



ARISTOTLE UNIVERSITY OF THESSALONIKI, SCHOOL OF MEDICINE
SECOND SURGICAL PROPEDEUTIC DEPARTMENT
Professor Theodoros E Pavlidis MD, PhD
Hippokration General Hospital, Konstantinoupoleos 49, 546 42, Thessaloniki, Greece
Tel: ++30 2310 992861, email: pavlidth@auth.gr

Editorial Bord ID: 00058511

Thessaloniki 19 December 2022

Dr. Lian-Sheng Ma, Founder and Chief Executive Officer
Baishideng Publishing Group, Inc.

Dear Editor:

Thank you for your preliminary decision regarding our invited paper entitled "Management of infected acute necrotizing pancreatitis" (Manuscript NO: 81037), which was sent to the *World Journal of Clinical Cases* for publication as a *Letter to the Editor*.

I would like to thank the reviewers for their earnest efforts in reviewing the manuscript. I accepted and responded step by step to all considerations by the reviewers improving the manuscript. The changes are highlighted by yellow.

Reviewer 1: Many thanks for his positive comments. No changes have been suggested.

Reviewer 2: Many thanks for his positive comments and the minor but considerable suggested change. It has been done by adding for the future directions four new references [23-26] and the following text: "*Serum pancreatic enzyme assessment and imaging for early detection of the disease course may be useful. Nanoparticles have been used as drug carriers and could be valuable for the application of both antibodies and antibiotics. Nanotechnology could be used to possibly overcome the resistance of microbes to antibiotics. In addition, it has been postulated that gene therapy may be more effective than drug therapy in severe acute pancreatitis [22].*

In addition to what has already been mentioned above, novel future directions include nanotechnology, the application of hydrogen peroxide (H₂O₂) in necrosectomy, 3D CT (3-dimensional computed tomography) cinematic, and anti-inflammatory monoclonal antibodies.

The preliminary use of H₂O₂ in endoscopic necrosectomy of walled-off necrosis showed excellent outcomes. Thus, prospective randomized controlled trials are necessary to precisely establish its role [23,24].

The novel volumetric 3D CT and cinematic rendering may improve further diagnosis and prognosis by precisely identifying infected necrotic tissue and local complications [25].

To date, there has not been etiopathogenic management of severe sepsis and septic shock consequences, despite the current considerable progress, unless patients undergo surgery and supportive intensive care. In infected pancreatic necrosis, proinflammatory factors, mainly tumor necrosis factor- α (TNF- α) but also interleukins (IL-6, IL-8) and monocyte chemotactic protein (MCP-1), activate the body's defense response to inflammation,



ARISTOTLE UNIVERSITY OF THESSALONIKI, SCHOOL OF MEDICINE
SECOND SURGICAL PROPEDEUTIC DEPARTMENT
Professor Theodoros E Pavlidis MD, PhD
Hippokration General Hospital, Konstantinoupoleos 49, 546 42, Thessaloniki, Greece
Tel: ++30 2310 992861, email: pavlidth@auth.gr

causing SIRS (systemic inflammatory response syndrome), which is called sepsis. If this initially beneficial reaction is not balanced by the CARS (compensatory anti-inflammatory response syndrome), then it will become uncontrolled and excessive, which leads to disseminated cell damage causing MODS (multiple organ dysfunction syndrome) and ultimately death [22,26]. Thus, the regulation of this balance by the use of antibodies or molecules against the most important inflammatory mediator of the cytokine cascade, TNF- α , would be crucial. The levels of TNF- α were increased within 1-2 hours of endotoxin injection in an experimental model [26]." (page 5, 10 last lines; page 6, lines 1-20)

Reviewer 3: Dr. Wu, thank you very much for accepting the paper. I agree absolutely with your extended comments which include your personal opinion reflecting your correct management strategy. Generally, this manuscript has been written having this in mind as the central idea and according to your point of view, and all the essence of your comments was included. However, your main valuable suggestions have been added in the conclusion to highlight the issue further. *"Percutaneous catheter drainage is the first step. Endoscopic debridement usually requires an elapsed time of three to four weeks. Transgastric debridement (laparoscopic or open) is suitable for central retrogastric collections. Laparoscopic transperitoneal debridement is suitable for isolated collections at the root of the mesentery. Open transperitoneal debridement is only performed when a collection is inaccessible to all other methods of drainage or after the step-up approach has failed."* (page 6, lines 22-28)

I am sending the revised manuscript and hope to receive a favorable final decision.

We look forward to hearing from you at your earliest convenience.

Sincerely,

Theodoros E Pavlidis MD, PhD

Professor of Surgery

School of Medicine, Aristotle University of Thessaloniki, Greece,

Hippokration Hospital, Konstantinoupoleos 49, 546 42, 2nd Surgical Propedeutic Department

Tel: ++302310 992861; e-mail: pavlidth@auth.gr

Editorial Bord ID: 00058511