Genetic mutations in BRCA or DNA-repair genes appear to favor longer survival in patients with pancreatic cancer

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Video Abstract

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Abstract

Pancreatic cancer is the fourth leading cause of cancer death among men and women and carries a poor prognosis; the percentage of patients living five years after diagnosis is just 5 to 10%. But certain patients with pancreatic cancer could fare better than others. A new study suggests that patients with a deficiency in genes responsible for responding to DNA damage could experience significantly superior outcomes compared with other patients following platinum-based chemotherapy. The findings support broader testing for germline mutations in patients with pancreatic cancer, as certain mutations could enhance the effects of anticancer therapeutics. The authors of the study reviewed medical records and genetic testing results to identify patients with pancreatic cancer who harbored mutations in DNA-damage response genes, including the breast cancer genes BRCA1 and 2. These genes help repair DNA breaks that can lead to cancer and uncontrolled tumor growth. Eleven patients matched the authors' search criteria, carrying a mutation in the genes BRCA-1 or -2, ATM, PALB2, and FANCC. Five patients had a prior history of other cancers. And four were still alive at the time of data review. Survival in the seven patients who had died ranged from approximately 14 months to more than 9 years. All patients with advanced disease had received platinum-based chemotherapy. Those survival figures are significantly longer than those reported in historical landmark studies, which range from 6 to 11 months for patients with metastatic pancreatic cancer. Response duration was also significantly longer than what's been reported, likely due to the patients' increased sensitivity to DNA-damaging drugs. An estimated 5 to 15% of all patients with pancreatic cancer harbor a detectable mutation in DNA-damage response genes. Based on the findings of the current study, that sizeable population could likely benefit from chemotherapies designed to eradicate tumors through DNA damage. The key is to detect these advantageous mutations with enough time to take action, which could present an obstacle to some patients. Insurance testing for germline mutations remains an issue despite guidelines endorsing universal testing for pancreatic cancer. Patient 2 of the current study, for example, was unable to complete such testing initially due to the high personal cost, even though they had a young diagnosis and a family history of pancreatic and other cancers. More work on larger samples across several institutions is needed to draw any definitive conclusions. But the overall message is clear. Universal germline testing should be required for all patients with pancreatic cancer; at the very least, somatic genetic testing should be made available for patients with advanced or metastatic cancer.