 97 (83.6%) | 0.379 |
| Multiple | 6 (25%) | 19 (16.4%) | |
| Involved segments | | | |
| ≤ 2 | 17 (70.8%) | 94 (81%) | 0.262 |
| > 2 | 7 (29.2%) | 22 (19%) | |
| Hilar compress | 5/24 (20.8%) | 8/116 (6.9%) | 0.048 |
| Liver vein compress | 16/24 (66.7%) | 27/116 (23.3%) | < 0.001 |

SD, standard deviation; BMI, body mass index; ASA, American Society of Anesthesiologists.
Univariate logistic regression analysis yielded four risk factors associated with the massive blood loss group: location of the hemangioma (P < .001), postcaval or hepatic venous compression (P < .001), hepatic hilar compression (P = .042), and BMI greater than 28 (P = .088). These four were then analyzed by the multifactorial logistic regression model. The specific location of the hemangioma (Couinaud I, IVa, VII, and VIII liver segments) was determined to be the single most important individual risk factor (P = .012) for intraoperative massive blood loss in laparoscopic surgery for hepatic hemangioma (**Table 2**).

**Table 2.**
Logistic Regression Results of Risk Factors for Intraoperative Massive Blood Loss

| Variables | Univariate | | | Multivariate (Entered) | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | P | OR | 95% CI | P |
| Age | 0.977 | 0.931–1.025 | 0.343 | | | |
| Gender | 0.847 | 0.320–2.242 | 0.738 | | | |
| BMI ≥ 28 | 2.789 | 0.858–9.072 | 0.088 | 3.607 | 0.891–14.606 | 0.072 |
| Abdominal surgery history | 0.609 | 0.211–1.761 | 0.360 | | | |
| ASA grading ≥ 2 | 0.741 | 0.271–2.022 | 0.558 | | | |
| Diabetes mellitus | 0.517 | 0.062–4.283 | 0.541 | | | |
| Hypertension | 0.662 | 0.140–3.126 | 0.603 | | | |
| Smoking | 0.662 | 0.140–3.126 | 0.603 | | | |
| Diameter ≥ 15 cm | 2.018 | 0.368–11.074 | 0.419 | | | |
| Location of HH | 9.558 | 3.296–27.711 | 0.000 | 6.781 | 1.526–30.128 | 0.012 |
| Number of HH ≥ 2 | 0.588 | 0.206–1.674 | 0.319 | | | |
| Involved liver segments ≥ 2 | 1.759 | 0.650–4.759 | 0.266 | | | |
| Hilar compress | 3.553 | 1.050–12.023 | 0.042 | 2.400 | 0.605–9.524 | 0.213 |
| Postcaval or hepatic venous compress | 6.593 | 2.545–17.075 | 0.000 | 1.481 | 0.377–5.822 | 0.574 |

OR, odds ration; CI, confidence interval; BMI, body mass index.

that in the low difficulty group. Another study[7] aimed to evaluate the feasibility and safety of laparoscopic HH resection compared to open hepatectomy, using a practical scoring system for surgical difficulty, assigning points for tumor location, the extent of hepatectomy, tumor size, proximity to major vessels and liver function. High points equated to high risk. There have been other difficulty scoring systems for laparoscopic liver resection intended to help surgeon decision-making regarding minimally invasive approaches.[11,12] However, the factors included in the scoring systems have been inconsistent and not fully assessed.[13] For example, a HH with a diameter greater than 15 cm located in the left lateral lobe might be assigned a high difficulty score based on size, but would actually not be difficult to resect laparoscopically. To address these deficiencies, we used the multifactorial logistic regression model for analysis in the present study. Of note, a BMI ≥ 28 was close to reaching statistical significance (P = .072). However, a recent systematic review that investigated the relationship between BMI and outcomes following laparoscopic liver resection found that the estimated blood loss rates were similar between obese and nonobese patients.[14] Although this outcome was not different, laparoscopic surgery is often more difficult in obese patients even if it can be completed safely. This factor might deserve further study. We did not address the effect of compromised liver function or cirrhosis in the present study as only three patients had cirrhosis, all with normal liver function.

Although rapid progress has been made in laparoscopic liver resection, lesions located in "difficult segments" remain challenging for surgeons, particularly lesions located in Couinaud I, IVa, VII, and VIII segments of the liver.[15–19] We posit two possible explanations for the above result. First, visualization in laparoscopic surgery is from caudal to cranial, known as the "caudal approach". For HHs located in the posterosuperior segments of the liver (Couinaud segments IVa, VII, and VIII), visualization is limited, and it is difficult to reach. And for HHs located in the caudate lobe (Couinaud segment I), because it is situated posteriorly in the liver, close to the liver hilum, and has several thin hepatic veins draining directly into the inferior vena cava, it is also less visible and accessible, and particularly dangerous from a surgical perspective. Once bleeding occurs in these "difficult segments", it is hard to control laparoscopically. Second, HH is essentially a big package of fragile blood vessels, obviously filled with blood that bleeds copiously if violated even if the portal triad is occluded. Even if sutured, the tissues are soft, and can tear, further complicating the bleeding, especially in the "difficult segments" of the liver.

Experience developed over years of open and laparoscopic hepatic surgery provides insights that cannot readily be quantitated or statistically analyzed but are valuable. First, enucleation of HH is our preferred surgical option. Because of the expansive growth characteristic of the HH, there is a boundary between the hemangioma and normal liver parenchyma. To find and follow that boundary is the key to enucleation and to avoid hemorrhage. Second, intermittent portal and hepatic artery blood flow obstruction can be performed when necessary. This procedure can not only reduce hemorrhage during the operation, but also can reduce the volume of blood within the HH, facilitating its identification and dissection. The hemi-hepatic inflow occlusion for hemi-hepatectomy and modified selective hepatic vascular occlusion can help to control the blood loss during operation.[20–21] And the size of HH can be reduced after occlusion, providing more space to mobilize and dissect the hemangioma.[20] We also use a self-made hilar occlusion band to encircle the portal triad and occlude blood flow as indicated. Most patients with HHs have normal liver function and can withstand longer periods of hilar occlusion. Third, especially for patients who would be anticipated to have a higher risk of bleeding, we routinely make adequate preparation before and during operation, such as preparing adequate blood products, marking the laparotomy incision before operation, using autologous blood reinfusion devices and hepatic vascular occlusion techniques during operation, as well as making the decision of conversion timely when encountering uncontrollable bleeding.

The present study has several limitations. First, although the sample size of the overall study is relatively large, the number in the massive blood loss group is relatively few. This is the clinical reality of a single-center study. Second, also relating to a single-center study, all procedures were performed by the same surgeon with extensive experience in laparoscopic hepatobiliary surgery. This minimizes the bias in learning curve effect that might be present in other publications. Third, this was a retrospective study extending over a long time period. The surgical technique continually improved over these years and may have influenced the outcomes. A well-designed multicenter study with a large sample size would be ideal in the future.

## CONCLUSION

In conclusion, the location of hepatic hemangiomas, specifically in Couinaud segments I, IVa, VII, and VIII, is statistically a critically important risk factor for massive blood loss during laparoscopic resection. Surgeons should be aware of this risk and, if the laparoscopic approach is chosen, they should take measures to avoid or minimize intraoperative massive blood loss.

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