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COMMENTARY

Future Directions to Limit Surgical Site Infections

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Surgical site infection (SSI) is defined as an infection that develops in superficial or deep soft tissues after surgery. We can classify superficial and deep SSI based on the timing and type of surgery. Superficial SSI is defined as an infection developing within 30 days after surgery that involves the skin and subcutis, while deep SSI can occur within one year after surgery and can also involve the deep soft tissue.

Regardless of classification, SSIs are a complex phenomenon with a considerable impact on health in terms of costs, management, time, and quality of life of the patient [1,2].

Recently, a group of researchers investigated three modifiable factors that increase SSI risk after elderly hip fracture surgery and concluded that smoking, preoperative albumin levels, and fasting blood glucose should be optimized preoperatively in order to reduce SSI risk in these patients [3].

Despite a reduction in prevalence, smoking is one of the most important health issues. Cigarette smoking has a negative impact on wound healing in orthopedic surgery with an increase in the incidence of SSI of 7% [4]. Many authors have also confirmed an increase in SSI after plastic surgery using multivariate analysis and shown that smoking suppresses the immune system [5]. Numerous studies have confirmed it as a complication for wound healing in terms of necrosis and infections due to the vasoconstricting and deoxygenating effects of nicotine and other tobacco-related chemicals. In plastic surgery specifically, smoking is related to an increase in complications and infections but not to an extension of the period of hospitalization [6]. Smoking causes hypoxia and reduces the protective response of the immune system, which increases infection rates; moreover, smoking alters the equilibrium between proteases and anti-proteases, resulting in deterioration of connective tissue [7].

Serum albumin concentration is one of the most easily assessed markers for malnutrition [8], and hypoalbuminemia is clearly linked to the development of acute postoperative infections after arthroplasty. Hypoalbuminemia is linked to SSI through impairment of wound healing, diminished fibroblast proliferation, and diminished collagen synthesis. Another described effect is impairment of the immune system, as albumin deficiency is related to lymphocytopenia [9]. A meta-analysis conducted by Yuwen et al. in 2017 showed a statistically significant correlation between SSI and hypoalbuminemia when the serum level of albumin is <3.5 mg/dl in orthopedic surgery [10].

The relationship between hyperglycemia and SSI has been investigated in numerous studies. In particular, hyperglycemia has been shown to be associated with SSI not only in diabetic patients (with constant hyperglycemia) but also in those patients who develop stress hyperglycemia after surgery [11], and control of blood glucose levels can reduce SSI by 50% [12]. Blood glucose levels impact wound healing by interfering with angiogenesis through modulation of growth factors and cytokines such as vascular endothelial growth factor (VEGF), transforming growth factor beta (TGF- β), platelet-derived growth factor (PDGF), and soluble fms-like tyrosine kinase 1 (sFlt-1) [13,14]. Authors have confirmed that these alterations in wound healing are increasingly complex and can also involve phagocytosis, chemotaxis, blood vessel adhesion, bactericidal activity of granulocytes, collagen synthesis, and fibroblast proliferation. The impact on the immune system and on bacterial survival is very interesting, and some evidence suggests an increase in the growth of Gram-positive bacteria in hyperglycemic serum [15]. In addition, nonenzymatic glycosylation can modify the function of plasma proteins, and this can further delay wound healing, predisposing the

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patient to bacterial colonization and infections. Diabetic patients, moreover, often have neuropathic and vascular diseases.

Based on the above, there are numerous studies indicating an important correlation between these factors (glucose, smoking, and hypoalbuminemia) and the risk of developing SSI. This evidence could play a role in determining further therapeutic measures for some types of patients. The importance of these data is notable especially in those surgical procedures involving prosthetic implantation.

WHICH PROCEDURES OR DEVICES ARE ABLE TO LIMIT THE RISK OF SSI? WHICH ARE CURRENTLY AVAILABLE TO PHYSICIANS?

The risk of developing SSIs can be reduced with highly specific medical devices.

We must remember that pathogenic microorganisms can colonize surgical wounds from the skin surface or they can be transported to the surgical site through blood circulation from another site (for example, after a dental infection a patient can develop an infection in a prosthetic implant). The bacteria present on the skin surface can be fought by thorough disinfection and by the use of medical devices such as cyanoacrylates. Cyanoacrylates are medical glues that seal the surgical site and shield it from bacteria colonization from the outside, even in cases of poor hygiene. In fact, when glues are used, patients can theoretically also wet the wounds because they will be completely impermeable [16].

Other useful devices include antibacterial, medicated sutures or the use of negative pressure therapy in the immediate postoperative period in order to remove excess of fluids and reduce the risk of wound dehiscence [17].

Negative pressure has shown good outcomes in these cases as it creates an isolated environment with low oxygen tension, removing any fluids and improving the vascular supply toward the edges of the wound, which helps reduce the risk of immediate SSIs.

Late infections, which occur when the surgical wound is closed, can be caused by bacteria that can colonize *locus minoris resistentiae*. In these cases, good planning of antibiotic therapy is very important and can limit the risks of bacteria colonization.

Research focused on identifying risk factors for SSI such as albumin levels, smoking, and fasting blood glucose levels could have a very strong impact in the future. It may one day be possible to limit the risk of infection by using not only disinfectants and antibiotics, but also by analyzing certain underestimated parameters that could pave the way

for treatments developed with great precision according to the type of patient.

For example, it may soon be possible to use certain kinds of disinfectants or medical devices during the postoperative period on a particular cohort of patients with low albumin levels, or the physician can opt for a different antibiotic regimen depending on fasting blood glucose levels.

In an environment so rich in variables, the key concept of more “tailor-made” surgeries is emerging. We could call it “precision surgery,” i.e., a surgery that is more focused on the type of patient and able to offer better results through the modulation of surgical techniques and technical expertise.

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