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EDITORIAL COMMENT

Optimal Dose of Running for Longevity

Is More Better or Worse?*

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Although it is well known that regular exercise and physical activity (PA) have health benefits, there is still an unanswered question: "Is it possible to have too much of a good thing?" In particular, is high-intensity PA, such as running, a healthful activity? The dose-response relationship between running and mortality is still subject to debate and controversy.

SEE PAGE 411

In this issue of the *Journal*, Schnohr et al. (1) report 3 major findings on jogging and all-cause mortality in 1,098 joggers and 3,950 nonjoggers from the Copenhagen City Heart Study. First, jogging even <1 h per week or 1 time per week is associated with significant mortality risk reduction compared with sedentary nonjoggers. Second, 1 to 2.4 h of jogging per week, with a frequency of 2 to 3 times per week, at a slow or average pace is most favorable as an optimal jogging time, frequency, and speed for reducing mortality. Third, higher jogging times (≥2.5 h per week), higher frequencies (>3 times per week), and faster paces are not associated with better survival compared with sedentary nonjoggers, suggesting a U-shaped association between jogging and mortality as well as loss of benefits with higher doses of jogging. Considering the current consensus of a linear dose-response relationship between total PA and health, indicating "the more the PA, the better for health and longevity," these findings are intriguing. The good news is that the mortality benefits of light jogging will encourage more people to jog for health benefits as a "practical, achievable, and sustainable" goal, as the authors have stated.

However, there are several important study limitations that should be considered in the interpretation of these interesting results. First, all analyses on the association between jogging and mortality included only 413 sedentary nonjoggers and excluded 3,537 active nonjoggers who are active in other types of PA. Considering other PA (sedentary vs. active) and jogging, we can think of 4 categories of overall PA: 1) sedentary nonjoggers, 2) active nonjoggers, 3) sedentary joggers, and 4) active joggers. Comparing mortality risk in joggers (both sedentary and active) with mortality risk in the least active, sedentary nonjoggers without active nonjoggers in the relative risk analyses likely contributed to more significant mortality benefits in joggers. In addition, sedentary nonjoggers were more obese, were nearly 20 years older, and had an approximately 5 to 6 times higher prevalence of hypertension and diabetes mellitus compared with joggers in this study, which could increase the risk of mortality irrespective of jogging status. Although the authors appropriately adjusted for age and diabetes mellitus in their analyses, statistical adjustment would not completely eliminate the confounding bias by these large differences, potentially leading to overestimation of the mortality benefits of jogging.

Second, Schnohr et al. (1) used a practical but somewhat arbitrary categorization of doses of jogging. This categorization resulted in a smaller sample size

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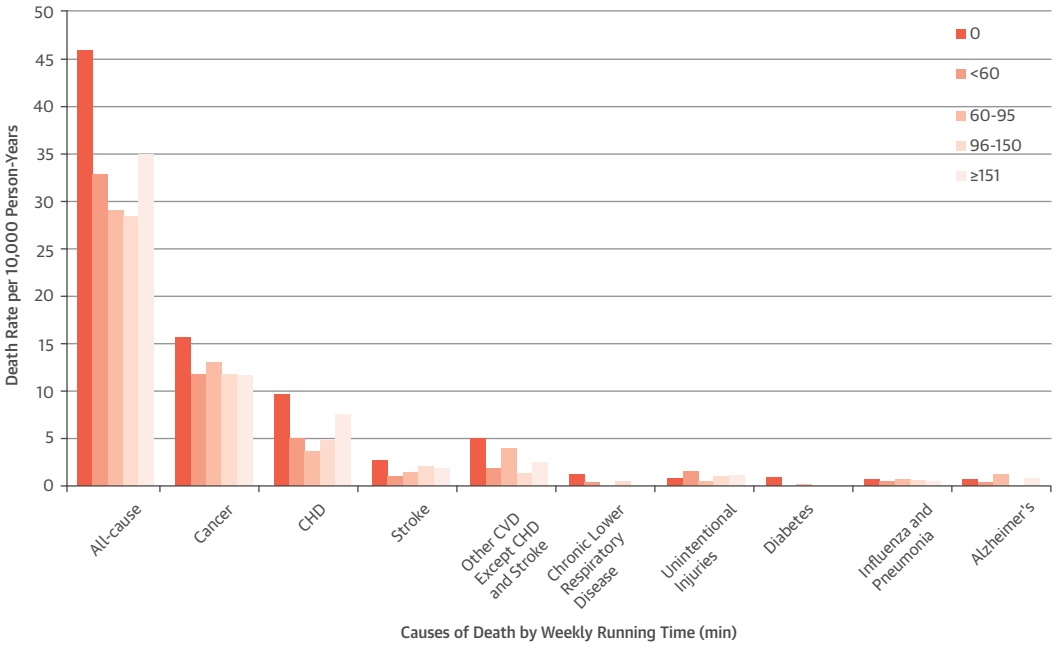
and lower statistical power for the higher doses of jogging, where no mortality benefits were found. For example, there were only 47 joggers (4%) with the highest jogging time (>4 h per week) and 80 joggers (9%) with the highest frequency (>3 times per week), with only 1 death and 5 deaths in the respective categories. However, the adjusted hazard ratios were 0.60 (95% confidence interval: 0.08 to 4.36) and 0.71 (95% confidence interval: 0.29 to 1.75) in each respective category, suggesting that significant mortality benefits would be possible even with these highest doses of jogging if these groups had sufficient sample sizes. In our recent study of running and mortality in 55,137 participants (13,016 runners) with 3,413 deaths (2), we used 5 quintiles so there would be an equal number of participants across different doses of running. We still found significantly lower risks of mortality even in the highest quintiles of running time (≥176 min per week) and frequency (≥6 times per week) compared with nonrunners. Therefore, it is possible that running even at high doses may provide mortality benefits compared with nonrunners.

Third, Schnohr et al. (1) did not fully take into account participation in other types of PA. Jogging is one type of PA, and it is possible that nonjoggers and joggers unequally participated in other types of PA. However, we found mortality benefits of running after adjusting for the total amount of other PA (2). We also found similar mortality benefits of running even after excluding subjects who reported participating in other PA besides running. Thus, it is likely that running provides mortality benefits independent of participating in other types of PA.

Fourth, Schnohr et al. (1) focused on the effects of jogging only on all-cause mortality because of the limited sample size. However, several studies have reported the potential adverse effects of excessive aerobic exercise specifically on cardiovascular diseases and mortality. In a recent long-distance (90-km) cross-country ski marathon study of 52,755 participants (3), the investigators found a higher risk of developing arrhythmias in those who had completed more races. In marathon runners, frequent marathon running and its required training also appeared to be correlated with myocardial damage (4,5). In addition, recent evidence suggests that high doses of PA (>30 miles per week of running and >46 miles per week of walking) in subjects with established coronary heart disease (CHD) were associated with loss of cardiovascular mortality benefit (6,7). In contrast, there are other studies showing opposite results, with lower risks of CHD with higher doses of running (8,9). In our

FIGURE 1 Death Rates for Major Causes of Death by Weekly Running Time



Participants were classified into 5 groups: nonrunners and 4 quartiles of weekly running time in minutes. Death rates were adjusted for baseline age, sex, and examination year. CHD = coronary heart disease; CVD = cardiovascular disease.

additional assessments of the effects of running and mortality, we also evaluated cause-specific mortality (**Figure 1**). It appears that mortality from all causes and cancer was lower in runners compared with nonrunners regardless of dose, although there was a slight nonsignificant trend for less benefit with higher doses of running compared with lower doses of running for all-cause mortality. On the other hand, CHD mortality appeared to be relatively higher in those with higher doses of running compared with lower doses, with a reverse J-shaped association. Thus, further studies are needed to better evaluate this controversial issue. Ideally, these studies will be well-controlled interventions, because we certainly agree that the goal is not to unnecessarily frighten people who wish to participate in more strenuous exercise (10).

In summary, the study by Schnohr et al. (1) adds to the current body of evidence on the dose-response relationship between running and mortality. However, further exploration is clearly warranted regarding whether there is an optimal amount of running for mortality benefits, especially for cardiovascular and CHD mortality. In addition, because self-reported doses of running may induce measurement error and bias, it would be preferable to use an objective assessment of doses of running in future studies.

The authors showed that even <1 h per week of jogging, below the current minimum guidelines of vigorous-intensity aerobic PA (≥75 min per week), may be sufficient for mortality benefits, consistent with other large studies (2,9,11). Therefore, as a better option for time efficiency, we should emphasize that even small amounts of running (<1 h per week) can provide significant mortality benefits for most healthy but sedentary people. The general consensus of the data certainly suggests that "more is not better!" regarding running and mortality. However, we still need more data to truly determine "is more actually worse?" regarding exercise dose and prognosis.

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REFERENCES

1. Schnohr P, O'Keefe JH, Marott JL, Lange P, Jensen GB. Dose of jogging and long-term mortality: the Copenhagen City Heart Study. J Am Coll Cardiol 2015;65:411–9.

2. Lee DC, Pate RR, Lavie CJ, Sui X, Church TS, Blair SN. Leisure-time running reduces all-cause and cardiovascular mortality risk. J Am Coll Cardiol 2014;64:472–81.

3. Andersen K, Farahmand B, Ahlbom A, et al. Risk of arrhythmias in 52 755 long-distance cross-country skiers: a cohort study. Eur Heart J 2013;34:3624–31.

4. Mohlenkamp S, Lehmann N, Breuckmann F, et al. Running: the risk of coronary events: prevalence and prognostic relevance of coronary atherosclerosis in marathon runners. Eur Heart J 2008;29:1903–10.

5. Neilan TG, Januzzi JL, Lee-Lewandrowski E, et al. Myocardial injury and ventricular dysfunction related to training levels among nonelite participants in the Boston Marathon. Circulation 2006;114:2325–33.

6. Williams PT, Thompson PD. Increased cardiovascular disease mortality associated with excessive exercise in heart attack survivors. Mayo Clin Proc 2014;89:1187–94.

7. O'Keefe JH, Franklin B, Lavie CJ. Exercising for health and longevity vs peak performance: different regimens for different goals. Mayo Clin Proc 2014;89:1171–5.

8. Williams PT. Reductions in incident coronary heart disease risk above guideline physical activity levels in men. Atherosclerosis 2010;209:524–7.

9. Chomistek AK, Cook NR, Flint AJ, Rimm EB. Vigorous-intensity leisure-time physical activity and risk of major chronic disease in men. Med Sci Sports Exerc 2012;44:1898–905.

10. Levine BD. Can intensive exercise harm the heart? The benefits of competitive endurance training for cardiovascular structure and function. Circulation 2014;130:987–91.

11. Wen CP, Wai JP, Tsai MK, et al. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. Lancet 2011;378:1244–53.

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