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REVIEW

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CT-derived adipose tissue characteristics and TAVI all-cause mortality and complications: a systematic review

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Abstract

Transcatheter Aortic Valve Implantation (TAVI) has revolutionized severe aortic stenosis treatment, but risk stratification remains challenging. This systematic review examined the association between computed tomography (CT)-derived adipose tissue parameters and TAVI outcomes. We searched major databases for studies on visceral (VAT), subcutaneous (SAT), and intramuscular (IMAT) adipose tissue parameters and post-TAVI outcomes. Fourteen studies (9692 patients) were included. Higher SAT area/volume was consistently associated with better survival (5 studies, HR range: 0.83–2.77, $p < 0.05$). Lower SAT and VAT density also correlated with better survival (5 and 4 studies, respectively, HR range: 1.31–1.46, $p < 0.05$). VAT area showed mixed results. A VAT:SAT ratio < 1 was associated with better cardiovascular outcomes in one study. Lower IMAT index correlated with shorter hospital stays in a single study. This review reveals complex relationships between adipose tissue parameters and TAVI outcomes. Lower adipose tissue density and higher subcutaneous adiposity were most consistently associated with better outcomes. These findings suggest that detailed analysis of adipose tissue characteristics may enhance risk stratification in TAVI candidates.

Keywords TAVI outcomes, Adipose tissue parameters, CT-derived body composition, Visceral fat, Subcutaneous fat, Risk stratification

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Introduction

Severe aortic stenosis is a life-threatening condition that demands prompt and effective intervention. In recent years, Transcatheter Aortic Valve Implantation (TAVI) has revolutionized the treatment landscape, expanding therapeutic options for patients who were previously considered too high risk for traditional open-heart surgery [1]. As TAVI indications continue to broaden, encompassing younger and lower-risk patients, the need for accurate risk stratification becomes increasingly crucial [2].

Traditionally, body mass index (BMI) has been used as a simple measure of obesity in cardiovascular risk assessment. However, BMI alone fails to capture the nuances of body composition and fat distribution, which are increasingly recognized as important determinants of cardiovascular risk [3]. This limitation is particularly relevant in the context of the "obesity paradox," a phenomenon observed in various cardiovascular conditions, including TAVI, where moderate obesity appears to confer a survival advantage [4–6].

Recent advancements in imaging technology and analysis techniques have opened new avenues for more detailed body composition assessment. Computed tomography (CT) scans, routinely performed for pre-TAVI planning, offer a wealth of information beyond just aortic and vascular anatomy. These scans can be leveraged to extract detailed data on adipose tissue distribution and quality, potentially providing valuable insights into a patient's metabolic status and overall health [7].

Studies have demonstrated that CT-derived body composition parameters at the level of the lumbar vertebrae correlate well with whole-body muscle and fat composition [8]. This allows for the extraction of eight key body composition parameters: the area and density of muscle, subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), and intramuscular adipose tissue (IMAT). Each of these parameters may offer unique prognostic information in the context of TAVI.

The importance of muscle-related parameters, particularly in the context of sarcopenia, has been well-established in TAVI outcomes [9]. However, the role of adipose tissue parameters remains less clear and potentially more complex. Adipose tissue, far from being a mere energy storage depot, is now recognized as a highly active endocrine organ that significantly influences systemic metabolism and inflammation [10].

Different adipose tissue compartments (SAT, VAT, IMAT) have distinct metabolic and inflammatory profiles. For instance, VAT is generally associated with increased cardiovascular risk, while SAT may have more beneficial effects [11]. Moreover, the density of adipose tissue, as measured by CT attenuation, may reflect the size and metabolic activity of adipocytes, potentially providing additional prognostic information beyond simple volumetric measurements [12, 13].

The complex interplay between these adipose tissue parameters and TAVI outcomes remains poorly understood. While obesity is generally considered a risk factor for cardiovascular disease, some studies suggest that in the specific context of TAVI, certain patterns of adiposity might be protective [14]. This highlights the need for a more nuanced understanding of how different aspects of body composition influence outcomes in this unique patient population.

This systematic review aims to elucidate the relationships between CT-derived adipose tissue parameters (SAT, VAT, and IMAT—both area and density) and outcomes following TAVI, with a primary focus on all-cause mortality. By synthesizing the available evidence, we seek to provide insights that could enhance risk stratification and potentially inform personalized management strategies for TAVI patients. Understanding these relationships may help decode the "obesity paradox" in TAVI and pave the way for more sophisticated, body composition-based risk assessment tools in the future.

Our focus on adipose tissue parameters, rather than other metabolic markers, is deliberate and pragmatic. These measures can be extracted from routine pre-TAVI CT scans without additional testing burden, represent stable indicators of metabolic health unaffected by acute illness, and directly address the 'obesity paradox' by examining fat distribution and quality beyond BMI alone. While comparing these parameters against established risk stratification tools (e.g., EUROSCORE) would be valuable, this comparison requires studies specifically designed for head-to-head predictive accuracy assessment—an important direction for future research but beyond the scope of this systematic review.

Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [15]. The protocol for this review was registered in PROSPERO (CRD42024549420) prior to the commencement of the study.

Search strategy

We conducted a comprehensive literature search in PubMed, Ebsco, Embase, Web of Science, and Cochrane databases on June 16th, 2024. The search strategy combined terms related to adipose tissue and TAVI using the following keyword combinations:

("Adipose Tissue"[Mesh] OR "Adipose Tissue"[Title/Abstract] OR "fat tissue"[Title/Abstract] OR "fat

attenuation"[Title/Abstract] OR "adipose tissue attenuation"[Title/Abstract]) AND ("Transcatheter Aortic Valve Replacement"[Mesh] OR "TAVI"[Title/Abstract] OR "TAVR"[Title/Abstract] OR "transcatheter aortic valve implantation"[Title/Abstract] OR "transcatheter aortic valve replacement"[Title/Abstract]).

Eligibility criteria

Studies were included if they met the following criteria: adult participants (>18 years) of any gender; patients undergoing TAVI for severe aortic stenosis; reported at least one CT-derived adipose tissue parameter (VAT, SAT, or IMAT); and evaluated the association between adipose tissue parameters and post-TAVI outcomes. We excluded studies if more than 10% of patients had unsuccessful TAVI procedures, pre-procedural CT scans at the level of the third lumbar vertebra were not available, body composition was assessed using modalities other than CT (e.g., DXA or MRI), or full text was not available in English.

While we included exclusion of studies with > 10% unsuccessful TAVI procedures as a pre-specified quality criterion in our protocol, no studies were ultimately excluded based on this parameter. This criterion was established to avoid procedural confounders from centers in early learning curve phases, which could potentially obscure the relationship between adipose tissue parameters and outcomes.

Study selection

Two reviewers (MP and PB) independently screened titles and abstracts of all identified articles. Full texts of potentially eligible studies were then assessed. Disagreements were resolved through discussion with a third reviewer (OJ). The study selection flowchart is depicted in Fig. 1 [16].

Data extraction

Data extraction was performed independently by two reviewers (JAM and IR) using a standardized form. The extracted information included study characteristics (author, year, country, design), patient demographics (sample size, age, gender, BMI), CT imaging details (scanner type, slice thickness, anatomical level), adipose tissue parameters (SAT, VAT, and IMAT—area and density), outcome measures (all-cause mortality, TAVI complications), and effect sizes (hazard ratios, odds ratios) with 95% confidence intervals.

Quality assessment

The quality of included studies was assessed using the Newcastle–Ottawa Scale for cohort studies [17]. Two reviewers (MP and PB) independently evaluated each study, with disagreements resolved by consensus.

Data synthesis and analysis

Due to the heterogeneity in adipose tissue measurement techniques and outcome definitions across studies, a meta-analysis was not feasible. Instead, we conducted a narrative synthesis of the findings, grouping results by adipose tissue compartment (SAT, VAT, IMAT) and measurement type (area/volume vs. density).

For each adipose tissue parameter, we summarized the direction and strength of associations with outcomes, noting consistencies and discrepancies across studies. Where possible, we reported pooled effect sizes for studies using similar methodologies.

While we initially considered performing subgroup analyses to mitigate heterogeneity (by BMI category, sex, or study quality), this approach was ultimately not feasible due to the unavailability of individual patient data, substantial variations in measurement techniques across studies, and insufficient stratified reporting for most subgroups of interest. Instead, we focused on identifying and describing patterns across methodologically similar studies while noting instances, where sex-specific or BMI-stratified results were available.

Subgroup and sensitivity analyses

We planned subgroup analyses based on patient characteristics (age, gender, BMI category), CT measurement location (L3 vs. other levels), and study quality (high vs. low). Sensitivity analyses were conducted by excluding studies with high risk of bias or those using non-standard adipose tissue measurement techniques.

Results

Study and patient characteristics

We evaluated 14 articles, comprising a total of 9692 patients (5316 females, 54.8%). The mean age ranged from 76.8 ± 7.8 years in the youngest cohort ($n = 258$) to 86.0 ± 5 years in the two oldest cohorts ($n = 234$ and $n' = 168$). The majority of studies were single-center, retrospective observational studies. The detailed data extracted from the studies are summarized in Supplementary Table S1.

CT imaging and analysis

Adipose tissue measurements were most commonly performed at the level of the third lumbar vertebra (L3) (8 studies), followed by umbilicus level (4 studies), L4 level (1 study), and L4/L5 level (1 study). Note that Guler et al. [4] measured at L3 level but used a formula to estimate whole abdominal fat volume for their analysis.The primary adipose tissue parameters assessed were the area

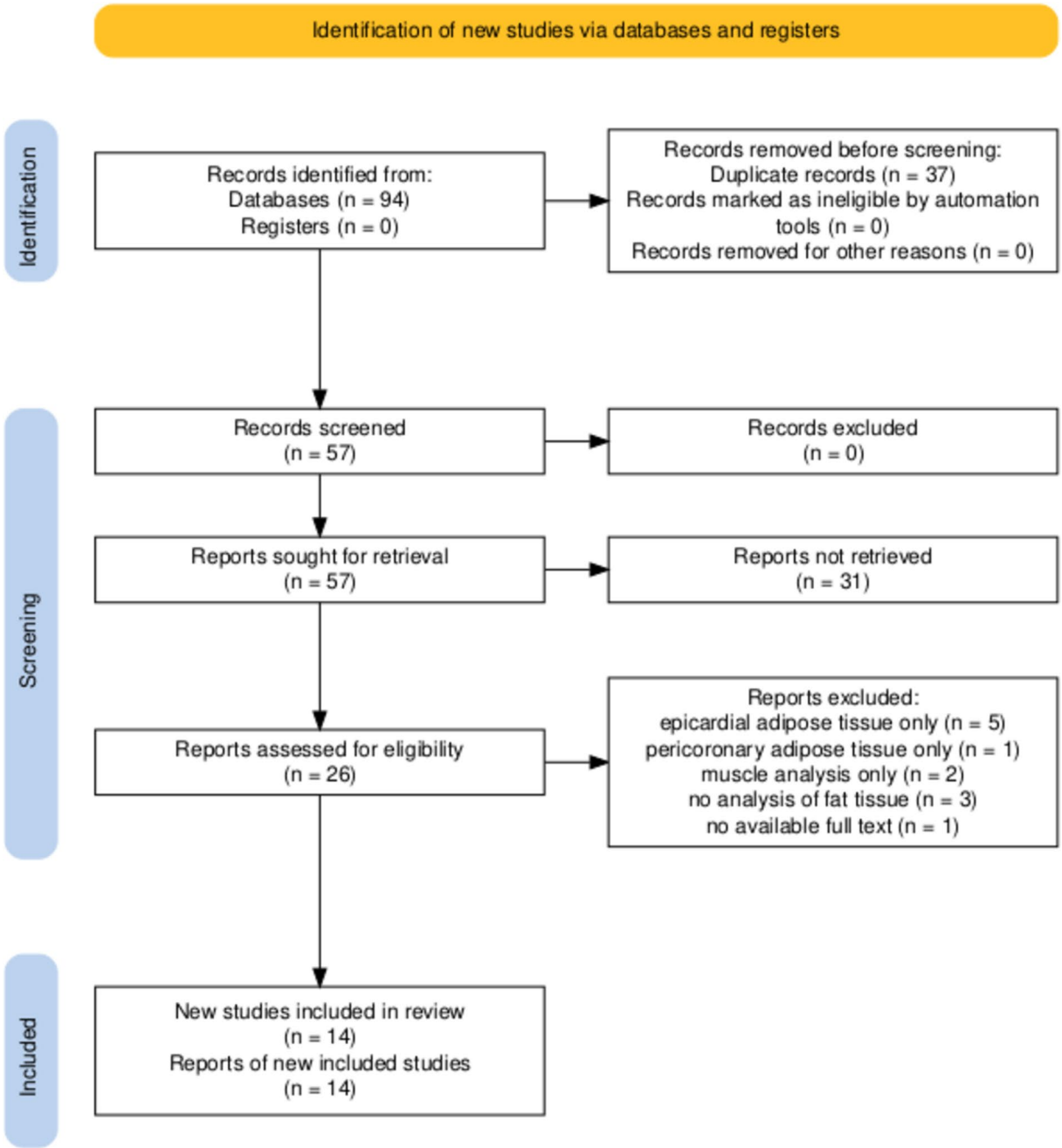

Fig. 1 PRISMA flow diagram of study selection process Diagram illustrates the identification, screening, and inclusion of studies for the systematic review. Initially, 94 records were identified from database searches, with no additional records from registers. After removing 37 duplicate records, 57 records were screened. All 57 reports were sought for retrieval, but 31 were not retrieved. Of the 26 reports assessed for eligibility, 12 were excluded for reasons including: epicardial adipose tissue only ($n=5$), pericoronal adipose tissue only ($n=1$), muscle analysis only ($n=2$), and no analysis of fat tissue ($n=3$). Finally, 14 new studies were included in the review, with 14 reports of new included studies

and density of subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), and intramuscular adipose tissue (IMAT).

Various methods were used to categorize patients into high- and low-risk groups, including median values, quartiles, and specific cutoff points determined by statistical methods, such as CART analysis or maximization of log-rank scores. Table 1 depicts the standardized CT measurement methodology across studies.

Table 1 Standardized CT measurement methodology across studies

Study	Sample size	CT level	Software used	Adipose parameters measured	HU threshold definitions	Follow-up period
Shibata et al	1372	Umbilicus	SliceOmatic v5.0	SAT/VAT area, density	SAT: − 90.7 HU (M), − 94.3 HU (F); VAT: − 71.2 HU (M), − 75.7 HU (F)	768 days
McInerney et al	3174	L3	NR	VAT:SAT ratio	VAT:SAT ratio ≥ 1	14.1 months
Pekar et al	866	L3	AutoMATiCA (NN)	SMI, VAT/SAT density	VAT: > − 93.27 HU (M), > − 95.02 HU (F); SAT: > − 94.03 HU (M), > − 96.87 HU (F)	5.89 years
Demirel et al	500	L3	SliceOmatic v5.0	TMA, VAT	Youden index	5 years
Heidari et al	415	L3	MATLAB-based	MFI, SMI	NR	Length of stay
Okuno et al	100	Umbilicus	320-row CT	TFA, VFA, SFA	SFA: 92.6 cm^2	665 days
Foldyna et al	403	L4	64 + slice CT	PM, SAT, VAT area/density	Lowest quartile for areas; Highest quartile for density	458 days
Somaschini et al	168	L3	Slice-O-Matic v5.0	VAT index	VATi: 57.5 cm^2/m^2	1 year
Guler et al	258	L3	128-detector CT	TFV, SFV, VFV	TFV: ≤ 9.1 L	12 months
Mancio et al	170	L4/L5	NR	NR	NR	1.2 years
Mok et al	460	L3	CT thresholds	SMMI	Sarcopenia: SMMI < 55.4 cm^2/m^2 (M), < 38.9 cm^2/m^2 (F)	12 months
Higuchi et al	234	Umbilicus	SOMATOM Force	SFA, VFA, MPM volume	Not specified	547 days
Van Erck et al	1404	L3	Deep-learning	SAT/VAT density	Highest tertile vs. middle/lowest tertiles	1,093 days

SAT Subcutaneous adipose tissue, *VAT* Visceral adipose tissue, *TMA* Total muscle area, *MFI* Muscle Fat Index, *SMI* Skeletal Muscle Index, *TFA* Total fat area, *VFA* Visceral fat area, *SFA* Subcutaneous fat area, *TFV* Total fat volume, *SFV* Subcutaneous fat volume, *VFV* Visceral fat volume, *SMMI* Skeletal Muscle Mass Index, *MPM* Major Psoas Muscle, *HU* Hounsfield units, *M* Male, *F* Female, *NR* Not reported, *L3/L4/L5* Lumbar vertebrae 3/4/5, *NN* Neural network

Adipose tissue parameters and survival after TAVI

We identified 41 reported relationships between adipose tissue parameters and outcomes across the 14 studies. Of these, 31 showed statistically significant associations with survival or adverse events. The most important findings for each adipose tissue parameter are summarized below and in Table 1 and Fig. 2.

Subcutaneous adipose tissue (SAT)

SAT area/volume

Among all studies examining SAT area/volume, McInerney et al. [21] was the only one that found no significant association with post-TAVI outcomes, while the other five studies consistently demonstrated better survival with higher SAT area/volume. The studies can be divided into two groups based on how they reported their results. The first group reported HR < 1 for SAT area/volume (indicating lower risk with higher SAT), including Shibata et al. [12] with HR 0.76 (95% CI 0.61–0.95), Higuchi et al. [14] with HR 0.87 (95% CI 0.77–0.98), and Guler et al. [4] with HR 0.83 (95% CI not provided, p = 0.045). The second group reported HR > 1 for low vs. high SAT area (also indicating lower risk with higher SAT), including Okuno et al. [18] with HR 2.77 (95% CI 1.27–6.02) and Foldyna et al. [19] with HR 1.99 (95% CI 1.19–3.33). It is important to note that this apparent discrepancy in HR values (some < 1, others > 1) is due to how the comparison groups were defined in each study (high vs. low or low vs. high). Despite this difference in reporting, all studies consistently show that higher SAT area/volume is associated with better survival outcomes after TAVI (Table 2).

SAT density

Lower SAT density was consistently associated with better survival in 4 studies (HR range: 1.01–1.46, p < 0.05). Shibata et al. [12] reported that higher SAT density was associated with increased mortality risk (HR: 1.41, 95% CI 1.06–1.88), while Foldyna et al. [19] demonstrated that higher SAT density was associated with increased mortality risk (HR: 1.35, 95% CI 1.10–1.67). Pekar et al. [13] found that higher SAT density was associated with slightly increased mortality risk (HR: 1.01, 95% CI 1.00–1.02), and Van Erck et al. [20] showed that higher SAT density was associated with increased mortality risk (HR: 1.46, 95% CI 1.23–1.73). It is important to note that all four studies consistently show that higher SAT density is associated with worse survival outcomes after TAVI. The hazard ratios are all greater than 1, indicating an increased risk of mortality with higher SAT density. The study by Van Erck et al. [20] reported the strongest association between SAT density and mortality, while Pekar

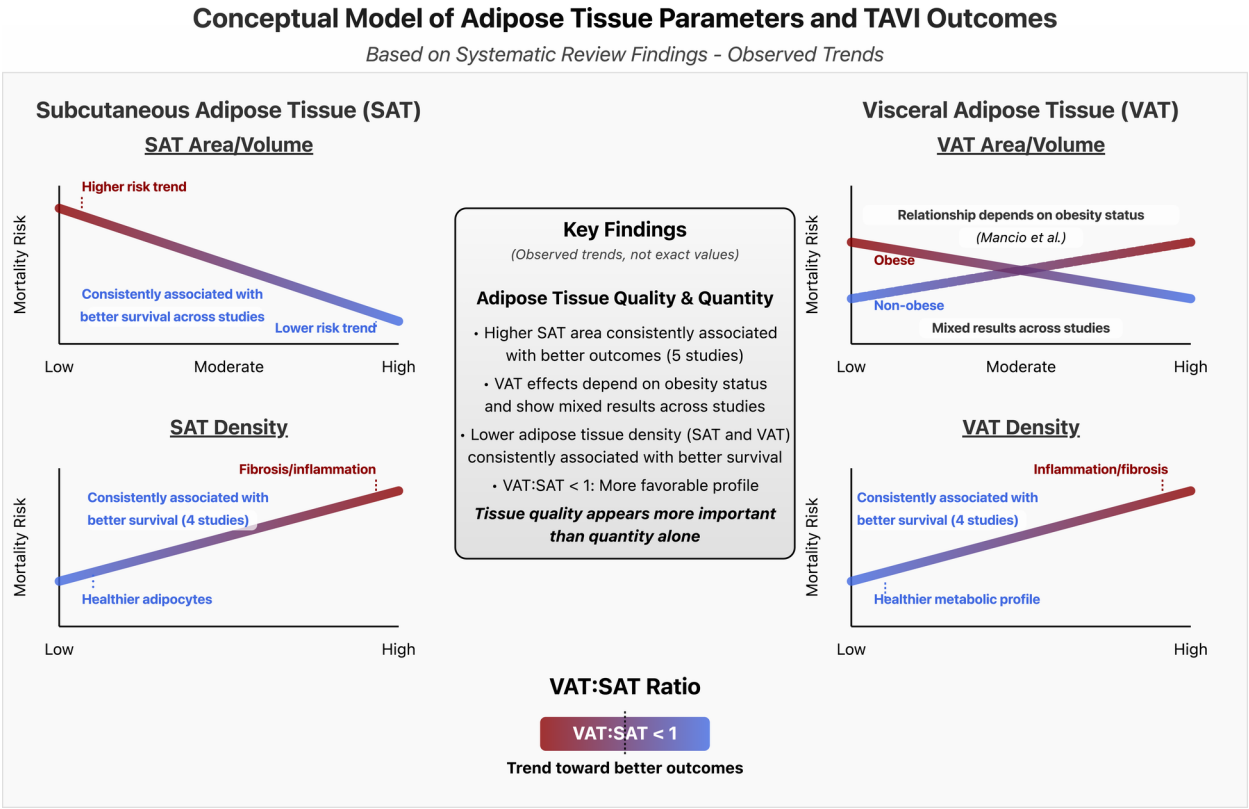

Fig. 2 Conceptual model of adipose tissue parameters and TAVI outcomes Observed trends in relationships between different adipose tissue parameters and mortality risk following Transcatheter Aortic Valve Implantation (TAVI), synthesized from our systematic review findings. *Important note: The curves represent conceptual relationships and observed trends across studies, not exact quantitative values*. The left panels show subcutaneous adipose tissue (SAT) parameters, while right panels show visceral adipose tissue (VAT) parameters. For SAT area/volume, higher values were consistently associated with better survival across multiple studies. VAT area/volume showed obesity-dependent effects, with different relationships in obese vs. non-obese patients (Mancio et al.). Both SAT and VAT density demonstrated consistent associations between lower density values and better survival outcomes, potentially reflecting healthier adipocyte morphology and metabolic profiles. *VAT*:SAT ratio < 1 was associated with more favorable outcomes in the limited studies examining this parameter. These relationships highlight the complex interplay between adipose tissue distribution, quality, and TAVI outcomes

et al. [13] found a more modest, but still statistically significant, association.

Visceral adipose tissue (VAT)

VAT area/volume

Six studies found significant associations between VAT area/volume and survival after TAVI, with mixed results. The studies can be divided into two groups based on how they reported their results. The first group reported better survival with lower VAT area/volume, including Shibata et al. [12] with HR 0.76 (95% CI 0.60–0.95) for high vs. low VAT, Okuno et al. [18] with OR 2.09 (95% CI 1.05–4.15) for lower VAT index and fewer cerebrovascular events, Foldyna et al. [19] with HR 1.73 (95% CI 1.12–2.67) for high vs. low VAT area, and Somaschini et al. [22] with OR 4.2 for low vs. high VAT index (95% CI not provided, p = 0.046). The second group reported better survival with higher VAT area/volume, with Mancio et al. [23] finding that in non-obese patients, HR 2.30 (95% CI 1.12–4.91) for low vs. high VAT. Higuchi et al. [14] reported no significant association. It is important to note that the apparent discrepancy in results is due to how the comparison groups were defined in each study (high vs. low or low vs. high) and the specific patient populations studied. Mancio et al. [23] found that the relationship between VAT and survival depended on obesity status: in non-obese patients, higher VAT was associated with better survival, while in obese patients, lower VAT was beneficial (HR: 2.5, 95% CI 1.10–5.84).

VAT density

Lower VAT density was consistently associated with better survival in 4 studies. Shibata et al. [12] reported that higher VAT density was associated with increased mortality risk (HR: 1.34, 95% CI 1.03–1.76), while Pekar et al. [13] found that higher VAT density was associated with

Table 2 Adipose tissue parameters and effect on survival after TAVI—a systematic review

Parameter	Measure Type	Study	CT Level	Comparison	Statistic	Forest Plot	Value (95% CI)	Effect on Survival
SAT	Area	[12]	Umbilicus	High vs Low	HR		0.76 (0.61-0.95)	Better survival - high SAT area
	Area	[21]	L3	N/A	NS		N/A	No significant effect
	Area	[18]	Umbilicus	Low vs High	HR		2.77 (1.27-6.02)	Better survival - high SAT area
	Area	[19]	L4	Lowest quartile vs Rest	HR		1.99 (1.19-3.33)	Better survival - high SAT area
	Area	[14]	Umbilicus	High vs Low	HR		0.87 (0.77-0.98)	Better survival - high SAT area
SAT	Volume	[4]	Abdominal vol.	High vs Low	HR		0.83 (0.83-0.83)	Better survival - high SAT volume
SAT	Density	[12]	Umbilicus	Low vs High	HR		1.41 (1.06-1.88)	Better survival - low SAT density
	Density	[13]	L3	Low vs High	HR		1.01 (1.00-1.02)	Better survival - low SAT density
	Density	[19]	L4	Low vs High	HR		1.35 (1.10-1.67)	Better survival - low SAT density
	Density	[20]	L3	Low vs High	HR		1.46 (1.23-1.73)	Better survival - low SAT density
VAT	Area	[12]	Umbilicus	High vs Low	HR		0.76 (0.60-0.95)	Better survival - high VAT area
	Area	[21]	L3	Per 40 cm2/m2	OR		2.09 (1.05-4.15)	Less frequent cerebrovascular events - low VAT index
	Area	[19]	L4	High vs Low	HR		1.73 (1.12-2.67)	Better survival - high VAT area
	Area	[23]	L4/L5	Low vs High (non-obese)	HR		2.30 (1.10-4.90)	Better survival - high VAT (non-obese)
	Area	[23]	L4/L5	Low vs High (obese)	HR		2.50 (1.10-5.80)	Better survival - low VAT (obese)
	Area	[14]	Umbilicus	N/A	NS		N/A	No significant effect
	Area	[22]	L3	Low vs High	OR		4.2	Better survival - low VAT index
VAT	Density	[12]	Umbilicus	Low vs High	HR		1.34 (1.03-1.76)	Better survival - low VAT density
	Density	[13]	L3	Low vs High	HR		1.01 (1.00-1.03)	Better survival - low VAT density
	Density	[20]	L3	Low vs High	HR		1.31 (1.09-1.58)	Better survival - low VAT density
	Density	[19]	L4	Low vs High	HR		1.57 (1.22-2.04)	Better survival - low VAT density (in men only)
VAT	Index	[21]	L3	Low vs High	HR		1.40 (1.05-1.86)	Better survival - low VAT index
	Index	[24]	L3	Low vs High	N/A		N/A	Better survival - low VAT index
TAT	Volume	[4]	Abdominal vol.	High vs Low	HR		0.82 (0.82-0.82)	Better survival - high TAT volume
	Volume	[5]	L3	Obese vs Non-obese	NS		N/A	No significant effect
IMAT	Area	[21]	L3	N/A	NS		N/A	No significant effect
IMAT	Index	[25]	L3	Low vs High	Beta		0.06	Shorter hospitalization - low IMAT index
VAT:SAT	Ratio	[21]	L3	< 1 vs > 1	HR		3.06 (1.20-7.77)	Better survival - VAT:SAT < 1

SAT Subcutaneous Adipose Tissue, *VAT* Visceral Adipose Tissue, *TAT* Total Adipose Tissue, *IMAT* Intramuscular Adipose Tissue, *HR* Hazard Ratio, *OR* Odds Ratio, *NS* Not Significant, *CI* Confidence Interval, *L3/L4/L5* Lumbar Vertebrae 3/4/5, *N/A* Not Available, *Abd. Vol.* abdominal volume

slightly increased mortality risk (HR: 1.01, 95% CI 1.00–1.03). Van Erck et al. [20] showed that higher VAT density was associated with increased mortality risk (HR: 1.31, 95% CI 1.09–1.58), and Foldyna et al. [19] demonstrated that higher VAT density was associated with increased mortality risk (HR: 1.57, 95% CI 1.22–2.04) in men, but not in women. It is important to note that all four studies consistently show that higher VAT density is associated with worse survival outcomes after TAVI. The hazard ratios are all greater than 1, indicating an increased risk of mortality with higher VAT density.

VAT index

Two studies found significant associations between VAT index and survival after TAVI. Okuno et al. [18] reported HR 1.40 (95% CI 1.05–1.86) for low vs. high VAT index, and Somaschini et al. [24] found significantly lower 1-year mortality (5.5% vs. 19.5%, $p=0.046$) for low vs. high VAT index. Both studies consistently show that a lower VAT index is associated with better survival outcomes after TAVI. It is important to note that while Okuno et al. provided a hazard ratio, Somaschini et al. reported their results as mortality percentages. Despite the difference in reporting methods, both studies indicate a survival benefit for patients with lower VAT index. Somaschini et al. [24] also found that after propensity score matching, low VAT index remained significantly associated with lower 1-year mortality (5.4% vs. 27%, $p=0.010$). This suggests that the association between low VAT index and better survival persists even after adjusting for potential confounding factors.

VAT ratio

One study found a significant association between VAT ratio and survival after TAVI. Okuno et al. [18] reported better survival with VAT ratio < 1, with HR 3.06 (95% CI 1.20–7.77) for VAT ratio < 1 vs. > 1. This study showed that a VAT ratio < 1 was associated with better outcomes, including lower cardiovascular mortality (HR: 4.11, $p<0.05$), fewer readmissions (HR: 1.81, $p<0.05$), and better overall survival (HR range: 2.78–3.06, $p<0.05$). It is important to note that this is the only study in our review that examined the VAT ratio in relation to TAVI outcomes. The results consistently indicate that a lower VAT ratio (< 1) is associated with better survival and fewer adverse events after TAVI.

Intramuscular adipose tissue (IMAT)

IMAT area and index

One study examined the association between IMAT area and outcomes after TAVI: Okuno et al. [18] found no significant association between IMAT area and outcomes. One study reported on the association between IMAT index and outcomes after TAVI: Heidari et al. [25] found that a lower IMAT index was associated with shorter hospital stays ($\beta=0.06$, $p=0.022$). It is important to

note that the evidence for IMAT's impact on TAVI outcomes is limited, with only two studies reporting on this parameter, and each examining a different aspect (area vs. index). The study on IMAT area [21] did not find any significant effect on outcomes, while the study on IMAT index [25] found a modest but statistically significant association with hospital stay duration.

Total adipose tissue (TAT)

Two studies examined the association between TAT volume and survival after TAVI, with mixed results. Guler et al. [4] reported better survival with higher TAT volume, with HR 0.82 (95% CI 0.71–0.95) for high vs. low TAT volume. However, Mok et al. [5] found no significant association between TAT volume and outcomes. Guler et al. [4] found that higher TAT volume was significantly associated with better survival outcomes after TAVI. This study used abdominal CT scans to measure TAT volume, providing a comprehensive assessment of total body fat. However, Mok et al. [5] did not find a significant association between TAT (referred to as fat mass in their study) and clinical outcomes. This study used CT scans at the L3 level to estimate total body fat mass. It is important to note that these studies used different methodologies to measure TAT (abdominal volume vs. L3 cross-sectional area), which may contribute to the differing results. In addition, Mok et al. [5] focused on comparing obese vs. non-obese patients, which may have impacted their findings.

Adipose tissue parameters and complications after TAVI

While the primary focus of most studies has been on mortality outcomes following TAVI, some researchers have also investigated the relationship between adipose tissue measurements and specific TAVI-related complications. These complications can significantly impact patient recovery and overall outcomes. Understanding how different adipose tissue compartments might influence the occurrence of complications could potentially help in risk stratification and patient management. However, it is important to note that the available data on this topic is limited, and findings are not always consistent across studies.

No specific associations between SAT and TAVI complications were reported in the studies we reviewed. For VAT, Okuno et al. [18] reported that lower VAT index was associated with fewer cerebrovascular events (OR: 2.09, 95% CI 1.05–4.15). Regarding IMAT, Heidari et al. [25] found that a lower IMAT index was associated with shorter hospital stays ($\beta = 0.06$, $p = 0.022$). Guler et al. [4] reported on some periprocedural complications but did not find significant differences between survivor and non-survivor groups for cerebrovascular events, need for permanent pacemaker, or major vascular complications. It is important to note that most studies focused on mortality outcomes rather than specific TAVI complications. The available data on the association between adipose tissue measurements and TAVI complications is limited, and more research is needed to establish clear relationships.

Discussion

This systematic review reveals complex relationships between adipose tissue parameters and outcomes following TAVI. The findings underscore the importance of considering both the quantity and quality of adipose tissue in different compartments when assessing risk in TAVI patients. However, a reliable explanation of these findings is complex and not at all clear. Methodological factors contributing to inconsistent findings across studies are described in Table 3. Now let us elaborate on the basics of fat metabolism.

Adipose tissue, both its quantity and quality, is closely tied to the metabolic state of a person. While subcutaneous adipose tissue is usually deemed as metabolically safe, when these fat stores are exceeded, the problem arises. When subcutaneous fat tissue adipocytes store ever more triglyceride molecules, they reach a genetically determined limit („personal fat threshold " [26]), after which point the cells become ischaemic. This process leads to adipocyte necrosis, leading to immune system activation and widespread inflammation [27]—a known cause of various medical complications, including cardiovascular disease, cancer, neurodegeneration etc.. Furthermore, when the personal fat threshold is reached, the subcutaneous adipocytes become more and more insulin resistant—resisting more fat to flow in. Insulin resistance by itself is one of the biggest risk factors for the development of the aforementioned diseases [28]. Since more fat cannot be stored into the subcutaneous compartment, the excess triglycerides find their way elsewhere, mainly in the visceral fat tissue. Visceral fat by itself is metabolically problematic. Cell necrosis and inflammation leads to fibrosis in both subcutaneous and visceral fat spaces [29].

It is also important to note, that patients with severe aortic stenosis usually have very similar comorbidities as patients with ischemic heart disease [30]. As in atherosclerosis and subsequently ischemic heart disease, endothelial inflammation seems to be paramount for the valve leaflets degeneration [31]. As metabolic syndrome, formerly known as „syndrome of insulin resistance ", is a causal factor of subclinical inflammation, it is of no surprise, that it is very prevalent in patients with aortic stenosis [32].

Table 3 Methodological factors contributing to inconsistent findings across studies

Methodological Factor	Studies Affected	Impact on Results	Recommendations for Standardization
CT measurement location	Umbilicus (Shibata, Higuchi, Okuno) vs. L3 (McInerney, Pekar) vs. L4 (Foldyna) vs. L4/L5 (Mancio)	Different anatomical levels yield different fat volumes and compositions	Standardize to L3 level (best correlation with total body composition)
Effect reporting direction	HR < 1 (Shibata, Higuchi, Guler) vs. HR > 1 (Okuno, Foldyna) for same parameter	Reverse comparison groups create apparent contradictions	Report all results as high vs. low for consistency
Patient population differences	Japanese cohorts (Shibata, Higuchi) vs. European/American (McInerney, Foldyna)	Ethnic differences in body composition affect outcomes	Stratify analyses by ethnicity or region
Statistical approaches	Different cutoff determination methods (median, quartiles, CART analysis)	Arbitrary thresholds yield different risk groups	Use standardized statistical approaches for threshold determination
Follow-up duration	Short-term (Okuno: 665 days) vs. long-term (Pekar: 5.89 years)	Short follow-up may miss late outcomes, leading to divergent conclusions	Report both short and long-term outcomes
Obesity-specific effects	Mancio found opposite effects in obese vs. non-obese patients	Non-linear, U-shaped relationships obscured by whole-population analysis	Analyze by BMI categories to detect non-linear relationships
CT scan quality and parameters	Slice thickness variations (1.0–10 mm)	Thicker slices may reduce measurement precision	Standardize scan parameters and quality control
Software and HU thresholds	Various software packages with different HU ranges for tissue classification	Different tissue classification leads to measurement inconsistencies	Adopt standardized HU ranges for tissue classification
Sex-specific differences	Foldyna found VAT density significant in men but not women	Sex-based differences in fat metabolism and distribution	Always perform sex-stratified analyses
Adjustment for confounders	Varying degrees of multivariate adjustment	Unadjusted or insufficiently adjusted analyses may show spurious associations	Define minimum set of covariates for adjustment

CT Computed Tomography, *BMI* Body Mass Index, *VAT* Visceral Adipose Tissue, *SAT* Subcutaneous Adipose Tissue, *L3/L4/L5* Lumbar Vertebrae 3/4/5, *HU* Hounsfield Units, *CART* Classification and Regression Tree

It is clear from our results, that larger area of subcutaneous fat is correlated with better survival. This conclusion deserves dissecting. First, most of the studies compared the lowest subcutaneous area quartile with the rest of the cohort. Second, in the study by McInerney et al. [21], the morbidly obese had a much worse prognosis than the non-obese patients. Thus, it cannot be stated that the larger the SAT area, the better the prognosis. It would be more accurate to conclude, that patients on both extremes (both lowest and highest SAT area) have worse prognosis, compared to the rest. While answering why morbidly obese patients have higher mortality is self-evident, it is not so clear why those with normal BMI, falling into the lowest quartile of SAT area, should fare worse as well. The explanation for this phenomenon (and even possibly for the „obesity paradox " itself) may lie in the metabolic characteristics of aortic stenosis patients. As we stated above, metabolic syndrome is prevalent in this cohort. Thus, we would expect a „normal " patient with aortic stenosis to be overweight, or obese. It is then possible, that patients from the lowest quartile of SAT area are not overweight, because they are already experiencing advanced heart failure induced cachexia, leading to worse outcomes. This applies to the parameter of total adipose tissue as well in our opinion. Potential mechanisms explaining the obesity paradox in TAVI based on adipose tissue parameters are explained in Table 4.

The presence of high amounts of visceral fat is classicaly regarded as „unhealthy ". It is not the primary storage space for fat in humans, and therefore, the area of VAT points to the degree of metabolic derangement [33]. It is also well-documented that VAT is producing certain cytokines and other compounds, further worsening the situation [34]. These are the reasons why, according to our metanalysis, VAT area is correlated negatively with outcome. It must be pointed, however, that a few studies showed that, similar to SAT area, patients in the lowest quartile of VAT area had worse prognosis than the rest of the cohort. The possible explanation for this may be the same as for SAT—a certain amount of visceral fat is expected in this metabolically unhealthy group of people and thus a low VAT area may be the sign of cardiac cachexia.

While the results for SAT and VAT amounts are more nuanced, the positive correlation of higher density of both SAT and VAT with mortality seems to be

Table 4 Potential mechanisms explaining the obesity paradox in TAVI based on adipose tissue parameters

Adipose parameter	Observed effect	Proposed physiological mechanism	Clinical and research implications
Higher SAT Area/Volume	Better survival (HR 0.76–0.87)	• Energy reserves during physiological stress • Reduced cardiac cachexia • Metabolically "safer" fat storage location • Potential endocrine benefits from subcutaneous adipokines	• Lowest quartile patients may benefit from nutritional intervention • Consideration of pre-TAVI nutritional optimization • SAT area may be useful addition to risk scores
Lower SAT/VAT Density	Better survival (HR 1.01–1.46)	• Lower density indicates less fibrosis and inflammation • Healthier adipocyte function with larger cell size • Reduced immune activation in adipose tissue • Less ectopic fat deposition in other tissues	• Higher density adipose tissue may indicate metabolic syndrome • Adipose tissue density could be a novel biomarker • Potential target for anti-inflammatory interventions
VAT:SAT Ratio < 1	Better cardiovascular outcomes (HR 3.06)	• Metabolically healthier fat distribution with predominant subcutaneous fat • Lower inflammatory cytokine production • Reduced ectopic fat in heart and vessels	• Simple ratio could serve as an easily calculated prognostic marker • Potential for body composition-guided personalized management
VAT Area	U-shaped relationship	• Too low: possible cachexia, insufficient energy reserves • Too high: metabolic dysfunction, inflammation • Optimal intermediate range may be protective	• Optimal VAT range may depend on BMI category • Non-linear relationships require careful statistical modeling • Different significance in obese vs. non-obese (Mancio)
Extreme BMI values	Worse outcomes	• Both cachexia and morbid obesity represent metabolic derangement • Central adiposity distribution may be more important than BMI alone • Personal fat threshold concept (genetically determined capacity)	• Suggests focus on body composition rather than BMI alone • Potential for identifying "metabolically healthy obese" TAVI candidates • Importance of considering frailty alongside adiposity
IMAT Index	Higher index related to longer hospital stay	• Intramuscular fat infiltration indicates poor muscle quality • Marker of sarcopenia and frailty • May impair post-procedural mobilization and recovery	• Could be used to identify patients needing enhanced rehabilitation • Combined assessment with muscle metrics may improve risk prediction

SAT Subcutaneous adipose tissue, *VAT* Visceral adipose tissue, *IMAT* Intramuscular adipose tissue, *BMI* Body mass index, *HR* Hazard ratio, *TAVI* Transcatheter aortic valve implantation

straightforward. As stated above, when subcutaneous adipocytes are fully saturated (the „personal fat threshold " is reached) and thus cannot store more fat, they start to become insulin resistant and ischemic, which leads to cellular necrosis. Inflammation sets in, followed by fibrosis—this causes the tissue to become more dense on a CT scan. Similar rationale applies for VAT. The whole issue can be summarized as follows—more dense fat on a CT scan is a hallmark of a more pronounced metabolic syndrome (insulin resistance), resulting in worse outcomes.

Only one study looked at intramuscular adipose tissue. It was expected that the less fat there is in the muscle, the better the outcomes would be. Again, it is of our opinion, that metabolic syndrome is the key to understand this phenomenon. Intramuscular storage of fat is known to be pronounced in the state of insulin resistance and, therefore, the amount of fat is again an indicator of metabolic syndrome severity [35]. The only instance in which the amount of intramuscular fat is increased physiologically is in athletes [36]—this is certainly not relevant for the TAVI cohort.

While the majority of studies used L3 as the reference level for adipose tissue assessment (8 studies), there was methodological heterogeneity in measurement locations across included studies, with some using L4/L5 level (1 study), umbilicus level (4 studies), or whole abdominal volume (1 study). We performed a qualitative assessment of results by measurement location, which revealed generally consistent patterns for adipose tissue density measures across different anatomical landmarks, with lower SAT and VAT densities and higher SAT area consistently associated with better outcomes regardless of measurement site. However, for area/volume measurements, findings varied more substantially, particularly

for VAT area. Studies using L3 measurements tended to show more consistent associations than those using other levels, likely reflecting the established status of L3 as the reference standard in body composition analysis. This anatomical heterogeneity represents an important limitation that may contribute to discrepancies in findings, as adipose tissue distribution can vary significantly between vertebral levels (Table 5).

Our findings regarding adipose tissue parameters and TAVI outcomes help explain the complex "obesity paradox" observed in cardiovascular procedures. Rather than a linear relationship, our review suggests a U-shaped association, where both extremes—lowest and highest adiposity quartiles—correlate with worse outcomes. Patients with extremely low SAT may be experiencing cardiac cachexia from advanced heart failure, explaining their poor prognosis despite "normal" BMI values. Conversely, morbidly obese patients face different complications. The protective effect of moderate adiposity likely depends on the underlying metabolic health status, with metabolically healthy obesity potentially offering protection through greater metabolic reserves and anti-inflammatory adipokines, but only up to a certain threshold. Beyond this threshold, metabolic syndrome, characterized by insulin resistance and increased inflammation, may negate these protective effects, particularly when visceral adiposity predominates over subcutaneous fat.

Table 5 Impact of CT measurement location on adipose tissue assessment

Anatomical Location	Studies Using This Level	Advantages	Limitations	Impact on Results	Recommendations
L3 Vertebra	Pekar et al. (*n* = 866) McInerney et al. (*n* = 3174) Somaschini et al. (*n* = 168) Guler et al. (*n* = 258) Mok et al. (*n* = 460) Van Erck et al. (*n* = 1404)	• Strong correlation with whole-body composition • Most validated in research • Consistent landmarks • Less affected by bowel content	• Requires specific reconstruction of pre-TAVI CT • May not be included in all acquisition protocols	• Most accurate reflection of total body adiposity • Better reproducibility across studies	• Recommended as standard location for adipose tissue assessment • Should be included in all TAVI planning protocols
L4 Vertebra	Foldyna et al. (*n* = 403)	• Slightly higher VAT content than L3 • Clear anatomical landmarks	• Less validated than L3 • May overestimate VAT relative to total body	• May show stronger VAT associations • Less comparable to L3-based studies	• Can be used if L3 unavailable • Results should note measurement level
L4/L5 Junction	Mancio et al. (*n* = 170)	• Historically used in early obesity research • Maximum VAT area in many patients	• Variable relationship to total body composition • Less reproducible positioning • Affected by pelvic anatomy	• Typically shows highest VAT:SAT ratio • May overemphasize VAT significance	• Not recommended for standardization • Less reliable for comparison across studies
Umbilical Level	Shibata et al. (*n* = 1372) Higuchi et al. (*n* = 234) Okuno et al. (*n* = 100)	• Easily identifiable external landmark • Can be used with limited scan ranges	• Variable relationship to vertebral levels • Affected by abdominal wall laxity • Less consistent in obese patients	• More variable measurements • Greater potential for misclassification • May show different associations with outcomes	• Not recommended as primary measurement location • Should specify vertebral level when using umbilical slices
Whole Abdominal Volume	Limited use	• Most comprehensive assessment • Not affected by single-slice variability	• Time-consuming analysis • Requires specialized software • No standardized protocols	• May be more sensitive but less specific • Difficult to compare across studies	• Valuable for research but impractical for routine use • Beneficial as validation for single-slice metrics

CT Computed tomography, *TAVI* Transcatheter aortic valve implantation, *SAT* Subcutaneous adipose tissue, *VAT* Visceral adipose tissue, *L3/L4/L5* Lumbar vertebrae 3/4/5, *HU* Hounsfield units

Technical considerations:

Slice thickness Studies used varying slice thicknesses (1.0–10 mm), with thinner slices providing more precise measurements but requiring more sophisticated image processing.

HU thresholds Different studies applied varying Hounsfield Unit ranges to define adipose tissue (− 190 to − 30 HU for SAT; − 150 to − 50 HU for VAT), affecting tissue classification and measurement.

Software variations Analysis software varied from manual segmentation to deep learning approaches, introducing methodological heterogeneity.

Clinical implications

These indings have several potential implications for clinical practice. Adipose tissue parameters derived from routine pre-TAVI CT scans could enhance risk stratification beyond traditional measures like BMI. In addition, understanding the protective role of certain adipose tissue characteristics could inform patient selection for TAVI procedures. Awareness of the potential protective effects of adiposity might influence peri-procedural nutritional management strategies. Furthermore, the insights into adipose tissue quality and distribution could inform long-term management approaches for TAVI patients, potentially improving outcomes through more personalized care.

Limitations and future directions

This review has several limitations. The included studies were largely observational, precluding causal inferences. The heterogeneity in measurement techniques and outcome definitions limits direct comparisons between studies caused the inability to perform subgroup analyses by factors, such as BMI category or sex. This restricted our capacity to fully explore potential effect modifiers and sources of heterogeneity in the relationship between adipose tissue parameters and TAVI outcomes. Future research should focus on standardizing adipose tissue measurements in TAVI patients and investigating the underlying mechanisms of the observed associations.

Prospective studies are needed to validate the prognostic value of these adipose tissue parameters and to explore whether interventions targeting adipose tissue quantity or quality could improve outcomes in TAVI patients.

The heterogeneity in measurement locations across studies (L3, L4/L5, umbilicus) represents an important methodological limitation. Adipose tissue distribution varies between anatomical levels, with L3 measurements showing strongest correlation with whole-body composition in validation studies. Future research should standardize measurement protocols at the L3 level to enhance comparability across studies and facilitate meta-analysis. When we examined patterns by measurement location, adipose tissue density findings were relatively consistent across anatomical sites, while area/volume measurements showed greater variation, suggesting density may be a more robust predictor regardless of measurement location.

Despite the potential prognostic value of adipose tissue parameters identified in this review, a significant limitation is the gap between these research findings and current clinical practice. While our analysis suggests that parameters such as SAT ratio and adipose tissue density might provide valuable prognostic information, clinicians predominantly rely on simpler metrics like BMI for risk stratification and patient selection in TAVI. The implementation of more sophisticated adipose tissue measurements in routine clinical workflows faces several challenges, including the need for specialized software, standardized protocols, and additional radiological expertise. Furthermore, the added value of these parameters over traditional risk factors needs to be established through dedicated validation studies with consistent methodologies before they can be incorporated into clinical decision-making algorithms. Although the technology to extract these parameters from routine pre-TAVI CT scans exists, the translation of these findings into practical clinical tools that influence patient selection and management remains a significant hurdle to be addressed in future research.

In conclusion, this systematic review highlights the complex relationships between adipose tissue parameters and outcomes following TAVI. The findings challenge simplistic notions of obesity as uniformly harmful and underscore the need for a nuanced understanding of body composition in this high-risk population. Incorporating detailed adipose tissue analysis into pre-TAVI assessment may enhance risk stratification and inform personalized patient management strategies.

Author contributions
M.P. and P.B. contributed equally to this work. M.P. and P.B. independently screened titles and abstracts of all identified articles. O.J. served as the third reviewer to resolve disagreements. J.A.M. and I.R. performed data extraction independently using a standardized form. M.P. and P.B. independently evaluated the quality of included studies, with disagreements resolved by consensus. O.J. and J.N. supervised the project and provided critical revisions. R.S., B.J.G., A.C.K., M.K., J.H., R.N., L.S., and J.N. contributed to the interpretation of results and manuscript revision. All authors reviewed and approved the final version of the manuscript.

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