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Original Article

Microparticle levels after exercises in healthy and obese individuals: A systematic review and meta-analysis

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Abstract

Aim: Microparticles (MPs) are 0.1-1 µm vesicles linked to endothelial dysfunction, particularly in obese and hypertensive patients. As exercise is suggested to reduce circulating MPs, this systematic review and meta-analysis evaluated MP level changes in healthy and obese individuals after physical exercise interventions.

Material and Methods: Following PRISMA guidelines, a systematic search (2000-2024) was conducted across five major databases. Inclusion criteria covered studies (RCTs, cohorts, retrospectives) documenting MP expression in healthy or obese individuals post-exercise. A random-effects model was applied for heterogeneous data (I2 > 50%).

Results: Thirteen observational studies (n=335) were included in the quantitative analysis. A pooled analysis of all MP types across the entire population showed no statistically significant change after exercise (p=0.36). However, subgroup analysis revealed a critical difference: healthy participants showed a significant decrease in MP levels post-exercise (p=0.009).

Conclusion: Physical exercise significantly reduces endothelial microparticles in healthy individuals, a change associated with improved vascular function. In contrast, this adaptive response appears attenuated in obese individuals, suggesting their metabolic status decreases vasculogenic reactivity.

Keywords: Microparticle, exercise, healthy and obese subjects

INTRODUCTION

Microparticles (MPs) are diverse diminutive membranous vesicular entities that arise from a multitude of cellular origins. They are characterized by the absence of a nucleus and exhibit a size range of 0.1 to 1 micrometer [1]. Microparticles are endowed with membrane-associated proteins that are a reflection of their progenitor cells. Although virtually all cellular types have the capacity to release these structures, the majority of investigative efforts have been directed towards microparticles derived from platelets, leukocytes, and endothelial cells. The quantification of endothelial microparticles (EMPs) present in circulating blood serves as an indicator of the in vivo condition of the endothelium, with these microparticles being evaluated via specific antibodies in conjunction with flow cytometry methodologies. The process of MP release is prompted by events such as cellular activation, injury, stress, or as a consequence of cellular apoptosis or necrosis [2].

Numerous empirical investigations have substantiated that physical exercise influences platelet functionality, the interaction between platelets and leukocytes, hemostasis, and fibrinolytic

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processes. Scholarly research suggests an association between the engagement in exercise and the incidence of cardiovascular events, often exhibiting an insufficient differentiation among the distinct modalities of exercise undertaken. The duration and intensity of physical activity are the principal determinants that characterize a specific type of exercise; consequently, more meticulous delineations of the particular exercise intervention are warranted [3].

Platelet-derived microparticles (Plt-MPs) constitute the predominant circulating microparticle population, accounting for 70-90% of the total. Exocytosis involves the production of vesicles through the budding of the plasma membrane. Following their release, MPs contain proteins characteristic of their originating cells and facilitate the transport of various enzymes, RNA, and miRNA. Many studies reveal phosphatidylserine on their external leaflet (Annexin V+) [4-6].

Recent studies suggest that exercise is a powerful behavioral strategy for lowering circulating microparticle levels. However, the mechanisms underlying this reduction remain poorly understood, and current knowledge is still in its early stages. Findings across studies are not entirely consistent, highlighting the need for further clarification. Based on the literature reviewed, we propose that exercise generates distinct physiological stimuli capable of influencing angiogenesis and driving mitochondrial remodeling within adipose tissue [6-8].

This systematic review and meta-analysis aim to analyze microparticle level of platelet, neutrophil, and monocyte in patients who exercise regularly. Our secondary objective is to analyze microparticle level in healthy subjects after exercise and microparticle level in obese individuals after exercise. In vascular surgery, the release of microparticles (MPs) from blood cells is an important consideration, as it may influence both intraoperative processes and postoperative outcomes. These small vesicles, shed by red blood cells, platelets, and endothelial cells, play active roles in regulating coagulation, inflammation, and endothelial function.

MATERIAL AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were utilized to conduct this meta-analysis. A systematic search was conducted across PubMed, SCOPUS, EuropePMC, ProQuest, and Cochrane Central Databases using the search terms “Microparticle” or “MPs” or “Platelet” or “Endothelial Dysfunction” or “Flowcytometry” “Granulocyte” or “Monocyte” AND “Exercise” or “Exercise Sessions,” AND “Obesity”, or “Healthy” focusing on publications from the year 2000 to 2024. Duplicate results were removed. Only abstract studies and studies not using English were also excluded. The remaining articles were independently screened for relevance based on their abstracts by all authors. The full text of the selected abstracts was thoroughly reviewed, and those meeting our criteria were included in the study. The final selection of studies was determined by the consensus of all investigators. If disagreements occurred, the solution was solved through consensus among all authors. Ethical approval is not necessary for this article as we only made secondary data analysis. Methodological variability was not assessed in this study as MPs expression was the main objective in this analysis.

Ethics committee approval is not necesseray as our meta-analysis use secondary data and approved by faculty policy.

Article eligibility and selection

The titles and abstracts of the retrieved articles underwent a meticulous examination to ascertain their potential relevance and eligibility for inclusion in the review. For an article to be considered for inclusion, it was required to satisfy stringent criteria, as delineated in Table 1, with the search and inclusion parameters predominantly focusing on published studies that document microparticle expression in individuals classified as healthy or patients possessing the capability to engage in physical exercise. Additionally, pre-printed materials and grey literature journals were incorporated into the scope of this search.

The results of the conducted searches were systematically compared to discern any common findings; subsequently, the six authors undertook a re-evaluation of the unmatched results to ascertain their adherence to the established inclusion eligibility criteria. No further instances of discord among the physicians were noted. In cases of any disagreement, the pertinent articles would have been excluded from the analytical framework. Among the articles identified as conforming to the selection criteria, complete versions or pre-proof journals were employed for the purpose of data analysis, and an ancillary search of the cited references was performed to guarantee the inclusion of all pertinent publications. This systematic review exclusively encompassed articles that were authored or translated into the English language. The searches were executed during the period from January 2000 to December 2024.

Data Appraisal and Extraction

The information derived from the designated publication encompassed: the methodological framework and results, the total number of participants, the duration of follow-up during the intervention, details regarding microparticles, and the results of the procedures conducted. A tabular representation was employed wherein each piece of information was articulated in a descriptive manner (Table 2).

Quality Assessment

The quality of the investigations was independently evaluated by the authors using the Risk of Bias (RoB) tool in Robvis [9]. Each study was assessed for risk of bias across four domains: patient selection, index test, reference standard, and study flow/timing. The potential for bias was carefully examined through a thorough

review of the articles and discussed before assigning scores. Any discrepancies in the quality assessment were resolved through discussions among all authors.

Statistical Analysis

A meta-analysis was performed utilizing Review Manager (RevMan) version 5.4 and Comprehensive Meta-Analysis (CMA) version 3.3 for all statistical evaluations. The presence of heterogeneity was considered significant with a p-value falling below 0.05, and its extent was regarded as substantial when I2 surpassed 50%. A random-effects model was adopted for the examination of heterogeneous data; conversely, a fixed-effects model was applied when the data were homogeneous. Dichotomous variables were evaluated through the Mantel-Haenszel statistical technique, with the risk ratio (RR) serving as the summary statistic, and these findings were presented in conjunction with 95% confidence intervals (CI). Heterogeneity assessment was shown in the forest plot analysis. Funnel plots were utilized to evaluate the potential for publication bias.

RESULTS

Characteristics of the studies included

A preliminary search identified 602 potentially relevant papers, with 320 excluded at the outset due to duplication. Following the initial review of titles and abstracts, 254 papers were excluded. Following a comprehensive full-text review, 15 additional papers were excluded, including 13 studies in this systematic review and meta-analysis (Figure 2).

Table 1 presents the baseline characteristics, methods of microparticle examination, and outcomes of the included studies. Sixteen publications were included, all categorized as observation studies (evidence level II-III). Authors of each study examined microparticles under different parameters, but few assessed the impact of microparticles on endothelial cells. A total of 335 participants were included across all studies, with the highest number of patients being 75. All studies were checked for risk of bias (Figure 1) and NOS score in Table 1.

The attributes of all 13 studies are delineated in Table 1. A total of 335 participants were incorporated into the analysis, and the gathered data was employed for evaluation purposes. The primary methodology utilized for the detection of microparticles (MPs) was flow cytometry, as referenced in sources [8,10-22]. Conversely, a singular study employed the enzyme-linked immunosorbent assay (ELISA) for the detection of MPs, as indicated in reference [14] which was excluded. The CD62+ antigen, recognized as a marker of platelet degranulation, is the most extensively studied microparticle, while CD34 serves as the predominant microparticle examined in endothelial contexts. The parameters pertaining to centrifugal conditions, sample dosage, antibody concentrations, and the measurement units for MPs exhibited variability across the studies. Further specifics are provided in Table 1.

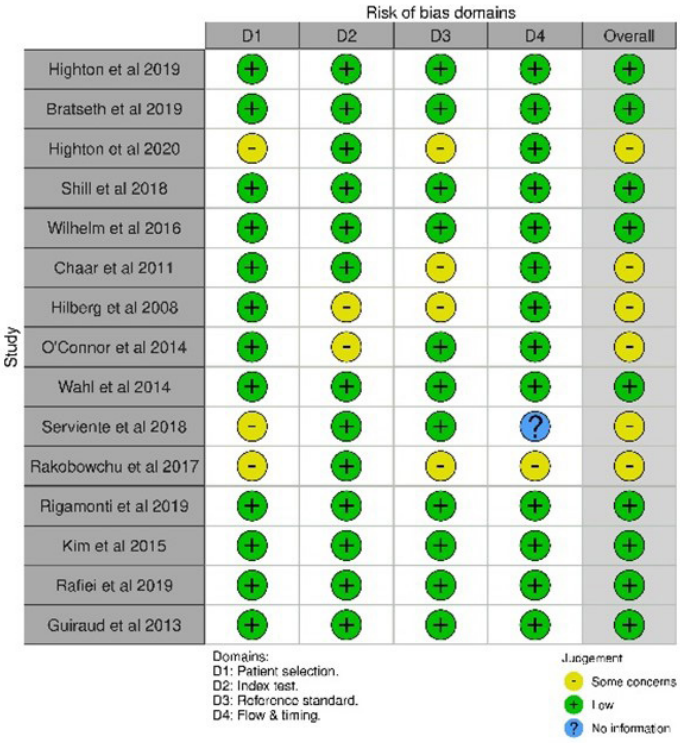

Figure 1. Risk of bias which comprehends all studies. No studies have a high concern of publication

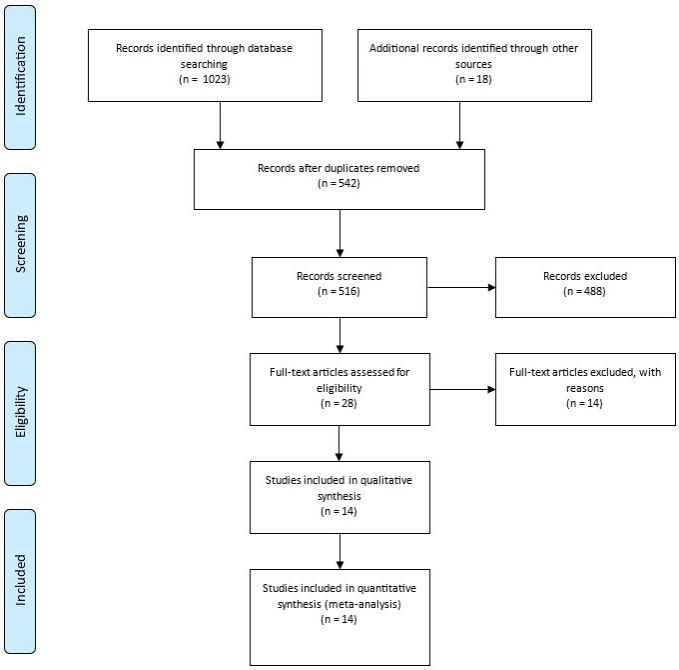

Figure 2. PRISMA flow diagram for the included studies and exclusion of other studies

Table 1. Article inclusion and exclusion criteria

Description	Inclusion Criteria	Exclusion Criteria
	Randomized controlled trial, cohort, retrospective, or descriptive study providing microparticle data in healthy or obese individual or with comorbid which do not delay the exercise.	Microparticle data is not clear enough or not using standard method of examination. Patient had comorbid which delay or did not finish the particular exercise protocol
Types of studies	All evidence levels, including safety data were acceptable for safety analysis inclusion.	**a.** Reviews, editorials, opinions, case reports, case series, comments, and correspondence lacking original data are excluded from consideration **b.** Non-clinical investigations, encompassing experimental, animal, or in vitro studies, are similarly excluded **c.** Clinical trials characterized by significant quality deficiencies and elevated potential for bias were omitted from efficacy assessment; however, they may be incorporated into safety evaluations
Age (per year)	Patients (irrespective of age, sex or race)	Patients with severe clinical condition or comorbid which can affect the microparticle data such as hematologic disease
Types of intervention	Exercise therapy	**a.** Exercise is less than 24 hours observation
Types of comparators	Obesity or patient with comorbid disease	
Types of Efficacy Outcome Measures	Could include (but not limited to): **a.** Microparticle regarding endothelial, granulocyte, monocyte, or platelet **b.** Combination of microparticle with acceptable methodology of review	
Safety Outcome Measures	Could include (but not limited to): Qualitative and quantitative assessment of microparticle before and after exercise	

Microparticle Analysis

To test the exercise effect on circulating microparticle, we included 9 studies that examined the microparticle with CD62+ expression. Microparticles were examined using flow cytometry with similar events in every study. Not all the studies reviewed all types of microparticles. Four studies examined neutrophil microparticles; seven studies examined monocyte microparticles; subgroup analysis was conducted within endothelial microparticles between healthy and obese subjects. All data were heterogeneous, with I2 > 50%, and we used random effect to determine the significance of the mean difference. The pooled analysis of all cell types across both obese and non-obese populations showed a non-significant reduction in microparticle levels ($p = 0.36$; 95% CI: −2.27 to −0.80) (Figure 3). However, when each subtype was analyzed individually combining data from obese and non-obese participants, platelet-, neutrophil-, and monocyte-derived microparticles showed no significant change in levels before and after exercise (Figure 4).

Subgroup for microparticle analysis

A subgroup analysis was conducted to compare the effects of exercise on microparticle levels in healthy versus obese individuals. In healthy participants, microparticle levels decreased significantly ($p = 0.009$; 95% CI: −7.87 to −1.12). In contrast, data for obese participants limited to two studies assessing endothelial microparticles showed no significant change (Figure 5).

Publication Bias

Figure 5 illustrates the funnel plot derived from the analysis of endothelial microparticles conducted in the present study. A potential bias in publication regarding mortality was identified, as several studies were found to lie outside the 95% confidence interval (CI) of the funnel plot. A potential source of bias in this analysis is the notably higher microparticle levels reported in the studies by Rafiei, Shill, and O'Connor compared with other included studies. This discrepancy, coupled with the larger standard deviations observed in these studies, may have influenced the overall results, which are still acceptable for analysis [10-12].

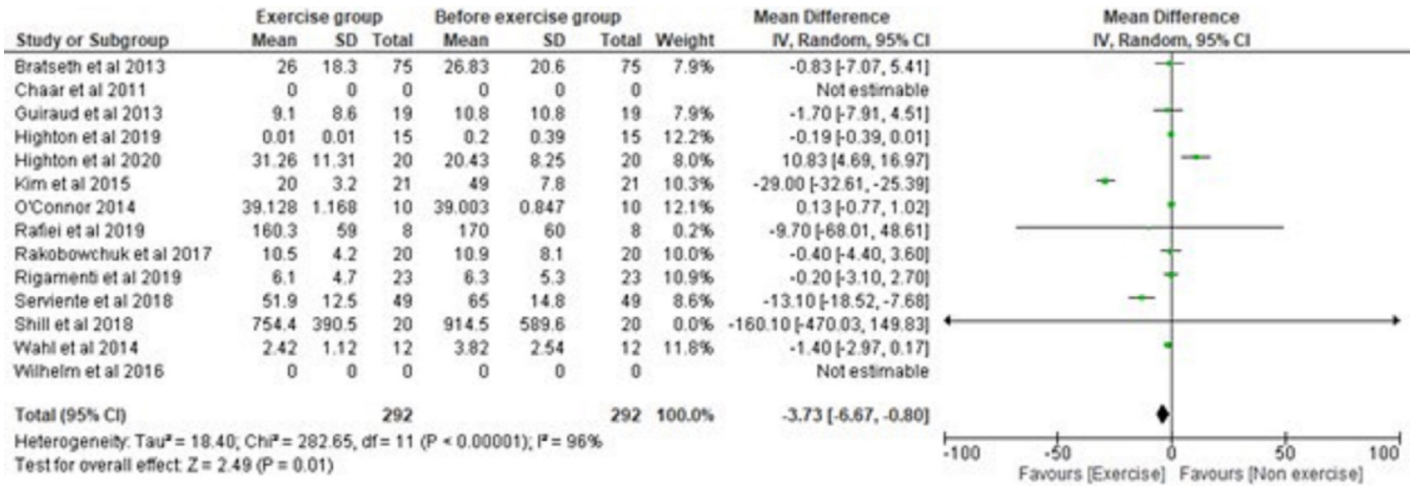

Figure 3. Microparticle forest plot of endothelial before and after exercise in all populations

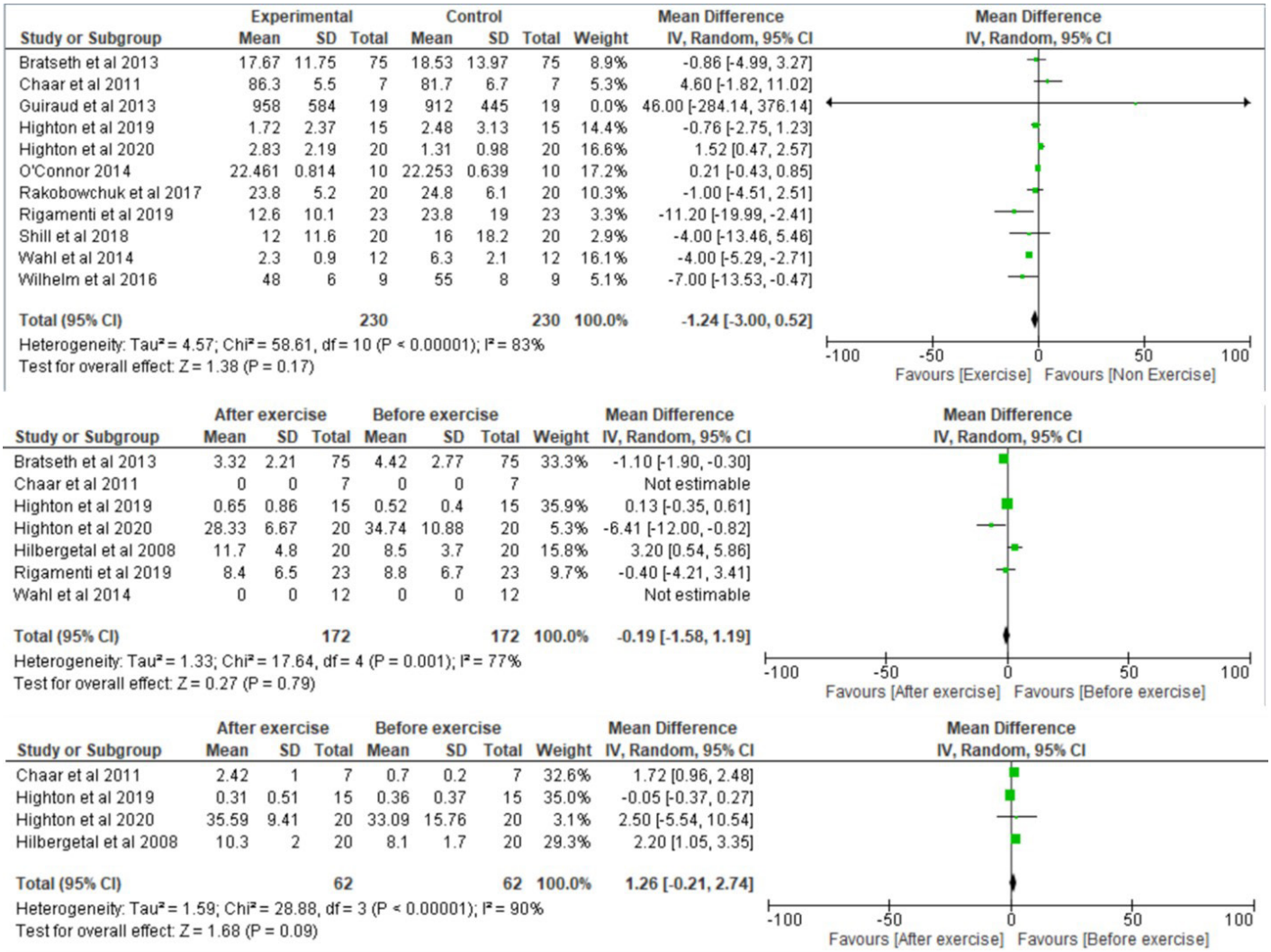

Figure 4. Microparticle forest plot of platelet (a), neutrophil (b), and monocyte (c) before and after exercise

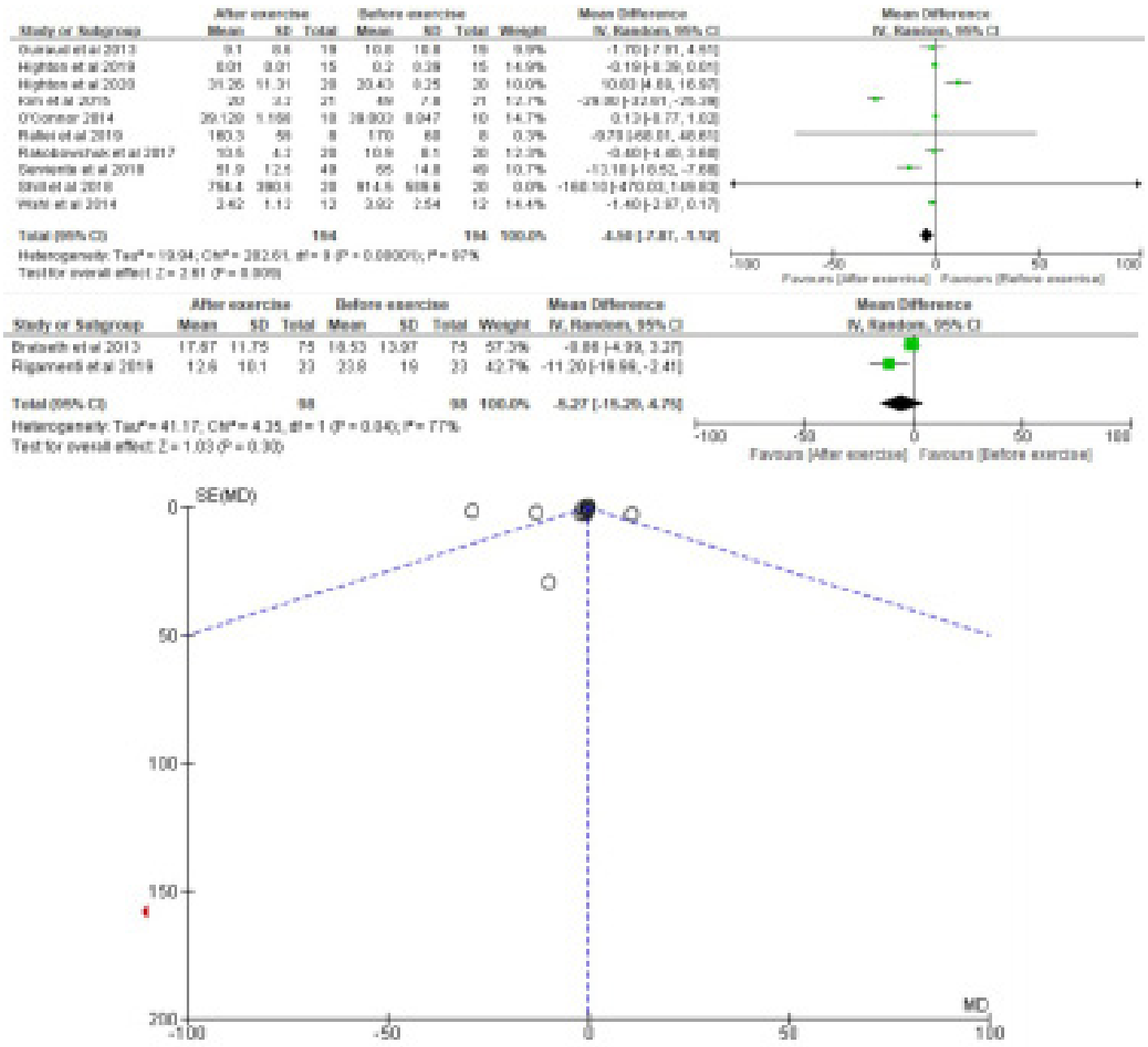

Figure 5. Microparticle forest plot of endothelial in healthy individual (a) and obese individual (b) before and after exercise (c) funnel plot study on endothelial microparticle analysis

DISCUSSION

This meta-analysis is the first to combine available evidence on how exercise influences circulating microparticles, particularly in healthy versus obese individuals. Across 13 studies, we found a consistent reduction in the microparticles after exercise in healthy participants, but little to no change in obese participants. This contrast suggests that metabolic health status plays a significant role in vascular responsiveness to exercise. This finding supports the potential role of MPs as biomarkers for early endothelial dysfunction [10-12].

From a methodological perspective, flow cytometry offers high-resolution profiles of particle-size distribution as well as concentration assessments of microparticles (count/ml in plasma), which may influence the outcomes. The ELISA technique was referenced in only a single investigation, potentially impacting the results. ELISA provides more sensitive

Table 2. Characteristics of the studies related microparticles

Author and Year	Study Design	Country	Quality Score	Characteristic of participant	Age (mean)	N	Study Design	Microparticle examination	Outcome
Highton et al, 2019[10]	Cohort Study	United Kingdom	8	Adult male (>18 years old) which can run continuously for 60 minutes in moderate intensity of 70% maximum oxygen intake.	22.9 ± 3.3	15 participants	Participants engaged in one exercise session and one control trial, with a minimum interval of 5 days, utilizing a randomized crossover design.	The total quantifiable microvesicle (MP) population (0.3-1.0 µm) was evaluated (n = 15) by size gating and phosphatidylserine (PS) expression (An-V+) to ascertain the quantity of MP that were Annexin-V positive.	Running resulted in a notable decrease in %TF+ platelet and neutrophil microparticles, indicating a temporary reduction in cardiovascular risk through less TF-stimulated thrombosis.
Bratseth et al, 2019[11]	Randomized Controlled Trial	Norway	8	75 participants from the EXCADI cohort of 137 individuals with coronary artery disease and type 2 diabetes participated in exercise training.	63.3 ± 5.6	25 vs 50	The exercise intervention comprised a 12-month integrated aerobic and resistance training regimen. The overall exercise volume was 150 minutes per week, comprising two group-based sessions of 60 minutes each.	Microparticles were detected and quantified according to their binding to AV+ and their reactivity to cell-specific monoclonal antibodies.	Patients with concurrent coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM) exhibited significantly elevated levels of circulating endothelial-derived microvesicles and circulating MVs
Highton et al, 2020[8]	Case-Control	USA	8	Patient with renal function decrease without dyalisis and healthy people.	54.8±16.3 for renal patient, 52.2±16.2 for healthy patients	20	Participants executed the incremental shuttle walk test: The distance attained influenced the velocity at which they would finish the 20-minute endurance shuttle walk test.	Leukocyte subsets, MP characteristics, and TF expression were examined. The MP flow cytometry gating approach encompasses T lymphocyte (CD3+, CD4+/−, CD8+/−) and monocyte (CD14+/−, CD16+/−) subsets.	The expression of MP TF has been associated with thrombus formation, and circulating TF+ platelet-derived microparticles may contribute to thrombosis in patients with end-stage renal illness. Consequently, the decrease in the proportion of TF+ MPs signifies a positive impact of exercise.

Table 2. Characteristics of the studies related microparticles

Shill et al, 2018[12]	Descriptive study	Georgia	8	Healthy men and women between the ages of 18 and 40 years were recruited.	23.6 ± 4.45	20	Patients perform three bouts of acute exercise at different intensities.	Alterations in CD62E+ microparticles generated by exercise are both sex-specific and dependent on intensity. The variations in circulating CD62E+ and CD34+ microparticle concentrations in response to exercise are contingent upon intensity, differ by sex, and are not consistent among microparticle types.	Moderate intensity exercises reduces CD62E+ MPs immediately after exercise.
Wilhelm et al, 2016[13]	Descriptive study	United Kingdom	8	Nine healthy young participants (height 1.79 ± 0.03 m, weight 80.5 ± 4 kg, maximum oxygen uptake (V̇o2max) 3.3 ± 0.2 l/min) successfully completed all five visits.	25 ± 1	9	The exercise trials were conducted in a randomized sequence. In the moderate-intensity exercise trial (MI), participants engaged in 60 minutes of cycling at 80% of the work rate relative to their first ventilatory threshold (VT1), followed by a recovery period of 180 minutes. Conversely, in the heavy exercise intensity trial (HI), participants cycled at a work rate equivalent to VT1 plus 30% of the difference between their individual work rate at VT1 and their maximum oxygen uptake (V̇o2max).	Microparticle quantification involves anti-human CD62E [E-selectin] and PE/Cy5 anti-human CD41 [integrin-α2b] fluorescent antibodies.	There is a significant increase in circulating plasma microvesicles (PMVs) during intense physical exercise, and these exercise-derived microvesicles promote the stimulation of human endothelial cells by augmenting angiogenesis and cellular proliferation.

Table 2. Characteristics of the studies related microparticles

Chaar et al, 2011[14]	Descriptive study	France	8	Seven male healthy subjects	19.8 ± 0.4 yrs	7	All participants were instructed to refrain from physical activity for a minimum of two days prior to the commencement of the program. All exercise tests were conducted between 8 AM and 11 AM. The pedaling speed was maintained consistently at 70 rpm over the testing period. The assessment comprised three successive maximal ramp exercise tests, each followed by a 10-minute recovery period, which included 5 minutes of light cycling and 5 minutes of rest	The cellular origin of microparticles was determined using phycoerythrin (PE)-conjugated particular monoclonal antibodies (MoAbs). MoAbs-PE, comprising anti-CD235a-PE (glycophorin A, clone 11E4B-7-6, IgG1), anti-CD41 (GPIIb, clone P2, IgG1), anti-CD15 (LewisR, clone 80H5, IgM), anti-CD14 (LPS receptor, clone RM052, IgG2a), and anti-CD106 (VCAM1, clone 5110C9, IgG2a), were employed to evaluate microparticles derived from RBCs, platelets, PMNs, monocytes, and endothelial cells, respectively.	Intense exercise induces the formation of microparticles generated from platelets and polymorphonuclear leukocytes, perhaps indicating the activation of these two cell types.
Hilberg et al, 2008[15]	Descriptive study	German	8	20 healthy subjects	25 ± 3 yrs	20	One to two weeks prior to the test program, all subjects underwent an incremental graded exercise on a cycle ergometer (step test, commencing at 50 W, with a 25 W increase every 3 minutes until volitional exhaustion) to assess peak oxygen consumption (VO2 peak).	The direct immunofluorescence approach was employed to assess alterations in platelet activity and their response to agonists: anti-CD62P-FITC (clone CLB-Thromb/6), anti-CD41-PE (clone P2), anti-CD14-ECD (clone RM052), and anti-CD45-PC5 (clone J33).	Moderate exercise resulted in heightened platelet reactivity and the production of platelet-leukocyte conjugates. The alterations in conjugate formation were markedly less pronounced than those observed during severe exercise.

Table 2. Characteristics of the studies related microparticles

O;Connor et al, 2014[16]	Case control study	Ireland	8	10 healthy subjects or subjects without limitation prior to exercise	21.6 ± 1.0 yr	10	Exercise sessions lasted 60 minutes and incorporated aerobic activity along with resistance training. Sessions began with a 10-minute warm-up at a low exercise level, followed by 40 minutes at moderate intensity.	Endothelial microparticles were characterized as CD31+/CD41a- and CD62E+, while platelet microparticles were identified as CD41a+ and CD31+/CD41a+.	Aerobic exercise training for 14 consecutive days elicits a significant increase in aerobic fitness. Circulating EMPs decrease 13 h following training. Endothelial function is significantly improved and circulating MPs are unchanged in men and women with CVD
Wahl et al, 2014[17]	Descriptive study	Germany	8	Twelve healthy, non-smoking male triathletes and cyclists	24.7 ± 3.4	12	The step test involved cycling at a minimum of 80 rpm, beginning with a workload of 100 W for 5 minutes, followed by incremental increases of 40 W every 5 minutes until the participant reached volitional exhaustion.	To determine EMP, monocytic microparticles (MMP), and platelet-derived microparticles (PMP), 8 mL of heparinized blood was collected at baseline, and at 0, 60, and 180 minutes. Extracellular microparticles (EMPs) were quantified (number/µl) via flow cytometry following the staining of platelet-poor plasma with cell surface markers. Events that were positive for Annexin-V and CD31, and negative for CD42b, were categorized as EMPs. Refer to the detailed information provided. Events that tested positive for Annexin-V, CD31, and CD42b were categorized as PMP, while those positive for Annexin-V, CD14, and CD16 were categorized as MMP.	Physical exercise results in reduced EMP levels and facilitates a phosphatidylserine-dependent uptake of EMP into target endothelial cells, correlating with enhanced protection of these cells against apoptosis.

Table 2. Characteristics of the studies related microparticles

Serviente et al, 2018[18]	Cohort study	United States of America	7	The study involved healthy, habitually active women aged 40 to 65 years. Participants were classified according to menopausal status based on the STRAW+10 guidelines.	45 - 60 years old differ in categoric menopausal	49	Participants were directed to choose either a brisk walking pace or a comfortable jogging pace. The incline was elevated by 2% every 2 minutes, with speed adjusted as required, until volitional fatigue was reached. Heart rate and rhythm were continuously monitored using a 12-lead ECG	CD31+/42b− and CD62E+ EMPs were identified utilizing fluorescent minus one gating strategies. Total events per microliter of plasma were determined using established protocols for CountBright beads, and the proportion of EMP events relative to total MP events (EMP%) was calculated.	Moderate-intensity exercise effectively reduces CD62E+ and CD31+/42b− endothelial microparticles, along with total microparticles, in healthy midlife women. These effects manifested regardless of variations in menopausal status and fitness levels.
Rakobowchuk et al, 2017[13]	Cohort study	Canada	8	Nine out of twelve healthy male participants provided adequate quality data (ultrasound images) for the complete protocol in the study.	29.2 ± 6.1 years	20	Twelve healthy males participated in two experimental sessions, engaging in either 45 minutes of eccentric or concentric cycling at a matched aerobic power output below the ventilatory threshold.	Objects within the specified size threshold were gated based on SSC intensity in relation to PE/Cy5 mean fluorescence intensity for CD41+ or PE mean fluorescence intensity for CD62E+.	Eccentric endurance exercise resulted in macrovascular endothelial dysfunction; however, the absence of endothelial activation, as indicated by endothelial microvesicles, suggests that this form of exercise may induce oxidative stress without causing significant endothelial damage. The rise in platelet microvesicle concentrations may promote advantageous microvascular adaptations, as indicated by prior studies

Table 2. Characteristics of the studies related microparticles

Rigamonti et al, 2019[19]	Cohort study	Italy	8	Obese individuals (BMI > 40 kg/m2) hospitalized in Italy were recruited for this study to participate in a multidisciplinary integrated program for body weight reduction. Healthy subjects of normal weight, matched for age, were recruited from among the friends and relatives of the medical and nursing staff to serve as the control group.	21.2 ± 8.8 years	15 vs 8	Each participant engaged in an incremental treadmill exercise protocol until reaching voluntary exhaustion. Specifically, following a 3-minute rest period, subjects walked for 2 minutes at a speed of 4 km/h on a 0% incline. This was succeeded by incremental increases in speed of 0.5 km/h per minute until a maximum of 6 km/h was achieved. Additionally, slope increments of 1% were introduced each minute, reaching a maximum of 15% incline.	CD14-APC (clone TUK4) is utilized for identifying monocyte/macrophage-derived extracellular vesicles (EVs), CD105-APC (clone 43A4E1) for total endothelium-derived EVs, CD62E (clone REA280) for activated endothelium-derived EVs, and CD61-APC (clone Y2/51) for platelet-derived EVs.	An acute exercise session influences the release of extracellular vesicles in circulation, which are specific to tissue type, sex, and body mass index, indicating that the benefits associated with exercise may rely on a complex interplay of tissue, endocrine, and metabolic factors.
Kim et al, 2015[20]	Cohort study	United states of America	8	Male and female subjects were recruited based on specific inclusion criteria: a sedentary lifestyle (defined as engaging in regular aerobic exercise less than two days per week), non-smoking status, absence of lipid-lowering medication, blood pressure below 160/100 mmHg, body mass index below 40 kg/m², and no history of diabetes, cardiovascular, liver, kidney, or lung disease.	52.1 ± 1.4 years	21	Qualified subjects engaged in a supervised aerobic exercise training session three times per week for a duration of six months. Each exercise session comprised 40 minutes of aerobic activity at an intensity of 65% of the individually predicted maximal heart rate.	Total and activated microparticles from endothelial cells were characterized as CD62E+ and CD31+/CD42a−, respectively, with vesicle sizes of less than 1.0 μm. A logarithmic scale was applied to the forward scatter signal, side scatter signal, and each fluorescent channel	After a 6-month supervised aerobic exercise training program, circulating levels of total (CD31+/CD42a−) and activated (CD62E+) microparticles released by endothelial cells were significantly reduced by approximately 40% in individuals with prehypertension.

Table 2. Characteristics of the studies related microparticles

Rafiei et al, 2019[21]	Cohort study	Canada	8	Women classified as inactive, determined through a standard seven-day physical activity recall interview conducted during screening, are defined as engaging in fewer than two 30-minute sessions of moderate-to-vigorous physical activity per week and are at an increased risk of developing type 2 diabetes (T2D).	48.9 ± 10.7 years	8 vs 7	Both groups completed baseline testing, followed by a 10-session exercise training intervention, with post-testing occurring approximately 48-72 hours after the final training session. The healthy control group underwent only baseline testing, which was the same as that of the intervention groups.	Extracellular microvesicles (EMPs) were evaluated in platelet-poor plasma collected from an EDTA tube, following two consecutive centrifugation steps at 1550 g, utilizing the upper two-thirds of plasma after each spin. Flow cytometry was utilized to assess CD62E+ and CD31+/CD42b− EMPs.	Two weeks of high-intensity training and medium-intensity training are comparably effective in reducing glycaemic variability and CD62E+ EMPs in overweight or obese women at increased risk of type 2 diabetes.
Guiraud et al, 2013[22]	Cohort study	Canada	7	Male patients with coronary heart disease participated in a randomized study involving a single session of high-intensity exercise characterized by 15-second intervals at 100% of peak power output, interspersed with 15-second passive recovery periods, as well as an isocaloric medium-intensity session.	62 ± 11 years	19	High intensity and medium intensity protocol not mentioned	Extracellular microparticles (EMPs) are characterized as particles with a diameter less than 0.9 mm, exhibiting negativity for CD42b and positivity for either CD31 (EMP31), CD62E (EMP62E), or both markers. PMPs are characterized as particles with a diameter less than 0.9 mm that exhibit positivity for CD42b.	A single high-intensity session featuring brief exercise and passive recovery periods seems to be safe and does not alter markers of endothelial function.

A: Healthy patient; B:comparator such as diseased patient; MP: Microparticle; CD: Cluster of differentiation; N/A, not available

quantification compared with flow cytometry, which detects microparticles using antibody-coated beads and may yield different measurement values. This variation can influence the interpretation of results in a meta-analysis. We did exclude the study using ELISA because the number of available studies on microparticles within the scope of this systematic review and meta-analysis was limited [14].

Our findings expand on earlier single-centre studies that have reported mixed results. While some reported increases in microparticles after acute exercise, others observed reductions or no change at all. By pooling data, we show a more coherent pattern: in healthy individuals, exercise appears to enhance vascular homeostasis, potentially by stimulating uptake of EMPs by endothelial cells, protecting them from apoptosis, and improving nitric oxide-mediated vasodilation. The blunted response seen in obese participants may reflect chronic low-grade inflammation, endothelial dysfunction, or altered shear stress signaling, all of which are common in obesity. These mechanisms could explain why obese individuals do not gain the same microparticle-mediated vascular benefits from exercise as their healthy counterparts. This difference is a key addition to the literature, highlighting the need for tailored exercise strategies in populations with metabolic risk [3,13,14].

Apoptosis experiments indicated a decrease in target cell apoptosis following treatment with serum obtained post-exercise, relative to pre-exercise condition. However, serum collected after physical exercise did not influence endothelial target cells' migration capacities compared to pre-exercise conditions. Both conditions, pre and post-exercise, significantly enhanced endothelial cell migration. The notable induction of migration in both groups may obscure potential differences between them. [2,15] In theoretical frameworks, microparticles are liberated by activated monocytes, lymphocytes, granulocytes, or platelets, thereby facilitating the detection of microparticle remnants. Engaging in aerobic exercise augments the magnitude of unidirectional laminar flow while concurrently mitigating the presence of disturbed or turbulent flow that manifests in specific arterial configurations, including bifurcations, branch points, and curvatures. The stimuli associated with the formation of microparticles from endothelial cells encompass reactive oxygen species, elevated glucose levels, angiotensin II, hypertension, along with pro-inflammatory and pro-coagulant factors prevalent in peripheral arterial disease [14]. This suggests microparticle analysis can be obtained for early detection of inflammation marker and evaluation of exercises.

Despite contradicting findings, obese individuals often demonstrate elevated plasma levels of MPs at rest, roughly tenfold higher than those of normal-weight individuals, with size profile indicating that exosomes constitute 20% and microvesicles 80% of the MPs. The post-exercise vesiculogenic reactivity in obese individuals may be less compared to their normal-weight counterparts, attributable to unidentified metabolic variables [16,17].

Our pooled analysis did not reveal clear, consistent patterns for neutrophil-, platelet-, and monocyte-derived microparticles after exercise, suggesting that the effects of physical activity on these subtypes are more complex, variable, or subtle than those observed for endothelial microparticles. This complexity becomes particularly relevant when comparing healthy and obese individuals, as our results indicate potential differences in how these groups respond at the microparticle level. In obesity, microparticle responses may be altered or blunted, possibly reflecting underlying endothelial dysfunction, chronic inflammation, or metabolic disturbances. If confirmed, these differences could have important implications for understanding how obesity modifies the systemic effects of exercise, especially in pathways involving inflammation, coagulation, vascular health, and cell-to-cell communication processes in which microparticles play a pivotal role.

After exercise, both obese and healthy individuals show changes in microparticle (MP) levels. Obese individuals generally have higher baseline MP levels and often respond differently to exercise compared to healthy counterparts. In healthy subjects, exercise tends to improve endothelial function and may lower certain MP levels. In contrast, obese individuals may exhibit a blunted response, although some studies report exercise-related reductions in specific MP types, such as CD105+ and CD62+ MPs, suggesting possible improvements in endothelial health. The outcomes appear to vary depending on exercise type, duration, and individual characteristics, underscoring the complex interplay between obesity, exercise, and MP responses [20,21].

In healthy adults, a single session of moderate-intensity continuous exercise reduces endothelial microparticles. Serviente et al. demonstrated significant decreases in $CD62E^{+}$ (activated EMPs), $CD31^{+}/CD42b^{-}$ (apoptotic EMPs), and total MPs after approximately 45 minutes of moderate cycling or walking, regardless of menopausal status or baseline fitness. These results support the view that moderate aerobic exercise can transiently alleviate endothelial activation and apoptosis in otherwise healthy vasculature [22,23].

In individuals with obesity, however, the response is more heterogeneous. Moderate treadmill or cycling protocols often produce immediate, cell-specific shifts in extracellular vesicles and MPs, with obese participants showing higher baseline levels and distinct recovery kinetics which involve platelet- and monocyte-derived MPs. This pattern suggests altered sensitivity of MP release pathways in obesity. Although study methodologies differ, the overall evidence indicates that MICE can reduce certain activated EMP subtypes in obese individuals, but the magnitude and timing of these effects are generally less

pronounced compared with healthy counterparts [22].

There are several limitations to this meta-analysis. First, all studies are not randomized and do not have the same protocol of exercise and examination timing of microparticles, which may affect the results of concentrations of microparticles. Second, the type, frequency, duration, and intensity of exercise, together with sex, age, and training status of subjects, exerted a multifaceted influence on outcomes, and every study has a different model of exercise either moderate intensity or high intensity. Third, we cannot do subgroup analysis in MP related neutrophil, platelet, and monocyte in obese and healthy subject individually due to limited data from the studies. Furthermore, the methodology for studying MPs required additional enhancement and similar method.

CONCLUSION

This study demonstrate that exercise significantly reduces endothelial microparticles in healthy individuals, a change linked to improved vascular function. In contrast, the response is attenuated in obese individuals, suggesting reduced vasculogenic reactivity. These findings position MPs as promising biomarkers for monitoring vascular adaptation to exercise and point to the importance of metabolic health in achieving optimal vascular benefits. Future research should focus on standardizing microparticle measurement and exploring targeted interventions to restore endothelial responsiveness in obesity.

Ethics Committee Approval: Ethics committee approval is not necesseray as our meta-analysis use secondary data and approved by faculty policy.

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