Pancreatic Cancer: Recognizing an Hereditary Predisposition

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Genetic screening of at-risk groups, such as the Ashkenazi Jewish population and recognized high-risk families (such as shown in Figure 2), is the currently recommended genetic testing approach to identify patients at risk of hereditary cancer.[1,2] However, since genes such as BRCA2 have a relatively low penetrance for causing cancer, this approach will miss many carriers. Even the technically straightforward process of screening Ashkenazi Jewish patients with pancreatic cancer for the 6174 delT BRCA2 mutation[3] is limited by the fact that the Ashkenazi population harbors other BRCA2 mutations.[4]

Once technological advances permit, it might be preferable to screen all consenting pancreatic cancer patients for germline BRCA2 mutations. The main immediate benefit of such an approach would be to identify carriers at risk of breast and other cancers so that preventive measures could be initiated.

Finally, it is still not clear how carriers of germline BRCA2 mutations should be screened for cancer. Females who are BRCA2 carriers could be offered an appropriate breast and ovarian cancer screening regimen. Yet many BRCA2 carriers might inquire whether cancer screening protocols were available specifically to detect early pancreatic cancer.

Despite improvements in the imaging of the pancreas, the low penetrance and late age of presentation of pancreatic cancer in BRCA2 carriers imply that screening for pancreatic cancer is probably not currently justifiable. Using the predicted estimates of the sensitivity and specificity for a pancreatic cancer screening test, and a low estimated risk of pancreatic cancer in BRCA2 carriers, screening would yield far more false-positive than true-positive test results. Since a positive test would likely require confirmation with an invasive procedure, the consequences of a false-positive test are currently unacceptable. Furthermore, even a "confirmatory" test such as pancreatic biopsy currently suffers from low sensitivity.

The development of a highly sensitive and specific screening test to detect early pancreatic cancer would greatly benefit patients at risk of hereditary disease.

**Conclusion**

Over the next few years, technologic advances such as DNA chip technology[5] will facilitate the identification of hereditary cancer families. Legislation to protect carriers of germline mutations and regulatory controls to oversee genetic testing services are expected to be in place. These developments should enable clinicians to genetically screen the majority of consenting patients with cancer.

Along with these developments, it is anticipated that additional clinical data on the potential benefits and risks of offering genetic testing to families with cancer will become available to assist clinicians. For certain cancers, such as pancreatic cancer, cancer screening programs will need to be developed to diagnose presymptomatic neoplastic lesions before gene testing can hope to have an impact on pancreatic cancer morbidity.

Advances in molecular genetics are bringing the goal of reducing the mortality and morbidity of hereditary cancer closer to realization.

**References:**

1. The American Society of Human Genetics: Statement of the American Society of Human Genetics


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