

# Research advance in the diagnosis of pancreas divisum

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## ABSTRACT

**Pancreas divisum is a kind of congenital anatomic abnormality; its diagnostic basis depends mainly on imaging examination. With the development of medical science, imaging technology has been improved and added, and a complete examination system including ERCP, B-Ultrasound, MRCP, S-MRCP and CT, etc. has been formed. There are even researcher, through further analysis of pancreas divisum on the level of genes, found that CFTR is a risk factor causing such disease. This paper is focused on the value of these examination methods in the diagnosis of pancreas divisum.**

**Keywords:** Pancreas Divisum; Endoscopic Retrograde Cholangiopancreatography (EPCR); Magnetic Resonance Cholangiopancreatography (MRCP); Computed Tomography (CT); Cystic Fibrosis Transmembrane Conductance Regulator (CFTR)

## 1. SUMMARY

Pancreas divisum originally referred to the double-pancreas formed as the dorsal pancreas cannot be fused with the ventral pancreas, a rare congenital malformation. While in nowadays its definition is broadened to be a kind of congenital dysplasia, the most common congenital variation in the development process of pancreatic duct, and usually refers to the infusion of ventral pancreatic duct and dorsal pancreatic duct in the process of development [1]. Initially, researchers found that the probability of PD among idiopathic pancreatitis patients is higher. Cotton [2] once reported that it is found that there were 3.6% of 169 patients who took pancreatography examination because of biliary tract diseases have got pancreas divisum; in addition, there is 25.6% of idi-

opathic pancreatitis patients have got pancreas divisum found through pancreatography examination [3]. And someone thought that PD may occur at any age and the incidence of PD among crowds is at a rate of about 10% [4]. The clinical manifestations of PD, a congenital anatomic abnormality, include non-symptom, relapsing pancreatitis, chronic pancreatitis and severe acute pancreatitis, and its diagnostic methods rely mainly on the imaging examination technologies such as ERCP, B-Ultrasound, MRCP, S-MRCP and CT, etc. Through research on the level of genes, it is found that CFTR is a risk factor causing PD. This paper will discuss the research progress of these diagnostic methods of PD.

## 2. DIAGNOSTIC APPLICATION OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (EPCR) IN PANCREAS DIVISUM

Although PD has been recognized by anatomist a few hundred years ago, it was not until 1970, with the emergence of ERCP, there were some researchers proposed that pancreas divisum and pancreatitis are associated with each other. People often think that relatively narrow occurs as PD patients draining pancreatic juice through dorsal pancreatic duct and minor papilla, and thus led to the occurrence of pancreatitis. Until now, however, the relationship between pancreas divisum and pancreatic diseases is not yet clear. The incidence of pancreatic diseases among pancreas divisum patients does not has a significant increase compared with that of normal people. However, studies show that a large number of pancreas divisum patients can indeed progressed to pancreatic diseases. As a result, the clinical value of this link is particularly important. Endoscopic retrograde cholangiopancreatography (EPCR) can provide clear and direct image of pancreatic duct; and with a higher rate of correct diagnosis of lesions in biliary cavity and wall, it can

clearly display the size, number, narrow scope and position of the lesions. And for papilla lesion, it can carry out biopsy, this technology is one of the main means of diagnosing pancreas and bile duct disease at present. EPCR presents a significant role in the diagnosis of PD [6-10]. Freeman ML, Nelson DB [11], and some others believe that the uppermost danger of ERCP is the complications of acute pancreatitis, the incidence of which is up to 20% among SOD patients and also 5%-6% among general population. For this reason, in the past 10 years, ERCP is replaced by endoscopic ultrasound (EUS) in diagnosing biliary calculi, tumor, pancreas divisum and pancreatic cyst. As EUS is characterized by high accuracy and high security [12-15], and the same, it also has limitations as can not make clear diagnosis of SOD (Sphincter of Oddi Dysfunction). The research of Coyle *et al* [16] shows while take the diagnostic application of ERCP in SOM (sphincter of Oddi manometry) and bile analysis, there are 80% of the patient can be diagnosed, of which 20% are diagnosed as PD; in comparison, EUS is quite useful in diagnosing biliary diseases and monitoring tumors, it can diagnose that there are 9 cases of patients suffering from chronic pancreatitis while ERCP cannot do. But EUS cannot diagnose any patients with SOD. Compared with EUS, one of the main advantages of ERCP is its ability to monitor and show the pressure, and once required interventional therapy can be taken to make diagnosis and treatment, without the need for such traumatic diagnosis means as sphincterotomy [17]. Napoleon [18] and some others think that EUS diagnosis can be made to replace ERCP in diagnosis of common bile duct stones.

### 3. DIAGNOSTIC APPLICATION OF MAGNETIC RESONANCE CHOLANGIOPANCREATOGRAPHY (MRCP) IN PANCREAS DIVISUM

MRCP is an up-to-date technology for the observation of the systematic anatomy and pathology forms of pancreatic duct. The anatomy and lesions of pancreaticobiliary duct system could be shown perfectly in physical circumstances with it. MRCP is safe, non invasive, has got no contraindications and complications. In the experiment on assessing outflow obstruction in pancreatic duct with primary acute recurrent pancreatitis, Khalid *et al* [19] apply MRCP of pancreatic exocrine response to secretin to 10 patients with primary acute recurrent pancreatitis, followed by EPCR, divided into two groups of with manometry and without manometry. The MRCP finding pancreatic exocrine response to secretin can provide high-quality imaging and be able to make diagnosis of high specificity to pancreatic duct obstruction by us-

ing pressure gauge measurement standard and clinical standard. All these illustrate the advantages of MRCP in observing pancreatic duct abnormality and diagnosing PD. The coincide rate of ERCP and MRCP is 83%-100% for lumen expansion, 70%-92% for lumen stenosis and is 92%-100% for filling defect [20]. In evaluation of the common diseases of the pancreas, MRCP is a non-traumatic substitute method for ERCP, and can make sure that there is no complication in the anatomical structure of the lumen. For the determination of common anatomic variation, conditions of pancreatic duct with pancreatitis, MRCP is quite valuable, especially combined with MRI imaging. However, MRCP has its limitations: 1) all patients not suitable for MRI (such as the patients wear cardiac pacemakers) are not suitable for applying MRCP; 2) severe bile-pancreas duct stenosis often manifested as the signal interruption of certain section, it cannot find the lesions accompanied with stenosis; 3) the images after reconstructed with maximum intensity projection reconstruction technology is easy to cover up minimal lesions. Ueno, etc. [21] also have reported the MRCP's difficulty in displaying short, thin ventral pancreatic duct while it is relatively easy to show thicker ventral pancreatic with a length over 2.8 cm. In recent years, the researchers also suggested that secretin-enhanced dynamic CPCR (S-MRCP) can clearly show the infused dorsal and ventral pancreatic ducts of PD patients, and so as to enhance the image quality of the pancreatic duct, reduce the false negative rate in MRCP diagnosis, as well as improve the detection rate [22-26]. Secretin-enhanced ultrasound examination is also a non-invasive examination method, which could get consecutive ultrasonic images of pancreatic duct. But due to the limitation of the patients' somatotype and the gas inside the site, it cannot show very clearly anatomy abnormality of pancreas divisum.

### 4. DIAGNOSTIC APPLICATION OF CT IN PANCREAS DIVISUM

Computed tomography (CT) is usually used to analyze the pancreas size, outline and focal lesions of patients with chronic pancreatitis or chronic abdominal pain. It is much more difficult for CT to show pancreatic duct structures than showing substantial pancreatic structure. By using three-dimensional reconstruction thin-slice spiral CT can get 3-D images of high quality, the diagnostic criteria of which is the infuse of the dorsal and ventral pancreatic duct and the direct connection of dorsal pancreatic duct and common bile duct. As conventional CT cannot display the duct system of the entire pancreas, conventional CT has little action in diagnosis of PD [27]. It is feasible for the multi-detect row computed tomography (MDCT) to take assessment of PD

when the pancreatic duct can be seen clearly. With MDCT, Soto JA, Lucey *et al* [28] found 10 PD patients among 73 patients with pancreatic diseases, in comparison, there are 9 PD patients found with ERCP. In addition, there is 1 false positive case included in experimental group 1 with MDCT while there are 2 in group 2. Therefore, experimental group 1 shows that in the diagnosis of PD, MDCT's sensitive rate is 95% and its specificity is 95%; experimental group 2 shows that in the diagnosis of PD, MDCT's sensitive rate is 95% and its specificity is 97%. Therefore, MDCT is very valuable in the diagnosis of PD, subject to the pancreatic duct is clearly visible.

## 5. APPLICATION OF GENE DETECTION IN THE DIAGNOSIS OF PD

Dray X [29] and someone else studied the relationship between Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) and recurrent pancreatitis caused by pancreas divisum. Their results suggest that even mild decline of CFTR function can lead to significant changes in pancreatic exocrine function, that is, to arise the increases of the viscosity of exocrine of pancreas and the formation of protein precipitation through the secretion of images chloride and bicarbonate, and the function decrease of this gene may also result in excessive inflammatory response and thus causing local tissue edema. Taken together, CFTR dysfunction leads to the occurrence of pancreatitis through the duct and inflammatory edema caused by. They also pointed out that the occurrence of pancreatitis caused directly by itself is accidental, but when combined with CFTR dysfunction, pancreas divisum becomes an important factor causing pancreatitis. CFTR dysfunction itself is not an important factor for the onset of pancreatitis, but when combined with modifier gene abnormality, alcohol consumption or and other congenital anomalies, it may cause pancreatitis. It is very important to know pancreas divisum, a kind of congenital abnormality, since its existing ratio is relatively high among the population. Although the possibility of pancreatic diseases being caused directly by CFTR itself is low, the CFTR abnormality could serve as a foundation for pancreatic diseases. The abnormality of CFTR often leads to pancreatitis increasing the density of pancreatin, which in turn gives rise to or be accompanied by local inflammation, making the accessory nipple narrow, and finally results in total and relative blockage of major drainage pancreatic ducts, and thus brings about pancreatic disease symptoms, namely pancreas divisum [29]. In other words, CFTR is a dangerous factor contributing to pancreas divisum, so it can be used as an auxiliary diagnosis standard for assessing the pancreas divisum.

## 6. CONCLUSION

Pancreas divisum, the most common congenital mutation in the development of pancreatic duct, was not recognised until the 1970s when EPCR was invented and applied. EPCR is the golden criteria for diagnosing pancreas divisum, and also a main treatment for it. In recent years, the rapid development of the photography technology has improved the role of technologies such as Ultrasound, Thin-slice CT, MDCT, MRCP in diagnosing pancreas divisum. Especially, the present S-MRCP with noninvasive and highspecific characteristics is the most promising diagnostic means [30]. The above-mentioned diagnostic means have their own limitations in clinical application. The gene diagnosis also supplies the patients suffering pancreas divisum with another choice. And as an alternative method in diagnosis and research, it leads us to an in-depth understanding of pancreas divisum at molecular level.

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