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Manuscript NO: 79519

Title: Effectiveness and safety of endoscopic resection for duodenal gastrointestinal stromal tumors: a single center analysis

Responses for reviewer's comments

Reviewer's code: 06267313

Comment:

Remove page breaks

Author's response:

Thanks for your comment. We have removed the page breaks in the revised manuscript.

Reviewer's code: 00724887

Comment:

This study is well written I have suggestion Kindly provide pathological details of the cases Few histological images to be added Also, immunohistochemistry work-up What about molecular studies.

Author's response:

Thank you for your kind attention to consider our manuscript. We have carefully read the comments, and added histological figures in our revised manuscript.

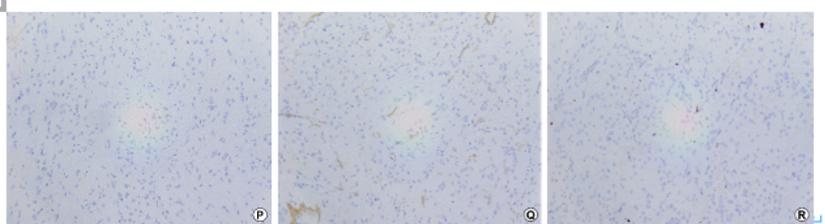
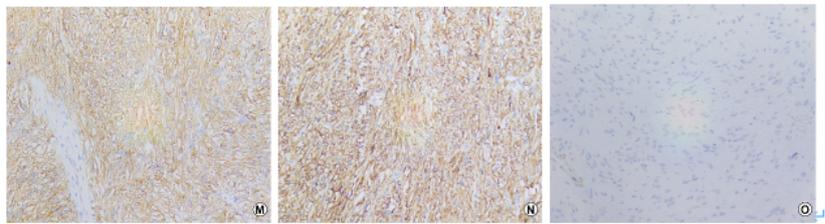
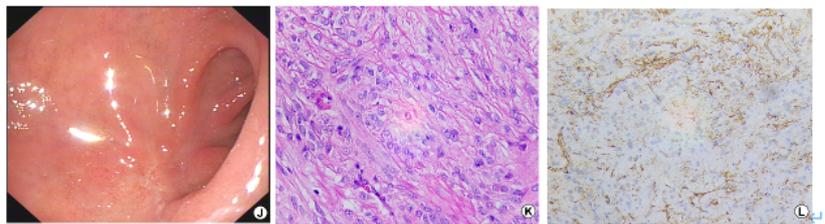
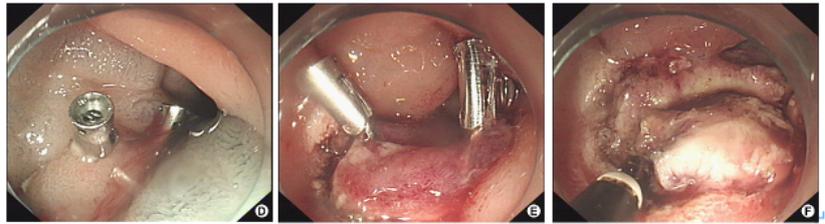
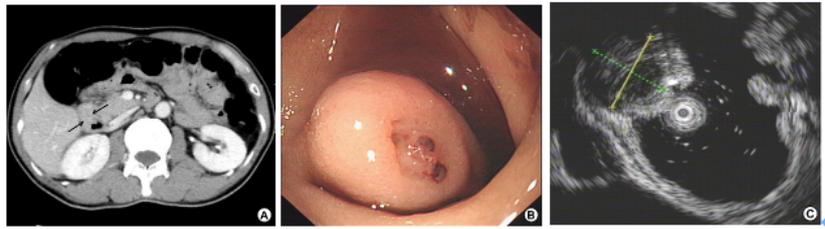
Pathologically, the diagnosis of GIST relies on morphology and immunohistochemistry, the latter typically being positive for CD117 (KIT) and/or DOG1. A proportion of GISTs (in the range of 5%) are CD117-negative^[1]. In our case series, immunohistochemistry of all lesions showed that CD117 and DOG1 were positive. Mutational analysis for known mutations involving KIT and PDGFRA can confirm the diagnosis of GIST, if doubtful (particularly in rare CD117/DOG1

immunohistochemically negative GISTs ^[1]. CD34 is not a specific marker of GIST. CD34 positive tumors also include isolated fibrous tumors, angiogenic tumors, dermatofibrosarcoma protuberans, liposarcoma and other soft tissue tumors. 70-80% of gastrointestinal stromal tumors are positive, which are often used as auxiliary diagnosis of GIST. In our study, all lesions showed that CD34 were positive. Ki-67 is a DNA binding nucleoprotein, which can be detected in all stages of cell proliferation (G1, S, G2 and M stages). Its expression is low in G1 and early S stages, and gradually reaches its peak during mitosis. Patients with high Ki-67 have worse clinical outcome and higher risk of recurrence ^[2]. Li et al. took Ki-67 5% as the cut-off value. The results showed that Ki-67>5% increased the risk grade of GIST and had a higher rate of metastasis and recurrence ^[3]. However, Ki-67 analysis does not replace the mitotic count and is not part of established prognostic systems in this disease ^[1]. In In our study, Ki-67 were all <5%. No local recurrence or distant metastasis were detected during the follow-up period (14-80 months). These contents have been modified in the revised manuscript.

References

- [1] P. G. Casali, N. Abecassis, S. Bauer, R. Biagini et al. Gastrointestinal stromal tumors: ESMO–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2018 Oct 1;29(Suppl 4): iv68-iv78.
- [2] PYO JS, KANG G, SOHN JH. Ki -67 labeling index can be used as a prognostic marker in gastrointestinal stromal tumor: a systematic review and Meta-analysis. *Int J Biol Markers.* 2016 May 28;31(2): e204-10.
- [3] LI H, REN G, CAIR, et al. A correlation research of Ki-67 index, CT features, and risk stratification in gastrointestinal stromal tumor. *Cancer Med*, 2018,7(9) : 4467-4474.

Figure Legends



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Figure 1 EETR for a duodenal GIST in the descending junction of the duodenal bulb. A: CT revealed a tumor of approximately 3 cm in diameter, with enhancement in the arterial phase. B: A tumor located in the descending junction of the duodenal bulb with ulcer and exposed blood vessels on the surface. Titanium clips were used to stop the bleeding. C: EUS showed that the lesion was a hypoechoic structure originating from the MP layer, with uniform echo and a clear boundary. D: Submucosal injection after making several marking dots around the lesion. E: A circumferential incision was made outside the border. F: The submucosa and MP around the lesion were circumferentially dissected. G: The duodenal defect after tumor resection. H: The wound was occluded with several titanium clips + an endoloop + an OTSC. A jejunal nutrition tube was placed near the wound for drainage. I: The resected tumor with the intact capsule. J: The wound healed well at 3 months after the procedure. K: Hematoxylin and eosin staining (original magnification ×40). L: Immunohistochemistry showed that the tumor was positive for CD34. M: Immunohistochemistry showed that the tumor was positive for CD117. N: Immunohistochemistry showed that the tumor was positive for Dog-1. O: Immunohistochemistry showed that the tumor was negative for Desmin. P: Immunohistochemistry showed that the tumor was negative for S-100. Q: Immunohistochemistry showed that the tumor was negative for SMA. R: Immunohistochemistry showed that Ki67 was about 2%.↵

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