Extended Abstract

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Pancreatic Cancer Screening: Attempts and Possibilities

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ABSTRACT

Pancreatic cancer has one of the highest disease specific mortality of any malignancy, despite significant advances in diagnosis and treatment over the past decade. Currently there are no efficient screening tools available that can be recommended outside a high-risk population. Screening of high-risk populations has been suggested for early detection of curable pancreatic cancer to improve outcome. There is still however, a lack of an ideal screening method. Efficient and reliable screening methods to achieve early detection of pancreatic cancer are therefore required.

Abbreviations: CT: Computed Tomography; EUS: Endoscopic Ultrsonography; FAMMM: Familial typical Multiple Mole Melanoma syndrome; FPC: Familial Pancreatic Cancer; HBOC: Hereditary Breast Ovarian Cancer; HNPCC: Hereditary Non-Polyposis Associated Colorectal Cancer; HP: Hereditary Pancreatitis; IPMN: Intraductal Papillary Mucinous Neoplasia; MRCP: Magnetic Resonance Cholangiopancreatography; PCMS: Pancreatic Carcinoma Melanoma Syndrome; PJS: Peutz Jeghers Syndrome Introduction Mortality rates for pancreatic cancer in developed nations steadily increased from 1950 to 1980. It is predicted that by 2030 pancreatic cancer will be the second leading cause of cancer mortality in the US In Europe, pancreatic cancer is the 7th most common cancer and accounts for around 138,100 global deaths a year in men and 127,900 deaths a year in women Baltic countries, and some central/eastern and northern European countries exhibit the highest incidence of pancreatic cancer in the world with rates of over 9.5 per 100 000 in men and 6 per 100 000 in women. Japan, the USA, Russia and the rest of Europe have similar incidence rates of around 7 to 9 per 100 000 men and 5 to 6 per 100 000 in women Pancreatic cancer carries a very bad prognosis despite advances in diagnosis and management; with an overall 1-year survival rate up to 28.3% From 2004 to 2010 the 5 year survival of patients diagnosed with pancreatic cancer in the US was 7%. His is a statistically signiٹcant improvement when compared to the seventies when the 5 year survival was as little as 3% however pancreatic mortality rates are markedly worse than most other malignancies Here are numerous factors why pancreatic cancer is synonymous with a terrible prognosis but the absence of clinical symptoms oien leads to late presentation. Patients oien have metastatic or unresectable disease at the time of primary presentation. Like all malignancies it is hoped that if a viable screening tool is available it may be possible to identify the precursor to invasive malignancy or early invasive malignancy. In turn interventions can be put in place to potentially improve survival. Currently screening for pancreatic cancer is limited to a very select population with a high risk of developing pancreatic malignancy. High risk individuals include those with hereditary pancreatitis who have a cumulative risk of 40% of developing pancreatic cancer which may increase further to 75% with a paternal inheritance pattern [6]. Hereditary pancreatitis is due to a defect in chromosome 7q35 that causes a mutation in trypsinogen which in turn predisposes patients to pancreatitis and pancreatic cancer. Peutz Jegher syndrome is associated with an 11% risk of pancreatic cancer at the age of . Hereditary breast and ovarian cancer syndromes, familial melanoma, and Lynch syndrome are all associated with an increased risk of pancreatic cancer. Screening at present for high risk populations includes a combination of both endoscopic ultrasound. (EUS) and magnetic resonance imaging (MRI) which are both expensive and invasive and therefore not appropriate for lower risk populations Ductal adenocarcinoma of the pancreas encompasses 80% of all pancreatic malignancies and therefore most malignancies are exocrine in origin. 5% to10% of patients have an underlying germ line disorder, while the remaining cases are thought to be caused by somatic mutations. Some individual studies suggest that mutations in various polymorphic genes can lead to small increases

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in the risk of pancreatic cancer, but these ثndings need to be replicated Mutation of KRAS is detected in more than 80% of pancreatic cancer. KRAS mutations are mostly a G12V or G12D mutation of which more than 80% exhibit deletions, mutations or epigenetic alterations principally the CDKN2 gene. Up to 50% of pancreatic cancers have mutations in the tumour suppressor gene p53 and 50% will also exhibit mutations or homozygous deletions in the DPC4/Smad4 gene

Keywords: Screening; Pancreatic cancer; Endoscopic ultrsonography; Magnetic resonance cholangiopancreatography; Hereditary cancer