Letter to the editor

To the Editor:

I read with interest and appreciated the article by De Manzoni et al. [1] recently published in this journal. They reported, in a retrospective series of 117 patients with a pT3 cancer of the distal stomach, an equivalence between subtotal and total gastrectomy, thus replicating the results of our randomized clinical trial [2] comparing the two procedures in a total number of 618 patients — of whom about 50% belonged to the pT3-pT4 class.

Although our conclusions are quite similar, that is, in early cancer, subtotal gastrectomy appears to be, in general, adequate and in pT3-pT4 patients total gastrectomy is unable to further improve the oncologic outcome, there are some points worthy of further consideration.

First, readers should realize that the patient populations included in surgical randomized clinical trials really exist because they have been identified *before* surgery according to the criteria of eligibility/exclusion of the protocol, whereas the patient population in a retrospective study is selected *after* surgery, and we are not sure to be able to identify it preoperatively.

This means, in general, that the results of such retrospective investigations are less reproducible in current practice than those of prospective studies.

Up to now, in fact, endoscopic ultrasonography represents the best way for staging the T class and has an accuracy, in experienced hands, of 74%–86% and 85%–93% in pT1 and pT3/4 classes, respectively [3,4].

Unfortunately, this tool and the associated medical expertise are only available in a few institutions. There is, therefore, some doubt that results in patients identified *a posteriori* may be properly applied to patients who, *a priori*, are expected to belong to the same T class.

Second, even for early gastric cancer (EGC) the option of total gastrectomy should not be, in principle, rejected. Apart from multicentric EGC, which may occasionally require a total gastrectomy, it is well known

that EGC is associated with a high frequency of second primaries (not only gastric-stump carcinoma), especially in the Western literature, where values of up to 34% are reported [5–7].

A possible mechanism is continuous nitrosification in the gastric stump, retained in subtotal gastrectomy, by bacteria producing N-nitroso compounds [8–11], which finally have different distant target organs.

The similar 5-year oncologic results of the two procedures are worth reconsidering when a longer follow up of the patients will be available.

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Authors' reply

To the Editor:

First of all, we need to clarify the statement by Dr. Bozzetti that our study was retrospective. Indeed, our study was prospective, as information on patients (TNM, histology, site of cancer) was collected at the time of the intervention and subsequently patients were subjected to regular follow up.

However, the statement by Dr. Bozzetti is correct in that patients were included in the present analysis if they were in the T3 tier, according to intra/postoperative staging. In this respect, Dr. Bozzetti's study [1] better reflects current clinical practice, where the surgeon has to choose the surgical procedure before the final assessment of the T stage.

Nevertheless, we think that our study is closer to current clinical practice than that of Dr. Bozzetti for the reasons we have already mentioned in the "Introduction" and in the "Discussion" in our article. During the 1980s, when most of the surgery was performed in Bozzetti's trial, splenectomy was routinely associated with gastrectomy, and D2 lymphadenectomy had just been introduced in Europe from Japan, while nowadays splenectomy is regarded as a complication of gastric surgery and quality controls for D2 have become mandatory.

This is a great problem of many surgical trials: surgical technique may improve rapidly, making the study protocol obsolete before the trial results are published. Also, our observational study lasted too long (11 years of recruitment).

Moreover, in Bozzetti's trial [1], the volume of intervention per center per year was rather low, while our study is based on series from three specialized centers (27.9 gastrectomies per center per year). Given recent

indications that morbidity and mortality associated with all surgical procedures for cancer are highly dependent on the number of such procedures performed in an institution and by each surgeon [2], we think that, in the future, gastrectomy for gastric cancer will be progressively concentrated in major hospitals and in major surgeries.

As far as "the option of total gastrectomy in principle, even for early gastric cancer" is concerned, the incidence of remnant recurrence after subtotal gastrectomy is 1.7% in European experiences [3–5] and 1.1% in the Japanese experience [6], and these data do not justify a rationale for routine total gastrectomy. We agree that early gastric cancer is associated with a high incidence of second primaries; however, in our opinion, the use of total or subtotal gastrectomy does not influence the natural history, the diagnosis, and the management of these second cancers during the follow up.

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