lek. Przemysław Kasiak

Ocena predykcji i wzajemnych zależności między wybranymi zmiennymi krążeniowo-oddechowymi w kardiologii sportowej

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu

w dyscyplinie nauki medyczne

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Obrona rozprawy doktorskiej przed Radą Dyscypliny Nauk Medycznych

Warszawskiego Uniwersytetu Medycznego

Warszawa, 2026 r.

Słowa kluczowe: Sercowo-płucne testy wysiłkowe; Wydolność organizmu; Kardiologia sportowa; Sportowiec wytrzymałościowy; Wartości normatywne, Fizjologia wysiłku fizycznego

Key words: Cardiopulmonary exercise test; Cardiorespiratory fitness; Sports cardiology; Endurance athlete; Reference values, Exercise physiology

Wykaz publikacji stanowiących pracę doktorską

Cykl stanowi 6 publikacji

4 artykuły oryginalne, 2 przeglądy narratywne

Sumaryczny Impact Factor cyklu publikacji: 16,2

Artykuły oryginalne

1. **Przemysław Kasiak***, Tomasz Kowalski, Kinga Rębiś, Andrzej Klusiewicz, Maria Ładyga, Dorota Sadowska, Adrian Wilk, Szczepan Wiecha, Marcin Barylski, Adam Rafał Poliwczak, Piotr Wierzbiński, Artur Mamcarz, Daniel Śliż. *Is the Ventilatory Efficiency in Endurance Athletes Different?—Findings from the NOODLE Study*
   DOI: 10.3390/jcm13020490

Journal of Clinical Medicine: IF=2,9 | kwartyl JCR Q1 | centyl JCR 80,6

**Przemysław Kasiak jest pierwszym i korespondującym autorem*

Artykuł wybrany jako *Editor's Choice* na okres drugiego kwartału 2025 r. dla badań o szczególnie wysokiej wartości naukowej

2. **Przemysław Kasiak***, Tomasz Kowalski, Kinga Rębiś, Andrzej Klusiewicz, Michał Starczewski, Maria Ładyga, Szczepan Wiecha, Marcin Barylski, Adam Rafał Poliwczak, Piotr Wierzbiński, Artur Mamcarz, Daniel Śliż. *Below or all the way to the peak? Oxygen uptake efficiency slope as the index of cardiorespiratory response to exercise—the NOODLE study*
   DOI: 10.3389/fphys.2024.1348307

Frontiers in Physiology: IF=3,4 | kwartyl JCR Q1 | centyl JCR 77,6

**Przemysław Kasiak jest pierwszym i korespondującym autorem*

3. **Przemysław Kasiak***, Tomasz Kowalski, Kinga Rębiś, Andrzej Klusiewicz, Dorota Sadowska, Adrian Wilk, Szczepan Wiecha, Marcin Barylski, Adam Rafał Poliwczak, Piotr Wierzbiński, Artur Mamcarz, Daniel Śliż. *Oxygen uptake efficiency plateau is unaffected by fitness level - the NOODLE study*
   DOI: 10.1186/s13102-024-00939-w

BMC Sports Science, Medicine and Rehabilitation: IF=2,8 | kwartyl JCR Q1 | centyl JCR 86,0

**Przemysław Kasiak jest pierwszym i korespondującym autorem*

4. **Przemysław Kasiak***, Tomasz Kowalski, Andrzej Klusiewicz, Ryszard Zdanowicz, Maria Ładyga, Szczepan Wiecha, Artur Mamcarz, Daniel Śliż. *Recalibrated FRIEND equation for peak oxygen pulse is accurate in endurance athletes: the NOODLE study*
   DOI: 10.1038/s41598-024-73730-z

Scientific Reports: IF=3,9 | kwartyl JCR Q1 | centyl JCR 82,0

**Przemysław Kasiak jest pierwszym i korespondującym autorem*

Artykuły przeglądowe

1. Tomasz Kowalski[#], **Przemysław Kasiak[#]***, Tomasz Chomiuk, Artur Mamcarz, Daniel Śliż. *Optimizing the Interpretation of Cardiopulmonary Exercise Testing in Endurance Athletes: Precision Approach for Health and Performance*
   DOI: 10.1155/tsm2/5904935

Translational Sports Medicine: IF=1,9 | kwartyl JCR Q2 | centyl JCR 55,6

[#]*Tomasz Kowalski i Przemysław Kasiak są równorzędnymi pierwszymi autorami*
**Przemysław Kasiak jest autorem korespondującym*

2. Tomasz Chomiuk, **Przemysław Kasiak***, Artur Mamcarz, Daniel Śliż. *Specificity and Areas of Usage of Cardiovascular Prediction Models Among Athletes—State-of-the-art Review*
   DOI: 10.31083/RCM37493

Reviews in Cardiovascular Medicine: IF=1,3 | kwartyl JCR Q3 | centyl JCR 27,9

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Spis treści

Wykaz stosowanych skrótów

Skrót	Rozwinięcie w języku angielskim / rozwinięcie w języku polskim*
ACCP	American College of Chest Physicians / Amerykańskie Towarzystwo Lekarzy Chorób Klatki Piersiowej
ATS	American Thoracic Society / Amerykańskie Towarzystwo Chorób Klatki Piersiowej
CHEER	Cardiopulmonary Health and Endurance Exercise Registry
CPET	Cardiopulmonary exercise test / Sercowo-płucny test wysiłkowy
CRF	Cardiorespiratory fitness / Wydolność fizyczna
EKG	Electrocardiogram / Elektrokardiogram
FRIEND	Fitness and the Importance of Exercise: A National Data Base
HR	Heart rate / Tętno
HR_{max}	Maximal heart rate / Tętno maksymalne
$ICC_{3,1}$	Two-way mixed effects intraclass correlation coefficient / Dwukierunkowy współczynnik korelacji wewnątrzklasowej o efektach mieszanych
NOODLE	predictioN mOdels fOr enDurance athLetEs
O_2P_{peak}	Peak oxygen pulse / Szczytowy puls tlenowy
OUEP	Oxygen uptake efficiency plateau / Plateau efektywności zużycia tlenu
OUES	Oxygen uptake efficiency slope / Krzywa efektywności zużycia tlenu
RER	Respiratory exchange ratio / Współczynnik wymiany oddechowej
RMSE	Root mean square error / Błąd średniokwadratowy
R^2	Coefficient of determination / Współczynnik determinacji
$\dot{V}E/\dot{V}CO_2$	Ventilatory efficiency / Współczynnik wentylacji do produkcji dwutlenku węgla
$\dot{V}E$	Minute ventilation / Wentylacja minutowa
$\dot{V}O_2$	Oxygen uptake / Pobór tlenu

$\dot{V}O_{2max}$	Maximal oxygen uptake / Maksymalny pobór tlenu

***Rozwinięcie w języku polskim podano, jeżeli dane pojęcie ma swoje specyficzne polskie rozwinięcie**

Streszczenie

Wstęp: Złotym standardem do oceny wydolności fizycznej pozostaje CPET, a najczęściej wyznaczanym parametrem jest $\dot{V}O_{2max}$. Wyniki CPET obserwowane u sportowców mogą różnić się w porównaniu z populacją ogólną/niewytrenowaną. Dotychczas powstał szereg danych normatywnych i równań predykcyjnych dla CPET oraz $\dot{V}O_{2max}$ dla populacji ogólnej lub sportowców rekreacyjnych. Mimo wartości diagnostycznej płynącej z innych zmiennych wysiłkowych, brakuje dla nich wartości referencyjnych dostosowanych do sportowców zaawansowanych, ze szczególnymi uwzględnieniem parametrów dwuczynnikowych. Mimo że choroby układu krążenia dotyczą również sportowców oraz wpływają na wyniki CPET, ich epidemiologia różni się od populacji ogólnej.

Cele: Pierwszorzędowym celem badania NOODLE było opracowanie specyficznych wartości referencyjnych i równań predykcyjnych przeznaczonych do analizy wyników CPET wśród sportowców wyczynowych ze szczególnym uwzględnienie zmiennych dwuczynnikowych. Wtórnymi celami były: (1) omówienie epidemiologii chorób układu krążenia i zastosowań pośrednich metod ich oceny wśród sportowców, (2) optymalizacja interpretacji wyników CPET w populacji sportowców, (3) podsumowanie zbiorów wartości referencyjnych i równań predykcyjnych dla CPET w populacji osób aktywnych fizycznie i sportowców.

Materiał i metody: Maksymalny CPET przeprowadzono na ergometrze rowerowym wśród 140 sportowców zaawansowanych (55% mężczyzn; wiek=22,7±4,6 lat; BMI=22,6±1,7 $kg \cdot m^{-2}$; $\dot{V}O_{2max}$=55,2±8,6 $mL \cdot kg^{-1} \cdot min^{-1}$) oraz na bieżni mechanicznej wśród 94 sportowców (66% mężczyzn; wiek=27,5±5,3 lat; BMI=22,4±2,5 $kg \cdot m^{-2}$; $\dot{V}O_{2max}$=56,7±8,6 $mL \cdot kg^{-1} \cdot min^{-1}$). Wyselekcjonowano oraz przeprowadzono walidację zewnętrzną 25 równań predykcji dla $\dot{V}E/\dot{V}CO_2$, OUES, OUEP oraz O_2P_{peak}. Po potwierdzeniu spełnienia założeń dla wieloczynnikowej kroczącej regresji liniowej, opracowano nowe równania referencyjne, skalibrowano już istniejące oraz przeprowadzono dodatkową walidację wyprowadzonych równań. Wyselekcjonowano ilustratywne i wiodące badania w obszarze kardiologii sportowej i CPET, które zostały umówione narratywnie.

Wyniki: $\dot{V}E/\dot{V}CO_2$ było znamiennie wyższe wśród sportowców zaawansowanych u kobiet niż u mężczyzn (27,7±2,6 vs. 26,1±2,0, $p<0,001$) oraz różne między poszczególnymi metodami wyznaczania ($p<0,001$–$0,043$). $\dot{V}E/\dot{V}CO_2$ rosło wraz z wiekiem u młodych sportowców, niezależnie od metody pomiaru (β=0,066–0,127). OUES był znacząco wyższy u sportowców, ale nie wykazał znamiennych różnic między 75%, 90% i 100% czasu CPET u mężczyzn ($p=0,65$) i u kobiet ($p=0,69$). Ponadnormatywna wydolność fizyczna miała minimalny wpływ

na wartości referencyjne dla OUEP wśród mężczyzn (−0,42 $mL \cdot L^{-1}$; p=0,39) oraz wśród kobiet (+0,33 $mL \cdot L^{-1}$; p=0,59). Kalibracja oryginalnego równania FRIEND o wartość dla O_2P_{peak} zredukowała błąd u mężczyzn z 2,9 ± 2,9 $mL \cdot beat^{-1}$ (p<0,001) do 0,1±2,9 $mL \cdot beat^{-1}$ (p=0,82) oraz u kobiet z 2,2 ± 2,1 $mL \cdot beat^{-1}$ (p<0,001) do 0,2±2,1 $mL \cdot beat^{-1}$ (p=0,65). Obecne równania predykcyjne w oryginalnej formie nie zaprezentowały zadowalającej dokładności dla $\dot{V}E/\dot{V}CO_2$ (R^2=0,003-0,031; –3,6, +0,2), OUES (R^2=0,004–0,388; $ICC_{3,1}$=0,062–0,529), OUEP (R^2=0,099; RMSE=4,16–4,84 $mL \cdot L^{-1}$) oraz O_2P_{peak} (R^2=0,62; p<0,001). Nowe równania predykcyjne dla sportowców były lepiej sprofilowane do tej populacji i prezentowały zaniedbywalny błąd w walidacji (R^2 [OUES]=0,36; R^2 [OUEP]=0,129; R^2 [O_2P_{peak}]=0,62).

Wnioski: Zależności między wybranymi zmiennymi w CPET różnią się znamiennie między sportowcami zaawansowanymi a populacją ogólną. Zastosowanie ogólnych wartości referencyjnych i równań predykcyjnych do populacji sportowców rodzi ryzyko błędnej interpretacji wyników CPET. Prognostyczne/diagnostyczne modele predykcji mogą zostać zastosowane wśród sportowców. Należy stosować specyficzne normy i zasady, aby prawidłowo intepretować wyniki CPET u sportowców zaawansowanych.

Angielska wersja tytułu rozprawy

Investigation of the predictions and relationships between selected cardiopulmonary variables in sports cardiology

Streszczenie w języku angielskim

Introduction: CPET is a gold standard to assess CRF, with its main indicator being $\dot{V}O_{2max}$. Results of athletes' CPET differ from those of the general population. Despite a substantial number of normative values and prediction equations for CPET and $\dot{V}O_{2max}$ having been developed, the majority focused on the general population or recreational athletes. The normative values tailored for competitive athletes are limited, with particular emphasis on variables other than $\dot{V}O_{2max}$ and bivariate parameters. Athletes also suffer from cardiovascular diseases, which aggravate CRF. However, the epidemiology of cardiovascular diseases in those populations differs from that of the untrained subjects.

Aims: The primary aim of the NOODLE study was to develop specific reference values and prediction equations for CPET tailored for competitive athletes, with particular emphasis on bivariate indices. Secondary objectives were: (1) to discuss the epidemiology of cardiovascular diseases and the application of indirect methods for their assessment among athletes, (2) to optimize the interpretation of CPET results in the athlete's population, and (3) to summarize reference values and prediction equations for CPET in the physically active population with particular emphasis on athletes.

Materials and methods: Maximal CPET was performed on a cycle ergometer by 140 elite athletes (55% males; age=22.7±4.6 years; BMI=22.6±1.7 $kg \cdot m^{-2}$; $\dot{V}O_{2max}$=55.2±8.6 $mL \cdot kg^{-1} \cdot min^{-1}$) and on a treadmill by 94 elite athletes (66% males; age=27.5±5.3 years; BMI=22.4±2.5 $kg \cdot m^{-2}$; $\dot{V}O_{2max}$=56.7±8.6 $mL \cdot kg^{-1} \cdot min^{-1}$). 25 prediction equations for $\dot{V}E/\dot{V}CO_2$, OUES, OUEP, and O_2P_{peak} were selected and externally validated. The assumptions for the multivariate stepwise linear regression were tested and found to be acceptable. Therefore, this method was used to derive new prediction equations and calibrate the existing ones. Developed equations were additionally validated. The most illustrative and promising studies in the area of CPET and sports cardiology were selected and discussed narratively.

Results: $\dot{V}E/\dot{V}CO_2$ was significantly higher in females than in males (27.7±2.6 vs. 26.1±2.0, P<0.001) and differed between the plotting methods (P<0.001–0.043). $\dot{V}E/\dot{V}CO_2$ increased with age in young endurance athletes, regardless of the plotting method (β=0.066–0.127). Although OUES was significantly higher in athletes, there were no significant differences between 75%-

, 90%-, and 100%-time intervals during CPET in males (P=0.65) and females (P=0.69). Extreme fitness had minimal effect on OUEP in males (−0.42 mL·L^{-1}; P=0.39) and females (+0.33 mL·L^{-1}; P=0.59). Calibration for endurance athletes of the original FRIEND equation for O_2P_{peak} reduced the bias in males from 2.9±2.9 mL·beat^{-1} (P<0.001) to 0.1±2.9 mL·beat^{-1} (P=0.82) and in females from 2.2±2.1 mL·beat^{-1} (P<0.001) to 0.2±2.1 mL·beat^{-1} (P=0.65). The available prediction equations in their original form presented limited accuracy for $\dot{V}E/\dot{V}CO_2$ (R^2=0.003–0.031; –3.6, +0.2), OUES (R^2=0.004–0.388; $ICC_{3.1}$=0.062–0.529), OUEP (R^2=0.099; RMSE=4.16–4.84 mL·L^{-1}), and O_2P_{peak} (R^2=0.62; P<0.001). The new prediction equations tailored for athletes were accurate and presented negligible bias (R^2 [OUES]=0.36; R^2 [OUEP]=0.129; R^2 [O_2P_{peak}]=0.62).

Conclusions: The relationships between selected CPET variables differ significantly between endurance athletes and the general population. Direct adaptation of general reference values and prediction equations to the athletic population poses a risk of misinterpretation of CPET results. Prognostic/diagnostic prediction models can be implemented in the cardiovascular care of athletes. Specific principles should be applied to optimize the interpretation of CPET results among athletes.

Wstęp uzasadniający połączenie wskazanych publikacji w jeden cykl, jak i komentujący osiągniecie naukowe kandydata na tle dotychczasowego stanu wiedzy

CPET stanowi złoty-standard oceny wydolności fizycznej, a także pozwala na wszechstronną ocenę układu krążenia (1). CPET może być wykorzystywany w diagnostyce chorób układu krążenia, kiedy inne metody diagnostyczne (np. EKG, echokardiografia, badanie fizykalne) nie pozwalały na postawienie definitywnej diagnozy. Wartość CPET wykracza również ponad medycynę, obejmując diagnostykę sportową i badania w zakresie fizjologii wysiłku fizycznego (1). W szczególności może być wykonywany wśród sportowców w trakcie sezonu i w okresach przygotowawczych do monitorowania wydolności oraz programowania treningu. W praktyce CPET najczęściej prowadzi się na bieżni lub ergometrze rowerowym, jednak w literaturze spotyka się prace na innych urządzeniach, np. ergometrze wioślarskim (2). Stąd, jego zastosowanie jest szczególnie wartościowe w dyscyplinach wytrzymałościowych, w których odzwierciedla rzeczywistą formę wysiłku występującą w trakcie treningu czy zawodów (1).

Wartości referencyjne stanowią zbiór danych, które powinny wystąpić w danej populacji w prawidłowych warunkach (3, 4). Są punktem odniesienia, wobec którego można porównywać wyniki otrzymywane w rzeczywistości. Różnice między faktycznym pomiarem, a danymi normatywnymi powinny skłaniać ku dalszej diagnostyce mogąc sugerować patologię. Wartości normatywne są opracowywane dla szeregu testów diagnostycznych i mogą przyjmować różne formy, zwykle tabelaryczne, prezentując jedynie absolutne wartości.

Jednak wartości tabelaryczne dla CPET powinny być prezentowane razem z równaniami predykcyjnymi (określanymi również jako modele predykcyjne czy równania predykcyjne), aby zapewnić prawidłowe dopasowanie danych normatywnych (5, 6). Równania referencyjne dla CPET wykorzystują komponenty antropometryczne (tzn. wiek, wzrost, masa ciała itp.), aby bez konieczności wykonywania testu wysiłkowego możliwie precyzyjnie oszacować, jakie wyniki powinny wystąpić u danej osoby (3, 4). Niekiedy, wykonywane są również analizy porównawcze na ile równania predykcyjne mogą odzwierciedlać lub zastępować bezpośrednie pomiary (np. CPET) oraz jaki jest błąd w danych przewidywanych (7). Należy podkreślić że, modele powinny przechodzić również walidację wewnętrzną i/lub zewnętrzną, aby ocenić ich uniwersalne zastosowanie (8).

Dane normatywne różnią się znacząco między populacjami i są podatne na czynniki zaburzające (5, 9). Liczne zmienne mogą wpływać na wartości normatywne: dane antropometryczne, poziom wydolności fizycznej i regularny trening. Intensywny trening, a w konsekwencji nieprzeciętna wydolność fizyczna, prowadzą do specyficznych adaptacji,

w tym krążeniowo-oddechowych. Zmiany są widoczne dla różnych testów diagnostycznych, nie tylko CPET. Ponadto, adaptacje w układzie krążenia są głównie przypisywane dyscyplinom wytrzymałościowym (np. bieganie, kolarstwo). Przykładem jest EKG, w którym mogą pojawić się m.in. cechy większego woltażu w kompleksie QRS będące wariantem normy. Ilustrują one adaptację fizjologiczną (tzw. Serce Sportowca – Athlete's Heart) i są naturalną zmianą wynikającą z kontynuowania treningu u osób bezobjawowych, bez historii rodzinnej czy wrodzonych chorób serca (10). Podobne zmiany u osób nieaktywnych fizycznie mogłyby sugerować przerost patologiczny i kierunkować dalszą diagnostykę na poszukiwanie ich przyczyn (11, 12). Należy tutaj zauważyć, że CPET (podobnie jak echokardiografia) może być wykorzystywany w celu różnicowania adaptacji wysiłkowych względem zmian patologicznych u sportowców i jest to jedno z jego szczególnych zastosowań (13).

Dotychczas powstał szereg wartości normatywnych dla CPET. Jednak, głównie są to opracowania dla populacji ogólnych i niewytrenowanych – rejestr FRIEND, równania Wasserman'a i pochodne mu prace (3, 4, 13). Obecnie nawet ¾ laboratoriów CPET na świecie używa u sportowców równań predykcyjnych pochodzących z populacji ogólnych (13). W ostatnich latach ukazały się dane z rejestru CHEER sprofilowanego dla sportowców (5). Jednak, w dużej mierze byli to sportowcy rekreacyjni w wieku około 40 lat, a niektórzy z uczestników mieli choroby współistniejące. Stąd, populacja nie do końca odzwierciedlała uniwersalną definicję sportowca preferowaną przez towarzystwa medyczne/naukowe (14, 15). Ponadto, dotychczasowe równania predykcyjne w znakomitej większości skupiały się na podstawowych zmiennych jednoczynnikowych – $\dot{V}O_{2max}$ czy HR_{max} (w przytoczonym wyżej rejestrze CHEER zaprezentowano jedynie równania dla $\dot{V}O_{2max}$ dla sportowców rekreacyjnych) (6, 16).

Jednak, w CPET można wyznaczyć szereg innych zmiennych, które rozszerzają analizę wydolności fizycznej. Znacząco ograniczona pozostaje wiedza w obszarze zmiennych stanowiących ilorazy kilku czynników. Przykładami pozostają: $\dot{V}E/\dot{V}CO_2$ (iloraz minutowej wentylacji i produkcji dwutlenku węgla), OUES (iloraz $\dot{V}O_2$ oraz logarytmu z $\dot{V}E$), OUEP (szczytowa 90-sekundowa ciągła wartość w ilorazie $\dot{V}O_2$ oraz $\dot{V}E$), a także O_2P_{peak} (szczytowa wartość ilorazu $\dot{V}O_2$ i HR z jednego interwału uśredniania) (17-20). Każda z opisanych zmiennych dwuczynnikowych wzbogaca wartość diagnostyczną CPET i stanowi uzupełnienie dla klasycznego złotego standardu jakim pozostaje $\dot{V}O_{2max}$.

Poza opisywanym rejestrem CHEER spotykane były publikacje na mniejszych grupach sportowców, badania pozostające w obszarze analiz $\dot{V}O_{2max}/HR_{max}$ lub prace bez jasno

zdefiniowanego celu opracowania wartości normatywnych i analizy dokładności równań predykcyjnych. Stąd, wciąż pozostawał szereg parametrów, dla których brakowało wysokiej jakości danych normatywnych sprofilowanych dla sportowców (spełniających przesłanki przytoczonej uniwersalnej definicji), a także opracowanych w oparciu o rzetelną metodologię.

Mimo, że zastosowanie powyższych zmiennych dwuczynnikowych nie jest rozpowszechnione, pojawiają się przesłanki, że mogą mieć one swoją wartość diagnostyczną również w grupach sportowców. W 2023 r. ukazały się wartości normatywne dla $\dot{V}E/\dot{V}CO_2$ z tego samego ośrodka co rejestr CHEER (21). Stąd, również metodologia i dobór uczestników były podobne i nie do końca pokrywały się z uniwersalną definicją sportowca. $\dot{V}E/\dot{V}CO_2$ można wyznaczać na różne sposoby: do pierwszego progu wentylacyjnego (slope) jako najniższa średnia z interwału uśredniania (nadir) czy z całego wysiłku (total) (17). Wyniki sugerowały, że przynajmniej część sportowców może przekraczać zalecane, bezpieczne punkty odcięcia (tzn. 30 i 34) dla każdej z metod wyznaczania $\dot{V}E/\dot{V}CO_2$. Biorąc pod uwagę przesłanki z przytoczonych prac, które wskazują że $\dot{V}E/\dot{V}CO_2$ może być nieznacznie zawyżone w trakcie wysiłku u sportowców rekreacyjnych, można spodziewać się dalszego trendu wzrostowego wraz ze wzrostem poziomu zaawansowania sportowca (tzn. bardziej wytrenowani uczestnicy mogą wykonywać większy wysiłek w CPET i tym większy odsetek może przekraczać punkty odcięcia lub zawyżenie może być bardziej znaczące) (21). Jednakże, taka hipoteza wymagała dalszej inwestygacji. Ponadto, zachodzą zasadne przesłanki, że $\dot{V}E/\dot{V}CO_2$ prezentuje istotne uzupełnienie do $\dot{V}O_2$ w ocenie młodych osób z kardiomiopatią przerostową, w tym sportowców (22). Mimo że, $\dot{V}O_2$ może niekiedy pozostawać zachowane bez jego znamiennej redukcji, $\dot{V}E/\dot{V}CO_2$ zwykle rośnie. Stąd, w ostatnim czasie rekomenduje się równoległą analizę $\dot{V}O_2$ i $\dot{V}E/\dot{V}CO_2$ u sportowców z potwierdzoną lub podejrzewaną kardiomiopatią przerostową (22). Pozostaje to w korespondencji z zasadnością przeprowadzenia badań własnych, w których przeanalizowano podstawowe zależności w $\dot{V}E/\dot{V}CO_2$ u sportowców. Podkreśla się również konieczność, aby wartości normatywne stosowane w praktyce pochodziły z populacji o podobnej charakterystyce. Stąd, zastosowanie wyników z populacji sportowców rekreacyjnych (niekiedy z chorobami współistniejącymi) w grupie zaawansowanych sportowców (regularnie startujących w zawodach i poddawanych pełnym kwalifikującym badaniom medycznym) rodzi ryzyko błędów.

Ponadto, w ostatnich latach pojawiły się prace, w których zasugerowano, że dalece ponadprzeciętna wydolność fizyczna ma zaniedbywalny wpływ na OUEP (19). Najczęściej $\dot{V}O_{2max}$ rośnie wprost proporcjonalnie do osiąganych wyników w sportach wytrzymałościowych (3). Powoduje to konieczność poszukiwania uniwersalnych wskaźników,

które mogłyby pozostawać stosowane zarówno w populacji sportowców, jak i osób nieaktywnych fizycznie, a ich zmienność między oboma grupami byłaby niewielka. Xing Guo-Sun wraz z zespołem, będący twórcą koncepcji dotyczącej OUEP, zasugerował, że może on nie rosnąć w przypadku wysokiej wydolności fizycznej, ale spadać w przypadku patologii (19, 23). Jednak, podkreślono, że opisana zależność wymaga potwierdzenia, a liczba uczestników określanych jako „*very fit*" (w badaniach autorów odpowiednik sportowców zaawansowanych/elitarnych) była niewielka i została sparowana w analizach z niewytrenowaną populacją ogólną. Stąd, ocena opisywanej zależność wymagała dalszych badań na wyselekcjonowanej szerszej grupie sportowców zaawansowanych.

Wartość diagnostyczna jest najczęściej przypisywana maksymalnemu CPET. Wysiłek maksymalny jest potwierdzany przez szereg czynników, jak plateau w $\dot{V}O_{2max}$, RER, skala Borga czy punkt odcięcia przewidywanego HR_{max} (7). Jednakże, żadne z przytoczonych kryteriów nie jest determinujące i każde może być różnie interpretowane. Plateau w $\dot{V}O_{2max}$ nie zawsze występuje, szczególnie u sportowców i osób młodych (24). Punkty odcięcia dla RER są różne – typowo 1.10 wg wytycznych ATS/ACCP (25), ale spotyka się również 1.05 (w rejestrze CHEER i niektórych pracach na sportowcach) (5), czy 1.00 (wśród dzieci) (26). Skala Borga ma swoje ograniczenia ze względu na subiektywny charakter i duży wpływ indywidualnej motywacji uczestnika (27). Procentowe punkty odcięcia są często stawiane na podstawie HR_{max} szacowanego ze wzorów (popularnych równań z ujemną komponentą wiekową, np. 220 – wiek), które same pozostają metodą niedoskonałą (28). Pozostaje to w korespondencji z faktem, że HR_{max} wykazuje dużą zmienność między osobami, nawet o podobnej charakterystyce demograficznej (28, 29). Ponadto, testy maksymalne nie zawsze mogą zostać wykonane (np. po kontuzji u sportowców). Podsumowując przytoczone przesłanki, zachodzi zauważalna potrzeba poszukiwania zmiennych submaksymalnych, które mogłyby wiarygodnie odzwierciedlać i/lub potwierdzać maksymalny wysiłek. Uwagę zwraca tutaj OUES, który u osób niewytrenowanych może nie wykazywać znamiennych różnic między różnymi interwałami wysiłku (np. 50% vs. 75% vs. 90% vs. 100% czasu trwania CPET lub RER<1.00 vs. RER≥1.10), a wartości submaksymalne OUES mogą być silnie skorelowane z $\dot{V}O_{2max}$ (18, 30). Jednakże, nikt dotychczas nie analizował zależności w OUES dla populacji sportowców, w szczególności sportowców zaawansowanych. Ponadto, nie ma prac analizujących powtarzalność i korelację maksymalnego i submaksymalnego OUES względem $\dot{V}O_{2max}$ u sportowców, a także relacji OUES względem parametrów demograficznych w tej populacji.

Jak podkreślono wcześniej, zasadnym jest, aby wartości referencyjne, które są stosowane do danej populacji pochodziły z grupy o podobnej charakterystyce (3). Do pewnego stopnia kwestionuje to cel obszernych badań rejestrowych, np. FRIEND, które miały stanowić uniwersalne źródło danych normatywnych. Wśród modeli prognostycznych/diagnostycznych często spotyka się tzw. *kalibrację* (31). Wśród pozostałych zmiennych dwuczynnikowych istnieją ograniczone dane dotyczące O_2P_{peak}, mimo jego wartości uzupełniającej CPET i do pewnego stopnia odzwierciedlającej objętość wyrzutową serca (32). Jedyne równanie predykcyjne dla O_2P_{peak} pochodziło dotychczas z rejestru FRIEND i zostało wyprowadzone z grupy testów wysiłkowych na bieżni (20). Dostęp do podobnych danych testów wysiłkowych na bieżni dla sportowców na zaawansowanym poziomie (tzn. odbiegających charakterystyką od populacji pierwotnej) skłaniałby do adaptacji tego równania. Bazując na modelu O_2P_{peak} można zaprezentować pewien schemat metodologiczny adaptujący *kalibrację* do równań regresji liniowej.

Obserwacje płynące z powyżej przytoczonych badań skłaniają ku ocenie możliwości adaptacji istniejących zbiorów wartości normatywnych do sportowców zaawansowanych i ewentualnym opracowaniu nowych równań referencyjnych. Występuje zauważalna potrzeba, aby udoskonalić interpretację CPET u sportowców i określić granice normy dla mniej popularnych zmiennych krążeniowo-oddechowych, w tym wskaźników wieloczynnikowych zyskujących w ostatnim czasie coraz więcej uwagi w analizie CPET.

W badaniach własnych analizie zostały poddane $\dot{V}E/\dot{V}CO_2$, OUES, OUEP i O_2P_{peak}. Opracowano wartości normatywne dla elitarnych sportowców i poszerzono je o walidację istniejących i/lub nowe równania referencyjne wykorzystujące zmienne demograficzne (tzw. modele predykcji). Zarówno dotychczasowe, jak i nowoopracowane równania przeszły walidację z wykorzystaniem zróżnicowanych metod statystycznych – walidacji krzyżowej (ang. *cross-validation*), metod samowspornych (ang. *bootstapping*), wizualizacji Blanda-Altmana, wzajemnej regresji, bezpośredniego porównania średnich, kalkulacji błędu absolutnego i pierwiastka z błędu średniokwadratowego. Pokrywa się to z większością głównych metod walidacji stosowanych dotychczas w literaturze, aby pozostać w zgodzie z ugruntowanymi standardami.

Publikacje oryginalne zostały poszerzone o dwie narratywne prace przeglądowe, w tym jeden przegląd *State-of-the-art*. Wyniki badań własnych NOODLE podkreśliły rozbieżności między wynikami CPET u sportowców zaawansowanych względem sportowców rekreacyjnych i populacji nieaktywnej fizycznie. Obserwacje w dalszej kolejności skłoniły ku przygotowaniu

poradnika podsumowującego zasady interpretacji CPET u sportowców – stanowiącego pierwszy z artykułów poglądowych. Stąd, zaprezentowane zostały metody optymalizacji analizy testów wysiłkowych ze szczególnym uwzględnieniem wyników badania NOODLE. Choroby układu krążenia nie omijają również populacji sportowców (33), jednak ich epidemiologia różni się od populacji ogólnej. Wśród ludzi nieaktywnych fizycznie dominują choroby przewlekłe, np. nadciśnienie tętnicze czy dyslipidemie, a wśród sportowców i osób młodych spotyka się zaburzenia rytmu serca oraz wrodzone anomalie (33-35). Przegląd *State-of-the-art* zbiera najnowszą literaturę w zakresie chorób układu krążenia wśród sportowców, a także komentuje zastosowanie pośrednich metod diagnostycznych (tj. diagnostycznych i prognostycznych modeli predykcji) w kardiologii sportowej. Jest to pierwsze tego typu podsumowanie, które w dużym stopniu skupiło się na modelach diagnostycznych/prognostycznych u sportowców, a także szeroko dyskutowało obszary ich zastosowania ponad populacje kliniczne i nieaktywne fizycznie.

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Założenia i cele prac

Celami publikacji wchodzących do niniejszego cyklu były:

- Ocena różnic w wartościach normatywnych dla wybranych parametrów krążeniowo-oddechowych u sportowców zaawansowanych trenujących dyscypliny wytrzymałościowe w porównaniu do populacji ogólnej.
- Opracowanie wartości normatywnych dla wybranych zmiennych krążeniowo-oddechowych w populacji sportowców zaawansowanych trenujących dyscypliny wytrzymałościowe.
- Określenie dokładności obecnych równań referencyjnych w populacji sportowców zaawansowanych trenujących dyscypliny wytrzymałościowe.
- Opracowanie i walidacja nowych równań referencyjnych sprofilowanych na populację sportowców zaawansowanych trenujących dyscypliny wytrzymałościowe.
- Opracowanie i prezentacja nowej metody kalibracji ogólnych równań referencyjnych do populacji o specyficznej charakterystyce korzystając z przykładu grupy sportowców zaawansowanych trenujących dyscypliny wytrzymałościowe i wybranej zmiennej.
- Aktualizacja obecnych wartości normatywnych dla CPET, ze szczególnym uwzględnieniem osób uprawiających sport.
- Podsumowanie epidemiologii chorób układu krążenia wśród sportowców.
- Podsumowanie obszarów zastosowania klasycznych modeli predykcji do oceny układu krążenia wśród sportowców oraz osób aktywnych fizycznie.

Kopie opublikowanych prac

Publikacja nr 1

Tytuł:

Is the Ventilatory Efficiency in Endurance Athletes Different?—Findings from the NOODLE Study

Autorzy:

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Typ publikacji:

Artykuł oryginalny

DOI:

10.3390/jcm13020490

Czasopismo:

Journal of Clinical Medicine

IF=2,9 | kwartyl JCR Q1 | centyl JCR 80,6

Artykuł wybrany jako *Editor's Choice* na okres drugiego kwartału 2025 r. dla badań o szczególnie wysokiej wartości naukowej

Journal of
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Article

Is the Ventilatory Efficiency in Endurance Athletes Different?—Findings from the NOODLE Study

Przemysław Kasiak [1,*], Tomasz Kowalski [2], Kinga Rębiś [2], Andrzej Klusiewicz [3], Maria Ładyga [2], Dorota Sadowska [2], Adrian Wilk [4], Szczepan Wiecha [3], Marcin Barylski [5], Adam Rafał Poliwczak [5], Piotr Wierzbiński [1], Artur Mamcarz [1] and Daniel Śliż [1]

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Abstract: Background: Ventilatory efficiency (VE/VCO_2) is a strong predictor of cardiovascular diseases and defines individuals' responses to exercise. Its characteristics among endurance athletes (EA) remain understudied. In a cohort of EA, we aimed to (1) investigate the relationship between different methods of calculation of VE/VCO_2 and (2) externally validate prediction equations for VE/VCO_2. **Methods:** In total, 140 EA (55% males; age = 22.7 ± 4.6 yrs; BMI = 22.6 ± 1.7 $kg \cdot m^{-2}$; peak oxygen uptake = 3.86 ± 0.82 $L \cdot min^{-1}$) underwent an effort-limited cycling cardiopulmonary exercise test. VE/VCO_2 was first calculated to ventilatory threshold (VE/VCO_2-slope), as the lowest 30-s average (VE/VCO_2-Nadir) and from whole exercises (VE/VCO_2-Total). Twelve prediction equations for VE/VCO_2-slope were externally validated. **Results:** VE/VCO_2-slope was higher in females than males (27.7 ± 2.6 vs. 26.1 ± 2.0, $p < 0.001$). Measuring methods for VE/VCO_2 differed significantly in males and females. VE/VCO_2 increased in EA with age independently from its type or sex (β = 0.066–0.127). Eleven equations underestimated VE/VCO_2-slope (from −0.5 to −3.6). One equation overestimated VE/VCO_2-slope (+0.2). Predicted and observed measurements differed significantly in nine models. Models explained a low amount of variance in the VE/VCO_2-slope (R^2 = 0.003–0.031). **Conclusions:** VE/VCO_2-slope, VE/VCO_2-Nadir, and VE/VCO_2-Total were significantly different in EA. Prediction equations for the VE/VCO_2-slope were inaccurate in EA. Physicians should be acknowledged to properly assess cardiorespiratory fitness in EA.

Keywords: prediction equation; cardiac physiology; cardiopulmonary exercise testing; VE/VCO_2-slope; cardiorespiratory fitness; exercise ventilation

Citation: Kasiak, P.; Kowalski, T.; Rębiś, K.; Klusiewicz, A.; Ładyga, M.; Sadowska, D.; Wilk, A.; Wiecha, S.; Barylski, M.; Poliwczak, A.R.; et al. Is the Ventilatory Efficiency in Endurance Athletes Different?—Findings from the NOODLE Study. *J. Clin. Med.* **2024**, *13*, 490. https://doi.org/10.3390/jcm13020490

Academic Editor: Birna Bjarnason-Wehrens

Received: 9 December 2023
Revised: 13 January 2024
Accepted: 14 January 2024
Published: 16 January 2024

1. Introduction

Ventilatory efficiency (VE/VCO_2) describes the relationship between pulmonary ventilation (VE) and carbon dioxide production (VCO_2) [1]. To keep acid–base balance during exercise, VE grows simultaneously with VCO_2 [2]. VE/VCO_2 merges circulatory and respiratory functions [1,3]. Several ways of measuring VE/VCO_2 have been proposed including VE/VCO_2 from start to first ventilatory threshold (VT1) (VE/VCO_2-slope), as the minimal continuous value (VE/VCO_2-Nadir) and across whole physical effort (VE/VCO_2-Total) [4].

Professional and elite athletes are exposed to high training loads [5]. Thus, more endurance athletes can be referred to with suspected cardiovascular diseases (CVD) [5]. Knowledge of cardiorespiratory indicators among endurance athletes remains important [6]. Precise risk stratification is of critical importance to ensure safe physical activity because it enables medical professionals to adjust clinical management and exercise intensity [5]. An

important prognostic role in CVD has been assigned to the VE/VCO_2-slope [7]. VE/VCO_2-slope is elevated in pulmonary hypertension, chronic obstructive pulmonary disease, interstitial lung disease, and other diseases. The pivotal role of the VE/VCO_2-slope was noted in heart failure (HF) [2,8].

Despite the VE/VCO_2-slope being a submaximal parameter, its prognostic power is comparable to peak oxygen uptake (VO_2peak) [1,9]. Studies on untrained populations reported lower VE/VCO_2 measurements in males and its increase with aging [10]. During clinical assessment, a cutoff below 30 is considered normal, and values above 34 to 36 suggest a high risk of mortality [7,11,12].

Previous research focused mainly on univariable measurements [13,14]. VE/VCO_2 is a ratio of two variables, i.e., VE and VCO_2. In other words, it is calculated by dividing one parameter by another. VE grows simultaneously with VCO_2 during continued physical effort to ensure efficient excretion of the produced metabolites [15]. The link between VE and VCO_2 is multifactorial. The slope continuously and stably increases from the start to VT1 [16]. Above this, VE is forced by lactate accumulation and the slope begins to steepen [10]. However, the physiology of VE/VCO_2 in endurance athletes is understudied.

Prediction equations provide several benefits. They allow for indirect calculation and facilitate the determination of the participant's health based on the comparison of direct measurements with predicted reference values [13]. There were some attempts to predict VE/VCO_2-slope with regression models [8,10,17–20], but there is no validation of those models. Previous research suggests that the usage of unified equations might not be optimal both in untrained individuals and athletes [8,21]. Few studies evaluated VE/VCO_2 in athletes [22–24]. However, none of them verified the underlying dependency of different VE/VCO_2 measurements. Potentially, well-trained endurance athletes could maintain strenuous physical effort well beyond VT1, where VE/VCO_2-slope increases nonlinearly [25]. The use of inaccurate prediction models has negative consequences. Underestimated or overestimated values may lead to incorrect monitoring of training and disregard of potential risk factors. In turn, overestimated values may unnecessarily increase awareness and prevent demanding physical activity [3,13,21].

Research suggests that in athletes, VE/VCO_2 could be independent of the type of exercise testing, body mass, or endurance capacity [23]. Based on our recent studies on well-trained individuals [14,21], we stipulate that current prediction models do not allow for a transferable calculation of cardiorespiratory parameters from the general population. Moreover, the underlying relationship between several measuring options for VE/VCO_2 in athletic cohorts is still controversial. This study aimed to (1) externally validate prediction equations for the VE/VCO_2-slope in the athletic population and (2) explain the relationship between the VE/VCO_2-slope, VE/VCO_2-Nadir, and VE/VCO_2-Total.

2. Materials and Methods

2.1. Study Design

This study was conducted following the guidelines of the EQUATOR Network for observational studies: Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement [26]. The STROBE Checklist for Cross-Sectional Studies is provided in the Supplementary Material (Table S1). Research has been reviewed and approved by the Bioethics Committee of the Medical University of Warsaw (AKBE/277/2023). Participants provided their written informed consent. All study procedures were in line with the Declaration of Helsinki.

Healthy endurance athletes were referred to the standardized CPET. An endurance athlete was defined as having at least four years of regular training and competitive experience (at local and international levels). Participants held a membership in a sports association or training club and were also members of elite or development national teams. The tests were carried out in the years 2022–2023 at the Institute of Sport—National Research Institute in Warsaw (https://insp.pl; accessed on 22 October 2023). To be included, all

participants underwent a medical evaluation by a physician (physical examination, medical and family history) according to the routine procedures of the testing center.

We applied a rigorous selection process to obtain a group free of disturbing factors to test the raw relationships of VE/VCO_2 and ensure safe exercise tests. The preliminary exclusion criteria were any of the following: (1) respiratory diseases, (2) CVD, (3) neurological and psychiatric conditions, (4) musculoskeletal injuries limiting performance during CPET, (5) deviations in complete blood count, and (6) being a smoker. The final selection criteria were (1) age $\geq$ 18 years and (2) maximum CPET. For a visual presentation of the recruitment procedures, see Figure 1, and for exact definitions of exclusion criteria, see the Supplementary Material (Table S2).

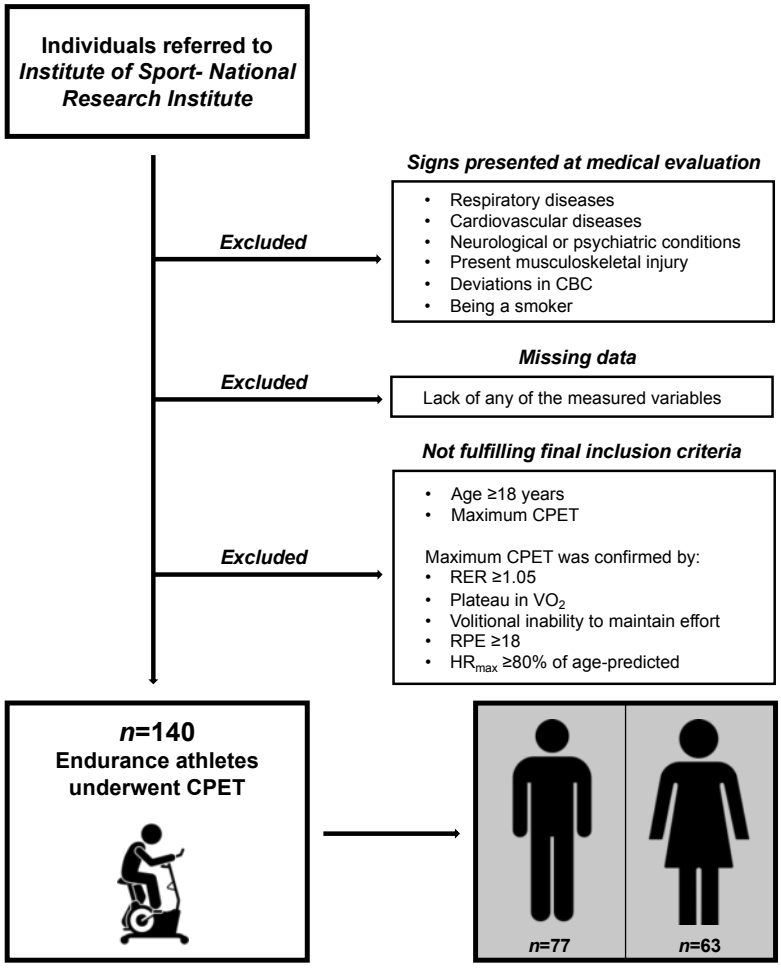

Figure 1. Visual presentation of participant recruitment procedures. CBC, complete blood count; CPET, cardiopulmonary exercise test; RER, respiratory exchange ratio; VO_2, oxygen uptake; RPE, rating of perceived exertion; HR_{max}, maximal heart rate.

2.2. CPET Protocol

CPETs were conducted following the same unified protocol. All tests were performed under unified laboratory conditions. According to the reference values for CPET in endurance athletes, the maximal effort was confirmed by the following: (1) respiratory exchange ratio (RER) $\geq$ 1.05, (2) plateau in VO_2 (stable VO_2 for $\geq$30 s), (3) volitional inability to maintain effort, (4) Borg rating of perceived exertion $\geq$ 18, and (5) maximal heart rate (HR) $\geq$ 80% of age-predicted [13,27]. The physiologist supervised each CPET. Participants were verbally encouraged to achieve peak performance.

CPET was performed on an upright cycle ergometer (Cyclus II Ergometer, RBM, Leipzig, Germany) in a ramp protocol. The tests began with a 2–3 min warm-up in the form of light pedaling without resistance. Participants completed an incremental test starting from 55 to 70 W, gradually increasing the load by 0.17–0.28 $W \cdot s^{-1}$. The working loads were individually adjusted in all provided ranges according to the performance capabilities of each athlete.

2.3. Study Endpoints

We measured basic demographic data: sex, age, height, weight, body mass index (BMI), and exercise performance. We obtained weight with the usage of a TANITA device (TANITA Corporation, Arlington Heights, IL, USA) and height with the usage of a SECA stadiometer (SECA GmbH & Co., Hamburg, Germany). Both weight and height were measured in the morning before breakfast. HR was measured with the Polar H10 chest strap (Polar Electro Oy, Kempele, Finland), continuously synchronized with the Cortex B3 Metamax. VE, VCO_2, oxygen uptake, respiratory rate, and tidal volume were measured by the Cortex B3 Metamax using the breath-by-breath method (Hans Rudolph V2 Mask, Hans Rudolph, Inc., Shawnee, KS, USA). Variables were averaged in 15-s intervals. All measurement devices were calibrated for each usage in line with the producer's instructions.

The v-slope method has been previously used to find VT1 [28]. VT1 was identified in all endurance athletes enrolled in this study. VE/VCO_2-slope was defined as the linear relationship between VE and VCO_2 from the start to VT1, excluding the first minute of the protocol, where noise values emerged. VE/VCO_2-Nadir was defined as the lowest continuous 30 s average. VE/VCO_2-Total was calculated across the whole CPET protocol without the first minute of the protocol.

2.4. Sample Characteristics

In total, 140 healthy, well-trained individuals fulfilled the study criteria. Sample characteristics stratified by sex are presented in Table 1. There were 77 (55.0%) males and 63 (45.0%) females. Participants represented the following endurance sports: 56 (40.0%) trained triathlon or cycling, 59 (42.1%) chose speedskating, and 25 (17.9%) preferred other disciplines. VO_2peak was 3.21 $\pm$ 0.48 $L \cdot min^{-1}$ for females and 4.40 $\pm$ 0.64 $L \cdot min^{-1}$ for males. Females noted a higher VE/VCO_2-slope than males (27.7 $\pm$ 2.6 vs. 26.1 $\pm$ 2.0). Two (2.6%) males exceeded the cutoff of 30 both for VE/VCO_2-slope and VE/VCO_2-Total, while all males maintained normal VE/VCO_2-Nadir. Eleven (17.5%) females exceeded the cut off of 30 both for VE/VCO_2-slope and VE/VCO_2-Total. Four (6.3%) of them had VE/VCO_2-Nadir above 30. There were no males with any $VE/VCO_2 > 34$; however, it was present for 4 (6.3%) females in VE/VCO_2-Total.

2.5. Selection of Prediction Models for Validation

Prediction equations for the VE/VCO_2-slope were collected based on Paap and Takken reference values for CPET [29,30] and by additional searches in 5 databases: PubMed, Web of Science, Scopus, Google Scholar, and Embase. Applied keywords were "ventilatory efficiency", "VE/VCO_2-slope", "prediction model", "prediction equation", "reference values", and "linear regression". To ensure similarity with our group, we excluded models primarily derived from pediatric or geriatric populations (<18 or >70 years old) and clinical samples with coexisting medical conditions. Finally, 12 models from 6 studies met the selection criteria, and their detailed description is presented in Table 2. All selected equations predicted the VE/VCO_2-slope to the first ventilatory threshold.

Table 1. Participant characteristics.

Variable		Total (n = 140)	Sex	
			Females (n = 63)	Males (n = 77)
Age (years)		22.7 ± 4.6	23.8 ± 4.2	21.8 ± 4.8
Height (cm)		174.8 ± 9.9	166.3 ± 6.2	181.6 ± 6.3
Weight (kg)		69.3 ± 10.1	61.0 ± 5.5	76.1 ± 7.6
BMI ($kg \cdot m^{-2}$)		22.6 ± 1.7	22.1 ± 1.6	23.1 ± 1.7
Primary sport	Speedskating	59 (42.1)	26 (41.3)	33 (42.9)
	Triathlon or cycling	56 (40.0)	30 (47.6)	26 (33.8)
	Other	25 (17.9)	7 (11.1)	18 (23.3)
HR ($beats \cdot min^{-1}$)		190.9 ± 8.9	191.0 ± 9.1	190.8 ± 8.7
VE ($L \cdot min^{-1}$)		154.5 ± 34.1	127.8 ± 21.1	176.3 ± 26.3
VO_2peak ($L \cdot min^{-1}$)		3.86 ± 0.82	3.21 ± 0.48	4.40 ± 0.64
VCO_2 ($L \cdot min^{-1}$)		4.36 ± 0.96	3.57 ± 0.52	5.00 ± 0.73
VO_2peak ($mL \cdot kg^{-1} \cdot min^{-1}$)		55.2 ± 8.6	52.1 ± 7.0	57.8 ± 9.0
RR ($breaths \cdot min^{-1}$)		60.0 ± 7.6	60.2 ± 6.7	59.9 ± 8.3
VT (L)		2.81 ± 0.64	2.30 ± 0.32	3.22 ± 0.53
RER (VO_2/VCO_2)		1.14 ± 0.05	1.13 ± 0.05	1.15 ± 0.05
VE/VCO_2-slope		26.8 ± 2.4	27.7 ± 2.6	26.1 ± 2.0
VE/VCO_2-Nadir		25.2 ± 2.3	26.2 ± 2.4	24.5 ± 2.0
VE/VCO_2-Total		28.0 ± 2.5	28.7 ± 2.7	27.3 ± 2.2
O_2P (VO_2/HR)		20.7 ± 4.4	17.3 ± 3.0	23.5 ± 3.3
Testing duration (minutes)		21.3 ± 2.6	21.1 ± 2.7	21.4 ± 2.6
Workload (watts)		320.4 ± 76.2	266.7 ± 40.8	364.4 ± 70.0

BMI, body mass index; HR, peak heart rate; VE, peak minute ventilation; VO_2peak, peak oxygen uptake; VCO_2, peak carbon dioxide output; RR, peak respiratory rate; VT, tidal volume; RER, peak respiratory exchange ratio; VE/VCO_2-slope, ventilatory efficiency from start to the first ventilatory threshold; VE/VCO_2-Nadir, the lowest 30-s continuous average for ventilatory efficiency; VE/VCO_2-Total, ventilatory efficiency from start to peak effort; O_2P, peak oxygen pulse. Data are presented as mean ± standard deviation for continuous variables or number (percentage) for categorical variables.

Table 2. Prediction equations selected for validation.

Reference	Model		Testing Protocol	Sample Size (Total/Males/Females)	Age (Years)
	Males	Females			
Salvioni et al. [8]	20.227 + 0.095 · age	23.808 + 0.052 · age	• Cycling CPET; ramp protocol. • Running CPET; Bruce protocol.	1136/773/363	13–83
	21.413 + 0.08 · age				
Kleber et al. [17]	19.9 + 0.13 · age	24.4 + 0.12 · age	Running CPET; modified Naughton protocol with increases in gradient and speed of 1 MET every 2 min.	101/45/56	16–75
Neder et al. [18]	21 + 0.12 · age	25.2 + 0.08 · age	Cycling CPET; ramp protocol with increases in power of 10–25 $W \cdot min^{-1}$ in females and 15–30 $W \cdot min^{-1}$ in males.	120/60/60	20–80
Loe et al. [20]	23.897 + 0.072 · age + 0.826	25.549 + 0.072 · age	Running CPET; ramp protocol with increase in speed of 1 $km \cdot h^{-1}$ or gradient of 2% every 2–3 min.	4631/2261/2370	20–90
Ashikaga et al. [19]	22.4 + 0.07 · age	22.467 + 0.07 · age	Cycling CPET; ramp protocol with increases in power of 10 $W \cdot min^{-1}$ or 20 $W \cdot min^{-1}$.	529/274/255	20–78
Sun et al. [10]	34.38 + 0.082 · age − 0.0723 · height		Running or cycling CPET; incremental maximal protocols with varying duration.	474/310/164	37–74

CPET, cardiopulmonary exercise test; MET, metabolic equivalent. For all models, age is expressed in years. All models apply to the ventilatory efficiency slope from the start to the first ventilatory threshold.

2.6. Statistical Analysis

Data distribution was examined by the Shapiro–Wilk test and quantile–quantile plots. Due to parametric distribution, continuous variables are presented as mean ± standard deviation. Categorical variables are presented as numbers (percentages). In cases of missing data in any of the measured variables, participants were excluded from the analysis to ensure maximum precision. The sample was evaluated in the G*Power Software (version 3.1.9.6) [31] to obtain significance ($p < 0.05$) and large effect sizes for each applied statistical test. All achieved statistical powers were >0.8.

Differences between VE/VCO_2-slope, VE/VCO_2-Nadir, and VE/VCO_2-Total or observed and predicted VE/VCO_2-slope were calculated using the Student *t*-test or Wilcoxon test, as appropriate. The precision of the equations was examined by the mean absolute percentage error (MAPE) and root mean square error (RMSE). RMSE was adjusted to percentage by dividing the errors by the mean of observed VE/VCO_2-slope (%RMSE). Two-way mixed effects interclass correlation coefficients ($ICC_{3,1}$) with 95% confidence intervals (CI) [32,33] were calculated to test agreement between the observed and predicted VE/VCO_2-slope. The relationship between observed and predicted values was visually presented by Bland–Altman plots. We regressed the predicted VE/VCO_2-slope against direct measurements and presented it by the coefficient of determination (R^2).

Data are presented following the AMA *Manual of Style*. A two-sided *p*-value < 0.05 was considered as significant. Analyses were performed in the IBM SPSS Statistical Software (version 29.0, IBM, Chicago, IL, USA). Figures were derived via GraphPad Prism (version 10.1, GraphPad Software, San Diego, CA, USA).

3. Results

3.1. Interdependency of VE/VCO_2 Measurements

Relationships between the VE/VCO_2-slope, VE/VCO_2-Nadir, and VE/VCO_2-Total are shown in Figure 2. In males, VE/VCO_2-slope (26.1 ± 2.0) was significantly higher than VE/VCO_2-Nadir (24.5 ± 2.0, $p < 0.001$) and lower than VE/VCO_2-Total (27.3 ± 2.2, $p < 0.001$). The same relationship was observed among females, where VE/VCO_2-slope (27.7 ± 2.6) was significantly higher than VE/VCO_2-Nadir (26.2 ± 2.4, $p < 0.001$) and lower than VE/VCO_2-Total (28.7 ± 2.7, $p = 0.043$). Between sexes, female athletes observed higher VE/VCO_2-slope ($p < 0.001$), VE/VCO_2-Nadir ($p < 0.001$), and VE/VCO_2-Total ($p = 0.001$). In univariable analysis, VE/VCO_2 increased with age: VE/VCO_2-slope ($\beta = 0.093$, $p = 0.27$), VE/VCO_2-Nadir ($\beta = 0.127$, $p = 0.14$), and VE/VCO_2-Total ($\beta = 0.066$, $p = 0.44$).

3.2. Validity of VE/VCO_2-Slope Predictions

The accuracy of prediction equations stratified by sex is presented in Table 3. Predicted and observed values differed significantly in 9 from 12 models. Models underestimated the VE/VCO_2-slope from −0.5 for the Loe et al. [20]. model in females up to −3.6 for the females' formula by Ashikaga et al. [19] and the general formula by Salvioni et al. [8]. Only the model for males by Loe et al. [20] overestimated predictions, by +0.2. RMSE ranged from 2.0 to 4.5, while MAPE varied from 6.3% to 13.0%. Alignment was poor, with all $ICC_{3,1}$ far under 0.5. Equations explained a low amount of variance, with R^2 ranging between 0.003 and 0.031. The model's agreement is visualized with Bland–Altman plots in Figure 3.

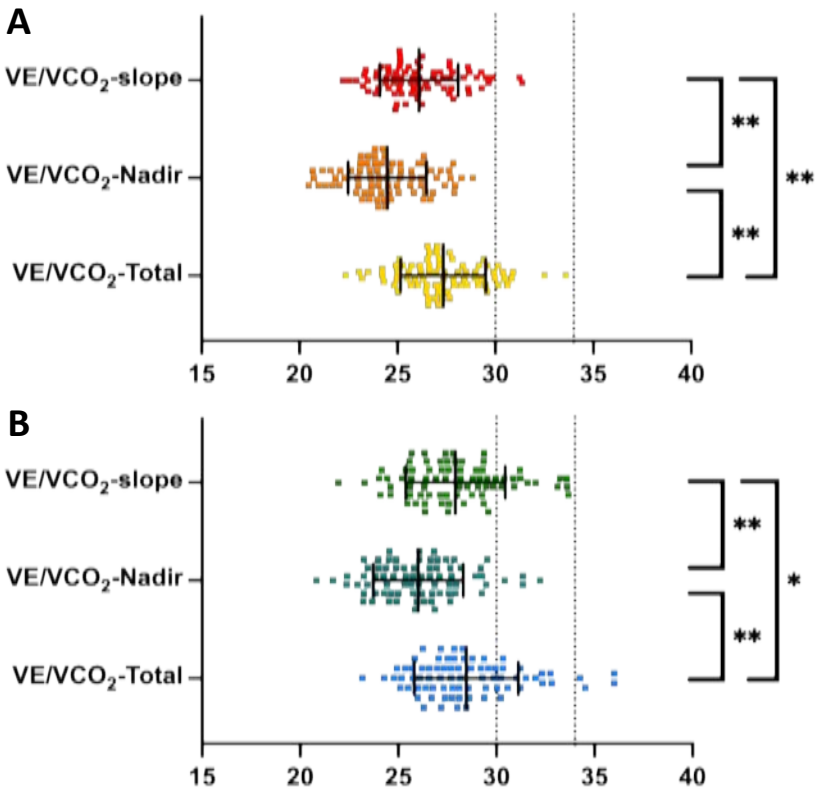

Figure 2. Interdependency in methods measuring ventilatory efficiency among endurance athletes. VE/VCO_2-slope, ventilatory efficiency from start to the first ventilatory threshold; VE/VCO_2-Nadir, the lowest 30 s continuous average for ventilatory efficiency; VE/VCO_2-Total, ventilatory efficiency from start to peak effort. Panel (**A**) illustrates a comparison for males, and panel (**B**) illustrates a comparison for females. Error bars present mean with standard deviation. Black dotted lines represent the recommended cutoffs of 30 and 34. Significant differences with $p < 0.001$ are marked with (**) and significant differences with $p < 0.05$ are marked with (*).

Table 3. Validity of ventilatory efficiency slope predictions.

Prediction Equation	Predicted VE/VCO_2-Slope	Difference	RMSE (%RMSE)	MAPE	*p*-Value	$ICC_{3,1}$ (95% CI)	R^2
Salvioni et al. (general model) [8]	23.2 ± 0.4	−3.6 ± 2.4	4.3 (16.2)	13.0	**<0.001**	0.028 (0.002, 0.053)	0.009
Salvioni et al. (males) [8]	24.3 ± 0.4	−1.8 ± 2.0	2.7 (10.3)	7.5	**<0.001**	0.043 (0.017, 0.069)	0.010
Salvioni et al. (females) [8]	25.1 ± 0.2	−2.7 ± 2.6	3.8 (13.5)	10.1	**<0.001**	<0.001 (−0.026, 0.026)	0.004
Kleber et al. (males) [17]	22.7 ± 0.6	−3.4 ± 2.0	3.9 (15.1)	12.5	**<0.001**	0.056 (0.031, 0.082)	0.010
Kleber et al. (females) [17]	27.3 ± 0.5	−0.5 ± 2.7	2.7 (9.8)	7.5	0.44	<0.001 (−0.026, 0.026)	0.004
Neder et al. (males) [18]	23.6 ± 0.6	−2.5 ± 2.0	3.2 (12.3)	9.4	**<0.001**	0.052 (0.027, 0.078)	0.010
Neder et al. (females) [18]	27.1 ± 0.3	−0.6 ± 2.6	2.7 (9.8)	7.5	0.20	<0.001 (−0.026, 0.026)	0.004
Loe et al. (males) [20]	26.3 ± 0.3	+0.2 ± 2.0	2.0 (7.6)	6.3	**0.03**	0.036 (0.010, 0.062)	0.010
Loe et al. (females) [20]	27.3 ± 0.3	−0.5 ± 2.6	2.7 (9.6)	7.4	0.33	<0.001 (−0.026, 0.026)	0.004
Ashikaga et al. (males) [19]	23.9 ± 0.3	−2.2 ± 2.0	2.9 (11.3)	8.5	**<0.001**	0.033 (0.007, 0.059)	0.010
Ashikaga et al. (females) [19]	24.1 ± 0.3	−3.6 ± 2.6	4.5 (16.1)	12.6	**<0.001**	<0.001 (−0.026, 0.026)	0.003
Sun et al. (general model) [10]	23.6 ± 0.9	−3.2 ± 2.4	4.0 (15.1)	11.7	**<0.001**	0.112 (0.087, 0.138)	0.031

VE/VCO_2-slope, ventilatory efficiency slope from start to the first ventilatory threshold; RMSE, root mean square error; %RMSE, percentage root mean square error; MAE, mean absolute error; MAPE, mean absolute percentage error; $ICC_{3,1}$, two-way mixed effect interclass correlation coefficient; CI, 95% confidence interval; R^2, adjusted coefficient of determination. The observed VE/VCO_2-slope was 27.7 ± 2.6 for females, 26.1 ± 2.0 for males, and 26.8 ± 2.4 for the total population. %RMSE was calculated by dividing RMSE by the mean of the observed VE/VCO_2-slope. Significant *p*-values (<0.05) are bolded. Negative values (−) of difference mean underestimation, i.e., predicted values were lower than observed values. Positive values (+) mean overestimation, i.e., predicted values were higher than observed values.

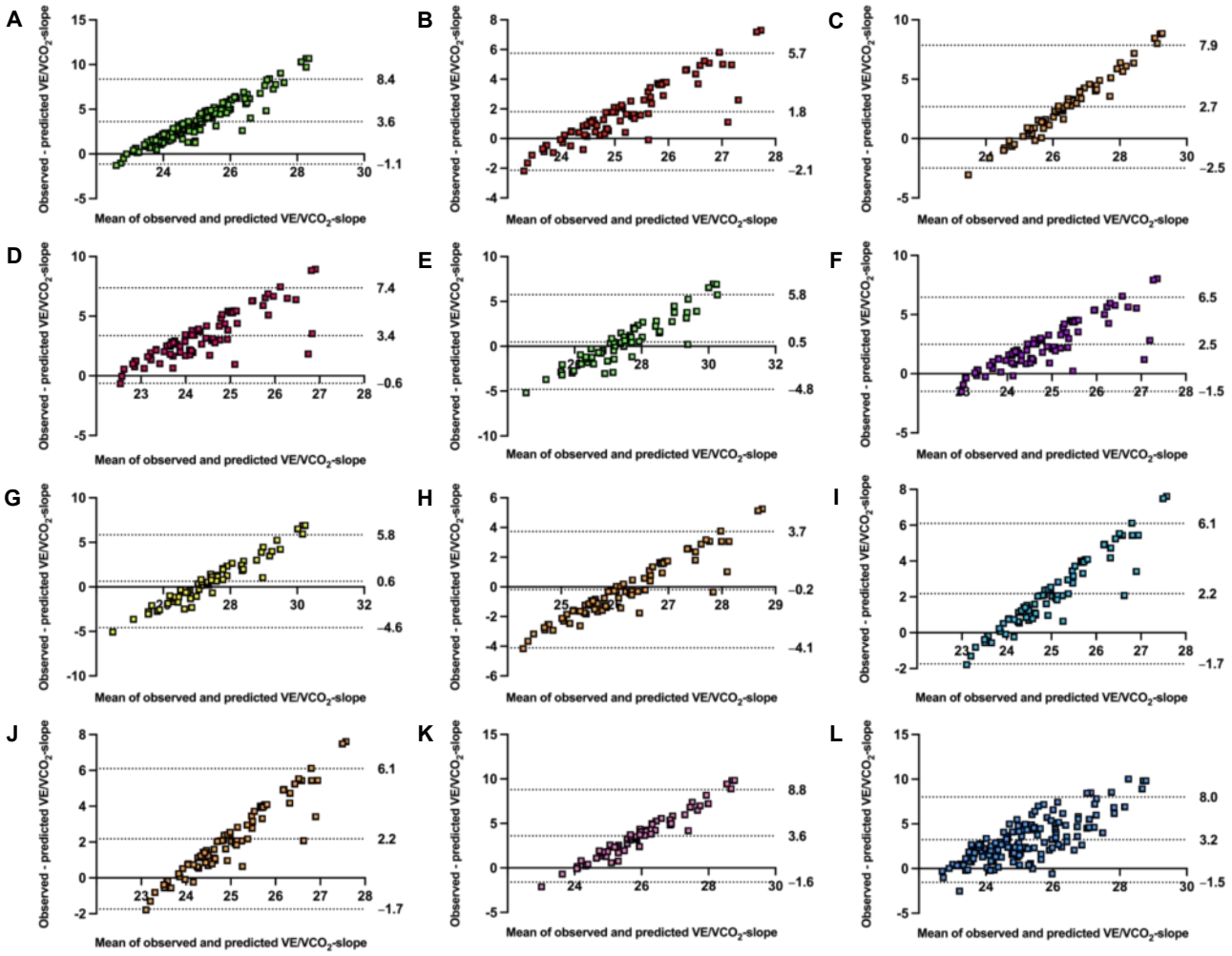

Figure 3. Bland–Altman plots comparing observed with estimated ventilatory efficiency slope by validated models. VE/VCO_2-slope, ventilatory efficiency slope from start to first ventilatory threshold. Panel (**A**) general model by Salvioni et al. [8], panel (**B**) male model by Salvioni et al. [8], panel (**C**) female model by Salvioni et al. [8], panel (**D**) male model by Kleber et al. [17], panel (**E**) female model by Kleber et al. [17], panel (**F**) male model by Neder et al. [18], panel (**G**) female model by Neder et al. [18], panel (**H**) male by Loe et al. [20], panel (**I**) female by Loe et al. [20], panel (**J**) male by Ashikaga et al. [19], panel (**K**) female model by Ashikaga et al. [19], and panel (**L**) general model by Sun et al. [10]. All models were validated for the VE/VCO_2-slope from the start to the first ventilatory threshold. The central dotted line represents mean bias. The upper and lower dotted lines represent 95% confidence intervals.

4. Discussion

We conducted a comprehensive analysis of VE/VCO_2 among athletes with above-average endurance levels. We examined the perspectives of estimating the important indicator of cardiorespiratory health. Our main findings are as follows: (1) prediction equations are not transferable for VE/VCO_2-slope and do not allow for precise estimation in the athletic group, (2) predicted VE/VCO_2-slope shows strong variability in healthy participants, and (3) several measuring methods (-slope, -Total, and -Nadir) are different both for female and male endurance athletes.

Endurance athletes are a unique population [13]. They differ from general, nonathletic individuals in the majority of cardiorespiratory indices [34]. Physical activity provides a brilliant effect on health, but demanding endurance training could even raise the risk of

CVD [5]. To mention only some differences from the untrained population, endurance athletes have higher cardiac output, their heart recovers faster, arterial hypoxemia occurs more often, and the breathing reserve is lower [34]. However, it is unknown what adaptive mechanism leads to elevation in VE/VCO_2 among healthy athletic populations [34].

The variability of VE/VCO_2 in endurance athletes and its indirect estimations are an understudied area. Our study filled this research gap and supplemented the knowledge of calculating bivariate cardiac indicators, especially for young adult endurance athletes. Variation associated with using prediction equations would allow a physician to compare how close the VE/VCO_2-slope of endurance athletes is to normal reference individuals. The advantage of this study is the unique reference sample, with above-average physical levels and free of health-disturbing factors. Additionally, this is the first study that externally validated current prediction equations.

Assuming a normal response to exercise, the VE/VCO_2 obtained from the full CPET should be higher and nonlinear. Previous studies derived regression prediction models up to VT1 [16,35]. Our results confirmed this physiological difference in healthy endurance athletes (VE/VCO_2-slope = 26.8 ± 2.4 vs. VE/VCO_2-Total = 28.0 ± 2.5). VE/VCO_2 usually grows with age. This trend is observed in untrained, healthy subjects and those with CVD [8,10]. We also noted that VE/VCO_2 increased with age in athletic subjects independently from sex (β = 0.066–0.127). This relationship with age was the strongest for VE/VCO_2-Nadir (β = 0.127, p = 0.14). However, it was not significant in either VE/VCO_2-slope, VE/VCO_2-Nadir, or VE/VCO_2-Total. Some explanation is provided by the work of Salazar-Martinez et al. [23]. In their study, the VE/VCO_2-slope was slightly higher in older endurance athletes (25.6 ± 3.7) compared to younger ones (24.3 ± 3.8). However, the authors noted that this difference was not significant between endurance athletes at the age of 16–25 years old and those at the age >45 years old (p = 0.146) [23]. Our study provided a wider view of other types of VE/VCO_2, i.e., VE/VCO_2-Nadir and VE/VCO_2-Total.

Derivation studies reported a low explanation of VE/VCO_2-slope by covariates expressed as R or R^2. Loe et al. reported R^2 = 0.08 [20], while Salvioni et al. reported R = 0.303 for the general model, R = 0.192 for females, and R = 0.371 for males [8]. In external validation, we performed a three-step analysis. Firstly, we checked how the models for VE/VCO_2-slope transfer above the original population. We selected a unique population—healthy, free of disturbing comorbidities, and with high endurance capacity. Based on previous studies on athletic cohorts for the remaining CPET variables, we stipulated that there would be an underestimation [13,14,21]. Reduced calculations are more often noticed among physically active subjects than in general groups [14,21]. Overall, equations provided values from −3.6 for Ashikaga et al. (in females) [19] and Salvioni et al. (general model) [8] to +0.2 for Loe et al. (in males) [20]. Differences were large enough that they reached significance in 9 of 12 models (75%). A transfer error of 6.3–13.0% in our athletic cohort is lower than that reported by Salvioni et al. (approximately 24.0%) when transferring from the general to clinical sample [8]. Some clarification was reported by Petek et al., who noted that endurance athletes could continue the physical effort longer and with higher intensity. Thus, their VE/VCO_2-slope increases significantly [3]. Even up to 33% of them could exceed the recommended normal cutoff of 30, while up to 13% could fall beyond 34 [3]. However, our subjects have only slightly elevated VE/VCO_2: the majority of them fell within the recommended ranges, and only four (6.3%) females exceeded the cutoff of 34 for VE/VCO_2-Total. Even though some of our athletes fall above the recommended cutoff, the average VE/VCO_2-slope was comparable to those observed by Brown et al. in juvenile cyclists (26.8 ± 2.4 vs. 28.14 ± 3.89) [22].

Secondly, we aimed to evaluate how the predicted slopes explained variance in the observed measures. To verify deeper relationships in the VE/VCO_2 course, we enriched our analysis by regressing predictions against directly measured slopes. R^2 ranged between 0.003 and 0.031 (0.03–3.1%). We noted that the trend of predictions is generally consistent; however, the covered amount of variance was still poor.

Finally, by low ICC, we noted that VE/VCO_2 variability remains large, and agreement was low between predicted and observed measures (all ICC < 0.5) [32,33]. The least accurate was a general model by Salvioni et al. [8]. Interestingly, the general model by Sun et al. [10] showed the highest accuracy. A plausible explanation could be that it was because that model was derived from a numerous, reliable population of 474 individuals with varied fitness levels. Moreover, an additional advantage of the Sun et al. [10] model is the inclusion of body height as a covariate, which could add to the prediction value. For precise descriptions of all selected models, see Table 2. To summarize, the VE/VCO_2-slope may have good visit-to-visit repeatability in a single athlete [22]. However, it is poorly transferable between populations. This observed variability in VE/VCO_2-slope predictions could emerge from improved breathing control with regular physical training [24].

4.1. Practical and Clinical Implications

Knowledge of the patient's endurance capacity remains important in the athletic assessment [6]. Our findings enable the evaluation of VE/VCO_2 as a factor related to cardiovascular functions and facilitate clinical decision making. Results can be a valuable supplement to the CPET assessment. Additionally, we confirmed that slightly elevated VE/VCO_2 can also be observed among younger individuals during strenuous physical effort, especially females. It is not unusual for VE/VCO_2 values to be increased in endurance athletes during efforts above VT1, especially at the maximal levels. Our findings are in line with the report by Petek et al. [3] and correspond with the results of Brown et al. [22]. Increased VE/VCO_2 should be an indicator for further, more precise medical evaluation to ensure safe physical activity.

Another practical implication of this study is the assessment of how the well-trained participant fits into the reference values [5]. Further determination of the degree of cardiorespiratory weakness or abnormalities is facilitated. What is more, we see that prediction equations could be used only to supplement the comprehensive diagnostic process, but not to make a definitive diagnosis. Comparing all three measurements provides a more comprehensive picture of cardiorespiratory health [16]. If one type of VE/VCO_2 is elevated, the physician could recalculate the remaining two to avoid over-awareness and misdiagnosis [16].

The present research confirms that reference values have limited repeatability between populations. The universal use of prediction equations for VE/VCO_2-slope between athletic and untrained populations is not recommended. In general, the prediction equations for VE/VCO_2-slope explained only minimal individual variance. The underlying reason should be confirmed by future studies. However, we stipulate that training specificity or additional somatic indices could individually contribute to the variability in predictions. All of the variance cannot be explained by available simple models, at least in endurance athletes.

Moreover, we underline that the most reliable and repeatable VE/VCO_2 index is the Nadir. It is calculated from a precisely defined time interval, so it avoids the subjective susceptibility of the VT1 assessment or the athlete's motivation to push to maximum effort [36]. Nevertheless, our results facilitate the selection of the most accurate equation for indirect prediction when full CPET is unavailable.

4.2. Limitations and Interpretation

The investigated population in the majority consisted of younger individuals. However, our age distribution fitted in the ranges of the original studies. Our cohort meets the required size to ensure reliable results, but previous models were developed based on broader samples. This study also guides the thoughts to reconsider the VE/VCO_2 in other populations, e.g., master athletes. Our testing center does not provide lactate measurements. Thus, all the thresholds were assessed based on the gas exchange responses. It should be acknowledged that ethnicity could influence endurance capacity because all of our athletes were Caucasians [37]. We did not consider the training period of our participants. However,

assuming their high fitness level, the performance of enrolled athletes should not vary significantly over the season [38].

Our group consisted of healthy individuals with a high fitness level. Above-average endurance of our athletes should be considered when interpreting the results of the present study. According to our knowledge, it is the first and largest validation study to date comparing predicted and observed VE/VCO_2-slopes in the athletic population. Independent replication on other populations, including clinical samples, would be intriguing.

4.3. Further Research Directions

Original derivation studies merge different testing protocols and modalities. The type of CPET could significantly contribute to the final measurements [16,39]. Novel, more advanced models should be created under unified CPET conditions and report testing modality. Additional confirmation for groups with more varied age distribution, including pediatric and master athletes, is always welcome. It is worth underlining that such variability between the observed and predicted VE/VCO_2-slope occurs in a healthy population. We stipulate that differences could become even more significant among clinical conditions when other comorbidities emerge [40]. Perhaps, supplementing future models with other covariates would enrich their accuracy. Moreover, clinical guidelines should consider methods of calculation and distinguish between athletic and nonathletic individuals. Future research on other sports disciplines should be also conducted.

5. Conclusions

VE/VCO_2-slope, VE/VCO_2-Nadir, and VE/VCO_2-Total significantly differed in young endurance athletes. The differences were stronger in male than female endurance athletes. Female endurance athletes observed higher VE/VCO_2 than male endurance athletes in all measuring methods. VE/VCO_2-slopes were significantly downgraded by 11 from 12 predicted equations. Prediction inaccuracies were higher in males than in females. Indirect calculations are not transferable for VE/VCO_2-slope between trained and untrained individuals. Estimated VE/VCO_2-slopes should be carefully used for clinical practice and sports diagnostics. Physicians should take care to properly assess cardiorespiratory responses to exercises in specific populations.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/jcm13020490/s1, Table S1: STROBE Statement—checklist of items that should be included in reports of cross-sectional studies, Table S2: abnormal health findings considered as the exclusion criteria.

Author Contributions: Conceptualization, P.K., T.K., A.K. and D.Ś.; data curation, P.K., M.Ł. and A.W.; formal analysis, P.K.; funding acquisition, S.W., M.B., A.R.P., P.W. and D.Ś.; investigation, P.K., T.K., K.R., A.K., M.Ł. and D.S.; methodology, P.K. and T.K.; project administration, P.K., T.K., A.M. and D.Ś.; resources, P.K., T.K., K.R., A.K., M.Ł., D.S. and A.W.; supervision, A.K., A.M. and D.Ś.; validation, P.K.; visualization, P.K.; writing—original draft, P.K. and T.K.; writing—review and editing, P.K., T.K., A.K., S.W., M.B., A.R.P., P.W. and D.Ś. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: This study was reviewed and approved by the Bioethics Committee of the Medical University of Warsaw (AKBE/277/2023, approval date: 9 October 2023). All study procedures were in line with the Declaration of Helsinki.

Informed Consent Statement: Participants provided their written informed consent.

Data Availability Statement: The raw data supporting the conclusions will be made available on a reasonable request to the corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest.

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Kopie opublikowanych prac

Publikacja nr 2

Tytuł:

Below or all the way to the peak? Oxygen uptake efficiency slope as the index of cardiorespiratory response to exercise—the NOODLE study

Autorzy:

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Typ publikacji:

Artykuł oryginalny

DOI:

10.3389/fphys.2024.1348307

Czasopismo:

Frontiers in Physiology

IF=3,4 | kwartyl JCR Q1 | centyl JCR 77,6

frontiers | Frontiers in Physiology

TYPE Original Research
PUBLISHED 26 January 2024
DOI 10.3389/fphys.2024.1348307

OPEN ACCESS

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RECEIVED 02 December 2023
ACCEPTED 15 January 2024
PUBLISHED 26 January 2024

CITATION
Kasiak P, Kowalski T, Rębiś K, Klusiewicz A, Starczewski M, Ładyga M, Wiecha S, Barylski M, Poliwczak AR, Wierzbiński P, Mamcarz A and Śliż D (2024), Below or all the way to the peak? Oxygen uptake efficiency slope as the index of cardiorespiratory response to exercise—the NOODLE study.
Front. Physiol. 15:1348307.
doi: 10.3389/fphys.2024.1348307

Below or all the way to the peak? Oxygen uptake efficiency slope as the index of cardiorespiratory response to exercise—the NOODLE study

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Background: The ratio of oxygen uptake (VO_2) to minute ventilation (VE) is described as the oxygen uptake efficiency slope (OUES). OUES has been suggested as a valuable submaximal cardiorespiratory index; however, its characteristics in endurance athletes remain unknown. In this study, we a) investigated OUES between different time intervals, b) assessed their prediction power for VO_2peak, and c) derived new prediction equations for OUES tailored for well-trained individuals.

Materials and Methods: A total of 77 male (age = 21.4 ± 4.8 yrs; BMI = 22.1 ± 1.6 kg·m^{-2}; peak oxygen uptake = 4.40 ± 0.64 L·min^{-1}) and 63 female individuals (age = 23.4 ± 4.3 yrs; BMI = 23.1 ± 1.6 kg·m^{-2}; peak oxygen uptake = 3.21 ± 0.48 L·min^{-1}) underwent the cycling cardiopulmonary exercise test. OUES was measured at 75%, 90%, and 100% of exercise duration. Prediction power and new models were derived with the multiple linear regression method.

Results: In male subjects, OUES [mL·min^{-1}/L·min^{-1}] from 75% = 4.53 ± 0.90, from 90% = 4.52 ± 0.91, and from 100% = 4.41 ± 0.87. In female subjects, OUES [mL·min^{-1}/L·min^{-1}] from 75% = 3.50 ± 0.65, from 90% = 3.49 ± 0.62, and from 100% = 3.41 ± 0.58. OUES did not differ between time intervals in male (p = 0.65) and female individuals (p = 0.69). OUES strongly predicts peak VO_2 independently from the measuring interval (β = 0.71–0.80; R^2 = 0.50–0.63). The prediction model designed for elite athletes was OUES [mL·min^{-1}/L·min^{-1}] = −1.54 + 2.99; BSA [m^2]—0.0014; (age [in years]; sex [1 = male, 2 = female]) (R^2 = 0.36).

Conclusion: OUES enables an accurate prediction of peak cardiorespiratory fitness in elite endurance athletes. OUES is a feasible alternative to maximal

exercise testing. A new prediction equation should be used for highly trained individuals. Physicians should understand OUES physiology to properly assess the cardiorespiratory response to exercise in athletic cohorts.

KEYWORDS

cardiopulmonary exercise test, endurance athletes, exercise physiology, oxygen uptake efficiency slope, prediction equation

Introduction

Maximal symptom-limited cardiopulmonary exercise testing (CPET) is a gold standard of assessment of an individual's endurance capacity, and its diagnostic value is most often assigned to maximal effort (Balady et al., 2010). However, Baba et al. introduced a new submaximal exercise performance indicator, the oxygen uptake efficiency slope (Baba et al., 1996). OUES has previously been evaluated in a clinical context to stratify the risk for cardiovascular diseases (Hollenberg and Tager, 2000).

OUES is plotted as the course of oxygen uptake (VO_2) relative to the logarithm of minute ventilation (VE) (Baba et al., 1996). VE is mostly affected by the partial pressure of carbon dioxide and further acidemia, and VO_2 reflects the oxygen absorption of the body (Baba et al., 1996). Similarly to peak VO_2 (VO_2peak), OUES is determined by the integrated functions of several different physiological systems: musculoskeletal, cardiac, and respiratory (Baba et al., 1996). A key advantage of OUES is the stable, linear course throughout the whole exercise duration (Sun et al., 2012). This is possible by the logarithmic transformation of the curvilinear relation of VE to VO_2 (Akkerman et al., 2010). OUES represents an almost excellent linear course during the whole physical effort, and OUES determines how effectively oxygen is transported (Baba et al., 1996). Previous research has suggested that, in the general population, OUES may correlate well with VO_2peak and allows for its accurate prediction only with the submaximal CPET (Ashikaga et al., 2021).

OUES enables a comprehensive assessment of the cardiac response to physical exercise (Baba, 2000; Akkerman et al., 2010). Individuals with higher fitness levels had a steeper OUES (Sun et al., 2012). VO_2 and OUES measure a close physiological mechanism (Hollenberg and Tager, 2000). OUES and VO_2peak correlate well with each other (Baba et al., 1999a). VO_2 and OUES increase simultaneously with growing exercise intensity (Baba et al., 1996). Moreover, the linear relationship between OUES and VO_2 should be maintained independently from the performance achieved during the exercise test (Baba et al., 1996; Baba et al., 1999a). A reduced slope is found in individuals with limited functional capacity or suggested pathology (Baba, 2000; Sun et al., 2012). OUES has been most often determined with 75% ($OUES_{75}$), 90% ($OUES_{90}$), and 100% ($OUES_{100}$) of data from the CPET protocol (Baba et al., 1996; Hollenberg and Tager, 2000). Among normal, healthy populations, all measuring intervals provide comparable values (Hollenberg and Tager, 2000), and OUES also maintains this relationship under clinical conditions (Baba et al., 1999b).

Moderate endurance training has several health benefits (Kim and Baggish, 2017). However, elite athletes are subjected to strenuous physical demands (Wasfy and Baggish, 2016). This results in a higher risk of cardiovascular diseases (CVDs) (Andersen et al., 2013; Schnohr et al., 2015). Athletes usually do not fit well into the general cardiopulmonary reference values (Petek et al., 2021; Wiecha et al., 2023b). Moreover, no studies so far compared the prediction powers of different OUES intervals on VO_2peak among well-trained endurance athletes (Akkerman et al., 2010). We stipulate that all those relationships could be more complex than in untrained individuals. Therefore, determining the underlying response profile of OUES for the athletic population remains crucial to avoid controversies and misdiagnosis.

In this study, we a) explained the relationship between OUES intervals for endurance athletes, b) assessed the prediction power of OUES for VO_2peak in well-trained participants, c) derived and internally validated new prediction equations for OUES, and d) externally validated current prediction equations in a highly trained reference cohort.

Materials and methods

Study design

We applied the recommendations for observational studies by the EQUATOR Network–STROBE Guidelines for cross-sectional studies (Supplementary Table S1). CPET was performed by endurance athletes in the years 2022–2023. Exercise tests took place at the Institute of Sport–National Research Institute in Warsaw. The study was reviewed and approved by the Bioethics Committee of the Medical University of Warsaw (AKBE/277/2023). Written informed consent was obtained for each subject. In particular, we did not initially refer to the CPET potential study candidates who had past medical or family histories and evident medical conditions (diagnosed during pre-participation physical examination).

Only adult subjects of age ≥18 years were included. To be eligible for this study, endurance athletes had to be free from a) cardiovascular or pulmonary conditions, b) psychiatric or neurological diseases, d) orthopedic conditions restricting effort at CPET, e) divergences in complete blood count, f) and tobacco smoking. All athletes had at least a 4-year experience in regular endurance training and were members of a training club and elite or development national teams in Olympic sports. They periodically participated in both national and international competitions, including the Olympic Games. The participants of this study belonged to tiers 3–5, according to the McKay classification system (McKay et al., 2022). The full participant selection process is detailed in Figure 1.

Cardiopulmonary exercise testing

All endurance athletes performed maximal-graded symptom-limited CPET. We considered the maximal exercise response when

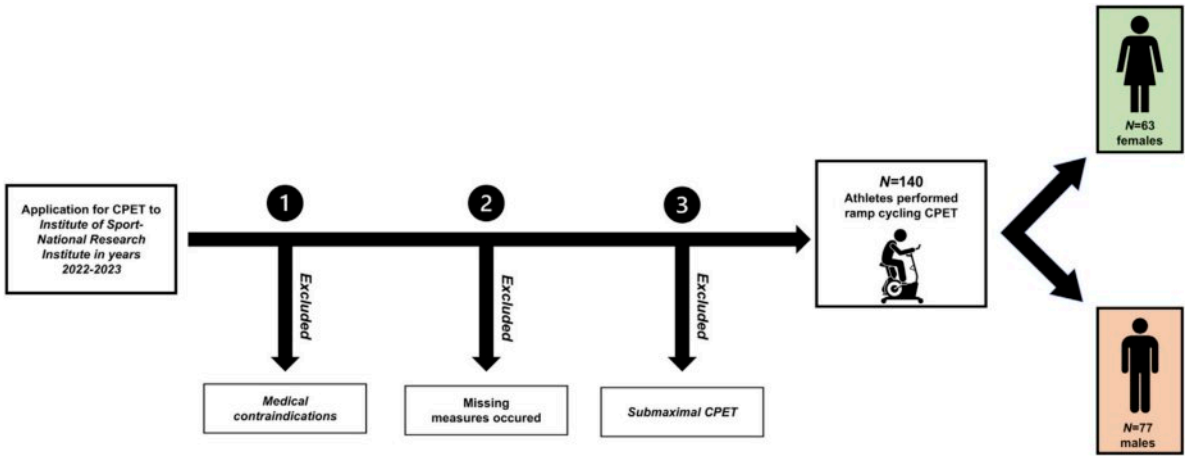

FIGURE 1
Flowchart for the study recruitment process. Abbreviation: CPET, cardiopulmonary exercise test. Note: only adult endurance athletes were enrolled in the study. A 3-step recruitment process was performed. During the first step, medical contraindications considered as mandatory exclusion criteria were: cardiovascular conditions, respiratory conditions, actual psychiatric or neurological disease, orthopedic conditions restricting effort at CPET, divergences in complete blood count, and tobacco smoking. At the second step, if any missing variables occurred, participants were excluded from the analysis to ensure the highest reliability of the analyses. Finally, in the third step, athletes with submaximal performance were not included, and the peak effort was defined as plateau in oxygen uptake, respiratory exchange ratio ≥1.05, declaration of volitional exhaustion with a rating of perceived exertion ≥18 according to the Borg scale, and maximal heart rate was ≥80% of the age-predicted value.

there was a a) ≥30-s VO_2 plateau, b) respiratory exchange ratio (RER) ≥1.05, c) declaration of fatigue confirmed by a Borg's RPE ≥18, and d) measured heart rate ≥80% of the age-predicted value. Experienced physiologists supervised the CPET, and the athletes were verbally motivated to reach maximal effort.

The athletes underwent ramp cycling CPET on a Cyclus2 Ergometer (RBM, Leipzig, Germany). At the beginning of CPET, there was a brief 2–3 min warm-up of freewheeling pedaling. The initial load began with 55–70 W and was progressively raised by 0.17–0.28 W s^{-1}. The resistance was modified individually in provided ranges to adjust the intensity in agreement with each participant.

Body measurements

We obtained the following anthropometric measurements: age, weight, height, and body mass index (BMI). The weight was measured prior to breakfast by a TANITA weight scale (TANITA Corporation, Arlington Heights, IL, United States). The height was measured in the morning (in the same time as weight) with a stadiometer (Seca GmbH and Co., Hamburg, Germany).

Cardiopulmonary fitness outcomes

Polar H10 (Polar Electro Oy, Kempele, Finland) was used to monitor the heart rate (HR). Gas-exchange variables were taken breath-by-breath with a V2 Mask (Hans Rudolph, Inc., Shawnee, KS, United States) and a Cortex B3 Metamax system (CORTEX Biophysik GmbH, Leipzig, Germany). All the pieces of equipment used were calibrated according to the manufacturer's guidelines before each CPET. We applied 15-s intervals to average the measurements. The measured VO_2peak was compared with the VO_2peak predicted by the Wasserman and Hansen equation (Wasserman et al., 1987).

OUES was defined according to the method of Baba et al. (1996): $VO_2 = a \cdot \log_{10} \cdot VE + b.$, where "a" represents the OUES. OUES was calculated at 75%, 90%, and 100% of the exercise duration. The first minute of the loaded protocol was not included in the analysis, as recommended by Hollenberg and Tager (2000). The body surface area was calculated using the Du Bois and Du Bois formula: $0.007184 \cdot \text{height (cm)}^{0.725} \cdot \text{weight (kg)}^{0.425}$ (Burton, 2008). We additionally calculated the HR (both absolute and percentage of peak HR) for each intensity zone ($OUES_{75}$, $OUES_{90}$, and $OUES_{100}$).

Prediction models for external validation

Prediction equations for external validation were chosen from the review by Akkerman et al. (2010) up to year 2010 and through additional search for studies published in years 2010–2024. The applied keywords were "oxygen uptake efficiency slope," "OUES," "prediction model," "prediction equation," "cardiopulmonary exercise testing," "reference values," and "linear regression" in the scientific literature. Equations derived from clinical cohorts (with comorbidities) were excluded to ensure maximal similarity. To sum up, 11 reference equations from seven studies fulfilled the inclusion criteria. Their characteristics are provided in Table 1.

Statistical analysis

First, data distribution was evaluated with the Shapiro–Wilk test and quantile–quantile plots. The continuous measures have been shown as mean (standard deviation [±]). The categorical measures

TABLE 1 Prediction models selected for validation.

Study	Model's type	Prediction equation		Exercise protocol	Study population [all/female subject/male subject]
		Male subject	Female subject		
Hollenberg and Tager (2000) [mL·min^{-1}/L·min^{-1}]		1,320–26.7 · age + 1,394 · BSA	1,175–15.8 · age + 851 · BSA	Running CPET; Cornell variation in the Bruce protocol	998/579/419
Buys et al. (2015)	1 [mL·min^{-1}/L·min^{-1}]	3,930–12.5 · age	3,013–15 · age	Cycling CPET; stepwise protocol with initial workload 20 W and increases of 20 W · min^{-1} until termination	1,411/877/534
	2 [mL·min^{-1}/L·min^{-1}]	1,093—18.5 · age + 1,479 · BSA	842–18.5 · age + 1,280 · BSA●		
	3 [mL·min^{-1}/L·min^{-1}]	1897–18.3 · age—631 · sex + 1,394 · BSA●			
Milani et al. (2023)	1 [mL·min^{-1}/L·min^{-1}]	2,682 + 45.47 · age—0.7658 · age^2	1,436 + 38.02 · age—0.5565 · age^2	Running CPET; ramp protocol with an initial speed of 2–4 km · h^{-1} and individually graded increases	3,544/1574/1970
	2 [mL·min^{-1}/L·min^{-1} · weight^{-1}]	36.80 + 0.2968 · age—0.005726 · age^2	26.11 + 46.90 · age—0.007472 · age^2●		
	3 [mL·min^{-1}/L·min^{-1} · BSA^{-1}]	1,450 + 17.47 · age—0.3011 · age^2	895.2 + 20.58 · age—0.3043 · age^2●		
Ashikaga et al. (2021) [mL·min^{-1}/L·min^{-1}]		2,841–12 · age	2,841–12 · age–753 + 4 · age	Cycling CPET; ramp protocol with increases in the power of 10 W · min^{-1} or 20 W · min^{-1}	529/274/255
Sun et al. (2012) [L·min^{-1}/L·min^{-1}]		–0.610–0.032 · age + 0.023 · height + 0.008 · weight	–0.610–0.032 · age + 0.023 · height + 0.008 · weight - 0.568	Running and/or cycling CPET; ramp protocol with 3-min resting and 3-min warm-up, followed by maximal effort and terminated with at least 2-min recovery	474/136/281
Marinov et al. (2007) [mL·min^{-1}/L·min^{-1}]		–398 + 1958.1 · BSA	–398 + 1958.1 · BSA—199.5	Running CPET; ramp modified Balke protocol with an initial grade of 6% and increase of 2% · min^{-1} and a fixed speed 5.4 km · h^{-1}	114/56/58
Marinov and Kostianev. (2003) [mL·min^{-1}/L·min^{-1}]		–3,346.9 + 28.08 · height + 794.2 · BSA		Running CPET; ramp modified Balke protocol with an initial grade of 6% and an increase of 2% · min^{-1} and a fixed speed 5.4 km · h^{-1}	60/30/30

Abbreviations: BSA, body surface area; CPET, cardiopulmonary exercise test.
Note: age is expressed in years, BSA is calculated in m^2, weight is presented in kg, and height is shown in cm. Sex was computed as 1 for male subjects and 2 for female subjects.

have been shown as numbers (percentage [%]). An athlete was removed from the analysis when there were any missing measurements, with the aim of supporting maximal credibility of the results. The significance borderline was set at a two-sided p-value < 0.05.

For applied statistical tests, we verified the cohorts' sizes. The whole population or particular subgroups (males and females) fulfilled the required numbers to achieve a large effect size, statistical significance (p < 0.05), and high power (>0.8).

Differences between all measurements ($OUES_{75}$, $OUES_{90}$, and $OUES_{100}$) were compared by one-way ANOVA. Additionally, Student's t-test for independent means was conducted to compare differences between paired measurements ($OUES_{75}$ and $OUES_{90}$, $OUES_{75}$ and $OUES_{100}$, and $OUES_{90}$ and $OUES_{100}$). Linear regression was used to examine the prediction power of $OUES_{75}$, $OUES_{90}$, and $OUES_{100}$ on VO_2peak. Each calculation was carried out independently for male and female individuals.

The model's derivation was preceded by an assessment of the data assumptions (correlations, collinearity, independence of observations, analysis of residuals, and leverage or influence plots). We used multiple linear regression to derive new prediction equations. The performance of new models was presented with the root-mean-square error (RMSE) and two-way mixed-effects interclass correlation coefficient ($ICC_{3,1}$) (Koo and Li, 2016). The Bland–Altman plots and 10-fold cross-validation were used to evaluate the model's agreement (Jung and Hu, 2015). Linear models were developed to externally validate equations by regressing the predicted OUES against the observed OUES. In analysis, the coefficient of determination (R^2) was considered as the adjusted R^2.

The results have been shown in line with the APA style guidelines. IBM SPSS (version 29.0, IBM, Chicago, IL, United States) was used for analysis, and GraphPad Prism (version 10.1.0, GraphPad Software, San Diego, California, United States) was used to prepare figures.

Results

OUES relationships among elite athletes

A total of 140 healthy endurance athletes were qualified. A total of 45.0% (n = 63) of the study population were female individuals, and 55.0% (n = 77) of the population were male individuals. The participants represented sports from endurance-oriented Olympic

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TABLE 2 Demographic and exercise characteristics.

Measurement		Whole group [n = 140]	Female subject [n = 63]	Male subject [n = 77]
Demographic characteristic				
Age [years]		22.7 ± 4.6	23.8 ± 4.2	21.8 ± 4.8
Height [cm]		174.8 ± 9.9	166.3 ± 6.2	181.6 ± 6.3
Weight [kg]		69.3 ± 10.1	61.0 ± 5.5	76.1 ± 7.6
BMI [$kg{\cdot}m^{-2}$]		22.6 ± 1.7	22.1 ± 1.6	23.1 ± 1.7
BSA [m^2]		1.84 ± 0.12	1.68 ± 0.10	1.97 ± 0.18
Sport discipline	Triathlon/cycling	56 (40.0)	30 (47.6)	26 (33.8)
	Speedskating	59 (42.1)	26 (41.3)	33 (42.9)
	Other	25 (17.9)	7 (11.1)	18 (23.3)
Exercise performance				
HRpeak [$beats{\cdot}min^{-1}$]		190.9 ± 8.9	191.0 ± 9.1	190.8 ± 8.7
VEpeak [$L{\cdot}min^{-1}$]		154.5 ± 34.1	127.8 ± 21.1	176.3 ± 26.3
VO_2peak [$L{\cdot}min^{-1}$]		3.86 ± 0.82	3.21 ± 0.48	4.40 ± 0.64
VO_2peak [$mL{\cdot}kg^{-1}{\cdot}min^{-1}$]		55.2 ± 8.6	52.1 ± 7.0	57.8 ± 9.0
VO_2peak [% predicted]		144.5 ± 25.9	161.4 ± 21.8	130.6 ± 20.2
VCO_2peak [$L{\cdot}min^{-1}$]		4.36 ± 0.96	3.57 ± 0.52	5.00 ± 0.72
RRpeak [$breaths{\cdot}min^{-1}$]		60.0 ± 7.6	60.2 ± 6.7	59.9 ± 8.3
VT [L]		2.81 ± 0.64	2.30 ± 0.32	3.22 ± 0.53
RER [VO_2/VCO_2]		1.14 ± 0.05	1.13 ± 0.05	1.15 ± 0.05
O_2Ppeak [VO_2/HR]		20.7 ± 4.4	17.3 ± 3.0	23.5 ± 3.3
Exercise time [minutes]		21.3 ± 2.6	21.1 ± 2.7	21.4 ± 2.6
Workload [watts]		320.4 ± 76.2	266.7 ± 40.8	364.4 ± 70.0
$OUES_{75}$ [$mL{\cdot}min^{-1}/L{\cdot}min^{-1}$]		4.07 ± 0.95	3.50 ± 0.65	4.53 ± 0.90
HR at $OUES_{75}$ [$beats{\cdot}min^{-1}$]		173.0 ± 10.5	175.1 ± 10.1	171.3 ± 10.5
HR at $OUES_{75}$ [%HRpeak]		90.6 ± 2.7	91.7 ± 2.1	89.8 ± 2.8
$OUES_{90}$ [$mL{\cdot}min^{-1}/L{\cdot}min^{-1}$]		4.06 ± 0.95	3.49 ± 0.62	4.52 ± 0.91
HR at $OUES_{90}$ [$beats{\cdot}min^{-1}$]		183.1 ± 9.3	184.5 ± 9.4	182.0 ± 9.1
HR at $OUES_{90}$ [%HRpeak]		95.9 ± 1.4	96.6 ± 1.1	95.4 ± 1.4
$OUES_{100}$ [$mL{\cdot}min^{-1}/L{\cdot}min^{-1}$]		3.96 ± 0.90	3.41 ± 0.58	4.41 ± 0.87

Abbreviations: BMI, body mass index; BSA, body surface area; HRpeak, peak heart rate; VEpeak, peak minute ventilation; VO_2peak, peak oxygen uptake; VCO_2peak, peak carbon dioxide output; RRpeak, peak respiratory rate; VT, tidal volume; RER, peak respiratory exchange ratio; O_2Ppeak, peak oxygen pulse; $OUES_{75}$, oxygen uptake efficiency slope from 75% of exercise duration; HR, heart rate; $OUES_{90}$, oxygen uptake efficiency slope from 90% of exercise duration; $OUES_{100}$, oxygen uptake efficiency slope from 100% of exercise duration.
Note: values are presented as mean ± standard deviation or number (%). HR for OUES was considered the peak HR, which occurred directly at the end of $OUES_{75}$ and $OUES_{90}$. HR at $OUES_{100}$ was HRpeak. Predicted VO_2peak has been calculated according to the Wasserman and Hansen equation.

disciplines. A total of 40.0% (n = 56) were specified in triathlon or cycling, 42.1% (n = 59) in speedskating, and 17.9% (n = 25) chose other disciplines. Percent-predicted VO_2peak equals 144.5% ± 25.9% according to the Wasserman and Hansen equation. The demographic characteristics and exercise results are stratified by sex in Table 2.

For males, the mean $OUES_{75}$ (4.53 ± 0.90 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$) was not significantly different than $OUES_{90}$ [(4.52 ± 0.91 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$); t (152) = 0.08, p = 0.94] or $OUES_{100}$ [(4.41 ± 0.87 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$); t (152) = −0.85, p = 0.398]. Similarly, $OUES_{90}$ did not differ significantly from $OUES_{100}$ [t (152) = −0.76, p = 0.45]. The same relationship was observed among female subjects. Average $OUES_{75}$ (3.50 ± 0.65 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$) did not differ significantly from $OUES_{90}$ [(3.49 ± 0.62 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$); t (124) = 0.07, p = 0.95] or $OUES_{100}$ [(3.41 ± 0.58 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$); t (124) = 0.79, p = 0.43]. Moreover, $OUES_{90}$ did not differ significantly from $OUES_{100}$ [t (124) = 0.73, p = 0.46]. One-way ANOVA revealed that there was no significant difference in all OUES measurements both for male [F

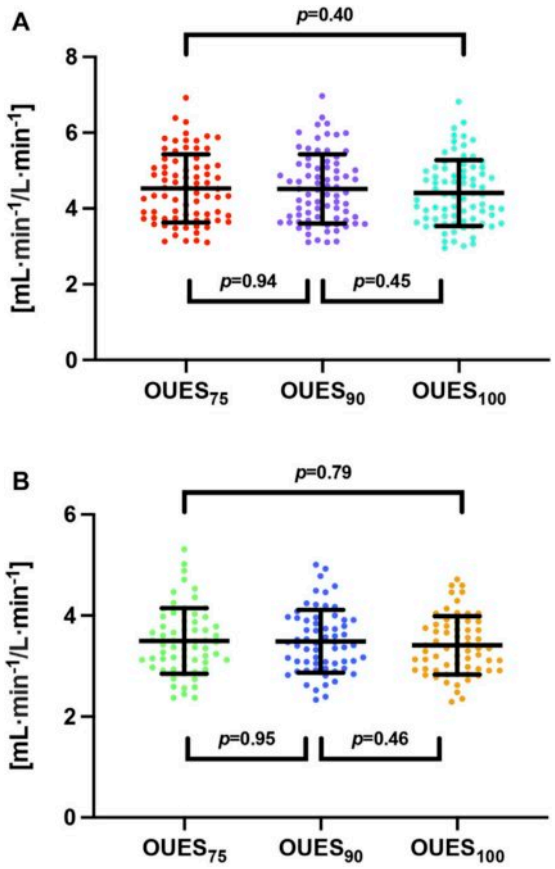

FIGURE 2
Oxygen uptake efficiency slope variability among endurance athletes. Abbreviations: $OUES_{75}$, oxygen uptake efficiency slope from 75% of exercise duration; $OUES_{90}$, oxygen uptake efficiency slope from 90% of exercise duration; $OUES_{100}$, oxygen uptake efficiency slope from 100% of exercise duration. Note: **(A)** represents male subjects, while **(B)** represents female subjects. There were no significant differences in independent bivariable comparisons or comprehensive multivariable comparisons.

(2,228) = 0.43, $p = 0.65$] and female subjects [F (2,168) = 0.38, $p = 0.69$]. On average, the difference between $OUES_{75}$ and $OUES_{90}$ was 0.11 ± 0.11 mL·min^{-1}/L·min^{-1} for male individuals and 0.12 ± 0.12 mL·min^{-1}/L·min^{-1} for female individuals, that between $OUES_{75}$ and $OUES_{90}$ was 0.21 ± 0.19 mL·min^{-1}/L·min^{-1} for male individuals and 0.18 ± 0.20 mL·min^{-1}/L·min^{-1} for female individuals, and that between $OUES_{90}$ and $OUES_{100}$ was 0.13 ± 0.11 mL·min^{-1}/L·min^{-1} for male individuals and 0.10 ± 0.12 mL·min^{-1}/L·min^{-1} for female individuals. OUES dependencies among the endurance athletes are shown independently for male and female individuals in the lower rows of Table 2 and Figure 2.

Prediction power of OUES for VO_2peak

Univariable models were developed to examine OUES prediction power on VO_2peak. OUES presented a high ability to predict VO_2peak. OUES explained up to 63% of the variance in VO_2peak in male subjects and up to 62% of the variance in VO_2peak in female subjects. VO_2peak increased simultaneously with OUES calculated from all time intervals. This relationship was more noticeable in male individuals (β = 0.73–0.80) than in female individuals (β = 0.71–0.79). The RMSE was consistently lower in female individuals than in male individuals. For the presented models, the predicted VO_2peak is in L·min^{-1} and OUES should be calculated in mL·min^{-1}/L·min^{-1}.

The fitted univariable models for male subjects were expressed as follows:

(a) $VO_2peak = 2.07 + 0.51 \cdot OUES_{75}$

The regression model covered 52% of the variance in VO_2peak ($R^2 = 0.52$, F (1, 75) = 83.6, $p < 0.001$), and $OUES_{75}$ significantly predicted VO_2peak ($\beta = 0.73$, $p < 0.001$). The RMSE was 0.44 L·min^{-1}.

(b) $VO_2peak = 1.97 + 0.54 \cdot OUES_{90}$

The regression model covered 59% of the variance in VO_2peak ($R^2 = 0.59$, F (1, 75) = 108.2, $p < 0.001$), and $OUES_{75}$ significantly predicted VO_2peak ($\beta = 0.77$, $p < 0.001$). The RMSE was 0.44 L·min^{-1}.

(c) $VO_2peak = 1.81 + 0.59 \cdot OUES_{100}$

The regression model covered 63% of the variance in VO_2peak ($R^2 = 0.63$, F (1, 75) = 131.5, $p < 0.001$), and $OUES_{75}$ significantly predicted VO_2peak ($\beta = 0.80$, $p < 0.001$). The RMSE was 0.39 L·min^{-1}.

The fitted univariable models for female subjects were expressed as follows:

(a) $VO_2peak = 1.36 + 0.53 \cdot OUES_{75}$

The regression model covered 50% of the variance in VO_2peak ($R^2 = 0.50$, F (1, 61) = 63.0, $p < 0.001$), and $OUES_{75}$ significantly predicted VO_2peak ($\beta = 0.71$, $p < 0.001$). The RMSE was 0.34 L·min^{-1}.

(b) $VO_2peak = 1.18 + 0.58 \cdot OUES_{90}$

The regression model covered 56% of the variance in VO_2peak ($R^2 = 0.56$, F (1, 61) = 79.2, $p < 0.001$), and $OUES_{75}$ significantly predicted VO_2peak ($\beta = 0.75$, $p < 0.001$). The RMSE was 0.32 L·min^{-1}.

(c) $VO_2peak = 0.96 + 0.66 \cdot OUES_{100}$

The regression model covered 62% of the variance in VO_2peak ($R^2 = 0.62$, F (1, 61) = 100.1, $p < 0.001$), and $OUES_{75}$ significantly predicted VO_2peak ($\beta = 0.79$, $p < 0.001$). The RMSE was 0.30 L·min^{-1}.

Plots visualizing the prediction powers are shown in Figure 3.

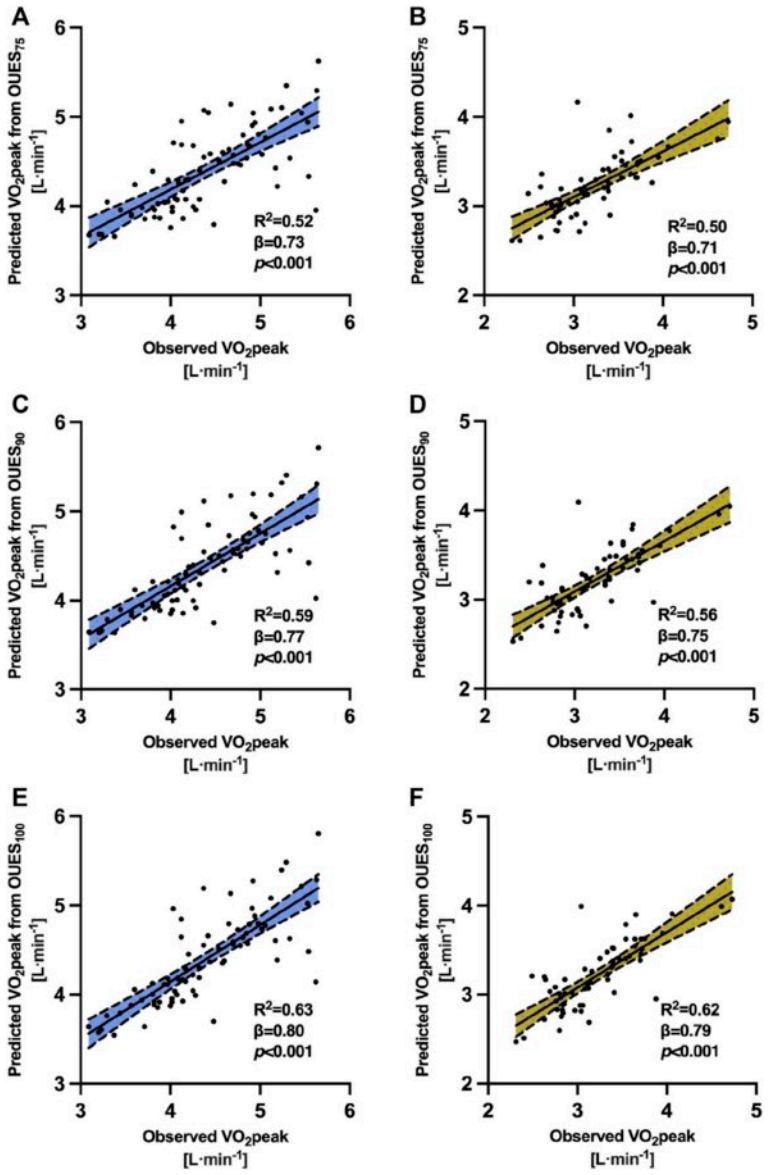

FIGURE 3
Prediction power of oxygen uptake efficiency slope on peak oxygen uptake. Abbreviations: VO_2peak, peak oxygen uptake; R^2, adjusted coefficient of determination; $OUES_{75}$, oxygen uptake efficiency slope from 75% of exercise duration; $OUES_{90}$, oxygen uptake efficiency slope from 90% of exercise duration; $OUES_{100}$, oxygen uptake efficiency slope from 100% of exercise duration. Note. **(A)** Prediction power of the oxygen uptake efficiency slope from 75% of exercise duration on VO_2peak for male subjects. **(B)** Prediction power of the oxygen uptake efficiency slope from 75% of exercise duration on VO_2peak for female subjects. **(C)** Prediction power of the oxygen uptake efficiency slope from 90% of exercise duration on VO_2peak for male subjects. **(D)** Prediction power of the oxygen uptake efficiency slope from 90% of exercise duration on VO_2peak for female subjects. **(E)** Prediction power of the oxygen uptake efficiency slope from 100% of exercise duration on VO_2peak for male subjects. **(F)** Prediction power of the oxygen uptake efficiency slope from 100% of exercise duration on VO_2peak for male subjects. In each model, the regression was significant with $p < 0.001$. The *x*-axis presents directly measured VO_2peak in cardiopulmonary exercise tests. The *y*-axis presents predicted VO_2peak by oxygen uptake efficiency slopes from 75%, 90%, and 100% portions of exercise data. The continuous central line represents a trend line. The upper and lower dashed lines represent upper and lower 95% limits of normal.

Developed prediction equations for OUES

We predicted OUES using several variables: age, sex, and BSA. Models for $OUES_{75}$, $OUES_{90}$, and $OUES_{100}$ showed similar and promising accuracy. In the developed equations, BSA should be in m^2, age in years, and the sex coefficients are 2 if female and 1 if male. The RMSE was similar in all three equations (0.72–0.77 $mL{\cdot}min^{-1}$/$L{\cdot}min^{-1}$) developed to predict OUES obtained from different portions of the exercise data.

The new prediction equations for OUES are as follows:

TABLE 3 Reliability of OUES prediction models.

Reference model		$OUES_{75}$					$OUES_{90}$					$OUES_{100}$				
		ICC	95% CI		R^2	% Predicted	ICC	95% CI		R^2	% Predicted	ICC	95% CI		R^2	% Predicted
			LL	UL				LL	UL				LL	UL		
Hollenberg and Tager (2000)		0.505	0.486	0.524	0.289	142.4	0.506	0.486	0.525	0.289	142.1	0.524	0.505	0.542	0.300	138.8
Buys et al. (2015)	1	0.431	0.411	0.453	0.267	127.5	0.431	0.410	0.452	0.264	127.2	0.449	0.428	0.469	0.272	124.2
	2	0.488	0.469	0.508	0.310	131.0	0.490	0.470	0.509	0.311	130.7	0.510	0.491	0.529	0.323	127.7
	3	0.493	0.474	0.513	0.311	131.1	0.495	0.475	0.514	0.312	130.8	0.515	0.496	0.534	0.324	127.7
Milani et al. (2023)	1	0.510	0.491	0.529	0.298	153.7	0.512	0.492	0.531	0.299	153.4	0.529	0.511	0.548	0.310	149.8
	2	0.062	0.037	0.088	0.004	160.0	0.064	0.038	0.090	0.004	159.6	0.066	0.040	0.092	0.004	155.9
	3	0.229	0.205	0.254	0.064	153.2	0.234	0.210	0.259	0.067	152.8	0.246	0.221	0.270	0.069	149.2
Ashikaga et al. (2021)		0.332	0.309	0.355	0.261	179.8	0.331	0.308	0.354	0.258	179.3	0.348	0.325	0.371	0.266	175.1
Sun et al. (2012)		0.447	0.426	0.468	0.241	137.3	0.446	0.425	0.467	0.240	137.1	0.464	0.444	0.484	0.249	133.8
Marinov et al. (2007)		0.321	0.298	0.344	0.188	186.8	0.326	0.303	0.349	0.193	186.3	0.350	0.327	0.373	0.209	181.9
Marinov and Kostianev. (2003)		0.443	0.422	0.463	0.357	134.6	0.451	0.430	0.472	0.369	134.2	0.477	0.457	0.497	0.388	131.0

Abbreviations: $OUES_{75}$, oxygen uptake efficiency slope from 75% of exercise duration; $OUES_{90}$, oxygen uptake efficiency slope from 90% of exercise duration; $OUES_{100}$, oxygen uptake efficiency slope from 100% of exercise duration; ICC, interclass correlation coefficient; CI, confidence interval; LL, lower limit; UL, upper limit; R^2, coefficient of determination.Note: coefficient of determination (R^2) is considered as the adjusted R^2. $OUES_{75}$ was 3.50 ± 0.65 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$ for female subjects, 4.53 ± 0.90 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$ for male subjects, and 4.07 ± 0.95 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$ for the total population. $OUES_{90}$ was 3.49 ± 0.62 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$ for female subjects, 4.52 ± 0.91 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$ for male subjects, and 4.06 ± 0.95 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$ for the total population. $OUES_{100}$ was 3.41 ± 0.58 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$ for female subjects, 4.41 ± 0.87 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$ for male subjects, and 3.96 ± 0.90 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$ for the total population. All reference models underestimated OUES. Significant p-values (<0.05) were marked with *, while p-values (<0.001) were marked with †.

10.3389/fphys.2024.1348307

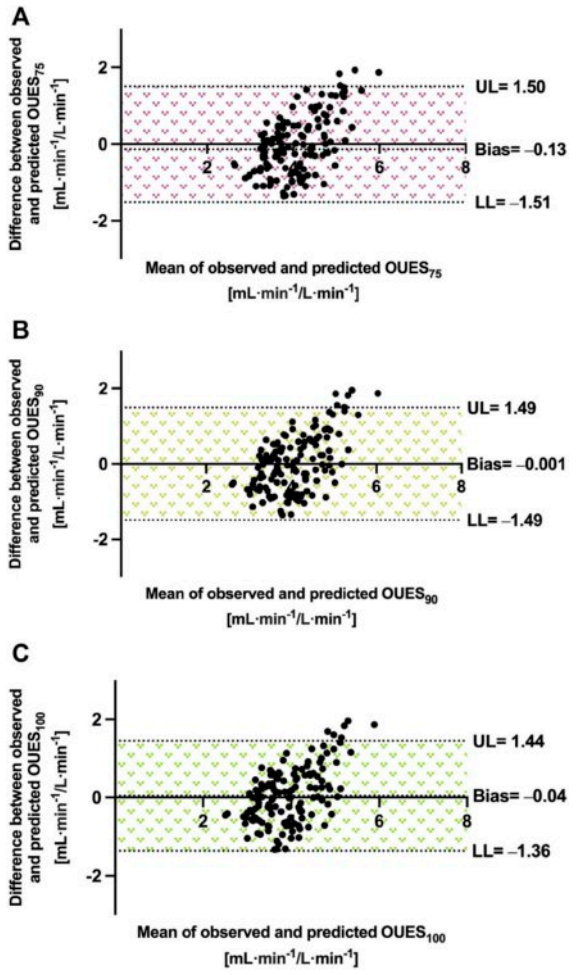

FIGURE 4
Precision of OUES equations in endurance athletes. Abbreviations: $OUES_{75}$, oxygen uptake efficiency slope from 75% of exercise duration; $OUES_{90}$, oxygen uptake efficiency slope from 90% of exercise duration; $OUES_{100}$, oxygen uptake efficiency slope from 100% of exercise duration; UL, upper 95% limit of agreement; LL, lower 95% limit of agreement. Note: the means and differences are calculated in mL·min^{-1}/L·min^{-1}. **(A)** Prediction performance for $OUES_{75}$. **(B)** Prediction performance for $OUES_{90}$. **(C)** Prediction performance for $OUES_{100}$. The area between LL and UL represents the limit of agreement and is indicated as the measure of the model's fit.

(a) $OUES_{75}$ = 1.09 + 2.87 · BSA—0.0030 · (age · sex)

The prediction equation explained 34% of variance in $OUES_{75}$ (R = 0.59, R^2 = 0.34, F (2, 137) = 36.1, $p < 0.001$). The overall RMSE was 0.77 mL·min^{-1}/L·min^{-1}.

(b) $OUES_{90}$ = 1.46–3.02 · BSA—0.0010 · (age · sex)

The prediction equation explained 35% of variance in $OUES_{75}$ (R = 0.60; R^2 = 0.35, F (2, 137) = 37.5, $p < 0.001$). The overall RMSE was 0.77 mL·min^{-1}/L·min^{-1}.

(c) $OUES_{100}$ = 1.54–2.99 · BSA—0.0014 · (age · sex)

The prediction equation explained 36% of variance in $OUES_{75}$ (R = 0.61; R^2 = 0.36, F (2, 137) = 40.3, $p < 0.001$). The overall RMSE was 0.72 mL·min^{-1}/L·min^{-1}.

Model validation

In all external models, a high variability was observed between the observed and predicted data sets (only 4 out of 11 models have ICC>0.5). The best alignment was noted in Milani et al. (2023) (equation adjusted to age) (ICC = 0.510 [0.491, 0.529] for $OUES_{75}$, ICC = 0.512 [0.492, 0.531] for $OUES_{90}$, and ICC = 0.529 [0.511, 0.548] for $OUES_{100}$). The equations underestimated all $OUES_{75}$, $OUES_{90}$, and $OUES_{100}$. Underestimation ranged up to 186.8% for the formula proposed by Marinov et al. (2007). However, the overall prediction trend in endurance athletes was maintained. The predicted values followed those directly observed, but the degree of explained variance was wide (R^2 = 0.004–0.388). For detailed external validation, see Table 3. The agreement was lower in equations for $OUES_{90}$ (R^2 = 0.290) and $OUES_{75}$ (R^2 = 0.346). Bland–Altman plots showing the validity of our models are shown in Figure 4. All the equations slightly underestimated OUES. The best-performing model was the one for $OUES_{90}$, with the bias of only −0.001 mL·min^{-1}/L·min^{-1}. The next was the model for $OUES_{100}$ (bias = −0.04 mL·min^{-1}/L·min^{-1}). The least-performing model was for $OUES_{75}$, with an error of −0.13 mL·min^{-1}/L·min^{-1}. The limits of agreement were narrow and similar in all models. For $OUES_{75}$, it ranged between −1.51 and 1.50 mL·min^{-1}/L·min^{-1}. The limit of agreement in the equation for $OUES_{90}$ was from −1.49 to 1.49 mL·min^{-1}/L·min^{-1}. Finally, in the model for $OUES_{100}$, it ranged between −1.36 and 1.44 mL·min^{-1}/L·min^{-1}. As presented in Figure 4, some athletes exceeded the upper limits of agreement, but no one exceeded the lower limits.

Discussion

We have shown that OUES is a valuable submaximal parameter in elite athletes as well. The key findings of this study are as follows:

- First, the new prediction equations provide promising but moderate precision for endurance athletes and explain between 34% and 36% of the variance in OUES.
- Second, the overall association between $OUES_{75}$, $OUES_{90}$, and $OUES_{100}$ was similar to those observed in untrained and elderly subjects.
- Third, we observed a strong relationship between OUES and VO_2peak, even in well-trained endurance athletes, and its predictive impact was comparable for all time intervals.
- Finally, the findings from this study confirm our hypothesis that prediction equations derived from the general population perform poorly in a cohort of endurance athletes.

We noticed that even when OUES is elevated in high-performance endurance athletes, the overall trend and lack of significant differences were still maintained. Previous studies have not assessed such relationships in trained participants or merged trained and untrained subjects (Akkerman et al., 2010; Sun et al.,

2012). We confirmed that even if an athlete can continue strenuous exercises for a prolonged time, the OUES remains stable across its duration. On the other hand, when one of the time intervals ($OUES_{75}$, $OUES_{90}$, or $OUES_{100}$) is underestimated or overestimated and presents a high difference from others, it should raise awareness (Hollenberg and Tager, 2000). Thus, monitoring OUES can valuably contribute to the assessment of the response profile to exercise (Hammond and Froelicher, 1985; Akkerman et al., 2010). Medical professionals can add OUES to their testing portfolio when challenging CPET results in this unique patient population.

Furthermore, our results show that OUES is a comparable predictor of VO_2peak independently from the measuring interval. In univariable models, we noticed that the relationship remained very strong, regardless of sex, age, and other covariates. For all prediction models, the overall regression was statistically significant (R^2 = 0.50–0.63, all $p < 0.001$), and OUES showed high prediction abilities (β = 0.71–0.80, all $p < 0.001$). Both submaximal $OUES_{75}$ and $OUES_{90}$ explained up to 60% of the variance in VO_2peak. Previously, Brown et al. reported a weaker correlation between OUES and VO_2peak, with R^2 = 0.09–0.15 (Brown et al., 2013). Perhaps, their research was conducted on youngsters (mean age was 14.7 years) and with fewer athletes (n = 25) than in ours (mean age 22.3 years, n = 140). The present study strongly advocates the conclusions made by Sun et al. that OUES and VO_2peak measure analogous mechanisms in athletes (Sun et al., 2012). Each may be complementary and supplementary to the other.

External validation of the prediction models for OUES confirmed the results of our previous studies that equations derived from the general population showed limited agreement when applied to endurance athletes (Wiecha et al., 2023a; Kasiak et al., 2023). Although the general trend was maintained, the variability between the observed and predicted values was high. Only 4 of the 11 models achieved at least ICC ≥0.5, which is considered the lowest borderline of moderate compliance (for precise data, see Table 3) (Koo and Li, 2016). Adjusting models to BSA or weight provides some additional benefits. The simple equations by Marinov and Kostianev (2003) using only BSA covered the highest amount of variance (R^2 = 0.388). The model by Marinov and Kostianev (2003) is a model derived from a pediatric sample. The athletic cohort of this study consisted of younger individuals with a mean age of roughly 22.3 years. We stipulate that this is the underlying reason for why the use of the age covariate provided only a slight predictive value in our participants. However, future studies should confirm our findings and externally examine our equations as this is the first study prediction of OUES among endurance athletes.

We adjusted OUES to BSA, as recommended by Baba et al. (1996) and Hollenberg and Tager (2000). Our model performed more accurately or with similar precision than that proposed by previous authors. The R^2 was approximately 34%–36%. Comparably, Milani et al. (2023) observed R^2 between 7.7% and 10.4%. A study by Milani et al. (2023) was conducted among healthy individuals, although with wider age ranges and with other ethnicity than in our participants. A model partially derived from trained subjects by Sun et al. (2012) provided R = 0.701, which was slightly higher than the R-value achieved in this study (between 0.59 and 0.61). To enrich the quality of the analysis, we additionally validated each of our models. It is worth underlining that our models performed comparably during the development and validation. The mean bias was −0.13 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$ for the predicted $OUES_{75}$, −0.001 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$ for $OUES_{90}$, and −0.04 $mL{\cdot}min^{-1}/L{\cdot}min^{-1}$ for $OUES_{100}$. This shows that the model fits well, as presented in Figure 2.

Perspectives and significance

So far, the diagnostic value of submaximal cardiorespiratory fitness has been mostly discussed in clinical populations when the maximal strenuous effort is not recommended, e.g., in heart failure (Metra et al., 1998). However, among healthy, highly trained individuals, the holistic approach should include an evaluation of the whole exercise duration (Shushan et al., 2022). Submaximal performance could also deteriorate in elite endurance athletes, e.g., after a viral infection (Sliz et al., 2022). Sheridan et al. noticed limited prediction power of OUES for VO_2peak when measured from the start to the ventilatory threshold in endurance athletes (Sheridan et al., 2021). OUES measured from the percentage of exercise duration is a more objective and replicable index because it includes the precisely truncated parts of exercise data (in our study, 75%, 90%, and 100%, respectively) (Baba, 2000). Even in elite athletes, OUES links well with the most reliable index of cardiorespiratory fitness, i.e., VO_2peak. Therefore, considering OUES as a prognostic indicator is justified when we suspect CVD in the athletic population. Furthermore, comparing OUES of a single participant between 75%, 90%, and 100% intervals would be beneficial to determine how an athlete's heart responds to increasing intensity. Furthermore, the developed new prediction equations could be applied when direct CPET is not possible.

Limitations and interpretation

Our study also has some points that have to be mentioned to ensure correct interpretation. The population was homogenous in age and ethnicity. The other studies for OUES prediction models included a higher number of participants than our study. In this research, the average age of the participants was roughly 22 years. The subjects were younger and had above-average endurance capacity when compared to other studies in this field. Our athletes were healthy. Thus, the results have limited application in patients with pathologies. We conducted CPET on cycle ergometry. Testing modality could influence the achieved performance, and exercise tests performed on other machines (treadmill and rowing ergometry) could provide slightly different results (Price et al., 2022). The participants usually achieve a lower performance on the cycle ergometer than on the treadmill, and our models are mostly tailored for cycling exercise tests. We expect that applying the presented models to other testing protocols could cause some inaccuracies. Therefore, we recommend considering all the above-mentioned aspects when deriving future reference equations. This is the first study of OUES predictions in highly fit participants, so we recommend careful extrapolation when considering the results. The external validation of our equations is welcome. Moreover, the development of formulas from other testing machines is also needed.

Conclusion

OUES remains stable between 75%, 90%, and 100% of exercise duration even in highly trained individuals. OUES was comparable between the measurements for endurance athletes. The prediction models derived from the general population demonstrated poor alignment. We do not recommend them for endurance athletes. New equations explained up to 36% of the variance and were inaccurate for only up to −0.13 $mL \cdot min^{-1}/L \cdot min^{-1}$. The proposed equations are internally validated and designed for endurance athletes. Medical professionals and physicians should be acknowledged to precisely adjust the training and properly interpret the specific cardiovascular response profile in athletes.

Data availability statement

The raw data supporting the conclusion of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the Bioethics Committee of the Medical University of Warsaw (Pawińskiego 3C Street, 02-106 Warsaw). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

PK: conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, validation, visualization, writing–original draft, and writing–review and editing. TK: conceptualization, investigation, methodology, project administration, resources, validation, writing–original draft and writing–review and editing. KR: investigation, resources, and writing–review and editing. AK: conceptualization, investigation, resources, supervision, and writing–review and editing. MS: data curation, investigation, resources, and writing–review and editing. MŁ: investigation, resources, and writing–review and editing. SW: methodology and writing–review and editing. MB: funding acquisition and writing–review and editing. AP: funding acquisition and writing–review and editing. PW: funding acquisition and writing–review and editing. AM: project administration, supervision, and writing–review and editing. DŚ: conceptualization, funding acquisition, project administration, supervision, and writing–review and editing.

Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fphys.2024.1348307/full#supplementary-material

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Kopie opublikowanych prac

Publikacja nr 3

Tytuł:

Oxygen uptake efficiency plateau is unaffected by fitness level - the NOODLE study

Autorzy:

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Typ publikacji:

Artykuł oryginalny

DOI:

10.1186/s13102-024-00939-w

Czasopismo:

BMC Sports Science, Medicine and Rehabilitation

IF=2,8 | kwartyl JCR Q1 | centyl JCR 86,0

Kasiak *et al. BMC Sports Science, Medicine and Rehabilitation* (2024) 16:151
https://doi.org/10.1186/s13102-024-00939-w

BMC Sports Science, Medicine and Rehabilitation

RESEARCH Open Access

Oxygen uptake efficiency plateau is unaffected by fitness level - the NOODLE study

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Abstract

Background Endurance athletes (EA) are an emerging population of focus for cardiovascular health. The oxygen uptake efficiency plateau (OUEP) is the levelling-off period of ratio between oxygen uptake (VO_2) and ventilation (VE). In the cohort of EA, we externally validated prediction models for OUEP and derived with internal validation a new equation.

Methods 140 EA underwent a medical assessment and maximal cycling cardiopulmonary exercise test. Participants were 55% male ($N=77$, age = 21.4 ± 4.8 years, BMI = 22.6 ± 1.7 kg·m^{-2}, peak VO_2 = 4.40 ± 0.64 L·min^{-1}) and 45% female ($N=63$, age = 23.4 ± 4.3 years, BMI = 22.1 ± 1.6 kg·m^{-2}, peak VO_2 = 3.21 ± 0.48 L·min^{-1}). OUEP was defined as the highest 90-second continuous value of the ratio between VO_2 and VE. We used the multivariable stepwise linear regression to develop a new prediction equation for OUEP.

Results OUEP was 44.2 ± 4.2 mL·L^{-1} and 41.0 ± 4.8 mL·L^{-1} for males and females, respectively. In external validation, OUEP was comparable to directly measured and did not differ significantly. The prediction error for males was − 0.42 mL·L^{-1} (0.94%, $p=0.39$), and for females was + 0.33 mL·L^{-1} (0.81%, $p=0.59$). The developed new prediction equation was: 61.37–0.12·height (in cm) + 5.08 (for males). The developed model outperformed the previous. However, the equation explained up to 12.9% of the variance ($R=0.377$, $R^2=0.129$, RMSE = 4.39 mL·L^{-1}).

Conclusion OUEP is a stable and transferable cardiorespiratory index. OUEP is minimally affected by fitness level and demographic factors. The predicted OUEP provided promising but limited accuracy among EA. The derived new model is tailored for EA. OUEP could be used to stratify the cardiorespiratory response to exercise and guide training.

Keywords Oxygen uptake efficiency plateau, Cardiopulmonary exercise testing, Endurance athletes, Prediction equation, Cardiorespiratory fitness, Cardiovascular health

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Introduction

Endurance athletes (EA) regularly participate in competitions and are exposed to high physical loads [1]. Cardiovascular diseases (CVD) are still a significant problem in the health care system [2]. Strenuous exercise could elevate the risk of CVD [3]. Hence, the development and validation of novel, reliable indices remain crucial to enable a comprehensive interpretation of cardiorespiratory fitness [4]. The gold-standard metric of athletic performance is oxygen uptake (VO_2) [5]. However, VO_2 is not the only one, and the usefulness of the other measures should be investigated [6, 7].

EA usually does not fit into the cardiorespiratory reference values from general population [8–10]. Both, the VO_2 and ventilation (VE) are poorly predicted and mostly underestimated by common prediction equations in EA [8, 11]. Moreover, measurements of absolute value of variables are often an insufficient source of knowledge about cardiovascular physiology in EA [12, 13]. Recent focus has been applied to ratios of oxygen uptake efficiency measures which is described by the correspondence between VO_2 and VE [14, 15]. Moreover, it is sometimes not feasible to perform cardiopulmonary exercise test (CPET) and directly measure cardiorespiratory fitness. Thus, the importance of prediction equations based on non-exercise and body measures emerge [16].

The oxygen uptake efficiency plateau (OUEP) was originally introduced by Sun et al. [17]. OUEP relates to different periods of exercise than the oxygen uptake plateau [17, 18]. OUEP explains the levelling-off between VO_2 and VE [17]. OUEP can be plotted in the majority of exercise tests because it occurs early, just before the aerobic threshold [17, 19]. OUEP occurs before hyperventilation due to demanding exercise leads to acidemia [17]. If OUEP falls below 65% of the predicted value, there is a suspected pathology [19]. However, among numerous cardiorespiratory indices, EA often noted an underestimation when compared to the untrained subjects [20, 21]. As it merges cardiac and respiratory systems, it may be superior to previous risk indicators (i.e. heart rate, ventilatory efficiency, oxygen pulse, etc.) [19].

The issues of prevention and diagnosis of cardiovascular diseases (CVD) among EA are increasingly gaining attention [3]. Adjustment between VE and VO_2 emerge as a valuable, interesting direction in sports cardiology. Hypo- or hyper- ventilation is influenced mostly by cardiovascular functions, however, peripheral and pulmonary factors also contribute here [22]. Merge between VE and VO_2 could be used in clinical setting to grade the CVD and in the sports cardiology to stratify impairment in physical training or to assess fitness [23–25].

OUEP should be stable even in highly fit athletes and varies only slightly [17]. However, no studies have confirmed its replicability in the EA population so far. Moreover, the prediction equation for OUEP has never been externally validated on other populations. We noticed a significant understudied area of knowledge. This research corresponds and complements to the previous NOODLE studies about ventilatory efficiency and oxygen uptake efficiency slope in EA [10, 26].

In this research, we aimed to: (1) clarify whether OUEP remains reproducible in a group of EA by external validation of the previous prediction equation, and (2) systemize the usefulness of OUEP in EA by development and internal validation of a new non-exercise model.

Materials and methods

Study setting

This study received approval from the Bioethics Committee of the Medical University of Warsaw. Participants provided their written informed consent. We applied the STROBE statement of EQUATOR Network guidelines [27]. The checklist is included in the Supplementary Material 1 (Table S1). The recruitment period was 2022–2023.

Eligibility criteria

Firstly, we applied the following inclusion criteria for EA: (1) age ≥ 18 years, (2) ≥ 4-year experience in regular endurance training, (3) membership in a sports association and national elite or development teams, and (4) regular participation in competitions on the regional and international levels. Participants were assigned to Class 3–5 in McKay classification framework [28].

Further, we ensured a consultation with a medical doctor to confirm the overall health of our participants. We used rigorous exclusion criteria that considered past medical history and ongoing symptoms. The physician looked for the presence of any of the following: pulmonary diseases, CVD, neurological and mental disorders, haematological deviations, and orthopaedic injuries; and we asked about habitual tobacco smoking. If we confirmed a past medical history, the physician refused the subject from CPET. Precise definitions of examined abnormal health criteria are described in Table 1.

Finally, we considered effort as maximal when there was a: (1) ≥ 30-s VO_2 plateau, (2) respiratory exchange ratio (RER) ≥ 1.05, (3) maximal heart rate ≥ 80% of the age-predicted, (4) EA declined further exercises, and (5) declared exhaustion was ≥ 18 points on the Borg scale. We chose these criteria from cardiopulmonary reference data for endurance athletes [8, 29]. All listed criteria of maximal effort were obligatory to include the EA in this study. If the CPET was submaximal the participant was not included in the analysis. The CPET was defined as submaximal when EA did not reach all of the previously listed criteria. Failure to meet any of these criteria excluded the participant.

Table 1 Abnormal health findings considered as the exclusion criteria

1. Pulmonary diseases

- *Chronic obstructive pulmonary disease*
- poorly controlled bronchial asthma
- blood saturation < 95%

2. Cardiovascular diseases

- significant heart rhythm disturbances in the 12-lead ECG (e.g., ventricular and supraventricular arrhythmias, atrial fibrillation)
- features of myocardial ischemia,
- prolongation of the QT interval in the 12-lead ECG
- structural heart disorders detected in cardiac echocardiography (e.g., hemodynamically relevant valvular defects, hypertrophic cardiomyopathy, systolic dysfunction of the right or left ventricle),
- decompensated blood pressure (with increases above 160/100 mmHg).

3. Neurological and mental disorders

4. Significant deviations found in CBC

- Leukocytosis above 10 000 · mm^{-3}
- Anaemia with Hb level < 10 g · d^{-1}

5. Exercise-limiting musculoskeletal injuries

Note Any of the above health conditions were considered as the mandatory exclusion criteria during pre-participation medical follow-up. Abbreviations: 12-lead ECG, 12-lead electrocardiography; CBC, complete blood count; Hb, blood haemoglobin concentration

Table 2 Study population

Variable		All EA [*N* = 140]	Males [*N* = 77]	Females [*N* = 63]
A. Baseline characteristics				
Age (years)		22.7 ± 4.6	21.8 ± 4.8	23.8 ± 4.2
Height (cm)		174.8 ± 9.9	181.6 ± 6.3	166.3 ± 6.2
Body weight (kg)		69.3 ± 10.1	76.1 ± 7.6	61.0 ± 5.5
BMI ($kg·m^{-2}$)		22.6 ± 1.7	23.1 ± 1.7	22.1 ± 1.6
BSA (m^2)		1.84 ± 0.12	1.97 ± 0.18	1.68 ± 0.10
Sport discipline	Triathlon or cycling	56 (40.0)	30 (47.6)	26 (33.8)
	Speedskating	59 (42.1)	26 (41.3)	33 (42.9)
	Other endurance sports	25 (17.9)	7 (11.1)	18 (23.3)
B. Exercise performance				
HR ($beats·min^{-1}$)		190.9 ± 8.6	190.8 ± 8.7	191.0 ± 9.1
VE ($L·min^{-1}$)		154.5 ± 34.1	176.3 ± 26.3	127.8 ± 21.1
VO_2peak ($L·min^{-1}$)		3.86 ± 0.82	4.40 ± 0.64	3.21 ± 0.48
VO_2peak/kg ($mL·kg^{-1}·min^{-1}$)		55.2 ± 8.6	57.8 ± 9.0	52.1 ± 7.0
% pred. VO_2peak		144.5 ± 25.9	130.6 ± 20.2	161.4 ± 21.8
OUES ($mL·min^{-1}/L·min^{-1}$)		3.96 ± 0.90	4.41 ± 0.87	3.41 ± 0.58
OUEP ($mL·L^{-1}$)		42.7 ± 4.7	44.2 ± 4.2	41.0 ± 4.8

Abbreviations BMI, body mass index; BSA, body surface area; HR, peak heart rate; VE, peak minute ventilation; VO_2peak, peak oxygen uptake; OUES, oxygen uptake efficiency slope; OUEP, oxygen uptake efficiency plateau

Note Upper rows (Part A) present characteristics of study group and lower rows (Part B) present exercise performance. OUES was calculated from VO_2/VE_{log} during the whole exercise effort. OUEP was considered the highest continuous 90-second average from the VO_2/VE ratio. Measures are presented as mean ± standard deviation or number (percentage). Predicted VO_2peak was calculated from the Wassermann and Hansen Eq. (31)

The flowchart presenting recruitment process is presented on the Fig. 1.

Cardiopulmonary exercise testing

Continuous ramp CPET was performed on a Cyclus II Cycling Ergometer (RBM, Leipzig, Germany). All CPET was conducted in unified procedures of the Institute of Sport - National Research Institute in Warsaw (https://insp.pl, accessed on 6th March 2024). The exercise began with pedalling without load for 2–3 min to warm up. The incremental protocol started with a workload between 55 and 70 W and increased by 0.17–0.28 $W·s^{-1}$. The starting workload and grading of workload during CPET were set after reaching agreement between the supervising physiologist and each single EA in the aforementioned ranges. Participants were guided by the physiologist and encouraged verbally to achieve maximum results.

Measuring procedures

We obtained several body indices: height, body weight, BMI, and body surface area (BSA). We measured body weight with the TANITA scale (TANITA Corporation, Arlington Heights, IL, USA) before breakfast. We measured height using the stadiometer (Seca GmbH & Co., Hamburg, Deutschland) in the morning (along with body weight). We calculated BSA from Du Bois & Du Bois Eq. [49]. Raw breath-by-breath data for ventilatory measures were collected using the Hans Rudolph V2 Face Mask (Hans Rudolph, Inc, Shawnee, KS, USA). During the data collection process, we used the Cortex B3 Metamax metabolic system (CORTEX Biophysik GmbH, Leipzig, Germany). We recorded: VE, VO_2, VCO_2, respiratory rate, and tidal volume. Gas analysing devices were calibrated individually for all participants before CPET. A Polar H10 heart rate sensor with a chest strap was used to measure heart rate. The heart rate sensor was continuously paired with the Cyclus II Cycling Ergometer. All obtained indices were averaged in the 15-second intervals. We excluded the first minute of loaded protocol to minimize noise variables and determined OUEP as the highest continuous 90-second average of VO_2/VE ratio plotted against time [17]. We excluded all the enrolled individuals with missing data to ensure the maximal credibility of the results.

Screening for prediction equation for OUEP

To select previous prediction equations for OUEP, we examined the 5 databases: PubMed, Scopus, Web of Science, Google Scholar, and Medline. Applied keywords were: "OUEP", "oxygen uptake efficiency plateau", "cardiopulmonary exercise tests", "prediction equation", "reference values", and "oxygen uptake efficiency". We included only models which were derived from healthy, adult

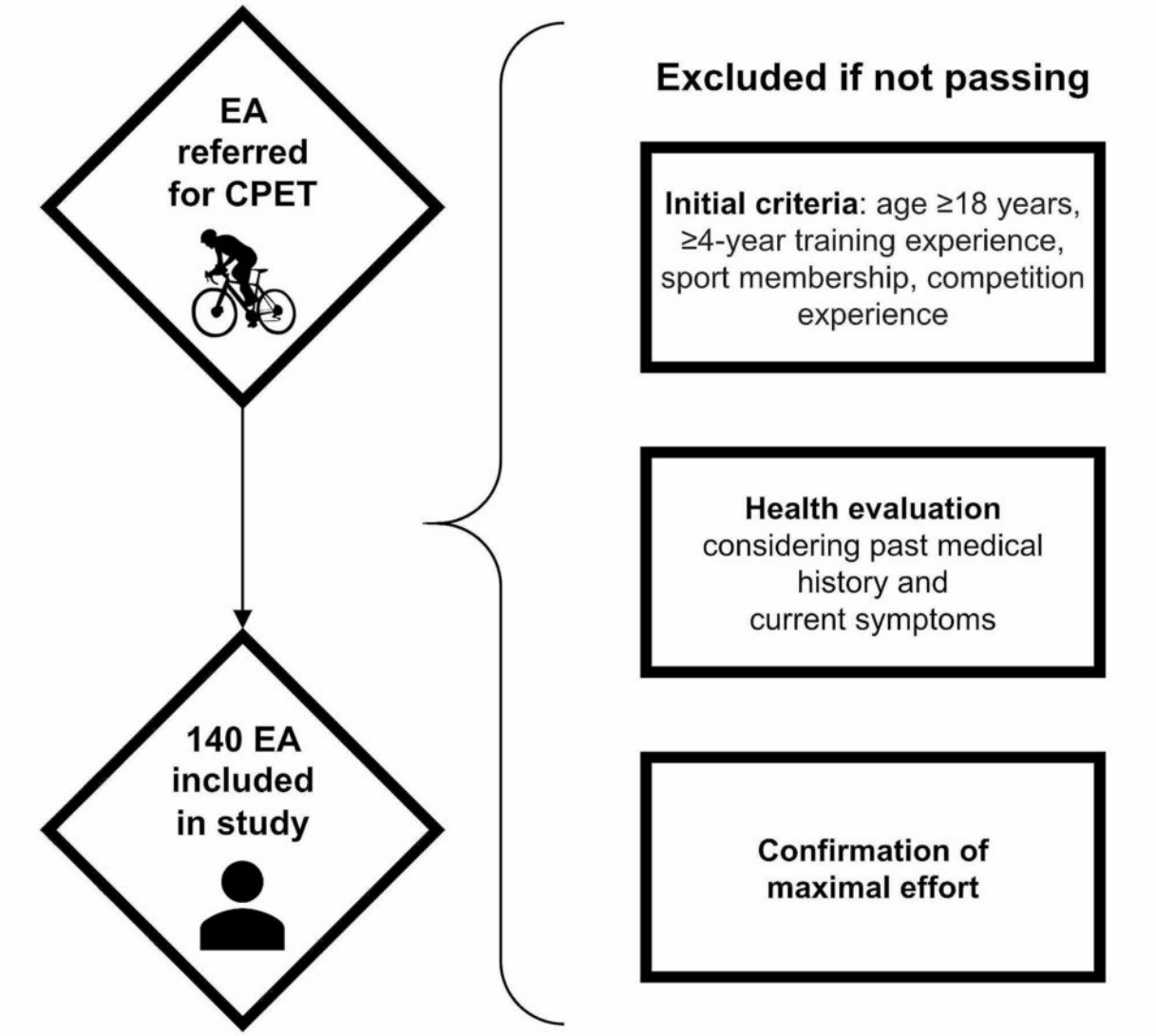

Fig. 1 Schematic representation of the participants recruitment procedure. *Abbreviations* EA, endurance athlete; CPET, cardiopulmonary exercise test

populations (age≥18 years, no existing co-morbidities). One prediction equation for OUEP has been found [17]:

$$\begin{aligned}\mathrm{OUEP}\,[\mathrm{mL}\cdot\mathrm{L}^{-1}] = & 42.18 - 0.189\cdot \mathrm{age}\,[in\ years] \\ & + 0.036\cdot \mathrm{height}\,[in\ cm]\ ] - 3.02[if\ female]\end{aligned}$$

The equation was derived from the mixed treadmill and/or cycling protocol from a healthy population of 417 participants aged 17–74 years. The population of the derivation study also had well-trained athletes (N=57) with >140% of predicted VO_2peak according to the Wasserman & Hansen Eq. (31) and those well-trained athletes were not included in the model derivation process. The CPET started with a 3-min resting and 3-min warm-up followed by an incremental ramp cycling protocol and terminated with at least 2-min recovery.

Statistical analysis

To determine the data distribution, we used the Shapiro-Wilk test and visually examined the corresponding Q-Q plots. We presented categorical variables as number (percentage) and continuous variables as mean±standard deviation. We used IBM SPSS (version 29.0, IBM, Armonk, NY, USA) for analyses and GraphPad Prism (version 10.1, GraphPad Software, San Diego, California USA) to develop the plots. We set $p<0.05$ as significant.

The external validation of the prediction equation for OUEP was determined by comparing observed and predicted values by Student's t-test for independent samples

and calculating root-mean-square error (RMSE). The compliance of predicted to observed OUEP was shown in Bland-Altman plots. The variance explained by the previous model was examined by regressing observed OUEP against predicted OUEP and presented as an adjusted coefficient of determination (R^2). The correlation of OUEP and VO_2peak was assessed by the Pearson Correlation Coefficient (R). The new model was derived with the stepwise multiple linear regression. The method for model derivation was selected by assessment of data assumptions (collinearity, correlations, independence of observations, residuals, and leverage plots). Especially, we included only significant variables with $p<0.05$. Finally, the model was internally validated with the bootstrapping from 10,000 iterations [30].

The sample size was evaluated post-hoc in the G*Power software [31]. For all applied statistical methods, the study population achieved significance, a large effect size, and a power of 0.99. Results were presented following the current 11th Edition of guidelines of the American Medical Association Manual of Style: A Guide for Authors and Editors [32].

Results

Study population

Of 140 EA, 77 (55.0%) were male and 63 (45.0%) were female. Table 2 presents the brief participants' basic demographic and exercise characteristics, while a detailed description of the study population is provided in the Supplementary Material (Table S2). Participants represented the following endurance disciplines: 56 (40.0%) triathlon or cycling, 59 (42.1%) speedskating, and 25 (17.9%) other disciplines. The predicted VO_2peak was 144.5±25.9% and ranged from 90.6 to 216.2% according to Wasserman and Hansen equation. Females had lower OUEP than males for an average of 3.2 $mL{\cdot}L^{-1}$ ($p<0.001$). OUEP was 44.2±4.2 $mL{\cdot}L^{-1}$ (range 36.2–54.2 $mL{\cdot}L^{-1}$) and 41.0±4.8 $mL{\cdot}L^{-1}$ (range 29.4–53.0 $mL{\cdot}L^{-1}$) for males and females, respectively. VO_2peak was significantly correlated with OUEP ($R=0.32$, $p<0.001$).

Derivation of the new model

We evaluated several non-exercise measures (sex, age, height, body weight, BMI, and BSA) for their suitability in building the model. The parsimonious bivariable model included the height and was adjusted to sex. The derived equation for OUEP is presented in Table 3.

The model was responsible for 12.9% of the variance in OUEP ($R=0.377$, $R^2=0.129$). Overall regression was significant ($F(2, 137)=11.33$, $p<0.001$). In Fig. 2 we compared observed and predicted OUEP by regressing one against another. As expected by the limited R^2 the data were scattered both for males and females. The model's RMSE was 4.39 $mL{\cdot}L^{-1}$. Predicted OUEP equals 42.67 $mL{\cdot}L^{-1}$ which was 100.2% of the observed values. The difference was 0.07 $mL{\cdot}L^{-1}$ for the whole population. Bland-Altman plots presenting the agreement between observed and predicted OUEP are in Fig. 3. In both males and females, the OUEP was slightly underestimated. The bias was −0.77 $mL{\cdot}L^{-1}$ and −0.53 $mL{\cdot}L^{-1}$ for males and females, respectively. The limit of agreement was wider in females (–9.25 $mL{\cdot}L^{-1}$ to 9.38 $mL{\cdot}L^{-1}$) than in males (–7.99 $mL{\cdot}L^{-1}$ to 7.85 $mL{\cdot}L^{-1}$).

External validation of prediction equation for OUEP

The external model overestimated OUEP by only 0.08 $mL{\cdot}L^{-1}$. The total difference was 0.19% and RMSE was 4.48 $mL{\cdot}L^{-1}$. In the whole population, values did not differ significantly ($t(278)= -0.18$, $p=0.86$). The external model contributed to the 9.9% of the variance in the directly observed OUEP ($R^2=0.099$).

Briefly, higher bias was noted for males than females. For males, the OUEP was underestimated by 0.42 $mL{\cdot}L^{-1}$ (0.94%). As in the total population, predicted values also did not differ significantly in males ($t(152)= -0.86$, $p=0.39$). RMSE for males was 4.16 $mL{\cdot}L^{-1}$. A similar relationship was observed among females. However, the model overestimated OUEP by 0.33 $mL{\cdot}L^{-1}$ (0.81%) in females. The error was not significant ($t(124)=0.54$, $p=0.59$). RMSE for females was 4.84 $mL{\cdot}L^{-1}$. A visual representation of model prediction capacity stratified by sex is presented in Fig. 4. As expected, the limits of agreement were wider than in the developed model. The limit of agreement for males was −8.59 $mL{\cdot}L^{-1}$ to 7.76 $mL{\cdot}L^{-1}$. For females, the limit of agreement ranged between −9.21 $mL{\cdot}L^{-1}$ to 9.87 $mL{\cdot}L^{-1}$.

Table 3 Multivariable prediction equation for OUEP

Covariate	Estimate	Standard Error	β	95% CI		*p*-value
				LL	UL	
Intercept	61.369	9.92	---	41.747	80.991	< 0.001
Sex	5.078	1.18	0.539	2.749	7.407	< 0.001
Height	–0.123	0.06	–0.257	–0.240	–0.005	0.041

Abbreviations 95% CI, 95% confidence interval; LL, lower limit; UL, upper limit

Note Sex is 1 for males and 0 for females

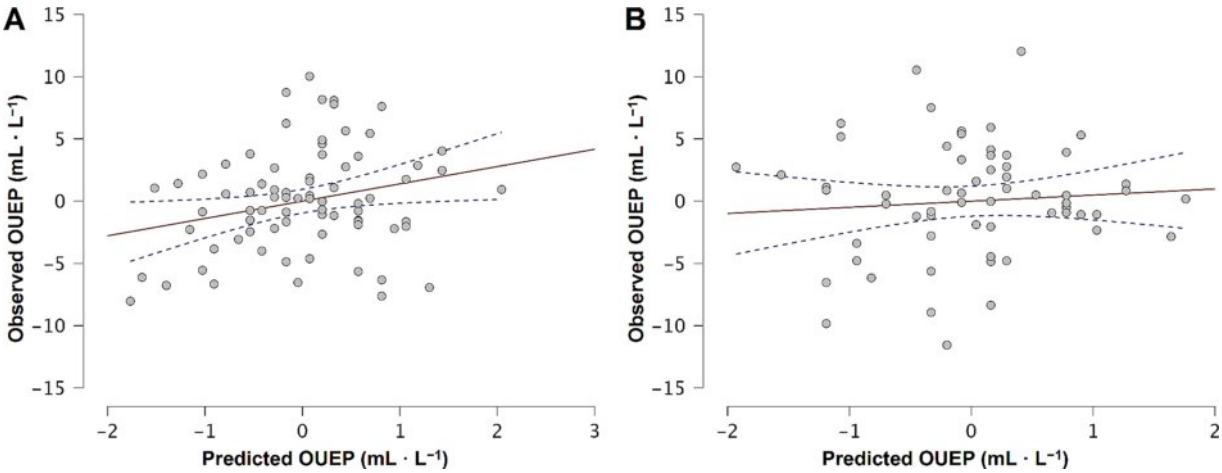

Fig. 2 Correlation between observed and predicted OUEP. *Abbreviations* OUEP, oxygen uptake efficiency plateau. *Note* Panel A represents males and panel B represents females. The central red line represents the trend. The blue dotted lines represent 95% confidence intervals. The plot presents univariable regression analysis of observed OUEP against predicted OUEP

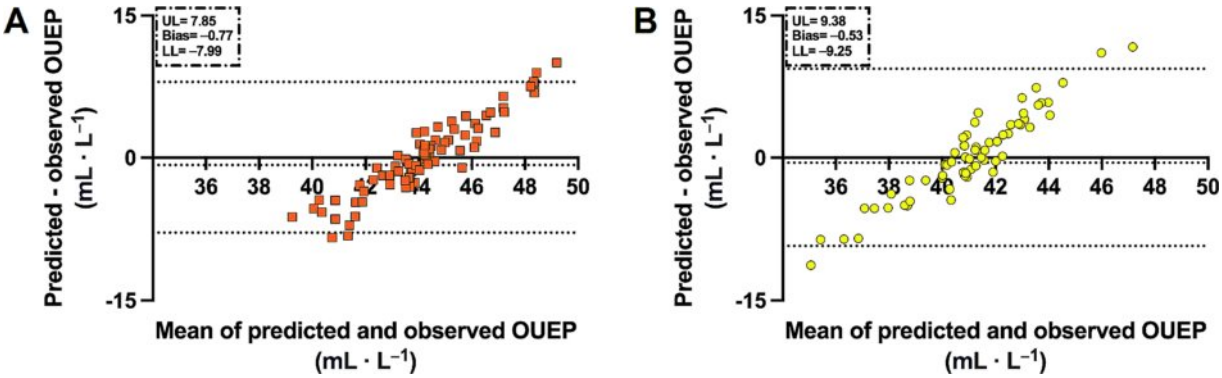

Fig. 3 Bland-Altman plots of the prediction accuracy of derived models. *Abbreviations* UL, upper limit of agreement; LL, lower limit of agreement. *Note* Panel A (orange color) represents males and panel B (yellow color) represents females. Upper dotted line represents upper limit of agreement and lower dotted line represent lower limit of agreement. Area between dotted lines represent model's accuracy

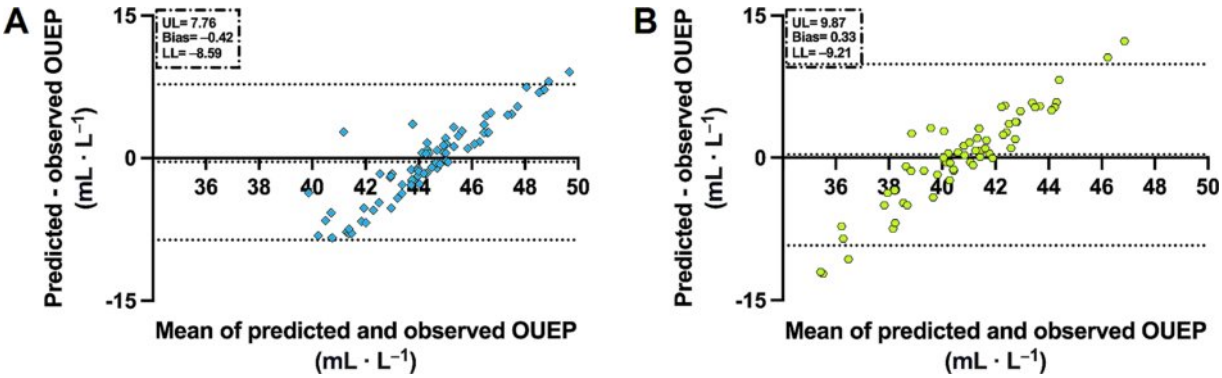

Fig. 4 Bland-Altman plots for external validation of previous models. *Abbreviations* UL, upper limit of agreement; LL, lower limit of agreement. *Note* Panel A (blue color) represents males and panel B (green color) represents females. Upper dotted line represents upper limit of agreement and lower dotted line represent lower limit of agreement. Area between dotted lines represent model's accuracy

Discussion

To the best of our knowledge, this is the first external validation of prediction equations for OUEP. Moreover, there is no research so far that has evaluated the stability of OUEP in EA. In this article we found that following areas: (1) OUEP is a replicable cardiorespiratory measure between EA and untrained healthy individuals, (2) OUEP predicted by somatic measurements provided promising but limited accuracy and (3) OUEP is a valuable marker when stratifying cardiorespiratory response profiles in EA.

EA is a unique population. They do not fit into the general reference values for the majority of cardiovascular measurements [33]. Regular physical activity has a brilliant preserving effect on the cardiovascular system. Endurance training causes a slower decline of fitness with aging (e.g. VO_2peak or maximal heart rate) [8, 34]. Our previous studies showed significant inaccuracies in prediction models for VO_2peak or heart rate when applied to athletic individuals [20, 21]. So far as we know, OUEP was never deeply analyzed in context of sports cardiology in EA.

OUEP remains a relatively understudied marker. Sun et al. found that, when OUEP drops below 65% of the predicted value, it can suggest pathology [19]. In our EA, no one observed such a difference. Only two females showed a difference of 11.3 $mL{\cdot}L^{-1}$. For all the remaining participants calculated OUEP did not differ more than 10 $mL{\cdot}L^{-1}$, i.e. around 25% error. What is more, no one exceeded the 35%. The highest calculated underestimation was 27.7% (11.3 $mL{\cdot}L^{-1}$ in both females). The variance explained by the derived model was 12.9% (R^2=0.129). Comparably, the variance explained by the external model [17] was 9.9% (R^2=0.099). Although those values are limited, both are comparable, even though the models were developed from different populations.

It is worth noting that the only variable missing from the original equation presented by Sun et al. is age [17]. This probably results from our cohort age distribution (22.7±4.6 years old). Age had only minor variance in our homogenous sample and did not reach significance. This is an emerging point in the discussion of our results and a great recommendation for further studies on OUEP predictions in populations of EA with a wider age distribution. Moreover, the original derivation study by Sun et al. included only 57 well-trained participants [17]. Our study has a wider population of 140 EA. Therefore, the provided results seem to be more reliable.

Moreover, OUEP has further advantages. Assuming other measures of cardiorespiratory fitness, VO_2peak may be different if a verification retest is used and the ventilatory efficiency slope depends largely on the plotting method [35, 36]. OUEP is an objective measure because it is an averaged time interval; thus, OUEP seems reliable and should be easier to compare between studies [17, 19]. An interesting finding from our study is presented on the Figs. 3 and 4 where bias grow simultaneously with increasing OUEP [37]. This indicate that agreement between measured and estimated OUEP could not be constant but varies with fitness level. Perhaps, prediction of OUEP with a universal equation could not be the most valid method. Therefore, it is justified to derive the models tailored for particular populations (i.e. trained and untrained) [8, 37].

The relationship of OUEP to basic demographic parameters such as sex and age remained mostly similar between EA and the general population [17]. However, findings from our study should be discussed as some relationships to other demographic measures with OUEP seem to be complex. We highlight the very strong impact of sex as reflected by the high β-coefficient (β=0.54). As expected, males had higher OUEP than females. Even though our study population was younger (age approximately 22.3±4.6 years), OUEP also declined with increasing age (β= −0.048, p=0.57). This relationship was not significant; thus, we do not include age covariate in our models. Our model indicates that OUEP could decrease with height (β=–0.257, p=0.041). Finally, we did not find a significant relationship between OUEP and other somatic measurements such as body weight, BMI, or BSA.

In young people, maximal effort is strongly dependent on the motivation to continue effort despite fatigue [38]. This does not mean that if CPET was submaximal, it did not provide valuable data. OUEP is most often found close to the first ventilatory threshold [17]. Our study indicates that it is a robust cardiorespiratory verifier, no matter whether the maximum effort has been achieved or not. Since OUEP is measured during submaximal, not peak, exercise, It does not cause strenuous fatigue and is safer for clinical purposes or to avoid overtraining [39]. OUEP can be repeated frequently and regularly to monitor cardiorespiratory health. What is more, OUEP is easier to reliably determine because it is calculated from a time interval and does not include finding the ventilatory threshold which could be affected by interobserver variability [40, 41].

Limitations

To ensure that our conclusions will be correctly interpreted, some points should be raised. We gathered a population of high-performance well-trained individuals, which is difficult. According to Wasserman & Hansen, the predicted VO_2peak in our subjects was on average 144.5±25.9% [42]. Therefore, we were able to conduct external validation on EA. Participants with VO_2peak>140% predicted were assigned to 'very fit' in the original study by Sun et al. [17]. We also emphasize

the equal ratio of males to females (55–45%). Therefore, the influence of sex is balanced and reliably modelled.

The study group appears to be homogeneous, and in the majority consisted of younger Caucasian EA [43]. Further studies with a wider age distribution should be conducted. Those studies should include both pediatric EA and master EA. CPET was conducted in a cycling protocol. The modality of CPET could influence the results. In other protocols (e.g. running or rowing) there could be some different values [44]. In the original derivation study from Sun et al. the participants also underwent CPET on the treadmill [17]. CPET results are usually slightly higher during running than cycling [44]. We stipulate that this should not have wide impact on results of our study because OUEP is a ratio of two variables. However, this relationship should be verified by further researchers. Therefore, we highlight that derived models are specified for cycling CPET.

It is worth noting that there is some ambiguity of the maximum effort criteria used for studies on EA. Wagener et al. suggest that the most appropriate RER for individuals aged 20–39 is ≥1.13 [45]. On the other hand, the American Thoracic Society and with American College of Chest Physicians recommend a RER of 1.10 [4]. Finally, Petek et al. found that the most suitable RER for EA equals 1.05 [8]. In our study, we used RER of 1.05 as a cutoff (i.e. similar to Petek et al.) because these criteria are the latest ones and were provided after consideration and evaluation of previous reports [8]. However, if any future study will choose other criteria of maximal CPET, we underline that the OUEP results could be slightly different. We underline the need to derive further models to predict OUEP from other testing modalities and under other testing criteria. In summary, all the results should be extrapolated carefully.

Clinical implications

Some practical and clinical applications should also be discussed. CPET can be performed for sports diagnostics to guide training and in a clinical setting when pathology is suspected [46, 47]. However, clinicians need a certain reference point (i.e., a value or formula to compare with directly measured results). Retrospective evaluation of achieved OUEP could facilitate the assessment of cardiorespiratory fitness [17]. Furthermore, the prospective calculation of OUEP enables the setting of the target ranges when planning the CPET intensity [17]. Our prediction equations are a valuable part of a clinician's toolbox when assessing cardiorespiratory health. However, the provided equations should not be used to make a definitive diagnosis. Nevertheless, the models could be used to guide further steps. This study facilitates the implementation of OUEP among apparently healthy subjects and those with suspected CVD.

Future perspectives

Previous studies tested OUEP in predicting the VO_2peak [38, 48]. Most often there was a weak or limited correlation between OUEP and VO_2peak (17, 50). However, in our study, both parameters were significantly correlated ($R=0.32$, $p<0.001$). OUEP and VO_2peak describe different elements of exercise physiology and complement each other but do not replace one another [17, 19]. Future research on wider populations should clarify how OUEP links with VO_2peak. OUEP certainly constitutes an interesting supplement to VO_2peak [48]. OUEP is emerging as an interesting additional cardiorespiratory variable [19]. Future studies should verify whether OUEP remains stable in extreme age groups. Therefore, further research about OUEP could be conducted on junior and master EA. Another unanswered point is whether OUEP has any discriminative power when CVD is suspected in EA or could help to identify athletes in a state of overtraining.

Conclusions

OUEP remains stable and is only minimally influenced by endurance level. It is transferable between untrained individuals and EA. OUEP could be modelled in EA with basic demographic parameters: height and sex. Prediction equations for OUEP were replicable and provided promising, however limited accuracy. Medical professionals and fitness practitioners should consider OUEP when evaluating CPET results to determine cardiorespiratory fitness and monitor training.

Abbreviations

BSA	Body surface area
CPET	Cardiopulmonary exercise test
CVD	Cardiovascular diseases
EA	Endurance athletes
OUEP	Oxygen uptake efficiency plateau
OUES	Oxygen uptake efficiency slope
R	Pearson correlation coefficient
R^2	Coefficient of determination
RER	Respiratory exchange ratio
RMSE	Root-mean-square error
VCO_2	Carbon dioxide output
VE	Minute ventilation
VO_2	Oxygen uptake
VO_2 Peak	Peak oxygen uptake

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13102-024-00939-w.

Supplementary Material 1

Supplementary Material 2

Acknowledgements

Nothing to acknowledge.

Author contributions

Conceptualization, P.S.K., T.K., A.K. and D.Ś.; data curation, P.S.K. and A.W.; formal analysis, P.S.K.; funding acquisition, S.W., M.B., A.R.P., P.W. and D.Ś.; investigation, P.S.K., T.K., K.R., A.K. and D.S.; methodology, P.S.K. and T.K.; project

administration, P.S.K., T.K., A.M. and D.Ś.; resources, P.S.K., T.K., K.R., A.K., D.S. and A.W.; supervision, A.K., A.M. and D.Ś.; validation, P.S.K.; visualization, P.S.K.; writing—original draft, P.S.K. and T.K.; writing—review and editing, P.S.K., T.K., A.K. and S.W. All authors have read and agreed to the published version of the manuscript.

Funding
No funding was received for conducting this study.

Data availability
The data were be made available for a reasonable request to the corresponding author.

Declarations

Ethics approval and consent to participate
This study received approval no. AKBE/277 from the Bioethics Committee of the Medical University of Warsaw (Pawińskiego 3 C Street, 02-106 Warsaw). Participants provided their written informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 7 March 2024 / Accepted: 1 July 2024
Published online: 10 July 2024

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Publisher's Note

Kopie opublikowanych prac

Publikacja nr 4

Tytuł:

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Typ publikacji:

Artykuł oryginalny

DOI:

10.1038/s41598-024-73730-z

Czasopismo:

Scientific Reports

IF=3,9 | kwartyl JCR Q1 | centyl JCR 82,0

scientific reports

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Recalibrated FRIEND equation for peak oxygen pulse is accurate in endurance athletes: the NOODLE study

Przemysław Kasiak[1,2]✉, Tomasz Kowalski[3], Andrzej Klusiewicz[4], Ryszard Zdanowicz[3], Maria Ładyga[3], Szczepan Wiecha[5], Artur Mamcarz[1] & Daniel Śliż[1]

Peak oxygen pulse (O_2P_{peak}) is an important index of cardiorespiratory fitness (CRF). The FRIEND database is a global source of reference values for CRF. However, no reference equation is tailored for endurance athletes (EA) to predict O_2P_{peak}. Here, we adjusted the well-established FRIEND equation for O_2P_{peak} to the characteristics of the EA population. 32 (34.0%) female EA and 62 (66.0%) male well-trained EA underwent maximal cardiopulmonary exercise test on a treadmill. $\dot{V}O_{2max}$ was 4.5 ± 0.5 L min^{-1} in males and 3.1 ± 0.4 L min^{-1} in females. O_2P_{peak} was 23.6 ± 2.8 mL beat^{-1} and 16.4 ± 2.0 mL beat^{-1} for males and females, respectively. Firstly, we externally validated the original FRIEND equation. Secondly, using multiple linear regression, we adjusted the FRIEND equation for O_2P_{peak} to the population of EA. The original FRIEND equation underestimated O_2P_{peak} for 2.9 ± 2.9 mL beat^{-1} ($P < .001$) in males and 2.2 ± 2.1 mL beat^{-1} ($P < .001$) in females. The updated equation was 1.36 + 1.07 (23.2 · 0.09 · age − 6.6 [*if female*]). The new equation explained 62% of the variance and significantly predicted O_2P_{peak} ($R^2 = 0.62$, $\beta = 0.78$, $P < .001$). The error of the EA-adjusted model was 0.1 ± 2.9 mL beat^{-1} ($P = .82$) and 0.2 ± 2.1 mL beat^{-1} ($P = .65$) for males and females respectively. Recalibration of the original FRIEND equation significantly enhances its accuracy among EA. The error of the EA-adjusted model was negligible. A new recalibrated equation should be used to predict O_2P_{peak} in the population of EA.

Keywords Peak oxygen pulse, Endurance athletes, Cardiopulmonary exercise test, Cardiorespiratory fitness, Reference values, O_2pulse

Maximal oxygen uptake (VO_{2max}) obtained from a cardiopulmonary exercise test (CPET) is the gold-standard measure of cardiorespiratory fitness[1]. However, other variables also provide valuable information and give a more precise and comprehensive view[2]. One such index is the peak oxygen pulse (O_2P_{peak}), the ratio of VO_{2max} and maximal heart rate (HR_{max})[3,4]. The athletic population exhibits different physiological characteristics than patients or the untrained healthy population[5]. A key component of the O_2P_{peak}, i.e. VO_{2max} is significantly higher in endurance athletes[6]. Similarly, the HR_{max} declines slower with age in endurance athletes[7].

Therefore, we should underline several sex and fitness-driven interactions in endurance athletes that could influence the O_2P_{peak}[5]. Athletes in dynamic endurance disciplines, such as running, could observe a more rapid increase in O_2P_{peak} than untrained individuals[5]. Cardiorespiratory fitness, and particularly O_2P_{peak}, deteriorates slower with age or during periods of untraining[5,8]. Moreover, females adapt differently to males to endurance training and the changes include hormone levels, athletic performance, electrocardiogram, and cardiovascular imaging[9]. Other cardiac adaptations resulting from endurance training include increased cardiac output, improved cardiac dimensions, and better contractility[10,11]. All those changes lead to bigger stroke volume and higher oxygen transport[10]. O_2P_{peak} mirrors the function of the athlete's heart which works as a synergistic unit and O_2P_{peak} is especially related to the stroke volume. The stroke volume is higher in endurance athletes[12].

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Summing up, O_2P_{peak} should also be higher in endurance athletes than in normal, untrained subjects[12–14]. All above changes in cardiac adaptations to exercise suggest that the variability of O_2P_{peak} could be more complex than VO_{2max} or HR_{max} alone[4]. Therefore, understanding differences in cardiac physiology between athletes and untrained individuals is crucial to further investigate relationships between exercise variables properly.

Despite its several benefits, CPET is not always possible[15]. The most important limitations that should be acknowledged are the lack of qualified personnel, the high cost of procedures, and no properly equipped diagnostic centers[15,16]. Therefore, numerous prediction equations are developed to estimate cardiorespiratory fitness indirectly[17]. The comparison of values recorded during CPET to predicted is used to stratify the individual's fitness level[18]. However, there is limited knowledge about predictions of O_2P_{peak} in endurance athletes.

The "Fitness Registry and the Importance of Exercise: A National Data Base" (FRIEND) provides universal reference values for cardiorespiratory fitness[6]. So far, there have been only a few studies that tried to develop prediction equations for O_2P_{peak}[4,19]. However, in the majority, they have limited practical application besides the derivation group. Those equations include variables that most laboratories do not measure in standard CPET, e.g. systolic blood pressure or resting heart rate[19]. Furthermore, previous equations were usually developed from populations of a few hundred people. Arena et al. proposed the prediction equation for O_2P_{peak} from the FRIEND database for the general population based on widely available variables[4]. There are no more prediction equations for O_2P_{peak} which include universal, easy-accessible demographic variables. Moreover, there is a lack of prediction equations for O_2P_{peak} for endurance athletes despite that O_2P_{peak} is a useful index in trained individuals[12].

Moreover, elite endurance athletes are subjected to constantly growing training loads and competition demands[20]. It leads to significant physiological adaptations and sometimes may increase the risk of adverse cardiovascular events[20,21]. Hence, a precise assessment of cardiorespiratory fitness specific to well-trained endurance athletes is of vital importance[22]. To properly apply prediction equations in sports diagnostics and for clinical purposes in endurance athletes, their accuracy must be first validated and adjusted[23]. Such validation and assessment of differences between observed and predicted data allows for a correct understanding of CPET results[24].

This highlights the need to revise and adapt the standard reference equation for O_2P_{peak} to the endurance athlete population. To address those issues, here we: (1) externally validated the well-established FRIEND prediction equation for O_2P_{peak} on the cohort of endurance athletes and (2) recalibrated the prediction equation for O_2P_{peak} for endurance athletes.

Materials and methods

Study design

We obtained approval from the Institutional Review Board of the Medical University of Warsaw (Pawińskiego 3C Street, 02-106 Warsaw, approval no. AKBE/277) for this study. Then, after written informed consent, we analyzed the data of well-trained endurance athletes admitted in 2022–2023 to the Institute of Sport—National Research Institute, Warsaw, Poland. We followed the Declaration of Helsinki and the STROBE statement for cross-sectional studies[25].

Exercise tests were part of routine periodic performance evaluations during the season. The participants were elite athletes from national or development teams in endurance sports (medium or long-distance running, triathlon, ski mountaineering, cross-country skiing, and biathlon). All endurance athletes were in the 75th, 90th, or 95th percentile according to *Reference Standards for Cardiorespiratory Fitness* by Kaminsky et al.[6]

Only healthy adult individuals $\geq$ 18 years old underwent CPET. We ensured the health and safety of all endurance athletes by rigorous medical evaluation during their admission. Briefly, the health-related exclusion criteria were the same as in previous research from our lab[26]. The medical doctor assessed their 12-lead ECG, echocardiography, complete blood count, past medical history, and family history. The physician also performed auscultation, and neurological and orthopedic examinations to confirm the lack of any contraindication for maximal exercise tests. Moreover, all the endurance athletes had to deny smoking.

Exercise tests

Participants performed maximal interval CPET in a step protocol on the treadmill (h/p/cosmos Saturn treadmill, h/p/cosmos sports & medical gmbh, Nussdorf-Traunstein, Germany). To ensure similarity with the derivation study we selected only running CPET. Endurance athletes were familiar with the specificity of running CPET, as everyone has performed it multiple times before. The test started with a brief warm-up of easy walking or jogging. The proper part began from the 8 km h^{-1} (for females) and 10 km h^{-1} (for males) and consisted of 4-min intervals. We increased the speed by 1.5–2.0 km h^{-1} for each interval. Running speed was individually adjusted for each CPET after consultation of an individual athlete with the supervising physiologist. We implemented a 60-s recovery between intervals. We set the treadmill inclination of 1.5% for the whole CPET protocol. Endurance athletes continued the grading interval protocol until CPET termination. All the following endpoints had to be fulfilled to consider the maximal effort: [1] 30-s plateau in VO_2, [2] respiratory exchange ratio $\geq$ 1.10, [3] rating of perceived exertion $\geq$ 18, and [4] $\geq$ 80% of age-predicted maximal heart rate according to Fox equation (220-age [*in years*])[27]. Figure 1 presents the process of selecting participants who underwent maximal effort during CPET.

Measured cardiorespiratory indices

We considered VO_{2max} as the highest 30-s stable oxygen uptake directly before the end of CPET. We measured all the gas exchange variables in the breath-by-breath method with the usage of Hans Rudolph V2 Mask (Hans Rudolph, Inc., Shawnee, KS, United States) and the Cortex MetaLyzer B3 (CORTEX Biophysik GmbH, Leipzig, Germany). We calibrated all the equipment for gasometry according to the manufacturer's instructions. The

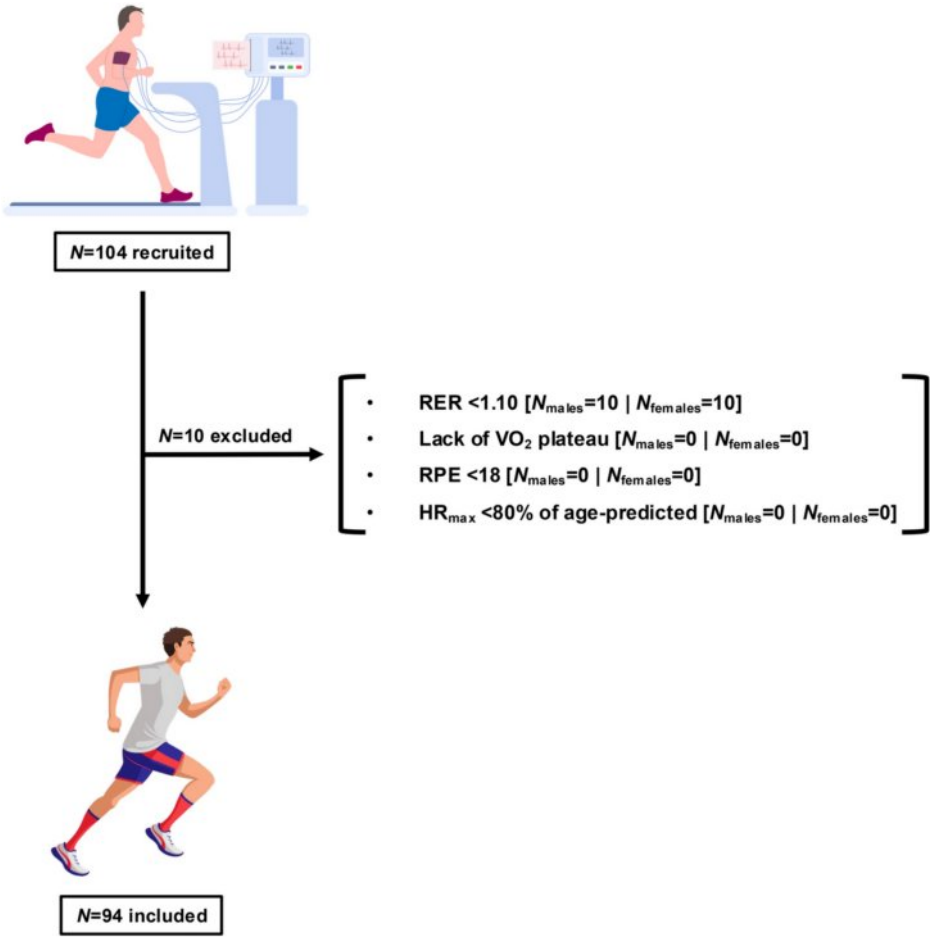

Fig. 1. Flowchart for selection of participants. *Abbreviations*: RER, respiratory exchange ratio; VO_2, oxygen uptake; RPE, rating of perceived exertion; HR_{max}, maximal heart rate.

participants wear Polar H10 (Polar Electro Oy, Kempele, Finland) chest straps to measure their heart rate (signal quality of 99.4%)[28]. We considered the HR_{max} as the highest value averaged in the 30-s intervals. Finally, we estimated the O_2P_{peak} by dividing the VO_{2max} by HR_{max} and presented it as a mL beat^{-1}[4].

Statistical analysis

We began the analysis by testing the data assumptions. For this purpose, we implemented the Shapiro–Wilk test and Q–Q plots. As all the data showed the parametric distribution, we presented continuous variables as mean ± standard deviation. We present categorical variables as numbers (percentages). In case of any missing variable, we exclude the participant from the analysis to ensure maximal data precision. The results presentation follows the 11th AMA *Manual of Style* guidelines[29].

O_2P_{peak} was the outcome variable, and age was an independent variable. The outcome and independent variable were the same as in the original FRIEND equation to ensure similarity between our study and the original derivation study. There were no interaction factors in the models, both basic and recalibrated. Further, we externally validated the FRIEND equation for O_2P_{peak}. We compared observed and estimated values using the Student t-test for independent means. Finally, we regressed the observed against the predicted peak O_2P_{peak} and estimated the equivalent of the previous model. Adjusted coefficient of determination (R^2) and root-mean-square error (RMSE) present regression results. On Bland & Altman plots, we visualized the performance of original and adjusted models.

We performed the post-hoc power analysis of the sample size in the G*Power Software (V3.1) for all applied statistical tests[30]. The whole population, subgroups of male endurance athletes or female endurance athletes reached power ≥ 0.8 and large effect size ($d \geq 0.8$) for the Student t-test and linear regression[31].

For calculations, we used SPSS Statistics (V29; IBM, Chicago, IL, USA) and we implemented GraphPad Prism (V10.2.2; GraphPad Software, San Diego, CA, USA) to derive figures. We considered two-tailed $P < 0.05$ as significant.

Results

Characteristics of participants

From 104 endurance athletes recruited for this study, 94 (90.4%) of them fulfilled all inclusion criteria. There were 32 females and 62 males. All the participants had > 4 years of competitive training experience. Briefly, O_2P_{peak} for male endurance athletes equals 23.6 ± 2.8 mL beat^{-1}, and for female endurance athletes, it was 16.4 ± 2.0 mL beat^{-1}. Males achieved VO_{2max} of 4.5 ± 0.5 L min^{-1} and females achieved 3.1 ± 0.4 L min^{-1}. In the majority, participants were in the 90th (N = 14, 14.9%) or 95th (N = 43, 45.7%) percentile for cardiorespiratory fitness. We presented the full characteristics of endurance athletes in Table 1.

Validation of original FRIEND equation

Briefly, the regression both for original and adjusted models explained 62% of the variance in the O_2P_{peak} ($R^2 = 0.62$, $F(1, 92) = 147.1$, $P < 0.001$). The RMSE was low and equals 2.6 mL beat^{-1}. We found that previous and recalibrated models significantly predicted the O_2P_{peak} to the same degree ($\beta = 0.78$). The original FRIEND equation underestimated O_2P_{peak} in male endurance athletes for 2.9 ± 2.9 mL beat^{-1} (11.0%) and in female endurance athletes for 2.2 ± 2.1 mL beat^{-1} (12.3%). In direct comparison among male endurance athletes, predicted O_2P_{peak} differed significantly for the original equation ($t(122) = -8.06$, $P < 0.001$). Moreover, the O_2P_{peak} estimated from the original equation differed significantly from directly measured values also in females ($t(62) = -6.06$, $P < 0.001$).

Performance of the modified model

The difference between directly observed and estimated O_2P_{peak} for the recalibrated model was negligible both in males (0.1 ± 2.9 mL beat^{-1}, 1.1%) and in females (0.2 ± 2.1 mL beat^{-1}, 2.4%). Furthermore, the recalibrated FRIEND equation outperformed the original model. In males, an updated equation did not present a significant difference between observed and estimated values ($t(122) = -0.23$, $P = 0.82$). As expected, a similar relationship occurred among female endurance athletes and the difference for the recalibrated model was insignificant ($t(62) = 0.46$, $P = 0.65$).

We present the original and recalibrated FRIEND equations for O_2P_{peak} in endurance athletes in Table 2. Finally, we compared observed and predicted values for both equations on the Bland & Altman plots in Fig. 2.

Discussion

This study provides several important findings. Firstly, the general reference equation provides limited accuracy and consistently underpredicts O_2P_{peak} in endurance athletes. Secondly, the recalibration with the adjustment of covariates significantly enhances the accuracy of predictions. Thirdly, we suggest a framework for adjusting the general reference equations for a population of endurance athletes. We highlight that there is not always a need to derive a completely novel equation for endurance athletes. The comparison of observed and predicted values

Variable	Total [N = 94]	Males [N = 62, 66.0%]	Females [N = 32, 34.0%]
Age [years]	27.5 ± 5.3	28.1 ± 5.5	26.4 ± 5.0
Weight [kg]	70.8 ± 12.1	76.1 ± 10.2	60.6 ± 8.3
Height [cm]	177.2 ± 9.3	181.2 ± 7.3	169.5 ± 7.9
BMI [kg m^{-2}]	22.4 ± 2.5	23.2 ± 2.5	21.0 ± 1.8
HR_{max} [beats min^{-1}]	189.6 ± 9.4	189.3 ± 9.7	190.1 ± 8.9
VO_{2max} [L min^{-1}]	4.0 ± 0.8	4.5 ± 0.5	3.1 ± 0.4
VO_{2max} [mL kg min^{-1}]	56.7 ± 8.6	59.2 ± 0.6	51.9 ± 6.3
VO_{2max} [percentile]			
95th	43 [45.7%]	25 [40.3%]	18 [56.3%]
90th	14 [14.9%]	10 [16.1%]	4 [12,5%]
75th	37 [39.4%]	27 [43.6%]	10 [31.2%]
RER	1.20 ± 0.06	1.20 ± 0.06	1.20 ± 0.06
f_R [breaths min^{-1}]	62.0 ± 10.0	63.1 ± 9.8	59.8 ± 10.3
O_2P_{peak} [mL beat^{-1}]	21.1 ± 4.2	23.6 ± 2.8	16.4 ± 2.0
Predicted O_2P_{peak} [mL beat^{-1}]	18.5 ± 3.1	20.7 ± 0.5	14.2 ± 0.4
Recalibrated predicted O_2P_{peak} [mL beat^{-1}]	21.1 ± 3.3	23.5 ± 0.5	16.6 ± 0.5
Maximal speed [km h^{-1}]	16.7 ± 2.1	17.3 ± 1.9	15.5 ± 1.9
Duration of test [minutes]	26.3 ± 3.8	26.9 ± 3.8	25.1 ± 3.7

Table 1. Description of the study population. We calculated O_2P_{peak} by dividing the VO_{2max} by HR_{max}. We estimated the predicted O_2P_{peak} from the FRIEND equation and further recalibrated the original models to be adjusted for endurance athletes. VO_{2max} percentiles were calculated based on *Reference Standards for Cardiorespiratory Fitness* by Kaminsky et al.[6]. *Abbreviations*: BMI, body mass index; HR_{max}, maximal heart rate; VO_{2max}, maximal oxygen uptake; RER, respiratory exchange ratio; f_R, breathing frequency; O_2P_{peak}, peak oxygen pulse.

Variable		Estimate	Standard error	β	95% CI		*P*-value
					UL	LL	
Intercept		1.36	1.65	–	−1.92	4.64	.41
Original FRIEND equation	23.2–0.09 age [*in years*]–6.6 [*if female*]	1.07	0.09	0.78	0.90	1.25	< .001

Table 2. Recalibrated FRIEND equation for O_2P_{peak} in endurance athletes. *Abbreviations*: CI, confidence interval; UL, upper limit; LL, lower limit. The updated model should be inputted as follows: $O_2P_{peak} = 1.36 + 1.07$ (23.2–0.09 age [in years]–6.6 [if female]). The model explained 62% of the variance in O_2P_{peak} in endurance athletes ($R^2 = 0.62$, $F(1, 92) = 147.1$, $P < .001$).

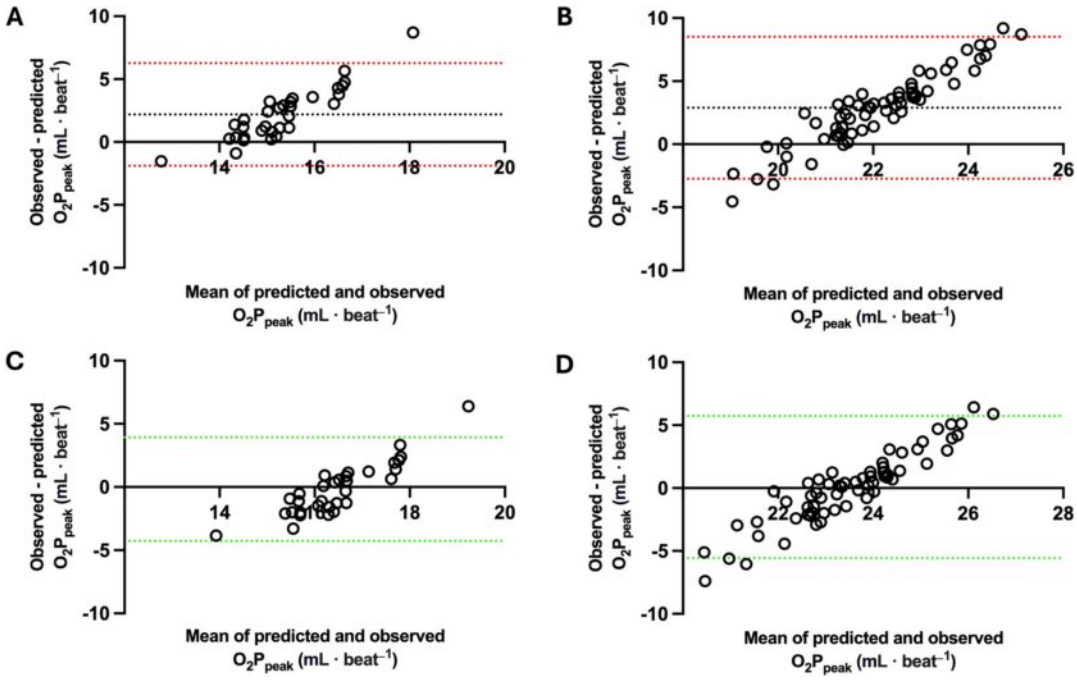

Fig. 2. Comparison of observed and predicted O_2P_{peak} for original and recalibrated FRIEND equations. *Abbreviations*: O_2P_{peak}, peak oxygen pulse. *Note*: In the Bland & Altman plots we compared observed and predicted O_2P_{peak} for both equations. Panel A presents the accuracy of the original model for females and panel B presents the original model for males. Panel C presents the accuracy of the recalibrated model for females and panel D presents the accuracy of recalibrated model for males. Green and red dotted lines present upper and lower limits of agreement. The black dotted line on panels A and B presents the bias of the original equation. The bias line covers the X axis on panels C and D for the recalibrated equation because the error was minimal.

with the usage of equivalents of the existing prediction models could be a valuable alternative to direct CPET for endurance athletes.

The FRIEND database includes several thousand individuals (the exact sample size depends on the study)[32,33]. Reference values from the FRIEND database constitute a universal reference point transferable across the laboratories and through the lifespan[34]. However, the FRIEND database in the majority included people with a moderate fitness level[35]. Thus, it may not be ideally suited for endurance athletes. Therefore, the FRIEND database is a valuable basis and starting point for predicting the cardiorespiratory fitness indices in endurance athletes. However, it requires some adjustments to the physiology of individuals with above-average fitness levels.

Previous studies indicate that the most appropriate way to estimate cardiorespiratory fitness in specific populations is to derive novel equations for them[17]. In the present study, we present a simpler approach. We do not derive a completely new model but only adjust the coefficient of the existing one. Bland & Altman plots (see Fig. 2) support the idea of such a recalibration. As expected, the original FRIEND equation significantly underestimated the O_2P_{peak} in the cohort of well-trained endurance athletes (see panels A and B of Fig. 2). It was developed based on the untrained subjects and endurance athletes exhibited higher O_2P_{peak}[4]. However, panels C and D with adjusted models show minimal bias. The statistical analysis results confirmed the relationship visible in Fig. 2.

The observed and predicted values were significantly different for the original FRIEND equation but not for the adjusted one. It should be emphasized, that the only change was adding a multiplier, without modifying the existing FRIEND equation. This innovative way of recalibration is the new method to indirectly predict cardiorespiratory fitness in endurance athletes, as it enables the correct interpretation of cardiorespiratory fitness in this population. The constant growth of the amateur endurance athletes population and training loads among elite endurance athletes underline the significance of our findings and the applicability of the presented approach[20].

Clinical implications

Oxygen pulse is a valuable component of CPET. Its role is invaluable in diseased populations as well as in physically fit individuals[36]. Cardiovascular diseases do not omit athletes who are exposed to significant training and competition overloads[21]. The results of the present study facilitate confirmation of whether an endurance athlete should not be suspected of any pathology. Comparison of the achieved CPET results with the predictions from the adjusted FRIEND model verifies athletic cardiorespiratory fitness[17]. Moreover, retrospective evaluation of past CPET results considering the estimated values adds significant value to the clinician's toolbox when assessing the heart of endurance athletes. We assume that significantly lower actual O_2P_{peak} may suggest pathology whereas similar O_2P_{peak} suggests normal cardiac function in endurance athletes, but these relationships should be investigated by future studies.

Limitations

We must highlight some caveats of the present study to ensure its proper understanding. Even though the analyzed group fulfilled the required sample size criteria, it was strongly homogeneous. Our subjects were highly trained endurance athletes, therefore populations of different training statuses, i.e. novice amateur endurance athletes, may require further adjustment of the O_2P_{peak} model. Moreover, our participants were White Europeans and ethnicity could contribute to cardiorespiratory fitness[37]. As this is the first study to present such an approach to recalibrating a well-established prediction equation, we recommend further confirmatory studies on more demographically diverse (especially regarding race and age) populations or groups of lower fitness status.

Conclusions

To conclude, a recalibrated model for O_2P_{peak} was highly accurate in well-trained endurance athletes. There was no need to change the original FRIEND equation. It was enough to calculate the equivalent of the FRIEND equation to enhance its precision among endurance athletes significantly. We recommend using the model to compare direct and estimated O_2P_{peak} and to establish new reference values for O_2P_{peak} in well-trained endurance athletes.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request (Przemysław Kasiak; przemyslaw.kasiak@wum.edu.pl).

Received: 19 July 2024; Accepted: 20 September 2024
Published online: 04 October 2024

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Acknowledgements

This research is a part of the NOODLE Study – "predictioN mOdels fOr enDurance athLetEs". Previous research about the ventilatory efficiency, oxygen uptake efficiency slope, and oxygen uptake efficiency plateau in well-trained endurance athletes (cyclists).

Author contributions

Przemysław Kasiak: Conceptualization, Methodology, Validation, Formal Analysis, Investigation, Resources, Data Curation, Writing—Original Draft, Writing—Review & Editing, Visualization, Project administration, Funding acquisition. Tomasz Kowalski: Conceptualization, Methodology, Investigation, Resources, Writing—Original Draft, Writing—Review & Editing. Andrzej Klusiewicz: Investigation, Resources, Writing—Review & Editing, Supervision. Ryszard Zdanowicz: Resources, Writing—Review & Editing. Maria Ładyga: Resources, Writing—Review & Editing. Szczepan Wiecha: Writing—Review & Editing. Daniel Śliż: Conceptualization, Writing—Review & Editing, Supervision, Project administration. Artur Mamcarz: Conceptualization, Supervision, Project administration. All authors read and approved the final manuscript.

Funding

No funding was received for conducting this study.

Competing interests

The authors declare no competing interests.

Additional information

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Kopie opublikowanych prac

Publikacja nr 5

Tytuł:

Optimizing the Interpretation of Cardiopulmonary Exercise Testing in Endurance Athletes: Precision Approach for Health and Performance

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Typ publikacji:

Przegląd narratywny

DOI:

10.1155/tsm2/5904935

Czasopismo:

Translational Sports Medicine

IF=1,9 | kwartyl JCR Q2 | centyl JCR 55,6

Wiley
Translational Sports Medicine
Volume 2025, Article ID 5904935, 10 pages
https://doi.org/10.1155/tsm2/5904935

WILEY

Review Article

Optimizing the Interpretation of Cardiopulmonary Exercise Testing in Endurance Athletes: Precision Approach for Health and Performance

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Received 19 May 2025; Revised 25 July 2025; Accepted 4 August 2025

Academic Editor: Ylva Hellsten

The present review summarizes findings from the NOODLE ("predictioN mOdels fOr enDurance athLetEs") study. The research aimed to refine variables obtained during cardiopulmonary exercise testing (CPET) in a large cohort of highly trained endurance athletes by adjusting general reference values and predictive equations to better reflect the unique physiological profiles of this population. Ventilatory efficiency, oxygen uptake efficiency slope, oxygen uptake efficiency plateau, and peak oxygen pulse were analyzed, as they were recently applied in various models concerning risk stratification and treatment optimization. As more people engage in endurance sports, tailored CPET assessments are crucial for accurate performance evaluation and health monitoring. By characterizing differences between general formulas and those suited for endurance athletes, we offered improved tools for optimizing training and ensuring athlete safety. The findings are in line with the existing trend of precision medicine that tailors diagnostics, treatments, and interventions to individual patients' characteristics. Moreover, we review the recent advances from widely applied CPET-obtained indices, such as maximum oxygen uptake, maximum heart rate, and breathing reserve. We also gave the recommendation for a comprehensive CPET assessment based on the relationships between all of the variables.

Keywords: cardiopulmonary exercise testing; cardiorespiratory fitness; endurance athletes; exercise physiology; sports cardiology

1. Introduction

Cardiopulmonary exercise testing (CPET) plays a crucial role in assessing the health and performance of endurance athletes, offering insights into both cardiovascular and pulmonary function [1]. By measuring key parameters, CPET provides a detailed profile of an athlete's aerobic capacity, respiratory efficiency, and metabolic responses to exercise and may contribute to medical diagnosis and risk stratification, among many [2]. In athletic settings, the effort is typically continued until exhaustion to identify maximum variables such as oxygen uptake, heart rate, ventilation, and carbon dioxide production. Moreover, submaximal indices like ventilatory or lactate thresholds, as well as movement economy, are often defined as common performance determinants in endurance sports [3]. CPET results are usually interpreted in the context of reference values and predictive equations. They play a vital role in medicine and diagnostics, serving as benchmarks to interpret clinical data and assess individual health status. By comparing the obtained results to the established norms, deviations that may indicate underlying conditions or risks should be detected. Such an approach allows for precise evaluation of physiological function and helps to guide diagnosis, treatment, and

monitoring of various populations [1, 4]. For endurance athletes, reference values and predictive equations specifically tailored to their cardiorespiratory profile seem essential. Traditional CPET reference values may not apply because endurance athletes exhibit different characteristics compared to the general population [2]. The values are typically higher, especially for gold-standard measurement, i.e., peak oxygen uptake (VO_2peak), as presented in Table 1. When comparing reference values for CPET for general and athletic populations, the VO_2peak is higher among athletes in each case [5, 6]. Possible reasons may include exercise-induced electrical and structural cardiac remodeling, as well as specific functional adaptations [7–9]. Therefore, differentiation between normal physiological adaptations and potential pathology requires careful consideration [10]. Equations specifically developed for endurance athletes allow for a more accurate interpretation of their CPET results, ensuring that performance and health risks are appropriately assessed. Moreover, CPET application varies between particular sports disciplines. CPET could be used both for training and diagnostic purposes [11]. Most often, CPET is conducted up to the maximal exertion [12]. However, in several parts of the sports season for some disciplines (e.g., triathlon), intensity of the CPET could be downgraded to the submaximal to not overtrain the athlete [13]. It is especially useful in the final parts of the sport's season when exertion reaches its peak. CPET is usually performed on the treadmill or cycle ergometry [4]. For some disciplines like watersports, the most mirroring modality will be rowing ergometry [14]. To sum up, it is well recommended that the modality and intensity of CPET should be considered when interpreting the results.

Noteworthily, in recent decades, the number of endurance athletes has significantly increased [15–17]. Many individuals participate in endurance sports, both professionally and as amateurs, while undertaking significant training loads [18]. Although physical activity is associated with multiple health benefits and is an undisputed positive lifestyle factor, it may also bring noteworthy risks [19, 20]. Especially many amateurs perform strenuous training with limited medical screening and supervision, which may result in severe health issues, possibly leading to sudden cardiac fatalities [21]. Interestingly, only one year of endurance training may result in morphological adaptations like those in elite athletes [22]. As a result, there is a growing need for tailored CPET evaluations to support clinicians and coaches in monitoring an athlete's health, detecting early signs of overtraining, and optimizing training regimens to improve performance safely. Moreover, novel CPET-obtained variables have recently been suggested for inclusion in risk stratification and treatment optimization processes [23–26]. However, they were typically assessed in patients or the general population, and tools allowing for application in endurance athletes are lacking. Consequently, we developed the NOODLE ("predictioN mOdels fOr enDurance athLetEs") study, which resulted in a series of articles addressing the possible differences in reference values and predictive equations between the general population and endurance athletes [27–30].

In our research, we investigated whether there are significant differences between the well-established CPET-obtained variables used for the general population and those that apply specifically to endurance athletes. As the type of CPET impacts the analysis of results, we additionally stratified the interpretation by modality [11]. We hypothesized that general predictions and equations might not accurately reflect their unique physiological profiles. Through a detailed comparison, we assessed key parameters such as ventilatory efficiency (VE/VCO_2), oxygen uptake efficiency slope (OUES), oxygen uptake efficiency plateau (OUEP), and peak oxygen pulse (O_2P_{peak}) in highly trained endurance athletes. Where discrepancies were identified, we characterized these differences and created or adjusted the predictive equations to better suit the demands and capacities of endurance athletes. This tailored approach allows for more precise health assessments, performance evaluations, and the development of personalized training strategies, ensuring that endurance athletes are monitored with a higher degree of specificity and accuracy. The presented article reviews the already published outcomes of the investigation. Moreover, state-of-the-art findings regarding other CPET-obtained variables are summarized. The aim of this brief review is to (1) provide physiologists and physicians with fundamental knowledge about CPET interpretation in endurance athletes and (2) identify existing research gaps to guide further investigations regarding active and trained populations.

2. Methods

2.1. Study Design. The presented review summarizes the NOODLE study and is based on data collected during CPET carried out in the years 2022-2023 at the Institute of Sport—National Research Institute in Warsaw, Poland [27–30]. The approval from the Institutional Review Board of the Medical University of Warsaw (Pawińskiego 3C Street, 02-106 Warsaw, approval no. AKBE/277) was obtained for all the studies. Informed consent has been obtained from all the participants in this study. In total, 234 healthy members of National Teams in endurance sports (biathletes, cyclists, cross-country skiers, long-track speed skaters, middle- and long-distance runners, ski-mountaineers, and triathletes) were included in further analyses. All the participants were healthy and highly trained endurance athletes. Brief characteristics of the included participants are presented in Table 2. Well-established maximum effort criteria were fulfilled in all the included tests [30]. Depending on the study, CPET was performed on a cycloergometer as a continuous ramp test ($n = 140$) or on a treadmill as an intermittent step test ($n = 94$). All the athletes underwent CPET, and several demographic and exercise variables were analyzed to build the prediction equations. We considered the basic parameters: age, weight, height, body surface area, and body mass index, and paired them with exercise indices, e.g., VO_2. Our approach aimed to build robust and easily available models to facilitate their usage in practical settings. All the physiological variables analyzed in the NOODLE study were VE/VCO_2, OUES, OUEP, and O_2P_{peak}. The CPET was conducted to the maximal exertion according to the following criteria: participant declined to continue exercises with Borg scale ≥ 18, VO_2 plateau (< 100 mL increase lasting ≥ 30 s), respiratory exchange ratio ≥ 1.05, and HRmax ≥ 80% of age-predicted.

Table 1: Comparison of reference values for peak oxygen uptake.

Variable	Age group (years)	Males				Females			
		Cycling CPET		Running CPET		Cycling CPET		Running CPET	
		FRIEND [6]	CHEER [5]	FRIEND [6]	CHEER [5]	FRIEND [6]	CHEER [5]	FRIEND [6]	CHEER [5]
VO_2peak (mL/kg/min)	Younger EA	44.2 ± 12.4	56.7 ± 9.6	44.7 ± 11.5	62.0 ± 11.1	32.0 ± 10.1	44.7 ± 7.2	35.3 ± 9.7	52.0 ± 8.6
	Older EA	31.6 ± 11.1	52.1 ± 8.1	39.0 ± 11.4	52.8 ± 7.6	22.8 ± 7.7	37.8 ± 4.4	29.3 ± 8.6	46.9 ± 6.7

Note: Table summarizes data for individuals aged 18–45 to most exactly match the age of participants from the NOODLE study. FRIEND registry is the most recognized and widely used data source of reference values for CPET among general population. CHEER registry is the most recognized and widely used data source of reference values for CPET among endurance athletes. Data from FRIEND registry used the RER of 1.1 and data from CHEER registry used RER of 1.05. Younger EA were 18–30 years old in CHEER database and 20–29 years old in FRIEND database. Older EA were 30–45 years old in CHEER database and 30–39 in FRIEND database.

Abbreviations: CHEER, Cardiopulmonary Health and Endurance Exercise Registry; CPET, cardiopulmonary exercise testing; EA, endurance athletes; FRIEND, Fitness Registry and the Importance of Exercise: A National Data Base; VO_2peak, peak oxygen uptake.

Table 2: Participants' characteristics.

Variable	Type of CPET			
	Running ($N = 94$)		Cycling ($N = 140$)	
	Males ($N = 62$, 66.0%)	Females ($N = 32$, 34.0%)	Males ($N = 77$, 55.0%)	Females ($N = 63$, 45.0%)
Age (years)	28.1 ± 5.5	26.4 ± 5.0	21.8 ± 4.8	23.8 ± 4.2
Weight (kg)	76.1 ± 10.2	60.6 ± 8.3	76.1 ± 7.6	61.0 ± 5.5
Height (cm)	181.2 ± 7.3	169.5 ± 7.9	181.6 ± 6.3	166.3 ± 6.2
BMI (kg/m^2)	23.2 ± 2.5	21.0 ± 1.8	23.1 ± 1.7	22.1 ± 1.6
BSA (m^2)	2.0 ± 0.2	1.7 ± 0.2	2.0 ± 0.2	1.7 ± 0.1
VO_2max (mL/kg/min)	59.2 ± 0.6	51.9 ± 6.3	57.8 ± 9.0	52.1 ± 7.0

Note: Data are presented as mean (standard deviation).
Abbreviations: BMI, body mass index; BSA, body surface area; CPET, cardiopulmonary exercise testing; VO_2max, maximal oxygen uptake.

All the participants were familiar with the testing procedures and environment. CPET was performed by qualified and experienced staff, using well-established protocols, validated equipment, and manufacturers' guidelines. The detailed description of applied testing protocols may be found in the above-referenced NOODLE studies.

2.2. Statistical Analysis. In the first step of statistical analysis, we assessed the relationships between individual variables. We used Student's *t*-test to determine differences between different types of VE/VCO_2: slope (interval from start to first ventilatory threshold), total (interval from start to termination), and nadir (the lowest 30 s value). We also used Student's *t*-test to compare OUES calculated from different exercise intervals: from 75%, 90%, and 100% of the duration of the exercise test. Finally, with Student's *t*-test, we compared predicted and observed values for each model.

We implemented two-way mixed effects intraclass correlation coefficient ($ICC_{3,1}$) to confirm the agreement between predictions and direct measurements from CPET. Using $ICC_{3,1}$, we showed whether models reflect trends and relationships among endurance athletes that occur among the general population. We also used linear regression to compare observed and predicted values, and we calculated the coefficient of determination (R^2) and root mean square error (RMSE).

Then, we confirmed the choice of derivation method by analyzing data assumptions (collinearity, independence of observations, leverage plots, and autocorrelation) and aimed to generate specific models using multivariate linear regression. All the derived models and equations were subsequently validated with cross-validation.

3. Insights From the NOODLE Study

A summary of the NOODLE study outcomes is presented in Table 3 and visualized in Figure 1. More detailed explanations regarding each investigated variable will follow.

3.1. VE/VCO_2. VE/VCO_2, the ratio of pulmonary ventilation to carbon dioxide production, reflects right ventricular-pulmonary vascular function during exercise [32]. VE/VCO_2 is most often plotted to the first ventilatory threshold (i.e., VE/VCO_2-slope). Achieving the VE/VCO_2-slope does not require maximum effort. The VE/VCO_2-slope is widely used in heart failure patients, particularly those with reduced ejection fraction, predicting poor outcomes and identifying high-risk individuals during CPET [23]. In the NOODLE study, we found that the VE/VCO_2-slope is not significantly higher in endurance athletes during physical effort compared to the untrained individuals. However, the current prediction equations do not properly reflect the relationship between demographic variables and VE/VCO_2-slope in endurance athletes because none of the equations are exact. Additionally, we investigated the sex differences in VE/VCO_2 measured from several intervals of physical effort. The lowest 30 s VE/VCO_2, VE/VCO_2-slope, and total VE/VCO_2 were higher in female than male endurance athletes. Our findings shed new light on between-sex differences with the potential to influence training prescription regarding cardiovascular, muscular, hematologic, and pulmonary systems' interplay. As we underlined in Table 3, the new model is necessary for endurance athletes. The existing models were mostly univariable, with the inclusion of the age covariate. We observed that the impact of age on VE/VCO_2 is negligible in the endurance athletes [29]. However, body measurements, such as height and weight, have higher prediction value in endurance athletes. Therefore, the new models for endurance athletes should revise the set of covariates and minimize the impact of age in exchange for weight and height [29].

3.2. OUES. OUES reflects how efficiently the body uses oxygen during exercise. Unlike other exercise test variables, OUES can be measured even during submaximal exercise, making it particularly valuable in populations who cannot push themselves to peak effort, such as elderly or frail patients [33]. This makes it a versatile tool in both athletic performance assessment and clinical care. OUES may be used for evaluating patients with cardiovascular or pulmonary conditions regarding disease prognosis and risk stratification, especially when they cannot perform maximal exercise [24, 34, 35]. In the NOODLE study, we noted that OUES is significantly higher in endurance athletes. However, despite OUES being significantly higher in well-trained individuals, it still did not differ between time intervals taken from the CPET [28]. When considering 75%, 90%, and 100% of the CPET duration, there were no significant differences. Therefore, the OUES is a more universal measurement not

Table 3: A brief summary of the NOODLE study outcomes.

Variable	Athlete-specific data		Was it different between the general population and endurance athletes?	Statistical comparison between general population and endurance athletes	R^2 for general models applied to endurance athletes	Direction of differences in endurance athletes	Degree of change between the general population and endurance athletes	Solution proposed in NOODLE study
	Males	Females						
VE/VCO_2-slope [29]	26.1 ± 2.0	27.7 ± 2.6	Yes	ICC =< 0.001–0.44 $R^2 = 0.003–0.031$	0.003–0.031	Higher	↑	New model
OUES (mL/min/L/min) [28]	$OUES_{75} = 4.53 \pm 0.90$ $OUES_{90} = 4.52 \pm 0.91$ $OUES_{100} = 4.41 \pm 0.87$	$OUES_{75} = 3.50 \pm 0.65$ $OUES_{90} = 3.49 \pm 0.62$ $OUES_{100} = 3.41 \pm 0.58$	Yes	ICC = 0.062–0.529 $R^2 = 0.004–0.388$	0.004–0.324	Higher	↑↑	New model
OUEP (mL/L) [27]	44.2 ± 4.2	41.0 ± 4.8	No	Males: $t = -0.86$, $p = 0.39$ Females: $t = 0.54$, $p = 0.59$	0.099	Comparable	⟶	—
O_2P_{peak} (mL/beat) [30]	23.6 ± 2.8	16.4 ± 2.0	Yes	Males: $t = -8.06$, $p < 0.001$ Females: $t = -6.06$, $p < 0.001$	0.62	Higher	↑↑	Recalibrated equation

Note: The definitions of "moderately" and "significantly" higher were adapted based on Petek et al. [31]. R^2, adjusted coefficient of determination. Differences for OUES and VE/VCO_2-slope were conducted with the usage of ICC (intraclass correlation coefficient) and R^2. Differences between general population and untrained individuals for OUEP and O_2P_{peak} were analyzed with the usage of Student's t-test.
Abbreviations: O_2P_{peak}, peak oxygen pulse; OUES, oxygen uptake efficiency slope; $OUES_{75}$, oxygen uptake efficiency slope calculated from 75% of the duration of exercise test; $OUES_{90}$, oxygen uptake efficiency slope calculated from 90% of the duration of exercise test; $OUES_{100}$, oxygen uptake efficiency slope calculated from 100% of the duration of exercise test; OUEP, oxygen uptake efficiency plateau; VE/VCO_2, ventilatory efficiency.
↑, variable moderately higher in endurance athletes than in untrained population.
↑↑, variable significantly higher in endurance athletes than in untrained population.
⟶, variable comparable between endurance athletes and general population.

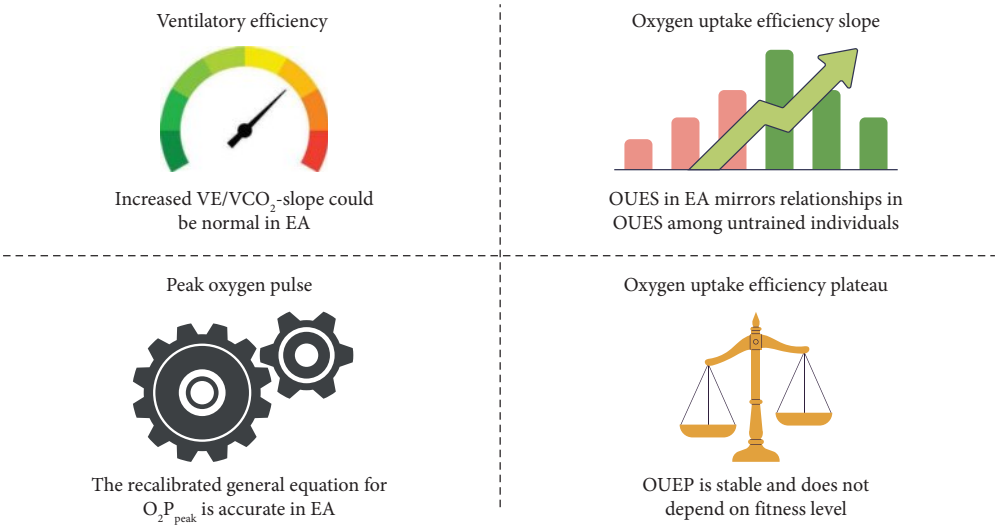

FIGURE 1: Visual summary of key findings for discussed cardiorespiratory variables among endurance athletes. Abbreviations: VE/VCO_2-slope, ventilatory efficiency slope; EA, endurance athletes; OUES, oxygen uptake efficiency slope; OUEP, oxygen uptake efficiency plateau; O_2P_{peak}, peak oxygen pulse.

only in clinical populations but also in endurance athletes because it does not require performing maximal-effort CPET to objectively assess the endurance capacity [28]. The existing prediction equations in the majority correctly reflected the trends, with significant underestimation of the predictions for well-trained individuals. However, we also observed a more complex relationship between previously used covariates (age and sex) in endurance athletes than in the general population. Therefore, we derived the novel equations tailored to the needs of endurance athletes. In new models for endurance athletes, we used the interaction factor (e.g., age × sex). Finally, we recommend the consideration of interaction factors for further studies.

The updated equations for OUES from the NOODLE study were as follows [28]:

a. OUES calculated from 75% of the CPET = 1.09 + 2.87 × BSA − 0.0030 × (age × sex).
b. OUES calculated from 90% of the CPET = 1.46 − 3.02 × BSA − 0.0010 × (age × sex).
c. OUES calculated from 100% of the CPET = 1.54 − 2.99 × BSA − 0.0014 × (age × sex).

Sex = 2 for males and = 1 for females. BSA is in m^2. Age is in years.

3.3. OUEP. OUEP represents a stable point where oxygen consumption becomes less responsive to increases in ventilation during exercise [36]. Clinically, it can provide valuable insights into a patient's cardiovascular and pulmonary health, offering a marker for early diagnosis of heart or lung diseases without requiring maximal exercise exertion [26, 37]. In the NOODLE study, we found that OUEP is not higher or even different in endurance athletes compared to the general population [27]. However, the prediction equations did not show satisfactory accuracy in athletes. In the NOODLE study, we did an external validation and created a new equation for OUEP. We emphasize that OUEP is a promising new understudied variable that is highly stable and does not depend on endurance capacity. We recommend OUEP to be routinely assessed during CPET in athletes, untrained individuals, and patients due to its feasibility and universal significance [27].

The updated equation for OUEP from the NOODLE study was as follows [27]:

61.369 + 5.078 × sex − 0.123 × height.

Sex = 1 for males and = 0 for females. Height is in cm.

3.4. O_2P_{peak}. O_2P_{peak} represents the oxygen uptake per heartbeat during peak exercise, serving as a proxy for stroke volume and overall cardiopulmonary performance [38]. Clinically, it can reveal abnormalities in cardiovascular function, particularly in patients with heart and pulmonary conditions or reduced exercise tolerance [25]. In the NOODLE study, firstly, we externally validated the common prediction equation for O_2P_{peak} derived from the "Fitness Registry and the Importance of Exercise: A National Data Base" (FRIEND database) on the cohort of endurance athletes. We observed a similar relationship as in OUES, i.e., the model significantly underestimated the O_2P_{peak} but generally reflected the relationships between exercise variables and body measurements [30]. Hence, we proposed a new method of calibration for prediction equations. We recalibrated the most recognized equation for O_2P_{peak} from the FRIEND database with the usage of multivariable linear regression [39]. This procedure allows us to adjust the prediction equation to any population by modifying the basic coefficients without changing the core of the model. The adjusting method that we proposed in the NOODLE

study allows for the transfer of equations between populations with different characteristics [30]. Hence, it is a simpler solution than creating a completely new equation, as was recommended in previous studies.

The updated equation for O_2P_{peak} from the NOODLE study was as follows [30]:

$$24.824 - 0.0963 \text{ age} - 7.062 \times \text{sex}.$$

Sex = 0 for males and = 1 for females. Age is in years.

4. Recommendations for Practitioners and Directions for Further Research

The NOODLE study exhibits limitations that should be acknowledged and addressed in further research regarding CPET. The presented study is a cross-sectional one. The longitudinal setting would be a valuable study design, allowing for exploration not only of associations, but also the influence of endurance training on the described variables. Only highly trained subjects took part in the study. Other trained populations, especially amateur endurance athletes who started training in middle or late life, and lifelong athletes, should be investigated. To date, studies on such groups remain scarce. Moreover, patients undertaking physical training simultaneously with existing conditions, especially lifestyle diseases, are understudied in the abovementioned context. Finally, near-infrared spectroscopy might be combined with CPET to identify central and peripheral exercise limitations and possibly improve diagnostic accuracy and risk stratification. This novel approach is becoming more popular in high-performance athletic settings in the context of training optimization. However, research regarding its application in clinical cardiopulmonary diagnostics remains lacking.

5. Other Variables

The rationale behind the NOODLE study was based on the hypothesis that general predictions and equations might not accurately reflect the unique physiological profiles of well-trained endurance athletes. As presented above, some of the CPET-obtained variables are significantly different in the general population and endurance athletes and others may be approached in a similar way in both groups. The presented research addressed the existing research gap and reported novel findings. Our work fits into the existing trend of precision medicine that tailors diagnostics, treatments, and interventions to individual patients' characteristics.

In recent years, such an approach gained noteworthy interest, and our findings should be reported in a wider context. Most importantly, the available literature suggests that other CPET-obtained indices differ between endurance athletes and the general population. Especially, predicted maximum oxygen uptake (VO_2max) and HRmax should reach only up to 84% and > 90%, respectively, in untrained individuals according to ATS/ACCP guidelines [12]. However, simultaneously, EACPR/AHA guidelines for well-trained individuals recommend more than 100% for VO_2max and ≥ 85% for HRmax [40]. Moreover, the breathing reserve is also different between aforementioned guidelines and should be > 15% in the general population compared to > 20% in athletes.

VO_2max is a key indicator of aerobic fitness, cardiovascular health, and a strong mortality and longevity predictor [41]. Typically, VO_2max is significantly higher in endurance athletes compared to other populations, although the exact difference may depend on trained sport, ethnicity, or exercise modality [42]. In healthy population, VO_2max typically decreases with age, is higher in males compared to females, and is higher on running treadmill compared to cycloergometry [6, 43, 44]. However, the extent of these differences is not thoroughly investigated in the trained athletic population. Multiple VO_2max prediction equations were already analyzed in recreational and elite athletes [45, 46]. The available models were characterized with moderate accuracy; therefore, predictive equations should not replace direct VO_2max determination during CPET in endurance athletes [46, 47]. Consequently, deriving improved specific models and equations addressing both recreational and elite endurance athletes is recommended.

Monitoring HRmax provides insights into a person's exercise capacity, heart function, and overall fitness [48]. Achieving or failing to achieve the predicted HRmax can indicate the presence of cardiovascular limitations, autonomic dysfunction, or potential exercise intolerance, all of which are important in diagnosing heart disease, evaluating treatment effectiveness, or determining exercise prescription [49, 50]. In healthy population, HRmax tends to decrease with age and level of fitness [44]. Since maximal exercise testing is not feasible in many settings, HRmax is often estimated using age-predicted equations with multiple options already presented in the literature [48–51]. Typically, HRmax in trained athletes is lower compared to their sedentary counterparts [52]. Noteworthy differences in HRmax depending on exercise modality were observed in trained athletes: higher values were obtained on rowing ergometer and running treadmill compared to kayak, skiing, and cycling ergometers [53]. Generally, the larger the muscle mass involved, the higher the VO_2max and HRmax. Compared to other parameters, HRmax may be well predicted in active and trained populations. Formulas from Tanaka et al. ($202.5–0.53 \times \text{age}$) and ($208–0.7 \times \text{age}$) yield acceptable accuracy and present relatively low mean errors [48, 51].

Breathing reserve reflects the capacity of the respiratory system to handle increased demand during exercise [54]. Monitoring breathing reserve during CPET is important because it helps determine if a patient's exercise limitation is due to respiratory factors. A low breathing reserve may indicate ventilatory impairment, such as in chronic obstructive pulmonary disease. In contrast, a high breathing reserve suggests that other systems, like the cardiovascular system, may be the limiting factor [54]. The analysis of breathing reserve may support identifying mechanical limits to exercise, associated with obstructive or restrictive lung disease [54]. Breathing reserve is typically lower in endurance athletes compared to the general population. In regular population, the lung capacity is rarely the limiting factor in

exercise [31, 55]. However, in trained subjects, the discrepancy in adaptation between cardiovascular, pulmonary hematologic, and muscular systems exists [56]. Even long-time and demanding endurance training is not sufficient to significantly improve pulmonary mechanical systems without additional respiratory muscle training [57]. Consequently, highly trained athletes may use all available lung mechanical capacity during peak exercise and even exhibit breathing reserve corresponding to 0% [31]. The percentage of breathing reserve may also be sport-dependent, since swimmers and rowers tend to exhibit increased lung volumes and pulmonary diffusion capacity when compared to other sports [14, 58]. Overall, large variability may be observed without clear physiological explanation. Further research might explore where this variability comes from, including differences between sexes and sports disciplines.

6. Conclusions

The presented review summarized state-of-the-art research regarding CPET-obtained variables for endurance athletes. When necessary, adjusted reference values and predictive equations that reflect unique physiological profiles of endurance athletes were presented. As more people engage in endurance sports with limited medical oversight, tailored CPET assessments are crucial for accurate performance evaluation and health monitoring. By characterizing differences between general formulas and those suited for endurance athletes, we offered improved tools for optimizing training and ensuring athlete safety.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Ethics Statement

The authors have nothing to report.

Consent

The authors have nothing to report.

Disclosure

All authors have read and approved the final version.

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Tomasz Kowalski: conceptualization, data curation, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, writing–original draft, and writing–review and editing. Przemysław Kasiak: conceptualization, data curation, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, writing–original draft, and writing–review and editing. Tomasz Chomiuk: writing–review and editing and funding acquisition. Artur Mamcarz: writing–review and editing and funding acquisition. Daniel Śliż: writing–review and editing and funding acquisition. Tomasz Kowalski and Przemysław Kasiak contributed equally to this study.

Funding

No funding was received for this research.

Acknowledgments

Dr Przemysław Kasiak, M.D. has been supported by the START Scholarship from the Foundation for Polish Science for outstanding young researchers under 30 years old. The authors would like to thank the team from the Institute of Sport—National Research Institute in Warsaw, Poland, for conducting the necessary testing and providing the data. Grammarly was used for linguistic correctness and clarity.

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Kopie opublikowanych prac

Publikacja nr 6

Tytuł:

Specificity and Areas of Usage of Cardiovascular Prediction Models Among Athletes—State-of-the-art Review

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Typ publikacji:

Przegląd narratywny (z elementami *State-of-the-art*)

DOI:

10.31083/RCM37493

Czasopismo:

Reviews in Cardiovascular Medicine

IF=1,3 | kwartyl JCR Q3 | centyl JCR 27,9

Reviews in Cardiovascular Medicine

Rev. Cardiovasc. Med. **2025**; 26(5): 37493
https://doi.org/10.31083/RCM37493

Review

Specificity and Areas of Usage of Cardiovascular Prediction Models Among Athletes—State-of-the-art Review

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Academic Editor: Hirofumi Tanaka
Submitted: 5 February 2025 Revised: 25 March 2025 Accepted: 31 March 2025 Published: 16 May 2025

Abstract

Cardiovascular diseases are a leading cause of mortality worldwide. Physical activity is linked with a reduced prevalence of cardiovascular diseases. However, excessive over-volume of training could negatively increase the risk of cardiovascular diseases. Prediction models are usually derived to facilitate decision-making and may be used to precisely adjust the intensity of physical activity and stratify individual exercise capacity. Incorporating prediction models and knowledge of risk factors of cardiovascular diseases allows for the accurate determination of risk groups among athletes. Due to the growing popularity of amateur physical activity, as well as the high demands for professional athletes, taking care of their health and providing precise pre-participation recommendations, return-to-play guidelines or training intensity is a significant challenge for physicians and fitness practitioners. Athletes with confirmed or suspected cardiovascular disease should be guided to perform training in carefully adjusted safe zones. Indirect prediction algorithms are feasible and easy-to-apply methods of individual cardiovascular disease risk estimation. Current knowledge about the usage of clinical forecasting scores among athletic cohorts is limited and numerous controversies emerged. The purpose of this review is to summarize the practical applications of the most common prediction models for maximal oxygen uptake, cardiac arrhythmias, hypertension, atherosclerosis, and cardiomyopathies among athletes. We primarily focused on endurance disciplines with additional insight into strength training. The secondary aim was to discuss their relationships in the context of the clinical management of athletes and highlights key understudied areas for future research.

Keywords: cardiovascular diseases; prediction model; athlete; physical activity; training

1. Introduction

For many years, research has shown that regular physical activity has a positive effect on health. Reports unequivocally indicate a reduced risk of all-cause mortality, including mortality due to cardiovascular diseases (CVDs) [1]. Physical and endurance training improves metabolism, especially in terms of the respiratory, circulatory, and muscular systems [2]. Although, in general, regular training provides health benefits, it can also have some negative consequences if done unadjusted or at too high of an intensity [3,4]. The training should be adjusted to individual needs and recovery potential. Among others, the possible methods include psychological measurements, biochemical measurements, and wearable devices [5]. If an athlete, both recreational and professional, does not use any monitoring method, the training could be named as unadjusted [5]. What's more; some athletes may have previously undiagnosed conditions in the circulatory system or belong to certain risk groups for particular CVDs (primarily amateurs, novices, and elderly athletes).

CVD prevalence and types differ across different age groups [4]. Types and frequencies of CVD that should be considered for advanced young athletes and master athletes are naturally different. Young athletes are usually engaged in more intensive physical training than older senior athletes [6]. Congenital cardiovascular diseases such as hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), and many types of coronary anomalies are a priority to discover [7]. On the other hand, for senior athletes, ischemic heart disease is the most important and frequent condition [8].

Recently, many prediction models have been derived to assess the risk of CVD [8]. The original studies are based on different populations, but so far, only a few of them have reported the use of prediction models among athletes [9]. Previous research is often focused only on the variables primarily used to measure exercise performance during cardiopulmonary exercise testing or competition (i.e., heart rate, oxygen uptake, or pulmonary ventilation) [10]. In turn, the clinical models for the prognosis and diagnosis of CVD remain understudied in athletic cohorts. There is a lack of comprehensive summaries for fitness practitioners, sports diagnostic specialists, or medical doctors.

Clinical prediction models are usually divided into prognostic and diagnostic. The first of them is designed to predict the occurrence of the disease in the future, based on the factors available at the time of the test [11]. The diagnostic model aims to calculate the risk that the disease already exists, considering the presented variables [11]. Both types include a plethora of predictors: demographic (age,

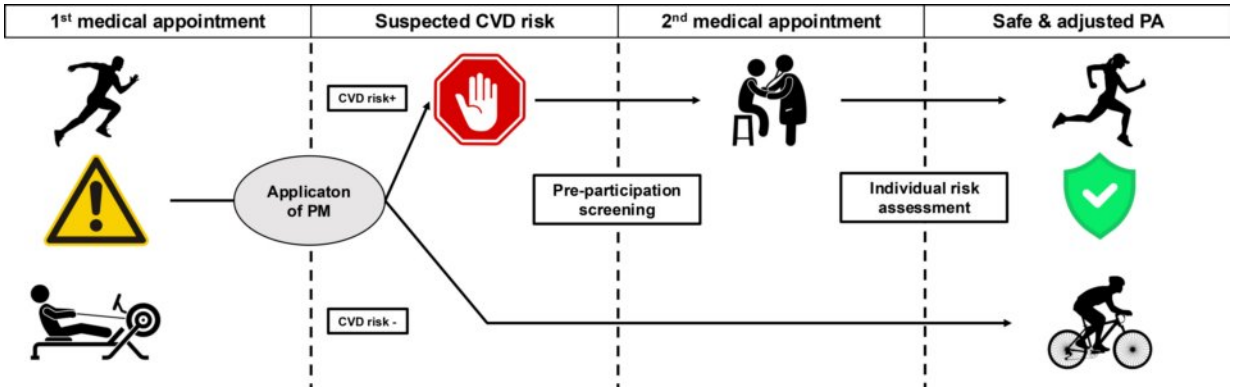

Fig. 1. Central take-home figure. Proposed protocol of application of prediction models for cardiovascular risk assessment among athletes. Abbreviations: CVD, cardiovascular disease; PA, physical activity; PM, cardiovascular risk prediction model.

weight, height), laboratory (serum biomarkers), past medical history, family history, smoking status, dietary habits, and genetics [12]. So far, usually just the existence of risk factors, rather than their crosstalk and relationship, is preferably considered to quantify the risk.

A novel, more individualized approach involves a constant balance between numerous predictors [13]. This flexible procedure enhances the accuracy of forecasted risks and improves the applicability of prediction algorithms for those with multiple diagnosed risk modulators.

A growing number of individuals above 35 years ("master athletes") and those without training experience ("amateur athletes"), engage in strenuous physical training in various sports disciplines [6]. It warrants increased attention to the weighting between the advantages of exercise and the risk of training-induced negative cardiovascular conditions [14,15]. Inactive individuals often start practicing endurance disciplines to improve their health and lose weight. Despite being considered healthy, many of them are at the beginning of their path to the burden of CVD risk factors, such as obesity, lipid disorders, hypertension, and diabetes [16]. The personalized risk stratification should provide valuable information to the medical and health professionals (e.g., general practitioner or personal fitness coach) on whether the individual could safely start regular progressive training [14]. Fig. 1 presents the proposed protocol for the use of clinical prediction models for athletes.

Professional athletes can afford regular comprehensive examinations assessing their health status [17,18]. However, such a complete package of medical testing is usually multistage and expensive. Thus, amateur athletes do not choose it. In consequence, there may be cases of undiagnosed conditions that pose a risk to regular participation in progressive endurance training [17]. The development of a new branch of sports medicine drives the research for alternative solutions. That is the moment when prediction models could be incorporated as a feasible and cost-effective prelude [9]. It is worth underlining that physical activity brings the best health outcomes when it is performed regularly and for a long time. CVD prediction models usually use a forecasting horizon for several years in the future (usually ranging from 2 to 45 years) [8]. They allow preparing guidance in advance for safe and effective long-term physical activity [17]. Both personal coaches and physicians can use such algorithms to properly adjust the intensity and frequency of training sessions.

With the development of numerous prediction models in cardiology, questions arise as to how, when, and which models should be used among athletes. So far, there have been no comprehensive reviews evaluating current knowledge about the practical applicability of CVD prediction algorithms in physically active cohorts. Our goal is to fill this gap. The following article summarizes the latest discoveries in this emerging area and presents them on the background of the most common CVD among athletes. We synthesized epidemiologic data, characteristics of prediction models, and risk factors in clinical cardiology and evaluated their applicability to athletes. Additionally, we outlined understudied areas which require further, more precise research.

2. Atrial Fibrillation and Other Minor Arrhythmias

Atrial fibrillation (AF) is described as the chaotic atrial electrical activity that can substitute regular sinus cadence and is one of the most popular dysrhythmias [19]. Usually diagnosed in older adults and individuals at cardiovascular risk (for our purposes — both veteran and amateur athletes), numerous case-controlled research studies have shown its link with a high amount of excessive endurance training [20,21]. Briefly, excessive training describes physical activity performed above the tolerance level of an individual [22]. The borderline is a subjective measure and depends on the individual's recovery, life demands, and stressors. An athlete could suspect overtraining when there is no mo-

tivation to work, sleep disturbances, elevated resting heart rate, or puissance [22]. Previous studies have noted a high prevalence of AF in middle-aged and master athletes ranging between 12% to 29%. However, despite the high rates of AF, most recommendations focused on other CVDs. It has been argued that AF carries a low risk of serious cardiac events when compared to other CVDs. However, undiagnosed can still lead to some health consequences [15,21,23].

Andersen *et al.* [24] illustrated the relationship between AF and overtraining. Skiers who completed $\geq$5 competitions (hazard ratio (HR) 1.29, 95% confidence interval (CI) 1.04–1.61) and those who had the fastest relative finishing time (HR 1.20; 95% CI 0.93–1.55) were exposed to the highest risk of AF [24]. Despite us knowing the existing relationship between strenuous exercises and AF, underlying mechanisms stay hypothetical and understudied [6]. Numerous preliminary assumptions include raised parasympathetic nervous system activity (so-called "vagal" tone), maladaptively enlarged and pathologically remodeled left atrium, hidden hypertension, inflammation/oxidative stress, periodic cardiac overload, alcohol, and caffeine (which is often supplemented as a performance-enhancing drug) [25,26]. The accurate dose and threshold of safe physical activity are still debated. We know that low-to-moderate sports did not increase the risk of AF. Although, there is a lack of exactitude for the consequences of chronic, prolonged exposure to over-volume of training demands (beyond which the risk of AF is higher) [6].

The occurrence of AF in the future can be predicted with substantial precision by clinical characteristics. AF risk estimates seem to be a practical go-to method. There are several common prediction scores- CHARGE-AF, C_2HEST, CHA_2DS_2-VASc, EHR-AF, and FHS-AF [27,28]. According to results from a large comprehensive meta-analysis of 21 AF predictive algorithms, the CHARGE-AF appeared to be most appropriate for preliminary screening, especially when applied to European populations [28]. Among the high heterogeneity of currently available equations, we recommend more unified protocols and cross-validation between different populations of existing models, rather than deriving new ones. This will allow physicians to select the most suitable type for athletes. Screening for the possibility of developing AF and other minor arrhythmias remains important. Cardiac rhythm disorders are common among athletes, primarily in endurance disciplines, and pose some dangers during exercises when undiagnosed [21]. Particularly noteworthy are the more ambitious amateurs who plan to practice high-intensity and high-frequency training and take part in competition events [24].

3. Blood Pressure and Hypertension

On average, about 25% of society suffers from elevated blood pressure and this is also mirrored in athletes, both amateur and professional [29]. High blood pressure is more often diagnosed among strength disciplines and bodybuilding. Although it has a lower prevalence among endurance athletes, they are also not excluded from hypertension [29]. It is the most common CVD in athletes and may present some problems with controlling the individual's eligibility for participating in regular training. Recent reports found an inverse association between endurance sports and blood pressure [30]. Accordingly, physical activity is advised during the treatment to control hypertension [30]. The number of cases of hypertension depends on sport discipline. There are some types of physical activity where the risk may be even higher than in the general population (e.g., powerlifting or bodybuilding) [30]. Undoubtedly, a precise clinical examination is required to make a definitive diagnosis of hypertension among athletes, stratify existing risks, and excluding secondary causalities [31].

In the largest research study of a European cohort, Caselli *et al.* [32] found that hypertension could be found in up to 3% of the athletic population (n = 2040, 64% men). Furthermore, in a wide review (n = 138,390) provided by Berge *et al.* [30], the authors claimed that hypertension prevalence in selected athletic cohorts is comparable to the inactive population. Although, results depend on the kind of discipline, and hypertension is more often seen in strength than endurance disciplines. Potential hypertension-predisposing risk factors are higher body mass index (often seen in amateurs and novices or bodybuilders with high muscle mass) and chronic misuse of illegal drugs or painkillers (predominantly found among professionals) [32]. Irregular circadian rhythm during competition season could also contribute to elevated blood pressure [32]. Tournaments or races during different phases of the day and on different continents could lead to sleep disorders which are related to hypertension [33]. Additional influencing variables may be a family history and genetic variables [34].

Thus, risk forecasting may be important in screening individuals with the highest possibility of current hypertension or developing it in the future [35]. Precise knowledge helps physicians select those who will benefit the most from regular medical follow-up [35]. Prediction models for hypertension are one of the most numerous in clinical cardiology [8]. The universal and thoroughly validated algorithm is the Framingham Risk Score and its derivatives [8,35–39]. Analyzing data from the Framingham cohort study, the researchers derived an uncomplicated scale with fair performance. The proposed algorithm classifies individuals into low (5%), medium (5% to 10%), or high (10%) likelihood of suffering hypertension in the following four years [35]. Calculations are based on points given for age, sex, blood pressure (both systolic and diastolic), body mass index, smoking status, and family history. Similar risk factors are common among other CVD, and athletes should be reassured about controlling them [8].

There are also regression equations to predict blood pressure variability during graded exercise. Two of them are provided by Mascherini *et al*. [40] and Szmigielska *et al*. [41]. Considering resting systolic and diastolic blood pressures, body mass index, age, and sex, it is possible to estimate peak blood pressure during workload. Such data and their comparison with resting measurements allows physicians and coaches to find those with abnormal blood pressure responses and refer them to further clinical evaluation [42].

To sum up, healthcare practitioners can utilize the Framingham scores or exercise regression equations to estimate an individual's chances of hypertension and monitor cardiac stress response [40]. Further steps are to inform the athletes of potential risks and assist during the choice of sport, threshold, amount and duration of physical activity. In addition, the proposed method of screening is relatively inexpensive, widely accessible, and uncomplicated. It is a viable tool for fitness practitioners to refer an athlete with suspected abnormal blood pressure to a medical appointment. This approach helps find so-called "red flags", i.e., athletes requiring precise intensity monitoring to safely participate in graded, progressive training. Furthermore, we recommend deriving new formulas with novel predictors of hypertension among athletes. Additional risk factors often found in sported cohorts are sleep assessments and primary sport discipline. Perhaps, their assessment could be completed using a questionnaire. New algorithms profiled for a specific population will be more useful for the medical team and coaching staff.

4. Coronary Artery Disease

Coronary artery disease (CAD) is one of the most common CVDs in the developed world and is associated with high morbidity [43]. Undoubtedly, endurance training reduces the risk of CAD [44]. However, current research has indicated a paradoxical association between excessive levels of conditioning and elevated CAD prevalence [45]. The underlying mechanism remains unclear, but existing findings documented raised serum levels of parathyroid hormone and consequently higher blood Ca^{2+} after workout bouts. It may explain to some degree the increased incidence of CAD [46,47].

In the general population, 2.4% to 6.6% of regular, symptomatic patients need noninvasive screening for possible high-risk CAD [48]. A simple set of preclinical factors enhances the prediction performance of CAD over the standard clinical examination. The identification of the highest-risk groups may facilitate decision-making related to additional tests, catheterization, or medical therapy [48]. For the athletic population, such a protocol may include adjusting and decreasing intensity to safe zones.

In a cross-sectional study on middle-aged and master athletes, Aengevaeren *et al*. [49] linked the occurrence of atherosclerotic plaques and elevated coronary artery calcification with prolonged, excessive conditioning. Training intensity but not amount, was correlated with aggravation of CAD in a six-year horizon. Strenuous training was responsible for greater CAD incidence and calcified plaque development. Whereas low-intensity exercise resulted in reduced CAD progression. Findings suggest that it is worth paying attention to the intensity prescribed to athletes and cardiac patients at a high risk of developing CAD [49].

Recently, Jang *et al*. [48] provided two prediction models of CAD. The algorithms consisted of practical, easy-to-obtain factors accessible from patients' medical history. There were seven variables, although particular importance in a sport-setting should be placed on family history, advanced age, and male sex. CAD risk factors correspond well with those described above for other CVDs [16]. Amateurs who start regular exercise and elderly veterans may suffer from them. Jang *et al*. [48] underlined that direct medical screening for individuals at high risk of CAD may be problematic. Hence, we shouldn't leave athletes unattended. Similar conclusions were provided by Hwang *et al.* [50]. Their findings confirmed results from previous studies. General practitioners and sports medicine physicians should be acknowledged with cohorts mostly exposed to CAD development to properly allow sports participation. Special attention should be paid to endurance disciplines among amateurs and the elderly.

To sum up, Lenselink *et al*. [51] examined the accuracy and transferability of 28 CAD prediction models on independent wide samples. Despite some inaccuracies, current algorithms are well-calibrated and replicable. They can be used by healthcare practitioners when conducting a comprehensive pre-participating medical evaluation or prescribing return-to-play guidelines [51].

5. Cardiomyopathies

Strenuous endurance conditioning can induce a specific pattern of functional and anatomical adaptations in the circulation [52]. In an unspecified ratio, an Athlete's Heart occurs. Precise diagnosis could strongly contribute to the prevention of particular athletes from sudden cardiac death [52]. However, those with an Athlete's Heart may continue their careers, even as competitors [52]. Recent reports related to the course of cardiac hypertrophy suggest that an individual approach may be the best management strategy [52]. Athlete's Heart results from biventricular hypertrophy [53]. There are also conditions with similar etiology, e.g., arrhythmogenic right ventricular cardiomyopathy (ARVC) [24]. Briefly, ARVC is a genetically acquired cardiomyopathy influencing tissue desmosomes and is described by the fibro-fatty substitute of typical cardiac myocytes, predominantly in the structure of the right ventricle [24].

Existing data suggest that endurance exercise accelerates the penetrance of the ARVC phenotype in those who are confirmed to carry the gene, consequently hurrying the evolution of severe ventricular arrhythmias and

heart failure [54]. It has been stipulated that numerous episodes of exercise-induced growth in pulmonary pressures may contribute to stronger afterload for the right ventricle and promote pathologic adaptation and cardiac remodeling which results in ARVC [24]. Currently, numerous unanswered queries and knowledge gaps have emerged. In the majority, conclusions are preliminary and based on observational studies from small populations [6]. Despite speculative mechanisms, undiagnosed myocardial fibrosis can occur in veterans after finishing a competitive career [6]. This condition results most likely from external factors, disconnected with training experience (perhaps post-career inappropriate lifestyle habits, alcohol consumption, unhealthy dietary preferences, periodical drug abuse, and performance-enhancing drugs during competitive times) [6]. It is worth noting that veterans or masters and amateurs are especially exposed to them.

A new risk prediction protocol for ARVC has been developed by Chen *et al*. [55] on an international cohort of 389 patients. Researchers analyzed popular clinical parameters such as left ventricular ejection fraction, serum creatinine levels, tricuspid regurgitation, and AF [55]. All of them could select athletes who are in danger of terminal events. They may advise physicians to consider and optimize follow-up procedures and rehabilitation exercise programs. This new prediction model also indicates the need for registering high-risk individuals and those with confirmed ARVC on the appropriate waiting lists [55].

The current prediction models mostly focus on ARVC. However, the HCM and DCM could also occur among athletes and are a serious issue. HCM could lead to fatal cases and is one of the most common cases of sudden cardiac death among athletes [7]. The diagnosis of HCM in physically active populations could not be easy and differential diagnosis is complex [7]. DCM could be similar to Athlete's Heart and prediction models could facilitate differential diagnosis [56]. The formulae could be considered the most common sign among athletes. For example, covariates for such a model could include ejection fraction, electrocardiography (ECG), echocardiography results, etc. Such a tool in a comprehensive diagnostic process could discriminate DCM and physiological left ventricular dilation in athletes [56]. Therefore, further prediction models could also be derived to stratify the risk of HCM and DCM.

Athlete's Heart and other cardiomyopathies are widely described syndromes [53]. However there is a lack of risk forecasting guidelines for safe exercises in those conditions. We recommend deriving novel prediction algorithms, perhaps including advanced contributing factors from radiological imaging and genetic testing.

6. Other CVDs

There are numerous prediction models derived for remaining the CVDs [8]. Among others, they concern stroke, myocardial infarction, or survival after invasive procedures [9]. It is worth highlighting that the majority of models are based on a common and replicable set of predictors [8,16]. Basic, universal CVD risk factors include nutrition quality, physical activity, nicotine exposure, sleep, body mass index, blood pressure, blood glucose, and lipid metabolism. The better the scores, the lower the risk of dying from CVD and all-cause mortality [57]. Actions that encourage optimal scores should be promoted among the athletes regardless of the level of advancement and age. Medical professionals and fitness practitioners should acknowledge the most common contributing variables to properly prescribe pre-participation guidelines and return-to-play protocols or adjust training. This is a universal tip to optimize results in other CVD risk estimations.

7. Maximal Oxygen Uptake (VO_{2max}) and its Role in Predicting CVD

VO_{2max} is a thoroughly described indicator of cardiovascular fitness and endurance capacity [58]. People with higher VO_{2max} have lower all-cause mortality, especially related to CVD [59]. Years of research in cardiology, epidemiology, and sports diagnostics have determined that a higher VO_{2max} is linked with a multitude of health benefits [60]. The impact of low cardiorespiratory fitness on cardiovascular and all-cause mortality is stronger than other predictors of CVD [61]. VO_{2max} is a parameter that merges the function of respiratory, muscular, and circulatory systems and gives an outlook of overall body physical performance [58]. Endurance training enables us to improve and maintain a high stable VO_{2max} with age [61]. Individuals who do not exercise regularly, experience a steeper VO_{2max} decline compared to active individuals [62]. In consequence, high VO_{2max} prevents CVD occurrence [61].

The gold standard for measuring $VO_{2max}$is the maximal symptom-limited cardiopulmonary exercise test [63]. However, due to practical reasons, such as lack of specialized testing equipment or personnel and the costs of the procedure [64], it is often infeasible to conduct studies on wider populations.

Hence, various equations for indirect VO_{2max} calculation have been derived. There are a significant number of VO_{2max} prediction models. We can classify them into linear regression models, which predict VO_{2max} level based on somatic and exercise variables [62], and prognostic-diagnostic models, which forecast cardiovascular events and mortality based on VO_{2max} [65].

Their accuracy is assessed in validation studies [62, 66,67]. VO_{2max} prediction models directed for all-cause and CVD mortality could be used as a valuable alternative to direct measurement, especially when recalibrated for the target population [62,68,69].

In recent years, there has been an emerging role of other cardiorespiratory parameters in predicting and diagnosing CVD. In particular, the oxygen uptake efficiency slope (OUES), oxygen uptake efficiency plateau (OUEP),

ventilatory efficiency (VE/VCO_2), and peak oxygen pulse (O_2P_{peak}) gained attention [70–73]. The comprehensive role of VO_{2max} and its interaction with other parameters is crucial to understanding the risk of CVD, especially in narrow and specific populations [59]. For example, higher VO_{2max} indicates a lower risk of CVD, but higher VE/VCO_2 suggests worse cardiorespiratory fitness [74]. OUES and OUEP are more attractive during the cardiopulmonary exercise test (CPET) because both do not require maximal effort to be derived [75]. Finally, O_2P_{peak} most precisely mirrors the function of the left ventricle responsible for ejection fraction, and is therefore a key measure for endurance athletes [76].

There is a lack of consensus on the discernable set of universal covariates for scaling cardiorespiratory fitness. Available models are often based on different predictors. This makes direct comparisons problematic. When choosing a predictive equation, determining characteristics should evaluate the precise level of exertion, previous medical history, drug history, derivation, validation cohorts, and testing modality [66]. Correct application of predicted VO_{2max} to stratify endurance capacity or CVD risk is a valuable method of guiding with precisely adjusted intensity for fitness training and medical rehabilitation [58].

Despite the unparalleled impact of VO_{2max} (both measured or estimated) on CVD prevalence, all the above-discussed CVD prediction models did not include it as a covariate. We recommend adding VO_{2max} and other indicators of cardiorespiratory fitness in future clinical prediction models to improve their predictive accuracy.

8. Discussion

This review examines the utility of CVD prediction models in athletes, emphasizing the need for individualized risk assessments in physically active populations. While regular exercise reduces CVD risk, excessive training can pose cardiovascular threats, particularly in amateur, veteran, and professional athletes. The study highlights gaps in research, such as the underuse of prediction models in athletic cohorts, and proposes protocols for integrating these tools into pre-participation screening. Specific CVDs are prevalent among athletes, including AF, hypertension, and cardiomyopathies, are discussed, alongside the role of VO_{2max} and other cardiorespiratory measures in risk prediction. Future directions include novel predictors, external validation, and ethnic adaptations. Overall, prediction models offer a cost-effective tool for preliminary CVD risk stratification, aiding safe training practices.

9. Challenges in Applying Prediction Models to Athletes

Currently, prediction models forecast the risk or diagnosis of CVDs and where these are likely to be fatal or non-fatal [8]. However, there are still emerging areas to discover. In clinical settings, numerous, already known variables are linked with CVD (e.g., albuminuria, education level, and coronary artery calcium). Despite having a confirmed predicting value, they are not employed to build more precise prediction algorithms. Perhaps the flexible incorporation of novel risk modeling factors will enrich the value of forecasting several clinically relevant cardiac conditions [77]. In addition, the proposed novel direction is to supplement existing formulas with cardiorespiratory fitness indicators, perhaps VO_{2max}.

The final decision of whether an athlete can be involved in training and competing is of crucial importance [78]. Prediction models cannot be used to draw a final diagnosis but could help during a comprehensive examination process and indicate the individuals at the highest risk [9]. This issue also depends on whether the decisive person is a medical doctor or not (e.g., a coach or a sports scientist) [78]. This is where the emerging role of shared decision-making allows avoidance of accidents during training or games and simultaneously prevents the unnecessary exclusion of an athlete from sport [78].

The preferred sports discipline is also a key factor when applying the prediction models as CVD risks may vary significantly across different sport disciplines [79]. For example, strength athletes more often suffer from hypertension than endurance athletes [29]. Moreover, endurance athletes have a higher risk of sarcopenia with aging, compared tostrength athletes [80]. The protective impact on the cardiovascular system of exercises is most often attributed for endurance sports (running, cycling, etc.) [81]. The cardiac effects of detraining are mostly visible in endurance disciplines rather than strength sports [81]. Moreover, the usage of doping substances that could aggravate the CVD risk is more common among strength sports [82]. Moreover, traditional risk factors could be subtle or temporary among athletes. For example, biochemical markers could grow due to strenuous training and some lipid disorders could even occur in strength athletes during dieting [83]. Finally, all the differences between types of sports or athletes and the general population should be acknowledged. Sports discipline should be considered when applying any diagnostic protocol.

Many of the above-discussed prediction models have not yet been externally validated. The most frequently examined models for general populations are: Framingham, SCORE, and QRISK [8,35,84,85]. It would be interesting to see their head-to-head performance among protocols in similar fields and direct validations on athletic samples. Moreover, studies most often include patients from Europe and North America [8,86]. However, athletes are all ethnicities. Body physiology and exercise capacity vary slightly between ethnic groups [87,88]. Thus, seeing the performance of the prediction formulae on other populations, e.g., African, Australian, or South American, would give valuable insights. The actual risk stratification approach sug-

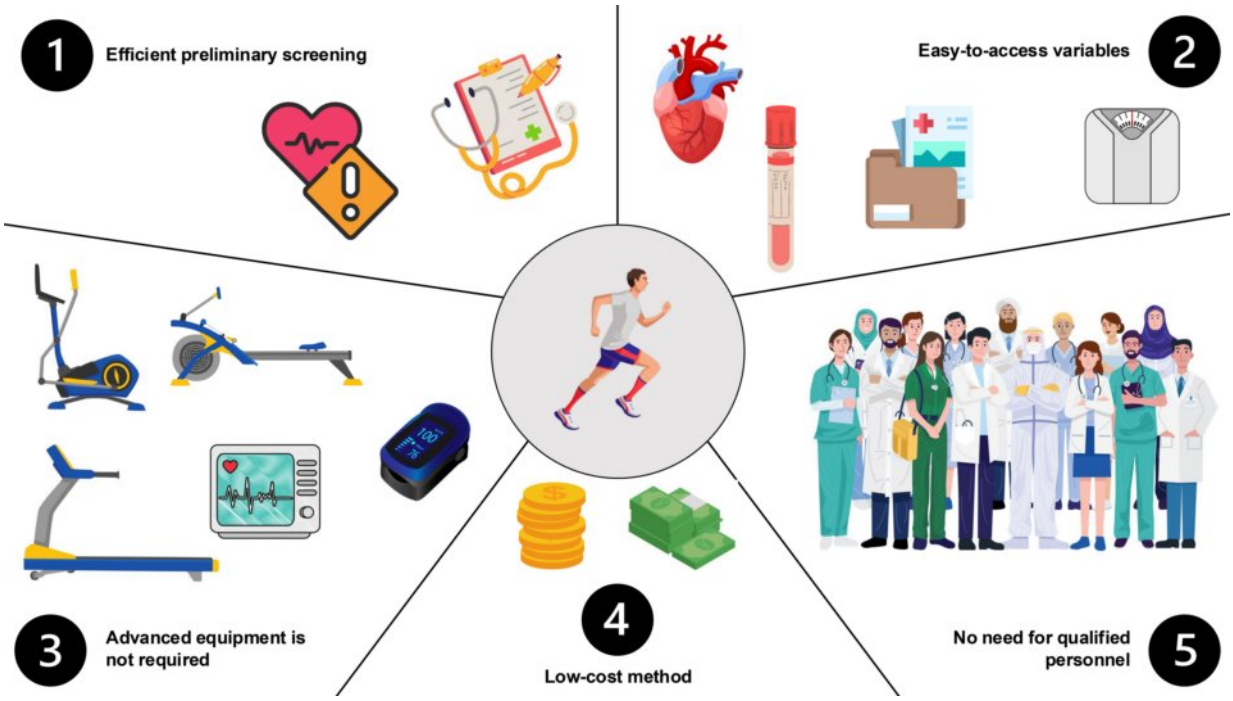

Fig. 2. Main advantages of using prediction models among athletes.

gests that the goal is to generate a clinically pertinent CVD prediction model and additionally combine current algorithms [8].

In particular, the criteria for participation in exercise with near-all-out intensity in seniors include factors which are often difficult to judge [89]. Master athletes should precisely monitor their efforts and recovery [5]. Any worrying signs such as breathlessness or chest pain should be the termination points of exercises [62]. Moreover, senior athletes must acknowledge the decrease in endurance capacity with aging (e.g., VO_{2max} decrease of about 6–8 mL/kg/min per decade) [60]. Older athletes should use monitoring methods and technologies, like wearables, to avoid overtraining [90]. Finally, regular medical follow-up supported by precise cardiopulmonary assessment (e.g., via CPET) could facilitate safe sport [59].

In Fig. 1 we proposed a protocol consisting of four phases. The first phase is illustrated in the left-lateral box. At this stage, CVD risk is unknown. A physician or fitness practitioner makes a preliminary CVD risk assessment based on estimation via prediction models. The second and third phases are illustrated in the central boxes (left and right respectively). If CVD is suspected (i.e., CVD risk +), the athlete is referred for precise medical evaluation. Additional diagnostic steps may include a medical appointment with a specialist, laboratory tests, cardiopulmonary exercise tests, etc. to make a definitive diagnosis. In the absence of suspicion of CVD (i.e., CVD risk –), the athlete is referred to basic diagnostic tests and regular health monitoring. The fourth step is illustrated in the right-lateral box. The process ends with approval for athletes with safe, adjusted, and precisely monitored physical activity (PA). The presented protocol enables feasible, inexpensive, and widely accessible forms of preliminary medical screening, in particular CVD risk assessment among athletes. Its usage enriches athletes' adherence to pre-participation screening and, in consequence, raises their diagnostic potential. It does not exempt athletes from periodic medical evaluation and health monitoring. However, it is an initiatory stage that facilitates the selection of athletes requiring deep, precise health assessment.

In Fig. 2, we illustrated the most important and emerging advantages of predictive models in cardiovascular risk stratification. Such algorithms provide a feasible and practical approach for physicians and fitness practitioners when guiding physically active individuals. (1) Early identification of increased risk of cardiovascular events during pre-participation screening is facilitated. Athletes with suspected elevated risk could be guided for a further, more comprehensive health assessment. (2) Most algorithms include widely available variables such as anthropometric measurements, demographic characteristics, or basic medical tests. Therefore, there is no need to undergo a complex medical examination if the preliminary risk is low or during periodic, regular health assessments. (3) Current prediction models limit the necessity to use specialized fitness equipment or medical devices. Initial risk stratification could be conducted during a brief appointment or by telemedicine advice. Subsequently, if an elevated risk is suspected, the athlete may be recommended to undergo a

Table 1. Characteristics of cardiovascular risk factors among athletes.

Risk factor category	Predictor	Type	Primary exposed group	Prediction model
Demographics and origin	Age	Non-modifiable	Veterans and masters athletes	• Framingham Anderson [37] • Framingham Wilson [91] • SCORE [85] • Framingham D'Agostino [36] • Framingham ATP III [38] • QRISK [84] • PROCAM [102] • Framingham Wolf [39] • Friedland *et al.* [92] • Keys *et al.* [93] • ASSIGN [94] • Chien *et al.* [95] • Asia Pacific cohort studies [96] • Framingham Risk Score [97] • Szmigielska *et al.* [41] • Mascherini *et al.* [40] • Hwang *et al.* [50] • Jang *et al.* [98] • CHARGE-AF [99]
	Sex		• Veterans and masters athletes • Amateurs and new athletes • Professional athletes	• Framingham Anderson [37] • Framingham Wilson [91] • SCORE • Framingham D'Agostino [36] • Framingham ATP III [38] • QRISK • ASSIGN • Chien *et al.* [95] • Asia Pacific cohort studies [96] • Szmigielska *et al.* [41] • Jang *et al.* [98] • CHARGE-AF
	Family history			• PROCAM • Framingham Risk Score • Hwang *et al.* [50] • Jang *et al.* [98]
	Ethnicity			• QRISK • CHARGE-AF
	Genetics			None
Comorbidities	Diabetes and glucose intolerance	Modifiable	Amateurs and new athletes	• Framingham Anderson [37] • Framingham D'Agostino [36] • QRISK • PROCAM • Chambless *et al.* [100] • Friedland *et al.* [92] • ASSIGN • Hwang *et al.* [50] • Jang *et al.* [98] • CHARGE-AF
	Atrial fibrillation		Professional athletes	• QRISK • Framingham Wolf [39] • Chen *et al.* [55]
	Past medical history		• Veterans and masters athletes • Amateurs and new athletes • Professional athletes	QRISK

Table 1. Continued.

Risk factor category	Predictor	Type	Primary exposed group	Prediction model
Lifestyle	BMI		Amateurs and new athletes	• QRISK • Chambless *et al.* [100] • Keys *et al.* [93] • Chien *et al.* [95] • Framingham Risk Score • Mascherini *et al.* [40] • CHARGE-AF
	Smoking			• Framingham Anderson [37] • Framingham Wilson [91] • SCORE • Framingham D'Agostino [36] • Framingham ATP III [38] • QRISK • PROCAM • Chambless *et al.* [100] • Friedland *et al.* [92] • Keys *et al.* [93] • Leaverton *et al.* [101] • ASSIGN • Chien *et al.* [95] • Asia Pacific cohort studies [96] • Framingham Risk Score • CHARGE-AF
	Stress and socioeconomic status			ASSIGN
	Diet			None
	Alcohol			None
Blood lipids and serum biomarkers	Total cholesterol		• Veterans and masters athletes • Amateurs and new athletes	• Framingham Anderson [37] • Framingham Wilson [91] • SCORE • Framingham D'Agostino [36] • Framingham ATP III [38] • Chambless *et al.* [100] • Friedland *et al.* [92] • Keys *et al.* [93] • Leaverton *et al.* [101] • ASSIGN • Chien *et al.* [95] • Asia Pacific cohort studies [96]
	HDL cholesterol			• Framingham Anderson [37] • Framingham Wilson [91] • Framingham D'Agostino [36] • Framingham ATP III [38] • PROCAM • Chambless *et al.* [100] • ASSIGN • Chien *et al.* [95]
	Non-HDL cholesterol			None
	LDL cholesterol			• PROCAM • Chien *et al.* [95]

Table 1. Continued.

Risk factor category	Predictor	Type	Primary exposed group	Prediction model
			• Veterans and masters athletes • Amateurs and new athletes	• Framingham Anderson [37] • Framingham Wilson [91] • Framingham D'Agostino [36] • Framingham ATP III [38] • PROCAM • Chambless *et al.* [100] • Keys *et al.* [93] • Leaverton *et al.* [101] • Chien *et al.* [95] • Asia Pacific cohort studies [96] • Framingham Risk Score [97] • Szmigielska *et al.* [41] • CHARGE-AF
BP	Systolic BP			
	Diastolic BP			• Framingham Anderson [37] • Mascherini *et al.* [40] • CHARGE-AF
	Hypertension and BP			• Framingham Wilson [91] • SCORE • Framingham ATP III [38] • QRISK • Chambless *et al.* [100] • Framingham Wolf [39] • Friedland *et al.* [92] • ASSIGN • Hwang *et al.* [50] • Jang *et al.* [98] • CHARGE-AF

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BP, blood pressure.

full diagnostic protocol. (4) There is no need to conduct a full exercise protocol, extensive laboratory examinations, etc. Thus, prediction models allow for higher compliance due to the simplification and reduction in costs to obtain basic pre-participation approval. As most athletes have to pay for medical appointments out of their own finances, it is one of the main reasons for non-adherence to medical screening. (5) The health assessment can be performed without the involvement of numerous medical staff (e.g., nurse, physician, lab technician, exercise physiologist). Thus, medical personnel can devote more time to individuals with severe health conditions.

Undoubtedly, the gold standard would always be to conduct a full screening and diagnostic examination of each athlete. In practical circumstances, this is difficult to implement due to the costs of the procedures, their complexity, and the availability of diagnostic centers. This is the moment when prediction models come for a preliminary screening assessment. They provide a cost-effective prelude to a thorough medical examination [9]. They help to find so-called "red flags", i.e., athletes who are most likely to develop certain diseases or have the highest risk of an ongoing condition. Those should be referred for more detailed diagnostic tests to ensure safe and effective training.

In Table 1 (Ref. [36–41,50,55,84,85,91–102]) we described the most common categories of CVD risk factors among athletes and indicated their type. Additionally, we propose major exposure groups with the highest probability where selected risk factors could occur. We provided the most often validated (>3 external validations) prediction models and prediction models described in this review which include particular variables in risk stratification. Three subgroups of athletes were proposed to facilitate risk stratification: (1) 'amateurs and new' refers to athletes with limited sports experience and those who started endurance training to improve their health who previously were inactive with an unhealthy lifestyle, (2) 'veterans and masters' refers to people who finished their competitive sports career or are amateurs at an advanced age, and (3) 'professionals' refers to individuals who competitively take part in sports events, are exposed to significant training demands and possibly use illicit performance-enhancing drugs.

10. Conclusions

Given the growing popularity of endurance disciplines and the increased number of amateur, veteran, and professional athletes, there is a need for individualized diagnostic and screening approaches. To prevent harmful, unforeseen effects of CVD, a promising method is provided by using prediction models. Existing equations require evaluation of transferability and should be adjusted for the specificity of the athletic cohorts. It must be highlighted that currently, such algorithms can only be a supplemental method despite promising results on general populations. Medical professionals and fitness practitioners could apply indirect predictions during screening, but these are not for definitive diagnoses or to prevent physical activity among athletes.

Author Contributions

Conceptualization, TC, PK, AM and DŚ; investigation, TC, PK, AM and DŚ; writing—original draft, TC, PK, AM and DŚ; writing—review and editing, TC, PK, AM, and DŚ; supervision, AM and DŚ. All authors contributed to editorial changes in the manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work. All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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Podsumowanie i wnioski (łączące wyniki zawarte w cyklu publikacji)

Cykl publikacji oryginalnych połączony został akronimem NOODLE. Badania prezentują nowatorskie podejście do analizy CPET u sportowców elitarnych. Publikacje łączą się w syntetyczny cykl prezentujący zarówno walidację zewnętrzną dotychczasowych równań predykcji, nowe równania referencyjne sprofilowane na sportowców wyczynowych, jak i tabularyczne wartości normatywne. Są to trzy główne obszary, które dotychczas były analizowane w obszarze norm dla CPET, jednak nigdy w tym kontekście – na populacji sportowców oraz dla wybranych zmiennych.

Artykuły prezentują nieznacznie inne, ale uzupełniające podejście do analiz statystycznych. Każdy z artykułów wykorzystywał indywidualnie: interakcję czynników (ang. *interaction factors*), walidację krzyżową (ang. *cross-validation*), metody samowsporne (ang. *bootstapping*) oraz kalibrację. Są to wiodące metody statystyczne wykorzystywane w poruszanej dziedzinie wiedzy i każda z nich w specyficzny sposób pozwala analizować zależności między zmiennymi CPET. Ponadto, metoda kalibracji może stanowić przykład skorygowania równań referencyjnych do innych populacji, nie tylko osób aktywnych fizycznie czy sportowców. W badaniu NOODLE wykorzystano model sportowców wytrzymałościowych – bazując na wcześniejszych wynikach badań własnych identyfikujących ją jako populację, której wyniki CPET odbiegają od populacji ogólnej. Jednakże, prezentowana metoda może być uniwersalnie stosowana również dla innych populacji.

Należy podkreślić, że wybór zmiennych był podyktowany dotychczasowymi lukami w literaturze oraz przesłankami opartymi w fizjologii wysiłku fizycznego. Wyselekcjonowano cztery zmienne będące współczynnikami dwóch podstawowych parametrów, co podkreśla połączenie powyższych prac w cykl. Wybrane zmienne płynnie integrują układ krążenia i inne układy, w szczególności układ oddechowy. Ponadto, parametry dwuczynnikowe były dotychczas reprezentowane w literaturze w ograniczonym stopniu, mimo potencjalnie bardziej złożonych zależności w ich fizjologii i wartościach referencyjnych. Stąd, przytoczone przesłanki poszerzają implikacje wyników badania NOODLE. Ponadto, znaczenie prac obejmowało nie tylko optymalizację analizy wyników CPET u sportowców, ale również opracowanie założeń teoretycznych istotnych z punktu widzenia badawczego. Ostatecznie, wnioski płynące z badania NOODLE mają zarówno wymiar praktyczny w obszarze kardiologii sportowej, jak i metodyczny.

Prezentowane podejście do wartości normatywnych może stanowić punkt wyjścia do oceny wyników CPET u sportowców, a porównanie wartości obserwowanych w testach wysiłkowych

do danych z badania NOODLE (w tym wartości przewidywanych) pozwoli identyfikować potencjalne niepokojące sygnały i patologie. Biorąc pod uwagę praktyczne wnioski z prac oryginalnych, zauważono znaczące luki w wiedzy w wybranych obszarach kardiologii sportowej. Stąd, przeglądy narratywne podsumowują ostatnie zmiany w literaturze i nowe trendy badawcze. Dyskutowane są również potencjalne tematy przyszłych badań, a także obszary zastosowań opracowywanych modeli. Wiodące opinie w epidemiologii i leczeniu najczęstszych chorób układu krążenia u sportowców również zostały opisane. Każda z publikacji przeglądowych wzbogaca prace oryginalne stanowiąc szerokie tło do interpretacji wyników badań własnych.

Publikacje stanowią efekt współpracy wiodących ośrodków w dziedzinie fizjologii i kardiologii sportowej – Warszawskiego Uniwersytetu Medycznego oraz Instytut Sportu – Państwowego Instytutu Badawczego w Warszawie. Artykuły wzbogacają dotychczasowe koncepcje prezentowane w literaturze będąc wstępem do kolejnych badań własnych.

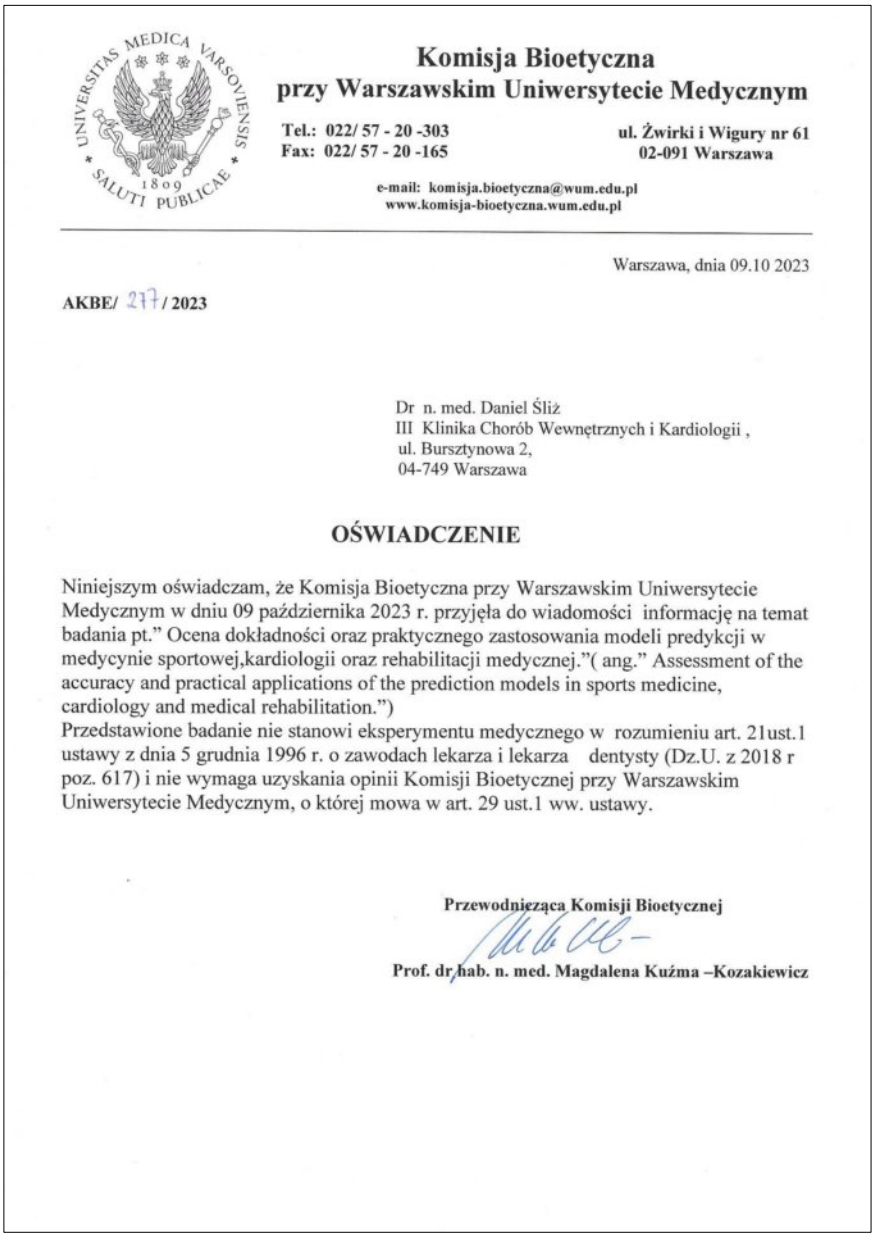
Wnioski:

- Zdrowi sportowcy elitarni w końcowych fazach maksymalnego wysiłku mogą doświadczać wartości $\dot{V}E/\dot{V}CO_2$ przekraczających przyjęte punkty odcięcia. Nie stanowią one o patologii, będąc wariantem normy. Typowe różnice między płciami pozostają zachowane – u kobiet wciąż obserwuje się wyższe wartości $\dot{V}E/\dot{V}CO_2$ niż u mężczyzn.
- W populacji osób młodych o ponadnormatywnym poziomie wytrenowania zmienna wieku w szacowaniu $\dot{V}E/\dot{V}CO_2$ ma zaniedbywalne znaczenie, mimo że typowe modele referencyjne wykorzystują wiek jako główny predyktor. Najdokładniejsze są modele wykorzystujące dane antropometryczne, tj. wzrost. Wysiłkowe zmienne krążeniowo-oddechowe w głównym stopniu są uzależnione od wymiarów ciała, a wpływ wieku pozostaje drugorzędny w populacji osób młodych uprawiających sport.
- Mimo że sportowcy wytrzymałościowi obserwują znacznie zawyżone wartości OUES, podstawowa relacja obserwowana u osób niewytrenowanych pozostaje zachowana – nie występują istotne różnice między OUES wyznaczanym z 75%, 90% czy 100% wysiłku. Zależność u sportowców pozostaje w zgodzie z wcześniejszymi pracami na populacjach ogólnych lub klinicznych.
- OUES z wysoką dokładnością i powtarzalnością pozwala przewidywać $\dot{V}O_{2max}$. OUES może stanowić wartościowy zamiennik dla $\dot{V}O_{2max}$ w populacji sportowców elitarnych, gdy maksymalne testy z pewnych względów mogą nie być rekomendowane (np. po powrocie po kontuzjach).

- Ogólne równania predykcyjne dla $\dot{V}E/\dot{V}CO_2$, OUES, OUEP i O_2P_{peak} prezentują znaczące błędy podczas walidacji zewnętrznej w populacji sportowców wytrzymałościowych i nie stanowią wartościowej alternatywny dla bezpośredniego CPET.
- Przygotowanie równań referencyjnych dla OUES stanowi większe wyzwanie u osób wytrenowanych niż w populacjach ogólnych. Do uzyskania satysfakcjonujących modeli wymagane jest zastosowanie zmiennych będących pochodną interakcji czynników.
- OUEP stanowi uniwersalny wskaźnik do oceny układu krążenia, ponieważ nie rośnie w przypadku wysokiego poziomu wytrenowania, a spada w sytuacji choroby. Różnice nie wykazują znamienności statystycznej, tak długo, jak obie komponenty pozostają w proporcjonalnej relacji.
- Kalibracja pozostaje mało skomplikowaną metodą skorygowania równań regresji do populacji o innej charakterystyce. Zaproponowana metoda pozwala na adaptację ogólnych równań referencyjnych do wąskich, homogennych populacji, jeżeli są one zbyt małe do osiągnięcia mocy statystycznej do przygotowania specyficznych równań.
- Modele predykcyjne mają szerokie zastosowania do oceny układu krążenia również u sportowców, stanowiąc nisko kosztowe i łatwo dostępne uzupełnienie dla tradycyjnych badań diagnostycznych; przy uwzględnieniu ich ograniczonej dokładności i pomocniczego charakteru.
- Dotychczasowe zbiory wartości normatywnych są opracowywane przy znacznych różnicach metodologicznych, co utrudnia ich bezpośrednie porównanie.
- Obszar badań nad CPET pozostaje dynamicznie rozwijającą się dziedziną wiedzy. Wartość diagnostyczna CPET jest wiodąca w ocenie wydolności fizycznej organizmu, jednak wymaga właściwych danych wyjściowych i uwzględnienia fizjologicznych różnic do prawidłowej interpretacji wyników.

Opinia Komisji Bioetycznej

Badanie przeprowadzono na danych zbieranych retrospektywnie we wcześniejszych latach podczas regularnej praktyki Instytutu Sportu – Państwowego Instytutu Badawczego w Warszawie polegającej na wykonywaniu CPET u sportowców w ramach monitorowania wydolności. Uczestnicy podpisywali świadomą zgodę na poddanie się wstępnym badaniom lekarskim, wykonanie CPET, a także wykorzystanie wyników na potrzeby badań naukowych w przyszłości w modelu retrospektywnym. Numer opinii komisji bioetycznej został podany w każdej z publikacji oryginalnych.



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AKBE/ 277 / 2023

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OŚWIADCZENIE

Niniejszym oświadczam, że Komisja Bioetyczna przy Warszawskim Uniwersytecie Medycznym w dniu 09 października 2023 r. przyjęła do wiadomości informację na temat badania pt." Ocena dokładności oraz praktycznego zastosowania modeli predykcji w medycynie sportowej,kardiologii oraz rehabilitacji medycznej."(ang." Assessment of the accuracy and practical applications of the prediction models in sports medicine, cardiology and medical rehabilitation.")
Przedstawione badanie nie stanowi eksperymentu medycznego w rozumieniu art. 21ust.1 ustawy z dnia 5 grudnia 1996 r. o zawodach lekarza i lekarza dentysty (Dz.U. z 2018 r poz. 617) i nie wymaga uzyskania opinii Komisji Bioetycznej przy Warszawskim Uniwersytecie Medycznym, o której mowa w art. 29 ust.1 ww. ustawy.

Przewodnicząca Komisji Bioetycznej
Prof. dr hab. n. med. Magdalena Kuźma –Kozakiewicz

Oświadczenia współautorów publikacji określające indywidualny wkład

Warszawa, 19.11.2025 r.
(miejscowość, data)

Przemysław Kasiak
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Is the Ventilatory Efficiency in Endurance Athletes Different?—Findings from the NOODLE Study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi*: opracowanie koncepcji, opracowanie danych, analiza formalna, inwestygacja, opracowanie metodologii, administracja projektem, zarządzanie zasobami danych, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór.

Przemysław Kasiak
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(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 19.11.2025 r.
(miejscowość, data)

Tomasz Kowalski
(imię i nazwisko)

OŚWIADCZENIE

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Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie danych, analiza formalna, inwestygacja, opracowanie metodologii, administracja projektem, zarządzanie zasobami danych, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek/~~mgr~~** Przemysława Kasiaka.

.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
(miejscowość, data)

Kinga Rębiś
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Kinga Rębiś
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Warszawa, 17.11.2025 r.
(miejscowość, data)

Andrzej Klusiewicz
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A. Klusiewicz
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Warszawa, 18.11.2025 r.
(miejscowość, data)

Maria Ładyga
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Warszawa, 18.11.2025 r.
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Dorota Sadowska
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Dorota Sadowska
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(miejscowość, data)

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OŚWIADCZENIE

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Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej lek/~~mgr~~ Przemysława Kasiaka.

.....
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*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
(miejscowość, data)

Szczepan Wiecha
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OŚWIADCZENIE

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Szczepan Wiecha
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*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
(miejscowość, data)

Marcin Barylski
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OŚWIADCZENIE

Jako współautor pracy pt. **Is the Ventilatory Efficiency in Endurance Athletes Different?—Findings from the NOODLE Study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: pozyskanie finansowania, redakcja manuskryptu – krytyczny przegląd i poprawki.

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***w szczególności** udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
(miejscowość, data)

Adam Rafał Poliwczak
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OŚWIADCZENIE

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Warszawa, 18.11.2025 r.
(miejscowość, data)

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OŚWIADCZENIE

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Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

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Warszawa, 09.12.2025 r.
(miejscowość, data)

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OŚWIADCZENIE

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Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie danych, analiza formalna, inwestygacja, opracowanie metodologii, administracja projektem, zarządzanie zasobami danych, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór.

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Warszawa, 09.12.2025 r.
(miejscowość, data)

Daniel Śliż
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OŚWIADCZENIE

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Warszawa, 19.11.2025 r.
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Przemysław Kasiak
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OŚWIADCZENIE

Jako współautor pracy pt. **Below or all the way to the peak? Oxygen uptake efficiency slope as the index of cardiorespiratory response to exercise—the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi*: opracowanie koncepcji, opracowanie danych, analiza formalna, inwestygacja, opracowanie metodologii, administracja projektem, zarządzanie zasobami danych, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki.

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Kinga Rębiś
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Andrzej Klusiewicz
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A. Klusiewicz
.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
(miejscowość, data)

Michał Starczewski
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Below or all the way to the peak? Oxygen uptake efficiency slope as the index of cardiorespiratory response to exercise—the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: opracowanie danych, inwestygacja, udostępnienie materiałów do badań, redakcja manuskryptu – krytyczny przegląd i poprawki.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie danych, analiza formalna, inwestygacja, opracowanie metodologii, administracja projektem, zarządzanie zasobami danych, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

.....

(podpis oświadczającego)

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Warszawa, 18.11.2025 r.
(miejscowość, data)

Maria Ładyga
(imię i nazwisko)

OŚWIADCZENIE

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Maria Ładyga

.....

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
(miejscowość, data)

Szczepan Wiecha
(imię i nazwisko)

OŚWIADCZENIE

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Szczepan Wiecha
.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
(miejscowość, data)

Marcin Barylski
(imię i nazwisko)

OŚWIADCZENIE

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(podpis oświadczającego)

***w szczególności** udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
(miejscowość, data)

Adam Rafal Poliwczak
(imię i nazwisko)

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(podpis oświadczającego)

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Warszawa, 18.11.2025 r.
(miejscowość, data)

Piotr Wierzbiński
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OŚWIADCZENIE

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*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 09.12.2025 r.
(miejscowość, data)

Artur Mamcarz
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Below or all the way to the peak? Oxygen uptake efficiency slope as the index of cardiorespiratory response to exercise—the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: administracja projektem, nadzór, redakcja manuskryptu – krytyczny przegląd i poprawki.

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Warszawa, 09.12.2025 r.
(miejscowość, data)

Daniel Śliż
(imię i nazwisko)

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Warszawa, 19.11.2025 r.
(miejscowość, data)

Przemysław Kasiak
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Oxygen uptake efficiency plateau is unaffected by fitness level - the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi*: opracowanie koncepcji, opracowanie danych, analiza formalna, inwestygacja, opracowanie metodologii, administracja projektem, zarządzanie zasobami danych, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór.

Przemysław Kasiak
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 19.11.2025 r.
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Tomasz Kowalski
(imię i nazwisko)

OŚWIADCZENIE

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Warszawa, 18.11.2025 r.
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Kinga Rębiś
(imię i nazwisko)

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Kinga Rębiś
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Andrzej Klusiewicz
(imię i nazwisko)

OŚWIADCZENIE

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A. Klusiewicz
.....
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Warszawa, 18.11.2025 r.
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Dorota Sadowska
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OŚWIADCZENIE

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Adrian Wilk
(imię i nazwisko)

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Warszawa, 18.11.2025 r.
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Szczepan Wiecha
(imię i nazwisko)

OŚWIADCZENIE

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Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

Szczepan Wiecha
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(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
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Marcin Barylski
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Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie danych, analiza formalna, inwestygacja, opracowanie metodologii, administracja projektem, zarządzanie zasobami danych, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek/~~mgr~~** Przemysława Kasiaka.

Marcin Barylski
.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
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Adam Rafał Poliwczak
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Oxygen uptake efficiency plateau is unaffected by fitness level - the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: pozyskanie finansowania.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie danych, analiza formalna, inwestygacja, opracowanie metodologii, administracja projektem, zarządzanie zasobami danych, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek/~~mgr~~** Przemysława Kasiaka.

.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
(miejscowość, data)

Piotr Wierzbiński
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Oxygen uptake efficiency plateau is unaffected by fitness level - the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: pozyskanie finansowania.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie danych, analiza formalna, inwestygacja, opracowanie metodologii, administracja projektem, zarządzanie zasobami danych, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek/~~mgr~~** Przemysława Kasiaka.

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PIOTR WIERZBIŃSKI
specjalista psychiatra
2034115

.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 09.12.2025 r.
(miejscowość, data)

Artur Mamcarz
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Oxygen uptake efficiency plateau is unaffected by fitness level - the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: administracja projektem, nadzór.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie danych, analiza formalna, inwestygacja, opracowanie metodologii, administracja projektem, zarządzanie zasobami danych, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 09.12.2025 r.
(miejscowość, data)

Daniel Śliż
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Oxygen uptake efficiency plateau is unaffected by fitness level - the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: opracowanie koncepcji, pozyskanie finansowania, administracja projektem, nadzór.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie danych, analiza formalna, inwestygacja, opracowanie metodologii, administracja projektem, zarządzanie zasobami danych, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 19.11.2025 r.
(miejscowość, data)

Przemysław Kasiak
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Recalibrated FRIEND equation for peak oxygen pulse is accurate in endurance athletes: the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi*: opracowanie koncepcji, opracowanie metodologii, walidacja wyników, analiza formalna, inwestygacja, zarządzanie zasobami danych, opracowanie danych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, wizualizacja wyników, pozyskanie finansowania.

Przemysław Kasiak

.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 19.11.2025 r.
(miejscowość, data)

Tomasz Kowalski
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Recalibrated FRIEND equation for peak oxygen pulse is accurate in endurance athletes: the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: opracowanie koncepcji, opracowanie metodologii, inwestygacja, udostępnienie materiałów do badań, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie metodologii, walidacja wyników, analiza formalna, inwestygacja, zarządzanie zasobami danych, opracowanie danych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, wizualizacja wyników, pozyskanie finansowania.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

T Kowalski

.....

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 17.11.2025 r.
(miejscowość, data)

Andrzej Klusiewicz
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Recalibrated FRIEND equation for peak oxygen pulse is accurate in endurance athletes: the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: inwestygacja, udostępnienie materiałów do badań, redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie metodologii, walidacja wyników, analiza formalna, inwestygacja, zarządzanie zasobami danych, opracowanie danych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, wizualizacja wyników, pozyskanie finansowania.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

A. Klusiewicz

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
(miejscowość, data)

Ryszard Zdanowicz
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Recalibrated FRIEND equation for peak oxygen pulse is accurate in endurance athletes: the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: udostępnienie materiałów do badań, redakcja manuskryptu – krytyczny przegląd i poprawki.
Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie metodologii, walidacja wyników, analiza formalna, inwestygacja, zarządzanie zasobami danych, opracowanie danych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, wizualizacja wyników, pozyskanie finansowania.
Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

Ryszard Zdanowicz
.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
(miejscowość, data)

Maria Ładyga
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Recalibrated FRIEND equation for peak oxygen pulse is accurate in endurance athletes: the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: udostępnienie materiałów do badań, redakcja manuskryptu – krytyczny przegląd i poprawki.
Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie metodologii, walidacja wyników, analiza formalna, inwestygacja, zarządzanie zasobami danych, opracowanie danych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, wizualizacja wyników, pozyskanie finansowania.
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Maria Ładyga
.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 18.11.2025 r.
(miejscowość, data)

Szczepan Wiecha
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Recalibrated FRIEND equation for peak oxygen pulse is accurate in endurance athletes: the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie metodologii, walidacja wyników, analiza formalna, inwestygacja, zarządzanie zasobami danych, opracowanie danych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, wizualizacja wyników, pozyskanie finansowania.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

Szczepan Wiecha
.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 09.12.2025 r.
(miejscowość, data)

Artur Mamcarz
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Recalibrated FRIEND equation for peak oxygen pulse is accurate in endurance athletes: the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: opracowanie koncepcji, nadzór, administracja projektem.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie metodologii, walidacja wyników, analiza formalna, inwestygacja, zarządzanie zasobami danych, opracowanie danych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, wizualizacja wyników, pozyskanie finansowania.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 09.12.2025 r.
(miejscowość, data)

Daniel Śliż
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Recalibrated FRIEND equation for peak oxygen pulse is accurate in endurance athletes: the NOODLE study** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: opracowanie koncepcji, redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór, administracja projektem.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, opracowanie metodologii, walidacja wyników, analiza formalna, inwestygacja, zarządzanie zasobami danych, opracowanie danych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, wizualizacja wyników, pozyskanie finansowania.

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.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 19.11.2025 r.
(miejscowość, data)

Tomasz Kowalski
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Optimizing the Interpretation of Cardiopulmonary Exercise Testing in Endurance Athletes: Precision Approach for Health and Performance** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: opracowanie koncepcji, zebranie literatury, pozyskanie finansowania, ekstrakcja danych z prac źródłowych, opracowanie kryteriów selekcji literatury, administracja projektem, zapewnienie dostępu do baz literatury, nadzór, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, zebranie literatury, pozyskanie finansowania, ekstrakcja danych z prac źródłowych, opracowanie kryteriów selekcji literatury, administracja projektem, zapewnienie dostępu do baz literatury, nadzór, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 19.11.2025 r.
(miejscowość, data)

Przemysław Kasiak
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Optimizing the Interpretation of Cardiopulmonary Exercise Testing in Endurance Athletes: Precision Approach for Health and Performance** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi*: opracowanie koncepcji, zebranie literatury, pozyskanie finansowania, ekstrakcja danych z prac źródłowych, opracowanie kryteriów selekcji literatury, administracja projektem, zapewnienie dostępu do baz literatury, nadzór, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki.

Przemysław Kasiak
.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 03.12.2025 r.
(miejscowość, data)

Tomasz Chomiuk
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Optimizing the Interpretation of Cardiopulmonary Exercise Testing in Endurance Athletes: Precision Approach for Health and Performance** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: redakcja manuskryptu – krytyczny przegląd i poprawki, pozyskanie finansowania.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, zebranie literatury, pozyskanie finansowania, ekstrakcja danych z prac źródłowych, opracowanie kryteriów selekcji literatury, administracja projektem, zapewnienie dostępu do baz literatury, nadzór, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

Tomasz Chomiuk

.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 09.12.2025 r.
(miejscowość, data)

Artur Mamcarz
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Optimizing the Interpretation of Cardiopulmonary Exercise Testing in Endurance Athletes: Precision Approach for Health and Performance** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: redakcja manuskryptu – krytyczny przegląd i poprawki, pozyskanie finansowania.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, zebranie literatury, pozyskanie finansowania, ekstrakcja danych z prac źródłowych, opracowanie kryteriów selekcji literatury, administracja projektem, zapewnienie dostępu do baz literatury, nadzór, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 09.12.2025 r.
(miejscowość, data)

Daniel Śliż
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Optimizing the Interpretation of Cardiopulmonary Exercise Testing in Endurance Athletes: Precision Approach for Health and Performance** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: redakcja manuskryptu – krytyczny przegląd i poprawki, pozyskanie finansowania.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, zebranie literatury, pozyskanie finansowania, ekstrakcja danych z prac źródłowych, opracowanie kryteriów selekcji literatury, administracja projektem, zapewnienie dostępu do baz literatury, nadzór, walidacja wyników, wizualizacja wyników, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

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(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 03.12.2025 r.
(miejscowość, data)

Tomasz Chomiuk
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Specificity and Areas of Usage of Cardiovascular Prediction Models Among Athletes—State-of-the-art Review** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: opracowanie koncepcji, zebranie literatury i ekstrakcja danych z prac źródłowych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki.

Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, zebranie literatury i ekstrakcja danych z prac źródłowych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki.

Jednocześnie wyrażam zgodę na wykorzystanie wyżej wymienionej pracy jako część rozprawy doktorskiej **lek**/~~mgr~~ Przemysława Kasiaka.

Tomasz Chomiuk

.....

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 19.11.2025 r.
(miejscowość, data)

Przemysław Kasiak
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Specificity and Areas of Usage of Cardiovascular Prediction Models Among Athletes—State-of-the-art Review** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi*: opracowanie koncepcji, zebranie literatury i ekstrakcja danych z prac źródłowych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki.

Przemysław Kasiak
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 09.12.2025 r.
(miejscowość, data)

Artur Mamcarz
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Specificity and Areas of Usage of Cardiovascular Prediction Models Among Athletes—State-of-the-art Review** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: opracowanie koncepcji, zebranie literatury i ekstrakcja danych z prac źródłowych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór.
Wkład **Przemysława Kasiaka** w powstawanie publikacji obejmował*: opracowanie koncepcji, zebranie literatury i ekstrakcja danych z prac źródłowych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki.
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.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 09.12.2025 r.
(miejscowość, data)

Daniel Śliż
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. **Specificity and Areas of Usage of Cardiovascular Prediction Models Among Athletes—State-of-the-art Review** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: opracowanie koncepcji, zebranie literatury i ekstrakcja danych z prac źródłowych, redakcja manuskryptu – wersja pierwotna, redakcja manuskryptu – krytyczny przegląd i poprawki, nadzór.

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*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników