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Role of Resection Following Focal Progression with Standard Doses of Imatinib in Patients with Advanced Gastrointestinal Stromal Tumors: Results of Propensity Score Analyses

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Gastrointestinal stromal tumor • Focal progression • Imatinib • Surgery

Abstract

Background. There are limited data on the clinical benefits of adding surgical resection in patients with focally progressive gastrointestinal stromal tumor (GIST). This study aims to compare the clinical outcomes of resection plus imatinib dose escalation or maintenance (S group) with imatinib dose escalation alone (NS group) in patients with advanced GIST following focal progression (FP) with standard doses of imatinib.

Materials and Methods. A total of 90 patients with advanced GISTs who experienced FP with standard doses of imatinib were included in this retrospective analysis. The primary endpoints were time to imatinib treatment failure (TTF) and overall survival (OS).

Results. Compared with the NS group (n = 52), patients in the S group (n = 38) had a higher proportion of primary tumor site involvement and lower tumor burden at FP. With a median follow-up duration of 31.0 months, patients in the S group had significantly better TTF and OS than patients in the NS group (median TTF: 24.2 vs. 6.5 months, $p < .01$; median OS: 53.2 vs. 35.1 months, $p = .009$). Multivariate analysis showed that S group independently demonstrated better TTF (hazard ratio [HR], 0.29; $p < .01$) and OS (HR, 0.47; $p = .01$). Even after applying inverse probability of treatment-weighting adjustments, S group demonstrated significantly better TTF (HR, 0.36; $p < .01$) and OS (HR, 0.58; $p = .049$).

Conclusion. Our results suggested that resection following FP with standard doses of imatinib in patients with advanced GIST provides additional benefits over imatinib dose escalation alone. ***The Oncologist*** 2019;24:e1443–e1449

Implications for Practice: This is the first study to compare the clinical outcomes of resection plus imatinib dose escalation or maintenance (S group) with imatinib dose escalation alone (NS group) in patients with advanced gastrointestinal stromal tumor (GIST) following focal progression (FP) with standard doses of imatinib. These findings suggest that resection can be safely performed following FP, and the addition of surgical resection provides further clinical benefit over imatinib dose escalation alone. Based on these results, the authors recommend resection following FP in patients with advanced GIST provided that an experienced multidisciplinary team is involved in the patient's treatment.

Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors arising from the gastrointestinal tracts, resulting most commonly from *KIT* or *PDGFRA* activating mutations [1]. The stomach (60%) and small intestine (30%) are the most common primary sites, but GISTs can arise anywhere along the gastrointestinal tract [2]. Localized GIST is a potentially curable disease if complete resection can be achieved. However, the risk of recurrence may be as high as 90% after curative surgery if high risk prognostic factors are present. Moreover, about 15% of patients initially present with metastatic disease [3].

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For patients with recurrent or metastatic GISTs, imatinib is the primary treatment of choice [4, 5]. However, although imatinib provides a durable period of disease control in these patients, with a median progression-free survival (PFS) of 2 years and median overall survival (OS) of 5 years, most patients eventually experience disease progression because of secondary resistance [5]. After disease progression with standard doses of imatinib (400 mg per day), the drug can be escalated up to 800 mg per day before switching to subsequent line tyrosine kinase inhibitors (TKIs) such as sunitinib malate and regorafenib [6–8], although its antitumor efficacy is modest with a disease control rate of 33% and a median PFS of 2.8 months [9, 10]. Sunitinib malate and regorafenib have been approved as second- and third-line TKIs for metastatic GIST [11, 12]. Nevertheless, responses to these TKIs are also limited, with a median PFS of 6.8 months for sunitinib and 4.8 months for regorafenib [11, 12], indicating that medical treatment using TKIs alone rarely achieves a complete response in patients with advanced GISTs.

In an effort to improve the survival outcomes of advanced GIST, several retrospective studies have demonstrated a survival benefit from adding surgical resection to imatinib at maximal response, including partial response and stable disease, or at focal progression in patients with unresectable, recurrent, or metastatic GIST. Here, some patients remained free from disease progression for a long time after surgery [13–17]. In contrast, An et al. demonstrated that initial debulking surgery before imatinib therapy was not beneficial, and surgery should be avoided as a primary approach prior to imatinib in the treatment of advanced GIST [18]. In addition, the survival outcomes of patients who receive surgery at general disease progression are disappointing, and surgery is also not recommended in these individuals [15–17]. Although the survival benefit has not been proven in randomized phase III trials because such trials have closed early from lack of accrual [19], the guidelines of the National Comprehensive Cancer Network, European Society of Medical Oncology, and Asian Consensus Guidelines suggest that surgery should be considered following maximal response to imatinib in patients with advanced GIST, based on the results of previous retrospective studies [6–8]. The clinical benefits of adding surgical resection in patients with focally progressive advanced GIST have been advocated in few retrospective studies, but these studies lack a control arm, limiting the level of evidence [16, 20].

The aim of this study was to compare the clinical outcomes of resection plus imatinib dose escalation or maintenance (S group) with imatinib dose escalation alone (NS group) in patients with advanced GIST following focal progression (FP) with standard doses of imatinib.

Materials and Methods

Patients

Between April 2003 and October 2016, 98 patients with histologically documented distant recurrent or initially metastatic GISTs experienced FP with standard doses of imatinib as first-line treatment at Asan Medical Center, Seoul, Republic of Korea. Eight patients who received sunitinib without imatinib dose escalation after FP were excluded, and a total of 90 patients were thus included in this retrospective analysis. FP was defined as follows: (a) one- or two-site progression with an increase in size of one or two of the pre-existing tumor masses; (b) appearance of single new lesion, including the development of a new enhancing focus enclosed within a preexisting tumor mass which was low in density and non-enhancing, described as a "nodule within a mass" [21]. Patients with pseudoprogression due to hemorrhage or cystic degeneration were excluded. The Institutional Review Board of Asan Medical Center approved this study.

Treatment and Evaluation

Patients who received surgery with maintenance of standard doses of imatinib or dose escalation of imatinib were classified as the surgery group (S group). Patients who were treated with escalated doses of imatinib first and then received surgery within 3 months were also classified as the S group. The nonsurgery group (NS group) included patients who were treated with escalated doses of imatinib only. Radiofrequency ablation (RFA) was regarded as a surgical intervention, and patients with liver metastases who were treated with RFA, either alone or with surgery, were also included in the S group.

All the patients included in this study were initially treated with standard doses of imatinib. At FP, the computed tomography (CT) scans were reviewed by the multidisciplinary team, including a medical oncologist, surgeon, and interventional radiologist to assess the probability of resection. Surgery was conducted only if all the focally progressive lesions were resectable. The extent of resection was defined as macroscopically complete with a negative microscopic margin (R0), macroscopically complete with a positive microscopic margin (R1), or macroscopically incomplete (R2). Postoperative complications were classified according to the Accordion Severity Grading System of Surgical Complications [22].

Generally, upon resumption of eating after surgery, imatinib treatment was restarted with standard or escalated doses of imatinib. For dose escalation of imatinib, the doses were escalated up to 800 mg day. CT scans were performed every 2–3 months and at any time when tumor progression was suspected. Responses were assessed according to the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.

Statistical Analysis

Time to treatment failure (TTF) was defined as the duration of time from FP date to the date of disease progression on last escalated dose level of imatinib, intolerance to imatinib, or death from any cause, whichever occurred first. OS was defined as the duration of time from FP date to the date of death from any cause. For patients who were treated with sunitinib after imatinib failure, PFS for sunitinib (PFS SU) was calculated from the start date of sunitinib to disease progression or death from any cause, whichever occurred first. OS for sunitinib (OS SU) was calculated from the start date of sunitinib to death from any cause. Survival rates and corresponding standard errors were estimated using the Kaplan-Meier method, and survival curves were compared using the log-rank test. Baseline characteristics of the groups were compared using Pearson's chi-square test or

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Fisher's exact test for categorical variables and Student's *t* test for continuous variables, as appropriate. To identify clinical prognostic factors for TTF and OS, univariate and multivariate analyses were performed using Cox proportional hazards regression modeling. Key baseline characteristics and candidate prognostic factors including age, sex, primary tumor site, disease status at the start of first-line imatinib, genotype of the primary tumor, best response to first-line imatinib, surgery before FP, number of involved metastatic organs at FP, involved organs at FP, initial tumor burden at FP, and treatment group (S vs. NS group) were included in the univariate analysis. In the multivariate analysis, variables exhibiting a potential association with survival ($p < .25$) in the univariate analysis, along with age, sex, and primary tumor site, were included.

To account for baseline differences between S and NS groups, we performed weighted Cox proportional hazards regression modeling using the inverse probability of treatment weighting (IPTW) [23]. The propensity to receive surgery (S group) vs. imatinib dose escalation alone (NS group) was estimated using a logistic regression model based on age, sex, primary tumor site, disease status at the start of first-line imatinib, genotype of the primary tumor, best response to first-line imatinib, surgery before FP, number of involved metastatic organs at FP, involved organs at FP, and initial tumor burden at FP. Here, weights for patients receiving surgery were the inverse of the PS, and weights for patients treated with imatinib dose escalation alone were the inverse of 1 − PS. The outcomes were compared by weighted Cox proportional hazards regression models with robust standard errors. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). All tests were two-sided, with $p < .05$ considered statistically significant.

Results

Patient Characteristics

The baseline characteristics of the patients with GIST in the S ($n = 38$) and NS ($n = 52$) groups are presented in Table 1. The baseline characteristics were similar between the two groups, but a higher proportion of patients in the S group had primary tumor site involvement at the time of FP (26.3% vs. 7.7%), and the largest tumor size at FP was smaller in the S group (median, 34 mm vs. 52 mm) compared with the NS group. Surgical interventions are described in Table 2. All RFA procedures completely ablated the target tumor masses. Even in patients who received R2 resection and/or RFA with visible residual lesions, all the focally progressive lesions were resected and/or ablated. The 30-day postoperative complication rate was 16.1 % ($n = 5$) in 31 evaluable patients of the S group, which includes ileus ($n = 4$) and ureteral injury ($n = 1$). Percutaneous nephrostomy for ureteral injury was required in one patient. There were no perioperative deaths. Pathologic reports for surgical specimens were available for 28 out of 38 patients in the S group (Table 2). Pathologic reports were not available in five patients who received only RFA as a surgical intervention and in five who received surgery at another hospital other than Asan Medical Center. The majority of patients had tumors with a mitotic

Table 1. Baseline patient and disease characteristics ($n = 90$)

Characteristics	S group ($n = 38$)	NS group ($n = 52$)	*p* value
Median age at FP (range), yr	59 (37–78)	62.5 (31–77)	.11
Sex			.29
Female	15 (39.5)	15 (28.8)	
Male	23 (60.5)	37 (71.2)	
Primary tumor site			.57
Stomach	13 (34.2)	22 (42.3)	
Small bowel	24 (63.2)	27 (51.9)	
Others	1 (2.6)	3 (5.8)	
Disease status at the start of first-line imatinib			.32
Initially metastatic	15 (39.5)	26 (50.0)	
Distant recurrence	23 (60.5)	26 (50.0)	
Genotype of primary tumor			.57
KIT exon 11 mutation	30 (78.9)	41 (78.8)	
Others	8 (21.1)	7 (13.5)	
Not available	0 (0.0)	4 (7.7)	
Best response to first-line imatinib			.316
Complete response	5 (13.2)	3 (5.8)	
Partial response	22 (57.9)	29 (55.8)	
Stable disease	8 (21.1)	15 (28.8)	
Disease progression	0 (0.0)	3 (5.8)	
Not evaluable	3 (7.9)	2 (3.8)	
Surgery before FP			.69
No	26 (68.4)	37 (71.2)	
Cytoreductive surgery before first-line palliative imatinib treatment[a]	8 (21.1)	12 (23.1)	
Residual lesion resection[b]	4 (10.5)	3 (5.8)	
Number of involved metastatic organs at FP			.34
1	25 (65.8)	39 (75.0)	
≥2	13 (34.2)	13 (25.0)	
Involved organs at FP			
Primary tumor site	10 (26.3)	4 (7.7)	.02
Liver	24 (63.2)	32 (61.5)	.88
Extra-liver	17 (44.7)	28 (53.9)	.39
Initial tumor burden at focal progression			
Median largest tumor size (range), mm	34 (8–127)	52 (10–136)	.04
Median sum of total tumor size (range), mm	60 (8–480)	79.5 (10–569)	.34

[a]Cytoreductive surgery before starting first-line palliative imatinib in distant recurrent or initially metastatic disease.
[b]Residual lesion resection following disease control with standard doses of imatinib in distant recurrent or initially metastatic disease.
Abbreviations: FP, focal progression; NS, nonsurgery; S, surgery.

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Table 2. Description of surgical intervention and pathologic reports for surgical specimens in S group (n = 38)

Surgical intervention and pathologic reports	No. of patients (%)
Types of intervention	
Surgery only	29 (76.3)
RFA only	5 (13.2)
Surgery + RFA	4 (10.5)
Types of surgery	
Hepatic resection	17 (44.7)
Peritoneal mass resection	13 (34.2)
Bowel resection	4 (10.5)
Gastrectomy	5 (13.2)
Extent of surgical intervention	
R0/1 resection and/or RFA without visible residual lesion	26 (68.4)
R2 resection and/or RFA with visible residual lesion	12 (31.6)
30-d postoperative complications[a]	
No	26 (68.4)
Grade 1	3 (7.9)
Grade 2	1 (2.6)
Grade 3	1 (2.6)
Not evaluable	7 (18.4)
Pathologic reports (n = 28)	
Mitotic index (mitoses per 50 HPF)	
≤5	6 (21.4)
>5	22 (78.6)
Histologic phenotype	
Spindle	15 (53.6)
Epithelioid	3 (10.7)
Mixed	10 (35.7)
Cellularity	
Low	1 (3.6)
Moderate	9 (32.1)
High	18 (64.3)
Necrosis extent, median (range), %	20 (0–90)
KIT expression	
Negative	2 (7.1)
Focal	3 (10.7)
Diffuse	23 (82.1)

[a]Complications were classified according to Accordion Severity Grading System of Surgical Complications.
Abbreviations: HPF, high-power field; R0, absence of tumor in resection margin; R1, microscopic presence of tumor in resection margin; R2, presence of any gross residual tumors; RFA, radiofrequency ablation.

index of more than 5 mitoses per 50 high-power field (n = 22, 78.6%), high cellularity (n = 18, 64.2%), and diffuse KIT expression (n = 23, 82.1%). Median necrosis extent was 20% (range, 0–90). Among 52 patients in the NS group, partial response and stable disease were achieved in 6 (11.5%) and 21 (40.4%) on escalated doses of imatinib, respectively,

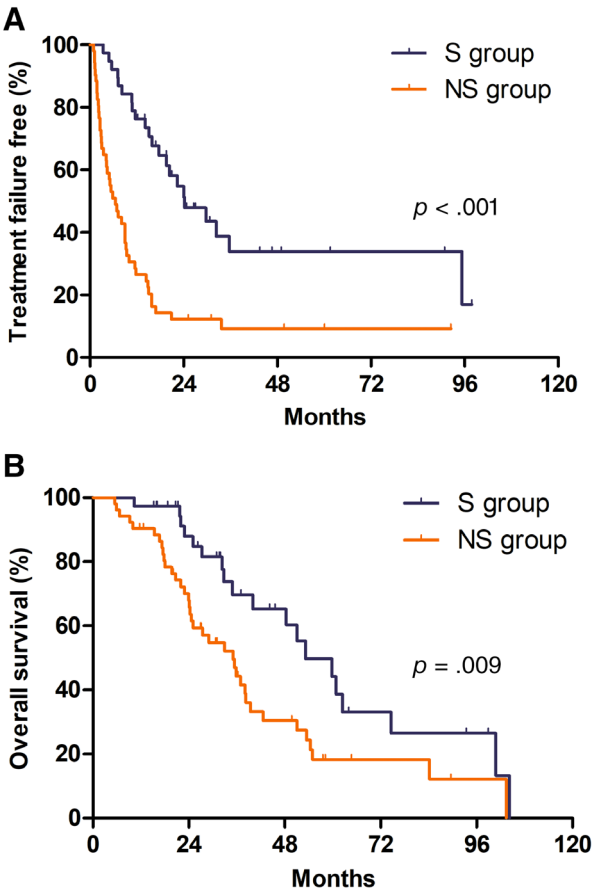

Figure 1. Kaplan-Meier curves of time to treatment failure **(A)** and overall survival **(B)**.
Abbreviations: NS, nonsurgery; S, surgery.

providing an overall response rate (ORR) of 11.5% and a disease control rate (DCR) of 51.9%.

Survival Outcomes

With a median follow-up duration of 31.0 months (range 11.7–99.0) in surviving patients, the median TTF for the S and NS groups was 24.2 months (95% confidence interval [CI], 13.3–35.1) and 6.5 months (95 % CI, 3.6–9.4), respectively (p < .001; Fig 1A). The median OS was 53.2 months (95% CI, 36.8–69.6) in the S group and 35.1 months (95% CI, 25.6–44.7) in the NS group (p = .009; Fig 1B).

Univariate and Multivariate Analyses of Survival Outcomes in All Patients

Table 3 summarizes the results of the univariate and multivariate analyses of the potential prognostic factors for TTF and OS. In the univariate analysis, sex showed potential association (p < .25) with TTF, and largest tumor size at FP, sum of total tumor size at FP, and treatment group (NS vs. S group) showed potential association with both TTF and OS. In the multivariate analysis, the S group was independently associated with better TTF (vs. NS group; HR, 0.29; 95% CI, 0.17–0.49, p < .001) and OS (vs. NS group; HR, 0.47; 95% CI, 0.27–0.83, p = .01). In addition, the sum of total tumor size was also independently associated with both TTF and OS.

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Table 3. Univariate and multivariate analysis for TTF and OS (n = 90)

	TTF				OS			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
Variables	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
Age at FP								
<60	Reference		Reference		Reference		Reference	
≥60	1.16 (0.71–1.87)	.56	1.31 (0.79–2.17)	.30	1.32 (0.77–2.27)	.31	1.52 (0.87–2.65)	.14
Sex								
Female	Reference		Reference		Reference		Reference	
Male	1.52 (0.88–2.61)	.13	1.37 (0.79–2.39)	.27	1.10 (0.61–1.99)	.75	1.06 (0.58–1.92)	.85
Primary tumor site								
Stomach	Reference		Reference		Reference		Reference	
Others	1.04 (0.63–1.72)	.87	1.07 (0.62–1.85)	.80	0.89 (0.51–1.54)	.67	0.86 (0.48–1.52)	.60
Largest tumor size at FP								
≤Median (46 mm)	Reference		Reference		Reference		Reference	
>Median (46 mm)	2.08 (1.27–3.39)	.004	1.47 (0.77–2.79)	.24	1.45 (0.85–2.47)	.17	0.84 (0.41–1.71)	.63
Sum of total tumor size at FP								
≤Median (77.5 mm)	Reference		Reference		Reference		Reference	
>Median (77.5 mm)	2.00 (1.22–3.28)	.006	2.07 (1.25–3.45)	.005	1.76 (1.03–3.01)	.04	1.78 (1.04–3.06)	.04
Treatment group								
NS group	Reference		Reference		Reference		Reference	
S group	0.29 (0.17–0.50)	<.001	0.29 (0.17–0.49)	<.001	0.48 (0.27–0.84)	.01	0.47 (0.27–0.83)	.01

Abbreviations: CI, confidence interval; FP, focal progression; HR, hazard ratio; NS, nonsurgery-surgery; OS, overall survival; S, surgery; TTF, time to treatment failure.

Propensity Score and Inverse Probability of Treatment Weighting Analyses

IPTW analysis was performed to evaluate the effects of surgery after adjustment for differences in baseline characteristics. Model discrimination was assessed with c statistics (0.83), and model calibration was assessed with Hosmer-Lemeshow statistics (Chi-square = 4.70, degrees of freedom = 8, p = .79). The absolute standardized differences were used to evaluate the balance, and all absolute standardized differences after weighting was less than 0.2. Even after applying IPTW adjustment, patients in the S group demonstrated significantly better TTF (covariate-adjusted HR, 0.36; 95% CI, 0.21–0.61, p < .001) and OS (covariate-adjusted HR, 0.58; 95% CI, 0.336–0.998, p = .049) compared with the NS group.

Survival Outcomes for Sunitinib Treatment in Patients Treated with Sunitinib After Imatinib Treatment Failure

Among the 90 patients enrolled in this study, 67 experienced imatinib treatment failure. Of those, 62 patients were subsequently treated with sunitinib (22 patients in the S group and 40 in the NS group). There was no significant difference in ORR (13.6% vs. 13.5%, p = .989) and DCR (72.7% vs. 83.8%, p = .308) between the S and NS groups. With a median follow-up duration of 20.2 months (range, 2.1–55.9) in surviving patients treated with sunitinib, the median PFS SU in the S and NS groups was 7.4 months (95% CI, 2.8–12.0) and 6.3 months (95% CI, 4.5–8.2), respectively (p = .487; Fig 2A). The median OS SU was 26.6 months (95% CI, 7.0–46.3) in the S group and 20.8 months (95% CI, 17.8–23.7) in NS group (p = .981; Fig 2B).

Discussion

The goal of surgery in focally progressive advanced GIST is to stop disease progression by removing lesions that have gained resistance to imatinib. Although several retrospective studies have reported clinical benefits associated with adding surgeries to the treatment plans of patients with focally progressive GIST, lack of control group (i.e. imatinib alone without surgery) limits the level of evidence [16, 20]. This is the first study to compare the clinical outcomes of resection plus imatinib dose escalation or maintenance with imatinib dose escalation alone in patients with advanced GIST following FP with standard doses of imatinib. The addition of resection was significantly associated with better TTF and OS compared with imatinib dose escalation alone.

In this study, the S group was significantly associated with better TTF and OS compared with the NS group in both univariate and multivariate analyses. Previous studies have used PFS instead of TTF to evaluate the benefits of surgery, in which disease progression at a certain dose of imatinib was regarded as a disease progression event [16, 20, 24, 25]. However, considering that the purpose of surgery in patients with FP on imatinib is to delay the time of switching to an alternative TKI from imatinib, TTF would be a more appropriate endpoint. The median TTF of the S group in the current study was 24.2 months (vs. 6.5 months in the NS group, p < .001), indicating that the addition of surgery provides longer disease control with imatinib in patients with focally progressive advanced GIST. Previous studies have reported a median PFS of 7.7–11.3 months in patients who received surgery for focally progressive advanced GIST, which is shorter

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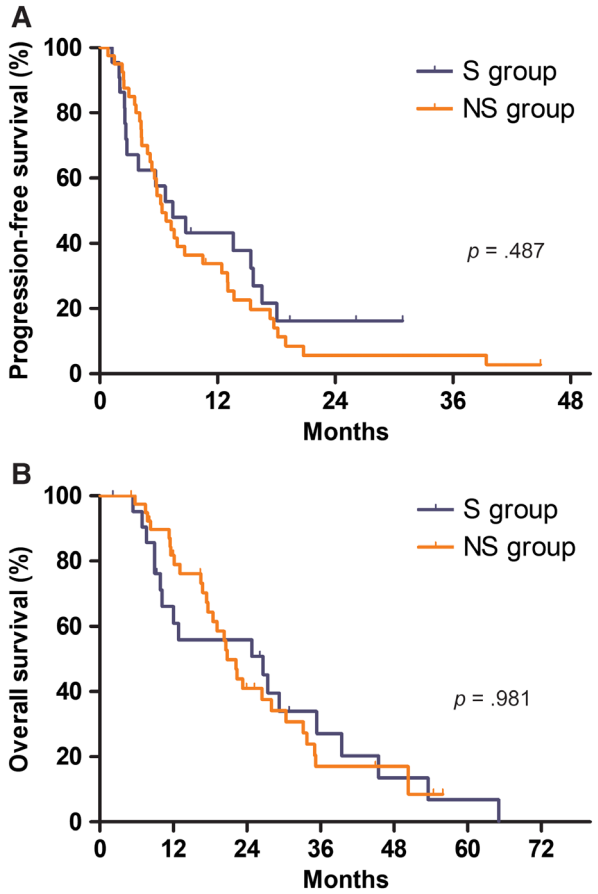

Figure 2. Kaplan-Meier curves of progression-free survival **(A)** and overall survival **(B)** in patients who were treated with sunitinib after imatinib treatment failure.
Abbreviations: NS, nonsurgery; S, surgery.

than the median TTF observed in the S group of the current study. The difference in outcome seems largely due to the inclusion of patients with focal progression on more later-line treatments such as imatinib dose escalation or sunitinib in the previous studies, whereas all of the patients in the current study were on standard doses of imatinib at the time of focal progression [15, 20]. Moreover, higher proportion of patients in the previous study (75%) had visible residual lesion after surgery including 16% of patients with bulky residual disease (presence of any residual disease ≥1 cm in diameter) [15]. By comparison, only 31.6% of patients had a visible residual lesion after surgical intervention in the current study, and even in these patients, all the focally progressive lesions have been successfully resected and/or ablated. The median OS of 53.2 months in the S group (vs. 35.1 months in the NS group, p = .009) was comparable to that reported in earlier studies (29.8–59.0 months) [15, 16, 24].

Although baseline characteristics between both the S and NS groups were similar, there were significant differences regarding the primary tumor site involvement and largest tumor sizes at FP. Tumor size is known to be a prognostic factor for both PFS and OS in patients with advanced GIST [26, 27]. Moreover, tumor size also affects the decision for surgery (i.e., patients with smaller tumors are more likely to be candidates for surgery). Thus, IPTW analysis was performed to account for the baseline differences between the two groups. Even after IPTW adjustment, TTF and OS were significantly better in the S group, compared with the NS group. This further supports that the addition of surgery provides survival benefits over imatinib dose escalation alone in patients with GIST following FP with standard doses of imatinib.

Among patients treated with sunitinib after imatinib treatment failure, there were no significant differences in PFS SU, OS SU, ORR, and DCR for sunitinib between the two groups, indicating that surgery had no influence on subsequent sunitinib treatment. Thus, it is likely that better OS in the S group was due to the prolongation of TTF by resection of imatinib-resistant clones.

One of the concerns associated with surgery for patients with metastatic or recurrent GIST is that complications may outweigh the clinical benefit in terms of survival. However, in this study, the rate of postoperative complications was low, with complications of any grade observed in less than 20% of evaluable patients in the S group. This is comparable to the results of a similar series (18%–33%) [15, 16, 24]. Most of the complications observed in this study were mild, and invasive intervention was required in only one patient with percutaneous nephrostomy for a left ureteral injury.

This study has several limitations. As anticipated for any retrospective study, selection bias was unavoidable. There were significant differences in baseline characteristics between the S and NS groups regarding primary tumor site and largest tumor size at FP. To minimize the impact of selection bias on the clinical outcomes of the current study, we used weighted Cox proportional hazards regression modeling with IPTW. In addition, the definition for FP varies among studies, and this might have affected the results of this study. However, to date, there is no standard definition for FP, and the definition used in this study was deemed acceptable following close review of definitions used in previous studies [15, 20, 21]. Moreover, our median follow-up duration was relatively short. Despite these limitations, this study has several strengths. The results of this study were based on one of the largest populations of patients with advanced GIST following FP with standard doses of imatinib. Furthermore, patients were uniformly treated with imatinib maintenance or dose escalation in both the S and NS groups. The relatively homogeneous patient population in the current study might have reduced potential confounding effects in the evaluation of the impact of surgery on survival outcomes.

Conclusion

Our findings suggest that resection plus imatinib dose escalation or maintenance can be safely performed following FP with standard doses of imatinib in patients with advanced GIST and provides additional benefits over imatinib dose escalation alone. Based on these results, resection following FP in patients with advanced GIST could be considered provided that an experienced multidisciplinary team including an experienced medical oncologist, surgeons, and interventional radiologists are involved in the patient's treatment.

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Although it would be ideal, recent experience shows that it is not feasible to conduct a randomized trial to evaluate the benefit of surgery in patients with focally progressive advanced GIST.

Acknowledgments

Presented in part at the American Society of Clinical Oncology annual meeting, Chicago, Illinois, June 2, 2018.

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Disclosures

The authors indicated no financial relationships.

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