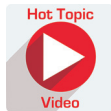


# Evidence-Based Perioperative Nutrition Recommendations: Optimizing Results and Minimizing Risks

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**Summary:** Plastic surgery patients span the nutritional spectrum from generally healthy, nutritionally competent patients to inherently catabolic, nutritionally deficient, and chronic wound patients. Therefore, plastic and reconstructive surgery affords the opportunity to investigate the impact of nutrition across a heterogeneous patient population following a wide variety of procedures. Although patients may be nutritionally deficient in certain vitamins warranting perioperative repletion, other supplements have the potential to benefit all patients, regardless of nutritional status. Despite these putative benefits, there is a dearth of information regarding nutritional optimization, with the limited, available literature focusing mostly on herbal supplements and their potential side effects. A significant barrier to supplement use is the lack of education and available supporting information regarding the indications, contraindications, and physiology of these adjuncts. The goal of this article is to provide a comprehensive, evidence-based review of available nutritional supplements that can be considered for the plastic surgery patient in the perioperative period to optimize surgical outcomes while minimizing risk. Prospective, well-designed studies using validated, high-quality supplements will be critical in determining the significance that perioperative supplementation can have for surgical outcomes. Until well-done prospective studies are performed, the supplement, dose, and duration should be determined on an individual, patient-per-patient basis at the discretion of the operating surgeon. (*Plast. Reconstr. Surg.* 146: 423, 2020.)

**M**alnutrition is a state of nutrient deficiency that results in an undesired change in physiology. It can lead to decreased immunity and an inability to tolerate and overcome stressors such as illness, trauma, infection, and surgery.<sup>1-4</sup> Prior studies have demonstrated that malnutrition is an independent risk factor for perioperative complications, including mortality, decreased wound healing, length of hospital stay, and cost.<sup>5-9</sup> However, the determination of malnutrition is not standardized and is typically measured using a variety of corollaries of nutrition such as body mass index, weight changes, subjective global assessments, or nutritional laboratory markers. Variations in measurements make global

application and nutritional meta-analyses fraught with inconsistent results and allow for misinterpretation. Although numerous reviews in plastic surgery have focused on wound healing and the importance of nutritional optimization,<sup>10-13</sup> there is a paucity of literature on how to safely overcome these deficiencies.

**Disclosure:** *The authors have no disclosures to report.*

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*Received for publication July 9, 2019; accepted February 11, 2020.*

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DOI: [10.1097/PRS.0000000000007004](https://doi.org/10.1097/PRS.0000000000007004)

Plastic and reconstructive surgery affords the opportunity to investigate the impact of nutrition across a heterogeneous patient population following a wide variety of procedures. Although patients may be nutritionally deficient in certain vitamins warranting perioperative repletion, other supplements have the potential to benefit all patients, regardless of nutritional status.<sup>14</sup> Although there are inherent differences in the goals and needs of different patient populations, the potential to improve patient outcomes is ubiquitous. Despite these putative benefits, there is a dearth of information regarding nutritional optimization, with the limited, available literature focusing mostly on herbal supplements and their potential side effects.<sup>15,16</sup> A significant barrier to supplement use is the lack of education and available supporting information regarding the indications, contraindications, and physiology of these adjuncts. Interestingly, prior studies have demonstrated that many plastic surgery patients are already taking herbal medicines or supplements but are not sharing this information with their surgeon or anesthesiologists preoperatively. Although previous studies have reviewed indications and potential adverse effects for the plastic surgery patient, perioperative recommendations were not provided.<sup>17</sup> The goal of this article is to provide a comprehensive, evidence-based review of available nutritional supplements that can be considered for the plastic surgery patient in the perioperative period to optimize surgical outcomes and minimize risk.

## SUPPLEMENTS OF INTEREST

### Vitamin A

Vitamin A is a fat-soluble vitamin that plays a significant role in wound healing. It increases collagen synthesis and cross-linking, augments the inflammatory response in wounds and increases the number of immune cells in the wound environment to allow for healing and epithelial cell differentiation.<sup>18–25</sup> It maintains the integrity of mucosal and epithelial surfaces by enhancing epithelialization and increasing collagen formation.<sup>21</sup> It also functions like a hormone by altering the activity of epithelial cells, melanocytes, fibroblasts, and endothelial cells by means of retinoic acid receptors.<sup>26</sup> It is most well known in wound healing because of its ability to reverse corticosteroid-induced inhibition of cutaneous wound healing.<sup>27</sup> However, there is a paucity of studies examining the singular impact that vitamin A has on wound healing in human studies.

### Vitamin C

Vitamin C (ascorbic acid) is a water-soluble vitamin with strong antioxidant properties that is also an essential cofactor for multiple enzymatic reactions. It promotes proinflammatory and antiinflammatory effects in various types of immune cells to augment healing and prevent infection.<sup>18,28–32</sup> It is crucial for collagen metabolism and regulation, as it is a cofactor in the hydroxylation of proline and lysine in collagen formation.<sup>18,32–36</sup> Animal studies have demonstrated that vitamin C supplementation results in reduced expression of proinflammatory mediators and higher expression of wound healing mediators to allow for early resolution of inflammation and tissue remodeling.<sup>37</sup> A randomized controlled trial found that supplementation with 500 mg of ascorbic acid daily led to improved healing in patients with pressure ulcers.<sup>38</sup> However, a study in nursing home patients with pressure ulcers who were supplemented with 500 mg of ascorbic acid daily found no improvement in wound healing.<sup>39</sup> Although a review article suggested that high-dose supplementation of vitamin C may improve the healing of surgical wounds in healthy subjects, the studies cited investigated combination supplementation.<sup>38,40–42</sup> In addition, supplementation with vitamin C demonstrated in a meta-analysis a decrease in the development of complex regional pain syndrome after wrist fracture.<sup>43</sup> As with vitamin A, there is a paucity of studies examining the singular impact that vitamin C has on wound healing in human studies.

### Vitamin D

It is estimated that 1 billion people worldwide are vitamin D insufficient or deficient, with postmenopausal women especially at risk. It has also been suggested that up to 36 percent of healthy 18- to 29-year-old adults are vitamin D deficient.<sup>44,45</sup> This is likely because of reduced sun exposure, low intake of dietary vitamin D, and comorbidities that can interfere with vitamin D synthesis or absorption.

Vitamin D and its receptor are ubiquitously expressed throughout the body and have a myriad of downstream effects that can influence wound healing. Vitamin D plays an important role in regulating infection and the associated inflammatory response. Potential mechanisms by which vitamin D modulates the immune system include suppression of interferon-mediated macrophage activation,<sup>46</sup> down-regulation of cytokine generation,<sup>47</sup>

phagocytosis stimulation,<sup>48</sup> decreasing production of T-helper type 1 cytokines, and promotion of T-helper type 2 cytokines.<sup>49</sup> This collectively leads to improvements in inflammatory biomarkers and oxidative stress levels.<sup>48</sup>

Vitamin D also plays a crucial role in modulating glycemic control through activation of insulin receptor expression and improved insulin sensitivity.<sup>47,50,51</sup> It is well established that poor glycemic control negatively impacts wound healing through a variety of downstream influences, including alterations in cytokine production that can lead to the development of chronic wounds.<sup>52</sup> In addition, vitamin D influences the metabolism of other nutrients such as calcium and phosphorus.<sup>47,50,51</sup>

The majority of studies investigating the role of vitamin D have been performed in the orthopedic literature because of its known role in bone healing.<sup>53</sup> However, vitamin D supplementation in patients with diabetic foot ulcers demonstrated to not only improve ulcer healing, but also to lead to beneficial effects on glucose homeostasis, total cholesterol, low-density lipoprotein cholesterol, total/high-density lipoprotein cholesterol, erythrocyte sedimentation rate, high-sensitivity C-reactive protein, and malondialdehyde levels, all of which have been associated indirectly with improved wound healing.<sup>54</sup>

Expert recommendations for vitamin D supplementation vary, with the Institute of Medicine recommending 400 IU daily and the Endocrine Society advocating for 200 IU daily to achieve optimal serum calcifediol levels.<sup>55</sup> However, these recommendations do not address the increased needs of surgical and/or chronic wound patients. For example, a multicenter trial of orthopedic trauma patients found that 2000 IU daily was more effective at achieving optimal calcifediol levels compared with 400 IU daily.<sup>56</sup> Other meta-analyses in the orthopedic literature have demonstrated that daily doses greater than 1000 IU may be more efficacious.<sup>57</sup> There may also be a dose-dependent response. In one study, it was demonstrated that for every additional 100 IU supplemented daily, there was an associated 8 percent reduction in risk of vitamin D deficiency.<sup>56</sup> Relevant to surgical planning, it has been shown that vitamin D–deficient patients with traumatic fractures who took oral vitamin D and calcium achieved normal calcifediol levels at a mean of 7 weeks.<sup>58</sup> This should prompt early identification and supplementation in patients that may be at risk for vitamin D deficiency.

## Glutamine and Arginine

Arginine and glutamine are two amino acids that have been shown to play important roles in wound healing.<sup>59</sup> Arginine impacts wound healing through several mechanisms.<sup>60</sup> It is a precursor to nitric oxide and proline, both of which are required for the inflammatory response, collagen synthesis, and neovascularization.<sup>61–63</sup> Arginine also stimulates the production and secretion of growth hormone and activation of T cells.<sup>64,65</sup> In healthy volunteers and rodents, arginine supplementation was able to enhance wound strength and collagen deposition in incisional wounds.<sup>63,66,67</sup> A meta-analysis of six studies and 397 head and neck cancer patients demonstrated that arginine-enriched enteral formulas led to a significant reduction in fistulas and improved wound healing.<sup>68</sup> Arginine is one of the crucial ingredients in IMPACT (Nestle, Arlington County, Va.), a nutrition formula, which was demonstrated in a systematic review to reduce infection rate and length of stay in high-risk elective surgical patients.<sup>69</sup> Pertinent to microvascular and plastic surgery, a randomized controlled trial demonstrated that arginine supplementation led to improved microcirculation in abdominally based free tissue transfers.<sup>70</sup>

Glutamine plays roles related to metabolic, enzymatic, antioxidant, and immune responses.<sup>60</sup> It is a fuel source for enterocytes, lymphocytes, fibroblasts, epithelial cells, and macrophages, all of which are required for wound healing.<sup>71</sup> In wounds, glutamine leads to the up-regulation of heat shock proteins, which provide antiinflammatory and immunomodulatory functions.<sup>72</sup> It also regulates leukocyte apoptosis, superoxide production, antigen processing, and phagocytosis in the inflammatory response.<sup>72,73</sup> Glutamine is a precursor of glutathione, a powerful antioxidant and cofactor for enzymatic reactions for cell membrane stabilization and amino acid transport.<sup>74</sup> In addition, glutamine is uniquely essential for the integrity of gut mucosa. When glutamine is broken down into  $\alpha$ -ketoglutarate, it acts as an energy substrate for enteric cells, including neutrophils, which leads to improved superoxide production, phagocytosis, and antigen processing.<sup>73,75,76</sup>

## Omega-3 Fatty Acids

Fats have numerous important physiologic roles in the human body. They are structurally important in the lipid bilayer of cell membranes

and serve as precursors for prostaglandins and mediators of inflammation and metabolism.<sup>77</sup>

Several studies have demonstrated that omega-3 fatty acids possess the ability to improve wound healing, glucose homeostasis, systemic markers of inflammation, infectious and noninfectious complications, length of hospital stay, readmissions, and mortality.<sup>78–81</sup> In a study of stage II to IV pressure ulcers, patients receiving an enriched fish oil formula had a decrease in the size of wounds and in blood C-reactive protein levels.<sup>81</sup> Omega-3 fatty acids given to patients with diabetic foot ulcers demonstrated beneficial effects on ulcer size, markers of insulin metabolism, serum high-sensitivity C-reactive protein, plasma total antioxidant capacity, and glutathione. It was proposed that the observed improved wound healing was attributable to its impact on optimizing metabolic profiles.<sup>78</sup>

Numerous studies have been performed investigating the role that immunonutrition supplying both omega-3 fatty acids and arginine in the form of IMPACT nutrition drink (reviewed in more detail in the Immunonutrition/Combination Treatment section). A recent meta-analysis demonstrated that this combination was able to reduce postoperative infections and length of hospital stay in patients following a variety of surgical procedures.<sup>82</sup>

There were originally concerns that omega-3 consumption resulted in increased bleeding times<sup>83</sup> and decreased platelet aggregation.<sup>83,84</sup> However, a recent meta-analysis of 52 publications (32 on healthy individuals and 20 on patients undergoing surgery) found that supplementation did not lead to increased bleeding or blood transfusions either during or after surgery.<sup>85</sup>

### Protein

For wound healing to occur, protein is required for skin integrity, growth, maintenance of cells, fluid and electrolyte balance, and to activate an appropriate immune response. It plays a role in fibroblast proliferation, collagen production, and angiogenesis to permit wound healing.<sup>18</sup> A delayed progression from the inflammation to proliferative phases leads to suboptimal wound healing. This is further compounded by the fact that protein deficiency decreases fibroblast activity, which delays angiogenesis and reduces collagen formation.<sup>86</sup>

In large, chronic wounds, significant amounts of protein are lost and protein requirements may increase as much as 250 percent.<sup>87,88</sup> Therefore, protein supplementation is critical to achieving

appropriate levels for wound healing. Pertinent to plastic surgery, a study demonstrated that whey protein supplementation led to decreased wound healing complications in postbariatric abdominoplasty patients.<sup>89</sup>

### Probiotics

The human gastrointestinal tract is home to an estimated 300 to 500 bacterial species.<sup>90</sup> When the normal flora of the intestines is disrupted (e.g., trauma, antibiotics), the balance of bacteria can be shifted to favor virulent species. In these instances, supplementation of commensurate bacteria can aid in restoring the desired balance. Probiotic supplements improve host defenses by producing antimicrobial agents, competing with pathogenic bacteria, stabilizing the integrity of the gut lining, and reducing anaerobic pathogenic bacteria through intestinal motility.<sup>91</sup> *Lactobacillus* bacteria are also able to produce cytokines that stimulate and augment the host immune response.<sup>92–101</sup>

Although probiotics are typically investigated for their role in mitigating disease of the digestive tract, large meta-analyses have supported their ability to decrease the incidence of abdominal distention, diarrhea, pneumonia, sepsis, surgical-site infections, urinary tract infections, duration of antibiotic therapy, and duration of hospital stay. In addition, there is evidence that they can improve wound healing, glucose homeostasis, systemic markers of inflammation, and cholesterol levels.<sup>102,103</sup> Probiotics have also shown utility in preventing fungal infections through similar mechanisms.<sup>104–109</sup>

Although probiotic safety is well documented in healthy subjects, there are isolated reports of systemic complications in immunocompromised populations. In a review of 1966 publications and 4131 patients, there were only 32 documented cases in which bacteremia or fungemia was associated with probiotic use. All 32 cases occurred in 20 patients with significant risk factors for bacterial and fungal septicemia.<sup>110</sup>

### Zinc

Zinc is a nutrient essential for DNA replication, especially in cells with high turnover rates such as inflammatory and epithelial cells and fibroblasts. In wound healing, it is required for collagen production, fibroblast proliferation, and epithelialization because of its critical role in enzymatic activity.<sup>86</sup> Zinc also promotes an immune response through lymphocyte activation.<sup>77</sup> This was clinically supported in patients with diabetic



foot ulcers where zinc supplementation led to reductions in ulcer size and improvements in fasting plasma glucose, serum insulin concentration, insulin resistance, high-density lipoprotein cholesterol, total antioxidant capacity, glutathione, high-sensitivity C-reactive protein, and plasma malondialdehyde concentrations.<sup>111</sup>

### Curcumin

Curcumin, a phenol from the rhizome of *Curcuma longa*, has been used in traditional medicine for the treatment of biliary and hepatic disorders, cough, diabetic ulcers, rheumatism, and sinusitis.<sup>112</sup> More recently, curcumin has been investigated for its putative positive effects in malignancies,<sup>113</sup> aging,<sup>114</sup> and wound healing.<sup>112</sup> Curcumin's mechanism of action is likely to be multifactorial, as it has been shown to improve inflammatory cell turnover,<sup>115–117</sup> reduce the expression of proinflammatory cytokines,<sup>118,119</sup> and augment antioxidant enzyme production and efficacy.<sup>119–121</sup> It has also been shown to facilitate hydroxyproline and collagen synthesis,<sup>122,123</sup> promote fibroblast differentiation into myofibroblasts,<sup>124–126</sup> reduce epithelialization time,<sup>123</sup> and enhance angiogenesis.<sup>127</sup> A recently published review summarized the potential beneficial effects of curcumin on wound healing.<sup>128</sup>

### Arnica and Bromelain

Arnica is a homeopathic medicine extracted from *Arnica montana*, which grows in the Swiss Alps. It is often recommended for its antiinflammatory effects and potential to decrease ecchymosis and edema.<sup>129</sup> A meta-analysis of eight studies demonstrated that in the majority of the studies, supplementation did not result in clinical improvements as compared to placebo.<sup>130</sup> However, as arnica is a homeopathic medication and relies on homeopathic dosing, interstudy comparisons and meta-analyses are difficult. A recently published systematic review analyzed studies that examined the perioperative efficacy of arnica with a focus on treatment regimen and outcomes. Twenty articles met inclusion criteria.<sup>131</sup> There was marked heterogeneity among the studies, but arnica appeared to have a mitigating effect on ecchymosis, most notably following rhinoplasty and face lifts/facial procedures.<sup>132–151</sup>

Bromelain is a homeopathic medicine isolated from pineapple cores and stems that has been shown to result in decreased postoperative edema, pain, and erythema. Procedures investigated included molar extraction and double-jaw

surgery with a variety of dilutions and dosing recommendations. A recently published systematic review analyzed studies that examined the perioperative efficacy of bromelain with a focus on treatment regimen and outcomes. Nine articles met inclusion criteria.<sup>131</sup> There was marked heterogeneity among the studies, but bromelain demonstrated in numerous studies the ability to reduce trismus, pain, and swelling following molar extractions.<sup>152–160</sup> Although fresh pineapple is not a concentrated source of bromelain, it does contain carotenoids, which have been shown to prevent lipid oxidation and oxidative stress.<sup>161,162</sup> Intake of bromelain supplements can be associated with nausea and emesis; therefore, consumption of whole fruit may be the optimal route of administration.<sup>162,163</sup>

### Immunonutrition/Combination Treatment

Malnourished patients suffer from a variety of protein, vitamin, and mineral deficiencies. To address this, immunonutrition can be used to address the myriad of nutritional deficiencies in the perioperative period. Three meta-analyses demonstrated that preoperative immunonutrition in well-nourished or mildly malnourished patients can significantly decrease the incidence of complications and shorten hospital lengths of stay.<sup>164–166</sup> A recent meta-analysis of 15 randomized controlled trials in 3831 patients found that perioperative nutritional support of malnourished patients decreased postoperative complications (infectious and noninfectious) and hospital lengths of stay.<sup>167</sup> Pertinent to plastic surgery, body contouring obese nonbariatric and postbariatric patients who received supplementation with ProCare (NutrEssential, Sushant Golf City, Lucknow, India) three times per day for 3 weeks were able to achieve similar complication profiles when compared to normal-weight patients. ProCare is a powder (complete profile in Agha-Mohammadi and Hurwitz<sup>168</sup>) composed of 20 g of protein; 3 g of free amino acid; 4 g of arginine; and 1 g of glutamine, folate, iron, copper, zinc, selenium, vitamin A, vitamin B<sub>12</sub>, vitamin B<sub>6</sub>, and vitamin C.<sup>169</sup>

Multiple studies have investigated the perioperative role that IMPACT nutrition drink has on operative outcomes and associated costs. A systematic review of 17 studies demonstrated that preoperative consumption of IMPACT contributed to improved outcomes in elective surgery patients, especially those undergoing gastrointestinal tract procedures. Specifically, it was shown to decrease infectious complications,

**Table 1. Proposed Preoperative and Postoperative Supplement Regimen for Plastic Surgery Patients\***

Supplement	Purpose	Suggested Dosing	Contraindications/Toxicity	Highest Level of Evidence	References
Vitamin A	Antiinflammatory, immunomodulatory, antioxidant	<ul style="list-style-type: none"> <li>• 3000 IU for men and 2300 IU for women</li> <li>• Higher doses required to reverse the impact of steroids on healing</li> </ul>	Patients with abnormal liver function or malnutrition can accumulate toxic doses; symptoms of toxicity include dryness of the mucous membranes, vomiting, headache, liver damage, alopecia, muscle or bone pain, bleeding, and coma	Animal/ in vitro studies	
Vitamin C	Antiinflammatory, immunomodulatory, antioxidant	<ul style="list-style-type: none"> <li>• 75 mg/day for women and 90 mg/day for men</li> <li>• 100–200 mg/day for stage I or II pressure ulcers</li> <li>• 1000–2000 mg (10× normal recommendations) for stage III or IV pressure ulcers, or for highly stressed, malnourished, cigarette smokers and seriously injured patients</li> </ul>	For patients with renal failure, current guidelines recommend giving no more than 60–100 mg per day because of the risk of renal oxalate stone formation; symptoms of toxicity include gastrointestinal disturbances, potential kidney stones	I	38, 43
Vitamin D	Antiinflammatory, immunomodulatory, antioxidant, glucose modulation	<ul style="list-style-type: none"> <li>• 2000 IU daily</li> </ul>	Symptoms of toxicity include kidney stones	I	53, 54
Glutamine	Antiinflammatory, immunomodulatory, antioxidant	<ul style="list-style-type: none"> <li>• No clear recommendations</li> <li>• Current maximum recommended dosage for adults is 0.57 g/kg daily</li> </ul>	Symptoms of toxicity include gastrointestinal tract disturbances	Animal/ in vitro studies	
Arginine	Immunomodulatory, antioxidant, precursor to nitric oxide	<ul style="list-style-type: none"> <li>• No clear recommendations</li> <li>• 14–17 g free arginine in some studies</li> </ul>	In critically ill patients, high doses can result in nitric oxide production and enhanced inflammation and hemodynamic instability in patients with sepsis	I	66–70
Omega-3 fatty acids	Glucose modulation, antiinflammatory, immunomodulatory	<ul style="list-style-type: none"> <li>• No clear recommendations</li> <li>• Some studies use 1–2 g daily</li> </ul>	Symptoms of toxicity include impaired wound healing	I	78–82
Protein	Building blocks for tissue repair, immunomodulatory	<ul style="list-style-type: none"> <li>• RDA 0.8–1.0 g/kg daily to prevent malnutrition</li> <li>• 90 g daily supplemented to improve wound healing</li> <li>• Up to 1.25–1.5 g/kg daily in pressure ulcers</li> </ul>	Patients with kidney disease can develop protein toxicity because of decreased excretion; symptoms of toxicity include kidney stones and hypercalciuria	III	89
Probiotics	Glucose modulation, immunomodulatory	<ul style="list-style-type: none"> <li>• No clear recommendations</li> <li>• Dosing as tolerated</li> </ul>	Can cause bloating, diarrhea	I	102, 103
Zinc	Immunomodulatory, antioxidant	<ul style="list-style-type: none"> <li>• Zinc sulfate 220 mg twice daily</li> </ul>	Symptoms of toxicity include copper and calcium binding, gastrointestinal irritation, and decreased immune response	I	111
Curcumin	Immunomodulatory, antioxidant, promote angiogenesis	<ul style="list-style-type: none"> <li>• No clear recommendations</li> </ul>	None known	Animal/ in vitro studies	
Arnica	Antiinflammatory, antioxidant, decrease edema and erythema	<ul style="list-style-type: none"> <li>• No clear recommendations and confused by homeopathic dosing</li> </ul>	None known	I	131–150
Bromelain	Antiinflammatory, antioxidant, decrease edema and erythema	<ul style="list-style-type: none"> <li>• No clear recommendations and confused by homeopathic dosing</li> </ul>	None known	I	151–159

RDA, recommended daily allowance.

\*All supplements should be taken at least 3 wk before and after surgery, except arnica and bromelain, which should both be taken for 3–5 days before and after surgery.

**Protein**

Why should I take this supplement? Protein is necessary for healing. Having an open wound and/or undergoing surgery increases your protein requirements.

Side effects: Avoid if you have kidney disease or are on dialysis.

**Glutamine and Arginine**

Why should I take this supplement? Glutamine and Arginine are amino-acids which help with wound healing.

Side effects: Common side effects include gastrointestinal issues. Arginine should be avoided in patients with low blood pressure.

**Omega-3 fatty acids**

Why should I take this supplement? Omega 3 fatty acids can help with wound healing, inflammation and preventing infection

Side effects: Common side effects include gastrointestinal issues.

**Vitamins and Minerals**

Why should I take this supplement? Certain vitamins and minerals help wound healing. Surgery can increase how much you need and they can be used to improve wound healing.

*Vitamin A*

Side effects: Patients with abnormal liver function or malnutrition can accumulate leading to side effects. Side effects include dry mucous membranes, vomiting, headache, muscle or bone pain, and hair loss.

*Vitamin C*

Side effects: This is relatively well tolerated except in patients with a history of kidney stones. Common side effects are gastrointestinal issues.

*Vitamin D*

Side effects: In patients with a history of kidney stones, Vitamin D can result in an increased risk.

*Zinc*

Side effects: Common side effects are gastrointestinal issues.

**Probiotics**

Why should I take this supplement? Your body's natural intestinal flora serves a wide range of functions including immunity, healing, and nutrition. Surgery and especially antibiotics can alter the normal function of your intestines leading to poor healing, immunity, nutrition, and motility.

Side effects: Common side effects are bloating and diarrhea.

**Homeopathic Therapies**

*Curcumin*-a natural compound found in turmeric, a spice

Why should I take this supplement? This supplement is an anti-oxidant that can help wound healing and prevent infection.

Side effects: None known

*Arnica*-extracted from *Arnica montana*, a plant that grows in the Swiss Alps

Why should I take this supplement? This supplement can decrease bruising and swelling.

Side effects: None known

*Bromelain*-an enzyme found in pineapples

Why should I take this supplement? This supplement can decrease bruising, swelling, and sometimes pain.

Side effects: None known

**Fig. 1.** Sample handout to be modified for the surgeon's practice.

surgical-site infections, length of stay, and readmission.<sup>69,170,171</sup> IMPACT provides 18 g of protein per carton along with numerous vitamins and minerals. A study examining InflammEnz (Enzymes, Inc., Kansas City, Mo.), an oral

enzyme product that contains proteases, bromelain, vitamin C, calcium, rutin, and grape seed extract, demonstrated the ability in a punch biopsy model to improve erythema and tissue healing compared with placebo.<sup>172</sup>

## Carbohydrate Loading

Carbohydrates play important roles in the perioperative period through stimulation of hormone and growth factor secretion, production of fibroblasts, and modulation of leukocyte activity.<sup>173,174</sup> Preoperative fasting in the surgical patient has been the standard recommendation in an effort to minimize the risk of pulmonary aspiration by decreasing gastric volume.<sup>175</sup> However, previous studies pooling the existing literature concluded that preoperative fasting limited to 6 hours for solids is safe.<sup>176</sup> Prolonged fasting carries the risk of exacerbating the surgical stress response and associated catabolic state by potentiating hyperglycemia, insulin resistance, hyperthermia, immunosuppression, and muscle breakdown.<sup>177,178</sup> Thus, the role that carbohydrate loading could have on postoperative recovery has been investigated. Studies have demonstrated a reduction in postoperative insulin resistance, hyperglycemia, muscle loss, and hospital stays with this intervention.<sup>179–184</sup> Liquid intake and carbohydrate loading up to 2 hours before a procedure also improve patient satisfaction by reducing subjective feelings of thirst and hunger.<sup>176,181,185–187</sup> A relative contraindication is the potential for hyperglycemia, which can lead to suboptimal wound healing. Therefore, healthy carbohydrate options should be used.<sup>173</sup>

## Importance of Quality Supplementation

Supplements are currently not regulated by the U.S. Food and Drug Administration. Thus, the importance of seeking out third-party-validated supplement companies cannot be overemphasized. This will ensure not only that the appropriate and desired dosing of supplement is provided, but also that additives that could potentially lead to undesired effects are not consumed. This is critical when performing prospective studies to ensure that the appropriate interventions are being used and analyzed.

Indications, suggested dosage, and contraindications/toxicity are summarized in Table 1. Suggested doses are provided based on analyzed studies. However, because of lack of third-party validation of supplement contents in many studies, this should be interpreted with caution and requires validation in well-done prospective studies. A sample patient handout is presented in Figure 1.

## CONCLUSIONS

This article provides a comprehensive, evidence-based approach to perioperative supplementation using the available literature. The supplements

addressed in this article are by no means a comprehensive assessment of the options available to nutritionally optimize patients. Additional supplements, such as copper and vitamin B<sub>12</sub>, are crucial for the healing process, and their roles in augmenting recovery after surgery have yet to be determined. There are numerous unanswered questions that remain regarding the optimal combination and duration of supplementation for the plastic surgery patient. With proper recognition of the role that nutritional optimization can play in surgical outcomes, surgeons possess a powerful tool that can augment the surgical experience. However, without an accurate appreciation of the potential impact, desirable and undesirable, of various supplements, potential harm could be delivered to a patient. Thus, nutritional optimization for surgery is a topic that plastic surgeons should commit themselves to understanding and appreciating, both as individual surgeons and as a specialty. Prospective, well-designed studies using validated, high-quality supplements will be critical in determining the significance that perioperative supplementation can have on surgical outcomes. Until well-done prospective studies are performed, the supplement, dose, and duration should be determined on an individual, patient-per-patient basis at the discretion of the operating surgeon.

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