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Review

Nutrition support in cardiac surgery patients - a narrative review

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Abstract: Nutrition support is increasingly recognized as a clinically relevant aspect of the intensive care treatment of cardiac surgery patients. However, evidence from adequate large-scale studies evaluating its clinical significance for patients' mid- to long-term outcome remains sparse. Considering nutrition support as a key component in the perioperative treatment of these critically ill patients, led us to review and discuss our understanding of the metabolic response to the inflammatory burst induced by cardiac surgery. In addition, we discuss how to identify patients who may benefit from nutrition therapy, when to start nutritional interventions, present evidence about the use of enteral and parenteral nutrition and the potential role of pharmaconutrition in cardiac surgery patients. Although the clinical setting of cardiac surgery provides advantages due to its scheduled insult and predictable inflammatory response, researchers and clinicians face lack of evidence and several limitations in the clinical routine, which are critically considered and discussed in this paper.

Keywords: cardiac surgery, cardiopulmonary bypass, systemic inflammatory response, nutrition risk stratification, underfeeding, postoperative nutritional management, supplemental parenteral nutrition, enteral nutrition, pharmaconutrition

1. Introduction: Cardiac Surgery, Inflammation and Current Standard of Nutrition

Cardiac surgery with the use of cardiopulmonary bypass (CBP) frequently triggers a systemic inflammatory response, which contributes to the development of postoperative organ dysfunctions. This further leads to a prolonged need of life-sustaining therapies and consequently longer stay on the intensive care unit (ICU) (Figure 1). The surgical trauma, ischemia/reperfusion (I/R)-injury and resulting inflammation may be aggravated by nutritional deficiencies due to reduced defense mechanisms in the patient. In this context, numerous observational studies demonstrated a significant depletion of macro- and micronutrients, as well as the importance of energy and protein metabolism in the early stage after cardiac surgery [1,2].

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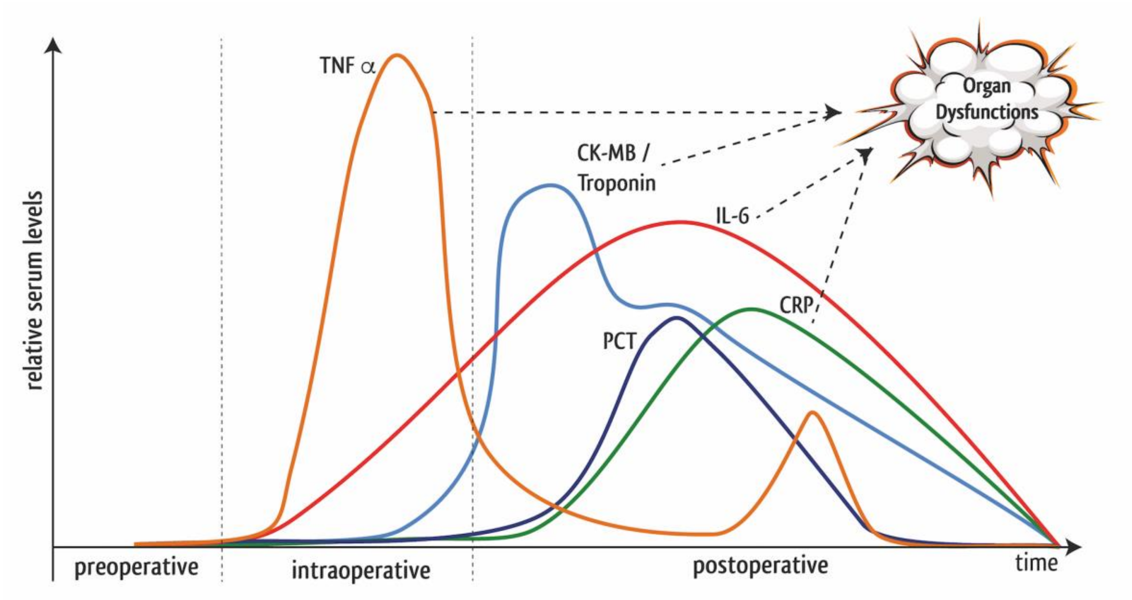

Figure 1. Time course of inflammation and development of organ dysfunction in cardiac surgery

Cardiac surgery patients who are well nourished prior to surgery show better outcomes, including morbidity and mortality as summarized in Figure 2 [1,2]. However, prior to surgery, a considerable percentage of these patients is malnourished, which is aggravated by preoperative fasting and the commonly observed postoperative delay of nutrition support. In the same vein, Drover et al. demonstrated in a retrospective analysis that patients after surgery are at an increased risk of malnutrition during the postoperative ICU stay [3].

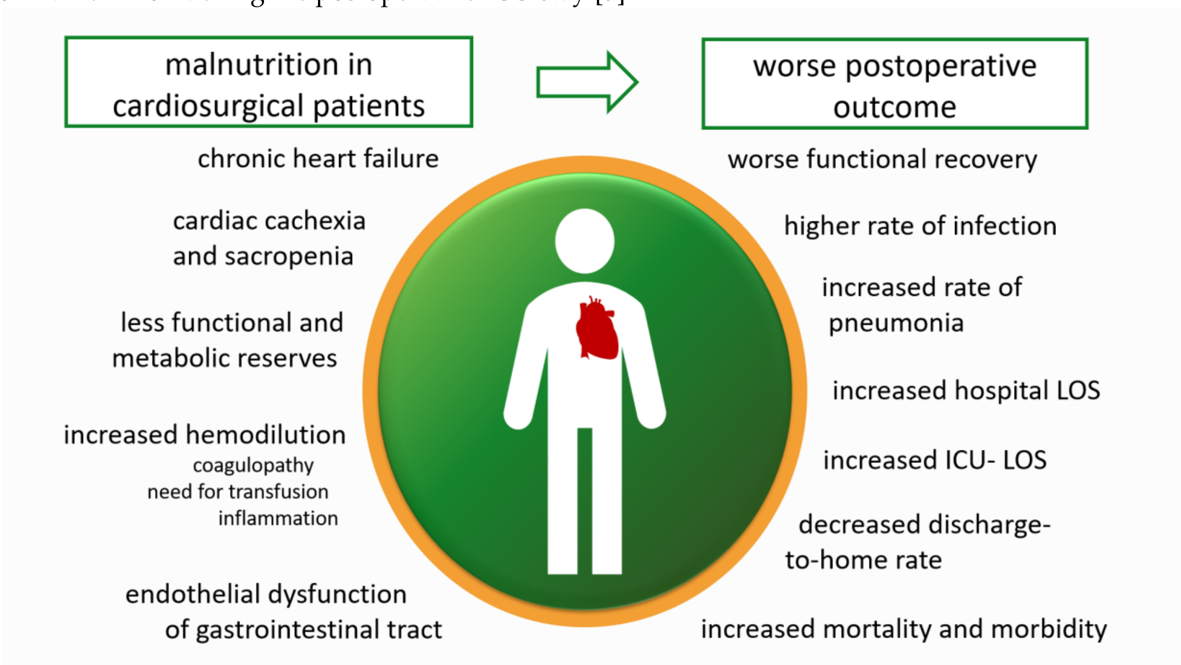

Figure 2. Influence of malnutrition on the outcome of cardiac surgery patients

Rahman et al. recently demonstrated that nutritional adequacy was low with respect to both energy and protein supplementation in cardiac surgery patients [4]. In addition, they confirmed that patients undergoing cardiovascular surgery were at the highest risk for iatrogenic malnutrition due to withholding of nutrition support during the early postoperative course. In a study including 787 patients cardiac surgery patients with an ICU stay of greater than 3 days, the authors found that 40 % of patients received no nutrition support at all and the mean time from ICU admission to initiation of enteral nutrition (EN) was 2.3 ± 1.8 days [5]. With EN alone, as well as with combined

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parenteral nutrition (PN), patients received less than a third of calories and protein as shown in Table 1. Furthermore, patients with later initiation of nutrition support have even lower total nutritional adequacy than other surgical or medical ICU patients, indicating the need to improve nutrition practice in that population [3].

Table 1. Current nutrition standard in cardiac surgery as reported by Rahman et al. [5]

Form of nutrition	Percentage of patients	Caloric adequacy	Protein adequacy
EN	78 %	25.5 %	24.9 %
EN + PN	17 %	32.4 %	28.8 %

Up to 8 % loss of body weight and a consistently positive nutrition risk screening (NRS 2002) were reported in patients scheduled for cardiovascular rehabilitation for 1 – 6 months after treatment for ischemic, valvular, or combined causes of heart diseases [6].

Given these findings, we can conclude that nutritional adequacy in cardiac surgery patients is low with respect to both energy and protein intake. However, improved nutritional adequacy was not associated with reduced overall mortality in all cardiac surgery patients per se. Given these findings, further work needs to be done to identify those cardiac surgery patients, who most likely to benefit from an intense nutrition support.

2. Nutrition Screening in Cardiac Surgery Patients

Nutritional status assessment scales are rarely used in cardiac surgery. Yet, they are critical component of intensive care and recommended by current international nutrition guidelines.

Studies evaluating the relevance of body mass index (BMI), albumin and prealbumin levels demonstrated that these are independent predictors of morbidity and mortality after coronary artery bypass graft (CABG) and valve surgeries [7,8]. In patients undergoing implantation of left ventricular assist devices, low pre-operative albumin levels –a non-specific biochemical marker of nutritional assessment– were associated with prolonged hospitalization and the development of acute kidney injury [9]. Furthermore, low prealbumin levels provide incremental information compared with BMI and albumin and were associated with prolonged duration of ventilation and increased incidence of postoperative infections [9,10]. However, the validity of serum albumin, prealbumin and BMI calculation using "dry" weight needs further validation as a way of identifying malnourished patients before surgery, as for example albumin has a turnover time of 20 days and its serum level is influenced by numerous factors. Yet, it is still recommended to be used as a component of the preoperative nutrition screening until a better marker is available.

In a recent study, Lomivorotov et al. demonstrated that the majority of well-established malnutrition screening tools (the Malnutrition Universal Screening Tool (MUST), the Nutrition Risk Screening 2002 (NRS-2002), the Short Nutrition Assessment Questionnaire (SNAQ), the Subjective Global Assessment (SGA) and the Nutrition Risk in the Critically Ill (NUTRIC) score) are insufficiently sensitive to the risk of developing postoperative complications [1]. The reasons for these findings are multifactorial and probably result from the different pathophysiology of postoperative cardiac surgery patients compared to other critically ill ICU patients.

As current findings indicate high malnourishment rates in cardiac patients [11,12], it is crucial to consider the patients' nutritional profiles preoperatively and to simultaneously devote further attention to the conception of individual diets for preoperative optimization in these patients [2]. Thus, the assessment of preoperative nutritional status may guide health care professionals to consider early nutrition interventions prior to surgery in patients at high risk of developing postoperative complications [13].

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3. Perioperative Nutrition in Cardiac Surgery Patients

3.1 Preoperative Nutritional Optimization in Cardiac Surgery Patients

Although the inflammatory response to cardiac surgery shares mechanisms with that observed in septic patients, the postsurgical inflammatory response is more predictable, mainly featuring the release of pro-inflammatory markers and reactive oxygen species. Therefore, the pre-operative period may represent an attractive time window in which to optimize nutritional status, correct deficiencies, and enhance immune defense mechanisms before surgery. This period is an especially effective time to act upon modifiable risk factors and potentially lower the risk of intra- and postoperative complications. The bulk of the literature on perioperative optimization in heart failure patients comes from anesthesiology and hence focuses on intra- and immediate postoperative management, when it may be too late to intervene and alter the outcome of a patient entering the operating room in a decompensated state [14]. Interestingly, guidelines on the cardiovascular evaluation and management of patients prior to non-cardiac surgery are available, but no comparable recommendations have been published concerning cardiac surgery [14,15], which is probably because the patients' outcome was thought to be mainly influenced by the surgical procedure itself.

In cardiac surgery patients with progressive heart failure, preoperative fasting further (i) aggravates commonly observed symptoms such as dyspnea, with a resulting increase in work of breathing, and (ii) it may worsen gut edema as well as (iii) hepatic congestion, which may further result in early satiety and nausea [16]. The chronic inflammatory state and the metabolic disturbances induced by chronic inflammation are shared by all disease-induced cachectic processes, including cancer, chronic obstructive pulmonary disease and advanced heart failure [17]. Clinically, this state is characterized by protein-calorie malnutrition, with systemic manifestations of lassitude, weakness, and poor wound healing, leading to frailty and significant comorbidities.

As it is generally accepted that preoperative medical and nutritional optimization is necessary and may provide beneficial effects if performed in patients scheduled for major surgery, multimodal approaches, such as enhanced recovery after surgery (ERAS) programs, may be useful in cardiac surgery patients to reduce surgical stress, maintain physiological functional capacity, and facilitate postoperative recovery by providing the best available evidence. However, while there several approaches available for other types of major surgery [18-20], evidence is lacking on how the principles of ERAS could be applied to cardiac surgery [21]. Further confirmation of the importance of a preoperative nutrition intervention is necessary. Besides, it must be acknowledged that a pre-operative nutrition risk assessment and timely intervention is hindered by logistical difficulties, as more than half of patients who undergo cardiac surgery are admitted as outpatients within 12 – 24 hours before surgery. Clinicians will need to overcome this problem and consider an interdisciplinary outpatient-approach to optimize the nutritional status prior to patient's admission in collaboration with surgeons, cardiologists and general practitioners. The potential areas of interest linked to therapeutic strategies to optimize nutrition practice are outlined in Figure 3.

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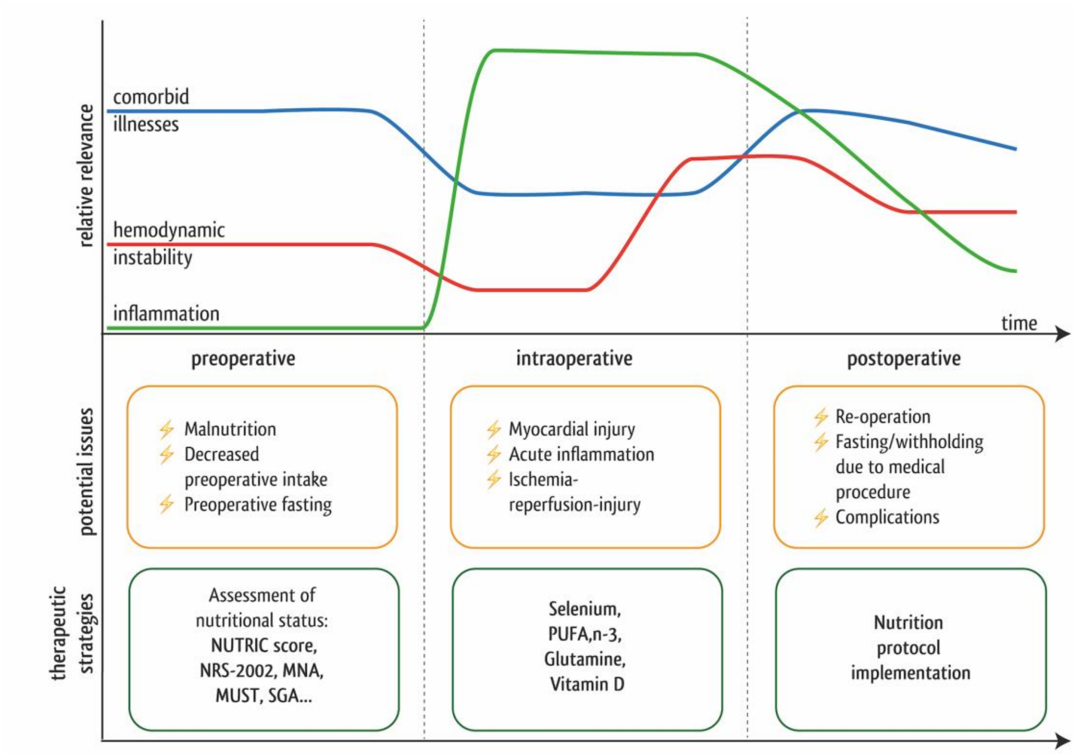

Figure 3. Possible areas of interest to optimize the nutritional status depending on the stages of hospitalization

3.2. Postoperative Nutrition Support in Cardiac Surgery Patients

While various large-scale randomized controlled studies evaluated different post-operative nutrition strategies in rather mixed cohorts of critically ill patients, only few small clinical studies specifically investigated its effects in cardiac surgery patients. In these studies, malnutrition has been reported to increase morbidity and mortality after cardiac surgery [22,23], as well as it may reduce the muscle mass of the left ventricle. Some cardiac surgery patients experience a complicated postoperative course, requiring pharmacological and/or mechanical cardiac support, as well as prolonged mechanical ventilation. These patients are frequently hypercatabolic, unable to feed themselves for more than 5 – 6 days and are in special need of intense nutrition support [24,25]. Besides, it was demonstrated that weight-loss in patients discharged after cardiac surgery was accompanied by a persistent inflammatory response resulting in decreased physical functioning [26]. However, most cardiac surgery patients stay briefly in the ICU and can resume oral feeding within 1 – 2 days after surgery, hence, they do not require an intense nutrition support.

Visser et al. studied the effect of perioperative nutrition in cardiac surgery on the myocardial inflammatory response, supplementing either no nutrition, EN or PN from 2 days before to 2 days after CABG. While both forms of nutrition contained comparable macro- and micronutrients, myocardial atrial tissue samples before and after revascularization demonstrated no significant differences in the myocardial inflammatory response [27].

The recent CoCoS trial evaluated the influence of nutrition therapy on possible alterations in caloric deficit, morbidity and mortality. No significant differences in patients, laboratory or mortality profile between the intervention group, which received intense nutrition support, and a retrospective control group were found. However, there were significantly less arrhythmias (7 % versus 31 %; p= 0.0056), and significantly less pneumoniae (7 % versus 22 %; p= 0.0183) in male intervention-group-patients receiving combined CABG and aortic valve surgery. In addition, survival was significantly higher in female patients receiving intense nutrition support than in the control group for both CABG (100 % versus 83 %; p= 0.0015) and aortic valve surgery (97 % versus 78 %; p = 0.0337) [28].

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The data derived from this trial support the hypothesis, that patients with either high nutrition risk or at elevated risk for prolonged ICU stay are the patient groups which will most likely benefit the most from a nutrition intervention and to determine the effect of prolonged EN on patients' clinical outcome. Despite well-established scoring systems for perioperative risk stratification, it is still challenging to identify patients at high nutrition risk early during their postoperative course, which may enable to start early an adequate nutrition support for these patients.

3.2.1. Enteral Nutrition

The role of postoperative nutrition support is to maintain nutritional status and energy requirements in the catabolic period after surgery. An interruption of nutritional intake is frequently observed after surgery, although it is evident that early oral and/or enteral food intake is possible, diminishes the risk of infectious complications and favors shorter hospital stays [29-31]. Therefore, early nutrition is encouraged by international nutrition societies to enhance recovery after surgery [18-20]. While the function of the gastrointestinal (GI) tract is the main determinant for initiation of EN after abdominal surgery, the key factor for initiation of nutrition in cardiac surgery patients may be hemodynamic stability, as the recently revised American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines recommend that EN should be withheld until the patient is hemodynamically stable [24].

Despite the lack of evidence, EN is commonly considered to be contraindicated as it may negatively affect gut integrity during a state of severe circulatory compromise in patients requiring high levels of vasopressor support, resulting in i) alteration of splanchnic perfusion and ii) an increased risk of GI complications, such as bowel ischemia. In addition, there are relevant practical hurdles such as the numerous interruptions of enteral feeding, pyloric dysfunction and intestinal atony, which are frequently seen in patients after major surgical procedures. In this context, there are several studies examining the GI response to enteral nutrition in the presence of compromised hemodynamics and evaluating intestinal intolerance in cardiac surgery patients (Table 2).

Table 2. Prospective observational cohort studies examining the gastrointestinal response to enteral nutrition in the presence of compromised hemodynamics by evaluating intestinal intolerance

Author, year	**№ of patients**	**Time to start of EN**	**Mean energy delivery**	**Vasopressor or inotropic drugs**	**Intestinal tolerance**
Berger 2005, [32]	70	<72 h	1360 ± 620 kcal/day	Median 5 days	• No serious GI complications • Prokinetics used in 12.9 %
Revelly 2001, [33]	9	12 – 16 h	1.1 ± 0.25 kcal/kg/h	dobutamine (mean 420 µg/min) and norepinephrine (6 – 30 µg/min)	Hemodynamic response • No change in catecholamine requirement • Significant increase of cardiac index • Transient decrease of mean arterial pressure Enteral and metabolic response • No gut distension or digestive ischemia • Increase in plasma glucose, decrease in fatty acids, increase in plasma lactate
Kesek 2002, [34]	62	<72 h	Depended individually as calculated by resting energy expenditure	n.a.[1]	• Vomiting: 20 % • Diarrhea: none 58 %; mild 18 %; moderate 21 %; severe 3 % • GRV[1]: none 47%, small 19 %; moderate: 11 %; large 23% • Aspiration pneumonia: 11 % • Prokinetics used in GRV > 400 ml
Flordelís Lasierra 2015, [35]	37	n.a.	1228.4 kcal/d	3 drugs: 38 % 4 drugs: 24 % 4 drugs + mechanical assistance in 16 %	• EN-related complications: 62 % • no serious GI complications • constipation 46 %, • 1 case ischemic colitis attributed to prior vascular disease

[1] GRV= Gastric residual volume, n.a.: not available

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In the prospective study of Berger et al., a mean energy delivery of 70 ± 35 % of the target could be achieved via EN, even though most patients were on vasoactive drugs for many days [32]. Dopamine and norepinephrine were significantly negatively correlated with enteral feeding, while there was a negative trend with dobutamine. No patient experienced any serious GI complications and EN was possible. Revelly [33] et al. studied nine patients requiring hemodynamic support in their hemodynamic and metabolic reaction to the initiation of EN. Physiological hemodynamic and metabolic reactions as well as no serious GI complications were observed.

In a comparable manner, Kesek et al. [34] started EN within 3 days in accordance to the patient's needs, which were calculated by the Harris–Benedict equation. The authors did not provide a detailed description or the duration and doses of vasoactive drugs. Diarrhea and gastric residual volumes were frequent, however the clinical relevance remains unclear [36]. Clinically significant GI complications were notably infrequent, and the authors concluded that early EN could be safely initiated in the cardiac surgery intensive care population.

A study by Flordelís Lasierra et al. including cardiac surgery patients with hemodynamic failure (dependence on 2 or more vasoactive drugs and/or mechanical circulatory support), EN was supplemented with a mean energy delivery 1228.4 kcal/d over a mean of 12.3 days. The mean energy target was achieved in 15 patients (40.4%). The most common EN-related complication was constipation, whereas no case of mesenteric ischemia was detected, further supporting the feasibility and safety of EN in these patients [35].

Despite the small number of patients included in these studies and the differences among their inclusion and application strategies, it is important to note that enteral nutrition has repeatedly been demonstrated to be feasible and that the circulatory and metabolic response to EN is adequate during the early postoperative course after operation in patients with acute severe circulatory failure. Furthermore, these studies indicated a potential beneficial effect of enteral nutrition due to its ability to maintain the splanchnic perfusion, which is of particular importance for cardiac surgery patients with an increased risk for postoperative mesenteric ischemia. However, all the mentioned studies also concluded that it was not possible to meet the nutritional requirements with EN alone and suggested the addition of supplemental parenteral nutrition (sPN), which need to be systematically investigated in future studies.

3.2.2. Parenteral Nutrition

As intestinal ischemia is a frequently fatal complication after cardiac surgery [37,38], the use of PN is often favored in cardiac surgery patients, especially within the first days after operation. However, there is no sufficient evidence available to evaluate the role of postoperative PN and its influence on clinically relevant outcome data, including survival, disease progression and morbidity in cardiac surgery patients. This lack of data may be due to the usually short duration of stays in the intensive care unit. Moreover, insufficient nutritional assessment prior to operation may prevent practitioners from starting parenteral nutrition in malnourished patients soon after surgery in accordance with actual guidelines.

PN may be used as sole nutrition or as sPN, as demonstrated almost 3 decades ago by Paccagnella et al in 1991 [39], who examined the hemodynamic, metabolic, and nutritional response to nutrition support of patients with severe cardiac cachexia before and after major cardiac surgery. Patients were allowed to eat ad libitum, and sPN was then provided in order to achieve a maintenance level of nutrition support. The results suggested that this approach is both safe and effective.

Existing guidelines recommend the initiation of PN in all critically ill patients within 3 – 7 days after admission if EN is contraindicated or cannot be tolerated in patients with low nutrition risk [37,38] and within 24 hours in patients with high nutrition risk. PN secures reaching energy and protein targets and avoids the potential complications of EN. Concerns regarding PN are the potential risk of overfeeding with hyperglycemia, elevated liver enzymes and increased rate of blood stream infections. Current evidence remains inconclusive, but there seems to be no difference regarding clinical outcome between EN and PN [40-42]. However, in the EPaNIC Trial of Casaer et al, a lower

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rate of infection was observed with a later achievement of caloric targets [43]. In any case, it is recommended to evaluate both provision as well as tolerance frequently and switch to the least invasive and most physiological route of administration of nutrition which is feasible for each individual patient.

Intravenous fish oil (FO)-based lipid emulsions (LEs) are of increasing interest as part of the parenteral nutrition support. FO is rich in ω-3 polyunsaturated fatty acids (ω-3-PUFAs), such as eicosapentanoic acid (EPA) and docosahexaenoic acid (DHA), which exhibit anti-inflammatory and immunomodulatory effects. Preliminary evidence received small phase II trials on FO-containing emulsions in cardiac surgery have demonstrated that preoperative FO infusion is a promising strategy to modulate the biological and clinical response to cardiac surgery with the use of CPB [44-47]. Various studies indicate that ω-3-PUFAs exert beneficial effects on the cardiovascular system that may ultimately reduce the risk of cardiac death and lower the incidence of perioperative atrial fibrillation (AF) in cardiac surgery, whereas current data on this topic are inconclusive, perhaps because of the different supplementation strategies and the dependence of the results on the type of surgical procedure [48]. Recently, Berger and colleagues demonstrated that three repetitive infusions of 0.2 g/kg FO emulsion, significantly increased PUFA concentrations in platelets and atrial tissue membranes within 12 hours of the first FO administration and reduced the inflammatory response [45].

Regarding the role of ω-3 PUFA supplementation in cardiac surgery patients, Christou et al. reviewed current trials in view of prevention of AF after cardiac surgery, but observed conflicting results [49], which probably occurred for 2 main reasons: (i) most studies applied n-3 PUFA treatment only postoperatively [48]. (ii) In the case of treatment before cardiac surgery, its duration was insufficient to result in adequate incorporation of n-3 PUFA in sarcolemmal myocardial membranes [47,48,50-53]. Moreover, DHA treatment appears to be more efficient than EPA treatment in reducing the incidence of postoperative AF [52,54,55]. However, a meta-analysis including all 6 placebo-controlled randomized controlled trials (RCT) [44,50,51,56,57] found a regression rate of 0.92 (95 % CI, 0.78 – 1.10) and could not detect a significant clinical relevant effect, as all included trials were limited by low statistical power, whereas other relevant postoperative complications have not been adequately evaluated. Furthermore, no data exists about its potential role in high-risk cardiac surgery patients, with complex surgical procedures, which are at increased risk for the development of postoperative complications. Given its outlined biological rationale and previously demonstrated beneficial effects in small clinical trials [44-47], following adequately designed studies focusing on functional outcomes are still needed to clarify the role of fish oil in these patients at high risk for the development of organ dysfunction.

4. Micronutrients in Cardiac Surgery Patients

4.1. Inflammation in Cardiac Surgery

Patients undergoing cardiac surgery experience a complex systemic inflammatory response syndrome, which manifests as pyrexia, tachycardia, leukocytosis, hypotension, edema, and organ failure. Several stimuli lead to systemic inflammation reactions during and after cardiac surgery. The surgical trauma induces the activation of neutrophils, endothelial cells and platelets and the release of mediators of the inflammatory response, such as tumor necrosis factor α (TNFα) and diverse interleukins (IL). The foreign surface contact during CPB leads to the activation of cellular components such as leukocytes and platelets and activates further humoral mediators, such as complement system, as well as kallikrein cascades, inducing a release of inflammatory mediators such as TNFα, IL-1, IL-6 and IL-8. After an ischemic period during the cross-clamping of the aorta, the reoxygenation of the tissues further triggers the inflammatory response. This I/R-injury can also be divided into leukocyte-dependent-mechanisms – through the interaction of neutrophils and endothelial cells – and non-leukocyte-dependent pathways, such as the release of reactive oxygen species, arachidonic-acid metabolites and cytokines, as well as increased nuclear factor kappa-light-chain enhancer of activated B cells (NFκB) activity. Hemodilution through large extracorporeal circuits and blood loss during surgery often create a need for blood transfusions, which may further trigger inflammatory reactions. Notably, the so called enteral hypoperfusion during cardiac surgery increases the permeability of the gut mucosae and the transferal of intestinal bacteria into the bloodstream. Bacterial lipopolysaccharides from gram-negative bacteria may further induce TNFα and IL-6 production, complement activation, and the release of cytokines and nitric oxide, which further increase the extent of organ dysfunctions (Figure 4, for comprehensive review please see: [58]). In particular, high-risk cardiac patients with extended surgical procedures and duration of CPB are exposed to a significantly higher inflammatory response with deleterious effects. For this reason, various clinical trials have attempted to reduce the perioperative inflammatory response by administration of different immune-modulatory agents, which are outlined in the following sections.

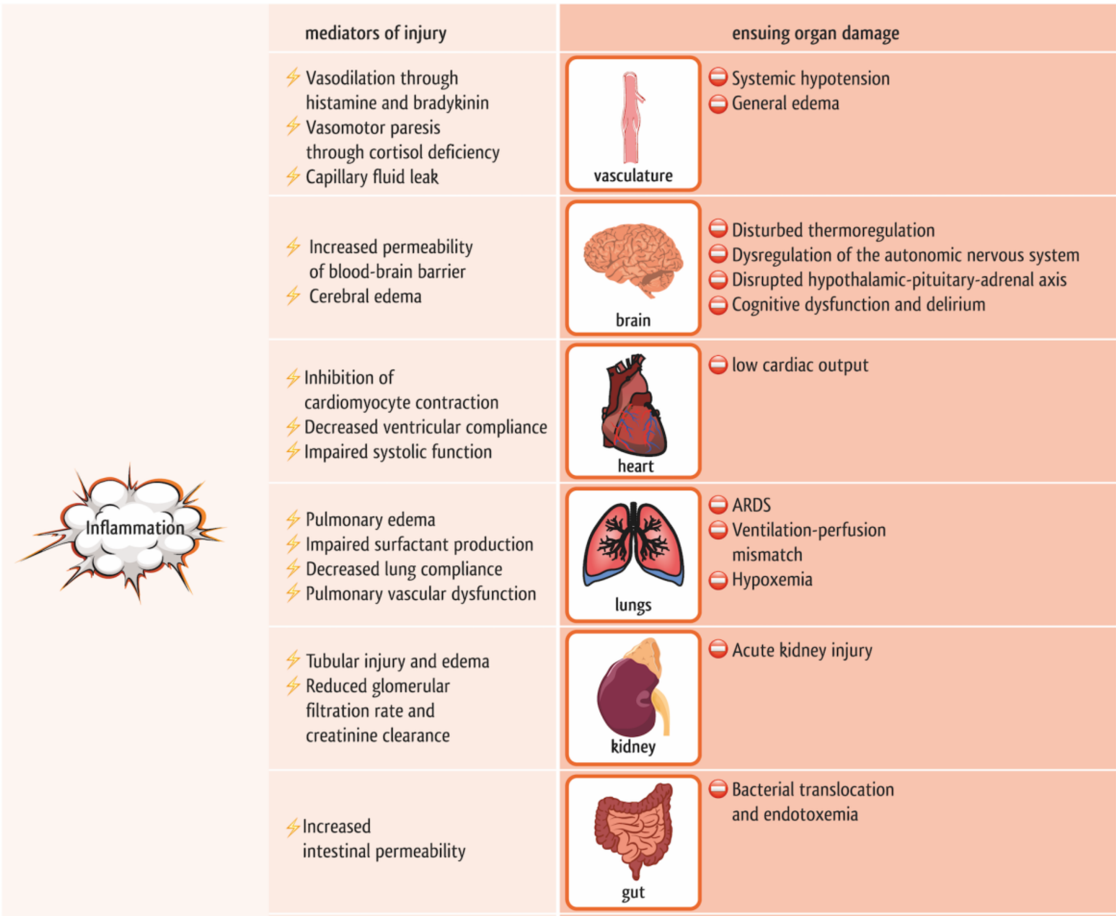

Figure 4. Effects of inflammation on different organs

4.2. Glutamine

One immune-active substance, the non-essential amino acid glutamine, is the most abundant amino acid in the human body and showed cardioprotective effects in several clinical trials. The perioperative administration of both parenteral (N(2)-L-alanyl-L-glutamine) [59] and enteral [60] forms of glutamine leads to reduced myocardial injury as assessed by reduced postoperative troponin I concentration among cardiac surgery patients.

However, in view of the insufficient evidence, recent guidelines state that routine supplementation with glutamine cannot be recommended due to the unproved clinical benefits in cardiac surgery patients and even a risk of harm, which has been demonstrated in critically ill patients [61].

4.3. Selenium

Selenium is a trace element that is important for many of the body's regulatory and metabolic functions, especially during times of stress [62,63]. In an observational study, the majority of patients undergoing cardiac surgery exhibited a significant selenium deficiency prior to CPB, which was further aggravated with increasing CPB time, leading to an insufficient capacity to withstand the stress of surgery [63]. In a subsequent non-randomized interventional trial, a high-dose selenium supplementation was effective in preventing this decrease of intraoperative circulating selenium levels and clinical outcomes were superior in this supplemented group compared with a historical control group [64]. Recently, a randomized controlled study demonstrated the safety and feasibility of high-dose selenium supplementation (4000µg) in cardiac surgery patients, whereas no significant clinical effects could be detected [65]. In view of these data, a large-scale multicenter trial is currently being performed to evaluate the clinical significance of high-dose (2000µg) perioperative sodium selenite supplementation in patients at high risk after cardiac surgery [66].

4.4. Vitamins

Few data are available regarding vitamin supplementation in cardiac surgery patients. Among the vitamins, thiamine and vitamins D and C are the most promising candidates and have been studied in several trials. Thiamine, the essential co-factor for pyruvate dehydrogenase function, is responsible for adequate aerobic metabolism. Preliminary studies demonstrated that thiamine levels are decreased after cardiac surgery and that low serum levels are inversely associated with blood lactate level [67,68], which, in turn, predicts postoperative mortality and morbidity [69,70]. However, recently published RCTs did not support the hypothesis that thiamine administration during cardiac surgery decreases postoperative blood lactate levels and improves clinical outcomes [71,72].

Vitamin D is known to affect the bones, the muscles, the blood vessels, cell proliferation and differentiation, autoimmune processes and the immune system in parallel with the regulation of calcium homeostasis [73]. Therefore, vitamin D deficiency leads to skeletal and non-skeletal diseases and is associated with various respiratory, immune, infectious, neurological and cardiovascular diseases. It is involved in numerous physiological mechanisms desirable for cardiac surgery patients, such as regulation of arterial stiffness and endothelial function [73]. However, in one retrospective study, low vitamin D concentrations before surgery were not associated with increased mortality and morbidity, while the significance of intraoperative changes and potential differences between the biological active (1,25OH) and inactive form (25OH) remained unknown [74].

Vitamin C shows pleiotropic functions in the human biology and reduced oxidative damage and resulting organ injury in critically ill patients with sepsis or septic shock [75]. In cardiac surgery patients, preliminary studies indicate a beneficial effect of Vitamin C supplementation on the occurrence of postoperative outcome [76]. Besides, a recent meta-analysis of small preliminary studies demonstrated that administration of vitamin C is effective as prophylaxis for prevention of postoperative AF [77]. Adequately designed studies are now encouraged to comprehensively investigate the effect of an appropriate Vitamin C supplementing strategy on the patients` inflammatory response and to evaluate its clinical effects on patients` mid- to long-term outcomes.

5. Conclusion

Despite substantial procedural advances, open-heart surgery continues to be associated with disconcerting complication rates, often necessitating a prolonged ICU stay until the organ functions recover, especially in high-risk cardiac surgery patients with significant comorbidities and complex cardiac surgical procedures. While the majority of patients generally stay briefly in the ICU and are able to recover within the first few days after surgery, intense nutrition support and early initiation of enteral nutrition seems of paramount importance, especially in high-risk cardiac surgery with prolonged ICU stays to allow for recovery, in order to reduce surgical stress, maintain physiological functional capacity, and facilitate postoperative functional recovery. Yet, adequate strategies are still needed for an early identification of these cardiac surgery patients with prolonged ICU stay. In

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addition, more research is warranted, to evaluate the effect of an intense nutrition support on functional outcomes in this cohort of critically ill patients. Considering the patients` perioperative inflammatory response, adequately designed studies are supported by smaller pilot studies and currently under way to evaluate the clinical significance of different anti-inflammatory strategies.

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List of Abbreviations

AF	Atrial Fibrillation
ASPEN	American Society for Parenteral and Enteral Nutrition
BMI	Body Mass Index
CABG	Coronary Artery Bypass Graft
CPB	Cardiopulmonary Bypass
DHA	Docosahexaenoic Acid
EN	Enteral Nutrition
EPA	Eicosapentanoic Acid
ERAS	Enhanced Recovery After Surgery
FO	Fish Oil
GI	Gastrointestinal
GRV	Gastric Residual Volume
ICU	Intensive Care Unit
IL	Interleukin
I/R	Ischemia/ Reperfusion
LE	Lipid Emulsions
LOS	Length of Stay
MUST	Malnutrition Universal Screening Tool
n.a.	not available
NFκB	nuclear factor kappa-light-chain enhancer of activated B cells
NRS 2002	Nutrition Risk Screening 2002
NUTRIC	Nutrition Risk in the Critically Ill
PN	Parenteral Nutrition
PUFA	Polyunsaturated Fatty Acids
RCT	Randomized Controlled Trial
SGA	Subjective Global Assessment
SNAQ	Short Nutrition Assessment Questionnaire
sPN	Supplemental Parenteral Nutrition
TNFα	Tumor Necrosis Factor α

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