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Magnetic resonance imaging for acute pancreatitis in type 2 diabetes patients

Ni YH *et al.* MRI for AP in T2DM

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Abstract

Type 2 diabetes mellitus (T2DM) and its complications have significantly increased the burden of mortality and disability globally, making diabetes one of the most dangerous and prevalent chronic diseases. ¹⁸ Acute pancreatitis (AP) is one of the most frequent gastrointestinal causes for hospital admission, which is a common exocrine pancreatic inflammatory disease that can cause severe abdominal pain and multiple organ dysfunction. There is an inseparable relationship between AP and diabetes. Diabetes is a high risk factor of AP, and patients with AP can develop pancreatogenic diabetes. In T2DM patients, the incidence rate of AP is significantly higher than that of the general population, and the clinical symptoms are more severe, with the majority of cases being moderate to severe AP. This review briefly introduces the pathogenesis and clinical features of AP in T2DM patients, focusing on the magnetic resonance imaging (MRI) manifestations of AP in T2DM patients. Our aim is to evaluate the severity of AP in patients with T2DM by MRI, so as to help clinicians assess the patient's condition and prognosis.

Key Words: Acute pancreatitis; Type 2 diabetes mellitus; Magnetic resonance imaging

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Core Tip: Up to present, a host of researchers focus on the type 2 diabetes mellitus (T2DM) clinical manifestations. However, there are currently few investigations on the imaging features of acute pancreatitis (AP) in patients with T2DM. This paper demonstrates that the patients with T2DM have a higher prevalence of AP and more severe clinical manifestations, showing the magnetic resonance imaging findings of AP in T2DM.

INTRODUCTION

Acute pancreatitis (AP) is one of the most frequent gastrointestinal causes for hospital admission^[1]. AP is a common exocrine pancreatic inflammatory disease that can cause severe abdominal pain and multiple organ dysfunction, with a mortality rate of 1% to 5%^[2]. Overall, it has a global incidence of 30-40 cases per 100000 people per year, including children, pregnant women and the elderly. Moderate to severe AP with effusions and/or necrotizing effusions can lead to serious complications, and severe AP with persistent organ failure can lead to significant mortality^[2,3].

Type 2 diabetes mellitus (T2DM) is a chronic, heterogeneous, systemic disease accompanied by varying degrees of insulin deficiency and/or insulin resistance^[4]. The epidemic condition of diabetes mellitus and its complications poses a major global health threat. The global prevalence of diabetes had reached pandemic proportions with the 9th edition of reporting a prevalence of 9% (463 million adults) in 2019. This estimated number will rise to 642 million by 2040^[5-7]. These studies^[8,9] have demonstrated that patients with T2DM have a greater prevalence of AP compared with the general population, and the clinical manifestations of AP secondary to T2DM are more serious (mostly moderate to severe AP). On magnetic resonance imaging (MRI), the incidences of pancreatic or peripancreatic hemorrhage and necrosis, pancreatic duct interruption, and peripancreatic infection are higher than those of non-diabetic individuals. To present, there has been little discussion about MRI for AP in T2DM patients. This review briefly introduces the pathogenesis and clinical features of AP in T2DM patients, focusing on the MRI manifestations of AP in T2DM patients.

PATHOGENESIS AND CLINICAL CHARACTERISTICS OF AP IN PATIENTS WITH T2DM

To our knowledge, the common causes of AP are gallstones, alcoholism, and hyperlipidemia. Previous studies show that T2DM may increase AP risk *via* hypertriglyceridemia^[10], cholelithiasis^[11]. Dyslipidemia is frequently encountered in diabetic patients. The characteristics of dyslipidemia in diabetic patients are

hypertriglyceridemia. T2DM increases low density lipoprotein cholesterol levels, and decreases apo-B, high-density lipoprotein cholesterol, and apo-A^[10,12]. Due to the hydrolysis of excess triglyceride by pancreatic lipase, a large amount of free fatty acids and free radicals are produced, resulting in acinar cell and pancreatic capillary damage and ischemia^[13,14]. Several other studies show that ⁷ the potential mechanisms of hypertriglyceridemia pancreatitis are the insolubility of the lipid triglycerides in the aqueous environment of blood resulting in microthrombi in the pancreatic vasculature and ischemia and pancreatic infarction^[15]. On the other hand, a previous study has found that diabetes is consistently associated with a higher risk of gallstones^[16]. Obesity is common in diabetics due to insulin resistance-related metabolic syndrome, which may impact gallstone formation by multiple mechanisms^[15]. This clinical study investigated people with T2DM have almost three times ⁶ the risk of gallstone formation, compared with people without diabetes^[17]. In addition, four large epidemiological studies suggest an etiological role for diabetes in AP. Hyperglycemia and insulin resistance are major important factors leading to increase production of reactive oxygen species in acinar cells. Moreover, infectious diseases are more frequent and severe in diabetics^[18,19]. In clinical settings, T2DM patients with AP are often complicated with hyperlipidemia, gallstone, obesity, long average hospital stay. The prevalence of ICU admission and mortality is higher in patients with T2DM with AP^[20].

IMAGING EVALUATION OF THE SEVERITY OF AP IN PATIENTS WITH T2DM

¹⁴ Computed tomography (CT) or MRI with contrast medium is usually the first-line ¹⁵ imaging examination for patients with AP. MRI and CT can specifically demonstrate the overall changes of the pancreas and the degree of necrosis of the pancreas. Also, imaging can indicate the etiology and pathological findings, which has certain guiding significance for clinical guidance of medication and patient prognosis. Although enhanced CT is considered the gold standard for evaluating AP, there are certain limitations in clinical application, such as repeated irradiation and injection of iodine contrast agents. Contrast-enhanced CT (CECT) is also avoided in patients with AP-

associated acute kidney injury. Moreover, scholars have found that contrast agents can exacerbate AP by damaging pancreatic microcirculation^[21]. However, MRI is a non-invasive and radiation free examination that can better display the morphology of pancreatic parenchyma and pancreatic duct, evaluate the degree of pancreatic and peripancreatic exudation, necrosis, bleeding, and detect early pancreatic duct rupture^[21]. And it can display the morphology of bile ducts, which is also helpful for evaluating the etiology of AP, such as cholelithiasis and tumors. Gadolinium in MRI contrast agents has fewer side effects, especially less nephrotoxicity^[22,23]. Besides, due to better soft tissue resolution and interreader agreement for the detection of debris within the collections compared with CECT, MRI may also have a prognostic implication in terms of risk stratification when diagnosing extrapancreatic necrosis without pancreatic parenchymal necrosis^[24]. Moreover, MRI has better sensitivity for detection of mild parenchymal and early inflammatory changes, better detection of pancreatic glandular necrosis on unenhanced examinations, improved identification of solid components in complex necrotizing collections before drainage^[23]. In a prospective study, scholars investigated the correlation between CT and MRI at similar time points of particular importance, namely immediately after admission, when it is most useful for predicting outcome, and 7 d later, MRI is helpful in confirming the presence of necrosis and excluding cases with reversible hypoperfusion of the pancreatic parenchyma. Last, another important time point is 30 d after admission, when therapeutic decisions have to be made for the management of complications in the most severe cases^[21]. On MRI, AP is classified as interstitial edematous pancreatitis or necrotizing pancreatitis. Pancreatic necrosis is often defined as an area of low signal on T1-weighted images and absence of enhancement after administration of gadolinium. The severity of AP is assessed and graded according to the MR severity index (MRSI) (Table 1), which is derived from the CT severity index^[25]. Depending on MRSI scores, the severity of AP on MRI is subdivided into mild pancreatitis (0–3 points), moderate pancreatitis (4–6 points), and severe pancreatitis (7–10 points). In addition, MRI can evaluate for vascular injury such as pseudoaneurysm and venous thrombosis^[26].

MR MANIFESTATIONS OF PANCREATIC CHANGES IN PATIENTS WITH AP IN PATIENTS WITH T2DM

Pancreatic necrosis and/or hemorrhage

MRI can better display the morphology of the pancreas and signal changes in pancreatic parenchyma. Edematous pancreatitis is characterized by an enlarged pancreas and T2-weighted hyperintense changes of pancreatic parenchyma (Figure 1). AP onset of T2DM presented more frequency of moderate-to-severe AP on MRI^[4]. Moderate-to-severe AP manifests as pancreatic enlargement, hemorrhage and necrosis of the pancreatic parenchyma. Hemorrhage is defined as hyperintense areas within the pancreatic parenchyma or outside the pancreas on T1-weighted images. ¹¹ Pancreatic necrosis is determined as a low-intensity area on T1-weighted images and parenchymal nonenhancement after injection of contrast media (Figures 2-4)^[27]. Our previous research^[4] have proved that the prevalence of pancreatic/peripancreatic hemorrhage was higher in AP patients with diabetes than in those without diabetes. In addition, we found that the incidence of necrotizing pancreatitis was higher in patients who presented with AP with diabetes, and there was greater parenchymal necrosis volume (greater than 30% of pancreatic necrosis) in AP patients with T2DM than in those without diabetes.

Disconnected pancreatic duct syndrome

¹³ Magnetic resonance cholangiopancreatography, a noninvasive modality, well demonstrates dilatation, stricture, and irregularity of the main pancreatic duct^[28-30]. Due to the higher incidence of acute necrotizing pancreatitis in T2DM, when a large area of pancreatic parenchyma necrosis in necrotizing pancreatitis involves the main pancreatic duct (leading to pancreatic duct necrosis), the pancreatic and peripancreatic ANC is often accompanied by rupture and interruption of the main pancreatic duct. That is so-called "disconnected pancreatic duct syndrome"^[31] (Figure 5).

MR MANIFESTATIONS OF PERIPANCREATIC CHANGES IN PATIENTS WITH AP IN PATIENTS WITH T2DM

The spread of AP inflammation most often involves the retroperitoneal space, and can also spread to the subperitoneal space (omentum, mesentery, *etc.*)^[32]. Peripancreatic changes of AP in patients with T2DM mainly include local complications of AP^[33]. According to the Revised Atlanta Classification, local complications are acute peripancreatic fluid collection (APFC), pancreatic pseudocyst, acute necrotic collection (ANC) and walled-off necrosis (WON). APFC (Figure 6) occurs in interstitial oedematous pancreatitis; and pancreatic pseudocyst forms as a delayed (usually > 4 wk) complication of interstitial oedematous pancreatitis. In contrast, necrosis may be an ANC (Figure 7) or WON (Figure 4). WON is a mature, encapsulated collection of pancreatic and/or peripancreatic necrosis and has a well-defined inflammatory wall. Usually, this maturation occurs ≥ 4 wk after onset of necrotising pancreatitis^[3]. Patients with AP with diabetes were at higher frequency of the development of fluid collections (especially walled-off necrosis) and infected collections compared with nondiabetic AP. These recognitions among physicians are of importance for appropriate clinical treatment strategies of T2DM-associated AP^[4].

MR MANIFESTATIONS OF ADJACENT OR DISTANT ORGAN CHANGES IN T2DM WITH AP

Liver injury

We found that liver injury could occur in patients with AP, including local liver inflammation, apoptosis, hepatocyte necrosis, and metabolic disorders^[34]. It may manifest as fatty liver (FL) on MRI. In a prior study, we found that FL on MRI occurred in a majority of patients with AP. The severity of the FL in MRI was related to the severity of the AP and to the serum triglyceride levels. Following the patient's recovery, the FL on MRI could subside for both mild and severe AP patients^[35].

Changes of renal and perirenal space

Previous studies have found that renal dysfunction caused by AP rarely exhibits renal parenchymal abnormalities on MRI (including asymmetrical renal enhancement, abnormalities of the renal collecting system and renal vascular abnormalities). However, perirenal space involvement is much more common and includes renal fascia thickening, perirenal space stranding and patchy fluid collections in the perirenal space. The prevalence of perirenal space involvement in AP patients on MRI has a positive correlation with the severity of AP based on the MRSI^[36].

CONCLUSION

Overall, this paper demonstrates that the patients with T2DM have a higher prevalence of AP and more severe clinical manifestations, showing the MRI findings of AP in T2DM. Up to present, a host of researchers focus on the clinical manifestations of AP in patients with T2DM. However, there are currently few investigations on the imaging features. Further research can be done on the imaging characteristics of AP exacerbated by diabetes, as well as whether diabetic medical histories and their blood sugar levels linked to the AP severity or not. In the future, it is expected that artificial intelligence methods, such as radiomics and deep learning, may be added to this field to detect pancreatic complications, severity prediction, and prognosis evaluation in patients with T2DM.

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