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Original Research

Age- and Sex-Based Differences in Exertional Heat Stroke Incidence in a 7-Mile Road Race

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Context: Sex, age, and wet-bulb globe temperature (WBGT) have been proposed risk factors for exertional heat stroke (EHS) despite conflicting laboratory and epidemiologic evidence.

Objective: To examine differences in EHS incidence while accounting for sex, age, and environmental conditions.

Design: Observational study.

Setting: Falmouth Road Race, a warm-weather 7-mi (11.26-km) running road race.

Patients or Other Participants: We reviewed records from patients treated for EHS at medical tents.

Main Outcome Measure(s): The relative risk (RR) of EHS between sexes and across ages was assessed with males as the reference population. Multivariate linear regression analyses were calculated to determine the relative contribution of sex, age, and WBGT to the incidence of EHS.

Results: Among 343 EHS cases, the female risk of EHS was lower overall (RR = 0.71; 95% confidence interval [CI] = 0.58, 0.89; $P = .002$) and for age groups 40 to 49 years (RR = 0.43; 95% CI = 0.24, 0.77; $P = .005$) and 50 to 59 years (RR = 0.31; 95% CI = 0.13, 0.72; $P = .005$). The incidence of EHS did not differ between sexes in relation to WBGT ($P > .05$). When sex, age, and WBGT were considered in combination, only age groups <14 years ($\beta = 2.41$, $P = .008$), 15 to 18 years ($\beta = 3.83$, $P < .001$), and 19 to 39 years ($\beta = 2.24$, $P = .014$) significantly accounted for the variance in the incidence of EHS ($R^2 = .10$, $P = .006$).

Conclusions: In this unique investigation of EHS incidence in a road race, we found a 29% decreased EHS risk in females compared with males. However, when sex was considered with age and WBGT, only younger age accounted for an increased incidence of EHS. These results suggest that road race medical organizers should consider participant demographics when organizing the personnel and resources needed to treat patients with EHS. Specifically, organizers of events with greater numbers of young runners (aged 19 to 39 years) and males should prioritize ensuring that medical personnel are adequately prepared to handle patients with EHS.

Key Words: heat illness, injury prevention, thermoregulation

Key Points

- Sex, age and environmental conditions are potential risk factors for exertional heat stroke (EHS) but are seldom considered in combination.
- During a 7-mi (11.26-km) running road race, females overall demonstrated a lower risk of EHS than males.
- However, when the combined effects of sex, age and environmental conditions were considered, only younger age significantly accounted for an increased risk of EHS.

Exertional heat stroke (EHS), an emergent medical condition, represents the pathologic state that results from increases in internal body temperature (>40°C) and concurrent neurocognitive impairments.[1] Exertional heat stroke is commonly the result of moderate- to high-intensity exercise, predominantly in hot, humid conditions. The predisposition to EHS is likely the result of both intrinsic and extrinsic factors,[1,2] including sex, age, and environmental conditions.[3]

Historically, females have demonstrated more blunted thermoregulatory responses than males, resulting in higher body temperatures while performing similar work.[4,5] In laboratory studies, researchers[6,7] have investigated potential physiologic mechanisms related to endogenous female sex hormones and their effects on temperature regulation. Whereas the luteal phase of the menstrual cycle prompts an increase in internal basal temperature (average = 0.3°C to 0.5°C),[8] evidence supporting differences in thermoregulation during exercise has been largely conflicted. Early studies demonstrated changes in sweat rate that depended on environmental conditions,[6] internal temperature variation at rest and during exercise,[9] and cutaneous vasodilation primarily related to expression of female sex hormones.[7] These physiological changes have been proposed to increase the risk of EHS. However, more recent investigators[10,11] found that subtle differences in thermoregulation across the menstrual cycle may be modified by environmental stress or behavioral responses (eg, reduction of work rate during self-paced exercise). Furthermore, morphologic factors (eg, body mass, surface area) appear to explain most of the differences in body-temperature responses between males and females, especially when controlling for metabolic heat production.[12,13]

From an epidemiologic standpoint, Gifford et al[14] performed a meta-analysis of reports of heat illness between sexes and noted a higher incidence rate in males than in females. However, the samples in the meta-analysis experienced either exertional or nonexertional heat illness, which are known to affect various segments of populations differently. Specifically, EHS is more commonly associated with young adults, whereas nonexertional heat stroke (ie, classical heat stroke) more often affects infants and the elderly.[15,16]

Across age ranges, thermoregulatory function in response to exercise heat stress changes. Older adults have been observed to have blunted sudomotor function and skin blood flow, which increased their heat strain compared with younger adults.[17,18] On the other end of the spectrum, adolescents are proposed to be at a greater risk for heat illness due to an altered body mass-to-surface area ratio.[19] Whether these age-related changes alter sex-based differences in thermoregulation and, as a result, the incidence of heat illness is unknown. Furthermore, it is important to consider these factors alongside environmental factors (ie, ambient conditions) in light of the strong influence of temperature and humidity on EHS incidence.[20,21]

Given the high incidence of EHS at the Falmouth Road Race (2.13 ± 1.62 cases per 1000 finishers),[22] the fact that EHS is the most severe of all exertional heat illnesses, and the approximately equal representation of sexes among registered racers, the purpose of our study was to examine differences in the incidence of EHS across sexes and ages in a setting with similar heat exposure. Specifically, we sought to test the hypothesis that differences would occur in the EHS risk between sexes when accounting for age and environmental conditions.

METHODS

We used a retrospective observational study design in which we examined the records of patients treated for EHS at the Falmouth Road Race from 2003 to 2018. The Falmouth Road Race is an annual 7-mi (11.26-km) running road race held in Falmouth, Massachusetts, in August. Medical records from the race medical tents, where medical staff treated all injured runners, were examined for the incidence of EHS and demographic information. Permission to review these records was provided by the University of Connecticut's Institutional Review Board.

Runners who presented with central nervous system dysfunction (eg, irrational behavior, collapse, or confusion) were identified by medical staff and triaged at the medical tent, where their rectal temperature (T_r) was assessed. Patients with a T_r greater than 40°C were diagnosed with EHS and treated with cold-water immersion.[1] They were cooled until T_r reached 38.8°C, at which point they were evaluated for discharge or follow-up at a local hospital.

Overall race data, including the number of participants and age distribution, were obtained from the race's public Web site. Age categorizations were determined using the race's groupings (ie, <14, 15–18, 19–39, 40–49, 50–59, 60–69, 70–74, and 75–100 years old) for results. For 2006, specific age data for race finishers were unavailable. Thus, we excluded EHS patients during this year from the age-specific analyses, but we included them for the sex and overall incidence analyses. Climatologic records were obtained for race days from the nearest weather station with irradiance data (Woods Hole, MA). We then estimated mean wet-bulb globe temperature (WBGT) during the race from these data using the model described by Liljegren et al.[23]

All data were analyzed using Prism (version 8.1.2; GraphPad Software, San Diego, CA). Data are reported as mean ± SD. We calculated the EHS incidence per 1000 race finishers. The relative risk (RR) of EHS by sex was determined with males as the reference population. The RR by age group and whether the EHS occurred at a medical tent along the course or at the finish line were compared using the Fisher exact test. Finish times were compared between sexes and across age groups using a 2-way analysis of variance. Initial T_r values were compared between sexes using a t test. Linear regression models that examined the relationship between EHS incidence and finish time across WBGTs were compared between sexes using F tests. Finally, we explored the relationship among sex, age, and WBGT using multiple linear regression to determine moderating factors. Significance for all statistical tests was set a priori ($P < .05$). Calculations of statistical power for our principal analysis—the comparison of risk between males and females—were performed post hoc to determine the adequacy of the sample size (G*Power, version 3.1.9.4; Heinrich Heine Universität, Dusseldorf, Germany).

RESULTS

From 2003 to 2018, race participation totaled 155 072 and ranged from 7532 to 11 103 finishers per year. We observed 343 EHS cases (n = 200 males, n = 143 females), which represented 0.2% of all race participants. The overall incidence of EHS was 2.57 (95% confidence interval [CI] = 1.52, 3.61) per 1000 finishers for males and 1.92 (95% CI = 1.28, 2.56) per 1000 finishers for females. The incidence of EHS by sex across age groups is shown in Figure 1. The RR of EHS for females compared with males across age groups is provided in Table 1. Females' risk of EHS was lower overall (RR = 0.71; 95% CI = 0.58, 0.89; $P = .002$), with an observed power of 0.92. Women aged 40 to 49 years (RR = 0.43; 95% CI = 0.24, 0.77; $P = .005$) or 50 to 59 years (RR = 0.31; 95% CI = 0.13, 0.72; $P = .005$) also exhibited lower incidences of EHS than their male counterparts.

We found a main effect of sex ($P = .003$) on EHS race finish time but no effect of age ($P = .395$) and no interaction effect between sex and age ($P = .719$; Table 2). Initial T_r was not different between sexes (males = 41.38°C ± 0.64°C, females = 41.33°C ± 0.65°C; $P = .481$). We also demonstrated no differences between sexes for the proportion of patients with EHS who presented at medical

Table 1. Relative Risk of Exertional Heat Stroke (EHS) by Sex

Age, y	Male Participants, n	Female Participants, n	EHS, n Males	EHS, n Females	Relative Risk[a] (95% Confidence Interval)
<14	2089	1706	5	4	0.98 (0.29, 3.36)
15–18	3565	3363	12	16	1.41 (0.68, 2.94)
19–39	29 997	40 638	72	76	0.78 (0.56, 1.07)
40–49	18 591	17 121	38	15	0.43 (0.24, 0.77)[b]
50–59	13 149	8446	29	6	0.31 (0.13, 0.72)[b]
60–69	4780	1691	9	2	0.63 (0.15, 2.59)
70–74	555	118	1	0	NA
75–100	257	43	0	0	NA
Overall	77 545[c]	77 527[c]	200[d]	143[e]	0.71 (0.58, 0.89)[b]

Abbreviation: NA, not applicable.

[a] Relative risk was calculated using males as the reference group.
[b] $P < .05$.
[c] One year of race data lacked participant age data.
[d] Age data were unavailable for 34 male patients with EHS.
[e] Age data were unavailable for 24 female patients with EHS.

tents along the course or at the finish line (finish-line tents: males = 91%, females = 95%; $P = .167$).

Race WBGT was 23.6°C ± 2.26°C across the years studied. The incidence of EHS by sex across WBGTs appears in Figure 2. Whereas the relationship between WBGT and EHS incidence was significant for females ($P = .007$), we noted no differences between the slope ($F = 0.06$, $P = .81$) or intercept ($F = 1.40$, $P = .24$) of the regression lines for males and females. Female EHS finish time decreased in response to a greater WBGT ($R^2 = .35$, $P = .031$), but male EHS finish time was unaffected by WBGT ($R^2 = .01$, $P = .696$). Accounting for sex, age, and WBGT, only age groups <14 years ($\beta = 2.60$, $P = .01$), 15 to 18 years ($\beta = 4.68$, $P < .01$), and 19 to 39 years ($\beta = 2.45$, $P = .01$) accounted for the variance in the incidence of EHS ($R^2 = .11$, $P < .01$).

DISCUSSION

The purpose of our study was to examine differences in the incidence of EHS based on age, sex, and environmental conditions. This work was unique in that we examined a scenario in which male and female participation was approximately equivalent and the exercise was self-paced. Our primary finding was that the RR of EHS for females (0.71; 95% CI = 0.58, 0.89) was lower than for males. This effect seemed to be magnified in individuals aged 40 to 59 years. However, when sex, age, and WBGT were considered concomitantly, the <14, 15 to 18, and 19 to 39 years age groups were the only significant variables to account for differences in EHS incidence.

It is useful to compare our results with those from other running road races. In a 12-year review of medical records from a marathon, Roberts[24] described approximately equivalent rates of exercise-associated collapse from hyperthermia between males and females (14 versus 8 cases), though the sample size was relatively small (n = 23). Across a broader population, our results are similar to those of Gifford et al[14]; their meta-analysis of epidemiologic reports of heat illness in men and women revealed an incidence rate ratio of 2.28 (95% CI = 1.66, 3.16) for males to females. Yet including both exertional and nonexertional heat illnesses in the same analyses makes it difficult to identify specific mechanisms of possible differences. With respect to other exertional heat illness research, our results (Table 1) contrast with those of Barnes et al,[25] who

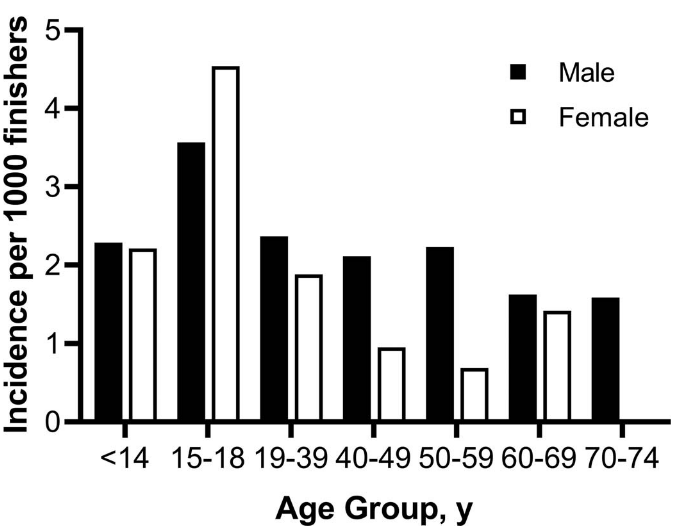

Figure 1. Incidence of exertional heat stroke by sex and age group.

Table 2. Race Finish Times by Sex (Mean ± SD)

Age, y	Finish Times of Runners with Exertional Heat Stroke, min: Males	Females
<14	51.77 ± 9.73	65.5 ± 13.58
15–18	57.30 ± 17.15	62.40 ± 11.10
19–39	53.43 ± 17.88	64.03 ± 15.23[a]
40–49	58.28 ± 14.00	62.14 ± 14.16
50–59	61.86 ± 9.86	77.23 ± 22.59
60–69	59.21 ± 5.50	77.53 ± 4.51
70–74	67.30	NA
75–100	NA	NA
Overall	58.45 ± 15.61	68.13 ± 14.53[a]

Abbreviation: NA, not applicable.

[a] $P < .05$.

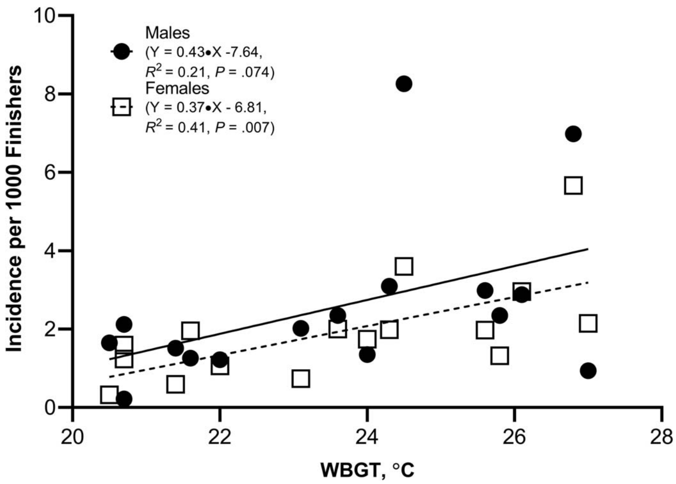

Figure 2. Incidence of exertional heat stroke by sex and wet-bulb globe temperature (WBGT).

determined that the RR of exertional heat illness in basic training was 2.3 (95% CI = 2.1, 2.6) for females. This finding may be confounded by the task-oriented nature of military basic training rather than individual physical performance. In a running road race, each individual runs within his or her own intrinsic limits, whereas military training tasks are not typically scaled to account for interindividual differences.

The authors of several laboratory studies evaluated differences in the thermoregulatory function of males and females. These studies[4,5] have typically demonstrated decreases in sudomotor function and greater body temperatures in females than in males performing similar work. These reported thermoregulation impairments in females have persisted through the literature on exertional heat illnesses, portraying females as at a greater risk of EHS[2] despite evidence demonstrating that sudomotor responses and body temperature during exercise are largely driven by physical characteristics rather than biologic sex.[5,26]

It is interesting that we did not observe sex differences for 2 of our studied factors of EHS presentation. Nearly all patients were treated at the finish-line medical tent (males = 91%, females = 95%; $P = .17$). In addition, both sexes presented with similar initial T_r (males = 41.38°C ± 0.64°C, females = 41.33°C ± 0.65°C; $P = .481$). We propose that the primary factor for increases in body temperature resulting in EHS in these road race participants was the balance between heat production and heat dissipation rather than a biologic sex factor. However, we did not have information on the menstrual status of female EHS patients, which would have allowed us to compare our results with the differences observed across the menstrual cycle.[7]

Although the overall effect of sex appears to result in a reduced risk for EHS in females, it is important to consider that our results appeared to be modified by age. We observed a significant risk reduction in women aged 40 to 59 years. These age groups are notable because Larose et al[27] showed that age-related decrements in heat dissipation appeared to occur in the same age range for men.[27] Thus, sex may play a role in the effects of ageing and is worthy of future investigation.

Both DeMartini et al[21] and Hosokawa et al[20] examined the influence of environmental conditions on EHS incidence during the Falmouth Road Race. Although an association was present between WBGT and EHS incidence, sex did not appear to modify this relationship in our study. This would contradict the suggestion that males and females express different responses to humid and dry heat stress,[6] at least to the extent that the EHS risk is altered.

Considering the influence of metabolic heat production on body temperature differences between males and females, the self-paced nature of a running road race should be incorporated into these observations. Several authors[28–30] have documented sex differences in running races that may influence the behavioral aspects of thermoregulation. Females typically demonstrated more effective pacing, slowing less throughout a race than males,[28] especially in the heat.[29] These differences in thermal behavior have also been observed in a laboratory environment, with females preferring cooler skin temperatures during exercise[30]; however, these results may not be generalizable across the studied population. Therefore, the EHS risk reduction in females may reflect differences in enteroception and pacing feedback rather than in a physiological thermoregulatory mechanism. We observed faster finish times for females with EHS as WBGT increased, whereas males with EHS had finish times that were unaffected by WBGT. Therefore, sex differences in pacing strategies or enteroception may have resulted in behaviors that reduced the risk of EHS; however, we lack specific data on the pacing used by runners to specifically address this possibility.

Limitations

These data were obtained from a road race with a volunteer medical staff who had limited documentation capabilities. As such, limited data are available on individual patients that would allow for a more complete analysis of the differences between populations (eg, anthropometrics, training history, menstrual status of females, past medical history, heat acclimatization). We also acknowledge that EHS is likely multifactorial in nature and the reported factors alone do not completely describe the risk of EHS in a specific population. Along with sex, age, and WBGT, numerous other factors contribute to an individual's predisposition to EHS.[1] Information on the characteristics of individual participants would have permitted us to explore other risk factors. Future investigators should characterize these risk factors in epidemiologic fashion.

We used the number of race finishers as the denominator for the incidence calculations. It would be ideal for the number of runners who began the race to be considered as well; however, these data were unavailable. Nevertheless, we believed that the proportion of individuals who dropped out of the race for non-EHS reasons would likely be consistent. The use of the race's specified age groups may also limit the applicability of our results. In particular, the nonuniform nature of the age groups (eg, 15–18 years, 19–39 years) complicates the identification of specific ages that may be at greater risk. Finally, these results apply to the limited circumstances of self-paced exercise; scenarios in which uniform exercise intensity is required, such as in military and occupational settings, may yield different outcomes. Future researchers should identify physiological and behavioral mechanisms that lead to variability in the EHS incidence between sexes and across ages.

Clinical Considerations

Our results support the notion that the risk for EHS differs between sexes. Although females had less risk of EHS than males, being younger than 40 years old was a greater risk factor than sex. This highlights the need to better understand the multifactorial nature of EHS risk, especially when applied to large populations. These data can be used by medical teams to better understand the resources and personnel necessary to provide adequate treatment to the populations they serve. Specifically, the organizers of events with greater numbers of young runners (aged 19–39 years) and males should prioritize ensuring that medical personnel are adequately prepared to handle patients with EHS.

CONCLUSIONS

We provide an analysis of the incidence of EHS in a warm-weather road race. Our principal finding was that the risk of EHS was lower in female participants, and age modified this relationship. Women aged 40 to 59 years were at less risk of EHS than males; yet when WBGT was factored alongside age and sex, being aged 19 to 39 years significantly accounted for an increased incidence of EHS. These results can help clinicians identify at-risk populations for targeted preventive measures.

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