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Original Article

Association of Monocyte Chemotactic Protein-1 and Dickkopf-1 with Body Composition and Physical Performance in Community-Dwelling Older Adults in Singapore

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Abstract

Objective: We aim to determine the association of monocyte chemotactic protein-1 (MCP-1) and dickkopft-1 (DKK-1) as potential biomarkers that may predict changes in body composition and physical performance in healthy older adults from Singapore. **Methods**: Two-hundred community-dwelling older adults (mean age: 67.9 years; 68.5% females) were classified into elevated versus non-elevated groups based on quintile cut-offs of MCP-1 and DKK-1 levels (156.02 pg/mL and 606.31 pg/mL, respectively). Multiple linear regression was performed to examine the relationship between MCP-1 and DKK-1 with body composition and physical performance, adjusted for age, gender and ethnicity. **Results**: MCP-1 was significantly associated with higher fat mass, fat mass index, percentage body fat, waist circumference and trunk-limb ratio for fat mass (all p<0.01), and repeated chair stand (p=0.004). DKK-1 was not associated with body composition and physical performance measures. Utilising the Asian Working Group for Sarcopenia (AWGS) 2019 criteria, there were 39 (19.5%) sarcopenia and 161 (80.5%) non-sarcopenia participants respectively, with MCP-1 levels significantly higher in sarcopenia compared with non-sarcopenia (p=0.046), but not for DKK-1 (p=0.525). **Conclusions**: Elevated MCP-1 are associated with changes in fat composition, physical performance and sarcopenia, suggesting its usefulness in identifying at-risk group with sarcopenic obesity.

Keywords: Body composition, Dickkopf-1, Monocyte chemotactic protein-1, Sarcopenia, Sarcopenic obesity

Introduction

Ageing leads to numerous physiological changes in muscle, fat and bone tissue. One such geriatric syndrome is sarcopenia, which is the progressive and generalised loss of muscle mass and function with advancing age[1]. With increased age, skeletal muscle fibre size and number decreases linearly at a rate of 3-5% per decade, accelerating up to 30-40% after the fifth decade of life[2]. Reduced strength, aerobic capacity and impaired functional capacity are resultant effects leading to adverse outcomes such

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as falls, disability, impaired quality of life and mortality[3]. Sarcopenia contributes to poor quality of life in older adults and increases social and health care costs[4].

With increasing recognition of its public health impact, sarcopenia was inaugurated as an independent condition with an International Classification of Diseases-10 code in 2016[5]. The impact of sarcopenia is expected to be even more significant in Asian countries due to rapid population aging and the rising prevalence of non-communicable chronic diseases with changes in lifestyle, diet and physical activity[6,7]. In a study of 3000 older Chinese with type II diabetes mellitus, it was found that they had lower muscle mass and weaker physical strength than African-American or Caucasians of the same age[8]. Moreover, body composition changes that occur with aging can lead to sarcopenic obesity, an emerging worldwide phenomenon that has been described as the confluence of two public health crises, namely the obesity epidemic and population aging[9].

Sarcopenia is a multi-factorial condition whose onset and progression are dependent on mechanisms that disrupt the normal physiology of skeletal muscles[10]. It is influenced not only by contemporaneous risk factors but also by genetic and lifestyle factors across the life course[11]. While the molecular and cellular aspects of the age-associated disease remain unclear, factors such as advancing age, underlying inflammation, endocrine dysfunction, chronic diseases, insulin resistance, nutritional deficiencies, cigarette smoking and physical inactivity are key contributors to the disease[3,12,13].

There is increasing interest in the pathogenesis role of various immune pathways through which an equilibrium between catabolic and anabolic processes in muscle homeostasis is maintained. Monocyte chemotactic protein 1 (MCP-1) is a proinflammatory cytokine secreted by adipocytes and adipose tissue leukocytes[14]. MCP-1 is one of the key chemokines that regulate migration and infiltration of leukocytes to inflammatory sites[15]. In addition, MCP-1 plays a role in "inflammaging", characterized by low-grade, chronic, systemic inflammation due to ageing[16]. The inflammatory state mediated by MCP-1 has been associated with skeletal muscle and bone loss[17]. Exposure of muscle tissue to physiologic concentrations of MCP-1 has been observed to induce insulin resistance, leading to impairment of glucose uptake which may similarly affect muscle contractility[18]. Dickkopf-1 (DKK-1) is a protein-coding gene that antagonizes Wnt/β-catenin signalling pathway through the reduction of β-catenin, and play an important role in regulating cell proliferation, cell fate determination and apoptosis. Elevated DKK-1 activity is implicated in osteoporosis, arthritis, and malignancy and possibly sarcopenia[19]. In this study, we aim to examine the association of MCP-1 and DKK-1 with body composition changes and physical performance in a cohort of functionally independent, community-dwelling older adults. A secondary objective is to compare the levels of MCP-1 and DKK-1 between sarcopenic and non-sarcopenic participants.

Methods

Study population

This retrospective study was conducted in 200 community-dwelling adults aged between 51 to 93 years who were generally healthy, independent in activities of daily living, and cognitively intact. These participants were recruited as part of a longitudinal cohort study (GeriLABS: Longitudinal Assessment of Biomarkers for characterisation of early Sarcopenia and predicting Frailty and Functional Decline in community-dwelling Asian older adults Study) at the Tan Tock Seng Hospital, Singapore. The study was approved by the Domain Specific Review Board (DSRB) of the National Healthcare Group (NHG) and informed written consent was obtained from each participant.

Inclusion and exclusion criteria

Subjects were included if they were (i) aged 51 to 93 years at study enrolment, (ii) community-dwelling, and (iii) independent in both basic and instrumental activities of daily living (ADLs).

Participants were excluded if they had cognitive impairment (prior diagnosis of dementia or modified Chinese version of Mini-Mental State Examination (CMMSE) score ≤21)[20], unable to walk 8 metres (m) independently, or were living in a long-term residential care facility. Participants with central nervous conditions, presence of any active neuropsychiatric conditions producing disability, history of inflammatory conditions, or current use of immune-suppressants were also excluded.

Determination of body composition and biomarker levels

Body composition measures were obtained via dual energy X-ray absorptiometry (DXA) (Discovery™ APEX 13.3; Hologic, Bedford, MA, USA), and performed by trained radiographers (Department of Diagnostic Radiology, Tan Tock Seng Hospital) in accordance with the advice provided in the International Society of Clinical Densitometry Adult Official Positions 2015[21]. A weekly automatic calibration was performed for Body Composition in compliance with the manufacturer's guidelines and with the supplied phantom from the manufacturer (Hologic). Variables obtained from DXA include appendicular lean mass, fat mass, percentage body fat and trunk to limb fat ratio. We assessed muscle strength via maximal reading of hand grip strength from 2 trials per hand using a hydraulic hand dynamometer (North Coast Medical, Inc, Gilroy, CA, USA), and knee extension strength was measured using an electronic push/pull dynamometer (BASELINE - model 12-0342). Physical performance was assessed using the Short Physical Performance Battery (SPPB), which comprises the three components of balance, 3-m usual gait speed and 5-times repeated chair stand. Serum levels of DKK-1 (R&D Systems, Minneapolis, MN, USA), and MCP-1 (BD

Baseline Characteristics							
Variables	Overall (n=200)	Normal DKK-1 (n= 160)	Elevated DKK-1 [a] (n= 40)	*P*-value	Normal MCP-1 (n=160)	Elevated MCP-1 [a] (n=40)	*P*-value
Age (years)	67.9±7.9	67.8±7.7	68.6±8.7	0.478	67.8±7.8	68.7±8.2	0.524
Male, n (%)	63 (31.5)	49 (30.6)	14 (35.0)	0.594	54 (33.8)	9 (22.5)	0.238
Chinese ethnicity, n (%)	184 (92)	147 (91.9)	37 (92.5)	1.000	152 (95)	32 (80)	0.005 [b]
Serum Vitamin D (ng/mL)	29.37±9.60	29.4±9.29	29.2±10.9	0.209	29.56±9.85	28.86±8.67	0.645
C-reactive protein (mg/L)	1.00 (0.40-1.80)	0.90 (0.40-1.50)	1.10 (0.40-3.00)	0.058	1.00 (0.40-1.70)	1.00 (0.43-2.28)	0.435
Body composition							
Appendicular Lean Mass (kg)	14.23 ± 3.33	14.22 ± 3.40	14.19 ± 3.06	0.698	14.32 ± 3.41	13.81 ± 2.99	0.389
Appendicular Lean Mass Index (kg/m^2)	5.69 ± 0.98	5.66 ± 0.99	5.77 ± 0.94	0.954	5.71 ± 1.00	5.58 ± 0.88	0.432
Fat Mass (kg)	21.32 ± 6.34	21.43 ± 6.35	20.58 ± 6.34	0.894	20.71 ± 6.26	23.46 ± 6.24	0.014 [b]
Fat Mass Index (kg/m^2)	8.64 ± 2.70	8.66 ± 2.63	8.54 ± 2.98	0.487	8.40 ± 2.67	9.58 ± 2.62	0.013 [b]
Body Mass Index (kg/m^2)	23.89 ± 3.72	23.80 ± 3.63	24.00 ± 4.12	0.209	23.70 ± 6.36	24.70 ± 6.94	0.136
Percentage Body Fat (%)	36.57 ± 6.94	36.78 ± 6.89	35.77 ± 7.16	0.635	35.93 ± 6.94	39.15 ± 6.36	0.008 [b]
% Fat Trunk/% Fat Leg	1.06 ± 0.20	1.07 ± 0.21	1.05 ± 0.14	0.421	1.06 ± 0.19	1.07 ± 0.23	0.852
Trunk/Limb Fat Mass Ratio	1.26 ± 0.28	1.26 ± 0.30	1.22 ± 0.22	0.288	1.24 ± 0.28	1.32 ± 0.29	0.102
Waist circumference(cm)	86.49 ± 9.05	86.20 ± 8.98	87.73 ± 9.36	0.521	85.73 ± 9.02	89.58 ± 8.61	0.016 [b]
Physical performance							
Knee-extension strength (kg)	38.65 ± 8.27	38.40 ± 7.99	39.80 ± 9.33	0.592	39.0 ± 8.32	37.40 ± 8.06	0.293
Hand grip strength (kg)	24.04 ± 7.64	23.85 ± 7.47	24.63 ± 8.33	0.279	24.47 ± 7.95	22.16 ± 5.94	0.044 [b]
Repeated Chair Stand (sec)	10.42 ± 2.57	10.44 ± 2.69	10.38 ± 2.04	0.111	10.26 ± 2.47	11.07 ± 2.86	0.077
Gait speed (m/s)	1.14 ± 0.21	1.13 ± 0.21	1.16 ± 0.23	0.452	1.14 ± 0.21	1.14 ± 0.21	0.955
Repeated Chair Stand Test Score=4, n (%)	136 (68.0)	107 (66.9)	29 (72.5)	0.495	114 (71.3)	22 (55.0)	0.049 [b]
Balance Test Score =4, n (%)	182 (91.0)	147 (91.9)	35 (87.5)	0.3807	146 (91.3)	36 (90.0)	0.805
Gait Speed Test Score =4, n (%)	186 (93.0)	149 (93.1)	37 (92.5)	0.890	149 (93.1)	37 (92.5)	0.890
SPPB Total Score (0-12) [c]	12 (11 - 12)	12 (11 - 12)	12 (11 - 12)	0.905	12 (11 - 12)	12 (11 - 12)	0.084

[a]Elevated versus non-elevated MCP-1 and DKK-1 levels based on quintile cut-offs (156.02 pg/mL and 606.31 pg/mL, respectively). [b]P<0.05. [c]Median (IQR). Values expressed as mean ± SD unless otherwise indicated. DKK-1: Dickkopf-1; MCP-1: Monocyte Chemotactic Protein-1; SPPB: Short Physical Performance Test.

Table 1. Comparison of baseline characteristics between elevated and normal MCP-1, DKK-1 levels respectively[a].

Biosciences, San Diego, CA, USA) were assayed via ELISA as previously described[22]. All biomarkers were measured in duplicates according to manufacturers' recommendations, and the average value was reported for all assays. The lower detection limits were as follows: DKK-1, 30 pg/mL and MCP-1, 10 pg/mL. Serum levels of C-reactive protein and Vitamin D were also assayed.

Determination of sarcopenia and sarcopenic obesity

Sarcopenia was defined by the presence of low gait speed and/or handgrip strength, and low muscle mass in accordance with the Asian Working Group for Sarcopenia (AWGS) criteria[6]. The cutoff for usual gait speed is <1.0 m/s, and cutoffs for handgrip strength are <28 kg for men and <18 kg for women. The cutoffs for height-square adjusted appendicular lean mass via DXA are 7.0 kg/m^2 for men and 5.4 kg/m^2 for women respectively. Using gender-specific cut-offs of waist circumference to define obesity (>90 cm for Asian man and >80 cm for Asian women)[23], we further classified subjects who fulfilled AWGS criteria as sarcopenic non-obese or sarcopenic-obese. We chose waist circumference as among the various obesity definitions, central adiposity has been shown to be best associated with poorer muscle function in sarcopenic obesity[9].

Statistical Analysis

Continuous variables were expressed as means (standard error) or as medians (interquartile range, IQR). Categorical variables were expressed as counts and percentages. As there is no universally accepted cutoff value for MCP-1 and

DKK-1, we employed an empirical data-driven approach of quintile cutoffs to denote elevated MCP-1 and DKK-1 levels (156.02 pg/mL and 606.31 pg/mL respectively). We performed univariate analysis to compare baseline demographics, body composition and physical performance parameters between elevated and non-elevated groups for MCP-1 and DKK-1 respectively. We further compared levels of MCP-1 and DKK-1 between non-sarcopenic, sarcopenic non-obese and sarcopenic-obese participants. Independent sample *t*-tests and one-way ANOVA were used for parametric data and Mann-Whitney *U* test for non-parametric continuous variables. Chi-square tests were used for categorical variables. We performed multiple linear regression to examine the relationship between MCP-1 and DKK 1 serum levels with body composition and physical performance, adjusted for age, gender and ethnicity. Age and gender are adjusted for a priori due to theoretical justification, whereas we further adjusted for ethnicity to account for the significant difference in ethnicity between normal and elevated MCP-1 groups. For regression analyses, we report β (unstandardized coefficient), Beta (standardized coefficient) and p-values. Data analyses were conducted using IBM SPSS Statistics Version 22.0 (IBM, Armonk, NY, USA), with p-value <0.05 considered statistically significant.

Results

Baseline characteristics (Table 1)

There was a total of 200 participants with a mean age of 67.9±7.9 years. Majority of the participants were of Chinese ethnicity (n = 184, 92%), and predominantly female (n = 137, 68.5%). Comparing between elevated and non-elevated groups, with the exception of a higher proportion with Chinese ethnicity in the elevated MCP-1 group (95% vs 80%, p < 0.005), there was otherwise no difference in age and gender. There was a trend towards higher CRP levels in the elevated DKK-1 group (Median, IQR: 1.10, 0.40–3.00 vs 0.90, 0.40–1.50) but no difference was observed for MCP-1. There was no difference in vitamin D between normal and elevated groups for both MCP-1 and DKK-1.

Body composition and Physical Performance (Table 1)

There was no difference in appendicular lean mass and appendicular lean mass index. Participants with elevated MCP-1 had significantly higher fat mass (kg) (20.71±6.26 vs 23.46±6.24, p=0.014); fat mass index (kg/m^2) (9.58±2.62 vs 8.40±2.67, p=0.013); percentage body fat (39.2±6.36 vs 35.9±6.94, p=0.008); and waist circumference (cm) (89.6±8.61 vs 85.7±9.02, p=0.016) compared with the non-elevated group. In contrast, for DKK-1, there was no difference in lean mass or fat-related body composition parameters.

For physical performance, the elevated MCP-1 group had weaker hand grip strength (kg) (22.16±5.94 vs 24.47±7.95, p=0.044) and lower proportion who scored 4 (equivalent to 11.19s or less) in the repeated chair stand test (55.0% vs 71.3%, p=0.049). There was no difference in physical performance between elevated and non-elevated DKK-1 groups (p>0.05).

MCP-1 and DKK-1 levels by sarcopenia status

Using the Asian Working Group for Sarcopenia 2019 consensus criteria, there were 39 (19.5%) sarcopenic and 161 (80.5%) non-sarcopenic participants respectively. The MCP-1 levels were significantly higher in sarcopenia compared with non-sarcopenia (mean±SD, pg/mL: 141.32±62.30 vs 122.23±50.89, p=0.046) but not for DKK-1 (mean±SD, pg/mL: 501.44±195.17 vs 475.98±230.51, p=0.525).

We further delineated sarcopenic subjects by gender-specific cutoffs for waist circumference into two groups: sarcopenic non-obese (N=20) and sarcopenic-obese (N=19). One-way ANOVA analysis revealed significant differences across non-sarcopenic, sarcopenic non-obese and sarcopenic-obese groups for MCP-1 (mean±SD, pg/mL: 122.23±50.89 vs 125.37±48.57 vs 158.11±71.58, p=0.022), with post-hoc analysis showing a significant difference only in the comparison between non-sarcopenic and sarcopenic-obese groups (p=0.017, Bonferroni correction).

Multiple Linear Regression (Table 2)

We performed multiple linear regression analysis of DKK-1 and MCP-1 against body composition for fat-related parameters and waist circumference, as well as physical performance. Even after adjustment for age, gender and ethnicity, MCP-1 was significantly associated with higher fat mass, fat mass index, percentage body fat and waist circumference (Beta: 0.153–0.230, all p<0.01). In addition, MCP-1 was also significantly associated with trunk-to-limb ratio for percentage fat (Beta: 0.134, p=0.04) and fat mass (Beta: 0.192, p=0.002). In contrast, no significant association in fat parameters and waist circumference was noted for DKK-1. Amongst the physical performance measures, the only significant association was between MCP-1 and repeated chair stand (Beta: 0.151, p=0.004).

Discussion

Our study demonstrates that elevated MCP-1 was associated with body parameters concerning fat, namely higher fat mass index, percentage body fat and waist circumference. This is consistent with other studies where MCP-1 was found to be elevated in the subcutaneous adipose tissue of obese patients and supports the existing notion that MCP-1 signalling has a direct role in the development of obesity[24]. Obesity is associated with low grade chronic inflammation, with MCP-1 being one of the key mediators in adipose tissue inflammation. MCP-1 is released by adipocytes as a pro-inflammatory adipokine to induce activation in macrophages[25], which in turn recruits additional monocytes from circulation into the site of adipose tissue to perpetuate the chronic inflammatory response. Binding of

Variables	Body Composition					
	DKK-1			MCP-1		
	β	Beta	*P*-value	β	Beta	*P*-value
Fat Mass Index (kg/m^2)	-0.001	-0.091	0.161	0.010	0.201	0.002 [b]
Fat Mass (kg)	-3.383	-0.119	0.081	24.022	0.203	0.004 [b]
Percentage Body Fat (%)	-0.003	-0.086	0.098	0.020	0.153	0.004 [b]
Waist circumference(cm)	-0.001	-0.033	0.636	0.004	0.230	0.001 [b]
% Fat Trunk/% Fat Leg	-6.085	-0.069	0.273	0.000	0.134	0.040 [b]
Trunk/Limb Fat Mass Ratio	-7.153	-0.057	0.359	0.001	0.192	0.002 [b]
	Physical Performance					
Variables	DKK-1			MCP-1		
	β	Beta	*P*-value	β	Beta	*P*-value
Repeated Chair Stand (sec)	-0.001	-0.081	0.246	-0.002	0.151	0.004 [b]
Hand grip strength (kg)	0.000	0.008	0.879	-0.011	-0.075	0.177
SPPB Total Score	0.000	-0.029	0.681	-0.002	-0.070	0.331
Knee-extension strength (kg)	0.001	0.029	0.643	0.008	0.054	0.405
Gait speed (m/s)	-0.000	0.068	0.326	-9.389	-0.024	0.742

[a]Adjusted for age, gender and ethnicity. [b]P<0.05. DKK-1: Dickkopf-1; MCP-1: Monocyte Chemotactic Protein-1; SPPB: Short Physical Performance Test.

Table 2. Multiple Linear Regression Analysis: Body Composition and Physical Performance [a].

MCP-1 to its receptor CCR2 leads to activation of "MCP-1-induced protein (MCPIP)" and promote 3T3-L1 cells to differentiate into an adipocyte-like phenotype *in vitro*[26,27].

Another interesting observation was the pattern of fat distribution, with the elevated MCP-1 group possessing abdominal fat accumulation as evident by the larger waist circumference. This is corroborated by the higher trunk-to-limb ratio for percentage fat and fat mass even after adjustment for age, gender and ethnicity in regression analysis. Taken together, this could be indicative of abdominal obesity, and the elevated trunk-to-limb fat ratio suggests lipodystrophy secondary to redistribution of adipose tissues from peripheral to central sites. Such central adiposity has been linked to conditions such as insulin resistance and metabolic syndrome[28,29]. Abdominal obesity may increase the risk of chronic diseases such as atherosclerotic vascular diseases and type 2 diabetes mellitus[30], as visceral adipose tissue can release higher amounts of MCP-1 compared to subcutaneous adipose tissue[31]. Thus, elevated MCP-1 levels as a result of abdominal fat accumulation can predispose to a pro-inflammatory state which forms the patho-physiological basis for insulin resistance and metabolic syndrome[32].

Along with higher fat measures, the elevated MCP-1 group also displayed weaker muscle strength in both upper (handgrip strength) and lower (repeated chair stand) limbs. Our observation of highest MCP-1 amongst sarcopenic-obese is consistent with earlier studies which implicate MCP-1 in the pathogenesis of sarcopenic obesity, which refers to the combined presentation of increased adiposity along with decreased muscle function[33]. Obesity contributes to a state of low-grade chronic inflammation which has been shown to impede muscle mass formation, promote accelerated muscle loss and facilitate fat accumulation in skeletal muscle[12]. Lipids ectopically accumulated in skeletal muscle may induce mitochondrial dysfunction which can in turn induce apoptosis and atrophy of muscle tissue[34]. Furthermore, the inflammatory state mediated by elevated MCP-1 leads to impaired muscle anabolism and accelerated muscle catabolism, further contributing to the impairment of muscle strength[35]. To this end our findings suggest that the influence of MCP-1 on impaired muscle strength may be driven by fat instead of lean mass per se. We earlier reported the association of MCP-1 with intermuscular adipose tissue (IMAT), supporting the putative role of adipose tissue inflammation in the ectopic infiltration of fat in muscle tissue. IMAT in turn has been associated with poorer physical performance[36]. Taken together, MCP-1 is a promising biomarker of adipose tissue inflammation that may have potential for identifying the at-risk group with sarcopenic obesity.

Our results demonstrate an overall lack of association between serum DKK-1 with body composition and physical performance. A recent study amongst African males reported significantly higher DKK-1 levels with total and

central adiposity as measured using DXA, in contrast to our findings[37]. Wnt/β-catenin signaling pathway is observed to decrease regenerative ability of muscle progenitor cells and promotes ageing phenotype[38,39], the lack of association with DKK-1 may indicate the role of other myokines such as DKK-3[40]. Yin et al. reported that DKK-3 level is significantly increased in serum and skeletal muscles of sarcopenic patients[41]. These findings suggest that DKK-3 may serve as a critical factor produced by skeletal muscle and play a role in muscle mass changes and pathogenesis of sarcopenia.

A limitation of this study was the higher female to male ratio in this study. On average, women typically present with 10% higher body fat compared to men due to the oestrogen induced effect of reduced ability to burn less energy after food consumption. Nonetheless, the associations for MCP-1 with body fat parameters and chair stand remained significant even after adjustment for gender. Because our study is underpowered for further sub-group analyses by gender, we recommend future larger longitudinal studies with a higher representation of male participants adequately powered to examine if the effects of MCP-1 are gender-specific.

In addition, alterations in physical performance may also be attributed to diseases commonly associated with aging in older adults such as reduced bone density, respiratory and joint pathologies. Altered endurance, biomechanics, and muscle function occurring as a result of obesity could also have contributed to poorer physical function and performance of participants in the elevated MCP-1 group. With the multi-layered mechanisms underlying sarcopenia, both intrinsic and extrinsic factors contribute to defective myogenesis, muscle atrophy and weakness[42]. As such, exploration of additional novel biomarkers is paramount to study the biological pathways associated with sarcopenia disease activity. Data on menopausal status of female subjects, smoking and alcohol intake were not quantified, contributing to other limitations in this study due to self-reporting biases. The cross-sectional design of the study also precludes definitive conclusion about causality in the observed associations. Finally, we did not employ additional imaging techniques such as magnetic resonance spectroscopy to study intramyocellular lipid[43].

Conclusion

Our study has identified the association of increased body fat, higher trunk to limb fat ratio, and weaker physical strength in individuals with elevated MCP-1, a promising biomarker of adipose tissue inflammation that may have potential for identifying the at-risk group with sarcopenic obesity. The potential of serum MCP-1 to monitor muscle function changes or to predict the risk of sarcopenia needs to be further validated in gender-stratified studies with longitudinal follow-up. The lack of association with DKK-1 suggest other myokines such as DKK-3 may serve as more sensitive biomarker in the ageing of muscle and sarcopenia.

Authors' contribution

LT, BPL and WSL: Study concept and design. NOA, HSL, AY, SY and WSL: Acquisition of data. NOA, HSL, LT and WSL: Analysis and Interpretation of data. NOA, HSL, LT, BPL and WSL: Drafting of the manuscript. All authors: critical revision of the manuscript.

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