Radiofrequency ablation vs. hepatectomy for liver metastases from gastrointestinal stromal tumors

YI ZENG*, YUDONG LING*, XIAOJIANG CHEN*, CHAO DING, YUKAI JIN, SHOUCHENG FENG, ZHENCHONG CHEN, JIANRONG GUO and HAIBO QIU

Department of Gastric Surgery, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-Sen University Cancer Center, Guangzhou, Guangdong 510060, P.R. China

Received August 31, 2023; Accepted January 12, 2024

DOI: 10.3892/ol.2024.14266

Abstract. For patients with gastrointestinal stromal tumors (GISTs) and liver metastases, there is still debate about whether radiofrequency ablation (RFA) or hepatectomy is preferable. The present study aimed to compare the clinical outcomes of RFA with hepatectomy in patients with GISTs and liver metastases. The present retrospective study consisted of a cohort of 43 patients who had been diagnosed with liver metastases from GISTs between January 2010 and December 2022. The study included 18 patients who received RFA combined with tyrosine kinase inhibitor (TKI) therapy (RFA group) and 25 patients who underwent hepatectomy combined with TKI therapy (hepatectomy group). For the patients with liver metastases, the progression-free survival (PFS) rates at 1, 3 and 5 years were 66.5, 38.2 and 33.9%, respectively. Notably, patients in the hepatectomy group exhibited significantly improved PFS times compared with those in the RFA group (median PFS, 42.7 months vs. 14.3 months; P=0.034). Furthermore, the time to imatinib treatment failure (TTF) was notably improved in the hepatectomy group compared with that in the RFA group, and this difference was statistically significant (median TTF, 71.1 vs. 38.0 months; P=0.041). However, the overall survival (OS) times of patients who received RFA and those who had hepatectomy did not differ significantly (median OS, not reached vs. not reached, P=0.120). There was no statistically significant distinction in PFS and TTF between patients who underwent hepatectomy combined with postoperative TKI and those who underwent hepatectomy combined with perioperative TKI (median PFS, 29.5 vs. not reached; P=0.520; median TTF, 66.4 months vs. 71.1 months; P=0.430). The univariate and multivariate analyses consistently identified the sole prognostic factor affecting PFS as hepatectomy combined with TKI therapy (hazard ratio, 0.379; 95% CI, 0.159-0.899; P=0.028). In conclusion, hepatectomy combined with TKI therapy improved prognosis for patients with liver metastases to a greater extent than RFA combined with TKI therapy. For this type of patient, hepatectomy may be a preferable option.

Correspondence to: Dr Jianrong Guo or Dr Haibo Qiu, Department of Gastric Surgery, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-Sen University Cancer Center, 651 Dongfeng East Road, Guangzhou, Guangdong 510060, P.R. China
E-mail: guojr1@sysucc.org.cn
E-mail: qiuhb@sysucc.org.cn

*Contributed equally

Abbreviations: GIST, gastrointestinal stromal tumor; TKI, tyrosine kinase inhibitor; RFA, radiofrequency ablation; PFS, progression-free survival; TTF, time to imatinib treatment failure; OS, overall survival

Key words: GIST, liver metastasis, RFA, hepatectomy, TKI

Introduction

Gastrointestinal stromal tumors (GISTs) represent the most prevalent mesenchymal tumors within the gastrointestinal tract and the incidence rate of GISTs is 10-15 cases per million per year, which varies by region and time (1,2). These tumors are primarily driven by mutations in KIT or platelet-derived growth factor receptor α, which serve as oncogenic drivers (1,3). Notably, GISTs can metastasize distantly, with reported incidence rates of metastases ranging from 15 to 50% (4-6). Among these metastatic sites, the liver and peritoneum are the most frequently affected (7). For patients with recurrent or metastatic GISTs, the primary treatment of choice is imatinib (8,9). Even though imatinib markedly increases the overall survival (OS) rate of these patients, with a median OS time >5 years and a median progression-free survival (PFS) time of ~2 years, a substantial portion of patients ultimately encounter disease progression, often due to secondary resistance to imatinib (8,10). In cases of imatinib resistance, alternative treatments come into play. Sequentially, sunitinib, regorafenib and ripretinib are employed as second-, third- and fourth-line treatments, respectively. These therapies have demonstrated noteworthy therapeutic effects, providing viable options for patients who do not respond to imatinib (11). Nonetheless, a challenge persists in deriving long-term benefits from subsequent lines of treatment for patients with GISTs who experience progression following first-line therapy with

imatinib (12). Consequently, an urgent and unmet need exists for the development of effective methods to treat advanced GISTs cases, aiming to extend survival times and improve the quality of life for these patients.

Hepatectomy and radiofrequency ablation (RFA) are considered potential and effective treatment methods for patients with liver metastases from GISTs due to their potential for a complete tumor resection or minimal surgical trauma. There are currently several studies, albeit with limited sample sizes or imbalanced patient characteristics, which suggest that hepatectomy or RFA is effective in treating these patients, but widely agreed standardized treatment methods for such cases have not yet been established (13-16). Considering this gap, the current study aimed to directly compare the clinical benefits of hepatectomy with those of RFA in patients with liver metastases from GISTs.

Patients and methods

Patients. Patients who were diagnosed with liver metastases from GISTs at Sun Yat-Sen University Cancer Center (Guangzhou, China) between January 2010 and December 2022 were identified from the institutional medical records. Ethical approval for the present study was granted by the Institutional Review Board of Sun Yat-sen University Cancer Center. The inclusion criteria encompassed the following conditions: i) Pathological confirmation of the GIST as the primary tumor site and removal of the tumor; ii) diagnosis of liver metastases from GIST through post-operative pathology, biopsy, imaging and clinical data; and iii) radiofrequency ablation or hepatectomy being used as a treatment for liver metastases. Exclusion criteria were as follows: i) Patients <18 years of age; ii) the presence of other malignancies; iii) the existence of other distant metastases from GIST; and iv) incomplete patient data. Liver metastases identified concomitantly with the primary tumor diagnosis or within the initial 6 months were classified as synchronous metastases. By contrast, metachronous metastases were classified by the detection of liver metastases >6 months after the primary tumor diagnosis. Comprehensive data, including patient demographics, clinicopathological features and other pertinent information, were meticulously reviewed.

RFA and surgical management. A multidisciplinary team composed of gastrointestinal surgeons, hepatobiliary surgeons and interventional radiologists, based on a comprehensive assessment of the patient's condition, made the decision to perform either RFA or a hepatectomy. In cases involving patients with a large volume of liver metastases or those located near critical structures, the multidisciplinary team favored liver resection. Additionally, for patients at an unacceptable risk of liver dysfunction post-resection, the preference leaned towards RFA. If RFA or hepatectomy were deemed technically viable but no decision was made during a multidisciplinary discussion meeting, the patient and the surgeons would confer before making a final choice. For patients selected to undergo hepatectomy or RFA, the procedures were determined following a comprehensive evaluation. Percutaneous RFA was performed with the patient under local anesthesia and conscious sedation, guided by ultrasound imaging. The radio frequency system was chosen based on the operator's thorough assessment of the amount and location of liver metastases. The procedural objective for targeted RFA was to achieve an ablative margin measuring at least 0.5-1.0 cm. Surgical margins were categorized as follows: i) Microscopically complete (R0), indicating no observable tumor cells; ii) macroscopically complete with microscopic residual tumor cells; or iii) macroscopically incomplete.

Follow-up and endpoints. Patients usually went to the hospital for regular follow-up every 3 months, including physical examinations, laboratory tests and imaging evaluations. Imaging examinations included contrast-enhanced multiphase computed tomography or magnetic resonance imaging, while laboratory tests encompassed a complete blood count, liver and renal function assessments, and tumor marker analyses, among others. The key parameters of interest were PFS time and time to imatinib treatment failure (TTF). Specifically, PFS time was characterized as the duration spanning from the occurrence of RFA or hepatectomy for liver metastases to the point of disease progression or mortality due to any cause. TTF was defined as the duration from the initiation of imatinib treatment for liver metastases from GISTs to the point at which treatment discontinuation occurred due to therapeutic ineffectiveness, intolerable toxicity or other factors influencing treatment failure. The period from the date of hepatic resection or RFA for liver metastases until the final follow-up or death was referred to as the OS time.

Statistical analysis. Nominal data were analyzed through Pearson's χ^2 test or Fisher's exact test, as deemed appropriate. To depict survival trends, the Kaplan-Meier method was employed, and differences between groups were ascertained via the log-rank test. For examining the potential prognostic factors and their association with PFS time, variables with a P-value of <0.2 or those considered potentially associated with PFS in the univariate analysis were included in the subsequent multivariable Cox proportional hazards model. All statistical analyses were performed using R version 4.2.2 (R Core Team). A significance threshold was established at a two-tailed P-value of <0.05.

Results

Patient demographics and clinical and pathological characteristics. The present study was ultimately comprised of 43 patients with liver metastases from GISTs treated between January 2010 and December 2022. A comparative analysis of baseline clinicopathological characteristics between the RFA group (n=18) and the hepatectomy group (n=25) is detailed in Table I. Notably, there were no statistically significant differences in the baseline attributes between these two groups. The patient age range was 19-68 years, with a median age of 50.5 years. The majority of patients (60.5%) were male.

Regarding the primary GIST site, 25 patients (58.1%) had tumors not located in the stomach, while 18 patients (41.9%) had tumors in the stomach. Liver metastases occurred beyond 6 months after the removal of the original tumor in 21 patients (48.8%; metachronous), whereas 22 patients (51.2%) initially

Table I. Baseline clinical characteristics of patients in the RFA (n=18) and hepatectomy (n=25) groups.

Characteristic	RFA group, n (%)	Hepatectomy group, n (%)	P-value
Age, years			0.455
<60	13 (72.2)	21 (84.0)	
≥60	5 (27.8)	4 (16.0)	
Sex			0.941
Female	7 (38.9)	10 (40.0)	
Male	11 (61.1)	15 (60.0)	
Primary GIST location			0.359
Stomach	9 (50.0)	9 (36.0)	
Non-stomach	9 (50.0)	16 (64.0)	
Metastatic phase			0.067
Synchronous	6 (33.3)	16 (64.0)	
Metachronous	12 (66.7)	9 (36.0)	
Largest metastasis diameter, cm			0.847
<4	11 (61.1)	16 (64.0)	
≥4	7 (38.9)	9 (36.0)	
Number of metastases			0.736
Solitary	4 (22.2)	7 (28.0)	
Multiple	14 (77.8)	18 (72.0)	
Mitotic rate, mitoses per 50 HPFs			0.681
≤5	6 (40.0)	7 (33.3)	
>5	9 (60.0)	14 (66.7)	
Mutation			0.860
KIT 9 mutation	2 (16.7)	3 (20.0)	
KIT 11 mutation	7 (58.3)	10 (66.7)	
Wild-type	3 (25.0)	2 (13.3)	

RFA, radiofrequency ablation; GIST, gastrointestinal stromal tumor; HPF, high-power field; KIT, c-kit proto-oncogene.

presented with metastatic GISTs (synchronous). Among the analyzed patients, mutational analysis was conducted in 27 patients, revealing KIT 11 mutations in 17 patients (63.0%), KIT 9 mutations in 5 patients (18.5%) and wild-type variants in 5 patients (18.5%).

Treatment. Following the diagnosis of liver metastases from GISTs, all patients underwent TKI treatment tailored to the nature of their condition. Initially, 41 patients were administered first-line imatinib therapy, while 2 patients received second-line sunitinib treatment following their initial diagnosis of liver metastases from GISTs. In the current study, the treatment approaches were diversified. Among the participants, 25 patients (58.1%) underwent hepatectomy combined with TKI therapy, while 18 patients (41.9%) received RFA combined with TKI treatment (Table I). Within the hepatectomy group, 15 patients (60.0%) underwent resection and received perioperative TKIs, whereas 10 patients (40.0%) underwent hepatic resection and exclusively received postoperative TKI therapy. Notably, all resections within the hepatectomy group achieved R0 status. Conversely, the RFA group experienced entirely ablative RFA procedures to eliminate target liver metastases.

Survival analysis. With a median follow-up duration of 38.1 months (range, 8.5-131.6 months), the 1-, 3- and 5-year PFS rates for all patients with liver metastases were 66.5, 38.2 and 33.9%, respectively. Specifically, patients with hepatic metastases exhibited 1-, 3-, and 5-year TTF rates of 95.1, 70.5 and 54.7%, respectively. Recurrence was observed in 11 patients (61.1%) in the RFA group and 12 patients (48.0%) in the hepatectomy group. Notably, patients who underwent hepatic resection alongside TKI therapy demonstrated significantly improved PFS and TTF times compared with those who received RFA combined with TKI therapy (median PFS, 42.7 months vs. 14.3 months, P=0.034; median TTF, 71.1 months vs. 38.0 months, P=0.041) (Fig. 1). Furthermore, no statistically significant disparity in OS time was observed between patients who underwent hepatectomy and those who underwent RFA (median OS, not reached vs. not reached, P=0.120) (Fig. 2). There was no statistically significant difference in PFS and TTF times between patients who received hepatectomy combined with postoperative TKI and those who received hepatectomy combined with perioperative TKI (median PFS: 29.5 months vs. not reached, P=0.520; median TTF, 66.4 months vs. 71.1 months, P=0.430) (Fig. 3). Table II outlines the outcomes

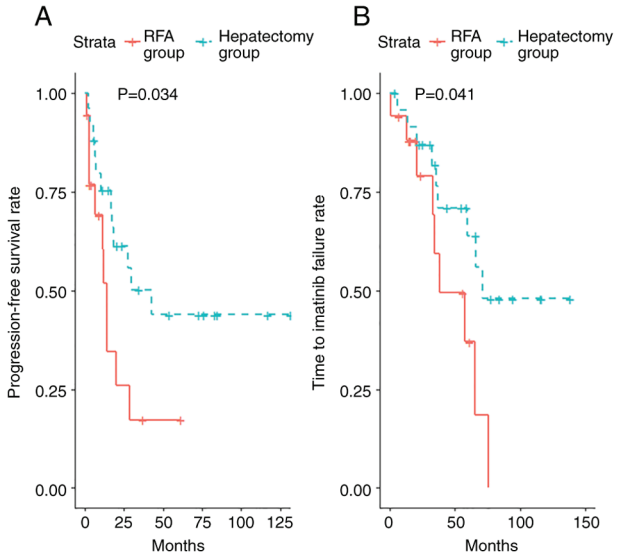

Figure 1. (A) Progression-free survival for patients with RFA vs. patients with hepatectomy. (B) Time to imatinib treatment failure for patients with RFA vs. patients with hepatectomy. RFA, radiofrequency ablation.

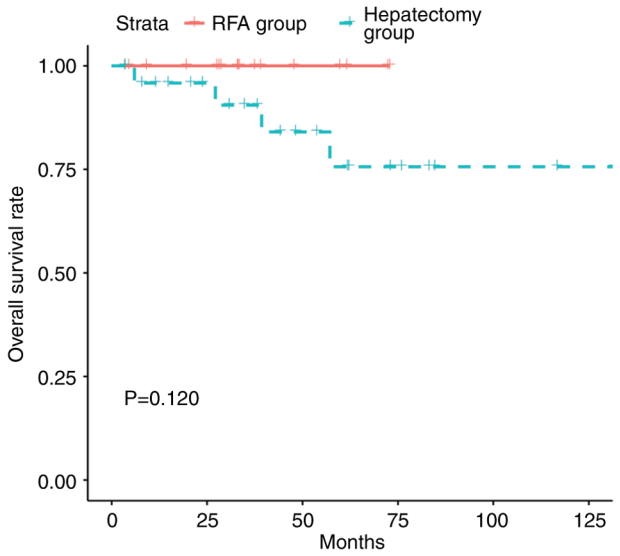

Figure 2. Overall survival for patients with RFA vs. patients with hepatectomy. RFA, radiofrequency ablation.

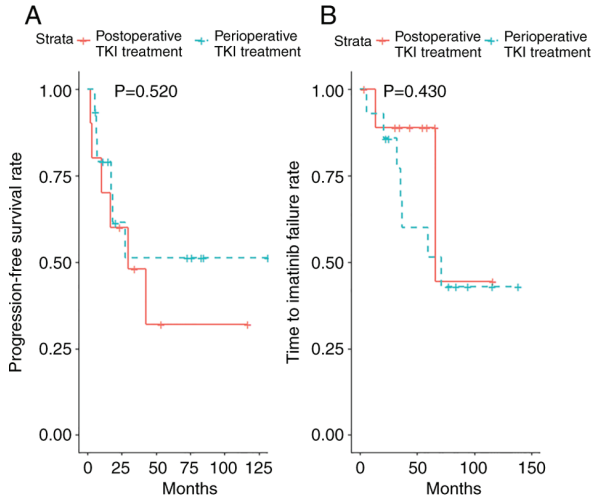

Figure 3. (A) Progression-free survival for patients with postoperative TKI treatment vs. patients with perioperative TKI treatment. (B) Time to imatinib treatment failure for patients with postoperative TKI treatment vs. patients with perioperative TKI treatment. TKI, tyrosine kinase inhibitor.

of univariate and multivariate analyses for a comprehensive view of potential prognostic factors affecting PFS. These analyses identified the hepatectomy group as being independently associated with longer PFS time (HR, 0.379; 95% CI, 0.159-0.899; P=0.028).

Discussion

GIST predominantly metastasizes to the liver and peritoneum (17). Despite the substantial increase in OS time following imatinib treatment, resistance mutations often lead to disease progression (10). Furthermore, for patients with GISTs who relapse after initial imatinib therapy, achieving sustained benefits from subsequent lines of treatment can be challenging (18). The absence of a standardized therapeutic model for liver metastases from GISTs compounds the issue, making it a complex challenge in the TKI era.

The combination of RFA and TKI therapy seems to be a viable, less invasive option for managing liver metastases from GISTs, as indicated by several retrospective studies (13,19,20). Similarly, other retrospective investigations suggested survival advantages with the inclusion of hepatectomy in the treatment of metastasis from GISTs (21,22). A retrospective study conducted by Xue *et al* (15) demonstrated that hepatectomy improved the PFS time in patients with hepatic metastases from GISTs. Notably, to the best of our knowledge, the present study is the largest comparative analysis of RFA and hepatectomy for liver metastases from GISTs.

The present findings indicated that hepatectomy surpasses RFA as the preferred approach for managing liver metastases from GISTs. Several factors support this conclusion. Firstly, patients who underwent hepatectomy in combination with TKI therapy achieved notably higher median PFS and TTF times compared with those treated with RFA (median PFS, 42.7 months vs. 14.3 months; median TTF, 71.1 months vs. 38.0 months). Secondly, the current analyses revealed that hepatectomy was as an independent prognostic factor for improved PFS time in both univariate and multivariate assessments. Lastly, hepatectomy may offer the opportunity for pathological examination of the resected tissue, enabling a more detailed understanding of the disease characteristics and informing subsequent therapeutic strategies. The retrospective analysis conducted by Chen *et al* (13) showed that patients with liver metastases from GISTs who underwent a liver resection had higher PFS times but similar OS times, which is consistent with the results in the present study. Additionally, the higher median PFS time in both patient groups in the present study compared with those in previous studies may be attributed to the inclusion of more advanced cases in previous studies, including those with extrahepatic metastases.

The utilization of hepatectomy combined with TKI therapy raises debates about the optimal approach for achieving

Table II. Prognostic factors for progression-free survival.

	Univariate analysis		Multivariate analysis	
Factor	HR (95% CI)	P-value	HR (95% CI)	P-value
Age, years				
<60				
≥60	1.060 (0.393-2.860)	0.908		
Sex				
Female				
Male	0.890 (0.390-2.031)	0.781		
Primary GIST location				
Stomach				
Non-stomach	1.162 (0.503-2.687)	0.725	1.250 (0.529-2.950)	0.613
Metastatic phase				
Synchronous				
Metachronous	1.279 (0.555-2.946)	0.564		
Largest metastasis diameter, cm				
<4				
≥4	1.964 (0.846-4.559)	0.116	1.930 (0.812-4.590)	0.137
Number of metastases				
Solitary				
Multiple	0.558 (0.236-1.322)	0.185	0.626 (0.261-1.500)	0.294
Treatment				
RFA group				
Hepatectomy group	0.416 (0.180-0.957)	0.039	0.379 (0.159-0.899)	0.028
Mitotic rate, mitoses per 50 HPF				
≤5				
>5	1.270 (0.468,3.450)	0.638		
Mutation				
KIT 9 mutation				
KIT 11 mutation	0.763 (0.201-2.894)	0.691		
Wild-type	1.634 (0.362-7.379)	0.524		

RFA, radiofrequency ablation; GIST, gastrointestinal stromal tumor; HR, hazard ratio; CI, confidence interval; HPF, high-power field; KIT, c-kit proto-oncogene.

improved survival benefits and the appropriate timing for surgical intervention. Turley *et al* (23) found that survival rates were higher with hepatectomy followed by TKI therapy, as opposed to hepatectomy combined with perioperative TKI therapy. Conversely, two other studies indicated that patients treated with preoperative TKI in conjunction with hepatic resection exhibited superior survival compared with those receiving hepatic resection followed by TKI postoperatively (24,25). The present study observed that there was no statistically significant difference in PFS time and TTF between patients who underwent hepatectomy combined with perioperative TKI therapy and those who underwent hepatectomy combined with postoperative TKI therapy. This lack of significance in outcomes can be attributed to several factors. Firstly, inherent disparities at the baseline level reduced comparability between the two patient groups. Predominantly, the patients undergoing preoperative TKI therapy were those with larger or multiple liver metastases, and such cases are associated with heightened recurrence risks, consequently impacting PFS time and TTF. This contributed to the absence of statistical significance for PFS and TTF between the two therapeutic strategies. Furthermore, the median treatment duration for patients receiving preoperative TKI therapy was 15 months, substantially exceeding the recommended preoperative neoadjuvant therapy course (26-28). This prolonged treatment period might have led to a missed optimal surgical window.

The present study, despite achieving generally balanced baseline data for both groups, does have certain limitations. Primarily, the limited prevalence of metastatic GIST translated to a small sample size, a constraint inherent to the low incidence. Furthermore, the retrospective nature of the present study unavoidably introduced selection bias. Additionally, due to a lack of radiographic response data at the time of hepatectomy or RFA in certain cases, it was not possible to delve

into the optimal timing for these procedures to yield optimal clinical outcomes. Lastly, the present study did not delve into the analysis of subsequent line treatments for recurrent patients, a facet crucial for a comprehensive evaluation of the benefits associated with RFA and hepatectomy.

In conclusion, the present findings indicated that hepatectomy could potentially extend both PFS time and TTF for patients with liver metastases. Specifically, the findings suggested that in clinical practice, for patients with liver metastases from GISTs, hepatectomy should be prioritized over RFA. Further research and clinical studies are necessary to explore the specific patient populations that would benefit the most from hepatectomy and to refine the surgical technique for improved long-term outcomes.

Acknowledgements

Not applicable.

Funding

This project was supported by the Natural Science Foundation of Guangdong Province (grant no. 2022A1515012347) and the Beijing CSCO-ROCHE Research Fund (grant no. Y-2019Roche-157).

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

HBQ and JRG contributed to the conception and design of this retrospective study. YZ, YDL and XJC performed most of the data extraction, the quality evaluation and the statistical analyses, and wrote the draft manuscript. CD, YKJ, SCF and ZCC contributed to the collection, analysis and interpretation of data. YZ and YDL confirm the authenticity of all the raw data. All authors contributed to the writing or editing of the manuscript, and have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The study was approved by the Institutional Review Board of Sun Yat-sen University Cancer Center (Guangzhou, China; approval no. B2022-764-01), and was conducted in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The requirement for informed consent was waived by the Institutional Review Board due to the retrospective nature of the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Hirota S, Isozaki K, Moriyama Y, Hashimoto K, Nishida T, Ishiguro S, Kawano K, Hanada M, Kurata A, Takeda M, *et al*: Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors. Science 279: 577-580, 1998.
2. Søreide K, Sandvik OM, Søreide JA, Giljaca V, Jureckova A and Bulusu VR: Global epidemiology of gastrointestinal stromal tumours (GIST): A systematic review of population-based cohort studies. Cancer Epidemiol 40: 39-46, 2016.
3. Heinrich MC, Corless CL, Duensing A, McGreevey L, Chen CJ, Joseph N, Singer S, Griffith DJ, Haley A, Town A, *et al*: PDGFRA activating mutations in gastrointestinal stromal tumors. Science 299: 708-710, 2003.
4. Miettinen M and Lasota J: Gastrointestinal stromal tumors. Gastroenterol Clin North Am 42: 399-415, 2013.
5. Nilsson B, Bümming P, Meis-Kindblom JM, Odén A, Dortok A, Gustavsson B, Sablinska K and Kindblom LG: Gastrointestinal stromal tumors: the incidence, prevalence, clinical course, and prognostication in the preimatinib mesylate era-a population-based study in western Sweden. Cancer 103: 821-829, 2005.
6. Joensuu H: Gastrointestinal stromal tumor (GIST). Ann Oncol 17 (Suppl 10): x280-x286, 2006.
7. Miettinen M and Lasota J: Gastrointestinal stromal tumors: Pathology and prognosis at different sites. Semin Diagn Pathol 23: 70-83, 2006.
8. Blanke CD, Demetri GD, von Mehren M, Heinrich MC, Eisenberg B, Fletcher JA, Corless CL, Fletcher CD, Roberts PJ, Heinz D, *et al*: Long-term results from a randomized phase II trial of standard- versus higher-dose imatinib mesylate for patients with unresectable or metastatic gastrointestinal stromal tumors expressing KIT. J Clin Oncol 26: 620-625, 2008.
9. Blay JY, Kang YK, Nishida T and von Mehren M: Gastrointestinal stromal tumours. Nat Rev Dis Primers 7: 22, 2021.
10. Antonescu CR, Besmer P, Guo T, Arkun K, Hom G, Koryotowski B, Leversha MA, Jeffrey PD, Desantis D, Singer S, *et al*: Acquired resistance to imatinib in gastrointestinal stromal tumor occurs through secondary gene mutation. Clin Cancer Res 11: 4182-4190, 2005.
11. Al-Share B, Alloghbi A, Al Hallak MN, Uddin H, Azmi A, Mohammad RM, Kim SH, Shields AF and Philip PA: Gastrointestinal stromal tumor: A review of current and emerging therapies. Cancer Metastasis Rev 40: 625-641, 2021.
12. Kurokawa Y, Honma Y, Sawaki A, Naito Y, Iwagami S, Komatsu Y, Takahashi T, Nishida T and Doi T: Pimitespib in patients with advanced gastrointestinal stromal tumor (CHAPTER-GIST-301): A randomized, double-blind, placebo-controlled phase III trial. Ann Oncol 33: 959-967, 2022.
13. Chen Q, Li C, Yang H, Zhao H, Zhao J, Bi X, Li Z, Huang Z, Zhang Y, Zhou J and Cai J: Radiofrequency ablation versus resection for resectable liver metastases of gastrointestinal stromal tumours: Results from three national centres in China. Clin Res Hepatol Gastroenterol 43: 317-323, 2019.
14. Yoon IS, Shin JH, Han K, Kim PN, Kim KH, Kang YK and Ko HK: Ultrasound-guided intraoperative radiofrequency ablation and surgical resection for liver metastasis from malignant gastrointestinal stromal tumors. Korean J Radiol 19: 54, 2018.
15. Xue A, Gao X, He Y, Shu P, Huang X, Sun J, Lu J, Hou Y, Fang Y and Shen K: Role of surgery in the management of liver metastases from gastrointestinal stromal tumors. Front Oncol 12: 903487, 2022.
16. Yamanaka T, Takaki H, Nakatsuka A, Uraki J, Fujimori M, Hasegawa T, Sakuma H and Yamakado K: Radiofrequency ablation for liver metastasis from gastrointestinal stromal tumor. J Vasc Interv Radiol 24: 341-346, 2013.
17. DeMatteo RP, Lewis JJ, Leung D, Mudan SS, Woodruff JM and Brennan MF: Two hundred gastrointestinal stromal tumors: Recurrence patterns and prognostic factors for survival. Ann Surg 231: 51-58, 2000.
18. Mazzocca A, Napolitano A, Silletta M, Spalato Ceruso M, Santini D, Tonini G and Vincenzi B: New frontiers in the medical management of gastrointestinal stromal tumours. Ther Adv Med Oncol 11: 1758835919841946, 2019.
19. Jung JH, Won HJ, Shin YM and Kim PN: Safety and efficacy of radiofrequency ablation for hepatic metastases from gastrointestinal stromal tumor. J Vasc Interv Radiol 26: 1797-1802, 2015.

20. Jones RL, McCall J, Adam A, O'Donnell D, Ashley S, Al-Muderis O, Thway K, Fisher C and Judson IR: Radiofrequency ablation is a feasible therapeutic option in the multi modality management of sarcoma. Eur J Surg Oncol 36: 477-482, 2010.
21. Keung EZ, Raut CP and Rutkowski P: The landmark series: Systemic therapy for resectable gastrointestinal stromal tumors. Ann Surg Oncol 27: 3659-3671, 2020.
22. DeMatteo RP, Shah A, Fong Y, Jarnagin WR, Blumgart LH and Brennan MF: Results of hepatic resection for sarcoma metastatic to liver: Ann Surg 234: 540-548, 2001.
23. Turley RS, Peng PD, Reddy SK, Barbas AS, Geller DA, Marsh JW, Tsung A, Pawlik TM and Clary BM: Hepatic resection for metastatic gastrointestinal stromal tumors in the tyrosine kinase inhibitor era. Cancer 118: 3571-3578, 2012.
24. Chen Q, Li C, Yang H, Zhao H, Wu J, Zhao J, Bi X, Li Z, Huang Z, Zhang Y, *et al*: Resection combined with TKI therapy for resectable liver metastases of gastrointestinal stromal tumours: Results from three national centres in China. J Gastrointest Surg 24: 1330-1341, 2020.
25. Seesing MF, Tielen R, van Hillegersberg R, van Coevorden F, de Jong KP, Nagtegaal ID, Verhoef C, de Wilt JH and Dutch Liver Surgery Working Group: Resection of liver metastases in patients with gastrointestinal stromal tumors in the imatinib era: A nationwide retrospective study. Eur J Surg Oncol 42: 1407-1413, 2016.
26. DeMatteo RP, Maki RG, Singer S, Gonen M, Brennan MF and Antonescu CR: Results of tyrosine kinase inhibitor therapy followed by surgical resection for metastatic gastrointestinal stromal tumor. Ann Surg 245: 347-352, 2007.
27. Haller F, Detken S, Schulten HJ, Happel N, Gunawan B, Kuhlgatz J and Füzesi L: Surgical management after neoadjuvant imatinib therapy in gastrointestinal stromal tumours (GISTs) with respect to imatinib resistance caused by secondary KIT mutations. Ann Surg Oncol 14: 526-532, 2007.
28. Vassos N, Agaimy A, Hohenberger W and Croner RS: Management of liver metastases of gastrointestinal stromal tumors (GIST). Ann Hepatol 14: 531-539, 2015.