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DE DOCTEUR EN MEDECINE

Evaluation de la morbi-mortalité chez les patients obèses sarcopéniques hospitalisés en réanimation chirurgicale

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Avertissement

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Avant-propos

Cette thèse d'exercice a été réalisée au sein du service de réanimation chirurgicale de l'hôpital Claude Huriez au CHRU de Lille.

Les résultats de ce travail seront soumis pour publication dans une revue scientifique.

Résumé

Objectif L'obésité et la dénutrition peuvent coexister chez un même individu, cependant il n'est pas rare de méconnaitre ce diagnostic chez les patients atteints d'obésité. Une technique récente assistée par tomodensitométrie (TDM) permet de prédire la composition régionale en masse maigre et grasse. Cette méthode n'a pas encore été validée chez les patients de réanimation mais pourrait être facilement mise en œuvre afin de faire le diagnostic d'obésité sarcopénique. L'obésité sarcopénique est caractérisée par un excès de masse grasse associé à une faible musculature squelettique, délétère particulièrement lors de stress aigu comme la réanimation. Les objectifs de cette étude étaient : i- d'évaluer l'impact de l'obésité sarcopénique sur la mortalité à 90 jours chez les patients admis en réanimation chirurgicale, ii- d'évaluer la morbidité associée à l'obésité sarcopénique, et iii- d'étudier la mortalité à 1 an chez ces patients.

Méthodes. Cette étude rétrospective menée dans le service de réanimation chirurgicale de l'hôpital Claude Huriez de Lille a inclus 203 patients dont 58 patients atteints d'obésité sarcopénique, diagnostiquée grâce à l'index musculaire squelettique mesuré au TDM à l'aide du logiciel MYRIAN. Une régression logistique a été réalisée pour identifier l'association et l'effet de l'obésité sarcopénique sur la mortalité à 90 jours et à 1 an de l'admission ajustée sur les facteurs de confusion potentiels.

Résultats. Le taux de mortalité à 90 jours et à 1 an après l'admission était respectivement de 18,2 % et 27,6%. Il n'y avait pas d'impact significatif de la sarcopénie sur la mortalité à 90 jours après l'admission. En revanche, la sarcopénie était associée à un risque plus élevé de mortalité à un an après l'admission, même après ajustement (OR = 2,25 [1,05-4,88] ; p=0,04). Les variations de poids estimées entre l'admission et la sortie de réanimation étaient statistiquement différentes (perte de 2,8 kg chez les obèses sarcopéniques vs gain de 3,4 kg chez les obèses non sarcopéniques (p=0,003)).

Conclusions. L'obésité sarcopénique est associée à une augmentation significative de la mortalité à l'admission en réanimation à un an. L'analyse quantitative de la composition corporelle par TDM pourrait être généralisée afin de permettre le dépistage de l'obésité sarcopénique dans

les unités de réanimation. D’autres études sont nécessaires pour évaluer les approches nutritionnelles adaptées à la population des obèses sarcopéniques.

Abstract

Objective. Obesity and undernutrition are not incompatible and frequently coexist in the same patient. Recently, a new CT-assisted procedure, widely used in oncology, used for accurate prediction of regional muscle and fat composition has emerged but has not yet been validated in intensive care unit (ICU) patients. This procedure is reproducible and could easily be implemented in these units to assess sarcopenic obesity diagnosis. Sarcopenic obesity is characterized by an excess of fat mass associated with low muscle mass and function, that has multiple harmful consequences especially in situations of acute stress such as in intensive care. Therefore, the aims of this study were: i- to assess the impact of sarcopenic obesity on 90-day mortality in patients admitted in surgical intensive care unit, ii- to evaluate the morbidity associated to sarcopenic obesity, and iii- to study the mortality at 1 year in these patients.

Methods. This study is a single-center retrospective study conducted in the surgical ICU of the Claude Huriez Hospital at the Lille University Hospital. It included 58 patients with sarcopenic obesity, diagnosed with skeletal muscle index measured on CT using the MYRIAN software, and 145 patients with obesity alone. A logistic regression was performed to identify the association and effect of sarcopenic obesity on mortality at 90 days and at 1 year from admission adjusted on potential confounding factors.

Results. Thirty-seven (18.2%) patients died at 90-day post-ICU admission. The rate of mortality at 1 year was 27.6%. There was no significant impact of sarcopenia on 90-day mortality after ICU admission. In contrast, sarcopenia was associated with a higher risk of mortality at one year after ICU admission for obese patients, even after adjustment (OR = 2.25 [1.05-4.88]; p=0.04). Weight variation estimated between admission and discharge from ICU were statistically different, indeed, patients with sarcopenic obesity lost, on average, 2.8 kg meanwhile non-sarcopenic obese patients gained 3.4 kg (p=0.003).

Conclusions. Sarcopenic obesity is associated with a significant increase in 1-year ICU admission mortality. The use of quantitative analysis of body composition by computed tomography imaging should probably be generalized to allow screening for sarcopenic obesity in

ICU. There is also an urgent need for interventional studies that include nutritional approaches adapted to the sarcopenic obese population.

Liste des abréviations

BMI	Body Mass Index
ASA	American Society of Anesthesiologists
DEXA	Dual Energy X-ray Absorptiometry
CHRU	Centre Hospitalier Régional Universitaire
CI	Confidence Interval
CPK	Créatine Phosphokinase
CRP	Protéine C-réactive
CT-scan	Computed Tomography
GFR	Glomerular Filtration Rate
HAS	Haute Autorité de Santé
ICU	Intensive Care Unit
IGS2	Indice de Gravité Simplifié, deuxième version
IMC	Indice de Masse Corporelle
INSEE	Institut National de la Statistique et des Etudes Economiques
KDIGO	Kidney Disease: Improving Global Outcomes
L3	3ème vertèbre lombaire
OMS	Organisation Mondiale de la Santé
OR	Odds Ratio
OSA	Obstructive Sleep Apnea
PY	Package-Year
SFA	Subcutaneous Fat Area
SFNCM	Société Francophone de Nutrition Clinique et de Métabolisme
SFNEP	Société Française de Nutrition Entérale et Parentérale
SMI	Skeletal Muscle Index
SOFA	Sepsis-related Organ Failure Assessment

TAMA	Total Abdominal Muscle Area
TDM	Tomodensitométrie
VFA	Visceral Fat Area

Table des illustrations

Contexte

I- Obésité sarcopénique

L'obésité est définie selon la classification de l'Organisation Mondiale de la Santé (OMS) par un indice de masse corporel (IMC) supérieur ou égal à 30 kg/m². Elle correspond à une surcharge pondérale par excès de masse grasse associée à une modification du tissu adipeux (1). L'obésité concernait 17 % des adultes en France en 2015 et constitue un problème de santé publique majeur (2).

L'obésité et la dénutrition ne sont pas incompatibles et peuvent coexister chez un même individu. Cependant, il n'est pas rare de méconnaitre ce diagnostic chez la personne atteinte d'obésité car les outils fréquemment utilisés en clinique sont mis à défaut.

La dénutrition est définie par la Société Française de Nutrition Entérale et Parentérale (SFNEP) comme un déséquilibre entre les apports et les besoins protéino-énergétiques de l'organisme entrainant des pertes tissulaires involontaires avec des conséquences fonctionnelles délétères. Le diagnostic de dénutrition nécessite la présence d'au moins un critère phénotypique et un critère étiologique. Il ne repose que sur des données cliniques, la biologie étant utilisée uniquement pour en caractériser la sévérité (Annexe 1).

Chez le sujet obèse, les critères phénotypiques sont difficilement applicables. En effet, l'IMC ne peut pas être utilisé pour faire le diagnostic, tout comme une perte de poids peut être interprétée comme non pathologique même si celle-ci est involontaire (3). De plus, le poids peut rester stable voire augmenter malgré une perte de la masse musculaire, masquée par une augmentation de l'adiposité (4).

La dénutrition est cependant présente chez un grand nombre de patients atteints d'obésité (5,6). Afin de la mettre en évidence, des travaux récents ont étudié la composition corporelle d'une population en surpoids et obèse (7) et ont mis en évidence une grande diversité de phénotypes corporels, tout âge confondu (Figure1). Ainsi est défini un profil dit optimal avec une masse

maigre musculaire élevée et une faible adiposité. À l'inverse, une adiposité excessive avec une masse maigre conservée favorise le développement de comorbidités (diabète, maladies cardiovasculaires, troubles respiratoires). Mais il a surtout été mis en évidence un nouveau phénotype : l'obésité sarcopénique. Celui-ci est caractérisé par une masse grasse excessive associée à une faible musculature squelettique notamment au niveau du tronc et des membres inférieurs, tout comme on peut le rencontrer dans certaines endocrinopathies (syndrome de Cushing par exemple).

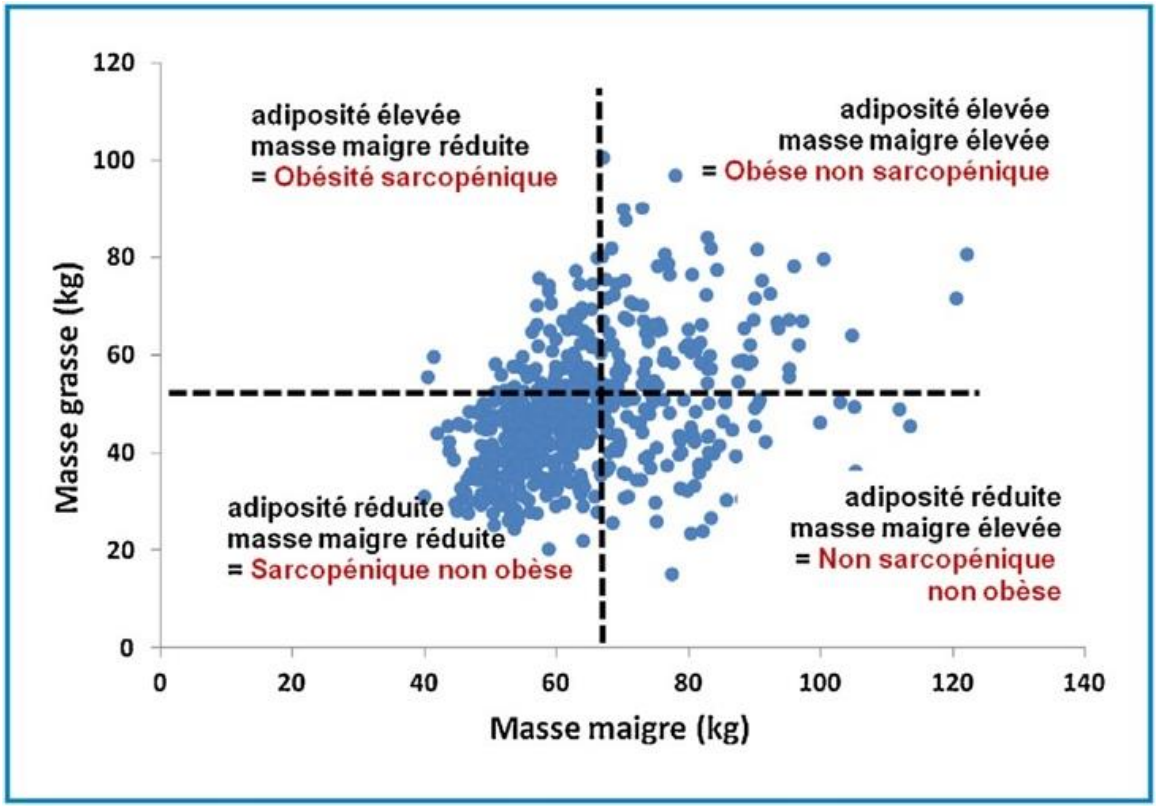


Figure 1: Phénotypes de composition corporelle selon la quantité de masse maigre et grasse. (8)

Dans le cadre d'une obésité sarcopénique, l'augmentation de poids est souvent la conséquence d'une malnutrition (augmentation des apports énergétiques totaux, mais carence des apports protéiques et des micronutriments essentiels au développement musculaire) associée à une baisse des dépenses énergétiques quotidiennes. Ce phénotype corporel est une particularité déjà bien connue lors du processus de vieillissement, au cours duquel existe de façon physiologique une augmentation du tissu adipeux au niveau viscéral, conduisant à une infiltration lipidique intra-

musculaire et à une fonte musculaire majeure (9–12). Ce phénomène de « lipotoxicité » de la personne âgée peut être transposé chez le sujet obèse et explique la cascade pathologique conduisant à un état de sarcopénie de manière précoce. Cette perte musculaire, conséquence de la malnutrition et de la réduction de la mobilité, favorise la diminution de la dépense énergétique et ce malgré la présence d'un bilan énergétique largement positif. Ce « surplus » énergétique de tissu adipeux est lui-même un facteur favorisant l'apparition d'une insulinorésistance et d'un hypercatabolisme lié à un stress inflammatoire qui peut à son tour amplifier le phénomène de perte musculaire (Figure 2) (13). Ainsi, l'obésité et la sarcopénie se potentialisent, entrainant à leur tour une majoration des limitations physiques et des troubles métaboliques de manière synergique.

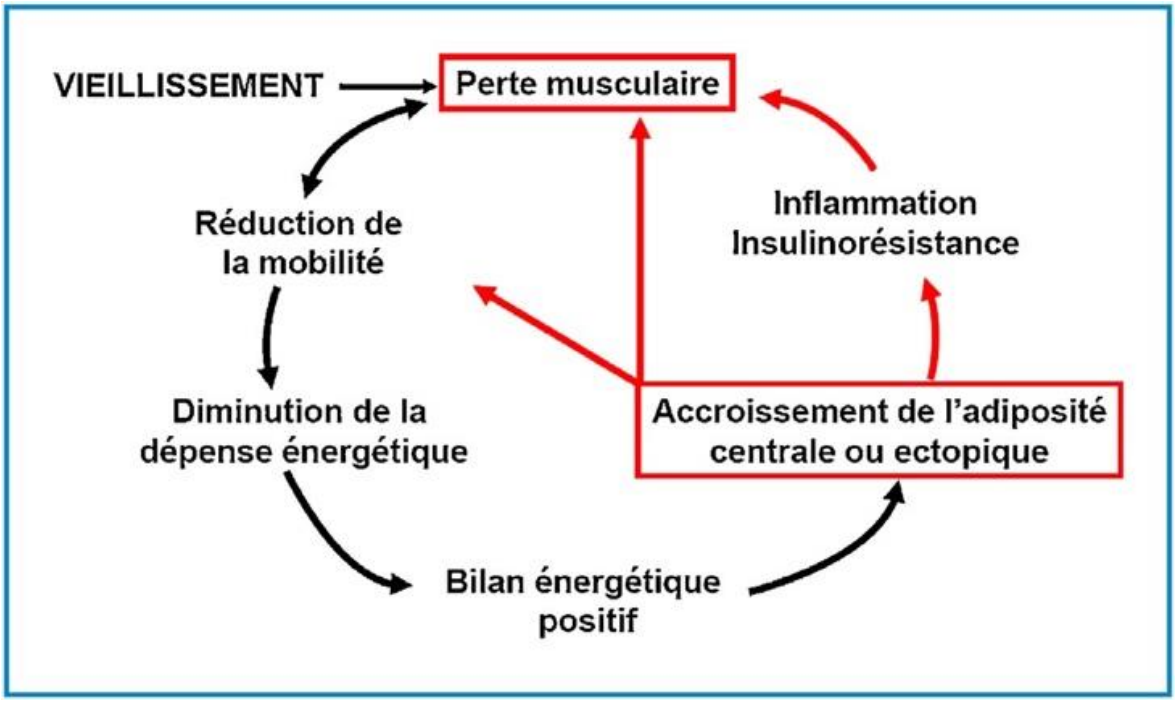


Figure 2 : Illustration de la relation entre la perte musculaire et le gain de tissus gras à l'origine de la cascade pathologique "lipotoxique".(8)

Ces nouvelles données ont abouti à la réactualisation des recommandations sur le diagnostic de la dénutrition. Ainsi les dernières recommandations de la Haute Autorité de Santé (HAS) en collaboration avec la Société Francophone de Nutrition Clinique et de Métabolisme (SFNCM) prennent en compte la sarcopénie en tant que critère phénotypique majeur pour le diagnostic de dénutrition.

II- Diagnostic de la sarcopénie assistée par imagerie

Les conséquences de l'obésité sarcopénique sont nombreuses (6,8) et si l'obésité est une comorbidité reconnue dans de nombreuses situations cliniques (14), la sarcopénie associée est un facteur indépendant de mortalité (15,16), d'autant plus dans les situations de stress aiguë comme l'hospitalisation en réanimation (17).

L'évaluation chez les patients obèses des données anthropométriques à l'aide d'outils adaptés pourrait permettre de dépister facilement ceux atteints d'obésité sarcopénique dès leur arrivée en réanimation.

En pratique clinique, l'absorptiomètre biphotonique aux rayons X (DEXA) est la méthode de référence pour mesurer la composition corporelle (18). Cependant, sa mise en place de manière courante est impossible en service de réanimation. Récemment, une nouvelle technique assistée par TDM permettant de prédire avec autant de précision que la DEXA la composition régionale en masse maigre et grasse a été mise en place (19–22). Déjà largement utilisée en cancérologie, cette méthode n'a pas été validée pour le moment chez les patients de réanimation (23–25). Elle est pourtant reproductible et peut être facilement mise en œuvre puisque le scanner est un examen réalisé de façon courante (26).

L'analyse de la composition corporelle par TDM consiste à réaliser sur une coupe scanographique standardisée au niveau de la 3e vertèbre lombaire (L3) des mesures de surface par contourage manuel (Figure 3). On peut ainsi réaliser la mesure de surface de la ceinture musculaire abdominale (TAMA) incluant le muscle transverse de l'abdomen, les muscles obliques, le muscle grand droit, les muscles psoas et paravertébraux. De la même manière la surface graisseuse viscérale (VFA) et sous-cutanée (SFA) peuvent être mesurées.

L'indice de surface musculaire (SMI) est ensuite calculé par la formule : TAMA en cm^2 / taille au carré en m^2. Un patient atteint d'obésité est défini comme sarcopénique si, chez les femmes le SMI < 38,5 cm^2/m^2 et si le SMI < 52,4 cm^2/m^2 chez les hommes (25,27,28).

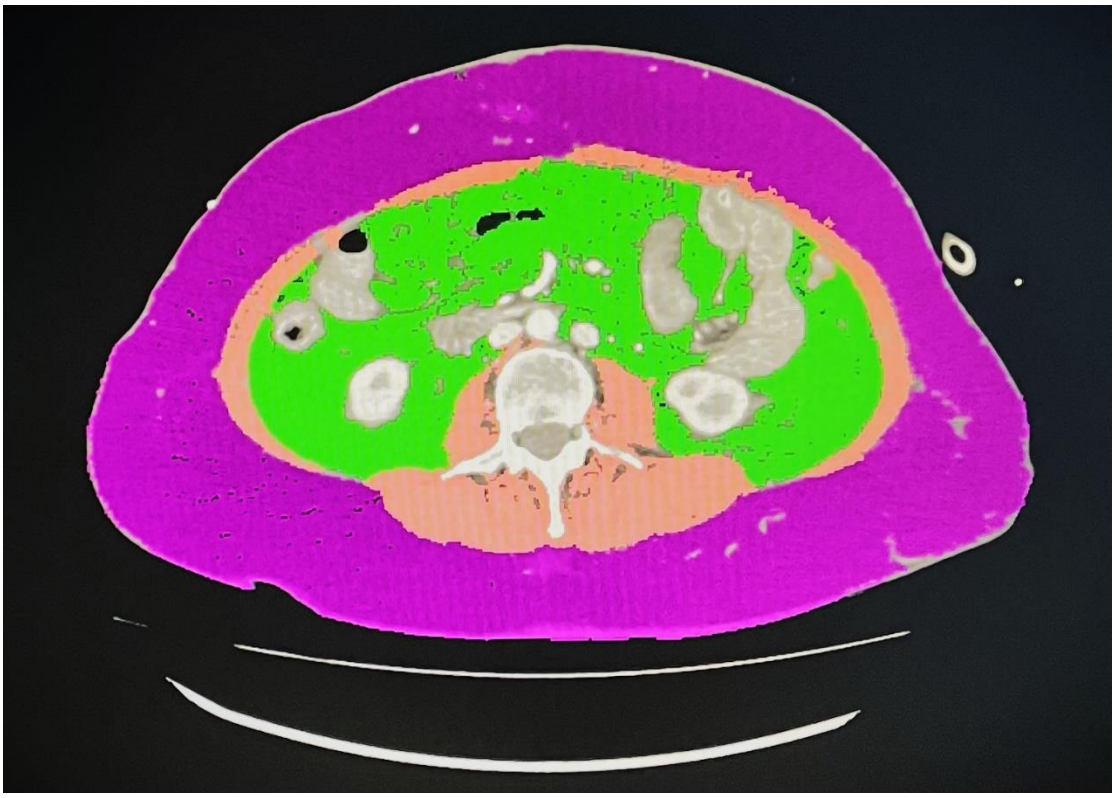


Figure 3 : Coupe TDM centrée en L3 analysée avec le logiciel Myrian

Légende : en rose: surface musculaire (TAMA); en vert: surface graisseuse viscérale (VFA); en violet: surface graisseuse sous-cutanée (SFA).

III- Objectifs

L'objectif principal de cette étude est d'analyser l'impact de l'obésité sarcopénique sur la mortalité à 90 jours chez des patients atteints d'obésité (définie par un IMC ≥ 30 kg/m²) hospitalisés en réanimation chirurgicale au CHRU de Lille.

Les objectifs secondaires sont d'étudier la morbidité associée à l'obésité sarcopénique et la mortalité à 1 an.

Article

I- Introduction

Obesity and undernutrition are not incompatible and frequently coexist in the same patient (5,6). While the body mass index (BMI) provides the most useful population-level measure of obesity, the diagnosis of undernutrition requires the use of phenotypic criteria (27) (Appendix 1). However, this diagnosis is often unrecognized in obese subjects because the tools routinely used are inappropriate for these patients. Indeed, a low BMI is a criterion that is used in several undernutrition screening tools. Conversely, BMI can no longer be used for diagnosis of undernutrition in obese patients. Also, weight loss can be interpreted as non-pathological even if it is involuntary (3) and weight can remain stable or increase despite a loss of muscle mass hidden by an increase in adiposity (4).

Thus, new research has revealed a body phenotype called sarcopenic obesity characterized by an excess of fat mass associated with low muscle mass and function (7). This phenotype is a well-known characteristic of aging, which involves an increase in adipose tissue at the visceral level and intra-muscular lipid infiltration, concomitant with major muscle loss (8–11). This phenotype is the result of a "lipotoxic" pathological cascade that induces a state of early sarcopenia in the obese subject through inflammatory stress and the development of insulin resistance (13).

Sarcopenic obesity has multiple harmful consequences (6,13) especially in situations of acute stress such as in intensive care (16,17). Recently, a new CT-assisted procedure for accurate prediction of regional muscle and fat composition has emerged (19–22). Already widely used in oncology, this method has not yet been validated in intensive care patients (23–25). It is reproducible and can easily be implemented in an intensive care unit because CT-scan is widely used for diagnosis evaluation (26).

The use of anthropometric data collected by CT-scan in obese patients in intensive care would allow reliable identification of patients with sarcopenic obesity and thus allow optimization of their overall management to reduce associated morbidity and mortality.

The aims of this study were: i- to assess the impact of sarcopenic obesity on 90-day mortality in patients admitted in surgical intensive care unit, ii- to evaluate the morbidity associated to sarcopenic obesity, and iii- to study the mortality at 1 year in these patients.

II- Methods

1. Study design

This is a single-center retrospective study conducted in the surgical intensive care unit of the Claude Huriez Hospital at the Lille University Hospital. We included patients aged 18 years or over with BMI ≥ 30 kg/m² admitted to the surgical intensive care unit between 01/01/2016 and 01/31/2020. The exclusion criteria were length of stay less than 24 hours, absence of abdominal CT-scan performed within 7 days of admission.

Data were retrospectively collected from hospital patient records. The current study complied with the "reference methodology" MR004 adopted by the ‘’Commission nationale de l'informatique et des libertés’’ (CNIL). We also verified that patients did not object to the use of their clinical data for research purposes.

2. Data collection

Data were collected via local clinical database (ICCA software (IntelliSpace Critical Care and Anesthesia, Philips) and Sillage software (computerized patient record, SIB)).

Clinical data included demographics, height, weight at admission, comorbidities, ASA (American Society of Anesthesiology) score, clinical frailty score (29), biological data, and sequential organ failure assessment score (SOFA score) at day 0 (30). Patients were also classified according to the reason (hemorrhagic shock, septic shock, acute vascular, abdominal, respiratory, renal or cardiological pathology, polytrauma with or without severe head trauma) and type of admission to the intensive care unit (ICU) (medical, emergency or planned surgery, carcinological or not). During the stay, the simplified acute physiology score (SAPS II or IGS2 score) (31), the KDIGO AKI staging (32), the 7-day SOFA score, glycemic imbalance, enteral and parenteral nutrition were assessed. Complications during the stay in the ICU were sought, such as mechanical ventilation, recourse to extra-renal purification, the use of amines, a thrombo-embolic events and the occurrence of septic shock or pneumopathy under mechanical ventilation. In addition, weight

change at discharge from the ICU, length of stay in the ICU, and overall length of stay in the hospital were also collected.

The mortality was evaluated at 90 days and 1 year after admission.

3. CT measurements of muscle, visceral and subcutaneous fat aeras

Using the MYRIAN software we analyzed a single cross-sectional CT-slice at the level of the 3rd lumbar vertebra. Using semi-manual contouring, we measured the total abdominal muscle area (TAMA). The skeletal muscle index (SMI) (cm^2/m^2) was calculated by dividing the TAMA (cm^2) by the square of the height (m^2). We also measured the fat area using the same method at the visceral (VFA) and subcutaneous (SFA) sites.

According to the latest recommendations, a threshold of SMI < 38.5 cm^2/m^2 in women and < 52.4 cm^2/m^2 in men defined sarcopenia in the obese patient (25,27,28). Visceral obesity was defined as an VFA > 130 cm^2 (33).

4. Statistical analysis

Usual descriptive analysis (frequency and percentages for categorical variables; mean, standard deviation for quantitative variables) were performed in the two groups: individuals with sarcopenic obesity and individuals without sarcopenic obesity separately and combined. These two groups were compared with a Chi-squared or a Fisher exact test for categorical variables; a Student's test or a Wilcoxon test was applied to quantitative variables.

A logistic regression was performed to identify the association and effect of sarcopenic obesity on mortality (at 90 days and at 1 year from admission) adjusted on the variables found in the literature and thought to be potential risk factors: age, sex, KDIGO score, clinical frailty scale, IGS2 score and SOFA score at admission.

Overall survival was estimated in the two groups using Kaplan Meier method (from the date of admission to one year after admission) and were compared by the Logrank test.

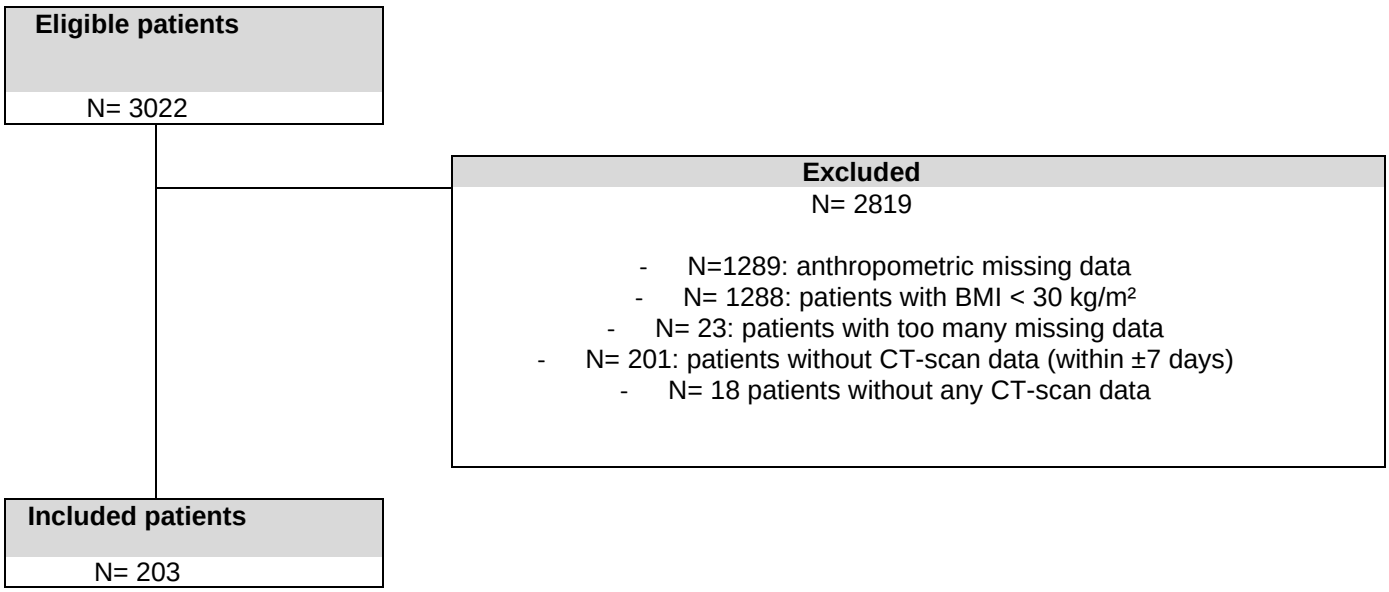
Sensitive analyses were performed to identify the association and effect of individuals with sarcopenic obesity associated with visceral obesity (compared to individuals without this

association) on mortality at 1 year from admission adjusted on the variables found in the literature and thought to be potential risk factors: age, sex, KDIGO score, clinical frailty scale, IGS2 score and SOFA score at admission.

III- Results

1. Flow chart

The following figure shows the study flow chart of this retrospective study. Out of the 3022 eligible patients, 203 patients were included for the final analysis.



2. Characteristics at admission in ICU according to sarcopenic status

In overall, 203 obese patients were identified in the study period. The sociodemographic and severity at admission data for the 58 patients with sarcopenic obesity and the 145 patients with obesity alone are summarized in Table 1. Considering the overall population, mean age was 58.6 years old and no statistical difference was found between the two groups. Compared to the group without sarcopenia, sarcopenic patients were more commonly females (31% vs. 54.4%, p=0.03). Also, sarcopenic patients did not differ statistically from those without sarcopenia on the different severity criteria measured at admission except for CPK blood measure. In patients with sarcopenic obesity, CPK was, on average, three times lower than in patients without sarcopenia (836 vs. 2 659 UI/L, respectively; p=0.02).

Table 1: Sociodemographic and severity characteristics at admission according to sarcopenic status

	Total population (N=203)		**No sarcopenia (N=145)**		**Sarcopenia (N=58)**		***P-value***
	n	**mean ± SD or %**	**n**	**mean ± SD or %**	**n**	**mean ± SD or %**	
Age, years	203	58.6 ± 14.8	145	58.1 ± 14.4	58	59.9 ± 15.7	0.44
Females	97	47.8%	79	54.5%	18	31.0%	**0.03**
IGS2	203	54.9 ± 22.2	145	54.6 ± 21.8	58	55.8 ± 23.5	0.74
ASA score							
1	8	3.9%	8	5.5%	0	-	
2	33	16.3%	25	17.2%	8	13.8%	
3	144	70.9%	100	69.0%	44	75.9%	0.29
4	16	7.9%	10	6.9%	6	10.3%	
5	2	1.0%	2	1.4%	0	-	
Clinical Frailty Scale							
Fit or managing well	137	67.5%	98	67.6%	39	67.2%	
Mild/moderate frailty	34	16.7%	26	17.9%	8	13.8%	0.62
Severe frailty or terminally ill	32	15.8%	21	14.5%	11	19.0%	
Score SOFA at day 0	203	11.9 ± 4.7	145	11.9 ± 4.7	58	11.8 ± 4.8	0.88
CPK (UI/l) - *(MD=11)*	192	2 146.6 ± 7 049.5	138	2 659.4 ± 8 149.3	54	836.0 ± 2 233.6	**0.02**
Serum creatinine (mg/l)	203	21.5 ± 17.6	145	22.1 ± 17.0	58	19.9 ± 19.1	0.10
Blood lactate (mmol/l) - *(MD=42)*	161	2.3 ± 2.3	118	2.2 ± 2.0	43	2.5 ± 2.8	0.86

IGS2 (International score : Index de Gravité Simplifié II) is a score used to evaluate the severity of a patient and is part of the scores used in intensive care unit. ASA : American Society of Anaesthesiologists (ASA) physical status classification ; SOFA : Sepsis-related Organ Failure Assessment ; CPK : Creatinine phosphokinase blood measure.

MD : Missing data

Regarding medical history, as shown in Table 2, no statistically significant difference was found between the two groups expect for smoking status and chronic alcohol consumption. Indeed, sarcopenic patients were more frequently smokers and active alcohol consumers than non-sarcopenic ones (21.1% vs. 12.4% and 24.1% vs. 4.1%, respectively; p=0.04).

Table 2 : Medical history at intensive care admission according to sarcopenic status

	Total population (N=203)		No sarcopenia (N=145)		Sarcopenia (N=58)		*P-value*
	n	mean ± SD or %	n	mean ± SD or %	n	mean ± SD or %	
Smoking status (> 5 PY)							
Non smoker	125	61.6%	96	66.2%	29	50.0%	
Smoker	32	15.8%	18	12.4%	14	24.1%	**0.04**
Quit smoking <2 years	9	4.4%	8	5.5%	1	1.7%	
Quit smoking >2 years	37	18.2%	23	15.9%	14	24.1%	
Chronic alcohol consumption							
None	170	83.7%	132	91.0%	38	65.5%	
Active	20	9.9%	6	4.1%	14	24.1%	**<0.001**
Former drinker	13	6.4%	7	4.8%	6	10.3%	
High blood pressure, yes	138	68.0%	102	70.3%	36	62.1%	0.25
Diabetes							
No	137	67.5%	96	66.2%	41	70.7%	
Non-insulin dependent diabetes	47	23.2%	35	24.1%	12	20.7%	0.83
Insulin dependent diabetes	19	9.4%	14	9.7%	5	8.6%	
Dyslipidemia, yes	92	45.3%	66	45.5%	26	44.8%	0.93
Major cardiovascular disease, yes	87	42.9%	62	42.8%	25	43.1%	0.96
Chronic respiratory disease, yes	44	21.7%	30	20.7%	14	24.1%	0.59
Equiped OSA, yes	54	26.6%	40	27.6%	14	24.1%	0.62
Long-term oxygen therapy, yes	11	5.4%	8	5.5%	3	5.2%	1
Cirrhosis, yes	14	6.9%	8	5.5%	6	10.3%	0.23
Chronic kidney disease							
No	165	81.3%	118	81.4%	47	81.0%	
GFR > 30 ml/min/1.73 m2	22	10.8%	18	12.4%	4	6.9%	0.26
GFR < 30 ml/min/1.73 m2	7	3.4%	3	2.1%	4	6.9%	
Chronic dialysis	9	4.4%	6	4.1%	3	5.2%	
Neoplasia, active vs. non or in remission	56	27.6%	43	29.7%	13	22.4%	0.30
Other immunodeficiency[1], yes	19	9.4%	13	9.0%	6	10.3%	0.76

PY : package-year ; OSA : Obstructive Sleep Apnea; GFR : Glomerular Filtration Rate.

[1] chemotherapy / corticosteroid therapy > 20 mg/day / other immunosuppressant / solid organ or bone marrow transplant / HIV / Neutropenia < 500/mm3.

The anthropometric data at ICU admission according to sarcopenic status are detailed in the Table 3. The BMI was significantly lower in sarcopenic obese patients compared to individuals without sarcopenia (35.9 vs. 38.7 kg/m², respectively; p=0.01). Similarly, the muscle/total fat ratio was also different between these two groups, with a lower mean ratio in sarcopenic obese patients (23.6 vs 28.2%, p<0.01). By contrast, biological measures associated to severe undernutrition did not significantly differ between the two groups.

Table 3 : Anthropometric and biological data according to sarcopenic status

	Total population (N=203)		No sarcopenia (N=145)		Sarcopenia (N=58)		*P-value*
	n	mean ± SD or %	n	mean ± SD or %	n	mean ± SD or %	
BMI (kg/m²)	203	37.9 ± 7.5	145	38.7 ± 8.0	58	35.9 ± 5.7	**0.01**
Muscle/total fat ratio (%)	203	26.9 ± 10.4	145	28.2 ± 10.0	58	23.6 ± 10.5	**<0.01**
Albumin (g/l) - *(MD=1)*	202	27.8 ± 4.9	144	28.1 ± 5.0	58	27.1 ± 4.7	0.19
Pre-albumine (g/l) - *(MD=46)*	157	0.1 ± 0.1	110	0.1 ± 0.1	47	0.1 ± 0.1	0.68
Total protein (g/l)) - *(MD=1)*	202	55.2 ± 7.1	144	55.4 ± 6.9	58	54.8 ± 7.8	0.59
CRP (mg/l) - *(MD=8)*	195	200.6 ± 139.6	138	207.1 ± 141.7	57	184.9 ± 134.4	0.28

BMI : Body mass index ; CRP : C-reactive protein.

MD : Missing data

In overall population, septic shock was the most common indication for ICU admission (33.5%). Considering the care prior to ICU admission, the majority of patients underwent non carcinologic emergency surgery (46.3%). When we analyzed data according to sarcopenic status, the reasons for ICU admission were globally comparable between obese sarcopenic and non-sarcopenic patients (Appendix 2).

3. Characteristics during ICU stay according to sarcopenic status

Characteristics during intensive care stay, such as for example: SOFA score at day 7, KDIGO score, proportion of time spent under invasive or non-invasive mechanical ventilation, are detailed in the following Table 4. No statistical differences were found between obese patients with and without sarcopenia. On average, patients spent around 39% of their time under invasive mechanical ventilation, spent 5 days on acute dialysis and 27% presented a septic shock acquired in ICU.

Considering nutritional management and glycemic imbalance, no difference was found between the two groups (Appendix 3).

Table 4 : Comparison between patients with and without sarcopenia on characteristics during intensive care stay

	Total population (N=203)		No sarcopenia (N=145)		Sarcopenia (N=58)		*P-value*
	n	mean ± SD or %	n	mean ± SD or %	n	mean ± SD or %	
Score SOFA at day 7 - *(MD=79)*	124	6.6 ± 5.4	87	6.7 ± 5.1	37	6.3 ± 6.1	0.45
KDIGO - *(MD=1)*							
No renal deficiency	39	19.3%	23	16.0%	16	27.6%	
1	37	18.3%	25	17.4%	12	20.7%	0.10
2	28	13.9%	24	16.7%	4	6.9%	
3	98	48.5%	72	50.0%	26	44.8%	
Time spent under invasive mechanical ventilation (%)	203	38.6 ± 30.6	145	38.9 ± 30.9	58	37.9 ± 30.2	0.87
Time spent under non-invasive ventilation (%)	203	26.3 ± 30.9	145	27.1 ± 31.7	58	24.2 ± 28.9	0.73
Days spent on acute dialysis	203	5.2 ± 10.0	145	4.7 ± 9.2	58	6.5 ± 11.9	0.98
Time spent on acute dialysis (%)	203	32.4 ± 39.2	145	31.3 ± 38.1	58	35.3 ± 42.1	0.85
Time spent on noradrenaline (%)	203	36.0 ± 31.0	145	34.7 ± 31.0	58	39.3 ± 31.2	0.31
Average dose of noradrenaline (mg/h)	203	0.8 ± 1.6	145	0.8 ± 1.8	58	0.8 ± 1.1	0.86
Time spent on dobutamine (%) - *(MD=1)*	202	1.1 ± 8.7	144	1.6 ± 10.3	58	0.0 ± 0.0	0.20
Time spent under antibiotic therapy (%)	203	81.6 ± 29.7	145	78.8 ± 32.3	58	88.5 ± 20.4	0.17
Time spent on corticosteroid therapy (%)	203	34.7 ± 34.7	145	34.2 ± 34.6	58	36.0 ± 35.3	0.72
Septic shock acquired in intensive care, yes	55	27.1%	36	24.8%	19	32.8%	0.25
Pulmonary disease acquired under mechanical ventilation, yes	50	24.6%	37	25.5%	13	22.4%	0.64
Deep vein thrombosis/Pulmonary embolism, yes	27	13.3%	20	13.8%	7	12.1%	0.74

SOFA : Sepsis-related Organ Failure Assessment ; KDIGO : Kidney Disease Improving Global Outcomes.

4. Patient characteristics on discharge from ICU according to sarcopenic status

Weight variation estimated between admission and discharge from ICU were statistically different between obese sarcopenic and non-sarcopenic patients. Indeed, patients with sarcopenic obesity lost, on average, 2.8 kg meanwhile patients without sarcopenia gained 3.4 kg (p=0.003). Importantly, the sarcopenic patients had significantly higher weight loss compared to the other group (-11.6 kg; p=0.049). Considering length of stay in ICU and overall hospital stay, no difference was shown between the two groups.

Table 5: Patient characteristics on discharge from ICU according to sarcopenic status

	Total population (N=203)		No sarcopenia (N=145)		Sarcopenia (N=58)		*P-value*
	n	mean ± SD or %	n	mean ± SD or %	n	mean ± SD or %	
Weight variation (kg) - *(MD=10)*	193	1.7 ± 13.2	140	3.4 ± 12.9	53	-2.8 ± 13.0	**0.003**
Evolution of the weight during ICU stay - *(MD=10)*	193		140		53		
Stable	5	2.6%	3	2.1%	2	3.8%	
Loss	83	43.0%	55	39.3%	28	52.8%	0.25
Gain	105	54.4%	82	58.6%	23	43.4%	
Average weight loss in patients who lost weight	83	-9.2 ± 10.2	55	-8.0 ± 9.4	28	-11.6 ± 11.5	**0.049**
Average weight gain in patients who gained weight - (MD=10)	105	10.4 ± 8.2	82	11.20 ± 8.80	23	7.7 ± 4.9	0.20
Length of stay in intensive care (days)	203	12.3 ± 13.4	145	11.6 ± 10.4	58	14.9 ± 19.0	0.60
Length of stay in hospital (days)	203	33.1 ± 29.3	145	32.7 ± 29.0	58	34.1 ± 30.2	0.85

ICU : Intensive care unit.

5. Association between sarcopenic status and mortality

Thirty-seven (18.2%) patients died at 90-day post-ICU admission. The rate of mortality at 1 year was 27.6%. There was no significant impact of sarcopenia on 90-day mortality after ICU admission (Table 6).

Table 6 : Risk of mortality at 90 days from admission according to sarcopenic status

	Crude OR		OR[1]	
	OR [95% CI]	*P-value*	OR [95% CI]	*P-value*
Sarcopenia	1.46 [0.67-3.07]	0.33	1.18 [0.47-2.85]	0.72

OR : Odds ratio ; CI : Confidence interval.

[1]OR adjusted for age, sex, KDIGO, frailty, IGS2 and SOFA at day 0.

In contrast, sarcopenia was associated with a higher risk of mortality at one year after ICU admission for obese patients (OR = 2.49; 95%CI: [1.29-4.80]; p=0.006) (Table 7). After adjustment for age, sex, KDIGO, frailty, IGS2 and SOFA score at day 0, sarcopenia remained associated with the risk of mortality at one year (OR = 2.25; 95%CI: [1.05-4.88]; p=0.04).

Table 7 : Risk of mortality at one year from admission according to sarcopenic status

	Crude OR		OR[1]	
	OR [95% CI]	***P-value***	**OR [95% CI]**	***P-value***
Sarcopenia	2.49 [1.29-4.80]	**0.006**	2.25 [1.05-4.88]	**0.04**

OR : Odds ratio ; CI : Confidence interval.

[1]OR adjusted for age, sex, KDIGO, frailty, IGS2 and SOFA at day 0.

6. Overall survival at one year from admission to ICU

At one year after admission to ICU, one hundred and forty-seven (72.4%) patients were alive. Global survival curves for each group (obese sarcopenic and obese non-sarcopenic patients) are represented in the following Figure 4. Overall survival median was not reached at one year. Individuals with sarcopenic obesity had an increased hazard of death at one year after ICU admission compared to obese individuals without sarcopenia (HR = 2.02; 95%CI: [1.12-3.65]; p=0.008).

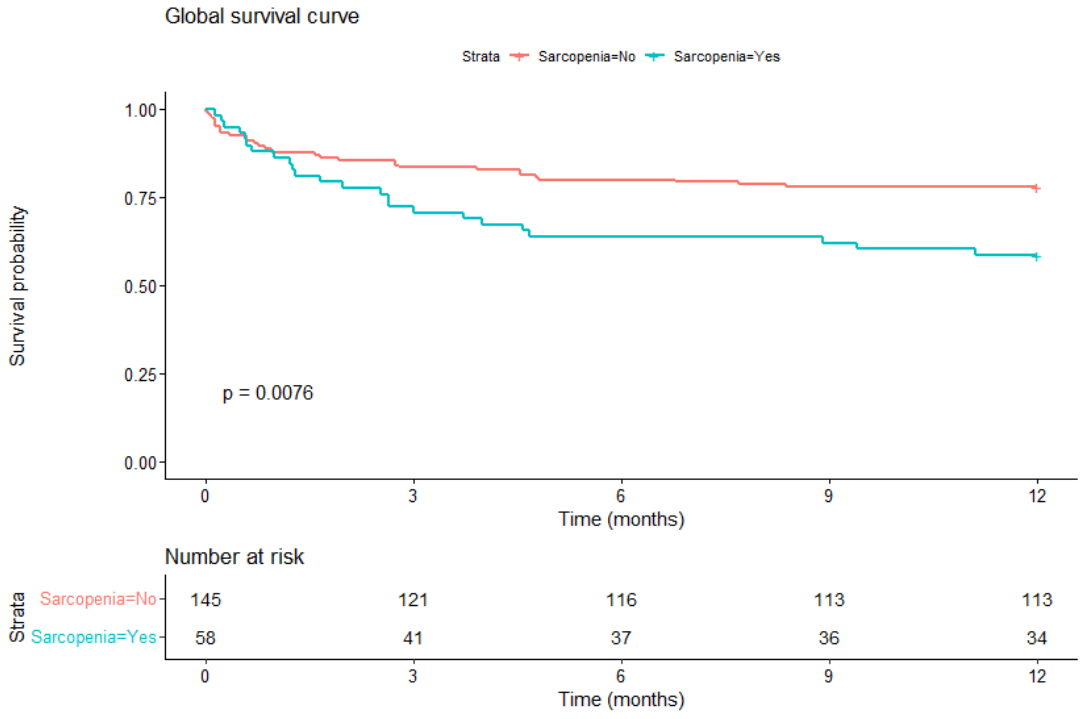


Figure 4: Global survival curves at one year after admission according to sarcopenic status

7. Sensitive analyses

The following Table 8 show the results of sensitive analyses. These identified that individuals with sarcopenic obesity and visceral obesity had a higher risk of mortality at one year from admission compared to individuals without these characteristics (OR = 3.40; 95%CI: [1.72-6.78]). This association remained statistically significant after adjustment on potential risk factors: age, sex, KDIGO score, clinical frailty scale, IGS2 score and SOFA score at admission (OR = 2.52; 95%CI: [1.15-5.58]).

Table 8 : Risk of mortality at one year from admission according to visceral obesity with sarcopenia status

	Crude OR		**OR[1]**	
	OR [95% CI]	***P-value***	**OR [95% CI]**	***P-value***
Sarcopenia with visceral obesity	3.40 [1.72-6.78]	**<0.001**	2.52 [1.15-5.58]	**0.02**

OR : Odds ratio ; CI : Confidence interval.

[1]OR adjusted for age, sex, KDIGO, frailty, IGS2 and SOFA at day 0.

IV- Discussion

This study is the first to investigate the impact of sarcopenic obesity on morbi-mortality after admission in ICU. While we did not find any correlation between sarcopenic obesity and mortality at 90 days after ICU admission, we showed that this nutritional status was an independent risk factor for 1-year mortality. Interestingly, the current study demonstrated that increased visceral fat in sarcopenic obese patients was associated with a significant increase of 1 year mortality. All of these findings suggest that quantitative analysis of skeletal muscle mass and visceral fat could be used to discriminate patients with sarcopenic obesity, which appears to be one of the prognostic factors after ICU admission.

In this study, there was no evidence of a relationship between sarcopenic obesity and 90-day mortality or the occurrence of resuscitation-specific complications. We believe that this may be related to a lack of statistical power in the study. Nevertheless, it is important to note that non-sarcopenic patients were admitted to the ICU more often for postoperative complications, whereas sarcopenic obese patients were admitted in larger proportion for medical conditions. Therefore, the growing prevalence of surgical patients in sarcopenic group could overestimate the rate of mortality. Nevertheless, we found that sarcopenic obesity was associated with a significant increase in 1 year mortality after ICU admission (OR = 2.49; 95%CI: [1.29-4.80]).

Recently, a large cohort study reported that the prevalence of sarcopenic obesity in the entire population ranged from 5 to 10% (34). In the current study, we focused only on obese population which proportion of sarcopenic obesity was 28%. Our study supports the emerging knowledge about the impact of sarcopenic obesity in the ICU. It now seems necessary to no longer consider obese patients as a homogeneous group of individuals, but rather to differentiate them according to their prior physical conditions. We found a mean length of hospital stay of approximately 1 month in both groups. However, analysis of 1-year survival shows that deaths in the non-sarcopenic obese group appear to occur mainly in the first 2 months after admission before stabilizing, whereas in the obese and sarcopenic group, the number of deaths continues to

increase several months later. Thus, sarcopenia associated with obesity seems to increase the vulnerability of patients to the acute stress imposed by their ICU stay with a negative effect on mortality several months after admission to the ICU. Some authors suggest several mechanisms underlying this association. During the stay in intensive care, the organism is exposed to important aggressions, particularly at the cellular level. As a result, there is a very significant increase in energy and protein requirements to enable the defense response. Hypercatabolism leads the organism to first draw on its reserves and then to use the autophagy process when these are exhausted (35,36). While the annual decline in muscle mass during aging is approximately 0.37 to 0.47% per year, it can be lost in one day in intensive care patients (17,37). Patients with low baseline skeletal muscle mass undergo a massive acceleration of this decline. Importantly, fat excess in the obese patient increases the propensity of adipose tissue to store lipids and thereby exacerbating the catabolic muscle protein response secondary to the aggression (38). Thus, in patients previously suffering from sarcopenia, accelerated muscle wasting induced by intensive care precipitates a loss of muscle strength below the threshold value necessary for independence and ADLs resulting in disability and further death (39).

In this study, we also reported the impact of visceral obesity associated with sarcopenia. Another study reported an excess of mortality for visceral obese patients admitted in ICU (40). Abdominal obesity induces an increased cardiometabolic risk leading to coronary heart disease, hypertension or diabetes and increased mortality (41,42). One of the proposed explanations is that while subcutaneous fat is mainly involved in rapidly mobilizable energy storage, visceral fat is rather involved in metabolic activities (43). Via the secretion of pro-inflammatory adipokines, visceral fat influences the immune system and increases cortisol secretion and insulin resistance in stressful situations (44–46). These results suggest that body fat distribution plays also a substantial role in the poor prognosis of sarcopenic obesity.

It is noteworthy that smoking, chronic alcohol consumption, and low CPK levels were strongly associated with sarcopenic obesity status in patients admitted to ICU. In contrast, albumin and

pre-albumin levels, classically used to characterize the severity of undernutrition, were not different between the two groups. But albumin and prealbumin levels are largely dependent on multiple parameters such as inflammation and their relevance in the intensive care setting is limited. In addition, we did not expect to find a significant difference in weight change at discharge. Similarly, there was no difference in the duration and caloric intake of enteral and parenteral nutrition between the two groups (Appendix 3). However, we found that patients with sarcopenic obesity tended to lose weight during their stay in the ICU, while non-sarcopenic patients gained weight (-2.0% vs +3.7%, respectively; p=0.003). These results are consistent with a decreased ability to face energy and protein hypercatabolism related to acute metabolic stress (38).

Limitations

The main strength of our study is its singular approach. Until now, few studies have focused on the impact of sarcopenic obesity in the ICU and, to our knowledge, this is the first to have used the definition of sarcopenic obesity based on the SMI in patients admitted to ICU.

Our study also has some limitations. It was a retrospective and monocentric study that could lead to a selection bias and a loss of information. Indeed, a significant number of patients could not be included in the study because we did not have reliable data on weight, height or CT-scan. However, it seems complex to carry out a prospective study to answer our hypothesis.

Concerning the collection of anthropometric data by imaging, the measurements were performed semi-manually but not fully-automatically (47), which could lead to a measurement bias. Nevertheless, the semi-manual contouring method is the most widespread in other studies and remains reliable (26). Finally, there are different cut-offs to define sarcopenia and visceral obesity in the literature. However, despite the lack of consensus, we used the SMI cut-off recommended by the HAS (27) and the most frequently used cut-off to define visceral obesity (33).

We believe it is important to investigate the nutritional status of obese patients as much as that of non-obese patients. The evaluation of sarcopenia by imaging can be easily implemented in the ICU and would allow a reliable detection of patients with sarcopenic obesity. In a second time, it

appears necessary to evaluate and implement adapted nutritional protocols for these patients in order to reduce mortality. A hypocaloric (< 70% of the usual recommended requirements) and hyperprotein diet seems to be able to reduce protein catabolism and hyperglycemia in these patients (17,36,48). The contribution of rapidly metabolizable proteins such as lactoserum (49) and non-protein sources such as omega-3 fatty acids (50) or vitamin D (51) also seem promising. However, prospective randomized studies including these strategies in patients with sarcopenic obesity are lacking. Finally, the most interesting part of the management of these patients could be focused on the outcome of post-intensive care. As has been demonstrated in geriatrics, the implementation of a post-hospital transition program focusing on nutritional status, frailty, and functional capacity with a multidisciplinary approach would allow patients with sarcopenic obesity to recover and maintain acceptable physical capacity for as long as possible (52).

Conclusion

In conclusion, this study demonstrates that sarcopenic obesity is associated with a significant increase in 1-year ICU admission mortality. Furthermore, the association of visceral obesity with sarcopenia further increases mortality. The use of quantitative analysis of body composition by computed tomography imaging should probably be generalized to allow screening for sarcopenic obesity in ICU. There is also an urgent need for interventional studies that include nutritional approaches adapted to the sarcopenic obese population.

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Appendix

Appendix 1 : Critères diagnostiques de la dénutrition chez le sujet adulte (> 18 ans) (Source : HAS, novembre 2019)

Le diagnostic de dénutrition nécessite la présence d'au moins : **1 critère phénotypique et 1 critère étiologique**. Ce diagnostic est un préalable obligatoire avant de juger de sa sévérité. Il repose exclusivement sur des critères non biologiques.

Les critères phénotypiques sont les suivants :

- perte de poids ≥ 5 % en 1 mois ou ≥ 10 % en 6 mois ou ≥ 10 % par rapport au poids habituel avant le début de la maladie ;
- IMC < 18,5 kg/m2 ;
- réduction quantifiée de la masse et/ou de la fonction musculaires ;

Méthodes de mesure	Hommes	Femmes
Force de préhension (dynamomètre) en kg	< 26	< 16
Vitesse de marche (m/s)	< 0,8	< 0,8
Indice de surface musculaire en L3 en cm^2/m^2 (scanner, IRM)	52,4	38,5
Indice de masse musculaire en kg/m^2 (impédancemétrie)	7,0	5,7
Indice de masse non grasse (impédancemétrie[a]) en kg/m^2	< 17	< 15
Masse musculaire appendiculaire (DEXA) en kg/m^2	7,23	5,67

Les critères étiologiques sont les suivants :

- réduction de la prise alimentaire ≥ 50 % pendant plus d'1 semaine, ou toute réduction des apports pendant plus de 2 semaines par rapport :
  - à la consommation alimentaire habituelle quantifiée,
  - ou aux besoins protéino-énergétiques estimés ;

- absorption réduite (malabsorption/maldigestion) ;

- situation d'agression (hypercatabolisme protéique avec ou sans syndrome inflammatoire)
  - pathologie aiguë
  - pathologie chronique évolutive
  - pathologie maligne évolutive.

Appendix 2 : Reasons for admission in ICU according to sarcopenic status

	Total population (N=203)		No sarcopenia (N=145)		Sarcopenia (N=58)		*P-value*
	n	%	n	%	n	%	
Reason for admission to intensive care							0.15
Hemorrhagic shock	22	10.8%	16	11.0%	6	10.3%	
Septic shock	68	33.5%	49	33.8%	19	32.8%	
Acute vascular pathology	4	2.0%	3	2.1%	1	1.7%	
Acute abdominal pathology	62	30.5%	38	26.2%	24	41.4%	
Acute respiratory failure	19	9.4%	14	9.7%	5	8.6%	
Acute renal failure	9	4.4%	9	6.2%	0	0.0%	
Acute cardiac failure	3	1.5%	2	1.4%	1	1.7%	
Polytrauma with severe head trauma	1	0.5%	1	0.7%	0	0.0%	
Polytrauma without severe head trauma	10	4.9%	10	6.9%	0	0.0%	
Other	5	2.5%	3	2.1%	2	3.4%	
Type of admission							0.06
Medical	30	14.8%	16	11.0%	14	24.1%	
Non-carcinologic surgery	40	19.7%	33	22.8%	7	12.1%	
Emergency non- carcinologic surgery	94	46.3%	66	45.5%	28	48.3%	
Carcinologic surgery	34	16.7%	27	18.6%	7	12.1%	
Urgent surgery with neoplastic lesion found in anatomopathology	5	2.5%	3	2.1%	2	3.4%	
Type of admission – carcinologic surgery grouped together							0.06
Medical	30	14.8%	16	11.0%	14	24.1%	
Non-carcinologic surgery	134	66.0%	99	68.3%	35	60.3%	
Carcinologic surgery	39	19.2%	30	20.7%	9	15.5%	
Type of admission – urgent surgery grouped together							**0.02**
Medical	30	14.8%	16	11.0%	14	24.1%	
Non-urgent surgery	134	66.0%	60	41.4%	14	24.1%	
Urgent surgery	39	19.2%	69	47.5%	30	51.8%	

Appendix 3 : Characteristics of nutrition management during ICU stay according to sarcopenic status

	Total population (N=203)		No sarcopenia (N=145)		Sarcopenia (N=58)		*P-value*
Time spent on enteral nutrition < 20 KCal/kg/j (%)	N=203		N=145		N=58		0.62
Median - (Range)	0.0	(0.0 ; 100.0)	0.0	(0.0 ; 100.0)	0.0	(0.0 ; 88.9)	
Mean - SD	12.1	22.1	12.3	21.6	11.8	23.4	
Time spent on enteral nutrition > 20 KCal/kg/j (%)	N=203		N=145		N=58		0.24
Median - (Range)	0.0	(0.0 ; 83.3)	0.0	(0.0 ; 83.3)	0.0	(0.0 ; 75.0)	
Mean - SD	5.9	15.6	4.5	12.9	9.3	20.8	
Time spent on parenteral nutrition < 20 KCal/kg/j (%)	N=203		N=145		N=58		0.86
Median - (Range)	0.0	(0.0 ; 100.0)	0.0	(0.0 ; 100.0)	0.0	(0.0 ; 100.0)	
Mean - SD	16.6	25.4	16.3	25.1	17.5	26.4	
Time spent on parenteral nutrition > 20 KCal/kg/j (%) - *(MD=1)*	N=202		N=144		N=58		0.80
Median - (Range)	0.0	(0.0 ; 100.0)	0.0	(0.0 ; 100.0)	0.0	(0.0 ; 100.0)	
Mean - SD	16.2	27.5	16.4	27.2	15.7	28.3	
Hours of glycemic imbalance	N=197		N=142		N=55		0.29
Median - (Range)	18.0	(0.0 ; 316.0)	20.0	(0.0 ; 316.0)	12.0	(0.0 ; 274.0)	
Mean - SD	34.7	48.0	36.9	49.4	28.9	43.8	

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Titre de la thèse : Evaluation de la morbi-mortalité chez les patients obèses sarcopéniques hospitalisés en réanimation chirurgicale

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Mots-clés : obésité sarcopénique, réanimation chirurgicale, index musculaire squelettique

Résumé :
Objectif L'obésité et la dénutrition peuvent coexister chez un même individu, cependant il n'est pas rare de méconnaitre ce diagnostic chez les patients atteints d'obésité. Une technique récente assistée par tomodensitométrie (TDM) permet de prédire la composition régionale en masse maigre et grasse. Cette méthode n'a pas encore été validée chez les patients de réanimation mais pourrait être facilement mise en œuvre afin de faire le diagnostic d'obésité sarcopénique. L'obésité sarcopénique est caractérisée par un excès de masse grasse associé à une faible musculature squelettique, délétère particulièrement lors de stress aigu comme la réanimation. Les objectifs de cette étude étaient : i- d'évaluer l'impact de l'obésité sarcopénique sur la mortalité à 90 jours chez les patients admis en réanimation chirurgicale, ii- d'évaluer la morbidité associée à l'obésité sarcopénique, et iii- d'étudier la mortalité à 1 an chez ces patients.
Méthodes. Cette étude rétrospective menée dans le service de réanimation chirurgicale de l'hôpital Claude Huriez de Lille a inclus 203 patients dont 58 patients atteints d'obésité sarcopénique, diagnostiquée grâce à l'index musculaire squelettique mesuré au TDM à l'aide du logiciel MYRIAN. Une régression logistique a été réalisée pour identifier l'association et l'effet de l'obésité sarcopénique sur la mortalité à 90 jours et à 1 an de l'admission ajustée sur les facteurs de confusion potentiels.
Résultats. Le taux de mortalité à 90 jours et à 1 an après l'admission était respectivement de 18,2 % et 27,6%. Il n'y avait pas d'impact significatif de la sarcopénie sur la mortalité à 90 jours après l'admission. En revanche, la sarcopénie était associée à un risque plus élevé de mortalité à un an après l'admission, même après ajustement (OR = 2,25 [1,05-4,88] ; p=0,04). Les variations de poids estimées entre l'admission et la sortie de réanimation étaient statistiquement différentes (perte de 2,8 kg chez les obèses sarcopéniques vs gain de 3,4 kg chez les obèses non sarcopéniques (p=0,003)).
Conclusions. L'obésité sarcopénique est associée à une augmentation significative de la mortalité à l'admission en réanimation à un an. L'analyse quantitative de la composition corporelle par TDM pourrait être généralisée afin de permettre le dépistage de l'obésité sarcopénique dans les unités de réanimation. D'autres études sont nécessaires pour évaluer les approches nutritionnelles adaptées à la population des obèses sarcopéniques.

Composition du Jury :

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