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## The challenge of treating older patients with pancreaticobiliary malignancies

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### ABSTRACT

Pancreatic and biliary tract cancers are aggressive malignancies. They commonly present with metastatic or unresectable disease. Those that do present with resectable cancer have high rates of recurrence. Despite recent advances in surgical technique, chemotherapy, and radiotherapy regimens, they are associated with poor survival outcomes. These cancers represent an exception to the trend of improved overall survival evident in most malignancies in recent decades. Depending on the goal of treatment, active management of pancreatic and biliary cancers involves surgery, chemotherapy, and radiation therapy, either alone or in combination. Both pancreatic and biliary tract cancers have a preponderance in the older population. Older patients are a heterogeneous group; although tolerability of multimodality treatment may be a challenge for some, many fit older patients may be undertreated based on their age alone. The growing field of geriatric oncology has highlighted the importance of a comprehensive assessment of these patients, and not relying on age alone as a discriminating factor for treatment. Management of older patients with pancreaticobiliary cancers is particularly challenging owing to limited prospective data in this population. As such, there is uncertainty with regard to optimal treatment approaches for these patients. In this article, we outline the therapeutic options available to patients with localized or advanced

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pancreatic and biliary tract cancers, and the evidence for specified treatment options in the elderly. We examine the inclusion and outcomes of elderly patients in relevant clinical trials; the morbidity that may be encountered by elderly patients receiving specified treatments and the tools that may assist the physician in selecting elderly patients for particular treatments.

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## Introduction

Pancreatic cancer (PC) is a disease of the elderly. The median age at diagnosis is 70 years and two-thirds of those diagnosed between 2010 and 2014 in the United States were >65 years.<sup>1</sup> Despite the preponderance of PC in the older adult, many have been excluded from large randomised trials.<sup>2</sup> A similar trend is seen with cancers of the biliary tract (BTC) comprising carcinomas of the gallbladder (GBC), intrahepatic and extrahepatic cholangiocarcinomas (CCA). The median age of diagnosis is 67 years (intrahepatic CCA and GBC) and 72 years (extrahepatic CCA), however, the majority of trials have focused on the management of younger patients.<sup>3,4</sup>

The management of these cancers is multimodal with curative therapy based around R0 surgical resection and consideration for adjuvant therapy. There are a number of factors, however, that complicate treatment decisions in the older population. Aging is associated with a decline in the functional reserve of multiple organ systems which may impact pharmacokinetics and pharmacodynamics of chemotherapeutic agents.<sup>5,6</sup> This has the potential to increase the risk of toxicity owing to altered drug absorption, metabolism, and excretion.<sup>6,7</sup> Older patients are more likely to have comorbidities and functional deficits which may impact suitability for aggressive surgical, radiation, or chemotherapy approaches. In addition, poorer social supports may make compliance to treatments, particularly chemotherapy, more challenging.

Therapeutic decisions in the older patient should thus consider all of these factors. Multidimensional, comprehensive clinical assessments should be used to better estimate the risks and benefits of interventions and guide treatment decisions in this population.

In this article, we will review the data addressing the management of older patients with pancreaticobiliary malignancies. In addition, we will outline the clinical assessment tools that may facilitate more individualized treatment decisions for this population.

## Pancreatic cancer

Pancreatic ductal adenocarcinoma represents approximately 85% of pancreatic malignancies. It is associated with a high mortality and represents an exception to the trend of improved overall survival (OS) evident in most malignancies in recent decades. The majority of patients present with inoperable or metastatic disease. In the 15%-20% of patients who present with operable disease, the 5-year OS rate in optimally staged patients is 20%.<sup>8</sup> Five-year OS rates for those > 65 years are less than half of those who are < 65 years (5.6 and 12.2%, respectively), reflecting the challenge regarding optimal management of this heterogeneous group.<sup>1</sup>

## Surgery

Resection of PC offers the only chance at cure. The conventional surgery for tumors of the head or uncinate process is a pancreaticoduodenectomy (Whipple procedure). Tumors in the body or tail may be resected with a partial pancreatectomy, however, these often present at a later stage when curative resection is not feasible. Despite surgery, 5-year OS rates remain poor at 15%-20%.<sup>9</sup>

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