ORIGINAL RESEARCH

Nonexercise Measurements as Predictors of Chronotropic Response to Exercise

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ABSTRACT

Background: Chronotropic response to exercise is a clinically important health indicator. Direct assessment of chronotropic response to exercise is problematic in many clinical settings because of lack of access to required exercise equipment. Also, abnormal chronotropic response to exercise is often asymptomatic, which hinders the ability to identify individuals who require exercise-based chronotropic response evaluation. The purpose of this study was to investigate a set of nonexercise, contemporary assessments as predictors of chronotropic response to exercise.
Methods: This prospective, cross-sectional study investigated nonexercise predictors of chronotropic response to exercise. Forty participants (19 women, 21 men; mean age = 34.3 years, SD = 14.5) performed a graded exercise work rate protocol while heart rate was continuously monitored. Chronotropic response to exercise was recorded as the heart rate-work rate slope. Data on a variety of nonexercise measures were also collected.
Results: Multivariable regression analysis indicated that sex, self-reported physical activity, body mass index, waist circumference, and isometric grip strength were independent predictors of chronotropic response to exercise and, as a subset, resulted in the strongest prediction model ($R = 0.80$, $R^2 = 0.64$, $P < 0.001$).
Conclusion: The results of this study suggest that a group of nonexercise measurements are predictive of chronotropic response to exercise. These findings provide a basis for future research to determine if these nonexercise predictors can be used to screen for chronotropic response to exercise abnormalities. Also, exercise interventions that target physical activity, body composition, and muscle strength may improve chronotropic response to exercise. *J Clin Exerc Physiol*. 2022;11(1):19–26.

Keywords: assessment, predict, heart rate response

BACKGROUND

Chronotropic response to exercise reflects the ability of an individual's heart rate to increase as a result of incremental increases in exercise work rate and is a health indicator for both symptomatic and asymptomatic individuals (1). For example, an abnormal heart rate response to increased exercise work rate (also known as chronotropic incompetence) is strongly associated with diseases like type 2 diabetes (2) and is a risk factor for major adverse cardiovascular events (3). Further, abnormal chronotropic response to exercise is significantly correlated to early death, even after adjusting for established cardiovascular risk factors (4).

Direct measurement of chronotropic response to exercise is performed by evaluating heart rate response to graded exercise work rates and has been reported as outcomes such as achieving a percentage of predicted maximum heart rate, the chronotropic index, and the slope of heart rate change relative to exercise work rate change (5–7). Although chronotropic response to exercise is a clinically meaningful outcome measure, many clinical settings (for example, Primary

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Care) do not have readily available access to exercise equipment nor qualified personnel that are needed for direct measurement of chronotropic response to exercise.

In addition, individuals with chronotropic response to exercise abnormalities are often asymptomatic (8,9). Gulati et al. (8) found that asymptomatic women with chronotropic incompetence were at a higher risk of early death, when compared to asymptomatic women without chronotropic incompetence. Jouven et al. (9) conducted a retrospective study of asymptomatic men who completed a graded exercise work rate protocol and found that study participants with abnormal chronotropic response were at a higher risk of mortality. The asymptomatic nature of irregular chronotropic response to exercise indicates the need for identification of nonexercise, clinical assessments that are predictive of chronotropic response to exercise.

Like chronotropic response to exercise, cardiorespiratory fitness is also a clinically important variable because low cardiorespiratory fitness is correlated to outcomes such as sudden cardiac death (10). Interestingly, Jurca et al. (11) conducted a study to examine nonexercise predictors of cardiorespiratory fitness, which included variables that are relatively easy to measure and are frequently evaluated in contemporary practice. Their findings indicated that the variables of sex, age, body mass index (BMI), resting heart rate, and self-reported physical activity were independently associated with cardiorespiratory fitness and that the combination of these variables could be used to predict cardiorespiratory fitness (11). Similarly, nonexercise measurements may also be predictive of chronotropic response to exercise.

A problem exists in that examination of chronotropic response to exercise is not feasible in many clinical settings because of the lack of access to requisite exercise equipment and qualified personnel. In addition, no studies have been conducted to investigate a group of nonexercise assessments as predictors of chronotropic response to exercise. If contemporary, nonexercise measurements are predictive of chronotropic response to exercise, such measurements may be further investigated to potentially screen individuals who are at risk of a cardiovascular event and serve as a basis for conducting a more in-depth, exercise-based cardiovascular evaluation. Further, some predictors may be modifiable with exercise and other lifestyle changes, which would provide clinicians with a rationale for prescribing exercise and lifestyle interventions. The research hypothesis was that selected nonexercise variables can predict chronotropic response to exercise. The primary purpose of this study was to investigate nonexercise measurements as predictors of chronotropic response to exercise. A secondary aim was to examine the nonexercise assessments as predictors of cardiorespiratory fitness.

METHODS

Study Design

This prospective, cross-sectional study investigated nonexercise measurements as predictors of chronotropic response to exercise. All data collection procedures were conducted by personnel who were trained on the study protocol. Each study participant completed a valid graded exercise work rate protocol while heart rate was continuously monitored. Data on a variety of nonexercise measures were also collected. Regression analysis was used to construct a prediction model where nonexercise measurements were entered as independent variables and chronotropic response to exercise was entered as the dependent variable.

Study Setting, Recruitment, and Participant Criteria

This study was approved by the institutional review boards of the University of Arkansas for Medical Sciences, University of Central Arkansas, and Harding University. This investigation was conducted on the campuses of both of these universities. Participants were recruited from the northwest Arkansas and central Arkansas geographic areas by posting study recruitment announcements and by word-of-mouth. To be included in this study, participants had to be between the ages of 18 to 69 years and fluent in the English language. A detailed health history was collected from any person who volunteered to participate in this study using a standardized health history questionnaire created specifically for this investigation. History of a medical condition identified by the American Heart Association as an absolute contraindication to exercise was a study exclusion criterion (12). Additional exclusion criteria were: angina (stable or unstable), uncontrolled hypertension, proliferative retinopathy, severe peripheral neuropathy, nephropathy, autonomic neuropathy, history of coronary artery disease, history of myocardial infarction, taking a beta-blocker drug, and pregnancy. Further, no participant reported using a supplement that affected heart rate. Volunteers with a physical impairment that precluded participation in this study were also excluded. Before being enrolled in this study, all participants were informed of the experimental procedures and completed a written informed consent document.

Data Collection of Nonexercise Variables

Jurca et al. (11) found that age, sex, BMI, resting heart rate, and self-reported physical activity level were correlated to cardiorespiratory fitness. Thus, these nonexercise variables were hypothesized to potentially be predictive of chronotropic response to exercise. Age and sex data were obtained as part of baseline data collection.

On the same day of chronotropic response to exercise assessment, body anthropometric data were collected. Body mass (in kilograms) was measured using a digital, calibrated scale. Height (in centimeters) was measured using a stadiometer. BMI was then calculated using the formula BMI = body mass ÷ (height [in meters])^2.

Resting heart rate (in beats per minute) was recorded immediately prior to chronotropic response to exercise assessment. Participants assumed a seated position in a chair, and resting heart rate was assessed using a wireless heart rate monitor (Polar H7, Polar Electro Oy, Kempele, Finland) after 5 minutes of rest.

Self-reported physical activity data was collected using a physical activity questionnaire, as described by Jurca et al. (11). Participants were asked to choose 1 of 5 levels that best describe their usual pattern of daily physical activity, including activities related to home and family care, transportation, occupation, exercise and wellness, and leisure or recreation. The levels were defined as follows:

a. Level 1: inactive or little activity other than usual daily activities;
b. Level 2: regularly (≥ 5 days per week) participate in physical activities requiring low levels of exertion that result in slight increases in breathing and heart rate for at least 10 minutes at a time;
c. Level 3: participate in aerobic exercises such as brisk walking, jogging or running, cycling, swimming, or vigorous sports at a comfortable pace or other activities requiring similar levels of exertion for 20 to 60 minutes per week;
d. Level 4: participate in aerobic exercises such as brisk walking, jogging, or running at a comfortable pace, or other activities requiring similar levels of exertion for 1 to 3 hours per week; or
e. Level 5: participate in aerobic exercises such as brisk walking, jogging, or running at a comfortable pace, or other activities requiring similar levels of exertion for over 3 hours per week.

Physical activity data were based on participants' responses to the physical activity questionnaire. Physical activity was recorded as Level 1, 2, 3, 4, or 5.

Since waist circumference has been associated with cardiorespiratory fitness (13) and cardiovascular conditions (14), waist circumference was postulated to be a predictor of chronotropic response to exercise. On the same day of chronotropic response to exercise evaluation, waist circumference (in centimeters) was determined by measuring the circumference around the waist in standing, where a tape measure was positioned at the level of the umbilicus and the measurement was taken after the participant exhales, as described by Earnest et al. (13).

Blood pressure and chronotropic response to exercise have a commonality in that both are modulated by the autonomic nervous system (15,16). Data from previous studies also suggest that cardiorespiratory fitness is an independent correlate in the development of hypertension (17). Thus, resting blood pressure was hypothesized to be a potential predictor of chronotropic response to exercise. Resting blood pressure of each study participant was examined immediately prior to chronotropic response to exercise measurement using a sphygmomanometer, and a single blood pressure measurement was taken after participants sat for 5 minutes in a chair, as performed in contemporary clinical practice (18).

Isometric grip strength is another nonexercise measurement and is a common component of a physical examination (19). Thus, isometric grip strength was investigated as a potential predictor of chronotropic response to exercise. Isometric grip strength was assessed using a handgrip dynamometer. The dominant hand (the hand that the study participant uses for throwing) was used for testing. Each participant assumed a seated position with the shoulder in neutral (approximately 0 degrees of abduction and external rotation). Participants maintained their elbows in about 90 degrees of flexion. The forearm was in a neutral position (0 degrees of supination) with the wrist in a neutral position (0 degrees of extension and ulnar deviation). Participants were instructed to grip the hand dynamometer with their fingers around the second handle position. Afterward, participants were instructed to grip the device as hard as possible for 5 seconds. Relative isometric grip strength was recorded as the maximum force produced after a single trial (in kilograms) divided by BMI. Previous research suggests that these procedures for measuring isometric grip strength are reliable (20).

Assessment of Chronotropic Response to Exercise

Evaluation of chronotropic response to exercise was performed in a climate-controlled laboratory environment, maintained at approximately 70°F (21°C). The participants were informed of the procedures and donned a wireless, chest strap heart rate monitor (Polar H7, Polar Electro Oy, Kempele, Finland). Lauer et al. (4) analyzed data from the Framingham Heart Study and found that an impaired increase in heart rate in response to submaximal graded exercise was associated with a higher risk of coronary heart disease. After individual adjustments of the seat and handlebars of the cycle ergometer and an introduction of the Borg rating of perceived exertion scale (21), participants performed a submaximal graded exercise work rate protocol using a calibrated cycle ergometer, as described by Björkman et al (22). The procedure included 4 minutes of cycling at a work rate of 30 watts and a pedal frequency of 60 revolutions per minute (stage 1), directly followed by 4 minutes of cycling at a higher individually chosen work rate (in watts) and a pedal frequency of 60 revolutions per minute (stage 2). The individually chosen work rate was based on a rating of perceived exertion of 14 on the Borg scale and achieving a heart rate of at least 120 $b \cdot min^{-1}$. Previous research indicates that this protocol is valid for measuring chronotropic response to exercise in that the quotient of heart rate increase divided by work rate increase is a predictor of maximum oxygen uptake (22).

Chaudhry et al. (6) reported chronotropic response to exercise as the slope of increase in heart rate relative to increase in work rate (heart rate-work rate slope). The mathematical basis for assessing chronotropic response to exercise using the heart rate-work rate slope is that heart rate response can be evaluated across 2 or more time points of graded exercise and is a function of work rate change. This method also normalizes heart rate response based on differences in individually chosen work rate during stage 2 of the protocol. To examine heart rate response to the graded exercise work rate protocol, each participant's heart rate and work rate data were recorded at 3 periods: (a) rest, (b) during the final minute of stage 1, and (c) during the final minute of stage 2. The slope of heart rate increase relative to work rate increase was calculated for each participant using linear regression. To address the secondary aim of this study, cardiorespiratory fitness was reported as maximum oxygen uptake (milliliters of oxygen uptake per kilogram of body mass per minute), determined using the validated prediction equation of Björkman et al. (22) ($R^2 = 0.83 - 0.86$, standard error of the estimate = 0.28 liters of oxygen uptake per minute).

Data Analysis

The primary purpose of this investigation was to examine nonexercise measurements as predictors of chronotropic response to exercise. An a priori power analysis was conducted to estimate the number of participants needed to obtain a statistical power of at least 0.90 at an alpha level of 0.05. For multivariable regression analysis, a coefficient of determination (R^2) of 0.50 was considered as reflective of the model having moderate prediction strength. An a priori power analysis estimated a total sample size of 30 participants would detect a coefficient of determination (R^2) of 0.50 when using 9 independent variables.

Descriptive statistics were computed and reported as counts, means, and standard deviations, as appropriate. Multivariable regression analysis, using the best subset selection approach, was performed to construct a prediction model for chronotropic response to exercise. In best subset selection, every possible combination of variables is examined to determine the best subset of predictors that results in the strongest prediction model (23). Best subset selection was based on the lowest Akaike information criterion (24). Nonexercise measurements were entered as potential independent (predictor) variables and chronotropic response to exercise as the dependent variable. A second multivariable regression analysis was conducted by entering nonexercise measurements as possible predictor variables and cardiorespiratory fitness as the dependent variable. Normality of residuals was evaluated with probability-probability (P-P) plots. The Pearson correlation coefficient (r) was used to investigate the association between chronotropic response to exercise and cardiorespiratory fitness. An alpha level of 0.05 was used for statistical analyses. Data were analyzed using IBM SPSS Statistics 27 (SPSS Inc, Chicago, Illinois).

RESULTS

A total of 40 participants were enrolled in this study. No participants withdrew from this investigation. Participant descriptive statistics are reported in Table 1. Multivariable regression analysis indicated that sex, self-reported physical activity, BMI, waist circumference, and isometric grip strength were independent predictors of chronotropic response to exercise and, as a subset, resulted in the strongest prediction model ($P < 0.001$). Figure 1 is a scatter plot with a line of regression that illustrates the prediction strength of the chronotropic response to exercise prediction model. The standardized regression coefficients (beta weights) for sex, self-reported physical activity, BMI, waist circumference, and isometric grip strength were −0.490, −0.270, −0.574, 0.425, and −0.316, respectively. The absolute values of beta weights determined that the relative order of importance of these variables in predicting chronotropic response to exercise (from least important to most important) was self-reported physical activity, isometric grip strength, waist circumference, sex, and BMI. The coefficient of determination (R^2) was 0.64, meaning that 64% of the total variance in chronotropic response to exercise was explained by the predictor variables.

Multiple regression analysis also revealed that age, sex, waist circumference, resting heart rate, systolic blood pressure, and diastolic blood pressure were independent predictors of cardiorespiratory fitness, and as a subset, resulted in the most powerful prediction model ($P < 0.001$). Figure 2 is a scatter plot with a line of regression that depicts the prediction strength of the cardiorespiratory fitness prediction model. The beta weights for age, sex, waist circumference, resting heart rate, systolic blood pressure, and diastolic blood pressure were −0.357, −0.477, −0.692, −0.255, 0.207, and −0.126, respectively. According to the absolute values of beta weights, the relative order of importance of these variables in predicting cardiorespiratory fitness (from least important to most important) was diastolic blood pressure, systolic blood pressure, resting heart rate, age, sex, and waist circumference. The R^2 was 0.84, meaning that 84% of the total variance in cardiorespiratory fitness was explained by the predictor variables.

For both models, P-P plots indicated that residuals were normally distributed, and multicollinearity was not identified. Refer to Table 2 for a summary of the regression

TABLE 1. Participant descriptive data.

Parameter	Value[a]
Sex, women:men	19:21
Age, y	34.3 ± 14.5
BMI, $kg \cdot m^{-2}$	26.5 ± 4.2
Resting heart rate, $b \cdot min^{-1}$	73.2 ± 9.4
Waist circumference, cm	89.9 ± 13.8
Systolic blood pressure, mm Hg	122.1 ± 10.4
Diastolic blood pressure, mm Hg	73.5 ± 8.4
Isometric grip strength, $kg \cdot BM^{-1}$	1.4 ± 0.5
Physical activity level	3.8 ± 1.1
Estimated cardiorespiratory fitness, $\dot{V}o_2 \cdot kg\ BM^{-1}$	46.5 ± 11.5
Chronotropic response to exercise, heart rate-work rate slope	0.5 ± 0.1

BMI = body mass index

[a]Sex data are presented as counts. All other data are presented as mean ± standard deviation.

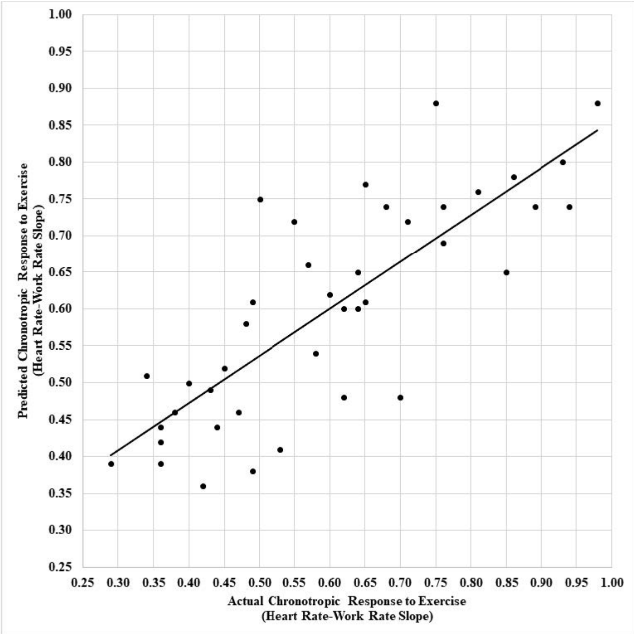

FIGURE 1. Scatter plot of actual vs predicted chronotropic response to exercise. Actual values are based on the chronotropic response to exercise assessment protocol. Predicted values are based on the multiple regression model using nonexercise predictors. Black-filled circles represent the intersection of actual and predicted values. The solid black line represents the regression line. Prediction equation:
$1.165 - (0.179 \times A) - (0.043 \times B) - (0.025 \times C) + (0.006 \times D) - (0.108 \times E)$.
A = sex (0 for women and 1 for men); B = self-reported physical activity level; C = body mass index; D = waist circumference (centimeters); E = isometric grip strength (kilograms of force divided by body mass index).

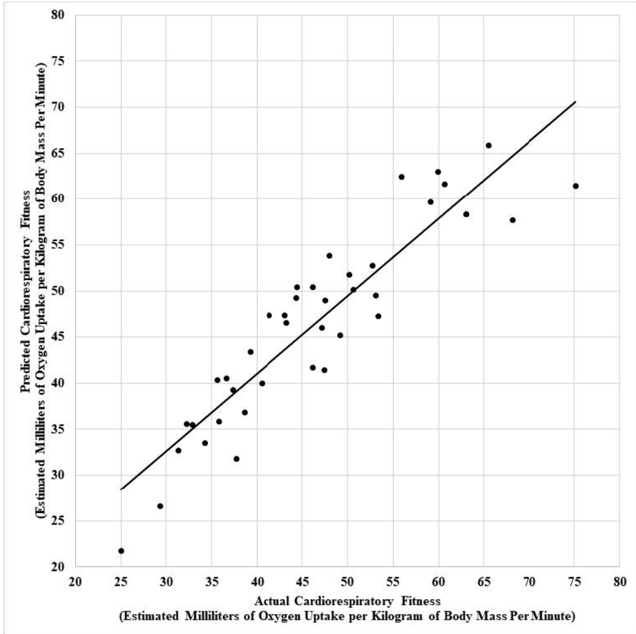

FIGURE 2. Scatter plot of actual vs predicted cardiorespiratory fitness. Actual values are based on estimated cardiorespiratory fitness from the graded exercise work rate protocol. Predicted values are based on the multiple regression model using nonexercise predictors. Black-filled circles represent the intersection of actual and predicted values. The solid black line represents the regression line. Prediction equation:
$110.137 - (0.284 \times A) + (10.908 \times B) - (0.580 \times C) - (0.311 \times D) + (0.230 \times E) - (0.172 \times F)$.
A = age (years); B = sex (0 for women and 1 for men); C = waist circumference (centimeters); D = resting heart rate (beats per minute); E = systolic blood pressure (millimeters of mercury); F = diastolic blood pressure (millimeters of mercury).

analyses findings. Also, a statistically significant correlation was found between chronotropic response to exercise and cardiorespiratory fitness ($r = -0.42$, $P = 0.006$).

DISCUSSION

To our knowledge, this study is the first investigation of a group of nonexercise measurements as predictors of chronotropic response to exercise. The research hypothesis was that selected nonexercise variables can predict chronotropic response to exercise. The findings of this study indicated that sex, self-reported physical activity, BMI, waist circumference, and isometric grip strength were independent predictors of chronotropic response to exercise and that the subset of these predictors resulted in the strongest prediction model. Individually, sex, self-reported physical activity, and BMI were statistically significant predictors ($P < 0.05$)

The order of importance of these variables in predicting chronotropic response to exercise (from least important to most important) was self-reported physical activity, isometric grip strength, waist circumference, sex, and BMI. In a practical sense, men with higher scores on self-reported physical activity, isometric grip strength, and BMI, along with smaller waist circumferences, were more likely to have less of an incline in heart rate-work rate slope. In our study, heart rate-work rate slope and estimated cardiorespiratory fitness were negatively correlated, meaning a lower heart rate-work rate slope was associated with higher cardiorespiratory fitness levels. One could interpret the combination of these findings as men with characteristics of greater overall physical fitness had a higher likelihood of a more favorable chronotropic response to exercise.

Chronotropic response to exercise has been reported as outcomes such as achieving a percentage of predicted maximum heart rate, the chronotropic index, and the heart rate-work rate slope (5–7). In our study, the heart rate-work rate slope was selected as the method for measuring chronotropic response to exercise. A strength of assessing chronotropic response to exercise using the heart rate-work rate slope is that heart rate response can be evaluated across 2 or more time points of graded exercise. This method also normalizes heart rate response based on differences in individually chosen work rates during a graded exercise protocol. Chaudhry et al. (6) also measured chronotropic response to exercise as the heart rate-work rate slope. Specifically, Chaudhry et al. (6) calculated the percent change in heart rate-work rate slope from the early phase (slope 1) of a graded exercise protocol to the slope during the late phase (slope 2). Slope 1 represented the heart rate-work rate slope during the 2

TABLE 2. Multivariable regression results

Prediction Model	Nonexercise Predictor Unstandardized Regression Coefficients (B)	Nonexercise Predictor Standardized Regression Coefficients (Beta)	Multiple Correlation Coefficient (*R*)	Coefficient of Determination (R^2)	Standard Error of the Estimate (SEE)
Chronotropic Response to Exercise			0.80	0.64	0.11
Sex	−0.179, ($P < 0.001$)	−0.490			
SRPA	−0.043, ($P = 0.02$)	−0.270			
BMI	−0.025, ($P = 0.03$)	−0.574			
WC	0.006, ($P = 0.12$)	0.425			
IGS	−0.108, ($P = 0.06$)	−0.316			
Cardiorespiratory Fitness			0.91	0.84	5.03
Age	−0.284, ($P < 0.001$)	−0.357			
Sex	10.908, ($P < 0.001$)	0.477			
WC	−0.580, ($P < 0.001$)	−0.692			
RHR	−0.311, ($P = 0.002$)	−0.255			
SBP	0.230, ($P = 0.06$)	0.207			
DBP	−0.172, ($P = 0.18$)	−0.126			

BMI = body mass index; DBP = diastolic blood pressure; IGS = isometric grip strength; RHR = resting heart rate; SBP = systolic blood pressure; SRPA = self-reported physical activity; WC = waist circumference

minutes before the ventilatory anaerobic threshold. Slope 2 represented the heart rate-work rate slope during the last 2 minutes of the graded exercise protocol. The study by Chaudhry et al. (6) also included participants with nonobstructive coronary artery disease. In comparison, we used a graded exercise protocol that does not require the measurement of the ventilatory anaerobic threshold and has been validated as a measure of chronotropic response to exercise in that change in heart rate as a function of change in work rate is an independent predictor of maximum oxygen uptake (22). Other differences between Chaudhry et al. (6) and our study was that we reported heart rate-work rate slope across the entire duration of the graded exercise protocol, as opposed to percent change in slope between 2 different phases of graded exercise, and our study included healthy individuals without a history of coronary artery disease.

Although published data are limited regarding nonexercise measurements, previous research studies have examined correlations between exercise-based outcome measures and various assessments of chronotropic response to exercise. The relationship between heart rate response to exercise and cardiorespiratory fitness is well established in healthy populations and in people with various diagnoses (19). In our study, we used the graded exercise protocol described by Björkman et al. (22), who found that the quotient of heart rate increase divided by work rate increase was negatively associated with cardiorespiratory fitness (maximum oxygen uptake). Brubaker et al. (25) conducted a study to investigate the relationship between chronotropic response to exercise and maximum oxygen uptake in patients with heart failure. The findings of Brubaker et al. (25) indicated a positive correlation between heart rate reserve (a measure of chronotropic response to exercise) and maximum oxygen uptake. Witte et al. (26) reported a positive association between maximum oxygen uptake and heart rate reserve in patients with heart failure who were not taking beta blocker medications. Like Björkman et al. (22), we found a negative correlation between cardiorespiratory fitness (estimated maximum oxygen uptake) and chronotropic response to exercise (heart rate-work rate slope). The differences between studies in direction of correlation can be explained by the differences in assessment and mathematical expression of chronotropic response to exercise. Cardiorespiratory fitness was not included in the regression analysis to develop the chronotropic response to exercise prediction model since cardiorespiratory fitness was estimated and not directly measured. Also, the primary aim of this study was to investigate correlations between nonexercise variables and chronotropic response to exercise, which was the reason for not including directly measured cardiorespiratory fitness as a possible predictor. Because of possible reader interest, we reported nonexercise predictors of estimated cardiorespiratory fitness and the associated prediction model, which was the secondary aim of this study.

The results of this study could be explained by the relationship between chronotropic response to exercise and cardiorespiratory fitness, along with a common subset of nonexercise predictors. As mentioned, data from previous research suggest that chronotropic response to exercise and cardiorespiratory fitness are correlated. Similarly, we also found an association between chronotropic response to exercise and cardiorespiratory fitness. The findings of Jurca et al. (11) indicated that the nonexercise variables of sex, age, BMI, resting heart rate, and self-reported physical activity were predictors of cardiorespiratory fitness and that the combination of these variables resulted in a considerably strong prediction model ($R = 0.76 - 0.81$, $R^2 = 0.57 - 0.65$). In our investigation, the variables of sex, self-reported physical activity, BMI, waist circumference, and isometric grip strength were predictive of chronotropic response to exercise and the subset of these variables resulted in a prediction model with marked prediction strength ($R = 0.80$, $R^2 = 0.64$). Because of the association between chronotropic response to exercise and cardiorespiratory fitness, one could expect a common subset of predictors for both assessments.

The clinical relevance of this investigation was considered. Chronotropic response to exercise is important in that an abnormal chronotropic response has been linked to outcomes such as cardiovascular events and mortality (3,4). However, direct assessment of chronotropic response to exercise is problematic in many situations because of a lack of access to necessary exercise equipment and qualified personnel. Also, patients with abnormal chronotropic response to exercise are often asymptomatic (8,9), limiting a clinician's ability to identify patients who require exercise-based chronotropic response evaluation. Our study identifies a subset of nonexercise assessments that are part of a contemporary clinical examination and were predictive of chronotropic response to exercise. A noteworthy point is that physical activity, BMI, waist circumference, and isometric grip strength are modifiable predictors, meaning these variables can be changed through exercise and other lifestyle modifications. Previous studies have also shown the correlation between chronotropic response to exercise and cardiorespiratory fitness. Thus, exercise interventions that target physical activity, body composition, muscle strength, and cardiorespiratory fitness may be beneficial for improving chronotropic response to exercise. Lastly, logical next steps for future research would be to investigate the ability of these nonexercise variables to predict chronotropic response to exercise abnormalities and to conduct this study in at-risk populations.

A limitation of this study was the inconsistent methodologies for assessment of chronotropic response to exercise that have been reported in previous research (5–7). As discussed in the literature, a standardized method for measuring chronotropic response to exercise would allow comparison of data between different studies (27). Similar to Chaudhry et al. (6), we reported chronotropic response to exercise as the heart rate-work rate slope. Readers should also interpret the cardiorespiratory fitness prediction model with caution in that estimated maximum oxygen uptake was entered as the dependent variable, which possibly added prediction error. As previously stated, the cardiorespiratory prediction model was related to the secondary aim of this study and the findings were included because of potential reader interest.

Participants were not asked to refrain from caffeine consumption prior to assessment of chronotropic response to exercise. Previous studies that have investigated the effect of caffeine on heart rate response to exercise have reported conflicting results (28). Glaister and Gissane (28) stated that such discrepancies could be caused by statistical error related to small sample sizes. Because of such conflicting data, Glaister and Gissane (28) conducted a meta-analysis with the purpose of examining the effect of caffeine on various physiological responses to exercise, including heart rate. Glaister and Gissane (28) found that caffeine increased minute ventilation, blood lactate, and blood glucose, but they found it had a suppressive effect on ratings of perceived exertion. Caffeine had no effect on respiratory exchange ratio, oxygen consumption, nor heart rate.

In our study, blood pressure data were collected using a single measurement, whereas an average of multiple measurements would have likely improved accuracy. Yet, calculating an average of multiple blood pressure measurements is not a method used in routine clinical practice (18). Because the method of blood pressure assessment in our investigation is contemporary practice, the study findings are more generalizable to clinical environments. A point to consider is that the multivariable regression analysis did not identify blood pressure as a predictor of chronotropic response to exercise and blood pressure was not entered into the prediction model. Therefore, blood pressure data did not add error to the prediction model.

CONCLUSION

Chronotropic response to exercise has been correlated to meaningful clinical outcomes. However, barriers exist for assessing chronotropic response to exercise in many practice settings. The results of this study suggest that a subset of nonexercise, contemporary measurements are predictive of chronotropic response to exercise. These findings provide context for future research to determine if these nonexercise predictors can be used to screen for chronotropic response to exercise abnormalities. Clinicians also have a basis for prescribing exercise interventions to target physical activity, body composition, and muscle strength to improve chronotropic response to exercise.

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