The Impact of Obesity on Gallstone Disease, Acute Pancreatitis, and Pancreatic Cancer

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KEYWORDS

• Obesity • Gallstone disease • Pancreatitis • Pancreatic cancer

KEY POINTS

- Obesity is frequently associated with gallstone disease, acute pancreatitis, liver steatosis, and gastrointestinal cancers.
- The formation of gallstones in patients with obesity is multifactorial. A rapid weight loss in obesity also predisposes patients to gallstone formation.
- Obese patients are at increased risk of severe acute pancreatitis. Multiple local and systemic factors contribute to poor outcomes in patients with obesity.
- Although recognized as a risk factor for pancreatic cancer, obesity is also associated with poor outcomes after surgery for pancreatic cancer.

INTRODUCTION

Obesity is increasing worldwide and the World Health Organization has confirmed this as a global epidemic.[1] Approximately 30% of the world's population is overweight or obese, and no country has reduced its obesity rates in 33 years.[2] In the United States, approximately 78.6 million (34.9%) of adults are obese, a statistic that has doubled over the past 2 decades.[3] In particular, the prevalence of morbid obesity has rapidly increased with an approximate 70% increment from 2000 to 2010.[4] Furthermore,

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childhood obesity has more than doubled in children and quadrupled in adolescents in the past 3 decades and this has led to increases in disease rates associated with obesity.[3]

Other than contributing to the metabolic syndrome and cardiorespiratory comorbidities, obesity is frequently associated with gallstone disease, acute pancreatitis, liver steatosis, and gastrointestinal cancers.[5–7] Gallstone disease is highly prevalent (10%–15% of population) in the Western population and is increasing. In the United States, there were 389,180 hospitalizations in 2012 due to cholelithiasis with cholecystitis.[8,9] Acute pancreatitis is the most common single gastrointestinal diagnosis for inpatient hospitalization (275,170 hospitalizations in 2012) and costs an estimated 2.6 billion dollars per year in inpatient costs.[10] The prevalence of inpatient hospitalization for acute pancreatitis is increasing annually, which parallels the rising prevalence of obesity.[4,11] There is an established association between obesity and the development of complications in acute pancreatitis.[12,13] In addition, obesity increases the risk of developing pancreas cancer in particular, pancreatic ductal adenocarcinoma (PDAC).[14–16] PDAC is a devastating disease, with a dismal long-term survival.[17,18] Surgery offers the only possibility of approximating a cure; however, only 20% of patients are eligible because the cancer tends to be detected at a late stage and has already metastasized at diagnosis. In 2016, PDAC became the third leading cause of cancer-related death in the United States and it is projected to become the second by 2030, due to both an aging population and the obesity epidemic.[2,17,19,20]

The aim of this review is to describe the pathophysiology and outcomes of obesity and the association with gallstone disease, acute pancreatitis, and pancreatic cancer.

CHOLELITHIASIS AND OBESITY

There are multiple risk factors for gallstones in patients with obesity (**Table 1**). Although elevated body mass index (BMI) is associated with gallstone disease, a causal association has been demonstrated between increasing BMI and symptomatic gallstones using a mendelian randomization approach.[21] Furthermore, increasing BMI was associated with a 3-fold increment in the risk of cholelithiasis as evidenced in the Nurses' Health Study involving women between 30 and 55 years of age followed over a total of 18 years.[22] A 2.5-fold increase in risk has also been demonstrated among men between 40 and 55 years of age.[23] As an outcome of obesity-associated gallstone disease, the risk of gallbladder cancer also increases with BMI.[24] The lithogenic mechanisms of obesity are multifold and are depicted in **Fig. 1**. These mechanisms can either act alone or contribute in combination. It is of relevance that the presence of components of metabolic syndrome increases the risk of gallstones; a risk of 5% without the presence of metabolic syndrome increases to 25% when all the components are present in a patient.[25]

CHOLELITHIASIS AFTER WEIGHT LOSS IN OBESITY

The trend of bariatric surgeries and simultaneous cholecystectomies in the United States (2005–2011) is shown in **Fig. 2**. Concomitant cholecystectomy during gastric bypass surgery is no longer the routine practice because the operative time, postoperative hospital stay, and postoperative morbidity and mortality are higher with prophylactic cholecystectomy.[26] Several studies have indicated its use only in cases of symptomatic gallbladder disease, in particular cholelithiasis.[27] Concomitant