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Peculiarities of Coronary Artery Disease in Athletes

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1. Introduction

Intense physical activity increases the risk of acute coronary syndrome but regular physical training is a cardio vascular protective factor (Shepard & Balady, 1999).

Sport related myocardial infarctions (SMI) are rare but serious. They present angiographic features that explain some clinical characteristics, the limits of the detection of coronary disease in this population and encourage decision making in order to have a better regulation of sport such as rules of good practice and dissemination of defibrillators on sports sites.

However, athletes could be asymptomatic despite tight coronary stenosis as in the three clinical cases presented. The reasons for the asymptomatic nature of these coronary diseases are probably due to cardiovascular adaptation to regular training. These athletes are at risk of major cardiac events and the place of stress testing remains important in this population.

2. Sport related myocardial infarctions

2.1 Clinical cases

2.1.1 Methods

We report a retrospective study of twelve cases of SMI. All patients had myocardial infarction (MI) defined as ischemic symptoms and ST segment elevation on ECG. MI was considered to be related to sport if it occurred during sport with vigorous exertions (METs > or = 6) or within 2 hours afterward according to the definition of Von Klot et al (Von Klot et al, 2008). All patients had emergent coronary angiography.

2.1.2 Results

A total of twelve patients are studied, all men. The mean age is 47.7 years (24 to 64). Eight of these patients considered themselves as insufficiently trained. Chest pain is the most

common presentation (11/12) with initial collapse in one case (case 12). SMI occur after exercise in 3 cases and during in 9 cases with unusual very vigorous exertion in 5 cases. One patient returned to sport after a year off (case 12). In this series, the most common sport was running (33%). The clinical characteristics of patients are presented on table 1.

Only two patients had multivessel diseases. Primary coronary intervention (PCI) was performed in nine patients, fibrinolysis in two patients (cases 1 and 4). The last patient (case 7) had normal coronary angiography just after relief of chest pain but elevated markers of myocardial necrosis. Coronary angiographic findings are presented on table 2.

N°	Age (years)	Sex	Risk factors	Sports	Symptoms	Circumstances
1	40	M	S, FC	Swimming	Chest pain	After sport
2	51	M	0	Running	Syncope	During sport
3	52	F	H, FC	Running	Chest pain	During sport
4	45	M	0	Triathlon	Chest pain	During sport
5	40	M	FC	Running	Chest pain	During sport
6	24	M	S, FC	Football	Chest pain	After sport
7	39	M	0	Rugby	Chest pain	During sport
8	63	M	0	Cycling	Chest pain	During sport
9	48	M	S, FC	Karate	Chest pain	During sport
10	64	M	H, FC	Running	Chest Pain	After sport
11	50	M	D, FC	Tennis	Chest Pain	During sport
12	33	M	D	Football	Chest pain	During sport

Table 1. M: male; F: Female; S: cigarette smoking; FC: family history of coronary artery disease; D: dyslipidemia; H: hypertension; 0 : no risk factor

N°	Ter	CA	TIMI flow	Collaterals	Thrombus	AL
1	Ant	LAD	3	0	0	0
2	Ant	LAD	2	0	0	0
3	Ant	LAD	2	0	+	0
4	Ant	LAD	3	0	+	0
5	Ant	LAD	2	0	+	0
6	Glob	LM	2	0	+	CD
7	Inf	0	3	0	0	0
8	Inf	RCA	1	0	+	0
9	Inf	RCA	2	0	+	0
10	Inf	RCA	0	0	+	LAD
11	Inf	RCA	2	0	+	0
12	Inf	RCA	0	+	+	Mg *

Table 2. Ter: territory ; Ant: anterior wall ; Inf: inferior wall, Glob: global; CA: culprit artery; LM: left main; LAD: left anterior descending artery; RCA : right coronary artery; Mg: marginal branch of circumflex artery; AL: associated lesion, * lesion < 70 %

Thus the most common angiographic presentation is a single-vessel disease with thrombus as case N°11.

This patient had inferior SMI. Chest pain occurred during tennis training and he arrived in our cath lab three hours after symptom onset. Cardiac catheterization was performed using a 6 French sheath via right radial artery access. Pharmacotherapy included 70 U/Kg unfractionated heparin and 250 mg aspirin intravenous and clopidogrel 600 mg loading dose. The left coronary artery was normal (figure 1). The right was occluded, flow TIMI 0 (Figure 2). PCI was performed with use of a thrombus aspiration catheter. Fresh clots were retrieved from the filtered aspirated blood (Figure 3).

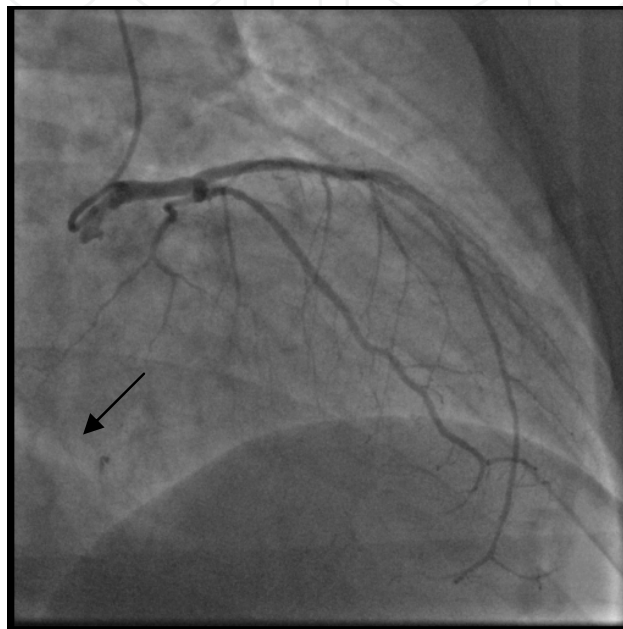


Fig. 1. Left coronary artery with collateral flow in the right coronary artery (black arrow)

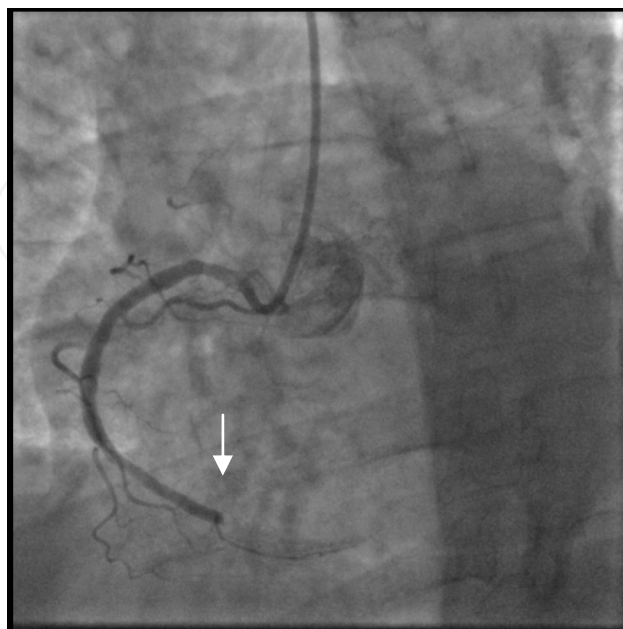


Fig. 2. Right coronary artery with thrombus (white arrow)

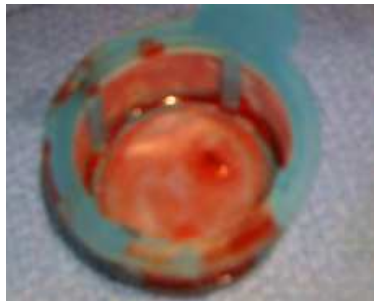


Fig. 3. Fresh clot removed by aspiration

Although after thromboaspiration only a limited stenosis remained (figure 4) a bare metal stent was placed to optimize the result (Figure 5).



Fig. 4. Result after thrombus aspiration

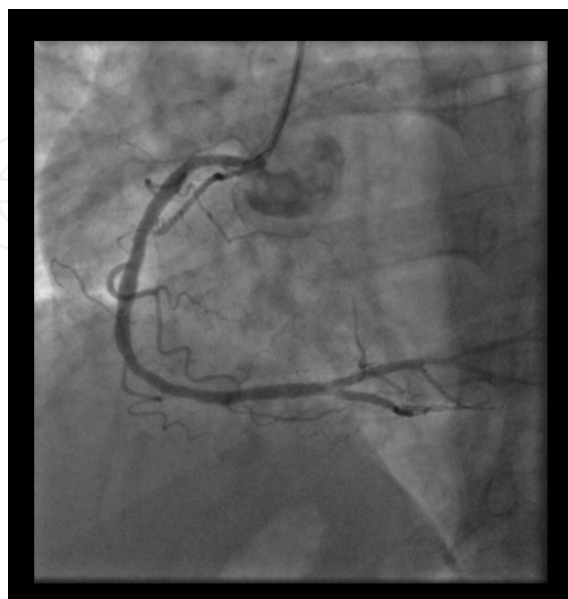


Fig. 5. Final result

2.2 Discussion and literature review

2.2.1 Prevalence of SMI

It is well reported that MI risk is increased during and after vigorous exercise (Gibson et al, 1980; Mittelman et al, 1993; Willich et al, 1993; Von Klot et al 2008). Ciampriccotti and Taverne reported even one case of MI twice during sporting activities (Ciampriccotti and Taverne, 1992). Mittelman et al reported that 4.4 % of MI were related to exercise which would represent more than 5000 MI per year in France. In addition, the majority of sport-related sudden deaths (SSD) are due to coronary artery disease and mainly MI.

The prevalence of SSD is more often evaluated, in retrospective studies (Maron et al, 1996; Peddoo, 2007), that of SMI. The SSD rates are between 1/50000 to 1/80000 athletes in these studies. SSD are most commonly related to coronary disease in the general population contrary to young competitive athletes (Marijon et al 2011).

Chevallier et al reported in a prospective study a yearly SMI incidence of 2.6/100000 persons. (50 SMI, lethal in 3 cases) (Chevallier et al, 2009).

So, SMI are rare but occur in a supposedly healthy population and shock the public opinion and the medical profession especially as the clinical presentation can be severe particularly when it comes to a sudden death.

2.2.2 Which athletes and which sports?

Running is the most commonly practiced sport in our study, reflecting European trends. Indeed the number of runners who completed the Paris Marathon has increased from 9000 to 30000 from 1990 to 2010. We have previously reported data for European studies about the type of sport during SMI (figure 6). The most commonly practiced sports in Europe are present. The number of runner is low as this is old data.

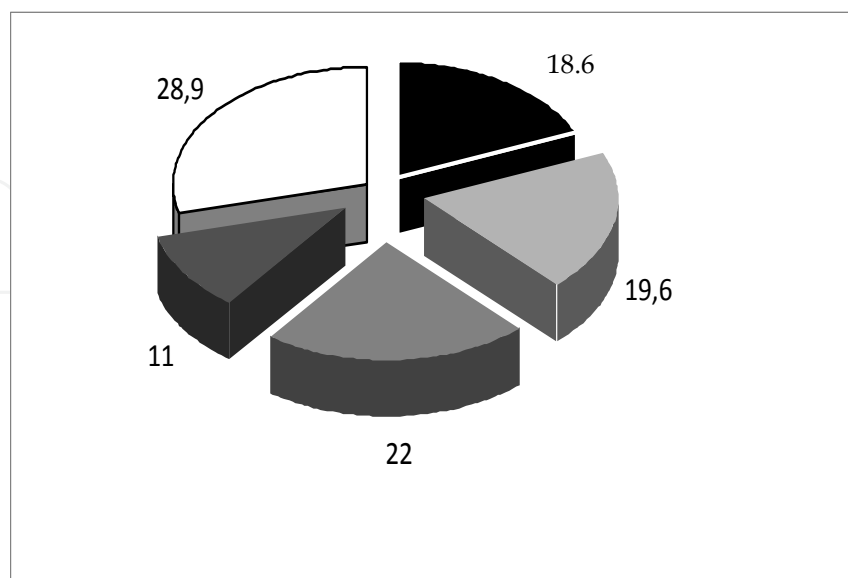


Fig. 6. Sports practiced during SMI : Tennis : ■; Cycling: ■; Football : ■; Running : ■; Other : □. (Halna du Fretay and Gerardin, 2008)

Recently, Marijon et al reported that cycling (30.6 %), running (21.3 % and football (13 %) were the most common sports related to sudden death (Marijon et al, 2011).

Hiltgen et al reported that SMI occurred most commonly after exertion and that the recovery period was particularly at high risk of SMI (Hiltgen et al 1989). The vagal stimulation may be the cause of coronary spasm, especially if the athlete smokes at this time. On the contrary, among runners, cardiac events occur in one third of cases at the end or after exercise and the rest during exercise (Robert and Maron, 2005; Pedoe, 2007; Gerardin, 2009). Gerardin reported even one case of SSD just at the start of the Paris Marathon.

SMI concern most often men aged over 35 years as in our study (10/12 patients) and is previously well reported (Roberts & Maron, 2005; Chevallier et al, 2009). Giri et al reported that patients with an exertion-related MI were more likely to have risk factors including male sex, hyperlipidemia, hypertension and current cigarette smoking (59 % versus 37 % in non exertion-related MI) but in a population of which had known coronary artery disease and older than that of our study (Giri et al 1999). There were 28 cigarette smokers in a population of 42 patients in one study on unstable angina, SMI and SSD related to sport (Ciampricotti et al, 1990). We find in our study, with a small number of patients, few risk factors in this population but often family history of coronary disease and 4/12 patients without risk factor. This is similar to those who suffer MI at young age (Kanitz et al 1996; Bajaj et al, 2011).

High frequency of exertion is a protection factor against SMI as reported by Giri and Mittelman. The latter showed that the risk of MI during exertion or within one hour afterward was elevated 107 times for subjects who usually exercise less than one a week and only 2.4 times for those having more than 5 times (Mittelman et al, 1993). So the subject most at risk of SMI is an untrained man over 35 years, current smoker and SMI can occur throughout or after exercise.

2.2.3 Clinical characteristics

The existence of prodromata before SMI or SSD is variable in studies. Chest pain is most commonly reported in high cardiac risk population or in case of known ischemic heart disease (Opie, 1975; Northcote et al, 1986). Several studies reported the existence of symptoms neglected before SMI (Droniou et al, 1987; François et al, 1989). In the study of Droniou and all, symptoms were present in 45 % of cases particularly after the age of 40 years with angina in 11/20 cases. The prevalence of risk factor was high in this study.

In a population with few or no (23.8 % of patients) coronary risk factor, Ciampricotti et al reported only 3 patients with prodromata in their study of 42 cases of SSD, SMI or unstable angina related to sport (Ciampricotti et al, 1990). Pedoe and Gerardin reported very few or no symptom in cases of SSD most commonly due to ischemic heart diseases (Pedoe, 2007; Gerardin, 2009).

Giri and all found ventricular fibrillation in 20 % of exertion-related MI and 11 % in non exertion-related MI (Giri and all, 1999).

Thus SSD appears to be a common mode of SMI or unstable angina related to sport presentation, as reported by Ciampricotti (28 % of cases), Gerardin (all cases) (Ciampricotti et al, 1990; Gerardin, 2009). We find in our study just one case of possible ventricular arrhythmia. It may be due to the small number of patients and the fact that SMI

occurred during trainings. Mental stress caused by a competitive situation leads to an greater increase in the heart rate during exertion (Lindholm et al, 2006;) and Viru et al reported that competitive conditions increase the cortisol response to exercise, suggesting that sympatho-adrenal system activation occur in such situations (Viru et al, 2010). Such complications are probably explained by high heart oxygen consumption during exertion at the time of SMI, the activation of the sympathoadrenergic system with increase of plasma nor epinephrine and epinephrine (Strobel et al, 1999), the absence of myocardial preconditioning due to the features of coronary disease in SMI wich could promote malignant ventricular arrhythmias.

2.2.4 Angiographic characteristics

In our study, 1 patient had normal coronary angiography, 8 patients had single vessel disease, and 3 multivessel disease. We had previously reported data from European studies showing the prevalence of single-vessel disease (Figure 7).

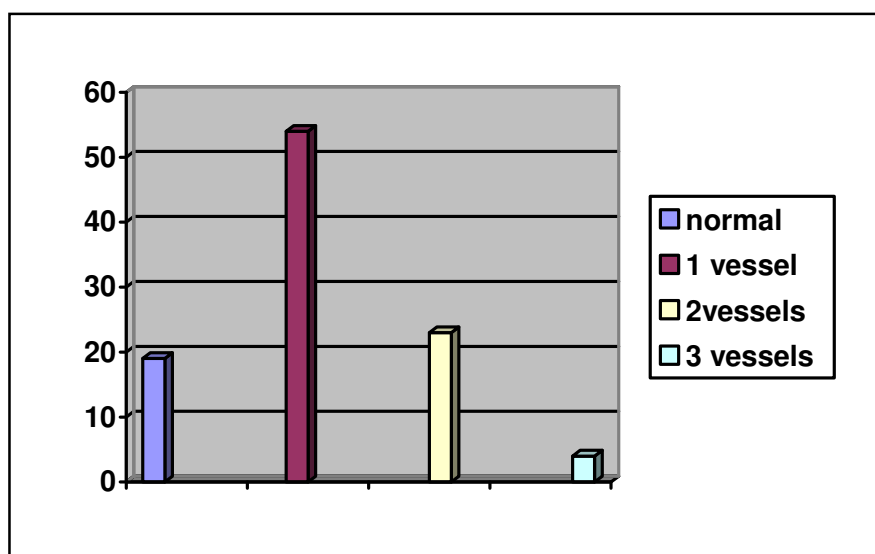


Fig. 7. Angiographic characteristics of SMI in European studies, percentage value of 97 patients, Halna du Fretay and Gerardin, 2008.

These angiographic characteristics are similar to those of MI in the young (Kanitz et al, 1996; Bajaj et al, 2011) despite a mean age of 45.7 years in our study.

Giri et al reported in their study 50 % of single-vessel disease in case of MI related to exertion and 28 % in case of MI none related to exertion. Three vessels disease was finding respectively in 8 % and 41 % of cases. Nevertheless, in the first group the population was more likely to have risk factors but was also more likely regular exertions with its probable beneficial effect (Giri et all 1999).

Most of the studies on SMI, usually with a younger population, show in more than 50 % of cases single vessel disease. Ambrose et al reported that MI frequently develops from previously non severe lesions (Ambrose et al, 1988). It is recognized that plaque rupture is the most common substrate for coronary thrombosis and occurs in case of vulnerable plaques as thin-caps fibroatheroma (Fuster et all, 2005). During exertion several phenomena

occur as increased coronary flow, adrenergic activity, blood pressure and heart rate causing a shearing effect of the coronary arteries and favouring plaque rupture, intimal haemorrhage. Platelets are also implicated in the participation of acute coronary syndromes particularly in exercise (Hilberg et al, 2003) and strenuous exercise is associated with a transient hypercoagulability state (Lippi and Maffulli, 2009). In vivo platelet activation is reported in marathon runners (Kratz et al, 2006). Exertion can be the trigger of a vulnerable plaque rupture and thrombosis promoted by modifications of haemostasis. Another possible pathophysiological mechanism is the occurrence of spasm (Hiltgen et al, 1989) and could explain the case N° 7 of our study. Few cases of spontaneous coronary dissection (Kalaga et al, 2007) and congenital coronary artery anomalies (Corrado et al, 1998) are also reported but concern young athletes with a different pathophysiological mechanism.

We can suppose that most of these patients with single-vessel disease had no severe coronary stenosis before SMI and that would explain the limits of stress testing to prevent SMI. Gerardin reported in their study 3 SMI with negative stress testing a few months before in 2 cases (Gerardin, 2009).

The patient of case N° 11 is a typical example of the probable pathophysiological mechanism of SMI.

2.2.5 Which specific treatment?

There is no specific treatment of SMI but some features should be noticed.

2.2.5.1 Prevention rules

Smoking is not only a risk factor of coronary disease but has also deleterious effects in the short term as an increased level of carboxyhemoglobin reducing the amount of haemoglobin available to carry oxygen, increased heart rate and blood pressure but with a decrease in coronary blood flow. It follows in an increase in myocardial consumption but a decreased supply. Smoking is also associated with an increased risk of vasospastic angina (Caralis et al, 1992). This can be mediated by increased catecholamines or during the recovery phase by acetylcholine release with vasospastic paradoxical effect in case of endothelial dysfunction. Chevallier et al reported that 73 % of young athletes smoke a cigarette in the last hour or two hours after a strenuous exercising (Chevallier et al, 2005). So educational measures against smoking are a priority.

Because of platelet activation during exercise aspirin use was discussed by some authors (Mittelman et al, 1993, Burtscher et al, 2007) but criticized by other and not recommended in case of exertion in hot weather (Fred, 1981) or with risk of body collision. Its use should be clarified by further studies, especially in athletes at risk of SMI.

2.2.5.2 Reperfusion therapy

Reperfusion strategies in SMI must be consistent with the recommendations of ESC for the treatment of STEMI but although the use of manual catheter thrombus aspiration during PCI is only class II a in the recent guidelines on myocardial revascularization (The Task Force on Myocardial Revascularization of ESC/EACTS, 2010), the advantage of this technique seems to be especially great in case of SMI.

2.2.5.3 Management of complications

We have previously emphasized the risk of sudden death or serious ventricular arrhythmias in SMI. Roberts and Maron reported nine cardiac events occurring during marathons, with SD (5 cases) and non fatal cardiac arrest (NFCA) (4 cases) from 1976 to 2004. Seven of the nine runners had underlying atherosclerotic coronary disease. The four patients with NFCA had external defibrillation performed promptly within 5 min. These authors observed a decrease in mortality since 1995, which was largely attributable to the expanded access to external defibrillators (figure 8).

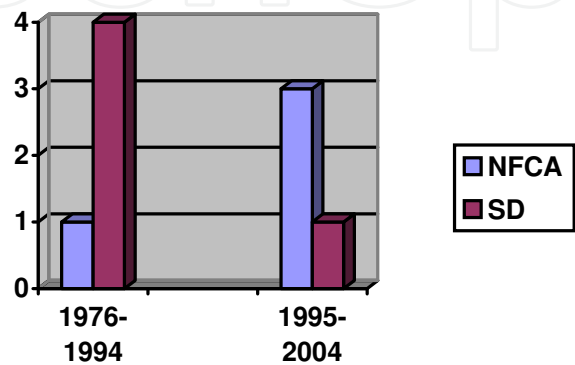


Fig. 8. Cardiac events occurring during marathons from 1976 to 2004, (Roberts and Maron, 2005)

Gerardin reported four cardiac arrests related to sport, with proven coronary diseases and no deaths. Sport events were marathons or running races of 20 km with a medical supervision by mobile intensive care units (ambulances). These four athletes had external defibrillation for ventricular fibrillation (SMI in 3 cases) (Gerardin, 2009).

So for these competitions the organization of medical teams including physicians, paramedics and emergency medical technicians trained to use defibrillators is saving-life.

3. Unrecognized coronary disease among athletes

In France 75 % of people aged 40 to 60 years report taking part in sporting competitions or recreational sport. A proportion of these people will have coronary artery disease either known or unknown. These athletes with unknown ischemic heart disease, sometimes asymptomatic, should be screened.

3.1 Case reports

Case N°1: A 43-year-old man presented with discomfort after running to catch his train. His risk factors were smoking and dyslipidemia. He was a well trained athletes, previous professional basketball player, and tennis player at a regional level with training at least three times per week. He was examined in emergency department a few hours later with a normal examination including ECG and troponin. The diagnosis was a vagal discomfort and consultation from a cardiologist was requested. ECG showed negative T waves in leads II,

III and aVF. Conventional ECG exercise testing showed late but profound ST segment depression in leads V1- V4, asymptomatic and coronary angiography was performed showing two vessel disease (figures 9, 10 and 11).



Fig. 9. Left coronary artery with short stenosis of LAD

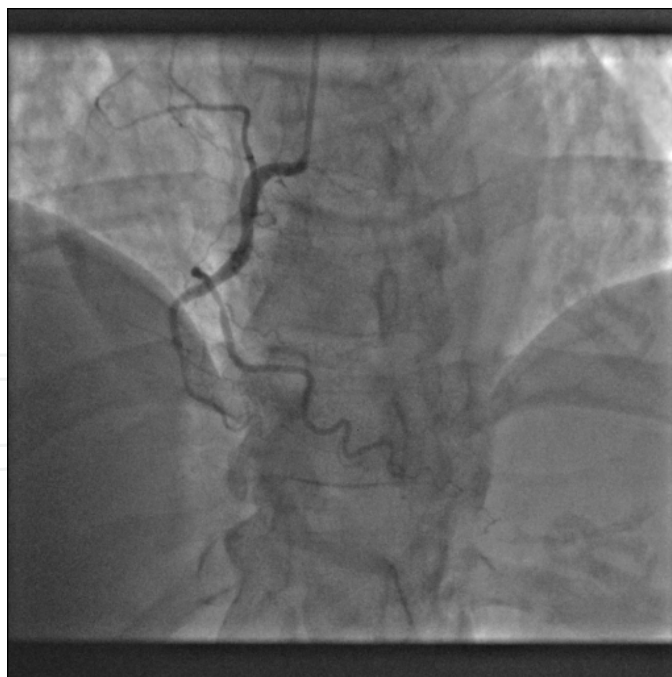


Fig. 10. RCA occlusion

This athlete was able to play tennis in competition despite at least one chronic lesion (occlusion of the RC may be recent and the cause of the discomfort). Coronary artery bypass grafting was performed in this patient who seeks now to return the competitive sport.

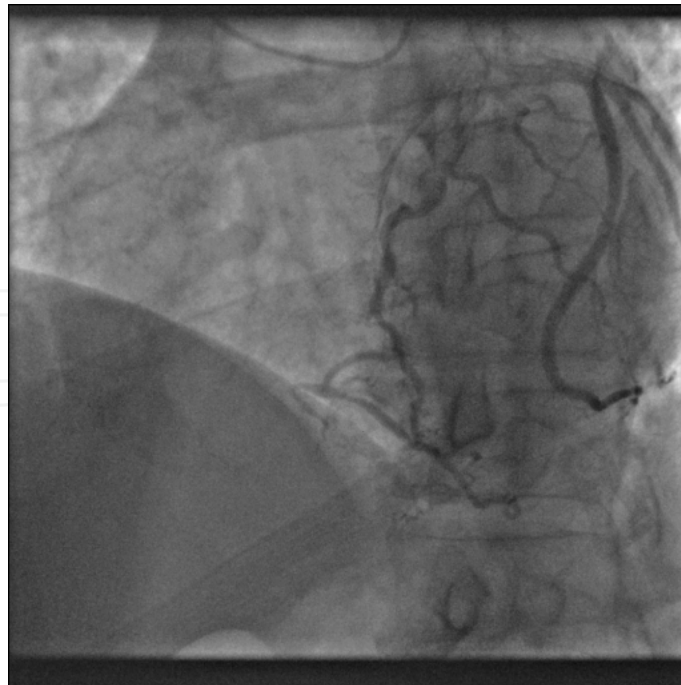


Fig. 11. Distal RCA perfused by collaterals from LAD

Case N° 2: A 54-year-old man had myocardial perfusion scintigraphy for the exploration of abnormal routine ECG. He had FC and dyslipidemia as risk factor and had stopped smoking 10 years before. He ran 10 km twice a week and had completed several marathons and a 100 km race. He was asymptomatic but myocardial perfusion scintigraphy showed defect in the anterior wall. Coronary angiography was performed showing 2 vessel disease (figures 12 and 13).



Fig. 12. Very tight lesion of marginal branch



Fig. 13. LAD stenosis including septal and diagonal branches

Coronary angioplasty was performed to LAD and Mg with a good result. This athlete returns to recreational sport and remains asymptomatic.

Case N ° 3: A 50-year-old man presented inaugural anterior STMI revealed by severe chest pain at rest. His risk factors were smoking and dyslipidemia. He was a well trained runner and had performed the Paris marathon two weeks before. Pre-hospital treatment included unfractionated heparin and GPIIb/IIIa antagonist. Coronary angiography was performed 90 mn after onset symptoms via right radial artery access showing 3 vessel disease (Figures 14, 15 and 16).

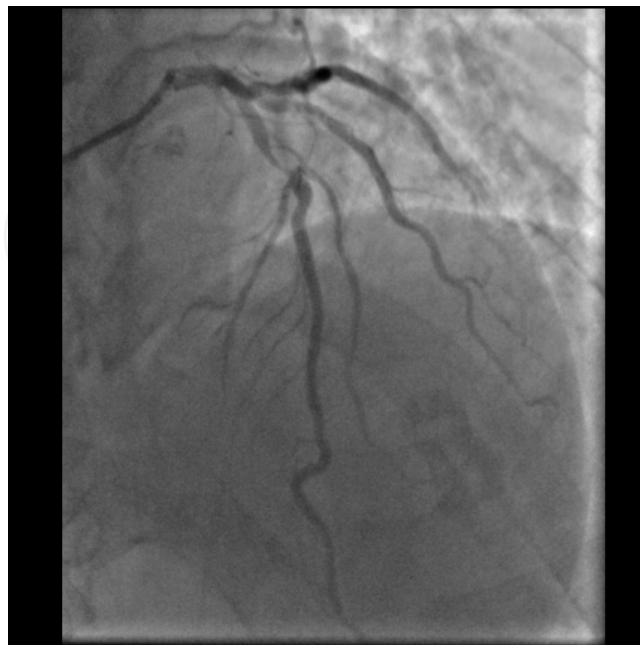


Fig. 14. Stenosis on proximal LAD



Fig. 15. Stenosis on mild RCA and occlusion of distal RCA

PCI was performed to the LAD requiring predilatation. Angioplasty of RCA and Mg was performed few days later.

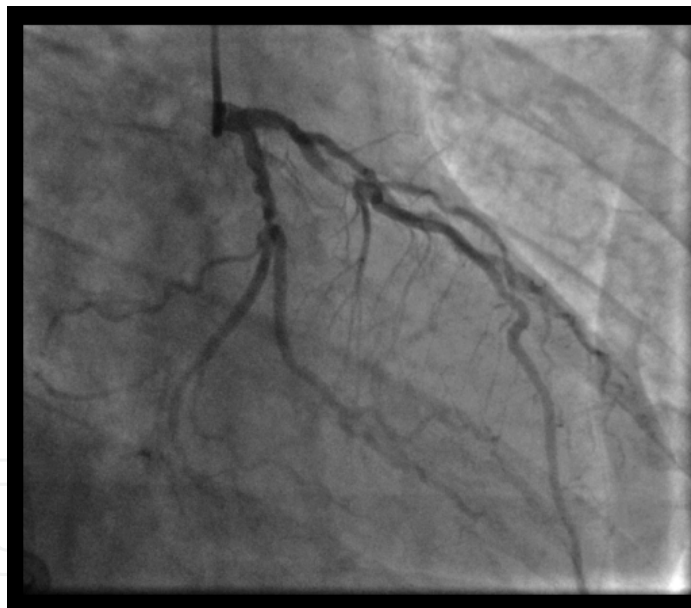


Fig. 16. Stenosis on Cx

In this case lesions of LAD, Mg and mild RCA seemed to be chronics, were very tight and had not stopped this athlete completing a marathon. The real culprit lesion was probably the distal occlusion of the RCA reperfused previously the LAD below of the tight stenosis.

In these three different cases of patients with chronic coronary lesions, strenuous exercise was possible without symptom even in competition. Cardiovascular adaptation to regular exercise may explain this fact but these patients have high risk of major cardiac events and should be screened.

3.2 Discussion

3.2.1 Why a lack of symptom in these three athletes?

Firstly, the athletes appear casual in their approach to possibly cardiac symptoms (Chevallier et al 2005). Secondly, silent ischemia in chronic ischemic heart disease has been commonly reported but is usually associated with angina (Rogers et al, 1995). At last, exercise training improves clinical symptoms of patients with stable coronary artery disease and increase maximal exercise tolerance (Wannamethee et al, 2000; Hambrecht et al, 2004). Explanation could be that moderate exercise training improve left ventricular function due to a decrease of blood pressure and an increase in myocardial contractile response to beta adrenergic stimulation. It also promotes coronary collateral development (Belardinelli et al, 1998) and improves peripheral endothelial function (Gokce et al, 2002). However, in these three cases the patients made frequent strenuous exertions. Zbinden et al reported a direct demonstration of coronary collateral flow by intense physical endurance exercise. The subject was a 46 year old healthy cardiologist who had performed long distance running. This invasive study including coronary angiography with measurement of coronary flow reserve showed increase of collateral flow index after regular training and one ultra marathon run (Zbinden et al 2004).

So the lack of symptoms in these patients could be due to cardiovascular adaptation to regular training and a development of coronary collateral particularly important.

3.2.2 What consequences?

It is recognized that ischaemia is a factor of poor prognosis even if it is silent (Rogers, 1995). Secondly although the major acute coronary syndromes occur more on moderate coronary stenosis, small luminal area is a predictor of events at lesion site (Stone et al, 2011). It can be assumed that these patients were at risk of serious cardiac events either acute coronary syndrome through occlusion of tight stenosis or plaque rupture but also severe ischemic arrhythmias related to strenuous exercises (6 or more metabolic equivalents as in practice of football, running, cycling, tennis). However increasing levels of habitual physical activity is associated with progressively lower relative risks of SMI.

Finally, these patients should not have been allowed to practice sports in competition (except low-moderate dynamic and low static sports, I A, B as bowling, golf, table tennis, doubles tennis, volleyball) and could be screened as recommended by ESC because of their risk factors (Pelliccia et al, 2005). Indeed these three athletes are men over 40 years with at least two risk factors.

4. Conclusions

SMI are rare but can have a severe clinical presentation and are the primary cause of SD in athletes over 35 years. The probable pathophysiological mechanism of SMI is a rupture and thrombosis of a vulnerable plaque often in a patient with single vessel coronary disease. These features may have some therapeutic consequences such as the use manual catheter thrombus aspiration during PCI and may explain the limits of the effectiveness of stress testing for the prevention of these events. This prompts us to determine rules of good practice, including information on the risks of smoking and promote equipment defibrillator on sports sites.

However some athletes have unknown severe coronary disease probably detectable by a stress test and should be screened. So athletes with multiple risk factors could benefit from screening for coronary artery disease, must respect rules of good practices and be advised of the possibility of SMI despite a negative stress test.



Fig. 17. Personal photo in the famous Mont Saint Michel which is held every year a marathon

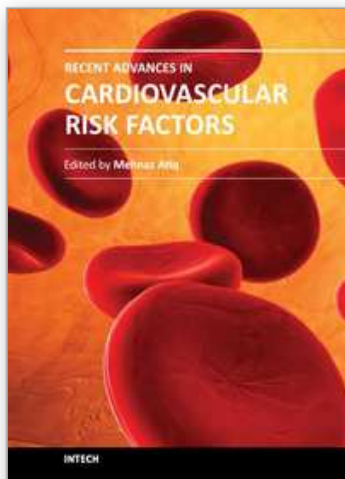
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Among the non-communicable diseases, cardiovascular disorders are the leading cause of morbidity and mortality in both the developed and the developing countries. The spectrum of risk factors is wide and their understanding is imperative to prevent the first and recurrent episodes of myocardial infarction, stroke or peripheral vascular disease which may prove fatal or disabling. This book has tried to present an update on risk factors incorporating new research which has thrown more light on the existing knowledge. It has also tried to highlight regional diversity addressing such issues. It will hopefully be resourceful to the cardiologists, general practitioners, family physicians, researchers, graduate students committed to cardiovascular risk prevention.

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