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REVIEW ARTICLE

Association of lipid accumulation product with type 2 diabetes mellitus, hypertension, and mortality: a systematic review and meta-analysis

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Abstract

Purpose Novel anthropometric measures are simple, applicable, and inexpensive tools for cardiovascular risk assessment. This study evaluates the association of lipid accumulation product (LAP) with hypertension, type 2 diabetes mellitus (T2DM), and all-cause mortality, and compares it with other anthropometric measures.

Methods PubMed, Web of Science, EMBASE, and Scopus were systematically searched for articles published until May 15, 2021. We included all the studies that had measured LAP predictability for T2DM, all-cause mortality, and hypertension with no limitation in comorbidities and follow-up duration. We assessed the predictability measures of LAP for the aforementioned outcomes. We also performed a meta-analysis on four articles on mortality using an inverse variance method by the "meta" package in R software.

Results Twenty-nine studies were included in the review after applying the eligibility criteria. The hazard ratio for all-cause mortality per one standard deviation increment of LAP was 1.24 (95% confidence interval [CI]: 1.00–1.53; P = 0.0463) in females, and 1.07 (95% CI: 0.74–1.57; P = 0.709) in males. All included studies found a direct association between LAP with T2DM and hypertension. However, studies used different cut-off points for LAP. Most studies found that LAP was superior in predicting T2DM and hypertension compared to conventional indices, e.g., body mass index and waist circumference. We found that LAP may have higher prognostic significance in females compared to males.

Conclusion LAP is an inexpensive method to evaluate the risk of all-cause mortality, T2DM, and hypertension, and could outperform conventional anthropometric indices in this regard.

Keywords Lipid accumulation product · LAP · Type 2 diabetes mellitus · Hypertension · Mortality · Anthropometric measure

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Introduction

Obesity and overweight are among the principal modifiable risk factors for coronary heart disease (CHD), ischemic stroke, hypertension, metabolic syndrome, and type 2 diabetes mellitus (T2DM) [1, 2]. According to World Health Organization (WHO), 39% of adults were overweight, as 11% of males and 15% of females were obese in 2016 globally; therefore, more than half a billion adults suffer from obesity and overweight worldwide [1]. Moreover, hypertension and T2DM are global health concerns since their global prevalence has an increasing trend [3, 4]. Screening and early detection of the high-risk populations for chronic diseases could contribute to controlling their morbidity and mortality [5].

Anthropometric measures are applicable tools for screening and early detection of weight-related disorders, having the advantages of simplicity. Notable among these are body mass index (BMI) [5], waist circumference (WC), hip circumference (HC), waist-to-hip ratio (WHR; the ratio of WC to HC), and waist to height ratio (WHtR; the ratio of WC to height) [6]. While BMI is the best known and most widely used anthropometric index, it has major limitations for the determination of body fat mass. For instance, BMI is not able to show fat distribution and is affected by age and sex; therefore, there is a need to investigate more powerful indices [7, 8].

Several new anthropometric measures have recently been recommended, and different studies have evaluated their performances in predicting chronic diseases. Abdominal volume index (AVI), body adiposity index (BAI), body shape index (ABSI), body roundness index (BRI), and lipid accumulation product (LAP) are a few examples that are associated with CHD [9, 10]. LAP was introduced by Kahn in 2005 [11]. Kahn suggested that "BMI may not be the best marker for estimating the risk of obesity-related disease", and LAP could be a better predictor of the incidence of cardiovascular diseases than BMI. Studies have reported a correlation between LAP and insulin resistance [12]. Moreover, the accuracy of LAP for predicting metabolic syndrome has been validated, and it was demonstrated that LAP is superior to other indices in this regard [13]. There is evidence that LAP can be used in predicting long-term cardiometabolic diseases among females with higher accuracy than other anthropometric and central obesity markers [14]. Furthermore, the results of a retrospective study revealed that LAP is associated with mortality, but that in some cases like diabetic patients, this association is not present [15].

Although many studies have evaluated and compared the predictability of different anthropometric measures, contradictory findings are confusing and complicate choosing an appropriate obesity index for practice and screening. Systematic reviews and meta-analyses might help us to determine which anthropometric measures are more appropriate for screening a specific subgroup of the population. We aimed to systematically review the literature and perform a meta-analysis to establish the correlation between LAP and T2DM, mortality, and hypertension.

Methods

This review was conducted in compliance with the review protocol registered on PROSPERO, PROSPERO 2019 CRD42019142239 [16]. It is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [17].

Study eligibility criteria

Studies were included if: (1) they were conducted among adults above 18 years of age; (2) used LAP (calculated by the following formula: male LAP = [WC (cm) − 65] × Triglyceride (TG) concentration (mmol/l) and female LAP = [WC (cm) − 58] × TG concentration (mmol/l)) as an exposure variable; (3) described the desired outcomes: hypertension, T2DM, and mortality; (4) studies that have evaluated the predictability of LAP for the above-mentioned health outcomes; (5) published in the English language; (6) published in peer-reviewed journals before May 15, 2021 (search date). The following studies were excluded: (1) case reports, letters, editorials, commentary articles, review articles, abstracts, and protocols; (2) articles that have reported no health outcome related to LAP. The selected studies were not limited due to comorbidities and follow-up duration.

Search strategy

Two authors (S.K. and A.A.) systematically and independently searched the electronic databases PubMed, Web of Science, EMBASE, and SCOPUS for related studies from inception to May 15, 2021. We developed our search strategy in PubMed and subsequently searched other databases through the following medical subject headings (MeSH) terms and free keywords: "Lipid Accumulation Product", "Hypertension", "Blood Pressure", "Diabetes Mellitus", "Diabetes Mellitus Type 2", and "Mortality". The search strategy is provided in the Supplementary Material. All records were transferred to EndNote software, and the duplicates were removed.

Data extraction and preparation

Three authors (S.K., H.T., and A.A.) independently screened the titles and abstracts to apply inclusion/exclusion criteria. The full text was reviewed thoroughly if any article's admissibility remained unclear. Following the selection of eligible studies, a comprehensive full-text review and data extraction were conducted by two authors (S.K. and H.T.) independently. Standardized data extraction forms were used to compile the variables comprising of methodological features (first author and year of publication, country, study type, source of data, population size, percentage of females, comorbidities, age of population, follow-up duration, method of LAP determination, statistical analysis, adjustment for confounders), outcome (T2DM, hypertension, and mortality), predictability measure (odds ratio [OR], area under receiver operating characteristic curve [AUC], hazard ratio [HR], relative risk [RR], and Poisson regression) and predictability of other anthropometric measures (BMI, WC, WHR, WHtR, VAI, BAI, and others). Disagreements in any of the steps were resolved through discussion and a third author's opinion.

Quality assessment

Study quality was evaluated with the National Institutes of Health's (NIH) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies [18]. This tool has 14 criteria to evaluate each study, and each criterion should be answered with "Yes", "No", or "Other" (cannot determine, not applicable, not reported). After determining the answer to each question, each study was scored as good, fair, or poor. Two authors (S.K. and H.T.) independently rated included articles according to the NIH checklists. The quality assessment was not used to exclude studies but made the robustness of the evidence clear. Discordance in ratings was resolved through discussion or arbitration by a third author.

Statistical analyses

Meta-analysis was performed to assess the predictability of LAP for the desired outcomes if two or more studies reported the same outcome measure. According to sex differences in LAP, the meta-analysis was done for each sex separately. The meta-analysis was done on mortality papers using an inverse variance method, and the random-effects model was reported. Heterogeneity was evaluated by I^2 and τ^2 tests with a $P < 0.1$ as evidence of heterogeneity. We used R statistical software version 4.0.3 and the "meta" package, including "metagen" command for this purpose.

Results

Study selection

Our search identified 684 publications, including 185 articles from Embase, 169 articles from Web of Science, 138 articles from PubMed, and 192 articles from Scopus. After removing duplicates, 301 records were screened through title and abstract, and 267 citations were removed. We reviewed the full-text of 34 articles, and five articles were excluded due to the following reasons: (1) Insufficient data (three articles), (2) Combination with undesired data (one article), and (3) Different LAP formula (one article). Finally, 29 articles were included in our study (Table 1). Figure 1 shows a flow diagram of study selection.

Study characteristics

The baseline characteristics of included records are illustrated in Table 2. Studies have been conducted in 14 countries (China = 12, Iran = 3, Korea = 2, Brazil = 1, Serbia = 1, USA = 2, Italy = 1, Romania = 1, Japan = 2, Mongolia = 1, Germany = 1, Poland = 1, Thailand = 1, Netherlands = 1).

Table 1 Excluded articles after full-text evaluation

Author/Year	Title	Reason of exclusion
H. S. Kahn, 2006 [19]	The Lipid Accumulation Product Is Better Than BMI For Identifying Diabetes: A Population-Based Comparison	Insufficient data
Hamsaveena, 2014 [20]	Lipid Accumulation Product As A Novel Index To Predict Diabetes In Women	Insufficient data
Wanderley Rocha, 2017 [21]	Visceral Adiposity Measurements, Metabolic and Inflammatory Profile in Obese Patients with and Without Type 2 Diabetes Mellitus: A Cross-sectional Analysis	Insufficient data
N. Ahn, 2019 [22]	Visceral Adiposity Index (VAI), Lipid Accumulation Product (LAP), And Product Of Triglycerides And Glucose (Tyg) To Discriminate Prediabetes And Diabetes	Combined with undesired data (Diabetic and prediabetic patients were not separated)
Y. Wang, 2020 [23]	A Novel Indicator, Childhood Lipid Accumulation Product, Is Associated With Hypertension In Chinese Children And Adolescents	Different LAP formula (childhood LAP)

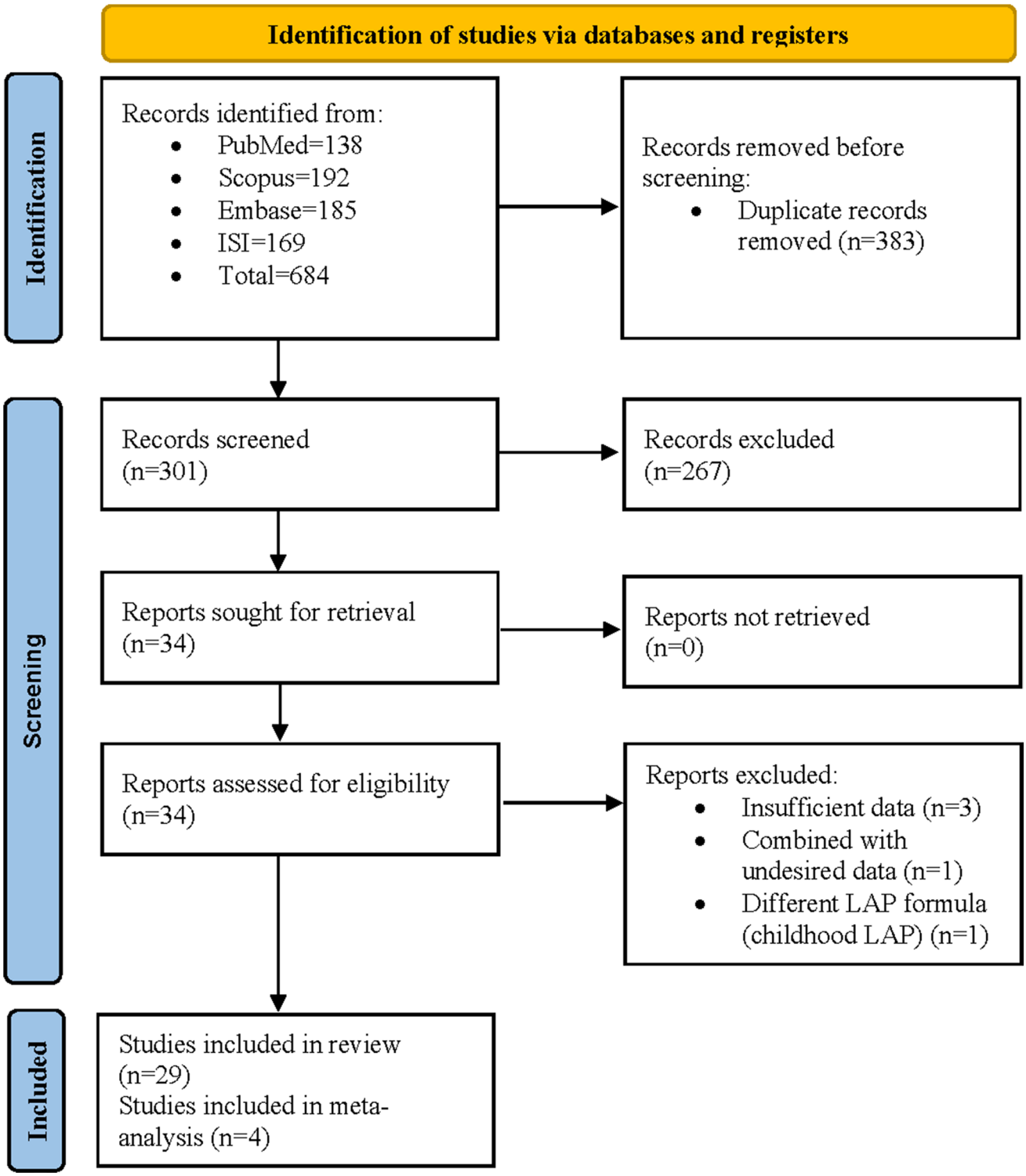

Fig. 1 PRISMA flowchart

Eighteen studies were cross-sectional, and 12 studies were prospective or retrospective cohorts. The sample size in the studies varied from 264 to 215,651, and the range of follow-up duration in cohort studies was from 5 to 18.1 years. The sample of 26 studies was the general population, and the others had evaluated people with specific conditions like menopausal women, post-menopausal women, and people with hypertension. In all the studies, LAP was measured

Table 2 Baseline characteristics of the included studies

Study ID	Author, year	Country	Study design	Data source	Sample size (%F)	Specific subgroup	Age range	Age (Mean ± SD)	Follow-up (years)	LAP determination	Statistical analysis	Adjustment
1	Bozorgmanesh, 2010	Iran	Cross-sectional and prospective cohort	Tehran lipid and glucose study	8671 (57.2) for cross-sectional and 3242 (57.8) for longitudinal		≥ 20	42.9 ± 15(cross sectional), 41.6 ± 13.2(longitudinal)	6	Objectively	Linear and logistic regression	Baseline mean arterial pressure, family history of DM
2	Bozorgmanesh, 2010	Iran	Prospective cohort	Tehran lipid and glucose study	6751(56.1)		≥ 30	NA	8.6	Objectively	General linear model, Cox's proportional hazards regression	Age, smoking, SBP, family history of premature CVD, DM, antihypertensive drug use, HDL and non-HDL-C, FPG, 2hPCPG, Tehran Lipid and Glucose (TLGS) intervention measures (whether a patient was or was not assigned to lifestyle intervention measures in the TLGS study)
3	Gao, 2013	Mongolia, china	Cross-sectional	Originally designed	2589(58.9)		20–84	HTN = 52.03 ± 12.05, Non-HTN = 43.21 ± 11.46	N/A	Objectively	Student's t-tests, χ2-test, Logistic regression, Wilcoxon rank-sum test	Age, current cigarette smoking, alcohol consumption, family history of HTN, FPG

Table 2 (continued)

Study ID	Author, year	Country	Study design	Data source	Sample size (%F)	Specific subgroup	Age range	Age (Mean ± SD)	Follow-up (years)	LAP determination	Statistical analysis	Adjustment
4	Ioachimescu, 2010	USA	Retrospective cohort	preCIS database (Preventive Cardiology Information System)	5924(39.2)		NA	55 ± 13	5.3	Objectively	Cox's proportional model	Age, sex, smoking status, history of DM, SBP, DBP, and fasting LDL-C and HDL-C
5	Kavaric, 2018	Serbia	Cross-sectional	Originally designed	299(58.5)		NA	Control = 55.0, DM = 63.0	N/A	Objectively	Mann–Whitney U test, Student's t-tests, χ2-test, Spearman's correlation analysis, Logistic regression	Age, LAP, hsCRP, ALT, GGT, uric acid, bilirubin, creatinine, eGFRMDRD, gender, smoking status, hypolipemics, and antihypertensive therapies
6	Kim, 2018	Korea	Prospective cohort	AnsungAnsan cohort database	7643(52.9)		40–69	51.7 ± 8.8	10	Objectively	De Long's test, Cox's proportional hazards regression	Age, sex, BMI, smoking, HTN, physical activity, energy intake
7	Lee, 2018	Korea	Prospective cohort	Korean Genome and Epidemiology Study	7708(52.8)		40–69	51.4 ± 8.6(M), 52.0 ± 8.9(F)	10	Objectively	χ2-test, Student's t-tests, Multiple logistic regression	Age, BMI, HTN, family history of DM, current smoking and alcohol consumption status, and regular exercise

Table 2 (continued)

Study ID	Author, year	Country	Study design	Data source	Sample size (%F)	Specific subgroup	Age range	Age (Mean ± SD)	Follow-up (years)	LAP determination	Statistical analysis	Adjustment
8	Malavazos, 2015	Italy	Cross-sectional	Originally designed	381(77)		18–70	41.3 ± 12.5	N/A	Objectively	ANOVA, Kruskal–Wallis test, Logistic regression	Age, smoking status
9	Marcadenti, 2017	Brazil	Cross-sectional	Originally designed	430(66.3)	HTN	18–80	58.3 ± 11.7	N/A	Objectively	Student's t-tests, Pearson's $\chi 2$-test, Shapiro-Wilks, Levene, C-statistics, Poisson regression	Gender, age, physical activity, smoking, and BMI
10	Namazi Shabestari, 2016	Iran	Cross-sectional	Originally designed	264(100)	Menopausal women	≥ 40	53.98 ± 5.57	N/A	Objectively	Student's t-tests, Man-Whitney U test, Pearson's correlation, Kolomogrov-Smirnov test	Age

Table 2 (continued)

Study ID	Author, year	Country	Study design	Data source	Sample size (%F)	Specific subgroup	Age range	Age (Mean ± SD)	Follow-up (years)	LAP determination	Statistical analysis	Adjustment
11	Song, 2018	China	Cross-sectional	Originally designed	1777(57.9)		NA	Non-HTN = 60.33 ± 11.38, HTN = 62.31 ± 10.64	N/A	Objectively	Wilcoxon rank-sum test, Student's t-tests, Kruskal–Wallis H, χ2-test, Multivariate logistic regression, Statistic of Z	Age, BMI, WHtR, smoking status, family history of HTN, educational level, marital status, and family income
12	Wakabayashi, 2014	Japan	Cross-sectional	Originally designed	54,477□ (34.5)		35–70	48.5 ± 7.7	N/A	Objectively	χ2-test, Student's t-tests, ANOVA, Sheffe F test, Kruskal–Wallis H, Post-hoc test, Mann–Whitney U test, Steel–dwass, Jonckheere-terpstra, Pearson's correlation	History of smoking, alcohol drinking, regular exercise, and drug therapy for DM

Table 2 (continued)

Study ID	Author, year	Country	Study design	Data source	Sample size (%F)	Specific subgroup	Age range	Age (Mean ± SD)	Follow-up (years)	LAP determination	Statistical analysis	Adjustment
13	Wakabayashi, 2014	Japan	Cross-sectional	Originally designed	10,170(32.1)		35–40	37.5 ± 1.8(F), 37.4 ± 1.7(M)	N/A	Objectively	Mann–Whitney U test, Student's t-tests, $\chi 2$-test, Logistic regression	Age, smoking, alcohol consumption, regular exercise
14	Wang, B., 2018	China	Prospective cohort	Originally designed	11,113(61.6)		≥ 18	50 ± 9	6	Objectively	Wilcoxon rank-sum test, Cox's proportional hazards regression	Age, family history of DM, family history of HTN, education level, marital status, smoking, alcohol consumption, physical activity, SBP
15	Wang, H., 2018	China	Cross-sectional	Originally designed	11,258(54.0)		≥ 35	54	N/A	Objectively	Mann–Whitney U test, Student's t-tests, $\chi 2$-test, Linear regression	Age, race, educational status, family income, salt intake, cigarette smoking, alcohol consumption, and physical activity, FPG, eGFR, history of CVD, and any medication used

Table 2 (continued)

Study ID	Author, year	Country	Study design	Data source	Sample size (%F)	Specific subgroup	Age range	Age (Mean ± SD)	Follow-up (years)	LAP determination	Statistical analysis	Adjustment
16	Wehr, 2011	Germany	Prospective cohort	LUdwigshafen RIsk and Cardiovascular Health (LURIC) study	875(100)	Post-menopausal women (who were scheduled for coronary angiography or presenting with coronary angiography)	NA	NA	7.7	Objectively	Kolmogorov–Smirnov test, ANOVA, $\chi 2$-test	Age, BMI, DM, arterial HTN, HDL, LDL, active smoking, CRP, and lipid-lowering medication
17	Rotter, 2017	Poland	Cross-sectional	Originally designed	313(0)		50–75	61.3 ± 6.3	N/A	Objectively	Shapiro–Wilk test, Mann–Whitney U test, ANOVA, Pearson's correlation, Logistic regression, Linear regression	Age, SHBG, HOMA-IR
18	Bala, 2019	Romania	Cross-sectional	Originally designed	1730(53.4)		18–80	Non-HTN = 41.3 ± 16.2, HTN = 54.4 ± 16.0	N/A	Objectively	Student's t-tests, Mann–Whitney U test, $\chi 2$-test, Logistic regression	Age, gender, smoking, drinking, and sedentary lifestyle, eGFR, urinary sodium (spot), urinary albumin creatinine ratio

Table 2 (continued)

Study ID	Author, year	Country	Study design	Data source	Sample size (%F)	Specific subgroup	Age range	Age (Mean ± SD)	Follow-up (years)	LAP determination	Statistical analysis	Adjustment
19	Ngoc, 2019	Thailand	Cross-sectional	National Health Examination Survey 2009	15,842(52.6)		≥ 35	59.3 ± 13.2	N/A	Objectively	Student's t-tests, χ2-test, Man-Whitney U test, Linear regression	Age, living area, education background, cigarette smoking within 12 months and regular smoking, alcohol consumption, alcohol consumption level, and physical activity, log of FPG, HDL-C, and LDL-C level
20	Kahn, 2012	USA	Cohort	Third National Health and Nutrition Examination Survey	11,437(51.79)		18–64	38.1 ± 0.3	Up to 18.1	Objectively	Cox's proportional model, χ2-test	Age, black ancestry, tobacco exposure, and socioeconomic position
21	Brahimaj, 2019	Netherlands	Prospective cohort	Rotterdam study	9564(58.3)		≥ 55	65.1 ± 10.3(F), 64.3 ± 9.5(M)	6.5	Objectively	χ2 test, Cox's proportional hazards models	Age, cohort, BMI, SBP, treatment for HTN, smoking and prevalent CVD, HDL-C, TG and serum lipid-reducing agents, FPG

Table 2 (continued)

Study ID	Author, year	Country	Study design	Data source	Sample size (%F)	Specific subgroup	Age range	Age (Mean ± SD)	Follow-up (years)	LAP determination	Statistical analysis	Adjustment
22	Shi, 2018	China	Cross-sectional	Originally designed	11,478(53.8)		≥ 35	NA	N/A	Objectively	Student's t-tests, Mann–Whitney tests, $\chi 2$-test, Wilcoxon rank-sum tests	Age, race, education levels, income levels, and physical activity
23	Sun, 2019	China	Cross-sectional	Originally designed	9496(71.65)		≥ 40	55.9 ± 8.1	N/A	Objectively	$\chi 2$-test, ANOVA, Linear regression, Pearson's correlation	Age, sex, current smoking and drinking status, physical activity level, SBP, LDL-C, γ-GGT, eGFR, and antidiabetic treatment
24	Wang, 2019	China	Retrospective cohort	Originally designed	687(41.92)		NA	48.1 ± 6.2(1992), 63.1 ± 6.2(2007)	15	Objectively	Mann–Whitney U test, Student's t-tests, $\chi 2$-test, Cox's proportional regression	Age, gender, cigarette consumption, alcohol intake, log10-SBP, log10-total cholesterol, and log10-TG

Table 2 (continued)

Study ID	Author, year	Country	Study design	Data source	Sample size (%F)	Specific subgroup	Age range	Age (Mean ± SD)	Follow-up (years)	LAP determination	Statistical analysis	Adjustment
25	Yan, 2019	China	Retrospective cohort	Originally designed	4508(45.9)		> 18	42	5	Objectively	ANOVA	Baseline age, gender, race, current smoking, current alcohol drinking, and married status, baseline diagnosis of HTN, use of antihypertensive, total cholesterol, HDL, hemoglobin, creatinine, and uric acid, Baseline blood glucose, and family history of DM
26	Huang, 2019	China	Cross-sectional	Originally designed	2079(51.8)		NA	41.06	N/A	Objectively	Kruskal–Wallis H, $\chi 2$-test, Multivariate logistic regression	Age, sex, marital status and educational level, physical activity, smoker, drinker, BMI, WHR, FPG, family history of HTN
27	Tian Tian, 2020	China	Cross-sectional	National Physical Examination Project	215,651(55.86)		NA	50.02	N/A	Objectively	Pearson's $\chi 2$, Student's t-tests, Logistic regression	Age, gender, education, smoking, and alcohol consumption

Table 2 (continued)

Study ID	Author, year	Country	Study design	Data source	Sample size (%F)	Specific subgroup	Age range	Age (Mean ± SD)	Follow-up (years)	LAP determination	Statistical analysis	Adjustment
28	Xu, 2020	China	Prospective cohort	Originally designed	15,717(58.2)		> 35	52.70 ± 11.58	7.77	Objectively	Cox's proportional regression	Age, sex, smoking status, drinking status, physical activity, family history of DM, family income, and education
29	Wang, 2021	China	Cross-sectional	Chinese National Stroke Prevention Project	162,880(54.47)		≥ 40	59.24 ± 11.04	N/A	Objectively	$\chi 2$ test, two-level logistic regression model, Student's t-tests	Age, physical exercise, smoking, alcohol consumption, BMI, WC, LAP, VAI, and BAI

2hPCPG, 2 h post-challenge plasma glucose; ALT, Alanine transaminase; BAI, Body adiposity index; BMI, Body mass index; CRP, C-reactive protein; CVD, cardiovascular diseases; DBP, Diastolic blood pressure; DM, Diabetes mellitus; eGFR, Estimated glomerular filtration rate; FPG, Fasting plasma glucose; GGT, Gamma-glutamyl transferase; HDL, High-density lipoproteins; HDL-C, HDL cholesterol; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; hsCRP, high-sensitivity C-reactive protein; HTN, Hypertension; LAP, Lipid accumulation product; LDL, Low-density lipoproteins; LDL-C, LDL cholesterol; SBP, Systolic blood pressure; SHBG, Sex hormone binding globulin; TG, Triglyceride; VAI, Visceral adiposity index; WC, Waist circumference; WHR, Waist-hip ratio; WHtR, Waist-to-height ratio;

objectively, and none of them were self-report. The minimum age in the studies was 18. All of the studies were adjusted for some health-related items (e.g., age; smoking; systolic blood pressure; family history of premature CVD; diabetes; antihypertensive drug use; HDL and non-HDL cholesterol; FPG (fasting plasma glucose); 2hPCPG (2 h post-challenge plasma glucose); socioeconomic status (rural/urban setting; region; education level; family income); alcohol use; ALT; Apo-lipoprotein A1; Apo-lipoprotein B; uric acid; bilirubin, creatinine, eGFRMDRD (continuous variables); VAI; hsCRP, WC, TG, WHR, Hypolipemics, BMI, physical activity, SHBG, physical activity level, race, marriage status, eGFR, and antidiabetic treatment).

Table 3 illustrates study outcomes with their statistical measures. Study outcomes are hypertension, mortality, and diabetes. Statistical measures include OR, AUC, HR, RR, and Poisson regression.

Study quality assessment

The result of the study quality assessments is summarized in Table 4. Overall, based on the NIH criteria, 16 studies scored as good, nine studies as fair, and three studies as poor. However, we decided to include all the studies.

Mortality

Four articles studied the association of LAP with all-cause mortality [15, 24–26]. Two of them also assessed other adiposity indicators to compare their predictability power for mortality with each other [24, 26]. One of the studies showed an inverse association between LAP and all-cause mortality after adjustment [24], while the others showed positive association only in specific subgroups [15, 25, 26]. Bozorgmanesh et al. (2010) evaluated the predictive performance of LAP for all-cause mortality and compared LAP with other anthropometric measures. They assessed HR to describe the contribution of LAP to the risk of all-cause mortality for one SD increment, and LAP was in natural logarithm transformed. The results surprisingly revealed that LAP after adjustment is inversely associated with all-cause mortality, which was only statistically meaningful for males. Besides, LAP was no better predictor in comparison with other anthropometric measures [24]. Ioachimescu et al. (2010) examined the association of LAP with all-cause mortality among patients with high cardiovascular risk and compared it with BMI. They assessed HR to describe the contribution of LAP to the risk of all-cause mortality for one SD increment, and LAP was in natural logarithm transformed. The results indicated that after adjustment, LAP is significantly associated with all-cause mortality. Moreover, LAP in nondiabetic subgroups showed a statistically meaningful association with all-cause mortality, and no strong association in diabetic groups was detected. Also, the results revealed that LAP is a better predictor for all-cause mortality than BMI (8.2 vs. 5.4% mortality at 6 years) [15]. Kahn et al. (2012) compared the power of different anthropometric measures for predicting all-cause mortality in non-elderly adults. They assessed quartiles and SD for their statistical analysis. In multiple adjusted models, in black females, LAP showed a positive association with mortality at p75. In addition, Tobacco exposure in both sexes showed the highest mortality risk for LAP at p75. It is worth mentioning that in this article, considering all the results, LAP had a weak association with all-cause mortality [26]. Wehr et al. (2011) studied the association of LAP with mortality in post-menopausal women and men. They measured HR for tertile, first tertile as a reference, and HR for one SD increase in LAP. In model 1 and model 3, LAP showed a statistically significant association with all-cause mortality in post-menopausal women. However, there was no significant association between LAP and all-cause mortality in men. Moreover, they did not detect any association between BMI and all-cause mortality at all [25].

The meta-analysis was done for four studies [15, 24–26] in females and three studies in males [15, 24, 26] (Fig. 2). We found that the HR of all-cause mortality per one SD increment in LAP in females is 1.24 (95% CI [1.00–1.53]; P = 0.0463). We found a marginally non-significant heterogeneity between the four included studies ($I^2 = 50\%$, $\tau^2 = 0.0231$; P = 0.11) [15, 24–26]. Except for one study [24], others found a positive association between LAP increments and all-cause mortality in females. In the male subgroup, three studies [15, 24, 26] were included, and we found that one SD increment in LAP non-significantly increases the hazard of all-cause mortality (HR: 1.07; 95% CI [0.74–1.57]; P = 0.709); however, significant heterogeneity was detected ($I^2 = 91\%$, $\tau^2 = 0.1004$; P < 0.01). Similar to females, except for one study, others reported a positive association between LAP and all-cause mortality in males.

Hypertension

Ten studies evaluated the association of LAP with hypertension [27–36]. All of them found a positive and significant association between LAP and hypertension. All included studies measured OR for LAP. In addition, five articles also analyzed AUC for the association of anthropometric measures with hypertension [30, 32, 34–36].

For the association of LAP and hypertension, Song et al. reported the highest OR for the fourth quartile vs. The first quartile in both sexes (unadjusted OR: 6.35; 95% CI [4.39–9.12]) and for Q4 vs. Q1. Huang et al. similarly reported the highest OR for males (OR: 17.82; 95% CI (9.21–34.46]) and for females (Model 1 OR: 20.06 95% CI [11.37—35.38]) [28, 32, 34, 35]. The lowest OR for

Table 3 Reported outcomes and measures of the included studies

Study ID	Study outcome	Outcome assessment	LAP	BMI	WC	WHR	WHtR	VAI	BAI	Other
1	DM prevalence	AROC	M (20–49 years): 0.75 M(≥50 years): 0.81 F(20–49 years): 0.81 F(≥50 years): 0.72	M(20–49 years): 0.7 M(≥50 years): 0.76 F(20–49 years): 0.76 F(≥50 years): 0.65		M(20–49 years): 0.74 M(≥50 years): 0.78 F(20–49 years): 0.78 F(≥50 years): 0.68	M(20–49 years): 0.74 M(≥50 years): 0.79 F(20–49 years): 0.79 F(≥50 years): 0.68			
	DM incidence	AROC	M(20–49 years): 0.66 M(≥50 years): 0.71 F(20–49 years): 0.78 F(≥50 years): 0.65	M(20–49 years): 0.66 M(≥50 years): 0.69 F(20–49 years): 0.76 F(≥50 years): 0.63		M(20–49 years): 0.67 M(≥50 years): 0.70 F(20–49 years): 0.77 F(≥50 years): 0.64	M(20–49 years): 0.66 M(≥50 years): 0.69 F(20–49 years): 0.79 F(≥50 years): 0.65			
	DM prevalence	OR(95%CI)	M(20–49 years): 1.4[1.2–1.6] M(≥50 years): 1.5[1.3–1.8] F(20–49 years): 2.1[1.8–2.5] F(≥50 years): 1.5[1.3–1.8]	M(20–49 years): 1.3 [1.1–1.5] M(≥50 years): 1.6 [1.3–1.9] F(20–49 years): 1.6 [1.5–1.9] F(≥50 years): 1.3 [1.1–1.4]		M(20–49 years): 1.7 [1.4–2.1] M(≥50 years): 1.6 [1.3–1.9] F(20–49 years): 1.8 [1.6–2.1] F(≥50 years): 1.1 [1.0–1.3]	M(20–49 years): 1.5 [1.3–1.8] M(≥50 years): 1.6 [1.3–1.9] F(20–49 years): 1.9 [1.3–2.1] F(≥50 years): 1.3 [1.1–1.5]			
	DM incidence	OR(95%CI)	M(20–49 years): 1.7[1.2–2.5] M(≥50 years): 1.7[1.1–2.6] F(20–49 years): 2.6[1.9–3.6] F(≥50 years): 2.1[1.3–3.3]	M(20–49 years): 1.3 [0.9–1.8] M(≥50 years): 1.5 [1.0–2.2] F(20–49 years): 1.9 [1.5–2.4] F(≥50 years): 1.5 [1.1–2.1]		M(20–49 years): 1.7 [1.0–2.7] M(≥50 years): 1.5 [0.9–2.4] F(20–49 years): 2.2 [1.7–2.9] F(≥50 years): 1.6 [1.1–2.3]	M(20–49 years): 1.4 [1.0–2.1] M(≥50 years): 1.5 [1.0–2.3] F(20–49 years): 2.3 [1.8–3.0] F(≥50 years): 1.9 [1.3–2.8]			
2	All-cause mortality	HR(95% CI)	M: 0.74 [0.61–0.90] F: 0.88 [0.60–1.30]							
3	Hypertension	OR(95%CI)	M Q1: Ref Q2: 1.85 [1.23–2.79] Q3: 2.20 [1.47–3.28] Q4: 4.21 [2.78–6.38] F Q1: Ref Q2: 1.90 [1.28–2.81] Q3: 2.29 [1.56–3.36] Q4: 3.33 [2.26–4.89]	F Q1: Ref Q2: 2.06 [1.40–3.03] Q3: 2.03 [1.39–2.96] Q4: 4.51 [3.10–6.55]	F Q1: Ref Q2: NS Q3: 1.84 [1.28–2.65] Q4: 2.89 [2.03–4.13]					
4	All-cause mortality	HR(95% CI)	M: 1.38 [1.15–1.66] F: 1.61 [1.19–2.16]							
5	DM	AUC(95% CI)	0.716 [0.657–0.776]	0.667 [0.603–0.732]	0.715 [0.653–0.777]			0.707 [0.647–0.776]		
	DM development	OR(95%CI)	1.016 [1.010–1.021]	1.140 [1.079–1.205]	1.068 [1.046–1.091]			1.292 [1.133–1.474]		
6	DM	AUC(95% CI)	0.642 [0.625–0.658]					0.622 [0.605–0.639]		TyG index: 0.672 [0.656–0.687]
	DM	HR(95% CI)	1.87[1.64–2.14]					1.75 [1.55–1.96]		TyG index: 2.17 [1.92–2.45]

Table 3 (continued)

Study ID	Study outcome	Outcome assessment	LAP	BMI	WC	WHR	WHtR	VAI	BAI	Other
7	DM	AUC(95% CI)	M: 0.602 [0.586–0.618] F: 0.623 [0.607–0.637]		M: 0.579 [0.563–0.595] F: 0.576 [0.561–0.592]					TyG index M: 0.623 [0.607–0.638] F: 0.644 [0.629–0.659]
	DM incidence	OR(95%CI)	M Q1: ref Q2: 1.04 [0.79–1.36] Q3: 1.70 [1.28–2.25] Q4: 2.47 [1.82–3.34] F Q1: ref Q2: 1.26 [0.97–1.64] Q3: 1.35 [1.03–1.78] Q4: 2.44 [1.82–3.26]		M Q1: ref Q2: 1.07 [0.81–1.40] Q3: 1.35 [1.00–1.83] Q4: 1.64 [1.13–2.38] F Q1: ref Q2: 1.14 [0.88–1.48] Q3: 1.27 [0.95–1.69] Q4: 1.17 [0.83–1.65]					TyG index: M Q1: ref Q2: 1.26 [0.97–1.64] Q3: 1.82 [1.41–2.36] Q4: 2.79 [2.16–3.60] F Q1: ref Q2: 1.19 [0.91–1.55] Q3: 1.97 [1.53–2.53] Q4: 2.85 [2.22–3.66]
8	DM	AUC(95% CI)	0.77 [0.72–0.81]		0.66 [0.61–0.71]					
	DM identifying abnormalities	OR(95%CI)	3.17 [1.75–5.77]		1.33 [0.83–2.15]					
9	DM	Poisson regression (95% CI)	M Q1: 1.07 [0.47–2.41] Q2: 0.69 [0.33–1.42] Q3: 1.42 [0.85–2.37] Q4: 1 F Q1: 0.34 [0.19–0.62] Q2: 0.53 [0.34–0.82] Q3: 0.55 [0.35–0.85] Q4: 1						M(< P75): 1 M(> P75): 1.61 [1.04–2.49] F(< P75): 1 F(> P75): 0.89 [0.62–1.30]	NC: M Q1: 1 Q2: 1.07 [0.55–2.07] Q3: 1.23 [0.62–2.44] Q4: 1.44 [0.69–3.03] F Q1: 1 Q2: 1.51 [0.82–2.79] Q3: 1.67 [0.90–3.11] Q4: 3.30 [1.78–6.14]
10	Hypertension	OR(95%CI)	2.07 [1.24–3.47]							
11	Hypertension risk	AUC(95% CI)	M: 0.66 [0.62–0.69] F: 0.70 [0.67–0.73]	M: 0.61 [0.57–0.64] F: 0.63 [0.60–0.66]			M: 0.67 [0.63–0.70] F: 0.66 [0.63–0.69]			
	Hypertension risk	OR(95%CI)	Q1: ref Q2: 1.91 [1.26–2.90] Q3: 2.32 [1.44–3.74] Q4: 3.31 [1.76–6.25]							

Table 3 (continued)

Study ID	Study outcome	Outcome assessment	LAP	BMI	WC	WHR	WHtR	VAI	BAI	Other
12	DM prevalence	OR(95%CI)	M(35–39 years): 6.36 [4.11–9.82] M(40–49 years): 3.43 [2.84–4.15] M(50–59 years): 2.05 [1.81–2.34] M(60–70 years): 1.53 [1.28–1.82] F(35–39 years): 7.00 [4.44–11.04] F(40–49 years): 5.33 [4.42–6.42] F(50–59 years): 2.99 [2.63–3.40] F(60–70 years): 1.89 [1.47–2.41]							
13	DM prevalence	OR(95%CI)	M: 7.40 [5.10–10.75] F: 19.09 [6.57–55.50]							
	Hypertension	OR(95%CI)	M: 7.31 [6.20–8.62] F: 10.66 [7.77–14.63]							
14	DM	AUC(95% CI)	M: 0.653 [0.638–0.667] F: 0.693 [0.682–0.704]		M: 0.654 [0.640–0.669] F: 0.669 [0.657–0.680]			M: 0.622 [0.607–0.636] F: 0.654 [0.642–0.665]		TyG index: M: 0.625 [0.610–0.639] F: 0.669 [0.657–0.680]
	DM	HR(95% CIs)	M Q1: 1 Q2: 1.59 [0.84–3.01] Q3: 2.12 [1.15–3.91] Q4: 5.02 [2.85–8.85] F Q1: 1 Q2: 2.42 [1.23–4.74] Q3: 3.65 [1.92–6.92] Q4: 6.49 [3.48–12.12]		M Q1: 1 Q2: 1.06 [0.58–1.94] Q3: 1.49 [0.82–2.69] Q4: 4.25 [2.51–7.21] F Q1: 1 Q2: 1.74 [0.96–3.16] Q3: 1.97 [1.09–3.56] Q4: 4.07 [2.36–7.03]			M Q1: 1 Q2: 1.65 [0.94–2.89] Q3: 1.49 [0.84–2.64] Q4: 2.89 [1.72–4.87] F Q1: 1 Q2: 1.75 [0.99–3.10] Q3: 2.13 [1.22–3.74] Q4: 4.40 [2.61–7.42]		TyG index: M Q1: 1 Q2: 1.59 [0.88–2.88] Q3: 2.22 [1.27–3.88] Q4: 3.54 [2.08–6.03] F Q1: 1 Q2: 2.50 [1.36–4.60] Q3: 3.12 [1.72–5.67] Q4: 6.15 [3.48–10.85]

Table 3 (continued)

Study ID	Study outcome	Outcome assessment	LAP	BMI	WC	WHR	WHtR	VAI	BAI	Other
15	Hypertension	AUC(95% CI)	M: 0.627 [0.614–0.641] F: 0.678 [0.666–0.690]	M: 0.620 [0.607–0.634] F: 0.637 [0.625–0.649]	M: 0.638 [0.625–0.652] F: 0.655 [0.643–0.667]			M: 0.564 [0.550–0.577] F: 0.621 [0.608–0.633]	M: 0.639 [0.625–0.652] F: 0.654 [0.642–0.666]	CMI: M: 0.574 [0.560–0.587] F: 0.635 [0.622–0.647]
	Hypertension	OR(95%CI)	M Q1: ref Q2: 1.643 [1.385–1.949] Q3: 2.302 [1.934–2.741] Q4: 3.892 [3.238–4.677] per SD: 1.651 [1.503–1.813] F Q1: ref Q2: 1.562 [1.325–1.841] Q3: 2.264 [1.919–2.670] Q4: 3.548 [2.985–4.217] per SD: 1.631 [1.501–1.771]						M Q1: ref Q2: 1.673 [1.412–1.982] Q3: 2.420 [2.039–2.873] Q4: 3.288 [2.754–3.927] per SD: 1.528 [1.427–1.637] M Q1: ref Q2: 1.636 [1.390–1.926] Q3: 2.130[1.808–2.508] Q4: 3.004 [2.537–3.557] per SD: 1.555 [1.454–1.662]	CMI: M Q1: ref Q2: 1.024 [0.864–1.214] Q3: 1.420 [1.197–1.685] Q4: 2.200 [1.838–2.635] per SD: 1.310 [1.204–1.425] F Q1: ref Q2: 1.279 [1.087–1.504] Q3: 1.641 [1.394–1.932] Q4: 2.318 [1.956–2.745] per SD: 1.356 [1.259–1.459]
16	All-cause mortality	HR (95% CI)	F T1: 1 T2: 1.23 [0.82–1.84] T3: 1.43 [0.91–2.25] per SD: 1.19 [0.86–1.64]							
	DM	OR(95%CI)	M T1: 1 T2: 1.39 [1.09–1.78] T3: 2.16 [1.66–2.81] F T1: 1 T2: 2.29 [1.50–3.50] T3: 5.03 [3.21–7.89]							
17	DM	OR(95%CI)	1.012 [1.006–1.017]							
	Hypertension	OR(95%CI)	1.014 [1.007–1.020]							
18	Hypertension	OR(95%CI)	2.09 [1.60–2.73]					1.94 [1.48–2.53]		TyG index: 1.83 [1.39–2.41]

Table 3 (continued)

Study ID	Study outcome	Outcome assessment	LAP	BMI	WC	WHR	WHtR	VAI	BAI	Other
19	Hypertension	AUC(95% CI)	M: 0.632 [0.620–0.645] F: 0.646 [0.634–0.658] total: 0.636 [0.627–0.645] M(35–49 years): 0.660 [0.631–0.689] M(50–64 years) 0.665 [0.644–0.687] M(≥65) 0.647 [0.628–0.667] F(35–49 years) 0.707 [0.681–0.733] F(50–64 years) 0.646 [0.625–0.666] F(≥65 years) 0.609 [0.589–0.629] total(35–49 years): 0.681 [0.661–0.701] total(50–64 years): 0.653 [0.638–0.668] total(≥65): 0.630 [0.616–0.644]	M: 0.624 [0.611–0.637] F: 0.591 [0.579–0.604] total: 0.603 [0.594–0.612] M(35–49 years): 0.653 [0.622–0.683] M(50–64 years): 0.674 [0.652–0.695] M(≥65 years): 0.654 [0.635–0.674] F(35–49 years): 0.685 [0.657–0.712] F(50–64 years): 0.638 [0.617–0.658] F(≥65 years): 0.616 [0.597–0.636] total(35–49 years): 0.657 [0.636–0.678] total(50–64 years): 0.651 [0.636–0.666] total(≥65 years): 0.636 [0.622–0.650]	M: 0.651 [0.638–0.664] F: 0.615 [0.603–0.628] total: 0.633 [0.624–0.641] M(35–49 years): 0.660 [0.630–0.689] M(50–64 years): 0.683 [0.662–0.704] M(≥65 years): 0.658 [0.638–0.677] F(35–49 years): 0.689 [0.662–0.717] F(50–64 years): 0.632 [0.612–0.653] F(≥65 years): 0.608 [0.588–0.628] total(35–49 years): 0.677 [0.656–0.697] total(50–64 years): 0.656 [0.642–0.671] total(≥65 years): 0.632 [0.618–0.645]	M: 0.650 [0.637–0.662] F: 0.605 [0.593–0.618] total: 0.620 [0.611–0.629] M(35–49 years): 0.652 [0.622–0.681] M(50–64 years): 0.663 [0.641–0.684] M(≥65 years): 0.623 [0.604–0.643] F(35–49 years): 0.649 [0.620–0.677] F(50–64 years): 0.590 [0.569–0.612] F(≥65 years): 0.568 [0.547–0.588] total(35–49 years): 0.657 [0.637–0.677] total(50–64 years): 0.612 [0.597–0.627] total(≥65 years): 0.585 [0.570–0.599]	M: 0.658 [0.646–0.671] F: 0.632 [0.620–0.644] total: 0.640 [0.631–0.649] M(35–49 years): 0.662 [0.633–0.692] M(50–64 years): 0.680 [0.659–0.701] M(≥65 years): 0.651 [0.631–0.670] F(35–49 years): 0.686 [0.659–0.714] F(50–64 years): 0.635 [0.614–0.656] F(≥65 years): 0.610 [0.590–0.630] total(35–49 years): 0.661 [0.640–0.681] total(50–64 years): 0.653 [0.638–0.667] total(≥65 years): 0.632 [0.618–0.645]	M: 0.555 [0.542–0.569] F: 0.618 [0.606–0.630] total: 0.586 [0.577–0.595] M(35–49 years): 0.594 [0.564–0.625] M(50–64 years): 0.564 [0.542–0.587] M(≥65 years): 0.557 [0.537–0.578] F(35–49 years): 0.650 [0.622–0.677] F(50–64 years): 0.589 [0.568–0.610] F(≥65 years): 0.551 [0.531–0.572] total(35–49 years): 0.623 [0.602–0.644] total(50–64 years): 0.577 [0.562–0.593] total(≥65 years): 0.559 [0.545–0.574]	M: 0.614 [0.601–0.627] F: 0.607 [0.595–0.620] total: 0.578 [0.569–0.587] M(35–49 years): 0.618 [0.587–0.648] M(50–64 years): 0.628 [0.606–0.650] M(≥65 years): 0.617 [0.597–0.637] F(35–49 years): 0.640 [0.610–0.670] F(50–64 years): 0.616 [0.595–0.637] F(≥65 years): 0.599 [0.579–0.619] total(35–49 years): 0.560 [0.538–0.582] total(50–64 years): 0.593 [0.578–0.609] total(≥65 years): 0.597 [0.583–0.611]	CI: M: 0.649 [0.636–0.662] F: 0.614 [0.601–0.626] total: 0.630 [0.621–0.639] M(35–49 years): 0.637 [0.607–0.667] M(50–64 years): 0.646 [0.624–0.668] M(≥65 years): 0.617 [0.597–0.637] F(35–49 years): 0.624 [0.594–0.654] F(50–64 years): 0.588 [0.567–0.610] F(≥65 years): 0.556 [0.535–0.576] total(35–49 years): 0.634 [0.614–0.655] total(50–64 years): 0.614 [0.599–0.629] total(≥65 years): 0.584 [0.570–0.599]
	Hypertension	OR(95%CI)	Q1: 1 ref Q2: 1.804 [1.621–2.008] Q3: 2.704 [2.425–3.015] Q4: 4.251 [3.792–4.765] per SD: 1.602 [1.535–1.671] cutoff > 24.44: 2.461 [2.277–2.660]		Q1: 1 ref Q2: 1.527 [1.375–1.697] Q3: 2.289 [2.060–2.544] Q4: 3.742 [3.355–4.174] per SD: 1.688 [1.623–1.756] cutoff > 81.58: 2.360 [2.191–2.542]		Q1: 1 ref Q2: 1.616 [1.453–1.797] Q3: 2.343 [2.105–2.607] Q4: 3.525 [3.162–3.931] per SD: 1.629 [1.567–1.694] cutoff > 0.52: 2.170 [2.016–2.336]			CI: Q1: 1 ref Q2: 1.251 [1.129–1.387] Q3: 1.705 [1.540–1.888] Q4: 2.140 [1.929–2.373] per SD: 1.343 [1.293–1.394] cutoff > 1.21: 1.693 [1.576–1.818]

Table 3 (continued)

Study ID	Study outcome	Outcome assessment	LAP	BMI	WC	WHR	WHtR	VAI	BAI	Other
20	All-cause mortality	HR(95%CI)	M per SD linear: 1.22 [0.95–1.55] M(at p25): 1.03 [0.72–1.49] M(at p75): 1.11 [0.66–1.85] F per SD linear: 1.27 [1.02–1.57] F(at p25): 1.26 [0.75–2.15] F(at p75): 1.48 [0.90–2.43]							
21	DM incidence	HR(95% CI)	F: 1.08 [0.93- 1.26] M: 0.96 [0.81- 1.15]							
22	discriminate DM	AUC(95% CI)	F: 0.717 [0.706–0.729] M: 0.683 [0.670–0.696]							
23	DM prevalence	AUC(95% CI)	0.658 [0.645–0.671]							
24	DM incidence	HR(95% CI)	univariate per SD: 2.16 [1.65–2.84] Q1: 1 ref Q2: 1.11 [0.45–2.74] Q3: 1.71 [0.75–3.91] Q4: 4.98 [2.42–10.26] multivariate per SD: 2.06 [1.56–2.73] Q1: 1 ref Q2: 1.17 [0.47–2.89] Q3: 1.66 [0.72–3.83] Q4: 4.70 [2.20–9.952]							
25	DM incidence	RR(95% CI)	T1: (< 12.7): ref T2: (12.7 ≤ ~ < 29.3): 1.03 (0.52–2.03) T3: (≥ 29.3):1.91 (0.97–3.74)							
26	Hypertension	AUC(95% CI)	M: 0.677 [0.640–0.713] F: 0.721 [0.680–0.761]	M: 0.707 [0.672–0.742] F: 0.698 [0.658–0.737]	M: 0.734 [0.700–0.769] F: 0.725 [0.686–0.766]					
	Hypertension	OR(95% CI)	M Q1: ref Q2: 1.61 [0.89–2.94] Q3: 1.75 [0.94–3.26] Q4: 2.79 [1.43–5.44] F Q1: ref Q2: 1.015 [0.51–2.03] Q3: 1.19 [0.60–2.38] Q4: 3.15 [1.56–6.39]							

Table 3 (continued)

Study ID	Study outcome	Outcome assessment	LAP	BMI	WC	WHR	WHtR	VAI	BAI	Other
27	DM prevalence	AUC(95% CI)	total: 0.655 [0.652–0.658] M: 0.625 [0.621–0.630] F: 0.679 [0.674–0.684]	total: 0.604 [0.600–0.607] M: 0.580 [0.576–0.586] F: 0.618 [0.614–0.623]						
	DM prevalence	COR(95%CI)	Q1: ref Q2: 1.28 [1.22–1.34] Q3: 1.86 [1.78–1.95] Q4: 4.67 [4.49–4.86]							
	DM prevalence	AOR(95%CI)	Q1: ref Q2: 0.97 [0.92–1.02] Q3: 1.28 [1.23–1.34] Q4: 3.24 [3.11–3.37]							
28	DM incidence	HR(95% CI)	total Q1: ref Q2: 1.169 [0.857–1.595] Q3: 2.903 [2.226–3.784] Q4: 6.298 [4.911–8.077] M Q1: ref Q2: 1.123 [0.719–1.752] Q3: 1.839 [1.230–2.748] Q4: 4.773 [3.324–6.854] F Q1: ref Q2: 1.633 [1.073–2.485] Q3: 4.150 [2.865–6.013] Q4: 8.063 [5.645–11.516]							
29	Hypertension	OR(95%CI)	Total: 1.289 [1.275–1.303] M: 1.316 [1.294–1.338] F: 1.294 [1.266–1.313]	Total: 1.539 [1.514–1.566] M: 1.439 [1.413–1.465] F: 1.510 [1.479–1.543]	Total: 1.389 [1.372–1.406] M: 1.733 [1.685–1.782] F: 1.435 [1.413–1.459]			Total: 1.146 [1.133–1.159 M: 1.141 [1.120–1.162] F: 1.131 [1.115–1.147]	Total: 1.317 [1.301–1.333] M: 1.297 [1.271–1.323] F: 1.343 [1.322–1.365]	
		AUC(95%CI)	Total: 0.679 [0.675–0.683] M: 0.670 [0.666–0.674] F: 0.688 [0.684–0.691]	Total: 0.695 [0.690–0.699] M: 0.679 [0.675–0.683] F: 0.709 [0.706–0.713]	Total: 0.696 [0.693–0.700] M: 0.693 [0.689–0.696] F: 0.698 [0.695–0.702]			Total: 0.654 [0.650–0.658] M: 0.645 [0.641–0.649] F: 0.662 [0.659–0.666]	Total: 0.675 [0.672–0.679] M: 0.661 [0.658–0.665] F: 0.689 [0.679–0.693]	

95%CI, 95% confidence interval; AOR, adjusted odds ratio; AUC, area under receiver operating characteristic curve; BAI, body adipose index; BMI, body mass index; CI, conicity index; CMI, cardiometabolic index; COR, crude odds ratio; DM, diabetes mellitus; F, female; HR, hazard ratios; LAP, lipid accumulation product; M, male; NC, neck circumference; OR, odds ratio; Q, quartile; T, tertile; TyG, triglyceride-glucose; VAI, visceral adiposity index; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio;

Table 4 Quality assessment of the included studies

Study ID Criteria	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
1. Was the research question or objective in this paper clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Was the study population clearly specified and defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Was the participation rate of eligible persons at least 50%?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table 4 (continued)

Study ID Criteria	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
5. Was a sample size justification, power description, or variance and effect estimates provided?	NR	No	No	No	NR	NR	NR	NR	Yes	NR	No	NR	NR	NR	Yes	NR	No	No	No	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	Yes	Yes	No	Yes	No	Yes	Yes	No	No	No	No	No	No	Yes	No	Yes	No	No	No	Yes	Yes	No	No	Yes	Yes	No	No	Yes	No
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	Yes	Yes	No	CD	No	Yes	Yes	No	No	No	No	No	No	Yes	No	Yes	No	No	No	Yes	Yes	No	No	Yes	Yes	No	No	Yes	No

Table 4 (continued)

Study ID Criteria	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
10. Was the exposure(s) assessed more than once over time?	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	Yes	No	No	No	No	No

Table 4 (continued)

Study ID Criteria	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
12. Were the outcome assessors blinded to the exposure status of participants?	NR	NR	NA	NR	NR	NR	NR	NR	NR	NA	NA	NR	NA	NR	NA	NR	CD	NA	NA	NR	NR	NR	NR	NR	NR	NR	NR	NR	Yes
13. Was loss to follow-up after baseline 20% or less?	No	Yes	NA	Yes	Yes	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes	No	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	No	Yes	Yes	Yes	Yes	CD	CD	No	Yes	No	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Result: Study Quality	Fair	Good	Fair	Good	Poor	Good	Good	Fair	Good	Poor	Good	Fair	Fair	Fair	Good	Good	Poor	Good	Good	Good	Good	Good	Good	Fair	Good	Fair	Fair	Good	Good

*CD, Cannot determine; NA, Not applicable; NR, Not reported

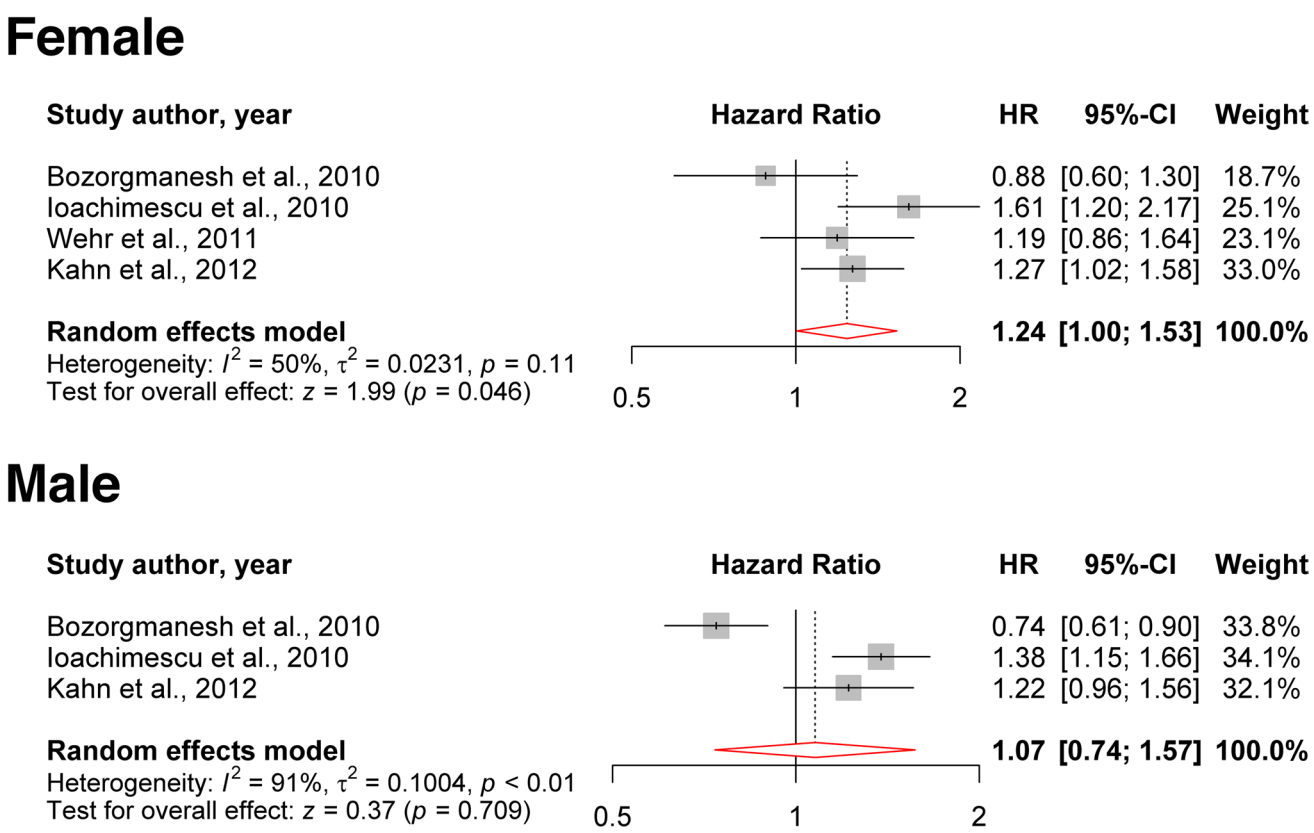

Fig. 2 The HR of all-cause mortality per one SD increment of LAP in females and males

Q4 vs. Q1, for the association of LAP with hypertension, was reported by Huang et al. for males (Model 3 OR: 2.79; 95% CI [1.43—5.44]) and females (Model 3 OR: 3.15; 95% CI [1.56—6.39]) [35]. Ngoc et al. reported the lowest OR for 1 SD increase in both sexes (Model 3 OR: 1.602; 95% CI [1.535–1.671]). Ngoc et al. also analyzed AUC in each sex and different age subgroups. They reported the highest AUC for 35–49 years old females (AUC: 0.707; 95% CI [0.681–0.733]) and the lowest AUC for over 65 females (AUC:0.609; 95% CI [0.589–0.629]) [30]. Although the results of Gao (2013) et al. (in males) and Song (2018) et al. (in both sexes) studies indicated that LAP has a stronger association with hypertension in comparison to BMI, Bala et al. (2019) revealed that LAP has no better power than BMI and WC [27, 28, 32]. Song (2018) et al. demonstrated that LAP is a stronger index for hypertension than WHtR in females [32]. However, Ngoc (2019) et al. indicated that WHtR has a stronger association with hypertension (AUC: 0.640 95% CI [0.631– 0.649]) in comparison with other anthropometric measures (BMI, WC, WHR, VAI, BAI, CI, LAP) and LAP (AUC: 0.636; 95% CI [0.627–0.645]) is the second strong index in association with hypertension [30]. Moreover, another study revealed that LAP is a stronger index for hypertension than WC and VAI in females [34]. It is also worth mentioning that Song et al. found an association between LAP and hypertension family history [32].

Except for two papers, the others had a good or fair quality based on our quality assessment. Considering all the included papers, LAP is an appropriate predictor of hypertension in both males and females, but it seems that it has better predictability for hypertension in females compared with males. Additionally, most studies reported that LAP is a better predictor of hypertension than other anthropometric measures in at least one sex. LAP also has interactive effects with smoking and a family history of hypertension.

Diabetes mellitus

Eighteen articles assessed the association of LAP with incidence or prevalence of T2DM, and all of them revealed that LAP has a significantly positive association with T2DM [3, 25, 33, 37–51], with the exception of one study which demonstrated that LAP has a statistically meaningful association with diabetes only in hypertensive female groups [51]. The lowest OR for the association of LAP with the prevalence of diabetes was 1.012 (95% CI [1.006–1.017]) [43]. Lee et al. reported the lowest OR for Q4 vs. Q1 for females (adjusted OR: 2.44; 95% CI [1.82–3.26]) and males

(adjusted OR: 2.47; 95% CI [1.82–3.34]) [41]. Wakabayashi et al. reported the highest OR in the prevalence of diabetes in females (adjusted OR:19.09; 95% CI [6.57–55.50]) [33]. Wakabayashi et al. and Bozorgmanesh et al. assessed the association of LAP with the prevalence of diabetes in specific age subgroups. In both studies, ORs were highest in the youngest age sub-groups in females. The OR for females in the first study is 7.00 (95% CI: 4.44–11.04) and 2.1 (95% CI: 1.8–2.5) in the latter. Also, OR in males was higher in younger age subgroups in the first study (crude OR: 6.85; 95% CI [4.45–10.56]) [37, 46]. Five studies evaluated HR for predicting diabetes with LAP [38, 40, 47, 48, 50]. The lowest HR in males and females was 0.96 (Model 5; 95% CI [0.81, 1.15]) and 9.058 (unadjusted; 95% CI [6.377–12.867]), respectively [38, 50]. In AUC analysis, the highest AUC for incidence of diabetes in females was 0.78 in the 20–49 years old age sub-group, and the highest prevalence of diabetes in males was 0.81 in the ≥ 50 years old age sub-group [37]. Three studies compared anthropometric measures with each other, and all of them revealed that the triglyceride glucose (TyG) index is the strongest index for predicting diabetes [38, 40, 41]. Seven articles found that LAP has a stronger association with diabetes in females in comparison with males [25, 33, 38, 42, 44, 46, 48]. Four articles reported that LAP is a stronger index than WC in association with diabetes, whereas Kavaric et al. analyses suggest that LAP and VAI are not better than WC and HDL-c, and Wang B et al. reported that AUC for LAP and WC is similar [39, 41, 44, 45, 47, 48]. Different articles reported that LAP has a stronger association with the incidence or prevalence of diabetes in comparison to HOMA-IR, BMI, CMI, BAI, VAI, WHtR, and WHR [42, 44, 45]. Meanwhile, it is worth mentioning that Bozorgmanesh et al. suggested that LAP is only better for the prevalence of diabetes in females in comparison to BMI, WHtR, and WHpR. In contrast to BMI, WHR, and WHtR, LAP showed only a statistically stronger positive association with the incidence and prevalence of diabetes in males in compere to BMI [37].

Except for two studies, the others had good or fair quality based on our quality assessment. Considering all the studies, LAP is positively and significantly associated with the incidence and prevalence of T2DM. It appears that LAP is a better predictor of T2DM in females than males. Most of the studies confirm the superiority of LAP over traditional anthropometric measures, such as BMI and WC, in predicting T2DM.

Discussion

This systematic review evaluated the predictability of LAP for T2DM, hypertension, and all-cause mortality. We also conducted a meta-analysis on the correlation of LAP with all-cause mortality. Our result showed that LAP is an appropriate predictor of all-cause mortality, hypertension, and T2DM with different predictabilities per sex. Most of the studies reported higher predictability measures for LAP in females in comparison with males. Although there are contradictory findings regarding the superiority of LAP over traditional anthropometric measures, evidence shows that LAP could be a better predictor of hypertension and T2DM than other indices like BMI, WC, CMI, etc. LAP could be used as an inexpensive method to determine the risk of developing T2DM and hypertension.

The ability of LAP to predict T2DM and hypertension has several reasons. LAP considers both anatomic and physiologic changes since it has WC and TG in its formula. LAP is an indicator of visceral adipose tissue which is correlated with insulin resistance [50]. Therefore, LAP as a predictor of insulin resistance is associated with the development of T2DM [50]. "Ectopic" lipid accumulation (e.g., liver, blood vessels, and heart) alters the metabolism of the human body. Insulin resistance as a result can lead to the development of T2DM [11]. TG in the LAP formula is an independent risk factor for T2DM [3]. Moreover, LAP is also a good indicator of hypertension. As mentioned before, TG, and therefore LAP, is associated with visceral adipose tissue that has more harmful effects than subcutaneous fat tissue. Adipocytokines secreted from adipose tissue can alter endothelial cells, consequently increasing the risk of hypertension [28, 32]. Considering both abdominal fat and visceral fat tissues in its formula, LAP can be a strong predictor of T2DM and hypertension.

Our findings suggested that LAP is significantly associated with all-cause mortality in females; however, it failed to reach statistical significance in males. As mentioned before, LAP can predict many diseases, such as T2DM, insulin resistance, metabolic syndrome, hypertension, cardiovascular diseases, and chronic kidney disease [25, 52, 53]. Considering the fact that people with higher LAP have an increased risk of developing metabolic disorders and cardiovascular disease, the association of LAP with all-cause mortality could be explained [15, 25]. Different predictability power of LAP for males and females could be explained by different patterns of lipid over-accumulation in each sex with aging [15] and scarcity of data on the association between LAP and all-cause mortality.

The higher strength of LAP in predicting T2DM and hypertension than BMI, WC, etc., can have several explanations. Unlike LAP, the traditional anthropometric measures like BMI and WC only assess obesity, and they are unable to distinguish between visceral adipose tissue and subcutaneous adiposity tissue. Visceral adipose tissue is more harmful than subcutaneous tissue. Thus, fat distribution plays an important role in the risk of diseases, such as hypertension and T2DM [30, 49, 50]. Also, BMI is unable to differentiate between adipose tissue and

lean mass. For instance, there are some patients with high LAP that still have a normal BMI. TG and WC are both independent risk factors for T2DM and hypertension. Combining TG and WC in the LAP formula can increase our insight regarding the fat distribution of the patients and the risk of developing diabetes or hypertension [30, 49, 50]. Since LAP considers both, it can be a better predictor for T2DM and hypertension in comparison with common anthropometric measures.

Discrepancies in the prediction power of LAP and different cut-off values could be due to the differences in the mean age, ethnicity of the study population, or sample size between the included articles. Additionally, most of the studies reported a stronger association of LAP with T2DM and hypertension in females than males [30, 35, 50, 54], but there are other studies that had different results [28, 32]. The outperformance of traditional anthropometric measures by LAP has been proved in several studies [32, 45, 55] but not all of them [56–58]. Different TG levels, WC, sample size, ethnicity, disease status, and confounding bias could explain the contradictory findings.

To the best of our knowledge, our study is the first systematic review and meta-analysis on the association of LAP with hypertension and all-cause mortality. We have compared the prediction power of LAP for T2DM, hypertension, and all-cause mortality by sex and age. Another strength of our study is the comparison of LAP with other anthropometric measures. However, our study has several limitations. Due to different cut-off values, we were unable to conduct a meta-analysis on T2DM and hypertension papers. Studies had a different adjusted model that complicates the pooling of studies. Some of the included studies had poor quality, and we cannot ignore the probability of confounding bias or poor methodology. Moreover, some of the studies were conducted on populations with a specific condition, such as post-menopausal women, which may call for caution in generalizing the findings of this study. Besides, most of the LAP measurements were done once in the follow-up years. Not all the studies had reported the predictability measures by sex.

Conclusion

In conclusion, LAP is associated with all-cause mortality, T2DM, and hypertension. The result of the meta-analysis showed that LAP is directly correlated with all-cause mortality in females; however, this association was not significant in males, probably due to scarcity of data. LAP is positively associated with T2DM and hypertension. Most of the studies showed that LAP is a better predictor of T2DM and hypertension in comparison to traditional anthropometric measures, such as BMI, WC, and WHR, especially in females. Overall, LAP has a higher prognostic significance in females compared to males. It also has interactive effects with smoking and a family history of hypertension. LAP is a cheap method to determine the risk of chronic diseases, such as hypertension, T2DM, or cardiovascular diseases. Different cut-off values in studies complicate using LAP in population-level health surveillance. Therefore, further studies are required to determine specific cut-off values for sexes, age sub-groups, and different populations.

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Author Contributions SK was responsible for designing the review protocol, screening eligible studies, extracting data, and writing the primary draft. HT was responsible for designing the review protocol, writing the review protocol, screening the eligible studies, extracting data, and writing the draft. AA was responsible for designing the review protocol, conducting meta-analysis, interpreting results, and writing the draft. YR was responsible for conducting meta-analysis, interpreting results, and writing the draft. HA contributed to designing the review protocol and revising the draft. AV was responsible for designing the review protocol, conceptualization, revising the draft and providing feedback on the review. All the authors approved the final version of the manuscript.

Data availability All data generated or analyzed during this study are included in this published article and its supplementary information files.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication Not applicable.

Conflicts of interest The authors have no competing interests to declare that are relevant to the content of this article.

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