CLINICAL—PANCREAS

Efficacy of Conservative Treatment, Without Necrosectomy, for Infected Pancreatic Necrosis: A Systematic Review and Meta-analysis

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BACKGROUND & AIMS: Conservative treatment (intensive care, a combination of antimicrobial agents, and nutritional support, with or without drainage of the infected fluid) has recently been shown to be effective for patients with infected pancreatic necrosis (IPN), but the data from individual studies are not robust enough to recommend it as the standard of care. We performed a systematic review and meta-analysis of studies related to primary conservative management for IPN. **METHODS:** We performed a literature search of MEDLINE/PubMed from January 1990 to March 2012 for studies of a priori protocols for primary conservative treatment, without necrosectomy, for consecutive patients with IPN. We analyzed data from 8 studies, comprising 324 patients with IPN who received primary conservative management. We then analyzed an additional 4 studies (comprising 157 patients) that reported the efficacy of percutaneous drainage in nonconsecutive patients with IPN. Outcome measures were the success of conservative management strategy, need for necrosectomy, and mortality. **RESULTS:** There was significant heterogeneity in results among the studies. Based on a random effects model, conservative management was successful for 64% of patients (95% confidence interval [CI], 51%–78%); mortality was 12% (95% CI, 6%–18%), and 26% of patients required necrosectomy or additional surgery for complications (95% CI, 15%–37%). A separate analysis of 4 studies that reported outcomes of nonconsecutive patients with IPN following percutaneous drainage had comparable results; 50% had successful outcomes (95% CI, 43%–58%), mortality was 18% (95% CI, 6%–30%), and 38% of patients required surgery (95% CI, 20%–56%). **CONCLUSIONS: Conservative management without necrosectomy is a successful approach for 64% of patients with IPN. This approach has low mortality and prevents surgical necrosectomy.**

Keywords: Acute Pancreatitis; Necrosis; Therapy; Infection.

Acute pancreatitis is a potentially lethal disease with considerable morbidity and 10% to 40% mortality.[1] There are 2 major forms of acute pancreatitis: interstitial and necrotizing. Acute necrotizing pancreatitis usually runs a severe course and is the cause of most of the morbidity and mortality.[2] Although patients with sterile pancreatic necrosis may have a severe course and die, infection of the nonviable necrotic pancreatic tissue is an ominous development during the course of acute pancreatitis. We and others have shown that the extent and infection of pancreatic necrosis correlate with the development of organ failure and mortality in acute pancreatitis.[3,4] Infected pancreatic necrosis (IPN) is the cause of most of the late mortality during the course of acute pancreatitis. Although conservative treatment is recommended for sterile necrosis, surgical necrosectomy has generally been considered the standard of care for IPN according to various practice guidelines.[5–7] Conservative treatment has not been considered a viable option in patients with IPN. However, in addition to a few anecdotal case reports, 2 case series have shown that conservative treatment might be successful in a substantial percentage of patients with infected necrosis.[8–12] We showed in a comparative study that conservative treatment is effective and comparable to surgical necrosectomy.[13] However, the data from individual studies are not robust enough to change the practice recommendations for patients with infected necrosis from surgical necrosectomy to conservative treatment. To derive a meaningful conclusion from these studies, we performed a systematic review and meta-analysis of all published studies that have reported management of patients with IPN primarily with conservative treatment without necrosectomy. Conservative therapy for IPN included intensive care, combination antimicrobials, and nutritional support, with or without drainage of the infected fluid collections in the reported studies. Although percutaneous drainage is a form of intervention and not truly conservative, it has been considered a part of medical conservative treatment because it does not involve surgery or formal necrosectomy. Our objective was to determine the effectiveness of therapy for IPN without necrosectomy; thus, for the purpose of this systematic review and meta-analysis, we included studies that used a conservative management protocol for consecutive patients with IPN that allowed for percutaneous drainage but not any form of necrosectomy: percutaneous, endoscopic laparoscopic, or open surgical.

Abbreviations used in this paper: APACHE II, Acute Physiology and Chronic Health Evaluation II; CI, confidence interval; CTSI, computed tomography severity index; IPN, infected pancreatic necrosis.

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Subjects and Methods

Study Selection

A systematic literature search was conducted to locate the relevant published articles on treatment of IPN through MEDLINE/PubMed from January 1990 to March 2012. The keywords used for the search included a combination of "infected pancreatic necrosis," "organized pancreatic necrosis," "walled off pancreatic necrosis," or "acute pancreatitis" AND "conservative treatment," "necrosectomy," or "nonsurgical treatment." Studies published as full articles in any language were eligible, but those published only as abstracts were not included. Cross-references were also searched manually. The authors of the selected articles were contacted to provide any missing relevant information and data. Attempts were made to contact the authors of respective studies that were published in languages other than English. The authors of a Korean study published in the Korean language provided data in English.[14]

Inclusion Criteria

Studies in which conservative treatment was reported as the primary management modality for consecutive patients with IPN were included in this meta-analysis. Conservative treatment was defined as supportive treatment, including care in an intensive care unit and antimicrobial therapy with or without percutaneous drainage but without any form of necrosectomy (ie, surgical, endoscopic, laparoscopic, retroperitoneal, or nephroscopic). Nonresponse (ie, failure of conservative treatment) was defined as the need for any form of necrosectomy and/or mortality. A few studies reported endoscopic drainage alone without necrosectomy in some patients, and that has been mentioned separately.

Exclusion Criteria

Studies with a small sample size (≤5 in number), studies in which any form of necrosectomy or endoscopic drainage was performed as the primary treatment modality, and studies that included patients with chronic pancreatitis were excluded.

There have been a few published studies with a sizeable number of patients with IPN that reported the efficacy of the percutaneous drainage procedure but did not include consecutive patients with IPN. Although these studies did not exactly fulfill our inclusion criteria, we have summarized and analyzed them separately because these studies also highlighted the principle of conservative management for IPN.

Data Extraction

Data regarding the following variables were extracted from the final selected studies: total number of patients with acute necrotizing pancreatitis during the study period, age, sex, etiology of pancreatitis, severity of pancreatitis, organ failure, computed tomography severity index (CTSI), severity scores (Acute Physiology and Chronic Health Evaluation II [APACHE II], Ranson), number of patients with IPN, criteria for diagnosing IPN, type of treatment, reason for offering a particular type of treatment (particularly conservative treatment) for infected necrosis, need for additional treatment (ie, necrosectomy in any form or surgery) for complications pertaining to percutaneous drainage/conservative management, type of necrosectomy (open surgical, minimally invasive surgical, endoscopic, or percutaneous), and mortality. The data were extracted, collated, and analyzed by 2 of the authors independently. Any difference was resolved by consensus.

Outcome Measures

The outcomes measures were (1) successful outcome of patients with IPN with conservative treatment (antibiotics and/or percutaneous drainage) without necrosectomy, (2) need for any form of necrosectomy or surgical intervention for complications related to percutaneous drainage/conservative management, and (3) mortality.

Statistical Analysis

The relevant extracted data were entered into an Excel sheet (Microsoft Corp, Redmond, WA). Stata version 11.1 (Stata Corp, College Station, TX) was used for statistical analysis. Analysis was performed using the command metan. I^2 test was used to assess heterogeneity of results among the studies. The random effects model was used for the meta-analysis when there was significant heterogeneity among the included studies. Random effects weights were estimated based on the DerSimonian and Laird method. Publication bias was assessed by Egger test.

Results

Characteristics of the Included Studies

The literature search revealed 965 articles, of which 932 were excluded after reviewing the title and abstract. A complete review of the full text was conducted for the remaining 33 articles, and 21 were excluded (Figure 1). The reasons for exclusion were as follows: conservative management not being the primary treatment (6 studies),[15–20] studies without characterization of patients into sterile or infected pancreatic necrosis (4 studies),[21–24] studies including ≤5 patients (3 studies),[8,9,25] percutaneous debridement (2 studies),[26,27] duplication of part of data (2 studies),[28,29] short reviews of other relevant studies (2 papers),[30,31] combined percutaneous and endoscopic drainage with high-volume lavage (1 study),[32] and inability to procure the results of a Chinese study in the English language (1 study).[33] Eight studies fulfilled completely the criteria for inclusion in the current meta-analysis, and these are presented as the group A studies.[11–14,34–37] In addition, 4 studies that reported the results of only those patients who underwent percutaneous drainage for the management of IPN are summarized in group B because they reflected the principle of conservative management for IPN.[38–41] The patients included in the group B studies were not consecutive, but rather were se-

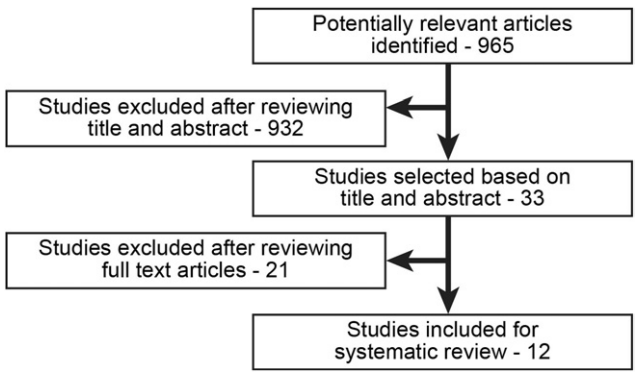

Figure 1. Flow-chart regarding selection of relevant studies.