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Can PEN A Type Early Gastric Cancer be Considered as Advanced Cancer?

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Abstract

Although early Gastric Cancer (EGC) generally has a very good prognosis, this is not the case for a subset of patients defined as PEN A type according to Kodama's microscopic classification. In 530 patients operated on in our surgical department between 1976-2006, the EGC survival rate was 94%. The 5-year survival of Pen A patients was 83%, decreasing to 69.7% when there was lymph node involvement. Moreover, survival rates for PEN A patients continued to decrease with respect to other EGC types (10-year survival 73% *vs*. 94%, respectively). PEN A EGC should thus be considered as advanced cancer.

Keywords: EGC; PEN A type

Introduction

Early Gastric Cancer (EGC) is defined as a tumor confined to the mucosal or submucosal layers irrespective of its size, lymphatic diffusion or presence of metastases [1]. When radically treated, it has usually a good prognosis in eastern and western centers (5-year survival >90%) [2,3]. However, some EGC patients show a poorer prognosis and differentiating between the 2 kinds of EGC is not always an easy task.

Early lesions can be classified into 5 macroscopic groups on the basis of their appearance (protruded, elevated, flat, depressed or excavated) or defined according to microscopic features, such as Kodama's classification, which considers tumor size (> or <4 cm) and growth pattern [4]. In Kodama's classification, massive submucosal infiltration <4 cm is divided into 2 types on the basis of local tumor invasion: PEN A tumors extensively infiltrate one area of the muscularis mucosae, whereas PEN B tumors infiltrate several areas near each other [4].

The most important prognostic factor in any type of gastric cancer s universally acknowledged as the extent of lymphatic invasion. Traditionally, risk factors for lymphatic involvement are tumor size, submucosal invasion, grade of differentiation, and the presence of ulceration. Very few studies have considered the Kodama PEN A type as a prognostic factor [5-8].

In previous studies published by our group [6] and in a follow-on work published by the Italian Research Group for Gastric Cancer (GIRCG) [5] on 652 EGCs, PEN A type tumors represented 19.6% and 22.5% of all EGCs, respectively, with a 5-year cancer-related survival rate of 83% compared to 94% for the entire EGC cohort [6]. In both studies the PEN A subgroup proved to be an independent risk factor for lymph node infiltration and a prognostic factor. Notably, 42.3% of all positive nodes were collected from PEN A patients who represented only a small percentage of the population. PEN B extended submucosal infiltration was not as aggressive as that of PEN A. The cancer-related survival rate was 97% (range 92-100) for PEN B patients, similar to that of other submucosal tumors (95%, range 86-100). The PEN A EGCs showing lymphatic involvement had a poorer 5-year overall survival in our 530 patients (69.72%) (data not shown in the original article) [6].

It is also interesting to observe that 10-year survival rates decreased in the PEN A group from 83% (range 76-90) to 73% (range 63-83), while those of PEN B patients showed only a slight reduction, from 97% (range 92–100) to 94% (range 87-100). The 10-year survival rate for Pen A N+ patients dropped to 62.34% (data not shown in the original article). In multivariate analysis of Kodama PEN

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A *vs.* non PEN A, patients in the former group had a fourfold higher risk of death (HR, 3.91; 95 % CI, 2.08–7.33; p <0.0001), which was recognized as a significant prognostic factor [6].

Conclusion

PEN A type is a particularly aggressive form of EGC showing the poorest overall survival, a higher risk of lymph node involvement, and lower 5-year survival rates than other EGC types. These tumors cannot be considered as early gastric cancer and thus gastrectomy with D2 dissection is probably not a sufficient measure o eradicate the disease. A multimodal approach comprising surgery and adjuvant chemotherapy should be contemplated, especially in N+ patients.

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