Endoscopic Treatment of Recurrent Acute Pancreatitis and Smoldering Acute Pancreatitis

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KEYWORDS

• Recurrent acute pancreatitis • Smoldering acute pancreatitis • Endoscopic therapy
• Pancreatic divisum • Idiopathic recurrent acute pancreatitis

KEY POINTS

- In pancreas divisum–associated recurrent acute pancreatitis (RAP) data from uncontrolled retrospective studies point toward a benefit from minor papillary endoscopic intervention.
- The literature around idiopathic RAP (IRAP), although generally prospective, is heterogeneous, with differing cohort compositions and endoscopic interventions. Randomized data do not support the use of endotherapy in IRAP associated with elevated pancreatic sphincter pressures.
- Smoldering acute pancreatitis (AP) is a poorly defined entity. The role of endotherapy in smoldering AP needs further investigation.

INTRODUCTION

RAP is a challenging condition, because it leads to significant patient morbidity, has potential for progression to chronic pancreatitis (CP), and has limited management options in many patients. Endoscopic therapy, in the form of papillary sphincterotomy and/or pancreatic duct stenting, is often used as a treatment modality for patients with RAP in the setting of pancreas divisum or idiopathic etiology, aiming to eliminate recurrent attacks and progression to CP.[1–17] The goal of this review is to discuss the role of endoscopic therapy in RAP related to pancreas divisum and IRAP, focusing on the methodology, findings, and limitations of available literature. The endoscopic management of smoldering AP, a poorly defined entity related to AP, also is discussed later.

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RECURRENT ACUTE PANCREATITIS

RAP is defined as the occurrence of 2 or more episodes of AP in a given patient, without concurrent clinical or imaging evidence supportive of CP.[18–20] In natural history studies examining the long-term outcomes of patients after an index episode of AP, the incidence of RAP is estimated to be between 3% and 5% per 100 patient-years, with an overall prevalence of 17% to 20%.[19,20] RAP has a variable etiology, with the most common causes alcohol abuse and gallstone disease.[18–20] Pancreatobiliary malformation, specifically pancreas divisum, has also been associated with the development of RAP.[2,20] A significant proportion of patients with RAP, despite thorough work-up, have no etiology identified,[21] and their disease is thus labeled idiopathic.

Irrespective of etiology, RAP is independently associated with the development of CP, although the true incidence and prevalence of this complication, outside of recurrent alcoholic pancreatitis, is unclear.[18–20] Given the socioeconomic impact of CP,[22] alleviation and/or cessation of RAP with etiology-based treatment may have an impact on health care costs and patient morbidity. As discussed previously, endoscopic therapy has been studied as a management option specifically within the context of divisum-associated RAP and IRAP and is the focus of this article.

Pancreas Divisum–Associated Recurrent Acute Pancreatitis and the Utility of Endoscopic Therapy

During embryologic development of the foregut, the pancreatic parenchyma is formed from the rotation and eventual fusion of the ventral and dorsal anlages. Parenchymal fusion is also associated with ductal fusion in greater than 90% of individuals, and failure of the ventral and dorsal ductal systems to fuse is termed, *pancreas divisum*.[23] Pancreas divisum is the most common congenital anomaly of the pancreas, with a prevalence of 6% to 8% based on prior autopsy and endoscopic retrograde cholangiopancreatography (ERCP) series.[24,25] Pancreas divisum has traditionally been diagnosed via ERCP, although secretin-enhanced magnetic resonance cholangiopancreatography (MRCP) has recently allowed for an accurate, noninvasive mode of diagnosis.

It is controversial as to whether pancreas divisum by itself is a causative factor for the development of RAP. Pathophysiologically, this is thought related to impaired pancreatic ductal drainage through the smaller minor papillary orifice. Retrospective studies have supported this hypothesis and found pancreas divisum significantly more common in patients with RAP compared with normal controls or patients with obscure abdominal pain.[24,26]

In the most recent study investigating this issue, Bertin and colleagues[27] examined the prevalence of pancreas divisum, as diagnosed by MRCP, in patients with RAP and/or CP deemed idiopathic or associated with *CFTR, SPINK1*, and/or *PRSS1* mutations. The frequency of pancreas divisum in the idiopathic group was 5%, not significantly different from the frequency found in both control groups and patients with *SPINK1 or PRSS1* mutations. The frequency of pancreas divisum in patients with concurrent *CFTR* mutation–associated RAP and/or CP was significantly higher at 47%. This finding suggests that pancreas divisum increases the risk of pancreatitis only in combination with another source of pancreatic injury, specifically *CFTR* dysfunction.

Characteristics of Available Studies for Endoscopic Therapy in Divisum-Associated Recurrent Acute Pancreatitis

The hypothesis of pancreas divisum as an obstructive cause of recurrent pancreatitis and clinical improvement with minor papillary endoscopic intervention were first described by Cotton in 1980[28]. This has subsequently led to numerous studies