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Original article

Preoperative cardiac screening using NT-proBNP in obese patients 50 years and older undergoing bariatric surgery: a study of 310 consecutive patients

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Abstract

Background: Obesity is associated with cardiovascular (CV) risk factors and diseases. Because bariatric surgery is increasingly performed in relatively elderly patients, a risk for pre- and postoperative CV complications exists.
Objectives: We aimed to assess the value of plasma N-terminal-probrain natriuretic peptide (NT-proBNP) as a CV screening tool.
Setting: High-volume bariatric center.
Methods: Between June 2019 and January 2020, all consecutive bariatric patients 50 years and older underwent preoperative NT-proBNP assessment in this cohort study to screen for CV disease. Patients with elevated NT-proBNP (≥125 pg/mL) were referred for further cardiac evaluation, including electrocardiography and echocardiography.
Results: We included 310 consecutive patients (median age, 56 years; 79% female; body mass index = 43±6.5 kg/m^2). A history of CV disease was present in 21% of patients, mainly atrial fibrillation (7%) and coronary artery disease (10%). A total of 72 patients (23%) had elevated NT-proBNP levels, and 67 of them underwent further cardiac workup. Of these 67 patients, electrocardiography (ECG) showed atrial fibrillation in 7 patients (10%). On echocardiography, 3 patients had left ventricular ejection fraction (LVEF) <40%, 9 patients had LVEF 40%–49%, and 13 patients had LVEF ≥50% with structural and/or functional remodeling. In 2 patients, elevated NT-proBNP prompted workup leading to a diagnosis of coronary artery disease and consequent percutaneous coronary intervention in 1 patient.
Conclusions: Elevated NT-proBNP levels are present in 23% of patients 50 years and older undergoing bariatric surgery. In 37% of them, there was echocardiographic evidence for structural and/or functional remodeling. Further studies are needed to assess if these preliminary results warrant routine application of NT-proBNP to identify patients at risk for CV complications after bariatric surgery. (Surg Obes Relat Dis 2021;17:64–71.)

Keywords: Bariatric surgery; Preoperative evaluation; N-terminal-pro hormone BNP; Heart failure; Cardiovascular disease; Cardiac complications

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Obesity is associated with many cardiovascular (CV) risk factors such as hypertension, type 2 diabetes, dyslipidemia, and systemic inflammation [1–4]. The long-term consequences of these risk factors are increasingly recognized, and CV diseases such as heart failure, atrial fibrillation, coronary artery disease, but valvular heart disease and stroke are also common, particularly in elderly persons. Obesity has become one of the largest healthcare problems worldwide. The prevalence of obesity (i.e., body mass index [BMI] $\geq$30 kg/m^2) is currently around 40% and is still increasing [5]. As a result, obesity is increasingly recognized as a serious and potentially treatable risk factor for CV disease [1,2].

Treatment of obesity is difficult, and currently, bariatric surgery is the only treatment option that renders significant and durable weight loss in obese patients with relatively low peri- and postoperative complications rates [6–8]. Anastomotic leakage and bleeding are the most common complications early after surgery, but vascular or cardiopulmonary problems can also occur [9]. The latter were reported to be present in up to 1.3% of all bariatric patients [9], although a larger study showed that during 90-day follow-up the percentage of CV deaths was much higher than those caused by leakage or bowel obstruction: 10 of 36 deaths were heart related (28%) and strongly related to CV risk factors and increasing age [8]. Although the majority of patients undergoing bariatric surgery are relatively young, a significant proportion of patients are older than 50 years, and these patients have a risk for CV diseases [10]. Given the significant number of patients with CV disease who will undergo bariatric surgery, screening for subclinical or unrecognized CV disease in patients 50 years and older may be beneficial.

Despite several review articles that have described possible diagnostic procedures in patients who undergo bariatric surgery, current bariatric guidelines do not provide details regarding preoperative cardiac workup [6,11,12].

In the present study, we therefore aimed to determine the prevalence and incidence of CV diseases in patients 50 years and older who were undergoing bariatric surgery. Because cardiac examinations are not routinely performed in patients referred for bariatric surgery, we investigated whether a simple marker could provide useful information. Therefore, we measured N-terminal probrain natriuretic peptide (NT-proBNP) levels in consecutive patients 50 years and older who were scheduled to undergo bariatric surgery. This biomarker is one the most sensitive markers to detect early CV disease [13] and has proven to be of important diagnostic value in patient groups undergoing noncardiac (vascular) surgery [14,15].

Methods

All patients in the present study were referred to the Department of Bariatric Surgery, Rijnstate Hospital, Arnhem, the Netherlands, between June 2019 and January 2020, which is a high-volume bariatric center performing around 1300 bariatric procedures per year. For this prospective cohort study, only patients who were 50 years and older and who fulfilled the International Federation for the Surgery of Obesity and Metabolic Disorders criteria (BMI $\geq$35 kg/m^2 with an obesity-related co-morbidity or BMI $\geq$40 kg/m^2) were considered eligible.

The cardiac screening protocol was approved by the Local Ethics Committee, and all patients gave informed consent. The present study was in concordance with the principles outlined in the Declaration of Helsinki. In patients who were deemed eligible, plasma NT-proBNP samples were collected and NT-proBNP concentrations in blood samples were measured by the Atellica IM PBNP Essay, using the Atellica IM Analyzer (Siemens Healthineers, Erlangen, Germany). If the NT-proBNP value was $\geq$125 pg/mL, patients were referred to the Department of Cardiology, Rijnstate Hospital for further cardiac workup. This cutoff point is advocated by the European Society of Cardiology for excluding heart failure. Although several confounders for NT-proBNP levels are known, including age, fat mass, and sex, this cutoff point has been shown to provide a reasonable performance [16,17].

If patients were referred to the cardiologist, a 12-lead standard ECG was performed as well as an echocardiogram. Transthoracic 2- and 3-dimensional echocardiography was performed using Epiq Philips (EPIQ 7 C Hardware en software version 5.02). HeartModel software was used to measure left ventricular (LV) and left atrial global volume at end-diastole and at end-systole and to calculate the left ventricular ejection fraction (LVEF). All measurements were assessed according to the current recommendations for cardiac chamber quantification and assessment of diastolic function [18] and included LV systolic function (in particular LVEF), tricuspid annular plane systolic excursion for right ventricular function and left ventricular diastolic function (E, A, E/A ratio, e', and E/e' ratio), valvular stenosis and/or regurgitation, and the peak pressure gradient across the tricuspid valve. Left atrial enlargement was defined as $\geq$34 mL/m^2, LV hypertrophy as LV mass index $>$95 g/m^2 for women and $>$115 g/m^2 for men, and diastolic dysfunction as mean septal and lateral 'e $<$9 cm/s and/or E/e' $>$13, all according to the current European Society of Cardiology criteria [19].

Heart failure was documented if patients had LVEF $<$40% (heart failure with reduced LVEF, or systolic heart failure), they had LVEF 40%–49% (heart failure with mid-range ejection fraction), or they fulfilled the criteria of heart failure with preserved LVEF, that is, $\geq$50%, and additional echocardiographic evidence for relevant structural heart disease, including LV hypertrophy and/or left atrial enlargement and/or diastolic dysfunction, as described earlier in this section [19].

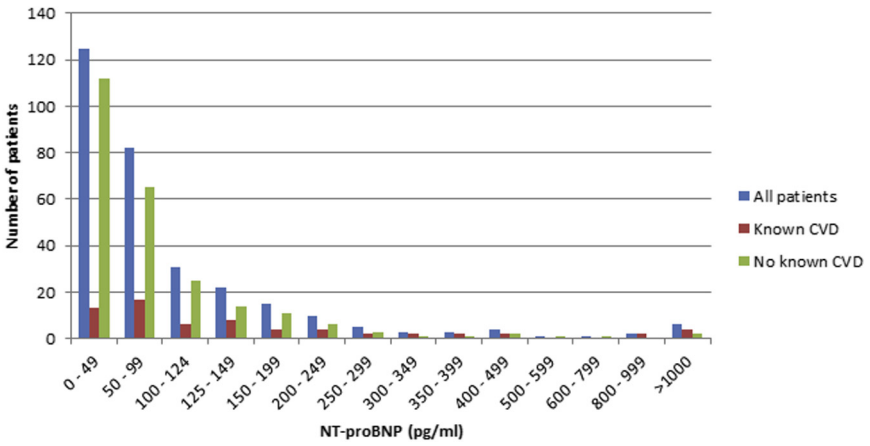

Fig. 1. Distribution of NT-proBNP levels. NT-proBNP = N-terminal probrain natriuretic peptide; CVD = cardiovascular disease.

Besides ECG and echocardiography, additional diagnostic tests or interventions were performed when deemed necessary. Adverse events during the first 30 days after surgery were documented. We had particular interest in CV and pulmonary adverse events, including severe arrhythmias, acute heart failure, acute coronary syndrome, stroke or transient ischemic attack, pneumonia, deep vein thrombosis or pulmonary embolism, acute renal failure, and reintubation. Severity of adverse events were scored according to the Clavien-Dindo Classification; minor and major complications were respectively defined as class 1–2 and class ≥3A [20].

Normally and nonnormally distributed data were described using means with SDs and medians with interquartile ranges. Continuous data were analyzed using independent *t* tests, Mann Whitney *U* test, or a Fisher exact test, depending on the distribution. A P value $< .05$ was considered statistically significant. Statistical analyses were performed by using SPSS version 25.0 for Windows (IBM, Armonk, NY).

Results

Patient characteristics

Between June 2019 and January 2020, NT-proBNP levels were assessed in 310 consecutive patients referred for bariatric surgery (Fig. 1). The median age of patients was 56 years, 72% were female, and mean BMI was 42.6 kg/m^2. Patients had a high prevalence of CV risk factors such as hypertension (58%), dyslipidemia (35%), and type 2 diabetes (28%) (Table 1).

Elevated NT-proBNP levels were observed in 72 patients (23%); the distribution of NT-proBNP levels is shown in Fig. 1. A history of CV disease was present in 64 of the 310 patients (21%) (Table 1). Patients with elevated NT-proBNP levels more often had a history of CV disease (42% versus 14%) and also used more CV drugs. There were 31 patients with a history of coronary artery disease, but in general NT-proBNP levels were not increased in these patients. A history of atrial fibrillation was present in 22 patients, and 17 of them had elevated NT-proBNP levels. A history of heart failure was present in only 6 patients, and 5 of them had elevated NT-proBNP levels. Use of CV drugs, in particular angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, beta-blockers, and diuretics was more common in patients with elevated NT-proBNP than patients with normal NT-proBNP values (all $P <$ .05). Of the 72 patients who had elevated NT-proBNP levels, 67 patients were referred for further cardiac workup (Fig. 2). Two patients dropped out of the study (1 patient with a BMI of 83 kg/m^2 who was not considered eligible for surgery and 1 lost to follow-up). In 3 other patients in whom NT-proBNP was marginally increased (between 125 and 150 pg/mL) further cardiac workup was not performed at the discretion of the treating physician.

Findings during cardiac workup

Of the 67 patients who were referred for further cardiac workup, current atrial fibrillation/flutter was observed in 7 patients on their ECG, which was in line with their medical history. In addition, 8 patients had a history of these arrhythmias but were in sinus rhythm on ECG.

On echocardiography, 3 of the 67 patients had systolic dysfunction, that is, LVEF <40%, and 9 patients had LVEF of 40%–49%, that is, mild systolic dysfunction, whereas the majority of patients had LVEF ≥50%. A total of 25 of 67 patients (37%) had evidence of structural and/or functional abnormalities on echocardiography. Only 4 of these 25 patients had a previous medical history of heart failure.

Of the 55 patients with LVEF ≥50%, 13 had evidence for structural heart disease on echocardiography: left atrial enlargement (n = 9), left ventricular hypertrophy (n = 4), and/or evidence of diastolic dysfunction (n = 3; patients

Table 1
Baseline characteristics and postoperative outcomes

	Total (N = 310)	Elevated NT-proBNP (n = 72)	Normal NT-proBNP (n = 238)	*P* value
Age, median (IQR), yr*	55.9 (53–61)	57 (54–62)	56 (53–60)	.406
Sex, female, n (%)	224 (72.3)	57 (79.2)	167 (70.2)	.088
BMI, mean ± SD, kg/m^2	42.6 ± 6.5	43.7 ± 7.8	42.1 ± 6.0	.445
Abd. circumference, (mean, SD)	128 ± 13	127 ± 15	128 ± 13	.171
Smoking, n (%)				.828
• Current smoking	21 (6.8)	6 (8.3)	15 (6.3)	
• History of smoking	151 (48.7)	34 (47.2)	117 (49.2)	
Medical history, n (%)				
• Hypertension	179 (57.7)	47 (65.3)	132 (55.5)	.173
• Hypercholesterolemia	107 (34.5)	26 (36.1)	81 (34)	.425
• Diabetes	88 (28.4)	18 (25)	70 (29.4)	.312
• Obstructive sleep apnea	84 (27.1)	18 (25)	66 (27.7)	.272
• Chronic kidney disease	13 (4.2)	8 (11.1)	5 (2.1)	.003
• Chronic obstructive pulmonary disease	19 (6.1)	7 (9.7)	12 (5)	.163
History of cardiovascular disease, n (%)*	64 (20.6)	30 (41.7)	34 (14.3)	<.001
• Atrial fibrillation	27 (8.7)	17 (23.6)	10 (4.2)	<.001
○ History of AF	20 (6.4)	10 (13.9)	10 (4.2)	
○ Current AF	7 (2.3)	7 (9.7)	0	
• Heart failure	6 (1.9)	5 (6.9)	1 (.4)	.003
• Coronary artery diseases	31 (10)	9 (12.5)	22 (9.2)	.126
○ Angina pectoris/no significant abnormalities on CAG	13 (4.2)	5 (6.9)	8 (3.4)	
○ MI/PCI/CABG	18 (5.8)	4 (5.6)	14 (5.9)	
• Valvular disease	6 (1.9)	3 (4.2)	3 (1.3)	.140
• Other cardiovascular disease	5 (1.6)	2 (2.8)	3 1.3)	.330
Medications, n (%)				
• ACEI or ARB	144 (46.5)	42 (58.3)	102 (42.9)	.023
• Beta-blocker	81 (26.1)	30 (41.7)	51 (21.4)	.001
• Diuretics	102 (32.9)	31 (43.1)	71 (29.8)	.045
• Lipid lowering agents	109 (35.2)	27 (37.5)	82 (34.5)	.673
• Oral anticoagulants	24 (7.7)	13 (18.1)	11 (4.6)	.001
• Platelet aggregation inhibitors	48 (15.5)	9 (12.5)	39 (16.4)	.464
• Insulin	33 (10.6)	7 (9.7)	26 (10.9)	.772
• GLP-1 agonist	11 (3.5)	3 (4.2)	8 (3.4)	.180
• Oral antidiabetic drugs	73 (23.5)	13 (18.1)	60 (25.2)	.267
Procedure, n (%)	266 (85.8)	57 (79.2)	209 (87.8)	.646
• LRYGB	223 (83.8)	46 (80.7)	177 (84.7)	
• LSG	26 (9.8)	6 (10.5)	20 (9.6)	
• Conversion LAGB to LRYGB	14 (5.3)	4 (7.0)	10 (4.7)	
• Conversion LAGB to LSG	2 (.8)	0	2 (1.0)	
• Conversion LSG to SADI	1 (.4)	1 (1.8)	0	

NT-proBNP = N-terminal probrain natriuretic peptide; IQR = interquartile range; BMI = body mass index; Abd. = abdominal; AF = atrial fibrillation; CAG = coronary angiography; MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; GLP-1 = glucagon-like peptide-1 receptor agonist; LRYGB = laparoscopic Roux-en-Y gastric bypass; LSG = laparoscopic sleeve gastrectomy; LAGB = laparoscopic adjustable gastric band; SADI = single-anastomosis duodenal-ileal bypass.

* Patients may have >1 cardiovascular disease.

may have >1 criterion). Using our workup, we found that the observed increased NT-proBNP levels in concert with the echo data resulted in newly found biochemical and echocardiographic evidence for heart failure with preserved ejection fraction [19] in 13 of these 55 patients (Fig. 3).

In 6 of the 67 patients, additional diagnostic tests were done. One patient with a history of coronary artery bypass surgery had recurrent cardiac events of chest pain and myocardial ischemia and underwent percutaneous coronary intervention. In 2 additional patients, coronary angiography was performed, which showed no coronary lesions, but both were found to have heart failure. Three patients had abnormalities on ECG, which led to 24-hour Holter ECG in 2 of them and a cardiac magnetic resonance imaging in the other; none of these 3 patients were diagnosed as having a new CV disease. All 6 patients were subsequently accepted for surgery.

As a result of cardiac workup, CV drug regimens were adjusted in 9 patients. In 7 patients, new drugs were prescribed (diuretics n = 2, statins n = 2, beta-blocker n =

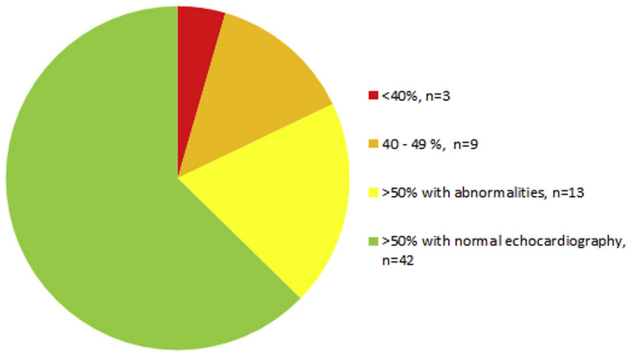

Fig. 2. Distribution of LVEF in patients who underwent preoperative echocardiography. LVEF = left ventricular ejection fraction.

1, angiotensin-converting enzyme inhibitor n = 1, calcium channel blocker n = 1). In the remaining 2 patients, adjustment of beta-blocker dosage was instructed for one, and a diuretic was ceased in another. In 5 other patients, the treating cardiologist ordered perioperative instructions on CV drugs, fluid balance, or oral anticoagulants.

Surgical outcome

Of the 310 patients, 266 patients underwent bariatric surgery. In patients with an increased NT-proBNP, 57 of the 72 patients were operated on, whereas 209 of the 238 with normal NT-proBNP were operated on. Of the 44 patients who did not undergo operation, surgery was either cancelled (n = 12) or postponed (n = 32). Reasons for postponement of surgery were need for further lifestyle changes or psychological management (n = 10), additional cardiac workup (n = 2), and the coronavirus disease 2019 pandemic (n = 20). During 30-day follow-up, no cardiac adverse events occurred. Total adverse events were found in 4 patients with elevated NT-proBNP levels and in 15 with normal NT-proBNP levels, at 7.0% and 7.2%, respectively, and none had a fatal outcome. Major adverse events occurred only in the group with normal NT-proBNP levels (5 of 209 patients; 2.4%), and were all surgical complications: stenosis of jejunojejunostomy (n = 2), postoperative hemorrhage (n = 1), anastomotic leakage (n = 1), and internal herniation (n = 1).

Discussion

The main purpose of this study was to determine the prevalence and incidence of subclinical or unrecognized CV disease in patients 50 years and older scheduled for bariatric surgery using plasma NT-proBNP. NT-proBNP was increased in 72 of 310 patients (23%). Of the 67 patients who underwent thorough cardiac evaluation, echocardiographic evidence of structural and/or functional remodeling was present in 25 patients (37%), and only 4 of these 25 patients had a medical history of heart failure. This means that this noninvasive, simple, and inexpensive diagnostic tool could be used to detect new of structural and/or functional remodeling in a high-risk patient population that is evaluated for bariatric surgery.

Natriuretic peptides such as NT-proBNP and brain natriuretic peptide (BNP) are most often used for monitoring patients with established heart failure, and both have important clinical and prognostic value for long-term outcome [21]. In addition, these biomarkers are powerful tools to predict

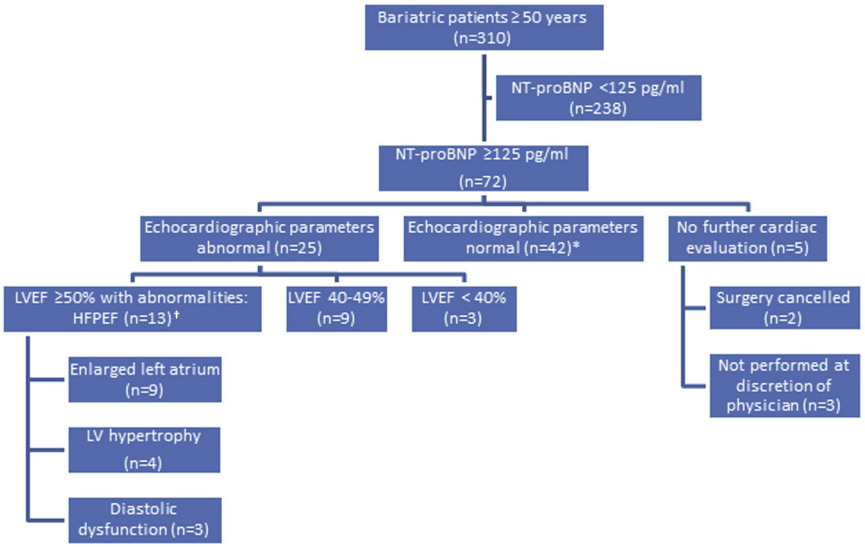

Fig. 3. Flowchart and main outcomes of cardiac preoperative evaluation. *Normal was defined as "no significant abnormalities found on echocardiogram" after current European Society of Cardiology guidelines. † Patients may have >1 criterion. NT-proBNP = N-terminal probrain natriuretic peptide; LVEF = left ventricular ejection fraction; LV = left ventricle.

new-onset heart failure [22]. Interestingly, in addition to heart failure and atrial fibrillation, NT-proBNP levels also strongly predict other CV events, such as myocardial infarction and stroke [23]. Therefore, NT-proBNP could be a reliable screening tool for CV disease. However, in our results we mainly observed elevated plasma NT-proBNP in patients with heart failure or atrial fibrillation, and to a lesser extend in patients with coronary artery disease. Therefore, the use of NT-proBNP as a screening tool for CV diseases may be best used for new-onset heart failure.

NT-proBNP and BNP have been evaluated for their prognostic value as cardiac screening tools to predict the development of (major) cardiac events [14,24]. In our cohort, no CV events occurred in the postoperative phase; though unlikely, this might have been influenced by alterations in CV drugs during cardiac workup. In general, there are limited data available on the incidence of cardiac complications after bariatric surgery, but in general the incidence is low, ranging between .1%–1.7% [25,26]. So far, no studies have examined the association between preoperative cardiac screening and outcome after bariatric surgery. Two meta-analyses concluded that single preoperative measurements of either NT-proBNP or BNP are both good predictors for CV complications [14,24]. These meta-analyses examined patients who were undergoing noncardiac surgery, and several studies did evaluate patients undergoing (major) abdominal procedures but not specifically patients undergoing bariatric surgery. Procedures that were examined in these meta-analyses were mainly classified as high risk for development of cardiac complications, while bariatric surgery is classified as a procedure with intermediate risk [14]. Elevated BNP or NT-proBNP levels were associated with an increased risk for the development of CV complications (odds ratio, 19.3 [95% CI, 8.5–43.7]) [24], and an area under the curve of the relative operating characteristic for the predictive value of elevated BNP or NT-proBNP levels was .70 (95% CI, .66–.74) [14]. In a more recent prospective study including more procedures with an intermediate risk of cardiac complications, the area under the curve was .88 (95% CI, .82–.93) for preoperative NT-proBNP measurements [27]. Outcomes consistently show that heart failure is an independent predictor for major adverse cardiac events [28]. As an alternative for a single measurement screening tool for major cardiac adverse events, several risk assessment tools have been tested in noncardiac surgery patients, such as the 6-item Revised Cardiac Risk Index that indicates whether preoperative cardiac assessment should be performed [29]. Two newer prediction models are available as online tools for risk assessment of major adverse cardiac events and integrate 23 and 30 items [30,31]. However, none of these prediction tools are validated in bariatric study patients and might not be sensitive enough. Given the lack of a validated screening tool for CV disease and high prevalence of occult LV dysfunction (and heart failure) in our cohort, it is somewhat surprising that in the recently reported Clinical Practice Guidelines for patients undergoing Bariatric Surgery, standard preoperative evaluation of (high-risk) patients to detect occult CV disease in selected patients is also not discussed [6].

With current acceptably low morbidity and mortality rates in the early phase after bariatric surgery and the evident long-term improvements in weight loss and CV disease, it is likely that the number of patients eligible for bariatric surgery will further increase. Moreover, it is conceivable that obese patients with specific CV diseases, such as heart failure and atrial fibrillation, will be considered candidates for bariatric or metabolic surgery, not just to induce weight loss but specifically to treat these co-morbidities [6]. Especially for these patients at high risk of developing CV complications, accurate preoperative CV screening is important. Therefore, NT-proBNP assessment could prove to be the first choice as a screening tool because it is inexpensive, easy, and noninvasive.

There are some limitations that merit emphasis. First, this is a single-center study with a relatively small sample size. Therefore, the results may not provide conclusive evidence whether cardiac screening is beneficial in terms of reducing CV morbidity and mortality. Second, patients with normal NT-proBNP levels were not referred for ECG or echocardiography, therefore the presence of CV disease is unknown in these patients. However, a normal BNP or NT-proBNP makes it very unlikely that a patient has CV disease, especially heart failure [19]. It should also be noted that NT-proBNP is a stronger predictor for heart failure than coronary artery disease and stroke, albeit we did identify 2 patients in our cohort who required intervention for coronary artery disease while using NT-proBNP [13,23]. Third, the aim of our study was to examine the value of NT-proBNP as a screening tool for CV disease and was consequently not powered to examine a potential association with postoperative CV outcome. Fourth, NT-proBNP has an inverse relation with BMI [32], which means that patients with potential CV disease could have false-negative outcome of cardiac screening with NT-proBNP. This implies that the reported 23% of patients with elevated NT-proBNP in our study is probably an underestimation of the actual number of patients with CV disease. Fifth, use of NT-proBNP as a single screening tool might be less predictive for CV disease than a prediction model that combines NT-proBNP with levels of additional laboratory measurements (such as troponins or highly sensitive C-reactive protein) and presence of co-morbidities such as diabetes. However, we aimed to investigate NT-proBNP as a simple and stand-alone diagnostic tool, and we thus did not add other parameters to the decision whether or not patients should be referred for cardiac workup. Last, it is likely that our cohort of patients is slightly different than the general obese population. General practitioners may be reluctant to refer a patient for bariatric surgery if they have CV disease such as congestive heart failure or recent myocardial infarction because of a

higher risk of fatal complications after bariatric surgery [33].

Conclusions

Elevated levels of NT-proBNP levels are present in almost one fourth of obese patients 50 years and older undergoing bariatric surgery. In more than one third of them, there was echocardiographic evidence for LV structural and functional remodeling. Further studies are needed to assess if these preliminary results warrant routine application of NT-proBNP to identify patients at risk for CV complications after bariatric surgery.

Disclosures

The authors have no commercial associations that might be a conflict of interest in relation to this article.

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