INTRODUCTION

Hill and Lupton [1] described maximal oxygen uptake (VO2max) as the level of oxygen intake during exercise beyond which no physical effort can raise it. Since then, numerous studies have used it to indicate the status of and predict changes in cardiovascular health and physical performance. A PubMed search performed in February 1, 2019, resulted in 3,925 scientific articles on humans (1953–2018) mentioning ‘maximal oxygen uptake’ in the title or abstract. Indeed, VO2max has established itself as a valid measure of cardiorespiratory fitness.
fitness (CRF), the upper limit for the cardiorespiratory system to transport oxygen from the air to the tissues [2]. From epidemiological and public health perspectives, VO2max is an important measure, as it predicts the risks of cardiovascular conditions and mortality [3]. A meta-analysis of 33 studies and over 100,000 participants concluded that one metabolic equivalent higher CRF corresponding to 1-km/h higher running speed associates to 0.87 times the risk of all-cause mortality and 0.85 times the risk of a cardiovascular disease event [4].

An accurate direct measurement of VO2max requires expensive equipment and trained staff and is time-consuming. Moreover, the direct measurement using a graded aerobic exercise test to exhaustion is not convenient or even completely safe for patients with severe cardiovascular diseases and other high-risk individuals. Consequently, there is a need for indirect methods to estimate VO2max [5] in clinical practice. One of these indirect methods is to divide the heart rate at maximal exercise (HRmax) by the heart rate at rest (HRrest) and, then, multiply this quotient by a coefficient. This coefficient, termed as the proportionality factor in the text hereafter, corresponds to a theoretical value of about 15 in healthy well-trained young adult men and women [6,7]. By and large, the maximal accuracy of VO2max estimations based on HR is approximately ±15% mainly because of normal day-to-day variations in HR [8].

Chronological age per se is the main explanator of the relationship between VO2max and HR. Both VO2max and HRmax are tightly related to age due to the natural aging process [9,10]. In addition to age, many health-related behaviors have potential to affect the relationship between VO2max and HR. Indicators of these behaviors could include, at least, smoking habits and physical activity as well as obesity that indirectly associates with diet. Alcohol consumption, excluding patients with severe alcohol-related diseases [11], on the contrary, appear not to have evident short- or long-term effects on VO2max [12,13].

So far, the proportionality factor has been verified only in young adults and very little is known about effects of common health-related behavior on the relationship between VO2max and HR.

In this study, our purpose was to estimate the maximum mass-specific oxygen uptake (VO2max) from the ratio of the HRmax to HRrest in middle-aged men representing the general population. We also aimed at demonstrating effects of age, body mass index (BMI), smoking, and the daily total physical activity (TPA) on the relationship between VO2max and the ratio of HRmax to HRrest. To describe and compare strengths of these effects, we utilized the proportionality factor.

### MATERIALS AND METHODS

#### 1. Ethics statement

The Research Ethics Committee of Kuopio University approved the Kuopio Ischemic Heart Disease Risk Factor Study (KIHD) on December 1, 1983. All participants have given an informed written consent at KIHD baseline in 1980s.

#### 2. Study design and sample

This was a population-based cross-sectional study. We used data from the KIHD study that is an ongoing follow-up study originally designed to investigate risk factors for cardiovascular diseases among men living in the city of Kuopio and surrounding areas in Eastern Finland [14]. The KIHD study consists of two parts, the first including only 54-year-old men (n=1,166), and the second part including men from four different age cohorts, 42, 48, 54, and 60, at baseline examina-

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**Fig. 1.** Flow chart of the Kuopio Ischemic Heart Disease Risk Factor Study. Bold fonts indicate the starting and end points for this study. VO2max: maximum mass-specific oxygen uptake, HRmax: ratio of the heart rate at maximal exercise, HRrest: heart rate at rest, BMI: body mass index.
tions carried out 1984–1989 (n=1,516). Our data excerpt consisted of men belonging to the second part. We did not combine the first and second parts because they applied different methods to measure VO₂max. After excluding 882 participants from the second part based on their condition and measurements available, see Fig. 1 for detailed reasons, the final number of them included in the analysis was 634. Specifically, we excluded men with cardiovascular illnesses, as these conditions per se affect CRF and may distort VO₂max estimations based on HR. All KIHD participants underwent a thorough cardiovascular examination at baseline and self-reported their diseases and medications. Register data regarding the use of medication for high blood pressure including beta blockers completed self-reports (Kela license 35/522/2014). Table 1 shows number and mean±standard deviation values for height, weight, BMI, systolic blood pressure, diastolic blood pressure, VO₂max, HRmax, HRrest, and TPA in each age cohort together with smoking habits.

3. Measurements

CRF tests were carried out at the Kuopio Research Institute of Exercise Medicine (Kuopio, Finland). An electrically braked cycle ergometer (400L; Medical Fitness Equipment, Mearn, the Netherlands) with a linear increase in the workload by 20 W/min was used for the assessment of the amount of physical work done and a breath-by-breath method (MGC 2001; Medical Graphics, St. Paul, MN, USA) for the measurement of VO₂max referring to the average of values recorded over 8 seconds. An ECG recorder (Kone, Turku, Finland) recorded a standard 12-lead ECG before, during, and after the exercise test. Lakka et al [15] explain the test techniques in detail.

Weight and height were measured, and BMI calculated at KIHD baseline. We distributed study participants into three groups referring to normal weight (BMI<25 kg/m², n=240), overweight (BMI=25–30 kg/m², n=312), and obesity (BMI>30 kg/m², n=82).

Smoking status is based on study participants’ own reports. Non-smokers reported that they have never smoked (n=240), former smokers reported that they have not smoked within a month (n=184), and current smokers reported that they smoke (n=210).

In this study, the daily TPA refers to metabolic equivalent hours (MET-h). One MET approximates the rate of energy expenditure at rest that corresponds to 1 kcal/kg/h and 3.5 mL O₂ kg/min. For example, resting for 14 hours (14×1 MET) plus walking to work for 2 hours (2×3.5 MET, about 3.5 times harder than rest) plus working for 8 hours at light intensity (8×2 MET) result in 37 MET-h/d [15]. We distributed study participants into tertiles referring to moderately active (less than 43 MET-h/d, n=211), active (43–50 MET-h/d, n=212), and highly active (51 or more MET-h/d, n=211). This distribution is in accordance with TPA quantiles in similar cohorts, such as 40,708 Swedish men aged 45–79 [16]. No participants were sedentary. In KIHD, participants self-recorded all physical activities for 24 hours.

| Variable                                      | Age group (y) | p for trend* |
|-----------------------------------------------|---------------|--------------|
| No. of subject                                | 226           | 179          | 134          | 95            | <0.001 |
| Height (cm)                                   | 175.7±5.8     | 174.8±6.0    | 173.1±5.4    | 170.7±5.2    | <0.001  |
| Weight (kg)                                   | 81.5±11.8     | 79.5±10.5    | 79.9±12.1    | 76.3±10.8    | 0.001   |
| Body mass index (kg/m²)                       | 26.4±3.3      | 26.0±2.9     | 26.6±3.5     | 26.2±3.4     | 0.733   |
| Maximum mass-specific oxygen uptake (mL/kg/min) | 36.3±7.2      | 34.8±7.4     | 31.8±6.8     | 27.9±6.3     | <0.001  |
| Heart rate at maximal exercise (beats/min)    | 177.0±12.3    | 171.8±13.1   | 165.0±14.4   | 157.4±17.4   | <0.001  |
| Heart rate at rest (beats/min)                | 63.2±11.3     | 62.9±9.3     | 63.0±11.1    | 64.8±11.9    | 0.426   |
| Daily total physical activity (MET-h/d)       | 48.3±9.9      | 49.0±9.8     | 48.4±10.7    | 48.1±10.6    | 0.626   |
| No. of never-smokers                          | 85 (37.6)     | 65 (36.3)    | 59 (44.0)    | 31 (32.6)    | 0.977   |
| No. of former smokers                         | 62 (27.4)     | 51 (28.5)    | 40 (29.9)    | 31 (32.6)    | 0.362   |
| No. of current smokers                        | 79 (35.0)     | 63 (35.2)    | 35 (26.1)    | 33 (34.7)    | 0.363   |

Values are presented as number only, mean±standard deviation, or number (%).
MET-h: metabolic equivalent hours.
*The Jonckheere trend test.
hours and researchers determined their MET-h in each 30-minute period. Lakka and Salonen [17] explain the measurement of TPA in detail.

To describe the relationship between VO_{2max} and the HR_{max} to HR_{rest} ratio, we applied the proportionality factor that, in this study specifically, refers to a number used to multiply the HR_{max} to HR_{rest} ratio to yield an estimate of VO_{2max}.

4. Statistical analysis

To discover the proportionality factor, we performed a regression through the origin (RTO) in which VO_{2max} served as a dependent variable, and the HR_{max} to HR_{rest} ratio served as an independent variable. To determine effects of age, BMI, smoking status, and TPA on the proportionality factor, we carried out simple and multiple linear regressions. To detect trends in baseline characteristics across age cohorts, we used the Jonckheere trend test. IBM SPSS Statistics 25 (IBM Corp., Armonk, NY, USA) and GraphPad Prism 5 for Windows (GraphPad Software, Inc., San Diego, CA, USA) served as statistical platforms.

RESULTS

There were statistically significant (p<0.05) trends in height, weight, VO_{2max}, and HR_{max} across age cohorts. Younger men were taller and heavier, and they had higher VO_{2max} and HR_{max} (Table 1).

The equation for the estimated VO_{2max} based on the HR_{max} to HR_{rest} ratio was: VO_{2max}=10.46+8.43×(HR_{max}/HR_{rest}). The p-values for the constant and coefficient of the HR_{max} to HR_{rest} ratio were <0.001. The equation for an RTO was: VO_{2max}=12.11×(HR_{max}/HR_{rest}) with a p-value of <0.001. The coefficient of the HR_{max} to HR_{rest} ratio in the RTO expresses the proportionality factor.

The proportionality factor related inversely with age (Fig. 2). The mean (95% CI) proportionality factor was 12.79 (95% CI=12.47–13.10) in the youngest group, 12.55 (95% CI=12.19–12.90) in the second youngest group, 11.99 (95% CI=11.57–12.40) in the second oldest group, and 11.32 (95% CI=10.82–11.82) in the oldest group. To sum, in around 50-year-old men

![Fig. 2. The relationship between the proportionality factor expressing the association of maximal oxygen uptake to heart rate (y-axis) and age (x-axis). The dots indicate means, the errors bars indicate their 95% confidence intervals (CIs), the solid line indicates a linear regression, and the dotted lines indicate its 95% CI. The black square indicates 10 well-trained 30-year-old men [6].](image)

![Fig. 3. Effects of body mass index, smoking status, and total physical activity on the relationship between maximal oxygen uptake and heart rate expressed as the proportionality factor (y-axis) at different age groups (x-axis). The dots indicate means and the lines indicate linear regressions.](image)

MET-h: metabolic equivalent hours.
with no cardiovascular diseases, the ratio of HR_{max} to HR_{rest} should be multiplied by approximately 12 to create estimates of VO_{2max}.

Based on simple linear regressions, being overweight or obese as well as being a former or current smoker modified the effect of age on the proportionality factor (Fig. 3). The decrease from 42 to 60 years in the proportionality factor was among obese participants (slope -0.125/y) nearly twice as large than among normal weight participants (-0.065). The phenomenon was almost as strong between current smokers (-0.118) and non-smokers (-0.065). The level of physical activity did not affect the slope of the relationship between the proportionality factor and age, it was -0.08 at all TPA levels.

Based on a multiple regression, one year in age, one step change in BMI (normal weight, overweight, obese), smoking status (never, former, current), and TPA (moderately active, active, highly active) altered the proportionality factor used to multiply the ratio of HR_{max} to HR_{rest} by 0.08, 0.59, 0.40, and 0.14, respectively. The equation was: the proportionality factor=17.27-0.08×age-0.59×BMI category-0.40×smoking status+0.14×TPA. The p-values for the constant and coefficients of age, BMI, and smoking were <0.001, and that for the coefficient of TPA was 0.237.

Within the age range studied, 42–60, the negative effect of being obese exceeded those of smoking and being only moderately active. The change from normal weight to obese decreased the proportionality factor by 1.2, whereas the change from a never-smoker to a current smoker decreased it by 0.8, and the change from highly active to moderately active only by 0.3.

**DISCUSSION**

Uth et al [6] and Uth [7] demonstrated that in healthy well-trained 30-year-old men (n=46) and women (n=27) the ratio of HR_{max} to HR_{rest} should be multiplied by approximately 15 to predict VO_{2max}. In this study, we showed that this proportionality factor relates inversely to age and, therefore, the factor of 15 is invalid in the case of middle-aged men representing the general population.

The present sample of 634 middle-aged Finnish men resembles other Finnish and Swedish cohorts with respect to TPA, living habits, and common sociodemographic and health factors [16,18,19] Consequently, we suggest that as a rule of thumb, in 50-year-old men with no cardiovascular diseases, bronchial asthma, or cancer the proportionality factor is 12.

BMI affects the relationship between VO_{2max} and HR. From the viewpoint of CRF, being obese roughly corresponds to being 10 years older. This denotes that BMI could be more often considered a predictor of mortality and morbidity in cohort studies involving middle-aged men. Moreover, BMI is an important covariate in mortality and morbidity analyses because it, per se, does not correlate with age, as many other typical covariates do. Regarding the relationship between VO_{2max} and HR it is worth noticing that in indirect VO_{2max} estimations, age is considered as chronological age but also via HR_{max} that is strongly related to age [20].

Studies have proven, already decades ago, the negative effect of smoking on VO_{2max} in all age groups from adolescence to early senescence [13,21]. Our results agreed with the existing knowledge, the negative effect of smoking becomes stronger with increasing age [22], and suggest that smoking habits can be considered to create more precise estimates of VO_{2max} based on HR. Although the effect of smoking on the relationship between VO_{2max} and HR appears to be slightly weaker than the effect of being obese, in practice, smoking reduces the proportionality factor by one, likewise obesity does.

Our finding that the effect of physical activity on the relationship between VO_{2max} and HR is minor, indirectly, strengthens the opinion that self-reported physical activity, specifically, non-vigorous activity, and VO_{2max} do not strongly associate with each other [23,24]. A probable reason for this somewhat surprising finding is that mainly genetic factors determine VO_{2max} [25], which for its part means that a sedentary lifestyle does not inevitably lead to a low VO_{2max}. The association between VO_{2max} and vigorous physical activity [23,24], on the contrary, is stronger and, possibly, reflects the self-evident fact that if a person has a genetically determined high VO_{2max} it is easier for him or her to do vigorous activities.

Clinical practice can apply our results as follows. A 40-year-old normal weight never-smoking man serves as a starting point. His VO_{2max} can be estimated by multiplying the ratio of HR_{max} to HR_{rest} by 14. Every 10 years of age reduces the factor by one, or every year by 0.1. Similarly, the change in body weight from normal weight to obese as well as the change from never-smokin...
er to current smoker decrease the factor by one. As a result, VO\textsubscript{max} of a 60-year-old obese current smoker should be estimated by multiplying the ratio of HR\textsubscript{max} to HR\textsubscript{rest} by 10. TPA is ignored because the difference in the proportionality factor between moderately and highly active men was almost negligible, and because our data do not include physically inactive men.

The main strength of this study is the sample size (n=634). Typically, studies investigating the relationship between VO\textsubscript{max} and HR enrolls dozens of participants [6,7]. As a potential limitation we acknowledge that the linear estimation of VO\textsubscript{max} based on HR is not an optimal method, because HR increases linearly with VO\textsubscript{max} only at submaximal, circa 90\%–95\%, level [8]. We chose the linear approach nevertheless for practical reasons, to contribute applicability of results. Another limitation of this study relates to self-reporting with questionnaires as a data collection method. For example, the measurement method may significantly affect the observed level of physical activity [26].

CONCLUSIONS

Based on our findings, in around 50-year-old men with no cardiovascular diseases, bronchial asthma, or cancer, the ratio of HR\textsubscript{max} to HR\textsubscript{rest} should be multiplied by approximately 12 to yield an estimate of VO\textsubscript{max}. This number considerably differs from that related to well-trained 30-year-old men and women reported in earlier studies. BMI and smoking status can be considered in calculations to improve accuracy.

ACKNOWLEDGEMENTS

This research was supported by the Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio, Finland.

Conflict of Interest

The authors have nothing to disclose.

Author Contribution

Conceptualization: TPT, AV, MOS. Data curation: AV, TPT. Formal analysis AV. Investigation: AV, TPT, MOS. Methodology: AV, TPT. Supervision: TPT. Validation: TPT, MOS. Visualization: AV. Writing – original draft: AV. Writing – review & editing: AV, MOS, TPT.

Data Sharing Statement

The data required to reproduce these findings cannot be shared at this time as the data also forms part of an ongoing study.

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