Su1984

Long Term Prognosis After Non-Curative Endoscopic Submucosal Dissection for Gastric Cancer

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Objective Endoscopic Submucosal Dissection (ESD) has been accepted and established as a standard treatment for early gastric cancer (EGC) without distant metastasis. With increase of elderly population, many aged patients have chance to receive ESD for their EGC. However, some patient resulted in unsuccessful non-curative ESD, and followed-up without additional surgery by limitation of various risks of comorbid disease and low performance status or patients' refusal for additional treatment. The aim of the present study is to assess the long-term clinical outcomes of non-curative ESD with or without additional surgery and effect of additional surgery for non-curative ESD. Methods We reviewed chart data on all patients who had undergone ESD for EGC at two foundation hospitals of Saga Medical school hospital and Saga prefectural Hospital between 2001 and 2012. A total of 957 cases (1047 lesions) of EGC underwent ESD, and a total of 99 cases resulted in non-curative ESD. We excluded 20 cases because un-enough follow-up period less than 36 months. As to the target 79 cases, we divided into observation group and additional surgery group. We compared overall and disease-specific survival rate between two groups Results After unsuccessful non-curative ESD, 28 patients (35.4%) underwent additional surgery and 51 patients (64.6%) were followed without surgery. Average age of patients without additional surgery was higher than that of additional surgery group (75.8 y.o. vs. 71.6 y.o.; P=0.03). There was no significant difference in gender ratio. The incidence of complicated hypertension was significantly higher in the observation group compared to additional surgery group (49.0% vs. 25.9%; P=0.04). Incidence of other comorbid diseases, such as cardiac disease, cerebrovascular disease, chronic liver disease, chronic kidney disease, and diabetes did not differ between the two groups. There was no significant difference in pathological feature except for ulcer findings. Mean follow-up period of patients with additional surgery was 60.2 months and that of patient observation alone was 57.0 months. Overall survival rate of additional surgery group was longer than observation group. However, only one patient died from gastric cancer in the observation group. Main causes of death were their comorbid diseases. Disease-specific survival rate was not significantly different between the two groups. Conclusions It is acceptable to follow up without additional surgery for EGD patients with comorbid disease and low performance resulted in non-curative ESD.

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Impact of Surveillance Interval in Patients Who Underwent Radical Gastrectomy for Gastric Cancer

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Background: Although patients who undergo gastrectomy for gastric cancer are recommended to be followed up systematically, benefits of surveillance imaging study with short interval have not been evaluated. We aimed to clarify whether short-term surveillance would help to increase post-recurrent survival or overall survival. **Methods:** We retrospectively reviewed the clinical records of patients who underwent radical gastrectomy with R0 resection for gastric cancer between January 2006 and December 2008. In order to determine intra-abdominal recurrences and surveillance intervals, we evaluated dates that esophagogastroduodenoscopy and abdominal computed tomography (CT) scan were performed. **Results:** Of 2,792 patients who underwent radical gastrectomy with R0 resection for gastric cancer, 32 and 383 showed recurrences at stomach and abdomen other than stomach, respectively. The median follow-up duration was 58.7 months (interquartile range, 29.9-68.6 months). In terms of recurrence at stomach, 5-year disease-free survival was 98.6% (95% confidence interval (CI), 98.1-99.1%). In cases of recurrence at abdomen other than stomach, 5-year disease-free survival was 85.0% (95% CI, 83.6-86.5%). Multivariable analyses showed that cancer stage and recurrence time were independently associate factor for both post-recurrent and overall survival in patients with recurrence at abdomen other than stomach. However, surveillance interval did not affect both post-recurrent and overall survival in patients with recurrence at abdomen other than stomach (hazard ratio (HR) [95% CI] for death after recurrence: ≤3 months, 0.985 [0.710-1.365]; 3-6 months, 1.032 [0.770-1.381]; 6-12 months, reference; HR [95% CI] for death after gastrectomy: ≤3 months, 0.996 [0.719-1.380]; 3-6 months, 1.024 [0.762-1.376]; 6-12 months, reference). **Conclusion:** Short-term surveillance imaging study within 3 months or 6 months in patients who underwent gastrectomy with R0 resection for gastric cancer increased neither post-recurrent survival nor overall survival. Prognosis of patients with gastric cancer depended on cancer stage and recurrence time rather than surveillance interval.

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Epigenetic and Genetic Inactivation of the E-Cadherin Gene in Sporadic Diffuse-Type Gastric Garcinoma

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E-cadherin is a calcium dependent cell-cell adhesion glycoprotein comprised of five extracellular cadherin repeats, a transmembrane region and a highly conserved cytoplasmic tail. Loss of E-cadherin has been observed in a variety of human carcinomas. It is well accepted that loss of expression of E-cadherin might contribute to the diffuse phenotype of Gastric Cancer. Furthermore, abundant evidence links a great variety of germ-line mutations of CDH-1 gene to the development of hereditary diffuse-type gastric carcinoma (HDGC). However the mechanisms of this inactivation in sporadic diffuse-type gastric carcinoma (SDGC) are unknown. To identify a major silencing mechanism in SDGC, we evaluated 32 SDGCs cases by immunohistochemical, mutational and methylation-specific PCR analysis. Among SDGCs, total loss of E-cadherin expression or aberrant pattern (granular cytoplasmic staining) was observed in 10 (31%) cases. Mutational analysis revealed 2 polymorphisms (codon 751 CxT and codon 879 CxT), 2 intronic mutations (Int 2 TxG and Int 15 CxG) and only 1 point mutation (codon 824 GxT). Aberrant hypermethylation of the CDH-1 promoter region, by methylation-specific PCR, was found in all cases with loss of E-cadherin expression. This was also observed in 9 out of 20 (45%) cases with no loss of E-cadherin expression. Taken together, aberrant hypermethylation of the CDH-1 promoter region was observed in 59% (19) of all cases. Our results show that aberrant hypermethylation of the CDH-1 promoter region is the most common mechanism of inactivation of E-cadherin gene in SDGC and that mutation is an infrequent event. In addition, the presence of aberrant cytoplasmic staining suggests a post-transcriptional mechanism of inactivation for CDH-1 gene. Grant Support: Fondap 15130011 and Fondecyt 1111014 from CONICYT-Government of Chile to AH Corvalan

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Methylated Reprimo in Cell-Free DNA (RPRM) in Comparison With CEA and CA 19-9 As a Tumor Marker in Gastric Cancer

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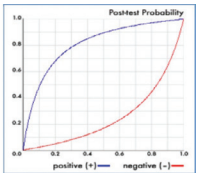
Background: Gastric Cancer (GC) is still a big problem of public health due to delay in the diagnostic. The non-invasive detection in blood has great advantages compared with invasive screening programs. However most of the available blood tumor markers such as CEA and CA 19-9 have poor specificity and sensitivity.. We performed analysis of RPRM in plasma in patients with GC and healthy controls and compare it with CEA and CA19-9 levels. Our outcome was looking a more valuable tumor marker of GC than CEA and CA19-9. **Methods:** A total of 31 healthy controls and 39 patients with GC were enrolled in this study. Peripheral blood samples were collected in GC and control subject (CS). DNA was purified from 0.5 mL of plasma by QIAamp DNA Blood Mini Kit (Qiagen), according to manufacturer's instructions. 20uL of previously extracted DNA underwent bisulfite conversion by del EZ ADN Methylation-GoldTM Kit (Zymo Research, according to manufacturer's instructions. For each sample, bisulfite-converted DNA was used for Reprimo (RPRM)-specific assay Methylight. Methylight primers and probes were obtained from integrated DNA technologies (IDT). CEA and CA19-9 were measured by ELISA in plasma of GC patients. Sensitivity, specificity, Predictive Positive Value (PPV), Negative Predictive Value (NPV) and likelihood ratio (LR) were calculated through test diagnostic strategy and compared between RPRM, CEA and CA19-9. **Results:** Among 39 patients with histological diagnoses of GC, average age was 64 y.o.(38-81 y.o.), male/female ratio 1.3/1, with stages I to IV. Patients were treated total gastrectomy, palliative chemotherapy and neoadjuvant chemotherapy. RPRM, CEA and CA19-9 were altered in 82, 18 and 20% of plasma of GC patients. RPRM was elevated in 10% of healthy controls. Relative to RPRM, the post-test probabilities were: the sensitivity was 82% (0.673 to 0.91), the specificity 90% (0.751 to 0.967), PPV 92% (0.776 to 0.97), PNV 8% (0.641 to 0.9) LR(+) 8,479 (2.864 to 25.102) and LR (-) 0.199 (0.101 to 0.393) (Table 1 and Figure 1). **Conclusions:** RPRM was better that CEA and or CA19-9 for non-invasive diagnosis of GC. The sensitivity, specificity, PPV, PNV, and LR positive may suggest the development of a large trial to evaluate the diagnostic efficacy of RPRM for non-invasive diagnosis of GC.

Post-Test probability RPRM	Estimate	95% CI
Sensitivity	0.821	[0.673 to 0.91]
Specificity	0.903	[0.751 to 0.967]
PPV	0.914	[0.776 to 0.97]
NPV	0.8	[0.641 to 0.9]
LR+	8.479	[2.864 to 25.102]
LR-	0.199	[0.101 to 0.393]



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Establishment and Characterization of Isogenic Invasive Subclones From a Gastric Cancer Cell Line

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Background: Investigating the mechanisms of gastric cancer invasion is an important issue clinically and scientifically. However, previous *in vitro* studies were based on genetically heterogeneous cell lines. In the present study, we aim to establish and characterize isogenic invasive subclones from a single gastric cancer cell line. **Experimental design:** The AGS cells were used as the parental cell line. We used the Matrigel Invasion Chambers to select the invading cells repeatedly. The collected invading cells were denominated as IN-1, IN-2, through IN-10, according to their generations of invading through the Invasion Chambers. The migration, invasion, cell proliferation, colony formation, and soft agar colony forming assay were used to examine the characteristics of these selected isogenic cells. Then we injected these selected cells into BALB/c mice to confirm their invasive characteristics. **Results:** We found the isogenic subclones had faster migration ability (up to 50% increase), higher invasive speed (up to 5 folds), faster cell proliferation rate (up to 6 folds), and more colony forming (up to 4.5 folds) compared with their parental AGS cells. The later isogenic subclones had more invasive characteristics. In the tumorigenicity assay, we found the IN-2, IN-6, IN-10 subclones had higher soft agar colony forming speed compared to AGS cells, with an incremental trend. In the xenograft experiments, we injected AGS cells and IN-10 cells subcutaneously into BALB/c mice. We found IN-10 cells injection led to higher successful rate of tumor development in BALB/c mice (80%) compared to the AGS cells injection (0%). Conclusion: Through the Matrigel Invasion Chamber selection, we have established serial isogenic subclones with an incremental invasive ability. These subclones are helpful for future studies of gastric cancer invasiveness.