Editorial Commentary

Optimal timing of intervention in pancreatic necrosis-current status

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Acute necrotizing pancreatitis (ANP) is observed in 20–40% of cases with episode of acute pancreatitis (AP) (1). Secondary infection of pancreatic or peripancreatic necrosis may result in significant morbidity and mortality in course of AP (2). The treatment of patients in early and late phase of ANP depends on the clinical condition of patients (3-5). In majority of patients with ANP the best therapeutic strategy is intensive conservative treatment in the early stage alternatively followed by interventional treatment in the late stage of AP if required. The word "required" is of a very important meaning here, because according to many publications in some patients with ANP it is possible to avoid interventional treatment. In pancreatic or peripancreatic necrosis intervention should be delayed by at least first four weeks of ANP (3-6). In almost half of the patients with ANP, pancreatic or peripancreatic necrosis will spontaneously regress. In the remaining patients, after four weeks of ANP the necrotic tissues become liquified, necrosis becomes walled-off and necrotic collection is created (*Figure 1*) (3-6). According to medical reports, postponed intervention in ANP improves the therapeutic results and reduces complications and mortality rates (3,7,8). Nevertheless, these reports were describing the surgical treatment only (9). Data concerning early intervention with use of minimally invasive techniques in managing the consequences of ANP are sparse. Involvement of minimally invasive techniques in treatment of ANP consequences largely reduces the complications compared with surgical open necrosectomy (10). Despite this knowledge, the optimal timing of intervention in ANP is unclear and mostly depends on experience of medical center.

In POINTER trial (11,12) the authors were trying to estimate the optimal timing of intervention in case of ANP. To achieve this, they divided patients with infected pancreatic necrosis into two groups (11,12). The first group of patients with immediate drainage included treatment with antibiotics and catheter drainage in first 24 hours after randomization (which occurred as soon as infected necrosis was diagnosed) (11,12). The second group that consisted of patients with postponed catheter drainage consisted of antibiotic treatment and supportive treatment to postpone the drainage procedure until the phase of walled-off pancreatic necrosis (at this stage necrotic collections were liquefied or fully encapsulated) (11,12). Additionally, in late stage of ANP the pancreatic necrosis gradually liquifies, which improves draining conditions. In both groups of patients with infected pancreatic necrosis, image-guided percutaneous or endoscopic transluminal drainage were performed (11,12). The authors compared the results of treatment in both groups (11,12). It should be stressed that only patients with infected pancreatic necrosis participated in POINTER trial (11,12). Patients with sterile necrosis were excluded from the study (11,12).

The publication titled "Long-Term Outcome of

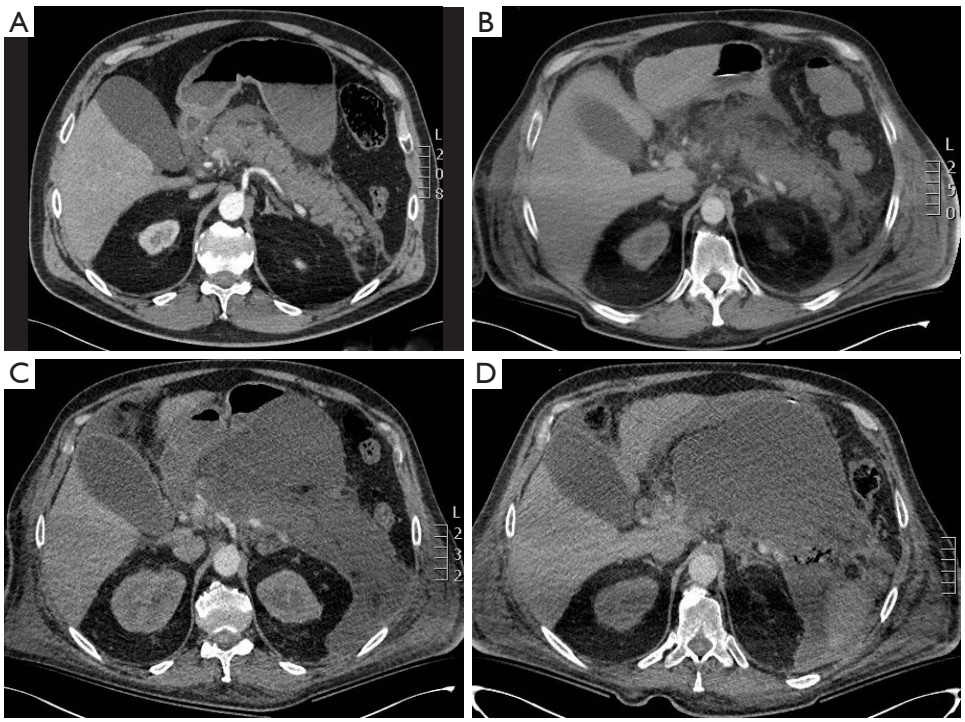

Figure 1 The course of ANP in the same patient in consecutive abdominal contrast-enhanced computed tomography: from pancreatic necrosis (A) in form of acute necrotic collection (B) to infected walled-of pancreatic necrosis (C,D). Scale bar is a radiological reference. L, left side; ANP, acute necrotizing pancreatitis.

Immediate Versus Postponed Intervention in Patients With Infected Necrotizing Pancreatitis (POINTER): Multicenter Randomized Trial" (11) is a continuation of previous study by Boxhoorn *et al.* (12). In the multicenter, randomized superiority trial from 2021 titled "Immediate versus Postponed Intervention for Infected Necrotizing Pancreatitis" the authors did not show superiority of immediate drainage over postponed drainage with regard to complications in patients with infected ANP (12). Moreover, in this trial Boxhoorn *et al.* show that the postponed-drainage strategy requires fewer invasive interventions compared to immediate drainage (12). In the randomized POINTER trial, patients with the postponed-drainage approach using antibiotic treatment did not require intervention in one third of all cases (12). The main result of POINTER study is conclusion, that the postponed drainage of pancreatic necrosis is a favorable approach (12). In the study from 2021 huge limitation was short follow-up period (6 months) (12). In the current study (11) the authors showed results of long-term follow-up of patients from POINTER study (12). During long-term follow-up (median 51 months), the authors (11) confirmed outcomes from the previous study (12) concluding that postponed drainage approach using antibiotic therapy in patients with infected ANP results in fewer interventions as compared to immediate drainage approach (12). For this reason, the postponed drainage should be preferred choice as long as clinical condition of patient is suitable (12). The authors concluded that postponing or even omitting drainage does not lead to long-term adverse outcomes in patients with infected ANP (12). One must not forget, that some patients with infected pancreatic necrosis may still benefit from an immediate approach, as in general the duration of organ failure impacts clinical outcomes. Moreover, some patients will still require interventional treatment within first 4 weeks of ANP (7-10).

POINTER trials clearly showed that postponed intervention in patients with infected necrotizing pancreatitis results in better outcomes than immediate intervention (1,2). These are the first studies reporting use of minimally invasive techniques in ANP, which resulted with better outcomes than with use of postponed intervention (1,2). Before these studies, most information about efficiency of delayed interventions in ANP, came

from studies concerning open surgery (8-10). For reasons mentioned above, the POINTER trials are a breakthrough in management of patients with ANP (1,2). Earlier we only had isolated reports about postponed endoscopic intervention in patients with pancreatic necrosis (mainly retrospective ones) (13,14).

In conclusions, we have to agree that optimal strategy of management of pancreatic necrosis is postponing of interventional treatment after four weeks from onset of ANP and the strategy of choice is "step-up approach" (3-16), especially in the patients with infected pancreatic necrosis (11,12). Nevertheless, the question of optimal timing of intervention in pancreatic necrosis remains unanswered. On the one hand we know that postponing improves the outcomes of intervention, but on the other hand we know that too long persistence of pancreatic necrosis may cause development of the pancreatic fistulas and in the course of long-term impression on blood vessels leads to development of thrombosis. It should be noted that above-mentioned complications of ANP appeared in patients from POINTER trial in both arms, but patients with postponed intervention did not show worse results than immediate intervention patients (11,12). Even in case of long-term follow-up (Boxhoorn *et al.*) there was no significant difference between two groups of patients (12). Despite many studies the question of optimal timing of intervention in ANP is still open and further randomized trials are required. The next question is necessity of drainage of sterile pancreatic and peripancreatic necrosis, because POINTER trial (11,12) concerns infected pancreatic and peripancreatic necrosis only.

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