Survival in patients with hypoechoic muscularis propria lesions suggestive of gastrointestinal stromal tumors in gastric wall

Ender Gunes Yegin[1], Tarik Kani[3], Munkhtsetseg Banzragch[2], Cem Kalayci[4], Ercan Bicakci[2], Deniz Guney Duman[2]

(1) Department of Gastroenterology, Bozyaka State Hospital, Izmir, Turkey ; (2) Department of Gastroenterology, (3) Department of Internal Medicine, Marmara University Faculty of Medicine, Istanbul, Turkey ; (4) Department of Gastroenterology, Florence Nightingale Hospital, Istanbul, Turkey.

Abstract

Background : **Subepithelial lesions (SEL) on upper gastrointestinal endoscopy are frequently encountered and referred to endoscopic ultrasound (EUS). Management of small gastric hypoechoic SELs of muscularis propria (MP) is controversial since EUS-assisted fine needle aspiration may be inconclusive, and surgical excision may be too invasive. We aimed to analyze our gastric MP-SELs in terms of survival and confounding factors.**

Methods : **Data from gastric hypoechoic MP-SELs suggestive of gastrointestinal stromal tumor (GIST) by EUS were retrospectively reviewed. Surgically resected GISTs were stratified according to the current pathological risk criteria.**

Results : **Sixty-one patients were identified. The mean age was 55.5 ± 13.2 years and 45.6% were male. Mean follow-up duration was 53.4 ± 26.7 (12-110) months. Twenty-eight (45.9%) patients were managed conservatively (diameter 15.3 ± 10.1 mm). There were no metastasis- or tumor-related deaths and no significant size changes (≥ 5 mm) in this group during follow-up. Thirty-three (54.1%) patients underwent complete resection (diameter 34.2 ± 14.1 mm) among which 25 (75.8%) had the final diagnosis of GIST ; 2 (8.0%), 14 (56%) and 6 (24%) patients were classified in no-risk, very-low-risk, low-risk categories respectively, while 2 (8.0%) were in moderate-risk and only 1 (4.0%) was in high-risk category.**

Conclusions : **The excellent survival of patients with small hypoechoic gastric MP-SELs with conservative management represents indolent course of those lesions. We suggest re- consideration of the recommendations in the current guidelines towards extending the follow-up intervals for small MP-SELs.** (Acta gastroenterol. belg., **2015**, 78, **12-17**).

Key words : survival, GIST, hypoechoic muscularis propria lesion, surveillance, surgery.

Introduction

Since upper gastrointestinal endoscopy is widely performed, clinicians encounter incidental bulges arising beneath the surface epithelium more often than before, and endoscopic biopsies are frequently non-diagnostic. Evaluation with endoscopic ultrasound (EUS) procedure is recommended for subepithelial lesions (SEL) to ascertain the size, layer of origin, echogenicity, and high-risk features. These high-risk features include irregular border, cystic spaces, ulcerations, echogenic foci, and heterogeneity (1). Although EUS alone is not sufficient to differentiate gastrointestinal stromal tumor (GIST)s from other less common etiologies originating from the muscularis propria (MP) layer of the gastric wall, such as leiomyoma, schwannoma etc, GIST is the most common cause (2), affecting the whole population with an estimated frequency of as high as 35%, as reported by the data from total gastrectomy and autopsy series (3,4). However, management of SELs less than 20 mm in diameter arising from the MP of the gastric wall is a matter of debate. Tissue sampling with EUS can reveal an inadequate tissue yield in 33.3% of the cases (5). Furthermore, even in the case when the tissue is obtained by EUS assisted fine needle aspiration (FNA), the quantity is often insufficient to assess the mitotic index to define the pathologic risk category for malignancy. Although surgical resection is the mainstay of curative treatment for similar lesions of > 20-30 mm diameter (6,7), clinical decision towards smaller lesions including the follow-up strategies are not clear in guidelines. Most of the survival data pertinent to GIST come from surgical series involving patients with large tumors (larger than 20 or 30 mm) some of which have positive resection margins or already metastasized locally/distantly or received adjuvant therapies (8-10). Thus, it is not plausible to exclude lead-time bias regarding the malignant potential of GISTs from those studies. Additionally, most series include GISTs from any location rather than those in stomach only.

In our center, we take the 20 mm diameter as the cut-off limit to offer surveillance for asymptomatic patients with small hypoechoic gastric MP-SELs with no high-risk EUS features. If the lesion has EUS features that raise suspicion for malignancy, we perform EUS-FNA and react accordingly, otherwise if the lesion is symptomatic, ulcerated, or larger we advise for surgical resection directly.

In this study, we aimed to evaluate the effects of conservative approach strategy in our institute as described above for small hypoechoic MP-SELs originating from stomach. We did not include the esophageal lesions owing to the fact that most of those lesions in that area are non-GIST tumors (11,12). The duodenal lesions were also excluded due to their heterogeneous etiologies and smaller incidence compared to gastric lesions. We also aimed to compare these small lesions with the larger diameter hypoechoic MP-SELs which we referred to

Correspondence to : Ender Gunes Yegin, M.D., Saglik Bakanligi Bozyaka E.A.H., Gastroenteroloji Bilim Dalı, Saim Çıkrıkçı Cad. No : 59, Bozyaka, Izmir, Turkey. E-mail : drendergunes@hotmail.com

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surgery. We discuss the factors influencing the long-term clinical course and overall survival in those patients.

Methods

Among the patients who underwent EUS examinations from March 2005 to May 2013, those with hypoechoic SELs originating from MP of gastric wall suggestive of GIST were identified. Relevant data were retrieved from medical records, outpatient visits, and phone- call interviews with patients or families of deceased patients, and included sex, age, location, largest diameter and sonographic features of the lesion, EUS-FNA procedure, operation records, surgical specimen histopathological results, and clinical progress until the review time. Survival data of patients at the time of review visit were verified from the Civil Registration System.

EUS examinations were performed by two experienced endosonographers in the same session (D.G.D. and C.K.) using either a radial (Pentax EG-3670URK or Pentax EG-3630UR ; Pentax, Tokyo, Japan) or a linear echoendoscope (Pentax EG-3870UTK or Pentax EG-3630U ; Pentax, Tokyo, Japan) connected to an ultrasound scanning system (EUB-525 or HI VISION Preirus, Hitachi Medical Corp., Tokyo, Japan). EUS-FNAs were performed for those patients showing high-risk features in their lesions. All aspirations were performed by 22-gauge EUS aspiration needles from different companies (EchoTip Ultra, ECHO-22 ; Cook Endoscopy, Winston-Salem, NC, USA ; Expect 22 gauge Flex™ , Boston Scientific, Natick, MA, USA). On- site pathologist was not available at the time of the intervention. Patients were advised to repeat their EUS surveillance initially at 6 months, and then, annually to monitor any progression for small (⩽ 20 mm) hypoechoic MP-SELs of stomach wall with benign EUS features unless they elected surgery. In those patients who underwent EUS surveillance, any change in tumor size and EUS characteristics were reviewed from their reports. An increase of 5 mm or more in the diameter of the mass was considered as significant enlargement. Irregular borders, heterogeneous echo patterns, presence of anechoic spaces, and echogenic foci on EUS were considered features suspicious of malignancy as described previously (7). Patients with lesions larger than 20 mm, symptoms such as bleeding, pain or significant change in size during follow up were offered surgical resection. Lesions located in esophagus, duodenum or extragastric sites were excluded. Small lesions having EUS features of malignant behavior underwent EUS-FNA. A definite diagnosis of GIST was based on positivity for CD117 or DOG1 immunocytochemical stainings with a consistent cytopathological appearance. Postoperative follow-up consisted of physical and laboratory examination and imaging mainly by contrast enhanced computed tomography.

GISTs confirmed by surgical specimens were evaluated according to the pathological criteria defined by Miettinen and Lasota (13) who stratified tumors according to their location, size, and mitotic index into no-, very low-, low-, moderate-, and high-risk categories for progressive disease. In cases with unresectable, metastatic or recurrent disease, tyrosine-kinase inhibitor imatinib was started. The cause of death was considered to be the GIST lesion, if the patient died from a consequence attributable to primary or metastatic tumor.

The study protocol was approved by our Institutional Ethics Committee.

Statistical Analyses

Primary end point was regarded as the overall survival. The survival interval was defined as the time period from the index EUS examination to the review visit or patient's death. Descriptive statistics were used to define the baseline characteristics and clinical data of patients. Quantitative values were reported as mean with standard deviation (SD). Continuous variables were compared using independent samples t-test, and categorical variables were compared with chi-square or Fisher's exact test, as appropriate. A p value of < 0.05 was considered statistically significant.

Results

We identified 61 gastric MP-SELs in the study period. The mean age of these patients at diagnosis was 55.5 ± 13.2 years (range 21–81 years), and the female-to-male ratio was 1.4:1 (36/25). Mean time from index EUS to the review visit was 53.4 ± 26.7 (12-110) months. In Table 1, the characteristics of patients with surgically managed hypoechoic gastric MP-SELs having confirmed GIST diagnosis (n = 25) and those conservatively managed with presumed GIST diagnosis based on endosonographic appearance (n = 28) were given. The latter group except 2 patients who yielded GIST after EUS-FNA were not histologically proven cases but they had small lesion size (75% of lesions were ≤ 20 mm) with no high -risk features and no significant enlargement during follow up. Ten (16.4%) patients had at least one endosonographic high-risk feature for malignancy and among them 9 were sent to surgery.

EUS-FNA biopsies were obtained from 17 (27.9%) of the 61 patients. Biopsy material was insufficient for diagnosis in 7 (41.2%) patients ; 3 of these lesions were continued to be conservatively managed, while the 3 of the remaining 4 were confirmed to be GIST after surgical resection, and the last one was diagnosed as inflammatory fibroid polyp. Adequate specimen was obtained from 10 (58.8%) biopsies, 9 of which were GIST and 1 was leiomyoma. Among GIST lesions, 8 were immunocytochemically positive for CD117, and one was CD117 negative but DOG1 positive. Endosonographic picture of a hypoechoic gastric MP-SEL with a cytopathological diagnosis of GIST by EUS-FNA biopsy from our study is

Table I. — **Characteristics of hypoechoic gastric muscularis propria subepithelial lesions of patients managed conservatively, or surgically with a final diagnosis of GIST**

		MP SELs managed conservatively (n = 28)	MP SELs managed surgically with a final diagnosis of GIST (n = 25)	p
Age, years- mean ± SD (range)		54.1 ± 14.4 (21-81)	60.2 ± 8.7 (39-78)	0.064
Gender, male- no. (%)		12 (42.9%)	8 (32%)	0.416
Follow-up, months- mean ± SD (range)		48.5 ± 23.5 (12-99)	56.7 ± 30.0 (12-110)	0.270
Long diameter of lesion on initial EUS, mean ± SD (range), mm		14.7 ± 9.7 (4.5-44)	36.7 ± 12.4 (13.6-63) mm	0.000
Long diameter category of lesion on EUS examination/ on surgical specimen - no.(%)	⩽ 20 mm	21(75%)	1 (4%)/ 2 (8.0%)	0.000***
	> 20-⩽ 50 mm	7 (25%)	21 (84%)/ 15 (60%)	
	> 50 mm-⩽ 100 mm	0 (0%)	3 (12%) / 8 (32%)	
	> 100 mm	0 (0%)	0 (0%)/ 0 (0%)	
Patients with at least one endosonographic high-risk feature suggestive of malignancy*- no. (%)		1 (3.5%)	9 (36%)	0.003
EUS-FNA no. (%)		6 (21.4%)	10 (40%)	0.142
Diagnosis after EUS-FNA	Inadequate material	3 (50%)	3 (30%)	0.424
	GIST diagnosis by IHC**	2 (33.3%)	7(70%)	0.227
	Leiomyoma	1 (16.7%)	NA	NA
Patients undergoing EUS or endoscopic surveillance without surgical resection (no (%))		11 (39.3%)	NA	NA
Patient with local recurrence or metastasis		0 (0%)	1 (4.0%)	0.271

EUS ; endoscopic ultrasonography, EUS-FNA ; endoscopic ultrasonography guided fine needle aspiration, GIST ; gastrointestinal stromal tumor, IHC ; immunohistochemistry, MP SEL ; muscularis propria subepithelial lesion, NA ; not applicable, SD ; standard deviation.

*Irregular extra-luminal border, heterogeneous echopattern, presence of anechoic cystic spaces, echogenic foci.

**Immunohistochemistry by CD117 and/or DOG1 staining.

***Comparison of long diameters on EUS examination.

illustrated in Figure 1. The largest diameter of lesions were greater, although statistically insignificant, in patients with adequate material from EUS-FNA than those with insufficient material for diagnosis (34.4 ± 12.6 vs 26.9 ± 10.4, respectively, p = 0.219).

Seven of 9 patients with GIST diagnosis underwent surgical resection, and GIST diagnosis was confirmed on histopathology of the surgical specimens. Two patients with 33.4 mm and 44 mm gastric GISTs rejected surgery and any endosonographic or radiological follow-up, and they had no disease-related complaints at the review visit of the study at 48th month and 99th month after their initial diagnosis, respectively.

Twenty-eight (45.9%) patients who had small hypoechoic MP-SELs or larger masses (> 20 mm) but rejected surgery, were managed conservatively. Mean largest diameter of those lesions was 14.7 mm (4.5-44) at the index EUS examination. Eleven patients in conservative follow-up group were compliant and underwent at least one follow-up EUS examination to monitor the tumor progression, none of which showed significant change in size more than 5 mm or developed high-risk sonographic features. After a mean follow-up of 48.5 (12-99) months from the initial EUS examination, there were no complaints attributable to mass lesion or tumor-related death in the conservatively managed group.

Thirty-three (54.1%) patients underwent surgery within a few weeks of the initial EUS.

The largest diameter of SELs managed surgically were greater than those of managed conservatively (34.2 ± 14.1 mm vs. 14.7 ± 9.7 mm, respectively, p < 0.001). None of the cases was considered unresectable due to local infiltration or metastatic disease. Twenty-five (75.8%) had the final definitive diagnosis of GIST. The surgical procedures were wedge resection in 50.0 % and partial gastrectomy in the remaining. On histopathology of surgical specimens, 24 of 25 (96%) of cases were positive for CD117, and one gastric GIST with a negative CD117 staining was positive for DOG-1. Positive stainings for CD34, smooth muscle actin (SMA), desmin and S100 were 96%, 58.8%, 31.1%, and 21.2%, respectively. The majority of the tumors were spindle-shaped (66.7%) in morphology, the others were mixed (23.8%) or epithelioid (9.5%) type. A positive microscopic margin was reported in two GIST patients on final pathologic analysis, but complete resection of macroscopic disease were achieved for all GIST cases. The two patients with microscopically positive margins did not develop any evidence of recurrence on their review visits at 48 and 51 months after the operation.

The other post-operative pathological diagnosis for MP-SELs were : 1 (3%) leiomyoma, 2 (6.1%) pancreatic rests, 1 (3%) lymphoma, 1 (3%) neuroendocrine tumor, 1 (3%) inflammatory fibroid polyp, 1 (3%) gastric tuberculosis ; surgical exploration revealed extraluminal compression in the stomach from the adjacent aneurysmatic

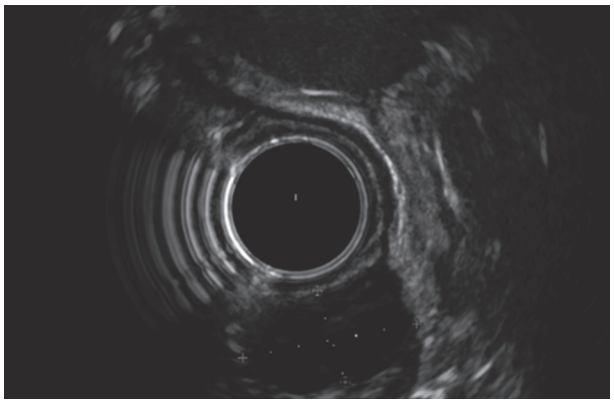

Fig. 1. — An incidental small hypoechoic lesion originating from muscularis propria layer in gastric wall having diameters of 15.3 × 8.2 mm. EUS-assisted fine needle aspiration was performed due to the presence of echogenic foci and the cytopathologic result was gastrointestinal stromal tumor.

hepatic vessel mimicking a SEL in the remaining patient.

The largest diameter of postoperative GISTs were 48.3 ± 20.1 mm (range : 20 to 90 mm) ; 2 (%8), 15 (60%) and 8 (32%) patients had largest tumor diameters of 20 mm, > 20-≤ 50 mm and > 50 mm-≤ 100 mm, respectively. Mitotic index was reported ≤ 5/50 high-power fields (HPF) in 87% of GISTs. According to the risk stratification system based on the largest tumor diameter and mitotic index proposed by Miettinen *et al*. (13), tumors from surgical specimens were classified into no-risk (2 tumors, 8%), very-low-risk (14 tumors, 56%), low- risk (6 tumors, 24%), moderate-risk (2 tumors, 8%), and high-risk groups (1 tumor, 4%).

After the surgical removal of the tumor, only one patient in moderate-risk category

(completely resected 64 × 50 mm gastric GIST with microscopically negative margins and mitotic rate of 8/50 HPF) developed metastasis to liver seven years after the primary surgery. She underwent partial segmentectomy for the metastasis involving three different segments and started tyrosine kinase inhibitor imatinib. This was the only patient who received imatinib in our series. At the time of the review visit, 28 months after the surgery for hepatic metastasis, this patient was alive without any sign of recurrence upon endoscopic or imaging evaluations.

Two patients among the conservatively managed patients with gastric MP-SELs of 20.3 and 15.5 mm size died of cardiac disease at ages of 74 and 83 years, respectively. There was no tumor- or metastasis- related death in our whole series during the mean follow-up time of 54.4 (12-110) months after the index EUS examination.

Discussion

Our study shows that patients with small gastric hypoechoic MP-SELs less than 20 mm, endosonographically suggestive of GIST, have survived disease-free for at least a mean duration of 4 years, although most patients in our series had much longer surveillance. We referred larger lesions (>20 mm) to surgery even they were asymptomatic ; despite this approach is a matter of debate, only one patient developed metastasis after a surgical resection during follow-up.

The National Institutes of Health (NIH) consensus (14) classified GISTs into very low-, low-, intermediate-, and high-risk categories by using the size and mitotic count of the lesions. Furthermore, Miettinen and Lasota indicated that GISTs ≤ 20 mm with a mitotic index of ≤ 5/50 HPF have no metastasis risk, thus they defined these lesions as benign, although NIH has avoided such a category. Nevertheless, obtaining sufficient material from a small SEL in an attempt to scrutinize its malignant potential by assessing the mitotic count may be technically difficult. To overcome some of the limitations of EUS-FNA in such small lesions, new techniques and equipments have been proposed, but it remains to be elucidated from prospective studies whether any improvement will be achieved to obtain better tissue sampling. In our study, yield of tissue acquisition was higher, though not statistically significant, in tumors with larger diameter. Consistent with our results is the study by Akahoshi *et al*., whereby the reported diagnostic rates for tumors with diameters less than 20 mm, 20 mm to 40 mm, and 40 mm or more were 71%, 86%, and 100%, respectively (15). On the other hand, by conservative follow-up approach of small hypoechoic SELs in stomach, we cannot exclude etiologies other than GIST. Nevertheless, no patient in this group developed any sign of progression or metastasis linked with his/her primary SEL lesion in our series, and we performed EUS-FNA from the lesions having suspicious echogenic features even if the size was less than 20 mm diameter.

The frequency of follow-up duration of small SELs suggestive of GIST is controversial in different guidelines. The American Gastroenterological Association (AGA) recommends surveillance for < 30 mm lesions without concerning the endosonographic features (2). The US National Comprehensive Cancer Network (NCCN) avoids making a clear statement for the small gastric GISTs (< 20 mm) because of the insufficient data, but recommends resection of the small lesions with high-risk EUS features, and endoscopic surveillance at 6- to 12-month intervals for the lesions without high-risk features (16). European Society for Medical Oncology (ESMO) guidelines suggest a short-term first control (e.g. at 3 months) continuing with a longer interval follow-up schedule in case of no growth, if follow-up strategy is chosen for small lesions (17). Japanese guidelines recommend that lesions < 20 mm in size and without ulceration or surface depression can be managed with endoscopic follow-up once or twice a year (18). There are no large scale investigations providing evidence for the effectiveness of these follow-up schedules, mostly due to the fact that GISTs are rare tumors. Our findings suggest that scheduling for much more extended intervals for

EUS follow-up may be more appropriate. Similarly, the follow-up schedule the operated patients with low-risk gastric GISTs is another dilemma since some guidelines suggest consideration of serial CT investigations exposing those post-operative patients to the risks of X-ray which deserves further research (17). All of our operated GIST patients with no-, very-low, and low-risk categories survived disease-free more than a mean duration of 4 years. So, our study paves the way for new studies evaluating the safe post- operative follow-up strategies in patients with low-risk categories of gastric GISTs.

Among 28 patients with MP-SELs managed conservatively, there were no tumor-related death, or any progressive or new symptom related to progressive disease after a mean of 48.5 (12-99) months. Seventy-five percent of these lesions were ⩽ 20 mm at index EUS. However, we also enrolled those patients with hypoechoic MP-SELs having larger diameters who denied surgery. Among the patients compliant for surveillance, we did not detect any significant change in tumor size or newly developed high-risk sonographic feature similar to the results of many prior studies. In one retrospective analysis by Lok *et al*., among 23 patients with small MP-SELs (mostly gastric with a median size of 12.9 ± 6.9 mm) without high-risk EUS features, only 3 patients (13.0%) showed an increase in tumor size over a mean period of 17.3 ± 10.2 months follow-up with EUS but no change in echogenic features (19). In another study by Kim *et al*., 8.5% of small gastric SELs (< = 30 mm) showed changes in size or echo pattern over a median follow-up of 24 months with regular endoscopic or EUS surveillance (20). Lachter *et al*. (21) found that the majority of small (< 17 mm) GISTs did not change in echogenicity or size during a median period of 5 years, and enlargement was significantly more common with GISTs over 17 mm at initial diagnosis ($p < 0.018$). So, if an increase in size is a factor predicting malignancy, those small hypoechoic MP-SELs are not subject to change for durations of at least 2 years of follow-up as supported in the literature. Moreover, the size of minimal tumor growth to distinguish the potentially malignant SELs from their benign counterparts that can be considered significant during surveillance has not been defined in literature and stands for another issue to be resolved in future studies. On the other hand, follow-up strategy may still carry the risk of missing a small GIST acquiring genetic mutations and rapidly evolving into clinically evident metastasizing lesion without any significant increase in the tumor size. Small GISTs are very common in population and frequently harbor an oncogenic activation in the c-KIT or PDGFRA gene (22). Agaimy *et al*. grossly identified small GISTs (1 to 10 mm) in 22.5% of consecutive 98 autopsy cases performed in a population of older than 50 years of age and also demonstrated c-KIT mutations in 11 cases (46%) and PDGRFA mutations in one case (4%) (4). Most small or microscopic GISTs are indolent, remain small or regress, however, some are thought to be the precursors of clinically overt GISTs (23). Factors causing the progression from benign to malignant behavior after acquisition of c-KIT mutations still have to be identified, but it is now known to be related with cytogenetic aberrations like chromosomal depletion and molecular mutations in tumor suppressor genes (22,24,25). We believe that other molecular surrogate markers should be researched for the follow-up of those small hypoechoic SELs suggestive of GIST which acquire aggressive mutations rather than following-up solely by size in short periods.

With the widespread use of endoscopy, it is likely that these types of SELs will be encountered even more frequently. Surveillance for all small lesions is costly in terms of healthcare, and increases the hospital workload. Additionally, surveillance procedures may impose emotional distress and give rise to frustration in many patients, which was reflected by the high rate (60.7%) of poor compliance in our study. Similar to ours, in a prospective study, more than 50% of patients were lost to follow-up after 1 year (26) ; in another study, only 46.9% of patients agreed regular EUS follow-up (19). A more extended follow-up interval than the current recommendations is more likely to be adopted by the patients ; the reduction of the visit burden over time may improve patient adherence, increasing the efficiency of the protocol overall and would be more safe and cost-effective. Also other less invasive, less costly, and more comfortable strategies should be studied for surveillance.

Among our 25 surgically managed GIST patients, complete macroscopic resection was achieved for all, and a good long-term prognosis was revealed except for one patient (4%) experiencing metastasis, and there was no tumor-related death during the mean 56.7 months (12-110) of follow-up. Our results showed higher survival rates compared to other studies revealing overall 5 year survival rates ranging from 54% to 78.5% with recurrence rates of 21% to 40% after complete macroscopic resection (8,9). This can be explained by the fact that in our study, 68.0% of cases were less than 50 mm, and none had diameters of more than 100 mm ; as De Matteo *et al*. (8) demonstrated that tumor size > 100 mm was the only significant predictor of poor survival on multivariate analyses (RR : 2.5, confidence interval 1.2-5.5) after the complete gross removal of disease. Additionally, most of our lesions (88%) were in no-risk, very-low-risk or low-risk category according to Miettinen classification, and the recurrence rate of our series was very low (4%), similar to those of the corresponding Miettinen categories (13). The prognosis of low-risk GIST after complete resection has been known to be excellent with the 5-year survival rate of approximately 95% (27,28), while high-risk GIST cases revealed poorer disease-free survival rates even after complete surgical resection could be achieved (14,29,30). The proportion of patients in the moderate- and high-risk groups in our study (8.0%, 4.0% respectively) was much lower than those reported by other series. In our series, only one case having 64 mm gastric GIST of moderate-risk category who was resected

completely with negative margins recurred and developed liver metastasis seven years later. By the time this patient underwent primary GIST resection surgery, postoperative adjuvant therapy using imatinib which is now known to decrease the recurrence risk (16) was not approved for reimbursement in our country thus she did not receive it.

The major limitations of our study were its limited sample size, retrospective design, low rates of histological sampling, and poor compliance of patients to attend their follow-up EUS visits. Nevertheless, our results reflect the experience of a single unit following the same unique rules on hypoechoic MP-SELs up to 9 years. In fact, our low EUS-FNA rates represent the daily practice of many centers.

In conclusion, our findings provide further support to the notion of conservative management of small asymptomatic MP-SELs without any high-risk echogenic features in gastric wall detected incidentally. Further research is needed to identify the optimum schedule with regard to the impacts on outcome, patient adherence and cost-effectiveness. Finally, based on our retrospective data, we evaluated the utility of EUS on survival of patients with small hypoechoic gastric MP-SELs. Their excellent survival with conservative management represents indolent course of those lesions. We suggest reconsideration of the recommendations in the current guidelines towards extending the follow-up intervals for small MP-SELs.

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