Multiple organ dysfunction syndrome (MODS) is the presence of altered organ function in acutely ill patients, when homeostasis cannot be maintained without intervention. MODS has been extensively studied in sepsis, trauma or abdominal surgery patients, but not subsequently to cardiac surgery. The aim of this study was to investigate the incidence, risk factors and the clinical, paraclinical and pathomorphological particularities of multiple organ dysfunction syndrome and the importance of the systemic inflammatory response syndrome (SIRS) in the pathogenesis of MODS after cardiac surgery with the use of cardiopulmonary bypass.

The thesis is consisted of two main parts: a general part and personal contributions. The general part presents discussions about the etiology, physiopathology, cellular and subcellular injuries and the involved mediators. Some clinical aspects and controversies in the treatment of this syndrome were also presented.

The second part comprises two studies. „Study A” is a retrospective, clinical observational study of 1908 cardiac surgical patients operated during 01.01. 2004 - 31.12. 2006.

This study presents the investigation of incidence and risk factors for MODS and the particularities of organ injuries. 131 patients suffering from multiple organ dysfunction syndrome were investigated. MODS developed more frequently in women (p=0,0837), in elderly (p=0,0213), in patients with different comorbidities (hypertension, renal and hepatic dysfunctions, diabetes, endocarditis) subsequently to complex surgical procedures. Emergency operations and reinterventions significantly increase the incidence of multiple organ dysfunction (p<0,0001). The prolonged myocardial ischemia and cardiopulmonary bypass time had a significant contribution in the development of MODS (p<0,0001).

The intraoperative administration of Aprotinin presenting antifibrinolytic and antiinflammatory properties, showed no benefits, but increased the number of renal and neurological complications, the number of patients with multiple organ dysfunction syndrome. The postoperative mortality rate didn’t change. Corticoids, administrated because of their anti-inflammatory properties increased the incidence of sepsis and MODS, as well as mortality.

Following cardiac surgery the incidence of MODS caused by tissue hypoperfusion was higher than multiple organ dysfunction developed after sepsis. It was demonstrated the role of tissue hypoperfusion caused by low cardiac output syndrome and the administration of high doses of inotropics and vasoconstrictors. Sepsis was uncommon, but when being present, it significantly increased the rate of mortality.

The evolution of patients with MODS was followed by the SOFA (Sequential Organ Failure Assessment) score, which had a good prognostic value, being higher with increasing tendency in patients who died and lower, with decreasing tendency in survivors. Mortality was significantly, more than 10 times higher in patients with MODS,
higher in men, at extreme ages, in patients with sepsis and increased almost linearly as the number of dysfunctional organs increased.

The incidence of diverse organ dysfunction was different after cardiac surgery, probably because of the peculiarities of cardiac surgical intervention, the use of cardiopulmonary bypass. In our setting the incidence of hematological, cardiac and renal dysfunction were higher than in general intensive care units.

Hematologic disorders were frequent, but usually not severe: posthemorrhagic anemia and dilutional thrombocytopenia could be corrected rapidly. Coagulation disorders and disseminated intravascular coagulopathy appeared only in very severe cases, in case of sepsis. The cardiogenic shock, the low cardiac output syndrome were more frequent after prolonged myocardial ischemia and cardiopulmonary bypass, they appeared almost in all cases immediately after surgery, only in few cases in sepsis. The acute renal insufficiency was caused by low cardiac output, high doses of cathecolamines and sepsis. Respiratory complications were frequent and various (acute respiratory distress syndrome, acute lung injury, atelectasia, pleural effusion) and required prolonged mechanical ventilation, which predisposed the patient to other complications (ventilator induced pneumonia, dysthelectasia). Neurological dysfunctions were frequent, but generally mild, there were only a few cases with coma caused by cerebral hemorrhage or toxico-metabolic disturbances. Gastro-intestinal and liver dysfunctions were infrequent, usually due to splanchnic hypoperfusion caused by low cardiac output and/or high doses of cathecolamines.

Concerning the pathomorphological aspects of injured organs, the most frequent lesions that appeared in the heart were severe diffuse or subendocardic ischemic injuries with the fragmentation of myocardial cells and the incipient diffuse fibrosis which is present due to high doses of cathecolamines. In patients with acute respiratory distress syndrome of the lung the presence of hyaline membrane was constant, but we also found dystelectasia, bronchopneumonia, pseudomembranous tracheitis in patients with prolonged mechanical ventilation. Regarding the brain cerebral edema was frequent, but we observed massive hemorrhage, microthrombosis and leptomeningitis. Within the liver mild hypoxic injuries caused pericentral lobular dystrophia, severe centrolobular ischemic necrosis. In the kidney the tubular dystrophia and tubular necrosis were the most frequent injuries. During the autopsies we found 6 cases with severe pancreatic steatonecrosis; none of them having suggestive clinical signs for acute pancreatitis.

The immunohistochemical examinations revealed important changes in critical cases. The expression of VEGF is the consequence of generalized hypoxia and tries to counteract the tissue hypoperfusion. The expression of HSP70 in almost all cells reflects the presence of the defence mechanisms. The expressions of apoptosis regulatory proteins (bcl-2, bax) demonstrate the regenerating capacity of the cells after injury. We can conclude that the expression of the studied immunohistochemical markers suggest the mobilisation of defence and regenerative capacity of the whole organism in critical cases.

"Study B" tries to demonstrate the magnitude of systemic inflammatory response induced by cardiopulmonary bypass and its importance in the development of MODS. The systemic inflammation was monitored by clinical signs (fever, leukocytosis, increased heart rate and respiratory frequency) and measured with the semi-quantitative procalcitonine tests preoperatively, immediately after the operation and in day 1, 3 and 5. The incidence of SIRS was high after cardiac surgery (66.7%), with maximums in day 1-3, decreasing in patients without complications, remaining at high levels in those who
developed MODS. In the third day the procalcitonine level was higher in patients with SIRS and MODS than in patients with only SIRS and it was also higher in patients with bad prognosis, so we could conclude that it has a good prognostic value.

The acquired results suggest the importance of preventing multiple organ dysfunction by aggressive treatment of comorbidities, lowering the myocardial ischemic and cardiopulmonary bypass time, avoiding the use of aprotinin and corticoisteroids and treating low cardiac output states with newer inotropics, avoiding cathecolamines.