Modern Medicine. 2015, Vol. 22, No. 1 : 31-38 

**Review**

# SIRS and MODS in Acute Pancreatitis

**C.C. Popa[1,2], Octavia Cristina Rusu[1], Alexandra Kocsis[1], S.I. Neagu[1,2], C.R. Strugaru[2,3]**

[1]2nd Surgery Clinic, University Emergency Hospital Bucharest, Romania
[2]10th Clinical Department - Surgery, Faculty of Medicine, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
[3]Discipline of Medical Genetics, Bucharest, Romania

## REZUMAT

***SIRS și MODS în pancreatita acută***

Pancreatita acută reprezintă o boală gravă, caracterizată prin inflamația acută a celulelor acinare glandulare pancreatice. Pierderea controlului local sau exagerarea reacției inflamatorii va determina din partea organismului un răspuns inflamator, care poate fi de două feluri: sindromul răspunsului proinflamator sistemic, respectiv sindromul răspunsului antiinflamator compensator. Dezechilibrul provocat de influențele celor două tipuri de răspunsuri asupra organismului produc numeroase consecințe clinice și biologice grave. În stadiul final de evoluție a bolii, datorită unei reacții compensatorii antiinflamatorii ineficiente sau excesive, se instalează imunosupresia și disfuncția multiplă de organe (MODS), cu morbiditate și mortalitate crescută. Disfuncțiile întâlnite în MODS sunt numeroase: cardiovasculară, respiratorie, renală, hepatică, hematologică, intestinală, neurologică și metabolică.

**Concluzii:** Pentru clinicieni este important de înțeles mecanismul fiziopatologic complex ce apare în evoluția unei pancreatite acute severe, în vederea instituirii cât mai precoce a tratamentului corespunzător.

**Cuvinte cheie:** sindromul răspunsului inflamator sistemic, insuficiență multiplă de organe, pancreatita acută

## ABSTRACT

Acute pancreatitis is a serious illness characterized by acute inflammation of the pancreatic acinar gland cells. Loss of local control or exaggerated inflammation will cause an inflammatory response of the body that can be of two kinds: systemic pro-inflammatory response syndrome or compensatory anti-inflammatory response syndrome. The imbalance caused by the influences of two types of body responses produces numerous serious clinical and biological consequences. In the final stage of the disease, due to inefficient or excessive compensatory anti-inflammatory reaction, immunosuppression and multiple organ dysfunction (MODS) with increased morbidity and mortality set in. Dysfunctions encountered in MODS are numerous: cardiovascular, respiratory, renal, hepatic, hematological, intestinal, neurological and metabolic. Conclusion: It is important

**Corresponding author:** Assist. Prof. Cristian Constantin POPA, MD, PhD
Specialist in General Surgery
169 Splaiul Independentei Street, 050098, Bucharest, Romania
e-mail: cristianconstantinpopa@yahoo.com

for clinicians to understand the complex pathophysiological mechanism occurring in the evolution of severe acute pancreatitis in order to apply the appropriate treatment as early as possible.

**Key words:** systemic inflammatory response syndrome, multiple organ failure, acute pancreatitis

Acute pancreatitis is the acute inflammation of the glandular pancreatic acinar cells, the consequence of parenchymal enzyme activation. Acinar local autodigestion which determines tissue destruction and ischemic necrosis sets in. Simultaneously, the local inflammatory reaction is followed by the release of pancreatic enzymes in the systemic circulation. In this situation, inflammatory cells appear, which stimulates the production of inflammatory mediators (1,2).

The loss of local control or exaggerated inflammatory reaction triggers the systemic inflammatory response syndrome (SIRS). The factors involved in determining the systemic response may be infectious (bacteria, viruses, fungi, parasites etc.), noninfectious (trauma, pancreatitis, burns etc.), or a combination of all the above (**Fig. 1**). In clinical and paraclinical terms, the systemic inflammatory response syndrome is defined by the presence of at least one of the following criteria: heart rate > 90 beats/min.; hyperventilation objectified by respiratory rate > 20/min. or Pa CO2 < 32 mmHg; body temperature > 38°C or < 36°C; WBC > 12,000/mm$^3$ or < 4,000/mm$^3$ (3,4,5). The international conference to define sepsis has found that clinical signs are nonspecific SIRS and for a more precise definition of sepsis adding several important biological elements is necessary: adrenomoduline, CD14 (S), ELAM-1 (S), extracellular phospholipase A2, interleukin (IL-6), MIP (S), C-reactive protein, all these elements showing significant increases. Following the consensus of the International Conference to define sepsis in 2001 the following terminology was proposed and approved:

- SIRS is the systemic inflammatory response of the body to a variety of infectious and non-infectious causes;
- sepsis is SIRS due to infection (infection represents a pathological process due to invasion of tissues or fluids or body cavity by pathogenic or potentially pathogenic micro-organisms);
- severe sepsis occurs as a result of sepsis complicated by organ dysfunction or hypoperfusion or hypotension;
- hypotension occurs due to sepsis;
- septic shock is manifested by persistent tissue alteration and refractory hypotension;
- multiple organ dysfunction syndrome (MODS) is the final stage (**Fig. 2**) (6).

After producing cellular injury, the body's inflammatory response may result in one of the following two ways: systemic inflammatory response syndrome

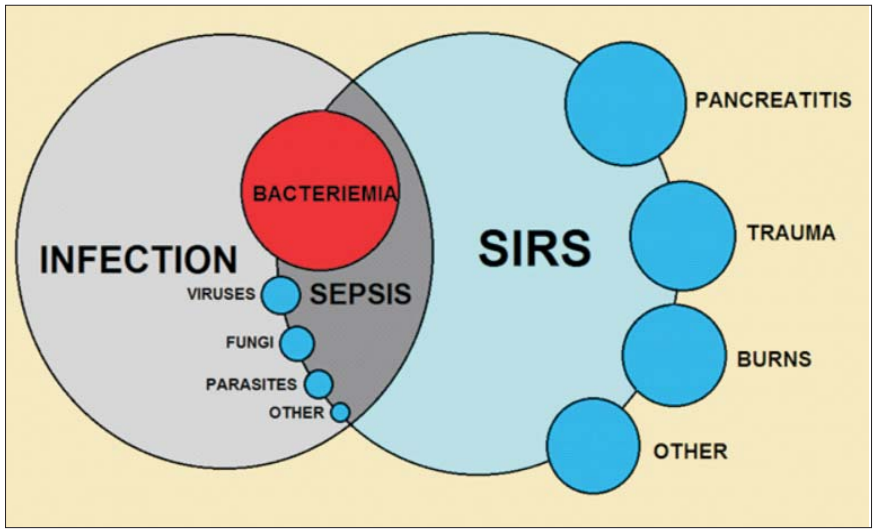


**Figure 1.** Interrelation between SIRS, infection and sepsis

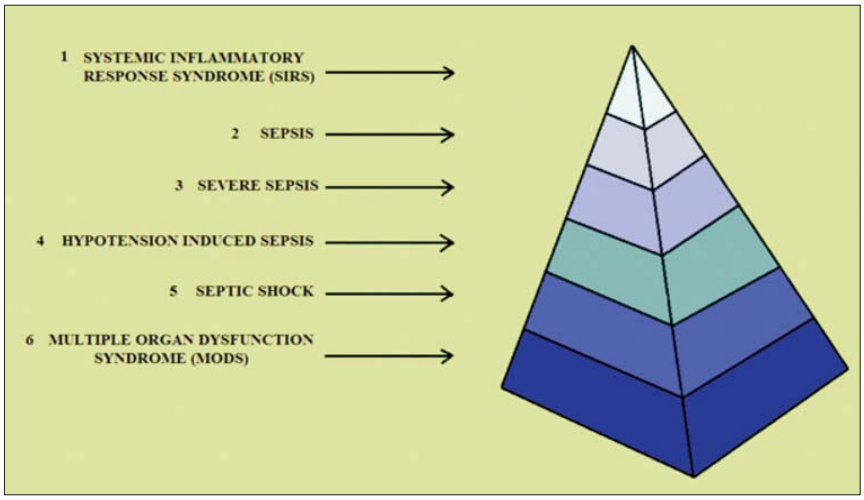


**Figure 2.** Definitions of sepsis

(SIRS) and compensatory anti-inflammatory response syndrome (CARS), as shown in **Fig. 3**. The patient being in a serious condition adapts with difficulty to the whole complex pathophysiological changes that occur in a relatively short period of time and, therefore all the premises for progressive development of MODS are insured. The imbalance caused by the influences of the two types of responses in the body, SIRS or CARS, produce many serious consequences: cardiovascular shock, altered homeostasis, apoptosis, organ dysfunction and immune suppression (5,7). A dark spectrum, called CHAOS (C-cardiovascular shock, H-homeostasis, A-apoptosis, O-organ dysfunction, S-immune suppression) will result (8). Complex cell response to injury can be seen in **Fig. 4**. Severe sepsis is accompanied by the development and duration of visceral dysfunction, which is variable, depending on the organ affected. Pulmonary dysfunction sets in early and remains persistent, and the most severe form, ARDS, occurs early and lasts for about 9 days. Simultaneously shock and oliguria occur at the onset of severe sepsis and lasts for about two days and it either gets better or becomes fatal. On the other hand, coagulation, liver and central nervous system dysfunctions are promptly instituted, within hours or days after the onset of severe sepsis and are maintained over a long period of time. If these pathological changes are added to any other visceral dysfunction, mortality risk increases by 15-20% (9).

SIRS develops in several stages. Initially, the body defends itself by releasing of mediators in affected and/or infected tissues. The appearance of the inflammatory response is intended to limit the actions of pro-inflammatory mediators. In a later stage, especially if injuries and/or infections are severe, pro-inflammatory and anti-inflammatory mediators are released into the systemic circulation.

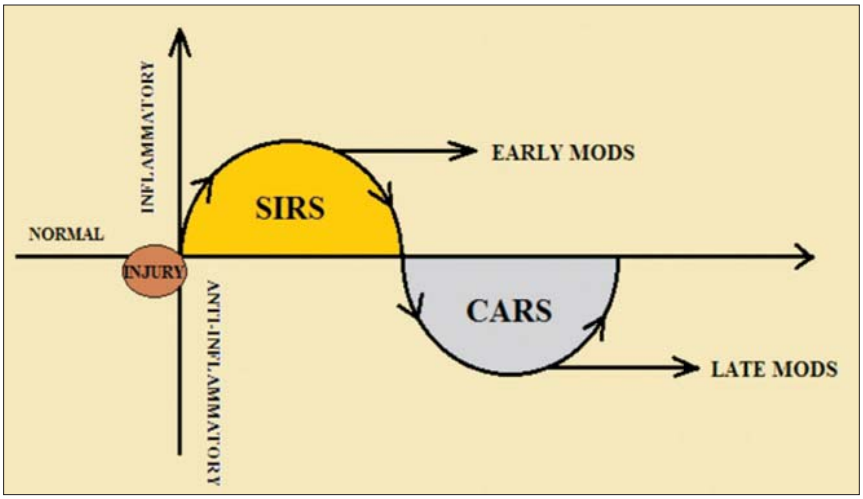


**Figure 3.** The inflammatory response depending on SIRS and CARS

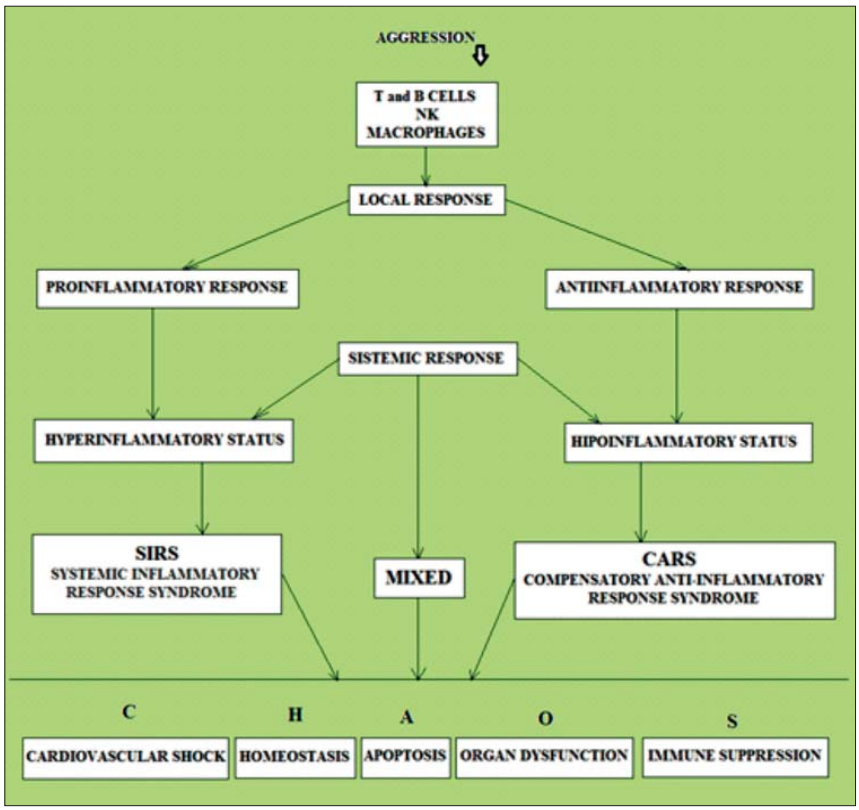


**Figure 4.** Interrelation between systemic inflammatory response and compensatory anti-inflammatory response

At this time, clinically and biologically confirmed SIRS appears. In the third stage, while reducing pro-inflammatory response regulation through excess or failure, systemic reaction occurs, with clinical and laboratory evidence of SIRS, comprising: organization of platelet sludge with shortened microcirculation, possibly with the advent of cellular ischemia and hypoxia; impaired endothelial cells function, with increased permeability of microcirculation; coagulation system activation; intense vasodilatation; transudative fluids; improper distribution of blood flow; all these pathological changes eventually leading to alterations in circulatory function and shock installation. Unless a prompt rebalance of homeostasis is being done, organ dysfunction or failure will occur. In the last phase an inefficient or excessive compensatory anti-inflammatory response occurs, which results in the end in immunosuppression and in MODS with increased morbidity and mortality (3,4,10,11,12,13,14,15).

Known by different terminologies, MODS (multiple organ dysfunction syndrome), MOF (multiple organ failure), MSOF (multiple systems organ failure), MOFS (multiple organ failure syndrome) or MOSF (multiple organ system failure) is characterized by affecting the function of two or more organs in a patient whose homeostasis may not be maintained without the imposition of a conservative therapeutic behavior (4,6,16). We present the system and organ dysfunctions and pathophysiological changes that occur for each individual dysfunction:

Cardiovascular dysfunction presents the following changes:

- pro-inflammatory cytokines influencing the vascular endothelium and nitric oxide are produced;
- nitric oxide diminishes the myocardial contractility and decreases the response to $\beta$-adrenergic agents, producing refractory hypotension;
- myocardial contractility decreases by the action of the endotoxin;
- baroreceptor stimulation produces tachycardia which, in time, leads to the development of hypovolemia and reduced cardiac output;
- shock may be due to hypovolemia by fluid loss or release of vasoactive substances (12).

Respiratory dysfunction is manifested by:

- hypoxia caused by impaired alveolar-capillary membrane;
- inflammatory exudate with numerous proteins, polymorphonuclear and mononuclear;

- pulmonary capillary endothelium alteration;
- reduced diaphragm muscle movements caused by the presence of pain and pleural effusion;
- respiratory failure due to surfactant degradation by the action of phospholipase A2;
- acute respiratory distress syndrome, expressed in two phases: exudate initially appears accompanied by diffuse alveolar and microvascular changes and recruitment of inflammatory cells (12,17,18).

Renal dysfunction is characterized by the following pathological changes:

- thromboxanes and leukotrienes decrease renal blood flow;
- renin-angiotensin-aldosterone system produce intrinsic vasoconstriction with impaired renal blood flow autoregulation; on the other hand, cytokines produce systemic vasodilation and relative hypovolemia;
- cytokines and free radicals leading to aggregation of neutrophils;
- peripancreatic inflammation fused perirenal space may cause hydronephrosis;
- ischemia followed by acute tubular necrosis leading to renal failure;
- acute renal failure occurs in 50% of patients with sepsis, and frequently,in turn, numerous complications including acute pancreatitis with the occurrence of a vicious circle occur (12,19).

Hepatic dysfunction is pathological landmarks:

- hepatic hypoperfusion;
- endothelial cell and liver changes;
- cytokines (TNF-$\alpha$, IL-6) by activated Kupffer cells are released into the circulation;
- the presence of liver lesions reperfusion mediators;
- presence of hyperbilirubinemia and cholestasis (12).

Hematological dysfunction presents following characteristics:

- coagulopathy induction by circulating proteases;
- occurrence of disseminated intravascular coagulation, evidenced by hemorrhages and microthrombi;
- the extrinsic pathway of coagulation activation by cytokines;
- inhibition of blood coagulation and fibrinolysis activation by thrombomodulin (low in sepsis);
- inflammation in the spleen can cause hematoma or even splenic rupture;
- decreased number of lymphocytes, which implies a low immune function; remaining lymphocytes have increased activity, objectified by elevated IL-2 receptor;
- vascular complications: pseudoaneurysms, portal vein thrombosis, arteriovenous fistula;
- increased mortality due to decreased antithrombin III (20,21,22,23).

Gut barrier dysfunction is characterized by:

- increased paracellular permeability of intestinal epithelium, with increased absorption of macromolecules;
- reduction of intestinal and systemic microcirculation will produce ischemia, reperfusion disorders and oxygen free radicals the release;
- immunocompetent cells in the intestinal wall along the adjacent lymph nodes (gut associated lymphoid tissue - GALT) and liver participate in immune defense;
- Gram-negative aerobe bacteria and/or endotoxin from the intestinal lumen arrive by translocation to mesenteric lymph nodes;
- various microorganisms and toxic products entering in portal and systemic circulation of the host contributing to SIRS and MODS, causing death;
- occurrence of gastrointestinal bleeding due to local ulceration, gastric varices or even eventual ruptures of pseudoaneurysm; local ulcerations are most commonly caused by stress or gastrointestinal ischemia; gastric varicose veins occur secondary to splenic vein obstruction; pseudoaneurysm rupture can be derived by vessels erosion in the vicinity of the pancreas (12, 23).

Neurological dysfunction is represented by the following pathological changes:

- polyneuropathy, represented by neuromuscular blockade;
- septic encephalopathy;
- retinopathy appeared consecutively obstruction of retinal arterioles;
- psychosis due to demyelination or cerebral hypoperfusion (12).

Metabolic dysfunction:

- decreased glucose intolerance;
- hyperglycemia due to low levels of insulin or increased glucagon release;
- metabolic acidosis due to low tissue perfusion;

- hypocalcaemia, secondary to hypoalbuminemia or citosteatonecrosis stains (12, 24).

Other symptoms:
- generalized heterotopic ossification;
- subcutaneous nodules due to metastatic fat necrosis;
- increase in intra-abdominal pressure, frequently produced in acute pancreatitis;
- abdominal bacterial and fungal infections (12,25,26,27,28).

In the international literature, for better clinical use in everyday medical practice, MSOF criteria were synthesized differently according to the authors.

a) after Knaus, MSOF criteria are:

Respiratory failure (presence of one or more):
- Respiratory rate <5 or >49 (> two years of life);
- Alveolar-arterial O2 difference >350 mmHg or PaO2/FiO2 <200 (without congenital heart lesions);
- Requires mechanical ventilatory support >24 h;
- PaCO2 >50 mmHg and arterial pH <7.25.

Circulatory failure (presence of one or more):
- Heart rate <50/min. or episode of ventricular tachycardia / fibrillation;
- Mean arterial pressure <50 mmHg and/or systolic blood pressure <60 mmHg;
- Cardiac index <2 l/min./m2 body surface area (acute onset) and/or arterial pH <7.25, PaCO2 <35 without respiratory failure.

Renal failure (presence of one or more):
- Urinary volume 9.3 ml/kg/h for 8 h;
- Serum creatinine >266 μmol/l;
- Urea Nitrogen >1.00 g/l or urea >0.60 g/l.

Hepatic failure (presence of both):
- Bilirubin >60 mg/l or greater twofold increase in serum alkaline phosphatase and
- Prothrombin time >4 times the upper limit of normal or two-fold increase of aspartate aminotransferase (AST) levels.

Hematological failure (presence of one or more):
- WBC <1500/mm$^3$ or> 40,000/mm$^3$;
- Platelets <20,000/mm$^3$ or evidence of disseminated intravascular coagulation.

Neurological failure:
- Glasgow coma score <6 (without sedation).

Uncontrolled sepsis (presence of one or more):
- Positive blood culture under antibiotic therapy;
- Fever >39.5˚C (rectal temperature) for >24 h or febrile crochet hooks for three days successively (29).

Depending on the number of organ failure and mortality a correlation was established (**Table 1**) and was found that the presence of three organ failure occurred in less than 3 days after admission is accompanied by a mortality rate of 98%.

b) After Tran and Cuesta, the criteria for each organ affected by MOSF can be seen in **Table 2**. Severity score is determined by summing organ failure with reference to one day of hospitalization, and can range from 0-7 (30).

c) Conference consensus on the classification of acute pancreatitis, which was held in 1992 in Atlanta, define single or multiple organ failure, represented succinctly: shock (BP <90 mmHg), respiratory failure (PaO2 <60 mmHg), renal failure (creatinine >17μmol/l after rehydration) or gastrointestinal bleeding (>500 ml/24h) (3.31). The organ failure present at admission must persist for at least 48 hours under proper medical treatment in order to be considered diagnostic criterion of severity (5).

According to studies from the international literature, the most common systemic complications were pulmonary (58.82%), renal (26.47%) and cardiovascular (36.76%) (32), in others, in a decreasing order of frequency, were: respiratory, cardiovascular and renal (11). Other authors indicate that MODS was present simultaneously in all three systems (respiratory, renal and cardiovascular) in 26.47% of cases (32). Later these three systems underlie the future design of multiple organ failure in the most recent classification of acute pancreatitis' severity, Atlanta revised, in 2012 (5).

MODS are the most common cause of death in severe acute pancreatitis (4.17). Of all the organ failures, taken individually, respiratory together with renal failure are the main causes of early mortality,

**Table 1. The correlation between the number of organ failures and mortality**

| No. organ failures | one > one day | two > one day | three > three days |
|---|---|---|---|
| Mortality | 40% | 60% | 98% |

**Table 2. Criteria for Multiple Organ System Failure (by Tran and Cuesta)**

| ORGAN /SYSTEM | CRITERIA |
|---|---|
| Cardiovascular | Mean arterial blood pressure ≤ 50 mmHg.<br>Fluid administration and / or vasoactive drugs are required to maintain systolic blood pressure of 100 mmHg.<br>Pulse ≤ 50 beats/min.<br>Tachycardia / ventricular fibrillation.<br>Cardiac arrest.<br>Acute myocardial infarction. |
| Respiratory | Respiratory frequency ≤ 5/min. or ≥ 50/min.<br>Mechanical ventilation for 3 or more days or FiO2 >0.4 and/or PEEP (positive end-expiratory pressure) >5 mmHg. |
| Renal | Serum creatinine ≥ 3.5 mg/dl (280 mmol/l).<br>The need for dialysis / ultrafiltration. |
| Neurologic | Glasgow coma score <6 (without sedation). |
| Haematologic | Hematocrit ≤ 20%.<br>WBC ≤ 300/mm$^3$ (0,3 x109/l).<br>Platelet count ≤ 50x10$^3$/ml (50 x109/l).<br>Disseminated intravascular coagulation. |
| Hepatic | Total bilirubin level ≥ 3.5 mg/dl (51 mmol/l) in the absence of hemolysis.<br>ALT (alanine aminotransferase) >100 U/l. |
| Gastrointestinal | Stress ulcer requiring transfusion of more than 2 units of blood per 24 hours.<br>Alithiasic cholecystitis.<br>Necrotizing enterocolitis.<br>Intestinal perforation. |

and infections and adding organ insufficiencies (MODS) are important causes of late mortality (33). Studies have revealed that the most critical period in which organ dysfunction may occur is the first week after admission, the percentage of deaths being about 50% of those with severe acute pancreatitis (5,34). And on the other hand, referring to the patients with acute pancreatitis that do not develop organ failure (NOF) (35,36).

## CONCLUSIONS

Acute pancreatitis represents acute inflammation of the pancreatic gland acinar cells. The organism responds to aggression on pancreatic acinar cell through an inflammatory response that can cause serious biological and clinical consequences. In the final stage of the disease immunosuppression and multiple organ dysfunction with increased morbidity and mortality settles in. It is important for clinicians to understand the complex pathophysiological mechanism occurring in the evolution of severe acute pancreatitis in order to apply the appropriate treatment as soon as possible.

## REFERENCES


1. Al Mofleh I.A. Severe acute pancreatitis: pathogenetic aspects and prognostic factors. World J Gastroenterol. 2008;14(5):675-84
2. Siqin D., Wang C., Zhou Z., Li Y. The key event of acute pancreatitis: pancreatic duct obstruction and bile reflux, not a single one can be omitted. Med Hypotheses. 2009;72(5):589-591
3. Bradley E.L. A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, G.A., September 11 through 13, 1992. Arch Surg 1993; 128(4):586-590
4. Kaye A.D., Hoover J.M., Baluch A.R. A contemporary review of multiple organ failure. Middle East J Anaesthesiol. 2005 Jun;18(2):273-92
5. Banks P.A., Bollen T.L., Dervenis C., Gooszen H.G., Johnson C.D., Sarr M.G., Tsiotos G.G., Vege S.S.; Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013 Jan;62(1):102-111
6. Ferreira A.M., Sakr Y. Organ dysfunction: general approach, epidemiology, and organ failure scores. Semin Respir Crit Care Med. 2011 Oct;32(5):543-51. doi: 10.1055/s-0031-1287862
7. Schlag G., Redl H. Pathophysiology of Shock, Sepsis and Organ Failure, Springer Verlag, New York, 1993
8. Oberholzer A., Oberholzer C., Moldawer L.L. Cytokine signaling – Regulation of the immune response in normal and critically ill states. Crit. Care Med, 2000, 28, 4(suppl.):N3-N12
9. Paunescu V. Progrese înregistrate în tratamentul peritonitelor acute difuze. În: Tendinte actuale de diagnostic si tratament în practica medicala. Ed. Ministerului de Interne, Bucuresti, 2002, 364-397
10. Banks P., Freeman M. and the Practice Parameters Committee of the American College of Garstoenterology: Practice guidelines in acute pancreatitis. Am J Gastroenterol 2006; 101(10):2379-2400
11. Mofidi R., Duff M.D., Wigmore S.J., Madhavan K.K., Garden O.J.,

Parks R.W. Association between early systemic inflammatory response, severity of multiorgan dysfunction and death in acute pancreatitis. Br. J. surg. 2006 Jun; 93(6):738-744
12. Paunescu V., Bordânca I., Popa C., Pop-Began V., Pop-Began D. Ce operam? Când operam? Cum operam? pancreatita acuta. Jurnalul de chirurgie, Iasi, 2006; 2(4):378-391
13. Wu B.U., Johannes R.S., Sun X., Tabak Y., Conwell D.L., Banks P.A. The early prediction of mortality in acute pancreatitis: a large population-based study. Gut 2008; 57(12):1698-1703
14. Jha R.K., Ma Q., Sha H., Palikhe M. Acute pancreatitis: a literature review. Med Sci Monit. 2009 Jul;15(7):RA147-56
15. Singh V.K, Wu B.U., Bollen T.L., Repas K., Maurer R., Mortele K.J., Banks P.A. Early systemic inflammatory response syndrome is associated with severe acute pancreatitis. Clin Gastroenterol Hepatol. 2009 Nov;7(11):1247-51
16. Marshall J.C., Cook D.J., Christou N.V., Bernard G.R., Sprung C.L., Sibbald W.J. Multiple organ dysfunction score: A reliable descriptor of a complex clinical outcome. Crit Care Med. 1995;23:1638–1652
17. Kong L., Santiago N., Han T.Q., Zhang S.D. Clinical characteristics and prognostic factors of severe acute pancreatitis. World J Gastroenterol. 2004; 10(22):3336-8
18. Zhou M.T., Chen C.S., Chen B.C., Zhang Q.Y., Andersson R. Acute lung injury and ARDS in acute pancreatitis: mechanisms and potential intervention. World J Gastroenterol. 2010 May 7; 16(17):2094-2099
19. Santoro A., Mancini E. Epidemiology of acute renal failure. G Ital Nefrol. 2006;23(Suppl 36):S3-12
20. De Perrot M., Berney T., Bóhler L., Delgadillo X., Mentha G., Morel P. Management of bleeding pseudoaneurysms in patients with pancreatitis. Br J Surg. 1999 Jan;86(1):29-32
21. Raat H., Stockx L., De Meester X., Van Steenbergen W., Marchal G. Percutaneous embolization of a splenic arteriovenous fistula related to acute necrotizing pancreatitis. Eur Radiol. 1999; 9(4):753
22. Dörffel T., Wruck T., Rückert R.I., Romaniuk P., Dörffel Q., Wermke W. Vascular complications in acute pancreatitis assessed by color duplex ultrasonography. Pancreas. 2000 Aug;21(2):126-33
23. Hagiwara A., Miyauchi H., Shimazaki S. Predictors of vascular and gastrointestinal complications in severe acute pancreatitis. Pancreatology 2008;8(2):211-8
24. Kaya E., Dervisoglu A., Polat C. Evaluation of diagnostic findings and scoring systems in outcome prediction in acute pancreatitis. World J Gastroenterol 2007;13(22):3090-4
25. Jacobs J.W., De Sonnaville P.B., Hulsmans H.M., van Rinsum A.C., Bijlsma J.W. Polyarticular heterotopic ossification complicating critical illness. Rheumatology (Oxford). 1999 Nov;38(11):1145-9
26. Garnacho-Montero J., Madrazo-Osuna J., Garcva-Garmendia J.L., Ortiz-Leyba C., Jimınez-Jimınez F.J., Barrero-Almodovar A., Garnacho-Montero M.C., Moyano-Del-Estad M.R. Critical illness polyneuropathy: risk factors and clinical consequences. A cohort study in septic patients. Intensive Care Med. 2001 Aug;27(8):1288-96
27. Rosas J.M., Soto S.N., Aracil J.S., Cladera P.R., Borlan R.H., Sanchez A.V., Ros F.B., Posa L.G. Intra-abdominal pressure as a marker of severity in acute pancreatitis. Surgery 2007; 141(2):173-8
28. Vege S.S., Gardner T.B., Chari S.T., Baron T.H., Clain J.E., Pearson R.K., Petersen B.T., Farnell M.B., Sarr M.G. Outcomes of intra-abdominal fungal vs. bacterial infections in severe acute pancreatitis. Am J Gastroenterol. 2009 Aug; 104(8):2065-70
29. Knaus W.A., Draper E.A., Wagner D.P., Zimmerman J.E. Prognosis in acute organ-system failure. Ann Surg. 1985 Dec;202(6):685-93
30. Tran D.D., Cuesta M.A. Evaluation of severity in patients with acute pancreatitis. Am J Gastroenterol 1992 May; 87(5):604-8
31. Balthazar E.J. Acute Pancreatitis: Assessment of Severity with Clinical and CT Evaluation. Radiology 2002; 223(3):603-613
32. Rau B., Baumgart K., Paszkowski A.S., Mayer J.M., Beger H.G. Clinical relevance of caspase-1 activated cytokines in acute pancreatitis: high correlation of serum interleukin-18 with pancreatic necrosis and systemic complications.Crit Care Med. 2001 Aug; 29(8): 1556-62
33. Sun B., Dong C.G., Wang G., Jiang H.C., Meng Q.H., Li J., Liu J., Wu L.F. Analysis of fatal risk factors for severe acute pancreatitis: a report of 141 cases. Zhonghua Wai Ke Za Zhi. 2007, 45(23):1619-22
34. Buter A., Imrie C.W., Carter C.R., Evans S., McKay C.J. Dynamic nature of early organ dysfunction determines outcome in acute pancreatitis. Br J Surg. 2002; 89(3):298-302
35. Bollen T.L., van Santvoort H.C., Besselink M.G., van Leeuwen M.S., Horvath K.D., Freeny P.C., Gooszen H.G.; Dutch Acute Pancreatitis Study Group. The Atlanta Classification of acute pancreatitis revisited. Br J Surg. 2008;95(1):6-21
36. Vege S.S., Gardner T.B., Chari S.T., Munukuti P., Pearson R.K., Clain J.E., Petersen B.T., Baron T.H., Farnell M.B., Sarr M.G. Low mortality and high morbidity in severe acute pancreatitis without organ failure: a case for revising the Atlanta classification to include "moderately severe acute pancreatitis". Am J Gastroenterol 2009; 104(3):710-5