

# Nutritional Considerations of Cardiovascular Diseases and Treatments

---

**Boban, Marko; Bulj, Nikola; Kolačević Zeljković, Matea; Radeljić, Vjekoslav; Krčmar, Tomislav; Trbušić, Matias; Delić-Brkljačić, Diana; Alebić, Tamara; Včev, Aleksandar**

*Source / Izvornik:* **Nutrition and Metabolic Insights, 2019, 12, 1 - 9**

**Journal article, Published version**

**Rad u časopisu, Objavljena verzija rada (izdavačev PDF)**

<https://doi.org/10.1177/1178638819833705>

*Permanent link / Trajna poveznica:* <https://urn.nsk.hr/urn:nbn:hr:239:930712>

*Rights / Prava:* [Attribution-NonCommercial 4.0 International/Imenovanje-Nekomercijalno 4.0 međunarodna](#)

*Download date / Datum preuzimanja:* **2024-11-22**



*Repository / Repozitorij:*

[Repository UHC Osijek - Repository University Hospital Centre Osijek](#)

# Nutritional Considerations of Cardiovascular Diseases and Treatments

Marko Boban<sup>1,2,3,4</sup>, Nikola Bulj<sup>1,5</sup>, Matea Kolačević Zeljković<sup>6</sup>, Vjekoslav Radeljić<sup>1</sup>, Tomislav Krčmar<sup>1</sup>, Matias Trbusić<sup>1</sup>, Diana Delić-Brkljačić<sup>1,5</sup>, Tamara Alebić<sup>3</sup> and Aleksandar Vcev<sup>3,4</sup>

<sup>1</sup>Department of Cardiology, University Hospital Centre "Sestre Milosrdnice," Zagreb, Croatia.

<sup>2</sup>Department of Rehabilitation and Sports Medicine, Faculty of Medicine, University of Rijeka, Rijeka, Croatia. <sup>3</sup>Department of Internal Medicine, Medical Faculty, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia. <sup>4</sup>Department of Internal Medicine and Physiology, Faculty of

Dental Medicine and Health, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia.

<sup>5</sup>Department of Internal Medicine, School of Medicine, University of Zagreb, Zagreb, Croatia.

<sup>6</sup>Department of Internal Medicine, University Hospital Centre "Sestre Milosrdnice," Zagreb, Croatia.

Nutrition and Metabolic Insights

Volume 12: 1–9

© The Author(s) 2019

Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/1178638819833705



**ABSTRACT:** Nutritional considerations of many chronic diseases are not fully understood or taken into consideration in everyday clinical practice. Therefore, it is not surprising that high proportion of hospitalized patients with cardiovascular diseases remains underdiagnosed with malnutrition. Malnourished patients have increased risk of poor clinical outcomes, complications rate, prolonged hospital stay, more frequent rehospitalizations, and lower quality of life. The purpose of this review is to recapitulate recent data on nutritional considerations in cardiovascular medicine.

**KEYWORDS:** nutritional risk, cachexia, unintentional loss of weight, ischemic heart disease, cardiomyopathy

**RECEIVED:** January 19, 2019. **ACCEPTED:** January 28, 2019.

**TYPE:** NMI-20 Nutrition, Metabolism, & Exercise—Expert Review

**FUNDING:** The author(s) received no financial support for the research, authorship, and/or publication of this article.

**DECLARATION OF CONFLICTING INTERESTS:** The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**CORRESPONDING AUTHOR:** Marko Boban, Department of Cardiology, University Hospital Centre "Sestre Milosrdnice," Vinogradska 29, 10000 Zagreb, Croatia. Email: marcoboban@yahoo.com

## Nutritional Risk

Increased nutritional risk is frequently found among hospitalized or institutionalized patients.<sup>1,2</sup> Prevalence of increased nutritional risk varies from 20% to 30% in large case registries, to significantly higher proportions, in dependence of type of studied population. Malnutrition was found to be connected with prolonged hospital stay, increased rate of hospitalizations, readmissions, increased prevalence of treatment-related complications, increased prevalence of hospital infections, and mortality.<sup>3–5</sup> Disease-related malnutrition increases significantly the costs of treatment.<sup>6</sup>

Main pathophysiologic issues of increased nutritional risk include changes in appetite and dietary intake, development of catabolism, manifested through loss of proteins, immunoglobulins, muscle tissue, adipose tissue, and eventually leads even to bone loss. Due to these complex reasons, functional changes develop, which are seen as changes in muscle strength and impairment of physical performance, where the latter is significantly different between the genders, in addition to age-based effects.<sup>7–9</sup>

Disease-related unintentional loss of weight or one occurring during the course of treatment is the most important parameter of health-related malnutrition. Beside the absolute extent of the unintentional loss of weight of at least 5%, the timeline of wasting process within 6 to 12 months is of pivotal importance.<sup>10</sup> Cachexia represents clinical condition with significant weight loss defined primarily by reduction in skeletal muscle mass to an amount that is 2 standard deviations below

gender-specific normal values for young adults. Unlike cachexia, sarcopenia represents loss of muscle tissue but does not require the presence of weight loss. Whereas most people with cachexia are sarcopenic, most sarcopenic individuals are not considered cachectic. Muscle loss without the loss or fat gaining is known as sarcopenic obesity.<sup>11,12</sup>

Sarcopenia is commonly prevalent in elderly population and is associated with increased mortality.<sup>13,14</sup> A recent retrospective study of elderly patients showed that the prevalence of sarcopenia in the general population ranged from 12.6% (Poland) to 17.5% (India) and that of sarcopenic obesity ranged from 1.3% (India) to 11.0% (Spain).<sup>15</sup> Recent studies also showed that sarcopenia increases the risk for cardiovascular diseases in non-obese men<sup>16</sup> and is also independently associated with insulin resistance, increased risk of nonalcoholic fatty liver disease, and hypertension and arterial stiffness.<sup>17–20</sup> Co-existing sarcopenia and obesity (sarcopenic obesity) further increase the risk of morbidity and mortality, especially in male subjects in whom sarcopenic obesity is associated with a 24% increased risk of all-cause mortality.<sup>21</sup>

## Clinical Assessment of Nutritional Risk

In general, clinical assessment of nutritional risk is a complex task, with no highly specific test available. The most convenient tool for identifying nutritional risk is using complex screening tools, made up from several sets of clinical data, which commonly include the extent and timeline of unintentional loss of



weight, age of patient, and disease severity and/or invasiveness of treatment.

Working group of European Society for enteral and parenteral nutrition (ESPEN) developed the Nutritional Risk Screening tool in 2002 (NRS-2002) for detection of malnutrition in health care settings.<sup>22</sup> This screening tool was tested in multicenter randomized settings and was shown to be of high sensitivity and specificity for detection of malnutrition. Furthermore, it was shown to be reproducible for frequent repeated re-testing and closely connected with clinical endpoints such as rate of readmissions, duration of hospitalization, complications rate, treatment costs, and mortality.<sup>23</sup> The NRS-2002 is one of the most widely used tools for screening of malnutrition in hospitalized or institutionalized patients.<sup>23,24</sup> NRS-2002 is made up from summation of up to 3 points for disease severity, up to 3 points for degree of unintentional loss of weight, and 1 point in case patient is more than 70 years of age.<sup>24</sup> NRS-2002 being equal or greater than 3 points is regarded as increased nutritional risk.

One must also mention that there are numerous other screening tools existing, which as well could be used in clinical settings like the Malnutrition Universal Screening Tool (MUST),<sup>25,26</sup> Nutrition Risk Index (NRI),<sup>27</sup> nutrition risk score,<sup>27</sup> subjective global assessment (SGA),<sup>28</sup> and mini nutritional assessment.<sup>29</sup>

Various anthropometric methods are easy available, widely used, and could be considered as the cornerstone for assessment of nutritional status.<sup>30</sup> Conventional measurements in terms of body mass index (BMI) or waist-to-hip ratio were identified as important parameters for detection of malnutrition and on the other side being closely connected with clinically relevant endpoints in numerous studies.<sup>31-33</sup> Bioelectrical impedance analyses were shown to be solidly connected with nutritional status, however, of controversial connects with composited prognostic endpoints.<sup>34</sup> Assessment of body composition is made using skinfold caliper, a convenient tool with solid accuracy.<sup>35,36</sup> The dual-energy X-ray absorptiometry (DEXA) scan as well as other imaging modalities like ultrasound, computerized tomography, or magnetic resonance have the utility of highly precise estimation of lean body mass, adipose tissue share, and offer other relevant information on body composition.<sup>37-39</sup> Muscle function tests like hand grip offer valuable information on nutritional status and mortality.<sup>40,41</sup> There is still no availability of highly specific laboratory test for detection of malnutrition, particularly in terms of connection with clinically relevant prognostic outcomes. Nevertheless, several tests can point toward malnutrition like B<sub>12</sub> and D-vitamin status.<sup>42,43</sup> Albumin is a parameter that is frequently discussed in connection with nutritional status. It is however closely related to worse prognostic outcomes in numerous health conditions; the long half-life (20 days) of plasma is not very sensitive for the detection of malnutrition or fine-tuned day-to-day changes in nutritional status.<sup>44</sup> The calorimetric assessment of nutritional status is

complex and difficult to perform in large case series of patients; due to variable accuracy regarding numerous external factors and complicated diagnostic machinery, it is not widely available as a clinical tool for the detection of malnutrition.<sup>45,46</sup>

The assessment of nutritional status, and taking notion of metabolic disturbances that occurred due to severe illness or major invasive treatment, is commonly overlooked in routine clinical practice, in contrast to both guidelines of the American and European society for enteral and parenteral nutrition which based on clinical evidence unanimously agreed on absolute necessity to detect malnutrition in any medical contact point.<sup>24,47,48</sup>

### Nutritional Risk and Cardiovascular Risk Factors and Comorbidities

Cardiovascular diseases (CVDs) are among the most important public health burden worldwide.<sup>49</sup> They are the very common chronic comorbidities, and ischemic heart disease being the first cause of death in most of the developed nations, as well as in great part of developing world.<sup>50</sup> There are numerous chronic risk factors that are related to development or more severe course of the CVDs and nutritional risk as well.<sup>40,51</sup> Most of the disease scoring systems in cardiology include those factors as well. In particular, the most commonly used risk scoring systems like congestive heart failure, hypertension, age, diabetes mellitus, stroke or transitory ischemic attack, vascular disease; sex categorie (CHADS-VASCII), thrombolysis in acute myocardial infarction (TIMI) score, Syntax II score, surgical Euroscore II, and 10-year Systemic Coronary Risk Estimation (SCORE) include age of patient, prevalence of hypertension, dyslipidemia, chronic renal disease or diabetes mellitus, and chronic obstructive pulmonary disease, which are at the same time disease severity cofounders for NRS-2002.<sup>51,52</sup> Severe acutization of cardiac condition on a perplexed ground of several chronic risk factors can indeed become life-threatening situation, with development of catabolism and significant increase to the nutritional risk as well. In addition, disease severity parameter could also be significantly enhanced by highly invasive treatment as cardiac surgery or critically ill patients on cardiac intensive care units (ICUs) who have cardiac or multiple organ failure, systemic infections, using mechanic ventilation, extracorporeal membrane oxygenation, mechanic circularity support, dialysis, or others.<sup>53,54</sup> On the other hand, in most of the disease entities from the *cardiovascular disease continuum* observed better survival of obese patients when compared with their peers of normal weight in terms of the obesity paradox, which could be, in part, explained through the confounding effects of lesser nutritional risk in the obese patients.<sup>55</sup>

### Nutritional Risk and Pharmacotherapy

Medications have the potential to affect nutritional status in many different ways. A large number of drugs are potentially associated with negative effect on nutrition status through

alterations in taste, intestinal absorption, metabolism, etc. Recent review on nutrition places polypharmacy as one of the crucial determinants of disease-related malnutrition (DRM).<sup>56</sup> Drug interactions with food can be of mechanical origin due to altered absorption, gastrointestinal transport, and metabolism, or due to systemic distribution, liver metabolism, and (liver or renal) excretion.<sup>57</sup> Moreover, several populations have greater risk of drug-nutrient interactions: undernourished, those with severe chronic multimorbidity, children, and pregnant women.<sup>57,58</sup> The causes of most clinically significant drug-nutrient interactions are usually multifactorial; therefore, failure to identify and properly manage these interactions can lead to very serious adverse events with negative impact on clinical outcomes.<sup>58</sup>

Cardiovascular patients often require prescription of several medications to slow down disease progression and to control different symptoms. Despite the fact that the use of multiple drugs can be very important in the treatment, it can increase the risk of potential “drug-drug” and/or “drug-nutrient” interactions.<sup>57,59</sup> Even therapy with single drug can be associated with nutrition issues and adverse reactions.<sup>60</sup>

It is well known that diuretics can cause electrolyte imbalance, and in the context of CVDs, the greatest concern are hypokalemia and hypomagnesemia associated with increased frequency of malignant arrhythmias and sudden cardiac death.<sup>61,62</sup> Furthermore, thiazides are frequently associated with severe hyponatremia, especially in older patients.<sup>63-65</sup> Angiotensin-converting enzyme (ACE) inhibitors usually raise concern because of the potential to cause hyperkalemia, but according to studies, it is safe to use new-generation ACE inhibitors in patients with normal renal function without worrying about potential hyperkalemia.<sup>66,67</sup> Hyperkalemia can also be caused by aldosterone antagonists, beta-blockers, and potassium supplements which are the mainstay in heart disease treatment, especially optimal medical therapy for heart failure (HF).<sup>68</sup> When talking about nutritional risk, the protective role of ACE inhibitors now becomes a well-known fact. The mechanism of ACE inhibitors action on the prevention of cardiac cachexia is not fully clarified, but it could be related to modification of the neurohormonal axis and decrease in circulating catecholamines and inflammatory cytokines such as tumor necrosis factor (TNF)- $\alpha$  and interleukin 6.<sup>69-72</sup> Similar beneficial effects have been shown with beta-blockers.<sup>73-75</sup> Maximal tolerated dosages of ACE inhibitors or beta-blockers in patients with HF are first-line strategy for preventing sarcopenia and malnutrition; however, it is difficult to recommend other pharmacological agents as part of routine treatment.<sup>75</sup>

On the other hand, according to review articles, few antihypertensive agents, including angiotensin receptor blockers (ARB), ACE inhibitors, and potassium-sparing as well as thiazide diuretics, have been associated with lower levels of zinc, which can lead to dysgeusia and anorexia and also worsen wound healing.<sup>56</sup> Despite the fact that proton pump inhibitors

(PPIs) are not drugs for the treatment of CVD, they are often prescribed in these patients, especially in elderly and are significantly associated with parameters of NRS.<sup>76</sup> According to some studies, 25% to 86% of elderly patients have been overprescribed with PPIs, mostly because of the antiaggregation therapy commonly used by cardiovascular patients.<sup>76-78</sup> In addition, in cardiovascular patients, PPIs seem to be negatively connected with nutritional risk, mostly due to increase in gastric malabsorption and anemia.<sup>76</sup> While, as mentioned above, ACE inhibitors may have protective role on nutritional risk, PPIs and loop diuretics might be associated with increased nutritional risk and unintentional weight loss.<sup>79</sup>

### Nutritional Risk and Cardiac Surgery

Malnutrition is prevalent in cardiac surgery. Malnutrition risk factors comprise 3 different clinical groups: psychosocial and lifestyle factors, laboratory findings, and disease-related factors. Patients who are most likely to be malnourished are those who have decreased mobility and food intake with valve pathology, severe systolic dysfunction, chronic renal dysfunction, and high inflammatory markers.<sup>80,81</sup>

Disease-related malnutrition is a serious problem for patients undergoing cardiac surgery because it not only results in higher risk of postoperative infections and other complications but also prolongs hospital stay and consequently higher mortality rates.<sup>82-84</sup> Due to these undesirable outcomes, early recognition of patients with suboptimal nutritional status in perioperative time is of pivotal importance to assure optimal nutritional assessment and interventions.<sup>85,86</sup>

Despite the existence of numerous tools for assessing nutritional risk, such as Nutritional Risk Screening tool in 2002 (NRS 2002), MUST, NRI, and others mentioned earlier, there was a need for a more specific tool for assessing nutritive risk before cardiac surgery. For that purpose, tools like Cardiac Surgery-Specific Malnutrition Universal Screening Tool (CSSM) and Cardiac Surgery-Specific Undernutrition Screening Tool (CSSUST) were created.<sup>87,88</sup> CSSUST proved to be superior to other tools in identifying poor nutritional status in patients undergoing cardiac surgery and is clinically widely accepted.<sup>88</sup> Cardiac surgery patients with a prolonged ICU stay (>5 days) may benefit most from early nutrition support.<sup>81,89,90</sup> Stoppe et al<sup>90</sup> proved in a prospective trial that combined use of different clinical scores including nutrition risk screening tool (NRS 2002) helps in prediction of prolonged ICU stay in these patients which could help to identify those who will benefit the most of early postoperative nutrition therapy.

Several studies implied that high dietary intakes of saturated fatty acids and cholesterol in candidates for coronary artery bypass graft (CABG) surgery were related to low serum albumin and high HbA1C concentration which is associated with worsening of chronic kidney disease, prolonged wound healing, and consequently higher short- and long-term mortality.<sup>91,92</sup>



Obesity is widely accepted to complicate anesthesia and surgery, being a risk factor for mediastinitis after CABG.<sup>93,94</sup> Patients with morbid grade obesity undergoing CABG and underweight patients slightly more than morbidly obese suffer increased crude mortality.<sup>94,95</sup> Despite many patients undergoing cardiac surgery being overweight and obese, significant proportion display clinical signs of malnutrition.<sup>96</sup> This implies the need for regular assessment of nutritional status and appetite which should be conducted regularly as well as interventions to improve nutritional status should be started preoperatively and be more aggressive.<sup>94-96</sup>

In the CoCoS trial, the investigators aimed to assess whether nutrition therapy could alter caloric deficit, morbidity, and mortality in patients scheduled for non-emergency CABG or aortic valve surgery. Results suggested that nutrition therapy deserves to be implemented as a standard-of-care supportive therapy in these patients.<sup>97</sup>

### NRS in Ischemic Heart Disease

Traditional risk factors for endothelial dysfunction (age, gender, total cholesterol, high-density lipoprotein cholesterol, arterial hypertension, and smoking) are included in scores for evaluation of the 10-year cardiovascular risk in everyday clinical practice (eg, Framingham score and SCORE). Nonetheless, pro-inflammatory mediators are deeply involved in the initiation and the progression of coronary artery disease (CAD) and can act independently of metabolic risk factors.<sup>98</sup>

Back in the late 1980s, 2 prospective trials were performed in male population with prophylactic aims including nutritional interventions in a group of high CVD risk: lowering of the total caloric intake, consumption of food cholesterol and refined sugar, as well as rise of animal protein, poly-unsaturated fatty acid (PUFA) and monounsaturated fatty acid (MUFA), and complex carbohydrates consumption. After 3 years of follow-up, these interventions resulted in reduction of risk factors for coronary disease, mostly on the drop of blood plasma cholesterol and the decrease of arterial pressure provided by weight reduction.<sup>99,100</sup> On the other hand, increased consumption of refined carbohydrates and alcohol consumption enhanced the impact of common risk factors (eg, overweight, arterial hypertension, and dyslipidemia) on CVD development.<sup>100</sup> Several trials proved that patients with CVD tend to delay lifestyle modification until symptoms occur.<sup>101</sup> Despite the knowledge of hyperlipidemia and obesity as significant risk factors in coronary heart disease (CHD), attention to healthy nutrition significantly decreases over time in patients who have undergone CABG.<sup>102</sup> Thus, patients who have undergone CABG, especially male patients >50 years old would benefit from supplementary nutrition counseling education.<sup>102</sup> Moreover, counseling based on different models seems to be effective in improving nutritional knowledge and most importantly nutritional behavior, which could improve long-term outcomes in cardiac surgery patients through controlling cardiovascular risk

factors: for example, reducing blood pressure through low salt diet and lowering blood cholesterol through Mediterranean diet.<sup>103-105</sup>

In addition, nutrition is a modifiable risk factor for systemic inflammation which ensues CHD, and its optimization may reduce post-cardiac surgery mortality, atrial fibrillation, and cognitive decline.<sup>106</sup> Dutch group showed that share of patients with CHD undergoing surgery with dietary intakes below recommendations were 62% for fruits, 87% for vegetables, 73% for dietary fiber, 98% for vitamin D, as well as patients with dietary intakes above recommendations were 95% for saturated fat. Unbalanced pre-operative diets put them at risk of unfavorable surgical outcomes, because they promote a pro-inflammatory state.<sup>106</sup> Undesirable changes in nutrition happens after CABG surgery with increase in fat consumption which occurred despite the provision of dietary advice and highlights the need to understand better the barriers to nutritional advices and education.<sup>106,107</sup>

There have been a number of studies proving the prognostic effects of poor nutritional status and cardiac cachexia on CAD. However, no nutritional index has been firmly established yet in patients with CAD.<sup>108,109</sup> The Prognostic Nutritional Index (PNI) is a well-accepted nutritional status parameter in patients with cancer and those undergoing gastrointestinal surgery, and lower PNI was associated with worse long-term cardiovascular outcomes in patients with stable CAD.<sup>109</sup> Also, previous studies have reported the prognostic value of objective nutritional indices such as the Controlling Nutritional Status (CONUT) score, Geriatric Nutritional Risk Index (GNRI), and PNI.<sup>109,110</sup> The Combined Objective Nutritional Score comprised high CONUT score, low GNRI, and low PNI, and patients with a Combined Objective Nutritional Score of 3 showed 3-fold increases in risk of mortality and 2-fold increase in cardiac mortality compared with patients with score of 0.<sup>110</sup> Doi et al<sup>108</sup> introduced TCBI (Triglycerides [TG] × Total Cholesterol (TC) × Body Weight (BW) Index) in clinical usage in patients with CAD who underwent percutaneous coronary intervention (PCI), as a novel and easy to calculate nutrition index which proved to be useful prognostic indicator. Another score, Controlling Nutritional Status (CONUT; range 0-12, higher = worse, consisting of serum albumin, cholesterol, and lymphocytes), is commonly used in patients with CAD. Patients with high CONUT scores had higher rates of major adverse cardiovascular events (MACE) and pre-PCI assessment of the CONUT score may provide useful prognostic information.<sup>111</sup> Moreover, the combination of CONUT score and BMI was an even more useful predictor of MACE in CAD population: high CONUT score + normal BMI showed a 2.72-fold increase in the incidence of MACE compared with low CONUT score + normal BMI.<sup>112</sup> Geriatric nutritional risk index <92 is associated with 7-fold and 3-fold increase in the incidences of cardiac death or non-fatal myocardial infarction compared with GNRI >98.<sup>113</sup>

Beside general malnutrition, deficit of some specific nutrients and some specific malnourishment can influence different CAD risk factors producing CAD advancement and MACE, for example, folic acid and vitamin B<sub>12</sub> deficiency causes hyperhomocysteinemia leading to acute myocardial infarction.<sup>114</sup> In addition, You et al<sup>115</sup> proved that pre-procedural prealbumin levels  $\leq 185.5$  mg/L were significantly associated with contrast-induced acute kidney injury in geriatric patients undergoing elective PCI and consequently with increase in long-term mortality.

On the contrary, despite strong association between body weight and mortality in the general population, clinical evidence suggests better outcome of overweight or obese patients with established CAD. This inverse association between obesity and CVD prognosis has been termed “obesity paradox,” but its existence remains a point of debate because it is mostly observed when BMI is used to define obesity.<sup>116,117</sup>

According to ESPEN guidelines on definitions and terminology of clinical nutrition, chronic DRM is commonly described in patients with chronic HF defining it as non-intentional and non-edematous weight loss  $>7.5\%$  of the pre-morbid normal weight.<sup>1</sup> Patients with terminal HF are the most complex population with multiple comorbidities and multiple organ dysfunction affecting appetite, intestinal absorption, aerobic metabolism, immunocompetency, neuro-hormonal axis, as well as protein and enzyme production at cell level.<sup>69,72,118</sup> Whether alone or in combination, micronutrient supplementation improves outcomes of patients with HF by ameliorating symptoms, work capacity, and left ventricular ejection fraction, thus increasing the quality of life.<sup>119</sup> As expected, malnourished patients with HF who received heart transplantation had a significantly higher incidence of post-transplantation complications (infection, late weaning from mechanical ventilation, stroke) as well as longer postoperative intensive care stay and higher mortality.<sup>120</sup> Similar results have been proven in patients who are candidates for continuous flow left ventricular assist device (LVAD) therapy.<sup>121</sup> Hospitalized patients with advanced HF are at high risk of malnutrition and death, and the Nutritional Risk Index (NRI) is a simple, well-validated tool for identifying patients at risk of nutrition-related complications.<sup>122</sup> Advanced HF is frequently associated with severe muscle wasting, termed as cardiac cachexia, which significantly decreases the quality of life and survival in this population.<sup>123,124</sup>

### Nutritional Risk in Heart Failure and Cardiac Cachexia

Chronic HF has prevalence of 1% in general population.<sup>125</sup> Due to its symptoms, it has profound effects on the quality of life; it is common reason for hospitalizations and greater overall mortality than numerous cancers like breast or colon cancer.<sup>125</sup> Patients with impairment of systolic function were shown to have higher prevalence of increased nutritional risk

than controls, although patients with HF and preserved systolic function eventually develop tissue wasting as well.<sup>126</sup> Complex perplexed mechanisms of neurohumoral, inflammatory processes with lower perfusion of multiple organs drive the chronic state of catabolism that ends up with cardiac cachexia.<sup>127</sup> Patients with HF who develop tissue wasting and cardiac cachexia have much higher mortality rate than their peers without cachexia.<sup>128,129</sup> Cachexia as systemic tissue wasting syndrome in HF could be found in 10% to 15% of patients and it continues to progress in extent as disease severity rises.<sup>130</sup> Even the subtle changes in body composition, such as loss of muscle tissue in lower limbs, could be found in nearly half of patients with New York Heart Association (NYHA) grade II-IV.<sup>127</sup> Even the decrease of cardiac muscle tissue could be found on conventional transthoracic echocardiography.<sup>131</sup> It is noteworthy to mention that this inconspicuous muscle loss happens while the overall loss of weight still did not develop, and it precedes clinically overt cachexia and that it is prognostically relevant for patients.<sup>132</sup> Therapeutic interventions for cardiac cachexia in HF include physical training and pharmaceuticals like testosterone, growth hormone, ghrelin, supplementation of iron, and enteral substitution of essential nutrients.<sup>132-134</sup>

### Nutritional Risk in Cardiovascular Rehabilitation

Despite many advances in acute management of patients with CVD, secondary prevention still remains essential and should necessarily include cardiac rehabilitation (CR).<sup>135</sup>

According to the American Association of Cardiovascular and Pulmonary Rehabilitation and the American Heart Association (AHA), CR is a comprehensive multidisciplinary program individually tailored to the needs of patients with CVD to slow down or reverse the CVD process.<sup>136</sup> The core components of CR are patient assessment, nutritional counseling, optimization of drug therapy, and weight management.<sup>136</sup>

Increased nutritional risk is common in patients starting rehabilitation after cardiac surgery and it is usually related to severity of underlying disease, age group, and renal function. Recognizing nutritional risk by routine application of nutritional risk scores improves patient evaluation.<sup>53,137</sup>

Suboptimal nutrition status before cardiovascular surgery has been related not only to increased morbidity and prolonged hospital stay but also to delay of postoperative rehabilitation.<sup>135,138</sup>

According to Arai et al,<sup>139</sup> who classified patients in 2 groups according to GNRI, patients in good nutrition group had earlier progression to walking after postoperative rehabilitation, higher rate of discharge home, and shorter postoperative hospitalization.

Screening patients scheduled for cardiovascular rehabilitation after treatment of ischemic or valvular heart disease (using NRS-2002 tool) revealed that more invasive treatments lead to greater nutritional risk due to increased metabolic demands,

stress, tissue damage or healing, infections, and inflammatory reaction. Also, greater weight loss was associated with surgery when compared with conservative treatments or PCI.<sup>137</sup>

Poorer nutritional risk in patients with CVD scheduled for CR can also be related to overuse of PPI and consequent malabsorption and anemia.<sup>76</sup>

### Treatment of Nutritional Risk

Considering the fact that malnutrition exists in patients with different types of CVD, it is common and significant risk factor associated with worse clinical outcome. Thus, it is very important not to neglect the nutritional risk and its factors.<sup>140-142</sup> CoCos trial, as a first randomized prospective trial on nutritional risk, proved useful in nutritional treatment in patients undergoing cardiac surgery.<sup>97</sup> Furthermore, nutrition treatment deserves to be implemented as primary treatment of CVD diseases.<sup>97</sup> In addition to cardioprotective drugs that are an integral part of CVD therapy and which have a positive nutritional effect (eg, ACE inhibitors), care should be taken on drug-nutrition interactions, especially in patients with poly-therapy. Also, one should be aware of the negative influences of some drugs, especially diuretics, and to keep their dosage as low as possible. Very important is patients' CR and their mobility, which prevents significantly muscle wasting and cachexia. It is also very important to invest efforts and resources in educating not only patients and their families but also medical personnel on nutritional risks. This leads to a better nutritional behavior and consumption of healthy diet which helps to better risk factor control (hypertension, dyslipidemia). All aforementioned is important in primary CVD prevention, but especially in secondary prevention. Also, by controlling large and well-known risk factors through dietary nutrition and physical activity, we can control the nutritional risk factors we initially were not aware of and significantly contribute to better survival and better quality of life.

In the end, it is important to stress the lack of prospective, randomized, controlled trials on nutritional risk and moreover on nutritional treatment and interventions to improve nutritional status and prevent sarcopenia and cardiac cachexia, especially in patients with prolonged ICU stay. This results in no guidelines on nutritional risk treatment in patients with CVD and chronic diseases in general, except those undergoing thoracic surgery (ESPEN guidelines).<sup>1</sup> However, although many clinicians are not aware of nutritional treatment importance, these interventions have high cost-benefit potential and are mostly easy to implement in everyday clinical work.

### Author Contributions

MB and NB are equally contributed first authors.

### REFERENCES

- Munro EL, Hickling DF, Williams DM, Bell JJ. Malnutrition is independently associated with skin tears in hospital inpatient setting—findings of a 6-year point prevalence audit. *Int Wound J*. 2018;15:527–533.

- Sorensen J, Kondrup J, Prokopowicz J, et al. EuroOOPS: an international, multicentre study to implement nutritional risk screening and evaluate clinical outcome. *Clin Nutr*. 2008;27:340–349.
- Correia MI, Waitzberg DL. The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. *Clin Nutr*. 2003;22:235–239.
- Wedick NM, Barrett-Connor E, Knoke JD, Wingard DL. The relationship between weight loss and all-cause mortality in older men and women with and without diabetes mellitus: the Rancho Bernardo study. *J Am Geriatr Soc*. 2002;50:1810–1815.
- Sharma Y, Miller M, Kaambwa B, et al. Factors influencing early and late readmissions in Australian hospitalised patients and investigating role of admission nutrition status as a predictor of hospital readmissions: a cohort study. *BMJ Open*. 2018;8:e022246.
- Correia M, Perman MI, Pradelli L, Omarasaleh A, Waitzberg DL. Economic burden of hospital malnutrition and the cost-benefit of supplemental parenteral nutrition in critically ill patients in Latin America. *J Med Econ*. 2018;21:1047–1056.
- Izawa KP, Watanabe S, Oka K. Relationship of thresholds of physical performance to nutritional status in older hospitalized male cardiac patients. *Geriatr Gerontol Int*. 2015;15:189–195.
- Izawa KP, Watanabe S, Oka K, et al. Differences in daily in-hospital physical activity and geriatric Nutritional Risk Index in older cardiac inpatients: preliminary results. *Aging Clin Experiment Res*. 2014;26:599–605.
- Izawa KP, Watanabe S, Oka K, et al. Differences in physical performance based on the Geriatric Nutritional Risk Index in elderly female cardiac patients. *Aging Clin Experiment Res*. 2015;27:195–200.
- Wong CJ. Involuntary weight loss. *Med Clin North Am*. 2014;98:625–643.
- Kim TN, Yang SJ, Yoo HJ, et al. Prevalence of sarcopenia and sarcopenic obesity in Korean adults: the Korean sarcopenic obesity study. *Int J Obesity*. 2009;33:885–892.
- Rolland Y, Lauwers-Cances V, Cristini C, et al. Difficulties with physical function associated with obesity, sarcopenia, and sarcopenic-obesity in community-dwelling elderly women: the EPIDOS (EPIDemiologie de l'OSteoporose) Study. *Am J Clin Nutr*. 2009;89:1895–1900.
- Brown JC, Harhay MO, Harhay MN. Sarcopenia and mortality among a population-based sample of community-dwelling older adults. *J Cachexia Sarcopenia Muscle*. 2016;7:290–298.
- Ebner N, von Haehling S. Unlocking the wasting enigma: highlights from the 8th Cachexia conference. *J Cachexia Sarcopenia Muscle*. 2016;7:90–94.
- Tyrovolas S, Koyanagi A, Olaya B, et al. Factors associated with skeletal muscle mass, sarcopenia, and sarcopenic obesity in older adults: a multi-continent study. *J Cachexia Sarcopenia Muscle*. 2016;7:312–321.
- Abe T, Thiebaud RS, Loenneke JP, Bemben MG, Loftin M, Fukunaga T. Influence of severe sarcopenia on cardiovascular risk factors in nonobese men. *Metab Syndrome Relat Disord*. 2012;10:407–412.
- Kim TN, Park MS, Yang SJ, et al. Prevalence and determinant factors of sarcopenia in patients with type 2 diabetes: the Korean Sarcopenic Obesity Study (KSOS). *Diabetes Care*. 2010;33:1497–1499.
- Hong HC, Hwang SY, Choi HY, et al. Relationship between sarcopenia and nonalcoholic fatty liver disease: the Korean Sarcopenic Obesity Study. *Hepatology*. 2014;59:1772–1778.
- Han K, Park YM, Kwon HS, et al. Sarcopenia as a determinant of blood pressure in older Koreans: findings from the Korea National Health and Nutrition Examination Surveys (KNHANES) 2008–2010. *PLoS ONE*. 2014;9:e86902.
- Zeidler H, Mau W, Khan MA. Undifferentiated spondyloarthropathies. *Rheum Dis Clin North Am*. 1992;18:187–202.
- Tian S, Xu Y. Association of sarcopenic obesity with the risk of all-cause mortality: a meta-analysis of prospective cohort studies. *Geriatr Gerontol Int*. 2016;16:155–166.
- Kondrup J, Allison SP, Elia M, et al. ESPEN guidelines for nutrition screening 2002. *Clin Nutr*. 2003;22:415–421.
- Kondrup J, Rasmussen HH, Hamberg O, Stanga Z; Ad Hoc ESPEN Working Group. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. *Clin Nutr*. 2003;22:321–336.
- Rasmussen HH, Holst M, Kondrup J. Measuring nutritional risk in hospitals. *Clin Epidemiol*. 2010;2:209–216.
- Scott A. Screening for malnutrition in the community: the MUST tool. *Br J Community Nurs*. 2008;13:406, 408, 410–402.
- Pouliou KA, Klek S, Doundoulakis I, et al. The two most popular malnutrition screening tools in the light of the new ESPEN consensus definition of the diagnostic criteria for malnutrition. *Clin Nutr*. 2017;36:1130–1135.
- Corish CA, Flood P, Kennedy NP. Comparison of nutritional risk screening tools in patients on admission to hospital. *J Human Nutr Diet*. 2004;17:133–139; quiz 141–143.
- Detsky AS, Baker JP, Mendelson RA, Wolman SL, Wesson DE, Jeejeebhoy KN. Evaluating the accuracy of nutritional assessment techniques applied to hospitalized patients: methodology and comparisons. *JPEN*. 1984;8:153–159.



29. Vellas B, Guigoz Y, Garry PJ, et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. *Nutrition*. 1999;15:116–122.
30. Castillo-Martinez L, Castro-Eguiluz D, Copca-Mendoza ET, et al. Nutritional assessment tools for the identification of malnutrition and nutritional risk associated with cancer treatment. *Rev Invest Clin*. 2018;70:121–125.
31. Borek P, Chmielewski M, Malgorzewicz S, Debska Slizien A. Analysis of outcomes of the NRS 2002 in patients hospitalized in nephrology wards. *Nutrients*. 2017;9:E287.
32. Ramos R, Nadal E, Peiro I, et al. Preoperative nutritional status assessment predicts postoperative outcomes in patients with surgically resected non-small cell lung cancer. *Eur J Surg Oncol*. 2018;44:1419–1424.
33. Bembenek JP, Karlinski M, Niewada M, Kurkowska-Jastrzebska I, Czlonkowska A. Measurement of nutritional status using body mass index, waist-to-hip ratio, and waist circumference to predict treatment outcome in females and males with acute first-ever ischemic stroke. *J Stroke Cerebrovasc Dis*. 2018;27:132–139.
34. Boban M, Persic V, Zulj M, Petricevic M, Kramaric RP, Vcev A. Bioelectrical impedance analyzes offers clinically relevant appraisal of body composition, but fails to recognize nutritional risk or differences between surgery and percutaneous coronary interventions treatments—a non-randomized cohort. *Coll Antropol*. 2014;38:979–985.
35. Ozeraitiene V, Butenaite V. The evaluation of bone mineral density based on nutritional status, age, and anthropometric parameters in elderly women. *Medicina*. 2006;42:836–842.
36. Orphanidou C, McCargar L, Birmingham CL, Mathieson J, Goldner E. Accuracy of subcutaneous fat measurement: comparison of skinfold calipers, ultrasound, and computed tomography. *J Am Diet Assoc*. 1994;94:855–858.
37. Leong KG, Chee JL, Karahalios A, Skelley A, Wong K. Accuracy and utility of estimating lean body mass and nutritional status in patients with chronic kidney disease on long-term hemodialysis using anthropometric skinfold thickness measurements. *Nephrol Nurs J*. 2018;45:35–40.
38. Shah RV, Anderson A, Ding J, et al. Pericardial, but not hepatic, fat by CT is associated with CV outcomes and structure: the multi-ethnic study of atherosclerosis. *JACC Cardiovasc Imaging*. 2017;10:1016–1027.
39. Wu CK, Tsai HY, Su MY, et al. Pericardial fat is associated with ventricular tachyarrhythmia and mortality in patients with systolic heart failure. *Atherosclerosis*. 2015;241:607–614.
40. Boban M, Barisic M, Persic V, et al. Muscle strength differ between patients with diabetes and controls following heart surgery. *J Diabetes Complicat*. 2016;30:1287–1292.
41. Leong DP, Teo KK. Predicting cardiovascular disease from handgrip strength: the potential clinical implications. *Exp Rev Cardiovasc Ther*. 2015;13:1277–1279.
42. Vojinovic J, Tincani A, Sulli A, et al. European multicentre pilot survey to assess vitamin D status in rheumatoid arthritis patients and early development of a new Patient Reported Outcome questionnaire (D-PRO). *Autoimmunity Rev*. 2017;16:548–554.
43. Green R. Vitamin B12 deficiency from the perspective of a practicing hematologist. *Blood*. 2017;129:2603–2611.
44. Fuhrman MP. The albumin-nutrition connection: separating myth from fact. *Nutrition*. 2002;18:199–200.
45. Bedogni G, Bertoli S, Leone A, et al. External validation of equations to estimate resting energy expenditure in 14952 adults with overweight and obesity and 1948 adults with normal weight from Italy. *Clin Nutr*. 2017;38:457–464.
46. Witvliet-van Nierop JE, Lochtenberg-Potjes CM, Wierdsma NJ, et al. Assessment of nutritional status, digestion and absorption, and quality of life in patients with locally advanced pancreatic cancer. *Gastroenterol Res Pract*. 2017;2017:6193765.
47. Arends J, Baracos V, Bertz H, et al. ESPEN expert group recommendations for action against cancer-related malnutrition. *Clin Nutr*. 2017;36:1187–1196.
48. Jensen GL, Mirtallo J, Compher C, et al. Adult starvation and disease-related malnutrition: a proposal for etiology-based diagnosis in the clinical practice setting of the International Consensus Guideline Committee. *Clin Nutr*. 2010;29:151–153.
49. Prabhakaran D, Anand S, Watkins D, et al. Cardiovascular, respiratory, and related disorders: key messages from Disease Control Priorities, 3rd edition. *Lancet*. 2018;391:1224–1236.
50. Townsend N, Nichols M, Scarborough P, Rayner M. Cardiovascular disease in Europe—epidemiological update 2015. *Eur Heart J*. 2015;36:2696–2705.
51. Claeys MJ, Mullens W, Vandekerckhove Y, Duytschaever M, De Maeyer C, Pasquet A. Summary of 2016 ESC guidelines on heart failure, atrial fibrillation, dyslipidaemia and cardiovascular prevention. *Acta Cardiol*. 2017;72:610–615.
52. Boban M, Laviano A, Persic V, Rotim A, Jovanovic Z, Vcev A. Characteristics of NRS-2002 Nutritional Risk Screening in patients hospitalized for secondary cardiovascular prevention and rehabilitation. *J Am College Nutr* 2014;33:466–473.
53. Boban M, Persic V, Miletic B, Kovacicck K, Madzar Z. Heart surgery stems increased nutritional risk, expressed during the course of stationary rehabilitation. *Ann Nutr Metab*. 2013;63:17–24.
54. Stoppe C, Nesterova E, Elke G. Nutritional support in patients with extracorporeal life support and ventricular assist devices. *Curr Opin Critical Care*. 2018;24:269–276.
55. Boban M, Persic V, Jovanovic Z, et al. Obesity dilemma in the global burden of cardiovascular diseases. *Int J Clin Pract*. 2014;68:173–179.
56. Little MO. Updates in nutrition and polypharmacy. *Curr Opin Clin Nutr Metab Care*. 2018;21:4–9.
57. Otles S, Senturk A. Food and drug interactions: a general review. *Acta Sci Pol Technol Aliment*. 2014;13:89–102.
58. Chan LN. Drug-nutrient interactions. *JPEN*. 2013;37:450–459.
59. Noh K, Kang YR, Nepal MR, et al. Impact of gut microbiota on drug metabolism: an update for safe and effective use of drugs. *Arch Pharm Res*. 2017;40:1345–1355.
60. Boullata JL, Hudson LM. Drug-nutrient interactions: a broad view with implications for practice. *J Acad Nutr Diet*. 2012;112:506–517.
61. Ahmed A, Zannad F, Love TE, et al. A propensity-matched study of the association of low serum potassium levels and mortality in chronic heart failure. *Eur Heart J*. 2007;28:1334–1343.
62. Ceremuzynski L, Gebalska J, Wolk R, Makowska E. Hypomagnesemia in heart failure with ventricular arrhythmias. Beneficial effects of magnesium supplementation. *J Intern Med*. 2000;247:78–86.
63. Huwyler T, Stirnemann J, Vuilleumier N, et al. Profound hyponatraemia in the emergency department: seasonality and risk factors. *Swiss Med Weekly*. 2016;146:w14385.
64. Liamis G, Filippatos TD, Elisaf MS. Thiazide-associated hyponatremia in the elderly: what the clinician needs to know. *JGC*. 2016;13:175–182.
65. Liang W, Ma H, Cao L, Yan W, Yang J. Comparison of thiazide-like diuretics versus thiazide-type diuretics: a meta-analysis. *J Cell Molec Med*. 2017;21:2634–2642.
66. Malta D, Arcand J, Ravindran A, Floras V, Allard JP, Newton GE. Adequate intake of potassium does not cause hyperkalemia in hypertensive individuals taking medications that antagonize the renin angiotensin aldosterone system. *Am J Clin Nutr*. 2016;104:990–994.
67. Reardon LC, Macpherson DS. Hyperkalemia in outpatients using angiotensin-converting enzyme inhibitors. How much should we worry? *Arch Intern Med*. 1998;158:26–32.
68. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016;37:2129–2200.
69. Hornig B, Arakawa N, Drexler H. Effect of ACE inhibition on endothelial dysfunction in patients with chronic heart failure. *Eur Heart J*. 1998;19:G48–G53.
70. Anker SD, Negassa A, Coats AJ, et al. Prognostic importance of weight loss in chronic heart failure and the effect of treatment with angiotensin-converting-enzyme inhibitors: an observational study. *Lancet*. 2003;361:1077–1083.
71. Adigun AQ, Ajayi AA. The effects of enalapril-digoxin-diuretic combination therapy on nutritional and anthropometric indices in chronic congestive heart failure: preliminary findings in cardiac cachexia. *Eur J Heart Fail*. 2001;3:359–363.
72. Lam PH, Dooley DJ, Fonarow GC, et al. Similar clinical benefits from below-target and target dose enalapril in patients with heart failure in the SOLVD Treatment trial. *Eur J Heart Fail*. 2018;20:359–369.
73. Lainscak M, Keber I, Anker SD. Body composition changes in patients with systolic heart failure treated with beta blockers: a pilot study. *Int J Cardiol*. 2006;106:319–322.
74. Clark AL, Coats AJS, Krum H, et al. Effect of beta-adrenergic blockade with carvedilol on cachexia in severe chronic heart failure: results from the COPELNICUS trial. *J Cachexia Sarcopenia Muscle*. 2017;8:549–556.
75. Saitoh M, Ebner N, von Haehling S, Anker SD, Springer J. Therapeutic considerations of sarcopenia in heart failure patients. *Exp Rev Cardiovasc Ther*. 2018;16:133–142.
76. Boban M, Persic V, Petricevic M, et al. Connections between nutritional status and proton pump inhibitor therapy in patients scheduled for cardiovascular rehabilitation after treatment for ischaemic and valvular heart disease. *Kardiol Pol*. 2016;74:461–468.
77. Forgacs I, Loganayagam A. Overprescribing proton pump inhibitors. *BMJ*. 2008;336:2–3.
78. Delcher A, Hily S, Boureau AS, Chapelet G, Berrut G, de Decker L. Multimorbidities and overprescription of proton pump inhibitors in older patients. *PLoS ONE*. 2015;10:e0141779.
79. Boban M, Persic V, Petricevic M, Manola S, Boban L, Vcev A. Impact of cardiovascular treatments and systolic dysfunction on nutritional risk in patients with ischemic and valvular heart disease. *J Am Coll Nutr*. 2015;34:159–166.



80. Ringaitiene D, Gincityte D, Vicka V, et al. Preoperative risk factors of malnutrition for cardiac surgery patients. *Acta Med Lituan*. 2016;23:99–109.
81. Rahman A, Agarwala R, Martin C, Nagpal D, Teitelbaum M, Heyland DK. Nutrition therapy in critically ill patients following cardiac surgery: defining and improving practice. *JPEN*. 2017;41:1188–1194.
82. Thourani VH, Keeling WB, Kilgo PD, et al. The impact of body mass index on morbidity and short- and long-term mortality in cardiac valvular surgery. *J Thorac Cardiovasc Surg*. 2011;142:1052–1061.
83. van Venrooij LM, de Vos R, Zijlstra E, Borgmeijer-Hoelen MM, van Leeuwen PA, de Mol BA. The impact of low preoperative fat-free body mass on infections and length of stay after cardiac surgery: a prospective cohort study. *J Thorac Cardiovasc Surg*. 2011;142:1263–1269.
84. van Venrooij LM, de Vos R, Borgmeijer-Hoelen MM, Haaring C, de Mol BA. Preoperative unintended weight loss and low body mass index in relation to complications and length of stay after cardiac surgery. *Am J Clin Nutr*. 2008;87:1656–1661.
85. Ogawa M, Izawa KP, Satomi-Kobayashi S, et al. Effects of postoperative dietary intake on functional recovery of patients undergoing cardiac surgery. *NMCD*. 2019;29:90–96.
86. Izawa KP, Watanabe S. Relation of nutritional status to physiological outcomes after cardiac surgery in elderly patients with diabetes mellitus: a preliminary study. *Aging Clin Experiment Res*. 2016;28:1267–1271.
87. van Venrooij LM, van Leeuwen PA, Hopmans W, Borgmeijer-Hoelen MM, de Vos R, De Mol BA. Accuracy of quick and easy undernutrition screening tools—Short Nutritional Assessment Questionnaire, Malnutrition Universal Screening Tool, and modified Malnutrition Universal Screening Tool—in patients undergoing cardiac surgery. *J Am Diet Assoc*. 2011;111:1924–1930.
88. van Venrooij LM, Visser M, de Vos R, van Leeuwen PA, Peters RJ, de Mol BA. Cardiac surgery-specific screening tool identifies preoperative undernutrition in cardiac surgery. *Ann Thorac Surg*. 2013;95:642–647.
89. Xu J, Ge Y, Pan S, Liu F, Shi Y. A preoperative and intraoperative predictive model of prolonged intensive care unit stay for valvular surgery. *J Heart Valve Dis*. 2006;15:219–224.
90. Stoppe C, Ney J, Lomivorotov VV, et al. Prediction of prolonged ICU stay in cardiac surgery patients as a useful method to identify nutrition risk in cardiac surgery patients: a post hoc analysis of a prospective observational study [published online ahead of print December 2, 2018]. *JPEN*. doi:10.1002/jpen.1486.
91. Farhangi MA, Najafi M, Jafarabadi MA, Jahangiri L. Mediterranean dietary quality index and dietary phytochemical index among patients candidate for coronary artery bypass grafting (CABG) surgery. *BMC Cardiovasc Disord*. 2017;17:114.
92. Farhangi MA, Najafi M. Dietary inflammatory index: a potent association with cardiovascular risk factors among patients candidate for coronary artery bypass grafting (CABG) surgery. *Nutrition J*. 2018;17:20.
93. Ardeshiri M, Faritus Z, Ojaghi-Haghighi Z, Bakhshandeh H, Kargar F, Aghili R. Impact of metabolic syndrome on mortality and morbidity after coronary artery bypass grafting surgery. *Res Cardiovasc Med*. 2014;3:e20270.
94. Milano CA, Kesler K, Archibald N, Sexton DJ, Jones RH. Mediastinitis after coronary artery bypass graft surgery. Risk factors and long-term survival. *Circulation*. 1995;92:2245–2251.
95. Protopoulos AD. Does body mass index affect mortality in coronary surgery? *Open Cardiovasc Med J*. 2016;10:240–245.
96. Jagielak D, Wernio E, Kozaryn R, et al. The impact of nutritional status and appetite on the hospital length of stay and postoperative complications in elderly patients with severe aortic stenosis before aortic valve replacement. *Kardiologiya i Torakochirurgiya Pol*. 2016;13:105–112.
97. De Waele E, Nguyen D, De Bondt K, et al. The CoCoS trial: Caloric Control in Cardiac Surgery patients promotes survival, an interventional trial with retrospective control. *Clin Nutr*. 2018;37:864–869.
98. Persic V, Bastiancic AL, Rosovic I, et al. Correlation between immunological-inflammatory markers and endothelial dysfunction in the early stage of coronary heart disease. *Med Hypotheses*. 2018;115:72–76.
99. Khaltaev NG, Timofeeva TN, Zhukovskii GS, Bulin VA, Ievlev AS. Nutritional and risk-factor dynamics of ischemic heart disease during a 3-year prophylactic intervention in an organized population. *Ter Arkh*. 1989;61:102–107.
100. Khalataev NG, Birlutskii GI, Deev AD, Zhukovskii GS, Zinenko GI. Comparative study of the effect of basic risk and nutritional factors on the development of ischemic heart disease in a population. *Ter Arkh*. 1985;57:60–66.
101. Vasudevan AR, Ballantyne CM. Cardiometabolic risk assessment: an approach to the prevention of cardiovascular disease and diabetes mellitus. *Clin Cornerstone*. 2005;7:7–16.
102. Vachenaer R, Grunenfelder J, Plass A, et al. Changing lifestyle habits as secondary prophylaxis after coronary artery bypass grafting. *Heart Surg Forum*. 2008;11:E243–E247.
103. Shojaei S, Farhadloo R, Acin A, Vahedian M. Effects of the Health Belief Model (HBM)-based educational program on the nutritional knowledge and behaviors of CABG patients. *J Tebran Heart Center*. 2016;11:181–186.
104. Delgado-Lista J, Perez-Martinez P, Garcia-Rios A, Perez-Caballero AI, Perez-Jimenez F, Lopez-Miranda J. Mediterranean diet and cardiovascular risk: beyond traditional risk factors. *Crit Rev Food Sci Nutr*. 2016;56:788–801.
105. Grosso G, Mistretta A, Frigiola A, et al. Mediterranean diet and cardiovascular risk factors: a systematic review. *Crit Rev Food Sci Nutr*. 2014;54:593–610.
106. Ruiz-Nunez B, van den Hurk GH, de Vries JH, et al. Patients undergoing elective coronary artery bypass grafting exhibit poor pre-operative intakes of fruit, vegetables, dietary fibre, fish and vitamin D. *Br J Nutr*. 2015;113:1466–1476.
107. Hartwell D, Henry J. Dietary advice for patients undergoing coronary artery bypass surgery: falling on deaf ears? *Int J Food Sci Nutr*. 2003;54:37–47.
108. Doi S, Iwata H, Wada H, et al. A novel and simply calculated nutritional index serves as a useful prognostic indicator in patients with coronary artery disease. *Int J Cardiol*. 2018;262:92–98.
109. Wada H, Dohi T, Miyauchi K, et al. Relationship between the prognostic nutritional index and long-term clinical outcomes in patients with stable coronary artery disease. *J Cardiol*. 2018;72:155–161.
110. Wada H, Dohi T, Miyauchi K, et al. Combined effect of nutritional status on long-term outcomes in patients with coronary artery disease undergoing percutaneous coronary intervention. *Heart Vessels*. 2018;33:1445–1452.
111. Wada H, Dohi T, Miyauchi K, et al. Prognostic impact of nutritional status assessed by the Controlling Nutritional Status score in patients with stable coronary artery disease undergoing percutaneous coronary intervention. *Clin Res Cardiol*. 2017;106:875–883.
112. Kunimura A, Ishii H, Uetani T, et al. Impact of nutritional assessment and body mass index on cardiovascular outcomes in patients with stable coronary artery disease. *Int J Cardiol*. 2017;230:653–658.
113. Kunimura A, Ishii H, Uetani T, et al. Impact of Geriatric Nutritional Risk Index on cardiovascular outcomes in patients with stable coronary artery disease. *J Cardiol*. 2017;69:383–388.
114. Shamkani WA, Jafar NS, Narayanan SR, Rajappan AK. Acute myocardial infarction in a young lady due to Vitamin B12 deficiency induced hyperhomocysteinemia. *Heart Views*. 2015;16:25–29.
115. You ZB, Lin KY, Zheng WP, et al. Association of prealbumin levels with contrast-induced acute kidney injury in elderly patients with elective percutaneous coronary intervention. *Clin Intervent Aging*. 2018;13:641–649.
116. Carbone S, Lavie CJ, Arena R. Obesity and heart failure: focus on the obesity paradox. *Mayo Clin Proc*. 2017;92:266–279.
117. Goyal A, Nimmakayala KR, Zonszein J. Is there a paradox in obesity? *Cardiol Rev*. 2014;22:163–170.
118. Rosenthal M, Gabrielli A, Moore F. The evolution of nutritional support in long term ICU patients: from multisystem organ failure to persistent inflammation immunosuppression catabolism syndrome. *Minerva Anestesiol*. 2016;82:84–96.
119. Dragan S, Buleu F, Christodorescu R, et al. Benefits of multiple micronutrient supplementation in heart failure: a comprehensive review [published online ahead of print December 3, 2018]. *Crit Rev Food Sci Nutr*. doi:10.1080/10408398.8.2018.1540398.
120. Barge-Caballero E, Garcia-Lopez F, Marzoa-Rivas R, et al. Prognostic value of the Nutritional Risk Index in heart transplant recipients. *Rev Esp Cardiol*. 2017;70:639–645.
121. Uribarri A, Rojas SV, Hanke JS, et al. Prognostic value of the Nutritional Risk Index in candidates for continuous flow left ventricular assist device therapy [published online ahead of print August 2, 2018]. *Rev Esp Cardiol*. doi:10.1016/j.rec.2018.05.029.
122. Adejumo OL, Koelling TM, Hummel SL. Nutritional Risk Index predicts mortality in hospitalized advanced heart failure patients. *J Heart Lung Transplant*. 2015;34:1385–1389.
123. Rahman A, Jafry S, Jeejeebhoy K, Nagpal AD, Pisani B, Agarwala R. Malnutrition and cachexia in heart failure. *JPEN*. 2016;40:475–486.
124. Pasini E, Aquilani R, Gheorghide M, Dioguardi FS. Malnutrition, muscle wasting and cachexia in chronic heart failure: the nutritional approach. *Italian Heart J*. 2003;4:232–235.
125. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail*. 2016;18:891–975.
126. Bekfani T, Pellicori P, Morris DA, et al. Sarcopenia in patients with heart failure with preserved ejection fraction: impact on muscle strength, exercise capacity and quality of life. *Int J Cardiol*. 2016;222:41–46.
127. Mancini DM, Walter G, Reichek N, et al. Contribution of skeletal muscle atrophy to exercise intolerance and altered muscle metabolism in heart failure. *Circulation*. 1992;85:1364–1373.
128. Saitoh M, Dos Santos MR, Emami A, et al. Anorexia, functional capacity, and clinical outcome in patients with chronic heart failure: results from the Studies Investigating Co-morbidities Aggravating Heart Failure (SICA-HF). *ESC Heart Fail*. 2017;4:448–457.

129. Rossignol P, Masson S, Barlera S, et al. Loss in body weight is an independent prognostic factor for mortality in chronic heart failure: insights from the GISSI-HF and Val-HeFT trials. *Eur J Heart Fail.* 2015;17:424–433.
130. Morley JE, Anker SD, von Haehling S. Prevalence, incidence, and clinical impact of sarcopenia: facts, numbers, and epidemiology—update 2014. *J Cachexia Sarcopenia Muscle.* 2014;5:253–259.
131. Boban M, Laviano A, Persic V, et al. Influence of transiently increased nutritional risk on a left ventricle myocardial mass assessed by echocardiography. *Ann Nutr Metab.* 2016;68:197–202.
132. von Haehling S, Ebner N, Dos Santos MR, Springer J, Anker SD. Muscle wasting and cachexia in heart failure: mechanisms and therapies. *Nat Rev.* 2017;14:323–341.
133. van Veldhuisen DJ, Ponikowski P, van der Meer P, et al. Effect of ferric carboxymaltose on exercise capacity in patients with chronic heart failure and iron deficiency. *Circulation.* 2017;136:1374–1383.
134. Springer J, Springer JI, Anker SD. Muscle wasting and sarcopenia in heart failure and beyond: update 2017. *ESC Heart Fail.* 2017;4:492–498.
135. Ogawa M, Izawa KP, Satomi-Kobayashi S, et al. Poor preoperative nutritional status is an important predictor of the retardation of rehabilitation after cardiac surgery in elderly cardiac patients. *Aging Clin Experiment Res.* 2017;29:283–290.
136. Smith SC Jr, Allen J, Blair SN, et al. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart, Lung, and Blood Institute. *Circulation.* 2006;113:2363–2372.
137. Boban M, Persic V, Laviano A, et al. Nutritional risk screening of patients scheduled for rehabilitation after treatment for ischemic or valvular heart disease. *Eur J Clin Nutr.* 2013;67:1116.
138. Lomivorotov VV, Efremov SM, Boboshko VA, et al. Prognostic value of nutritional screening tools for patients scheduled for cardiac surgery. *Inter Cardiovasc Thorac Surg.* 2013;16:612–618.
139. Arai Y, Kimura T, Takahashi Y, Hashimoto T, Arakawa M, Okamura H. Preoperative nutritional status is associated with progression of postoperative cardiac rehabilitation in patients undergoing cardiovascular surgery. *Gen Thorac Cardiovasc Surg.* 2018;66:632–640.
140. Maruyama K, Nakagawa N, Koyama S, Maruyama JI, Hasebe N. Malnutrition increases the incidence of death, cardiovascular events, and infections in patients with stroke after rehabilitation. *J Stroke Cerebrovasc Dis.* 2018;27:716–723.
141. Maruyama K, Nakagawa N, Saito E, et al. Malnutrition, renal dysfunction and left ventricular hypertrophy synergistically increase the long-term incidence of cardiovascular events. *Hypertens Res.* 2016;39:633–639.
142. Tennant IA, Barnett AT, Thompson DS, et al. Impaired cardiovascular structure and function in adult survivors of severe acute malnutrition. *Hypertension.* 2014;64:664–671.