wound infection, as presented in a retrospective study managing 1,320 elbow fractures [25] and a case-control study from 318 calcaneal fractures [26]. In the first study, only smoking was found to have an association with infection after multivariate analysis (adjusted OR = 2.2; p = 0.023); the second study revealed that higher body mass index, delayed operation and active smoking (OR 19.497, p < .001) represented an increased risk for wound infection after ORIF.

Despite the conflicting evidence found in the literature, smoking seems to have a negative effect on overall complications and health and could potentially lead to an increased risk of infection. It is well-established that smoking has a detrimental effect on tissue healing and cellular pathways. Nonetheless, the current literature lacks the high-level evidence to state a direct relationship between these two factors. The recommendation provided here is inconclusive.

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QUESTION 2: What is the role of nutritional supplementation (NS) in avoiding infection in acute fracture cases?

RECOMMENDATION: (1) Evidence does not support the role of NS for avoiding infections in well-nourished individuals. (2) However, the literature has stated that in patients with a nutritional deficiency or catabolic state restoring nutritional parameters might reduce the risk of infection.

LEVEL OF EVIDENCE: (1) Limited, (2) Moderate

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Evidence in the available literature demonstrats that malnutrition is a significant clinical and public health problem. Several clinical trials present NS as a global effort in medicine, with applications in different specialties to improve the general condition of patients

with malnutrition or metabolic stress secondary to trauma or infection and to modulate the inflammatory response and potentially mitigate negative outcomes. Although there are controversial results, in spite of several studies with evidence level I on both supporting and refuting this initiative [1–7]. The literature has shown certain indications for prescription of NS in surgery, most recently defined by the European Society for Clinical Nutrition and Metabolism (ESPEN) guideline in 2017 [2]. There are two published meta-analyses concerning the effect of perioperative oral NS on elderly patients after hip surgery. The first combined 10 randomized control trials (RCTs) involving 986 elderly patients, which showed that oral NS had a positive effect on the serum total protein ($p < 0.00001$) and led to a significantly decreased number of complications ($p = 0.0005$). Furthermore, data from the infection subgroups showed significant decreases in wound infection (odds ratio (OR) = 0.17; 95% confidence interval (CI): 0.04, 0.79; $p = 0.02$), respiratory infection (OR = 0.26; 95% CI: 0.07, 0.94; $p = 0.04$), and urinary tract infection (OR = 0.22; 95% CI: 0.05, 0.90; $p = 0.03$) [6]. The second pooled the results from 11 RCTs (multinutrient, oral, nasogastric and intravenous supplementation), with an NS group of 370 elderly people controlled with a group of 357 elderly, non-NS patients. This study demonstrated a reduction in complication rates (e.g., pressure sores, chest infection) at 1-12 months in the NS group (123/370 versus 157/ 367; relative risk (RR) 0.71; 95% CI 0.59 to 0.86) [7], but not on rates of surgical site infection (SSI). However, NS use in an elderly population with acute fractures remains controversial and the prescription is reserved for underfed or malnourished patients in an attempt to reduce complications during hospitalization [2,6]. According to the World Health Organization (WHO) and ESPEN, malnutrition is considered when a patient has a 10-15% weight loss within six months, 5% in three months and/or has a Body Mass Index (BMI) under 18.5 kg/m^2. There are hematologic parameters evaluated throughout the literature, such as a serum albumin/globulin ratio below 1.5 (normal range), albumin below 3.0 g/dl, lymphocyte count below 1,500 cells/mm^3 and a lymphocyte//monocyte ratio below five versus one that allows selective screening of suspected malnutrition [3,5,8–10]. This is a special topic of interest in patients with factures, due to the fact that approximately 50% of patients with orthopaedic infections had some degree of malnutrition and immunosuppression regardless of age [3].

Evidence favoring NS has revealed that supplementation containing protein could produce beneficial effects by reducing the risk of infection in patients with fractures and nutrition deficiencies, regardless of age [2,4,5,11]. In a 2012 clinical trial, Myint et al. describe significant differences in BMI comparing the supplementation arm versus a control group [4]. Also, NS also prevents weight loss during a prolonged hospital stay, improving the general state of the muscles and muscular strength, which could reduce hospitalization periods and thus lead to shorter exposure to nosocomial microorganisms [7,12]. Long et al. reported that patients with poor nutritional status and with infections lose a higher amount of protein during postoperative states through urine [13]. Furthermore, an altered nutritional status reflects a depleted physiological state that affects humoral and/or cellular immunity, limiting an effective response to infection [3]. These findings might explain why early enteral administration of NS reduces the risk of septic shock with an active infectious process [12]. NS also seems to prevent long periods of delirium, which in turn is associated with an increased mortality rate [14].

Despite the previous evidence, there is also available literature against the use of NS [7,12,15]. For instance, NS administration near the time of surgical intervention does not seem to have an important effect, as it cannot effectively change the traditional nutritional markers such as albumin or transferrin [8]. However, in a 2012 clinical trial, Gunnarsson et al. reported evidence of the utility of monitoring the insulin-like growth-factor 1 to evaluate the response of nutritional support in the short term [9].

Some studies report that NS should be used with caution, considering metabolic phenomena such as refeeding syndrome, a condition associated with quick NS in patients with severe malnutrition. In this case, a sudden increase in insulin stimulates hypophosphatemia and produces a decrease in the extracellular adenosine triphosphate (ATP) and two to three diphosphoglycerate on erythrocytes producing arrhythmia, respiratory failure and hematologic alterations. Prevention, monitoring and adequate dosage are key to the success of preventing such complication [16–18]. Standard nutritional supplements containing arginine, omega-3 fatty acid, glutamine and other components (immunonutrition) have level I evidence supporting its use in avoiding infection after colorectal resection [1].

Another meta-analysis (eight RCTs and two observational studies) showed that multiple nutrient-enhanced formulas demonstrate a benefit in reducing the risk of SSI compared to standard NS (very low-quality evidence) [19]. The population studied included adult patients undergoing major surgical procedures (mainly cancer and cardiac patients). Orthopaedic surgical procedures, however, were not included in this meta-analysis.

In conclusion, these results suggest that NS can have positive effects on avoiding wound infection and other infectious complications (respiratory infection, urinary tract infection) only in elderly patients after hip surgery. There are several limitations in the current literature with respect to recommending NS in acute fractures for every patient. It would be necessary to conduct further research to investigate the role of immunonutrition in orthopaedics, especially with respect to fractures.

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QUESTION 3: Do preoperative pneumonia/urinary tract infections (UTIs)/trophic ulcers increase periprosthetic joint infection/surgical site infection (PJI/SSI) risk in femoral neck fracture patients treated by partial/total hip arthroplasty (THA)?

RECOMMENDATION: There is a paucity of literature examining whether pneumonia/UTI/trophic ulcers increase SSI/PJI risk for patients with femoral neck fractured treated by hemi- or THA.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 91%, Disagree: 0%, Abstain: 9% (Super Majority, Strong Consensus)

RATIONALE

Infection after femoral neck fracture treated with hemiarthroplasty/THA is an uncommon but devastating problem. The current literature cites a 1.7 to 7.3% risk of SSI after hemiarthroplasty for femoral neck fracture [1]. Commonly-cited risk factors for PJI/SSI after hemiarthroplasty for femoral neck fracture include higher Body Mass Index (BMI), prolonged surgery time, preoperative elevation in C-reactive protein (CRP) levels, surgeon experience level, reoperation and hematoma formation [2,3].

For patients undergoing primary total joint arthroplasty, pneumonia, UTIs and skin ulceration were shown to be predisposing factors for developing PJI [4–8]. However, there remains a lack of publications that specifically examine the risk of PJI/SSI related to the preoperative presence of pneumonia, UTI or skin ulceration in patients with femoral neck fracture treated with hemiarthroplasty or THA. One small prospective study demonstrated that UTI preoperatively was a significant risk factor for infection (odds ratio = 10; p = 0.04) [9]. A systematic review of the literature indicated that two or more urinary tract catheterizations during hospitalization was identified as a risk factor for SSI [1]. After a thorough investigation, we could not find any existing evidence of an association between preoperative pneumonia or trophic ulcers with the development of PJI/SSI after hemiarthroplasty or total hip replacement for femoral neck fractures.

In summary, there is scant or no evidence to suggest that preoperative pneumonia/UTI/trophic ulcers result in an increase in PJI/SSI risk in femoral neck fracture patients treated by partial/THA. The little evidence that is available is low quality and suggests that preoperative urinary tract infection increases the odds of PJI after hemiarthroplasty. Higher quality and larger scale studies are necessary in this subset population to make valid conclusions on this possible relationship.

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