759 POSTER

Relative risk according to the DNMT3B C → T promotor polymorphism in gastric cancer

B.J. Song, S.S. Jung, J.S. Kim, S.T. Oh, J.H. Park, S.N. Kim, W. Kim, H.M. Jeon. *Kangnam St. Mary's Hospital, The Catholic University, Department of Surgery, Seoul, Korea*

Background: As the recent research about methylation is gone, the methylation of CpGisland was reported to important pathway of tumorigenesis as another epigenetic modification. This methylation process is mediated by DNA-methyltransferase (DNMTs) and DNMT1, DNMT3B was confirmed as active subtypes. It was reported that the activity of DNMT3B increased in bladder, colorectal, renal and pancreas cancer. DNMT3B genc increases activity of promotor about 30% in cases of C → T promotor polymorphism in vitro. Exact pathway of promotor polymorphism is undefined, but Tvariant increases translation of DNMT3B and derives hypermethylation of tumor suppressor gene and cause functional inactivity in human. In this study we recognize about correlation between the rate of C → T promotor polymorphism of DNMT3B gene and susceptibility in gastric cancer.
Materials and methods: 176 patients who was diagnosed of gastric cancer was case group and control group was 70 patients woho was identitied H.pylori infection in gastrofiberoscopic examination. All patient group and control groups picked 10cc blood sample and extracted DNA and performed PCR, we extracted 380 bp target DNA and performed restriction reaction rsing Avrll enzyme (New England Biolab, Inc). In case there is T variant, we could confirm two bands that have 207 bp and 173 bp. We analysed data using SPSS statistically.
Results: In case there is T variant, it is 150 cases (85.2%) – CT (71.6%), TT (13.6%), CT+TT (85.2%) in cancer group and is significantly higher in the cancer group than the control group (42 cases (60.0%) – CT (42.9%), TT (17.1%), CT+TT (60.0%) ($p < 0.05$). In multivariant analysis, relative risk in CT (heterozygote type) was high 4.523 times than cc (wild type), and it was high 2.154 times in TT (homozygote type), and increased 3.846 time in case is CT+TT (T variant) ($p < 0.05$). However, If there was T variant, we can assume that the relative risk of gastric cancer increases 3.846 times. But, there was no significance correlation with stage, differentiation and Lauren's classification by T variant. The infection rate of H. pylori was 34.6%, the rate of gastric cancer is higher in H. pylori positive groups (87.1%) than negative groups (63.4%). In case of T variant, H. pylori infection rate was increased about 1.19 times, but there was no statistical significance.
Conclusions: In these results, we can conclude that T variant of CNMT3B promotor gene shows about 1.42 times higher than normal and the relative risk increase 3.846 times if there is the T variant of DNMT3B promotor gene in gastric cancer. However, there is no relation between T variant and pathologic status and H.pylori infection rate.

760 POSTER

Duplex RT-PCR improves accuracy in detecting lymph node micrometastasis in early gastric cancer

H. Sonoda[1], K. Yamamoto[2], R. Kushima[3], H. Yamamoto[1], H. Naitoh[1], Y. Endo[1], Y. Kurumi[1], H. Okabe[2], T. Tani[1]. *[1]Shiga University of Medical Science, Department of Surgery, Otsu, Japan; [2]Shiga University of Medical Science, Department of Clinical Laboratory Medicine, Otsu, Japan; [3]Shiga University of Medical Science, Division of Clinical Pathology, Otsu, Japan*

Background: We previously reported that MUC2 is a useful marker in the detection of lymph node micrometastasis (LMM) in gastric cancer *(J surg oncol. 2004; 88: 63–70)*. However, MUC2 is rarely expressed in early poorly-differentiated adenocarcinoma. To improve accuracy in detection of LMM in gastric cancer, we paid attention to a novel gene, *TFF1*, which is preferentially expressed in diffuse-type gastric cancer cells. We have examined its potential as a novel marker for the detection of lymph node micrometastasis in gastric cancer, and investigated a novel method for LMM detection in gastric cancer.
Material and methods: We selected 33 histologically node negative (pN0) early gastric cancer patients who underwent curative surgery in our surgery department between July 2002 and June 2004. This study group consisted of 22 mucosal cancer and 11 submucosal cancer patients. Each lymph node was dissected into two pieces. One piece was formalin fixed and paraffin embedded for histological examination. The other was used for duplex (MUC2 and TFF1) reverse transcriptase-polymerase chain reaction (RT-PCR) assay.
Results: MUC2 and TFF1 were expressed in 22 of 33 (66.7%) and 30 of 33 (90.9%) of the gastric carcinoma specimens. MUC2 and TFF1 were expressed in 5 of 13 (38.5%) and 13 of 13 (100%) undifferentiated carcinoma specimens. The positive rate of TFF1 was significantly higher than that of MUC2 in the undifferentiated carcinoma specimens ($P = 0.002$). All carcinoma specimens were positive for MUC2 and/or TFF1. MUC2 was expressed in 15 of 310 lymph nodes (4.8%) from 6 patients (18.2%). TFF1 was expressed in 9 of 310 lymph nodes (2.9%) from 6 patients (18.2%). The detection rate of LMMs was raised until 6.8% (21 lymph nodes) and 33% (11 patients) by using duplex RT-PCR assay. We were able to detect LMMs in 7 of 22 patients (31.8%), especially in mucosal cancer. In the 7 cases, 3 cases were MUC2 positive/TFF1 negative and the other 4 cases were MUC2 negative/TFF1 positive. Duplex assay revealed no false positive results in the control specimens.
Conclusions: Duplex RT-PCR assay provides higher accuracy than either MUC2 or TFF1 alone to detect LMM in early gastric cancer.

761 POSTER

Gastric cancer susceptibility in the P53 codon 72 polymorphism

B. Song, S. Jung, J. Kim, S. Oh, J. Park, S. Kim, W. Kim, H. Jeon. *Kang-Nam St. Mary's Hospital, The Catholic Univers, Department of Surgery, Seoul, Korea*

Background: The P53 codon 72 polymorphism results in either arginine or proline, there are many studies to clear the relationship between P53 codon 72 genotypes and specific cancer risk and susceptibility. Recently, the P53 codon 72 polymorphism has been extensively studied to determine the risk factors responsible for carcinogenesis. The purpose of this study was to investigate the association of the genotype distribution of the P53 codon 72 polymorphism and gasric cancer susceptibility via in comparison of gastric cancer group and normal control genotypes. We also studied the relation between the distribution of P53 codon 72 genotypes and the state of P53 immunohistochemical staining, infectivity of Helicobacter pylori and the clinicopathologic findings in gastric cancer patients.
Materials and methods: In our study, the samples consisted of 145 gastric cancer patients and 77 normal controls. The analysis was performed by polymerase chain reaction (PCR), restriction fragment length polymorphism (RFLP) method using DNA extracted from gastric cancer patients blood and normal controls blood.
Results: The frequency of three genotypes arg/arg, arg/pro and pro/pro in gastric cancer patients was 41.1%, 38.6% and 20.0%. In controls, it was 36.3%, 53.2% and 10.3%. There was no statistical significance ($p = 0.312$, 0.665). There was no correlation between the frequency of the three genotypes and the state of P53 immunohistochemical staining infectivity of H. pylori. The pro/pro homozygote was more frequent in lymph node metastasis (25.6% vs 7.3%, $p = 0.026$).
Conclusions: The P53 codon 72 polymorphism does not contribute to gastric cancer susceptibility. The P53 codon 72 polymorphism is not associated with the state of P53 immunohistochemical staining and the infectivity of H. pylori but pro/pro genotype is associated with the lymph node metastasis in gastric cancer patients.

762 POSTER

Value of elevated Ki67 index (>10%) and p53 protein expression as prognostic factors in GIST

B. Song, S. Jung, J. Kim, S. Oh, J. Park, S. Kim, W. Kim, H. Jeon. *Kangnam St. Mary's Hospital, The Catholic Universi, Department of Surgery, Seoul, Korea*

Background: Gastrointestinal stromal tumors are the most common mesenchymal tumors and express CD117. But the prediction of the malignant potential of GISTs is still difficult. The aim of this study is to evaluate the prognostic accuracy of elevated Ki67 index and p53 overexpression in combination with classical prognostic factors(tumor size and mitotic index.
Material and Methods: A retrospective study was conducted of 84 patients who had re-evaluated to confirm diagnosis based on immunohistochemical analysis with CD117 expression, between Jan 1991 and Dec 2001. Cases were classified and very low, low, intermediate and high risk group according to 2001 NIH consensus symposium. Elevated Ki67 index was assign to the lesion that displayed 10% or more of immunoreactive cells. And p53 expression is assign to the area with 5% or more of eosinophilic nucleus.
Results: The elevated Ki67 was noted in 37 (44.0%) out of 84 cases. High risk patients showed elevated Ki67 index frequently ($P < 0.0001$) and there was significant difference between elevated Ki67 and survival rate ($P = 0.0417$). The p53 expression was noted in 32 (38.1%) out of 84 cases. p53 expression was significantly higher in high risk patients ($P = 0.0081$). But, there was no significant difference between p53 expression and survival rate. As a result of multivariable analysis, tumor size ($P = 0.0059$), mitotic rate ($P = 0.0016$) and elevated Ki67 index ($P = 0.0384$) were proved as significant independent prognostic factors.