

Application and Discussion of Laparoscope in the Treatment of Gallbladder Carcinoma

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Research article

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Abstract

Background: To explore the clinical efficacy and long-term prognosis of laparoscopic technique in patients with gallbladder cancer.

Methods: Retrospective analysis and summary of the clinical data of 50 patients with gallbladder carcinoma treated by laparoscope from January 2010 to November 2018 in the Third Affiliated Hospital of Soochow University.

Results: The intraoperative or postoperative pathology of 43 cases were confirmed as the gallbladder carcinoma. Among them, 11 cases were confirmed as Tis stage, 12 cases as T1b stage, 20 cases as T2 stage and 7 cases as T3 stage. Follow up data of one patient was lost due to personal reason. During the follow-up period, no one at Tis stage died, two cases at T1b stage died, six cases at T2 stage died and six cases at T3 stage died.

Conclusion: Laparoscope is a secure and feasible way in the treatment of gallbladder carcinoma at an early stage, but a large number of clinical data is still required to demonstrate its long-term curative effect.

Background

Gallbladder carcinoma(GBC), which usually occurs in the body and bottom of the gallbladder, is one of the most common malignant disease of the biliary tract and accounts for 80%~85% of the biliary system malignancies[1]. 90% of the patients were over 50 years old, and females are more prone to develop the disease, with a male to female ratio of about 1:3~4. With the rapid development of laparoscopic technology, laparoscopy has become the gold standard for the treatment of benign gallbladder diseases[2]. However the laparoscopic treatment of gallbladder cancer has not reached a consensus. How to make better use of the laparoscopic technique to treat gallbladder cancer and improve the curative effect of GBC is worth further discussion. In this article, the clinical data and experience of laparoscopic treatment for GBC in the Third Affiliated Hospital of Soochow University from January 2010 to November 2018 were summarized to explore how to rationally utilize laparoscopic technique to treat GBC and improve its prognosis.

1. Methods

1.1 General Information

In this study, there were 20 males and 30 females, with a male to female ratio of 1:1.50, aged 30-90 years, with an average age of (63±13.52) years. Among them, 25 cases were preoperatively diagnosed as simple cholecystolithiasis, 1 cases were preoperatively diagnosed as gallbladder polyps (larger than 1cm in diameter and complicated with cholecystolithiasis), and 24 cases preoperatively examined by B-ultrasound and enhanced CT were suspected as malignant gallbladder tumors (including 10 cases

complicated with cholecystolithiasis at the same time). Besides, there were 8 patients with increased CA199 before the operation.

1.2 Therapy

Among them, 18 patients with simple cholecystolithiasis or gallbladder polyp were treated with Laparoscopic simple cholecystectomy, The other 32 cases (including 24 cases with suspected gallbladder malignancy before the operation and 8 cases with significantly thickened and stiffened gallbladder wall during operation) underwent rapid pathological sections during operation and all were indicating GBC. Among the 32 cases, 10 patients with negative cystic duct cutting edge and no liver invasion underwent laparoscopic cholecystectomy + lymph node dissection, The remaining 22 patients with tumor invasion above the muscle layer of the gallbladder or liver invasion to varying degrees underwent laparoscopic cholecystectomy + hepatic wedge resection (liver tissue over 2cm from the gallbladder bed) + lymph node dissection (Group 8/12/13) (Figure 1). The size and location of the trocar during surgery were shown in Figure 2. Specimens were removed entirely from the extended observation hole after the operation.

2. Results

The 50 patients were divided into three groups according to different surgical methods. The specific surgical conditions are shown in Table 1

Table 1
Operation of 50 patients with GBC

surgical method	number of cases	Average operating time(min)	Average intraoperative blood loss(ml)	Hospitalization days	Postoperative complications
LC	18	63.1±22.0	57.3±77.6	4.0±2.1	1(Bile leakage)
LC+lymph node dissection	10	150.0±83.7	71.7±65.9	5.8±2.9	0
LC+hepatic wedge resection+ lymph node dissection	22	163.9±60.8	194.1±174.3	6.3±4.4	1 infection of incisional wound

All patients were diagnosed with gallbladder cancer by intraoperative or postoperative pathology and underwent T staging according to the American Joint Committee on Cancer (AJCC) TNM Tumor Staging Criteria (7th edition). Postoperative survival was assessed by telephone and outpatient follow-up

(excluding lethal factors not due to GBC), and the follow-up deadline was 2019-01-01, The specific situation is shown in Table 2

Table 2
T staging and postoperative follow-up of 50 cases of GBC

surgical method	T staging	number of cases	Death cases	Survival time (deaths)
LC	Tis	9	0	
	T1b	4	1	28 months
	T2	5	3	7-8-9 months
LC+lymph node dissection	Tis	2	0	
	T1b	4	0	
	T2	4	1	10 months(1 case was lost to follow-up)
LC+hepatic wedge resection+lymph node dissection	T1b	4	0	
	T2	11	3	3-7-8 months
	T3	7	6	3-5-9-9-10-11 months

According to the T stage and postoperative survival of gallbladder cancer, Kaplan-Meier survival analysis was performed by using SPSS23.0 statistical software, and the log-rank test was used to test the differences between groups. $P < 0.05$ was considered statistically significant. (The survival curve is shown in Figure 3)

3. Discussion

Gallbladder cancer is the most common malignant tumor in the biliary tract, and its pathogenesis is related to chronic inflammation stimulation of gallbladder for a long time. Epidemiology showed that 70% of patients with GBC were complicated with cholecystolithiasis (36 cases in this group were complicated with cholecystolithiasis, accounting for 72.0%), it can take 10-15 years to vary from cholecystolithiasis to the occurrence of GBC, patients with cholecystolithiasis were 13.7 times more likely to develop GBC than those without. The risk of developing gallbladder cancer is 10 times if the stones are greater than 3cm than that if the stones are less than 1cm[3]. There are no specific symptoms in the early stage of gallbladder cancer. According to the literature, only 30% of patients were suspected or diagnosed as gallbladder cancer before surgery, The remaining 70% were confirmed as gallbladder cancer by intraoperative or postoperative pathology, so-called incidental gallbladder cancer(IGBC)(In this group,

there were 26 cases of IGBC, accounting for 52.0%)[4]. While preoperative diagnosis are benign gallbladder disease, the incidence of IGBC after the operation is about 0.19%~2.8%[5].

Due to the high degree of malignancy and aggressivity of gallbladder cancer, and its early local invasion and metastasis, the 5-year survival rate of gallbladder cancer patients is about 5%, and the median survival time is about 9.2 months[6]. At present, surgery is still the first choice for patients with gallbladder cancer. Due to its clear vision, small surgical trauma and quick postoperative recovery, laparoscope has been widely applied in benign diseases of the gallbladder. However, laparoscopic treatment of gallbladder cancer has not reached a consensus. The main problems are as follows: ¶During laparoscopic surgery, bile leakage due to surgical operations and other reasons can easily lead to the spread of malignant cells in the abdominal cavity; ¶The specimens or surgical instruments that touched the specimens can lead to the metastasis of malignant cells in the abdominal wall while crossing the punctured incision. ¶Gasification and the "Chimney" effect of CO₂ facilitate implantation and metastasis of tumor cells. ¶CO₂ pneumoperitoneum environment is more conducive to tumor growth. ¶CO₂ pneumoperitoneum can reduce immune function and so on.[7-13]

We believe that a well-coordinated team and advanced laparoscopic equipment are the prerequisites for laparoscopic radical gallbladder cancer surgery. Secondly, preoperative and intraoperative diagnosis is essential to reduce the occurrence of the above problems. For example, patients with suspected gallbladder malignancy or high-risk factors of gallbladder cancer were fully evaluated before and during surgery, including preoperative tumor markers[14], ultrasound, endoscopic ultrasonography, CT, MRI, PET-CT and other examinations, the specimen of gallbladder should be carefully examined and the quick pathological section should be made to confirm the diagnosis during the operation. Ouchi et al[15] reported that when the wall of gallbladder was ruptured or not, the incidence of incision implantation was 5.3% and 2.4% respectively. Therefore, for patients with suspected or confirmed gallbladder cancer, we should avoid rough separation during operation, especially for those with obvious edema of the gallbladder wall, dense adhesions and unclear anatomy or anatomical variation, to ensure the integrity of gallbladder specimens. Intraoperative or postoperative intraperitoneal perfusion therapy can be used for patients with intraoperative gallbladder rupture to prevent tumor spread[16]. Besides, measures such as timely elimination of smoke during surgery, proper fixation of Trocar, reduction of unnecessary pulling and insertion of Trocar, instruments being disinfected before reenter the abdominal cavity and the use of disposable specimen bags would be conducive to reduce the implantation of tumor cells in abdominal cavity and incision[17](No incisional planters were found in 50 patients). In addition, due to the disadvantages of CO₂ pneumoperitonum, such as beneficial to the growth of tumor cells and reduced immune function, some scholars proposed to replace CO₂ with helium[18]. This method has not been reported in China, and its effect needs to be verified by further clinical trials.

As for the range of laparoscopic radical resection of gallbladder carcinoma, the decision is made mainly according to the TNM stage of gallbladder cancer, so preoperative and intraoperative gallbladder cancer staging is crucial. For Tis or T1a gallbladder cancers, most of them are occult gallbladder carcinoma. Simple cholecystectomy can achieve R0 resection, and no further liver resection or lymph node dissection

is required, which has reached a consensus[19](In this study, 11 patients with gallbladder carcinoma at Tis stage underwent LC and no death is observed). For patients with gallbladder carcinoma invading the muscle at stage T1b, because there is no serosa on the side of the gallbladder bed, tumor cells can easily flow back to the liver through the gallbladder vein to cause micrometastasis in the liver bed and the distance of liver bed micrometastasis does not exceed 16mm[20]. Goetze et al.[21] reported that lymph node metastasis of gallbladder cancer at this stage firstly involved lymph nodes in the triangle of the gallbladder and lymph nodes distributed along the common bile duct, and the rate of lymph node metastasis was 15.7%. The rate of lymphatic vessel infiltration was 18%, and there were reports of lymph node metastasis in the upper back of the pancreatic head (group 13a)[22]. In our study, 4 patients with gallbladder carcinoma at stage T1b underwent simple LC, and 1 died 28 months after surgery. While 4 cases who underwent LC+ lymph node dissection and 4 case who underwent LC + liver wedge resection + lymph node dissection had no death. Therefore, we believe that simple LC is not sufficient for patients at T1b stage. Lymph node dissection is required for patients with tumors not located in gallbladder bedside, including hepatoduodenal ligament(group 12), common hepatic artery side(group 8) and posterior superior pancreatic head (group 13a) lymph nodes. In case of tumors located in gallbladder bedside, simultaneous hepatic wedge resection above 2cm from the gallbladder bed should be performed. For patients at stage T2, tumor cells returned to the liver through the gallbladder vein at an average distance of 2 ~ 5cm from the gallbladder bed, with a metastatic range >4cm in at least one direction[23]. Mekeel et al.[24] reported that the lymph node metastasis rate of T2 gallbladder cancer was as high as 46%, and 5-year survival rates of patients in the lymphadenectomy group and the undissection group were 50% and 10%, respectively. In this study, 5 patients at stage T2 received LC alone, 3 patients died at 7, 8 and 9 months after surgery, and the followed up period of the other two patients wasn't long enough. 4 patients at stage T2 received LC+lymph node dissection and 11 patients received LC+hepatic wedge resection+lymph node dissection, 1 case of the former group died at 10 months after operation (1 case was lost during follow-up), and 3 cases of the latter died at 3, 7 and 14 months after operation. Therefore, we believe that it is not enough only to perform hepatic wedge resection + lymph node dissection for patients at this stage. The hepatic resection range should be enlarged. We can try to remove the liver segment adjacent to the gallbladder (including S4b+S5) or even a wider range of liver resection to achieve R0 resection[25]. Patients with tumors at T3 or T4 stage that have broken through the serosal layer and invaded the liver or extrahepatic organs are considered to be at terminal stage. In this study, all the patients died except one whose followed up period was not long enough, with an average survival of 7.8±3.1 months. According to the above survival curve analysis, the prognosis is poor, extended laparoscopic radical resection of gallbladder carcinoma is required. Due to the serious difficulty of laparoscopic surgery, large surgical scope and long operation time, laparoscopic surgery is not recommended[26].

4. Conclusions

In summary, laparoscopic treatment of early gallbladder cancer (Tis, T1, T2) is technically safe and feasible. Due to its small surgical trauma, quick postoperative recovery, fewer postoperative

complications, reduced patients' pain, laparoscopic lymph node dissection being more advantageous than open surgery, it is worth promoting in clinical practice. Due to the limited study samples and follow-up time, the long-term efficacy of laparoscopic radical resection of gallbladder carcinoma still needs a large number of clinical research data to demonstrate.

Abbreviations

GBC: Gallbladder carcinoma

RHA: Right hepatic artery

LHA: Left hepatic artery

GDA: Gastroduodenal artery

CHA: Common hepatic artery

CBD: Common bile duct

PV: Portal vein

LC: laparoscopic cholecystectomy

AJCC: American Joint Committee on Cancer

IGBC: incidental gallbladder cancer

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional ethical committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. And all experimental protocols in the manuscript were approved by Ethics Committee of Changzhou First People's Hospital (Third Affiliated Hospital of Soochow University).

Informed consent was written and obtained from all individual participants included in the study.

Consent for publication

Written informed consent for publication was obtained from all authors.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors of this study declare no conflict of interest.

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Authors' contributions

DS and YL designed experiments. DS carried out experiments with the help of his colleagues. YC gathered results of each patient. YD analyzed the data. DW wrote the manuscript and took an active part in the procedures mentioned above. All authors have read and approved the manuscript.

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Figures

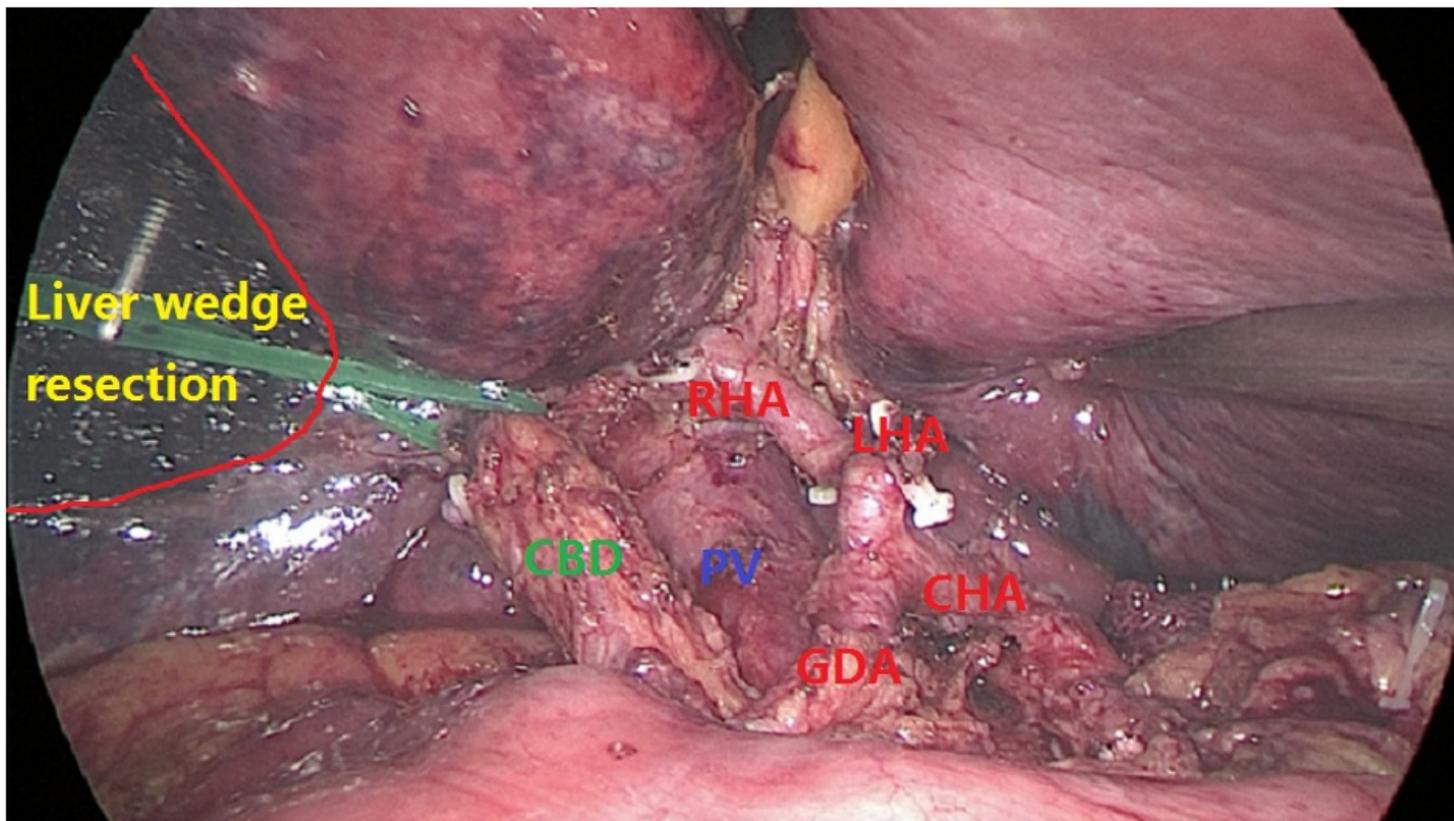


Figure 1

laparoscopic cholecystectomy + hepatic wedge resection + lymph node dissection. RHA: Right hepatic artery, LHA: Left hepatic artery, GDA: Gastroduodenal artery, CHA: Common hepatic artery, CBD: Common bile duct, PV: Portal vein

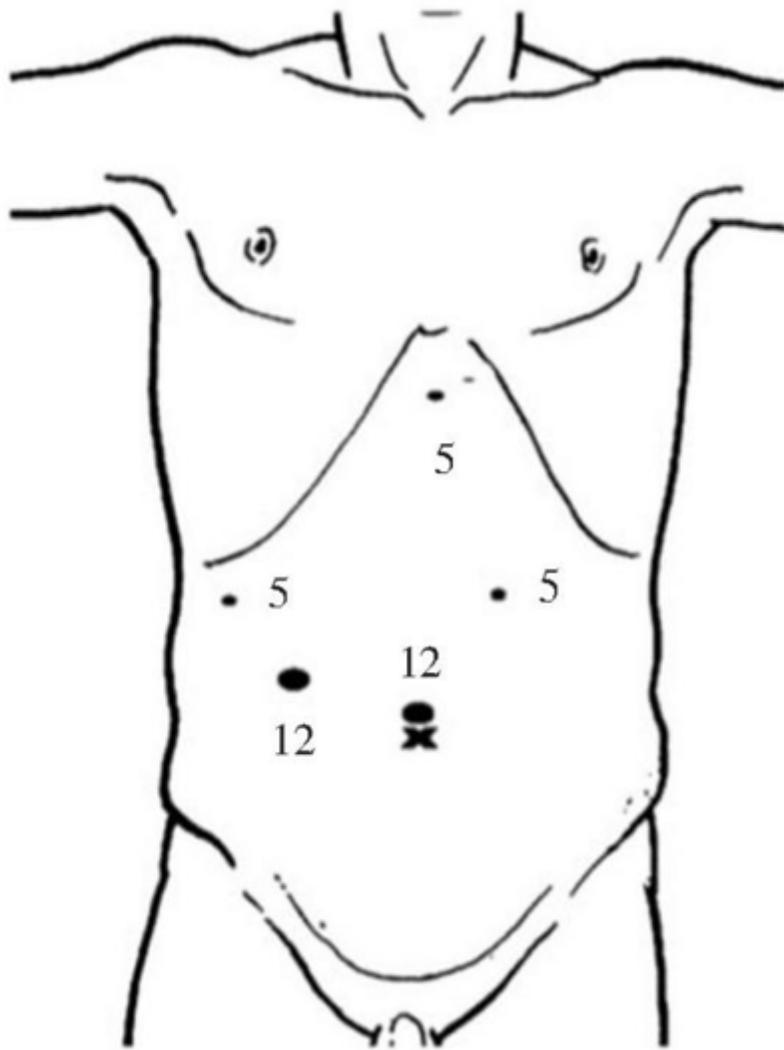


Figure 2

Trocar size and location distribution during surgery

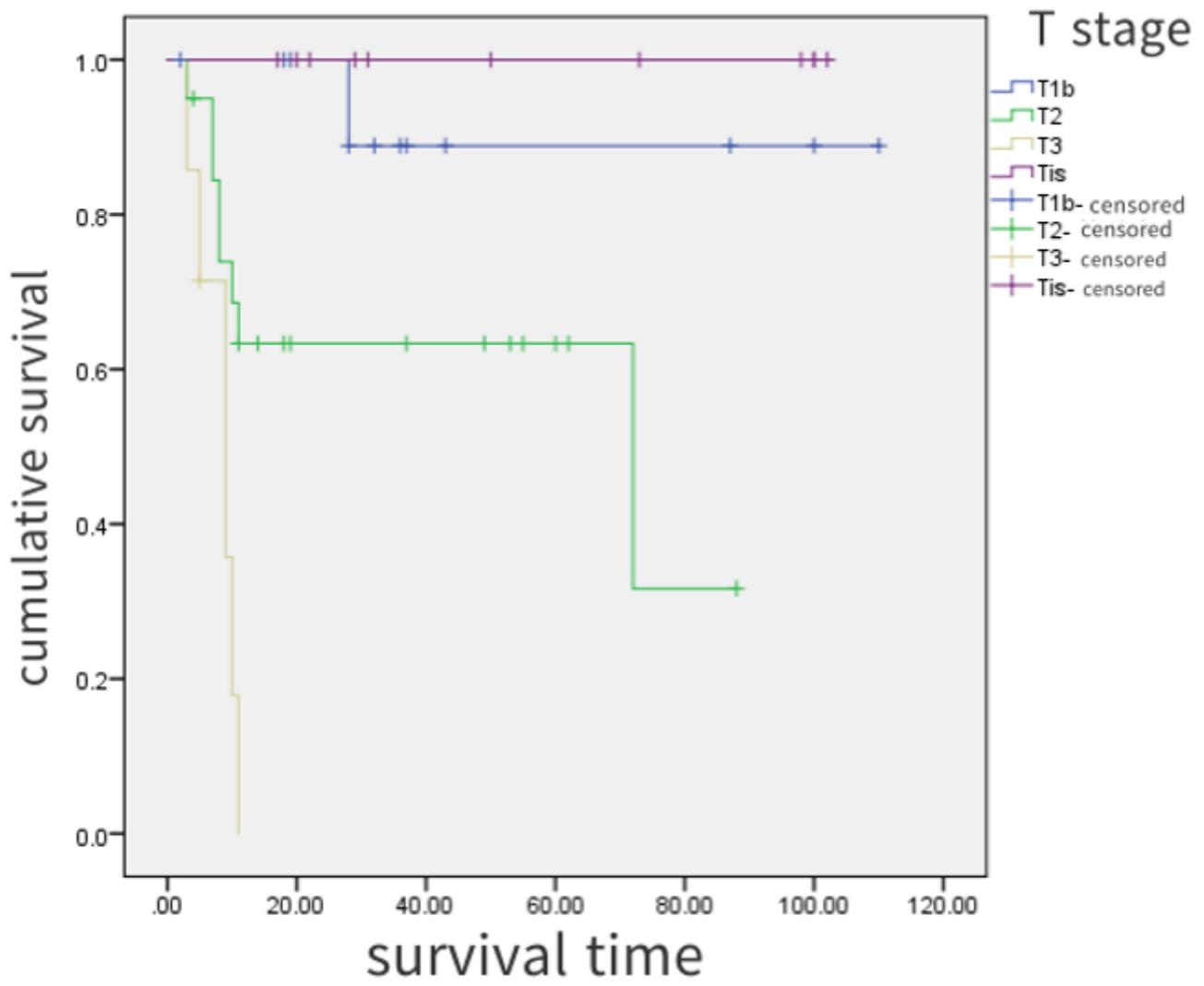


Figure 3

Postoperative survival curve of GBC at different T stages