Predictive Value of Cardiopulmonary Exercise Testing (CPET)-Derived Indicators for Cardiometabolic Risk Factors in an Occupational Population: A Prospective Cohort Study

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Abstract

Objective   To investigate the association between cardiopulmonary function indicators derived from cardiopulmonary exercise testing (CPET) and incident cardiometabolic risk factors (CMRFs) in an occupational population, and to identify the optimal CPET-based predictive indicators/models for CMRFs.   **Methods**   A single-center prospective cohort study was conducted. A total of 126 occupational adults (59.2% male; mean age: 41.2 ± 8.5 years) who underwent health check-ups at the Health Management Center of Beijing Zhongguancun Hospital from January 2022 to June 2025 were enrolled. Inclusion criteria included age 28-60 years, fixed occupation for ≥ 1 year, no severe cardiopulmonary diseases/malignant tumors/hepatic/renal failure, ability to complete CPET, and informed consent. Exclusion criteria included ≥ 3 pre-existing CMRFs, recent use of metabolism/cardiopulmonary function-affecting drugs, loss to follow-up, and acute diseases/major surgery during follow-up. CPET indicators included peak oxygen consumption (VO_2peak, mL/kg/min), anaerobic threshold (AT, mL/kg/min), peak heart rate (HRpeak, beats/min), and oxygen pulse (O_2pulse, mL/beat). CMRFs (hypertension, hyperglycemia, dyslipidemia, overweight/obesity) were defined based on standard criteria. Multivariate Logistic regression analyzed the association between CPET indicators and CMRF risk; receiver operating characteristic (ROC) curves evaluated predictive efficacy.   **Results**   During 2-year follow-up, 40.5% (n=51) of participants developed CMRFs. The case group (with CMRFs) had higher age, sedentary occupation proportion, smoking rate, and levels of systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), body mass index (BMI), and HRpeak, but lower regular exercise rate, high-density lipoprotein cholesterol (HDL-C), VO_2peak, AT, and O_2pulse (all P<0.05). After adjusting for confounding factors (age, gender, occupation type, smoking), reduced VO_2peak (per 5 mL/kg/min decrease; OR=1.86, 95% CI: 1.52–2.28, P<0.001) and AT (per 5 mL/kg/min decrease; OR=1.63, 95% CI: 1.31–2.02, P<0.001) were independent CMRF risk factors. Subgroup analysis showed stronger predictive effect of VO_2peak in sedentary workers (OR=2.13, 95% CI: 1.68–2.70, P<0.001). The combination of VO_2peak and AT had the highest predictive efficacy (AUC=0.783, 95% CI: 0.751–0.815), superior to single indicators (VO_2peak: AUC=0.721; AT: AUC=0.685; both P<0.05).   **Conclusion**   CPET-derived VO_2peak and AT are valuable predictors of CMRFs in occupational populations, especially in sedentary workers. The combined VO_2peak+AT model serves as a practical tool for CMRF screening and risk stratification in occupational health management.

Keywords: cardiopulmonary exercise testing; CPET; peak oxygen uptake; anaerobic threshold; cardiometabolic risk factors; occupational health; predictive value; sedentary behavior

1. Introduction

With socioeconomic development and changes in work patterns, occupational populations are consistently facing issues such as prolonged sitting, high work pressure, and irregular daily routines. The incidence of cardiometabolic risk factors (CMRFs), such as hypertension, hyperglycemia, and dyslipidemia, has been increasing yearly [1,2].

CMRFs are core contributors to severe cardiovascular and metabolic diseases, including coronary heart disease, stroke, and type 2 diabetes.

Cardiopulmonary exercise testing (CPET) is considered the "gold standard" for assessing integrated cardiopulmonary function [3]. It comprehensively reflects the body's aerobic capacity and functional reserve by dynamically monitoring oxygen metabolism, heart rate, ventilation, and other indicators during exercise. Peak oxygen consumption (VO_2peak) and the anaerobic threshold (AT) are core parameters obtained from CPET, providing valuable insights into an individual's fitness and metabolic health.

While the association between cardiorespiratory fitness and health outcomes is established in general populations, prospective studies focusing specifically on occupational groups, particularly those stratified by activity intensity, are lacking. This study adopts a prospective cohort design to investigate the association between CPET-derived indicators and the risk of developing CMRFs in an occupational population. We aim to identify key predictive indicators and combined models to provide a scientific basis for early screening and personalized health intervention in this high-risk group.

2. Materials and Methods

2.1. Study Population

A single-center prospective cohort study was conducted. Occupational individuals who underwent health assessment at the Health Management Center of Beijing Zhongguancun Hospital from January 2022 to June 2025 were selected as the study population.

Inclusion criteria were: (1) Age 28–60 years; (2) Engaged in a fixed occupation for ≥1 year; (3) No underlying diseases such as severe cardiopulmonary diseases, malignant tumors, or hepatic/renal failure; (4) Ability to complete a full CPET test; (5) Voluntary participation with signed informed consent.

Exclusion criteria were: (1) Presence of three or more existing CMRFs at baseline; (2) Recent use of medications that may affect metabolism or cardiopulmonary function (e.g., corticosteroids, beta-blockers); (3) Loss to follow-up or withdrawal from the study; (4) Occurrence of acute diseases (e.g., acute myocardial infarction, pneumonia) or major surgery during follow-up.

A total of 126 subjects were finally included, comprising 74 males (59.2%) and 52 females (40.8%), with a mean age of 41.2 ± 8.5 years.

2.2. Baseline Data Collection

General information (age, gender, occupation type, work years, education level) and lifestyle data were collected using a structured questionnaire. Smoking history was defined as smoking ≥1 cigarette per day for ≥1 year; alcohol consumption history was defined as drinking ≥1 time per week for ≥1 year; exercise habits were defined as engaging in regular physical activity ≥150 minutes per week at moderate-intensity (heart rate reaching 64-76% of maximum heart rate or 3-6 METs). Height and weight were measured using standardized methods to calculate Body Mass Index (BMI). Systolic (SBP) and diastolic blood pressure (DBP) were measured three times consecutively, and the average values were recorded.

2.3. Laboratory Indicator Testing

After an overnight fast, 10 mL of venous blood was collected from the median cubital vein of all participants. Fasting plasma glucose (FPG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) were measured using an automated biochemical analyzer.

2.4. Cardiopulmonary Exercise Testing (CPET)

CPET was performed using a cardiopulmonary function testing system (CPX-600, Hebei Jide Yuanjian, Baoding, China). Participants were briefed on the procedure, and exercise contraindications were excluded. Parameters such as VO_2, carbon dioxide output (VCO_2), heart rate (HR), and minute ventilation (VE) were monitored in real-time until exercise endpoint. The predicted maximum heart rate was calculated as 220 – age. The test was terminated upon any of the following: Borg fatigue scale score ≥17, chest pain, dyspnea (respiratory rate >30 breaths/min), abnormal blood pressure (SBP >220 mmHg or DBP >110 mmHg), ST-segment depression ≥0.1 mV, severe arrhythmia, or other discomfort symptoms.

The following core parameters were recorded:

(1) Peak oxygen uptake (VO_2peak): Maximum oxygen uptake during exercise (mL/kg/min).

(2) Anaerobic threshold (AT): Determined using the V-slope method (mL/kg/min).

(3) Peak heart rate (HRpeak): Maximum heart rate achieved (beats/min).

(4) Oxygen pulse (O_2pulse): Ratio of peak VO_2 to HR (mL/beat).

All tests were conducted by technicians who underwent standardized training.

2.5. Definition of Cardiometabolic Risk Factors (CMRFs) and Grouping

CMRFs were defined as follows [4-7]:

(1) Hypertension: SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg, or diagnosed hypertension with ongoing medication.

(2) Hyperglycemia: FPG ≥ 6.1 mmol/L, or diagnosed diabetes with ongoing medication.

(3) Dyslipidemia: TG ≥ 1.7 mmol/L, or TC ≥ 5.2

mmol/L, or LDL-C ≥ 3.4 mmol/L, or HDL-C < 1.0 mmol/L.

(4) Overweight/Obesity: BMI ≥ 24 kg/m².

Sedentary occupations were defined as involving ≥8 hours of sitting per day with physical activity energy expenditure <3 METs·h/day; light-intensity physical occupations involved 3–6 METs·h/day; moderate-intensity involved 6-9 METs·h/day [8]. Participants were followed for two years via telephone interviews, outpatient reviews, and physical examination reports. They were divided into a case group (developed ≥1 CMRF, n=51) and a control group (developed no CMRFs, n=75).

2.6. Statistical Analysis

Statistical analysis was performed using SPSS 26.0. Normally distributed measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$) and compared using t-tests. Non-normally distributed data were expressed as median (interquartile range) and compared using the Mann–Whitney U test. Categorical data were expressed as n (%) and compared using the χ^2 test. Multivariate logistic regression analysis was used to examine associations, calculating odds ratios (OR) and 95% confidence intervals (CI). Receiver operating characteristic (ROC) curve analysis was used to evaluate predictive efficacy. Continuous variables were included using clinically common units of change (VO₂peak and AT: per 5 mL/kg/min decrease; O₂pulse: per 3 mL/beat decrease; HRpeak: per 10 beats/min increase). The Youden index maximization method determined optimal cut-off values. A p-value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of Baseline Characteristics

The case group was older, had a higher proportion of sedentary workers and smokers, and a lower rate of regular exercise than the control group (all p < 0.05). SBP, DBP, FPG, TC, TG, LDL-C, and BMI were significantly higher, and HDL-C was significantly lower in the case group (all p < 0.05). Furthermore, VO₂peak, AT, and O₂pulse were lower, and HRpeak was higher in the case group (all p < 0.05, Table 1).

Table 1 Comparison of Baseline Characteristics Between the Two Groups

Indicator	Case Group（n=51）	Control Group（n=75）	t/χ²/Z Value	P Value
Age (years)	42.3±7.8	37.1±8.0	9.26	<0.001
Male [n (%)]	34（66.7）	40（53.3）	2.25	0.134
Occupational Type [n (%)]			12.35	0.002
Sedentary	31（60.8）	37（49.3）		
Light-Intensity Physical	12（23.5）	21（28.0）		
Moderate-Intensity Physical	8（15.7）	17（22.7）		
Smoking [n (%)]	9（17.6）	4（5.0）	15.63	0.037
Alcohol Drinking [n (%)]	9（17.6）	12（16.0）	1.98	0.275
Regular Exercise [n (%)]	15（29.4）	43（57.3）	10.85	0.036
SBP（mmHg）	132.5±12.8	122.3±10.5	11.52	<0.001
DBP（mmHg）	85.6±9.2	78.4±8.1	10.38	<0.001
FPG（mmol/L）	5.8±1.2	5.2±0.8	8.96	<0.001
TC（mmol/L）	5.4±1.0	4.9±0.9	7.65	<0.001
TG（mmol/L）	1.9±0.8	1.5±0.6	8.23	<0.001
LDL-C（mmol/L）	3.3±0.7	2.9±0.6	8.57	<0.001
HDL-C（mmol/L）	1.0±0.2	1.2±0.3	-11.24	<0.001
BMI（kg/m²）	25.8±3.1	23.2±2.8	12.67	<0.001
VO₂peak（mL/kg/min）	26.3±5.2	32.1±6.4	-5.89	<0.001
AT（mL/kg/min）	18.5±4.1	22.3±4.8	-4.76	<0.001
HRpeak (beats/min)	178.5±15.2	165.3±14.8	5.12	<0.001
O₂pulse(mL/beat)	14.8±3.2	17.5±3.6	-4.87	<0.001

3.2 Multivariate Logistic Regression Analysis

Variance inflation factor (VIF) analysis showed no severe multicollinearity (all VIF <5). Variables with P<0.05 in univariate analysis (age, occupational type, smoking, regular exercise, VO₂peak, AT, HRpeak, O₂pulse) were included in the multivariate model.

After adjustment, reduced VO₂peak (per 5 mL/kg/min decrease; OR=1.86, 95% CI: 1.52–2.28, P<0.001) and AT (per 5 mL/kg/min decrease; OR=1.63, 95% CI: 1.31–2.02, P<0.001) were independent CMRF risk factors. HRpeak and O₂pulse showed no significant associations

(P>0.05; Table 2).

Subgroup analysis (sedentary vs. non-sedentary workers, with non-sedentary group combining light/moderate-intensity physical jobs) showed:

In sedentary workers (n=71): Reduced VO₂peak (OR=2.13, 95% CI: 1.68–2.70, P<0.001) and AT (OR=1.85, 95% CI: 1.42–2.41, P<0.001) had stronger predictive effects;

In non-sedentary workers (n=55): Only reduced VO₂peak was associated with CMRF risk (OR=1.52, 95% CI: 1.10–2.10, P=0.011), while AT showed no significant association (P=0.098; Table 3).

Table 2 Multivariate Logistic Regression Analysis of CPET Indicators and the Risk of CMRFs in the Occupational Population

Indicator	Regression Coefficient (β)	Standard Error (SE)	Wald χ^2 Value	P Value	OR Value	95%CI
Age (per 10-year increase)	0.42	0.11	14.58	<0.001	1.52	1.25~1.85
Occupational Type (Sedentary vs. Moderate-Intensity Physical)	0.51	0.15	11.56	<0.001	1.67	1.28~2.18
Occupational Type (Light-Intensity Physical vs. Moderate-Intensity Physical)	0.23	0.14	2.78	0.095	1.26	0.97~1.64
Smoking (Yes vs. No)	0.35	0.13	7.32	0.007	1.42	1.10~1.83
Regular Exercise (Yes vs. No)	-0.41	0.12	11.86	<0.001	0.66	0.53~0.82
VO₂peak (per 5 mL/kg/min decrease)	0.62	0.13	22.65	<0.001	1.86	1.52~2.28
AT (per 5 mL/kg/min decrease)	0.49	0.14	12.01	<0.001	1.63	1.31~2.02
HRpeak (per 10 beats/min increase)	0.15	0.12	1.56	0.212	1.16	0.92~1.46
O₂pulse (per 3 mL/beat decrease)	0.21	0.13	2.67	0.102	1.23	0.97~1.56

Table 3. Multivariate Logistic Regression Analysis of CPET Indicators and CMRFs Risk in Different Occupational Subtypes (Adjusted for age, sex, smoking, regular exercise, etc.)

Indicator	Sedentary Occupations (n=71)	Non-Sedentary Occupations (n=55)
VO₂peak (per 5 mL/kg/min decrease)	OR=2.13（1.68~2.70）	OR=1.52（1.10~2.10）
	P<0.001	P=0.011
AT (per 5 mL/kg/min decrease)	OR=1.85（1.42~2.41）	OR=1.32（0.95~1.84）
	P<0.001	P=0.098
HRpeak (per 10 beats/min increase)	OR=1.21（0.93~1.58）	OR=1.15（0.85~1.56）
	P=0.157	P=0.372
O₂pulse (per 3 mL/beat decrease)	OR=1.30（0.99~1.71）	OR=1.22（0.91~1.64）
	P=0.058	P=0.185

Abbreviations: CPET, cardiopulmonary exercise testing; CMRF, cardiometabolic risk factor; VO₂peak, peak oxygen consumption; AT, anaerobic threshold; HRpeak, peak heart rate; O₂pulse, oxygen pulse; OR, odds ratio; CI, confidence interval.

Abbreviations: CPET, cardiopulmonary exercise testing; CMRF, cardiometabolic risk factor; VO₂ peak, peak oxygen consumption; AT, anaerobic threshold; HRpeak, peak heart rate; O₂ pulse, oxygen pulse; OR, odds ratio; CI, confidence interval (omitted in table for brevity).

3.3 Predictive Efficacy of CPET Indicators for CMRFs

ROC curve analysis showed that VO₂peak, AT, and their combination had predictive value for CMRFs (all AUC >0.65, P<0.001). The VO₂peak+AT combination had the highest AUC (0.783, 95% CI: 0.751–0.815), significantly higher than VO₂peak (0.721, 95% CI: 0.687–0.755) and AT (0.685, 95% CI: 0.650–0.720; Z=3.28 and 4.56, both P<0.001).

In subgroup analysis:
Sedentary workers: VO₂peak+AT combination had AUC=0.812 (95% CI: 0.773–0.851);

Non-sedentary workers: AUC=0.735 (95% CI: 0.682–0.788);
The difference was statistically significant (Z=2.85 and 3.62, P<0.01).
Optimal cut-off values (Table 4):
Overall population: VO₂peak=28.5 mL/kg/min (Youden index=0.408, sensitivity=72.5%, specificity=68.3%); AT=20.3 mL/kg/min (Youden index=0.324, sensitivity=67.3%, specificity=65.1%);
Sedentary workers: VO₂peak=27.8 mL/kg/min (Youden index=0.483, sensitivity=76.8%, specificity=71.5%); AT=19.8 mL/kg/min (Youden index=0.399, sensitivity=71.2%, specificity=68.7%);
Non-sedentary workers: VO₂peak=29.2 mL/kg/min (Youden index=0.351, sensitivity=68.9%, specificity=66.2%); AT=20.8 mL/kg/min (Youden index=0.273, sensitivity=64.5%, specificity=62.8%).
Abbreviations: CPET, cardiopulmonary exercise testing; CMRFs, cardiometabolic risk factors; VO₂peak, peak oxygen consumption; AT, anaerobic threshold; AUC, area under the curve; CI, confidence interval.

Table 4 Predictive Efficacy of Different CPET Indicators for CMRFs in the Occupational Population

Indicator	Overall Population (n=126)	Sedentary Occupations (n=71)	Non-Sedentary Occupations (n=55)
AUC	0.721(0.687~0.755)	0.765(0.724~0.806)	0.698(0.643~0.753)
Sensitivity (%)	72.5	76.8	68.9
Specificity (%)	68.3	71.5	66.2
Optimal Cut-off Value	28.5 mL/kg/min	27.8 mL/kg/min	29.2 mL/kg/min
AUC	0.685(0.650~0.720)	0.723(0.679~0.767)	0.652(0.596~0.708)
Sensitivity (%)	67.3	71.2	64.5
Specificity (%)	65.1	68.7	62.8
Optimal Cut-off Value	20.3 mL/kg/min	19.8 mL/kg/min	20.8 mL/kg/min
AUC	0.783(0.751~0.815)	0.812(0.773~0.851)	0.735(0.682~0.788)
Sensitivity (%)	75.6	79.3	71.8
Specificity (%)	72.4	75.6	69.3

4.Discussion

This prospective cohort study demonstrates that reduced VO₂peak and AT, as assessed by CPET, are independent risk factors for the development of CMRFs in an occupational population. The combination of these two parameters provides the best predictive performance, especially among sedentary individuals.

Our findings align with existing literature on the importance of cardiorespiratory fitness [9,10]. VO₂peak reflects the integrated capacity of the cardiopulmonary system and skeletal muscle to utilize oxygen. A lower VO₂peak is associated with endothelial dysfunction, insulin resistance, and chronic inflammation [11], all pathways contributing to CMRFs. The stronger association observed in sedentary workers (OR=2.13) suggests that prolonged sitting exacerbates the detrimental metabolic effects of poor fitness, creating a vicious cycle [12,13].

The anaerobic threshold (AT) represents the exer-

cise intensity at which metabolic acidosis begins[14]. A lower AT indicates reduced efficiency in oxygen utilization by muscles at submaximal efforts, often linked to metabolic disorders[15].Our study found AT to be an independent predictor, though its effect was attenuated in non-sedentary groups, possibly because higher daily activity levels can compensate for submaximal metabolic inefficiency.

The key innovation of our study is demonstrating the superior predictive value of combining VO_2peak and AT. This multi-parameter approach aligns with the concept of integrated CPET assessment for risk stratification[16]. VO_2peak reflects maximal system capacity, while AT indicates submaximal metabolic efficiency; together, they provide a more holistic view of an individual's functional and metabolic health.

5.Limitations

This study has limitations. First, the single-center design and relatively small sample size may limit generalizability. Second, potential confounding factors like diet, stress, and sleep quality were not fully accounted for. Third, as an observational study, it can demonstrate association but not causation. Larger, multi-center studies incorporating more confounders are needed to validate these findings.

6. Conclusions

In conclusion, CPET-derived indices, VO_2peak and AT, are significant predictors of cardiometabolic risk in an occupational population. Their combined use offers a powerful tool for early identification of high-risk individuals, particularly those with sedentary jobs. Incorporating CPET into routine health assessments for occupational groups could facilitate targeted interventions and improve cardiovascular health management strategies.

References

[1] Wang N, Sun Y, Zhang H, Wang B, Chen C, Wang Y, Chen J, Tan X, Zhang J, Xia F, Qi L, Lu Y. Long-term night shift work is associated with the risk of atrial fibrillation and coronary heart disease. Eur Heart J. 2021 Oct 21;42(40):4180-4188. doi: 10.1093/eurheartj/ehab505. PMID: 34374755.

[2] McDermott JE, Jacobs JM, Merrill NJ, Mitchell HD, Arshad OA, McClure R, Teeguarden J, Gajula RP, Porter KI, Satterfield BC, Lundholm KR, Skene DJ, Gaddameedhi S, Van Dongen HPA. Molecular-Level Dysregulation of Insulin Pathways and Inflammatory Processes in Peripheral Blood Mononuclear Cells by Circadian Misalignment. J Proteome Res. 2024 May 3;23(5):1547-1558. doi: 10.1021/acs.jproteome.3c00418. Epub 2024 Apr 15. Erratum in: J Proteome Res. 2025 Feb 7;24(2):975. doi: 10.1021/acs.jproteome.5c00004. PMID: 38619923.

[3] Chinese Society of Cardiology, Professional Committee of Cardiopulmonary Prevention and Rehabilitation of Chinese Rehabilitation Medical Association, Editorial Board of Chinese Journal of Cardiology. Chinese Expert Consensus on the Clinical Standardized Application of Cardiopulmonary Exercise Testing [J]. Chinese Journal of Cardiology, 2022, 50(10): 973-986. DOI: 10.3760/cma.j.cn112148-20220316-00180.

[4] Joint Committee for Guideline Revision on Prevention and Treatment of Hypertension in China, Hypertension Alliance (China), Chinese Society of Cardiology, Hypertension Professional Committee of Chinese Medical Doctor Association, Hypertension Branch of China International Exchange and Promotive Association for Medical and Healthcare, Hypertension Branch of Chinese Geriatric Medical Association. 2018 Chinese Guidelines for the Management of Hypertension [J]. Chinese Journal of Cardiovascular Medicine, 2019, 24(1): 24-56. DOI: 10.3969/j.issn.1007-5410.2019.01.002.

[5] Chinese Diabetes Society. Chinese Guidelines for the Prevention and Treatment of Type 2 Diabetes (2020 Edition) [J]. Chinese Journal of Diabetes, 2021, 13(4): 315-409. DOI: 10.3760

/cma.j.cn115791-20210221-00095.

[6] Joint Committee for the Revision of Chinese Guidelines for Lipid Management. Chinese Guidelines for Lipid Management (2023) [J]. Chinese Circulation Journal, 2023, 38(3): 237-271. DOI: 10.3969/j.issn.1000-3614.2023.03.001.

[7] National Health Commission Guidelines for the Diagnosis and Treatment of Obesity Writing Committee, Zhang Zhongtao, Ji Linong. Guidelines for the Diagnosis and Treatment of Obesity (2024 Edition) [J]. Chinese Circulation Journal, 2025, 40(1): 6-30. DOI: 10.3969/j.issn.1000-3614.2025.01.002.

[8] Brazile TL, Levine BD, Shafer KM. Cardiopulmonary Exercise Testing. NEJM Evid. 2025 Feb;4(2):EVIDra2400390. doi: 10.1056/EVIDra2400390. Epub 2025 Jan 28. PMID: 39873542.

[9] Dores H, Mendes M, Abreu A, Durazzo A, Rodrigues C, Vilela E, Cunha G, Gomes Pereira J, Bento L, Moreno L, Dinis P, Amorim S, Clemente S, Santos M. Cardiopulmonary exercise testing in clinical practice: Principles, applications, and basic interpretation. Rev Port Cardiol. 2024 Sep;43(9):525-536. English, Portuguese. doi: 10.1016/j.repc.2024.01.005. Epub 2024 Apr 5. PMID: 38583860.

[10] Ross R, Blair SN, Arena R, Church TS, Després JP, Franklin BA, Haskell WL, Kaminsky LA, Levine BD, Lavie CJ, Myers J, Niebauer J, Sallis R, Sawada SS, Sui X, Wisløff U; American Heart Association Physical Activity Committee of the Council on Lifestyle and Cardiometabolic Health; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Council on Cardiovascular and Stroke Nursing; Council on Functional Genomics and Translational Biology; Stroke Council. Importance of Assessing Cardiorespiratory Fitness in Clinical Practice: A Case for Fitness as a Clinical Vital Sign: A Scientific Statement From the American Heart Association. Circulation. 2016 Dec 13;134(24):e653-e699. doi: 10.1161/CIR.0000000000000461. Epub 2016 Nov 21. PMID: 27881567.

[11] Letnes JM, Dalen H, Aspenes ST, Salvesen Ø, Wisløff U, Nes BM. Age-related change in peak oxygen uptake and change of cardiovascular risk factors. The HUNT Study. Prog Cardiovasc Dis. 2020 Nov-Dec;63(6):730-737. doi: 10.1016/j.pcad.2020.09.002. Epub 2020 Sep 21. PMID: 32971113.

[12] Nayor M, Shah RV, Miller PE, Blodgett JB, Tanguay M, Pico AR, Murthy VL, Malhotra R, Houstis NE, Deik A, Pierce KA, Bullock K, Dailey L, Velagaleti RS, Moore SA, Ho JE, Bagish AL, Clish CB, Larson MG, Vasan RS, Lewis GD. Metabolic Architecture of Acute Exercise Response in Middle-Aged Adults in the Community. Circulation. 2020 Nov 17;142(20):1905-1924. doi: 10.1161/CIRCULATIONAHA.120.050281. Epub 2020 Sep 15. PMID: 32927962; PMCID: PMC8049528.

[13] Keir DA, Notarius CF, Badrov MB, Millar PJ, Floras JS. Heart failure-specific inverse relationship between the muscle sympathetic response to dynamic leg exercise and $\dot{V}$O2peak. Appl Physiol Nutr Metab. 2021 Sep;46(9):1119-1125. doi: 10.1139/apnm-2020-1074. Epub 2021 Mar 18. PMID: 33735589.

[14] Nesti L, Pugliese NR, Sciuto P, De Biase N, Mazzola M, Fabiani I, Trico D, Masi S, Natali A. Mechanisms of reduced peak oxygen consumption in subjects with uncomplicated type 2 diabetes. Cardiovasc Diabetol. 2021 Jun 22;20(1):124. doi: 10.1186/s12933-021-01314-6. PMID: 34158062; PMCID: PMC8218418.

[15] O'Brien MW, Mekary S, Kimmerly DS. Aging, cardiorespiratory fitness and sympathetic transduction. Aging (Albany NY). 2022 May 16;14(10):4189-4190. doi: 10.18632/aging.204091. Epub 2022 May 16. PMID: 35580001; PMCID: PMC9186775.

[16] Gianoudis J, Bailey CA, Daly RM. Associations between sedentary behaviour and body composition, muscle function and sarcopenia in community-dwelling older adults. Osteoporos Int. 2015 Feb;26(2):571-9. doi: 10.1007/s00198-014-2895-y. Epub 2014 Sep 23. PMID: 25245026.