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Interstitial lung edema triggered by marathon running

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ABSTRACT

The purpose of this study was to determine whether marathon running causes lung edema, and if so, to determine its effects on runners. Posterior/anterior (PA) radiographs were taken one day before the marathon and at 19, 55, and 98 min post-marathon in 26 runners. The pre and post exercise radiographs of each runner were collated, and then read simultaneously. Two physicians interpreted the images independently in a blinded fashion. The PA radiographs were viewed together at each time-point and findings suggestive for interstitial lung edema were rated as 'mild,' 'moderate,' or 'severe' based on four different radiological criteria. Forty-six percent of the runners presented radiographic findings suggestive of mild to severe interstitial lung edema. Radiographic findings persisted until 98-min post-marathon, with at least moderate degree increases found more frequently in women (55%) than men (6%) ($p < 0.01$). In conclusion, about half of the runners developed interstitial lung edema of varying degrees post-exercise with the incidence being higher in women compared to men.

1. Introduction

Since 1980, there has been almost a four-fold increase in the total number of marathon competitors in the United States, representing close to 0.2% of the U.S. population over 18 years of age in 2010. Its increasing popularity has been accompanied by a large body of research on the physiology of marathon running. It has been mentioned anecdotally that the normal levels of lung water (40–50 mL of water per L of lung at total lung capacity) (Milne and Pistolesi, 1993) may rise during marathon running. Different types of exercise such as an "all-out" 15-min cycling interval training session (Zavorsky et al., 2006a), a triathlon (Caillaud et al., 1995), an ultramarathon (McKechnie et al., 1979), and sustained heavy cycling exercise for 45 min (McKenzie et al., 2005) caused approximately 65% of subjects to show signs of increased lung water. Despite this evidence, argument continues both for and against the development of lung edema with exercise (Hopkins, 2010a,b; Sheel and McKenzie, 2010a,b).

Authors writing about this topic invariably refer to increases in lung water as "edema" which leads to some confusion, since "pulmonary edema" is usually considered condition secondary to an abnormal increase of liquid in the alveoli causing clinical symptoms, whereas smaller increases in lung water can be confined to the interstitial space of the lung. Since in these conditions there is no alteration in the alveolar–capillary interface (Weibel, 1973), the increase does not usually cause any subjective or objective clinical finding. Excess lung water can, therefore, be better detected and defined in its severity by chest radiography rather than by clinical evaluation or by indicator dilution techniques (Pistolesi and Giuntini, 1978). The level of accuracy of chest radiography in detecting and quantifying lung water accumulation has been determined in both animals and humans and has been accepted as the best technique available for this purpose (Pistolesi and Giuntini, 1978; Ware and Matthay, 2005). Although increases in lung water do not cause overt clinical symptoms, we hypothesized that they may have measurable effects on runners' race performance and post-race fitness. The purpose of this study was to investigate

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the development of radiographic findings suggestive of interstitial lung edema in marathon runners over a range of finishing times.

2. Methods

2.1. Study participants

Participants were selected based on projected marathon finishing times, such that about one third of the participants would finish in each of three time ranges: 3:00 h or less, 3:00–4:00 h, and 4:00–5:00 h. The inclusion criteria were as follows: any male or female ≤55 years of age, with the ability to complete the marathon under 5:00 h, and with no symptoms or known presence of heart disease. The exclusion criteria were signs or symptoms of cardiopulmonary disease or obstructive or restrictive lung diseases airways, determined by spirometry testing. The study was approved by the Institutional Review Board of Marywood University. Subjects who agreed to participate signed a written informed consent.

2.2. Imaging technique

Each subject had posterior/anterior (PA) radiographs taken pre-race, as well as 20, 45 and 90 min after crossing the finish line. All radiographic imaging was performed using a portable X-ray machine (Model SR-115, Source Ray Inc., Ronkonkoma, NY) and Digital Radiology ViZion DR imaging Software/flat panel detectors (Viztek Inc., Garner, NC). The X-ray tube-to-patient distance was six feet. Radiographic exposure was individualized using 90–125 kVp and 2.4 mAs (6 ms) to 9.8 mAs (24 ms) exposure time, depending on the subject's anthropometric characteristics, and using the lower kV levels to obtain optimum lung contrast. The image was obtained at total lung capacity. Each set provided an effective radiation dose ranging from 0.02 to 0.12 mSV. Thus, the maximum total exposure per subject was 0.48 mSv for the full study.

2.3. X-ray reading

The films were analyzed by two readers: a chest radiologist (ENCM) and a chest physician (MP), both of whom have previously published a textbook on chest radiograph reading (Milne and Pistolesi, 1993). Each X-ray set was randomly coded before being supplied to the readers. The readers were blinded as to the time each radiograph was taken.

Each reader was given the same set of instructions for interpreting the films and evaluated the films separately from the other readers. The radiographs from each runner were analyzed in a randomized order. Because of the randomization, it was not possible for the readers to know whether they were looking at pre or post exercise films, making it (deliberately) impossible for them to make comparative pre and post film analyses.

Films were analyzed for evidence of the following findings (Anholm et al., 1999; Gallagher et al., 1988; Giuntini et al., 1987; Milne, 1985; Milne and Pistolesi, 1993; Miniati et al., 1988; Pistolesi and Giuntini, 1978; Zavorsky et al., 2006a) considered suggestive of interstitial lung edema: (1) loss of sharp definition of pulmonary vascular markings; (2) hilar blurring; (3) peribronchial and perivascular cuffing; (4) obscuration of the smallest peripheral vessels. The first three radiographic findings were graded on a three-point scale: 0 when absent, 1 for minimally present, and 2 if there was a definite radiographic presence. For the fourth finding, this item was scored as 0 for normal visualization, 1 for partly obscured, and 2 for completely obscured. Therefore, the total score for each radiograph could range from 0 (absence of any radiographic findings suggestive of interstitial lung edema) to 8 (maximum total score attainable). For each subject, the scores of the two readers were then averaged for data analysis. Since the radiographic findings of interstitial lung edema in its early phase of accumulation could be subtle and non-specific, to avoid false positive readings and increase the specificity of the readings, we arbitrarily graded interstitial lung edema as "none" (total score of 2.0 or lower), "mild" (total score from 2.1 to 3), "moderate" (total score from 3.1 to 4) and "severe" (total score higher than 4).

2.4. Statistical analyses

Radiographic characteristics before and after exercise for all runners who finished the race in under 5 h were compared using the Friedman analysis of variance test. This test compared whether the median "edema" scores (ordinal data) amongst the four measurement points for all finishers significantly increased. A Wilcoxon-signed rank test determined where the differences were *post hoc.* As there were four combinations of pairs (pre *vs.* 20 min post, pre *vs.* 45 min post, pre *vs.* 90 min post, 45 min post *vs.* 90 min post), $p < 0.0125$ was used to signify statistical significance.

A Kruskal–Wallis ANOVA also compared the differences between edema scores obtained in males compared to females. If significant, a Wilcoxon Mann–Whitney *U* test then determined where the differences were *post hoc.* The level of inter-observer agreement on the quantification of radiological findings suggestive of interstitial lung edema was obtained from the weighted *kappa* statistical test (Jakobsson and Westergren, 2005; Kundel and Polansky, 2003), and the average weighted *kappa* coefficient was reported (Kundel and Polansky, 2003). Difference between quantification scores for two readers at every time-point was also assessed using a Kruskal–Wallis ANOVA, and when significant, a Wilcoxon Mann–Whitney *U* test then determined where the differences were *post hoc*, with significance declared at $p < 0.0125$. Forward binary logistic regression was conducted to determine which independent variables (marathon finishing time, age, gender) were predictors of developing moderate to severe interstitial pulmonary edema (yes or no) from marathon running. The data were analyzed by a statistical software package (SPSS Version 19.2, IBM SPSS Statistics Inc., Chicago, IL). Statistical significance was declared when $p < 0.05$ unless otherwise noted.

3. Results

The 2011 Steamtown Marathon began at 475 m above sea level and finished at 229 m above sea level. The ambient temperature increased from about 8 °C (96% humidity) at the 8:00 a.m. start to 21 °C (51% humidity) at the finish line by 1:00 p.m.

Twenty-six subjects with normal resting lung function values (as reported elsewhere in a study using the same subjects (Lavin et al., 2012)) completed the marathon in less than 5 h with times ranging from 2 h and 22 min to 4 h and 48 min. The average finishing time was 3 h and 38 min (40 min). Of the finishers, 17 were male, with a mean (SD) age of 40 (8) years, height of 178 (6) cm, weight of 76 (10) kg, and body surface area of 1.94 (0.15) m^2. Nine subjects were female and had a mean age of 33 (9) years, height of 164 (8) cm, weight of 57 (9) kg, and body surface area of 1.60 (0.16) m^2. Due to difficulty in organizing flow of runners through the chest X-ray triage, the films were not taken at the exact predetermined times. Instead, the average times for the three post-exercise X-rays were 19 (8) min, 55 (13) min, and 98 (16) min, post-finish, respectively.

Fig. 1 shows evidence of moderate to severe findings suggestive of interstitial lung edema in a subject at 58 min post-exercise.

Post-marathon, 12 out of the 26 (46%) runners (11 at the first post race time point, and 1 at the second post race time point)