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8

Obesity and the risk and prognosis of gallstone disease and pancreatitis



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A B S T R A C T

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Obesity is a risk factor for the formation of cholesterol gallstones and exposes patients to increased risk of gallstone-related complications and cholecystectomy. Rapid weight loss achieved by very low calorie diets or bariatric surgery is also a risk factor for cholelithiasis in obese patients, and therapy should take into account the higher prevalence of gallstones, the possibility of more frequent complications and the need for prophylactic treatment with oral ursodeoxycholic acid during weight loss. Obesity is also frequent in children and adolescents, and the burden of cholesterol cholelithiasis is increasing in this population. The chance to develop acute pancreatitis and the severity of the disease are higher in obese subjects because of specific pathogenic factors, including supersaturated bile and crystal formation, rapid weight

Abbreviations: AP, acute pancreatitis; BMI, body mass index; NSAIDs, nonsteroidal anti-inflammatory drugs; SIRS, systemic inflammatory response syndrome; TNF, tumour necrosis factor; UDCA, ursodeoxycholic acid.

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loss, and visceral obesity. All health policies aimed at reducing the incidence of obesity worldwide will decrease the incidence of gallstones and gallstone-related complications. The pathophysiological scenarios and the therapeutic implications for obesity, gallstone disease, and pancreatitis are discussed.

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Introduction

From 1980, a progressive shift toward obesity has been showed at any age, with a greater surge of obesity prevalence in lower- and middle-income developing countries rather than in higher-income countries. Whereas the differences in obesity prevalence across countries reflect the differences in national and local environments, the modifications in the global food system and increased sedentary life during the past 3–4 decades have created an obesogenic environment contributing to the increase of obesity epidemic worldwide.

Among many other comorbidities, obesity is also frequently associated with hepatobiliary diseases, including gallstone disease [1–3], pancreatitis and liver steatosis [4], three conditions reflecting abnormal cholesterol and triglyceride metabolism. Gallstone disease is one of the most prevalent and costly digestive diseases in Western countries [2]. The prevalence of gallstones in adults is 10–15% [2,5,6], and is rising. Around one million of new cases are diagnosed each year in the USA [7], and the 3rd National Health and Nutrition Examination Survey (NHANES III) reports that in the USA about 6.3 million of men and 14.2 million of women aged 20–74 might suffer from gallbladder disease [5].

During the development of gallstones, solid conglomerates of cholesterol monohydrate crystals, mucin gel, calcium bilirubinate, and proteins accumulate and grow in the gallbladder [8]. Depending on the chemical composition, gallstones are often classified as pure cholesterol, pure pigment, and mixed stones. The latter type contains some amounts of bilirubin salts and calcium. In developed countries, cholesterol gallstones account for about 75% of stones, black pigment stones for 20%, and brown pigment stones for about 5% [8]. Besides some genetic factors, in the majority of cases, gallstones can be induced by non-genetic risk factors [2,8] (Table 1). For cholesterol gallstones, factors comprise female gender (women exposed to a higher level of oestrogen than men), pregnancy, several conditions leading to gallbladder stasis, oral oestrogens and contraceptives, and hypomagnesaemia. The prevalence of both types of cholesterol and pigment stones increases with increasing age, smoking, and liver cirrhosis. Black pigment stones are associated with haemolytic anaemia, cystic fibrosis, high alcohol intake, biliary/intestinal infections, and vitamin B12/folic acid deficient diets.

It is the aim of this chapter to describe the pathophysiological scenarios and the therapeutic implications involving the association of obesity with gallstone disease and pancreatitis.

Obesity and gallstones

Obesity, body mass index (BMI) and gallstones

Obesity “*per se*” is a potent factor associated with the formation of cholesterol gallstones. A genetic predisposition is found in specific ethnic groups such as the Pima Indians of Arizona, in which obesity and non-insulin diabetes mellitus coexist, displaying the highest prevalence rate of cholesterol gallstones (about 80% in women by age 25–30) in the world [9]. Non-genetic risk factors for cholesterol gallstones associated with obesity are depicted in Table 2. Increased BMI is also a causal risk factor for symptomatic gallstone disease [10]. In the Nurses' Health Study, increasing BMI was associated with increased relative risk of cholelithiasis (3-fold), in women initially at 30–55 years of age and followed for up to 18 years [11]. A dramatic increase was observed in the incidence of symptomatic gallstones defined as cholecystectomy, or newly diagnosed symptomatic gallstones, and BMI [12]. The incidence of symptomatic gallstones increased from approximately 0.25% to >2% per year of follow-up in these

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