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Editorial

Current View on Elderly Hip Fracture and Inflammatory Response

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Editorial

Hip fractures represent one of the most common injuries in the elderly which are associated with a high incidence of complications and mortalities. Nearly 300000 hip fractures occur in the United States, and also, there are approximately 1.7 million patients suffering from this disease annually in worldwide [1]. Moreover, the number of elderly individuals and those with chronic healthy conditions is increasing and it is estimated that the prevalence of hip fractures will continue to increase with rising life expectancy. The occurrence of hip fractures is expected to increase concomitantly, with an estimated number of 6.3 million hip fractures which was predicted by 2050 in the worldwide [2].

Despite significant improvements of surgical procedures, anesthesia techniques and nursing care, concurrently with advancements in the quality and effectiveness of treatments for the elderly hip fractures, the current risk of Pneumonia and mortality induced by hip fracture are still high. Previous studies show that the estimated mortality of these complications take up between 7 and 10% (with an excess 30-day mortality of, an excess 1-year mortality of between 18% and 35%)which are at increased risk for premature death for many years after hip fracture [3-5].

Excess mortality after hip fracture may be linked to complications following by the fracture, such as pneumonia, and heart failure [6,7]. A review based on autopsy of people who died within 1 year of hip fracture surgery in 1995 indicated that pneumonia, cardiac failure, myocardial infarction and pulmonary embolism are the principal causes of death [8].

Excess mortality after fracture may depend on individual characteristics of the person sustaining the hip fracture, but the major causes of the high mortality are associated with the subsequent lung injury and lung infection of the fracture event. Our recent studies show that hip fracture and surgery in aged rats cause a systemic inflammatory response and lung injury which are associated with increased susceptibility to infection during the acute phase after injury and surgery [9].

Lung infections are the most common postoperative complications associated with this procedure, contributing to increased hospital stays and increased mortality rates [10,11]. Some previous researches report that the elderly possess a reduced physiological reserve and are more vulnerable to post-injury inflammatory cytokines release that is uncompensated by anti-inflammatory mediators [12,13]. Similar observation is previously reported the surgery lead to significant elevation of C-reactive protein level, (orosomucoid) and decrease in transferrin. The patients with intracapsular fractures had preoperatively highest values of inflammatory markers including fibrinogen, C-reactive protein, orosomucoid, white blood cells count, and lowest values of transferrin, as compared to intermediate values found in extra capsular fractures and lowest values in elective surgery groups [14]. Our previous study reported that inflammatory response played an important role in lung injury in elderly hip fracture patients after operation, and various cytokines including TNF-a, IL-6 and IL-10 concentrations represent independent outcome predictors for mortality and complications in elderly patients with hip fracture [15]. Subsequent researches have shown that fracture and surgery as a trigger which stimulate an immediate sterile systemic inflammatory response and lung injuries [16]. The evidences present that tumor necrosis factor alpha (TNF-α), interleukin 6 (IL-6), interleukin 1 (IL-1), and prostaglandin E2 increase in early stage during the process of elderly hip fracture and these are correlated with the severity of the SIRS and lung injury [17].

Aging is associated with chronic, low-grade, systemic inflammation characterized by an increasing level of inflammatory cytokines such as TNF-α, IL-6, and IL-1. This pro-inflammatory response has been linked to a wide range of chronic conditions associated with aging, including cardiovascular disease, diabetes, and dementia. There are mounting evidences implicating chronic systemic inflammation in osteoporosis and fracture risks in adults' patients. Hip fracture and surgery have a close associations with activation of systemic inflammatory response of the organism due to the individual heterogeneity and surgery invasiveness and timing [18,19]. Acute lung injury is the most serious and fatal complication of the elderly patients with hip fracture, but understanding of the pathophysiology and mechanism of systemic inflammatory response and lung injury in elderly hip fracture has developed remarkably in the past few years [20-22].

Zhang et al reported that cellular disruption by trauma releases mitochondrial damage is associated molecular patterns with evolutionarily conserved similarities to bacterial pathogen-associated molecular patterns into the circulation [23]. Mitochondrial DNA (mtDNA) has been detected in the plasma of patients with trauma and causes functionally important immune consequences. The release of mtDNA by cellular injury is a key link between trauma, inflammation, and systemic inflammatory response syndrome. These signals through innate immune pathways were identical to those activated in sepsis to create a sepsis-like state. The release of mtDNA by cellular injury was proven to be a key link both in blunt

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injury and hip fracture [23,24]. Our studies have demonstrated that hip fracture in the elderly rats and in elderly patients can induce systemic inflammatory response and lung injury, which increase the risk of lung infection and death during the post-injury period, and initiated in the absence of bacterial infection and is characterized by the activation of components of the complement system, a variety of cytokines and chemokines, and other acute phase proteins [9,25]. Our research showed that the lung injury induced by hip fracture may be involved with the mtDNA release and its TLR9/NF-kB pathway, and mtDNA induced inflammation and increased toll-like receptor 9 (TLR9)/nuclear factor kappa B (NF-kB) expression in lung tissue [24,25]. As shown by Larsson and co-workers, this inflammatory reaction may persist more than 6 weeks after the surgical procedure. Recent studies offer compelling evidence that inflammation could be a significant risk factor for bone loss and fracture in aging. The trials conducted by the University of Pittsburgh research team showed a 1.5-fold to 2.5-fold greater risk for fracture in older women with the highest levels of inflammation compared to those with the lowest levels [26].

The clinical practice guideline developed by AAOS showed that it would seem prudent to surgically treat elderly patients with hip fractures within the first 48 hours of admission and everything possible should be done to ensure the majority of patients are operated within one to two days [27]. This principle of early surgery is not applicable to all the patients with high risk and physiologically unstable patients clearly. Damage Control Orthopedics (DCO) is an approach that could contains and stabilizes orthopedic injuries so that the patient's overall physiology can get improvement. The purpose is to avoid aggravating the patient's condition by the "second hit", a major orthopedic procedure and how to delay definitive fracture repair until a time when the overall condition of the patient is optimized [28].

According to DCO theory, one of the most important issues in elderly hip fracture is the timing of the surgical procedures. Our study demonstrated significant inflammatory response was present in pulmonary and blood with chronic pulmonary disease after surgery, and associated with increase of MPO activity, and permeability. Late fixation in hip fracture with chronic pulmonary disease patients significantly reduced severity of inflammatory infiltration, myeloperoxidase activity, and permeability in pulmonary compared to early fixation, suggesting DCO validity to reduce damage of organs in elderly hip fracture with chronic pulmonary disease [29]. Clinical observation on the results of anti-inflammation treatment using COX-2 inhibitor to improve prognosis in our study showed the average length of hospitalization was significantly shorter in experimental group than the control group and survival rate of experimental group was slightly better.

The inflammatory response plays an essential role in postoperative organ dysfunction in elderly patients with hip fracture, and it is necessary to study further on patients who are based on their overall physiologic status and systemic inflammatory response, which should be treated with DCO instead of early fixation after hip fracture. Whether or not to reduce systemic inflammatory response and consequent lung organ injury through late surgery, and whether decreasing the inflammatory response through late surgery would decrease mortality and complication following hip fracture.

In general, Hip surgery represents a major intervention present a notable association in inflammatory response. Clinical data and emerging discoveries in molecular medicine may continue to provide answers to these questions of when and who should utilize DCO approach for the elderly hip fracture patients. Despite the lack of prospective clinical studies, an increasing number of scientists and orthopedic surgeons have already modified their approach to the treatment of the elderly patients with hip fracture by incorporating the principles of damage control orthopedics [30-32].

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