



Choledochoscopy combined with double-cannula lavage in the treatment of acute pancreatitis with encapsulated necrosis and the analysis of related inflammatory indexes

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Abstract

Objective This study aimed to evaluate the application of choledochoscopy combined with double-cannula lavage in the treatment of acute pancreatitis (AP) with encapsulated necrosis and analyzed related inflammatory indexes.

Methods Thirty patients with AP with encapsulated necrosis were enrolled and treated with choledochoscopy and double-cannula lavage. Serum white blood cell (WBC), procalcitonin (PCT), C-reactive protein (CRP), interleukin 6 (IL-6), IL-8, tumor necrosis factor alpha (TNF- α), and related inflammatory indexes were detected before and after surgery.

Results All of the participants who underwent the surgery recovered well and were discharged without serious complications; no deaths occurred. The serum WBC, PCT, and CRP of patients after surgery decreased compared with before the procedure, and the differences in WBC and CRP were statistically significant ($P < 0.05$); the difference in PCT was not statistically significant ($P > 0.05$). Postoperatively, IL-6, IL-8, and TNF- α levels were higher than before surgery, and the differences were statistically significant ($P < 0.05$).

Conclusion The surgical method presented herein effectively controlled and alleviated the infection of patients; it also did not increase the risk of infection and can thus be considered a safe and effective surgical method.

Keywords Choledochoscopy · Pancreatic encapsulated necrosis · Acute pancreatitis · Inflammatory factor

Pancreatic encapsulated necrosis is one of the late complications of severe acute pancreatitis (SAP) [1] and is also the primary cause of death in the late stage of AP [2]. The traditional surgical method for the treatment of pancreatic encapsulated necrosis is pancreatic necrosis clearance; however, the mortality of this surgical method is reportedly 4–25% [3–6]. Unlike other abscesses, pancreatic encapsulated necrosis is not easy to remove. In surgical treatment, intubation alone is difficult to drain completely, and abscess residues are likely to occur. However, traditional open surgery is gradually replaced by minimally invasive surgery because of its large trauma and high incidence of postoperative complications, and patients may not benefit from it under some circumstances. It is only used for the treatment of complications that cannot be solved by minimally invasive surgery. Percutaneous nephroscopy and laparoscopic retroperitoneal

approach are the main minimally invasive surgical methods at present. But there are still some problems when dealing with pancreatic encapsulated necrosis. First, since the material of laparoscope is hard, there are inevitably blind spots in surgical fields and small cavities are likely to remain after operation. Second, laparoscopic operations need to establish multiple approaches. It is difficult to establish approaches when lesions are small. Third, because the necrotic tissues are not very clear under the microscope, it is prone to removal excessive tissue, which may cause uncontrollable bleeding. A choledochoscope is a flexible mirror that can enter each abscess cavity smoothly, observe the abscess cavity in an all-round way, evaluate tissue activity at close range and debride thoroughly. As long as an access channel established, surgical operation can be performed without multiple approaches. Necrotic tissue removal instruments under choledochoscopy are soft instruments, which are not easy to cause uncontrollable hemorrhage. During choledochoscopy, lesions need to be filled with saline, cysts is in a full state, and abscesses can be clearly identified. These facilitate the entry of choledochoscope. In addition,

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with flowing water, floating necrotic tissue is easily distinguishable, which is helpful for judging the boundary of the necrotic tissue and avoiding excessive debridement. In the current authors' clinical department, choledochoscopy, combined with double-cannula lavage, was employed to treat pancreatic encapsulated necrosis. Furthermore, white blood cell (WBC), procalcitonin (PCT), C-reactive protein (CRP), interleukin 6 (IL-6), IL-8, and tumor necrosis factor alpha (TNF- α) levels were detected in patients' serum before and after surgery, and the changes in related inflammatory indexes were studied and analyzed.

Method and materials

Clinical data

A total of 30 patients who had been hospitalized in the authors' department from 2018 to 2021 were enrolled in the study, including 17 males and 13 females. The age of the patients ranged from 35 to 79 years (average, 53 years). A diagnosis of pancreatic encapsulated necrosis was based on the following: the patient's history of AP; the patient's symptoms, i.e., fever or abdominal pain; a laboratory examination showing elevated leukocytes, and abdominal computed tomography (CT) confirming obvious peripancreatic effusion. The inclusion and exclusion criteria are as follows. Inclusion criteria: severe pancreatitis secondary to peripancreatic encapsulated necrotic tissue infection; ineffective medical treatment of peripancreatic abscess, or residual abscess after drainage; pancreatic encapsulated effusion persisting for a long time, or with symptoms of compression; function of the heart, lungs and other organs can tolerate operations; normal blood coagulation; no other obvious contraindications to surgery. Exclusion criteria: function of the heart, lungs and other organs cannot tolerate operations; abnormal blood coagulation; abscesses confined to the lesser

omentum and cannot be drained by puncture. We evaluated all patients with acute physiology and chronic health evaluation-II (APACHE-II) score and computed tomography severity index (CTSI) before sinus expansion. APACHE-II scores of all patients were A/B. And CTSI were equal to or greater than 7 points.

Therapeutic methods

Treatment process is shown in Fig. 1.

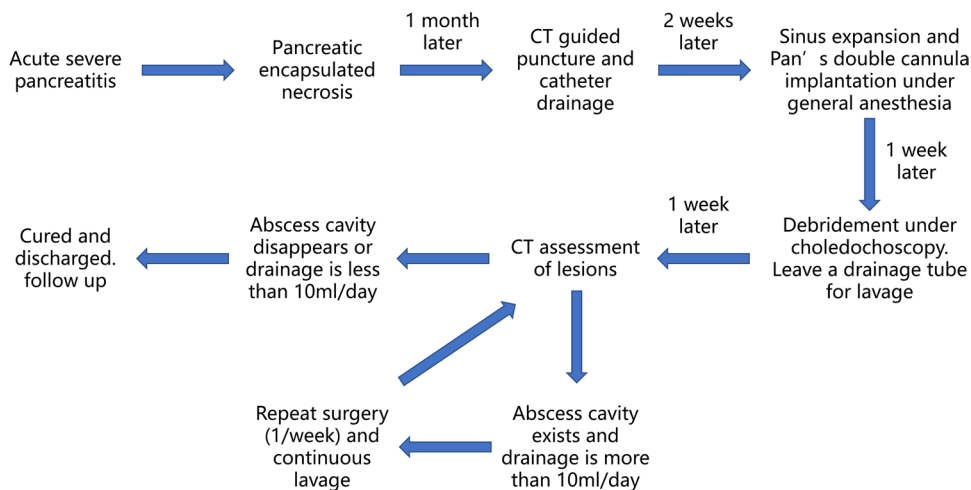
Computer tomography-guided puncture and catheter drainage

First, the abdomen was examined by non-enhanced CT scanning to determine the specific location, scope, and depth of the patient's focus, and a puncture path was designed. An 8F pigtail tube was inserted using the retroperitoneal approach under CT guidance. Large blood vessels and surrounding organs should be avoided when determining the puncture route. Following a successful puncture, the draining of purulent liquid could be observed if the drainage tube had been fixed properly.

Sinus expansion

Two weeks after a successful puncture and based on the assumption that the sinus tract had been completely formed, the patient was given general anesthesia; the original drainage tube was removed, and the sinus tract was expanded using the systematic dilator approach. A Pan's double cannula was placed and washed with hydrogen peroxide and normal saline. Following the surgery, the drainage bag was connected externally, and the saline irrigation and drainage were continued through the double cannula.

Fig. 1 Treatment process of the study



Debridement via choledochoscopy

One week after abdominal lavage, the necrotic tissue in the vicinity of the pancreas could be removed using a choledochoscope. The original drainage tube was removed, and the choledochoscope was guided through the sinus tract for exploration; the necrotic tissue was removed using a lithotomy net and biopsy forceps. Using the flexible characteristics of the choledochoscopy procedure, the entire pus cavity could be thoroughly explored.

Following exploration, the choledochoscope was placed in the deepest part of the purulent cavity; a super-sliding guide wire was placed, the choledochoscope was withdrawn, and a drainage tube was placed along the super-sliding guide wire. Irrigation and drainage were continued after completing the surgery. Due to the presence of a significant amount of necrotic tissue, the drainage tube could easily become blocked. Additionally, tissue necrosis in the vicinity of the pancreas was a gradual process, which often required multiple debridement procedures using the choledochoscope on average conducted once a week.

Test indexes

Blood samples were taken before and after each surgery to detect WBC, PCT, CRP, IL-6, IL-8, and TNF- α levels in the serum of all patients. Statistical analysis was also performed.

Statistical methods

Data were analyzed using the SPSS Statistics 21.0 software program. Measurement data were expressed as mean \pm standard deviation ($\bar{x} \pm SD$) or median (25%; 75%) and were compared with Student-*t* test or Mann–Whitney *U* test, respectively. $P < 0.05$ was considered statistically significant.

Results

Therapeutic effect

All patients underwent CT-guided puncture and drainage procedures. Choledochoscopic debridement was performed at least once and a maximum of six times. After treatment, the patients' general condition improved without fever, abdominal pain, or other symptoms. Once the patients resumed eating, they were discharged with a drainage tube, and regularly returned to the hospital for choledochoscopy and replacement of the drainage tube.

All the patients recovered well and were discharged without serious complications; no deaths occurred (see Fig. 2).

Analysis of related inflammatory indexes before and after surgery

The results (see Table 1) revealed that the serum WBC, PCT, and CRP of patients after surgery had decreased compared with before the procedure, and the differences in WBC and CRP were statistically significant ($P < 0.05$); the difference in PCT was not statistically significant ($P > 0.05$). Postoperative IL-6, IL-8, and TNF- α levels were higher than before the procedure, and the differences were statistically significant ($P < 0.05$).

Discussion

Acute pancreatitis is a serious inflammatory process of the pancreas. Its mortality rates range from 3% in patients with plexus stroma edematous pancreatitis to 17% in those with pancreatic necrosis [7, 8]. A large number of studies revealed that WBC, PCT, CRP, IL-6, IL-8, and TNF- α levels were positively correlated with the severity of infection and closely related to the occurrence and development of AP. C-reactive protein (CRP) is synthesized and secreted in the liver and will increase due to stress after infection; therefore, it is often considered to be a sensitive indicator for judging clinical acute inflammation [9]. An existing study revealed that CRP had a higher value for the early prediction and evaluation of SAP and could be used as an indicator for judging the severity of the disease [10]. Procalcitonin, a glycoprotein comprising 116 amino acids, serves as a precursor of calcitonin following a systemic inflammatory reaction due to severe infection and can be secreted by lung tissue, the pancreas, and colon tissue; the resulting increase in PCT level functions as a positive index following an inflammatory reaction. Chan et al. [11] confirmed that PCT was positively correlated with the severity of a bacterial infection, the incidence of complications, and mortality.

Tumor necrosis factor alpha (TNF- α), a mononuclear and important inflammatory response factor, is secreted primarily by mononuclear phagocyte system, can promote neutrophil phagocytosis, induce acute-phase protein synthesis of hepatocytes, and promote cell proliferation and differentiation [12]. In the early stages of AP, the elevation of TNF- α level can first be detected in the patient's serum; as such, TNF- α may be a trigger factor of AP [13]. In a study on the impact of TNF- α on the pathogenesis of AP, Satoh et al. [14] revealed that TNF- α participated in the development of AP, primarily through the protein kinase C-signaling and tyrosine kinase-2 signaling pathways. Gulcucuk et al. [15] further confirmed that when the concentration of

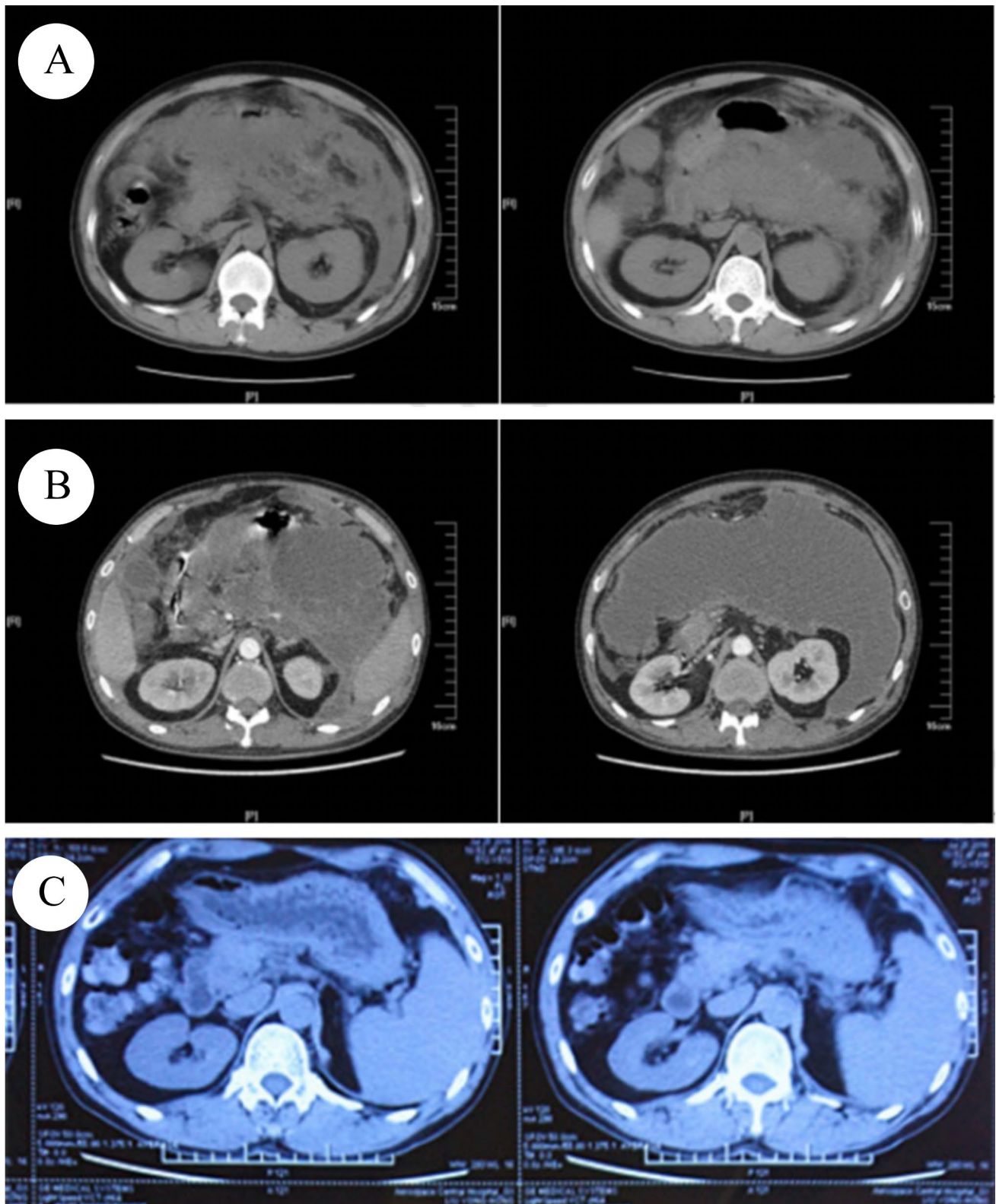


Fig. 2 CT shows pancreatic encapsulated necrosis before treatment (A), after 1 month of medical treatment (B), after 4 months of choledochoscopy treatment (C)

Table 1 Comparison of white blood cells and related inflammatory factors before and after operation

	WBC ($10^9/L$)	CPR (mg/L)	PCT (ng/mL)	IL-6 (pg/mL)	IL-8 (pg/mL)	TNF- α (pg/mL)
Before operation	9.41 (6.73; 11.79)	79.41 (47.5; 146.02)	0.22 (0.12–1.41)	23.85 \pm 2.17	24.07 (22.39–25.72)	23.88 \pm 2.19
After operation	7.29 (4.82; 8.37)	50.18 (33.65; 66.67)	0.17 (0.09–0.41)	115.27 \pm 12.08	112.58 (103.01–120.51)	115.59 \pm 12.16
<i>P</i>	<0.001 [#]	<0.001 [#]	0.110 [#]	<0.001*	<0.001 [#]	<0.001*

*Compared with Student-*t* test; [#]compared with Mann–Whitney *U* test

TNF- α is ≥ 8 –10 mol/L, it can induce the production of other cytokines, resulting in the gradual amplification of an inflammatory response.

Interleukin-6 is a major inflammatory factor that is released by a variety of cells and mediates acute-phase response under inflammatory stimulation. A recent study also found that IL-6 antibodies could induce the apoptosis of pancreatic acini in AP mice and, accordingly, reduce the severity of AP [16]. In addition, an increase in IL-6-level is related to the severity of AP and organ complications; clinically, it can be used to predict the severity and prognosis of AP [17].

Interleukin-8 (IL-8) is an inducer and chemokine of neutrophils. During AP, the active substances released by the pancreas and its surrounding tissue are absorbed into the blood and activate the monocyte–macrophage system, releasing a large number of cytokines and inflammatory transmitters (including IL-8) that further aggravate pancreatic damage and give rise to systemic complications [18]. In a study on the systemic complications of AP, Mayer et al. [19] found that the level of IL-8 in serum correlated with the severity of AP; the researchers also pointed out that IL-8 could predict fatal pancreatitis.

The results of the experiment presented in the current study revealed that postoperative serum levels of IL-6, IL-8, and TNF- α were higher than before surgery. The reason for this was considered to be related to the trauma of surgery. However, the WBC, PCT, and CRP serum levels of patients after surgery decreased compared with those before the procedure, and the differences in WBC and CRP were statistically significant ($P < 0.05$); the difference in PCT was not statistically significant ($P > 0.05$).

The authors analyzed the results of the current study and considered that the main reason for a lack of statistical difference in PCT had been the small number of cases. In future studies, the sample size can be increased to support the results of the current analysis.

Based on preliminary studies by Tong et al. [20], the preferred treatment for diagnosed SAP (severe acute pancreatitis) involves enhanced CT or ultrasound-guided percutaneous puncture drainage, complemented by a “double cannula” for continuous negative pressure suction to optimize drainage effects. Subsequently, percutaneous endoscopic necrosectomy (PEN) is conducted through the

double-cannula tract. Open surgery for pancreatic necrosectomy is considered only when there is no clinical improvement after these treatments and the patient meets surgical criteria. Also, existing literature [21–23] has demonstrated that laparoscopic surgery offers advantages over traditional open surgery in terms of complications and mortality rates when treating acute pancreatitis.

In this study, the intervention of PEN was applied at an early stage, resulting in significant improvement in all patients, who subsequently recovered well and were discharged without severe complications. This underscores the clinical efficacy of minimally invasive necrosectomy. Moreover, recent guidelines have recommended a progressive treatment approach based on minimally invasive techniques as the initial intervention. Therefore, traditional open surgical debridement was not employed for patients included in this study.

As a minimally invasive technique, PEN offers advantages such as less trauma, minimal bleeding, and faster recovery, which are primary reasons for investigating this method in treating related diseases. However, the main challenge in treating SAP lies in preventing acute abdominal bleeding related to the duration of intervention. Considering patients with extensive infected pancreatic necrosis who may require a longer period of PEN treatment and are generally in poor condition, surgical intervention might be necessary. This scenario was not encountered in our study population; hence, our conclusion that PEN is superior to traditional open surgery lacks certain data support and requires further exploration.

Nonetheless, by comparing the WBC and CRP results, as well as changes in clinical symptoms (e.g., patient temperatures), the authors considered that the surgical method presented herein could effectively control and alleviate the infection of patients. Furthermore, although IL-6, IL-8, and TNF- α serum levels were increased to some degree, the clinical symptoms of patients were improved. Considering that the surgical procedure itself had a stimulating effect on the body but did not increase the risk of infection, this surgical method can be considered as being safe and effective.

The revised Atlanta Classification of Acute Pancreatitis (2013) updated the terminology used to describe pancreatic effusion and divides inflammatory effusion into four categories, i.e., acute peripancreatic effusion, pancreatic

pseudocyst, acute necrotic accumulation, and pancreatic encapsulated necrosis [1]. The traditional management for pancreatic encapsulated necrosis is open debridement treatment.

However, due to the significant trauma (that is already present due to the condition) and based on the popularization of the concept of minimally invasive surgery and the progress of laparoscopic technology, management has gradually shifted to laparoscopic necrotic tissue removal [21, 22]. However, because the laparoscope is a hard mirror, the current authors considered choledochoscopy as being better suited to this type of surgery. Following drainage and lavage, the pus cavity generally becomes narrow and rugged; a laparoscope will encounter difficulties bypassing these deviations for in-depth observation, and a dead cavity can easily be overlooked. The advantage of a choledochoscopy is its “soft mirror” characteristics; experienced clinicians can use a choledochoscope to observe the pus cavity in an all-inclusive manner without the risk of “dead angles,” enabling them to fully clear all dead cavities. Furthermore, the drainage tube can be placed as deep as possible to achieve full lavage and drainage.

Conclusion

This experimental study found that choledochoscopy combined with double-cannula lavage could effectively treat pancreatic encapsulated necrosis without increasing the risk of infection, thereby presenting a feasible treatment method.

However, due to the small number of cases included in this trial, the data may differ in larger studies. In future studies, the authors aim to include larger sample sizes to gather more accurate data. This study presents several limitations that should be considered when interpreting the results. One significant limitation is the absence of patients requiring prolonged PEN treatment or those in poor general condition within our sample. This exclusion might limit the generalizability of our findings, as our conclusions about the superiority of PEN over traditional open surgery may not hold true for more complex or severe cases of SAP. Consequently, further studies involving a broader and more diverse patient population are necessary to validate our results comprehensively and to explore the efficacy and safety of PEN in managing more challenging SAP scenarios.

Additionally, by conducting follow-up appointments with patients who had previously undergone choledochoscopy, combined with double-cannula lavage surgery, the authors aim to investigate whether there were differences related to long-term complications.

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Data Availability The datasets used and/or analysed during the current study available from the corresponding author on reasonable request. We declared that materials described in the manuscript, including all relevant raw data, will be freely available to any scientist wishing to use them for non-commercial purposes, without breaching participant confidentiality.

Declarations

Disclosures All authors have nothing to disclose.

Conflict of interest Qiang Zhang, Xiangnan Ai, Tengfei Wang, Yugang Qin declare that they have no conflict of interest.

Ethics approval and consent to participate This study was conducted with approval from the Ethics Committee of Aerospace Center Hospital. This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

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