This is an interesting and well written paper. However, the statistical analyses need to be refined. In the current version, the authors proceed to do two embedded subgroup analyses: one subgroup analysis according to mucosa-submucosa classification (= 2 levels), and another subgroup analysis according to histological type (mixed, Undifferentiated, and Differentiated= 3 levels). This is a confusing and inefficient approach highly likely to cause spurious findings. In Table 2, n=17 cases for MT, and in Table 3, n= 24 for MT and n=20 for Pure U. The small size of these subgroups cause quizzical odds ratio. Thus, in Table 4, LV invasion present vs. absent is associated with an OR whose confidence interval is 1.75-106.28 (univariate) or 1.39-125.30 (multivariate). A hundred-fold confidence interval indicates unreliability. No test has been performed to compare whether the risk of LNM differ significantly between the mucosa and submucosa localisation. The discussion's statement that "the mixed-type group and pure U group showed similar aggressive behavior and LNM rate, regardless of if it was mucosal or submucosal EGC" is not supported by any test. This reviewer suggests that the statistical analyses might be reconsidered by modeling LNM as a function of localisation (mucosa-submucosa), of histological type (mixed, U and D), and other covariates, do interaction tests regarding localisation and histological type, then consider grouping the levels if the tests of interaction appear clearly non-significant.

Question: In the current version, the authors proceed to do two embedded subgroup analyses: one subgroup analysis according to mucosa-submucosa classification (= 2 levels), and another subgroup analysis according to histological type (mixed, Undifferentiated, and Differentiated= 3 levels). This is a confusing and inefficient approach highly likely to cause spurious findings.

Response: The reviewer provided good suggestions for improving our manuscript. We totally agree with your viewpoint. We set LNM as a function of invasion depth (mucosa-submucosa), of histological type and other covariates in all the patients. In a univariate analysis of risk factor for LNM of EGC, LNM was associated with younger age ($P = 0.005$), female sex ($P = 0.044$), tumor size ($P = 0.022$), middle/lower location

(P = 0.010), lymphovascular invasion (P = 0.013), flat/depressed gross type (P = 0.034), and depth of submucosal invasion (P = 0.001), pure U type (P = 0.005) and mixed-type (P = 0.001). (Table 2). Given the criteria for ESD treatment of EGC consists of the invasion depth, histological type, tumor size and ulceration, it's reasonalbe and meaningful to take these four covariates into a multivariate analysis to assess their main effect on the rate of LNM. We found that the submucosal invasion (OR = 4.58, 95%CI 1.23–16.97, P = 0.023), pure undifferentiated type (OR = 4.97, 95%CI 1.21–20.39, P = 0.026) and mixed-type (OR = 5.84, 95%CI 1.05–32.61, P = 0.044) were independent risk factors for LNM in EGC. There was no interaction effect between the invasion type and histological type (P = 0.822) (Table 2).

We have added these in our revised manuscript (Page 9).

Question: In Table 2, n=17 cases for MT, and in Table 3, n= 24 for MT and n=20 for Pure U. The small size of these subgroups cause quizzical odds ratio. Thus, in Table 4, LV invasion present vs. absent is associated with an OR whose confidence interval is 1.75-106.28 (univariate) or 1.39-125.30 (multivariate). Thus, in Table 4, LV invasion present vs. absent is associated with an OR whose confidence interval is 1.75-106.28 (univariate) or 1.39-125.30 (multivariate). A hundred-fold confidence interval indicates unreliability.

Response: Thank you for your question. Some previous studies have showed the relationship between the lymphovascular invasion and LNM, and similar wide confidence interval, such as 1.745-123.671 (Lee JH, Choi IJ, Han HS, Kim Y-W, Ryu KW, Yoon HM, Eom BW, Kim CG, Lee JY, Cho S-J, Kim Y-I, Nam B-H, Kook M-C. Risk of Lymph Node Metastasis in Differentiated Type Mucosal Early Gastric Cancer Mixed with Minor Undifferentiated Type Histology. *Ann Surg Oncol* 2015;**22**:1813–9) and 7.40–102.20 (Huo Z Bin, Chen SB, Zhang J, Li H, Wu DC, Zhai TS, Luan SF. Risk clinicopathological factors for lymph node metastasis in poorly differentiated early gastric cancer and their impact on laparoscopic wedge resection. *World J Gastroenterol* 2012;**18**:6489-93). According to the reviewer's suggestion, we have realized that the small sample size resulted to the wide confidence interval, and have added the following content in our discussion section, "Limited by the small sample sizes, our data showed considerable wide confidence interval of the OR ratio of lymphovascular invasion, in the univariate and multivariate analysis of mucosal EGC. Although similar data were reported in some

studies[28,29], it should be confirmed by additional clinical research with larger sample sizes" (Page 13).

Question: The discussion's statement that "the mixed-type group and pure U group showed similar aggressive behavior and LNM rate, regardless of if it was mucosal or submucosal EGC" is not supported by any test.

Response: We are deeply sorry for making the reviewer confused by this sentence. We have revised this to "the distribution of tumor size, location, gross type, ulceration, lymphovascular invasion and LNM rate were similar between the mixed-type group and pure U group in mucosa-confined EGC, and the histological mixed-type was not an independent risk factor for LNM in mucosal EGC"(Page 11). We also added the following content in our discussion section, "The mixed-type group and pure U group showed similar clinicopathologic features and aggressive behavior in mucosal EGC, including the distribution of age, gender, tumor size, location, gross type, ulceration, lymphovascular invasion and LNM rate" (Page 12).

We extremely appreciate you carefully review our manuscript again.

Response to Reviewer#2's comments

This is well designed and performed clinical retrospective study for analyzing the relationship between the histological type of early gastric cancer and lymph node metastasis. The authors investigated retrospectively the data of 298 patients who underwent gastrectomy. The rate of lymph node,metastasis (LNM) was compared in patients with histological mixed-type, pure undifferentiated and pure differentiated early gastric cancer in the mucosa and submucosa. The authors found that the rate of LNM was significantly higher in the mixed type as well as in the pure undifferentiated group regardless of the mucosal or submucosal type of early gastric cancer. The mixed-type group and pure undifferentiated group showed similar aggressive behavior in both mucosal and submucosal EGC. In submucosal EGC the pure undifferentiated as well as mixed type were independent predictors of LNM. The study is set up correctly. Introduction gives a good overview of the study

background and the authors raised clearly the aim of the study. The aim of the study is fulfilled. The material studied is large enough and allows to drawn the conclusions. The Figure and 5 Tables give a good overview about the results. However, the text of the Discussion is quite difficult to follow and the Conclusion is not clear.

Response: We extremely appreciate you carefully review our manuscript. We have carefully revised and reorganized the discussion section (Page 11-14). We hope the revised version will meet with your approval.

Response to Reviewer#3's comments

Dear Author, This article title with '"Endoscopic ultrasound-guided fine-needle aspiration for diagnosing a rare extraluminal duodenal gastrointestinal tumor'' it should be published at WJGO. It has new informations and it makes a new contribution for Gastroenterologists. Sincerely yours.

Response: We extremely appreciate you carefully review our manuscript.