

New model predicts patient survival after surgical resection for gastric cancer

A new prediction model has been developed by a team of researchers in Taiwan that uses gene expression profiling to predict patient survival after surgery for gastric cancer. As gastric cancer is one of the most common cancers and prognosis varies greatly for patients with different stages of the disease, the development of an accurate and reliable method to diagnose and predict outcome could help direct therapy more appropriately.

Chen *et al.* constructed a cDNA microarray that was used to profile 328 genes in RNA samples obtained from 18 patients with gastric cancer. Before the analysis, the patients were categorized according to their survival after surgery: good (>30 months; nine patients) and poor (<12 months; nine patients). Genes were identified that most accurately predicted outcome; the microarray data were used to develop a prediction model based on expression of three genes (*CD36*, *SLAMF1* and *PIM1*). The sensitivity and specificity of the prediction model were assessed in an independent cohort of 30 patients and were 73.3% and 80%, respectively. A positive prediction value of 75% and a negative prediction value of 78.57% were recorded. Furthermore, the model was shown to predict survival in patients more accurately than traditional staging methods. Larger prospective studies are needed to confirm the findings of this study and determine the clinical impact of this model for the diagnosis and treatment of gastric cancer patients.

Rachel Jones

Original article Chen C-N *et al.* (2005) Gene expression profile predicts patient survival of gastric cancer after surgical resection. *J Clin Oncol* 23: 7286–7295

Screening for hereditary hemochromatosis in the primary-care setting

Hereditary hemochromatosis is a common genetic disorder, and interest in the implementation of a screening program for this condition in the general population is increasing. The overall benefit of such a program, however, is not clear. This is mainly owing to the lack of

available evidence on the natural history and prevalence of the disease, the efficacy of treatments, and the accuracy of diagnostic tests (both phenotypic and genetic). A systematic review by Schmitt *et al.* and a corresponding set of guidelines by Qaseem *et al.*, both published on behalf of the American College of Physicians, highlight the need for greater clarity regarding this disorder and present some useful information regarding its management in the primary-care setting.

In their systematic review, Schmitt and colleagues performed a MEDLINE search for all literature relating to hereditary hemochromatosis that was published between 1966 and 2004. Several key screening issues were examined: prevalence of the disorder within the primary-care setting; the burden of illness for patients who do not receive treatment; the diagnostic usefulness of phenotypic screening methods, such as percentage saturation of transferrin and serum ferritin levels; the efficacy of early treatment; and the benefits and risks associated with screening for the disorder. The prevalence of hereditary hemochromatosis within the primary-care setting was reported to be 0.18–0.59% (1:169–1:556) of patients screened. Furthermore, the disease seems to have a higher prevalence in white men >40 years old (0.37–0.46% [1:185–1:219]). With regard to diagnostic accuracy, levels of serum ferritin were found to be strongly predictive of the absence of cirrhosis: a serum ferritin level <1 mg/l was indicative of the absence of cirrhosis. The utility of genetic screening was not formally evaluated. Assessment of the efficacy of therapeutic phlebotomy and the overall cost-effectiveness of screening were limited, owing to a lack of published evidence. The study concluded there was insufficient evidence to show that the benefits of screening outweighed the risks and costs.

The set of accompanying guidelines by Qaseem *et al.* interprets the data accrued by Schmitt *et al.* and presents guidelines for primary-care physicians on the management of hereditary hemochromatosis. It states four key recommendations. First, owing to a lack of sufficient evidence, a decision cannot yet be reached on whether to recommend screening the primary-care population for this disorder. Second, serum ferritin should be measured and transferrin-saturation tests should be performed in diagnostic testing for the

disorder (a serum ferritin level $>200\ \mu\text{g/l}$ in women or $>300\ \mu\text{g/l}$ in men with a transferrin saturation $>55\%$ is indicative of disease). Third, in patients with an inherent risk of hereditary hemochromatosis or those with raised serum ferritin levels or transferrin saturation, clinicians should discuss the risks and benefits of genetic testing with patients. Finally, further clinical research into hereditary hemochromatosis should be undertaken.

The systematic review and guidelines go some way to clarify the usefulness of various diagnostic measures. Further research is, however, needed in order to gain a clearer understanding of the natural history of this disease, and to standardize diagnostic criteria.

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Original articles Schmitt B *et al.* (2005) Screening primary care patients for hereditary hemochromatosis with transferrin saturation and serum ferritin level: systematic review for the American College of Physicians. *Ann Intern Med* **143**: 522–536

Qaseem A *et al.* (2005) Screening for hereditary chromatinosis: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* **143**: 517–521

OncoSurge: rating treatment for patients with metastatic colorectal cancer

A recent paper in the *Journal of Clinical Oncology* reports on OncoSurge, a new computer-based decision model for the treatment of metastatic colorectal cancer. An international, multi-disciplinary team created this model using RAM to determine the appropriateness of resection,

chemotherapy, and local ablation, and various combinations of these three treatment options, in various clinical scenarios. Patients with metastatic colorectal cancer usually present to oncologists and general surgeons, either of whom may lack the specialist knowledge required for the management of this disease. OncoSurge was created to assist in the decision-making process, determine resectability, and identify an individualized optimal treatment strategy for each patient.

A panel of 16 oncologists, surgeons, and radiologists rated the appropriateness of each possible treatment option in terms of patient characteristics and indications—a total of 1,872 ratings. The rated treatment strategies were then assimilated into a computerized decision matrix—OncoSurge. The model was tested using real and theoretical cases by comparing the panel's modal treatment choice with the OncoSurge appropriateness rating. Of the 48 theoretical cases, the treatment strategy was validated in 37; therefore, in 23% of clinical situations the optimal therapeutic regimen was unclear, representing areas of scientific uncertainty upon which future clinical trials could be focused. The authors conclude that, by combining the best scientific evidence with expert opinion, OncoSurge can assist medical practitioners at the primary and secondary level of care to determine the most appropriate treatment strategy and identify candidates for resection among patients with metastatic colorectal cancer.

Alexandra King

Original article Poston GJ *et al.* (2005) OncoSurge: a strategy for improving resectability with curative intent in metastatic colorectal cancer. *J Clin Oncol* **28**: 7125–7134

GLOSSARY

RAM

The RAND corporation/
University of California, Los
Angeles Appropriateness
Method