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GASTROINTESTINAL NEWS

Newsletter di aggiornamento sui tumori gastrointestinali

GASTROINTESTINAL NEWS nel 2007 si presenta rinnovato sia nella veste che nel contenuto. Nato per iniziativa del comitato scientifico e coordinato da Intermedia, mantiene la pubblicazione quindicinale e continua ad occuparsi di cancro gastrointestinale. Le news non verranno più tradotte in italiano, ma pubblicate in lingua inglese e, una volta al mese, verrà proposto un commento su un particolare articolo, preparato da un componente del comitato scientifico.

NEWS DALLA RICERCA

American Joint Committee on Cancer Staging System Does Not Accurately Predict Survival in Patients Receiving Multimodality Therapy for Esophageal Adenocarcinoma
Journal of Clinical Oncology 2007; Volume 25, No 5 (February 10): Pages 507-512 (abstract)

Gene Expression Signature in Advanced Colorectal Cancer Patients Select Drugs and Response for the Use of Leucovorin, Fluorouracil, and Irinotecan
Journal of Clinical Oncology 2007; Volume 25, No 7 (March 1): Pages 773-780 (abstract)

Prognostic and Predictive Roles of High-Degree Microsatellite Instability in Colon Cancer: A National Cancer Institute–National Surgical Adjuvant Breast and Bowel Project Collaborative Study
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Cigarette smoking and the risk of colorectal cancer among men: a prospective study in Japan
European Journal of Cancer Prevention April 2007; Volume 16 Issue 2: Pages 102-107 (abstract)

Results following resection for stage IV gastric cancer; are better outcomes observed in selected patient subgroups?
Journal of Surgical Oncology 2007; Volume 95, Issue 2, 1 February: Pages 118 - 122 (abstract)

APPUNTAMENTI

SECONDO CORSO NAZIONALE per il TEAM ONCOLOGICO di APPROFONDIMENTO sugli STRUMENTI ORGANIZZATIVO-GESTIONALI (leggi)

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NEWS DALLA RICERCA

American Joint Committee on Cancer Staging System Does Not Accurately Predict Survival in Patients Receiving Multimodality Therapy for Esophageal Adenocarcinoma

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Journal of Clinical Oncology 2007; Volume 25, No 5 (February 10): Pages 507-512

Purpose: In patients with adenocarcinoma of the esophagus who receive preoperative chemoradiotherapy (CRT), American Joint Committee on Cancer (AJCC) stage, pathologic complete response (pCR), and estimated treatment response are various means used to stratify patients prognostically after surgery. However, none of these methods has been formally evaluated. The purpose of this study was to establish prognostic pathologic variables after CRT.
Patients and methods: A retrospective review was performed of patients with esophageal adenocarcinoma who received CRT before esophagectomy. Data collected included demographics, CRT details, pathologic findings, and survival. Statistical methods included recursive partitioning and Kaplan-Meier analyses.
Results: Two hundred seventy-six patients were appropriate for this analysis. Kaplan-Meier analysis indicates that the current AJCC system poorly distinguishes between stages 0 to IIA ($P = 0.52$), IIB to III ($P = 0.87$), and IVA to IVB ($P = 0.30$). The presence of a pCR conferred improved survival over residual disease ($P = 0.01$). Recursive partitioning analysis indicates that involved lymph nodes and metastatic disease are the best predictors of survival and that depth of invasion and degree of treatment response are less predictive.
Conclusion: The current AJCC staging system is not a good predictor of survival after CRT. Although patients with a pCR do have improved long-term survival relative to patients with residual disease, this method places too much emphasis on residual depth of invasion and fails to identify patients with residual disease who have good long-term survival. Recursive partitioning analysis more accurately identifies nodal disease and metastatic disease as the most important prognostic variables. Degree of treatment response is less prognostic than nodal involvement.

TOP

Gene Expression Signature in Advanced Colorectal Cancer Patients Select Drugs and Response for the Use of Leucovorin, Fluorouracil, and Irinotecan

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Journal of Clinical Oncology 2007; Volume 25, No 7 (March 1): Pages 773-780

Purpose: In patients with advanced colorectal cancer, leucovorin, fluorouracil, and irinotecan (FOLFIRI) is considered as one of the reference first-line treatments. However, only about half of treated patients respond to this regimen, and there is no clinically useful marker that predicts response. A major clinical challenge is to identify the subset of patients who could benefit from this chemotherapy. We aimed to identify a gene expression profile in primary colon cancer tissue that could predict chemotherapy response.
Patients and Methods: Tumor colon samples from 21 patients with advanced colorectal cancer were analyzed for gene expression profiling using Human Genome GeneChip arrays U133. At the end of the first-line treatment, the best observed response, according to WHO criteria, was used to define the responders and nonresponders. Discriminatory genes were first selected by the significance analysis of microarrays algorithm and the area under the receiver operating characteristic curve. A predictor classifier was then constructed using support vector machines. Finally, leave-one-out cross validation was used to estimate the performance and the accuracy of the output class prediction rule.
Results: We determined a set of 14 predictor genes of response to FOLFIRI. Nine of nine responders (100% specificity) and 11 of 12 nonresponders (92% sensitivity) were classified correctly, for an overall accuracy of 95%.
Conclusion: After validation in an independent cohort of patients, our gene signature could be used as a decision tool to assist oncologists in selecting colorectal cancer patients who could benefit from FOLFIRI chemotherapy, both in the adjuvant and the first-line metastatic setting.

TOP

Prognostic and Predictive Roles of High-Degree Microsatellite Instability in Colon Cancer: A National Cancer Institute–National Surgical Adjuvant Breast and Bowel Project Collaborative Study

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Journal of Clinical Oncology 2007; Volume 25, No 7 (March 1): Pages 767-772

Purpose: The role of high-degree microsatellite instability (MSI-H) as a marker to predict benefit from adjuvant chemotherapy remains unclear.

Patients and Methods: To help define its impact, we conducted an analysis of National Surgical Adjuvant Breast and Bowel Project (NSABP) patients who were randomly assigned to a surgery-alone group (untreated cohort) and patients assigned to an adjuvant fluorouracil (FU) -treated group (treated cohort). MSI-H and other potential markers were assessed (*TGF-BRII*, p53, thymidylate synthase, and Ki67)

Results: In all, 98 (18.1%) of 542 patients exhibited MSI-H, and there was a strong inverse relationship between MSI-H and mutant p53 status ($P < 0.001$). The prognostic analyses showed increased recurrence-free survival (RFS) for MSI-H patients versus MSS/MSI-L patients ($P = 0.10$), but showed no difference in overall survival (OS; $P = 0.67$). There was a potential interaction between MSI-H and mutant p53 in terms of improved RFS ($P = 0.03$). In the predictive marker analysis, we observed no interaction between MSI status and treatment for either RFS ($P = 0.68$) or OS ($P = 0.62$). Hazard ratios (HR) for RFS for MSI-H versus MSS/MSI-L patients were 0.77 (95% CI, 0.40 to 1.48) in the untreated-patients group and 0.60 (95% CI, 0.30 to 1.19) in the treated-patients group. HRs for OS were 0.82 (95% CI, 0.44 to 1.51) and 1.02 (95% CI, 0.56 to 1.85) for the respective groups. There was a trend toward improved RFS in patients with MSI-H and mutant p53.

Conclusion: These results do not support the use of MSI-H as a predictive marker of chemotherapy benefit.

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Cigarette smoking and the risk of colorectal cancer among men: a prospective study in Japan

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European Journal of Cancer Prevention April 2007; Volume 16 Issue 2: Pages 102-107

*Abstract***:** The association between cigarette smoking and the risk of colorectal cancer remains controversial. We examined this association using a population-based prospective cohort study in Miyagi, Japan. In 1990, we delivered a self-administered questionnaire on cigarette smoking and other health habits to 25 279 men who were 40-64 years of age and lived in 14 municipalities of Miyagi Prefecture. A total of 22 836 men responded (90.3% response rate). During 7 years of follow-up (158 376 person-years), we identified 188 patients of colorectal cancer. Relative risks and 95% confidence intervals were estimated by the Cox proportional-hazards regression analysis with adjustment for potential confounders. The multivariate-adjusted relative risks (95% confidence interval) of colorectal cancer for past smokers and current smokers compared with those who had never smoked were 1.73 (1.04-2.87) and 1.47 (0.93-2.34), respectively. Among current smokers, both a higher number of cigarettes smoked per day and an earlier age at which smoking had started were associated with a significant linear increase in risk (P for trend <0.05). Our findings are consistent with the hypothesis that cigarette smoking is associated with a higher risk of colorectal cancer in men.

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Results following resection for stage IV gastric cancer; are better outcomes observed in selected patient subgroups?

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Journal of Surgical Oncology 2007; Volume 95, Issue 2, 1 February: Pages 118 - 122

Background Patients who present with stage IV gastric cancer are not commonly managed with surgical resection as effective palliation can usually be accomplished with systemic chemotherapy, endoscopic stenting, or surgical bypass procedures. Given the inherent morbidity and mortality associated with gastrectomy, palliative resection for stage IV gastric cancer should be reserved for ideal surgical candidates who are most likely to benefit from the procedure. The purpose of this study is to review outcomes following resection for stage IV gastric cancer, and to identify criteria predictive of improved outcomes following gastrectomy in this setting.
Methods A retrospective review of a prospective GI oncology database was conducted. Sixty-three patients with stage IV gastric cancer managed with surgical resection between 1989 and 2001 were identified. Variables including demographic data, patterns of distant spread (ex: peritoneal, lymphatic, hematogenous), location of tumor, and type of gastrectomy were utilized to conduct survival analyses.
Results Actuarial survival for all patients at one and 3-year intervals was 52% and 12%, respectively. Improved survival was observed for patients of East Asian race (median survival 20 vs. 12 months, $P < 0.05$, students *t*-test) and age less than 60 years (median survival 15 vs. 12 months, $P < 0.05$). This trend was also illustrated by Kaplan-Meier survival analysis. Other variables including pattern of distant spread, location of tumor, and type of gastrectomy were not associated with a significant difference in survival. Both East Asian race and age less than 60 years were statistically significant predictors of improved survival when assessed by univariate regression analysis. When variables were analyzed in a multivariate regression analysis, Asian race and age <60 both lost their statistical significance as independent predictors of improved survival.
Conclusions Long-term survival for patients with stage IV gastric cancer who are managed with surgical resection is achievable. Patient specific variables including East Asian race and age less than 60 years appear to be associated with prolonged survival when assessed by comparison of means, Kaplan-Meier analysis, and univariate regression analysis. However, multivariate regression analysis failed to demonstrate these factors as independent predictors of improved outcome. In conclusion, highly selected acceptable risk surgical candidates with stage IV gastric cancer should be considered for management with surgical resection in clinically appropriate scenarios.

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