



Original article

Body mass index as a biomarker for the evaluation of the “Obesity Paradox” among inpatients



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SUMMARY

Background: Overweight and obesity are, on the one hand, recognized as risk factors for many health-related disorders, and, on the other, as favorable prognostic factors in various patients treated for several different conditions; what is called the “obesity paradox”. Until now, the existence of this phenomenon among a general population of consecutive inpatients has not been evaluated. We decided, therefore, to perform an evaluation.

Patients and methods: Historical prospective analysis of the medical documentation of 23 603 hospitalizations during two consecutive years in one center was performed. The outcomes measured were as follows: length of stay, in-hospital all-cause mortality, and non-scheduled readmission in the 14-day, 30-day and one-year periods following discharge.

Results: Overweight and obese patients had a lower or similar prevalence of the measured outcomes than malnourished patients and those of normal weight. Adjustment of the standard WHO BMI ranges for patients aged ≥ 65 y (normal weight BMI range 23–33 kg/m²) made these differences more apparent. In logistic regression, the ratio of fat to fat-free body mass was a stronger and unfavorable risk factor compared with BMI for the measured outcomes.

Conclusions: The greatest risk of all-cause in-hospital death and readmission concerned malnourished inpatients. Compared to patients with a normal BMI range, overweight and obesity had a lower or similar (but not greater) risk of the outcomes measured. However, due to several BMI limitations, our observations should be interpreted as suggesting a “BMI paradox”, rather than an “obesity paradox”.

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1. Introduction

Overweight and obesity are recognized as risk factors in several health-related disorders, such as: atherosclerosis, myocardial infarction, stroke, type 2 diabetes mellitus, hypertension,

dyslipidemia, hyperuricemia, obstructive sleep apnea, arthrosis, liver steatosis, cholelithiasis, colorectal cancer, breast cancer, polycystic ovarian syndrome and other endocrinological disturbances, and lower back pain. On the other hand, it has been reported that overweight and class 1 obesity are favorable prognostic factors in the course of many diseases, such as: atrial fibrillation [1–3], diabetes mellitus [4,5], peripheral artery diseases and atherosclerosis of the aorta [6], heart failure [7,8], coronary artery disease after percutaneous coronary revascularization [9], stroke [5], colorectal and lung cancer [10], end-stage kidney disease [5],

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liver cirrhosis [11], acute respiratory distress syndrome (ARDS) [12] and other conditions treated in intensive care units [13], AIDS [14], osteoporosis, and in elderly patients [5,14,15]. This suggests that patients with these diseases have a better prognosis if they are overweight. This apparently contrary phenomenon, a reverse epidemiology of overnutrition, is known as the “obesity paradox”. Its existence has both many proponents and many opponents [15,16]. Opponents refer to it as the “BMI (body mass index) paradox” and suggest that this phenomenon results from: (a) methodological shortcomings of the studies, such as lack of initial nutritional status determination or analysis of body fat percentage and distribution, lack of control for intentional and unintentional body weight changes, lack of control for comorbidities, patients' age and degree of physical activity, short follow-up periods, confounding or detection bias, or a specific form of selection bias known as collider bias; (b) only taking BMI ranges into consideration, regardless of various clinical phenotypes of obesity and fat distribution (e.g. being metabolically healthy but obese); (c) earlier and more aggressive treatment of obese individuals, which improves prognosis; (d) reverse causality, especially in patients with cancer [17]; although (e) the potential protective effect of subcutaneous adipose tissue and adipokines, differences in immune responses, more metabolic reserves, the importance of cardiorespiratory fitness, skeletal muscle mass and strength are also taken into account [1,15,16,18–20].

A BMI greater than or equal to 25 kg/m² is the main criterion for overweight (BMI 25–29.9 kg/m²) and obesity (BMI ≥ 30 kg/m²) diagnosis [21]. BMI is also the most elementary and cheapest parameter to measure for nutritional risk and status assessment. However, BMI has several limitations, of which the most important are: (a) an inability to distinguish between fat and fat-free (lean) body mass, which may be a cause of obesity underestimation in older adults, and its overestimation in those with a muscular build (e.g. athletes); (b) the failure to determine fat distribution, such as waist circumference or waist-to-hip ratio; (c) a dependence on the accuracy of reported height, which frequently decreases as patients age; (d) its relation to body fluid fluctuations; and (e) the influence of age, gender, smoking status, and comorbidities, which is not taken into account by the rigid borders of BMI ranges [21–23]. These shortcomings of BMI as a parameter of nutritional status assessment are the reason why BMI determination is often omitted from studies. Therefore, in the context of the above-mentioned data showing that, on the one hand, overweight and obesity are risk factors for several health-related disorders, and, on the other, that morbidity and mortality are paradoxically lower in overweight and obese patients treated for a number of diseases, as well as the lack of confirmation of the existence of the “obesity paradox” or neutral risk linking being overweight among inpatients, we conducted this analysis to determine the association between BMI and all-cause mortality and readmissions in consecutive patients hospitalized in one hospital during a two-year period.

2. Materials and methods

We performed a historical prospective analysis of the electronic medical documentation of all non-selected, consecutive patients admitted to a university hospital during the course of two years, i.e. between July 1, 2014 and June 30, 2016. During this period, 70 076 hospitalizations were carried out, of which 64 856 (92.55%) concerned patients older than 18 years of age and 53 375 (76.17%) lasted more than one day. The latter inclusion criterion helped to exclude one-day hospitalizations, during which, in accordance with Polish regulations, routine nutritional risk screening and assessment are not obligatory. Pregnant women hospitalized in the Department of Obstetrics and data obtained during the rehospitalization of other

patients who were included in the study were also excluded from the analysis. Of the remaining 34 191 individuals, full BMI calculation data were not available for 10 588 (30.97%) of them and, therefore, an analysis was conducted of 23 603 (69.03%) patients. Every patient was identified on the basis of his or her personal identity number, and his or her clinical, anthropometric and laboratory data were taken for analysis only once.

The following parameters were analyzed: age, gender, number of hospitalization days, hospitalization mode (whether urgent or scheduled), in-hospital all-cause mortality, non-scheduled readmission, Nutritional Risk Screening (NRS)-2002 score (a score of at least 3 points in the questionnaire indicates a risk of malnutrition), body mass, height, BMI, blood concentration of hemoglobin, total low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol, triglycerides, glucose, albumin, C-reactive protein (CRP), and absolute lymphocyte count. For this analysis of associations between lymphocyte count and measured outcomes, 69 patients with hematological malignancies and a lymphocyte count above the laboratory norm (>4.5 g/l) were excluded. All the biochemical parameters included in the analysis (e.g. blood cholesterol, glucose concentration and lymphocyte count) were the first determinations during the respective hospitalizations.

In order to achieve a more detailed evaluation of the associations between the measured outcomes and the parameters mentioned above, the following secondary parameters were also calculated:

- BMI according to the following formula: actual body mass/patient's height expressed in kilograms per meter squared (kg/m²);
- BMI range was calculated in three ways: (1) according to the World Health Organization (WHO) categories (Underweight: <18.5 kg/m²; Normal weight: 18.5 ≤ BMI < 25 kg/m²; Overweight: 25 ≤ BMI < 30 kg/m²; and Obese: BMI ≥ 30 kg/m²) [21]; and according to the two ranges of BMI proposed in a recent meta-analysis by Winter et al. for people aged ≥65 y, which were as follows: (2): Underweight: <24 kg/m²; Healthy weight: 24–31 kg/m²; Overweight: >31 kg/m²; and (3): I (Underweight): <23 kg/m²; II (Healthy weight range): 23–33 kg/m²; and III (Overweight): >33 kg/m² [23]. Thus, according to formula (3), BMI range I included patients with BMI <18.5 kg/m² (<65 y) and <23 kg/m² (aged ≥ 65 y); BMI range II included patients with 18.5 kg/m² ≤ BMI < 25 kg/m² (aged < 65 y) and 23 kg/m² ≤ BMI ≤ 33 kg/m² (aged ≥ 65 y); and BMI range III included patients with BMI ≥ 25 kg/m² (aged < 65 y) and BMI > 33 kg/m² (aged ≥ 65 y);
- median as well as lower and upper quartiles and percentiles of BMI;
- percentage of body fat according to the following formula $(1.2 \times BMI) + (0.23 \times age) - (10.8 \times gender) - 5.4$, in which gender was accorded a value of “0” for females and “1” for males [24]. This formula is considered to be one of the best ways to adjust BMI for age and gender;
- fat mass (FM) as a product of actual body mass and the percentage of body fat;
- fat-free mass (FFM) as the difference between actual body weight and body fat mass;
- the quotient of FM to FFM;
- an “ideal weight” according to the Lorentz formula. For female patients: ideal weight = [height (cm)–100]–{[height (cm)–150]/2}; and for male patients: ideal weight = [height (cm)–100]–{[height (cm)–150]/4} [25];
- absolute (actual–ideal body weight) and proportional (100% × [actual–ideal body weight]/actual body mass) difference between actual and ideal body weight;

- the quotient of actual to ideal body mass/100%; the following intervals were analyzed: <70%, 70–80%, 80–90%, 90–110% (norm); 110–120%, 120–130%, 130–140%, >140%;
- deficit of body mass was defined as the negative difference between actual and ideal body mass;
- Geriatric nutritional risk index (GNRI) according to the following formula [26]: $\text{NRI} = 1.519 \times \text{blood albumin concentration} + 41.7 \times \text{actual body mass/ideal body mass}$ [25,26];
- instant nutritional assessment (INA) [27,28] using a classification of four degrees of malnutrition: 1st degree = albumin ≥ 3.5 g/l and lymphocyte count ≥ 1.5 G/l; 2nd degree = albumin ≥ 3.5 g/l and lymphocyte count < 1.5 G/l; 3rd degree = albumin < 3.5 g/l and lymphocyte count ≥ 1.5 G/l; and 4th degree = albumin < 3.5 g/l and lymphocyte count < 1.5 G/l;
- Onodera's (Preoperative) prognostic nutritional index (OPNI) according to the following formula: $10 \times \text{albumin blood concentration (g/l)} + 0.005 \times \text{lymphocyte count (G/l)}$ [29];
- blood CRP/albumin ratio;
- blood albumin in one of the following ranges: <2.5 g/l; 2.5–3.0 g/l; 3.0–3.5 g/l; ≥ 3.5 g/l;
- blood lymphocyte count in the following ranges: <800 G/l; 800–1200 G/l; 1200–1500 G/l; >1500 G/l.

The main and additional diagnoses on discharge were also checked. Cardiovascular diseases as a cause of hospitalization were recorded when a patient was discharged, using the International Classification of Diseases 10th revision (ICD-10) diagnosis from group "I", with the exception of I84 and I85, as well as G45, G46, H34, H35, and H36. Malignant neoplasm as a cause of hospitalization was recorded when the final diagnosis on discharge was derived from ICD-10 group "C".

2.1. Outcomes measured

The following outcomes were measured: length of stay (LOS; duration of hospitalization [number of days hospitalized]), in-hospital all-cause mortality and non-scheduled readmission (second and subsequent hospitalizations) in the 14-day, 30-day and one-year periods following discharge.

2.2. Bioethics

The investigation was conducted in compliance with the Declaration of Helsinki for medical research, after receiving permission from local Bioethical Committee No. 682/2016.

2.3. Statistics

Statistical analysis was conducted using licensed versions of statistical software STATISTICA (a data analysis software system), StatSoft, Inc. (2015), version 12. The normal distribution of the study variables was checked using the Shapiro–Wilk test. The results were mainly presented as the mean \pm standard deviation, or n, %. The statistical significance of differences between groups was verified using the Student's t-test and χ^2 test. The statistical significance level was set at a p-value <0.05. Logistic regression using a quasi-Newton estimation method was applied to check the relationships between the measured outcomes and the variables analyzed. The odds ratio (OR) was defined as the odds that an outcome would occur with the association of a particular BMI value interval, compared to the odds of the outcome occurring in the other BMI value intervals, and was calculated according to the following formula: the product of the number of subjects with the measured outcome (e.g. in-hospital death or rehospitalization) and

the presence of the variables analyzed (exposed cases = patients who died in hospital and upon admission had e.g. $\text{BMI} \geq 30 \text{ kg/m}^2$) and the number of subjects without the measured outcome and analyzed variable (unexposed non-cases = e.g. patients with $25 \text{ kg/m}^2 \leq \text{BMI} < 30 \text{ kg/m}^2$ upon admission who were discharged from hospital) divided by the product of the number of exposed non-cases (patients discharged from hospital who had upon admission e.g. $\text{BMI} \geq 30 \text{ kg/m}^2$) and the number of unexposed cases (e.g. patients with $25 \text{ kg/m}^2 \leq \text{BMI} < 30 \text{ kg/m}^2$ upon admission who died during hospitalization).

3. Results

3.1. Patients with and without available BMI values

Our analysis was performed based on the medical documentation of the general inpatient population in the university hospital, in which we assessed the relationships between different BMI ranges and measured outcome occurrence. BMI values were not available for 31% of the patients who completed the inclusion criteria (Tables 1 and 1a). Compared to patients with available BMI values, individuals for whom a BMI value was not available were statistically significantly ($p < 0.0001$) older, more prevalently male, had a significantly greater NRS-2002 score, were hospitalized for a significantly longer period of time, and had a higher prevalence of the measured outcomes, such as in-hospital death and readmission within 14 days, 30 days and one year. Of the patients with available BMI values, detailed demographic and clinical data are presented in Table 1 and biochemical data in Table 1a.

3.2. Crude analysis of BMI

In patients with BMIs measured according to the WHO cut-offs [21], those from the lowest interval were significantly younger, more prevalently female, had the greatest nutritional risk, and less frequently suffered from cardiovascular and neoplastic diseases (Table 2). Moreover, the prevalence of the outcomes measured was the greatest in this group, and the risk of in-hospital death due to all-causes was more than twice that of patients in the BMI range of $18.5\text{--}24.99 \text{ kg/m}^2$ ($\text{OR} \pm 95\% = 2.41 \pm 1.41\text{--}4.51$). Compared to patients with normal body mass, the risk of in-hospital death and one-year readmission in overweight and obese individuals was not significantly greater, the length of in-hospital stay was shorter and the prevalence of the remaining readmissions was lower. The trend for a lower prevalence of the outcomes measured in overweight patients was also marked when the patients studied were divided into groups according to BMI percentile (Fig. 1), into intervals of actual to ideal body mass percentages (Fig. 2), and into BMI quartiles (data not presented).

3.3. BMI adjusted for age ≥ 65 y

In the context of a recent publication which undermines the usefulness of the BMI ranges proposed by the WHO [21] in older patients [23], we adjusted our analysis of BMI ranges for patients aged ≥ 65 y (Table 3), who comprised 42.45% of the population studied (Table 1). For patients aged ≥ 65 y, we used two ranges of healthy normal BMI values: $24\text{--}31 \text{ kg/m}^2$ (data not presented) and $23\text{--}33 \text{ kg/m}^2$, which was suggested from the meta-analysis by Winter et al. [23], but more apparent differences were noted for the second, wider BMI interval. Finally in this analysis, we distributed all the patients into three groups in relation to criteria given in the commentary to Table 3. In this analysis, the values and prevalence of the measured outcomes decreased proportionally and

Table 1
Comparison of demographic and clinical data of the inpatients with available and unavailable BMI value.

Parameter	Patients with available BMI value (n = 23 603; 69.03%)	Patients with unavailable BMI value N = 10 588 (30.97%)	P=
Age (years)	59.88 ± 17.52	61.80 ± 18.59	<0.001
Age ≥ 65 years (n, %)	10 019 (42.45%)	5198 (49.09%)	<0.001
Male gender (n, %)	11 369 (48.17%)	4516 (42.65%)	<0.001
NRS-2002 ≥ 3 (n, %)	1030 (4.36%)	1013 (12.24%)	<0.001
Number of patients with body mass deficit (n, %)	3386 (14.35%)		
Height (cm)	167.88 ± 9.80		
Body weight (kg)	76.80 ± 17.26		
Average absolute difference between actual and ideal body weight (kg)	14.90 ± 15.08		
Average proportional difference between actual and ideal body weight (%)	16.43 ± 16.23		
Actual to ideal body weight ratio (%)	124.29 ± 24.79		
BMI (kg/m ²)	27.17 ± 5.43		
Average fat mass (kg)	27.93 ± 11.86		
Average fat-free mass (kg)	48.88 ± 10.90		
Fat to fat-free mass ratio	0.59 ± 0.27		
Number of patients with a diagnosis of cardiovascular disease on discharge (n, %)	7707 (32.65%)	2587 (24.43%)	<0.001
Number of patients with a diagnosis of neoplastic disease on discharge (n, %)	2428 (10.29%)	927 (8.76%)	<0.001
Length of hospital stay (days)	5.78 ± 6.61	7.12 ± 7.92	<0.001
Urgent admission (n, %)	11 801 (50.00%)	7140 (67.43%)	<0.001
In-hospital death (n, %)	273 (1.16%)	646 (6.10%)	<0.001
Number of non-elective rehospitalizations in the 14-day period after discharge (n, %)	454 (1.92%)	330 (3.12%)	<0.001
Number of non-elective rehospitalizations in the 30-day period after discharge (n, %)	1018 (4.31%)	616 (5.82%)	<0.001
Number of non-elective rehospitalizations in the one-year period after discharge (n, %)	2677 (11.34%)	1503 (14.20%)	<0.001

Commentary: data presented as the mean (M) ± standard deviation, median, lower and upper quartiles, and as a number and %.

Abbreviations: NRS-2002 = Nutritional Risk Screening 2002 questionnaire; BMI = body mass index.

Table 1a
Comparison of available biochemical parameters in the inpatients with available and unavailable BMI value.

Parameter	Patients with available BMI value (n = 23 603; 69.03%)	Patients with unavailable BMI value N = 10 588 (30.97%)	P=
Hemoglobin (g/dl) (n = 19 100 and 9589)	12.80 ± 2.40	12.63 ± 2.36	<0.001
Total cholesterol (mg/dl) (n = 2254 and 893)	177.42 ± 70.15	158.88 ± 66.87	<0.001
LDL cholesterol (mg/dl) (n = 7125 and 2224)	113.70 ± 43.18	110.13 ± 41.91	<0.001
LDL ranges (n = 7125 and 2224)	<70 mg/dl: 954 (13.39%); 70–100 mg/dl: 2049 (28.76%); 100–115 mg/dl: 909 (12.76%); >115 mg/dl: 3213 (45.09%)	<70 mg/dl: 375 (16.96%); 70–100 mg/dl: 610 (27.43%); 100–115 mg/dl: 320 (14.39%); >115 mg/dl: 919 (41.32%)	<0.001
HDL cholesterol (mg/dl) (n = 838 and 306)	53.85 ± 19.87	51.57 ± 23.30	0.019
Abnormal HDL cholesterol (n = 838 and 306)	220 (26.25%)	116 (37.39%)	<0.001
<40 mg/dl in males, < 45 mg/dl in females			
Non-HDL cholesterol (n = 769 and 282)	131.41 ± 46.27	120.51 ± 42.21	<0.001
Triglycerides (mg/dl) (n = 6149 and 1696)	130.55 ± 145.26	124.12 ± 143.51	0.040
Triglycerides > 150 mg/dl (n = 6149 and 1696)	1566 (25.47%)	394 (23.23%)	0.059
Blood glucose (mg/dl) (n = 12 873 and 6903)	125.75 ± 62.77	135.50 ± 74.50	<0.001
Lymphocyte count (G/l), (n = 5959 and 2401)	1.58 ± 0.78	2.05 ± 6.36	<0.001
Albumin (mg/dl) (n = 2830 and 1699)	3.47 ± 2.20	3.27 ± 3.45	<0.001

Commentary: data presented as the mean (M) ± standard deviation, median, lower and upper quartiles, and as a number and %. Biochemical data were not available for all inpatients; numbers of patients with determination of respective parameters were given in brackets.

Abbreviations: LDL = low-density lipoprotein; HDL = high-density lipoprotein.

significantly with the increase in BMI range. However, it must be underlined that this observation should be carefully interpreted, because, compared to individuals of normal weight (group II), the patients allocated to group III were significantly younger; the prevalence of patients aged ≥65 y was significantly lower, by approximately four times, although they had a greater percentage of body fat and a higher FM/FFM ratio (Table 3).

In our analysis, we also used another way to adjust our analysis of BMI for patients' age and gender through the calculation of fat mass percentage (according to one of the formulas mentioned above [24]) and derived parameters, such as FM, FFM, and FM/FFM ratio. The values of these parameters increased proportionally with an increase in WHO BMI range (Table 2), and BMI ranges adjusted for age ≥65 y and gender (Table 3).

3.4. Multifactorial analysis

Finally, we performed multifactorial analysis of factors determining the occurrence of the measured outcomes using the logistic regression method (Table 4). As the models obtained were for different measured outcomes, detailed data are only presented for in-hospital all-cause mortality. In this analysis, we confirmed the above-mentioned observation that the probability of survival during hospitalization and not being readmitted during the periods analyzed was positively related to a higher BMI value (suggesting the presence of an “overweight and obesity paradox”). Patients' age and male gender were also positively associated with the risk of in-hospital mortality, but FM/FFM ratio, which is recognized as a kind of BMI correction in relation to age and

Table 2
Parameters studied among patients divided in relation to BMI ranges according to the WHO.

Parameter	BMI <18.5 kg/m ² (n = 684; 2.90%)	18.5 ≤ BMI < 25 kg/m ² (n = 8254; 34.97%)	25 ≤ BMI < 30 kg/m ² (n = 8207; 34.77%)	BMI > 30 kg/m ² (n = 6458; 27.36%)	p=					
	A	B	C	D	A vs. B	A vs. C	A vs. D	B vs. C	B vs. D	C vs. D
Age (years)	49.14 ± 21.29	55.20 ± 19.19	60.96 ± 15.58	62.47 ± 13.35	±0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Age >65 years (n, %)	197 (28.80%)	3022 (36.61%)	3738 (45.55%)	3062 (47.41%)	<0.001	<0.001	<0.001	<0.001	<0.001	0.024
Male gender (n, %)	210 (30.70%)	3570 (43.25%)	4465 (54.40%)	3124 (48.37%)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
NRS-2002 ≥ 3 (n, %)	161 (23.54%)	418 (5.06%)	284 (3.46%)	167 (2.59%)	<0.001	<0.001	<0.001	<0.001	<0.001	0.002
Average absolute difference between actual and ideal body weight (kg)	-12.16 ± 3.92	1.91 ± 5.05	15.35 ± 4.49	33.79 ± 10.99	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Average proportional difference between actual and ideal body weight (%)	-26.23 ± 10.51	2.44 ± 8.02	19.54 ± 4.66	34.90 ± 6.69	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Actual to ideal body weight ratio (%)	79.72 ± 6.04	103.17 ± 8.20	124.70 ± 7.28	155.47 ± 18.32	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Number of patients with body mass deficit (n, %)	684 (100%)	2702 (32.74%)	0	0	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
BMI (kg/m ²)	17.22 ± 1.16	22.44 ± 1.74	27.35 ± 1.40	34.05 ± 3.83	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
% of fat mass	23.25 ± 6.76	29.56 ± 7.05	35.56 ± 6.97	44.06 ± 8.23	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Average fat mass (kg)	10.91 ± 2.96	18.57 ± 4.30	27.38 ± 4.52	42.40 ± 10.54	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Average fat-free mass (kg)	36.79 ± 6.96	45.00 ± 9.02	50.67 ± 10.33	52.85 ± 11.63	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Fat to fat-free mass ratio	0.31 ± 0.12	0.43 ± 0.14	0.57 ± 0.17	0.85 ± 0.32	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Number of hospitalizations with a diagnosis of cardiovascular disease on discharge (n, %)	96 (14.04%)	2076 (25.15%)	2866 (34.92%)	2669 (41.33%)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Number of hospitalizations with a diagnosis of neoplastic disease on discharge (n, %)	59 (8.63%)	887 (10.75%)	926 (11.28%)	556 (8.61%)	0.08	0.033	0.98	0.27	<0.001	<0.001
Length of hospital stay (days)	6.15 ± 7.04	5.16 ± 5.80	5.15 ± 5.81	5.11 ± 5.73	<0.001	<0.001	<0.001	0.93	0.62	0.68
Urgent admission (n, %)	402 (58.77%)	4203 (50.92%)	4017 (48.95%)	3179 (49.23%)	<0.001	<0.001	<0.001	0.011	0.041	0.73
In-hospital all-cause mortality (n, %)	16 (2.34%)	81 (0.98%)	100 (1.22%)	76 (1.18%)	<0.001	0.013	0.010	0.14	0.25	0.82
Risk of all-cause in-hospital mortality (OR ± 95% CI)	2.42 ± 1.41–4.56	1	1.24 ± 0.93–1.67	1.20 ± 0.88–1.65	–	–	–	–	–	–
Number of non-elective rehospitalizations in the 14-day period after discharge (n, %)	19 (2.78%)	184 (2.23%)	144 (1.75%)	107 (1.66%)	0.35	0.055	0.034	0.029	0.014	0.65
Number of non-elective rehospitalizations in the 30-day period after discharge (n, %)	36 (5.26%)	402 (4.87%)	307 (3.74%)	273 (4.23%)	0.65	0.047	0.21	<0.001	0.064	0.13
Number of non-elective rehospitalizations in the one-year period after discharge (n, %)	95 (13.89%)	982 (11.90%)	812 (9.89%)	788 (12.20%)	0.13	<0.001	0.20	<0.001	0.57	0.0

Commentary: data presented as the mean ± standard deviation or number (n) and % of subjects, as well as OR ± 95 CI (odds ratio ± 95% confidence interval). Deficit of body mass was defined as a negative difference between actual and ideal body mass. Percentage of fat mass, fat mass and fat-free mass were calculated from a BMI-based pattern [24]. OR ± 95% CI were calculated in relation to healthy normal BMI interval (18.5 ≤ BMI < 25 kg/m²). OR expresses the probability of the occurrence of an in-hospital death of a patient with a BMI value below or above normal range.

Abbreviations: BMI = body mass index; WHO = World Health Organization; NRS = Nutritional Risk Screening.

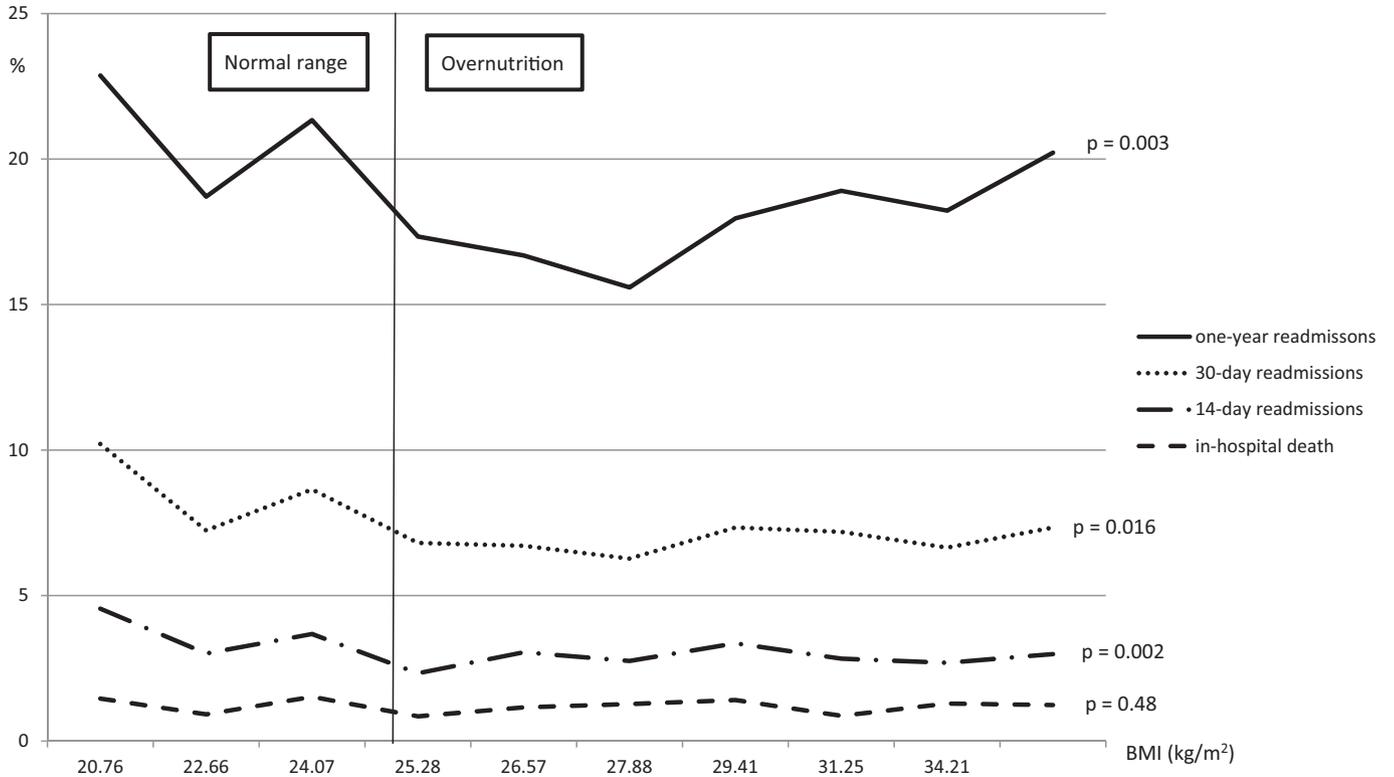


Fig. 1. Percentages of occurrence of the measured outcomes in respective percentiles of BMI (n = 23 603).

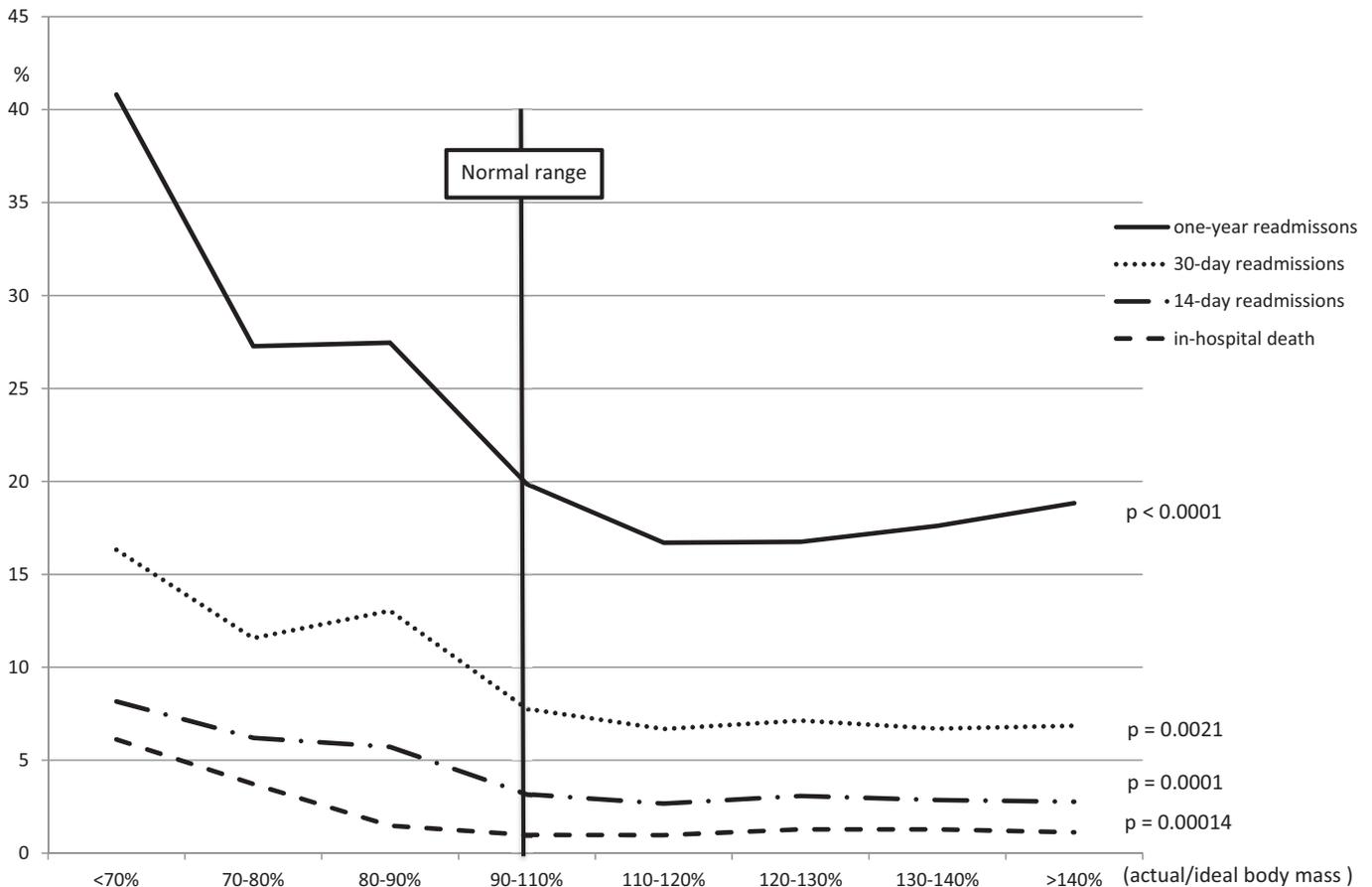


Fig. 2. Percentages of occurrence of the measured outcomes in respective ranges of actual to ideal body mass ratio (n = 23 603).

Table 3
Prevalence of some of the clinical data and measured outcomes in relation to modified BMI ranges (n = 23 603).

Parameter	BMI range I (Underweight) (n = 2126; 9.01%)	BMI range II (Healthy normal weight) (n = 12 175; 51.58%)	BMI range III (Overweight) (n = 9302; 39.41%)	p=		
	A	B	C	A vs. B	A vs. C	B vs. C
Age (years)	66.66 ± 18.03	61.11 ± 18.35	54.53 ± 12.23	<0.001	<0.001	<0.001
Age ≥ 65 years (n, %)	1639 (77.09%)	6943 (57.03%)	1437 (15.45%)	<0.001	<0.001	<0.001
Male gender (n, %)	882 (41.49%)	5482 (45.03%)	5005 (53.81%)	0.002	<0.001	<0.001
NRS-2002 ≥ 3 (n, %)	344 (16.18%)	560 (4.60%)	126 (1.35%)	<0.001	<0.001	<0.001
BMI (kg/m ²)	19.97 ± 2.24	25.29 ± 3.52	31.29 ± 4.8	<0.001	<0.001	<0.001
% of fat mass (%)	29.41 ± 7.50	34.14 ± 9.00	38.88 ± 9.81	<0.001	<0.001	<0.001
Fat to fat-free mass ratio	0.43 ± 0.15	0.55 ± 0.22	0.69 ± 0.33	<0.001	<0.001	<0.001
Number of hospitalizations with a diagnosis of cardiovascular disease on discharge (n, %)	632 (29.73%)	4025 (33.06%)	3050 (32.79%)	0.002	0.006	0.68
Number of hospitalizations with a diagnosis of neoplastic disease on discharge (n, %)	272 (12.79%)	1263 (10.37%)	893 (9.60%)	0.001	<0.001	0.062
Length of hospital stay (days)	5.83 ± 6.45	5.19 ± 5.80	5.01 ± 5.70	<0.001	<0.001	0.025
Urgent admission (n, %)	1278 (60.11%)	6133 (50.37%)	4390 (47.19%)	<0.001	<0.001	<0.001
In-hospital death (n, %)	43 (2.02%)	145 (1.19%)	85 (0.91%)	0.002	<0.001	0.051
Risk of in-hospital death (OR ± 95% CI)	0.97 ± 0.72–1.30	1	0.95 ± 0.63–1.44	–	–	–
Number of non-elective rehospitalizations in the 14-day period after discharge (n, %)	88 (4.14%)	220 (1.81%)	146 (1.57%)	<0.001	<0.001	0.18
Number of non-elective rehospitalizations in the 30-day period after discharge (n, %)	171 (8.04%)	531 (4.36%)	316 (3.40%)	<0.001	<0.001	<0.001
Number of non-elective rehospitalizations in the one-year period after discharge (n, %)	376 (17.69%)	1398 (11.48%)	903 (9.71%)	<0.001	<0.001	<0.001

Commentary: data presented as the mean ± standard deviation or number (n) and % of subjects. For patients aged <65 y, BMI range was assigned according to WHO recommendations [21] and for patients aged ≥ 65 y according to modified ranges: < 23 kg/m², 23–33 kg/m², >33 kg/m² [23], i.e. BMI range I (Underweight) included patients with BMI < 18.5 kg/m² (<65 y) and <23 kg/m² (aged ≥ 65 y); BMI range II (Healthy normal weight) included patients with 18.5 kg/m² ≤ BMI < 25 kg/m² (aged <65 y) and 23 kg/m² ≤ BMI < 33 kg/m² (aged ≥ 65 y); BMI range III (Overweight) included patients with BMI ≥ 25 kg/m² (aged <65 y) and BMI ≥ 33 kg/m² (aged ≥ 65 y). OR ± 95% CI (odds ratio ± 95% confidence interval) for all-cause in-hospital mortality was calculated in relation to healthy normal BMI range (II). OR expresses the probability of the occurrence of in-hospital death during hospitalization of a patient with a BMI value range below or above such defined normal.

Abbreviations: BMI = body mass index; NRS-2002 = Nutritional Risk Screening 2002 questionnaire.

Table 4
Factors determining the risk of in-hospital death in the logistic regression model. Chi² (5) = 143.19; p < 0.0001; n = 23 603.

Parameter	Constant	Age	Male gender	BMI	FM/FFM
OR for one unit	0.001	1.043	1.912	0.938	3.818
–95% CI	0.000	1.032	1.312	0.896	1.519
+95% CI	0.004	1.054	2.785	0.982	9.593
OR for study range		32.282	1.912	0.047	483.512
–95% CI		13.479	1.312	0.005	6.890
+95% CI		77.316	2.785	0.425	33929.890

Abbreviations: BMI = body mass index; FM/FFM = fat to fat-free mass ratio; CI = confidence interval; OR = odds ratio.

gender, had the greatest OR. It should be underlined that the representation of nutritional status by FM/FFM ratio was positively and BMI negatively related to the risk of in-hospital death, despite both variables being derivatives (Table 4). When cardiovascular and neoplastic comorbidities were added to the model, the effects of BMI and FM/FFM on the risk of in-hospital death were similar and still significant (Table 4a). The effect of FM/FFM ratio on all-cause in-hospital mortality (OR 4.10; 95%

confidence interval [CI] 1.64–10.24) was even greater than for cardiovascular diseases and neoplasm, although the effect of the FM/FFM ratio was less than that of cardiovascular diseases and neoplasm when nutrition-associated risk expressed by an NRS-2002 score of at least 3 was added to the model (Table 4b). NRS-2002 score in this model achieved the greatest OR of all the variables.

4. Discussion

To the best of our knowledge, our study is the first to analyze the BMI-associated risk among all consecutive patients hospitalized in one center over a two-year period. Our patients were divided into several groups in relation to different cut-off criteria for BMI: according to the WHO (Table 2), BMI median, quartiles and percentiles (Fig. 1), as well as percentiles of actual to ideal body mass (Fig. 2). We also tried to adjust BMI value by patients' age through a comparison of clinical data and the prevalence of the measured outcomes in the BMI ranges corrected for patients aged ≥ 65 years, in accordance with suggestions by Winter et al. [23] (Table 3), through the use of a formula proposed by Jackson et al. [24] and the

Table 4a
Factors determining the risk of in-hospital death in the logistic regression model after the addition of data concerning cardiovascular and cancerous co-morbidities Chi² (6) = 208.86; p < 0.0001; n = 23 603.

Parameter	Constant	Age	Male gender	BMI	FM/FFM	CVD	Cancer
OR for one unit	0.001	1.04	1.80	0.94	4.10	1.55	3.81
–95% CI	0.0003	1.03	1.24	0.89	1.64	1.16	2.80
+95% CI	0.004	1.05	2.63	0.98	10.26	2.06	5.19
OR for study range		24.54	1.80	0.046	669.31	1.55	3.81
–95% CI		9.74	1.24	0.005	9.70	1.16	2.80
+95% CI		61.82	2.63	0.41	46179.57	2.06	5.19

Abbreviations: BMI = body mass index; FM/FFM = fat to fat-free mass ratio; CVD = cardiovascular disease as a main diagnosis on discharge; cancer = malignant neoplastic disease as a main diagnosis on discharge; CI = confidence interval; OR = odds ratio.

Table 4b

Factors determining the risk of in-hospital death in the logistic regression model after the addition of data concerning nutritional risk, cardiovascular and cancerous comorbidities. $\text{Chi}^2(7) = 411.60$; $p < 0.0001$; $n = 23\ 603$.

Parameter	Constant	Age	Male gender	BMI	FM/FFM	CVD	Cancer	NRS-2002
OR for one unit	0.001	1.03	1.40	1.01	1.54	1.32	2.17	11.16
–95% CI	0.002	1.01	0.93	0.96	0.56	0.98	1.56	8.38
+95% CI	0.002	1.04	2.09	1.05	4.24	1.78	3.02	14.86
OR for study range		7.61	1.40	1.24	7.37	1.32	2.17	11.16
–95% CI		2.96	0.93	0.12	0.07	0.98	1.56	8.38
+95% CI		19.53	2.09	12.39	783.44	1.78	3.02	14.86

Abbreviations: BMI = body mass index; FM/FFM = fat to fat-free mass ratio; CVD = cardiovascular disease as a main diagnosis on discharge; cancer = malignant neoplastic disease as a main diagnosis on discharge; NRS-2002 = Nutritional Risk Screening 2002 questionnaire (the variable was introduced as a qualitative, dichotomous variable: ≥ 3 and < 3 score); CI = confidence interval; OR = odds ratio.

calculation of the FM/FFM ratio, which is a derivative of BMI, patients' age and gender (Tables 1–4). All the univariate and multivariate (Table 4) analyses showed a similar (Table 2) or better (Tables 3, 4 and 4a) prognosis for patients being overweight in comparison to normally nourished and malnourished patients (Table 4b), which may be recognized as the presence of the “obesity paradox” because BMI was the only variable favorably affecting the risk of the measured outcomes in the population studied. The variables related to increased risk of the occurrence of the established end-points were as follows: patients' age, male gender, FM/FFM ratio, comorbidities (cardiovascular diseases and neoplasm) and an NRS-2002 score amounting to ≥ 3 (Tables 4–4b).

Our results corroborate a number of papers which have indicated the presence of the “obesity paradox” in the general population [30]. In the recent meta-analysis by Winter et al. [23], performed on data published in 32 investigations concerning 197 940 individuals living in the community aged ≥ 65 y who were followed-up on average for 12 years, the association between BMI and all-cause mortality was non-linear and U-shaped. In this meta-analysis, the risk of death was the lowest among patients in the BMI range of 24–30.9 kg/m² and the favorable effect of increased BMI was marked even for patients with a BMI of 30.0–34.9 kg/m². Patients in the BMI range of 35.0–39.9 kg/m² had a 21% greater risk of mortality, but this was modified by comorbidities and smoking status [23]. Whereas, in a meta-analysis of 239 prospective studies which considered 10 625 411 participants from 32 countries, in Asia, Australia and New Zealand, Europe, and North America, the Global BMI Mortality Collaboration found that survival was the best in patients with a BMI of 20–25 kg/m² and decreased just below this range and through the overweight and obesity ranges [22]. However, in both the aforementioned publications, the authors excluded hospitalized patients from their review of published articles and the analysis, whereas this population of patients was the subject of our analysis. In the publications available, we did not find data concerning BMI-associated epidemiology among consecutive inpatients (the general hospital population), as in our analysis. In some articles the authors analyzed the associations between overweight and obesity and the outcome of concrete health disorder therapy in short-term follow-ups (in-hospital or 30 days). In the majority of these publications, the authors confirmed the existence of an “overweight paradox”, “obesity paradox”, “BMI paradox” or at least a similar risk of mortality and/or morbidity among inpatients with increased BMI in comparison with hospitalized patients of normal weight. These publications concerned the following conditions: adults undergoing cardiac surgery [5,31,32], patients with acute heart failure [33], patients with in-hospital cardiac arrest [34], patients with ST-segment elevation myocardial infarction (STEMI) [35], patients after percutaneous coronary intervention (PCI) [36], patients undergoing vascular surgery [37], patients undergoing hip replacement surgery [38],

older nursing-home residents [39], and patients with hyperglycemia and diabetes, regardless of glycemic status [40].

In our study, we modified BMI ranges for older patients and patients aged below 65 y (Table 3). This analysis seemed by us to be justified by the high representation of older patients in the population studied (42.45%) and the association of aging with a decrease in patients' height, and an increase in body weight and fat mass percentage [14,23,24]. This analysis was performed in three BMI categories, as stated in the commentary to Table 3, and range III included patients < 65 y who were overweight or obese in accordance with the standard WHO definition [21] and patients aged ≥ 65 y with BMI ≥ 33 kg/m² [23]. The modification of BMI ranges resulted in statistically significant differences between patients of normal weight, and not only those who are malnourished, but also overweight patients, in relation to length of in-hospital stay, as well as the prevalence of in-hospital death (23.5%), 30-day readmission (22%), and one-year readmission (15%) (Tables 2, 3, 4, 4a, 4b, Figs. 1 and 2). These observations, in spite of the suggestions of the Global BMI Mortality Collaboration concerning outpatients [22], confirmed the presence of an “obesity paradox” among inpatients. On the other hand, high body fat determined on the basis of BMI, patients' age and gender was a powerful risk factor for all-cause in-hospital mortality. Such apparently contrary observations corroborate the study results of Padwal et al. [30], who, in a population of 49 476 women and 4944 men aged 40 years or older referred for bone mineral density scans, found that low BMI and high body fat percentage were independent variables associated with increased mortality. Moreover, we also confirmed the well-known observation [23,41] that undernutrition is the strongest independent risk factor for unfavorable outcomes among hospitalized patients, which should be interpreted as a factor confirming the validity of our analysis.

Our study may have several limitations. First, BMI values were only available for 70% of the inpatients who fulfilled the inclusion criteria, which was mainly the result of the seriously ill clinical condition of the remaining inpatients, for whom the measurement of weight and height was impossible. Moreover, compared to individuals for whom BMI values were available, inpatients in whom BMI assessment was impossible significantly differed in relation to the majority of demographic, clinical and biochemical data and prevalence of the measured outcomes (Tables 1 and 1a), which may decrease the external validity of our analysis. However, the main conclusions were made on the basis of comparisons of demographic and clinical data among patients from each BMI categorization. Second, the prevalence of death and non-elective readmissions found might be biased by the accumulation of seriously ill patients who needed hospitalization [42], although knowledge concerning the clinical importance of BMI determination in this population is also relevant. On the other hand, it is obvious that our observations are not useful for the

general population and outpatients. Third, regular follow-up is lacking in our study, although an analysis of readmission risk can be considered its equivalent. Fourth, our analysis concerning risk of readmission may be biased because we analyzed only non-elective rehospitalizations in our hospital, but our patients might have been admitted to other medical centers which were not noted. Fifth, our analysis was performed historically on the basis of electronic documentation and, therefore, some clinical data might have been overlooked. Sixth, we did not analyze dynamic changes in body weight, and it is known that fluctuations in body mass, especially when unintentional, are factors in poor prognosis. Data from the NRS-2002 questionnaire could be considered as a substitute for this analysis, as inpatients were asked for their weight loss during each of the previous three months, where scoring ≥ 3 is one of the strongest risk factors for in-hospital death [41]. This was also confirmed in this study (Table 4b). Seventh, in our study, there is a lack of analysis of fat distribution measured by the determination of waist circumference, waist-to-hip ratio or body composition. However, the surrogate of this analysis was the calculation, from BMI value, of body fat percentage and its derivatives, such as FM, FFM and FM/FFM ratio, which seem to be better than BMI in the prediction of clinical outcomes [18] (Tables 1–3). Eighth, in our study, we analyzed only all-cause mortality, without disease-specific risk of death and readmission, but it is known that various disorders have different associations with BMI and clinical outcomes [23,30,43,44]. Moreover, in our study, comorbidities, other than cardiovascular diseases and neoplasm, their clinical advancement, as well as lifestyle considerations, e.g. smoking, were not taken into account and publications by Winter et al. [23] and the Global BMI Mortality Collaboration [22] show an influence of these factors on patients' BMI value and mortality.

In conclusion, the greatest risk of all-cause in-hospital death and readmission concerned malnourished inpatients. Compared to patients with a normal BMI range, overweight and obesity, which concerned 62.21% of the inpatients studied, were associated with a similar or lower (not greater!) risk of length of in-hospital stay, urgent admission, all-cause in-hospital mortality and readmission, regardless of the diagnostic criteria (BMI range or quotient of actual and ideal body mass) used and BMI categorization (use of WHO standard criteria, median, quartiles or shifting to the right and extending criteria for the normal range of BMI for patients aged ≥ 65 y). However, because BMI has a number of limitations as a biomarker of obesity, it was a favorable but only a weak prognostic factor for the outcomes measured, and its significant effect disappeared when nutritional risk (NRS-2002 score) was taken into account. Moreover, the FM/FFM ratio, which was calculated on the basis of BMI, was associated with an increased risk of all-cause in-hospital death and readmission compared to BMI and was stronger in effect. BMI seems to be too simple a prognostic parameter among inpatients and should probably be replaced by other markers of obesity. In this context, our observations should be interpreted as suggesting a “BMI paradox”, rather than an “obesity paradox”.

Conflict of interest

None declared.

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