BJA Open

BJA Open, 14 (C): 100391 (2025)

doi: 10.1016/j.bjao.2025.100391
Review Article

REVIEW ARTICLE

Beyond body mass index: exploring the role of visceral adipose tissue in intensive care unit outcomes

Maximilian R. Ralston[1,2,*], Gordan McCreath[2], Zoe J. Lees[1], Ian P. Salt[3], Malcolm A. B. Sim[2,4], Malcolm J. Watson[5,6] and Dilys J. Freeman[1]

[1]School of Cardiovascular & Metabolic Health, University of Glasgow, Glasgow, UK, [2]Academic Unit of Anaesthesia, Critical Care & Perioperative Medicine, University of Glasgow, Glasgow, UK, [3]School of Molecular Biosciences, University of Glasgow, Glasgow, UK, [4]Department of Critical Care, Queen Elizabeth University Hospital, Glasgow, UK, [5]School of Medicine, Dentistry & Nursing, University of Glasgow, Glasgow, UK and [6]Department of Anaesthesia, Queen Elizabeth University Hospital, Glasgow, UK

*Corresponding author. School of Cardiovascular & Metabolic Health, University of Glasgow, Glasgow, UK. E-mail: Maximilian.Ralston@glasgow.ac.uk

Abstract

Obesity is a worldwide health crisis and poses significant challenges in critical care. Many studies suggest an 'obesity paradox', in which obesity, defined by body mass index (BMI), is associated with better outcomes. However, the inability of BMI to discriminate between fat and muscle or between visceral adipose tissue and subcutaneous adipose tissue, limits its prediction of metabolic ill health. We suggest that the 'obesity paradox' may be more reflective of the limitations of BMI than the protective effect of obesity.

We explore the biological processes leading to visceral fat accumulation, and the evidence linking it to outcomes in critical illness. In the 'spillover' hypothesis of adipose tissue expansion, caloric excess and impaired expansion of storage capacity in the subcutaneous adipose tissue lead to accumulation of visceral adipose tissue. This is associated with a chronic inflammatory state, which is integral to the link between visceral adiposity, type 2 diabetes mellitus, and ischaemic heart disease.

We review the current evidence on visceral adiposity and critical illness outcomes. In COVID-19, increased visceral adipose tissue, irrespective of BMI, is associated with more severe disease. This is mirrored in acute pancreatitis, suggesting visceral adiposity is linked to poorer outcomes in some hyperinflammatory conditions. We suggest that visceral adiposity's chronic inflammatory state may potentiate acute inflammation in conditions such as COVID-19 and acute pancreatitis. Further work is required to investigate other critical illnesses, especially sepsis and acute respiratory distress syndrome, in which current evidence is scarce. This may give further insights into pathophysiology and inform tailored treatment and nutrition strategies based on body fat distribution.

Keywords: acute pancreatitis; body composition; body mass index; COVID-19; critical care outcomes; obesity; obesity paradox; visceral adipose tissue

Obesity has been declared a global pandemic by the World Health Organization, with an estimated worldwide prevalence of 13%, which has increased markedly in the past 50 yr.[1] The prevalence of obesity is higher in high-income countries, with 29.7% of adults in the UK classified as obese in 2016, up from 11.2% in 1975.[1] Rates of obesity in patients admitted to an intensive care unit (ICU) are ~20%, but vary between countries.[2] Obesity causes a number of pathophysiological, physical, and pharmacological challenges in caring for the critically ill, but its influence on their outcomes is less clear.[3,4] A number of meta-analyses of observational studies investigating the relationship between obesity and outcomes

Received: 20 June 2024; **Accepted:** 11 February 2025

in critical illness have found that patients who are overweight or obese may have better outcomes than those of a normal body mass index (BMI).[5–7] This somewhat surprising finding has been termed an 'obesity paradox'. However, whether the 'obesity paradox' is a true phenomenon, or a methodological artifact, remains a topic of debate.

The obesity paradox

Several pathophysiological mechanisms have been proposed to explain the 'obesity paradox'. Excess fat may act as a 'metabolic reserve', providing additional energy substrate during the hypercatabolic phase of acute critical illness, while potentially supporting preservation of muscle, allowing improved recovery. Adipose tissue, particularly subcutaneous adipose tissue, may have an immunomodulatory effect, producing anti-inflammatory adipokines, acting as a comparatively harmless 'inflammatory sink' for pro-inflammatory mediators released in acute critical illness, or both. In addition, chronic low-level inflammation in obesity may act as a form of 'inflammatory preconditioning', blunting the excessive inflammatory response often seen during critical illness.[8,9]

Conversely, it may be that the 'obesity paradox' remains a methodological artifact.[9,10] Biases introduced by confounding factors such as age, sex, ethnicity, smoking status, alcohol consumption, physical activity, and socioeconomic status may be inadequately controlled-for, particularly in large retrospective studies. Collider stratification bias may also play a role: if clinicians admit obese patients with less severe acute illness to the ICU for fear of poorer outcomes or more rapid deterioration, this would skew those analyses including only patients admitted to ICUs.[11] Misclassification bias may occur as heavier patients may be less likely to have been weighed, because of technical and physical difficulties, potentially leading to non-uniform study exclusion through missing data. Weight loss caused by comorbid conditions may also misclassify patients as of 'normal weight' when in fact they are in a compromised nutritional state, increasing the risk of poor outcomes in the normal weight group.

Some studies have attempted to address these biases. One study adjusting for nutritional status at ICU admission found no evidence of an 'obesity paradox', while another found no paradox when patients received early enteral nutrition.[12,13] Another study used a machine learning approach within a causal inference framework to replace a traditional logistic regression model, and found this mitigated the 'obesity paradox'.[11] Consequently, there must be significant doubt as to whether the 'obesity paradox' is a true effect, or a statistical artifact.

BMI, the most common measurement of obesity, may also contribute to the 'obesity paradox'. Although easy and cheap to measure and calculate, BMI provides no information about body composition, including the quantity and distribution of adipose tissue and muscle. Adipose tissue distribution is more strongly linked to increased metabolic risk than BMI or overall adipose tissue volume.[14,15] While BMI has been shown to be correlated with subcutaneous adipose tissue (SAT) quantity, it shows less correlation with visceral adipose tissue (VAT) quantity.[16] In a UK Biobank study, a higher VAT quantity was associated with coronary heart disease (CHD) and type 2 diabetes mellitus (T2DM).[17] South Asian populations at a given BMI have higher VAT in comparison to white populations, and this is associated with increased insulin resistance, earlier incidence of CHD and T2DM, and more severe complications of these conditions.[18–20] Body fat distribution also varies with age and sex, with increased VAT associated with increased age and male sex.[21] Nevertheless, this relationship between VAT and CHD and T2DM persists despite adjusting for these factors, suggesting it is an independent risk factor.[17] This has led to the suggestion that the 'obesity paradox' in cardiovascular disease may be more of a 'BMI paradox', and that fat distribution may be a more important predictor of disease risk and outcome than BMI.[22,23] It is possible that this is also true in critical illness. This has been reinforced by a recent revision of diagnostic criteria for obesity, which calls for BMI to be supplemented by additional measures of adiposity.[24]

This review will explore the hypothesis that body fat distribution, rather than obesity, may be associated with ICU outcomes.

Adipose tissue structure, function, and dysfunction

The structure and function of adipose tissue is key to understanding the health risks associated with increased adiposity. Adipose tissue is a loose connective tissue, composed of adipocytes and the stromal vascular fraction, which includes macrophages, mesenchymal stem cells, and pre-adipocytes. In humans, adipose tissue can be divided into white adipose tissue, brown adipose tissue, and beige adipose tissue. White adipose tissue can be further subdivided into SAT, found underneath the skin, and VAT, which surrounds the internal organs. SAT is mostly contained within abdominal and gluteofemoral deposits (with variation in distribution between individuals), while omentum is the major VAT depot. The major role of white adipose tissue is in energy storage, and white adipocytes are characterised by a large unilocular lipid droplet. In contrast, brown adipose tissue plays a crucial role in temperature regulation, critically at low temperatures, and is characterised by adipocytes with multilocular lipid droplets, significantly higher mitochondrial density, and the expression of uncoupling protein-1.[25] Beige adipose tissue is developed from white adipose tissue, and is formed when white adipocytes are exposed to a stimulus which causes them to develop many characteristics of brown adipocytes described above.[25]

Adipose tissue is the site of storage of triacylglycerol through lipogenesis under conditions of excess nutritional intake. In conditions of nutritional deficit, energy can be released from stored triacylglycerol in adipose tissue through lipolysis. However, adipose tissue is no longer thought of as just an inert energy store and is now known to be highly metabolically active. There is evidence it plays an integral role in inflammation and immunity both in healthy and in disease states.[26–28]

In response to caloric excess, adipose tissue can expand through two different processes: hyperplasia and hypertrophy. In hyperplastic expansion, pre-adipocyte differentiation into mature adipocytes is stimulated, increasing the number of mature adipocytes available for triacylglycerol storage. In contrast, in adipocyte hypertrophy, existing mature adipocytes expand in size to store excess triacylglycerol, as failure of pre-adipocyte differentiation and adipocyte maturation leads to a limited increase in adipocyte number.[29,30] Adipocyte hyperplasia is not associated with significant alterations in insulin sensitivity.[31] In contrast, adipocyte hypertrophy is associated with increased adipocyte insulin resistance, resulting in increased lipolysis.[32] This can lead to increased

circulating free fatty acids, which may promote ectopic fat deposition and the development of systemic insulin resistance. Adipocyte hypertrophy is also associated with reduced angiogenesis, tissue hypoxia, macrophage infiltration, and an inflammatory response.[33] This inflammatory response includes a shift to a proinflammatory cytokine secretion profile, with a positive correlation between cell size and secretion of leptin, interleukin-6 (IL-6), IL-8, monocyte chemoattractant protein-1, and granulocyte colony stimulating factor, and a negative correlation with the anti-inflammatory cytokine IL-10.[33]

It is now generally accepted that excess VAT is a marker of this failure in SAT expansion, brought about by factors such as genetic predisposition, ethnicity, sex, age.[34–36] Excess fatty acids are not securely retained in hypertrophied adipocytes.[37] As fatty acids cannot be retained as triacylglycerol in SAT, either because of an insufficient number of mature adipocytes or as a result of hypertrophic adipocyte insulin resistance, they 'spill over' and accumulate into other fat deposits, such as omentum and epicardial adipose tissue (EAT), or into ectopic storage as intracellular lipid droplets in the liver, heart, and pancreas.[38,39] Excess VAT is associated with the development of insulin resistance[40] and the metabolic syndrome.[29] The pathophysiology is thought to be that increased VAT is associated with increased lipolysis, resulting in increased free fatty acid delivery to the liver increasing hepatic ectopic fat, insulin resistance, and gluconeogenesis.[41,42] VAT is also more sensitive than SAT to catecholamine-induced lipolysis, which may be of particular relevance in states of elevated endogenous catecholamine release such as critical illness.[42,43] In addition, increased VAT has been associated with increased inflammatory mediators, such as tumour necrosis factor-α (TNF-α), IL-6, and plasminogen activator inhibitor-1.[44–46] Excess VAT is associated with poorer outcomes in cardiovascular diseases[23] and inflammatory conditions such as Crohn's disease.[47]

Measurement of adiposity/body fat distribution

Adipose tissue can be measured directly using computed tomography (CT), magnetic resonance imaging or ultrasound, or approximated using anthropometric techniques (such as waist circumference or sagittal abdominal diameter measurement) or bioelectrical impedance analysis.

Anthropometric measurements, such as waist circumference, waist:hip ratio, and sagittal abdominal diameter, are fast, simple, reproducible, low cost, and with minimal side-effects or complications. However, they are unable to separate abdominal SAT and VAT, there is significant variation in measurements by sex, age, and ethnicity, and there are no universally agreed measurement sites.[48]

Bioelectrical impedance involves measuring resistance (opposition to an alternating current through body compartments) and reactance (conduction delay by membranes). However, it is not clear how well bioelectrical impedance correlates with direct quantification (such as from CT), particularly at extremes of VAT, and larger studies are required to demonstrate this method is superior to anthropometric measurements.[48]

CT imaging is the most commonly used direct measurement technique in critical care studies. A number of analysis protocols have been published, using abdominal imaging to measure SAT and VAT, or thoracic imaging to measure SAT and EAT.[49] CT is widely available in well-resourced settings, and commonly used in the care of critically ill patients. This allows analysis of images acquired for clinical reasons, avoiding additional radiation exposure. MR imaging can be analysed in a similar manner, and does not expose patients to radiation, but is less widely used, is slower to perform, and the magnetic field poses challenges for clinical equipment and monitoring. Both modalities require transfer out of the ICU to an imaging department, exposing critically ill patients to increased risk relative to bedside tests. Ultrasound imaging, which can be performed at the bedside, has also been used to measure adipose tissue distribution.[50] Techniques have been developed to measure abdominal SAT and VAT thickness, and apply geometric models to estimate volume, but these have not been used in critically ill patients.

Composite indices of anthropometric, imaging-derived measures, biochemical parameters, or all can also be used to quantify metabolic risk. These include the visceral adiposity index (a model created using BMI, waist circumference, triglyceride, and high-density lipoprotein concentrations) and the combined adiposity-nutritional index (calculated using the visceral adiposity index, serum albumin concentration, and serum total lymphocyte count), which have been used to predict cardiovascular outcomes and complications.

Obesity, body fat distribution, and outcomes in critical illness

Several studies have examined CT-derived body fat quantification in general ICU populations. SAT was not associated with the need for invasive mechanical ventilation,[51] duration of invasive mechanical ventilation,[51,52] ICU length of stay,[52] disability at hospital discharge,[53] or mortality.[51,53] In contrast, VAT was associated with the requirement for invasive mechanical ventilation,[51] although the results were inconsistent regarding association with duration of invasive mechanical ventilation.[51,52] VAT was not associated with mortality,[51,54] apart from above a certain threshold (241 cm^2 at the L3 vertebral level).[51] None of these studies assessed the relative proportions of adipose tissue between visceral and subcutaneous compartments.

Other approaches yielded similar results. One study using bioelectrical impedance found that neither fat-free mass nor visceral fat area was associated with outcomes in ICU,[55] while another found no association between waist circumference and mortality.[56] In summary, evidence suggests no consistent association between body fat quantity or distribution and outcomes in a general ICU population.

The COVID-19 pandemic provides more information on adiposity and ICU outcome

Obesity rapidly emerged as a risk factor for severe COVID-19 and poorer patient outcomes.[57–59] As a result, studies investigated possible associations between adiposity, body fat distribution, and clinical outcomes. Three meta-analyses have investigated CT-derived body fat parameters and outcomes in COVID-19, showing a consistent association between increased VAT and disease severity.[60–62] Increased VAT was also associated with an increased risk of ICU admission and of requiring invasive mechanical ventilation.[60,61] SAT was not associated with ICU admission,[61] or

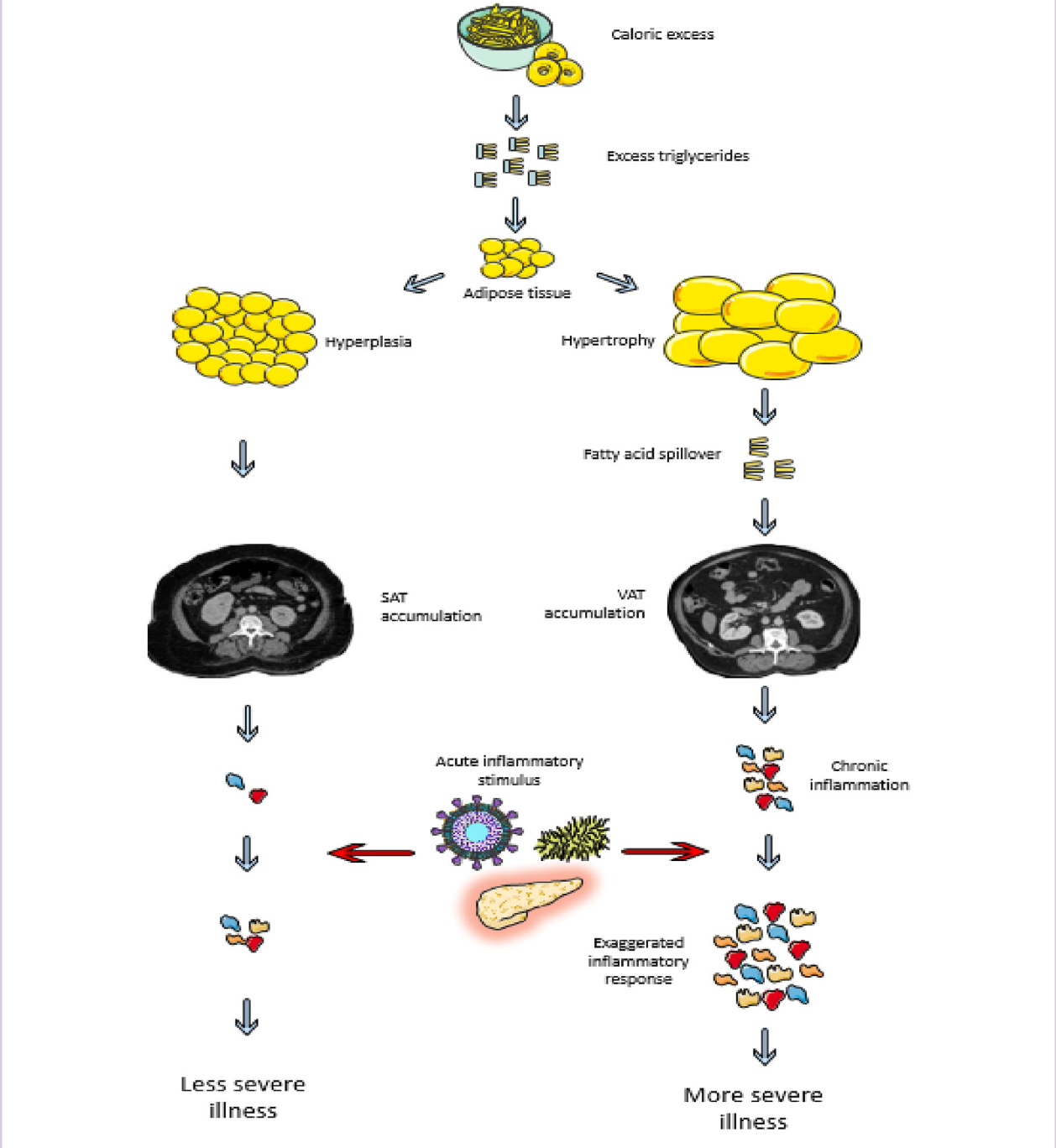

Fig 1. Why visceral obesity may be associated with more severe acute inflammatory illness. In response to caloric excess, adipose tissue may expand by either adipocyte hyperplasia, or hypertrophy. Expansion by hypertrophy is associated with fatty acid spillover and accumulation of VAT. This in turn is associated with a state of chronic inflammation. We hypothesise that in this setting, the response to an acute pro-inflammatory stimulus (such as infection or acute pancreatitis) may be exaggerated in those with greater VAT, leading to a higher severity of illness. Figure created using images from Servier Medical Art (https://smart.servier.com/) under creative commons licence 3.0. SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue.

severe disease in two meta-analyses.[62] These findings were reinforced by a subsequent systematic review, which included studies using a greater variety of body composition measurements.[63] Findings for other clinical outcomes were mixed, and no clear conclusions could be drawn. It should be noted that the largest meta-analysis only included five studies, with significant overlap between the meta-analyses, and most included studies were small. As such, neutral

results may reflect underpowering, rather than the true absence of effect.

Subsequent individual studies confirmed associations between VAT and disease severity,[64–66] ICU admission,[67] and the need for invasive mechanical ventilation.[68] However, while one study showed an association between increased VAT and mortality,[69] others found no evidence of association.[66,67,70] Bioelectrical impedance studies have shown that high or very high VAT may be associated with more severe disease,[71,72] and the need for invasive mechanical ventilation[73] but not mortality.[73] Waist:hip ratio was also positively correlated with the development of respiratory distress.[74] The visceral adiposity index was also associated with more severe disease, but not ICU admission or mortality.[75]

In subsequent studies SAT was not associated with disease severity,[65] ICU admission,[67,70] or the need for invasive mechanical ventilation,[68,70] and even had an inverse relationship with ICU admission[70] and mortality.[67]

The distribution of fat between subcutaneous and visceral depots can also be assessed. An increased ratio of VAT:SAT may be associated with increased ICU admission,[67,76] mortality[70] or a composite of the two.[77] An increased ratio of VAT:SAT was associated with increased disease severity[78] and hospitalisation, but not requirement for invasive mechanical ventilation.[79] However, one study found no difference in the ratio of VAT:SAT between patients who developed severe disease or died, and those who did not,[69] and another found no association between VAT:SAT and mortality.[67] Further studies are required to confirm whether fat distribution ratios provide additional prognostic information.

EAT has also been investigated in COVID-19, as it can be measured from a thoracic CT, which is more frequently undertaken than an abdominal CT. A meta-analysis concluded that patients with severe COVID-19 had higher EAT thickness, volume, and attenuation (a measure of inflammation) than patients with non-severe COVID-19.[80] EAT thickness and attenuation were both associated with ICU admission, but no EAT measures were associated with mortality.[80] Subsequent studies have also found an association between increased EAT and more severe COVID-19,[81–83] and requirement for ICU admission.[82,84–86] However, findings were inconsistent, with other studies finding no association with ICU admission,[87,88] need for invasive mechanical ventilation,[68] or severity[89] and one finding EAT quantity was only associated with ICU admission in those with T2DM.[90] Subsequent results have also been mixed with regards to an association between EAT quantity and mortality, with two studies finding a positive association,[91,92] and two finding no association.[82,88] EAT thickness >0.8 cm, measured using ultrasound, was also associated with mortality in patients in the ICU with COVID-19.[50]

There is a relatively consistent trend towards an association between ectopic fat depots (VAT and EAT) and more severe disease, as evidenced by the meta-analyses discussed.[60–62,80] These studies also suggest that SAT is not likely to be associated with more severe disease.[61,62] However, the majority of studies conducted have been small, retrospective, single-centre studies, and so are at high risk of bias. There is insufficient evidence regarding other outcomes, or in relation to fat distribution ratios, to suggest any associations.

The pathophysiology of COVID-19, characterised by immune dysregulation and hyperinflammation, to an extent mirrors that of obesity.[57,93] Adipose tissue is known to produce significant quantities of proinflammatory mediators, such as TNF-α and IL-6, which also play a role in the pathophysiology of critical illness syndromes.[45,94–96] Visceral adiposity in particular is strongly associated with increased cytokine and adipokine secretion, elevated inflammatory markers, and proinflammatory macrophage infiltration.[95,97,98] Concentrations of commonly-measured inflammatory markers, such as C-reactive protein, are also related to outcomes in critical illness, particularly when persistently elevated.[99–101] This may also be supported by a study showing an association between visceral adiposity and early and severe cytokine release syndrome after chimeric antigen receptor T-cell therapy.[102] Obesity-related inflammation is known to play a key role in the pathogenesis of cardiovascular disease and T2DM,[103,104] and is associated with a number of inflammatory diseases, including asthma, psoriasis, rheumatoid arthritis, and inflammatory bowel disease.[105–109] This may also be true of critical illnesses associated with high levels of inflammation. In visceral obesity, a chronically dysfunctional immune and inflammatory response may lead to an exaggerated response to a pro-inflammatory stimulus (Fig. 1). This may lead to an increased organ dysfunction, and more severe disease.

The association of body fat distribution and ICU outcome for specific disease groups

If the hypothesis that visceral obesity is linked to disease outcomes via the interaction of inflammatory and metabolic pathways is correct (Fig. 1), it may extend to other ICU conditions characterised by a dysregulated immune and inflammatory response, such as sepsis and ARDS.

Below, we review the existing literature on conditions that constitute a significant proportion of admissions to critical care units, in which studies of body composition have been carried out. We will focus on sepsis, ARDS, pancreatitis, and trauma. We will also discuss the literature regarding perioperative ICU patients and body composition.

Sepsis

Few studies have looked at body fat distribution as measured by CT and its association with sepsis outcomes. Two studies from the same group found an association between an increased VAT:SAT ratio and increased mortality, while finding no association between the absolute volume or mass of SAT or VAT and outcomes.[110,111] One small study of patients with carbapenem-resistant *Klebsiella pneumoniae* bacteraemia found an association between increased VAT and increased mortality.[112] Two other retrospective studies found that absolute volumes of VAT or SAT were not associated with outcomes in necrotising soft tissue infections or intra-abdominal infections.[113,114]

In contrast, a study of patients with solid organ malignancy and septic shock found no association between SAT, VAT, or VAT:SAT ratio and outcomes, though cancer cachexia may be a confounder.[115] A study using sagittal abdominal diameter, rather than by CT analysis found that while both BMI and sagittal abdominal diameter were positively correlated with length of stay and duration of invasive mechanical ventilation, only sagittal abdominal diameter was associated with increased multi-organ dysfunction, need for renal replacement therapy, and mortality.[116]

Overall, the evidence regarding a link between fat distribution and outcomes in sepsis remains limited and inconsistent. While the largest study did find an association between VAT:SAT ratio and outcomes,[111] other studies have been

relatively small, and conducted in heterogenous populations, which may explain the inconsistent results. Further research is therefore required to definitively characterise any relationship between visceral adiposity and sepsis.

Pancreatitis

A systematic review of 11 studies, involving 2529 patients, evaluated the evidence for an association between VAT and outcomes in acute pancreatitis.[117] This review found mixed evidence for an association between VAT and incidence, severity, complications, and outcomes. Four studies found VAT to be a risk factor for acute pancreatitis, while five did not. Nine studies found an association between increased VAT and increased severity, assessed using the Revised Atlanta Classification. In two of these studies this association was only present on univariate analysis, and did not persist in multivariate analysis, while another only noted this association in hyperlipidaemic pancreatitis.[118–120] Eight studies found an association between VAT and increased systemic complications, two found no association, and one did not assess for this. Two studies found an association between VAT and local complications,[121,122] while one found no association.[120]

Two of the studies found an association between VAT and mortality in acute pancreatitis,[123,124] while two others found no association.[120,125]

In addition to the studies included in this systematic review, four other studies found no association between VAT and mortality.[126–129] However, one found an association between VAT and complications, including requirement for vasopressor support, requirement for haemodialysis, respiratory failure, and need for endoscopic intervention or percutaneous drainage.[128] Increased severity was also associated with increased VAT in two studies using CT[129,130] and one using the visceral adiposity index.[131]

Overall, current evidence suggests that increased VAT may be a risk factor for increased severity of pancreatitis, using the Revised Atlanta Classification. The evidence is more mixed regarding complications of pancreatitis—both local and systemic—but there is some suggestion of an association with VAT. However, most studies suggest that there is not an association between VAT and mortality in acute pancreatitis. Given that both increased severity and increased complications are generally associated with increased mortality, it is not clear if this is a type II error as a result of relatively underpowered studies, or if the impact of VAT on disease severity is of insufficient magnitude as to translate into an association with mortality. Further large, multicentre, prospective studies are required to definitively answer this question.

Acute respiratory distress syndrome

Only one retrospective study looked at the association between CT-assessed body fat distribution and outcomes in ARDS. Higher VAT and SAT were associated with decreased mortality, but higher VAT:SAT ratio was associated with increased mortality, suggesting that distribution of adipose tissue, rather than absolute volume, may be important.[132] Given the very limited data, further studies are required to confirm or refute these findings and explore the role of visceral adiposity in ARDS. It may be prudent to focus on EAT in these patients, as they are more likely to undergo thoracic CT imaging than abdominal.

Trauma

Unlike other ICU conditions, trauma outcomes remain strongly associated with measures of severity of the initial injury, potentially limiting the impact of obesity-associated inflammation. For patients suffering traumatic injuries, existing evidence using BMI to define obesity suggests a positive association between BMI and mortality, and with in-hospital complications.[133,134]

Three studies found no association between VAT and mortality after major trauma,[135–137] while one other did find an association between VAT and mortality.[138] Two studies have found an association between higher SAT and increased ICU length of stay,[137,139] and complications,[137] though one of these studies found this association only for gunshot wounds, and not stab wounds.[139] There was no association between SAT and mortality in two studies.[137,140] One study using VAT:SAT ratio also found no evidence of an association between this and mortality after major trauma.[141] Two studies found that a higher waist:hip ratio was associated with increased complications, mortality, or both in a trauma population.[138,142]

The literature quantifying obesity by BMI has also suggested an association between obesity and an increased risk of acute kidney injury after trauma.[143] This was replicated using CT-based body fat distribution analysis in one study, which demonstrated that both SAT and VAT volumes were positively associated with the development of acute kidney injury.[144]

Studies in trauma suggest that volume or distribution of adipose tissue is not associated with mortality but may be associated with development of acute kidney injury and with other in-hospital complications. This stands in contrast to the evidence in which obesity is quantified using BMI. It may be that increased body mass is associated with different patterns of injury, contributing to poorer outcomes.[145,146] Studies conducted in trauma populations had a reasonable sample size, though were mainly retrospective and often conducted within a single centre or healthcare provider, and therefore remain at significant risk of bias.

Discussion

The relationship between obesity and outcomes for critically ill patients remains unclear. Existing research suggests that for the general ICU population, and for some specific conditions, an ‘obesity paradox’ may exist, but this remains a topic of debate. We hypothesise that the inability of BMI to accurately reflect the metabolic risk associated with visceral adiposity may contribute to this ‘obesity paradox’ and investigated the evidence that alternative measures can identify the true risks associated with adiposity.

In COVID-19, evidence suggests that increased VAT or increased EAT are associated with increased severity of disease. In contrast, SAT does not seem to be associated with outcomes. In acute pancreatitis, VAT also seems to be associated with increased severity of illness and increased incidence of complications, though the relationship with mortality remains unclear. This requires further exploration. It may be that this reflects the preponderance of relatively underpowered studies, which is a common feature of the literature in this area, and that larger studies are required. For other conditions that require ICU admission, the numbers of studies, and patient populations included, are too small, and too heterogenous, to draw firm conclusions.

The association between increased visceral adiposity and poorer outcomes in two conditions (COVID-19 and acute pancreatitis) associated with dysregulated inflammatory and immune responses suggests the possibility of shared aspects of pathophysiology. Both EAT and VAT are known to be highly metabolically active tissues, with important autocrine, paracrine, and endocrine functions, and significant roles in inflammation.[26,147] In these conditions, increased EAT or VAT depots may exacerbate the inflammatory response, contributing to more severe disease, and poorer patient outcomes (Fig. 1). It is not clear whether any detrimental pathophysiological effects of EAT/VAT depots are local effects on the primarily affected organ, or systemic effects triggered by the initial pathological insult. Further research on serum and tissue markers of inflammation and altered metabolism would be required to elucidate this.

In contrast, visceral adiposity was not strongly associated with clinical outcomes in trauma. This differs from studies demonstrating an association between increased BMI and poorer outcomes in this patient population. It may be that absolute body mass is more important in physical injury than body composition, in contrast with those primarily immune and inflammatory conditions such as COVID-19 and pancreatitis.

Few studies have been conducted in non-COVID-19 sepsis or in non-COVID-19 ARDS, two of the most common, and most severe conditions affecting patients in intensive care. Both conditions are, like COVID-19 and acute pancreatitis, characterised by dysregulated inflammatory and immune responses, hypermetabolic states, and cardiac dysfunction.[148,149] Indeed, despite their different triggers, it is possible that the multiorgan dysfunction syndrome seen in severe cases of these conditions share important pathophysiological aspects.[150] These similarities suggest a biological plausibility to a detrimental impact of visceral adiposity on patient outcomes, and thus further research is required to explore this possibility.

If confirmed, a link between visceral adiposity and hyperinflammatory critical illness syndromes may offer new potential therapeutic targets, and further support for measures to reduce obesity. In contrast, if there is no association between visceral obesity and critical illness (or it is demonstrated to be associated with improved outcomes), further research would be required to understand why this stands in contrast to many other conditions, what aspects of obesity may be protective to patients with critical illness, and how these insights can be harnessed to improve their treatment.

Further research is needed to address the significant limitations and gaps identified in the current literature. Most studies cited in this review were small, often single-centre, retrospective studies, and were at high risk of bias as a result. Larger studies are required, to reduce the risk that null results are a result of underpowering, rather than the absence of any effect, and to mitigate against random false-positive results in a small sample. Carrying these studies out prospectively would reduce the risk of selection bias, which is potentially present in the majority of studies cited in this review, which were conducted retrospectively. This would also allow evaluation of any systematic differences between patients who do and do not undergo CT imaging, to assess if this sample is representative of the population. It would also increase external validity if studies were conducted across multiple centres. To address potentially shared aspects of pathophysiology, particularly the hypothesis that visceral obesity may exaggerate the inflammatory response, these studies should ideally incorporate clinical and biochemical data available from patients' clinical care.

Conclusion

The relationship between obesity and outcomes in critical illness remains a source of debate. BMI, the most commonly used metric for defining obesity, is easy to measure and calculate, but provides insufficient information at an individual patient level. Alternative measures of adiposity, particularly body fat distribution analysis from CT imaging, may offer more information on the influence of adiposity on the outcomes of patients with critical illnesses. In COVID-19 and in acute pancreatitis, increased quantity of VAT is probably associated with more severe disease. In other conditions, and for other outcomes, the current evidence is insufficient to support any associations with body fat distribution. Further research is required to assess the proposed 'obesity paradox' in other ICU conditions using these methods, and this should be focused on conditions in which there is biological plausibility that visceral adiposity may impact outcomes.

Authors' contributions

Conceptualisation and design: all authors
Review of literature: MRR, GM, ZJL
Primary draft of the manuscript: MRR, GM, ZJL
Review and revision of the manuscript for important intellectual content: IPS, MABS, MJW, DJF
Supervision: IPS, MABS, MJW
Approval of the final version: all authors

Funding

This work was supported by NHS Greater Glasgow & Clyde Endowment. Fund Grant GN23ME009.

Declarations of interests

The authors declare that they have no conflicts of interest.

References

1. Abarca-Gómez L, Abdeen ZA, Hamid ZA, et al. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. *Lancet* 2017; **390**: 2627–42
2. Sakr Y, Alhussami I, Nanchal R, et al. Being overweight is associated with greater survival in ICU patients: results from the Intensive Care over Nations Audit. *Crit Care Med* 2015; **43**: 2623–32
3. Anderson MR, Shashaty MGS. Impact of obesity in critical illness. *Chest* 2021; **160**: 2135–45
4. Schetz M, De Jong A, Deane AM, et al. Obesity in the critically ill: a narrative review. *Intensive Care Med* 2019; **45**: 757–69
5. Pepper DJ, Sun J, Welsh J, Cui X, Suffredini AF, Eichacker PQ. Increased body mass index and adjusted mortality in ICU patients with sepsis or septic shock: a systematic review and meta-analysis. *Crit Care* 2016; **20**: 181

6. Zhao Y, Li Z, Yang T, Wang M, Xi X. Is body mass index associated with outcomes of mechanically ventilated adult patients in intensive critical units? A systematic review and meta-analysis. *PLoS One* 2018; **13**, e0198669
7. Zhi G, Xin W, Ying W, Guohong X, Shuying L. 'Obesity paradox' in acute respiratory distress syndrome: a systematic review and meta-analysis. *PLoS One* 2016; **11**, e0163677
8. Karampela I, Chrysanthopoulou E, Christodoulatos GS, Dalamaga M. Is there an obesity paradox in critical illness? Epidemiologic and metabolic considerations. *Curr Obes Rep* 2020; **9**: 231–44
9. Ludwig N, Hurt RT, Miller KR. The obesity paradox: validity and clinical implications. *Curr Pulmonol Rep* 2017; **6**: 58–63
10. Banack HR, Stokes A. The 'obesity paradox' may not be a paradox at all. *Int J Obes* 2017; **41**: 1162–3
11. Decruyenaere A, Steen J, Colpaert K, Benoit DD, Decruyenaere J, Vansteelandt S. The obesity paradox in critically ill patients: a causal learning approach to a casual finding. *Crit Care* 2020; **24**: 485
12. Robinson MK, Mogensen KM, Casey JD, et al. The relationship among obesity, nutritional status, and mortality in the critically ill. *Crit Care Med* 2015; **43**: 87–100
13. Harris K, Zhou J, Liu X, Hassan E, Badawi O. The obesity paradox is not observed in critically ill patients on early enteral nutrition. *Crit Care Med* 2017; **45**: 828–34
14. Fox CS, Massaro JM, Hoffmann U, et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. *Circulation* 2007; **116**: 39–48
15. Neeland IJ, Ross R, Després J-P, et al. Visceral and ectopic fat, atherosclerosis, and cardiometabolic disease: a position statement. *Lancet Diabetes Endocrinol* 2019; **7**: 715–25
16. Ping Z, Pei X, Xia P, et al. Anthropometric indices as surrogates for estimating abdominal visceral and subcutaneous adipose tissue: a meta-analysis with 16,129 participants. *Diabetes Res Clin Pract* 2018; **143**: 310–9
17. Linge J, Borga M, West J, et al. Body composition profiling in the UK Biobank imaging study. *Obesity (Silver Spring)* 2018; **26**: 1785–95
18. Lear SA, Kohli S, Bondy GP, Tchernof A, Sniderman AD. Ethnic variation in fat and lean body mass and the association with insulin resistance. *J Clin Endocrinol Metab* 2009; **94**: 4696–702
19. Misra A, Soares MJ, Mohan V, et al. Body fat, metabolic syndrome and hyperglycemia in South Asians. *J Diabetes Complications* 2018; **32**: 1068–75
20. Misra A, Khurana L. Obesity-related non-communicable diseases: South Asians vs White Caucasians. *Int J Obes* 2011; **35**: 167–87
21. Dai L, Huang X, Lu Y, et al. Defining reference values for body composition indices by magnetic resonance imaging in UK Biobank. *J Cachexia Sarcopenia Muscle* 2023; **14**: 992–1002
22. Antonopoulos AS, Oikonomou EK, Antoniades C, Tousoulis D. From the BMI paradox to the obesity paradox: the obesity–mortality association in coronary heart disease. *Obes Rev* 2016; **17**: 989–1000
23. Coutinho T, Goel K, Corrêa de Sá D, et al. Central obesity and survival in subjects with coronary artery disease. *J Am Coll Cardiol* 2011; **57**: 1877–86
24. Rubino F, Cummings DE, Eckel RH, et al. Definition and diagnostic criteria of clinical obesity. *Lancet Diabetes Endocrinol* 2025; **13**: e6
25. Rui L. Brown and beige adipose tissues in health and disease. *Compr Physiol* 2017; **7**: 1281–306
26. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. *J Clin Endocrinol Metab* 2004; **89**: 2548–56
27. Marques MB, Langouche L. Endocrine, metabolic, and morphologic alterations of adipose tissue during critical illness. *Crit Care Med* 2013; **41**: 317–25
28. Schäffler A, Müller-Ladner U, Schölmerich J, Büchler C. Role of adipose tissue as an inflammatory organ in human diseases. *Endocr Rev* 2006; **27**: 449–67
29. Bays HE, González-Campoy JM, Bray GA, et al. Pathogenic potential of adipose tissue and metabolic consequences of adipocyte hypertrophy and increased visceral adiposity. *Expert Rev Cardiovasc Ther* 2008; **6**: 343–68
30. Isakson P, Hammarstedt A, Gustafson B, Smith U. Impaired preadipocyte differentiation in human abdominal obesity. *Diabetes* 2009; **58**: 1550–7
31. Weyer C, Foley JE, Bogardus C, Tataranni PA, Pratley RE. Enlarged subcutaneous abdominal adipocyte size, but not obesity itself, predicts Type II diabetes independent of insulin resistance. *Diabetologia* 2000; **43**: 1498–506
32. Laforest S, Labrecque J, Michaud A, Cianflone K, Tchernof A. Adipocyte size as a determinant of metabolic disease and adipose tissue dysfunction. *Crit Rev Clin Lab Sci* 2015; **52**: 301–13
33. Skurk T, Alberti-Huber C, Herder C, Hauner H. Relationship between adipocyte size and adipokine expression and secretion. *J Clin Endocrinol Metab* 2007; **92**: 1023–33
34. Frank AP, Santos de RS, Palmer BF, Clegg DJ. Determinants of body fat distribution in humans may provide insight about obesity-related health risks. *J Lipid Res* 2019; **60**: 1710–9
35. Sniderman AD, Bhopal R, Prabhakaran D, Sarrafzadegan N, Tchernof A. Why might South Asians be so susceptible to central obesity and its atherogenic consequences? The adipose tissue overflow hypothesis. *Int J Epidemiol* 2007; **36**: 220–5
36. Tian S, Morio B, Denis J-B, Mioche L. Age-related changes in segmental body composition by ethnicity and history of weight change across the adult lifespan. *Int J Environ Res Public Health* 2016; **13**: 821
37. Gustafson B, Hedjazifar S, Gogg S, Hammarstedt A, Smith U. Insulin resistance and impaired adipogenesis. *Trends Endocrinol Metab* 2015; **26**: 193–200
38. Rutkowski JM, Stern JH, Scherer PE. The cell biology of fat expansion. *J Cell Biol* 2015; **208**: 501–12
39. Unger RH, Scherer PE. Gluttony, sloth and the metabolic syndrome: a roadmap to lipotoxicity. *Trends Endocrinol Metab* 2010; **21**: 345–52
40. Misra A, Garg A, Abate N, Peshock RM, Stray-Gundersen J, Grundy SM. Relationship of anterior and posterior subcutaneous abdominal fat to insulin sensitivity in nondiabetic men. *Obes Res* 1997; **5**: 93–9
41. Wajchenberg BL. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. *Endocr Rev* 2000; **21**: 697–738
42. Montague CT, O'Rahilly S. The perils of portliness: causes and consequences of visceral adiposity. *Diabetes* 2000; **49**: 883–8

43. Misra A, Vikram NK. Clinical and pathophysiological consequences of abdominal adiposity and abdominal adipose tissue depots. *Nutrition* 2003; **19**: 457–66
44. Hotamisligil GS. The role of TNFα and TNF receptors in obesity and insulin resistance. *J Int Med* 1999; **245**: 621–5
45. Yudkin JS, Kumari M, Humphries SE, Mohamed-Ali V. Inflammation, obesity, stress and coronary heart disease: is interleukin-6 the link? *Atherosclerosis* 2000; **148**: 209–14
46. Tchernof A, Després J-P. Pathophysiology of human visceral obesity: an update. *Physiol Rev* 2013; **93**: 359–404
47. Büning C, von Kraft C, Hermsdorf M, et al. Visceral adipose tissue in patients with Crohn's disease correlates with disease activity, inflammatory markers, and outcome. *Inflamm Bowel Dis* 2015; **21**: 2590–7
48. Fang H, Berg E, Cheng X, Shen W. How to best assess abdominal obesity. *Curr Opin Clin Nutr Metab Care* 2018; **21**: 360–5
49. Tolonen A, Pakarinen T, Sassi A, et al. Methodology, clinical applications, and future directions of body composition analysis using computed tomography (CT) images: a review. *Eur J Radiol* 2021; **145**, 109943
50. Millman M, Santos ABS, Pianca EG, Pellegrini JAS, Conci FC, Foppa M. Rapid prognostic stratification using Point of Care ultrasound in critically ill COVID patients: the role of epicardial fat thickness, myocardial injury and age. *J Crit Care* 2022; **67**: 33–8
51. Wirtz TH, Loosen SH, Schulze-Hagen M, et al. CT-based determination of excessive visceral adipose tissue is associated with an impaired survival in critically ill patients. *PLoS One* 2021; **16**, e0250321
52. Dusseaux MM, Antoun S, Grigioni S, et al. Skeletal muscle mass and adipose tissue alteration in critically ill patients. *PLoS One* 2019; **14**, e0216991
53. Jaitovich A, Dumas CL, Itty R, et al. ICU admission body composition: skeletal muscle, bone, and fat effects on mortality and disability at hospital discharge-a prospective, cohort study. *Crit Care* 2020; **24**: 566
54. Baggerman MR, Dekker IM, Winkens B, et al. Visceral obesity measured using computed tomography scans: No significant association with mortality in critically ill patients. *J Crit Care* 2023; **77**, 154316
55. Ko SJ, Cho J, Choi SM, et al. Phase angle and frailty are important prognostic factors in critically ill medical patients: a prospective cohort study. *J Nutr Health Aging* 2021; **25**: 218–23
56. Coşkun Musaoğlu I, Aksun M, Şencan A, Katırcıoğlu K, Karahan N. The effect of waist circumference/chest circumference ratio on mortality in intensive care units. *J Cardiovasc Thorac Anaesth Intensive Care Soc* 2018; **24**: 60–6
57. Sattar N, McInnes IB, McMurray JJV. Obesity Is a risk factor for severe COVID-19 infection: multiple potential mechanisms. *Circulation* 2020; **142**: 4–6
58. Sattar N, Valabhji J. Obesity as a risk factor for severe COVID-19: summary of the best evidence and implications for health care. *Curr Obes Rep* 2021; **10**: 282–9
59. Simonnet A, Chetboun M, Poissy J, et al. High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. *Obesity* 2020; **28**: 1195–9
60. Huang Y, Lu Y, Huang Y-M, et al. Obesity in patients with COVID-19: a systematic review and meta-analysis. *Metabolism* 2020; **113**, 154378
61. Foldi M, Farkas N, Kiss S, et al. Visceral adiposity elevates the risk of critical condition in COVID-19: a systematic review and meta-analysis. *Obesity (Silver Spring)* 2021; **29**: 521–8
62. Pranata R, Lim MA, Huang I, et al. Visceral adiposity, subcutaneous adiposity, and severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis. *Clin Nutr ESPEN* 2021; **43**: 163–8
63. Montes-Ibarra M, Orsso CE, Limon-Miro AT, et al. Prevalence and clinical implications of abnormal body composition phenotypes in patients with COVID-19: a systematic review. *Am J Clin Nutr* 2023; **117**: 1288–305
64. Sosna M, Mlynarska A, Stasiow B, Mlynarski R. Association between lung opacities and visceral fat in COVID-19 patients. *Pol J Radiol* 2023; **88**: e119–23
65. Vural M, Dolek BA, Ucar O, Ozkan E, Ozkaya UE. The evaluation of subcutaneous and visceral adipose tissue changes by computed tomography in coronavirus disease 2019 and comparison with quantitative analysis of lung involvement. *Curr Med Imaging* 2024 Jan; **20**(1), E100823219603
66. Yamamoto T, Sugimoto K, Ichikawa S, et al. Impact of body composition on patient prognosis after SARS-Cov-2 infection. *PLoS One* 2023; **18**, e0289206
67. Battisti S, Pedone C, Tramontana F, et al. Abdominal adipose tissue distribution assessed by computed tomography and mortality in hospitalised patients with COVID-19: a retrospective longitudinal cohort study. *Endocrine* 2024; **83**: 597–603
68. Dos Santos DMC, Liu L, Gerisch M, et al. Risk stratification based on a pattern of immunometabolic host factors is superior to body mass index-based prediction of COVID-19-associated respiratory failure. *Nutrients* 2022; **14**: 4280
69. Guarisco G, Fasolo M, Capoccia D, et al. Blood glucose and epicardial adipose tissue at the hospital admission as possible predictors for COVID-19 severity. *Endocrine* 2022; **75**: 10–8
70. Surov A, Thormann M, Kardas H, et al. Visceral to subcutaneous fat ratio predicts short-term mortality in patients with Covid 19. A multicenter study. *Br J Radiol* 2023; **96**, 20220869
71. Carvalho JB, de Andrade GKP, do Nascimento LA, *et al*. Visceral fat area measured by electrical bioimpedance as an aggravating factor of COVID-19: a study on body composition. BMC Infect Dis; 23: 826.
72. Zdravkovic V, Stevanovic D, Cicaric N, et al. Anthropometric measurements and admission parameters as predictors of acute respiratory distress syndrome in hospitalized COVID-19 patients. *Biomedicines* 2023; **11**: 1199
73. Graziano E, Peghin M, De Martino M, et al. The impact of body composition on mortality of COVID-19 hospitalized patients: a prospective study on abdominal fat, obesity paradox and sarcopenia. *Clin Nutr ESPEN* 2022; **51**: 437–44
74. van Zelst CM, Janssen ML, Pouw N, Birnie E, Cabezas MC, Braunstahl G-J. Analyses of abdominal adiposity and metabolic syndrome as risk factors for respiratory distress in COVID-19. *BMJ Open Respir Res* 2020; **7**, e000792
75. Yilmaz E, Sehmen E, Arslan H, Bolat M, Yigit Y. The effect of the visceral adiposity index on the severity of COVID-19 disease: results of a cross-sectional study. *Eur Rev Med Pharmacol Sci* 2023; **27**: 9446–53

76. Battisti S, Pedone C, Napoli N, et al. Computed tomography highlights increased visceral adiposity associated with critical illness in COVID-19. *Diabetes Care* 2020; **43**: e129–30
77. Bunnell KM, Thaweethai T, Buckless C, et al. Body composition predictors of outcome in patients with COVID-19. *Int J Obes (Lond)* 2021; **45**: 2238–43
78. Ogata H, Mori M, Jingushi Y, et al. Impact of visceral fat on the prognosis of coronavirus disease 2019: an observational cohort study. *BMC Infect Dis* 2021; **21**: 1240
79. Chandarana H, Dane B, Mikheev A, Taffel MT, Feng Y. Visceral adipose tissue in patients with COVID-19: risk stratification for severity. *Abdom Radiol* 2021; **46**: 818–25
80. Liu K, Wang X, Song G. Association of epicardial adipose tissue with the severity and adverse clinical outcomes of COVID-19: a meta-analysis. *Int J Infect Dis* 2022; **120**: 33–40
81. Marcucci M, Fogante M, Tagliati C, Papiri G. Cut-off point of CT-assessed epicardial adipose tissue volume for predicting worse clinical burden of SARS-CoV-2 pneumonia. *Emerg Radiol* 2022; **29**: 645–53
82. Bartoli A, Fournel J, Ait-Yahia L, et al. Automatic deep-learning segmentation of epicardial adipose tissue from low-dose chest CT and prognosis impact on COVID-19. *Cells* 2022; **11**: 1034
83. Topcu F, Temel S. Epicardial adipose and pre-sternal subcutaneous tissues associated with extent of pneumonia and hospitalization in COVID-19. *Eur Res J* 2023; **9**: 840–7
84. Erdol MA, Civelek Eser F, Aslan AN, et al. The predictive value of epicardial fat volume for clinical severity of COVID-19. *Rev Port Cardiol* 2022; **41**: 729–37
85. Luchian ML, Motoc AI, Lochy S, et al. Epicardial adipose tissue thickness in COVID-19 hospitalized patients: a tool for risk stratification. *Eur Heart J Cardiovasc Imaging* 2022; **23**: i633–4
86. Turker Duyuler P, Duyuler S, Demirtaş B, Çayhan V. Epicardial and pericoronary adipose tissue in severe COVID-19 infection. *Acta Cardiologica* 2023; **78**: 451–8
87. Calim A, Yanic U, Halefoglu AM, et al. Is there a relationship between epicardial adipose tissue, inflammatory markers, and the severity of COVID-19 pneumonia? *Sisli Etfal Hastan Tip Bul* 2023; **57**: 387–96
88. Meyer H-J, Aghayev A, Hinnrichs M, Borggrefe J, Surov A. Epicardial adipose tissue as a prognostic marker in COVID-19. *In Vivo* 2024; **38**: 281–5
89. Aydeniz E, Weberndorfer V, Brandts L, et al. Pericardial fat is associated with less severe multiorgan failure over time in patients with coronavirus disease-19: the Maastricht intensive care COVID Cohort. *J Thorac Imaging* 2024; **39**: W32–9
90. Charpentier E, Redheuil A, Bourron O, et al. Cardiac adipose tissue volume assessed by computed tomography is a specific and independent predictor of early mortality and critical illness in COVID-19 in type 2-diabetic patients. *Cardiovasc Diabetol* 2022; **21**: 294
91. Emekli E, Turkkani M, S Balli S. Is there a relationship between epicardial adipose tissue, inflammatory markers and prognosis in COVID-19 in patients under 65 years? *Biomark Med* 2022; **16**: 925–33
92. Rossi AP, Donadello K, Schweiger V, et al. Epicardial adipose tissue volume and CT-attenuation as prognostic factors for pulmonary embolism and mortality in critically ill patients affected by COVID-19. *Eur J Clin Nutr* 2023; **77**: 105–11
93. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: a review. *Clin Immunol* 2020; **215**, 108427
94. Bhatia M, Brady M, Shokuhi S, Christmas S, Neoptolemos JP, Slavin J. Inflammatory mediators in acute pancreatitis. *J Pathol* 2000; **190**: 117–25
95. Hotamisligil GS. Inflammation, metaflammation and immunometabolic disorders. *Nature* 2017; **542**: 177–85
96. Zizzo G, Tamburello A, Castelnovo L, et al. Immunotherapy of COVID-19: inside and beyond IL-6 signalling. *Front Immunol* 2022; **13**, 795315
97. Fontana L, Eagon JC, Trujillo ME, Scherer PE, Klein S. Visceral fat adipokine secretion is associated with systemic inflammation in obese humans. *Diabetes* 2007; **56**: 1010–3
98. Pou KM, Massaro JM, Hoffmann U, et al. Visceral and subcutaneous adipose tissue volumes are cross-sectionally related to markers of inflammation and oxidative stress. *Circulation* 2007; **116**: 1234–41
99. Lobo SMA, Lobo FRM, Bota DP, et al. C-reactive protein levels correlate with mortality and organ failure in critically ill patients. *Chest* 2003; **123**: 2043–9
100. Park JE, Chung KS, Song JH, et al. The C-reactive protein/albumin ratio as a predictor of mortality in critically ill patients. *J Clin Med* 2018; **7**: 333
101. Smilowitz NR, Kunichoff D, Garshick M, et al. C-reactive protein and clinical outcomes in patients with COVID-19. *Eur Heart J* 2021; **42**: 2270–9
102. Dos Santos DMC, Rejeski K, Winkelmann M, et al. Increased visceral fat distribution and body composition impact cytokine release syndrome onset and severity after CD19 chimeric antigen receptor T-cell therapy in advanced B-cell malignancies. *Haematologica* 2022; **107**: 2096–107
103. Esser N, Legrand-Poels S, Piette J, Scheen AJ, Paquot N. Inflammation as a link between obesity, metabolic syndrome and type 2 diabetes. *Diabetes Res Clin Pract* 2014; **105**: 141–50
104. Tracy RP. Emerging relationships of inflammation, cardiovascular disease and chronic diseases of aging. *Int J Obes* 2003; **27**: S29–34
105. Budu-Aggrey A, Brumpton B, Tyrrell J, et al. Evidence of a causal relationship between body mass index and psoriasis: a mendelian randomization study. *PLoS Med* 2019; **16**, e1002739
106. Gremese E, Tolusso B, Gigante MR, Ferraccioli G. Obesity as a risk and severity factor in rheumatic diseases (autoimmune chronic inflammatory diseases). *Front Immunol* 2014; **5**: 576
107. Harper JW, Zisman TL. Interaction of obesity and inflammatory bowel disease. *World J Gastroenterol* 2016; **22**: 7868–81
108. Martin S, Tyrrell J, Thomas EL, et al. Disease consequences of higher adiposity uncoupled from its adverse metabolic effects using Mendelian randomisation. *eLife* 2022; **11**, e72452
109. Sideleva O, Suratt BT, Black KE, et al. Obesity and asthma. *Am J Respir Crit Care Med* 2012; **186**: 598–605
110. Lee JGH, Genga KR, Pisitsak C, et al. Survival benefit of a low ratio of visceral to subcutaneous adipose tissue depends on LDL clearance versus production in sepsis. *Crit Care* 2018; **22**: 1–9
111. Pisitsak C, Lee JGH, Boyd JH, Coxson HO, Russell JA, Walley KR. Increased ratio of visceral to subcutaneous adipose tissue in septic patients is associated with adverse outcome. *Crit Care Med* 2016; **44**: 1966–73

112. Ying P, Chen J, Ye Y, Ye J, Cai W. Adipose tissue is a predictor of 30-days mortality in patients with bloodstream infection caused by carbapenem-resistant Klebsiella pneumoniae. *BMC Infect Dis* 2022; **22**: 173
113. Ji Y, Cheng B, Xu Z, et al. Impact of sarcopenic obesity on 30-day mortality in critically ill patients with intra-abdominal sepsis. *J Crit Care* 2018; **46**: 50–4
114. Zhao-Fleming H, Almekdash MH, Cook E, et al. Obesity is not an independent predictor of necrotizing soft tissue infection outcomes. *Surg Infect (Larchmt)* 2021; **22**: 187–92
115. Kim Y-J, Seo D-W, Kang J, Huh JW, Kim KW, Kim WY. Impact of body composition status on 90-day mortality in cancer patients with septic shock: sex differences in the skeletal muscle index. *J Clin Med* 2019; **8**: 1583
116. Chalkias A, Nitsotolis T, Papalexandrou A, Mikros S, Iacovidou N, Xanthos T. Sagittal abdominal diameter may effectively predict future complications and increased mortality in intensive care unit patients with severe sepsis. *J Crit Care* 2013; **28**: 964–9
117. Kuan LL, Dennison AR, Garcea G. Association of visceral adipose tissue on the incidence and severity of acute pancreatitis: a systematic review. *Pancreatology* 2020; **20**: 1056–61
118. Sternby H, Mahle M, Linder N, et al. Mean muscle attenuation correlates with severe acute pancreatitis unlike visceral adipose tissue and subcutaneous adipose tissue. *United Eur Gastroenterol J* 2019; **7**: 1312–20
119. Jin Z, Xu L, Wang X, Yang D. Risk factors for worsening of acute pancreatitis in patients admitted with mild acute pancreatitis. *Med Sci Monit* 2017; **23**: 1026–32
120. Ji T, Li X, Zhang X, et al. Evaluation of the severity of hyperlipidemia pancreatitis using CT-measured visceral adipose tissue. *J Clin Gastroenterol* 2019; **53**: e276–83
121. Yashima Y, Isayama H, Tsujino T, et al. A large volume of visceral adipose tissue leads to severe acute pancreatitis. *J Gastroenterol* 2011; **46**: 1213–8
122. Natu A, Stevens T, Kang L, et al. Visceral adiposity predicts severity of acute pancreatitis. *Pancreas* 2017; **46**: 776–81
123. O'Leary DP, O'Neill D, McLaughlin P, et al. Effects of abdominal fat distribution parameters on severity of acute pancreatitis. *World J Surg* 2012; **36**: 1679–85
124. Xie J, Xu L, Pan Y, et al. Impact of visceral adiposity on severity of acute pancreatitis: a propensity score-matched analysis. *BMC Gastroenterol* 2019; **19**: 1–8
125. Hall TC, Stephenson JS, Jones MJ, et al. Is abdominal fat distribution measured by axial CT imaging an indicator of complications and mortality in acute pancreatitis? *J Gastrointest Surg* 2015; **19**: 2126–31
126. van Grinsven J, van Vugt JLA, Gharbharan A, et al. The association of computed tomography-assessed body composition with mortality in patients with necrotizing pancreatitis. *J Gastrointest Surg* 2017; **21**: 1000–8
127. Higaki Y, Nishida T, Matsumoto K, et al. Effect of abdominal visceral fat on mortality risk in patients with severe acute pancreatitis. *JGH Open* 2021; **5**: 1357–62
128. Trikudanathan G, Vantanasiri K, Faizi N, et al. Decreased skeletal muscle density is an independent predictor of mortality in necrotizing pancreatitis- A single tertiary center experience in 507 patients. *Pancreatology* 2021; **21**: 1146–51
129. Wang S, Wang M, Jiang L, Zhao X. Low skeletal muscle quality extracted from CT is associated with poor outcomes in severe acute pancreatitis patients. *Eur J Radiol* 2024; **170**, 111215
130. Dawra S, Gupta P, Yadav N, et al. Association between the distribution of adipose tissue and outcomes in acute pancreatitis: a comparison of methods of fat estimation. *Indian J Radiol Imaging* 2022; **33**: 12–8
131. Xia W, Yu H, Huang Y, Yang Y, Shi L. The visceral adiposity index predicts the severity of hyperlipidaemic acute pancreatitis. *Intern Emerg Med* 2022; **17**: 417–22
132. Ni Y-N, Yu H, Xu H, et al. High visceral adipose tissue to subcutaneous adipose tissue ratio as a predictor of mortality in acute respiratory distress syndrome. *Am J Med Sci* 2019; **357**: 213–22
133. Liu T, Chen J, Bai X, Zheng G, Gao W. The effect of obesity on outcomes in trauma patients: a meta-analysis. *Injury* 2013; **44**: 1145–52
134. Hoebee S, Ron E, Alattar Z, Kang P, van Sonnenberg E. Assessing the cushion effect: a systematic review and meta-analysis of the role of obesity in motor vehicle injuries and fatalities. *J Intensive Care Med* 2021; **37**: 293–303
135. Moisey LL, Mourtzakis M, Cotton BA, et al. Skeletal muscle predicts ventilator-free days, ICU-free days, and mortality in elderly ICU patients. *Crit Care* 2013; **17**: R206
136. Poros B, Irlbeck T, Probst P, et al. Impact of pathologic body composition assessed by CT-based anthropometric measurements in adult patients with multiple trauma: a retrospective analysis. *Eur J Trauma Emerg Surg* 2021; **47**: 1089–103
137. Belger E, Truhn D, Weber CD, Neumann UP, Hildebrand F, Horst K. The impact of body mass composition on outcome in multiple traumatized patients-results from the fourth thoracic and third lumbar vertebrae: a single-center retrospective observational study. *J Clin Med* 2023; **12**: 2520
138. Oh JS, Ssentongo AE, Ssentongo P, et al. Image-based assessment of sarcopenic obesity predicts mortality in major trauma. *Am J Surg* 2022; **223**: 792–7
139. Mejias C, Hoegger M, Snyder J, Raptis C, Mellnick V. Subcutaneous and visceral fat are associated with worse outcomes in gunshot injuries but not stab injuries to the torso. *Trauma Surg Acute Care Open* 2023; **8**, e001072
140. Aktokmakyan TV, Gullu HF, Yavuz E. Are trauma victims with obesity lucky in penetrating trauma injuries? *Ulus Travma Acil Cerrahi Derg* 2024; **30**: 50–9
141. Collier B, Dossett L, Shipman J, et al. Visceral adiposity is not associated with inflammatory markers in trauma patients. *J Trauma* 2010; **68**: 57–61
142. Joseph B, Zangbar B, Haider AA, et al. Hips don't lie: waist-to-hip ratio in trauma patients. *J Trauma Acute Care Surg* 2015; **79**: 1055–61
143. Hakam N, Nabavizadeh B, Sadighian MJ, et al. The impact of obesity on renal trauma outcome: an analysis of the National Trauma Data Bank from 2013 to 2016. *World J Surg* 2021; **45**: 3633–42
144. Shashaty MGS, Kalkan E, Bellamy SL, et al. Computed tomography-defined abdominal adiposity is associated with acute kidney injury in critically ill trauma patients. *Crit Care Med* 2014; **42**: 1619–28
145. Evans DC, Stawicki SP, Davido HT, Eiferman D. Obesity in trauma patients: correlations of body mass index with outcomes, injury patterns, and complications. *Am Surg* 2011; **77**: 1003–8

146. Liu HT, Rau CS, Wu SC, et al. Obese motorcycle riders have a different injury pattern and longer hospital length of stay than the normal-weight patients. *Scand J Trauma Resusc Emerg Med* 2016; **24**: 50
147. Alexopoulos N, Katritsis D, Raggi P. Visceral adipose tissue as a source of inflammation and promoter of atherosclerosis. *Atherosclerosis* 2014; **233**: 104–12
148. Bhatia M, Moochhala S. Role of inflammatory mediators in the pathophysiology of acute respiratory distress syndrome. *J Pathol* 2004; **202**: 145–56
149. van der Poll T, Shankar-Hari M, Wiersinga WJ. The immunology of sepsis. *Immunity* 2021; **54**: 2450–64
150. Marshall JC. Why have clinical trials in sepsis failed? *Trends Mol Med* 2014; **20**: 195–203

Handling editor: Phil Hopkins