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Association between preoperative nutritional status and postoperative delirium in individuals with coronary artery bypass graft surgery: A prospective cohort study

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ABSTRACT

Objectives: The prevalence of delirium and undernutrition are both relatively high subsequent to coronary artery bypass graft (CABG) surgery. The aim of this study was to evaluate the association between preoperative malnutrition and the occurrence of delirium after CABG surgery.
Methods: In this prospective cohort study, body mass index, mid-upper arm circumference, triceps skinfold, and adductor pollicis muscle thickness of 398 adult patients before CABG surgery were measured by a single trained dietitian. Also, Nutritional Risk Screening 2002 (NRS-2002) and subjective global assessment (SGA) were obtained from patients. Delirium was defined by the confusion assessment method for the intensive care unit. SPSS software was used for performing the statistical analyses. Logistic regression analysis was applied to examine the effect of various factors on the development of delirium.
Results: Postoperative delirium was detected in 17% of patients (n = 68). Multivariate regression analysis adjusted by other risk factors indicated that risk for delirium was 1.56-fold higher in patients with NRS-2002 >3 (odds ratio [OR], 1.56; 95% confidence interval [CI], 1.20–3.24; $P = 0.001$). Severe undernutrition at admission as assessed by SGA was independently associated with the occurrence of delirium (OR, 2.58; 95% CI, 1.02–3.48; $P = 0.005$). Risk for delirium was 1.26-fold higher in patients with adductor pollicis muscle thickness <15 mm (OR, 1.26; 95% CI, 1.02–3.14; $P = 0.02$).
Conclusions: Since the prevalence of delirium is relatively high in CABG surgery and undernutrition is related to postoperative delirium, considering nutrition status with NRS-2002, SGA, or adductor pollicis muscle thickness before surgery could decrease the risk for postoperative delirium.

Introduction

Delirium is defined by the acute onset of fluctuating cognitive impairment and a disturbance of consciousness with reduced attention. Delirium is associated with frequent associated perceptual abnormalities, sleep–wake cycle disturbances, disorganized thought process, and abnormal psychomotor activity [1,2]. Postoperative delirium usually develops shortly after surgery and lasts for a few hours up to few days. It leads to adverse patient outcomes,

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increased hospital length of stay, less likelihood of being discharged from the hospital, decreased health-related quality of life, lowered functional abilities, higher postoperative resource use, and long-term mortality [2,3]. Many predisposing factors for postoperative delirium have been recognized. These include advanced age, illness severity, infection, cognitive impairment, visual or sensory impairment, alcohol abuse, and some electrolyte imbalances [4,5]. Malnutrition or nutritional deficiency is one of the risk factors proposed for delirium in older individuals in long-term care [6]. Additionally, malnutrition is a well-established and common condition in patients undergoing cardiac surgery [7,8]. In these patients, the prevalence of malnutrition varies and ranges from 3% to 47%, depending on the criteria used to determine it [9]. It has been reported that disease-related undernutrition is associated with higher postoperative risks for infectious and noninfectious complications, increased morbidity and mortality, impaired wound healing, and prolonged hospital stay in patients undergoing cardiac surgery [10–12]. Micronutrients and some vitamin deficiencies such as niacin or thiamine are known to have an effect on delirium onset due to impaired neurotransmission [13]. As undernutrition is prevalent in hospitalized patients, evaluating nutritional status could decrease adverse outcomes. Nutrition screening is a rapid procedure in which simple questions are used to detect who is malnourished or who is at risk for malnutrition to determine whether a detailed nutrition assessment is needed. Nutrition screening methods include the Nutritional Risk Screening-2002 (NRS-2002), the Malnutrition Screening Tool, and the Malnutrition Universal Screening Tool. A 2015 study showed that malnutrition defined by the NRS-2002 was an independent, preoperative risk factor of postoperative delirium that can be applied after coronary artery bypass graft (CABG) surgery [14]. Nutrition assessment, which is followed by nutrition screening, is a method that is applied by clinicians to diagnose the presence of malnutrition, determine its severity, and plan the interventions and follow-ups. Subjective global assessment (SGA) and the Mini Nutritional Assessment (MNA) are two widely applied assessment tools in this regard. A study on patients with hip fracture surgery showed that poor nutritional status measured by MNA Short Form (MNA-SF) was associated with the occurrence of postoperative delirium [15]. Because the prevalence of delirium and undernutrition are both relatively high after CABG surgery, and the relation between nutritional assessment tools and some anthropometric measurements in this group of patients has not been evaluated yet, the aim of the present study was to investigate whether SGA, NRS-2002, body mass index (BMI), mid-upper arm circumference (MAC), triceps skinfold (TSF), and adductor pollicis muscle (AMP) thickness were in association with the occurrence of postoperative delirium.

Methods

Study design and participants

This observational, single-center, prospective cohort study was approved by the local ethics committee and performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. From May 2017 to October 2018, patients referred to the Shahid Lavasani Hospital for open heart surgery were checked for eligibility criteria and selected with convenience sampling. The criteria for inclusion in the study included ≥18 y of age and undergoing elective CABG surgery with or without valvular procedure. Exclusion criteria included patients with preoperative diagnosed delirium, mental disease, dementia, emergency surgery, and death before 24 h in the intensive care unit (ICU). Of the 435 patients enrolled in the study 398 completed it. Written informed consent was obtained from all patients or their surrogates.

General characteristics

Participants underwent a comprehensive assessment 1 d before surgery. The assessment included demographic and general clinical characteristics such as age,; sex,; level of education; type of surgery (i.e., isolated CABG surgery with single-vessel disease, isolated CABG surgery with two-vessel disease, isolated CABG surgery with three-vessel disease, and valvular plus CABG surgery); and comorbidities including diabetes mellitus, hypertension, and hyperlipidemia. Subjective assessment using the SGA and NRS-2002 questionnaires and objective assessment through anthropometric measurements were done for all patients by a single trained dietitian to minimize errors in measurement.

Anthropometric measurements

Anthropometric measurements were weight, height, MAC, TSF, and AMP thickness. Participants were measured without shoes and wearing light clothes using digital scales and a portable stadiometer. Height and weight were measured to the nearest 1 cm and 0.1 kg, respectively. BMI was calculated as weight (kg) divided by the square of height (m). The MAC was the circumference of the upper arm at that same midpoint measured with a non-stretchable tape. The mid-arm muscle circumference (MAMC) was the circumference of the upper arm muscle at the same midpoint calculated using the MAMC (cm) = MAC (cm) − [$\pi \times$ TSF (cm)] formula or using a monogram. The measurement of TSF was taken with the individual standing upright and arms hanging down loosely. The skinfold was pulled away from the muscle and measured with the calipers, taking a 4s reading after the calipers were released. The measuring point was halfway between the olecranon process of the ulna and the acromion process of the scapula. Measurement of APM thickness was done by a caliper (Vogel, Germany) in the dominant hand. It was measured with the individual seated with the elbow flexed to approximately 90 degrees over the chair handle. The caliper was applied across the APM situated in a triangle formed by the extended thumb and the index finger, with a 10 g/mm pressure. The average of three consecutive measurements was considered as a measure of APM thickness for each individual.

NRS-2002

Nutritional risk was evaluated by the NRS- 2002 form proposed by the European Society for Clinical Nutrition and Metabolism for hospitalized patients within 1 d before surgery [16]. NRS-2002 form consists of two parts. In the first part, the severity of the disease, reduction of food intake, and weight loss within the previous 3 mo are questioned. If none of the questions are answered in the positive, the second part is not completed. If there was even one positive answer, the second part of the questionnaire is completed. In this section, patients are evaluated regarding malnutrition and its severity. To assess malnutrition, patients are scored based on BMI, recent weight loss percentage, and the recent reduction in food intake. The score of the severity of disease and age (>70 y) is added to get the final score. The total score is in the range of 0 to 7. Patients with a score of ≥3 are considered at risk for malnutrition.

SGA

Nutrition assessment was evaluated by SGA 1 d before surgery [17]. To perform the SGA, patients answered questions about weight loss, eating habits, gastrointestinal symptoms, functional capacity, and stress imposed by the disease. Also, physical examination to find loss of subcutaneous fat (measured in the orbital and triceps region and the midaxillary line at the level of the lower ribs) and muscle waste (measured in the temple, clavicle, shoulder, scapula, quadriceps, and back of hand areas) was performed on all patients. Categorization of SGA was as follows: well nourished (A), moderately malnourished (B), and severely malnourished (C).

Delirium assessment

In the present study, delirium development in the ICU was screened routinely according to Confusion Assessment Method for the ICU (CAM-ICU) criteria with a two-step method. The first step is to assess patient's consciousness using the Richmond Agitation-Sedation Scale (RASS) after surgery [18]. The RASS is a 10-point sedation scale that measures level of consciousness after surgery. If a patient's RASS score is from −3 to +4, the second step is performed. If the RASS score is −4 (responsive only to physical stimulus) or −5 (unresponsive to physical and verbal stimulus), the patient is ineligible for CAM-ICU assessment. In the present study, delirium was evaluated every day using the validated CAM-ICU [19] until the last day of admission to this unit. Delirium screening was performed by a trained nurse involved in the patient's ICU care. This method assessed the following features:

- Acute onset of changes or fluctuations according to mental status in last 24 h,
- Inattention,
- Disarranged thinking, and
- Altered level of consciousness.

Patients were followed up until discharge from hospital.

Confounders

The risk factors that were potentially related to postoperative delirium development were divided into preoperative, intraoperative, and postoperative classifications.

Preoperative risk factors included demographic data (age, sex, and education level), smoking (tobacco use during the 3 mo before surgery), alcohol use (during the 3 mo before surgery), impaired hearing or vision, hypertension (≥140/90 mm Hg), diabetes mellitus, New York Heart Association (NYHA) classification showing the stages of heart failure [20], and renal insufficiency (elevated serum creatinine concentration ≥1.2 mg/dL). Sensory impairments, including ear/language barrier and vision impairment are risk factors for delirium development. Deprivation of the patients from eye glasses and hearing aid in the ICU is a risk factor for delirium development.

Intraoperative risk factors included surgery type (isolated CABG surgery with single-vessel disease, isolated CABG surgery with two-vessel disease, isolated CABG surgery with three-vessel disease, and valvular plus CABG surgery), numbers of distal anastomoses, and surgery duration.

Postoperative predisposing risk factors were serum electrolyte disturbances (metabolic disturbance of serum sodium and potassium), renal insufficiency, poor sleep quality, early mobilization, and acute infection.

Sleep perception after surgery was assessed using five dichotomous questions on the self-reported sleep quality of the patient:

1 Did you sleep well?
2 Did you sleep better than expected?
3 Did you sleep better than at home?
4 Were you awake for a long time before falling asleep?
5 Do you feel sufficiently rested?

The score on question 4 was reversed. A higher total sum score on the five questions showed a better sleep perception. The scores were categorized as poor sleep (sum ≤3), and good sleep (>3). Mobilization after surgery was assessed as good, average, and bad according to the patient's willingness to mobilize soon after surgery.

Statistical analysis

SPSS software version 24 (IBM, Armonk, NY, USA) was used for performing the statistical analyses. Distribution normality of variables was examined by Kolmogorov–Smirnov test. Continuous variables are denoted as means ± SD or medians and interquartile ranges (IQR). Categorical data are presented as proportions (number and percentage). Between patients with and without delirium, continuous variables were compared by Student's t test or Mann–Whitney U test, depending on the distribution of data. Regarding the size of the group, χ^2 or Fisher's exact test was used for comparing the categorical variables. Univariate and then multivariate logistic regression analysis was applied to examine the effect of various factors on the development of delirium. Confounder variables with $P < 0.05$ were imported into multivariate models. Cutoff points used in these analyses were chosen based on the median of anthropometric parameters. In all analyses, $P < 0.05$ was considered statistically significant.

Results

During the study interval, 435 patients were admitted to the cardiac surgery ward. Of these patients, 37 were excluded due to decline to participate, death, discharge before assessment, incomplete data, and having preoperative diagnosed psychiatric disease (Fig. 1). Table 1 shows the basal characteristics of the patients. The mean ± SD age of the 398 included patients was 61 ± 9 y. The study population consisted of 92 women (23%) and 306 men (77%). Among these patients, 142 were illiterate (36%), 182 did not have a high school diploma (45%), 54 had a high school diploma (14%), and 20 had academic educations (5%). All patients underwent nonemergent cardiopulmonary bypass. The majority of patients (81%, n = 321) were NYHA functional class II (defined as slight limitation of physical activity; comfortable at rest; ordinary physical activity resulting in fatigue, palpitation, and dyspnea).

Table 2 shows the anthropometric and nutritional characteristics of patients. Median (IQR) of MAC and MAMC were significantly higher in patients with delirium. According to the SGA, 65% 260 patients (65%) were well nourished, 104 were moderately malnourished (26%), and 34 were severely malnourished (9%).

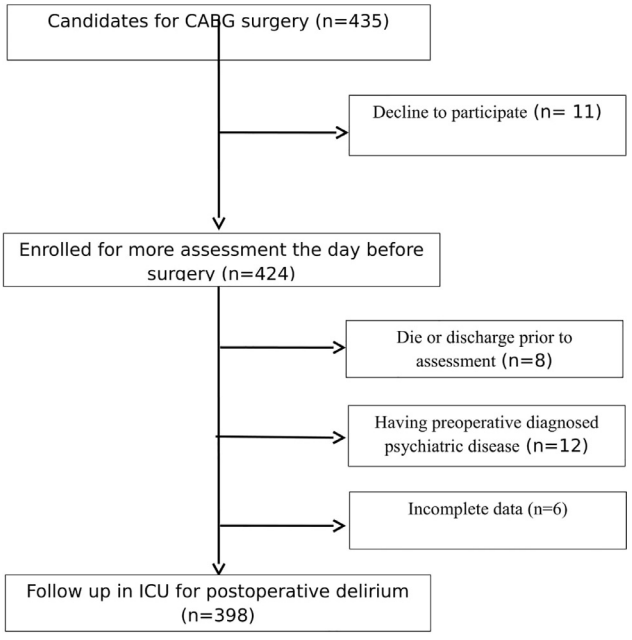

Fig. 1. Study flowchart.

NRS-2002 identified 184 patients with nutritional risk (46%). Postoperative delirium was detected in 68 patients (17%) of whom 16 were women (23%). Median (IQR) length of stay in the ICU and in the hospital were 4 d (2–5) and 7 d (6–9), respectively, in patients with delirium. This was significantly longer than for patients without delirium patients ($P < 0.001$).

Univariate logistic regression analysis was performed to examine the effect of various pre-, intra-, and postoperative risk factors along with nutritional variables on the development of delirium. For univariate logistic regression analysis of anthropometric variables, measures of MAC, APM, MAMC, and TSF were classified according to their medians. Results showed that low levels of APM and MAMC, obesity, NRS >3, SGA-B, and SGA-C were significantly associated with delirium (Table 3). As shown in Table 3, in a multivariate logistic model adjusted by age, hyperlipidemia, hypertension, vision impairment, and creatinine and serum sodium levels after surgery, patients with SGA-C, NRS >3, and APM thickness <1.5 cm had an increased risk for developing delirium.

Discussion

The importance of the association between poor nutritional status and postoperative delirium in the cardiac population is poorly predetermined in the literature, despite growing concern addressing malnutrition and surgical outcomes [21]. Results of the present study showed that SGA, NRS-2002, and APM thickness were independently associated with the risk for delirium. Risk for delirium was 1.56 times more in patients with NRS-2002 >3. This risk was 2.58 times more in patients with severe undernutrition as assessed by SGA. APM thickness <1.5 cm resulted in a 1.26-fold increase in the risk for development of delirium.

In a prospective cohort study, Ringeisen et al. reported an association between high scores for risk for undernutrition, assessed by NRS-2002 and postoperative delirium, in patients undergoing elective CABG surgery [14]. Also, Mazzola et al., in a prospective observational cohort study, used the MNA-SF to diagnose malnutrition in older adults undergoing hip fracture surgery. Mazzola et al. showed that those patients who were at risk for malnutrition and

Table 1
Baseline characteristics of patients

	Delirium (n = 68)	Non-delirium (n = 330)	Total (N = 398)	*P*-value
Age, y	65.62 ± 10.3	60.01 ± 8.8	60.9 ± 9.2	<0.001*
Sex, n (%)				0.92†
Male	52 (76)	254 (77)	306 (77)	
Female	16 (24)	76 (23)	92 (23)	
NYHA functional class, n (%)				0.23†
II	58 (85)	263 (80)	321 (81)	
III	6 (9)	56 (17)	62 (16)	
IV	4 (6)	11 (3)	15 (3)	
Charlson Comorbidity Index				0.64†
0–3	32 (47)	212 (64)	244 (61)	
4–6	34 (50)	116 (35)	150 (38)	
>7	2 (3)	2 (1)	4 (1)	
SOFA score	5 (4.12–5.59)	4 (4.15–4.98)	5 (4.20–5.46)	0.14‡
APACHE II	13.45 (12.78–14.33)	11.99 (11.45–12.36)	12 (11–13.75)	0.21‡
Presurgery hemoglobin, g/dL	13.39 ± 1.66	13.68 ± 1.8	13.63 ± 1.78	0.27*
Comorbidities				
Diabetes mellitus	30 (44)	138 (41)	168 (42)	0.65†
Hypertension	42 (62)	160 (48)	202 (51)	0.04†
Hyperlipidemia	18 (27)	136 (41)	154 (39)	0.02†
Smoker, n (%)	14 (21)	86 (26)	100 (25)	0.34†
Addiction, n (%)	14 (21)	70 (21)	84 (21)	0.90†
Vision impairment, n (%)	10 (15)	14 (4)	24 (6)	0.006†
Ear/language barrier, n (%)	8 (12)	26 (8)	34 (9)	0.29†
Alcohol use, n (%)	0	0	0	1
Type of surgery, n (%)				0.50†
SVD	2 (3)	15 (5)	17 (4)	
2 VD	14 (21)	81 (24)	95 (24)	
3 VD	50 (73)	209 (63)	259 (65)	
CABG + valvular	2 (3)	25 (8)	27 (7)	
CPB duration (h:min)	4:30 (4:15–4:45)	4 (3:45–5:30)	4:15 (4–5)	0.33‡
Serum sodium, mg/dL§	143 (141–145)	142 (139–144)	142 (139–144.75)	0.005‡
Serum potassium, mg/dL§	4.5 (4.3–4.7)	4.5 (4.2–4.7)	4.5 (4.2–4.7)	0.48‡
Serum creatinine, mg/dL§	1.21 (1–1.71)	1.11 (1–1.3)	1.13 (1–1.34)	0.005‡
Poor mobilization, n (%)	12 (18)	60 (18)	72 (18)	0.60†
Poor sleep, n (%)	8 (12)	40 (12)	48 (12)	0.50†
Acute infection, n (%)	2 (3)	4 (1)	6 (1)	0.40†

APACHE, Acute Physiology and Chronic Health Evaluation; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; IQR, interquartile range; NYHA, New York Heart Association; SOFA, Sequential Organ Failure Assessment; SVD, single-vessel disease; VD, vessel disease.
*Independent samples *t* test (mean ± SD).
†χ^2 n (%).
‡Mann–Whitney (median, IQR).
§Postsurgery.

Table 2
Anthropometric and nutritional characteristics of patients

	Delirium (n = 68)	Non- delirium (n = 330)	Total (N = 398)	*P*-value
BMI (kg/m^2)				0.15*
Underweight	0 (0)	2 (1)	2 (1)	
Normal	18 (26)	56 (17)	74 (19)	
Overweight	36 (53)	170 (51)	206 (52)	
Obese	14 (21)	102 (31)	116 (28)	
SGA				<0.001*
A	32 (47)	228 (69)	260 (65)	
B	22 (32)	82 (25)	104 (26)	
C	14 (21)	20 (6)	34 (9)	
NRS				0.056*
Well-nourished	28 (41)	186 (56)	214 (54)	
<3	34 (50)	128 (39)	162 (41)	
>3	6 (9)	16 (5)	22 (5)	
MAC (cm)	29 (26–31)	30 (28–32)	30 (28–32)	0.005†
TSF (cm)	1.1 (0.6–1.55)	1.2 (1–1.6)	1.2 (0.9–1.57)	0.14†
MAMC (cm)	23.93 (22.41–27.79)	25.8 (24.17–2.7)	25.7 (23.9–27.7)	0.007†
APM (cm)	1.4 (1–1.55)	1.5 (1.1–1.9)	1.5 (1.1–1.8)	0.058†

APM, adductor pollicis muscle; BMI, body mass index; IQR, interquartile range; MAMC, mid-arm muscle circumference; NRS, Nutritional Risk Screening; SGA, subjective global assessment; TSF, triceps skinfold.
*χ^2 n (%).
†Mann–Whitney (median, IQR).

Table 3
Univariate and multivariate logistic regression for delirium

Variables	OR	95% CI	*P*-value	OR*	95% CI	*P*-value
BMI, kg/m^2						
Normal	Reference					
Overweight (24–30)	0.65	0.34–1.25	0.2			
Obese (>30)	0.42	0.19–0.92	0.030			
SGA						
A	Reference					
B	1.91	1.05–3.47	0.034			
C	4.98	2.29–10.8	<0.001	2.58	1.02–3.48	0.005
NRS-2002						
Well-nourished	Reference					
>3	1.76	1.02–3.05	0.042	1.56	1.20–3.24	0.001
≤3	2.49	0.89–6.9	0.079			
MAC <30 cm	1.68	0.95–.9	0.07			
TSF <1.2 cm	1.34	0.78–2.28	0.28			
MAMC <25.7 cm	2	1.16–3.46	0.013			
APM <1.5 cm	2.02	1.1–3.7	0.02	1.26	1.02–3.14	0.02

APM, adductor pollicis muscle; BMI, body mass index; MAC, mid-arm circumference; MAMC, mid-arm muscle circumference; NRS, Nutritional Risk Screening; SGA, subjective global assessment; TSF, triceps skinfold.
*Adjusted by age, hyperlipidemia, hypertension, vision impairment, and creatinine and sodium levels after surgery.

those who were overtly undernourished were more likely to develop delirium after hip fracture surgery [15]. Results of the present research are in agreement with these studies. Furthermore, we performed nutrition assessment by SGA in all patients and observed a higher correlation with delirium after CABG surgery. Nutritional screening and assessment have different meanings and methods. Indeed, nutrition screening is a simple and quick process that identifies the risk factors of malnutrition in patients, whereas nutrition assessment is a more complex and longer procedure that provides deeper information. Nutrition screening questionnaires are subjective tools, whereas nutrition assessment tools are based on subjective and objective findings [22,23]. Accumulation of fluid in congestive heart failure, which affects weight and BMI, may interfere with the answers of the two first question of initial screening in the NRS-2002 because they may be incorrectly answered by patients. On the other hand, the NRS-2002 is designed with a series of questions that are scored by the patien's response and thus may be affected by answers. In the present study, 37% of patients were illiterate. Levels of education, cultural factors, and patient' alertness may influence the answers.

We found that low APM thickness was associated with the occurrence of postcardiac surgery delirium. Culp et al. showed an increased risk for delirium in long-term care of older patients who were leaner and had lower fat-free mass [6]. Also, Ganai et al., in a retrospective case study, showed that poor preoperative nutritional status, detected by serum albumin and precipitous weight loss, was correlated with postoperative delirium and mortality in older patients who underwent major abdominal surgery [24]. We did not find any independent association between other anthropometric variables with post-CABG delirium. The presence of edema in some cardiac patients interferes with accurate measurement of weight and BMI. As edema is controlled before surgery, its presence is mild and is in lower extremities or in the form of ascites, so measurement of other anthropometric variables are not affected. The superiority of APM thickness to other anthropometric measurements is due to its unique anatomic position, making it accessible for fast muscle thickness measurement. Among MAC, TSF, and MAMC, measurement of MAMC is most accurate, but requires the use of a formula that combines MAC and the TSF thickness with 33% calculating error between observers [25]. The superiority of the SGA to anthropometric measurements depends on obtaining history and subjective assessment in addition to a physical examination.

Overall, it seems that the SGA is a comprehensive tool that gathers subjective and objective findings to diagnose undernutrition and is superior to solely subjective assessments such as the NRS-2002 or objective assessments such as anthropometric measurements. On the other hand, the SGA is a complex and time-consuming procedure that must be performed by a trained dietitian. It seems that if SGA is available, it is superior to screening methods; otherwise, screening methods should be performed to detect patients at risk for delirium so preventive procedures can be performed.

The present study had some strengths and limitations. The strengths included the study's prospective design, which makes it more powerful than a retrospective study, using anthropometric measurements along with the SGA and the NRS-2002, using a strong method for delirium assessment applying the validated CAM-ICU [25], and finally considering potential non-nutritional risk factors. The limitation of the study was itsa single-center design, which reduces the generalizability of results. Another limitation of the present study was the presence of edema in cardiac patients, which could affect anthropometric measurements and associated results.

Conclusion

The present study showed that high scores for risk for undernutrition, assessed by NRS-2002 and SGA, in patients undergoing elective CABG are associated with the occurrence of delirium. Among anthropometric measurements, only AMP thickness was associated with postoperative delirium. Ppreoperative malnutrition should be considered as a risk factor for the occurrence of post-CABG delirium.

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