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Claudin-4/E-cadherin Index to Predict Prognosis in Breast Cancer

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Background: Different expression of claudins and E-cadherin was described in pathologic processes including cancer. Elevated expression of claudin-4 was found to correlate with poor prognostic features in adenocarcinomas of different origin.
Patients and Methods: Expression of claudin-1, -3, -4, -5, -7, -8, -10, -15, -18 and E-cadherin at mRNA level was evaluated for correlation with survival in datasets containing expression measurements of 1809 breast cancer patients. Another training set of breast cancer tissues of 197 patients were evaluated with tissue microarray technique and immunohistochemical method for claudin-1, -2, -3, -4, -5, -7 and E-cadherin protein expression. 387 independent samples were used to evaluate the performance of the claudin-4/E-cadherin (CC) index.
Results: Expression of certain claudins bears prognostic information in itself. The meta-gene of claudin-3, -4, -7 and E-cadherin has shown the most powerful predictive power for survival analyses in silico. An immunohistochemical protein profile consisting of claudin-2, -4 and E-cadherin was able to predict outcome in the most effective manner in the tissue based training set. Combining the overlapping members of the distinct methods resulted in the CC index, which was able to accurately predict relapse-free survival in the validation cohort ($p = 0.029$) in a more efficient way than its components (claudin-4, E-cadherin).
Conclusion: The defined claudin-cadherin index provides additional prognostic information besides the routinely utilized diagnostic approaches and factors.
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Treatment-related Changes in Systemic Inflammatory Status, Measured by Neutrophil-to-lymphocyte Ratio, is Predictive of Outcome in Metastatic Colorectal Cancer Patients

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Background: Systemic and local tumour-associated inflammatory status plays a key role in tumour growth and progression in colorectal cancer. Experimental evidences suggest that different myeloid derived cells associated with inflammation, such as neutrophils and macrophages, activate different cytokine/chemokine networks which in turn are able to promote tumour-escape from host's adaptive immunity, tumour growth and neo-angiogenesis. In this contest, we investigated, in metastatic colorectal cancer (mCRC) patients, the prognostic role of several clinical, laboratory and inflammatory-related parameters.
Material and Methods: In this retrospective multicentric study, including 247 mCRC patients who had received at least a line of chemo/bio-chemotherapy, we evaluated possible correlations among overall survival (OS), progression-free survival (PFS) and multiple parameters including sex, age, performance status, grading, serum CEA, CA19.9, LDH and CRP concentrations, ESR, lymphocyte, neutrophil and monocyte counts and neutrophil-to-lymphocyte ratio (NLR) at baseline and after six chemo/bio-chemotherapy courses. Kaplan Meier curves, Log-Rank test and Cox's regression analysis were used to perform statistical analysis.
Results: Median PFS and OS in the whole group were 9.0 (95% CI 7.794–10.206) months and 22.3 (95% CI 19.932–24.668) months respectively. Multivariate analysis revealed a significant prognostic value only for performance status (HR: 1.604; $p = 0.045$), serum CEA concentration (HR: 2.284; $p = 0.001$) and NLR (HR: 1.767; $p = 0.004$). Furthermore, in our statistical analysis the reduction of NLR under 3 during the treatment, predicted a significantly longer time to event when compared with those who did not show such reduction [21.5 (95% CI 19.171–23.763) vs 11.0 (95% CI 6.063–15.937) months; $p = 0.004$; HR: 2.009 vs 4.262, $p < 0.001$]. In the whole patient population, we were not able to find any correlation among PFS and treatment-related changes in NLR; however, those patients who presented NLR >3 at baseline, showed the worse treatment-related outcome. These events were independent by the kind of treatment regimen adopted for these patients.
Conclusions: These results suggest that possible treatment-related changes in systemic inflammatory status, indirectly measured throughout NLR, may affect prognosis of mCRC patients.

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Comparison of Prognostic Impact of Circulating Tumour Cells, Tumour Markers, and Radiological Tumour Assessment in Patients With Small-cell Lung Cancer

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Background: Little is known about the prognostic impact of circulating tumour cells (CTCs), tumour markers, and radiological tumour assessment in patients with small-cell lung cancer (SCLC).
Materials and Methods: In total, 51 consecutive patients with newly diagnosed SCLC, starting chemotherapy or chemoradiotherapy, were prospectively enrolled. Blood samples were drawn at baseline and after 1st-line chemotherapy. CTCs were isolated using the CellSearch System (Veridex LLC). Tumour response was assessed by RECIST criteria.
Results: Two or more baseline-CTCs were detected in 35 patients (68.6%). Area under the receiver operating curve (AUROC) for predicting 1-year survival was 0.8 (0.6−0.9) for baseline-CTC, 0.7 (0.5−0.8) for NSE, 0.5 (0.3−0.7) for Pro-GRP, and 0.7 (0.5−0.8) for radiological staging ($P = 0.018$). The Cox proportional-hazards ratios (HR) were 10.0 (3.3–37.2), 2.9 (0.9−7.9), 1.7 (0.4−5.4), and 3.6 (1.4–10.5), respectively. At post-treatment period, AUROC for predicting 6-months post-treatment survival was 0.7 (0.4−0.9) for post-treatment CTC, 0.8 (0.6−0.9) for NSE, 0.7 (0.4−0.9) for ProGRP, and 0.8 (0.6−0.9) for radiological tumour response ($P = 0.580$). HRs were 3.2 (1.0−8.9), 7.3 (2.5–26.4), 3.4 (1.2−9.8), and 7.0 (2.4–25.2), respectively.
Conclusions: CTC-count is sensitive and specific prognostic factor especially for the baseline measurement when compared with tumour markers and radiological tumour assessment.

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Prognostic Factors and Patterns of Recurrence After Resection of Primary Desmoids − a Single-institution Experience Over 10 Years

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Background: Local control of desmoids remains a significant problem, with the average recurrence rate of 24−77% no matter what therapeutic modality used. The aim of this study was to analize the prognostic factors for recurrence after macroscopically radical resection of desmoid tumours.
Material and Methods: From 2000 to 2010 40 patients (12 males, 28 females; mean age 37.6 years, range 16−69 years) underwent macroscopically radical removal of a primary desmoid tumour at the European Institute of Oncology, Milan. Tumour arose from the trunk wall in 27 cases (68%), from lower extremity in 5 (12%), from head and neck in 4 (10%), and was intrabdominal in another 4 (10%). Kaplan-Maier curves were employed to calculate actuarial disease-free survival (DFS) with comparison between groups using the log-rank test.
Results: In 32 patients pathological examination revealed a R0 situation and R1 in the remaining 8 (20%). Six patients developed tumour recurrence after a median 48 months follow-up period but no deaths caused by disease progression were registered. In 2 cases recurrence was at the surgical site and in 4 patients within the same anatomical region but not immediately near the surgical site. Five-years DFS was 76% for the whole group of patients. At univariate analysis only R0 vs R1 surgery (89% vs 45% 5-years DFS respectively; $p = 0.025$) and maximum tumour diameter $\geqslant$10 cm vs <10 cm (85% vs 33% 5-years DFS respectively; $p = 0.025$) were significantly correlated to DFS. According to desmoid location 5-years DFS rates were 81% for trunk vs 60% lower extremity vs 100% head and neck vs 66% intrabdominal ($p = 0.52$).