Temperature 1:2, 101–106; July/August/September 2014; © 2014 Landes Bioscience

The thermal-circulatory ratio (TCR)
An index to evaluate the tolerance to heat

Itay Ketko[1,2], Uri Eliyahu[1], Yoram Epstein[2,3], and Yuval Heled[1,2,*]

[1]The Warrior Health Research Institute; Israel Defense Forces; Medical Corps; Tel Hashomer, Israel; [2]Heller Institute of Medical Research; Sheba Medical Center; Tel Hashomer, Israel; [3]Sackler Faculty of Medicine; Tel Aviv University; Tel Aviv, Israel

Keywords: heat injury, core temperature, thermoregulation, exercise

Abbreviations: Bpm, beat per minute; HI, heat intolerant; HT, heat tolerant; HTT, heat tolerance test; SD, standard deviation; TCR, thermal circulatory ratio; T_{rec}, body core temperature (rectal temperature)

Introduction: The common practice in the Israel Defense Force is that all exertional heat related injuries victims undergo a heat tolerance test (HTT) as a part of the "return to duty" process. The purpose of this study was to develop a quantitative, supportive physiological index for the assessment of the HTT based on the understanding that heat strain level should combine the thermal and cardiovascular strains.

Materials and Methods: The HTT results of 104 individuals with a history of heat injuries were retrospectively analyzed after randomly divided into two groups (an analysis group and a validation group). Rectal temperature and heart rate were monitored continuously during the test. Using the ratio between those two variables we constructed the TCR (Thermal-Circulatory Ratio) index and defined thresholds for determining heat tolerance based on the HTT.

Results: Using a TCR value of 0.279 [°C/bpm] or less after completing the 120 min HTT can be used as a significant measure to distinguish between heat tolerance and heat intolerance individuals with sensitivity and specificity of 100% of 89%, respectively. In addition, a TCR value of 0.320 [°C/bpm] or less calculated after 60 min was found as a significant measure to determine heat tolerance with 100% sensitivity and 69% specificity. The latter threshold may assist in significantly shortening the HTT for those individuals whose TCR value matches this criterion.

Discussion and Conclusion: A new index (TCR) that combines the thermal and cardiovascular responses to exercise-heat stress was found to be a valid measure, with high sensitivity and specificity, to support the distinguishing between heat tolerance and heat intolerance individuals following a HTT. Furthermore, the suggested index may enable to shorten the HTT, which will make the test more efficient.

Introduction

Heat strain is the physiological response to thermal stress. The level of the physiological strain can be characterized by assessing the equivalent compensatory effort of the body to meet the external and internal thermal loads. When work is performed, blood flow is increased mainly in order to meet the additional oxygen requirements of the working muscles. A further increase in blood flow is required for the thermoregulatory purposes - conducting heat from the body core to the skin. Thus, heart rate can potentially be used as an indicator of the total circulatory response to thermal strain.[1] Surplus of body heat, the amount of heat that cannot be dissipated, is reflected by body core temperature; thus, during physical exercise, when a large amount of heat is generated by the working muscles, body core temperature will tend to rise. Therefore, the change in body core temperature is used as a criterion for the evaluation of body heat storage, which reflects the combined metabolic and environmental heat stresses.[1] Overall the total physiological strain is determined by the combination of the circulatory and thermal loads, which are complementary to each other.[2]

Exertional heat related injuries are a spectrum of clinical disorders that are typical to workers, athletes and soldiers. Two of the exertional heat related injuries are characterized by elevated body temperature; heat exhaustion and exertional heat stroke.[3] Among those two entities exertional heat strokes is considered a medical emergency, because of the rise of body core temperature to such a level that imposes tissue damage (above 40 °C) that may lead to a multi system failure.[3,4]

A common practice in the Israel Defense Force is that all exertional heat related injuries patients undergo a heat tolerance test (HTT) about 6 wk following the injury, as part of the "return to duty" process.[5,6] This test, which is in practice for over 3 decades, is based on the physiological responses - rectal temperature and heart rate - to an exercise-heat stress. The data obtained in the test is evaluated subjectively by an experienced staff member according to certain criteria.[6] Recently, the dynamics of change in rectal temperature during the HTT have been re-evaluated, in

*Correspondence to: Yuval Heled; Email; yuval.heled@sheba.health.gov.il
Submitted: 06/18/2014; Revised: 06/26/2014; Accepted: 06/26/2014; Published Online: 07/02/2014
http://dx.doi.org/10.4161/temp.29752

order to suggest a quantitative criterion in regard to the change in rectal temperature during the last part of the test, serving as a supportive diagnostic tool especially in borderline cases.[8] This criterion, however, is based on body core temperature alone. The purpose of this study was to develop a quantitative, physiological index for the assessment of HTT based on the fact that heat strain evaluation should include the measures of the entire physiological strain components that are involved in the thermoregulatory response to high heat load.

Materials and Methods

HTT protocol

The HTT protocol was described in details by Moran et al. 2007.[6] In short, the test is performed in a climatic chamber at a temperature of 40 °C and 40% relative humidity (extreme heat load). The exercise protocol includes walking, in a euhydrated condition, on a motor driven treadmill at a speed of 5 kph at a 2% grade for two hours. During the HTT, heat strain is assessed by continuously monitoring body core temperature (T_{rec}) and heart rate.[6,7] The current criteria for heat intolerance, which were set for young male adults, are determined when at the end of the test (120 min) body core temperature exceeds 38.5 °C, heart rate exceeds 150 beat per minute (bpm), or when either does not tend to reach a plateau.[6,8]

Database

The HTT results of consecutive 104 young (18–21 y.) male individuals with a history of heat injuries that performed the test as a part of the return to duty process, were retrospectively analyzed. Those individuals were randomly divided into two groups: an analysis group (39 heat tolerant (HT) and 20 heat intolerant (HI) subjects), defined according to common criteria in our Institute and a validation group (35 heat tolerant subjects and 10 heat intolerant subjects). Five of the heat intolerant subjects, that were part of the analysis group, ceased the test when reaching the safety limit of 39 °C (at 65, 84, 89, 100 and 111 min during the HTT).

Throughout the entire exercise-heat exposure, the subjects' body core temperature was measured with a rectal thermistor (YSI-401) inserted 10 cm beyond the anal sphincter. Temperatures were displayed continuously and automatically stored by the monitoring BIOPAC system. Heart rates were monitored continuously and stored by a Polar heart watch (POLAR RS800cx, Finland).

The construction of the index

Based on the concept that the expression of thermal strain relates to the cardiovascular and thermal responses, we suggest the following index to differentiate between heat tolerant and intolerant individuals during a HTT:

$$\text{Thermal} - \text{Circulatory Ratio (TCR)} = \frac{\text{Trec}}{\text{HR}}$$

Where: T_{rec} = rectal temperature (°C) and HR = heart rate (bpm).

The index was calculated retrospectively for each time point measurement (every minute) during the entire HTT, suggesting to reflect the dynamics of the physiological responses during the exercise-heat stress exposure. In order to minimize the index's fluctuations due to momentarily rapid changes in the heart rate, the mean of each consecutive 5 min of the TCR value along the test was used.

The minimal value to accept heat tolerance is based on two standard deviations (SD) above the mean value of TCR in the heat intolerant individuals, calculated at each time point along the test. With this threshold criterion, assuming a normal distribution of the TCR, 2.5% of heat tolerant individuals might be defined as heat intolerant (false positive), but no heat intolerant individual will be classified as heat tolerant bearing in mind that false negatives (see statistical analysis) are not allowed.

Model validation

The index applicability was validated by retrospectively applying it double blinded to determine the threshold on 45 random HTT results (post-factum: 35 subjects were heat tolerant and 10 subjects were heat intolerant). For this purpose, a computerized algorithm was developed to calculate sensitivity and specificity of the index, which enabled to compare post-hoc the experts' assessment of tolerance to heat with the prediction of heat tolerance using the TCR.

Statistical analysis

The Kolmogorov - Smirnov test was used to determine normal distribution of the TCR values. Continuous variables (TCR, heart rate and T_{rec}) were compared between HT and HI groups using student *t* test and categorical variable (moving average value of TCR in comparison to the cut off values and between the HI and HT groups) were compared using Pearson's chi-square.

In the context of the present study, sensitivity measures the proportion of actual positives (i.e., heat intolerant individuals) using the index and specificity measures the proportion of negatives (i.e., heat tolerant individuals). Sensitivity and specificity were calculated as follows:

$$\text{Sensitivity} = \frac{\text{True postives}}{\text{True positives} + \text{False negatives}}$$

$$\text{Specificity} = \frac{\text{True negatives}}{\text{True negatives} + \text{False positives}}$$

Where: True positives are heat intolerant individuals who were correctly identified using the TCR; True negative are heat tolerant individuals who were correctly identified; False positives are heat tolerant individuals who were incorrectly identified as heat intolerant; False negatives are heat intolerant individuals who were incorrectly identified as heat tolerant. Statistical analysis was conducted using the SPSS software (Ver. 20) and the JMP software (Ver. 7). Statistical significance was set at $P < 0.05$.

Results

The basic HTT results (mean ± SD values of T_{rec} and heart rate) of the analysis group are presented in **Figure 1**. The dynamics of

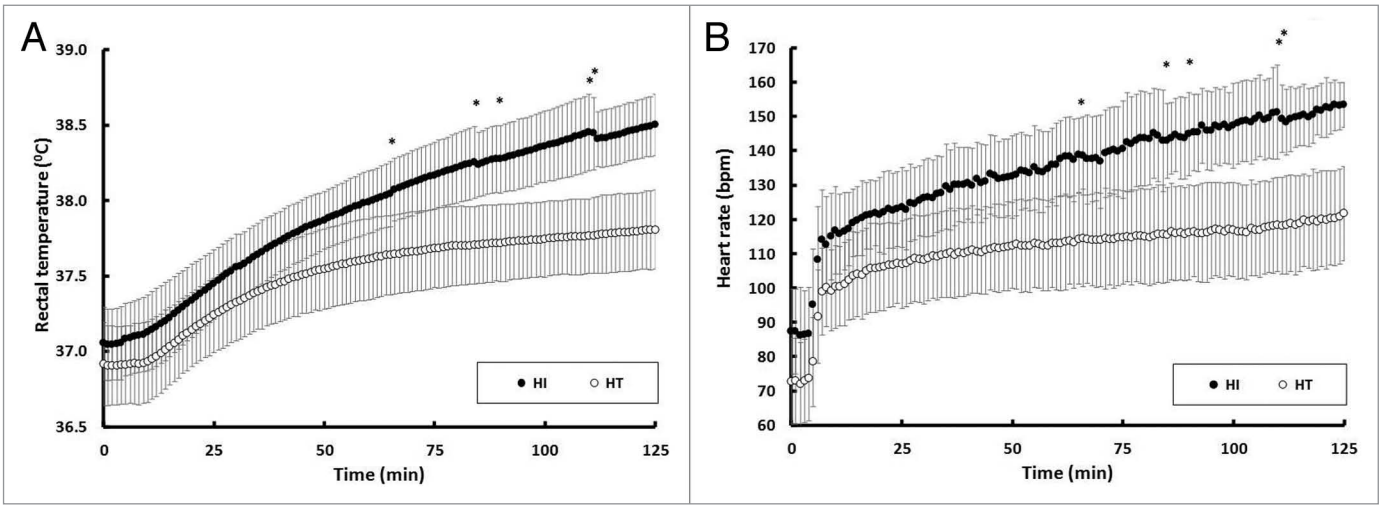

Figure 1. Changes in T_{rec} (1A) and heart rate (1B) (mean ± SD) during the HTT for the analysis group. HT - heat tolerant; HI - heat intolerant. * denotes the point in time 5 of the heat intolerant subjects ceased the test.

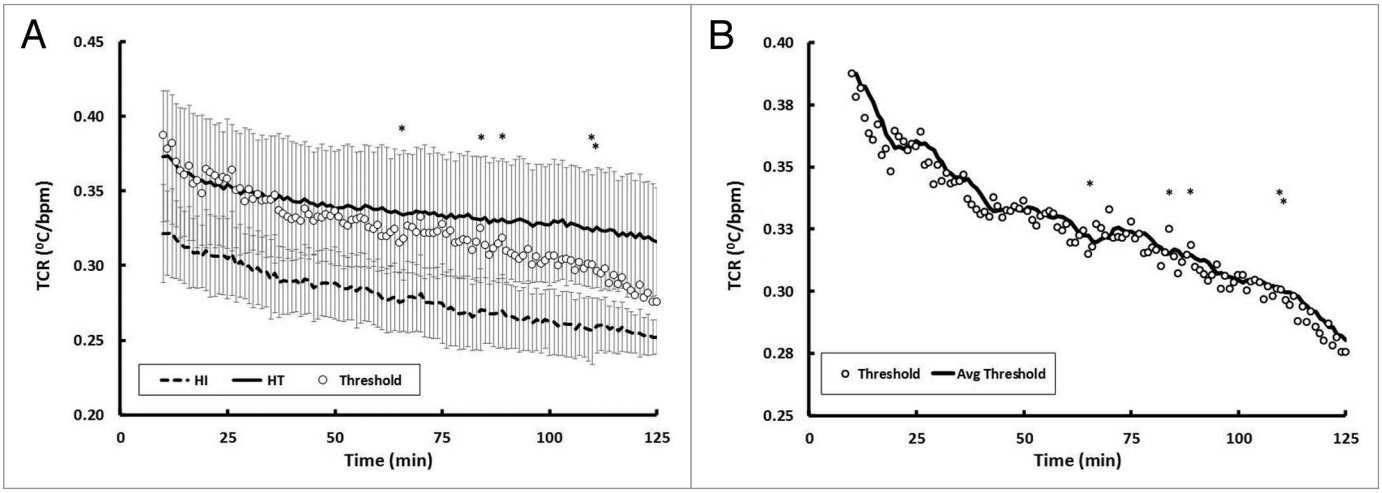

Figure 2. (**A**) Changes in TCR values (mean ± SD) during the HTT for the analysis group, (excluded the first 10 min of exposure). Heat tolerant (HT - solid line). Heat intolerant (HI - dashed line),. * denotes the point in time 5 of the heat intolerant subjects ceased the test. (**B**) threshold (open circles) and the moving average of TCR for each consecutive 5 min (line).

T_{rec} and heart rate of the HT group showed a tendency to plateau whereas among the HI group the tendency of both variables was steadily increasing. The HT group significantly differed from the HI group in both T_{rec} and heart rate at every time point during the exercise period ($P < 0.02$ and $P < 0.001$, respectively). The sudden changes in the T_{rec} and heart rate curves are due to five heat intolerance subjects who have ceased the test after reached the test's safety limit of 39 °C (marked by an asterisk). Those subjects were characterized with high values of T_{rec} and heart rate and therefore after they ceased the test, the average values were first decreased and then returned to the normal dynamics and markedly increased (at both T_{rec} and heart rate curves).

The mean ± SD values of TCR for the heat tolerance and heat intolerance individuals in the analysis group and the mean +2SD of the TCR calculated for the HI group in the analysis group at each time point are presented in **Figure 2A**. The mean value of TCR was significantly higher for the HT group compared with the HI group at each time point during the test ($P < 0.0001$).

The TCR mean value of the HI group +2 SD of the last 5 min. of the HTT was 0.279 °C/bpm. Tested in the validation group, this value yielded 100% sensitivity and 89% specificity. It was therefore set as a threshold value of TCR that enables to distinguish between heat tolerant and heat intolerant individuals.

The usage of the index was expanded in order to find a predicted TCR threshold earlier in the test in order to try and shorten the HTT for those who are defined as heat tolerant. The average TCR value of each consecutive 5 min. of the heat intolerant individuals and the specificity for those thresholds along the test are shown in **Figures 2B and 3**, respectively. Accordingly, the TCR mean value of the last 5 min. of the 1st hour - 0.320 °C/bpm was chosen, yielding 100% sensitivity and 69% specificity.

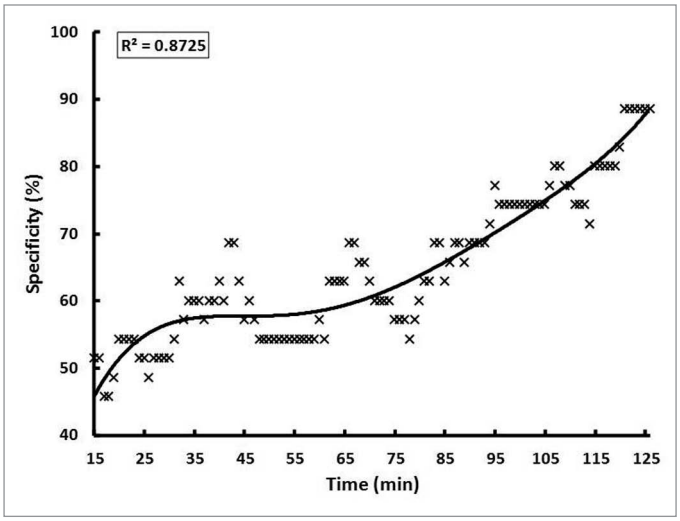

Figure 3. Specificity percentage results (marked as x) after applying our proposed method on the validation group. For that we used different thresholds calculated for each consecutive 5 min along the HTT. Presented here the results without the resting period (5 min) of the test. black line is the polynomial from 5th degree which fits best the model.

Table 1 summarizes the comparison between the mean TCR values calculated for the heat tolerant and heat intolerant individuals within the validation group after 60 min and 120 min of the HTT and in comparison to the mentioned above thresholds calculated for those cases. Significant differences were found in all cases.

Discussion

An index (TCR) that combines the thermal and cardiovascular response to exertional heat stress has been developed and was found to be a valid measure with high sensitivity and specificity to distinguish between heat tolerant and heat intolerant individuals during a HTT. The heat tolerance test is a common practice in our Institute and until recently the diagnosis of heat intolerance was mostly made by a professional examiner based on reference values that were set for this test; one of the criteria is the tendency of T_{rec} to plateau toward the end of the test.[6] Recently, Druyan et al. described mathematically the tendency of the T_{rec} to reach a plateau during the HTT.[8] This measure gives a supportive tool to the examiner providing a quantitative measure that is helpful in determining intolerance to heat, without the need to rely on an experienced staff member, whose judgment might rely on subjective qualitative approach. This is mostly helpful especially in borderline cases. Nevertheless, this proposed cut-off value is based only on the dynamics of T_{rec} and does not account for the cardiovascular system response (and strain).[1,2] Taking into account the importance of combining both thermal and cardiovascular responses to exertional heat stress and the need for a quantitative measure for heat intolerance, the TCR was developed as an additional physiological criterion for evaluating individuals who undergo a HTT.

The understanding that the physiological strain during exertional heat stress should be determined by a combined measure of the circulatory and the thermal mechanisms has resulted in many attempts to develop appropriate physiological indices.[10,11] In 1996, Frank et al. introduced the cumulative heat strain index (CHSI) that is based on the physiological cost of those components that are involved in maintaining the thermal balance of the body.[2,12] The index relies on the area under the hyperthermic curve (rectal temperature) and the circulatory strain (heart beats count). The CHSI was found to be a valid comparative index for differentiating between levels of strain but it is limited in its use for certain reasons.[11] First, CHSI has no threshold and thus cannot be used for comparing between individuals. For each individual other values will be calculated without the ability to compare between them. Second, the CHSI is a cumulative stain index that requires using an integrating operator for the rectal temperature (it is the area under the curve) and a summation operator for the cumulative heart beats, which are not commonly measured. The TCR is a simpler index in its nature and simple to use. It is based on a simple ratio between two straight-forward measurements (at a specific time point), core body temperature and heart rate, which can easily be read from commonly used devices.

Another index based on T_{rec} and heart rate is the physiological strain index (PSI) that was described by Moran et al. in 1998.[12] The PSI rates the physiological strain on a universal scale of 0–10. Unlike other indices that were valid only under certain specific conditions, the PSI was found to be a valid and simple physiological index under different protocols (climate and clothing), either online or when data analysis is applied. Nevertheless, this index also suffer from some backdraws; e.g., it simply adds heart rate and T_{rec} with the same weight and does not allow for determining physiological failure due to a safety limit in one of the parameters.

It should be emphasized however that the CHSI and PSI, among other indices, were developed in order to evaluate the induced heat strain during exertional heat stress rather than to define thresholds that distinguishing heat tolerant from heat intolerant individuals performing a HTT.

In our study a TCR value of 0.279 °C/bpm at the end of the 120 min test was found to be an effective measure to distinguish between heat tolerant and heat intolerant subjects with specificity and sensitivity of 89% and 100%, respectively. A thorough investigation of those 11% false positives individuals (4 individuals), revealed the following: in one individual heart rate did not tend to plateau at the upper acceptable value for this HTT. The second case was falsely identified as heat tolerant, although the dynamics of change in T_{rec} did not tend to plateau. The third case was borderline and only by using the criterion set by Druyan et al.[8] the expertise decision could be overruled. In the fourth case TCR indicated that the individual is heat intolerant according to the expert's decision, which could not be overruled, but according to all physiological parameters the subject should be categorized as heat tolerant. Those cases emphasize the difficulty in investigating physiological behavior based on multiple parameters and the importance of creating a valid mathematical tool especially for borderline cases. Nevertheless, the fourth case described above

Table 1. Comparison of the mean ± SD TCR values of heat tolerant (HT) and heat intolerant (HI) individuals after the 1st hour and at the end of the test, within the groups (*student's *t* test) and regard to the threshold values (**Pearson's chi-square test)

	Threshold	HT (mean ± SD)	HI (mean ± SD)	HT > HI	HT > Threshold	HI < Threshold
Average TCR @ t = 61–65 min.	0.320	0.343 ± 0.041	0.278 ± 0.021	< 0.0001*	< 0.05**	< 0.05**
Average TCR @ t = 121–125 min.	0.279	0.321 ± 0.039	0.243 ± 0.024	< 0.0001*	< 0.05**	< 0.05**

resembles the option for identifying false positives using the proposed index. For that reason it is recommended that, especially in borderline cases, to evaluate one's tolerance based on as much supportive methods as possible together with "classical" accepted T_{rec} and heart rate dynamics.[6,8]

A TCR value of 0.320 °C/bpm at 60 min of the HTT was found to be a reliable measure to determine heat tolerance with 69% specificity and 100% sensitivity. By using this threshold value the HTT can be shortened and only 31% of the heat tolerant individuals will need to complete a 120 min test, because in no heat intolerant individual such a high TCR value will be attained. Taking into account that the index is calculated online those individuals in whom such a value will be observed after 60 min of the test could be pulled out earlier, without the need to test them for 120 min. Only borderline cases and heat intolerant cases, which are the minority of the cases, will need to complete the 120 min test.

This is a significant advantage over the threshold set by Druyan et al. who showed that no significant differences between heat tolerant and heat intolerant individuals were found in either T_{rec} or heart rate during the 1st hour of the test.[8] Moreover, Moran et al. have also indicated that the PSI calculate at 60 min was unable to predict the PSI after 120 min.[7] The CHSI enabled to shorten the test, but since its complexity it is not feasible for daily use.[11,12] By using the TCR we can overcome the limitations of the PSI and CHSI and to predict the tolerance to heat in most cases.

False negative cases in our model refer to the misdiagnosis of heat intolerant individuals who might be at higher risk for developing exertional heat injury after returning to duty/play.[9,13-15] Therefore, 100% sensitivity is mandatory in this case, as well as negative predictive value of 100%. Specificity of 100% is not obligatory because it refers to those individuals in whom the 60 min time point results in the HTT are inconclusive to define them as heat tolerant. Therefore, in those cases the test cannot be shortened and a full 120 min test should be performed.

Specificity analysis (**Fig. 3**) showed a 3 phases curve: (1) the model's specificity is rising gradually until the 35th minute. (2) The curve tends to plateau until the end of the first hour of exercise. (3) The curve changes its trend from a logarithmic behavior (resembles the expected tendency for heat tolerant individuals) to a linear behavior. This follows the same tendency that was described for the T_{rec} and heart rate dynamics in the analysis group (**Fig. 1**). The dynamics of T_{rec} and heart rate of the HT group showed a tendency to plateau whereas among the HI group the tendency of both variables was steadily increasing. This was also verified by calculating the change in T_{rec} during the last 60 min of exercise according to Druyan et al., which was 0.17 and 0.46 for the curves that represent the HT and HI groups respectively.[8]

While using a simple ratio between T_{rec} and heart rate for assessing the HTT results, it is assumed that both physiological parameters have an important role on the thermoregulation process, while exercising in hot environment. Moreover, the TCR is highly sensitive to momentary changes in heart rate, which is a more dynamic measure than the T_{rec}. On the other hand, the changes in T_{rec} throughout the HTT are less dominant in comparison to the changes in heart rate. By using both variables momentarily fluctuations could be blunted and the index values stabilize. In order to further minimize the index's fluctuations due to rapid changes in the heart rate values, the mean TCR value of each consecutive 5 min should be taken.

In conclusion, the proposed new index was found to be highly sensitive in a way that prevents a misdiagnosis of heat intolerance (false negatives), with an adequate specificity to account for "false positives." Thus, the index is proposed as a supportive measure in the evaluation of the HTT results.

Study Limitations

This model was developed from a database including young, relatively fit individuals who underwent a HTT. The analysis and validation were based on a relatively small sample size: 59 and 46 subjects, respectively. Further examination on a larger group is required to validate the proposed model. The conclusions presented are therefore limited only to the environmental conditions and exercise protocol described. Therefore, at present, we cannot generalize the index and it's applicability for the use in other populations: e.g., age, body composition, gender and fitness. We can only suggest using this model for the specific population and conditions described here, which mostly represent young and relatively fit male population.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

References

1. Man Givoni B. Climate and Architecture. Elsevier Publishing Company Limited. 1969; Chapter 3:31-36.
2. Frank A, Belokopytov M, Shapiro Y, Epstein Y. The cumulative heat strain index--a novel approach to assess the physiological strain induced by exercise-heat stress. Eur J Appl Physiol 2001; 84:527-32; PMID:11482547; http://dx.doi.org/10.1007/s004210000368
3. Epstein Y, Moran DS, Shapiro Y, Sohar E, Shemer J. Exertional heat stroke: a case series. Med Sci Sports Exerc 1999; 31:224-8; PMID:10063810; http://dx.doi.org/10.1097/00005768-199902000-00004
4. Shapiro Y, Seidman DS. Field and clinical observations of exertional heat stroke patients. Med Sci Sports Exerc 1990; 22:6-14; PMID:2406546; http://dx.doi.org/10.1249/00005768-199002000-00003
5. Epstein Y. Heat intolerance: predisposing factor or residual injury? Med Sci Sports Exerc 1990; 22:29-35; PMID:2406544; http://dx.doi.org/10.1249/00005768-199002000-00006
6. Moran DS, Erlich T, Epstein Y. The heat tolerance test: an efficient screening tool for evaluating susceptibility to heat. J Sport Rehabil 2007; 16:215-21; PMID:17923727
7. Moran DS, Heled Y, Still L, Laor A, Shapiro Y. Assessment of heat tolerance for post exertional heat stroke individuals. Med Sci Monit 2004; 10:CR252-7; PMID:15173669
8. Druyan A, Ketko I, Yanovich R, Epstein Y, Heled Y. Refining the distinction between heat tolerant and intolerant individuals during a Heat tolerance test. J Therm Biol 2013; 38:539-542; http://dx.doi.org/10.1016/j.jtherbio.2013.09.005
9. O'Connor FG, Casa DJ, Bergeron MF, Carter R 3rd, Deuster P, Heled Y, Kark J, Leon L, McDermott B, O'Brien K, et al. American College of Sports Medicine Roundtable on exertional heat stroke--return to duty/return to play: conference proceedings. Curr Sports Med Rep 2010; 9:314-21; PMID:20827100; http://dx.doi.org/10.1249/JSR.0b013e3181f1d183
10. Epstein Y, Moran DS. Thermal comfort and the heat stress indices. Ind Health 2006; 44:388-98; PMID:16922182; http://dx.doi.org/10.2486/indhealth.44.388
11. Moran DS, Shitzer A, Pandolf KB. A physiological strain index to evaluate heat stress. Am J Physiol 1998; 275:R129-34; PMID:9688970
12. Frank A, Moran D, Epstein Y, Belokopytov M, Shapiro Y. The estimation of heat tolerance by a new cumulative heat strain index. Environmental Ergonomics: Recent Progress and New Frontiers, 1996; (Freund, London), pp 194–197.
13. Robinson S, Wiley SL, Myhre LG, Bondurant S, Mamlin JJ. Temperature regulation of men following heatstroke. Isr J Med Sci 1976; 12:786-95; PMID:977287
14. Shibolet S, Coll R, Gilat T, Sohar E. Heatstroke: its clinical picture and mechanism in 36 cases. Q J Med 1967; 36:525-48; PMID:6077230
15. Epstein Y, Shapiro Y, Brill S. Role of surface area-to-mass ratio and work efficiency in heat intolerance. J Appl Physiol Respir Environ Exerc Physiol 1983; 54:831-6; PMID:6841230