Heart Rate Index—An Alternative Exercise-Based Equation for Estimating Peak VO_2

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Purpose: Heart rate (HR)-derived variables (HR reserve [HR_{peak} – HR_{rest}], chronotropic indices [attenuated HR response to exercise], HR recovery [attenuated HR response to exercise recovery], and peak HR index [HR_{peak}/HR_{rest}]) together with peak oxygen uptake (VO_{2peak}) are potential prognostic variables for cardiovascular and all-cause mortality. However, heart rate index (HRI) has not been established as a surrogate for VO_{2peak}, whether measured (Meas) or estimated (Est), during cycle ergometry (CE) and/or treadmill testing (TT).

Methods: HR-derived prognostic variables to assess cardiovascular outcomes were identified from 150 studies obtained from MEDLINE and Google Scholar searches. The Meas CE/TT-VO_{2peak} was reported in 81 studies (21 773 participants) and Est CE/TT-VO_{2peak} in 69 studies (331 435 participants). Using the HRI equation with metabolic equivalent (METs) = 6 × HRI – 5 (where HRI = peak HR/resting HR), HRI-VO_{2peak} was calculated from HR data reported in the 150 studies. The HRI-VO_{2peak} was then compared against group mean data for both Meas CE/TT-VO_{2peak} and Est CE/TT-VO_{2peak}.

Results: The difference between Meas CE/TT-VO_{2peak} and HRI-VO_{2peak} was 1% (7.15 ± 3.25 METs vs 7.08 ± 3.02 METs [P = .833], respectively). By comparison, the difference between Est CE/TT-VO_{2peak} and HRI-VO_{2peak} was 25.6% (8.94 ± 2.36 METs vs 7.12 ± 2.27 METs [P < .001], respectively). Moreover, HRI equation estimation of VO_{2peak} showed greater overprediction for TT, 26.6%, than for CE, 11.9%.

Conclusions: The Meas-VO_{2peak} and HRI-VO_{2peak} agreed closely. When compared with HRI-VO_{2peak}, Est-VO_{2peak} from currently used exercise-based equations shows significant overprediction. Use of HRI and/or Fitness Registry and the Importance of Exercise National Database (FRIEND) registry equations warrant consideration for more accurately estimating VO_{2peak}.

Key Words: exercise-based equations • heart rate-derived variables • heart rate index • peak oxygen uptake

KEY PERSPECTIVES

What is novel?

- Use of peak heart rate index (HRI) (peak heart rate divided by resting heart rate) in the HRI equation where METs = 6 × HRI – 5, provides a simple method for estimating peak VO_2.
- This study suggests that exercise-based equations used to estimate peak VO_2 with treadmill testing may be associated with overprediction in excess of 20%.

What are the clinical and/or research implications?

- Prediction of peak VO_2 from the HRI equation may provide a simple alternative to currently used exercise-based equations.

Heart rate (HR) is the simplest variable of the oxygen transport system to measure. Maximal or peak oxygen uptake, expressed as VO_{2peak}, has prognostic significance both in relation to cardiovascular (CV) and all-cause mortality in individuals with and without CV diseases such as coronary artery disease and heart failure.[1-5]

Measurements of both resting and peak HR (HR_{rest} and HR_{peak}) have independent prognostic significance for all-cause and CV disease; for HR_{peak}, it is likely through the association with VO_{2peak}.[5-8] Commonly used HR-derived variables are heart rate reserve (HRres), chronotropic incompetence (CI), and heart rate recovery (HRrec). Karvonen et al introduced HRres (the difference between HR_{peak} and HR_{rest}) as a method of defining aerobic training intensity,[9] but more recently, the relationship between the percentage of HRres and the percentage of O_2 reserve has challenged what minimal training thresholds are required for both fit and unfit subjects.[9-11] The adverse prognostic significance of CI, defined as an inadequate HR response to incremental exercise to volitional fatigue, was first reported in 1975.[12] Therefore, CI is determined by the reduction in HRres and is commonly set at 85% of the age-predicted maximum HR.[13] However, different definitions for CI confounded its use leading to the chronotropic index, with beta blocker use in heart failure further compromising interpretation.[14-16] With HRrec, a variety of time intervals postexercise have been suggested, ranging from 10 seconds to 1 to

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2 minutes.[17-19] In a meta-analysis of 9 studies in which a 1 minute interval postexercise was chosen, for every 10 beats per minute decrement in HRrec, CV events increased by 13% and all-cause mortality by 9%.[19] None of these 3 variables, though widely used for decades, have an accepted universal definition.

An infrequently used HR-derived variable is the heart rate index (HRI) that, when defined as the highest HR at peak incremental exercise or physical activity divided by HR at rest is expressed as HRI_{peak}.[20-22] HRI-VO_2 has a robust linear association with directly measured submaximal and maximal levels of VO_2, the prediction equation being metabolic equivalents (METs) = 6 × HRI − 5, with 1 MET being defined as a VO_2 of 3.5 mL O_2/kg/min.[22-24]

The present study enabled us to compare the accuracy of VO_{2peak} determined from HRI_{peak} to both measured (Meas) and estimated (Est) VO_{2peak} during cycle ergometry (CE) or treadmill testing (TT), expressed as Meas CE/TT VO_{2peak} or Est CE/TT VO_{2peak}.

METHODS

STUDY SELECTION

MEDLINE, Google Scholar, and cross-referencing were used to identify search terms of "heart rate reserve," "chronotropic incompetence/index," "heart rate recovery," and "heart rate ratio," which is expressed as "heart rate index" in this manuscript.

ELIGIBILITY CRITERIA

The eligibility criteria for final selection of studies included in this study were as follows: (1) The publication used a HR-derived variable (HRres, CI, HRrec, HR ratio, or HRI) in the analysis of CV outcomes. The variable was either frequently listed in the publication title, defined in the methods, detailed in the results, or interpreted within the discussion. (2) Within the "Results," a patient cohort had to meet the following requirements: (a) both a group mean HR_{rest} and HR_{peak} associated with the HR-derived variable, (b) the VO_{2peak} of the HR-derived variable under comparison, eg, CI vs chronotropic competence, and (c) the group mean VO_{2peak} for the compared variables was expressed as either mL/kg/min or as METs.

To minimize selection bias and to ensure a comprehensive range of studies incorporating both healthy individuals and those with chronic disease, a large number of studies were sourced (upper limit set at 150 studies), which met the above-referenced search criteria. A supplementary table is included as Supplemental Digital Content, available at: http://links.lww.com/JCRP/A576.

Exercise capacity was determined either by CE, TT, or both. Measurements of VO_{2peak} were defined as being either directly measured (indirect calorimetry) or estimated (from predictive equations and/or nomograms for TT or CE). The testing protocol was recorded, and for Est VO_{2peak}, equations and/or nomograms used for prediction were categorized as: (1) American College of Sports Medicine (ACSM) equations, (2) non-ACSM equations and/or nomograms, or (3) not referenced.[25] To avoid redundancy or duplicative inclusions, study selections excluded publications having similar patient cohorts based on the date of publication or research centers involved.

A comparison of directly Meas and Est VO_{2peak} data was made against HRI-VO_{2peak} calculated from HR_{rest} and HR_{peak}. The MET value of HRI-VO_{2peak} was calculated from the HRI equation where METs = 6 × HRI − 5, and HRI = peak HR/resting HR, with 1 MET corresponding to the widely accepted VO_2 at rest, ie, 3.5 mL O_2/kg/min.[22]

STATISTICAL ANALYSES

Categorical variables were expressed as numbers and percentages with continuous variables expressed as mean ± standard deviation. Student's paired *t* test (2-tailed) was used to compare HR-derived variables. Excel Data Analysis was used to determine the linear relationship (least squares method) of HRI to METs of Meas VO_{2peak} data with the inclusion of the correlation coefficient (R) and the standard error of the estimate (SEE).

RESULTS

From the 150 studies used for data extraction, HRres was used in 42 studies, CI in 72, HRrec in 81, and HRI in 2, with many studies using multiple HR-derived variables for analysis. The details of each of the 150 studies included in the present analyses are shown in tabular form in the Supplemental Digital Content, available at: http://links.lww.com/JCRP/A576. These include author, year of publication, category (normal and specific pathology), number of subjects, sex, age, testing device (CE, TT, or both), and VO_{2peak} (Meas [indirect calorimetry] or Est from predictive equations for TT and CE).

From the 150 studies reporting either Meas or Est CE/TT-VO_{2peak}, a total of 416 data points were obtained for HR_{rest}, HR_{peak}, and VO_{2peak}. The Meas CE/TT-VO_{2peak} was reported in 81 studies with 216 data points; CE was used in 41 studies with 109 data points, TT in 33 studies with 90 data points, and with both devices in 7 studies with 17 data points. The Est CE/TT-VO_{2peak} was reported in a total of 69 studies with 200 data points; CE was reported in 4 studies with 12 data points, with TT in 64 studies with 184 data points, and with both modalities in 1 study with 4 data points (Table 1).

The total number of subjects in the 81 studies reporting Meas CE/TT-VO_{2peak} was 21 773 (median = 101; range = 9-2231) with 71% male (mean age = 52 years, range = 11-72 years). For the 69 studies reporting Est CE/TT-VO_{2peak}, the total number of subjects included was 331 435 (median = 490; range = 14-120 705) with 65% male (mean age = 52 years, range = 22-81 years).

Detailed results for both test methods, CE and TT, and VO_{2peak}, as either Meas or Est-METs in conjunction with HRI-derived VO_{2peak}, are also expressed as METs and shown in Table 2.

For the 81 studies reporting Meas CE/TT-VO_{2peak}, there was little difference (1.0%) between Meas CE/TT METs at 7.15 ± 3.25 METs and HRI-METs at 7.08 ± 3.02 METs (P = .833). However, modestly larger, but still insignificant, differences were noted with specific testing modalities. For CE (41 studies), the difference in METs was −3.6% with respective MET values being 6.41 ± 2.82 METs for Meas-VO_{2peak} and 6.65 ± 2.75 METs for HRI-VO_{2peak} (P = .523). For TT (33 studies), the difference was 5.5% with respective values being 8.22 ± 3.62 METs for Meas-VO_{2peak} and 7.79 ± 3.37 METs for HRI-VO_{2peak} (P = .409).

From the 69 studies using Est-VO_{2peak}, a large and significant 25.6% difference was observed between Est-METs at 8.94 ± 2.36 METs and HRI-METs at 7.12 ± 2.27 METs (P = .001). With CE (4 studies), there was a smaller (11.9%) and not significant difference in METs with Est-METs being 8.74 ± 2.59 METs compared to HRI-VO_{2peak} METs of 7.81 ± 2.26 METs (P = .357). On the other hand, for the 64 studies with TT, the difference in METs was also large and significant at 26.6%, with Est-VO_{2peak} MET values of 8.99 ± 2.35 METs and HRI-METs at 7.10 ± 2.27 METs (P = .001).

Table 1

Studies Reporting Measured CE/TT-VO_{2peak} or Estimated CE/TT-VO_{2peak}, VO_{2peak} Data Points and Subject Sex and Age

	Measured CE/TT-VO_{2peak}		Estimated CE/TT-VO_{2peak}	
	Number of Studies	**Data Points**	**Number of Studies**	**Data Points**
All studies	81	216	69	200
Cycle ergometry	41	109	4	12
Treadmill testing	33	90	64	184
Both	7	17	1	4
Subjects				
Total, n	21 773		331 435	
Median (range)	101 (9-2231)		490 (14-120 705)	
Sex				
Male, % (range)	71 (9-100)		65 (0-100)	
Mean age, yr (range)	52 (11-72)		52 (22-81)	

Abbreviations: CE, cycle ergometry; TT, treadmill testing; VO_{2peak}, peak oxygen uptake.

Because of the large degree of overprediction from 64 studies observed with TT, a sub-analysis based on the method of estimating VO_{2peak} (equations and/or nomograms used) and test protocol employed was undertaken. Three categories were used for estimation, namely: (1) ACSM equations, (2) non-ACSM equations and/or nomograms, and (3) not referenced.[25] With studies listing use of a single testing protocol, 32 studies used the standard Bruce protocol, 7 studies used a modified Bruce protocol, and 14 used a non-Bruce protocol, eg, ramp, Naughton, and Cornell. Results of equations/nomograms used for Est VO_{2peak} are listed in Table 3 with protocols (Bruce, modified Bruce, and non-Bruce) for both Est and Meas VO_{2peak} being listed in Table 4.

Using ACSM equations (Table 3) showed a moderate and significant overprediction of 27.2% with respective values of Est VO_{2peak} and HRI-VO_{2peak} being 10.10 ± 2.49 METs and 7.94 ± 2.52 METs ($P < .007$). Use of non-ACSM equations and/or nomograms showed the lowest, but still significant, overprediction of 21.1% with respective values of Est VO_{2peak} and HRI-VO_{2peak} being 9.20 ± 2.32 METs and 7.60 ± 2.55 METs ($P < .001$). Studies in which the method of estimation was not referenced showed the largest and significant overprediction of 35.4%, between Est VO_{2peak} and HRI-VO_{2peak}, with respective values of 8.38 ± 2.20 METs and 6.19 ± 1.36 METs ($P < .001$).

Of the 64 treadmill studies estimating VO_{2peak}, 40 studies (62%) provided a reference for estimation of VO_{2peak} (Table 3). However, from analyses of these references, including cross-referencing, it was only possible to identify specific equations in 14 studies (22%) with 8 studies having a single equation and 6 studies having multiple equations. For the 14 studies with identified equations and/or nomograms, Est VO_{2peak} was 9.47 ± 2.38 METs and HRI-VO_{2peak} 8.22 ± 2.97 METs ($P = .023$), a difference of 15.2%. For the remaining 50 studies with an unidentified equation method, Est VO_{2peak} was 8.81 ± 2.33 METs and HRI-VO_{2peak} was 6.69 ± 1.81 METs ($P = .001$), a difference of 31.8%.

In determining the effect of TT protocol (Table 4), use of the standard Bruce protocol was associated with a greater and significant overprediction of 28.4% between the Est VO_{2peak} of 8.87 ± 2.30 METs and the HRI-VO_{2peak} of 6.91 ± 1.64 METs ($P < .001$). The modified Bruce showed the largest overprediction of 38.3% with the Est VO_{2peak} being 9.42 ± 2.03 METs and HRI-VO_{2peak} at 6.81 ± 1.24 METs ($P < .001$). Use of a non-Bruce protocol showed a smaller and not significant overprediction of 15.9% with respective values being Est VO_{2peak} at 9.18 ± 2.75 METs and HRI-VO_{2peak} at 7.92 ± 3.54 METs ($P = .056$). No significant difference between Meas VO_{2peak} and HRI-VO_{2peak} was observed for the Bruce, modified Bruce, or non-Bruce protocols. For the Bruce protocol, Meas VO_{2peak} was 9.63 ± 1.57 METs and HRI-VO_{2peak} was

Table 2

Number of Studies and Data Points by Test Method for Measured and Estimated VO_{2peak} and the Associated HRI-VO_{2peak} Presented as METs ± SD

	Number of Studies	Data Points	Meas/Est METs	HRI-METs	*P*-Value	% Difference[a]
Measured CE/TT-VO_{2peak}						
All studies	81	216	7.15 ± 3.25	7.08 ± 3.02	.833	0.9
Cycle ergometry	41	109	6.41 ± 2.82	6.65 ± 2.75	.523	−3.6
Treadmill	33	90	8.22 ± 3.62	7.79 ± 3.37	.409	5.5
Both	7	17	6.15 ± 2.09	6.07 ± 1.75	.914	1.3
Est CE/TT-VO_{2peak}						
All studies	69	200	8.94 ± 2.36	7.12 ± 2.27	.001	25.6
Cycle ergometry	4	12	8.74 ± 2.59	7.81 ± 2.26	.357	11.9
Treadmill	64	184	8.99 ± 2.35	7.10 ± 2.27	.001	26.6
Both	1	4	7.40 ± 1.70	6.40 ± 2.54	.536	15.6

[a][(Meas/Est METs - HRI-METs) / HRI-METs] x 100

Abbreviations: CE, cycle ergometry; EST, estimated; HRI, heart rate index; Meas; measured; MET, metabolic equivalent; TT, treadmill testing; VO_{2peak}, peak oxygen uptake.

Table 3

Treadmill Studies With Estimated VO_{2peak} and HRI-VO_{2peak} Presented as METs ± SD and Categorized by Equations and/or Nomograms

Treadmill Equations Estimated VO_{2peak}	Number of studies	Data Points	Est METs	HRI-METs	*P*-Value	% Difference[a]
ACSM equations	9	22	10.10 ± 2.49	7.94 ± 2.52	.007	27.2
Non-ACSM equations and/or nomograms	31	91	9.20 ± 2.32	7.60 ± 2.55	.001	21.1
Not referenced	24	71	8.38 ± 2.20	6.19 ± 1.36	.001	35.4
Studies – equations	14	49	9.47 ± 2.38	8.22 ± 2.97	.023	15.2
Studies – no equations	50	135	8.81 ± 2.33	6.69 ± 1.81	.001	31.8

Abbreviations: ACSM, American College of Sports Medicine; EST, estimated, HRI, heart rate index; Meas; measured; MET, metabolic equivalent; $VO_{2peak,}$ peak oxygen uptake.
[a][(Est METs - HRI-METs / HRI-METs)] x 100.

9.52 ± 1.73 METs (P = .852); for the modified Bruce protocol, Meas VO_{2peak} was 6.61 ± 1.81 METs and HRI-VO_{2peak} was 5.88 ± 1.60 METs (P = .183); and for non-Bruce protocols, Meas VO_{2peak} was 8.46 ± 4.70 METs and HRI-VO_{2peak} was 8.14 ± 4.21 METs (P = .760).

To test the relationship of HRI to VO_{2peak} within this study, regression analysis was performed on data from the 81 studies containing Meas VO_{2peak} (Figure 1), with the relationship of HRI to METs being METs = 6.025x – 4.986 (R = 0.93, SEE 1.19 METs or 4.16 mL/kg/min). This closely approximates the regression analysis of the original data used to construct the HRI equation, which can simply be expressed as METs = 6 × HRI – 5 without any loss of accuracy.[22]

DISCUSSION

This study demonstrates a robust association of HRI-derived VO_{2peak} and Meas VO_{2peak}, determined by indirect calorimetry. The simplicity of HRI-derived VO_{2peak} is that it is determined from 2 routinely measured HR variables during exercise testing, HR_{rest} and HR_{peak}. However, only 2 of the 150 studies in this review used it to assess CV outcomes.

From the 81 reports analyzed in the present study, which employed Meas CE/TT-VO_{2peak} as determined by indirect calorimetry, the group mean value of the 216 data points of Meas CE/TT-VO_{2peak} was 7.15 ± 3.25 METs with the HRI-VO_{2peak} being 7.08 ± 3.02 METs (P = .833), a difference of as little as 1%. By comparison, in the 69 studies using Est CE/TT-VO_{2peak} prediction equations, the group mean value of the 200 data points was 8.94 ± 2.36 METs with the HRI-VO_{2peak} being 7.12 ± 2.27 METs ($P < .001$), an overprediction of 25.6%. The overprediction seen in the present study is similar to that previously reported in an analysis of treadmill testing where Est VO_{2peak} was 21.1% in excess of Meas CE/TT-VO_{2peak}.[26]

The present study indicates that overprediction of VO_{2peak} was greater with TT when using HRI-VO_{2peak} as a comparator, +26.6% for TT vs +11.9% for CE. In the 69 studies using Est VO_{2peak}, 326 475 subjects (99%) were assessed with TT compared with only 4043 subjects (1%) with CE; this bias indicates the need for improved accuracy of prediction of VO_{2peak} with TT.

The consistency of the HRI equation, y = 6.025x – 4.986 (R = 0.93, SEE 1.19 METs or 4.16 mL/kg/min) closely approximates the regression analysis from the original investigation of 60 studies where y = 6.018x – 4.928 (R = 0.98, SEE 0.64 METs or 2.24 mL/kg/min).[22] Reported SEE values associated with maximal treadmill testing assist with determining accuracy of prediction. Peterman et al examined linear correlation and SEE in 10 studies of commonly used treadmill protocols (Bruce, modified Balke-Ware, and individualized protocols) for maximal exercise prediction.[27] The SEE for these studies ranged from 2.5 to 5.6 mL/kg/min, with a mean of 4.14 mL/kg/min,[27] which is in close agreement with the reported SEE of our study, 1.19 METs or 4.16 mL/kg/min, supporting the validity of the HRI prediction method. As management of severe symptomatic heart disease may require complex surgical and medical intervention, determination of VO_{2peak} is of critical importance to assist with optimal decision making. However, prediction of VO_{2peak} in the least fit is associated with the greatest error (overprediction

Table 4

Treadmill Studies With Estimated and Measured VO_{2peak} and HRI-VO_{2peak} Presented as METs ± SD and Categorized by Treadmill Protocol

Treadmill Protocol	Number of Studies	Data Points	Est/Meas METs	HRI-METs	*P*-Value	% Difference[a]
Estimated VO_{2peak}						
Bruce	32	83	8.87 ± 2.30	6.91 ± 1.64	.001	28.4
Modified Bruce	7	20	9.42 ± 2.03	6.81 ± 1.24	.001	38.3
Non-Bruce	14	48	9.18 ± 2.75	7.92 ± 3.54	.056	15.9
Measured VO_{2peak}						
Bruce	5	17	9.63 ± 1.57	9.52 ± 1.73	.852	1.2
Modified Bruce	8	20	6.61 ± 1.81	5.88 ± 1.60	.183	12.4
Non-Bruce	13	36	8.46 ± 4.70	8.14 ± 4.21	.760	3.9

Abbreviations: EST, estimated; HRI, heart rate index; Meas; measured; MET, metabolic equivalent; $VO_{2peak,}$ peak oxygen uptake.
[a][(Est/Meas METs - HRI-METs / HRI-METs)] x 100

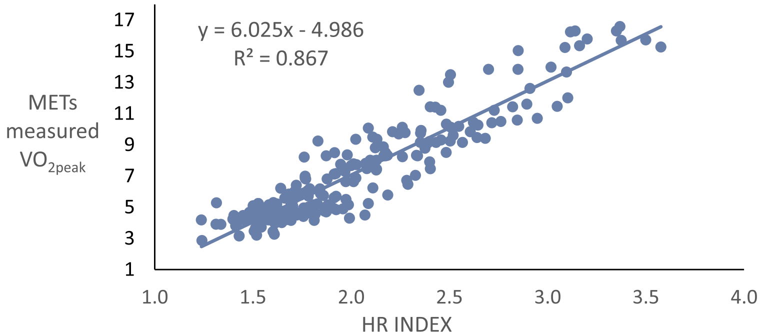

Figure 1. Regression analysis of HR Index vs METs of data derived from current study. Abbreviations: HR, heart rate; MET, metabolic equivalent; VO_{2peak}, peak oxygen uptake.

of 31.2%).[26] With an observed SEE of 4 mL/kg/min, the error of prediction in severely limited patients with a VO_{2peak} in a range of 10 to 18 mL/kg/min (New York Heart Association class 3 and 4) may be of an order of 20% to 40%, highlighting the need for direct measurement of VO_{2peak} in this group.[28]

Overprediction of Est VO_{2peak}, compared to studies using Meas VO_{2peak}, may be due to multiple factors, namely (1) hand holding of treadmill rails[29-31]; (2) need for population-specific equations for heart failure,[27,32,33] chronic obstructive pulmonary disease,[34] the elderly,[35] and cancer[36]; (3) use of protocols that fail to achieve steady-state values and an adequate test duration, ideally 8 to 12 minutes[37,38]; and (4) misuse of ACSM equations when incorporation of a time component (test duration) is ignored.[39-41] A recent development, likely to improve the accuracy of predicted values, is treadmill and CE equations developed from Fitness Registry and the Importance of Exercise National Database (FRIEND) registry data.[42-45]

In the present study, use of non-ACSM equations and/or nomograms was associated with less predictive error than reliance on either ACSM equations or failure to reference the method of prediction. The Bruce protocol is the most widely used exercise test method for general screening for CV disease and the associated cardiorespiratory fitness assessment supported by the frequency of use within this study.[46,47] Unlike other treadmill protocols such as Balke, Naughton, Cornell, and ramp testing, the Bruce protocol utilizes relatively large increments (2-3 METs) in work load every 3 minutes, as opposed to smaller increments every 1 to 2 minutes, when compared with other protocols.[37,38] The standard ACSM walking equation uses speed and incline grade to estimate VO_2. There is no time component. If this equation is used in conjunction with both the Bruce and modified Bruce protocols, estimation of VO_2 will therefore be the same at the commencement or completion of a 3-minute stage, thereby magnifying the error of estimate. Need for a time component when estimating VO_2 during the Bruce protocol became apparent from discrepancies noted in Meas VO_2 studies.[39,40] Inadequately detailed methodology for estimating VO_{2peak} was observed in a large percentage (78%) of treadmill studies within our analysis, which suggests a failure to understand the limitations of commonly used prediction equations.

Given the prognostic significance of VO_{2peak} for all-cause and CV mortality in healthy adults and those with chronic disease, future studies should evaluate HR-derived indices and other data obtained during exercise testing to improve CV risk assessments.[4,5,48,49] Data from this study suggest that, when compared against Meas VO_{2peak}, HRI-VO_{2peak} derived from the HRI equation appears to yield a more accurate measure of VO_{2peak} than that provided by currently used equations and nomograms, this estimate being independent of the test method and work intensity. As the derivation of the HRI equation was based on studies of subjects in sinus rhythm, its use in patients with cardiac pacing, arrhythmias such as atrial fibrillation, and heart transplantation remains unclear. The HRI-VO_{2peak}, with its utility as a surrogate of directly measured VO_2 as shown by this study, would suggest that HRI_{peak} warrants further investigation as a HR-derived prognostic variable.

STUDY LIMITATIONS

In using HR data from the database of 150 studies, no attempt was made to discriminate the method for measurement of HR. HR_{rest} may be recorded in a supine, seated, or standing position using various time intervals at rest before measurement. As such, this measurement lacks standardization. Similarly, HR_{peak} may relate to a single or time-averaged measurement. No restriction was placed on the method of estimation of VO_{2peak} with most authors citing reference equations or alternatively, "metabolic equivalents were estimated from treadmill speed and grade," without reference to the duration achieved at a given stage. Finally, as the derivation of the HRI equation was based on studies of subjects in normal sinus rhythm, its use in patients with cardiac pacing, atrial fibrillation, and heart transplantation remains unfounded. Accordingly, attempting to approximate exercise capacity, expressed as peak METs, using the HRI equation in these patient subsets is unwarranted.

CONCLUSIONS

In this review of HR-derived prognostic variables obtained from 150 studies involving a total of 353 208 subjects, HRI demonstrated a robust association with Meas VO_{2peak}. Because of its simplicity, HRI provides an ideal method for estimating VO_{2peak}, namely use of 2 HR variables (HR_{rest} and HR_{peak}), incorporated into the equation, $METs = 6 \times HRI - 5$, where HRI equals the ratio of HR_{peak}/HR_{rest}. These findings hold regardless of the presence of CV disease and/or beta-blocker therapy.[22] Further research to assess the usefulness of HRI for estimating VO_{2peak} is warranted as it may show closer agreement with equations derived from the FRIEND registry than that obtained from conventional published formulae referred to in this study.[43,50]

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