PANCREAS CANCER SCREENING STUDY UPDATE

As for other types of cancers, early detection is associated with a better prognosis or outcome. Unfortunately, the majority of pancreas cancer cases are diagnosed at late stages. This is mainly because the symptoms, if there are any, are non-specific. Different groups have been investigating various screening tools for detecting early stage pancreatic cancer, but unfortunately, there are no proven clinical screening recommendations available at this time.

The pancreas cancer screening program at Mount Sinai Hospital and the University Health Network in Toronto is an on-going study that began in 2003. The original goal of the study was to determine the effectiveness of MRI (magnetic resonance imaging) and transabdominal ultrasound for early detection of pancreatic cancer. We are looking for the most common type of pancreatic cancer, called adenocarcinoma. As of January 2009, we discontinued the use of abdominal ultrasound. This is based on previous findings that abdominal ultrasound does not detect potentially important pancreas lesions (abnormal changes) that have been identified on MRI.

Each participant is asked to return annually for magnetic resonance imaging (MRI) of the pancreas. Blood samples were being drawn at each visit and are now only being taken at the Year 1 baseline appointment. These samples will be used for future studies which may involve trying to find proteins (biomarkers) in the blood to aid in the detection and management of pancreatic cancer which will lead to improved outcomes for patients with this disease. Participants are also asked to complete questionnaires about environmental risk factors and psychosocial issues of interest, such as perceived risk of cancer and cancer related anxiety.

OBJECTIVES

Since primary prevention of pancreatic cancer is currently not possible, the key to improving survival rates of patients affected with pancreatic cancer will be to identify individuals who are at high risk of developing the disease and then detecting the disease at the earliest possible stage.

Our objective is to determine the effectiveness of abdominal ultrasound (currently discontinued) and magnetic resonance imagining (MRI) in detecting early stage pancreatic cancer in individuals identified at high risk for developing this disease.

INCLUSION CRITERIA

Our inclusion criteria were based on previous research describing groups at higher risk of pancreas cancer. These include individuals with familial pancreas cancer (FPC; at least two or more cases of pancreas cancer on the same side of the family), families with several well known hereditary cancer syndromes including hereditary breast and ovarian cancer, familial atypical multiple mole melanoma (FAMMM), Peutz-Jeghers Syndrome (PJS), and hereditary pancreatitis (HP). The genes corresponding to these syndromes are BRCA1 and BRCA2, p16, STK11, and PRSS1, respectively.

Familial Atypical Multiple Mole Melanoma (FAMMM): This inherited syndrome is associated with an increased risk for melanoma. Individuals with FAMM typically have numerous atypical nevi (moles) that are at risk of becoming melanoma. This syndrome is also associated with a slightly increased risk for pancreas cancer. Genetic testing is available.

Peutz-Jeghers Syndrome (PJS): This genetic syndrome is characterized by specific types of polyps called Peutz-Jeghers-type hamartomatous polyps, combined with specific patterns of skin pigmentation. PJS is associated with some cancer risks as well, including a very small increased risk for pancreas cancer. Genetic testing is available.

Hereditary Pancreatitis (HP): This is a genetic condition causing recurrent episodes of pancreas attacks consisting of abdominal pain, nausea and vomiting, and eventually chronic pancreatitis (inflammation of the pancreas). HP has also been linked to an increased lifetime risk of pancreatic cancer of up to 40%.

Hereditary Breast/Ovarian Cancer (*BRCA1* and *BRCA2*): Mutations in the *BRCA1* and *BRCA2* genes cause a hereditary breast/ovarian cancer syndrome. In addition to breast and ovarian cancers, individuals with *BRCA1/2* mutations also have an increased risk for pancreas cancer.

Eligible participants are asymptomatic and include:

1. individuals with FPC (≥2 blood relatives in the same lineage with pancreatic adenocarcinoma) who are in a first or second degree relationship to an affected case
2. BRCA2 or p16 carriers (family history of pancreatic cancer not required)
3. BRCA1 carriers (family history of pancreatic cancer required in at least one family member on the side at risk)
4. first degree relatives of individuals with multiple primary cancers (one is pancreatic)
5. individuals with a clinical diagnosis of Peutz-Jeghers Syndrome or with a known STK11 mutation
6. individuals with HP

Individuals are eligible to participate at age 50, or ten years younger than the youngest diagnosis of pancreatic cancer in the family for criteria 1-4, age 25 for PJS, and age 35 for individuals with HP.

GENETIC COUNSELLING

Genetic counselling is currently provided prior to the baseline MRI appointment; however participants have the option of speaking with a genetic counsellor at any point during the study. All participants are informed about the lack of clinical screening recommendations for pancreatic cancer, and have an opportunity to discuss the potential risks, benefits and limitations of the study protocol, general information about pancreatic cancer and familial pancreatic cancer, their estimated risk, and risk factors.

METHOD OF SCREENING

Abdominal Ultrasound (currently discontinued)

Pancreatic ultrasound is a safe, noninvasive imaging technique performed by placing an electrical device on the abdominal skin surface. Images are created with the use of high frequency sound waves. Scans were performed following a four hour fast. Standard abdominal curved array ultrasound probes were used on an ATL HDI 5000 or iU22 (Philips Medical Systems, Bothell, WA).

MRI

MRI is a safe and noninvasive technique used to obtain images of the body organs. The patient lies on a table that is surrounded by a cylindrical scanner that takes images with the use of a magnetic field. From 2003 to 2009, pancreatic MRI was performed on a 1.5T MRI system (Signa Excite HD, GE Medical Systems, Waukesha, WI, USA) using a four or eight channel surface phased array coil. The protocol was amended in January 2009 following installation of a stronger 3T MRI magnet and as a result, the abdominal ultrasounds were discontinued for all enrolled participants. The hardware for the 3T MRI, which was funded in part by generous donations from Pancreatic Cancer Canada, allows for a clearer and sharper image of the pancreas. By combining 3T technology and a new receiver coil under development in collaboration with Sentinelle Medical, also funded in part by generous donations from Pancreatic Cancer Canada, we can anticipate a 4-8 fold improvement in signal and a 2-4 fold improvement in image detail.

Follow Up

Participants with abnormal ultrasound and/or MRI results were followed by repeat ultrasound, MRI, and/or CT within three to six months.

NUMBER OF PATIENTS SCREENED/PATIENT CHARACTERISTICS

To date, 259 participants have been enrolled, with 196 subjects having undergone at least three sets of screening episodes. Ninety-one (35.1%) participants were recruited from our pancreatic cancer registry at Mount Sinai Hospital, 84 (32.4%) mutation carriers and PJS patients were recruited by mailings through the familial breast cancer, familial melanoma, and polyposis clinics, and 84 (32.4%) participants were self-referrals or referred by other physicians and local genetics clinics.

A total of 40 (15.4%) individuals dropped out of the study after at least one evaluation, 27.5% because participation was “too inconvenient”, 40% were non-responders, lost to follow up or were no longer interested in the study, and 12.5% were subsequently diagnosed with cancer, of which two were pancreatic adenocarcinoma.

We are no longer actively recruiting for the Pancreas Cancer Screening Study since we have almost reached enrollment capacity; however we have reserved a limited number of spots for high risk families that meet the inclusion criteria. We are hoping to increase the number of spots available for screening in the future so that we can actively enroll more participants.

FINDINGS

To date, two cases of pancreatic adenocarcinoma have been identified. One of these patients had surgery and is alive and well two and a half years later. Unfortunately, the other patient had more advanced disease detected and passed away a year ago. To our knowledge, no additional participants have been diagnosed with pancreatic cancer. Although the purpose of our screening study is to detect new pancreas adenocarcinomas, other cancer types that have been found during the study include a pancreatic neuroendocrine tumour, an ovarian cancer, a stomach tumour, and three kidney cancers. Benign pancreas lesions have been found in 15 patients and pancreas cysts in 79 patients. There is currently no consensus among surgeons and researchers when these benign pancreas lesions should be surgically removed; however all of these patients are being followed closely. One participant has had surgery to remove one of these benign lesions and is being followed annually.

FUTURE DIRECTIONS

The Pancreatic Cancer Screening Study has no foreseeable end date and we hope to enroll more participants in the future. Together with our other concurrent research, the objective of which is to identify environmental and genetic risk factors of pancreas cancer, we hope to identify the Familial Pancreas Cancer (FPC) gene(s) and genetic biomarkers which are urgently needed for disease detection and the improved clinical management of these patients. Once a genetic test for pancreas cancer is available, we will be able to screen the blood samples of the current participants to determine whether we are screening the correct cohort of individuals.

This study will lead to a better understanding of how pancreatic cancer can be detected at the earliest possible stage for individuals who are at increased risk for developing this disease. Detecting cancer early may also mean it is more likely to be curable which is the ultimate goal of this research.