

HIGHLIGHT ARTICLE

Clinical Outcome of Pancreatic Cancer Patients with Diabetes Mellitus: Is Diabetes a Poor Prognostic Factor?

Highlights from the “2010 ASCO Annual Meeting”. Chicago, IL, USA. June 4-8, 2010

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Summary

Diabetes mellitus and its related factors such as hyperinsulinemia have been linked to various cancer risks and outcomes. Previous research has offered inconsistent results in terms of relationship between diabetes and pancreatic cancers. Establishing clear association between these two entities may guide us in improving clinical outcomes of pancreatic cancer patients. Two abstracts that examined the association between diabetes mellitus and pancreatic cancer are updated in this paper. Herein, the authors report updated information from the 2010 American Society of Clinical Oncology (ASCO) Annual Meeting in association between pancreatic cancer and diabetes mellitus. The present paper illustrates insufficient knowledge base to draw a conclusion in this topic. However, validation and understanding of the association could have significant clinical implications with respect to cancer prevention, early detection, and treatment. As such, further investigations are warranted to explore the link diabetes and pancreatic cancers.

What We Knew Before ASCO 2010

Pancreatic cancer is one of the most lethal diseases in the United States. In year 2009, over 42,000 new cases were diagnosed and 35,240 patients did succumb to deaths due to pancreatic cancer [1]. Factors related to diabetes and insulin resistance, namely hyperglycemia and hyperinsulinemia, have often been associated with pancreatic cancer. However, the association remains unproven and poorly understood [2, 3, 4, 5].

Diabetes is considered a possible risk factor and/or a manifestation of early pancreatic cancer. A stronger relationship between pancreatic cancer and new onset diabetes (compare to long standing diabetes) suggests that type 2 diabetes might be an early clinical indicator of undiagnosed pancreatic cancer [6]. The majority of pancreatic cancer patients have unresectable disease at the time of diagnosis, and treatment outcomes of advanced pancreatic cancer with available chemotherapy agents remain poor. While the entity as common as diabetes will not be considered a screening

tool by itself, it may contribute to early diagnosis of pancreatic cancer when combined with other established risk factors.

A retrospective study by Busaidy *et al.*, showed that diabetes may be an independent prognostic factor in patients with resectable pancreatic cancers [7]. Busaidy *et al.* then sought translational implications by elucidating pathophysiology behind the association. Their *in vitro* study showed that hyperglycemia and hyperinsulinemia, both conditions commonly seen in diabetics, may promote pancreatic cancer growth and even confer resistance to gemcitabine. The study also suggested that metformin and rosiglitazone can be synergistic with gemcitabine by promoting apoptosis [8]. The study shows that epidemiological findings can be translated into effective interventions.

What We Leant at ASCO 2010

Evidence Against the Association between Diabetes Mellitus and Clinical Outcomes in Patients with Pancreatic Cancer

Olowokure *et al.* (Abstract #4114) conducted a retrospective study utilizing the Veterans Affairs Central Cancer Registry data accumulated between 1995 and 2008 in order to compare survival data between patients with and without diabetes mellitus [9]. In patients with stage I-IV pancreatic cancers, having diabetes mellitus did not confer worse prognosis, in fact diabetic had statistically significant superior median survival (Table 1) [9].

Key words Diabetes Mellitus; Pancreatic Neoplasms; Prognosis
Abbreviations AJCC: American Joint Committee on Cancer; ASCO: American Society of Clinical Oncology
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Table 1. Results of two retrospective studies presented at the 2010 ASCO Annual Meeting, examining association between diabetes mellitus and pancreatic cancer.

Abstract Author	Sample size		Endpoints in comparison	Comparison of patients with pancreatic cancer		
	Diabetics	Non diabetics		Diabetics		Non diabetics
#4114 Olowokure <i>et al.</i> [9]	1,326	3,402	Median survival	4.2 months	P=0.048	3.5 months
#4117 Shama <i>et al.</i> [10]	92	252	Frequency of perineural invasion	94.6%	P=0.037	86.5%
			Overall survival	30.2%	P=0.024	20.1%

Evidence Supporting the Association of Diabetes with Perineural Invasion and Overall Survival in Surgically Resected Patients with Pancreatic Cancer

A retrospective study (Abstract #4117) tested a hypothesis that there may be association between perineural invasion, diabetes, and survival of pancreatic cancer patients by reviewing medical records of 344 patients who underwent resection of pancreatic cancer between 2004 and 2008. Data captured included diagnosis, presence of perineural invasion, American Joint Committee on Cancer (AJCC) TNM stage, and overall survival. Perineural invasion was significantly more common in patients with diabetes. Perineural invasion and diabetes were independent predictors for survival after adjusting for AJCC TNM stage. This study further corroborates the suggestion that understanding the biology rendering the association between diabetes and perineural invasion may guide us in discovering novel therapeutic targets for pancreatic cancer (Table 1) [10].

Commentary

The association between diabetes and pancreatic cancers are intriguing as identification of modifiable prognostic factors can lead to better understanding of the biology of cancer. In turn, knowledge of tumor biology can result in discoveries of new therapeutic targets which will be instrumental in improving the clinical outcomes of pancreatic cancer patients.

The link between diabetes mellitus and pancreatic cancer has been largely unclear due to the paucity of available data. This year's abstracts, while adding to our knowledge base and being hypothesis generating, clearly do not provide compelling arguments in either direction. Further studies to validate this association would be a logical first step. At the same time, translational and clinical studies to identify appropriate interventions (i.e. aggressive diabetes mellitus

management and novel targeted therapy) will be necessary in exploiting this potentially important association between diabetes and pancreatic cancer for the benefit of our patients.

Conflict of interest The authors have no potential conflicts of interest

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