

## HIGHLIGHT ARTICLE

# Pancreatic Cancer: New Hopes for Early Detection and a Future Screening Tool?

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### ABSTRACT

Given the overall poor prognosis of patients with pancreatic cancer, there has always been an interest in early screening and primary prevention. An abstract presented in ASCO 2014 by Orłowski et al. introduced the potential use of an elevated serum procarboxypeptidase A (PCPA) and high ratios of PCPA to free carboxypeptidase A (FCPA) in enhancing the diagnostic efficacy of pancreatic cancer either alone or with CA19-9 (Abstract #4118).

### Introduction

Early detection allows diagnosis at an earlier stage which translates into better survival. This principle applies to cancers in general and more so to aggressive cancer that are usually detected late, many times too late for any therapeutic intervention to result in a statistically significant improvement in overall survival.

Pancreatic cancer is the fourth leading cause of cancer deaths in women and men in the United States [1], eight leading cause of cancer deaths in men and ninth in women worldwide [2]. Recent statistics have shown that most patients die within one year after diagnosis [3], this is in part attributed to the late detection of this aggressive cancer. Based on that, several attempts have been made to come up with a reliable and cost effective tool that can help in screening for pancreatic cancer.

### What Did We Know Before ASCO 2014?

Up to this date, Carbohydrate Antigen 19-9 (CA 19-9) has been suggested to play a role in pancreatic cancer screening. A recently published meta-analysis, that included 2, 316 individuals, CA 19-9 had a pooled sensitivity of 0.80 (95% confidence interval [CI] 0.77-0.82) and specificity of 0.80 (95% CI 0.77-0.82), in detection of pancreatic cancer [4].

Other studies evaluated the utility of one time screening with MRI, CT scan and EUS in high risk asymptomatic individuals [5], or EUS and/or MRI with CA19-9 and genetic testing in patients with family history of pancreatic cancer [6]. These studies however did not show a cost effective

benefit in detection of pancreatic cancer, with yield of these screening modalities not being uniformly high [5-9].

The U.S. Preventive Services Task Force (USPSTF) recommended against screening for pancreatic cancer in the guidelines published in 1996 (level D recommendation). The subsequent statements have been revised based on current rating of the strength of evidence. In summary, there were no clear guidelines regarding diet-based prevention. It has been suggested however, based on expert opinion, that avoiding tobacco products and having moderate alcohol intake along with a balanced diet with good fruit and vegetable intake could be some lifestyle modifications that can help in prevention of pancreatic cancer [10]. There were no guidelines recommending screening for people with hereditary pancreatitis, even though it was suggested that they might be at a higher lifetime risk for pancreatic cancer [11].

### What Did We Learn at ASCO 2014?

In an abstract presented in ASCO this year, Orłowski et al. evaluated the use of an elevated serum procarboxypeptidase A (PCPA) and high ratios of PCPA to free carboxypeptidase A (FCPA) in potentially enhancing the diagnostic efficacy of pancreatic cancer either alone or with CA19-9 in an independent cohort [12].

The investigators conducted their study at Maya Clinic where pre-treatment serum from 224 participating subjects were collected (74 early and 75 late stage clinically and/or histologically proven pancreatic adenocarcinoma patients, with 75 healthy primary care controls). Of these patients, 111 were found to have a head lesion and the 38 other patients had a body/tail lesion. A newly automated method was used to measure PCPA and FCPA levels and all patients had CA19-9 measured as well. The cutoff used in the study for a cancer diagnosis was CA19-9 >55 and/or PCPA/FCPA ratio either <1 or >33, based on previous studies [12]. The study showed that, when used as single biomarkers, CA19-9 and PCPA/FCPA ratio have similar

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sensitivity (73.2 vs. 72.5, respectively), but specificity was higher for CA19-9 (98.7 vs. 78.7, respectively) [12]. Interestingly, further analysis showed that the use of both the PCPA/FCPA ratio and CA19-9 improves sensitivity (73.2% to 87.2%, McNemar's test p-value < 0.0001) when compared to CA19-9 alone, while specificity is decreased (98.7% to 82.7%, McNemar's test p-value = 0.0005) but with an increased overall accuracy relative to CA19-9 alone (81.7% to 85.7%). The authors concluded based on this blinded, single draw independent sample of a heterogeneous patient population, that the combination of the PCPA/FCPA ratio and CA19-9 has a higher sensitivity and specificity (87.2% and 82.7% respectively) as a screening tool for the early detection of pancreatic cancer in high risk patients.

## Discussion

Several attempts have been made to find effective ways to detect pancreatic cancer. The aim would be to implement these screening tests into the routine care of high risk patients, such as those with inherited cancer susceptibility syndromes and patients with hereditary pancreatitis, with the goal to detect noninvasive precursor lesions to pancreatic cancers at a curative stage. Despite all previous attempts at finding a reliable screening modality for pancreatic cancer, no study to date has shown improved survival [13]. Based on the literature that miRNAs (miRNA) are related to many different cancers including pancreatic cancers [14, 15] Ding et al. recently conducted a meta-analysis that reviewed the literature on the use of miRNAs as novel biomarkers as a screening tool for pancreatic cancer [16]. This meta-analysis included 2, 036 patients and 1, 444 controls and showed that the use of multiple miRNA for discriminating pancreatic cancer patients from healthy individuals had a pooled sensitivity of 82% (95% CI, 78–86%) and specificity of 77% (95% CI, 73–81%), suggesting a potential diagnostic value of miRNAs for pancreatic cancer.

Despite the best attempts, it remains a general consensus that the early diagnosis of pancreatic cancer remains a clinical challenge and further research is needed to validate the utility of the newly suggested assays and biomarkers in the literature that could be used in the future as a screening tool for early detection and possibly monitoring the treatment of pancreatic cancer.

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## Conflict of Interest

The authors have no conflicts to disclose.

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