The Journal of Arthroplasty 31 (2016) 1631–1634

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

AAHKS Symposium: Modifying Risk Factors: Strategies that Work

Patient Optimization—Strategies That Work: Malnutrition

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ARTICLE INFO

Article history:
Received 13 March 2016
Accepted 14 March 2016
Available online 24 March 2016

Keywords:
malnutrition
optimization
arthroplasty
wound healing
infection

ABSTRACT

Background: Patient optimization is receiving increasing attention as outcomes monitoring and bundled payments have been introduced in joint arthroplasty. Optimization of nutrition is an important aspect of perioperative management.
Methods: This manuscript is a review of previously published material related to nutrition and the impact of malnutrition on surgical outcomes, with guidance for surgeons preparing patients for elective joint arthroplasty.
Results: Patients with optimized nutritional parameters have fewer complications, especially related to wound healing and infection.
Conclusion: Nutritional assessment and optimization should be a part of the perioperative management of patients undergoing lower extremity arthroplasty.

In an era of medicine in which outcomes are increasingly tied to data tracking and reporting as well as reimbursement, and bundled payments for joint replacement have begun, new emphasis has been placed on the concept of patient optimization before surgical intervention. Recognition and management of malnutrition is one facet of patient optimization that can positively impact outcomes in arthroplasty. Malnutrition has been associated with delayed wound healing, persistent drainage, and prosthetic joint infection in orthopedic patients [1-3].

The purpose of this review is to outline the definition of malnutrition, to aid the surgeon in identification of patients at risk, and to suggest appropriate assessments and interventions that can be used to optimize prospective arthroplasty patients.

Definition of Malnutrition

Malnutrition is defined as a state resulting from lack of uptake or intake of nutrition leading to altered body composition (decreased fat-free mass but specifically body cell mass) and diminished function [4]. This includes over nutrition as well as undernutrition. Malnutrition has not traditionally been a focus of intervention by orthopedic surgeons, but it has significant effects on surgical outcomes [4-7].

Malnutrition in these studies has been defined as serum albumin less than 3.5 or absolute lymphocyte count less than 1500, whereas other studies have used other markers such as transferrin or prealbumin. However, these values are not absolute and have been questioned in several studies [8-12]. In a consensus agreement reached through series of meetings held at the American Society for Enteral and Parenteral Nutrition and European Society for Parenteral and Enteral Nutrition congresses, malnutrition was classified into 3 groups: starvation-related, chronic disease–related, and acute injury– or disease state–related group [13]. Classifying malnutrition based on etiology simplifies the issue and also helps determine appropriate management strategies.

Prevalence of Malnutrition

Malnutrition has been reported to be as high as 20%-50% in hospitalized patients [14] and while the prevalence of malnutrition in orthopedic patients has been reported as 9%-39% [15,16]. Furthermore, malnutrition was identified in 26% of arthroplasty patients at an urban academic center [17], and other studies report this incidence as high as 50% [3,18].

Malnutrition and Immunity

Nutritional factors play a crucial role in regulating metabolic pathways and immune system functions. Various nutritional factors that have been implicated to play a role in patients undergoing arthroplasty include serum albumin, serum iron/transferrin, vitamin D, serum zinc, and adiposity.

Protein deficiency causes atrophy of lymphoid organs affecting several immune functions such as lymphocyte proliferation,

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http://dx.doi.org/10.1016/j.arth.2016.03.027
0883-5403/

antibody responses, Interleukin-2 (IL-2), and Interferon-gamma as well as delayed-type hypersensitivity reactions [19]. Recent study has shown human albumin has an immunomodulatory effect leading to an increased ability of antigen presenting cells to trigger T-cell activation [20]. Iron sequestration provides innate defense termed nutritional immunity, where a single substitution in transferrin reverses TbpA binding to counteract bacterial piracy [21]. Composition of adipose tissue is regulated by body weight status, feeding, and fasting. Hypertrophy and hyperplasia of adipocytes lead to decreased vascularity and subsequent necrosis followed by macrophage infiltration and inflammation. T cells infiltrating adipose tissue produce Th1 cytokines such as IL-1, Interferon gamma, IL-6, and leptins, which are responsible for chronic inflammation as well as insulin resistance [22]. The nutritional importance of zinc is well known, but its role in immunomodulation has been recognized more recently. Zinc deficiency affects both innate and adaptive immunity in acute situations, and chronic deficiency leads to an increase in the production of proinflammatory cytokines leading to inflammatory states [23].

Although vitamin D has a well-recognized role in bone health, it also plays an important role in innate immunity [24]. The immunomodulatory actions of vitamin D are well recognized and are a key factor in innate as well as adaptive immunity and immunity modulation [25]. Immunologically competent cells such as B and T lymphocytes, monocytes as well as dendritic cells display specific vitamin D receptors [26]. Circulating vitamin D levels have direct influence on macrophages and increase their oxidative burst potential [27] (maturation and production of cytokines, acid phosphatase, and hydrogen peroxide) and prevents excessive expression of inflammatory cytokines. Vitamin D may also improve outcomes by reducing both local and systemic inflammatory response as a result of modulating cytokine responses and reducing toll-like receptor activation [28]. It also stimulates expression of potent antimicrobial peptides, such as cathelicidin and beta-defensin 2. Similarly, vitamin C has also been implicated as an important nutritional parameter. Vitamin C has well-recognized antioxidant properties and has been used in arthroplasty to reduce systemic inflammatory response syndrome [29]. It is also known to have immunostimulant, antibacterial, and antiviral properties and has been advocated to reduce regional pain syndrome [30].

Malnutrition and Arthroplasty

Using an institutional computerized database, 11,785 consecutive total hip arthroplasty (THA) and total knee arthroplasty (TKA) were reviewed. Three hundred patients had persistent drainage, and 83 patients failed initial debridement. In this study, late debridement and malnutrition (35%) predicted failure of debridement with component retention and subsequent development of prosthetic joint infection [31].

In a more recent study, 49,603 primary THA or TKA patients were retrospectively reviewed using the American College of Surgeons National Surgical Quality Improvement Project database. Hypoalbuminemia was identified in 4.0% of cases and was associated with a 2-fold increase in the rate of surgical site infection. This study also demonstrated independent associations between hypoalbuminemia and pneumonia, prolonged hospital length of stay as well as readmission [7]. In a previous study by the same author, of 9230 revision THA or TKA patients in the ACS-NSQIP registry, 4517 had recorded serum albumin and 755 (15.8%) were found to have hypoalbuminemia. This cohort was 3 times more likely to have a septic indication for revision than patients with normal albumin [32]. A prospective study of 213 patients undergoing total knee replacement used triceps skinfold thickness as a marker for nutritional status. There was 5% risk of infection when triceps skinfold thickness was below 30 mm and 10% risk when it was below 20 mm [33]. Hypoalbuminemia has been identified as a more significant risk factor for postoperative complications than morbid obesity [34].

Nelson et al [35] using the NSQIP database, analyzed 77,785 surgical patients. They grouped patients as morbidly obese (body mass index [BMI] ≥40) or nonmorbidly obese (BMI ≥18.5-<40) or by low serum albumin level <3.5 mg/dL) or normal serum albumin (serum albumin level ≥3.5 mg/dL). They found that low serum albumin independently predicted higher mortality than the group with normal serum albumin (0.64% vs 0.15%; odds ratio [OR], 3.17; 95% confidence interval, 1.58-6.35; $P = .001$). They also found that patients in the low serum albumin group were more likely to have a superficial surgical site infection (1.27% vs 0.64%; OR, 1.27); deep surgical site infection (0.38% vs 0.12%; OR, 3.64); organ space surgical site infection (0.45% vs 0.15%; OR, 2.71); pneumonia (1.21 vs 0.29); require unplanned intubation (0.51% vs 0.17); and remain on a ventilator more than 48 hours (0.38% vs 0.07%). Malnourished patients were found to have a higher incidence of renal insufficiency (0.45% vs 0.12%; OR, 2.71); acute renal failure (0.32% vs 0.06%; OR, 5.19); cardiac arrest requiring cardiopulmonary resuscitation (0.19% vs 0.12%; OR, 3.74); and septic shock (0.38% vs 0.08%; OR, 4.4). Patients in the low serum albumin group also were more likely to require blood transfusion (17.8% vs 12.4%; OR, 1.56; 95% confidence interval, 1.35-1.81; $P < .001$).

Vitamin D insufficiency has been implicated with poor functional outcomes, an increase postoperative pain, and increased risk for periprosthetic infection [36,37]. Examining the National Health and Nutrition Examination Survey 2005-2006 using a cutoff of ≤20 ng/mL, the prevalence of vitamin D insufficiency was found to be 41.6% [38]. Johnson et al [39], comparing 448 patients with hip fractures and a control group of 1091 patients, all of whom underwent elective total hip or total knee replacement, showed that there was high rate of vitamin D insufficiency in both groups (cutoff of 30 ng/mL) with prevalence of 65.8% in the fracture group and 54% in the arthroplasty group. In a recent study [40], examining 9135 patients from the Australian Diabetes, Obesity and Lifestyle study, 201 hip arthroplasties for osteoarthritis were identified. In this study, they found that a one standard deviation increase in 25-hydroxy-vitamin D in males was associated with a 25% increase in incidence of arthroplasty. In a retrospective study, Maier et al [36] found 86% of patient undergoing revision arthroplasty for periprosthetic infection having vitamin D level below 20 ng/mL. In the same study, they also found 64% of primary arthroplasty patients and 52% of patients undergoing revision arthroplasty for aseptic loosening having vitamin D insufficiency.

Similarly, low serum zinc level has been correlated with delayed wound healing in total hip arthroplasty as well as hemiarthroplasty. The cutoff value is less than 95 microgram/dL. In a prospective study, Zorrilla et al [41] found that low serum zinc level and absolute lymphocyte count of less than 1500 significantly correlated with delayed wound healing in total hip arthroplasty patients.

Identification of Patients at Risk

Obesity, low BMI, prior gastric bypass, malabsorption states, and hyper metabolic states can increase risk of malnutrition. World Health Organization defines obesity as a BMI >30. The average BMI for patients undergoing arthroplasty in the United States is 33. The most common reason for obesity is excess caloric intake. Although excess calories lead to obesity, many obese patients do not have adequate nutrition, as high-calorie diets tend to contain foods high in carbohydrates and fat and limited true nutritional value. Many centers now set a cutoff of BMI 40 or lower before arthroplasty. Simple advice for patients to lose weight is inadequate. Calorie counting advice with a structured diet and a BMI goal as well as a referral to a dietitian for nutritional consultation may improve compliance. Referral to a bariatric center for counseling and potential surgical management of obesity may be appropriate in certain cases. However, some forms of bariatric surgery may lead to malabsorption, and monitoring and supplementation are important in these patients.

Physical examination should include BMI as well as inspection of skin turgor, hair and nail quality, and body fat distribution. Distribution of body fat may be more important in determining wound healing and infection risk in knee patients than in hip patients [42].

Routine laboratory studies should include a complete blood count with differential, to identify both anemia as well as to quantify absolute lymphocyte count. A reticulocyte count is also helpful to determine marrow response to anemia. A serum albumin and transferrin as well as a hemoglobin A1C should be obtained. Patients having anemia should have additional indices measured and intervention applied according to the results. Optimization of anemia can include iron and vitamin C supplementation and folate, and patients with preoperative hemoglobin <11 g/dL should have additional assessments to determine etiology. This may include referrals to hematology and gastroenterology for evaluation and management. A vitamin D (OH) 2 level may also be useful.

Malnutrition Assessment Tools

Various malnutrition screening tools have been reported in the literature. Some screening tools use combination of biochemical marks and clinical indices such as nutritional risk index [43] and geriatric nutritional risk index [44]. Some others use anthropometry, mobility, cognitive state, self perception of health and nutrition such as Mini Nutritional Assessment [45], its shorter version, the Mini Nutritional Assessment screening form [46] as well as the Malnutrition Universal Screening Tool (MUST) [47]. Subjective Global Assessment (SGA) [48], and Nutritional Risk Screening 2002 [43] use data from medical history, clinical and subjective evaluation of the patient. In a prospective study, enrolling 248 patients, Poulia et al [49] demonstrated that among the 6 screening methods using Nutritional Index, Geriatric Risk Index, SGA, Mini Nutritional Assessment-screening form, MUST, and Nutritional Risk Screening 2002, MUST seemed to be the most valid in the evaluation of risk for malnutrition in elderly hospitalized patients. Various markers have been used in orthopedic literature as a method for screening malnutrition. The most common serologic markers used include serum albumin of less than 3.5 gm/dL and absolute lymphocyte count of less than 1500 [31,41,50-52] and transferrin <200. Anthropometric measures [33,53] as well as nutritional screening tools have also been described in orthopedic literature as tools for screening [18,50]. Although anthropometric measures have been useful for nutritional screening, there are no standardized established cut off values and their usefulness has been limited.

Correction of Malnutrition in Elective Arthroplasty Patients

Literature is scant on nutritional intervention and its effects in orthopedic patients. In a randomized control trial, Ljunggren et al randomized 55 patients undergoing hip replacement either to preoperative fasting, oral ingestion of tap water, or oral ingestion of carbohydrate drink. They found no statistically significant effect on glucose clearance, insulin sensitivity, or postoperative complications in patients undergoing elective hip surgery [54]. In a randomized clinical trial, 60 elderly patients were randomized to receive energy-protein supplement perioperatively. They found that higher daily protein intake groups were associated with fewer postoperative complications [55]. Low serum albumin is reflective of chronic disease, and this should be addressed before surgery. In patients with normal liver and kidney functions, ESPEN guidelines are to be followed for enteral supplementation. Enteral nutrition should be used for 10-14 days before surgery on patients with severe nutritional risk factors. Severe nutritional factors are defined as patients with weight loss greater than 10%-15% in the last 6 months, SGA of grade C, serum albumin level less than 30gm/L, and BMI of less than 18.5 [56]. Protein supplementation for patients with protein deficiency can be accomplished with nutritional shakes, with a target intake of 1 gm/kg daily. Oral nutrition supplement should be enriched with immune-modulating substrates including arginine, omega 3 fatty acids, and nucleotides.

Table 1
Nutritional Interventions.

1. Protein Supplements	1 gm/kg/qd × 10-14 d
2. Iron supplementation	324 mg PO TID × 3-4 wk
3. Vitamin D	1000 IU daily unless deficient. If <20 ng/dL, 50,000 IU weekly × 8 wk. For levels 20-30 ng/dL, 5000 IU daily × 3-6 mo.
4. Vitamin C	500 mg qd × 2 wk
5. Zinc sulfate	220 mg/qd

TID, three times daily.

Simple interventions (Table 1) can include iron supplementation (324 mg po three times daily × 3-4 weeks) and vitamin C (500 mg po daily), to aid iron absorption as well as collagen cross linking, which aids wound healing. If absolute iron deficiency is identified based on low serum ferritin and transferrin saturation, referral to a gastroenterologist should be made. If absolute iron deficiency is not present, kidney function should be assessed and referral to a nephrologist should be made if abnormal renal function is present. If results are equivocal, a trial of iron therapy should be made. If there is no response to iron, further treatment for anemia of chronic disease should be considered with erythropoiesis stimulating agents. Hematologist referral is considered appropriate in this setting. Zinc (11 mg po daily) can aid in wound healing also. Vitamin D supplementation of 1000 IU daily is also recommended for routine maintenance. Patients with vitamin D levels <20 ng/mL should be given super supplementation with 50,000 IU weekly for 8 weeks followed by maintenance dose of 1500-2000 IU daily with yearly vitamin D level monitoring. Levels between 20 and 30 ng/dL should be treated with daily vitamin D supplementation of 5000 IU for 3-6 months followed by retesting [57].

Follow-up laboratory studies can be obtained 6-12 weeks after intervention to assess correction, although there is limited data at present to determine optimum timing of repeat assessment or timing of subsequent surgical intervention after optimization steps have been completed.

Conclusion

Understanding the impact of malnutrition on healing response and risk of wound healing and infection complications is an important step in the optimization of patients undergoing elective arthroplasty. Identification of patients at risk, performing physical and laboratory assessment, and instituting targeted interventions are simple steps that should be taken preoperatively to help minimize risk of adverse outcomes.

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