EDITORIAL

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Could assessment of genetic susceptibility be an effective solution to prevent pancreatitis from occurring after endoscopic retrograde cholangiopancreatography?

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Endoscopic procedures, particularly endoscopic retrograde cholangiopancreatography (ERCP), play a crucial role in the successful evaluation and treatment of pancreaticobiliary disease. However, alleviating the risk for acute pancreatitis, a potential complication of ERCP, remains a significant challenge for endoscopists. Post-ERCP pancreatitis (PEP) occurs in 1.6–15.7% of patients who undergo ERCP [1]. Although most cases are mild, severe cases can occasionally arise and some are fatal [2].

The causes of PEP have been identified as risk factors grouped into patient-related and procedural-related categories. Patient-related factors include being a young woman, having redundant peri-ampullary mucosal folds, and having a history of PEP [3]. Procedural-related factors consist of repeated intubation of the pancreatic duct, contrast injection into the pancreatic duct, and procedures performed by less-experienced doctors [3]. Numerous investigators have explored optimal preventive methods for PEP, and some techniques have proven effective in reducing its incidence. Traditional methods include rectal indomethacin, sufficient pre-hydration, and protease inhibitors [4]. Immunosuppressant drugs have recently been examined as potential preventive measures for PEP [5]. However, these methods have not been successful.

The cause and progression of PEP are not fully understood. Notably, even without apparent preexisting risk factors or precautions taken during ERCP, severe pancreatitis can sporadically develop, leading to unfavorable outcomes. Hence, hidden factors such as genetic mutations may be at play. Studies have highlighted an association between acute pancreatitis and genetic mutations to show their potential link with PEP. This genetic insight offers a new perspective on the onset and progression of the disease for cases of pancreatitis with indeterminate origin.

More than 30 genetic mutations linked to hereditary or idiopathic pancreatitis have been identified. These include mutations in genes such as serine protease 1 (*PRSS1*), serine protease inhibitor Kazal type 1 (*SPINK1*), cystic fibrosis transmembrane conductance regulator, chymotrypsin C, calcium-sensing receptor (*CASR*), and carboxypeptidase A1 [6]. However, it is inappropriate to view PEP and acute pancreatitis from identical perspectives considering the marked differences in etiology and clinical course between them. Previous studies that have focused on genes have reported no significant correlation in patients with PEP [7,8]. However, a recent multicenter study on the relationship between genetic factors and PEP produced compelling findings [9].

In addition to *PRSS1*, *SPINK1*, and *CASR*, that study prospectively investigated several genetic mutations suspected of being linked to pancreatitis in high-risk patient groups. They revealed that the *IRF2BP1* gene mutation is associated with PEP. The strength of the study lies in its multi-center approach, which generated robust data. Propensity score matching was employed during analysis to account for biases from operator differences and the various PEP-prevention methods across institutes. Although *CASR* mutations may affect the calcium concentration in pancreatic secretions

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due to contrast agents or physical stimuli, there was no significant difference in PEP risk. The significant difference in the *IRF2BP1* gene variant in PEP patients is a new finding. Additionally, even if there was no significant difference, the *CPAMD8* and *TUBGCP6* showed a potential relationship with PEP risk. Thus, identifying potential genetic variants that can be targeted in future pancreatic disease studies is noteworthy. However, while this study effectively identified a specific gene mutation associated with an increased risk for PEP, it did not thoroughly elucidate the potential pathogenesis and progression of PEP.

The exploration of genetic susceptibility and mutation analysis has emerged as a potential avenue to overcome the limitations of traditional approaches that rely on clinical factors and laboratory results. This paradigm shift holds the promise of revolutionizing current standardized evaluations, risk factor assessments, and treatment modalities. Although challenges, such as high cost and ambiguities in results, may hinder immediate implementation, many clinicians remain optimistic that technological and systematic advancements will address these concerns. Such progress will set the stage for future medicine to emphasize patient individuality, enabling more personalized treatment.

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