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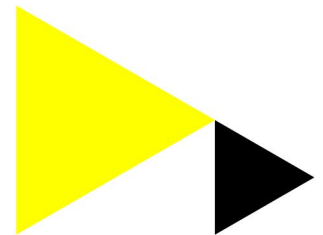
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Visceral obesity measured using computed tomography scans: No significant association with mortality in critically ill patients

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ABSTRACT

Introduction: The association between obesity and outcome in critical illness is unclear. Since the amount of visceral adipose tissue (VAT) rather than BMI mediates the health effects of obesity we aimed to investigate the association between visceral obesity, BMI and 90-day mortality in critically ill patients.

Method: In 555 critically ill patients (68% male), the VAT Index (VATI) was measured using Computed Tomography scans on the level of vertebra L3. The association between visceral obesity, BMI and 90-day mortality was investigated using univariable and multivariable analyses, correcting for age, sex, APACHE II score, sarcopenia and muscle quality.

Results: Visceral obesity was present in 48.1% of the patients and its prevalence was similar in males and females. Mortality was similar amongst patients with and without visceral obesity (27.7% vs 24.0%, $p = 0.31$). The corrected odds ratio of 90-day mortality for visceral obesity was 0.667 (95%CI 0.424–1.049, $p = 0.080$). Using normal BMI as reference, the corrected odds ratio for overweight was 0.721 (95%CI 0.447–1.164 $p = 0.181$) and for obesity 0.462 (95%CI 0.208–1.027, $p = 0.058$).

Conclusion: No significant association of visceral obesity and BMI with 90-day mortality was observed in critically ill patients, although obesity and visceral obesity tended to be associated with improved 90-day mortality.

1. Introduction

The association between body composition and outcome in critical illness is increasingly gaining interest. It is known that sarcopenia and low muscle quality are associated with increased mortality in critically ill patients [1,2]. In contrast, the relation between obesity and outcome in critical illness is less clear. In the general population, it is known that obesity is associated with increased health risks such as chronic inflammation, a procoagulant state, insulin resistance, type 2 diabetes, dyslipidemia, hypertension, cardiovascular disease, chronic kidney

disease and various types of cancer [3–8]. However, in critically ill patients several studies suggest that obesity is associated with better survival [3,9–14], although this so-called “obesity paradox” is not uniformly reproduced by other studies [3,15]. The metabolic consequences of obesity are also different between men and women [16–18]. There is increasing recognition that BMI is not the most factor that determines the impact of adiposity on health status, but that the distribution of the adipose tissue and in particular the amount of visceral adipose tissue mediates the metabolic consequences of obesity [19,20]. To shed further light on the association between obesity and outcome in

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critical illness it seems important to investigate in particular the association between the amount of visceral adipose tissue and outcome. The aim of the present study was to evaluate the association of visceral obesity and BMI with 90-day mortality in critically ill patients.

2. Methods

2.1. Patients

The study population consisted of patients admitted to the Intensive Care Unit (ICU) of the Amsterdam University Medical Center between September 2003 and February 2016. All patients had an abdominal CT scan suitable for body composition analyses between one day before to four days after admission to the ICU. Patients with an abdominal CT scan of sufficient quality to perform analyses were included in the study. Data on muscle mass and muscle quality originating from the same cohort have been published before [1,2]. For this analyses, we selected patients with a non-elective ICU admission as showed in Fig. 1.

2.2. Body composition analysis

CT-scan analysis of body composition was performed as described by Mourtzakis et al [21]. Briefly, a single slice of each individual CT scan was selected at the level of the 3rd lumbar vertebra. Using predefined Hounsfield Unit (HU) ranges, visceral adipose tissue (VAT) (−150 to −50 HU) was determined. The total area of VAT was estimated by assessing the total tissue area at vertebra L3 and indexed for height by dividing it by height squared, resulting in the Visceral Adipose Tissue Index (VATI) given in cm^2/m^2 . In a large number of CT scans the subcutaneous adipose tissue was cut off, whereby reliable analysis of subcutaneous adipose tissue was not possible. In addition we calculated the Skeletal Muscle area Index (SMI) (−29 to 150 HU). Muscle quality, assessed by Computed Tomography derived muscle density, is given as the mean Radiation Attenuation (RA), expressed in Hounsfield Units (HU) of the total skeletal muscle tissue area [2,22]. Body composition analyses were performed by 2 trained researchers. Each CT scan was analyzed by a single researcher who had frequent consultation with another trained researcher if there was any doubt about eligibility, landmarking, or analysis. Previous research shows a variability of <2% for this method [2,23]. CT scans were analyzed using SliceOmatic V4.3 and 5.0 (TomoVision, Magog, Canada) software for Microsoft

Windows®.

2.3. The definition of visceral obesity

Body composition and the Visceral Adipose Tissue Index (VATI) are ethnicity and sex dependent [24,25]. To define visceral obesity sex specific cut-off values for VATI from a healthy Caucasian population were used [25]. The cut-off value of VATI for visceral obesity in males was $\geq 38.7 \text{ cm}^2/\text{m}^2$ and for females $\geq 24.9 \text{ cm}^2/\text{m}^2$ [25].

2.4. The definition of sarcopenia

To define sarcopenia, a Skeletal Muscle area Index (SMI) below the 5th percentile of a healthy Caucasian population were used. For males, this was a SMI of $41.6 \text{ cm}^2/\text{m}^2$. For females, a SMI of $32.0 \text{ cm}^2/\text{m}^2$ was used as a cut-off value [26].

2.5. BMI categories

BMI was categorized according to the definition of the World Health Organization (WHO): 1) a BMI value of $<18.5 \text{ kg}/\text{m}^2$ indicating underweight, 2) BMI $18.5\text{--}24.9 \text{ kg}/\text{m}^2$ indicating a normal weight, 3) BMI $25\text{--}29.9 \text{ kg}/\text{m}^2$ indicating overweight and 4) BMI $\geq 30 \text{ kg}/\text{m}^2$ indicating obesity [27].

2.6. Statistical analysis

Categorical variables are presented as number of patients (%), where mean \pm standard deviation (SD) or median (interquartile range, IQR) were used for numerical variables.

Differences in categorical and numerical variables between groups (visceral obesity yes/no; died within 90 days yes/no) were assessed using chi-square and independent samples *t*-tests, respectively. In case of clear non-normality based on histograms, medians and IQRs were reported and a Mann-Whitney *U* test was performed instead of a *t*-test.

Multivariable logistic regression analysis were performed to test the association of visceral obesity and BMI with 90-day mortality, correcting for variables that may influence mortality such as disease severity using the APACHE II score [28], age, sex, the presence of sarcopenia and muscle quality. To assess potential effect-modification of sex, the interaction between sex and BMI, visceral obesity, sarcopenia and muscle quality were tested. In case of significant interaction with sex, the effects were reported separately for men and women. In case of non-significant interaction, the interaction term was removed from the model and the effects were reported for men and women combined. Collinearity was checked using Variation Inflation Factor (VIF). To check the robustness of the results, a Cox regression analysis assessing the time-to-event was included as a sensitivity analysis, where the same variables were included as in the logistic regression analysis model. Additionally, Kaplan Meier curves (and log-rank test) were used to visualize the association between visceral obesity and 90 day mortality.

Analyses were performed using IBM SPSS Statistics for Windows version 25 (Armonk, NY, USA; IBM Corp.). A *p*-value ≤ 0.05 was considered statistically significant. The statistical analyses were supervised by a statistician (BW).

2.7. Ethics

The study protocol was reviewed and approved by the Medical Ethics Committee of the Amsterdam University Medical Center, location VUmc (IRB00002991, decision 2012/243). The study has also been registered at [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT02817646). The need for informed consent was waived because of the retrospective nature of the study using coded data obtained from standard care. The Medical Research Involving Human Subjects Act does not apply to the study and the study was conducted in accordance with the Declaration of Helsinki.

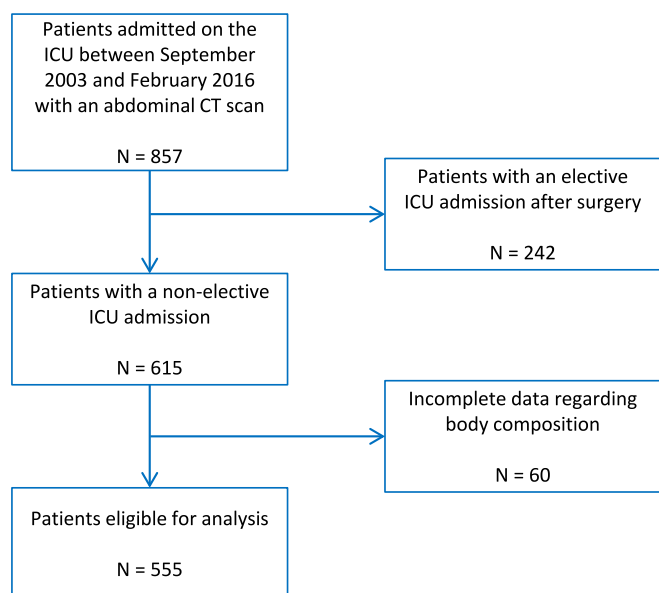


Fig. 1. Patient selection.

3. Results

3.1. Study population

A total number of 555 (378 male (68%) and 177 female (32%)) patients were included in the analysis. Mean (\pm SD) age was 55 (\pm 19) years and mean APACHE II [28] score was 24 (\pm 8). Median (IQR) duration of mechanical ventilation was 10.0 (6.0–18.0) days, median ICU stay was 12 (7–22) days and median hospital stay was 30 (17–52) days. The ICU mortality was 16% and overall mortality within 90 days after admission to the ICU was 26%. ICU and 90 day mortality was not different between sexes ($p = 0.287$ and $p = 0.261$ respectively). ICU mortality in females was 18.1% and 90 day mortality was 28.8%. In males, ICU mortality was 14.6% and 90 day mortality was 24.3%. More patient characteristics and characteristics of patients with visceral obesity and without visceral obesity are presented in Table 1.

3.2. The prevalence of visceral obesity and BMI categories

Mean (\pm SD) VATI was 42.2 cm²/m² (\pm 32.8) for males and 30.3 cm²/m² (\pm 25.6) for females. Using sex specific cut-off values from an otherwise healthy Caucasian population [25] visceral obesity was present in 183 (48%) males and 84 (47%) females. A comparison of patients with and without visceral obesity and their BMI is presented in Table 2. Twenty-nine percent of the patients with a normal weight according to BMI were classified as having visceral obesity.

3.3. Univariable analysis of 90-day mortality

In total, 143 patients (25.8%) died within 90 days after ICU admission. The presence of visceral obesity was not significantly associated ($p = 0.312$) with higher mortality (Table 3, Fig. 2). Also BMI ($p = 0.774$) and sex ($p = 0.261$) were not significantly associated with a higher mortality as shown in Table 3. The age of patients, disease severity using the APACHE II score, the presence of sarcopenia and muscle quality were significantly associated with a higher 90 day mortality following ICU admission ($p \leq 0.001$).

3.4. Multivariable analysis of 90 day mortality

The interaction terms between sex and BMI ($p = 0.469$), visceral obesity ($p = 0.949$), sarcopenia ($p = 0.654$ in model with BMI, $p = 0.537$ in model with visceral obesity) and muscle quality ($p = 0.997$ in model with BMI, $p = 0.837$ in model with visceral obesity) were not significant. Therefore, the effects of BMI or visceral obesity on 90-day mortality are presented for men and women combined using logistic regression analysis with correction for age, sex, APACHE II score, sarcopenia and muscle quality.

Visceral obesity was not significantly associated with 90-day mortality, although the 95% confidence interval was largely compatible with a favorable association between visceral obesity and 90-day mortality (OR 0.667 (0.424–1.049, $p = 0.080$) (Table 4). When defined by BMI category, obesity was not significantly associated with 90-day mortality, although also here the 95% confidence interval was largely compatible with a favorable association between obesity and 90-day mortality (Table 5). Of the factors included in the analyses age and APACHE II score were significantly associated with increased mortality ($p \leq 0.001$). Sarcopenia was significant in the model with visceral obesity ($p = 0.045$), but not with BMI ($p = 0.147$). Since there was a collinearity problem with BMI and visceral obesity (VIF values for normal weight and obesity were larger than 10), BMI and visceral obesity could not be analyzed in the same analyses and were therefore analyzed separately.

Table 1
Characteristics of the study population.

	Mean (\pm SD), median (IQR) or number (%)			P-value
	Overall (N = 555)	Visceral obesity (N = 267)	No visceral obesity (N = 288)	
Demographics and body composition				0.834 ^a
Sex (%)				
Male	378 (68.1%)	183 (68.5%)	195 (67.7%)	
Female	177 (31.9%)	84 (31.5%)	93 (32.3%)	
Age (years)	55 (\pm 19)	64 (\pm 14)	47 (\pm 20)	<0.001 ^b
Weight (kg)	77.5 (\pm 14.8)	82.6 (\pm 14.6)	72.7 (\pm 13.2)	<0.001 ^b
Height (m)	1.75 (\pm 0.1)	1.75 (\pm 0.1)	1.75 (\pm 0.1)	0.554 ^b
BMI (kg/m ²)	25 (\pm 4)	27 (\pm 4)	24 (\pm 3)	<0.001 ^b
Hospital stay before ICU admission (days)	0 (0–1)	0 (0–2)	0 (0–1)	0.042 ^c
Time between ICU admission and CT scan (days)	0 (0–1)	0 (0–1)	0 (0–0)	0.610 ^c
Admission diagnosis				<0.001 ^a
Cardiovascular	34 (6.1%)	24 (9.0%)	10 (3.5%)	
Metabolic/Renal	21 (3.8%)	16 (6.0%)	5 (1.7%)	
Neurologic	56 (10.1%)	26 (9.7%)	30 (10.4%)	
Post resuscitation	44 (7.9%)	26 (9.7%)	18 (6.3%)	
Respiratory insufficiency	86 (15.5%)	53 (19.9%)	33 (11.5%)	
Sepsis	61 (11.0%)	32 (12.0%)	29 (10.1%)	
Trauma	191 (34.4%)	59 (22.1%)	132 (45.8%)	
Other/unknown	62 (11.1%)	31 (11.6%)	31 (10.8%)	
Disease severity				0.008 ^b
APACHE II score	24 (\pm 8)	24 (\pm 8)	23 (\pm 8)	
Outcomes				
ICU stay (days)	12 (7–22)	13 (8–21)	12 (7–23)	0.058 ^c
Hospital stay (days)	30 (17–52)	30 (17–54)	31 (18–50)	0.559 ^c
Duration of mechanical ventilation (days) ^a	10.0 (6.0–18.0)	9.0 (6.0–18.3)	10.0 (6.0–18.0)	0.752 ^c
Mortality within 90 days after admission to the ICU	143 (26%)	74 (27.7%)	69 (24.0%)	0.312 ^a

Values are presented as mean (\pm SD), median (IQR) and absolute number (%). Normality was checked using histograms.

^a chi square test.

^b Independent sample t-test.

^c Mann-Whitney U test.

* 262 patients with visceral obesity and 287 patients without visceral obesity received mechanical ventilation.

3.5. Sensitivity analysis

To assess a potential difference in time-to-event, we performed a Cox regression analysis as a sensitivity analysis, including the same variables as for logistic regression analysis, namely visceral obesity or BMI category (underweight, normal weight, overweight, obesity), age, sex, APACHE II score, sarcopenia and muscle quality. The results were similar as the results of the logistic regression analysis (see supplemental Tables S1 and S2).

4. Discussion

The aim of the present study was to investigate the effect of visceral obesity

Table 2
Comparison of visceral obesity and BMI.

	Underweight	Normal weight	Overweight	Obese	Total
Visceral obesity	1 (7.7%)	83 (28.8%)	126 (66.3%)	49 (94.2%)	259 (47.7%)
No visceral obesity	12 (92.3%)	205 (71.2%)	64 (33.7%)	3 (5.8%)	284 (52.3%)
Total	13 (2.4%)	288 (53.0%)	190 (35.0%)	52 (9.6%)	

Visceral obesity was measured using Computed Tomography scans and defined as a VATI value of $\geq 38.7 \text{ cm}^2/\text{m}^2$ for males and $\geq 24.9 \text{ cm}^2/\text{m}^2$ for females [25]. Underweight is defined as a BMI $\leq 18.5 \text{ kg}/\text{m}^2$, normal weight is defined as a BMI of 18.5–24.9 kg/m^2 , overweight is defined as a BMI of 25.0–29.9 kg/m^2 and obesity is defined as a BMI $\geq 30.0 \text{ kg}/\text{m}^2$ according to the WHO [27]. * BMI of 12 patients is missing.

Table 3
Univariable analysis of 90-day mortality.

	Alive (N = 412)	Dead (N = 143)	P-value
Age (years) N = 555	52.0 (± 19.2)	64.1 (± 16.6)	<0.001 ^a
Sex			0.261 ^b
Male N = 378	286 (69.4%)	92 (24.3%)	
Female N = 177	126 (71.2%)	51 (28.8%)	
APACHE II * N = 553	22.0 (± 8.0)	27.5 (± 7.9)	<0.001 ^a
Sarcopenia			<0.001 ^b
Yes N = 85	47 (55.3%)	38 (44.7%)	
No N = 470	365 (77.7%)	105 (22.3%)	
Muscle quality (HU) N = 555	36.7 (± 12.8)	29.0 (± 12.0)	<0.001 ^a
Visceral obesity			0.312 ^b
Yes N = 267	193 (72.3%)	74 (27.7%)	
No N = 288	219 (76.0%)	69 (24.0%)	
BMI* N = 543			0.774 ^{b, **}
Underweight N = 13	9 (69.2%)	4 (30.8%)	
Normal weight N = 288	210 (72.9%)	78 (27.1%)	
Overweight N = 190	143 (75.3%)	47 (24.7%)	
Obesity N = 52	41 (78.8%)	11 (21.2%)	

Numerical data are presented as mean (\pm SD), categorical data are presented as number of patients (%). Statistical tests that were used were.

^a Independent sample t-test.

^b chi square test.

* Of 2 surviving ICU patients APACHE II score is missing and of 12 patients BMI is missing.

** The trend test for BMI categories was not significant ($p = 0.296$). Sarcopenia is defined as a SMI for males of $41.6 \text{ cm}^2/\text{m}^2$ and a SMI for females of $32.0 \text{ cm}^2/\text{m}^2$ [26]. Muscle quality, assessed by Computed Tomography derived muscle density, is given as the mean Radiation Attenuation (RA), expressed in Hounsfield Units (HU) of the total skeletal muscle tissue area [2,22]. Visceral obesity is defined as a VATI value of $\geq 38.7 \text{ cm}^2/\text{m}^2$ for males $\geq 24.9 \text{ cm}^2/\text{m}^2$ for females [25]. Underweight is defined as a BMI $\leq 18.5 \text{ kg}/\text{m}^2$, normal weight is defined as a BMI of 18.5–24.9 kg/m^2 , overweight is defined as a BMI of 25.0–29.9 kg/m^2 and obesity is defined as a BMI $\geq 30.0 \text{ kg}/\text{m}^2$ according to the WHO [27].

measured using CT scans, on 90-day mortality in critically ill patients, using sex specific cut-off values of a Caucasian cohort to define visceral obesity. This in order to gain more insight in the possible obesity paradox in critical illness. Univariable analysis revealed no significant association between visceral obesity or obesity (based on BMI) and 90-day mortality in critically ill patients with a non-elective ICU admission. After correction for age, sex, sarcopenia, muscle quality and APACHE II score, the association between visceral obesity and 90-day mortality and the association between obesity and 90-day mortality did not reach statistical significance, although the 95% confidence interval of the odds ratios for 90-day for mortality was largely compatible with better survival in patients with visceral obesity as well as in patients with obesity defined by BMI.

Of note, the proportion of patients classified as obese based on BMI was considerably smaller than the proportion of patients classified as having visceral obesity.

Previous research regarding the relationship of obesity with ICU outcome is contradictory. In general, obesity is associated with higher mortality [3–8]. In critically ill patients it has been reported that mild obesity is beneficial compared to normal BMI [3,9–14]. However, the existence of an obesity paradox in critical illness has been debated by recent studies [15,29,30]. In previous studies regarding obesity and outcome, BMI is most frequently used to define obesity. However, to address the relation between obesity and clinical outcomes it seems important to appreciate the pathophysiological processes that may mediate this relation. In particular, visceral adipose tissue is metabolically active and associated with increased health risks and various diseases [3,19,20]. This is in contrast to subcutaneous adipose tissue which is not metabolically active and may have benefits such as providing energy and lipid stores during the acute catabolic phase in critical illness [3]. This differentiated distribution of adipose tissue is not reflected when using BMI in the definition of obesity. Moreover, in the BMI the weight of muscle tissue is included and previous research shows that sarcopenia at ICU admission is an important predictor of increased mortality [1]. When using BMI to assess the relation between obesity and outcome, it is not possible to distinguish the separate effects of obesity and sarcopenia on mortality. Since, the distribution of visceral and subcutaneous adipose tissue differs between individuals, and typically between sexes, with males typically having a predominant visceral adipose tissue distribution and females a predominant subcutaneous distribution we used sex specific cut-off values to define visceral obesity [24,25]. Since body composition differs also per population, we used external reference values from a relatively healthy Caucasian population [25,31,32].

An earlier study showed that visceral obesity measured at the third lumbar vertebra using CT scans was a better predictor for metabolic risk than BMI [25]. We have explored whether using visceral adipose tissue area rather than BMI would better describe the obesity paradox, but found that neither BMI nor visceral adiposity was significantly associated with increased mortality risk in our population of critically ill patients with a non-elective ICU admission. In the present study mortality was not significantly associated with BMI or visceral obesity in critically ill patients. However, we observed a trend that was compatible with improved survival in patients with obesity and visceral obesity and therefore based on our current results we cannot definitely reject the obesity paradox.

There is data that suggest that the amount of visceral adipose tissue may protect against muscle weakness [33,34]. Unfortunately, data on functional outcome regarding muscle strength are not available in this cohort. In the present study muscle quality was not associated with mortality in multivariable in contrast to univariable analysis. An association between mortality and achievement of energy and protein targets has been described in patients from the current source population [35]. Unfortunately, we were not able to link the currently analyzed data to nutritional data.

Wirtz et al. and Yang et al. addressed the association between VAT and outcome in critically ill patients and COVID-19 patients, respectively, and found an association between the onset and duration of mechanical ventilation and VAT area [36,37]. They both included a substantial number of patients who did not receive mechanical ventilation which impairs comparability with our data. In addition, the use of cut-off values was different. Wirtz et al. used a cut-off value of 241.4 cm^2 , which was defined in the investigated population, and Yang et al. used a cut-off value of 100 cm^2 for both men and women, which was not indexed for height.

The present study has several strengths and weaknesses. The sample size was quite large in comparison to other body composition studies in critical illness. In addition, by excluding patients that were admitted in the ICU electively after surgery we selected a group of patients with “true critical illness”, albeit that considerable heterogeneity persists with respect to admission diagnosis and other baseline characteristics. However, it might be that the observed trends may become statistically significant in larger cohorts or systematic reviews or meta-analyses of multiple cohorts. To increase comparability amongst studies or data pooling of different studies, standardization of methods and definitions are required.

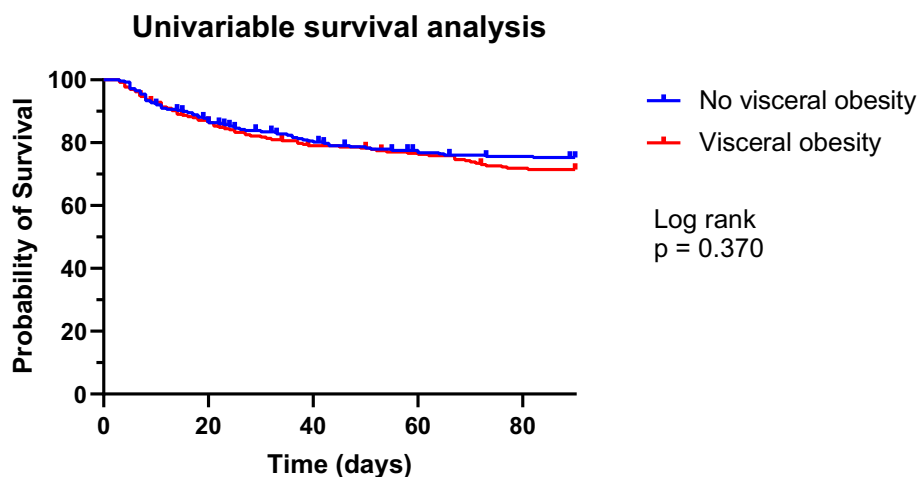


Fig. 2. Univariable survival analysis.

Univariable survival analysis using Kaplan Meier assessing the association between the presence of visceral obesity with 90-day mortality. Visceral obesity is defined as a Visceral Adipose Tissue Index (VATI) measured using Computed Tomography scans of $\geq 38.7 \text{ cm}^2/\text{m}^2$ for males $\geq 24.9 \text{ cm}^2/\text{m}^2$ for females [25].

Table 4

Univariable and multivariable logistic regression analysis of visceral obesity and 90-day mortality.

	Univariable analysis (N = 553)			Multivariable analysis (N = 553)			
	OR	95% CI	P-value	OR	95% CI	P-value	P-value
Visceral obesity	1.128	0.832–1.783	0.311	0.667	0.424–1.049	0.080	
Age (years)	–	–	–	1.027	1.012–1.043	<0.001	
Sex (male vs female)	–	–	–	1.037	0.659–1.630	0.877	
APACHE II score*	–	–	–	1.067	1.039–1.097	<0.001	
Sarcopenia	–	–	–	1.751	1.012–3.028	0.045	
Muscle quality	–	–	–	0.986	0.964–1.009	0.231	

Multivariable analysis using logistic regression analysis with 90 day mortality as outcome. Data are presented as Odds Ratio (OR), 95% Confidence Interval (CI) and p-value. Visceral obesity is defined as a VATI value of $\geq 38.7 \text{ cm}^2/\text{m}^2$ for males and $\geq 24.9 \text{ cm}^2/\text{m}^2$ for females [25]. Disease severity is defined using the APACHE II score (Acute Physiology and Chronic Health Evaluation) [28]. Sarcopenia is defined as a SMI for males of $41.6 \text{ cm}^2/\text{m}^2$ and a SMI for females of $32.0 \text{ cm}^2/\text{m}^2$ [26]. Muscle quality, assessed by Computed Tomography derived muscle density, is given as the mean Radiation Attenuation (RA), expressed in Hounsfield Units (HU) of the total skeletal muscle tissue area [2,22].* Of 2 surviving ICU patients APACHE II score is missing.

Table 5

Univariable and multivariable logistic regression analysis of BMI categories and 90 day mortality.

	Univariable analysis (N = 541)			Multivariable analysis (N = 541)			
	OR	95% CI	P-value	OR	95% CI	P-value	P-value
BMI*			0.758				0.234
Normal weight (reference)							
Underweight	1.185	0.355–3.959	0.782	0.884	0.240–3.261	0.854	
Overweight	0.876	0.576–1.334	0.538	0.721	0.447–1.164	0.181	
Obesity	0.715	0.350–1.462	0.358	0.462	0.208–1.027	0.058	
Age (years)	–	–	–	1.023	1.008–1.038	0.003	
Sex (male vs female)	–	–	–	1.104	0.691–1.762	0.679	
APACHE II score*	–	–	–	1.067	1.038–1.096	<0.001	
Sarcopenia	–	–	–	1.534	0.860–2.735	0.147	
Muscle quality	–	–	–	0.980	0.957–1.004	0.095	

Multivariable analysis using logistic regression analysis with 90 day mortality as outcome. Data are presented as Odds Ratio (OR), 95% Confidence Interval (CI) and p-value. Underweight is defined as a BMI $\leq 18.5 \text{ kg}/\text{m}^2$, normal weight is defined as a BMI of $18.5\text{--}24.9 \text{ kg}/\text{m}^2$, overweight is defined as a BMI of $25.0\text{--}29.9 \text{ kg}/\text{m}^2$ and obesity is defined as a BMI $\geq 30.0 \text{ kg}/\text{m}^2$ according to the WHO [27]. Disease severity is defined using the APACHE II score (Acute Physiology and Chronic Health Evaluation) [28]. Sarcopenia is defined as a SMI for males of $41.6 \text{ cm}^2/\text{m}^2$ and a SMI for females $32.0 \text{ cm}^2/\text{m}^2$ [26]. Muscle quality, assessed by Computed Tomography derived muscle density, is given as the mean Radiation Attenuation (RA), expressed in Hounsfield Units (HU) of the total skeletal muscle tissue area [2,22].

* Of 2 surviving ICU patients APACHE II score is missing and of 12 patients BMI is missing.

Moreover, the study concerns a single center experience over a prolonged period of time. Practice variation amongst different centers or practice changes over time may have affected the external validity of the results.

In the present study, for the definition of visceral obesity, sex specific cut-off values were used since body composition is sex dependent [38]. We used

external reference values which is important since the distribution of body composition in some selected populations may deviate substantially from that of the general population [39]. Also the distribution of adipose tissue and associated health risks is different between populations and therefore we used population specific reference values [31,32]. This is different from previous studies [36,37]. Body composition was measured using Computed

Tomography (CT) scans which is an established method with a high inter- and intra-observer reliability [21,23].

5. Conclusion

In a large heterogenous group of critically ill patients with a non-elective ICU admission, neither visceral obesity nor BMI was significantly associated with an increased or decreased mortality risk. Multivariable analysis showed a trend towards improved 90-day survival in patients with obesity and visceral obesity, therefore the existence of an “obesity paradox” cannot be ruled out based upon the present data.

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CRediT authorship contribution statement

Michelle R. Baggerman: Conceptualization, Investigation, Formal analysis, Writing – original draft, Visualization. **Ingeborg M. Dekker:** Investigation, Writing – review & editing. **Bjorn Winkens:** Formal analysis, Writing – review & editing. **Steven W.M. Olde Damink:** Writing – review & editing. **Sandra N. Stapel:** Writing – review & editing. **Peter J.M. Weijs:** Conceptualization, Resources, Writing – review & editing. **Marcel C.G. van de Poll:** Conceptualization, Formal analysis, Writing – review & editing, Resources, Supervision.

Declaration of Competing Interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jccr.2023.154316>.

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