Radical Versus Non-Radical Resection for Small intestinal Gastrointestinal Stromal Tumors: A Propensity Score-Matched Analysis

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Abstract

Surgical resection is the first choice for the treatment of small intestinal gastrointestinal stromal tumors (GISTs), but the best surgical method for small intestinal stromal tumors remains undefined. It is not clear whether there is a difference in the long-term survival of small intestinal GISTs between radical surgery and non-radical surgery. We included 877 patients with small intestinal stromal tumors who underwent surgery between 2010 and 2015 from the SEER database. They were divided into the radical resection group and the non-radical resection group. To minimized the selection bias and mixed bias in the comparison, propensity score matching (PSM) and multivariate regression analysis were carried out. In the entire cohort, 120 patients underwent radical surgery and 757 patients received non-radical resection. The 1, 3, and 5-year OS rates were 95.7%, 80.2%, and 69.6% in the radical resection group versus 94.3%, 86.8%, and 77.2% in the non-radical resection group, respectively. (p=0.069) Meanwhile, radical resection had the similar CSS rates of 1, 3 and 5-year compared with non-radical surgery. (1-year CSS rate: 97.4% vs. 98.0%, 3-year CSS rate: 86.1% vs. 93.2%, 5-year CSS rate: 81.6% vs. 88.3%; p =0.056) Besides, after adjusting for other clinical factors and PSM, the long-term OS and CSS did not significantly differ between radical surgery and non-radical surgery. Our study preliminarily found that for small intestinal GISTs, there was no significant difference in long-term survival between radical surgery and non-radical surgery.

Introduction

Gastrointestinal stromal tumors (GIST) are sarcomas that mainly originate from the spindle-shaped mesenchymal cells called interstitial cells of Cajal (ICCs) or stem cell precursors to these cells.[1] GISTs are rare gastrointestinal tumors with an incidence of about 1/100000/year, accounting for 0.1–3% of all gastrointestinal malignant tumors.[2,3] Gastrointestinal stromal tumors can occur in any part of the gastrointestinal tract, mainly in the stomach(60-65%) and small intestine (20-25%), while colorectal, esophagus and other parts are relatively rare.[4,5] Due to small bowel tumors are relatively rare and difficult to detect in imaging at an early stage, they are easy to be ignored and delayed diagnosis.[6] There are different clinicopathological and recurrence differences between small intestinal stromal tumors and gastric stromal tumors. In addition, small intestinal stromal tumors have higher invasiveness and worse prognosis with lower disease-free survival and overall survival.[7–9]

Radical resection is the first choice for the treatment of small intestinal stromal tumors.[10] The adequacy of radical resection was evaluated by boundary state and complete resection (no tumor spillover or rupture).[11,12] Limited resection of small bowel GIST is also an ideal surgical method from an oncology point of view.[13] However, there was a lack of relevant studies to evaluate whether radical resection and non-radical resection of small intestinal stromal tumors had a difference in long-term survival, so we conducted this retrospective study based on the American population.

Methods

Data Sources

We used the SEER database to identify patients with small intestinal stromal tumors according to the third edition of the International Classification of Diseases for Oncology (specific histologic subtype code: 8936; primary site code: C170-179). Inclusion criteria are (1) age ≥ 18 years old; (2) patients undergoing surgical resection (Radical surgery, simple/partial surgical removal of primary site or total surgical removal of primary site); (3) patients from 2010 to 2015. Exclusion criteria are (1) lack of TNM staging information; (2) patients with unknown tumor size; (3) lack of survival data or patients with "survival months=0"; (4) no cancer-directed surgery of primary site, local tumor destruction, or excision (photodynamic therapy; electrocautery; fulguration; cryosurgery; laser; polypectomy; excisional biopsy). The SEER database defines radical resection as partial or total removal of the primary site with an en bloc resection (partial or total removal) of other organs.

Variables and Outcomes of Interest

The primary endpoint of our study was overall survival (OS)and cancer-specific survival (CSS) after surgery. In our study, the clinicopathological characteristics of small intestinal stromal tumors extracted from the SEER database included age, race, sex, tumor grade, tumor size, mitotic rate, TNM stage, lymph node metastasis, distant metastasis, primary tumor resection (radical resection and non-radical resection) and chemotherapy, vital status, survival time, insurance status, and marital status.

According to the surgical methods of small intestinal stromal tumors, we divided the patients into radical resection and non-radical resection groups. Tumor size was divided into ≤2 cm,2-5 cm, 5-10 cm, and ≥10 cm, and the age variable was divided into < 65 or ≥ 65 years old. Meanwhile, the mitotic rate included the high mitotic rate group, low mitotic rate group, and unknown group.

Statistical analysis

The distributions of the baseline characteristics were described as percentages and Pearson's chi-squared test was used to compare the differences in clinical characteristics between the radical resection group and the non-radical resection group. (SPSS, version 21, IBM Corporation, Armonk, NY) Meanwhile, OS and CSS were calculated by the Kaplan-Meier method and the survival differences between the radical resection and the non-radical resection groups were compared by log-rank test. We also use GraphPad Prism 9.0 (San Diego, CA) to draw the survival curve. The hazard ratio of radical resection group and non-radical resection group was calculated by multivariate Cox proportional hazard regression model after adjusting for other variables (age, race, sex, tumor grade, tumor size, mitotic rate, TNM stage, lymph node metastasis, distant metastasis, chemotherapy, insurance status, and marital status) (SPSS21) Besides, a propensity score matching (PSM) analysis was done by R 4.0.5(Institute for Statistics and Mathematics, Vienna, Austria). One-to-one matching between the radical resection and the non-radical resection groups was performed with a caliper of 0.05. The propensity model included the following variables: age, race, sex, tumor grade, tumor size, mitotic rate, TNM stage, lymph node metastasis, distant metastasis, chemotherapy, insurance status, and marital status.

Ethics approval and consent to participate.

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. As data acquisition in the SEER database is de-identified and poses no risk for individual participants, our study was exempt from review by the ethics committee.

Results

Baseline Characteristics

We identified a total of 877 patients with small intestinal GISTs who met the inclusion criteria, of which 757 (86.3%) underwent non-radical resection and 120 (13.7%) received radical resection. (Figure 1) The detailed baseline characteristics for the overall population are summarized in Table 1. Before PSM, many factors significantly differed between the two groups including tumor grade, tumor size, mitotic rate, TNM stage, distant metastasis, chemotherapy. We found that the proportion of Stage IV (40.80% vs. 16.20%, P<0.001), distant metastasis patients (39.20% vs. 13.90%, P<0.001), high mitotic rate (40.80% vs. 23.40%, P<0.001), Grade III-IV (30.80% vs. 13.50%, P<0.001), tumor size≥ 10cm (51.70% vs. 26.20%, P<0.001) and patients receiving chemotherapy (72.50% vs. 50.30%, P<0.001) in the radical resection group was higher than that in the non-radical resection group. After PSM, 113 matched pairs of small intestinal GISTs were enrolled in our study, showing no significant difference in all factors between the two groups. (Table 1) Meanwhile, the histograms of propensity scores indicated that the two groups were well matched. (Figure 2)

Survival Outcomes

The 1, 3, and 5-year OS rates were 95.7%, 80.2%, and 69.6% in the radical resection group versus 94.3%, 86.8%, and 77.2% in the non-radical resection group, respectively; radical resection did not improve OS in small intestinal GISTs, with a median survival of 65 months in the radical resection group versus 70 months in the non-radical resection group. (P = 0.069; Figure 3A)

Radical resection had the similar CSS rates of 1, 3 and 5-year compared with non-radical surgery. (1-year CSS rate: 97.4% vs. 98.0%, 3-year CSS rate: 86.1% vs. 93.2%, 5-year CSS rate: 81.6% vs. 88.3%; p =0.056) The median cancer-specific survival time was 71 months in the radical resection group versus 76 months in the non-radical resection group, respectively. The cancer-specific survival curves were shown in figure 3B.

Multivariate Cox Analyses

Multivariate cox regression analysis was performed to adjust the confounding factors and identify the independent risk factors affecting the OS and CSS of small intestinal stromal tumors.

In terms of overall mortality, the hazard ratio (HR) of the radical resection group and non-radical resection group was 1.045 (95%CI 0.673-1.620; P = 0.846) after adjusting for other variables. (Table2) Besides, we found that older age>65 (HR:3.315, 95%CI 2.375-4.629; P<0.001), male (HR:1.408, 95%CI 1.023-1.937; P=0.036), Stage III (HR:1.827, 95%CI 1.126-2.962; P=0.015), Stage IV (HR:4.407, 95%CI 2.678-7.253; P<0.001) were independent risk factors for decreasing OS while receiving chemotherapy (HR:0.492, 95%CI:0.352-0.686, p<0.001) and married patients (HR:0.471, 95%CI:0.343-0.647, p<0.001) was conducive to reducing the overall risk of death. (Table2)

We did not observe a significant difference between the radical resection group and the non-radical resection group in the risk of cancer-specific death in the multivariate cox regression analysis (HR 0.892, 95%CI 0.500-1.591; P=0.699). (Table2) The multivariate cox regression analysis results showed that age>65 (HR:2.440, 95%CI 1.541-3.863; P<0.001), Stage III (HR:7.421, 95%CI 2.536-21.717; P<0.001), Stage IV (HR:19.650, 95%CI 6.655-58.021; P<0.001) were significant risk factors for CSS in small intestinal stromal tumors. The analyses for CSS showed that married patients (HR:0.400, 95%CI 0.183-0.872; P=0.021) and insured patients (HR:0.571, 95%CI 0.369-0.886; P=0.012) had lower a lower risk of death in multivariate analyses. (Table2)

Propensity Score Matching Analyses

After PSM, 113 matched pairs with similar baseline characteristics and propensity to undergo non-radical and radical surgery were included in our study. (Table 1)

Following the propensity-score analyses, the 1, 3, and 5-year OS rates were 95.4%, 80.2% and 70.4% in the radical resection group, compared with 95.5%, 80.8% and 73.2% in the non-radical resection group (p=0.430). (Figure 4A) The median overall survival was 65 months for the radical resection group versus 66 months for the non-radical resection group. There was no significant difference between the two groups (p=0.430). (Figure 4A) Meanwhile, there was no significant difference in the 1, 3, and 5-year CSS rates between the radical resection group and the non-radical resection group after adjusting by propensity score (1-year CSS rate: 97.2% vs. 98.1%, 3-year CSS rate: 85.3% vs. 85.7%, 5-year CSS rate: 80.6% vs. 79.6%; p =0.602). Besides, the median CSS of radical resection in small bowel stromal tumors was similar to that of non-radical resection. (70.7 months vs. 70.3 months; p =0.602). The cancer-specific survival curves were shown in Figure 4B.

After adjusting for confounding factors using a multivariate cox regression model, we found that the risk of death of small intestinal stromal tumors was comparable between radical resection and non-radical resection. (OS HR: 1.117, 95%CI 0.575-2.170, P=0.744; CSS HR: 0.984, 95%CI 0.434-2.232, P=0.969)

Subgroup Analyses

To further address whether different surgical methods (radical resection or non-radical resection) have different prognosis in different populations, we performed subgroup analyses according to age, sex,

tumor grade, mitotic rate, and chemotherapy. We also performed a test for the interaction between surgical methods and different subgroups (age, sex, tumor grade, mitotic rate, and chemotherapy).

In the subgroup of male patients, radical resection was associated with a significantly increased overall risk of death. (HR: 2.432, 95%CI 1.408-5.646; P=0.039) (Figure 5) Besides, we found a significant association between surgical methods and sex; the P values for interactions was 0.033. (Figure 5) Similarly, in patients with low mitotic index, radical resection significantly increased the overall risk of death compared with non-radical resection (HR: 3.150, 95%CI 1.134-8.751; P=0.028); the P values for interactions between surgical methods and mitotic rate was 0.045. (Figure 5) In other subgroups (different ages, grades, and whether receiving chemotherapy), radical resection had the same overall risk of death as non-radical resection. Meanwhile, our interaction tests showed that the P values for interactions between surgical methods and other variables (age, grade, and chemotherapy) were not significant.

The subgroup analyses results showed that the radical resection group had the same cancer-specific risk of death as the non-radical resection group in these different subgroups. Meanwhile, our interaction tests indicated that the P values for interactions between surgical methods and other variables (age, sex, tumor grade, mitotic rate, and chemotherapy) were not significant. (Figure 6)

Discussion

The standard treatment for gastrointestinal stromal tumors is surgical resection. The goal of surgery is to remove the primary tumor and its pseudo-capsule to achieve a negative microscopic margin.[14] Since gastrointestinal stromal tumors are inherently low invasive and rarely undergo lymph node metastasis, surgery does not require large margins and lymph node removal.[15] For GISTs with distant metastasis, it is not a contraindication to tumor resection. A recent study has shown that even in patients with distant GISTs, primary tumor resection can also significantly improve prognosis and survival.[16] With the development of laparoscopic surgery, for small intestinal stromal tumors, related studies have shown that there is no significant difference in survival prognosis between laparoscopic surgery and open surgery, and laparoscopic surgery has the advantages of the short operation time, early recovery, and low incidence of complications.[12,17,18] At the same time, NCCN guidelines also recommend laparoscopic resection of GIST less than 5 cm.[19] Endoscopic therapy, such as submucosal dissection, submucosal excavation, banding ligation, full-thickness resection, and submucosal tunnel endoscopic resection, are mainly used in gastric GISTs with a diameter smaller than 5cm, and many studies have shown that endoscopic resection has the advantages of lower incidence of complications, lower risk of operation-related death, less traumatic bleeding and shorter hospital stay.[20-23] Surgical resection is mainly used in small intestinal gastrointestinal stromal tumors because most of the small intestinal stromal tumors are located in the jejunum and ileum, which cannot be reached by the endoscope and cannot be resected under endoscope. Surgical resection can be divided into radical resection and non-radical resection. Considering that there were no previous studies to compare the difference of long-term survival between

radical resection and non-radical resection in small intestinal GISTs, we conducted this retrospective study based on the American population.

In our study, most patients chose non-radical resection (86.3%), and only about 13.7% of patients chose radical resection. Compared with non-radical resection, patients with Stage IV, distant metastasis, high mitotic rate, tumor size> 10cm, Grade III-IV, and receiving chemotherapy were more likely to undergo radical resection. Previous studies indicated that patients with high mitotic rate, high tumor grade, and tumor size> 5cm had a higher risk of recurrence, which may be part of the reason why surgeons were more likely to perform radical resection for these patients.[24] For patients with distant metastasis, radical surgery requires resection of the primary tumor and removal of the metastatic lesions, while for the small intestinal GISTs invading adjacent organs or tissues, the surrounding invasive lesions should be removed at the same time. This means that radical surgery for small bowel GISTs requires a larger resection range. Increasing the scope of resection leads to more intraoperative blood loss, longer hospital stays, and more postoperative complications.

Our study found that there was no significant difference in long-term survival between radical surgery and non-radical surgery for patients with small intestinal GISTs. When comparing the overall survival of the two groups, the median survival time and the 1, 3, and 5-year OS rates of the two groups were similar, meanwhile, the result was also observed in the analysis of cancer-specific survival. Similarly, after adjusting the confounding factors by using a multivariate COX regression model, there was no significant difference in OS and CSS between the two groups. Considering the imbalance of baseline data between the two groups, after adjusting the distribution of the two groups by PSM, we still found that the two groups had the same OS and CSS. In patients at high risk of recurrences, such as distant metastasis and poorly differentiated small intestinal gastrointestinal stromal tumors, radical resection did not achieve the desired prognosis compared with non-radical surgery.

In our multivariate cox regression analysis, we found that age > 65, male, TNM Stages III and IV were independent risk factors for reducing overall OS, while marriage and receiving chemotherapy were independent factors for improving overall survival and prognosis of small intestinal GISTs. In the CSS cohort, we found that age > 65 and TNM Stages III and IV were still independent factors that increased the risk of cancer-specific death, while married and insured status was beneficial to reduce the risk of cancer-specific death. Elderly patients have higher overall and cancer-specific mortality after surgery, which is consistent with the results of Gordo et al.[8] Considering that elderly patients are more likely to have basic diseases (cardiovascular and cerebrovascular diseases), insufficient physiological reserve capacity, and poor recovery ability after surgical trauma, these may be part of the possible reasons for the poor survival and prognosis of elderly patients after surgery. Patients with high TNM stages often have larger tumors, distant metastasis, lymph node metastasis, poor differentiation, and high mitotic rate. Gastrointestinal stromal tumors with these characteristics are often more aggressive and likely to recur, which affects the patient's long-term OS and CSS. The National Comprehensive Cancer Network (NCCN) currently recommends imatinib adjuvant therapy for patients with GISTs at moderate to high risk of recurrence after surgical resection.[19] Previous related studies have shown that compared with surgical

resection alone, postoperative adjuvant treatment significantly reduces the patient's risk of death and improves the recurrence-free survival rate.[25,26] A study on small intestinal GISTs showed that postoperative adjuvant therapy improved the overall survival rate of high-grade tumors with intermediate and large size, but had no significant effect on the low-grade tumors with small size.[24] The risk of long-term death of married patients was significantly lower than that of unmarried patients in our study. Many studies have shown that marital status has a significant correlation with the survival and prognosis of tumor patients.[27-29] In tumor diseases, the possible reasons for the low survival rate of unmarried patients are as follows. First of all, the early screening of unmarried patients is insufficient, and most of them are diagnosed in the late stage of the disease. Second, married patients' spouses may encourage them to undergo surgery and adjuvant treatment, while unmarried patients are undertreated. In addition, the diagnosis of cancer is thought to cause higher psychological stress, and the incidence of psychological distress, depression, and helplessness in unmarried patients is higher than that in unmarried patients. Meanwhile, patients with insurance have a better survival prognosis. Meanwhile, patients with insurance have a better survival prognosis. In the United States, 38 million people are still uninsured.[30] It is difficult for uninsured patients to have equal access to care in many areas of medicine, and accordingly, their survival in malignant and chronic diseases is worse than that of insured patients. This may be because uninsured patients did not receive the same monitoring or maintenance treatment as insured patients, resulting in a shorter survival time.

Although we use PSM and multivariate cox regression analysis to adjust selection bias and confounding factors, our study still has some inevitable limitations. First, the SEER database lacks related information about post-operative complications, tumor recurrence, and treatment after recurrence. Therefore, we cannot evaluate the safety of surgery (radical surgery and non-radical surgery) and the recurrence rate in patients with small bowel gastrointestinal stromal tumors. Besides, the SEER database does not provide information on the KIT gene, exon mutation, clinical symptoms, detailed chemotherapy information, comorbidities, and surgical margin status, which may cause potential confounding bias.

Conclusions

In summary, our study found that for small intestinal GISTs, there was no significant difference in long-term survival between radical surgery and non-radical surgery. However, in the male and low-mitotic subgroups, radical surgery will lead to a worse overall survival prognosis. At the same time, no significant survival benefits were observed in those high-risk subgroups (high mitotic rate, distant metastasis and poor differentiation).

Declarations

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Declaration of competing interest

All authors declare no conflicts of interest

Authorship contribution statement

Linlin Yin designed the study. Haihao Yan performed data mining. Jue Lin and Zuhong Ji analyzed the data. Linlin Yin and Haihao Yan drafted the initial manuscript. Guozhong Ji and Xiuhua Zhang contributed to the revision of the manuscript. All authors read and approved the final manuscript.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: Surveillance, Epidemiology, and End Results (SEER) database (https://seer.cancer.gov/).

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Tables

Table 1: Baseline characteristics of patients with small intestinal gastrointestinal stromal tumors before and after PSM

Variables	Before PSM		p	After PSM		p
	Non-radical resection n =757	Radical resection n=120		Non-radical resection n =113	Radical resection n=113	
Age group, years, %						
≤65	431(56.90%)	71(59.20%)	0.646	57(50.40%)	68(60.20%)	0.141
>65	326(43.10%)	49(40.80%)		56(49.60%)	45(39.80%)	
Race, %						
White	597(78.90%)	98(81.70%)	0.471	96(85.00%)	91(80.50%)	0.672
Black	57(7.50%)	6(5.00%)		5(4.40%)	6(5.30%)	
Others	94(12.40%)	16(13.30%)		12(10.60%)	16(14.20%)	
Unknown	9(1.20%)	0(0.00%)		0(0.00%)	0(0.00%)	
Gender, %						
Female	335(44.30%)	63(52.50%)	0.092	61(54.00%)	56(49.60%)	0.506
Male	422(55.70%)	57(47.50%)		52(46.00%)	57(50.40%)	
Marital status, %						
Married	315(41.60%)	42(35.00%)	0.171	42(37.20%)	40(35.40%)	0.782
Unmarried	442(58.4%)	78(65.00%)		71(62.80%)	73(64.40%)	
Insurance status, %						
Insured	715(94.50%)	116(96.70%)	0.312	111(98.20%)	109(96.50%)	0.408
Uninsured	42(5.50%)	4(3.30%)		2(1.80%)	4(3.50%)	
Tumor size, %						
≤20mm	45(5.90%)	4(3.30%)	<0.001	3(2.70%)	4(3.50%)	0.394
20-50mm	222(29.30%)	19(15.80%)		13(11.50%)	19(16.80%)	
50-100mm	292(38.60%)	35(29.20%)		44(38.90%)	33(29.20%)	
≥ 100mm	198(26.20%)	62(51.70%)		53(46.90%)	57(50.40%)	
Grade, %						
Grade I-II	318(42.00%)	41(34.20%)	<0.001	40(35.4%)	39(34.50%)	0.738
Grade III-IV	102(13.50%)	37(30.80%)		28(24.8%)	33(29.20%)	

Unknown	337(44.50%)	42(35.00%)		45(39.8%)	41(36.30%)	
TNM stage, %						
I	231(30.50%)	12(10.00%)	<0.001	10(8.80%)	12(10.60%)	0.748
II	185(24.40%)	16(13.30%)		21(18.60%)	16(14.20%)	
III	218(28.80%)	43(35.80%)		45(39.80%)	43(38.10%)	
IV	123(16.20%)	49(40.80%)		37(32.70%)	42(37.20%)	
N stage, %						
N0	726(95.90%)	116(96.70%)	0.692	110(97.35%)	109(96.50%)	0.867
N1	31(4.10%)	4(3.30%)		3(2.65%)	4(3.50%)	
M stage, %						
M0	652(86.10%)	73(60.80%)	<0.001	76(67.30%)	73(64.60%)	0.674
M1	105(13.90%)	47(39.20%)		37(32.70%)	40(35.40%)	
Mitotic rate, %						
Low	547(72.30%)	66(55.00%)	<0.001	62(54.90%)	61(54.00%)	0.991
High	177(23.40%)	49(40.80%)		47(41.60%)	48(42.50%)	
Unknown	33(4.40%)	5(4.20%)		4(3.50%)	4(3.50%)	
Chemotherapy, %						
No	376(49.70%)	33(27.50%)	<0.001	39(34.50%)	32(28.30%)	0.316
Yes	381(50.30%)	87(72.50%)		74(65.50%)	81(71.70%)	

Table 2: Overall survival and cancer-specific survival in multivariable analysis

Variables	OS		p	CSS		p
	HR	95% CI		HR	95% CI	
Age group, years						
≤65	Reference			Reference		
>65	3.315	(2.375-4.629)	<0.001	2.440	(1.541-3.863)	<0.001
Race						
White	Reference			Reference		
Black	1.058	(0.615-1.818)	0.839	1.345	(0.624-2.898)	0.449
Others	1.009	(0.602-1.691)	0.972	1.315	(0.690-2.506)	0.405
Unknown	1.345	(0.181-9.983)	0.772	1.012	(0.232-7.818)	0.972
Gender						
Female	Reference			Reference		
Male	1.408	(1.023-1.937)	0.036	1.460	(0.933-2.286)	0.098
Marital status						
Unmarried	Reference			Reference		
Married	0.471	(0.343-0.647)	<0.001	0.571	(0.369-0.886)	0.012
Insurance status						
Uninsured	Reference			Reference		
Insured	0.741	(0.362-1.52)	0.414	0.400	(0.183-0.872)	0.021
Tumor size						
≤20mm	Reference			Reference		
20-50mm	0.510	(0.249-1.044)	0.066	1.198	(0.143-10.057)	0.868
50-100mm	0.494	(0.183-1.331)	0.163	1.149	(0.122-10.81)	0.903
≥ 100mm	0.604	(0.234-1.554)	0.296	1.466	(0.162-13.297)	0.734
Grade,						
Grade I-II	Reference			Reference		
Grade III-IV	1.511	(0.973-2.346)	0.066	1.356	(0.728-2.526)	0.337
Unknown	0.895	(0.618-1.297)	0.558	0.648	(0.368-1.140)	0.132
TNM stage						

I	Reference			Reference		
II	1.089	(0.624-1.901)	0.763	2.867	(0.852-9.649)	0.089
III	1.827	(1.126-2.962)	0.015	7.421	(2.536-21.717)	<0.001
IV	4.407	(2.678-7.253)	<0.001	19.650	(6.655-58.021)	<0.001
N stage						
N0	Reference			Reference		
N1	1.614	(0.713-3.653)	0.251	1.874	(0.748-4.696)	0.180
M stage						
M0	Reference			Reference		
M1	2.709	(0.881-8.323)	0.082	3.745	(0.988-14.201)	0.052
Mitotic rate						
Low	Reference			Reference		
High	1.217	(0.781-1.897)	0.386	1.419	(0.806-2.501)	0.226
Unknown	1.206	(0.600-2.423)	0.598	1.341	(0.547-3.288)	0.521
Chemotherapy						
No	Reference			Reference		
Yes	0.492	(0.352-0.686)	<0.001	0.643	(0.407-1.016)	0.059
Surgical method*						
No-radical resection	Reference			Reference		
Radical resection	1.045	(0.673-1.620)	0.846	0.892	(0.500-1.591)	0.699

*Adjusting for age, race, sex, tumor grade, tumor size, mitotic rate, TNM stage, lymph node metastasis, distant metastasis, chemotherapy, insurance status, and marital status

Figures

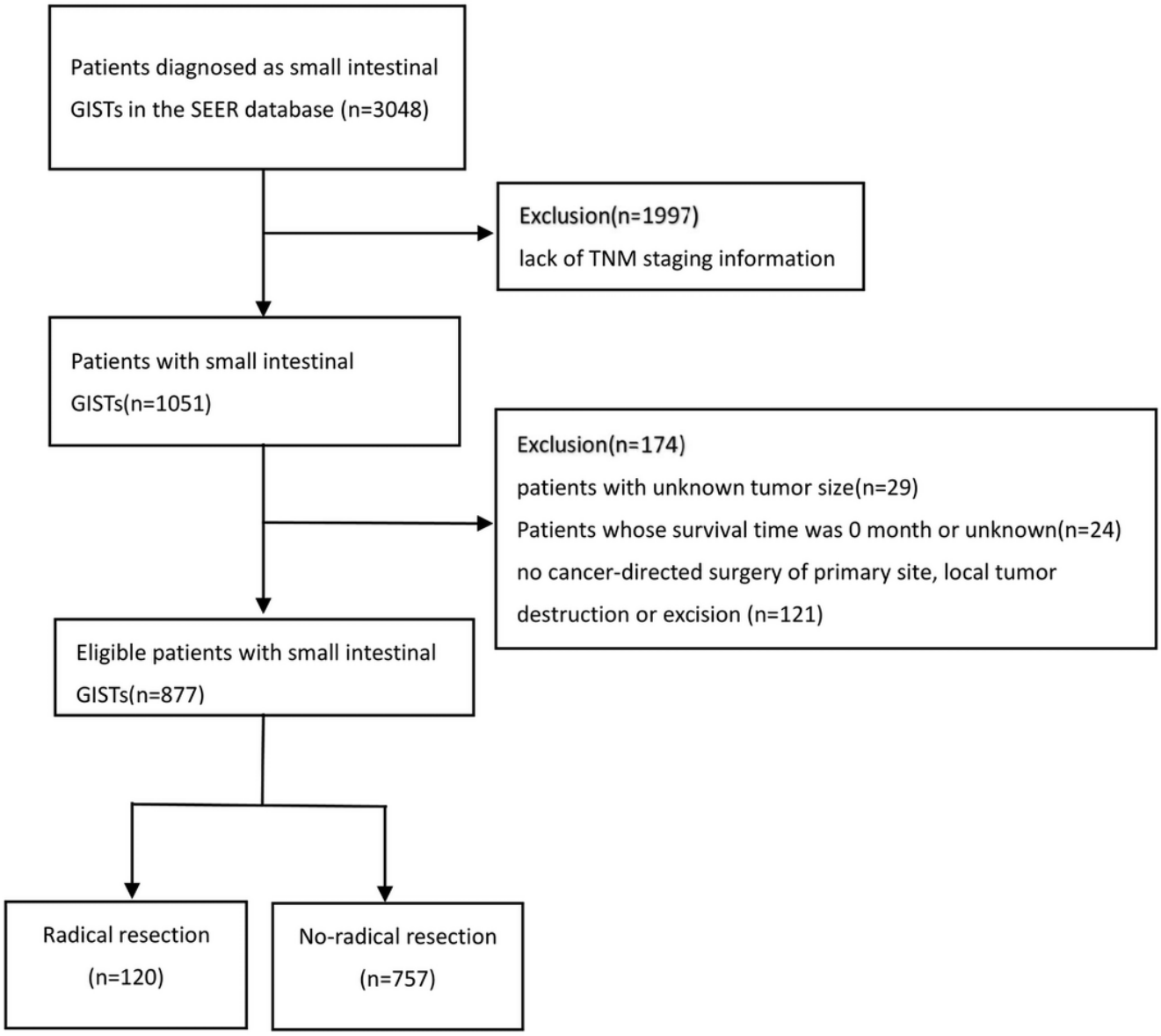

Figure 1

Flow diagram of eligible patients diagnosed with small intestinal gastrointestinal stromal tumors

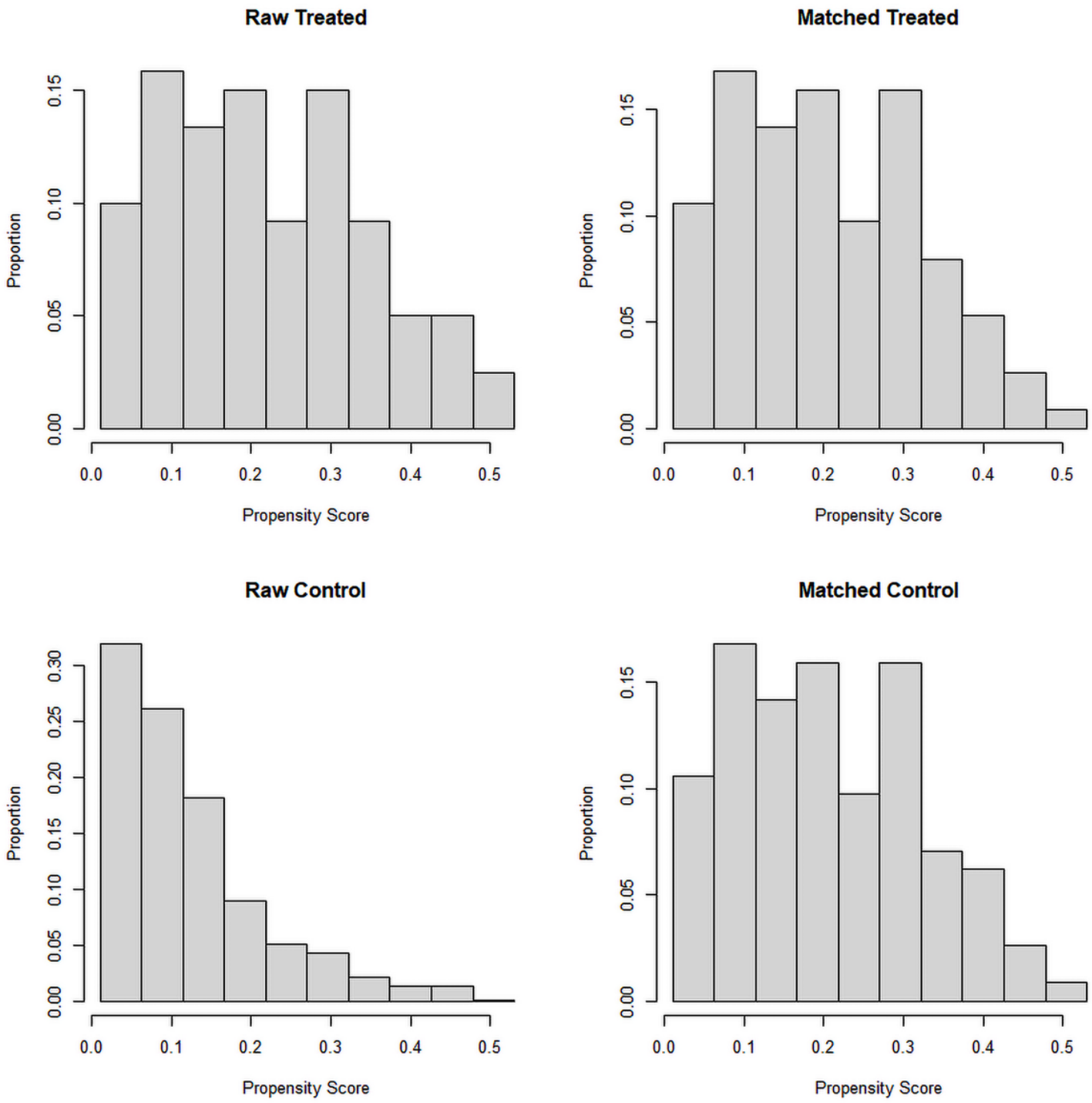

Figure 2

The histograms of propensity scores for the raw and matched case and controls

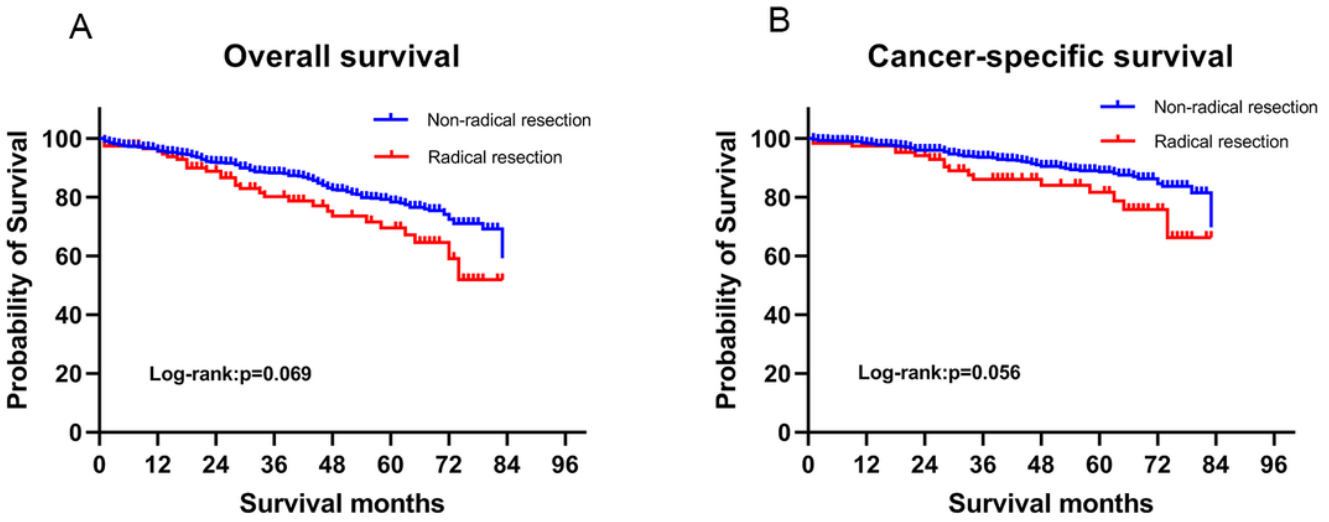

Figure 3

Kaplan-Meier curves of (A) overall and (B) cancer-specific survival according to treatment methods (radical surgery and non-radical surgery)

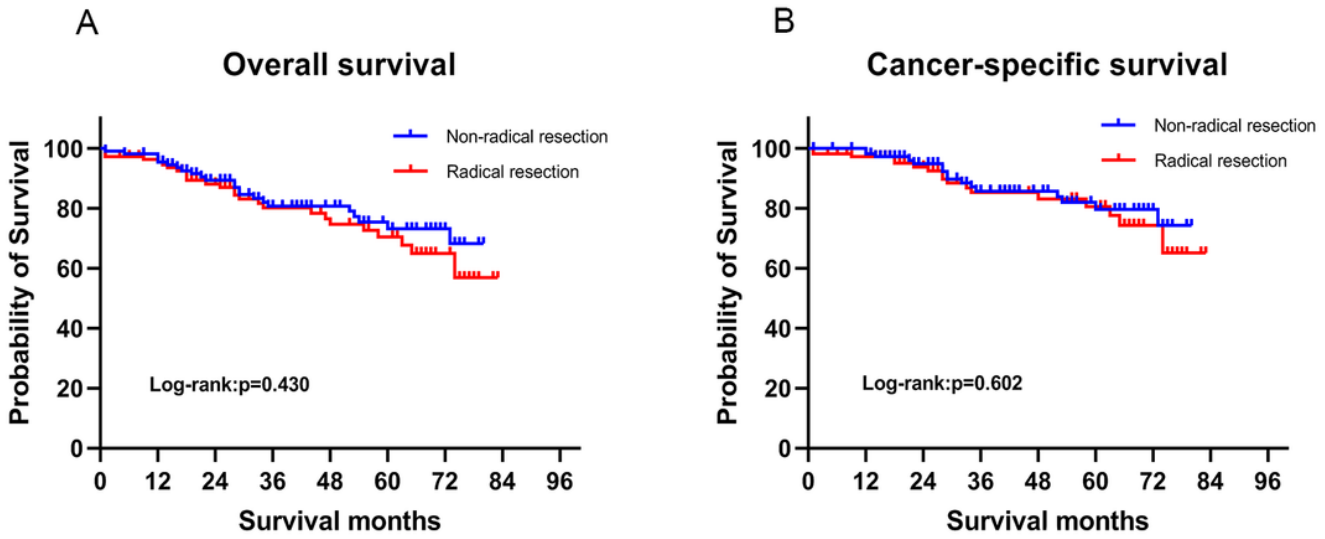

Figure 4

Kaplan-Meier curves of (A) overall and (B) cancer-specific survival according to treatment methods (radical surgery and non-radical surgery) after PSM

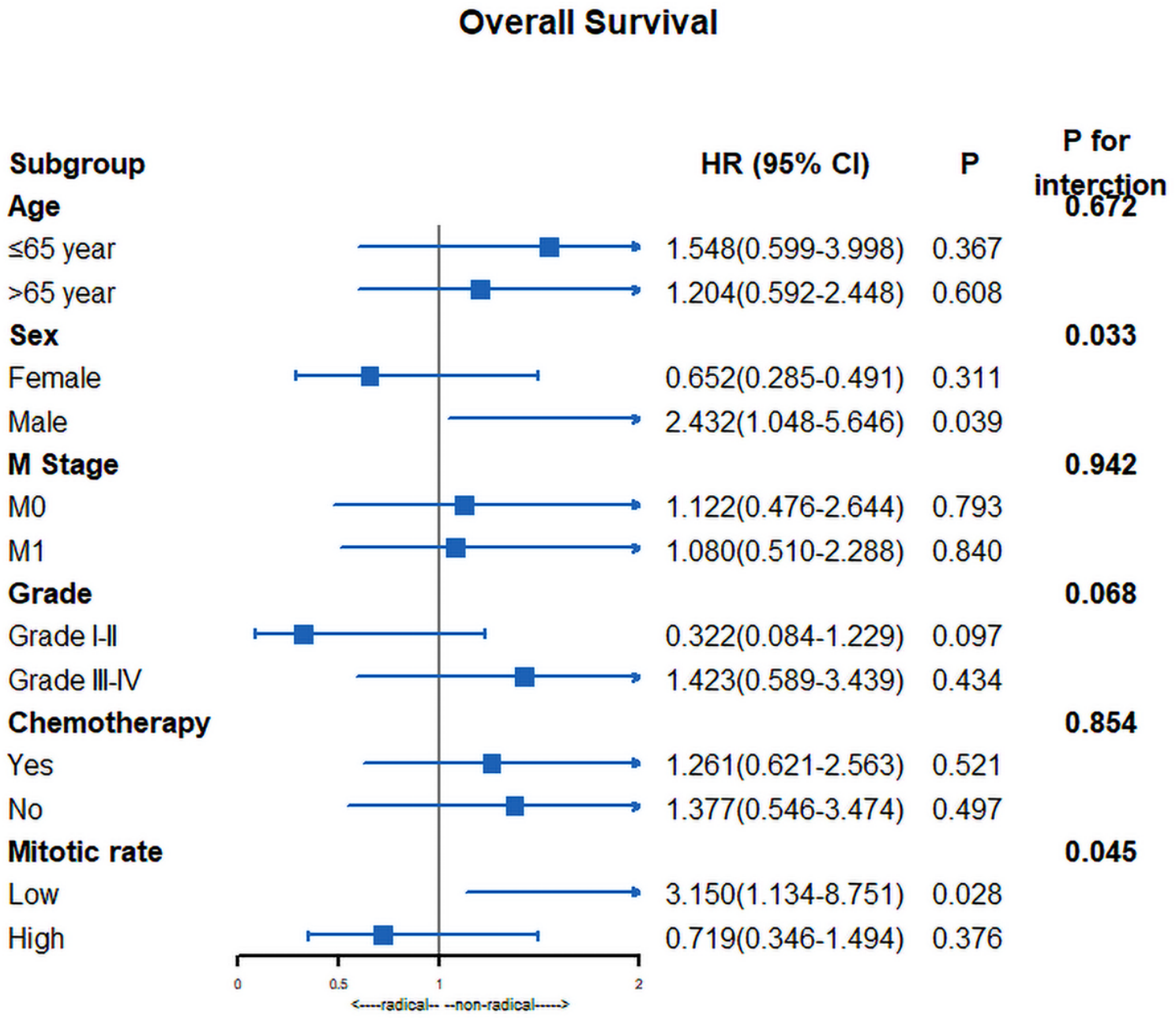

Figure 5

Forest plots summarize the HR and 95% CI of overall survival according to treatment methods

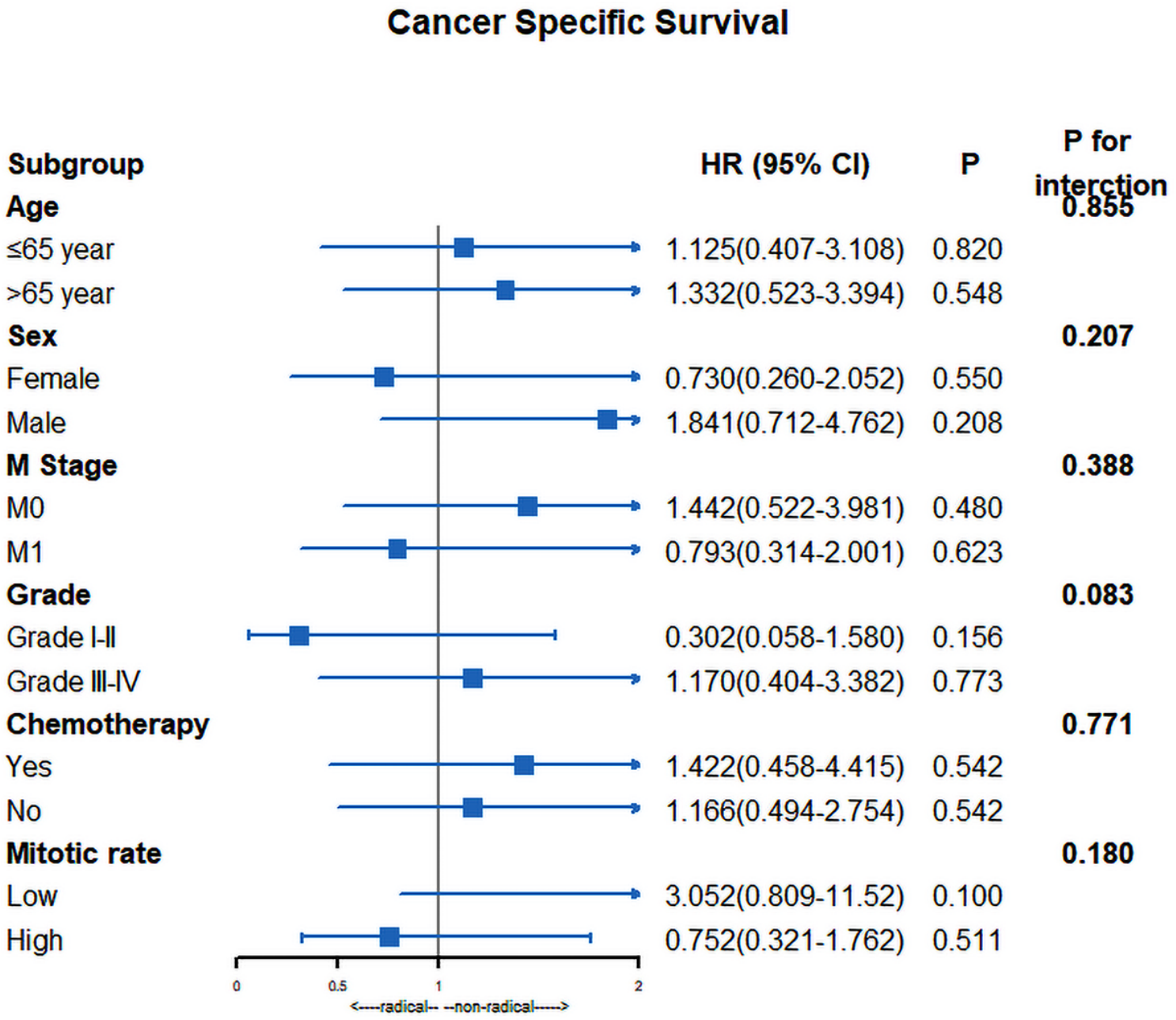

Figure 6

Forest plots summarize the HR and 95% CI of cancer-specific survival according to treatment methods