VILNIUS UNIVERSITY

Donata Ringaitienė

PREVALENCE, ASSESSMENT AND EFFECTS OF MALNUTRITION ON EARLY POSTOPERATIVE COMPLICATIONS IN CARDIAC SURGERY

Summary of Doctoral Dissertation

Biomedical Sciences, Medicine (06 B)

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The doctoral dissertation was prepared during the period of 2012–2016 at Vilnius University, in cooperation with Vilnius University Hospital Santariskiu Clinics.

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VILNIAUS UNIVERSITETAS

Donata Ringaitienė

MITYBOS NEPAKANKAMUMO PAPLITIMAS, VERTINIMAS IR ĮTAKA ANKSTYVOMS KOMPLIKACIJOMS PO ŠIRDIES OPERACIJŲ

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LIST OF ABBREVIATIONS

ASPEN	–	American Society for Parenteral and Enteral Nutrition
BIA	–	Bioelectrical impedance analysis
BMI	–	Body Mass Index
CABG	–	Coronary artery bypass grafting
CDC	–	Centers for Disease Control and Prevention
CI	–	Confidence interval
CPB	–	Cardiopulmonary bypass
C-RP	–	C-reactive protein
ESPEN	–	European Society for Parenteral and Enteral Nutrition
EuroSCORE	–	European System for Cardiac Operative Risk Evaluation
FFMI	–	Fat-Free Mass Index
NYHA FC	–	Heart failure classification based on the New York Heart Association Functional Classification
IABC	–	Intra-aortic balloon counter-pulsation
ICU	–	Intensive care unit
LVEF	–	Left ventricular ejection fraction
n	–	Sample
MN	–	Malnutrition
MNA	–	Mini Nutritional Assessment
NRS 2002	–	Nutritional risk screening for hospital patients
OR	–	Odds ratio
p	–	Level of significance
PA	–	Phase angle
STS	–	Society of Thoracic Surgeons
USA	–	United States of America
VUH SC	–	Vilnius University Hospital Santariskiu Clinics

1. Introduction

In Lithuania, just as in Europe and all over the world, cardiovascular disease is the largest cause of death (Haubner U, 2006).

In spite of modern conservative treatment, progressing symptoms of heart failure make surgical interventions unavoidable. The number of cardiac surgeries is growing all over the world. Worldwide, the total number of cardiac surgeries utilising CPB is estimated at 1.2–1.4 million patients per year, of which 700,000–800,000 cardiac operations are performed in the United States of America (USA) (Pezzella AT, 2004). As far as we know, in Lithuania this figure stands at about 2,000. The growing number of cardiac surgery volumes is accompanied by increasing attention to the perioperative care of patients. Effective and timely diagnostics of risk factors, reliable identification of the degree of risk and risk management become increasingly important for improving postoperative outcomes in cardiac surgery (Relman AS, 1988). Preoperative cardiovascular markers, diabetes, peripheral arterial disease, chronic pulmonary and renal diseases, infective endocarditis, and disease severely affecting ambulation are known as the factors increasing operative risks included in Scoring Systems for Cardiac Operative Risk Evaluation European – the System for Cardiac Operative Risk Evaluation (EuroScore) and the Society of Thoracic Surgeons' risk score (STS).

Malnutrition (MN) is a pathological state resulting from a deficiency of nutrients or the imbalance between the supply of nutrients and the body's demand for them. Nutritional deficiencies can lead to structural and functional changes in various systems, which cause metabolic and immune function impairments as well as determine treatment results not only for therapeutic but also for surgery patients: longer hospital stay, reduced quality of life, and increased mortality (Haubner U, 2006).

According to recent reports, nutritional deficiency is a common condition in cardiac surgery patients, with an incidence ranging from 1.2% to 46.4% (van Venrooij LM, 2008, 2011; Yu PJ, 2015; Visser M, 2012; Thouranj

VH 2011; Lim SL, 2012, Chermesh I, 2014). The prevalence of MN ranges depends on the criteria used to determine it. Extensive research is done in order to obtain diagnostic criteria of MN. Weight loss, low body mass index (BMI) and reduced food intake are known as the screening markers of MN (Lochs H, 2006). However, it is obvious that in specific patient groups these conventional methods of nutritional state evaluation might not be accurate enough in detecting MN (van Venrooij, 2011). Pathophysiological changes, prevalent in congestive heart failure, lead to fluid retention with the increase of body mass (Houston BA, 2015). This poses a problem to diagnose malnourished patients using conventional methods which are based on the decrease of body weight, or use questions about unintended weight loss, to which patients cannot always objectively answer (Cederholm T, 2015). Hence, MN is often underdiagnosed and not adequately treated. This results in a higher risk of postoperative infectious and non-infectious complications, as well as higher mortality rates, prolonged length of stay at hospital and intensive care unit (ICU) and consequently the poorer quality of life (van Venrooij, 2008; Chermesh I, 2014). Therefore, an accurate detection of preoperative MN is crucially important in predicting the outcomes after cardiac surgery.

In this study, we use a novel approach to evaluate the nutritional status of the patients. Bioelectrical impedance analysis (BIA) is a quick, easy-to-use, non-invasive and easily applicable method of body composition and cell health evaluation (Kyle UG, 2004). Subtle alterations on the cellular membrane and fluid imbalance can be detected earlier using BIA than using anthropometric measurements. We hypothesize that using a phase angle (PA) value derived from the BIA we can objectively differentiate malnourished patients from those well-nourished (Visser M, 2012; Barbosa-Silva MC, 2003; Kyle UG 2004, 15, 16). Therefore, it is a way of detecting MN at its first stages.

Moreover, the PA value is associated with worse clinical outcomes in some chronic diseases: chronic obstructive pulmonary disease, liver failure, haematology–oncology patients (Anker SD, 2006; Plauth M, 2009; Calleja

Fernandez A, 2015). However, only a couple of studies were conducted with cardiac surgery patients (Visser M, 2012; Chermesh I, 2014), but none of them dealt with low-operative-risk cardiac surgery patients. Thus, our aim is to determine whether PA is a marker of MN and postoperative morbidity in low-operative-risk patients undergoing cardiac surgery.

2. Research purpose

The purpose of the research is to identify the impact of preoperative malnutrition on early postoperative complications in cardiac surgery.

3. Research tasks

1. To identify the values of phase angle determined by bioelectrical impedance analysis, which can be used for the diagnosis of malnutrition:
   1.1. Identification of correlations between phase angle and nutritional status;
   1.2. Standardisation of phase angle values for diagnostic purposes.
2. To compare the sensitivity of nutritional screening tools for assessing the risk of malnutrition using bioelectrical impedance analysis as a control method.
3. To investigate the prevalence of preoperative malnutrition in cardiac surgery patients.
4. To identify the risk factors for preoperative malnutrition in cardiac surgery.
5. To identify the impact of preoperative malnutrition on early postoperative complications, mortality and the length of postoperative hospital stay in cardiac surgery patients.

4. Propositions to be defended

1. The degree of a phase angle from bioelectrical impedance reflects nutritional status and can be used for the diagnosis of malnutrition.
2. Malnutrition is diagnosed more frequently when the bioelectrical impedance phase angle is interpreted, as compared with the low preoperative fat-free mass index (FFMI) and the body mass index (BMI) as the malnutrition indicators in cardiac surgery patients.
3. The nutritional status of cardiac surgery patients is correlated with the severity of heart disease, co-morbidities, inflammatory processes, nutrition, and physical activity.
4. The preoperative nutritional status may increase the risk of early postoperative complications in cardiac surgery patients.

5. Significance and novelty of the research

The dissertation research assessed the impact of the preoperative nutritional status on postoperative complications in cardiac surgery. In previous studies, investigating effects of nutrition and metabolism on therapeutic outcomes of various surgeries, cardiac surgery patients represented a relatively small portion of patients, whereas the effect of MN on postoperative outcomes in cardiac surgery patients with a low operative risk has not been assessed at all. To the best of our knowledge, it is the first MN research in Lithuania, having the largest sample size of 712 patients who underwent cardiac surgery at the Vilnius University Hospital Santariskiu Clinics (VUH SC) from 7 March 2013 until 31 March 2014. It is the first time in Lithuania when the prevalence of MN was investigated using a BIA, i.e. a relatively low-cost, safe, quick-and-easy-to-use, non-invasive method for measuring body composition and nutritional status in patients. The dissertation research assessed nutritional status using a PA determined by BIA. The BIA-derived PA is still being considered a hypothetic MN criterion by the European Society for Parenteral and Enteral Nutrition (ESPEN), allowing a diagnosis of early nutritional status abnormalities. The research confirmed correlations between PA and MN criteria recommended by the ESPEN – BMI <18.5 kg/m², low FFMI (<17 kg/m² and <15 kg/m² in males and females, respectively), and unintentional loss of weight by >5% in the past 3 months. Within the framework of the research, a PA standardisation method was developed and presented for assessing nutritional status in cardiac surgery patients.

The analysis of demographic and preoperative indicators performed during the research complemented the spectrum of factors influencing preoperative MN development in cardiac surgery. Preoperative nutritional status was screened in order to determine the diagnostic sensitivity of screening tools and to identify the most accurate MN risk screening tool for cardiac surgery patients, i.e. Nutritional Risk Screening 2002 (NRS-2002).

The dissertation paper provides new knowledge beneficial not only for improving early diagnostics and prevention of MN in cardiac surgery patients, but also for determining correlations between MN and early postoperative complications in cardiac surgery.

6. Patients and methods

6.1. Patients

All patients with congenital and non-congenital heart diseases, who were admitted to the Department of Cardiac Surgery at VUH SC to undergo scheduled surgeries during the period from 7 March 2013 to 31 March 2014, were offered to participate in the research. All patients who agreed to participate and met the selection criteria in the table below were enrolled in a two-phase study. The study was authorised by the Vilnius Regional Committee of Bioethics (No. 158200-13-622-194, 14/5/2013).

Table 1. Selection of patients

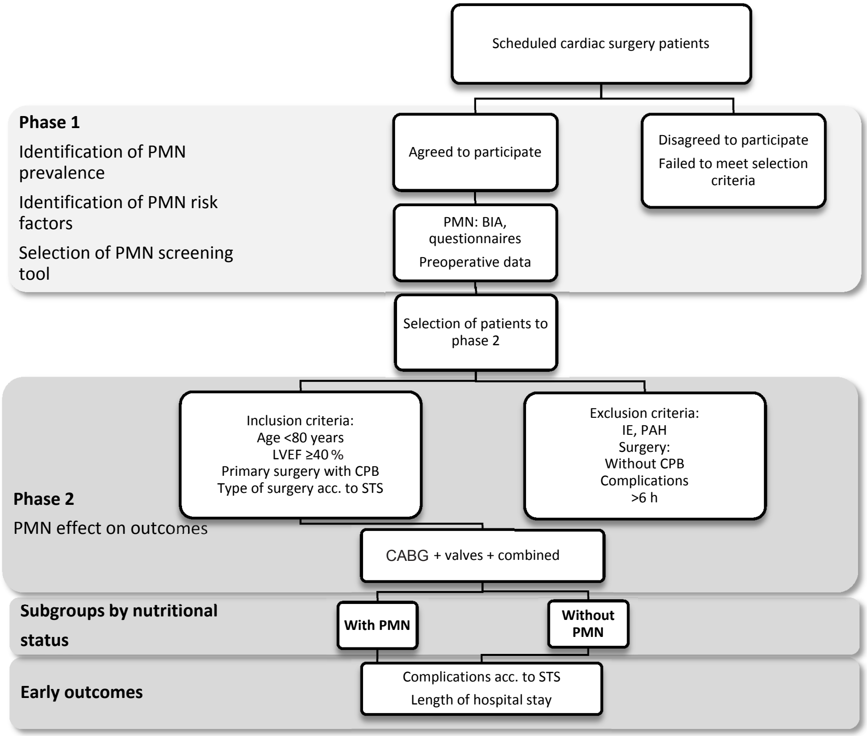
	Inclusion criteria	Exclusion criteria
Phase 1	**Cardiac surgery with pericardiotomy**	**Incapacitated**
	Age >18 years	**Implanted electric cardiac pacemakers**
	Informed consent of the patient to participate in the study	**Amputation of ≥ 1 extremity(ies)**
Phase 2	Age from 18 to 79 years	Unplanned intervention during the surgery
	On pump-cardiac surgery	Complication during the surgery
	Type of surgery: • coronary artery bypass surgery, • replacement of the aortic and mitral valves, • reconstruction of the mitral valve, • combined surgery LVEF more than 40%	Patients with an acute operative cardiac failure defined as at least one of the following: • repeated application of cardiopulmonary bypass, • application of IABC during the surgery, • infusion of a cumulative dose of more than 0.2, mcg/kg/min of two or more inotropic drugs. IABP application before surgery Diagnosis of infectious endocarditis Patients with severe pulmonary hypertension (> 55 mmHg).

6.2. Course and model of the study

The study was conducted in two phases (phase 1 and phase 2) (Diagram 1).

At phase 1, the prevalence of preoperative MN and determinant factors among cardiac surgery patients were identified using BIA-derived PA (degree), and the screening tool was selected which is the most accurate for MN diagnosis in cardiac surgery patients.

The preoperative nutritional status of patients was assessed using the BIA method to investigate body composition and by filling in the MN screening tool (questionnaires) on the eve of surgery.



PMN – preoperative malnutrition, BIA – bioelectrical impedance analysis, LVEF – left ventricular ejection fraction, CPB – cardiopulmonary bypass, STS – Society of Thoracic Surgeons, CABG – Coronary artery bypass grafting, IE – Infectious endocarditis, PAH – pulmonary hypertension (severe).

Diagram 1. Selection of patients and study phases

All patients underwent a standard preoperative screening, and the following data were recorded: demographic data, co-morbidities, laboratory and instrumental analyses in accordance with the standard protocol of examinations conducted at the cardiac surgery clinic to patients scheduled for cardiac surgery (chest X-ray, ECG, coronarography, duplex scan of extracranial arteries, visceral ultrasound, fibroesophagogastroduodenoscopy), addictions, and the preoperative length of hospital stay.

During phase 2, a homogenous cohort of cardiac surgery patients at a low operative risk was selected in accordance with the selection criteria and stratified basing on the STS criteria for assessing the effects of preoperative MN on postoperative complications, mortality and length of hospital stay in cardiac surgery patients.

During the study, the patients meeting the cohort selection criteria were registered by cardiac surgeries, cardiopulmonary bypass (CPB) time and complications. In order to assess correlations between preoperative MN with postoperative complications, mortality and the length of hospital stay, the patients were postoperatively registered according to complications, mortality and the length of stay in intensive care and cardiac surgery units in accordance with the definitions of early postoperative complications used in the STS operative risk model. The patients also underwent laboratory analyses and instrumental examination during the postoperative period.

6.3. Research methodology

6.3.1. Methods for assessing preoperative nutritional status

Preoperative nutritional status was assessed using **screening tools for nutritional risk assessment** recommended by the ESPEN (NRS-2002 (*Nutritional Risk Screening 2002*), MUST (*Malnutrition Universal Screening Tool*), MNA-SF (*Short Form – Mini Nutritional Assessment)* and filling the relevant forms on the eve of surgery, and the **bioelectrical impedance method (BIA)** for body composition measurements. Nutritional risks and MN in cardiac surgery patients were assessed, respectively, on the basis of the screening tools for assessing nutritional status and PA value derived from the BIA.

BIA is based on the principle that the electrical current passes at different rates through the patient's body. The low frequency electrical current (5 kHz) only flows through extracellular fluids thus creating body resistance, while the high frequency current (50 kHz, 200l kHz) also flows intracellularly, producing reactance and intracellular resistance. The values of the resistances are then put in population-specific reference equations, and a patient's body composition is measured: fat mass, fat-free mass, muscle mass, extracellular and intracellular waters. A PA, defined as the relationship between intracellular and extracellular resistance components, is expressed in degrees subject to changes of the current passing through a patient's body over time. The PA is measured at a high-frequency electrical current (50 kHz).

To confirm correlations between PA and nutritional status, the PA value was compared with BMI, FFMI and unintentional weight loss (UWL) (of >5% within 3 months), and confidence levels were determined.

As a measurement directly proportional to a patient's age and gender, PA has been standardised. The patients were split into two subcohorts grouped by age: 0–19 years, 20–29 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years, 70–79 years, and 80+. The subcohorts were then divided into two groups by gender: males and females. Hence, the entire cohort was split into two subcohorts, each grouped into 8 subgroups by age, i.e. into a total of 16 separate samples. Patients' PA value falling into each sample was assessed according to reference values for that sample, and the patients were then gradually redistributed by a decrease in the PA from the 45^{th} percentile down to the 5^{th} percentile. A total of 9 groups were defined by the PA decrease, where the group below the 45^{th} percentile represented the lowest PA decrease and the group below the 5^{th} percentile represented the highest decrease in PA. A specific PA percentile indicating MN was obtained by way of analysis of all percentile groups which were compared against FFMI cut-off values predicting MN: FFMI <15 kg/m² in women and 17 kg/m² in men. Then the statistical analysis was used to identify the PA percentile group best suited to reflect MN, and the patients were again divided into two groups: malnourished and well-nourished.

BIA was performed using the InBody S10 body composition analyser (Biospace, Seoul, Korea). The analyser was calibrated before the beginning of data collection and set to use standard equations adapted for the analysis of data on Caucasians. The analysis was performed on the eve of surgery in accordance with ESPEN (202) and manufacturer's recommendations (203).

6.3.2. Methods for determining factors associated with preoperative malnutrition

Preoperative factors likely to determine preoperative MN detected for cardiac surgery patients on the basis of a standardised PA (degree) were registered through patient interviews and on the basis of data collected from person's medical documents and electronic medical records (available at VUH SC since 2000). The registered factors were divided into three groups of risk factors:

1. Factors describing a patient's condition and the severity of disease.
2. Laboratory parameters.
3. Psychosocial factors associated with lifestyle and nutritional habits.

The group of factors describing a patient's condition and severity of disease included demographic indicators, all prevalent co-morbidities in cardiac surgery patients, and the length of hospital stay. Laboratory parameters of inflammations, haemopoietic disorders and other laboratory parameters relevant to cardiac surgery patients were considered to be risk factors for MN. Psychosocial factors associated with lifestyle and nutritional habits were described basing on definitions highlighted in nutritional screening tools, i.e. dietary intake, weight loss, psychological or mood disorders, depression, severity of chronic diseases, impaired ambulation.

The preoperative factors included in the study were compared between the malnourished and well-nourished groups. Factors were investigated further in a logistic regression analysis in each group (group of factors describing a patient's condition and severity of disease, group of laboratory parameters, group of psychosocial factors associated with lifestyle and nutritional habits) to determine correlations between the factors and PA (degree) as a marker of MN standardised for cardiac surgery patients.

6.3.3. Selection of the most accurate malnutrition screening tool for cardiac surgery patients

Nutritional risks were assessed a day before surgery, using MN screening tools: NRS-2002, MUST and MNA-SF. Basing on nutritional risk screenings and their recommendations for the monitoring of nutritional status, patients generating a score of ≥2 in accordance with MUST, a score of ≥3 in accordance with NRS-2002 or a score of ≤7 according to MNA-SF were considered to be malnourished. A screening tool specific to cardiac surgery patients was selected by way of comparison of the screening results against the value of BIA-derived PA (degree), as a marker of MN, standardised for cardiac surgery patients (low PA).

MN screening tools failing to meet the methods of filling in the forms were excluded from the study. It was required to assess the nutritional status of each patient in accordance with all three screening tools. In case of error or inappropriate filling of any of the three forms, an incorrectly filled-in form was removed from the study together with the other two screening tools and excluded from the selection of the MN screening tool specific to cardiac surgery patients.

6.3.4. Procedures for surgery and anaesthesia

The preparation of patients for cardiac surgery and premedication were in compliance with regular procedures followed in the Clinic. The patients were administered sedatives such as benzodiazepines on the evening before surgery and before transport to the operating room. General anaesthesia (endotracheal intubation) was used for all surgeries applied. Benzodiazepines, propofol and fentanyl were used for anaesthetic induction. Fentanyl, propofol, short-acting myorelaxants and volatile anaesthetic agents (sevoflurane) were used to maintain anaesthesia. Surgeries were performed by experienced surgeons in accordance with the regular procedures applied in the Cardiac Surgery Clinic. Cardiac surgeries with CPB were performed in accordance with the standard protocol of CPB, prepared by the VUH SC Second Department of Anaesthesiology and Intensive Care and approved at the Clinic of Anaesthesiology, Intensive Therapy and Pain Treatment. Nonpulsatile pumping and membrane oxygenation were used for CPB during the surgeries. A CPB circuit was primed with Ringer's acetate 1500 ml and 15% monnitol 250 ml, adding to each system cefazolin 1 g. During CPB, a pump flow rate was maintained at 2.2–2.4 l/min per m^2. The mean arterial pressure was maintained at ~60–80 mmHg, minimal venous oxygen saturation – 70%. Blood cardioplegia was used for myocardial protection. Unfractionated heparin was administered to prevent blood clotting during CPB, maintaining the activated coagulation time at a minimum value of 480 seconds. All patients were warmed up to the level of normothermia before the stop of CPB. After CPB, heparin was reversed by the administration of protamine sulphate. Postoperative patients were transferred to the ICU on mechanical ventilation for monitoring their vital functions.

6.3.5. Postoperative treatment procedures

After surgery, all postoperative patients were transferred to the ICU and applied treatment in accordance with therapeutic protocols valid at the VUH SC Second Department of Intensive Care. Postoperative sedation was maintained with propofol infusion at 20–25 μg/kg/min., morphine infusion at 1–2 mg/h; non-steroidal anti-inflammatory drugs (sol. ketolgan 30 mg 2–3 t/24 h) and acetaminophen (0.5–1 g 2 t/24 h) were administered postoperatively as analgesics. Intermittent mechanical ventilation was continued until a patient met the criteria for safe extubation. Red blood cell (RBC) transfusion was applied if the postoperative haemoglobin level fell below 80 g/l. RBC transfusions in case of higher haemoglobin levels as well as intravenous inotropic and vasoactive medications were administered at the doctor's discretion. Artificial nutrition was delivered in accordance with the feeding protocol of the unit. Patients were discharged from the ICU if they were conscious, adequate, breathing spontaneously, hemodynamic, diuretic and glycaemic control did not require intravenous infusions (sympathomimetics, diuretics, insulin), patients had the sinus rhythm or controlled atrial fibrillation, and no symptoms/signs of bleeding were diagnosed.

6.3.6. Methods for determining postoperative complications, mortality and the length of hospital stay after cardiac surgery

The postoperative course of treatment for patients enrolled in phase 2 of the study was assessed perspectively in order to identify postoperative complications, mortality rates and the length of postoperative treatment in cardiac surgery. Postoperative outcomes were recorded in accordance with the 9 standardised indicators recommended in the STS operative-risk model: operative mortality, ischemic (permanent) stroke, renal failure, prolonged ventilation (MV), mediastinitis (deep sternal wound infection), reoperation, major morbidity, length of stay (Table 2).

Table 2. Definitions for the STS clinical outcome endpoints

Clinical outcome	Definition
Operative mortality	Operative mortality includes both (1) all deaths occurring during the hospitalization in which the operation was performed, even if after 30 days; and (2) deaths occurring after discharge from the hospital, but within 30 days of the procedure.
Permanent stroke	Postoperative stroke (i.e. any confirmed neurological deficit of abrupt onset caused by a disturbance in blood supply to the brain that did not resolve within 24 hours.
Renal failure	Acute or worsening renal failure resulting in one or more of the following: 1. Increase of serum creatinine to ≥353.6 mcmol/l with an increase of at least 44.2 mcmol/l or 3x most recent preoperative creatinine level. 2. A new requirement for dialysis postoperatively.
Prolonged ventilation > 24 hours	Prolonged post-operative pulmonary ventilation > 24 hours. The hours of postoperative ventilation time include OR exit until extubation, plus any additional hours following reintubation.
Deep sternal wound infection	Deep sternal wound infection or mediastinitis (according to CDC definition) diagnosed within 30 days of the operation or at any time during hospitalization for the surgery.
Reoperation for any reason	Reoperation for bleeding/tamponade, valvular dysfunction, graft occlusion, other cardiac reason, or non-cardiac reason.
Major morbidity or operative mortality	A composite endpoint defined as any of the outcomes listed in the first six rows of this table.
Short Stay: PLOS < 6 days	Discharged alive and within 5 days of surgery.
Long Stay: PLOS >14 days	Failure to be discharged within 14 days of surgery.

6.4. Statistical analysis of data

A statistical analysis of data was carried out using the Statistical Analysis System SAS 9.2 and Statistical Package for the Social Sciences SPSS 21.0. Quantitative variables were presented as median and quantiles 25 to 75 percent; qualitative indicators are expressed in rates.

Descriptive statistics were used to assess key clinical characteristics. Differences between two independent groups were initially assessed using the Kolmogorov–Smirnov test for testing data normality of two datasets. Taking into account findings of the Kolmogorov–Smirnov test, the differences between the groups were then assessed using the Mann–Whitney–Wilcoxon in case of the abnormal distribution of data or the Student's t-test for normally distributed data. The Fisher's exact test was used to compare the independent qualitative datasets, and the Spearman's correlation coefficient was used to measure a relationship between the variables.

The Receiver Operating Characteristic (ROC) curve analysis was used to determine a critical degree as a marker of MN of the BIA-derived PA, to identify the most accurate nutritional risk screening tool for cardiac surgery patients and to test the relationship between PA and weight loss.

A univariate and multivariate logistic regression analysis was done using the stepwise method to assess preoperative MN, postoperative morbidity and prolonged hospital risk factors. The multivariate logistic regression model used statistically significant risk factors selected stepwise from the univariate logistic regression analysis.

The P value was set at the <0.05 significance level for statistical testing of hypotheses.

7. Research findings

7.1. General characteristics of the population

A total of 712 patients were enrolled in the study; Phase 2 cohorts included 342 cardiac surgery patients (Figure 1).

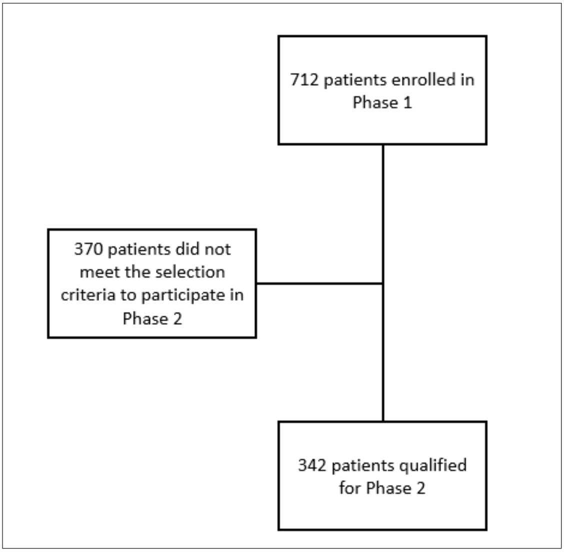


Figure 1. Patient groups and enrolment

7.1.1. General characteristics of the Phase 1 population

The majority of patients enrolled in Phase 1 were men aged 65 at a low operative risk. Two thirds of the patients had coronary artery bypass grafting (CABG) (Figure 2), and only 1% of the patients had reoperative cardiac surgery (Table 3).

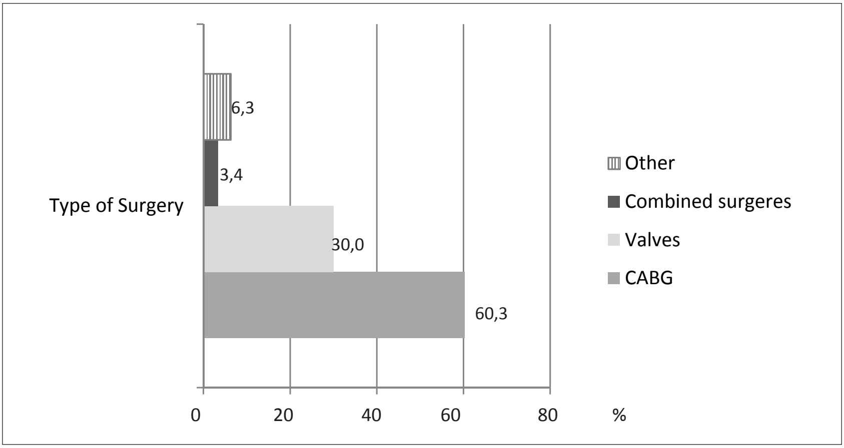


Figure 2. Distribution of Phase 1 patients by type of surgery

Three fourths of the patients were overweight or obese, and only 3 patients had BMI <18.5 kg/m² (Figure 3). On the other hand, a low FFMI (<15 m/kg² and <17 m/kg² for women and men, respectively) was diagnosed in 61 (8,6%) patients (Figure 3).

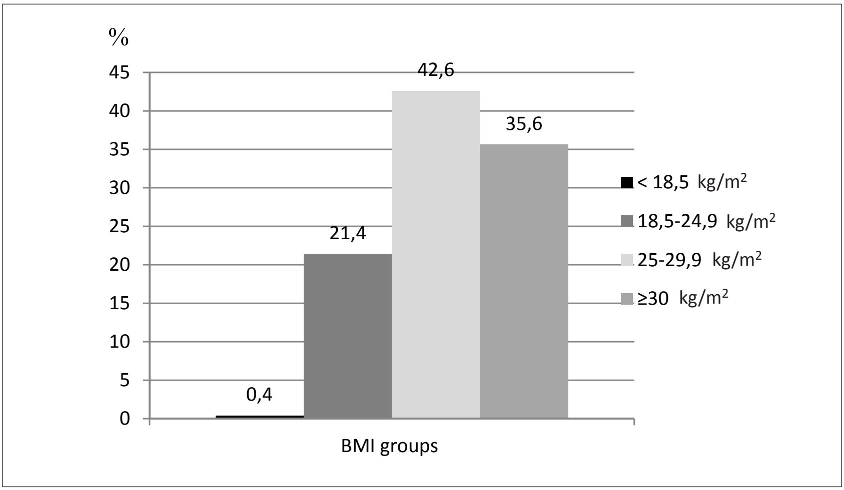


Figure 3. Distribution of Phase 1 patients among Body Mass Index (BMI) groups

The most frequent co-morbidities included primary arterial hypertension, myocardial infarction, rhythm abnormalities, and diabetes. Almost all patients had heart failure (NYHA class II or III), but a severe left ventricular dysfunction (ejection fraction <30%) was diagnosed only in 6% of the patients, and 3.1% of the patients were found to have a severe pulmonary hypertension.

The mean operative time was 205 min. Patients with a prolonged operative time (>6 hours) and complications accounted for 4.7% and 2.4%, respectively. During surgery, CPB was applied to 497 patients (70,9%); the average CPB time – 114 min; aortic clamping time – 73 min.

Intra-aortic balloon counter-pulsation (IABC) was used in 61 patients (8.7%) with a higher risk of perioperative myocardial damage for achieving heamodynamic stabilisation or preventive purposes (Table 3).

7.1.2. General characteristics of the Phase 2 (cohort) population

The selection criteria for enrolment in the Phase 2 cohort were satisfied by 342 patients of Phase 1 (48%). The cohort was composed of patients at a low operative risk (EuroScore II value of 1.46). The majority of the patients were overweight or obese men aged 65 (Table 3).

After assessing the preoperative cardiovascular status, the majority of patients were found to have a heart failure NYHA class III with the LVEF 55% (Table 3).

In comparison with the Phase 1 population, there was no difference in the range of co-morbid abnormalities between Phase 1 and Phase 2 populations, except for preoperative rhythm abnormalities which were at a lower range in the Phase 2 sample (Table 3).

The majority of the patients underwent CABG (Figure 4, Table 3) with a shorter mean time of surgery and CPB as compared with Phase 1 (Table 3).

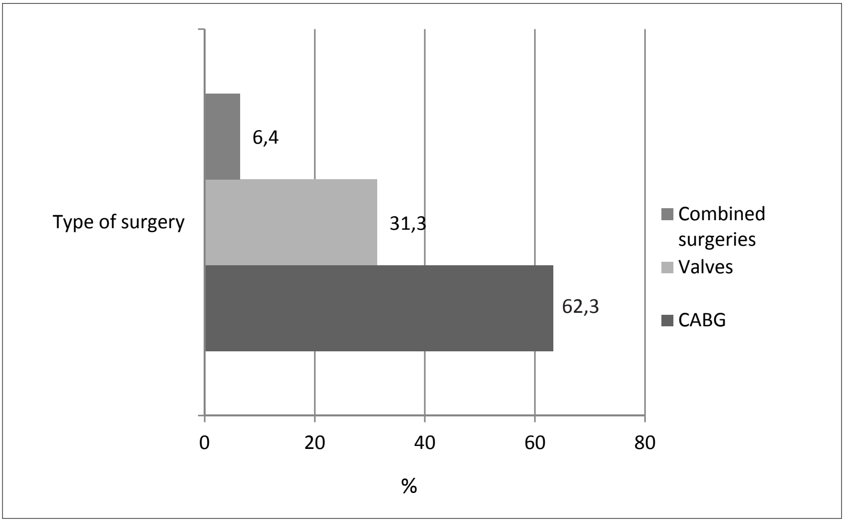


Figure 4. Distribution of Phase 2 patients by the type of surgery

These and other basic characteristics are described in Table 3 below.

Table 3. Comparative characteristics of patients in Phase 1 and Phase 2

Variable	**Phase 1 (n = 712)**	**Phase 2 (n = 342)**	**P**
	n (%) or median [IQR]	n (%) or median [IQR]	
Demographic indicators			
Age (years)	65 [58–73]	65[58–72]	0.202
Gender:			
Male	471 (66.2)	225(65.8)	0.844
Female	241 (33.8)	117 (34.2)	
Indicators of preoperative nutritional status			
Anthropometric indicators			
Body mass index (kg/m²)	28.23 [25.28–31.64]	28.39 [25.47–31.99]	0.303
Body mass index < 18.5	3 (0,4)	2 (0.6)	
Body mass index 18.5–24.9	150 (21.4)	69 (20.5)	
Body mass index 25–29.9 78	298 (42.6)	137 (40.1)	
Body mass index ≥30	249 (35.6)	134 (39.2)	

Table 3 (continuation). Comparative characteristics of patients in Phase 1 and Phase 2

Variable	Phase 1 (n = 712)	Phase 2 (n = 342)	P
	n (%) or median [IQR]	n (%) or median [IQR]	
Bioelectrical impedance analysis data			
Phase angle (°)	5.5 [4.9–6.14]	5.6 [5.08–6.16]	<0.001
Low phase angle (°)	163 (22.9)	61 (17.8)	0.002
Fat-free mass index (kg/m²)	19.26 [17.43–20.86]	19.39 [17.49–20.95]	0.480
Low fat-free mass index	61 (8.6)	27 (7.9)	0.594
Cardiovascular			
Heart function indicators			
NYHA class:			0.142
Class I	6 (0.9)	3 (0.9)	
Class II	77 (11.3)	42 (12.8)	
Class III	562 (82.3)	271 (82.6)	
Class IV	38 (5.6)	12 (3.7)	
Echocardiographic indicators			
Left ventricular ejection fraction	50.43 [45–55]	55 [50–55]	<0.001
Left ventricular ejection fraction <40%	72 (10.6)	0 (0)	<0.001
Left ventricular ejection fraction <30%	41 (6.0)	0 (0)	<0.001
Left ventricular ejection fraction ≤20%	2 (0.3)	0	<0.001
Left ventricle end-diastolic diameter (cm)	5.3 [5.0–5.8]	5.2[4.9–5.7]	<0.001
Dilatation of left ventricle	195 (29.0)	68 (20.9)	<0.001
Pulmonary artery mid-pressure (mmHg)	35 [30–50]	33.5 [27.0–38.8]	<0.001
Pulmonary artery mid-pressure >55 mmHg	22 (3.1)	0 (0)	<0.001
Co-morbidities			
Primary arterial hypertension	554 (78.1)	257(80.4)	0.234
Peripheral arterial disease	96 (13.6)	49 (14.3)	0.524
Chronic obstructive pulmonary disease	36 (5.1)	18 (5.3)	0.814
Renal failure	42 (5.9)	19 (5.6)	0.696

Table 3 (continuation). Comparative characteristics of patients in Phase 1 and Phase 2

Variable	Phase 1 (n = 712)	Phase 2 (n = 342)	P
	n (%) or median [IQR]	n (%) or median [IQR]	
Haemodialysis	3 (0.4)	2 (0.6)	0.611
Cancers	56 (7.9)	21 (6.1)	0.053
Myocardial infarction	255 (36.0)	114 (33.4)	0.176
Myocardial infarction <30 days	84 (11.9)	43 (12.6)	0.554
Myocardial infarction <90 days	69 (9.7)	25 (7,3)	0.067
Rhythm abnormalities	168 (23.7)	67 (19.6)	0.015
Diabetes	151 (21.2)	73 (21.4)	1.000
Diabetes requiring insulin therapy	65 (9.2)	31 (9.1)	0.848
Stroke	69 (9.7)	29 (8.5)	0.288
Hepatic failure	40 (5.6)	19 (5.6)	0.938
Erosive gastritis	170 (24.0)	88 (25.8)	0.272
Smoking	135 (19.0)	70 (20.5)	0.332
Infective endocarditis	11 (1.5)	0(0)	<0.001
Surgery-related			
EuroScore II	1.77 [1.06–2.49]	1.46 [0.97–2.03]	<0.001
Cardiac reoperation	7 (1.0)	0 (0)	<0.001
Intra-aortic balloon counterpulsation	61 (8.7)	0 (0)	<0.001
Type of surgery			
Surgery with CPB	497 (70.9)	342 (100)	
CABG: **with CPB** **without CPB**	423 (60.3) 219 (31.2) 204 (29.1))	213 (62.3) 213 (62.3) 0	0.306 <0.001
Valve surgery: **aortic valve replacement** **mitral valve replacement** **mitral valve reconstruction**	210 (30.0) 135 (19.3) 75 (10.7) 22 (3.1)	107 (31.3) 82 (24.0) 17 (5.0) 8 (2.3)	 0.002 0.011 0.282
combined surgeries	24 (3.4)	22 (6.4)	<0.001
other	44 (6.3)	0	<0.001
Failed surgery	11 (1.5)	0	<0.001
Complicated surgery	17 (2.4)	0	<0.001

Table 3 (continuation). Comparative characteristics of patients in Phase 1 and Phase 2

Variable	Phase 1 (n = 712)	Phase 2 (n = 342)	P
	n (%) or median [IQR]	n (%) or median [IQR]	
Time of surgery (min)	205 [180-240]	202.5 [180-240]	<0.001
Surgery >6 hours	33 (4.7)	0	<0,001
CPB time (min)	114 [92.00-150.75]	105 [88-131]	<0.001
Aortic clamping time (min)	73 [60-98]	69 [56-84]	<0.001

IQR – interquartile range, n – sample, CPB – cardiopulmonary bypass, CABG – Coronary artery bypass grafting, EuroScore II – European System for Cardiac Operative Risk Evaluation.

7.2. Preoperative malnutrition assessment

The preoperative nutritional status was correctly assessed using three screening tools in 549 patients (77.1%). The preoperative MN risk was determined for 4.74% to 47.54% of patients depending on the screening tool form (Table 4).

Table 4. Results of preoperative nutritional status assessment using different screening tools

Nutritional assessment screening tools/questionnaires	Patients (n=549); n (%)
NRS-2002: **No risk of malnutrition**	 119 (21.68)
MUST: **Medium risk of malnutrition** **High risk of malnutrition**	 103 (18.76) 26 (4.74)
MNA-SF: **Risk of malnutrition** **Malnutrition**	 261 (47.54) 122 (22.22)
Malnutrition or risk of malnutrition (in accordance with at least one nutritional status assessment questionnaire)	372 (67.75)

The MNA-SF showed the highest risk for MN. In accordance with the MUST criteria, 23.5% of patients were at the risk of MN, but clinical nutrition was recommended only for 4.74% of the patients. By contrast, NRS-2002 and MNA-SF screening results showed that more than one fifth of the patients required nutritional protocols and clinical nutrition (Figure 5).

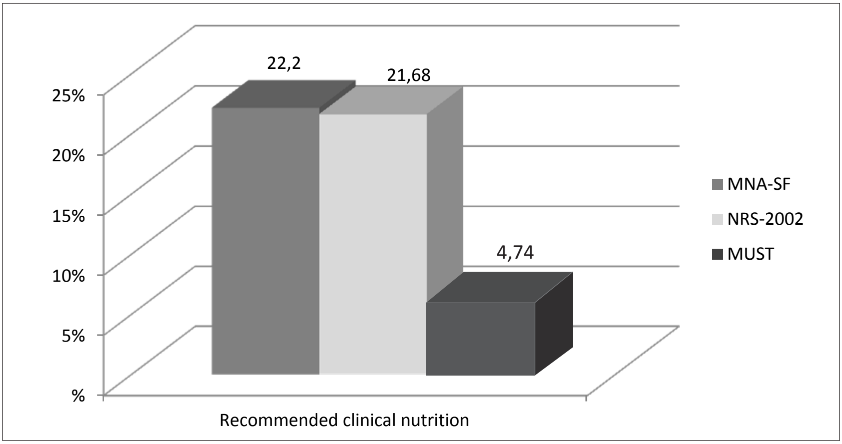


Figure 5. Range of patients (%) recommended clinical nutrition in accordance with the criteria of nutritional screening tools

What is interesting is that at least one of the screening tools used showed that two thirds of the patients were malnourished or at risk of MN (Table 4), even though the majority of the patients were overweight or obese: mean BMI = 28.23 kg/m^2; even 78.2% of the patients had BMI above 25 kg/m^2. By contrast, only 3 patients (0.4%) appeared in the group of malnourished patients by BMI (<18.5 kg/m^2) in accordance with the nutritional status classification, and 8.6% of the patients met the criteria of MN in accordance with a low FFMI (Table 3).

The analysis of the relationship between BIA PA and FFMI and the analysis of BMI showed a positive linear correlation between the above variables. A moderate correlation was found between PA and FFMI ($R = 0.458$ $p < 0.001$), and weak correlation was noted between PA and BMI ($R = 0.100$ $p = 0.08$). ROC analyses revealed a statistically significant correlation between the PA degree and body mass reduction by >5% within 3 months (AUC 0.613, $p = 0.001$).

The initial assessment of PA determinants had been conducted prior to the standardisation of the PA. The PA value was found to decrease gradually each decade ($p < 0.001$) and to be by 0.6 degree less on average in the female group (5.73 ± 0.95 vs. ± 5.13 0.722 $p < 0.001$) (Figure 6). These variables were used for the standardisation of PA. PA was not standardised using BMI due to a low correlation found between BMI and PA.

The rates of PA percentile groups are displayed in Table 5. The patients were proportionally distributed between the groups, from 11.0% (78 patients) in the < 5% group to 59.6% (424 patients) in the < 45% group.

The ROC AUC analysis demonstrated that the presence of MN may be identified on the basis of the cut-off values of all percentile groups, but the most accurate marker of MN, as defined by the FFMI cut-off values for women and men (< 15 (kg/m^2 and < 17 kg/m^2, respectively) was the PA < 15% group (AUC 0.679 PI 95%: 0.603–0.755 $p < 0.001$). The analysis is illustrated in Figure 7.

Table 5. Range of phase angle (PA) percentile groups

PA percentile group	n (%)
PA < 5%	78 (11.0)
PA < 10%	129 (18.1)
PA < 15%	163 (22.9)
PA < 20%	199 (279.9)
PA < 25%	254 (35.7)
PA < 30%	305 (42.8)
PA < 35%	340 (47.8)
PA < 40%	376 (52.8)
PA < 45%	424 (59.6)

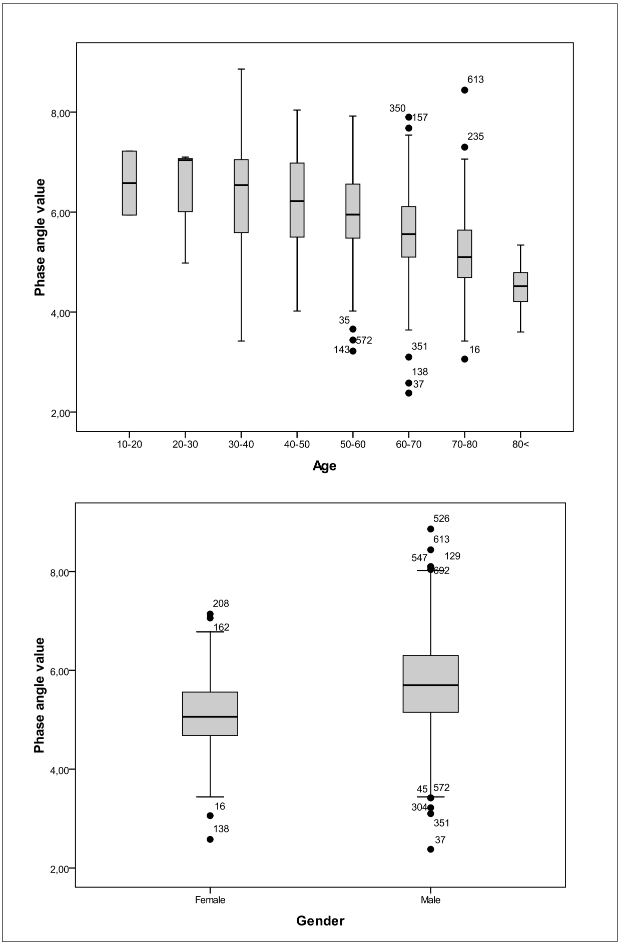
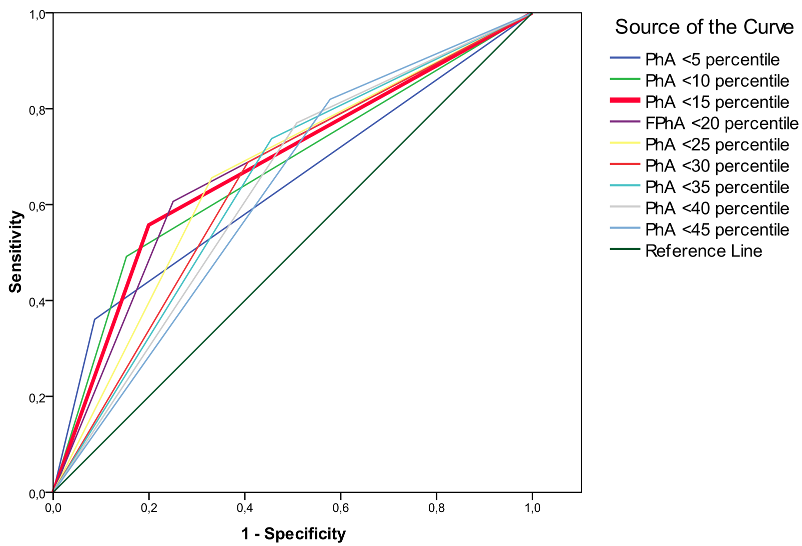


Figure 6. Initial assessment of phase angle (°) determinants



Percentile group	AUC	95% confidence interval		P value
		Lower limit value	Upper limit value	
PA < 5%	0.637	0.555	0.19	<0.001
PA < 10%	0.669	0.590	0.748	<0.001
PA < 15%	0.679	0.603	0.755	<0.001
PA < 20%	0.678	0.604	0.752	<0.001
PA < 25%	0.662	0.590	0.734	<0.001
PA < 30%	0.641	0.570	0.712	<0.001
PA < 35%	0.641	0.572	0.710	<0.001
PA < 40%	0.631	0.563	0.699	0.001
PA < 45%	0.621	0.554	0.688	0.002

Figure 7. Identification of the phase angle percentile group most accurately showing the presence of malnutrition

Basing on the findings, the values of the PA < 15% percentile group (low PA) were selected as the preoperative MN criterion, and patients were then divided into the groups of malnourished and well-nourished.

In order to improve the diagnostics of MN and its accuracy, a table of PA values was made, illustrating the values of the <15 percentile for men and women in each age group (Figure 8).

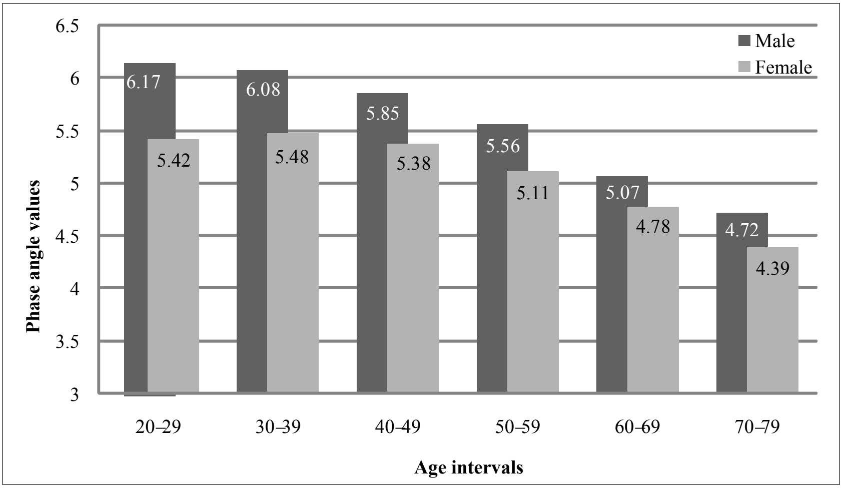


Figure 8. Phase angle (<15 percentile) values standardised to cardiac surgery patients with respect to gender and age group

7.3. Identification of the incidence of preoperative malnutrition in patients before cardiac surgery

Preoperative MN in the given population of cardiac surgery patients was identified using a low PA derived from BIA. MN was diagnosed to 163 patients (22.9%). This figure was lower within the cohort of patients at a low operative risk (17.8%, n = 61).

Phase 1 malnourished patients had a lower FFMI and higher ranges of unintentional weight loss. Low PA ranges were higher in women and in patients with a renal failure. Patients with a heart failure, infective endocarditis, severe left ventricular dysfunction (< 30 %) and the dilatation of the left ventricle were also found to have a lower PA. Patients with a low PA demonstrated higher markers of preoperative inflammation and anaemia and were at a higher operative risk in accordance with the EuroScore II system.

Uninterrupted preoperative hospital stay was longer in the group of malnourished patients, showing a 5.5-day difference (Table 6).

Table 6. Comparison of preoperative indicators in Phase 1 groups distributed by nutritional status

Variables	**Phase 1 (n = 712)** n (%) or median [IQR]			
	Total (n = 712)	Malnourished (n = 163)	Well-nourished (n = 549)	p
Demographic indicators				
Age (years)	65 [58–73]	67 [57–74]	65 [59–73]	0.584
Gender:				0.026
Men	471 (66.2)	96 (58.9)	375 (68.3)	
Women	241 (33.8)	67 (41.1)	174 (31.7)	
Anthropometric indicators				
Body mass index (kg/m²)	28.23 [25.28–31.64]	26.91 [23.8–30.4]	28.52 [25.8–32.0]	0.001
Body mass index < 18.5 kg/m²	3 (0.4)	1 (0.6)	2 (0.4)	<0.001
Body mass index 18.5–24.9 kg/m²	150 (21.4)	54 (33.8)	96 (17.8)	
Body mass index 25–29.9 78 kg/m²	298 (42.6)	60 (37.5)	238 (44.1)	
Body mass index ≥ 30 kg/m²	249 (35.6)	45 (28.1)	204 (37.8)	
Weight loss >5% within 3 months	165 (23.2)	50 (40.3)	115 (27.1)	0.005
Fat-free mass index (kg/m²)	19.26 [17.43–20.86]	17.49 [16.4–19.6]	19.63 [18.0–21.1]	<0.001
Low fat-free mass index	61 (8.6)	34 (20.9)	27 (5.0)	<0.001
Main surgical disease				
3-vessel coronary artery disease	423 (60.3)	87(53.37)	336(61.1)	0.038
Valve disease	210 (30.0)	59 (36.2)	151 (28.1)	0.051
Complex cardiac pathology (valve + ischemic heart disease)	24 (3.4)	4 (2.5)	20 (3.7)	0.623
Other	44 (6.3)	13 (8.0)	31 (5.8)	0.307

Table 6 (continuation). Comparison of preoperative indicators in Phase 1 groups distributed by nutritional status

Variables	Phase 1 (n = 712)			
	n (%) or median [IQR]			
	Total (n = 712)	Malnourished (n = 163)	Well-nourished (n = 549)	p
Cardiovascular indicators				
NYHA class:				<0.001
Class I	6 (0.9)	3 (1.9)	3 (0.6)	
Class II	77 (11.3	15 (9.6)	62 (11.8)	
Class III	562 (82.3)	120 (76.4)	442 (84.0)	
Class IV	38 (5.6)	19 (12.1)	19 (3.6)	
Left ventricle ejection fraction	50.43 [45–55]	55 [40–55]	55 [49–55]	0.055
Left ventricle ejection fraction < 30%	41 (6.0)	17 (11,0)	24 (4.6)	0.003
Left ventricle end-diastolic diameter (cm)	5.3 [5.0–5.8]	5.4 [5-6]	5.3 [4.9-5.8]	0.181
Dilatation of the left ventricle	195 (29.0)	56 (36.6)	139 (26.8)	0.019
Pulmonary artery mid-pressure (mmHg)	35 [30–50]	44 [29.8–60.0]	35 [30–45]	0.057
Co-morbidities				
Primary arterial hypertension	554 (78.1)	118 (72.8)	436 (79.7)	0.063
Peripheral arterial disease	96 (13.6)	23 (14.2)	73 (13.4)	0.787
Chronic obstructive pulmonary disease	36 (5.1)	9 (8.2)	27 (27.8)	0.689
Renal failures	42 (5.9)	19 (11.8)	23 (4.2)	<0.001
Haemodialysis	3 (0.4)	1 (0.6)	2 (0.4)	0.541
Cancers	56 (7.9)	16 (9.9)	40 (7.3)	0.288
Myocardial infarction	255 (36.0)	58 (35.8)	197 (36.0)	0.961
Myocardial infarction <30 days	84 (11.9)	20 (12.3)	64 (11.7)	0.829
Myocardial infarction <90 days	69 (9.7)	20 (12.4)	49 (9.0)	0.193
Rhythm abnormalities	168 (23.7)	47 (29.0)	121 (22.1)	0.070
Diabetes	151 (21.2)	40 (24.7)	111 (20.3)	0.230
Diabetes requiring insulin therapy	65 (9.2)	17 (10.5)	48 (8.8)	0.506
Stroke	69 (9.7)	20 (12.3)	49 (9.0)	0.201
Hepatic failure	40 (5.6)	6 (3.7)	34 (6.2)	0.252
Erosive gastritis, ulceration	170 (24.0)	32 (19.8)	138 (25.2)	0.152
Smoking	135 (19.0)	34 (21.0)	101 (18.5)	0.495
Infective endocarditis	11 (1.5)	6 (3.7)	5 (0.9)	0.022

Table 6 (continuation). Comparison of preoperative indicators in Phase 1 groups distributed by nutritional status

Variables	Phase 1 (n = 712)			
	n (%) or median [IQR]			
	Total (n = 712)	Malnourished (n = 163)	Well-nourished (n = 549)	p
Preoperative course of disease				
Preoperative length of stay	6 [3–9]	12,5 [3.75–19.75]	7 [4–10]	0.02
EuroScore II	1.77 [1.06–2.49]	2.44 [1.12–6.60]	2.00 [1.41–2.96]	<0.000

IQR – interquartile range, n – sample, NYHA – New York Heart Association, EuroScore II – European System for Cardiac Operative Risk Evaluation

There was no difference among groups distributed by nutritional status for patients at a low operative risk (Phase 2), except for gender. MN was more frequently diagnosed for women than for men (Table 7).

Table 7. Comparison of initial preoperative indicators in Phase 2 groups distributed by nutritional status

Variable	Phase 2			
	n (%) or median [IQR]			
	Total (n = 342)	Malnourished (n = 61)	Well-nourished (n = 281)	P value
Demographic indicators				
Age (years)	65 [58–72]	67 [56–71]	65 [58–73]	0.654
Gender: **Men (intragender)** **Women (intragender)**	 225(65.8) 117 (34.2)	 31 (13.8) 30 (25.6)	 194 (86.2) 87 (74.6)	 0.011
Body mass index (kg/m²)	28.39 [25.47–31.99]	27.51 [24.16–31.81]	28.69 [25.64–32.01]	0.110
Body mass index < 18.5 kg/m² **Body mass index 18.5-24.9 kg/m²** **Body mass index 25–29.9 78 kg/m²** **Body mass index ≥ 30 kg/m²**	2 (0.6) 69 (20.5) 137 (40.1) 134 (39.2)	0 (0) 19 (31.1) 20 (32.8) 22 (36.1)	2 (0.6) 50 (14.6) 117 (41.6) 112 (32.7)	0.110

Table 7 (continuation). Comparison of initial preoperative indicators in Phase 2 groups distributed by nutritional status

Variable	Phase 2 n (%) or median [IQR] Total (n = 342)	Malnourished (n = 61)	Well-nourished (n = 281)	P value
Operative risk				
EuroScore II	1.46 [0.97–2.03]	1.96 [1.04–2.28]	1.43 [0.96–1.96]	0.054
Nutritional status indicators				
Weight loss >5% within 3 months	69 (26.5)	20 (40.0)	49 (23.3)	0.016
Phase angle (°)	5.6 [5.08–6.16]	4.54 [4.19–5.08]	5.76 [5.36–6.32]	<0.001
Fat-free mass index (kg/m²)	19.39 [17.49–20.95]	17.49 [16.32–19.15]	19.72 [17.89–21.11]	<0.001
Low fat-free mass index	27 (7.9)	14 (23.0)	13 (4.7)	<0.001
Cardiovascular indicators				
Cardiac function indicators				
NYHA class:				0.756
Class I	3 (0.9)	0 (0)	3 (1.1)	
Class II	42 (12.8)	6 (10.2)	36 (13.4)	
Class III	271 (82.6)	51 (86.4)	220 (81.8)	
Class IV	12 (3.7)	2 (3.4)	10 (3.7)	
Echocardiographic indicators				
Left ventricular ejection fraction (%)	55 [50–55]	55.0 [478–55.0]	55 [50–55]	0.243
Left ventricle end-diastolic diameter (cm)	5.2 [4.9–5.7]	5.2 [5.0–5.6]	5.2 [4.9–5.7]	0.202
Dilatation of the left ventricle	68 (20.9)	12 (20.3)	56 (21.0)	0.914
Co-morbidities				
Primary arterial hypertension	275 (80.4)	49 (80.3)	226 (80.4)	0.986
Peripheral arterial disease	49 (14.3)	12 (19.7)	37 (13.3)	0.226
Chronic obstructive pulmonary disease	18 (5.3)	4 (6.6)	14 (5.0)	0.541
Renal failures	19 (5.6)	7 (11.5)	12 (4.3)	0.056
Haemodialysis	2 (0.6)	1 (1.6)	1 (0.4)	0.326

Table 7 (continuation). Comparison of initial preoperative indicators in Phase 2 groups distributed by nutritional status

Variable	Phase 2			
	n (%) or median [IQR]			
	Total (n = 342)	Malnourished (n = 61)	Well-nourished (n = 281)	P value
Cancers	21 (6.1)	6 (9.8)	15 (5.3)	0.234
Myocardial infarction	114 (33.4)	20 (32.8)	94 (33.6)	0.906
Myocardial infarction <30 days	43 (12.6)	9 (14.8)	34 (12.1)	0.531
Myocardial infarction <90 days	25 (7,3)	5 (8.2)	20 (7.1)	0.787
Rhythm abnormalities	67 (19.6)	14 (23.0)	53 (18.9)	0.474
Diabetes	73 (21.4)	16 (26.2)	57 (20.4)	0.306
Diabetes requiring insulin therapy	31 (9.1)	7 (11.5)	24 (8.6)	0.308
Stroke	29 (8.5)	5 (8.2)	24 (8.6)	1.000
Hepatic failure	19 (5.6)	2 (3.3)	17 (6.1)	0.545
Erosive gastritis, ulceration	88 (25.8)	12 (19.7)	76 (27.1)	0.227
Smoking	70 (20.5)	15 (24.6)	55 (19.6)	0.385

IQR – interquartile range, n – sample, NYHA – New York Heart Association, EuroScore II – European. System for Cardiac Operative Risk Evaluation

7.4. Identification of preoperative malnutrition risk factors

The study covered sixty factors analysed in order to identify relationships with preoperative MN diagnosed using the PA from BIA standardised for cardiac surgery patients. The group of factors describing the patient's status and the severity of disease consisted of thirty-eight preoperative factors: demographic, anthropometric, cardiovascular, and co-morbid. The analysis included ten preoperative laboratory parameters and twelve psychosocial factors related to lifestyle and nutritional habits.

An extensive analysis of preoperative factors, conducted within the framework of the study, revealed a relationship between the preoperatively worsening nutritional status and the cardiovascular system's condition, co-morbidities, appetite, ambulation and the immune system's condition (reflected by laboratory parameters) of patients.

The univariate and multivariate logistic regression carried out using the stepwise method in the group of factors describing the patient's condition and the severity of the disease has revealed that poor kidney function, heart failure in the functional NYHA class IV and mitral valve insufficiency ≥II° increase the odds for MN from 1.8 to 4 times and are associated with the BMI (Table 8). Multivariate stepwise logistic regression in the group of laboratory analyses has shown that the low PA is independently influenced by the haemoglobin levels, platelet count and C-reactive protein (C-RP). It has been calculated that a 30 g/l decrease in haemoglobin concentration and a 33 mg/l elevation in the C-RP level increase the MN risk by 50% (Table 8). Analysis of the psychosocial factors related to lifestyle and nutrition has revealed that the preoperative lack of appetite and impaired ambulation increase the risk of MN two to three times (Table 8).

Table 8. Univariate and multivariate stepwise regression analysis to identify factors associated with preoperative malnutrition diagnosed with phase angle standardised to cardiac surgery patients

Variable	**Odds ratio**			***P***	**Odds ratio**			***P***
	Value	Lower CI 95%	Upper CI 95%		Value	Lower CI 95%	Upper CI 95%	
	Univariate				Multivariate			
Factors determining disease severity								
Gender (male)	0.665	0.464	0953	0.0263				s.i.
Body Mass Index (kg/m²)	0.936	0.901	0.973	0.0008	0.928	0.890	0.968	<0.001
Ischemic heart disease	0.643	0.446	0.927	0.0179				s.i.
Renal failure	3.049	1.616	5.747	0.0006	4.091	1.995	8.389	<.0001
Preoperative hospitalisation	1.037	1.003	1.073	0.0316	1.037	1.001	1.076	0.050
LVEF < 30%	2.564	1.340	4.902	0.0044				s.i.
LV dilatation	1.577	1.078	2.315	0.0192				s.i.
AVI ≥ III°	2.353	1.168	4.739	0.0166				s.i.
MVI ≥ II°	1.842	1.241	2.732	0.0024	1.825	1.182	2.819	0.007
TVI ≥ II°	1.887	1.149	3.096	0.0119				s.i.

Table 8 (continuation). Univariate and multivariate stepwise regression analysis to identify factors associated with preoperative malnutrition diagnosed with phase angle standardised to cardiac surgery patients

Variable	**Odds ratio**			***P***	**Odds ratio**			***P***
	Value	Lower CI 95%	Upper CI 95%		Value	Lower CI 95%	Upper CI 95%	
	Univariate				Multivariate			
Infective endocarditis	4.158	1.252	13.805	0.020				s.i.
NYHA Class IV	3.681	1.898	7.136	<0.001	3.073	1.416	6.668	0.005
Laboratory parameters								
Haemoglobin (g/L)	0.964	0.951	0.976	<.0001	0.967	0.951	0.983	<.0001
Haematocrite	0.889	0.850	0.929	<.001				n.i.
Platelet count 109/L	1.004	1.001	1.007	0.0060	1.004	1.000	1.008	0.0338
Leukocyte count 109/L	1.092	1.013	1.178	0.0218				s.i.
C-RP (mg/L)	1.020	1.008	1.032	0.0007	1.015	1.002	1.028	0.0279
Psychosocial factors related to lifestyle and nutrition								
Decreased food intake (≥ 25 %) within the last week	1.669	1.038	2.681	0.0343				s.i.
Nutritional status:								
Good (1 point)	1.001	0.001	1.667	0.9978				s.i.
Medium (2 points)	3.077	1.603	5.882	0.0007				s.i.
Bad (3 points)	1.795	0.001	4.310	0.1883				s.i.
Disease severity								
Low (1 point)	2.105	1.294	3.165	0.0020				s.i.
Medium (2 points)	1.520	1.010	4.386	0.0469				s.i.
High (3 points)	10.753	0.000	14.925	0.7187				s.i.
Disease-related 5-day starvation	2.169	1.107	100.000	0.0406				s.i.
Lack of appetite:								
moderate loss of appetite	3.690	1.280	3.676	0.0040	1.848	1.068	3.205	0.0280
poor appetite	2.169	1.692	8.065	0.0010	3.030	1.353	6.757	0.0070
Weight loss within 3 months:								
1-3 kg	1.131	0.598	2.140	0.705				n.i.
not aware	2.328	1.333	4.066	0.003				
> 3 kg	1.490	0.876	2.534	0.141				
Impaired ambulation:								
active within a room	3.717	1.393	3.378	0.0006	1.802	1.131	2.874	0.0133
active in bed or chair	1.821	1.486	9.259	0.0050	2.770	1.067	7.194	0.0364

Table 8 (continuation). Univariate and multivariate stepwise regression analysis to identify factors associated with preoperative malnutrition diagnosed with phase angle standardised to cardiac surgery patients

Variable	Odds ratio			*P*	Odds ratio			*P*
	Value	Lower CI 95%	Upper CI 95%		Value	Lower CI 95%	Upper CI 95%	
	Univariate				Multivariate			
Psychological stress or acute disease	1.996	1.217	2.732	0.0036				s.i.
Neuropsychological disorders:								
medium depression/ dementia	1.272	1.149	3.460	0.0141				s.i.
Severe depression/ dementia	1.001	0.338	4.785	0.7219				s.i.

CI – confidence interval, LV – left ventricle, LVEF – left ventricle ejection fraction, AVI – aortic valve insufficiency, MVI – mitral valve insufficiency, TVI – tricuspid valve insufficiency, NYHA Class IV – cardiac functional class based on the New York Heart Association.

7.5. Identification of the most accurate range assessing preoperative malnutrition in cardiac surgery

Identification of the most accurate malnutrition screening tool for cardiac surgery patients

MN was assessed using three MN screening tools, each of which demonstrated different findings (Table 4). In order to identify the most accurate screening tool for the diagnosis of MN in cardiac surgery patients, the BIA-derived PA was used.

Findings of the nutritional status screening, standardised in accordance with the recommendation for the further treatment, revealed that the nutritional status abnormalities for which clinical nutrition is recommended was the least commonly diagnosed with MUST (≥2 points), whereas the range of MN reported by the NRS-2002 (≥3 points) and MNA-SF (≤7 points) questionnaires was similar and exceeded 20% (Figure 9).

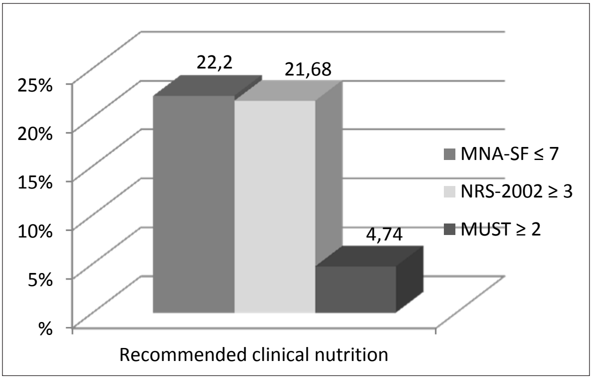


Figure 9. The incidence of MN assessed using the MN screening tools: MNA-SF, NRS-2002, MUST

These standardised values of nutritional status assessment were compared with the BIA-derived PA (low PA) as a marker of MN. A statistical analysis showed the maximum area under the ROC curve for the NRS–2002 questionnaire (AUC = 0.561, p = 0.39) (Figure 10, Table 9).

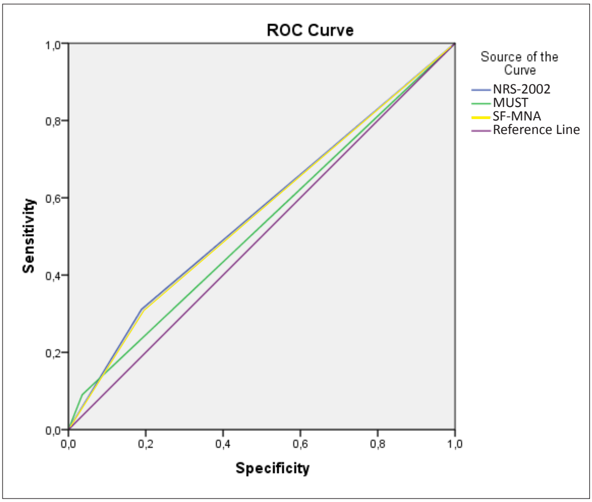


Figure 10. ROC curves for nutriotional status screening questionnaires

Table 9. The area under the ROC curves for nutrition screening tools

Variable	AUC	95% confidence interval		P value
		Lower limit	Upper limit	
NRS-2002	0.561	0.501	0.621	0.039
MUST ≥2	0.527	0.468	0.587	0.357
MNA-SF 7≤	0.558	0.498	0.617	0.052

AUC – area under curve

7.6. Correlations between preoperative malnutrition and postoperative complications

The overall range of postoperative complications (morbidity) in the Phase 2 group of patients was 12.6% (n = 43); malnourished patients had twice the range as compared with well-nourished patients (13 (21.3%) vs. 30 (10.7), p = 0.023) (Table 10).

Table 10. Comparison of ranges of postoperative complications (acc. to STS) and length of hospital stay among the groups distributed by nutritional status

Variable	**Phase 2**			
	n (%) or median [IQR]			
	Total (n = 342)	Malnourished (n = 61)	Well-nourished (n = 281)	P value
Postoperative outcomes under STS criteria				
STS mortality	2 (0.6)	0 (0)	2 (0.7)	1.000
STS stroke	11 (3.2)	3 (4.9)	8 (2.8)	0.421
STS ventilation	17 (5.0)	6 (10.0)	11 (4.0)	0.094
STS mediastinitis	7 (2.0)	1 (1.6)	6 (2.1)	1.000
STS rethoracotomy	18 (5.3)	5 (3.2)	13 (4.6)	0.335
STS renal failure	3 (0.9)	2 (3.7)	1 (0.4)	0.074
STS morbidity	43 (12.6)	13 (21.3)	30 (10.7)	0.023

IQR – interquartile range; STS – Society of Thoracic Surgeons; ICU – Intensive Care Unit.

The multivariate stepwise regression has shown that MN as diagnosed on the basis of a low PA value and the type of surgery (mitral valve reconstruction, combined surgery) are the independent factors of postoperative morbidity. MN (low PA) increases the likelihood of postoperative morbidity 2.5 times, similarly to the combined surgery type which increases the odds of postoperative morbidity 3.370 times (Table 11), whereas the mitral valve reconstruction increases the odds of postoperative morbidity 16.423 times (Table 11).

Table 11. Univariate and multivariate regression of preoperative and operative factors in relation to postoperative morbidity under STS criteria

STS morbidity								
Variable	Odds ratio			P value	Odds ratio			P value
	Value	Lower CI 95%	Upper CI 95%		Value	Lower CI 95%	Upper CI 95%	
	Univariate				Multivariate			
Demographic indicators								
Gender (male)	0.769	0.398	1.482	0.614				n.i.
Age	1.008	0.976	1.041	0.32				n.i.
Body mass index (kg/m²)	1.057	0.992	1.126	0.089				n.i.
Nutritional status indicators								
Fat-free mass index (kg/m²)	0.983	0.857	1.126	0.801				n.i.
Low fat-free mass index	0.542	0.124	2.376	0.417				n.i.
Phase angle	0.818	0.559	1.199	0.303				n.i.
Low phase angle	2.266	1.103	4.657	0.026	2.502	1.183	5.290	0.016
Cardiovascular indicators								
NYHA	0.930	0.443	1.953	0.848				n.i.
Left ventricular ejection fraction (%)	0.994	0.941	1.049	0.819				n.i.
Left ventricle end-diastolic diameter (cm)	0.698	0.416	1.169	0.172				n.i.

Table 11 (continuation). Univariate and multivariate regression of preoperative and operative factors in relation to postoperative morbidity under STS criteria

STS morbidity								
Variable	Odds ratio			P value	Odds ratio			P value
	Value	Lower CI 95%	Upper CI 95%		Value	Lower CI 95%	Upper CI 95%	
	Univariate				Multivariate			
Dilatation of left ventricle	0.782	0.330	1.855	0.577				n.i.
Co-morbidities								
Smoking	1.202	0.561	2.576	0.636				n.i.
Diabetes	1.308	0.624	2.742	0.476				n.i.
Diabetes requiring insulin therapy	1.029	0.342	3.100	0.959				n.i.
Primary arterial hypertension	1.076	0.474	2.440	0.862				n.i.
Peripheral arterial disease	0.958	0.381	2.406	0.927				n.i.
Stroke	1.120	0.370	3.390	0.841				n.i.
Depression	1.069	0.233	4.911	0.931				n.i.
Chronic obstructive pulmonary disease	2.081	0.652	6.640	0.216				n.i.
Renal failure	1.322	0.369	4.739	0.668				n.i.
Haemodialysis	7.071	0.434	115.196	0.169				n.i.
Hepatic failure	1.322	0.369	4.739	0.668				n.i.
Cancers	0.719	0.161	3.201	0.665				n.i.
Gastric erosions, ulcers	0.987	0.474	2.052	0.971				n.i.
Myocardial infarction	9.956	0.482	1.890	0.897				n.i.
Myocardial infarction <30 days	2.055	0.908	4.652	0.084				n.i.
Myocardial infarction <90 days	0.941	0.269	3.287	0.924				n.i.
Rhythm abnormalities	1.281	0.597	2.751	0.525				n.i.
Pre-operative hospitalisation (days)	1.028	0.957	1.104	0.447				n.i.
Operative indicators								
Coronary artery bypass grafting	0.660	0.347	1.256	0.205				n.i.

Table 11 (continuation). Univariate and multivariate regression of preoperative and operative factors in relation to postoperative morbidity under STS criteria

STS morbidity								
Variable	Odds ratio			P value	Odds ratio			P value
	Value	Lower CI 95%	Upper CI 95%		Value	Lower CI 95%	Upper CI 95%	
	Univariate				Multivariate			
Aortic valve replacement	0.820	0.375	1.789	0.617				n.i.
Mitral valve replacement	0.000	0.000	0.001	0.998				n.i.
Mitral valve reconstruction	12.982	2.983	56.501	0.001	16.423	3.671	73.473	<0.001
Combined surgery	2.868	1.056	7.788	0.039	3.370	1.212	9.372	0.020
Duration of surgery (min)	1.013	1.007	1.020	0.000				n.i.
Cardiopulmonary bypass								
Aortic clamping time (min)	1.012	0.999	1.025	0.060				n.i.
CPB time (min)	1.011	1.002	1.019	0.012				s.i.

STS – Society of Thoracic Surgeons, CI – confidence interval, n.i. – not included, s.i. – statistically insignificant, NYHA – cardiac functional class based on the New York Heart Association.

7.7. Correlations between preoperative malnutrition and postoperative length of hospital stay

The length of hospital stay showed that malnourished patients stayed in hospital longer after surgery (14[11–15] vs. 12[11–14], p = 0.036) (Figure 11), but there was no difference between the groups in the average length of stay in the ICU (2[2–4] vs. 2[1–3], p = 0.106) (Table 12).

Although no difference was found in the average length of stay in the ICU, the range of malnourished patients who stayed in intensive care for > 3 days was higher (Table 12). Such patients accounted for one third in the malnourished group versus one fifth in the well-nourished group.

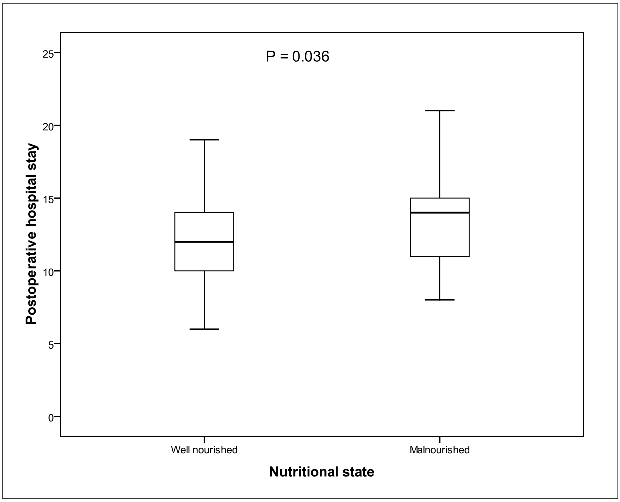


Figure 11. Overall length of postoperative hospital stays in nutritional status groups

Basing on the STS standardised criteria for early postoperative outcomes, only 2 patients (0.6%) were found to have a short hospital stay (< 6 postoperative days) as compared to two fifths of patients (136 patients, or 40.1%) in the Phase 2 cohort who had long hospital stays (>14 postoperative days) (Table 12). Half of malnourished patients were hospitalised for >14 postoperative days. This share was by 13% less in the well-nourished group, but the difference was not statistically significant (Table 12).

The logistic regression analysis has revealed that prolonged hospital stay after cardiac surgery depends on the type of surgery, CPB time and PA value (Table 13). Mitral valve replacement surgery increased the likelihood of prolonged hospital stay 6.113 times compared with patients who underwent other types of cardiac surgery under the STS criteria. One additional minute of CPB increased the odds of prolonged hospital stay 1.009 times (PI: 1.003–1.016, p = 0.006). A one-degree decrease in the BIA-derived PA increased the odds of prolonged hospital stay 1.6 times (PI 1.21–2.14), p = 0.001) (Table 13).

Table 12. Postoperative hospital stays and their comparison between groups divided by nutritional status

Variable	Phase 2			
	n (%) or median [IQR]			
	Total (n = 342)	Malnourished (n = 61)	Well-nourished (n = 281)	P value
Length of postoperative hospital stay under STS criteria				
Short length of stay (< 6 days)	2 (0.6)	0 (0)	2 (0.7)	1.000
Long length of stay (> 14 days)	136 (40.1)	31 (50.8)	105 (37.8)	0.063
Length of postoperative hospital stay				
Postoperative stay (days)	12 [10–15]	14 [11–15]	12 [11–14]	0.036
Postoperative stay in ICU (days)	2 [2–3]	2 [2–4]	2 [1–3]	0.106
Postoperative stay in ICU >3 days	76 (22.2)	20 (32.8)	56 (19.9)	0.029

IQR – interquartile range; STS – Society of Thoracic Surgeons; ICU – intensive care unit

Table 13. Univariate and multivariate regression analysis of risk factors for prolonged postoperative hospital stay

Prolonged hospital stay (>14 days) after cardiac surgery								
Variable	Odds ratio			P value	Odds ratio			P value
	Value	Lower CI 95%	Upper CI 95%		Value	Lower CI 95%	Upper CI 95%	
	Univariate				Multivariate			
Demographic indicators								
Gender (male)	0.540	0.343	0.850	0.008				s.i.
Age	1.015	0.993	1.037	0.185				n.i.
Body mass index (kg/m²)	1.020	0.976	1.066	0.381				n.i.
Nutritional status indicators								
Fat-free mass index (kg/m²)	0.897	0.816	0.985	0.023				s.i.
Low fat-free mass index	1.037	0.466	2.309	0.930				n.i.
Phase angle (°)	1.623	1.225	2.105	0.001	1.6	1.21	2.14	0.001
Low phase angle	1.732	0.992	3.024	0.053				n.i.

Table 13 (continuation). Univariate and multivariate regression analysis of risk factors for prolonged postoperative hospital stay

Prolonged hospital stay (>14 days) after cardiac surgery								
Variable	Odds ratio			P value	Odds ratio			P value
	Value	Lower CI 95%	Upper CI 95%		Value	Lower CI 95%	Upper CI 95%	
	Univariate				Multivariate			
Cardiovascular indicators								
NYHA	1.192	0.713	1.993	0.503				n.i.
Left ventricle end-diastolic diameter (cm)	0.862	0.612	1.213	0.393				n.i.
Dilatation of left ventricle	1.414	0.824	2.426	0.209				n.i.
Left ventricular ejection fraction (%)	0.971	0.936	1.008	0.120				n.i.
Co-morbidities								
Smoking	0.543	0.306	0.961	0.036				s.i.
Diabetes	1.083	0.640	1.834	0.767				n.i.
Diabetes requiring insulin therapy	1.113	0.526	2.353	0.779				n.i.
Primary arterial hypertension	0.774	0.451	1.327	0.351				n.i.
Peripheral arterial disease	1.302	0.707	2.398	0.396				n.i.
Stroke	1.265	0.588	2.723	0.574				n.i.
Chronic obstructive pulmonary disease	1.563	0.604	4.045	0.357				n.i.
Renal failure	2.196	0.859	5.609	0.100				n.i.
Haemodialysis	0.000	0.000	0.001	0.999				n.i.
Hepatic failure	1.751	0.692	4.429	0.237				n.i.
Cancers	1.407	0.581	3.410	0.450				n.i.
Erosive gastritis, ulceration	0.779	0.471	1.290	0.332				n.i.
Myocardial infarction	0.939	0.592	1.490	0.790				n.i.
Myocardial infarction <30 days	1.114	0.582	2.131	0.745				n.i.
Myocardial infarction <90 days	0.571	0.232	1.407	0.223				n.i.
Rhythm abnormalities	1.408	0.821	3.412	0.214				n.i.
Pre-operative hospitalisation (days)	1.025	0.975	1.078	0.336				n.i.

Table 13 (continuation). Univariate and multivariate regression analysis of risk factors for prolonged postoperative hospital stay

Prolonged hospital stay (>14 days) after cardiac surgery								
Variable	Odds ratio			P value	Odds ratio			P value
	Value	Lower CI 95%	Upper CI 95%		Value	Lower CI 95%	Upper CI 95%	
	Univariate				Multivariate			
Operative indicators								
Coronary artery bypass grafting	0.575	0.368	0.889	0.015				s.i.
Aortic valve replacement	0.897	0.539	1.495	0.677				n.i.
Mitral valve replacement	7.765	2.187	27.567	0.002	6,113	1.684	22,189	0.006
Mitral valve reconstruction	0.000	0.000	0.001	0.999				n.i.
Combined surgery	1.052	0.437	2.534	0.910				n.i.
Aortic clamping time (min)	1.010	1.001	1.019	0.038				n.i.
CPB time (min)	1.009	1.003	1.016	0.005	1.009	1.003	1.016	0.006
Duration of surgery (min)	1.010	1.005	1.014	<0.001				n.i.

IQR – interquartile range, n – sample, NYHA – New York Heart Association, EuroScore II – European System for Cardiac Operative Risk Evaluation, CPB – cardiopulmonary bypass.

8. Discussion of the findings

MN is defined as a nutritional state in which an imbalance of energy, protein and other nutrients causes measurable adverse effects on the shape of tissues and/or body (size, composition), body function and clinical outcomes.

MN has been recently identified as a public health problem in many developed and developing countries. The identification of the real range of MN is difficult in any country due to the lack of a universal method for the detection of MN. Being particularly widespread among ill patients, MN in hospitals and care homes may be several times higher than the community levels.

Our data confirm the hypothesis that the preoperative PA value derived from BIA can objectively distinguish malnourished from well-nourished patients undergoing cardiac surgery. Associations between low PA and low FFMI, BMI and unintended weight loss by >5% suggest that MN and low PA are interrelated. A PA lower than the 15th percentile identified 22.9 % of the patients as malnourished. As a result, those with a PA value lower than the 15th percentile had a higher risk of postoperative morbidity. Strict postoperative outcome definitions rendered by the STS were used to elude outcome variability and to objectify the evaluation. The prevalence of post-operative morbidity was two times higher in the malnourished group than in the well-nourished group (21.3% vs. 10.7%, $p = 0.023$). MN was associated with the overall postoperative morbidity but not with each STS-defined endpoint separately. This might be because the prevalence of each individual outcome was too low in our population.

The evaluation of hospitalisation length showed a tendency of prolonged postoperative hospitalisation (>14 days) rate (31 [50.8%] vs. 105 [37.8%], $p = 0.063$) in the malnourished group. The further analysis of hospitalisation length revealed statistically significant differences in the total time spent in the hospital postoperatively (median [IQR]: 14 vs. 12, $p = 0.036$). The dissertation thesis found out that a one-degree decrease in BIA-derived PA increased the odds of prolonged hospital stay 1.6 times, proving that the deteriorating preoperative status prolongs the postoperative hospital stay (Van Venrooij LM, 2008; 2011; Visser M, 2012; Lim SL, 2012).

The cardiac surgery population is very susceptible to MN; however, it is rarely detected. While it is relatively easy to suspect MN in patients with severe heart failure and cardiac cachexia (Pathirana AK, 2014), the problematic group of patients, in terms of MN detection, are those with the second and third NYHA class heart failure and, as a result, retention of water and an increased body weight. The median BMI in our study group was 28.23 kg/m^2, whereas the ESPEN diagnostic criteria suggest a BMI lower than 18.5 kg/m^2 as one of the MN markers. There were only 3 patients (0.4%) meeting this criteria. Unintended weight loss, the next suggested marker, is not accurate because patients rarely recall how many kilograms of weight they have lost; most of them do not keep the track of their weight at all. In light of these recommendations, FFMI is calculated only if unintended weight loss is reported. Low FFMI was diagnosed only for 8.6 % of patients. Overall, there were considerably less patients who would be considered malnourished using the ESPEN MN criteria than the percentage identified when using the low PA from BIA. These patients are not yet in such an advanced stage of MN compared to the cachectic ones. However, they ought to be diagnosed and accounted for preoperatively. Therefore, we propose the usage of PA to detect the first alterations of the nutritional status.

There is no approved and recommended cut-off value of PA for the diagnosis of MN. However, it is pointed out that the classification value should be different in various chronic conditions. To determine whether the patient is in a good nutritional state or not, researchers have to make their own cut-off points (Visser M, 2012; Lee JE, 2015). Most of these cut-off points are the values with the highest predictive accuracy and specificity for adverse clinical outcomes. However, one size does not fit all. Age, gender and BMI are the primary determinants of PA in healthy subjects (Barbosa–Silva MC, 2005). Having this evidence in mind, PA should be stratified in accordance with its determinants. In our study, PA was stratified by age and gender, because significant differences in the PA value were detected only among these determinants. These results are consistent with the results of the study by Paiva et al. (2012). Healthy subjects' age and gender reference values of PA were used to produce standardised measurements (Bosy-Westphal A, 2006). The standardised cut-off point of MN used in different studies varies, ranging from the 5th to the 20th percentile. In our study, patients who had a value lower than the 15th percentile or (-)1 standard deviation of the subgroup in question were classified as malnourished and accounted for 163 (22.9 %) of the patients.

We propose the use of the percentile method for PA standardisation. The standardisation process of PA measurements allows accounting for different reference values of different patient subgroups. To perform the standardisation, one has to use the equation: standardised PA = observed PA – mean PA (reference) / standard deviation PA (reference) (Cardinal

TR, 2010). However, the calculations of this ratio require looking into reference values each time. We propose to have the reference values stratified by age and gender in a diagram (Figure 1). This diagram would be composed of PA reference values plotted along the axis scaled for different age subgroups. To determine if the patient is malnourished and at a risk of postoperative morbidity, a physician has to use the diagram and to find whether the patients' PA value is below the 15^{th} percentile in the age and gender group. This diagram is easy to use and less complicated to interpret.

This study investigated the possible risk factors of preoperative MN in a group of cardiac surgery patients. Due to a vast variety of variables they were divided into three groups: the co-morbidity and disease-related group, laboratory values and psychosocial and lifestyle factors as described in the current research on MN development (Saunders J, 2010). All three groups were comprised of variables which were found to be statistically significant in the univariate regression analysis of low PA risk factors. A further analysis of the compounds of each group revealed the main risk factors of MN for cardiac surgery and, most importantly, provided the basis for early MN recognition and prevention for these patients. The results are concordant with the main mechanisms responsible for the development of MN and are discussed in literature: metabolic dysfunction and malabsorption, insufficient diet and the loss of nutrients via the digestive or urinary tracts (von Haehling S, 2008).

Amongst the co-morbidities and other disease-related factors, the most potent predictors of MN were renal and heart failure (Tevik K, 2015; Dumler F, 2005). Both of these conditions can be either the cause or the consequence of MN. Malnourished patients often have a decreased cardiac muscle mass, which results in a decrease of cardiac output and reduced renal perfusion. Furthermore, energy, micronutrient and electrolyte deficiencies cause changes in cytokines, glucocorticoids, insulin and insulin-like growth factors, which also result in decreased cardiac function. Congestive heart failure further reduces dietary intake and appetite sensation, creating the pathophysiological *circulus vitiosus* (Cicoira M, 2011).

There is an increasing evidence that neurohormonal and immune abnormalities play a crucial role in cardiac cachexia (von Haehling S, 2011). Studies have shown that this may be linked to raised plasma levels of inflammatory cytokines, such as tumour necrosis factor alpha, a possible result of cell hypoxia in heart failure (Hasper D, 1989). Laboratory values related to MN were blood serum levels of haemoglobin, CRP and platelet count. These relationships reflect the multifactorial genesis of MN (Jensen GL, 2010). The shortage of nutrients is reflected by the suppression of erythropoesis and thrombopoesis (Thakur N, 2014). The increase of CRP levels is related to the chronic inflammation state of the undernourished tissues. All of these findings are concordant with the research on the origins of MN, published in the American Society for Parenteral and Enteral Nutrition (ASPEN) recommendations (Jensen GL, 2010). Therefore, it is important to take into account these factors whilst preparing a patient for cardiac surgery and to adjust the nutrition care, which has been shown to increase the PA (Richter E, 2012).

Psychosocial and lifestyle alterations add up to the complex nature of MN. In our study, psychological stress and neuropsychological problems, such as dementia or depression, are reported as the risk factors of low PA (Ringaitienė D, 2015). These findings are in line with the conventional risk factors of MN. However, these variables are not independent from the mobility and food intake of the patient (Cicoira M, 2011). This emphasises the strength of the relationship between these conditions and implies a need for the proper psychological screening of patients before surgery.

This study investigated that a low preoperative PA is an indicator of malnutrition and leads to adverse outcomes in cardiac surgery patients, therefore it is crucial to identify the modifiable risk factors at an early stage of preoperative management. MN risk factors comprise three different clinical groups: psychosocial and lifestyle factors, laboratory findings and disease-associated factors. The patients who are most likely to be malnourished are those with severe heart failure, valve pathology, insufficient renal function and high inflammatory markers. Also these patients have decreased mobility and food intake before surgery.

9. Conclusions

1. A phase angle determined by bioelectrical impedance analysis is an indicator of nutritional status with the cut-off value of <15 percentile being a marker of malnutrition.
2. The most accurate screening tool to detect malnutrition risks in cardiac surgery patients is the Nutritional Risk Screening 2002 (NRS-2002) which may be used as an auxiliary tool for assessing nutritional status in cardiac surgery patients.
3. Malnutrition detected by bioelectrical impedance analysis derived phase angle is a more frequently diagnosed preoperative pathology in comparison with low fat-free mass index and body mass index and is diagnosed to one fourth of cardiac surgery patients and one sixth of low-risk cardiac surgery patients.
4. Preoperative malnutrition is associated with the structural and functional affection of the heart, co-morbidities, appetite, mobility and the immune system condition in cardiac surgery patients.
5. Preoperative malnutrition affects the overall postoperative morbidity leading to higher rates of early postoperative complications and prolongs the hospitalization length after cardiac surgery in spite of no association with operative mortality.

10. Practical recommendations

1. Preoperative assessment of nutritional status is recommended in order to reduce the range of postoperative complications and the length of hospital stay.
2. It is recommended to assess nutritional status in cardiac surgery using the method of bioelectrical impedance analysis or the Nutritional Risk Screening 2002 (NRS-2002).
3. For the purpose of accurate and early diagnostics of malnutrition, it is recommended to pay special attention to cardiac surgery patients with the following risk factors for malnutrition: heart failure in the functional NYHA class IV, faulty heart valves (particularly the mitral valve insufficiency ≥II°), preoperative renal failure, a low BMI or the loss of weight, the lack of appetite, impaired mobility, anemia and the elevated C-RP level.
4. Once malnutrition or risks for malnutrition are diagnosed, it is recommended to inform the clinical nutrition team and/or to establish protocols for nutritional monitoring and dietary adjustments.
5. Malnutrition prevention is recommended by encouraging patients to eat the whole portion served, ensuring support at mealtimes (for those who need it) and creating a cosy and comfortable environment for eating.
6. Within the framework of preoperative malnutrition prevention, to encourage patients to engage in physical activity or exercise preoperatively and apply early postoperative rehabilitation in cardiac surgery.

11. Publications and reports by the author of the doctoral dissertation

11.1. Publications

1. **Ringaitienė D**, Vicka V, Gineitytė D, Norkienė I, Šipylaitė J, Irnius A., Ivaškevičius J. Malnutrition assessed by phase angle determines outcomes in low-risk cardiac surgery patients. Clinical Nutrition. 2016 Feb 18. pii: S0261-5614(16)00067-4. doi: 10.1016/j.clnu.2016.02.010. *(ISI).*
2. **Ringaitienė D**, Vicka V, Gineitytė D, Šipylaitė J, Irnius A, Ivaškevičius J. Preoperative risk factors of malnutrition for cardiac surgery patients. Acta Medica Lituanica. 2016, Vol. 24, No. 2. P. 99-109. doi: http://dx,doi,org/10,6001/actamedica.v23i2,3326.
3. **Ringaitienė D,** Gineitytė D, Vicka V, Šipylaitė J, Ivaškevičius J, Stukas R. Importance of malnutrition for cardiac surgery patients. Visuomenės Sveikata 2015, Annex 1, pp. 5–11.
4. **Ringaitienė D,** Norkienė I, Žvirblis T, Šipylaitė J, Irnius A, Ivaškevičius J. Impact of malnutrition on postoperative delirium development after on-pump coronary artery bypass grafting. Journal of Cardiothoracic Surgery. 2015 May 20; 10:74. doi: 10.1186/s13019-015-0278-x. *(ISI).*

11.2. Scientific reports

1. **Ringaitienė D**, Gineitytė D, Vicka V, **Šipylaitė** J, Ivaškevičius J. Malnutrition assessed by phase angle determines outcomes in low-risk cardiac surgery patients**.** The International Symposium on Intensive Care and Emergency Medicine (ESICEM), Brussels, Belgium, 2016 March 15–18.

2. **Ringaitienė D**, Gineitytė D, Vicka V, Šipylaitė J, Ivaškevičius J. Bioelectrical Impedance Phase Angle as Indicator of Adverse Clinical Outcomes and Prolonged Hospitalization in Patients Undergoing Cardiac Surgery. Annual meeting of the European Association of Cardiothoracic Anesthesiologists (EACTA'15), Gothenburg, Sweden, 2015 June 24–26.

3. **Ringaitienė D**, Gineitytė D, Vicka V, Šipylaitė J, Ivaškevičius J. Preoperative phase angle: relation with outcome after cardiac surgery. Annual Congress of the European Society of Clinical Nutrition and Metabolism (ESPEN 15), Lisbon, Portugal, 2015 September 05–08. *(Publication of interim research findings).*

4. **Ringaitienė D**, Gineitytė D, Vicka V, Šipylaitė J, Ivaškevičius J. Malnutrition Screening Tool Accuracy in Patients Scheduled for Cardiac Surgery. Awarded to the ESPEN 2014 Travel fellowship. The ESPEN 2015 (European Society of Parenteral and Enteral Nutrition) congress. Geneva, Switzerland, 2014 September 06–09. *(Publication of interim research findings).*

5. **Ringaitienė D**, Gineitytė D, Vicka V, Šipylaitė J, Ivaškevičius J. The bioelectrical impedance phase angle as an indicator of malnutrition and adverse clinical outcomes in cardiac surgery patients. The international conference "Evolutionary medicine: perspectives in understanding health and disease", Vilnius, Lithuania, 2014 May 27 – June 30. Awarded under nomination "The Best E-Report". *(Publication of interim research findings).*

6. **Ringaitienė D**, Gineitytė D, Vicka V, Šipylaitė J, Ivaškevičius J. Prognostic value of preoperative bioelectrical impedance phase angle on hemotransfusion after cardiac surgery, ESICM LIVES 2014, 27th Annual Congress. Barcelona, Spain, 2014 September 27 – October 01.

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2013 – present	Member of the European Society for Clinical Nutrition and Metabolism (ESPEN)

Other publications

1. Norkienė I, **Ringaitienė D**, Ručinskas K, Samalavičius R, Baublys A, Miniauskas S, Sirvydis V. Intra-aortic balloon counterpulsation in decompensated cardiomyopathy patients: bridge to transplantation or assist device. Interactive Cardiovascular and Thoracic Surgery. 2007 Feb; 6(1): 66–70. PMID: 17669772.

2. Norkienė I, **Ringaitien**ė **D**, Misiūrienė I, Samalavičius R, Bubulis R, Baublys A, Uždavinys G. Incidence precipitating factors of delirium after coronary artery bypass grafting. Scandinavian Cardiovascular Journal, 2007; 3 (41) 180–185. PMID: 17487768

3. Norkienė I, **Ringaitien**ė **D**, Kuzmickaitė V, Šipylaitė J. Incidence and risk factors of early delirium after cardiac surgery. Biomed Res Int 2013; 2013: 323491. doi: 10.1155/2013/323491. Epub 2013 Sep 12.

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