with closure devices has been shown to reduce the risk of such complications. [14]

Another intravenous direct thrombin inhibitor is argatroban.[15] The efficacy of argatroban has been demonstrated among patients with acute coronary syndromes and stroke. However, this drug is currently approved by the FDA only for the treatment of patients with heparin-induced thrombocytopenia. Although newer intravenous direct factor Xa inhibitors have been developed, they are still in the testing phase.[16] Fondaparinux is a long-acting indirect factor Xa inhibitor,[17] but its use was associated with a high rate of catheter-related thromboses and thus has not been well received.

REFERENCES

1. Davis EM, Packard KA, Knezevich JT, Campbell JA. New and emerging anticoagulant therapy for atrial fibrillation and acute coronary syndrome. *Pharmacotherapy* 2011;31:975-1016.
2. Viles-Gonzalez JF, Fuster V, Halperin JL. New anticoagulants for prevention of stroke in patients with atrial fibrillation. *J Cardiovasc Electrophysiol* 2011;22: 948-955.
3. Katsnelson M, Sacco RL, Moscucci M. Progress for stroke prevention with atrial fibrillation: emergence of alternative oral anticoagulants. *Circulation* 2012;125: 1577-1583.
4. Eerenberg ES, Kamphuisen PW, Sijpkens MK, Meijers JC, Buller HR, Levi M. Reversal of rivaroxaban and dabigatran by prothrombin complex concentrate: a randomized, placebo-controlled, crossover study in healthy subjects. *Circulation* 2011;124:1573-1579.

5.http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm282820.Htm

6. Fox KAA, Piccini JP, Wojdylaet D, et al. Prevention of stroke and systemic embolism with rivaroxaban compared with warfarin in patients with non-valvular atrial fibrillation and moderate renal impairment. *Eur Heart J* 2011; 32: 2387–2394.
7. Lakkireddy D, Reddy YM, Di Biase L, et al. Feasibility and safety of dabigatran versus warfarin for periprocedural anticoagulation in patients undergoing radiofrequency ablation for atrial fibrillation: Results from a multicenter prospective registry. *J Am Coll Cardiol* 2012;59: 1168–1174.
8. Goldhaber SZ, Leizorovicz A, Kakkar AK. Apixaban versus enoxaparin for thromboprophylaxis in medically ill patients. *N Engl J Med* 2011;365:2167-2177.
9. Nikolsky E, Mehran R, Dangas GD, et al. Outcomes of patients treated with triple antithrombotic therapy after primary percutaneous coronary intervention for ST-elevation myocardial infarction (from the Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction [HORIZONS-AMI] Trial). *Am J Cardiol* 2012;109:831– 838.
10. Stone GW, Witzenbichler B, Guagliumi G, et al. Bivalirudin during primary PCI in acute myocardial infarction. *N Engl J Med* 2008;358:2218-2230.
11. Mehran R, Lansky AJ, Witzenbichler B, et al; HORIZONS-AMI Trial Investigators. Bivalirudin in patients undergoing primary angioplasty for acute myocardial infarction (HORIZONS-AMI): 1-year results of a randomised controlled trial. *Lancet* 2009; 374(9696):1149-59.
12. Kastrati A, Neumann F, Schulz S, for the ISAR-REACT 4 Trial Investigators. Abciximab and heparin versus bivalirudin for non–ST-elevation myocardial infarction. *N Engl J Med* 2011;365:1980-1989.
13. Abdel-Wahab M, Richardt G. Safety of bivalirudin in patients with coronary artery disease. *Expert Opin Drug Saf* 2012;11:141-150.
14. Romaguera R, Wakabayashi K, Laynez-Carnicero A, et al. Association between bleeding severity and long-term mortality in patients experiencing vascular complications after percutaneous coronary intervention. *Am J Cardiol* 2012;109:75– 81.
15. Boggio LN, Oza VM. Argatroban use in heparin-induced thrombocytopenia. *Expert Opin Pharmacother* 2008;9: 1963-1967.
16. Sabatine MS, Antman EM, Widimsky P, et al. Otamixaban for the treatment of patients with non-ST-elevation acute coronary syndromes (SEPIA-ACS1 TIMI 42): a randomised, double-blind, active-controlled, phase 2 trial. *Lancet* 2009; 374: 787–795
17. Mehta SR, Granger CB, Eikelboom JW, et al. Efficacy and safety of fondaparinux versus enoxaparin in patients with acute coronary syndromes undergoing percutaneous coronary intervention: results from the OASIS-5 trial. *J Am Coll Cardiol* 2007;50:1742-1751.

The Electrocardiogram (ECG) in the Athlete

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Athlete`s Heart or Athletic Heart Syndrome is a benign entity characterized by morphological changes of the heart muscle as a result of long-term adaptation to exercise. The hallmark of these alterations is a substantial enlargement of the heart due to both heart chamber dilatation and heart muscle mass hypertrophy. Although athlete's heart has long been considered as a benign condition, there are data suggesting an association with sudden cardiac death (SCD) which can occur in athletes during exercise or even during daily activities.[1] Indeed, hypertrophic cardiomyopathy (HCM), also characterized

by marked cardiac hypertrophy, is the most common cause of SCD in young athletes.[2,3] The association between HCM and athlete's heart has been a matter of extensive discussion and debate among clinicians since an eccentric biventricular hypertrophy is almost universally present in athletes with a left ventricular diastolic volume >58 mm. This conflict has not yet been resolved, but, we have nowadays evidence that the ECG, although commonly altered by athletic cardiac remodeling, can assist in selecting athletes who are at substantial risk for an episode of SCD.

The Electrocardiogram in the Athlete

The ECG is a simple and reproducible method to assess the risk of SCD and has been proposed as a useful tool for screening young persons who are willing to participate in high endurance training. ECG findings in athletes are divided in two categories: *common* or training related and *uncommon* or training unrelated changes (Table).[4] The majority of these ECG findings are of no clinical significance, e.g. sinus bradycardia or an early repolarization ST-pattern. Only a minority of young athletes demonstrate abnormalities which require further diagnostic work-up, such as negative T waves or bundle branch blocks. Athletes with the ECG abnormalities listed in the Table should be more thoroughly assessed to exclude any severe underlying heart disease.

Table 1. Classification of ECG Abnormalities in Athletes.[4]

Common ECG abnormalities (training related)	Uncommon ECG changes (training unrelated)
Sinus bradycardia	**Complete LBBB, RBBB**
First degree AV block	**T wave inversion & ST depression**
Incomplete RBBB	**Long QT**
Early repolarization	**Left atrial enlargement**
Increased QRS voltage	**Left axis deviation/LAHB**
	Right axis deviation/LPHB
	Pathological Q-wave
	Brugada-like ECG

AV = atrio-ventricular; ECG = electrocardiogram; LAHB = left anterior hemiblock; LBBB = left bundle branch block; LPHB = left posterior hemiblock; RBBB = right bundle branch block

Sinus bradycardia- Atrioventricular block

Sinus bradycardia is extremely common in athletes. However, in case of persistent severe bradycardia along with pauses >3 s, further testing is needed. Increased parasympathetic tone is also associated with first degree atrioventricular (AV) block. Athletes with no symptoms (syncope, presyncope) or structural heart disease can participate in all sports. Nevertheless, symptomatic first degree AV block requires further investigation (exercise stress test, echocardiogram).[5] On the other hand, the presence of Mobitz II AV block, 3^{o} AV block, persistent sinus bradycardia or pauses >3 s are indications for a permanent pacemaker.[6] Mobitz I (Wenckebach) 2^{o} AV block is a frequent benign finding in well trained athletes, esp. at sleep or at rest. Thus, in asymptomatic athletes with Mobitz I block further testing is not recommended.[5]

Right (RBBB) and Left Bundle Branch Block (LBBB)

Intraventricular conduction abnormalities, i.e. in the form of complete bundle branch block are not common in athletes. Accordingly, whenever these abnormalities are present, exercise stress testing, Holter monitoring, and imaging studies are recommended in order to exclude ischemic heart disease, myocarditis, hypertensive heart disease, restrictive cardiomyopathy (e.g. sarcoidosis) and congenital heart disease.

Athletes with no family history, negative physical examination and RBBB or LBBB, can participate in high endurance sports activities,[7] only under the condition that they do not develop any AV conduction abnormalities during an exercise stress test.[8]

Brugada syndrome

Brugada type 1 ECG is characterized by a 'coved' ST-segment elevation ≥2 mm (0.2 mV) followed by a negative T wave. Type 2 & 3 Brugada ECG shows a 'saddleback' morphology.[4] Brugada type 1 is not associated with SCD during exercise, but increased vagal tone at rest can trigger a malignant arrhythmic event. Nevertheless, athletes with Brugada type 1 ECG are not permitted to participate in competitive sports.[8]

Increased QRS voltage- T wave inversion

Highly trained athletes exhibit some degree of cardiac hypertrophy. On the other hand, HCM is an autosomal dominant genetic disease characterized by both myocardial hypertrophy and disarray. Increased QRS voltage without the presence of at least one other abnormality, such as ST segment depression, T wave inversion, or left axis deviation, is very rare in HCM.

T-wave inversion >2 mm in the inferior and lateral leads needs to be further investigated to rule out ischemic heart disease, aortic valve disease and cardiomyopathy. On the other hand, inverted T waves in leads V_1-V_3 may be a normal finding in athletes <16 years old.[9] Post-pubertal athletes with persistent negative T wave in V_1-V_6 require thorough investigation to exclude arrhythmogenic right ventricular cardiomyopathy (ARVC), including echocardiography, Holter monitoring, magnetic resonance imaging (MRI) and possibly genetic screening.

Ventricular Premature Beats (VPBs)

Young athletes with VPBs and no structural disease can participate in all competitive sports. If the number of VPBs increases during exercise and patient becomes

symptomatic, the athlete can participate in sports with the lowest total cardiovascular demand, i.e. <40% max O2 (billiards, bowling, cricket, golf).[10,11]

Wolff-Parkinson-White (WPW) Syndrome

WPW syndrome is present in 0.3% of athletes.[12] The ECG demonstrates short PR (<120 ms), wide QRS with delta wave and secondary ST-T changes.

Atrioventricular reentry tachycardia (AVRT), either orthodromic (narrow QRS) or antidromic (wide QRS), is the most common tachycardia (95%) in WPW. Atrial fibrillation can be a life-threatening arrhythmia in these patients, as a short refractory period (<220 ms) of the accessory pathway can lead to a very rapid ventricular rate and degeneration into ventricular fibrillation. In symptomatic young athletes (palpitations, syncope) with WPW, an electrophysiology study is recommended.[5] If an AVRT can be provoked during the study, ablation of the accessory pathway should be performed. On the other hand, even if the athlete with WPW is completely asymptomatic, an electrophysiology study is still required to give permission for participation in competitive sports.

Long QT Syndrome (LQTS)

QT prolongation may be transient in athletes due to acute electrolyte changes or abuse of specific substances and normalizes after de-conditioning. If QT prolongation persists, echocardiogram, Holter monitoring and exercise testing are recommended. Per the ESC guidelines, athletes with LQTS should be disqualified from sports.[8]

Conclusion

Cardiovascular remodelling in highly trained athletes is frequently associated with minor ECG abnormalities. ECG monitoring and classifying ECG findings into physiological or "common" or "training related" and pathological or "uncommon" or "training unrelated" changes, facilitates pre-participation screening. In the presence of ECG abnormalities not related to training, it is important to exclude any underlying heart disease associated with SCD (HCM, chanelopathies, etc) using more tests (e.g. MRI or eletrophysiology studies). Nevertheless, false –positive results that pose serious limitation to pre-participation screening also exist. Peliccia et al, in a study of 1005 young athletes, have demonstrated that the majority (60%) had no significant ECG changes.[13] The rest (40%) had ECG changes not related to cardiomyopathy. In fact, young athletes in cycling or rowing had most typical changess as a result of adaptation of the heart after high endurance training with no echo or MRI evidence of cardiomyopathy.

Thus, a new debate has been recently going on about whether an ECG should be part of the screening of apparently healthy young sporters. In Italy this screening is compulsory by law and the ESC supports this policy and has recently issued recommendations for the interpretation of the ECG in the athlete.[14] However, others[15] find the cost too high for its yield and an ECG is not included in the screening protocol of the AHA.[16,17]

REFERENCES

1. Thompson PD, Franklin BA, Balady GJ, et al. Exercise and acute cardiovascular events placing the risks into perspective: a scientific statement from the AHA Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology. *Circulation* 2007; 115: 2358-2368.
2. Corrado D, Basso C, Thiene G. Essay: Sudden death in young athletes. *Lancet* 2005; 366(Suppl 1): S47-S48.
3. Maron, BJ. Sudden death in young athletes. *N Engl J Med* 2003; 349: 1064-1075.
4. Corrado D, Pelliccia A, Heidbuchel H, et al. Recommendations for interpretation of 12-lead electrocardiogram in the athlete. *Eur Heart J* 2010;31:243-259.
5. Zipes DP, Ackerman MJ, Estes NA 3rd, et al. Arrhythmias. *J Am Coll Cardiol* 2005; 45:1354.
6. Venerando A, Rulli V. Frequency morphology and meaning of the electro-cardiographic anomalies found in Olympic marathon runners and walker. *J Sports Med Phys Fitness* 1964;4:135-141.
7. Langdeau JB, Blier L, Turcotte H, O'Hara G, Boulet LP. ECG findings in athletes: the prevalence of left ventricular hypertrophy and conduction defects. *Can J Cardiol* 2001*;17:*655-659.
8. Pelliccia A, Fagard R, Bjørnstad HH, et al. Recommendations for competitive sports participation in athletes with cardiovascular disease: a consensus document from the Study Group of Sports Cardiology of Cardiac Rehabilitation & Exercise Physiology and the Working Group of Myocardial & Pericardial diseases of the ESC. *Eur Heart J* 2005: 26:1422-1445.
9. Corrado D, Pelliccia A, Bjørnstad HH, et al. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol. *Eur Heart J* 2005;26:516-524.
10. Mitchell JH, Haskell W, Snell P, Van Camp SP. Classification of sports. *J Am Coll Cardiol* 2005 ; 45:1364-1367.
11. Zehender M, Meinertz T, Keul J, Just H. ECG variants and cardiac arrhythmias in athletes: clinical relevance and prognostic importance. *Am Heart J* 1990; 119:1378-1391.
12. Hiss RG, Lamb LE. Electrocardiographic findings in 122 043 individuals. *Circulation* 1962*;25:*947-961.
13. Pelliccia A; Maron BJ, Culasso F, et al. Clinical significance of abnormal ECG patterns in trained athletes. *Circulation* 2000, 102:278-284.
14. Corrado D, Pellicia A, Heidbuchel H, et al. Recommendations for interpretation of 12-lead electrocardiogram in the athlete. *Eur Heart J* 2010;31:243–259.
15. Chaitman BR. An ECG should not be included in routine preparticipation screening of young athletes. *Circulation* 2007;116:2610-2614.
16. Maron BJ, Thompson PD, Ackerman MJ, et al. Recommendations and consideration related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement for the AHA Council on Nutrition, Physical Activity and Metabolism: endorsed by the ACC Foundation. *Circulation* 2007;115:1643-1655.
17. Myerburg RJ, Vetter VL. ECGs should be included in preparticipation screening of athletes. *Circulation* 2007;116:2616-2626.