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ORIGINAL RESEARCH

Association of the Appendicular Skeletal Muscle Mass-to-Visceral Fat Area Ratio with Cause-Specific Mortality in Diabetes

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Abstract

The relationship between muscle mass and visceral fat with mortality risk in diabetes has been extensively studied. This study investigates the association between the appendicular skeletal muscle mass-to-visceral fat area ratio (SVR) and cardiovascular and cancer-related mortality in diabetic patients in the United States. A nationwide cohort study was conducted using NHANES data (2011–2018), including 1439 diabetic patients with dual-energy X-ray absorptiometry (DXA) measurements. Weighted Cox proportional hazards models and restricted cubic splines (RCS) were employed to evaluate the association between SVR and cause-specific mortality rates. Weighted receiver operating characteristic (ROC) curves were used to assess the diagnostic performance of SVR and other conventional indicators in predicting mortality. After adjusting for multiple confounding factors, SVR showed a linear negative association with cardiovascular and cancer-related mortality in diabetes. Each 0.01-unit increase in SVR was associated with a 3% reduction in the risk of cardiovascular death and a 2% reduction in cancer-related death. However, SVR demonstrated weak diagnostic performance for both cardiovascular and cancer mortality, with weighted AUCs of 0.520 and 0.527, respectively, compared to other metrics including BMI, WC, ASM, and VFA. Although SVR was significantly associated with cardiovascular and cancer mortality, its predictive performance was not superior to that of simpler or more established indicators, suggesting that it has limited clinical utility for predicting mortality in diabetic patients.

Keywords Appendicular skeletal muscle mass-to-visceral fat area ratio · Diabetes · Cardiovascular mortality · Cancer-related mortality · Dual-energy · X-ray absorptiometry

Introduction

In 2021, an estimated 529 million people worldwide were living with diabetes, and this number is projected to rise to 1.31 billion by 2050 [1]. In 2019, diabetes was the direct cause of 1.5 million deaths, nearly half (48%) of which occurred before the age of 70. Additionally, elevated blood glucose was responsible for approximately 20% of cardiovascular deaths [2]. The disparity in mortality rates between individuals with and without diabetes is closely linked to deaths caused by cardiovascular diseases (CVD) and cancer [3]. Reduced muscle mass and increasing visceral fat have been recognized as significant risk factors for increased mortality from both CVD and cancer [4–6]. Through mechanisms such as metabolic dysregulation, chronic inflammation, and immune suppression, the combination of reduced muscle mass and increasing visceral fat may accelerate the progression of diabetes complications, substantially increasing the risk of mortality, including deaths from CVD and cancer [7]. The appendicular skeletal muscle mass-to-visceral fat area ratio (SVR) has emerged as a key indicator of body composition and metabolic health, reflecting the balance between muscle mass reserves and the metabolic burden of fat accumulation. SVR is calculated by dividing appendicular skeletal muscle mass (ASM) by visceral fat area (VFA).

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A cross-sectional study involving 1326 patients with diabetes revealed that a reduced SVR was independently associated with impaired cognitive function [8]. Liu et al. observed that diabetic patients with lower SVR values were more likely to have an elevated risk of CVD. Moreover, SVR levels were found to have a significant negative correlation with the estimated 10-year CVD risk, particularly among men [9]. Xu et al. further demonstrated that SVR was independently and negatively associated with arterial stiffness, highlighting SVR as a superior risk assessment tool for identifying diabetic patients with higher cardiovascular risk in clinical practice [10]. Additionally, Su et al. reported that SVR was independently correlated with non-alcoholic fatty liver disease in female patients with diabetes [11]. These conditions are all major contributors to cardiovascular and cancer-related mortality. However, the association between SVR and cardiovascular and cancer-related mortality in diabetes remains unexplored. To address this knowledge gap, this nationwide cohort study investigates the relationship between SVR and cardiovascular and cancer-related mortality among diabetic patients in the United States. By clarifying this association, the study aims to deepen our understanding of the link between the muscle mass and visceral fat with the risk of cause-specific mortality.

Methods

Study Design and Participants

The National Health and Nutrition Examination Survey (NHANES) is a comprehensive research initiative aimed at assessing the health and nutritional status of adults and children in the United States. The study protocols were approved by the Research Ethics Review Board of the National Center for Health Statistics, and written informed consent was obtained from all participants to ensure that their rights were protected. Data were gathered from four survey cycles conducted between 2011 and 2018. Diabetes was diagnosed according to the American Diabetes Association (ADA) criteria, which include a self-reported diagnosis, use of insulin or oral hypoglycemics, fasting blood glucose (FBG) ≥ 126 mg/dL, or HbA1c $\geq 6.5\%$ [12]. The study initially included 4483 diabetic patients aged 20 years or older. After excluding individuals with missing data on survival status, ASM, or VFA, a total of 1439 participants were retained for the final analysis. The participant selection process is detailed in Fig. 1.

Body Composition Assessment by Dual-Energy X-Ray Absorptiometry

Whole-body dual-energy X-ray absorptiometry (DXA) scans were performed using Hologic Discovery model A densitometers (Hologic, Inc., Bedford, Massachusetts) with Apex 3.2 acquisition software. All scans were analyzed using Hologic APEX 4.0 software with NHANES body composition analysis (BCA) protocol by trained and certified radiology technologists. ASM was quantified as the sum of lean soft tissue mass from both arms and legs (kg), with radiation exposure maintained below 20 μSv per scan. VFA was specifically measured at the L4–L5 vertebral interspace level through automated analysis of intra-abdominal adipose tissue compartments. The APEX software algorithm differentiated visceral adipose tissue (VAT) from subcutaneous adipose tissue (SAT) by identifying anatomical boundaries of the abdominal cavity at this landmark location. This measurement protocol aligns with NHANES standardized body composition assessment guidelines. SVR was subsequently calculated as the ASM-to-VFA ratio (kg/cm^2), providing a composite index of musculoskeletal and metabolic health.

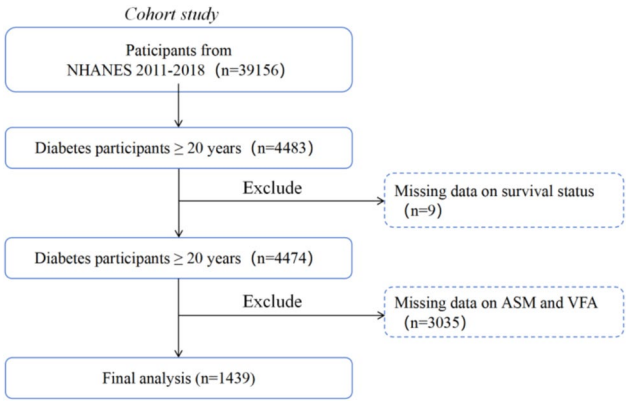

Fig. 1 Flowchart of participants' selection

Evaluation of Covariates

Demographic and health-related information—including sex, age, education level, marital status, income-to-poverty ratio, smoking habits, waist circumference (WC), body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), physical activity, and drug use—was gathered through household interviews conducted by NHANES. Current smoking was defined as having smoked at least 100 cigarettes in a lifetime and being a current smoker [13]. Physical activity (PA) was calculated as follows: PA (MET-h/wk) = MET × weekly frequency × duration [14, 15]. Participants with PA = 0 were defined as having no physical activity, while the rest of the participants were defined as engaging in physical activity. Clinical indicators, including total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FBG), HbA1c, and urine albumin-to-creatinine ratio (UACR) were measured in the NHANES laboratory. To enhance the accuracy

of the results, missing data were imputed using both the template method (R Package 'VIM') and multiple imputation (R Package 'mice').

Mortality Assessment

Mortality data were sourced from the National Death Index (NDI), maintained by the National Center for Health Statistics, and were updated through December 31, 2019. The primary outcomes were cardiovascular and cancer-related mortality, classified using ICD-10 codes. Cardiovascular mortality included deaths from heart disease (codes 054–068), while cancer-related mortality covered deaths from malignant neoplasms (codes 019–043). Follow-up time was measured from the initial interview date to the date of death or December 31, 2019, whichever occurred first.

Statistical Analysis

The analysis was performed using RStudio, with statistical significance set at a two-sided P value of < 0.05. To account for NHANES'complex sampling design, sample weights were applied, with adjustments made for clustering and stratification. Continuous variables were expressed as means (standard error [SE]), while categorical variables were presented as frequencies (percentages). To assess the relationship between SVR and cardiovascular and cancer-related mortality, weighted Cox proportional hazards regression models were used, with hazard ratios (HR) and 95% confidence interval (CI) reported. Three models were constructed. Model 1 did not adjust for any covariates. Model 2 was adjusted for sex and age. Model 3 was further adjusted for education level, marital status, income-to-poverty ratio, smoking status, WC, BMI, FBG, HbA1c, TC, TG, HDL-C, LDL-C, SBP, DBP, and UACR, using hypoglycemic drugs, using insulin, using antihypertensive drugs, and using lipid-lowering drugs and physical activity. The median of the quartiles of SVR was used as a continuous variable to test for a trend. Restricted cubic spline (RCS) analysis was used to investigate the dose–response relationship between SVR with cardiovascular and cancer-related mortality risks. Analyses were further stratified by sex (male vs. female), age (< 45 vs. ≥ 45), education level (under vocational school vs. vocational school and above), marital status (married or living with a partner vs. widowed, divorced, separated, or single), and BMI (< 30 vs. ≥ 30) to explore whether these factors influenced the associations and to assess potential interactions. We assessed the predictive performance of SVR and other related indices for cardiovascular and cancer-related mortality using weighted receiver operating characteristic (ROC) curves. The differences in weighted area under the curve (AUC) between indices were statistically analyzed using the roc.test function based on DeLong's test.

Results

Table 1 presents the characteristics of participants stratified by SVR quartiles (Quartile 1: SVR < 0.125, Quartile 2: SVR 0.125–0.169, Quartile 3: SVR 0.169–0.237, Quartile 4: SVR ≥ 0.237). Those in the highest SVR quartile (Quartile 4) were younger, more likely to be male, had more physical activity, and had higher educational attainment compared to those in the lowest SVR quartile (Quartile 1). Additionally, participants in Quartile 4 exhibited lower levels of WC, BMI, FBG, HbA1c, TC, TG, and SBP.

Table 2 summarizes the impact of SVR on cardiovascular and cancer-related mortality. In Model 3, SVR as a continuous variable was inversely associated with both cardiovascular and cancer-related mortality. For every 1-unit increase in SVR, the HRs and 95% CIs were 0.03 (0.00–0.29) for cardiovascular mortality and 0.13 (0.03–0.69) for cancer-related mortality. Additionally, for every 0.01-unit increase in SVR, the HRs and 95% CIs were 0.97 (0.94–0.99) for cardiovascular mortality and 0.98 (0.96–1.00) for cancer-related mortality. Relative to the SVR Quartile 1 group, individuals in the Quartile 4 group had a 52% decreased risk of cardiovascular mortality (HR: 0.48, 95% CI: 0.27–0.87, $P = 0.016$). RCS analysis indicated that lower SVR was linearly associated with an increased risk of cardiovascular and cancer-related mortality, as shown in Fig. 2.

In certain subgroups, the association between reduced SVR levels and the risk of cardiovascular or cancer-related mortality was not consistently observed, as detailed in Table 3. For cardiovascular mortality, this association was statistically significant among participants who were male, under 45 years old, had a vocational or higher education level, were widowed, divorced, separated, or single, or had a BMI < 30 ($P < 0.05$). For cancer-related mortality, the correlation was significant among participants with a vocational or higher education level, or with a BMI < 30 ($P < 0.05$). However, interaction tests indicated that these characteristics—including age, sex, educational level, marital status, and BMI—did not significantly modify the relationship between SVR and mortality (all P for interaction > 0.05).

As shown in Table 4 and Fig. 3, SVR demonstrated weak diagnostic performance for cardiovascular mortality compared to other metrics, including BMI, WC, ASM, and VFA, with a weighted AUC of 0.520 (95% CI: 0.485–0.555). The optimal cutoff value was 0.37, yielding a sensitivity of 0.976 and specificity of 0.084. For cancer mortality, SVR similarly showed weak diagnostic

Table 1 Participant characteristics stratified by SVR quartiles

Characteristics	SVR kg/cm^2			
	Quartile 1 (< 0.125)	Quartile 2 (0.125 ~ 0.169)	Quartile 3 (0.169 ~ 0.237)	Quartile 3 (≥ 0.237)
Age, years	50.44 (0.58)	48.80 (0.64)	45.56 (0.69)	41.78 (0.80)
Male, %	97 (26.9%)	181 (50.3%)	226 (62.8%)	234 (65.2%)
Education level				
Under vocational school, %	98 (27.2%)	98 (27.2%)	96 (26.7%)	68 (18.9%)
Vocational schools and above, %	262 (72.8%)	262 (72.8%)	264 (73.3%)	291 (81.1%)
Marital status				
Married or living with partner, %	228 (63.3%)	236 (65.6%)	244 (67.8%)	208 (57.9%)
Widowed, divorced, separated, or single, %	132 (36.7%)	124 (34.4%)	116 (32.2%)	151 (42.1%)
Income-to-poverty ratio	2.61 (0.14)	2.80 (0.14)	2.67 (0.12)	2.78 (0.12)
Current smoking, %	59 (16.4%)	57 (15.8%)	67 (18.6%)	69 (19.2%)
WC, cm	118.17 (0.90)	111.35 (1.17)	109.17 (1.41)	100.78 (1.48)
BMI, kg/m^2	36.15 (0.49)	33.70 (0.50)	32.89 (0.67)	29.95 (0.65)
FBG, mmol/L	8.07 (0.25)	8.35 (0.24)	8.04 (0.26)	7.94 (0.28)
HbA1c, %	7.38 (0.10)	7.36 (0.16)	7.17 (0.12)	7.03 (0.14)
TC, mmol/L	6.15 (0.29)	5.64 (0.25)	5.51 (0.15)	5.25 (0.12)
TG, mmol/L	2.81 (0.16)	2.84 (0.25)	2.51 (0.14)	1.81 (0.11)
HDL-C, mmol/L	1.16 (0.02)	1.14 (0.03)	1.17 (0.02)	1.34 (0.04)
LDL-C, mmol/L	2.97 (0.07)	3.13 (0.08)	3.05 (0.07)	3.12 (0.11)
SBP, mmHg	127.19 (1.44)	126.44 (1.49)	123.66 (1.01)	125.52 (1.18)
DBP, mmHg	74.89 (0.69)	75.64 (0.77)	75.45 (0.66)	73.88 (0.93)
UACR, mg/g	123.78 (31.28)	79.94 (17.06)	57.30 (13.79)	144.47 (42.41)
Using hypoglycemic drugs, %	239 (66.4%)	220 (61.1%)	224 (62.2%)	173 (48.2%)
Using insulin, %	66 (18.3%)	57 (15.8%)	39 (10.8%)	73 (20.3%)
Using antihypertensive drugs %	170 (47.2%)	140 (38.8%)	116 (32.2%)	119 (33.1%)
Using lipid-lowering drugs, %	147 (40.8%)	124 (34.4%)	90 (25.0%)	86 (23.9%)
Having physical activities, %	217 (60.2%)	255 (70.8%)	279 (77.5%)	297 (82.7%)
Cardiovascular mortality, %	84 (23.3%)	85 (23.6%)	90 (25.0%)	71 (19.8%)
Cancer mortality, %	84 (23.3%)	75 (20.8%)	85 (23.6%)	67 (18.7%)

SVR Appendicular skeletal muscle mass-to-visceral fat area ratio, *WC* Waist circumference, *BMI* Body mass index, *FBG* Fasting blood glucose, *TC* Total cholesterol, *TG* Triglyceride, *HDL-C* High-density lipoprotein cholesterol, *LDL-C* Low-density lipoprotein cholesterol, *SBP* Systolic blood pressure, *DBP* Diastolic blood pressure, *UACR* Urine albumin-to-creatinine ratio

performance, with a weighted AUC of 0.527 (95% CI: 0.492–0.563). The optimal cutoff value was 0.19, with a sensitivity of 0.688 and specificity of 0.400.

Discussion

This study is the first to examine the relationship between DXA-based SVR and both cardiovascular and cancer-related mortality among diabetic patients in the United States. The key findings are as follows: (1) SVR showed a linear negative association with cardiovascular mortality in diabetic patients, with each 0.01-unit increase in SVR reducing the risk of cardiovascular death by 3%; (2) SVR also demonstrated a linear negative association with cancer-related mortality, with each 0.01-unit increase in SVR lowering the risk of cancer-related death by 2%. (3) Compared to BMI, WC, ASM, and VFA, the predictive performance of SVR for cardiovascular mortality (AUC = 0.520) and cancer-related mortality (AUC = 0.527) was relatively limited.

Although prior studies have not specifically reported on the association between SVR and the risks of cardiovascular and cancer-related mortality, the relationships between muscle mass, visceral fat, and these mortality risks in diabetic patients have been widely explored. For instance, Guo et al., using data from the NHANES database, analyzed 1,417 adults aged ≥ 50 years with T2DM and found that a higher arm muscle mass index was associated with lower cardiovascular mortality [16]. Wei et al., in a study based on the UK Biobank, observed that skeletal muscle mass, measured via bioelectrical impedance analysis, may be linked to reduced cardiovascular mortality risk in diabetic patients [17]. A

Table 2 Weighted Cox Proportional Hazards Regression Analysis of Associations between SVR and Cause-Specific Mortality

	Model 1		Model 2		Model 3	
	HR 95% (CI)	P_{value}	HR 95% (CI)	P_{value}	HR 95% (CI)	P_{value}
Cardiovascular mortality						
Per 1-unit change	0.19 (0.06, 0.61)	0.006	0.08 (0.02, 0.31)	< 0.001	0.03 (0.00, 0.29)	0.002
Per 0.01-unit change	0.97 (0.96, 0.99)	0.002	0.96 (0.94, 0.98)	< 0.001	0.97 (0.94, 0.99)	0.002
Categorical						
Quartile 1	Reference		Reference		Reference	
Quartile 2	0.85 (0.62, 1.15)	0.280	0.74 (0.54, 1.02)	0.062	0.64 (0.41, 1.01)	0.053
Quartile 3	0.97 (0.72, 1.30)	0.817	0.81 (0.59, 1.12)	0.200	0.62 (0.32, 1.20)	0.154
Quartile 4	0.72 (0.52, 0.99)	0.041	0.58 (0.41, 0.83)	0.003	0.48 (0.27, 0.87)	0.016
$P_{for\ trend}$		0.065		0.007		0.038
Cancer-related mortality						
Per 1-unit change	0.29 (0.09, 0.93)	0.037	0.41 (0.11, 1.43)	0.160	0.13 (0.03, 0.69)	0.016
Per 0.01-unit change	1.00 (0.98, 1.01)	0.516	1.00 (0.99, 1.01)	0.968	0.98 (0.96, 1.00)	0.016
Categorical						
Quartile 1	Reference		Reference		Reference	
Quartile 2	0.77 (0.57, 1.06)	0.104	0.82 (0.60, 1.14)	0.236	0.92 (0.59, 1.44)	0.728
Quartile 3	0.92 (0.68, 1.24)	0.590	1.00 (0.73, 1.38)	0.991	1.00 (0.68, 1.47)	0.996
Quartile 4	0.69 (0.50, 0.95)	0.022	0.77 (0.54, 1.09)	0.140	0.64 (0.39, 1.04)	0.074
$P_{for\ trend}$		0.052		0.232		0.061

SVR Appendicular skeletal muscle mass-to-visceral fat area ratio, *HR* Hazard ratios, *CI* Confidence intervals

Model 1 did not adjust for any covariate

Model 2 was adjusted for sex, and age

Model 3 was further adjusted for education level, marital status, income-to-poverty ratio, smoking status, WC, BMI, FBG, HbA1c, TC, TG, HDL-C, LDL-C, SBP, DBP, UACR, using hypoglycemic drugs, using insulin, using antihypertensive drugs, using lipid-lowering drugs and physical activity

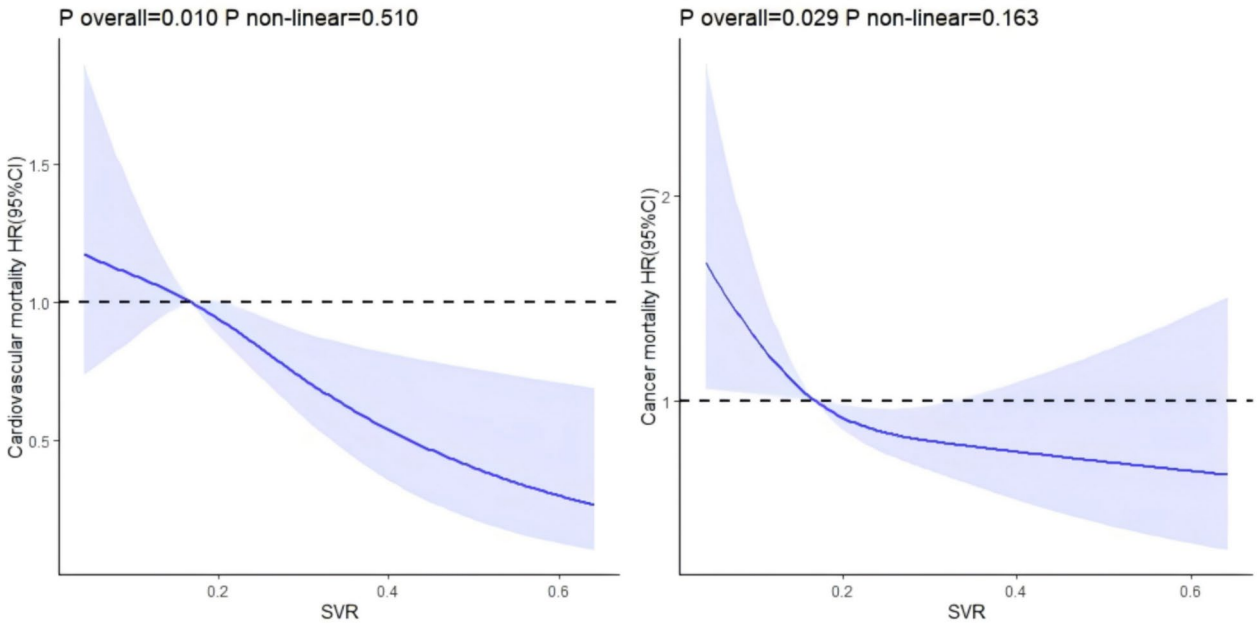

Fig. 2 RCS Analysis of Associations between SVR and Cause-Specific Mortality. SVR Appendicular skeletal muscle mass-to-visceral fat area ratio, *HR* Hazard ratios, *CI* Confidence intervals. Adjusted for sex, age, education level, marital status, income-to-poverty ratio, smoking status, WC, BMI, FBG, HbA1c, TC, TG, HDL-C, LDL-C, SBP, DBP, and UACR, using hypoglycemic drugs, using insulin, using antihypertensive drugs, and using lipid-lowering drugs and physical activity

Table 3 Subgroup analysis and interaction test

Subgroup	Cardiovascular mortality		Cancer-related mortality	
	HR 95% (CI)	$P_{for\ interaction}$	HR 95% (CI)	$P_{for\ interaction}$
Sex				
Male	0.07 (0.01, 0.36)	0.4173	0.65 (0.13, 3.12)	0.2316
Female	0.19 (0.03, 1.40)		0.16 (0.03, 1.05)	
Age				
< 45	0.10 (0.02, 0.62)	0.7906	0.31 (0.05, 1.79)	0.9379
≥ 45	0.30 (0.06, 1.55)		0.33 (0.06, 1.72)	
Education level				
Under vocational school	0.90 (0.06, 12.70)	0.2095	2.16 (0.16, 29.11)	0.1153
Vocational schools and above	0.13 (0.03, 0.51)		0.19 (0.05, 0.74)	
Marital status				
Married or living with partner	0.32 (0.07, 1.38)	0.3014	0.50 (0.12, 2.09)	0.2745
Widowed, divorced, separated, or single	0.08 (0.01, 0.66)		0.13 (0.02, 1.02)	
BMI				
< 30	0.07 (0.01, 0.51)	0.4489	0.14 (0.03, 0.69)	0.564
≥ 30	0.41 (0.09, 1.96)		0.16 (0.02, 1.14)	

BMI Body mass index, *HR* Hazard ratios, *CI* Confidence intervals

Table 4 Weighted ROC curves for predicting cause-specific mortality

Indices	Weighted AUC	Weighted AUC 95% CI	Cutoff value	Sensitivity	Specificity
Cardiovascular mortality					
SVR	0.520	0.485–0.555	0.37	0.976	0.084
BMI	0.531	0.496–0.566	32.55	0.512	0.556
WC	0.556[b]	0.522–0.591	100.55	0.736	0.358
ASM	0.572[b]	0.537–0.606	24.14	0.633	0.528
VFA	0.569[ab]	0.534–0.604	177.03	0.397	0.723
Cancer-related mortality					
SVR	0.527	0.492–0.563	0.19	0.688	0.400
BMI	0.590[a]	0.557–0.624	34.05	0.743	0.433
WC	0.605[a]	0.571–0.639	108.55	0.691	0.507
ASM	0.611[a]	0.577–0.646	21.14	0.669	0.559
VFA	0.547[bcd]	0.513–0.581	164.93	0.720	0.393

SVR Appendicular skeletal muscle mass-to-visceral fat area ratio, *BMI* Body mass index, *WC* Waist Circumference, *ASM* Appendicular skeletal muscle mass, *VFA* Visceral fat area, *AUC* Area under the curve, *CI* Confidence intervals

[a]Significantly different compared to SVR ($P < 0.05$)

[b]Significantly different compared to BMI ($P < 0.05$)

[c]Significantly different compared to WC ($P < 0.05$)

[d]Significantly different compared to ASM ($P < 0.05$)

[e]Significantly different compared to VFA ($P < 0.05$)

nationwide longitudinal population-based study found that the coexistence of diabetes and sarcopenia significantly increased cardiovascular mortality risk; however, neither condition alone was associated with an elevated risk [18]. Furthermore, Chang et al. highlighted that higher lean mass in the upper limbs, compared to other body regions, was associated with lower cardiovascular mortality in diabetic patients [18]. Additionally, muscle mass is associated with both diabetes and cancer-related mortality. Cong et al., in a prospective study involving 8247 cancer patients across 72 hospitals in China, found that cancer patients with diabetes had lower muscle strength and poorer survival outcomes [19]. Among pancreatic cancer patients, those diagnosed with diabetes were found to experience significantly greater

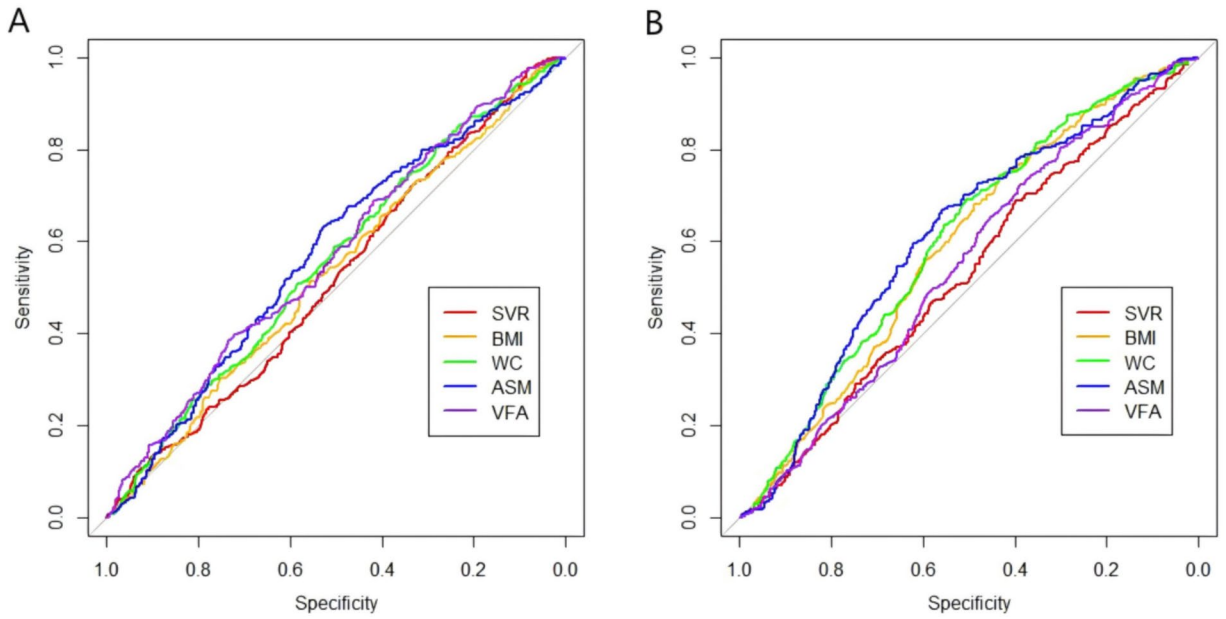

Fig. 3 Weighted ROC Curves for Predicting Cause-Specific Mortality. **A** Cardiovascular mortality, **B** Cancer-related mortality. SVR Appendicular skeletal muscle mass-to-visceral fat area ratio, *BMI* Body mass index, *WC* Waist Circumference, *ASM* Appendicular skeletal muscle mass, *VFA* Visceral fat area

loss of skeletal muscle compared to non-diabetic patients. Moreover, patients with higher rates of muscle loss exhibited worse survival outcomes [20]. The role of visceral fat in cardiovascular mortality among diabetic patients has also been explored. Zhu et al. reported that a higher visceral fat score was associated with an increased risk of cardiovascular mortality [21]. Ke et al. found that excessive visceral adipose tissue in patients with type 1 diabetes was linked to diastolic dysfunction and coronary artery calcification—both recognized risk factors for cardiovascular death [22]. While there are no direct studies examining the relationship between visceral fat and cancer-related mortality in diabetic patients, the link between visceral fat and cancer-related death is noteworthy. Jia et al., in a cohort study of 11,120 U.S. adults, observed that visceral fat score was positively associated with cancer mortality, illustrating how visceral fat impacts of visceral fat on cancer-related deaths [23]. These findings strongly support the premise of this study. By utilizing data from the NHANES database, this research investigates the relationship between SVR and the risks of cardiovascular and cancer-related mortality in diabetic patients. It addresses a critical knowledge gap and provides fresh insights into how body composition impacts long-term outcomes in the diabetic population.

SVR, which integrates ASM and VFA, has recently been used as a marker to identify the muscle mass and visceral fat. While the biological mechanisms linking reduced muscle mass and increasing visceral fat to the risks of cardiovascular and cancer-related mortality in diabetic patients are not yet fully understood, several potential explanations can be proposed. (1) Reduced muscle mass significantly impacts metabolic health, as muscle is the primary tissue for glucose metabolism. A decline in muscle mass reduces insulin sensitivity, exacerbating insulin resistance in diabetic patients [24]. This metabolic dysregulation not only promotes atherosclerosis and hyperglycemia-related vascular damage but also creates a 'glucotoxic' environment that facilitates cancer cell growth [25, 26]. Furthermore, reduced muscle mass impairs the clearance of metabolic by-products, such as lactate and free radicals, leading to increased oxidative stress, which directly damages cardiovascular function and promotes cancer development through mechanisms like DNA damage [27–30]. Muscle also serves as a critical source of anti-inflammatory cytokines, such as IL-10. When muscle mass decreases, chronic low-grade inflammation develops, accelerating the progression of both CVD and cancer [31]. (2) Excessive visceral fat plays a harmful role in this process. Visceral fat secretes pro-inflammatory cytokines, including IL-6 and TNF-α, which drive systemic inflammation, contributing to atherosclerosis, hypertension, and other CVD while promoting cancer cell proliferation and metastasis [32–34]. Metabolic by-products from visceral fat, such as free fatty acids, induce lipotoxicity, directly damaging cardiomyocytes and vascular endothelial cells. These by-products also activate signaling pathways that enhance cancer cell survival and growth [35]. The overexpression

of obesity-related adipokines, such as leptin, further exacerbates inflammation and cancer progression [36, 37], while reduced levels of anti-inflammatory adipokines, such as adiponectin, worsen cardiovascular, and tumor pathologies [38, 39]. (3) Lifestyle and behavioral factors also play a crucial role in the muscle mass and visceral fat. Patients with this condition often exhibit significantly reduced physical activity, which not only increases cardiovascular risk but also weakens the immune system's ability to combat cancer. Additionally, reduced muscle mass and increasing visceral fat are frequently associated with a high-calorie, high-fat diet combined with insufficient protein intake. This dietary pattern exacerbates metabolic stress and inflammation, further compounding the negative effects on cardiovascular and cancer-related outcomes.

Notably, ROC curve analysis revealed that the predictive performance of SVR was not superior to that of simpler or more established indicators such as BMI and WC. This finding suggests that although SVR theoretically captures the dual risk of reduced muscle mass and increased visceral fat, its utility in clinical practice may be limited. One possible explanation is that SVR is a ratio-based metric, making it susceptible to the influence of extreme values. When either the numerator (muscle mass) or the denominator (visceral fat) is abnormal, it may exaggerate or obscure the true body composition status, thereby reducing the stability and interpretability of the measure. The key strength of this study lies in its design as a large-scale, nationwide cohort study based on the NHANES database. It evaluates the impact of SVR on cardiovascular and cancer-related mortality in diabetic patients while accounting for a wide range of confounding factors. Moreover, SVR measured by DXA provides an objective and accurate assessment of body composition, offering greater reliability. However, several limitations should be noted. First, due to the inherent constraints of observational study designs, reverse causality cannot be entirely ruled out. Second, as this study focuses exclusively on the diabetic population in the US, the findings may not be generalizable to other ethnic groups due to potential environmental, genetic, and racial differences. Third, ASM in this study was quantified as the sum of lean soft tissue mass from both arms and legs using DXA. However, lean soft tissue mass includes not only skeletal muscle but also other tissues, so ASM may overestimate skeletal muscle mass. This should be considered when interpreting the results. Finally, it should be noted that SVR does not outperform other simpler or more established metrics, and its ROC performance suggests limited clinical relevance for predicting mortality in diabetic patients. Future research should explore the potential value of combining SVR with other biomarkers to enhance predictive accuracy.

Conclusion

Although this study identified a linear inverse correlation between SVR and the risks of cardiovascular and cancer-related mortality among diabetic patients in the United States, its predictive performance did not surpass that of commonly used clinical indicators. Therefore, there is currently insufficient evidence to support SVR as an independent prognostic marker. Future studies should explore its potential value in combination with other biomarkers to enhance prognostic accuracy.

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Author Contributions Shuwu Wei conceived the study and performed data analysis. Shuwu Wei and Jiale Zhang drafted the manuscript. Huijuan Zheng, Weimin Jiang, and Jie Yang assisted in data acquisition and preprocessing. Yaoxian Wang contributed to the research methodology and analysis. Weiwei Sun and Weihong Chen oversaw the study design and project administration. All authors reviewed and approved the final manuscript.

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Data Availability The datasets used and analyzed in this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest Shuwu Wei, Jiale Zhang, Huijuan Zheng, Weimin Jiang, Jie Yang, Yaoxian Wang, Weihong Chen, and Weiwei Sun declare no competing interests.

Ethical Approval and Consent to Participate The NHANES protocols were approved by the National Center for Health Statistics and the Ethics Review Board, with written informed consent obtained from all participants.

Human and Animal Rights and Informed Consent This study was based on publicly available data from the National Health and Nutrition Examination Survey (NHANES), which is conducted by the National Center for Health Statistics (NCHS). All participants provided written informed consent, and the survey protocols were approved by the NCHS Research Ethics Review Board. Since this research involved only secondary analysis of anonymized data, no additional ethical approval was required.

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