

Peer Review File

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Reviewer 1:

1. Would discuss the cause and changes implemented to reduce the rate if missed lesions. Do you have a tumor board and multidisciplinary team that guides treatment?

Reply: Time, magnification, narrow band, may help in biopsy site selection; discussion of suspected cases in multidisciplinary team and repeated endoscopy may improve the results.

2. Would also discuss the role of minimally invasive surgery and the rate of conversion.

Reply: We add our consideration on robotic surgery . After the first years, conversion rate consider only 5%.

3. May need to discuss the Barriers in replication your model and a flow diagram of how patients are triaged.

Reply: Few experience, short time for each endoscopy and inadequate instruments.

Reviewer 2:

The authors conducted a retrospective study to determine the accuracy of the endoscopy and the effectiveness of the early gastric cancer treatment in Western countries. The rate of the missed lesions decreased, indicating good technical skills and accuracy of the endoscopy are required. The treatments of early gastric lesions were performed in their hospital. This Italian study could be a real-world data in Western area but there are some queries to answer.

Major points

1. The aim of this study should be clarified. To present their experience of early gastric cancer/dysplasia, shown in the introduction section (line 61-63, page 3), may be one of the methods in this study.

Reply: In introduction the sentence "We present our experience of early gastric cancer (EGC)/dysplasia detection and treatment, which represents the end result of a close collaboration between different hospital Units such as Gastroenterology, Pathology and

General Surgery" has become " The aim of this study is to present our experience in early gastric cancer (EGC) or dysplasia detection and treatment suggesting a close collaboration between different hospital Units such as Gastroenterology, Pathology and General Surgery.

Moreover we underline the importance of the missing lesions as a quality index to be detected by endoscopic services.

2. Their histological classification need to be mentioned. Japanese gastric cancer treatment guidelines are not histological guidelines. WHO classification seems to be used in the manuscript.

Reply: In the text the use of Lauren's classification has been specified and the corresponding bibliographical reference has been added.

3. The numbers in the text did not correspond with the Figure 2. 60,907 patients underwent 51,381 gastroendoscopies?

Reply: Initially we decided to use a figure with data expanded to include an additional 2 years of evaluation. Encouraged by your evaluation, we have decided to harmonize text and figure to a single period (see modification of figure 1 and text).

4. Please mention the detail of the method to calculate the incidence of missed lesions (line 76-78, page 4). The detailed result should be shown in a table or a graph. The comparisons between 2003 and 2011 is insufficient (line 100-101, page 6).

Reply: We add information on missing lesions and fig 3 on incidence of missing lesions for each year.

5. Survival analyzed using Kaplan-Meier should be a figure. Judged from Patients and methods (line 91-94, page 5), Kaplan-Meier curves are required.

Reply: We add survival rate as requested.

Minor points

1. The 6 patients who did not fulfill JGCA criteria and underwent further surgical treatment were included in both group of the patients surgically treated and those underwent endoscopic resection. (Table 1, Figure 2) The 6 cases are overlapped.

Reply: Thank you, the 6 patients made 2 different procedures and are considered for each ones. We added in figure text.

2. The number of High-grade dysplasia in Histotype performed EMRs should be 7.

Reply: Thank you very much , done.

3. Mininvasive in line 173 page 9 may be a typo.

Reply: Thank you very much , done.

4. The retrospective study was permitted which committee?

Reply: We add the committee permission.

Reviewer 3:

Authors mentioned the importance of not overlooking early gastric lesions by improving endoscopic skills and accuracy and cooperating closely with each department in western area where gastric cancer screening program is not common. They showed the rate of missed early lesions was significantly reduced at intervals of about 10 years, and that in the cases found, a good prognosis was obtained by appropriate minimally invasive treatment.

However, the content of this article is very abstract and lacks impact for readers to be interested in, so revision of the content is desired.

Major comments are as follows.

1. If it is mentioned as an important point of this article that the number of missed lesions has decreased significantly, the characteristics of missed cases; such as location, macroscopic type, size, stage classification, approach to treatment and elapsed years from the last endoscopy to diagnosis; should be summarized in a table. It is desirable to show a graph of changes as a figure in the number of missed cases (not just the proportion) from 2003 to 2011.

Reply: We add information and graphic.

2. Is the definition of missed lesions appropriate? The authors defined it as “the rate of patients diagnosed with gastric cancer after at least 3 years of negative endoscopy (page 4, line 77),” but Yalamarathi et al. (ref 9) described it as “patients who had undergone an endoscopy within 3 years before the diagnosis.”

Reply: We changed the definition as correctly reported.

3. The procedure for endoscopic lesion evaluation was unclear. The authors stated that chromoendoscopy was performed as the first-step, but it is not clear whether the

pigment is applied to the entire stomach in all cases or only after suspicion of the presence of lesions. It should also describe the details of equipment such as the model of the scopes and specify whether Image-Enhanced Endoscopy such as FICE would be used only after the second look, not at the first time.

Reply: Chromoendoscopy was performed on suspected areas, we changed in the text.

4. I'm not sure what authors want to claim by showing figure 1. The authors should mention in the text that can be read from this figure, such as "the number of early cancer has increased over time because the number of missed lesions has decreased due to the improvement of endoscopic accuracy" (on the face of it, there does not seem to be any tendency in the change in the number of cases during the observational period).

Reply: We better explain fig 1. Even if we think to have a good number of EGC for a western center as shown in the figure, we think it is possible to improve.

5. The strength of mass screening programs is that it is possible to pick up asymptomatic early lesions by examining many subjects randomly. Although authors mentioned that the point of this initiative is to promptly guide "patients with suspicious symptoms to the Endoscopy service (page 4, line 71)," it could not be a substitute for screening programs unless a system is established to guide the patients to endoscopy service before they have symptoms. It is described as "Screening is not the only means of achieving good rates of EGC detection" in conclusions, but as mentioned above, although it is interesting as an effort to improve the accuracy of endoscopy in authors' facility, it seems impossible to compare it with the screening programs for picking up early lesions. Please answer what you think about this point. If there are any strengths in this effort compared to screening programs, it should be clearly stated.

Reply: Screening programs in our countries is not considered. Even if the continuous checkup of the missed lesions may not substitute the screening it can improve accuracy of the endoscopic service.

Minor comments.

1. Regarding the follow up after endoscopic treatment, it is described as "endoscopic check up every 3 months for the first year and every 2 years thereafter (page 4, line 83-84)," but it is desirable to show references as the basis for this being appropriate.

Reply: We add that this was our institution follow up. Being the beginning of our experience a frequent follow up was observed.

2. The limitations of this study should be mentioned.

Reply: We add limitations

3. It is stated twice with almost the same content that surgery was performed in 146 cases (page 6, line 114-119). It is desirable to summarize in one sentence concisely.

Reply: We summarized.