



Registry on acute cardiovascular events during endurance running races: the prospective RACE Paris registry

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Aim

Long distance running races are associated with a low risk of life-threatening events much often attributed to hypertrophic cardiomyopathy. However, retrospective analyses of aetiology lack consistency.

Methods and results

Incidence and aetiology of life-threatening/fatal events were assessed in long distance races in the prospective Registre des Accidents Cardiaques lors des courses d'Endurance (RACE Paris Registry) from October 2006 to September 2012. Characteristics of life-threatening/fatal events were analysed by interviewing survivors and reviewing medical records including post-mortem data of each case. Seventeen life-threatening events were identified of 511 880 runners of which two were fatal. The vast majority were cardiovascular events (13/17) occurring in experienced male runners [mean (\pm SD) age 43 ± 10 years], with infrequent cardiovascular risk factors, atypical warning symptoms prior to the race or negative treadmill test when performed. Acute myocardial ischaemia was the predominant aetiology (8 of 13) and led to immediate myocardial revascularization. All cases with initial shockable rhythm survived. There was no difference in event rate according to marathons vs. half-marathons and events were clustered at the end of the race. A meta-analysis of all available studies including the RACE Paris registry ($n = 6$) demonstrated a low prevalence of life-threatening events (0.75/100 000) and that presentation with non-shockable rhythm [OR = 29.9; 95% CI (4.0–222.5), $P = 0.001$] or non-ischaemic aetiology [OR = 6.4; 95% CI (1.4–28.8), $P = 0.015$] were associated with case-fatality.

Conclusion

Life-threatening/fatal events during long distance races are rare, most often unpredictable and mainly due to acute myocardial ischaemia. Presentation with non-shockable rhythm and non-ischaemic aetiology are the major determinant of case fatality.

Keywords

Acute coronary syndrome • Sudden death • Marathons • Sport cardiology

Introduction

Endurance running races (ERR) have become increasingly popular and the demonstration that physical exercise improves quality of life and life expectancy has reinforced this practice.¹ Scant data are

available on ERR-related life-threatening/fatal events, in particular with respect to their aetiology and type of races.² Event rates range from 1 per 200 000 up to 1 per 7500 participants and are higher in occasional runners (1 per 7500–18 000) when compared with marathon runners (1 per 50–200 000).^{3–10} Cardiomyopathy has

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been reported as the dominant aetiology in individuals aged <35,^{11,12} whereas atherosclerotic coronary artery disease (CAD) is usually reported in older individuals.^{13–15} However, the vast majority of case reports are retrospective without details on patients' characteristics, clinical presentation, and the outcome.

Our goal was to perform a prospective registry of life-threatening/fatal events occurring during the main Parisian ERR between October 2006 and April 2012. The objectives of the Registre des Accidents Cardiaques lors des courses d'Endurance à Paris (RACE Paris Registry) were to determine the rate of non-traumatic deaths and major cardiovascular events, to provide an accurate estimation of prevalence, event aetiology, patient risk profile, and the outcome. The results of the RACE Paris Registry were combined with all available cases previously reported in a meta-analysis to identify determinants of case fatality and to determine an accurate estimation of the prevalence of life-threatening events.

Methods

Study design

The RACE Paris registry is an investigator-initiated project led and supported by the Groupe de Réflexion sur la Cardiologie Interventionnelle (GRCI), an independent non-profit organization of interventional cardiologists (www.GRCI.fr). Five major Parisian ERR were included prospectively between October 2006 and April 2012, including the Paris marathon and half-marathon, the Boulogne-Billancourt half-marathon, the 20 km de Paris, and the Paris–Versailles. This former race is 16 km long but with 200 m elevation gain in a short distance and therefore classified as a half-marathon (Table 1). The protocol was approved by the organizing committees of each race and by the Service Aide Médicale Urgente (SAMU) of the Assistance Publique–Hôpitaux de Paris, responsible for the onsite medical emergency service. The study was conducted in accordance with the Helsinki declaration.

Selection of cases and data collection

Individuals aged of 18 years old or more participating in one of the forenamed races entered the RACE Paris Registry. According to the French legislation, medical examination with written approval issued by a physician was requested for all participants. Age, gender, and performance of runners were recorded together with the rate of discontinuation, weather conditions (temperature, rainfall, humidity level), and pollution index provided by AIRPARIF (<http://www.airparif.asso.fr>).

The workflow of the RACE Paris registry is summarized in Figure 1. Any death or life-threatening events occurring 30 min before, during and within 2 h after the end of the race were recorded. Participation of all emergency units involved in the organization of the races was obtained. All interventions performed by healthcare organizations were centralized by the SAMU. Any intervention which met the inclusion criteria was carefully followed up with direct contact with all hospital departments involved in the patients' care. A specific questionnaire was filled for each patient admission to collect information on sports practice and medical history (Supplementary material online, Table S1).

Study objectives

The primary study objective of the RACE Paris Registry was to determine the incidence of life-threatening/fatal cardiovascular and non-cardiovascular events occurring during five major Parisian races.

Secondary objectives were to identify the aetiology of these events and the potential predisposing factors related to the race environment (weather, pollution, distance run before occurrence of event) or to the runners (level of previous training/practice, hydration during the race, the use of energetic supplements, pre-existing condition, and medication).

Definition of endpoints

The primary endpoint was defined as a composite of any death or any life-threatening events requiring urgent on-site medical intervention with hospital admission for at least 24 h. Life-threatening events were categorized as requiring immediate on-site cardiopulmonary resuscitation (CPR) or not. Traumatic events and non-life-threatening events such as chest pain presentation with normal cardiovascular examination, temporary discomfort including vagal faint and moderate exertional heat illnesses were excluded.

Statistical analysis

Baseline characteristics were expressed by mean and standard deviation (SD) for continuous variables and frequencies and percentages and for categorical variables. Continuous variables were compared using Student's test in case of normal distribution and Wilcoxon–Mann–Whitney test otherwise. For categorical variables comparisons, the Pearson's χ^2 test was used if all theoretical sample sizes were ≥ 5 or using the Fisher test if < 5 . Incidence rates for the total number of cases were calculated as the simple proportion of events divided by the number of participants for stated time intervals. Ninety-five per cent confidence intervals for event rates were computed with the use of a Poisson distribution. All these analyses were performed with the SAS software, version 9.1 (SAS Institute, Cary, NC, USA).

To further identify determinants of case fatality and to determine an accurate estimate of the prevalence of life-threatening events, we performed a meta-analysis of all individual reported life-threatening/fatal events reported in ERR (Table 2). A full electronic search was conducted in PUBMED and the terms used for research were 'deaths', 'life-threatening', 'cardiac events', 'myocardial infarction', 'marathons or half-marathons'. Data were extracted using a standardized form. A meta-analysis was performed with Comprehensive Meta-analysis software, version 2.0 (Biostat, USA) to aggregate effect measures using a random-effects model. Effect measures were calculated to highlight potential predictive factors of life-threatening and cardiovascular events during races. Statistical heterogeneity across the studies was calculated by the I^2 statistic to quantify inconsistencies between studies. I^2 values of 25% or less, 50%, and 75% or more represent low, moderate, and high inconsistency, respectively. To assess the potential for publication bias, we added the Egger regression test P -value for funnel symmetry when possible (at least three studies), a P -value of < 0.05 is an argument for a potential publication bias. Four investigators (B.G., H.M., A.B.A., and J.P.C.) independently assessed reports for eligibility.

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Results

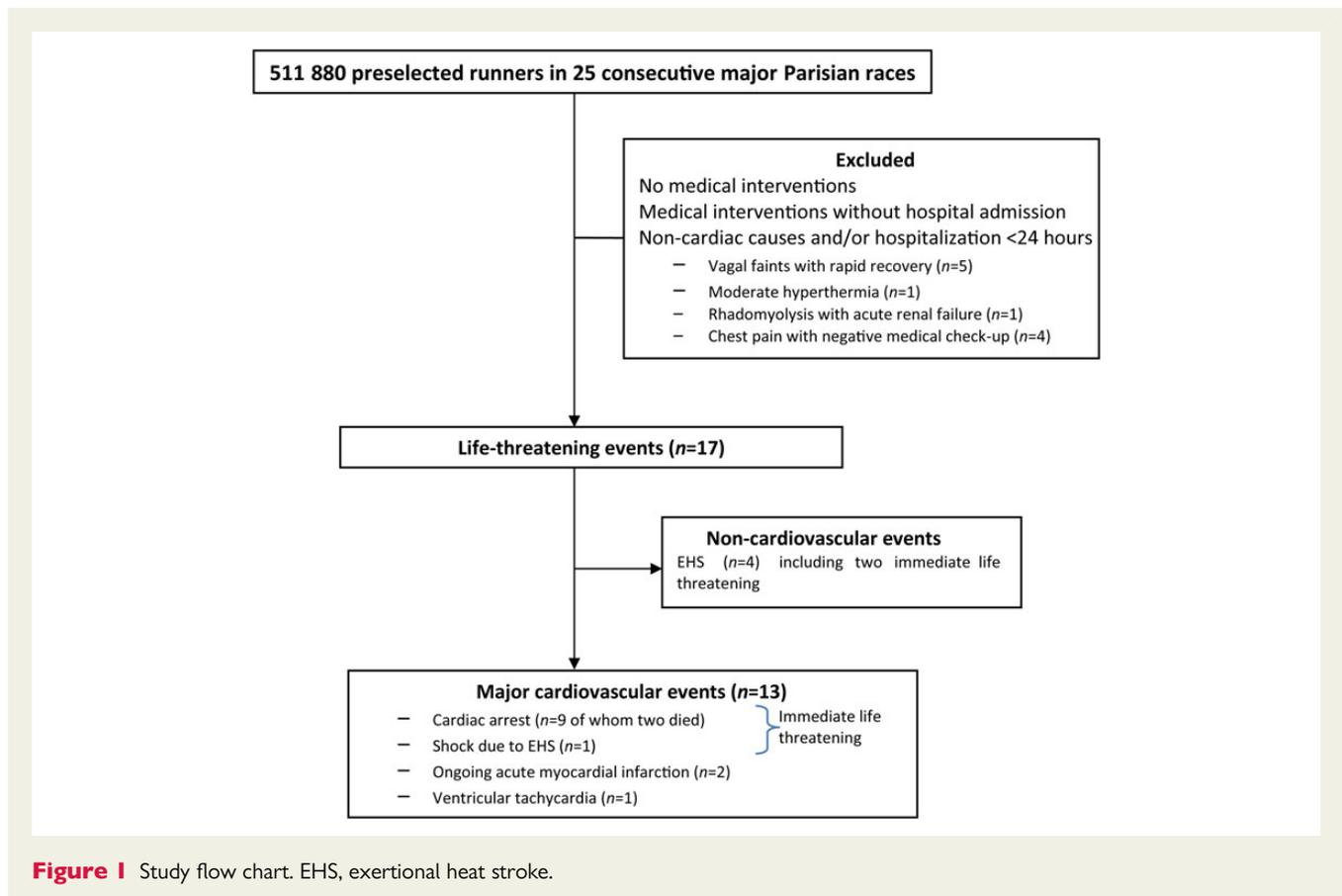
Demographic data

A total of 511 880 runners entered the RACE Paris registry representing 25 races (Table 1). Female participants accounted for 20% of the total number of participants. Mean age was < 40 years with 63% of participants aged of 35 years or more. Runners

Table 1 Selected races

RACES	Number of participants	Discontinuation (%)	Female %	Registered runners (%)	Average age	Age ≥35 (%)	Average duration	Average speed (km/h)	Degree Celsius	Weather	Pollution parameters	Hygrometry (%)	Events *
20 km Paris 2006	18 751	0.6	17	3.8	38.8	62	1h49	11.0	14–18	Sunny	5 (PM10)	82–69	0
Paris half-marathon 2007	18 780	0.8	20	9.1	38.1	57	1h54	11.1	10.5–14	Sunny	4 (NO2 PM10)	69–48	0
Paris marathon 2007	28 261	4.9	16	8.8	41.0	71	4h14	10.0	19–26	Sunny	8 (PM10)	69–42	2
Paris—Versailles 2007	18 434	3.3	18	6.6	40.4	68	1h31	10.5	14–19	Cloudy	4 (O3)	76–53	0
20 km Paris 2007	19 436	1.2	19	5.7	39.0	63	1h50	10.9	13–18	Sunny	5 (PM10)	75–55	1
Paris half-marathon 2008	18 831	1.0	21	6.9	37.6	53	1h55	11.0	12–15	Cloudy	3 (O3)	84–72	0
Paris marathon 2008	29 749	3.0	16	8.4	41.1	72	4h03	10.4	5–8	Bruin	4 (O3)	80–57	1
Paris—Versailles 2008	13 778	0.7	18	6.0	39.9	66	1h29	10.8	11–19	Sunny	5 (NO2)	70–39	2
20 km Paris 2008	21 141	1.8	20	5.2	39.2	64	1h51	10.8	13–19	Sunny	4 (PM10)	84–61	1
Paris half-marathon 2009	21 761	1.0	23	9.5	38.0	56	1h55	11.0	9–9	Rainy	4 (O3)	92–80	1
Paris marathon 2009	31 373	3.3	17	9.6	41.0	71	4h08	10.2	11–16	Cloudy	4 (O3 et PM10)	81–52	0
Paris—Versailles 2009	18 052	0.9	19	9.6	39.6	65	1h30	10.7	18–23	Sunny	5 (PM10)	57–46	0
20 km Paris 2009	22 260	1.5	20	4.3	39.0	63	1h50	10.9	15–16	Cloudy	3 (O3)	79–66	1
Boulogne half-marathon 2009	3920	2.7	15	16.0	39.6	67	1h47	11.8	12–14	Bruin	3 (NO2 et O3)	78–70	0
Paris half-marathon 2010	22 653	2.7	24	5.3	37.3	53	1h59	10.6	3–3.5	Sunny and Windy	3 (O3 et PM10)	48–36	1
Paris marathon 2010	31 596	2.5	18	9.4	40.7	69	4h08	10.2	9–14	Sunny and windy	4 (O3)	64–41	0
Paris—Versailles 2010	19 062	0.5	20	10.0	39.6	65	1h29	10.8	11–14	Cloudy	3 (O3)	68–67	0
20 km Paris 2010	21 607	1.3	23	2 (?)	39.2	63	1h58	10.2	13–17	Sunny	3 (O3 et PM10)	80–68	0
Boulogne half-marathon 2010	3916	2.2	16	18.0	39.9	70	1h48	11.7	13–13	Rainy	3 (O3)	82–83	0
Paris half-marathon 2011	23 983	1.3	24	ND	37.4	53	1h56	10.9	3–8	Sunny	4 (PM10)	66–49	1
Paris marathon 2011	32 092	3.0	20	ND	40.9	70	4h13	10.0	15–27	Sunny	5 (O3)	46–26	2
Paris—Versailles 2011	20 824	0.4	22	9.0	39.3	64	1h33	10.3	15–25	Sunny	4 (O3 et PM10)	84–50	2
20 km Paris 2011	21 166	1.5	23	15.0	39.0	62	1h59	10.1	14–16	Rainy	2 (O3)	92–80	1
Boulogne half-marathon 2011	5236	1.8	17	16.0	39.8	68	1h48	11.7	9–13	Cloudy	6 (PM10)	85–76	1
Paris half-marathon 2012	25 218	0.9	27	6.7	36.9	50	1h57	10.8	8–11	Cloudy	4 (PM10)	86–79	0
Total	5 11 880	1.9	20		39.3	63		10.7					17

PM10, high level of micro-particles of < 10µM; NO2, high level of nitrous oxyd; O3, high level of ozone.



were slightly older in marathons vs. half-marathons. There were more participants in half-marathons than in marathons (358 809 vs. 153 071).

The average running speed was 10.7 km/h (10.0 km/h up to 11.8 km/h) and was slower in marathons when compared with half-marathons (10.2 km/h vs. 10.9 km/h, $P = 0.005$). Discontinuation rate was 1.9% (0.4–4.9%) and was higher in marathons when compared with half-marathons (3.3 vs. 1.3%, $P = 0.00009$). Average outside temperatures were $>20^{\circ}\text{C}$ in four races (#3, 12, 21, and 22) and $<10^{\circ}\text{C}$ in four others (#7, 10, 15, and 20). The pollution index was high (global index of 8) in a single race (2007 marathon, #3) due to a high rate of micro particles ($<10 \mu\text{m}^3$).

Cases selection

Cases without medical intervention/hospital admission, cases with a hospital stay of <24 h and cases which did not require immediate admission in an intensive care unit were excluded (Figure 1). A total of 17 life-threatening events were selected [3.3/100.000; 95% CI (1.8–4.9)] including 13 major cardiovascular adverse events [2.5/100 000; 95% CI (1.2–3.9)] and 4 life-threatening exertional heat stroke (EHS) (Figure 1).

Individuals presenting with major ischaemic cardiovascular events were all male aged 40 years or more with few cardiovascular risk factors. Two were active smokers. All were trained and experienced

runners, defined as performance of one or more endurance race and/or weekly training of 2 h or more, except one (Table 3). Events were more likely clustered to the end of the races without difference between cardiac arrest and cardiovascular events (Figure 2). All individuals presenting with cardiac arrest ($n = 9$) were immediately witnessed and resuscitated by bystanders and/or mobile intensive care units staff. Rates of life-threatening events [3.3 per 100 000; 95% CI (0.4–6.1) vs. 3.3 per 100 000; 95% CI (1.5–5.2), $P = 0.82$] and of major cardiovascular adverse events [2.0 per 100 000; 95% CI (0–4.2) vs. 2.8 per 100 000; 95% CI (1.1–4.5), $P = 0.81$] did not differ between marathons and half-marathons. None of the selected individuals were exposed to any medical treatment or prohibited drugs prior to the race and all had proper hydration during the race.

Case aetiology and outcome

Cardiac arrest was the most frequent clinical presentation of runners with major cardiovascular adverse events (9 of 13) and was predominantly due to ventricular fibrillation ($n = 6$) and less frequently to asystole ($n = 3$). All cardiac arrests were successfully resuscitated except 2.

All individuals with initial shockable rhythm including ventricular fibrillation or ventricular tachycardia survived. Initial presentation with asystole led to death (2 of 3) despite early on-site haemodynamic support by extracorporeal membrane oxygenation implantation in

Table 2 Major reports

Studies and type of race (country)	Type of study and number of runners	Recorded events	Cardiac arrest N (rate)	Events				
				Death N (rate)	Mean age (years)	Male (%)	Timing	Aetiology
Maron (1976–1994) Marathons (USA)	Prospective 221 318	CVD and non-fatal CA	5 (2.3/100 000)	4 (1.8/100 000)	39	80	>50% within the last quarter	4 MI, 1 anomalous origin of LMCA from the right anterior sinus
Roberts—Maron (1995–2004) Marathons (USA)	Prospective 220 606	CVD and non-fatal CA	4 (1.8/100.000)	1 (0.5/100 000)	47	100	>50% within the last quarter	3 MI, 1 mitochondrial myopathy
Tunstall Pedoe (1981–2006) runners Marathons (UK)	Retrospective 650 000	All deaths, CVD and non-fatal CA	14 (2.5/100 000)	10 (1.5/100 000)	48	100	From km 10 to finish line	11 MI, 3 HCM, 2 cerebral haemorrhage
Kim 'RACER registry' (2000–2010) Marathon and half-marathons (USA)	Retrospective 10 871 000	All deaths, CVD and non-fatal CA	59 (0.5/100 000)	42 (0.4/100 000)	42	86	>50% within the last quarter	42 non-survivors (data on 23): 6 HCM, 2 HCM and myocarditis, 3 HCM and MI, 2 HCM and structural abnormalities, 1 HCM and EHS, 1 EHS, 1 ARVC and MI, 2 hyponatremia, 2 presumed cardiac dysrhythmia, 2 unknown (no autopsy). 17 survivors (data on 8): 7 MI and 1 unknown
Schwabe 'SAFER study' (2008–2011) 21 km and 56 km (South-Africa)	Prospective 65 865	Deaths and all medical complications	3 (4.6/100 000)	2 (3.4/100 000)	NA	NA	NA	Non-survivors: no data. Survivors (37 life-threatening): 3 MI, 2 myocarditis, 2 serious cardiac arrhythmias, 14 serious metabolic complications, 6 EHS, 1 hypothermia, 2 pulmonary oedema, 8 serious metabolic disorders, 2 bronchospasms, 1 convulsion
'RACE Paris Registry' (2006–2012) Marathons and half-marathons (France)	Prospective 511 880	All life-threatening events including deaths, CVD, and non-fatal CA	9 (1.8/100 000)	2 (0.4/100 000)	42.8	100	>50% within the last quarter	15 survivors: 7 MI, 3 arrhythmias, 5 EHS. 2 non-survivors: 1 MI and 1 ARVD

ARVC, arrhythmogenic right ventricular cardiomyopathy; CA, cardiac arrest; CVD, cardiovascular death; HCM, hypertrophic cardiomyopathy; EHS, exertional heat stroke; LMCA, left main coronary artery; MI, myocardial ischaemia; NA, not available; RCA, right coronary artery; VT, ventricular tachycardia.

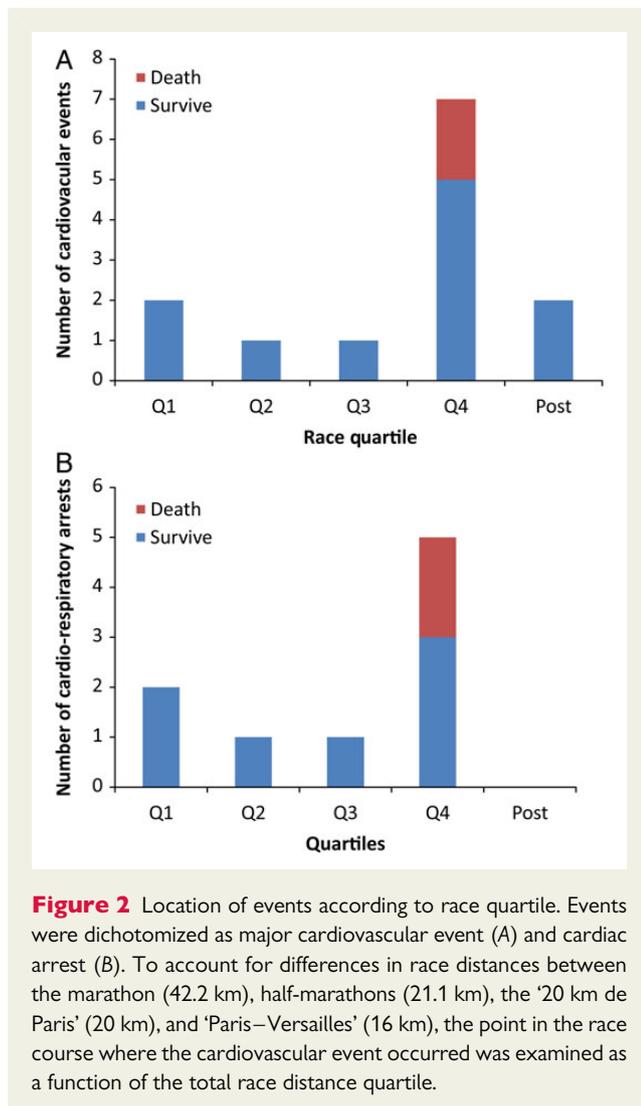
Table 3 Life-threatening cardiovascular events

Case	Gender	Age	CV risk factors	Training (h/week)	Prior races	Type of race	Timing	Event	Aetiology	Treatment	Discharge	Note
1	M	47	Yes (smoker)	7	1	Marathon	km 5–6	CA with VF	AMI	PCI	Alive	Prior high-level sportsman
2	M	56	No	6	20	Marathon	km 19	CA with VF	AMI	PCI	Alive	Recent negative treadmill test (250 W)
3	M	23	No	2	1	Half-marathon ^a	km 13	CA with VF	Brugada syndrome	ICD	Alive	Normal post-event EKG
4	M	54	No	5	25	Marathon	km 0	CA with VF	AMI	CABG	Alive	Recent negative treadmill test (180 W). Recent short of breath
5	M	23	No	6	3	Half-marathon	Arrival	Shock	EHS	Medically managed	Alive	Recent cold and race with a non-breathable garment
6	M	45	No	2	5	Half-marathon	Arrival	CA with VF	AMI	PCI	Alive	Recent negative treadmill test (270 W)
7	M	44	No	3	2	Half-marathon	Post-arrival	VT	Likely ARVC (MRI, releasable VT)	Medically managed	Alive	Documented normal EKG
8	M	45	No	2	6	Half-marathon	Arrival	CA with asystole	ARVC (autopsy)	ECLS	Death	
9	M	50	No	1.5–2	16	Half-marathon	Arrival	CA with VF	AMI	PCI	Alive	Recent negative treadmill test. Recent short of breath
10	M	48	No	4.5	>40	Half-marathon	km 18	CA with asystole	AMI	ECLS and PCI	Death	
11	M	46	Yes (HCT, heredity)	1	0	Half-marathon	Post-arrival	Chest pain	AMI	PCI	Alive	15 days ago, 1 h atypical rest chest pain
12	M	34	Yes (SD)	3.5	3	Half-marathon	km 19	CA with asystole	Unknown ^b	ICD	Alive	Familial history of sudden death
13	M	41	Yes (smoker)	2.5	5	Half-marathon	Post-arrival	Chest pain	AMI	PCI	Alive	2 typical effort chest pains since 1 month

AMI, acute myocardial ischaemia; ARVC, arrhythmogenic right ventricular cardiomyopathy; CA, cardiac arrest; ECLS, extracorporeal circulatory life support; EHS, exertional heat stroke; HCT, hypercholesterolaemia; ICD, implantable cardiac defibrillator; MRI, magnetic resonance imaging; PCI, percutaneous coronary intervention; SD, sudden death; VF, ventricular fibrillation; VT, ventricular tachycardia.

^aHalf-marathon or similar ('20 km de Paris' and 'Paris–Versailles').

^bAfter extensive investigation.



one patient. Fatality was due either to arrhythmogenic right ventricular cardiomyopathy (ARVC) leading to death within the first 3 h of medical management (Case #8) or to hypoxic-ischaemic brain injury 19 days after successful percutaneous coronary revascularization for cardiac arrest complicating acute myocardial ischaemia (AMI) (Case #10). There was only one cardiac arrest successfully resuscitated after asystole which remained of unknown origin despite extensive investigation (Case #12).

Among the four individuals without cardiac arrest on initial presentation, one was severe shock due to EHS (Case #5), one was dizziness due to ventricular tachycardia (Case #7), and the two remaining were symptomatic ST-elevation myocardial infarction occurring within 2 h after the end of the race and underwent percutaneous coronary intervention (Cases #11 and 13).

A total of five patients with EHS were identified, including one severe shock presentation. All except one were reported in races where the mean temperature was 20°C or more. Acute myocardial ischaemia was the leading cause of major cardiovascular events, identified in 8 of 13 patients aged of 48 ± 5 (mean \pm SD) and led to immediate myocardial revascularization by percutaneous

coronary intervention ($n = 7$) or coronary artery bypass surgery ($n = 1$). Only one reported typical chest pain on exercise 1 month before (Case #13) and three complained of shortness of breath and limitation of performance (Cases #4, 9, and 11). Finally, four patients had negative valid stress tests before the race (Cases #2, 4, 6, and 9) of whom two had atypical symptoms (Cases #4 and 9). All survivors were symptom-free at 1 month except one with light neurological damage.

Interpretation of the meta-analysis

Among the 147 citations extracted from PUBMED, consistent individual data were available in 10 studies including the RACE Paris Registry, of which 2 were duplicates and 2 had insufficient data (Figure 3). Among a total of 12 540 669 runners, 94 life-threatening events were selected including 61 deaths. The only statistically analysable item was fatality during ERR which was neither affected by age, length of races, prior experience in long distance running or gender. However, fatality was higher when non-shockable (asystole) vs. shockable rhythm at presentation [OR 29.9; 95% CI (4.0–222.5) $P = 0.001$] and in non-ischaemic vs. ischaemic aetiology [OR 6.4; 95% CI (1.4–28.8) $P = 0.015$] (Figure 4).

Discussion

Whether AMI is the dominant cause of life-threatening/fatal events during endurance races remains controversial. The RACE Paris registry prospectively collected all life-threatening/fatal events which had occurred within a 6-year time period in 25 major Parisian ERR totaling >500 000 runners. The main findings are below:

- Life-threatening events (3.3/100 000) and immediate life-threatening events (2.4/100 000) were rare and case-fatality very low (0.4/100 000).
- Events occurred over the whole length of the races with a peak at the end without differences according to marathons vs. half-marathons.
- Major cardiovascular events were the leading aetiology (2.5/100 000) among those AMI was the predominant cause (1.6/100 000).
- Major cardiovascular events were unpredictable in the vast majority and were not associated with races' characteristics.
- Cardiac arrests with non-shockable rhythm were associated with case fatality.

The absolute number of life-threatening events in the RACE Paris registry is low but the event rate is among the highest ever reported, ranging from 1.8 up to 2.3 per 100 000 runners according to the literature. This is accounted for by the design of the RACE Paris registry, an ongoing prospective study with an exhaustive report of all events and where missed case is virtually impossible.

The observed favourable outcome in the RACE Paris Registry is another particular finding. Although different from that reported from resuscitated sudden deaths occurring on city streets and during sports,^{16–18} it first contradicts the common idea that treatment of cardiac arrest induced by intense exertion is difficult. It also highlights that prompt medical management is an effective strategy, although specific to these endurance races.^{7,17} Survival rate after cardiac arrest during sport is usually <20%, bystander CPR and initial cardiac defibrillation being the strongest independent predictors

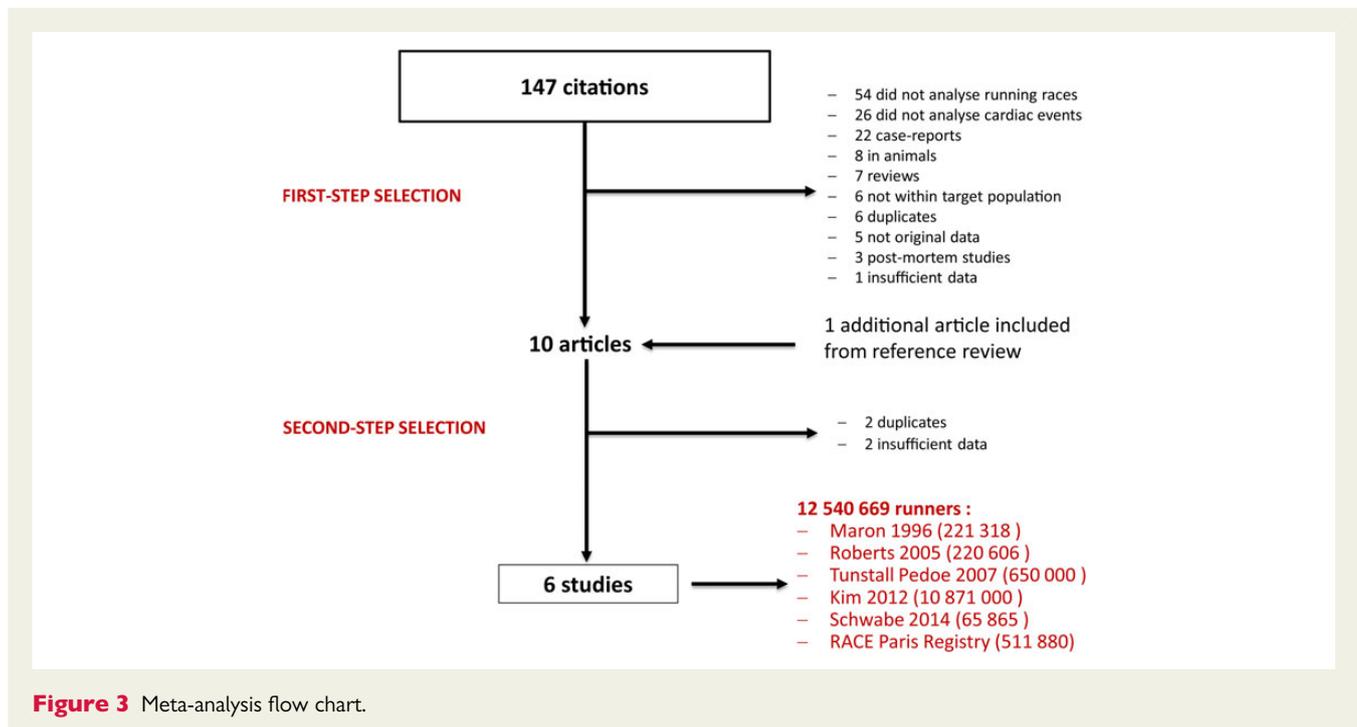


Figure 3 Meta-analysis flow chart.

of survival, and doubles in areas with active witnesses.^{17,18} However, unsuccessful resuscitation was extremely low (2 of 10) in the RACE Paris Registry and differs from previous reports.^{3,5,8} Although availability of on-site emergency might be seen as a confounder for these discrepancies, the aetiology should be viewed as a potential explanation for these discrepancies. Death occurred despite immediate on-site intervention with no low flow when asystole and ARVC were identified.

We found AMI to be the leading cause (50%) of immediate life-threatening events, as reported in the London survey.⁶ In addition, common angiographic features of acute coronary syndromes including either intracoronary visible thrombus or unstable plaque were reported in all patients of the RACE Paris Registry except one presenting with AMI, and myocardial revascularization was successfully performed in all of them. Our data differ significantly from the RACER survey where features of stable CAD were only reported.³ Finally, in the Paris Race Registry, a single life-threatening event was left without formal diagnosis despite extensive investigations further emphasizing atherothrombotic plaque rupture, described years ago in vigorous exercise,¹⁹ as one of the major mechanism of ischaemic events during running races.²⁰ Of note, ischaemic heart disease was clustered to aged runners above 35 years old as opposed to non-ischaemic heart disease or other causes of life-threatening events, including hypertrophic cardiomyopathy which was not reported in the present registry.

Poor predictability is another key finding of the RACE Paris registry. Only 2 of 17 life-threatening events could have been avoided, one EHS-related shock and one AMI with stress angina prior to the race. EKGs at rest or treadmill tests were available in half of runners who experienced an acute cardiovascular event during the race and were without abnormalities. A very low proportion of runners with an event (3 of 17) complained of recent mild functional signs—mainly performance limitation—which afterward should have been

considered as angina.^{14,21,22} Poor predictability does not preclude medical examination prior to endurance races. However, the lack of clinical symptoms or findings at examination including a normal EKG at rest as well as normal treadmill test is inconclusive with respect to prediction of further events. This further raises the issue of functional tests evaluating the physical capability and safety of individuals who are willing to perform ERR.²³ Whether a more aggressive approach as suggested by few authors²⁴ may help to further risk stratify asymptomatic runners remains a matter of debate.²⁵ There are counter-arguments to such approach showing that rest EKG combined with a careful clinical examination drastically reduce the rate of sudden death in competitors to that of individuals not practising any sports (0.9/100 000).^{26,27} Of interest, by using such approach, 9% of competitors underwent further medical tests and 2% were contra indicated for competitive sports. However, this study was restricted to young competitors aged <35.

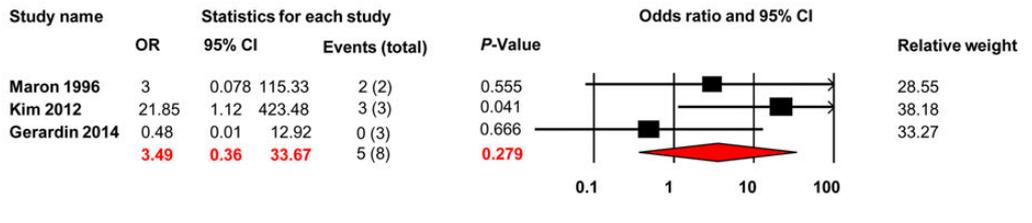
EHS was rare and less frequently reported than in warmer climates, but occurred preferentially when the mean temperature was over 20°C, although it can happen in the absence of high environmental temperatures.²⁸ We found no relationship between other weather conditions and life-threatening events. However, extreme weather conditions was rare and there was a single race with extreme values in air microparticles concentration, a condition known to be associated with hazard.²⁹ The RACE Paris registry population comprised experienced amateur sportsmen of a relatively advanced age but with only few females (20 vs. 47%) as compared to US surveys.^{3,30} This may account for the differences in event rates. In fact, none of the race or population characteristics of the RACE Paris Registry had a determinant impact on the outcome. This was further ascertained by the meta-analysis.

We acknowledged that the findings of the RACE Paris Registry cannot be extrapolated to extreme conditions of endurance running race, to 'week-end' joggers where medical attention is

much less but also to elite or professional runners in whom medical attention is mandatory. We cannot exclude that a selection bias may have accounted for the low incidence rate of events. The occurrence of symptoms during training session may have discouraged

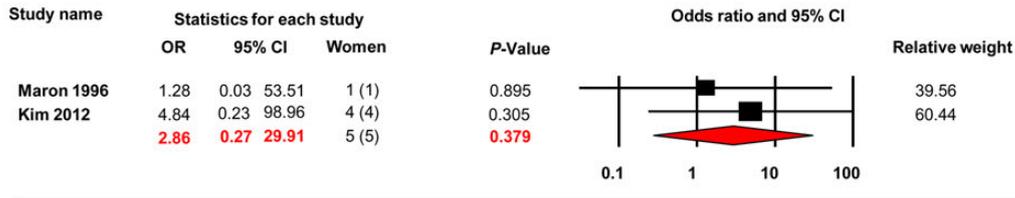
runners to participate to endurance races and to seek for medical attention. Likewise, no speculation can be made with respect to the potential prevented life-threatening events by a systematic medical screening prior to the race. Indeed, not all patients who suffered

A Lethality according to age (< 35 years vs. ≥ 35 years)



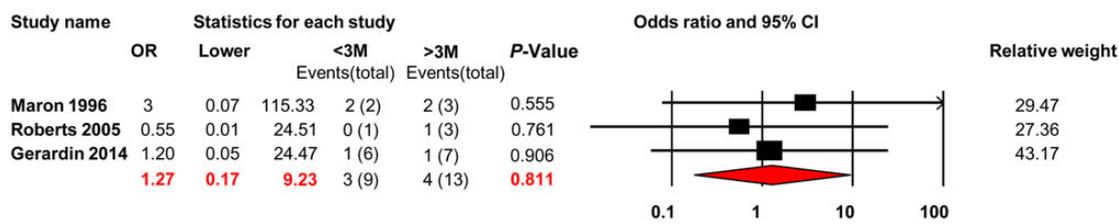
Heterogeneity: $I^2 = 30\%$
 Egger's regression test for publication bias argument: $P = 0.62$

Lethality according to gender (male vs. female)



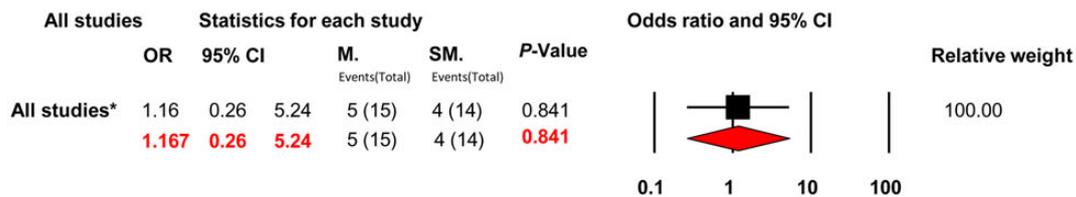
Heterogeneity: $I^2 = 0\%$
 Egger's regression test for publication bias argument: not estimable < 3 studies

B Lethality according to previous training (<3 marathons vs. ≥3 marathons)



Heterogeneity: $I^2 = 0\%$
 Egger's regression test for publication bias argument: $P = 0.95$

Lethality according to running race type (marathon vs. semi-marathon)



* Maron 1996, Schwabe 2014, Gerardin 2014
 Heterogeneity and Egger's regression test not estimable

Figure 4 Outcomes according to runner's characteristics (A), type of races and prior training (B), and clinical presentation of the life-threatening event (C). Odds ratio with (95% confidence interval) for lethality is presented.

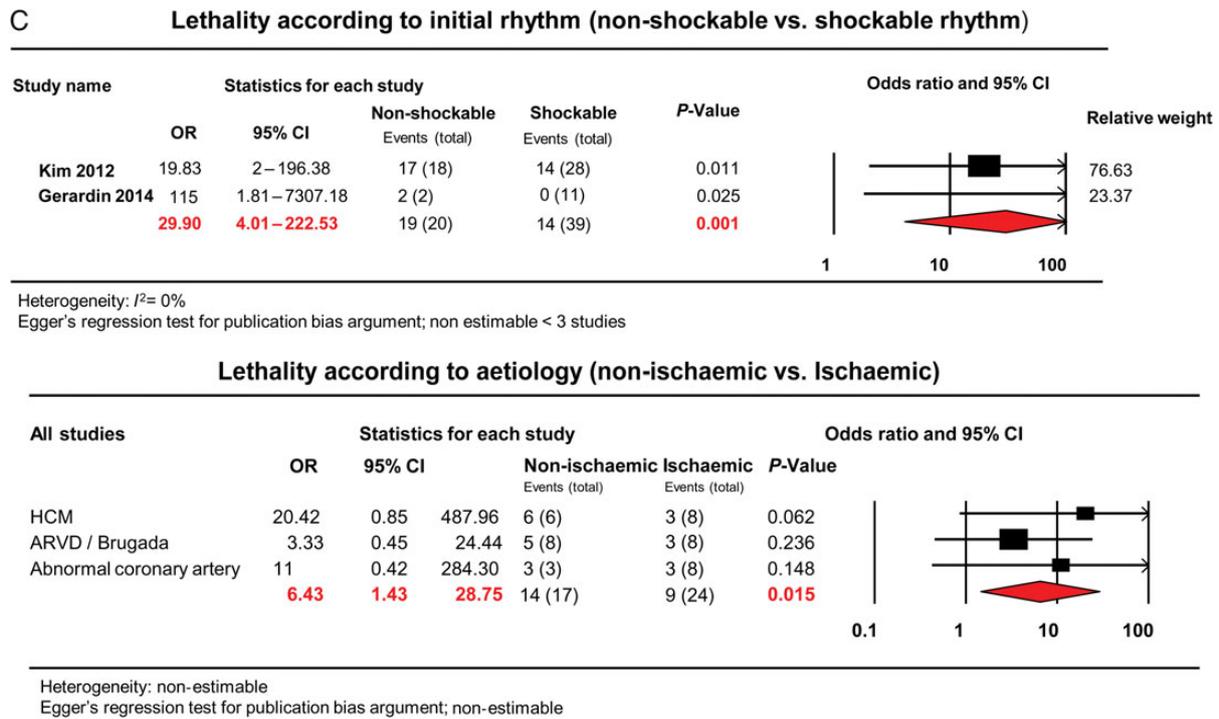


Figure 4 Continued

a life-threatening event had a baseline EKG and silent CAD cannot be excluded. However, the rate of life-threatening events that we report is not lower than that observed in places where medical certificate is not requested. Finally, the number of events is limited and the results of the meta-analysis should be taken with caution.

In conclusion, the prospective RACE Paris Registry confirms the very low prevalence of life-threatening events during endurance race, a finding further corroborated by the meta-analysis. We also demonstrate AMI as a consequence of atheroma plaque rupture to be the leading cause with good survival due to successful immediate on-site resuscitation and myocardial revascularization. These events were found unpredictable and refinement in the risk stratification using functional tests remains to be established. In particular, Whether identification of performance limitation and/or atypical symptoms is a helpful strategy remains to be demonstrated.

Supplementary material

Supplementary Material is available at *European Heart Journal* online.

Authors' contributions

H.M., A.B.-A. performed statistical analysis. B.G., J.-P.C., P.A. handled funding and supervision. B.G., J.-P.C., M.J., L.L., C.F., P.A. acquired the data. B.G., J.-P.C., H.B., J.M., E.T., L.B., P.A. conceived and designed the research. B.G., J.-P., C.H.B. drafted the manuscript. H.M., A.B.-A., H.B., J.M., E.T., L.B., M.J., L.L., C.F., P.A. made critical revision of the manuscript for key intellectual content.

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