Heterogeneity of new molecular gastric cancer classification. Clinico-pathological characteristic

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BACKGROUND

Today we have few genetical and molecular classification of gastric cancer (GC). In last few years we could find many examples of new GC divisions based on different genetical and molecular information. They were based on anatomic site, histopathology and anatomic site, gene expression, gene amplification, DNA methylation, numerous cancer relevant aberrations or oncogenic pathways. We performed an analysis of clinical utility of molecular classification based on anatomical and histological background and additionally we used that classification for microsatellite instability (MSI) patients.

MATERIALS & METHODS

We analyzed 457 patients treated because of gastric cancer. Clinical, pathological and follow up data were compared with molecular information like microsatellite instability (MSI). We differentiated 3 groups of molecular classification based on anatomical and histological background. Additionally we divided patients into three subgroups as proposed by Shah et al. Clin. Cancer Res. 2011.

- Type 1: proximally located, non-diffuse GC with a major part of the tumor (>80%) located in the upper third of the stomach (cardiac area), and presenting non-diffuse histopathology according to Lauren classification (intestinal and mixed).
- Type 2: diffuse GC, located anywhere in the stomach, presenting entirely diffuse pattern of infiltration.
- Type 3: distal non-diffuse GC, with the major part of the tumor located in the distal or middle part of the stomach and presenting non-diffuse histopathology according to Lauren classification (intestinal and mixed), with or without components of poorly differentiated carcinoma.

Classifying anatomical and histological factors together with molecular findings is one of the limitations of this simple classification. The authors also stress the fact that gene set analysis with the false discovery rate which were set at 0.25 allowed to identify several pathways. These pathways were differentially regulated when comparing each gastric cancer subtype to adjacent normal stomach.

RESULTS

By arranging the data according to this classification, we found that the 3 subgroups are different in terms of such factors as age, sex, T and N status, the stage of the disease, WHO histological type, and adjuvant treatments (Table 1).

The second analysis was based on the same division into 3 types, but with additional information on the MSI status. The patients were divided into MSI and microsatellite stable (MSS) groups. The results for MSI patients are presented in Table 2, and for MSS in Table 3.

For MSI group we found that the following factors were statistically significant: N, the stage of the disease, WHO histological type and adjuvant treatment usage. No differences were observed in sex, T status, R status, M status. From MSI patients difference was observed in sex (more females were seen in type 2, and more males in type 1 and 3). Other statistically significant differences were observed in T, N status, stage of the disease, WHO classification and adjuvant therapy.

Next, we analyzed cancer-free survival. Figure 1 shows the differences in survival rates between all 3 types (p=0.135). The 5-year survival rate for type 1 was at 31.4%, for type 2 at 37.6%, and for type 3 at 49%.

Finally, we analysed MSS and MSI subgroups for all 3 types (Figure 2). We observed a strong statistical correlation in terms of 5-year survival rate according to that division (p<0.001).

CONCLUSIONS

In summary, the new molecular classifications may help in better understanding of GC biology. We have presented clinical and pathological results that might also be used in molecularly based anatomical and pathological GC classification. We have found that this classification might find its place in the subdivision of MSI subgroup of GC, especially that this classification is simple and clinically useful. The question of detailed molecular analysis calls for further research.