

Can pre-race aspirin prevent sudden cardiac death during marathons?

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As if reprising the index case of Pheidippides in 490 BC, the sudden cardiac death of a 32-year-old modern-day warrior at mile 20 in the 2016 London marathon mandates an expedited search to prevent such tragic events based on novel insights

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into the underlying cause (figure 1).^{1,2} Although the cardiac findings in this case have not been released, an acute coronary event is most likely as the most common cause of sudden cardiac death in men over the age of 30 years including among experienced runners in that event.³⁻⁵

While the overall incidence of sudden cardiac death during marathons is low, cardiac arrests occur in roughly 1 in 50 000 finishers.⁶ Based on 59 cases with a mean age of 42 years in a 10-year prospective registry of American road

races since 2000, male sex and the marathon were the only significant risk factors for cardiac arrest.⁷ Atherosclerotic heart disease was the predominant underlying cause in same-aged runners in a concurrent Parisian registry.⁸ Marathon running thereby illustrates the triggering of acute myocardial infarction by strenuous exercise in middle-aged males with underlying non-obstructive coronary atherosclerosis.⁹

RATIONALE FOR TARGETED PREVENTION

Supported by a 44% reduction in first acute myocardial infarctions in healthy middle-aged men in the Physicians Health Study, a randomised controlled primary prevention trial,¹⁰ the International Marathon Medical Directors Association (IMMDA) has recommended prerace aspirin for males over the age of 40 years with approval by



Box 1 Rationale for using pre-race aspirin to prevent sudden cardiac death during marathons

- ▶ Aspirin reduces first acute myocardial infarctions in healthy males by 44%.
- ▶ Acute myocardial infarction is the most common cause of sudden cardiac death in males over the age of 30 including during marathons.
- ▶ Use of pre-race low-dose aspirin is prudent to prevent race-related sudden cardiac death.

Figure 1 Modern and ancient warriors.

their physicians after considering risks such as gastrointestinal bleeding or allergy.¹¹ This strategy is concordant with clinical guidelines endorsing aspirin for primary prevention in persons at high cardiovascular risk, which includes middle-aged males at increased short-term risk for acute myocardial ischaemia.¹²⁻¹³

IMMDA's advisory is analogous to that proposed for firefighters, who are at increased risk for sudden cardiac death during emergency duties in part related to procoagulant effects as shown in athletes after strenuous physical exercise.¹⁴⁻¹⁶ Attenuation of training-induced prothrombotic effects by aspirin in firefighters would apply as well to runners based on atherothrombosis as the shared pathogenic paradigm.¹⁷ In contrast to continuous prophylaxis to cover unpredictable risk in firefighters, pre-race use may suffice for marathoners who are at otherwise low cardiovascular risk as assessed by 10-year Framingham measures.

Assessment of coronary artery calcification, which independently predicts incident coronary heart disease and death in males aged 32 to 46 years,¹⁸ may be useful for stratifying the utility of aspirin for marathoners with such evidence for atherosclerosis.¹⁹ This strategy may be especially relevant for habitual marathoners whose paradoxically

higher scores correlate inversely with event-free survival.²⁰ This finding indicates short-term risk for acute cardiac events associated with atherosclerotic plaque burden, confounding the benefit of enhanced longevity with this lifestyle.²¹⁻²³

The case for using pre-race aspirin in middle-aged males

Given 285 040 US male marathoners over the age of 40 in 2015,²⁴ IMMDA's advisory warrants expedited attention given a greater than twofold increase in race-related cardiac arrests since 2005.⁷ We therefore encourage medical directors to follow Rio de Janeiro's lead by informing entrants of IMMDA's advisory, hoping to avert cardiac arrests as occurred at their last two races (personal communication, Paulo Alfono Loriga de Menezes, MD, medical director, Rio de Janeiro marathon).

Pre-race aspirin provides runners pre-emptively with the only pharmacological agent with a class 1A recommendation for pre-hospital administration in the event of an acute coronary syndrome. Such usage may reduce the increasing frequency of emergent post-race percutaneous coronary angioplasties and bypass surgery, as occurred after the most recent Boston and Chicago marathons.²⁵⁻²⁶ 'Just because the cardiac risk is low, doesn't mean it can't be lower', argues Amby Burfoot, Runners World's editor-at-large and former Boston marathon champion.²⁷

IMMDA's advisory enables middle-aged males to make more informed decisions regarding the cardiovascular benefits of marathon training and pre-race aspirin use for risk reduction during races (figure 2).²⁸ The lifetime benefit of reducing risk for sudden cardiac death through marathon training can be accomplished with attenuation of its transient risk during races (box 1).⁹⁻²⁹ In lieu of a randomised controlled primary prevention trial in marathoners, which lacks feasibility due to the low frequency of index events, prospective registries can be used to assess aspirin's efficacy once usage gains acceptance among runners contingent on wider support by the marathon medical community.

The goal of reducing sudden cardiac death in middle-aged males during marathons

is realistic in our view, having successfully curtailed race-related fatalities due to water intoxication in young females through a robust consensus process.³⁰⁻³¹ As it is safe, inexpensive and readily available worldwide, aspirin is ready for prime time in middle-aged males as a high-risk subgroup. Based on a predominance of current clinical evidence, this remedy, known to Hippocrates in the time of Pheidippides, may enhance the heroic dimensions of a sport celebrating his legacy by reducing re-enactments of his tragic demise.

Rationale

If aspirin conclusively prevents first myocardial infarctions in healthy middle-aged males, pre-race aspirin may reduce such events during marathons.

MMDA recommendation

Long-distance runners, especially men over the age of 40, are advised in the absence of specific contraindications to take pre-race aspirin if approved by their personal physician after discussion of its risks and benefits.

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Figure 2 Father Time running a marathon, by Peter de Sève, the New Yorker, 13 November 1995.

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