

Supplement Table 1. The results of the questionnaire for primary surgeon of each participant hospitals

Conditions	Yes	No	Yes/No	Pre or Intra[#]
Tumor fracture with blood-tinged ascites at laparotomy	25	0	0	Pre
Intestinal perforation on tumor with blood-tinged ascites at laparotomy	23	2	0	Pre
Microscopically direct tumor invasion into adjacent resected organs	10	15	0	Pre
Intraluminal tumor perforation	3	22	0	Pre
Piecemeal resection during operation	25	0	0	Intra
Iatrogenic fracture of tumors	25	0	0	Intra
Macroscopic injuries to the pseudocapsule exposing tumor cells into the peritoneal cavity	20	4	1	Intra
Minor or microscopic injuries to pseudocapsule without exposure of tumor cells	3	22	0	Intra
Open biopsy	21	4	0	Intra
Core needle biopsy without complications	7	18	0	Pre
Fine needle biopsy without complications	1	24	0	Pre

The questionnaire was sent to the 33 hospitals and institutions, and the answers were received from 25 primary investigators in each hospital and institution. (Valid Response Rate : 76%)

In the questionnaire, it was asked for investigators whether each listed item may be considered as tumor rupture. Yes: investigators consider that it is rupture; No: investigators do not consider; Yes/No: depending on circumstances and they had no clear answer.

indicates classification of preoperative or intraoperative rupture in the study; Pre: preoperative rupture, Intra: intraoperative rupture

Supplement Table 2. Comparison of between the two tumor rupture types (study cohort)

		Preoperative (N=12)	Intraoperative (N=9)	P value
Primary Location	Gastric	9 (75%)	4 (44%)	0.1536
	Non-gastric	3 (25%)	5 (56%)	
Median tumor size (cm)		7.5 (2.6-30.0)	10.6 (4.0-30.0)	0.7872
Symptoms	No	0 (0%)	1 (11%)	0.2367
	Yes	12 (100%)	8 (89%)	
Median Mitosis (/50 HPF)		2.5 (0.0-250)	16.6 (1.0-75.0)	0.2898
Recurrence	No	4 (33%)	1 (11%)	0.2367
	Yes	8 (67%)	8 (89%)	
Survival	Alive	10 (83%)	6 (67%)	0.3749
	Dead	2 (17%)	3 (33%)	

Supplement Table 3. Backgrounds of GIST patients with and without tumor rupture (Validation cohort)

		Non-ruptured (N=167)	Ruptured (N=5)	P value
Age (years)		62 (33-89)	75 (17-81)	<0.0001
Gender	Male	99 (59%)	1 (20%)	0.1624
	Female	68 (41%)	4 (80%)	
Primary Location [#]	Gastric	116 (69%)	3 (60%)	0.6442
	Non-gastric	51 (31%)	2 (40%)	
Association of cancer	No	130 (78%)	5 (100%)	0.5861
	Yes	37 (22%)	0 (0%)	
	Unavailable	0 (0%)	0 (0%)	
Median tumor size (cm)		5.0 (1.1-25.0)	5.0 (3.3-19.0)	0.4027
Neoadjuvant [#]	No	152 (91%)	5 (100%)	1.0000
	Yes	15 (9%)	0 (0%)	
	Unavailable	0 (0%)	0 (0%)	
Adjuvant therapy [#]	No	138 (83%)	4 (80%)	1.0000
	Yes	29 (17%)	1 (20%)	
	Unavailable	0 (0%)	0 (0%)	
Surgery	Open	112 (67%)	4 (80%)	0.0336
	Laparoscopic	51 (31%)	0 (0%)	
	Local	4 (2%)	1 (20%)	
R	R0	161 (96%)	1 (20%)	<0.0001
	R1	6 (4%)	4 (80%)	
Median mitosis (/50 HPF)		5 (0-250)	7 (4-50)	0.6353
Cell type	Spindle	79 (47%)	4 (80%)	0.7991
	Epithelioid	2 (1%)	0 (0%)	
	Mixed	7 (4%)	0 (0%)	
	Unavailable	79 (47%)	1 (20%)	
Median RFS	(95% CI; years)	8.4 (7.4-9.3)	3.2 (0.7-5.8)	0.0392
Estimated median 5-year RFS (median+SE)		73.7% _{+3.9%}	26.7% _{+22.6%}	
Recurrence	No	122 (73%)	2 (40%)	0.1333
	Yes	45 (27%)	3 (60%)	
Recurrence sites [#]	Liver	26 (58%)	2 (66%)	0.0392
	Lung	1 (2%)	2 (66%)	
	Local	5 (11%)	1 (33%)	
	Peritoneum	15 (33%)	1 (33%)	
	Others	4 (9%)	0 (0%)	
	Unavailable	1 (2%)	0 (0%)	
Estimated 5-year median OS (median+SE) [§]		91.9% _{+2.4%}	100%	
Survival	Alive	146 (87%)	5 (100%)	1.0000
	Dead	21 (13%)	0 (0%)	
	Death due to GIST	17 (81%)	0 (0%)	
	Death due to other diseases	4 (19%)	0 (0%)	

#: duplicated number

\$. Median OS could not be calculated.

Supplement Table 4. Multivariate analysis for RFS and OS (Validation cohort and integrated analysis)

Recurrence-free Survival

Independent Prognostic Factors	HR (95%CI)	P value
Size (cm)	1.013 (1.006 - 1.020)	0.0001
Mitotic Count (/50HPF)	1.020 (1.012 - 1.027)	<0.0001
Rupture (Ref: non-rupture)	12.08 (2.957 – 49.32)	0.0015

Other factors included in the analysis using a forward stepwise Cox proportional hazards model are age (P=0.318), gender (P=0.299), tumor location (P=0.469), neoadjuvant therapy (P=0.813), adjuvant therapy (P=0.0879; HR=0.409), and R (completeness of surgery) (P=0.293).

Overall Survival

Independent Prognostic Factors	HR (95%CI)	P value
Gender (Ref: female)	7.258 (1.222 – 43.10)	0.02919
Mitotic Count (/50HPF)	1.013 (1.003 - 1.024)	0.01330
Size (cm)	1.014 (1.002 – 1.025)	0.01999

Other factors included in the analysis using a forward stepwise Cox proportional hazards model are age (P=0.779), rupture (P=0.591), tumor location (P=0.717), neoadjuvant therapy (P=0.529), adjuvant therapy (P=0.3523) and R (completeness of surgery) (P=0.368).

The results of integrated analysis of the two data sets.

Recurrence-free Survival

Independent Prognostic Factors	HR	95%CI		P value
Gender	1.393	1.178	1.645	0.047
Rupture	6.539	4.998	8.525	<0.001
Tumor Size	1.006	1.004	1.008	0.003
Mitotic Count	1.013	1.011	1.015	<0.001
Location	1.495	1.254	1.782	0.022

Other factors included in the analysis using a forward stepwise Cox proportional hazards model are age (P=0.498), R (P=0.851), neoadjuvant therapy (P=0.943), and adjuvant therapy (P=0.126).

Overall Survival

Independent Prognostic Factors	HR	95%CI		P value
Age	1.025	1.013	1.038	0.031
Gender	2.445	1.859	3.216	0.001
Mitotic Count	1.012	1.001	1.015	<0.001

Other factors included in the analysis using a forward stepwise Cox proportional hazards model are

rupture (P=0.402), tumor size (P=0.206), R (P=0.245), tumor location (P=0.592), neoadjuvant therapy (P=0.646), and adjuvant therapy (P=0.4406).

Supplement Figure 1. Patient selection (Study cohort)

Study cohort

743 patients with locally diagnosed GISTs who underwent surgery in institutes and hospitals (2003-2007)

excluded

- Non-GISTs by immunohistochemistry (n=7)
- Pathologically not confirmed tumors (n=13)

723 patients with GIST

excluded

- Metastatic disease (n=43)
- No surgery for primary disease (n=11)
- R2 surgery (n=4)

665 patients included in this study

Validation cohort

182 patients with locally diagnosed GISTs who underwent surgery in institutes and hospitals (2000-2014)

excluded

- Non-GISTs by immunohistochemistry (n=0)
- Pathologically not confirmed tumors (n=0)

182 patients with GIST

excluded

- Metastatic disease (n=8)
- No surgery for primary disease (n=0)
- R2 surgery (n=2)

172 patients included in this study

Supplement Figure 2. Cumulative Incidence of Recurrence (Study Cohort)

