Oslo Sports Trauma
RESEARCH CENTER

Hilde Moseby Berge

The Norwegian athletes' heart

Cardiac screening of 595 professional soccer players

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Det er den svarte prikken

midt i skiva du skal treffa,

nett den, der

skal pila stå og dirra!

Men nett der treffer du ikkje.

Du er nær, nærare,

nei, ikkje nær nok.

Så lyt du gå og plukka upp pilene,

gå tilbake, prøva på nytt.

Den svarte prikken tergar deg.

Til du forstår pili

som stend der og dirrar:

Her er og eit midtpunkt.

Olav H. Hauge

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List of papers

This dissertation is based on the following original research papers, which are referred to in the text by their Roman numerals:

I. Berge HM, Gjerdalen GF, Andersen TE, Solberg EE, Steine K. Blood pressure in professional male football players in Norway. *J Hypertens* 2013;31:672-679.

II. Berge HM, Andersen TE, Solberg EE, Steine K. High ambulatory blood pressure in male professional football players. *Br J Sports Med* 2013;47:521-525.

III. Berge HM, Gjesdal K, Andersen TE, Solberg EE, Steine K. Prevalence of abnormal ECGs in male soccer players is still high, but decreases with the Seattle criteria. Submitted.

IV. Berge HM, Steine K, Andersen TE, Solberg EE, Gjesdal K. Visual or computer-based measurements: Important for interpretation of athletes' ECG. *Br J Sports Med* Published Online First: [22 February 2014] doi:10.1136/bjsports-2014-093412

Abbreviations

BMI	Body mass index
BP	Blood pressure
BSA	Body surface area
CV	Cardiovascular
ECG	Electrocardiography
ESC	European Society of Cardiology
HT	Hypertension
LV	Left ventricle
$LVmass_{BSA}$	Left ventricle mass indexed to BSA
MAP	Mean arterial blood pressure
PP	Pulse pressure
SCA	Sudden cardiac arrest
SCD	Sudden cardiac death
SPSS	Statistical Package of Social Sciences

Summary

Introduction

Preparticipation health examinations are recommended in athletes (1), and mandatory in professional soccer players (2). The main aim is to reduce the prevalence of sudden cardiac death (SCD), which is 2-3 times more common in athletes than in the general population (3). The most common cause of SCD is hypertrophic cardiomyopathy in the USA, arrhythmogenic right ventricular cardiomyopathy in Italy, but what causes the highest risk in the Nordic countries was unknown (4;5). Electrocardiography (ECG) is a diagnostic tool to detect athletes with increased risk of cardiovascular (CV) disease and SCD, but descriptions of methodology are scarce and interpretation has often been left to personal experience (6). "Abnormal" ECG findings related to training are common in athletes, and a challenge to distinguish from pathological ECG findings (6). Blood pressure (BP) is recorded during screening examinations, and high BP accounts for the highest prevalence of abnormal findings (7). This has neither been emphasized as an isolated finding, nor in association to other CV risk factors. Hence, the main aims of this thesis were to 1) see if high BP (≥140/90 mmHg) was associated with other CV risk factors, 2) follow-up players with high BP, 3) describe the male professional soccer players' electrocardiograms according to available recommendations and 4) to compare visual and computer-based ECG-measurements.

Methods

During a preparticipation training camp at La Manga in 2008, BP, ECG and echocardiography were recorded from 595 players aged 18-38 years. BP was registered as the mean of two consecutive resting BP recordings and related to heart rate (HR) and pulse pressure (PP) as indicators of increased sympathetic activity, and echocardiographic variables for left ventricle hypertrophy (LVH), left atrial enlargement (LAE) and systemic arterial compliance (SAC) (**Paper I**). Players with high BP still living in Norway were invited to a follow-up study of ambulatory BP (ABP) in 2010, and together with 26 matched controls with optimal BP (<120/70 mmHg), ABP was recorded during 24 hours without exercise (**Paper II**). ECGs from 587 players were interpreted according to the European Society of Cardiology's (ESC) recommendations from 2010, with specifications from Uberoi *et al* in 2011, and compared to the new Seattle criteria from 2013. Choice of method, technical specifications and visual measurements with callipers on-

screen of the averaged PQRST complex in each lead was described in detail (**Paper III**). Visual measurements were compared to computer-based measurements, to test for correlation and agreement between prevalence of abnormal ECGs. Based on the main differences, reference values for abnormal findings were adjusted, to tentatively increase the agreement between visual and computer-based measurements (**Paper IV**).

Figure 1. Picture from La Manga training camp in Spain, February 2008.

Results

BP was high in 39 (7%) of the players, and high normal (≥130/85 mmHg) in another 18% of the players. There was a significant association between increasing BP in groups, and increased HR, PP, indexed LV mass, LA volume, and decreased SAC. Two players with BP>160/100 mmHg and LV hypertrophy on echocardiography were temporarily restricted from activity (**Paper I**). High daytime ABP (≥135/85 mmHg) was unmasked in nine (35%) of the controls after ABP recording and more than half of the players had high ABP (≥120/70 mmHg) during the night (**Paper II**). The prevalence of abnormal ECGs was reduced from 29.3% to 11.2% by the new Seattle criteria. None of the players with abnormal ECGs according to the ESC's recommendations only, had abnormal echocardiograms. Echocardiography alone did not detect important abnormality. All players, except the two hypertensives already mentioned, got medical clearance. (**Paper III**). Abnormal ECG findings were more common after computer-based versus visual measurements both according to the ESC recommendations (51% versus 29.5%), and the Seattle criteria (22% versus 11%). The disagreements were mainly due to "borderline" abnormal findings or misclassifications by the computer. With small adjustments of reference

values, the agreement increased to moderate and good. None of the ECGs interpreted as normal by the computer-based algorithm was recommended follow-up after the initial screening (**Paper IV**).

Perspectives

The associations between BP and hypertensive subclinical organ damages in this young cohort of athletes emphasize the need for closer focus on BP measurements and standardized follow-up. The novel findings of masked HT and high BP during nighttime, together with lack of nocturnal dip in BP, are surprising in these young, slim and physically active athletes. Whether these, as in the general population, are independent risk factors for CV disease should be investigated in large prospective cohort-studies.

The Seattle criteria for interpreting ECG in athletes reduced the need for follow-up investigations, and based on echocardiographic evaluations this reduction increased the specificity of the Seattle criteria, without increasing the number of false negative ECGs. We experienced several difficulties when trying to decide the prevalence of abnormal ECGs in athletes, and revealed a need for new definitions of "standard" methodology. Reference values for abnormality should be adjusted dependent on measurement method. We can rely on normal computer-based interpretations according to the Seattle criteria, while abnormal computer-based ECG findings should be reread visually and maybe corrected. Echocardiographic evaluations seem unnecessary in all soccer players.

Introduction

Background

Sudden cardiac deaths (SCD) in sports are tragic events, especially for athletes and their relatives. But as great sport's events like professional soccer games are broadcasted worldwide, these events also affect millions of people. The true incidence of sports related SCD is hard to know, but is reported to be 0.3-3.6 per 100 000 persons per year, and is usually said to be two to three times more frequent in young athletes than in the general population (3). In attempts to prevent SCD, preparticipation health examinations are recommended in athletes (1), and mandatory in professional soccer players (2). The most common cause of SCD is hypertrophic cardiomyopathy in the USA, arrhythmogenic right ventricular cardiomyopathy in Italy, but what causes the highest risk in the Nordic countries is unknown (4;5). Some of the CV risk factors can be detected during screening and successfully treated, while others will lead to recommendations for restricted activity to reduce the risk of SCD (8-14). How many athletes who unnecessary have to abandon their career because of false positive screening results and how many athletes at risk eluding the wide mesh screening, is unknown. It is also dependent on type of investigations. The ESC recommends ECG to be part of the examinations because of an Italian study from 2006 which claims that inclusion of ECG reduces the incidence of SCD by 89% (15;16). On the contrary, the American Heart Association does not recommend inclusion of ECG, because of its low sensitivity and specificity (17). Whether echocardiographic evaluations of all athletes catch even more athletes at risk, and only them, has not been proven, but both ECG and echocardiography became mandatory parts of the preparticipation cardiac screening of soccer players in 2008 (2). To gain more knowledge about the Norwegian athlete's heart, the first mandatory screening of male professional soccer players in Norway was conducted as a research project in 2008.

Demographic data related to gender, ethnicity and sports discipline

SCD in young competitive athletes is five to nine times more common in males than females (18-21). Hypertrophic cardiomyopathy as cause of death is more common in Afro-American than in white athletes (19). Development of athlete's heart is related to gender and race, with different echocardiographic and electrocardiographic reference values for normality (22-25). Hence, ethnicity has great impact on screening results. As an increasing number of professional soccer

players in Norway are black, information of ethnicity is important when interpreting the results. Different athletic activities influence the formation of athlete's heart in different ways, and also the incidence of SCD (26;27). In a study of 134 sports related cardiovascular SCD in the US, altogether 68% occurred in basketball (n=47) and football (n=45) (20). Many studies of preparticipation cardiac screening seems to ignore these differences and mix participants with different age, gender, ethnicity and sports disciplines (15;20;28-33).The Norwegian project offered a unique opportunity to study the development of athlete's heart and prevalence of CV risk factors in a homogenous group of adult male professional soccer players, categorized by ethnicity. Screening is mandatory for both genders, but unfortunately the females were not included in this research project.

Blood pressure in athletes

Previous to the Olympic Games in London in 1948, the Nutrition Society on the nutrition of athletes realized they had few scientific data on the nutrition and physiology of athletes (34). So they performed a study of diet, hemoglobin and BP, while the athletes were gathered in London. Mean BP was 121/76±13/8 mmHg in participants from temperate countries. In western countries the prevalence of hypertension has been reported to be 14.4% and 21.2% in men aged 20-29 and 30-39 years, respectively (35). The prevalence in physically active people and athletes has been considered to be lower than in the general population (36), but no studies have been designed to actually compare this. Until 1993 hypertension was defined according to the World Health Organization's report from 1962, based on one BP recording (37). From 1993, repeated measurements of high BP are required for the diagnosis of hypertension (38).

Despite that high BP is the most common abnormal finding during preparticipation cardiac screening of athletes, there is little focus on measurement method, follow-up and CV consequences (7). OBP should be measured three times after 5-10 minutes sitting rest and registered as the mean of the last two measurements (38). ABP should be conducted on a day without exercise as an adjunct to OBP as it is superior to OBP in predicting CV events (38;39). The two measurement methods complement each other and define subgroups of white coat HT and masked HT (38). Athletes with high BP should be followed up according to national

guidelines for the general population as long as we don't know if hypertension in athletes is less serious (40). Increased LV mass is considered as subclinical organ damage in people with hypertension (41;42), and increased left atrium size has been linked to the increased prevalence of atrial fibrillation in endurance athletes (43;44). Several studies have demonstrated increased LV mass in athletes (23), but no studies have investigated if this is associated with high BP in athletes. In the general population left atrium size also increases with BP, and whether this occurs in athletes with high BP is unknown (42;45;46). Nor is systemic arterial compliance (SAC), which is reduced in hypertensive patients (47), studied in young athletes with high BP.

High heart rate (HR) and pulse pressure (PP) have shown to be strong predictors for CV disease, and are both associated with increased sympathetic activity (48;49). In addition, increased HR also predicts development of essential HT (48).

Electrocardiography

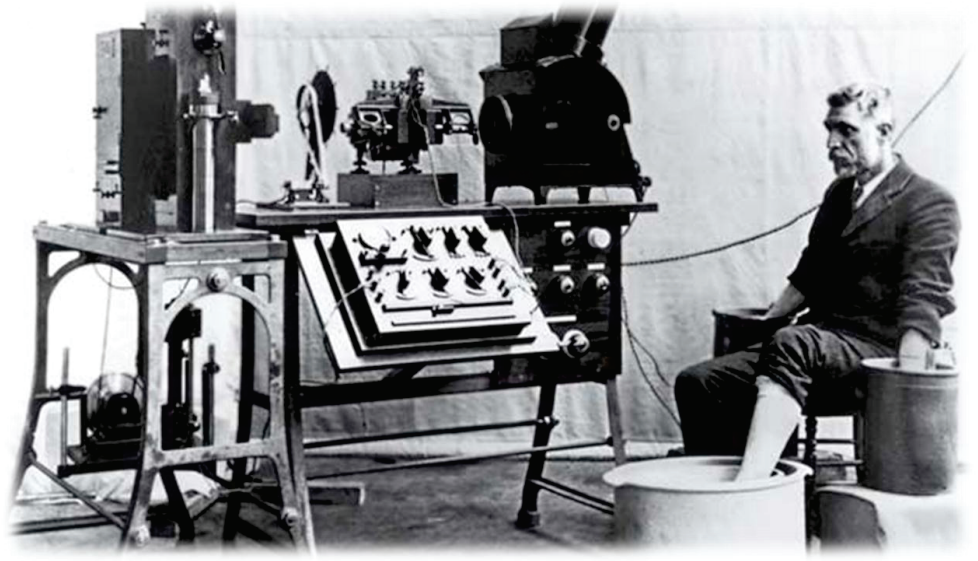

Figure 2. Professor Willem Einthoven invented the first practical ECG device, the string galvanometer, in 1903. The weight was 270 kilograms and it required five technicians to be operated. The person's arms and feet were dipped in salt solutions while the strength and rate of the heartbeat were registered on the chest. Einthoven was awarded the Nobel Prize in physiology and medicine in 1924, "for the discovery of the mechanism of the electrocardiogram". Photo: Google pics. FPG/Hulton Archive/Getty Images. http://www.nobelprize.org/nobel_prizes/medicine/laureates/1924/einthoven-bio.html

Today ECG devices are carried in one hand and operated by one person, Einthoven's original assignment of the letters P, Q, R, S and T to the various deflections as well as his equilateral triangle centered on the chest (figure 3), are still used. But to determine whether cardiac remodeling in athletes have a pathological component and if any ECG findings may help identify this type of remodeling, we need standards for all phases of the ECG procedure. The athlete's position, lead placements and technical specifications of the ECG device can all influence the measurements of amplitudes, intervals, and diagnostic statements (50). Recommendations for measurement standards in quantitative ECG were first published in 1938 and have been revised several times since (51). The International Society for Computerized Electrocardiography state that all ongoing studies used for criteria development must clearly document electrode placement with precision (50). The only widely accepted written recommendations for ECG interval measurement before the digital era were published in 1997 by the European Committee for Proprietary Products (CPMP). They were based on annotating three consecutive sinus complexes, preferably from lead II (52). It's reasonable to believe that during the last decade, when several studies of preparticipation screening have been published, digitalized ECG devices with built in algorithms for measuring intervals from the earliest onset to the latest offset of the waveform in all leads have gradually become more utilized. Small systematic differences in measurements, particularly with respect to diagnostically important global measures of QRS duration and QT interval, might be expected between different ECG devices, because of different methods for lead alignment and template formation (50). These differences in global measurement algorithms must be accounted for in comparative studies within individuals and between individuals (50). Since global PQRST measurements are systematically larger than measurements from representative complexes of individual leads, redefined normal values are also required (53).

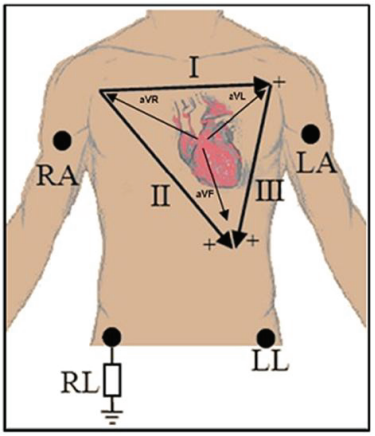

Figure 3. Einthoven's equilateral triangle

Measurements can be performed manually on paper or on-screen, or they can be derived from the ECG software. A number of studies of QT measurements has shown relatively poor agreement between manual and automated ECG measurement methods (54), though somewhat better in healthy participants (55). Whether choice of method influences the prevalence of abnormal ECG findings in athletes, is hitherto unknown. "Abnormal" ECG findings related to

training are common in athletes, and are a challenge to distinguish from pathological ECG findings (16). The ECGs in this study should be interpreted at La Manga according to the Minnesota Code Classification System for Electrocardiographic Findings, but was as usual left to personal experience (16;56). In 2010, the ESCs recommendations for interpretation of 12-lead ECG in the athlete were published (16), but detailed definitions of Q waves, axis deviations, right ventricular hypertrophy, ST-segment depressions, QT-abnormalities and ventricular extra systoles were lacking. In addition minor T wave inversions were not defined, even if the authors recommended further follow-up of these. Whether or not these minor alterations are included as abnormal ECG findings cannot be read in the paper. Therefore we chose to use Uberoi et al's recommendations for interpreting ECG in young athletes from 2011 since that paper is more specific than the ESC criteria from 2010. Seven of the authors contributed to both publications, and we therefore regarded Uberoi et al's paper as specifications to Corrado et al. (57). Finally, in the beginning of February 2013, the Seattle criteria for interpreting ECG in athletes were published in British Journal of Sports Medicine (58-61). These recommendations were developed in collaboration between the American Medical Society for Sports Medicine (AMSSM), the Section of Sports Cardiology of the European Association for Cardiovascular Prevention and Rehabilitation (EACPR), the FIFA Medical Assessment and Research Center (F-MARC), and the Pediatric & Congenital Electrophysiology Society (PACES). The ECGs in our study were interpreted as accurately as possible according to the specified ESC recommendations and Seattle criteria.

Echocardiography

Echocardiography is an important tool when studying the athlete's heart, which is recognized by eccentric symmetrical hypertrophy (thickening of the myocardial wall and increase of left ventricular chamber), as opposed to hypertrophic cardiomyopathy, which is usually recognized by asymmetrical concentric hypertrophy. Hypertrophy secondary to hypertension and aortic stenosis is recognized by concentric symmetrical hypertrophy. The athlete's heart is therefore not involved as a background-cause to sudden death in athletes, in the way congenital cardiac diseases, such as cardiomyopathies, are. It is of utmost importance to differentiate between physiological and pathological hypertrophy as suggested by Maron et al (62).

Echocardiographic evaluations were used as the best available "gold standard" in our project, since the Regional Ethical Committee did not allow results from recommended follow-up investigations to be part of the present study.

Descriptions of athlete's heart in Scandinavia are scarce, and with application of new technology, as 2-dimensional speckle tracking (2-D Strain) echocardiography, one of the main aims of this research project was to contribute to original knowledge of the Norwegian athlete's heart, as well as to international understanding of the field. This part of the project constitutes a separate PhD thesis, written by Gard Filip Gjerdalen.

Aims of the thesis

The general aim was to describe the Norwegian athletes' heart.

Specific aims

1. To describe the prevalence of high BP in male professional soccer players and the associations of BP to HR, PP, $LVmass_{BSA}$, LA size and SAC. Secondly, we wanted to investigate differences in these parameters between hypertensive versus normotensive soccer players, white European players versus controls, and white versus black players. (**Paper I**).
2. To identify the prevalence of high ABP in male professional soccer players in Norway and to examine the players' compliance to recommended follow-up of high BP. Second, we wanted to study if indicators of sympathetic activity were increased in players with high BP. (**Paper II**).
3. To compare the prevalence of abnormal ECG findings between ESC's recommendations as specified by Uberoi et al, with the new Seattle criteria for interpreting ECG, in male professional soccer players in Norway. We also wanted to show how slight differences in the criteria would affect our results, and to describe in detail the performance of the ECG procedure to facilitate meaningful comparison with other studies. (**Paper III**).
4. To compare the prevalence of abnormal ECG findings between visual and computer-based measurements, according to the ESC's recommendations as specified by Uberoi et al, and the new Seattle criteria for interpreting ECG, in male professional soccer players in Norway. The performance of the ECG sampling and visual and computer-based measurements are described in detail. (**Paper IV**).

Materials and methods

Participants

La Manga, Spain 2008

During the winter 2008, all Norwegian male professional soccer players underwent mandatory preparticipation cardiac screening when attending a training camp in La Manga, Spain (2). Players aged 18 to 40 years were invited to participate in the study, while players <18 years were excluded due to practical challenges with collecting parental consent. Male controls of the same age, exercising three or less times per week, were for practical reasons selected among the teams' staff and the remaining as volunteers from the Oslo region. All participants gave informed written consent. The study was approved by the Regional Ethical Committee (**Paper I- IV**).

Norway, 2010/2011

Based on the players' BP from the screening in 2008, we designed a case-control study and recorded ABP from October 2010 until February 2011. All available players with untreated high BP (n=37) were assessed for eligibility as cases, excluding players living abroad. Controls were randomly selected from players with optimal blood pressure (n=250) according to a predefined protocol, and individually matched for age group (or maximum age difference four years), ethnicity and professional soccer team. All participants gave informed written consent. The study was approved by the Regional Ethical Committee (**Paper II**).

Questionnaire

Athletes and controls responded to a questonnaire regarding their height and weight, if they used snuff every day and if their ethnicity was Caucasian, Afro-American or other. In addition they answered whether they had experienced chest pain, palpitations, syncope/near syncope or breathlessness during or in close proximity to exercise, and if SCD, CV disease, HT or diabetes had occurred in a first-degree relative under the age of 55 years (**Paper I&III**).

Athletes who participated in the follow-up study with ABP recordings were asked once again about symptoms during or in close proximity to exercise, family history of CV disease and if they used snuff every day. In addition they reported if they currently used any medications, if something extraordinary had occurred during the recording period, and if they had undergone additional OBP or ABP recordings after the screening in 2008 (**Paper II**).

Paper I, III and IV

Twenty-eight of the 30 Norwegian elite and 1st division leagues participated in the study, and 595 of 604 eligible players (99%) consented to participate. The players had a mean age of 25.1±4.5 years, mean body mass index (BMI) 23.7±1.2 kg/m^2 and mean BSA 2.0±0.1 m^2. Among the players, 493 (83%) were Europeans, 52 (9%) Africans, 29 (5%) Americans, four Asians, four Australians, and 13 (2%) were of unknown origin. The skin colour was white in 504 (85%), black in 49 (85), mixed for 13 (2%) and other for 29 (5%). BP results were available from 594 players. All the 47 included controls were white Europeans (**Paper I**). ECG of good quality was available from 587 players (99%), computerized for 579 and on paper only for eight (**Paper III**). Computerized ECG of good quality for visual and computer-based measurements was available from 579 players (97%) (**Paper IV**).

Paper II

Twenty-six of the 28 (93%) non-treated hypertensive players (cases) still living in Norway, and 26 controls were included in this study. Nine were excluded because they were living abroad, two because they had hypertension grade II and were on antihypertensive medication, one because he never had the time, and one because he did not want to participate.

Physical examination

Office blood pressure

The examinations were preferably conducted before exercise, and at least one hour rest was required. BP was measured after five minutes rest in a sitting position, using a validated automatic BP monitor (Dinamap ProCare DPC300N, GE, Milwaukee, USA). Systolic BP (SBP) and diastolic BP (DBP) were registered as the mean of two consecutive BP measurements and categorized according to European Society of Hypertensions' guidelines for BP (table 1) (38). High BP was defined as SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg. Mean arterial pressure (MAP) was defined as DBP + 1/3 (SBP-DBP), PP was calculated as the difference between SBP and DBP, and SAC as stroke volume (SV) from the two dimensional echo recordings divided with PP (**Paper I and II**)

Category	Systolic BP (mmHg)		Diastolic BP
Optimal	<120	and	<80
Normal	120 – 129	**and/or**	80 – 84
High normal	130 – 139	and/or	85 – 89
Hypertension grade I	140 – 159	and/or	90 – 99
Hypertension grade II	160 – 179	and/or	100 – 109
Isolated systolic HT	≥140	and	<90

Table 1. Definitions and classifications of office blood pressure levels. ESC 2013.

Ambulatory blood pressure

On the recording day, the players resigned from snuffing and exercise in the morning and all kinds of sport activities for the following 24 hours. Outside this, they engaged in normal activity in accordance with the guidelines from the European Society of Cardiology and European Society of Hypertensions.(38) The project leader (HMB) measured the upper-arm girth, fastened the appropriate cuff to the players' non-dominant arm, and the ABP device (Tonoport, CardioSoft, GE Healthcare, Oslo, Norway) was kept in a belt. The ABP device was programmed with software CardioSoft V6.61 to obtain blood pressure readings at 30-minutes intervals from 7:00 AM until 09:59 PM, and at 60-minutes interval during the night. Nighttime was later adjusted for reported time in bed, and daytime the rest of the time. Measurements were automatically repeated when registered as not valid (**Paper II**).

Data definitions

Among the 52 players, daytime ambulatory BP monitoring was successfully committed in all players, at nighttime in 51 players. The mean valid measurements were 26.9 ± 4.5 and 8.3 ± 3.4 during the day and night respectively. According to published guidelines, high office BP was defined as ≥ 140/90 mm Hg, high ambulatory BP during daytime ≥ 135/85 mm Hg, during 24-hour ≥ 130/80 mm Hg and during nighttime ≥ 120/75 mm Hg (38;63). We used daytime ambulatory BP, which is most common, when the players were categorized in four BP subgroups (64) (table 2).

After ambulatory BP monitoring, both players with true normotension and white-coat hypertension were defined as normotensive players, and both players with masked hypertension and sustained hypertension were defined as hypertensive players.

Nocturnal dip in BP was defined as a mean 10 % decline in average systolic or diastolic BP at night compared to daytime.(65) High HR, (48) increased PP and (49) nighttime ABP, and lack of nocturnal dip (65) were considered as indicators of increased sympathetic activity.

Subgroups	Office BP (mmHg)		Daytime BP (mmHg)
Sustained HT	≥140/90	and/or	≥135/85
White-coat HT	≥140/90	and/or	<135/85
Normotension	<140/90	and	<135/85
Masked HT	<140/90	and/or	≥135/85

Table 2. Definitions and classifications of blood pressure subgroup levels.

Electrocardiography

With the player supine the precordial ECG electrodes were placed according to recommendations (50), and the four limb lead electrodes were placed on the arms and legs just distal to the shoulders and hips. ClickECG (Cardiette Cardioline, Milan, Italy) with Real Click software version 3.2.10 collected the simultaneous ten seconds digital recordings with front-end sampling rate of 2000 per second and compression ratio 4:1. Paper speed was 25 mm/s with 10 mV gain. The frequency response was 0,05 Hz - 150 Hz, the baseline filter was always on, network filter was set at 50 Hz and muscular filter at 40 Hz. The filtered signals were stored. The software recognized waveforms with amplitudes of at least 25 μV and durations of at least 6 ms.

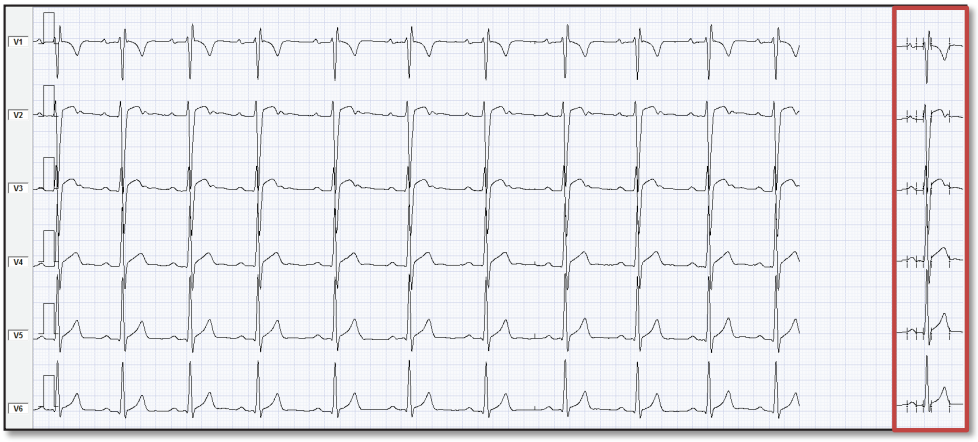

Figure 4. After QRS was detected and classified, a medium beat (red rectangle) for all leads was built from every sinus complex.

Lead Mesurement

	I	II	III	aVR	aVL	aVF	V1	V2	V3	V4	V5	V6
P Duration (ms)	110	106	98	0	0	104	54	70	98	106	108	110
PR Interval (ms)	244	244	234	0	0	239	234	234	234	234	246	234
QRS Duration (ms)	94	90	112	93	98	90	112	103	102	102	88	101
QT Interval (ms)	336	346	386	0	319	357	0	0	0	332	336	354
Q Duration (ms)	0	0	0	53	0	0	0	0	0	0	0	13
R Duration (ms)	47	57	112	40	30	70	18	28	41	63	55	59
S Duration (ms)	47	33	0	0	68	20	43	75	61	39	33	29
R' Duration (ms)	0	0	0	0	0	0	49	0	0	0	0	0
S' Duration (ms)	0	0	0	0	0	0	0	0	0	0	0	0
Q Amplitude (uV)	0	0	0	-1132	0	0	0	0	0	0	0	-67
R Amplitude (uV)	790	1542	962	512	177	1217	155	487	792	1977	2057	1602
S Amplitude (uV)	-660	-370	0	0	-557	-75	-1197	-2397	-1427	-747	-405	-217
R' Amplitude (uV)	0	0	0	0	0	0	510	0	0	0	0	0
S' Amplitude (uV)	0	0	0	0	0	0	0	0	0	0	0	0
J Amplitude (uV)	77	125	52	-92	15	92	37	185	190	125	85	65
P+ Amplitude (uV)	80	167	95	0	0	130	80	75	85	82	87	85
P- Amplitude (uV)	0	0	0	-122	0	0	0	0	0	0	0	0
T+ Amplitude (uV)	310	450	165	0	97	302	0	0	0	170	415	422
T- Amplitude (uV)	0	0	0	-377	0	0	-422	-215	-245	0	0	0
ST Slope (uV/s)	1190	1160	-27	-1190	595	565	-652	1220	1755	1755	1605	1070
P Morphology	0	0	0	0	0	0	0	0	0	0	0	0
T Morphology	0	0	0	0	0	0	0	0	0	0	0	0
I Segment (ms)	0	0	0	0	0	0	0	0	0	0	0	0
K Segment (ms)	0	0	0	0	0	0	0	0	0	0	0	0
Signal Quality	0	0	0	0	0	0	0	0	0	0	0	0
ST Amplitude at J+20	100	147	52	-115	25	102	30	225	237	162	110	82
ST Amplitude at J+60	147	197	55	-165	47	127	0	272	310	237	180	125
ST Amplitude at J+80	177	222	50	-192	65	140	-17	287	337	272	220	155

Close

Figure 5. Fiducial points and measurements were computed and stored in the measurement table.

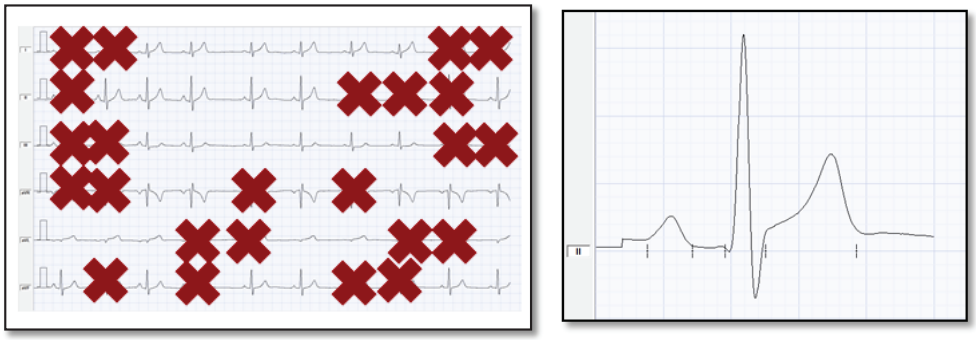

Figure 6. The averaged PQRST complex in each lead (right) was calculated by the trimmed mean, discarding the first and last quartile of the data (left).

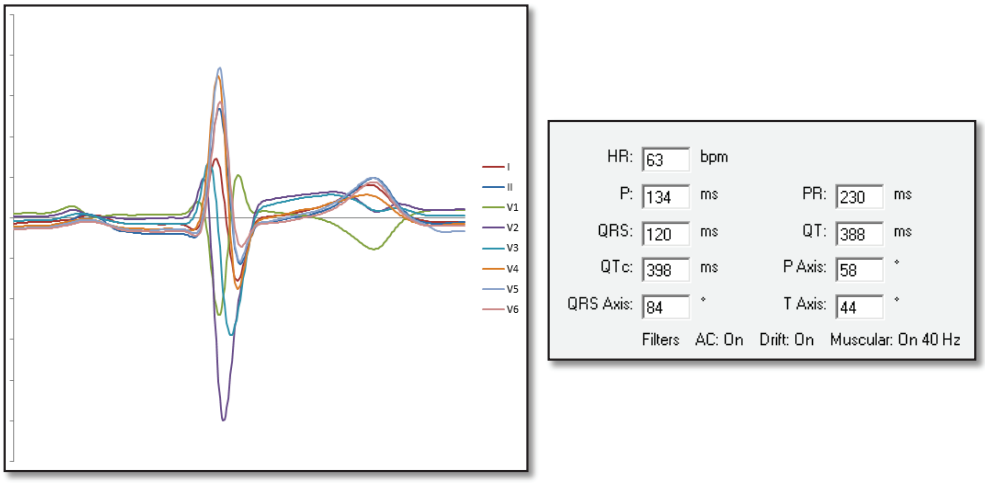

Figure 7. The superimposed global complex (SGC) was composed of 12 representative beats superimposed from each of 12 leads (left), and durations were measured from the earliest onset to the latest offset in the SGC and stored in the database (right). Heart rate in beats per minute (bpm) and QRS axis in degrees were derived from the computer and visually confirmed.

The visual analysis was performed on 100-400% magnified signals on a 24" screen with 1680x1050 MPixel resolution, using on-screen callipers (Real Click, software version 3.5.4.):

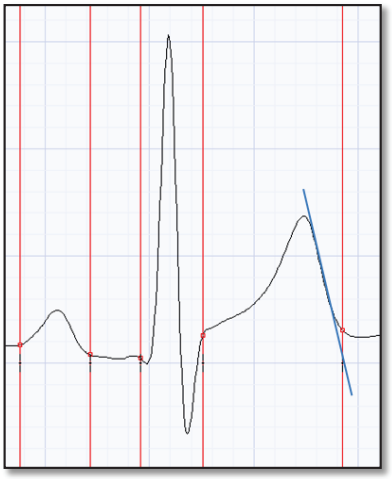

Figure 8. The P wave, PR interval and QRS duration were measured to the nearest 2 ms from the average PQRST complex in lead II. If the PR interval was <120 ms in lead II, all leads were measured. The PR interval was categorized as short if <120 ms in all leads. Intraventricular conduction delay was diagnosed if the QRS duration in lead II was >120 ms according to the specified ESC recommendations, or if the computer-derived QRS duration was ≥140ms after visual assessment of first onset to last offset in the SGC. The offset of the QT interval was adjusted visually using the intersection between a tangent drawn from the descending part of the T wave to the horizontal line drawn between the PR intervals in lead II, V_3 or V_5. QTc was defined according to Bazett's formula and categorized as prolonged if ≥470 ms in any lead. The QT duration was visually assessed in all leads if QT was ≤330 ms or QTc <340 ms (ESC recommendations), or ≤320 ms (Seattle criteria), and only regarded as short if these criteria were fulfilled in all leads.

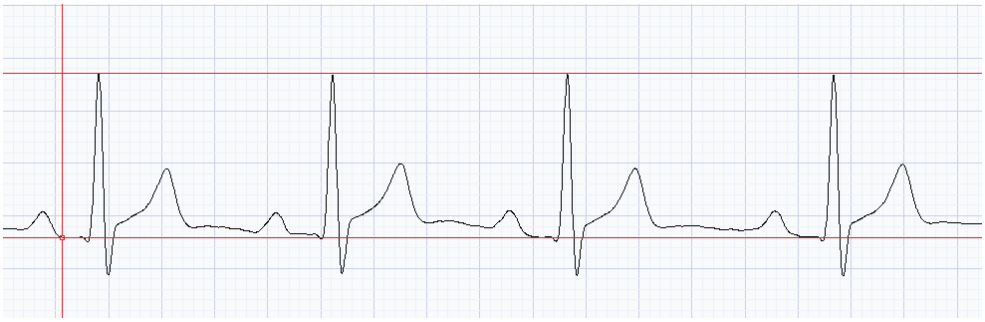

Figure 9. The R and S wave amplitudes were measured to the nearest 1 μV as the mean of the highest amplitudes in the QRS complexes, and the maximum P wave amplitude was measured in lead II.

The following amplitudes were visually assessed and measured with on-screen calipers in the separate leads if borderline: ST segment depression was categorized as >0.5 to 1.0 mm or >1.0 mm in any lateral leads (I, aVL, V_5 or V_6) and >1.0 mm in any other lead, ST segment elevation was categorized as >1.0 mm, pathological T wave inversion as >1.0 mm (or negative part of biphasic T wave >1 mm) and pathological Q wave amplitudes as ≥3.0 mm and/or 40 ms in duration. All amplitudes were related to the PR line.

For detailed differences between the specified ESC recommendations and the Seattle criteria, see table 1-3 in supplemental online material, **paper** IV.

Echocardiography

All echocardiographic recordings were performed by 13 cardiologists with a 2.5-MHz transducer (Vivid 7 and Vivid i; GE Vingmed Ultrasound AS, Horten, Norway) within 30 minutes after the BP and HR measurements. The digital data were transferred to a computer (Dell Optiplex 755) for off-line analysis at the core echolab, Oslo University Hospital, Aker, with the software EchoPAC (BT08) (GE Vingmed Ultrasound AS, Horten, Norway). The echocardiographic recordings were performed from standard parasternal long- and short-axis and apical views. LV internal dimensions (LVID) and posterior wall thicknesses (PWT), and LV mass were measured at end diastole as recommended by the American Society of Echocardiography (66;67), LV mass were calculated by the formula of Devereux (66). LV volumes were measured by modified Simpson's rule from biplane 2 and 4-chamber views (figure 10) (66;68). From these data, SV was calculated. Relative wall thickness (RWT) was calculated by 2xPWTd/LVIDd using the parasternal long-axis view (66;69).

LA size was measured as LA end-systolic volume (LA ESV) from the apical 2 and 4-chamber views by the method of area-length (66). Data regarding

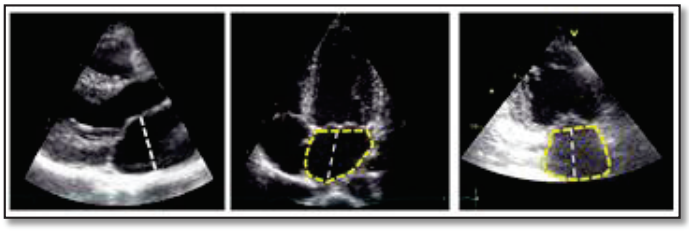

Figure 10. Echocardiographic measurements of left atrium.

chamber quantification were indexed to body surface area (BSA) according to recommendations (66) (**Paper I&III**).

The second assessment of echocardiographic analyses during the autumn 2009 were all conducted by one of the authors (GFG) who was blinded for the BP results and clinical status of the participants (**Paper I**).

Interpretation

On site, experienced cardiologists decided if the players were eligible for professional soccer based on their symptoms, family history, physical examination, ECG and echocardiographic evaluation (figure 14). After completion of the screening in 2008, three cardiologists reassessed all the examinations with remarks and recommended further follow-up. For **Paper III and IV**, all ECGs were assessed and measured by one investigator (HMB), who also developed separate syntaxes adjusted to the different criteria, and possible rhythm or conduction disturbances were discussed with a cardiac electrophysiologist (KG). The ECGs were categorized as normal, including common and training-related ECG changes, or abnormal. **(Paper IV)**.

Adjusted reference values for computer-based measurements

When the main differences between visual and computer-based measurements were displayed, reference values were adjusted for computer-based measurements to obtain better agreement to visual analyses (**Paper IV**).

Statistical analyses

All statistical analyses were conducted using SPSS (PASW Statistics 18, IBM Corporation 2010, NY, USA) (**Paper I, II and III**) and (PASW Statistics 21, IBM Corporation 2013, NY, USA) (**Paper IV)**. Differences between two subgroups were analyzed using t-tests for continuous variables, and χ^2 or Fisher's exact tests for categorical variables. $P<0.05$ was considered statistically significant, and all tests were two-tailed (**Paper I, II and III**).

Paper I and II

Differences in means between all BP categories/subgroups were calculated using analysis of variance test for trend for continuous variables, and linear-by-linear analysis for categorical variables. The significance levels of differences in means between the subgroups were adjusted by

the Bonferroni procedure to control the risk of a type I error. Data are presented as mean ± standard deviation or as numbers (percentages).

Paper I

The players were divided into four subgroups according to their office BP (38). All controls were white Europeans, and they were compared to white European players only to make the comparisons more homogenous. All white players were compared to all black players, but not to players of other or mixed ethnicity, since this category was too heterogeneous. The players were also divided according to their position in the team, as goalkeepers or outfield players. Based on the match-schedule from La Manga, they were also divided according to whether their team had played a match in the evening (4.00 pm or 7.00 pm) the day before their examinations or not.

LVID, PWT, LV mass, LA ESV, SV and SAC were all indexed to body surface area (BSA), calculated from height and weight. The outcome variables for this study were SBP, DBP, MAP, PP, HR, $LVID_{BSA}$, PWT_{BSA}, $LVMI_{BSA}$, RWT, LA ESV_{BSA}, SV_{BSA} and SAC_{BSA}. Linear regression analysis was used for correlation between two continuous variables.

Paper II

The outcome variables for this study were mean SBP, DBP, MAP, HR, PP and nocturnal dip in systolic and diastolic BP. Correlation between office and daytime ambulatory MAP was tested using Pearson's bivariate correlation analysis. Included cases and controls were compared with the remaining players with high and optimal OBP, respectively, to test for selection bias.

Paper III and IV

Since most of the ECG measurements had non-Gaussian distribution, all data are presented as medians and interquartile ranges (IQR), though mean ± standard deviations (SD) are presented as online data supplement to make comparisons with other studies easier.

Paper III

The Mann-Whitney U test was used to test for significant differences between two groups. Correlation between QRS duration from the SGC and visual analysis from the average PQRST complex in lead II was tested using Pearson's bivariate correlation analysis.

Paper IV

Intraclass correlations (ICC) were used to test correlations for continuous variables and kappa statistics ($\varkappa$) to test agreement between categorical variables. Intra-observer variability of visual analysis according to the Seattle criteria was tested nine months apart from 30 randomly selected players. K and ICC <0.2 represent poor, 0.21- 0.40 fair, 0.41- 0.60 moderate, 0.61 - 0.80 good and >0.8 very good correlation, respectively. Bland-Altman plots were performed between visual and computer-based measurements, and all outliers were visually assessed to decide if waves were misclassified by the computer.

Summary of results

Paper I

In this study we investigated the prevalence of high BP (≥140/90 mmHg) in players and controls, and in players of white and black ethnicity, and the association between increasing BP in groups and LV $mass_{BSA}$, LA volume and arterial compliance. The players' mean BP was 122/69 ± 11/8 mmHg. There were no significant differences in prevalence of high BP between all players, 39 (7%), and controls, 4 (9%), or between white, 32 (7%), and black, 5 (10%), players. There was a significant positive linear relationship between BP and LV $mass_{BSA}$, LA ESV_{BSA}, SV_{BSA}, HR and PP, and negative relationship to SAC_{BSA}.

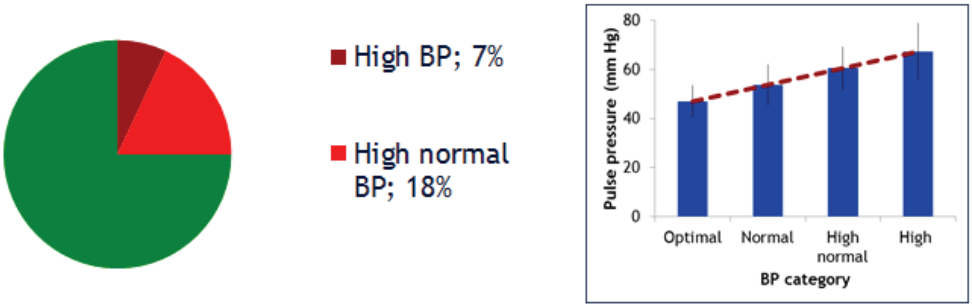

Figure 11. One quarter of the players had BP≥130/85 mmHg (left figure). The figure illustrates a significant linear relationship between increasing BP category and pulse pressure (right figure).

Paper II

This study sought to identify the prevalence of high ABP and examine the players' compliance with recommended follow-up of high OBP, and to study if indicators of sympathetic activity were increased in players with high BP. The prevalence in BP subgroups is shown in table 3.

Subgroups	Cases (n=26)	Subgroups	Controls (n=26)
Sustained HT	15 (58%)	**Normotension**	17 (65%)
White-coat HT	11 (42%)	**Masked HT**	9 (35%)

Table 3. Prevalence in BP subgroups of cases and controls after office and daytime BP recordings.

Mean nighttime ABP was high in 39, and 20 had no nocturnal dip. Ten (38%) of the cases had no follow-up of BP.

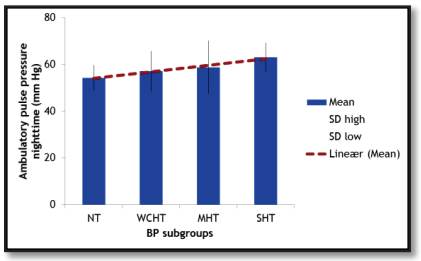

Figure 12. There was a linear relationship between increasing BP in the four subgroups and mean ambulatory PP (p<0.01).

Paper III

In this study we compared the prevalence of abnormal ECG findings between the ESC's recommendations as specified by Uberoi et al., with the new Seattle criteria for interpreting ECG in athletes. We also described the performance of the ECG procedure in detail to facilitate meaningful comparisons with other studies. The prevalence of abnormal ECG findings was reduced from 29.3% to 11.2% or 66 players by the new Seattle criteria. These 66 athletes were all included among the 172 (29.3%) players with abnormal ECGs according to the specified ESC recommendations (figure 13). Echocardiography alone detected one player with abnormalities. None of the players with abnormal ECGs according to the ESC's recommendations only, had abnormal echocardiograms. All players, except to with hypertension grade II and LV hypertrophy on echocardiography, were found eligible for competitive soccer. Based on echocardiographic evaluations this reduction increased the specificity of the Seattle criteria, without increasing the number of false negative ECGs.

We also showed that comparisons with previous studies were difficult due to imprecise descriptions of ECG recordings, analysis methods, and different reference values for abnormality in these studies.

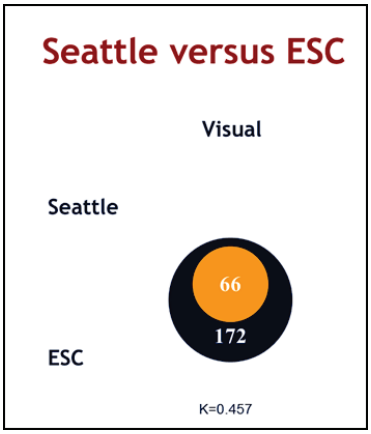

Figure 13. Overlapping circles illustrating level of agreement of visually abnormal ECG findings between the Seattle criteria (orange) and the specified ESC recommendations (blue).

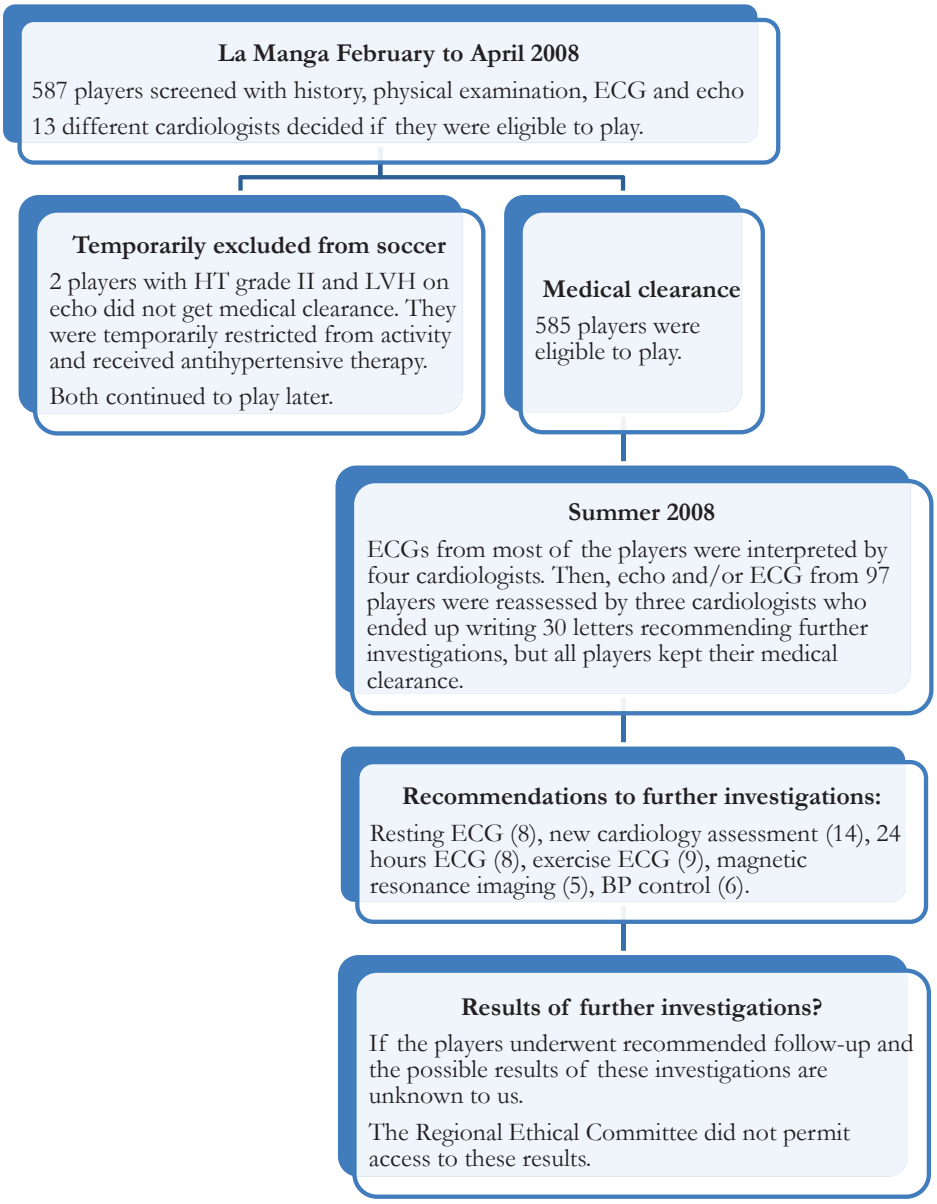

Figure 14. Flow chart explaining assessment of ECG screening results during and after screening in 2008.

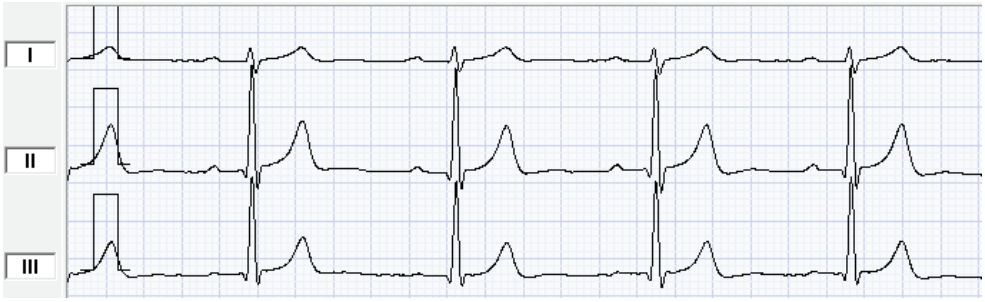

Figure 15. The PR interval in this ECG is between 201 and 220 ms. According to the specified ESC recommendations this is defined as a normal finding (PR interval ≤220 ms), and according to the Seattle criteria as a training-related finding of first degree atrioventricular block (PR interval >200 ms).

Paper IV

This study compared the prevalence of abnormal ECG findings between visual and computer-based measurements, according both to the European Society of Cardiology's (ESC) recommendations as specified by Uberoi et al, and the new Seattle criteria for interpreting ECG in athletes. When the main differences between visual and computer-based measurements were displayed, reference values were adjusted for computer-based measurements to obtain better agreement to visual analyses. According to the ESC's recommendations and Seattle criteria respectively, ECGs were categorized as abnormal in 171 (29.5%) versus 64 (11.1%) players after visual assessments and in 293 (50.6%) versus 127 (21.9%) players after computer-based measurements. Agreement between abnormal ECGs according to the Seattle and ESC criteria is illustrated in figure 16, and between visual and computerbased measurements with normal reference values in figure 17, and with adjusted reference values in figure 18. Intraclass correlation was very good for R and S wave amplitudes and moderate to very good for intervals (figure 19-20). K was very good for pathological Q wave amplitudes and moderate for T wave inversions.

Correlations for visual measurements of durations and amplitudes in ECG from 30 randomly selected players were very good, except for QRS duration in lead II with ICC 0.621 (supplementary online table 6). Five ECGs were interpreted abnormal each time according to the Seattle criteria (K=1.00).

Disagreements mostly regard "borderline" ECG findings without clinical significance, except for misclassifications of S as Q waves and vice versa.

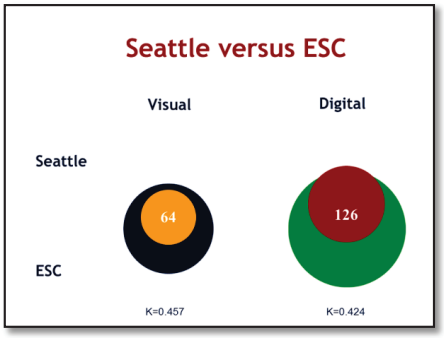

Figure 16. Overlapping circles illustrating level of agreement of abnormal ECG findings between the Seattle criteria (orange and red) and the specified ESC recommendations (blue and green).

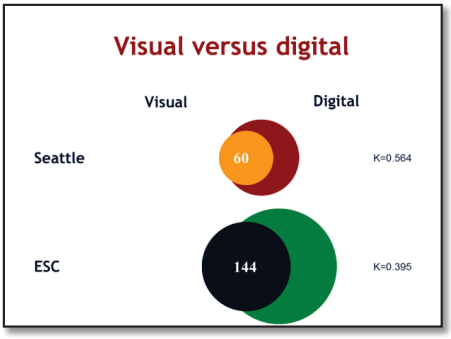

Figure 17. Overlapping circles illustrating level of agreement between visual and digital measurements according to the Seattle criteria (orange and red) and the specified ESC recommendations (blue and green).

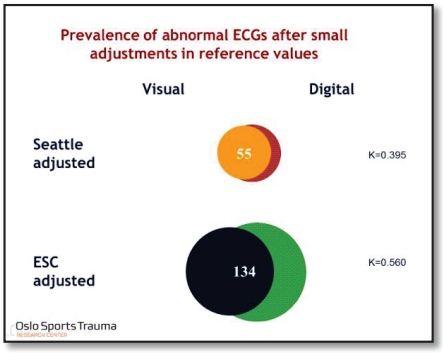

Figure 18. Overlapping circles illustrating level of agreement between visual and digital measurements after small adjustments of computer based reference values.

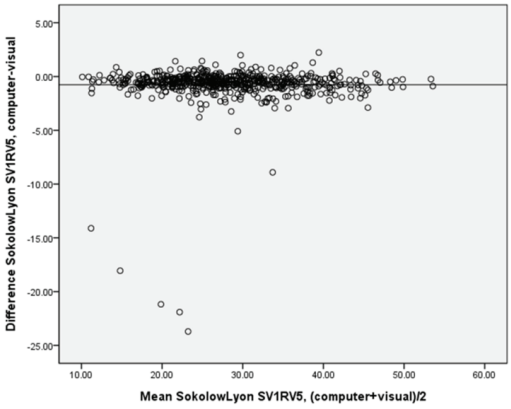

Figure 19. Bland-Altman plot of Sokolow-Lyon voltage criteria for LVH (SV_1+RV_5) in mm. Mean Sokolow-Lyon: 28.2±8.0 mm. Mean difference: -0.9±2.4 mm.

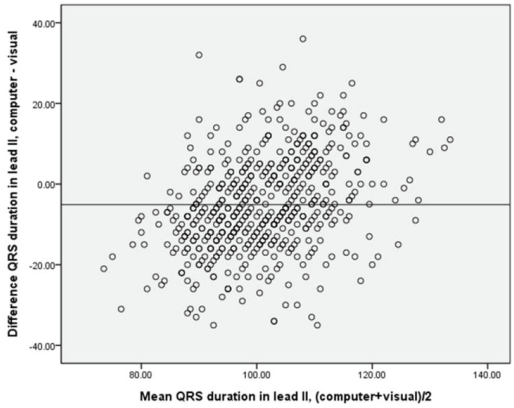

Figure 20. Bland-Altman plot of QRS duration in lead II measured by the computer versus visually in ms. Mean QRS duration: 101±9.8 ms. Mean difference: -5.1±11.7 ms.

Discussion

Setting and participants

The Norwegian Football Association (NFF) decided in 2008 that all players in "Tippeligaen" and "Adeccoligaen" should undergo cardiac screening in order to receive medical clearance to play professional soccer. Two of the teams organized the examinations locally (Tromsø and Rosenborg), while the remaining 28 teams were screened during a 1-2 weeks training camp at La Manga in Spain. Many soccer players in Norway change team each year, and the level of training and organization vary between the clubs. Some of the players have a part-time job or are studying in addition to their job as soccer players, while others are "just" playing soccer twice a day. Many of the players also have a family and have to follow children to nursery, school and activities. The level of stress in every-day life is therefore not limited to how much "play-time" they get, salary or new contracts. Some of the players felt that being away from home in Spain was quite relaxing. Some of the players who underwent ambulatory BP recordings later reported a higher level of stress when they were back in Norway, and that being away from home in Spain was quite relaxing. Significantly more players than controls used snuff every day, more than in the general population. The first 100 players were asked if they smoked, but this question was canceled, when it seemed they all preferred smokeless tobacco.

Several other factors related to participants can also influence the results in preparticipation cardiac screening studies, and some of them are presented in table 4, and discussed further here.

Age

Players <18 years of age were excluded due to lack of parental consent. If they had been included, we must have considered different reference values for hypertension and abnormal ECG findings (70;71). In a huge screening study by Pellicia *et al* they merged data from all athletes (from 8 to 78 years old) and presented an *overall* prevalence of markedly abnormal (4.8%) and abnormal (11.8%) ECGs in 32 652 *young* amateur athletes (72). The authors acknowledged the differences between age groups and presented significantly different prevalence of T wave inversions (among abnormal ECG findings) related to age: <20 years; 9.5%, 20-29 years; 38.6%, and ≥30 years; 37.9%. Since 84% of our cohort of professional soccer players were 20-34 years

old, compared to <30% in Pellicia *et al's* study, the overall prevalence of abnormal ECGs was higher in our study, with abnormal T wave inversions as the most frequent finding.

Ethnicity

The options for answers about ethnicity was; "Caucasian", "Afro-American", or "other". Some of the answers were obviously wrong. We learned that "Afro-American" means black American with African ancestry. Thus, there had been no option for black Africans – from Africa. We understood that ethnicity and race are imprecise terms, covering different concepts of nationality, religion, migrant status, language, country of birth, family origin and visible physical characteristics (73). Therefore, Bhopal recommended that researchers should explain their understanding of the concepts of race or ethnicity and the classification they use (73). Among 26 screening studies presented in table 4, eighteen had no definition of ethnicity, three used self-assigned questionnaires and five referred to descent. Interestingly, none of these studies describe how they define athletes descending from parents with different ethnicity. Since we especially wanted to study differences in cardiac adaptations between "Africans" and "Caucasians", we retrospectively defined ethnicity as parents' homeland and updated the database using internet and telephone. We also introduced "mixed" inheritance.

Several studies have demonstrated that African/Afro-Caribbean athletes have greater LV wall thickness than Caucasian athletes (22;30;74;75), while studies of Arabic athletes has demonstrated significantly smaller cardiac dimensions than in Black African and Caucasian athletes (76). In our cohort of professional soccer players, Gjerdalen *et al* showed that LV mass was equally enlarged in black and white players, but both left and right ventricular relative wall thickness were increased in Africans compared with Caucasian athletes (77). Both LV and right ventricle were smaller in Africans than in Caucasian athletes, while left and right atria increased similarly. As a consequence of these findings, African athletes had significantly more concentric remodeled LV and right ventricle than the Caucasian athletes. Japanese soccer players, on the other hand, showed more eccentric remodeling in a study by Kervio *et al* (78). With regard to distinctly abnormal ECG findings, Japanese (10.3%) and Caucasian (6%) soccer players were comparable, but differed significantly from African-Caribbean (21%) athletes.

A higher prevalence of abnormal ECG patterns in black than white athletes has also been demonstrated in highly-trained male American football players (79), in college athletes in Kansas (80), and in national level athletes in Qatar (33), among others (75). In Qatar, Riding *et al*, demonstrated a significantly greater prevalence of T wave inversions in black Africans compared

to Caucasian and West-Asian athletes (76). A higher prevalence of T wave inversions in black (14.3%) compared to white (3.7%) athletes was also shown by Zaidi *et al* (81). But even when anterior T wave inversions were concomitant with marked right ventricular enlargement, arrhythmogenic right ventricular cardiomyopathy was never diagnosed in any of these athletes.

In our study we found significant differences between black and white players in all measurements of durations, except QRS interval, and in half of the amplitude measurements. Contrarily, in a study of undergraduate students at Stanford University, no clinical meaningful differences between races were demonstrated, although race was not defined (82).

We realize that impact of "ethnicity" is very hard to decide, since environmental factors such as birthplace and migration also influence the results**.** Variations in cardiovascular diseases between African-born and Caribbean-born black people in New York, for instance, exceeded those between black and white people (83).

Sporting discipline and level of physical activity

Elite soccer players usually run 8-12 km during match play regardless of player position (T, E. Andersen, personal communication). Maximal oxygen consumption of players at elite level has remained constant for the last 20-30 years, between 60-65 ml/kg/min. However, the number of repeated sprints above 25 km/h has increased dramatically over the last decades.
Hence, physiologists do not regard soccer as a pure endurance sport, but as an intermittent intensity sport. Professional American football players who play at positions that require sprinting and similar bursts of physical activity associated with abrupt elevations in heart rate, like our outfield players, showed more abnormal ECGs than players at positions with lower levels of activity (79). And linemen had greater heart mass than other players, despite adjustments for body size (84).

Several studies have demonstrated the impact of different athletic activity on cardiovascular adaptation, as summarized by Pluim *et al* and Fagard (26;85). Still, the majorities of screening studies combine athletes from up to 38 different sporting disciplines together and present one common result (table 4). However, even to compare our results with the three other studies of only soccer players (table 4), causes concern because of different level of activity, age or ethnicity (32;78;86). Since athletes' hearts develop as a result of athletic activity over time, it is not meaningful to compare the prevalence of abnormal findings in our studies including children, and where the majority of athletes are entering athletic activity for the first time (72).

Controls

For practical reasons, most of the controls were recruited among the teams' support people, like physiotherapists, coaches and masseurs. They could not be physically active more than 3 h/week, but probably they were more fit than the general population because many of them were former soccer players. Still, they had significantly higher resting heart rate, and $LVmass_{BSA}$ and $LAESV_{BSA}$ were smaller.

Questionnaire

The players answered the questionnaire before BP recordings. This was the first screening in Norway, so they were unaware of questions about self experienced symptoms and cardiovascular disease in the family. Some players made extra comments, but in general they were not interrogated for their answers by the cardiologists

After the screening, three quarter of the players answered another questionnaire, assessing how distressed they had been during the screening and how they had experienced the situation (98). Sixteen percent were afraid that the screening result might have consequences for their own health, and 13% were afraid of losing their license to play soccer. Therefore, underreporting of self experienced symptoms or heart disease in the family cannot be excluded. We only asked about first degree relatives, while some investigators include second degree relatives (99). Relatives were regarded as "young" if < 55 years of age, while the Norwegian guidelines for assessment of cardiovascular disease risk extends this to 65 years for women (40). Others only ask for a history of SCD in relatives under the age of 35 years (99).

Physical examination

Height and weight were self-reported, and this might have influenced the echocardiographic variables which are indexed to body surface area (BSA). However, for example one centimeter or one kilo more or less has minimal impact on $LVmass_{BSA}$. To illustrate this, a player who reports 78 kilos and 181 cm, with LV mass 224.7 g, has a calculated LV $mass_{BSA}$ at 113.5 g/m^2 if the reported variables are correct, and 112.7 g/m^2 if his real weight were one kilo more, or 113.8 g/m^2 if his real height were one cm less.

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Table 4. Characteristics of participants and settings in studies of preparticipation cardiac screening in athletes

1st author (Ref)	Published	Country	Number of participants	Age, mean (median)	-range
Maron (87)	1987	US	501	19	17-30
Bjørnstad (88)	1991	Norway	1299	24	24
Pellicia (31)	2000	Italy	1005	(23)	9-55
Choo (89)	2002	US	1282	22	22
Corrado (15)	2006	Italy	42386	?	12-35
Pellicia (72)	2007	Italy	32652	22 (17)	8-78
Magalski (79)	2008	US	1959	23	20-29
Basavarajaiah (90)	2008	UK	3500	21	14-35
Thunenkotter (91)	2009	Germany	582	27	?
Baggish (92)	2010	US	510	19	(>18
Corrado (16)	2010	Italy	1005	(23)	9-55
Le (29)	2010	US	658	20	?
Malhotra (93)	2011	US	1473	19	?
Papadakis (30)	2011	UK & France	904	23	14-34
Magalski (80)	2011	US	964	?	18-21
Wilson (33)	2012	Qatar	1220	23	12-35
Gademan (82)	2012	US	653	20	?
Schmied (94)	2012	Switzerland	102	(34)	20-68
Kervio (78)	2013	Japan & France	282	24	17-35
Schmied (32)	2013	Gabon	210	19	18-22
Zaidi (81)	2013	UK	675	22	14-35
Riding (76)	2013	West Asia	1175	24	13-40
Brosnan (28)	2013	Australia	1078	20	16-35
Zaidi (95)	2013	UK	627	22	14-35
Riding (96)	2013	Qatar	1328	?	?
Gati (97)	2013	UK	2550	22	14-35

Table 4 continues

Gender	Ethnicity	Definition of ethnicity	Sport	Setting
Mixed	Mixed	?	Mixed	University of Maryland, athletes
Mixed	?	?	Mixed	National Sport College
Mixed	White	?	Mixed	National team members, Italy
Males	Mixed	?	Football	National Football League Players
Mixed	?	?	Mixed	Competitive athletes, Veneto
Mixed	Italian	?	Mixed	Young amateur athletes
Males	Mixed	?	Football	College, athletes
Mixed	Mixed	?	Mixed	Elite athletes
Males	Mixed	?	Soccer	World Cup Players, Germany
Mixed	Mixed	?	Mixed	Harvard University, athletes
Mixed	White	?	Mixed	National team members, Italy
Mixed	Mixed	?	Mixed	Stanford undergraduate students
Mixed	Mixed	?	Mixed	College athletes division I
Males	Black	Self-assigned	Mixed	Athletes, regional to international
Mixed	Mixed	?	Mixed	University of Kansas, athletes
Males	Mixed	Descent	Mixed	National level athletes
Mixed	Mixed	?	Mixed	Stanford undergraduate students
Mixed	?	?	Mixed	Competitive athletes
Males	Mixed	Descent	Soccer	First league soccer championship
Males	Black	Gabonian	Soccer	Competitive soccer, high level
Mixed	Mixed	Self-assigned	Mixed	Athletes, regional to international
Males	Mixed	Descent	Mixed	National level athletes
Mixed	Mixed	Descent	Mixed	Professional elite athletes
Mixed	Mixed	?	Mixed	Athletes, regional to international
?	Mixed	?	Mixed	Athletes exercising ≥6 h/week
Mixed	Mixed	Self-assigned	Mixed	Athletes, regional or national

The IOC Consensus Statement on periodic health evaluation of elite athletes (1) proposes that physical examinations should be performed according to best clinical care and should investigate the presence of:

- Musculoskeletal and ocular features suggestive of Marfan syndrome
- Diminished and delayed femoral artery pulses (co-arctation)
- Mid-or end-systolic clicks
- Abnormal second heart sound (single or widely split and fixed with respiration)
- Heart murmurs (Systolic grade >2/6, and any diastolic)
- Irregular heart rhythm

Players with Marfan's syndrome are more likely to be found in sports like basketball and volleyball, since these sports favor tall players. Average mean height in our study was 183±6 cm, and only two players were >200 cm. About 12-20 children are born with Marfan's syndrome each year in Norway, and in 75% of the cases they inherit the condition from one of their parents (100). We might debate whether to include stigmata for Marfan's syndrome in screening in all sports disciplines in Norway owing to low incidence and already known disease, but remember these athletes might develop serious aorta dissection and even rupture because of weak connective tissue. Dilatation of aorta might also lead to aorta regurgitation. High athletic activity is not recommended since this might lead to progression of the aortic dilatation. Cardiac auscultation was not performed in this screening because all players underwent echocardiography. Aortic diameter was not investigated though.

Office blood pressure

The cardiac examinations of >670 participants were performed during a few weeks, by thirteen cardiologists and six nurses. Most often the players exercised twice a day, so it was impossible to avoid physical activity prior to the investigations. The minimum time gap between exercise and examinations was one hour, but most often several hours.

Detailed description of each player's physical activity was not collected, and retrospectively it was only possible to compare players whose team had played a match the day before versus not played. No significant difference in BP was found, but there are several limitations to these assumptions of the players' prior activity. We have been questioned whether post exercise hypotension can explain a low prevalence of high office BP, and if this also can explain the corresponding increased prevalence of high ambulatory BP.

Post exercise hypotension has been known at least since 1898 (101). At that time, Leonard Hill of the London Hospital Medical College published the results of a subject who ran 400 yd "as rapidly as possible" and had a 10- to 15-mm Hg reduction after 10 min rest, and 30-35 mm Hg after 60 min (102). Hill concluded, "The arterial pressure becomes depressed below the normal resting pressure after severe muscular work". But still there is no widely accepted normal BP response to exercise (103), except for an initial physiologic rise in systolic BP. The magnitude and duration (seconds to 20 min) of the immediate post exercise hyperaemia is dependent on the time, type and intensity of exercise (104). An exaggerated BP response on the other hand, defined as systolic BP >210 mm Hg during a treadmill exercise test in men, might be a predictor of future HT (103;105). Diastolic BP, usually unchanged or decreased during exercise, was shown to be an independent predictor of masked HT in subjects with exaggerated BP response, and increased with 15 mm Hg in patients with masked HT compared to 4 mm Hg in normotensive patients. Likewise, an inadequate fall in diastolic nocturnal BP might also be associated with masked HT (105). Systolic BP decreases after exercise, but the level and duration of hypotension depends on type of exercise (106-108) and pre exercise BP levels (109). Recent laboratory studies have usually been conducted in small groups. Keese *et al* studied in 21 healthy men (mean age 20.7±0.7 years), the immediate BP lowering effects of resistance exercise, aerobic exercise, and concurrent (resistance and aerobic) exercise for 60 minutes, compared to control (table 5) (108).

	Decrease in systolic BP		**Decrease in diastolic BP**	
1st author (Ref) / Exercise	in mm Hg	in min	in mm Hg	in min
Keese (108)				
Control, seated rest 60 min				
Resistance*	4.1±2.0	80	1.8±1.1	20
Aerobic† 65% VO_2peak 50 min	6.3±1.3	>120	1.8±1.0	50
Concurrent‖ 65% VO_2peak 20 min	5.1±2.2	>120	1.6±0.6	40
Keese (106)				
Control, seated rest 60 min				
Concurrent‖ 50% VO_2peak 30 min	4.2±2.5	60-70	1.2±0.4	40
Concurrent‖ 65% VO_2peak 30 min	4.8±2.7	>120	1.5±0.6	40
Concurrent‖ 80% VO_2peak 30 min	6.0±2.0	>120	1.8±1.2	60

*Table 5. Exercise induced BP reduction in 21 healthy men, mean age 20.7±0.7 years and mean resting BP 111.5±2.6/73.9±3.6 mm Hg. *Resistance exercise; 3 sets at 80% 1 RM for 8 exercises, including upper and lower limb. †Aerobic exercise; cycle ergometer. ‖Concurrent exercise; 2 sets at 80% 1 RM for 6 exercises, plus cycle ergometer.*

The decrease in systolic and diastolic BP was similar after all exercise sessions and significantly different from control. The duration of decreased systolic BP was longer after aerobic and concurrent exercise versus resistance exercise, and for diastolic BP after aerobic exercise compared to concurrent and resistance exercise (table 5). Then they studied how resistance and aerobic concurrent exercise with different intensities influenced post exercise hypotension (106). The magnitude of SBP decrease was similar after all concurrent exercise sessions, but the post exercise hypotension lasted approximately 1 h longer following the highest intensities (table 5). The magnitude of DBP decrease was slightly greater after concurrent exercise at higher intensities and longest after concurrent exercise at the highest intensity (table 5). They concluded that concurrent exercise sessions elicited post exercise hypotension, especially when the intensity of the aerobic exercise was higher than 65% VO_2peak.

In another small group of eleven healthy prehypertensive subjects (mean age 28.3±8.0 years), Bhammar *et al* studied the effect of fractionized aerobic exercise (3x10 min during 8 h) and continuous exercise (1x30 min), versus control, and found that mean systolic 24 h ambulatory BP was significantly lower during fractionized training versus control (127 versus 130 mm Hg) (107). Both types of exercise reduced the systolic BP during daytime, but only fractionized exercise reduced BP during nighttime (118 versus 122 mm Hg). Prehypertensive subjects were defined as per Joint National Commission 7 guidelines (110), and were comparable to players with normal and high normal BP in our study (table 1). The subjects' mean BP at baseline was 126±5/72±7 mm Hg versus 127±6/71±7 mm Hg in the prehypertensive soccer players (n=305). It might be that the beneficial BP lowering effect of physical activity in general is more pronounced in people not engaged in so vigorous continuous exercise as professional soccer, and that the absence of nocturnal dipping in ambulatory BP recordings in 38% of the players, indicates an unfavorable effect of vigorous exercise. We are not aware of comparable studies of post exercise hypotension in elite athletes, and acknowledge several limitations to these assumptions. Besides, some studies do not demonstrate any post exercise hypotension (109;111). In a study of ten normotensive, recreationally active young men (mean age 25±1 year), no post exercise hypotension was found after four experimental exercise sessions (111). Finally, in a study of 32 participants, reduction in BP did not correlate with pre exercise BP, but with peak oxygen uptake and time of day (109). The authors concluded that if statistical artefacts (as regression to the mean) were not controlled for, the degree of post exercise hypotension could be spuriously exaggerated and mask other more important moderators of BP change.

Summarized, it was difficult to consider the effect of exercise in the individual soccer players during the screening programme, and only two of the 26 screening studies in table 6 describe that

Table 6. Description of blood pressure recordings and prevalence of hypertension in studies of preparticipation cardiac screening in athletes

1st author (Ref)	BP	Prior activity	Position	Hypertension N (%)	Definition of HT (mmHg)
Maron (87)	Yes	?	?	1 (0.2)	Mild systemic HT
Bjørnstad (88)	No	?			
Pellicia (31)	No	No			
Choo (89)	No	?			
Corrado (15)	Yes	?	?	202 (0.5)	>160/100 repeated
Pellicia (72)	Yes	?	?	?	?
Magalski (79)	No	?			
Basavarajaiah (90)	No	?			
Thunenkotter (91)	Yes	?	?	12 (2)	>140/90
Baggish (92)	Yes	?	?	2 (0.4)	Elevated BP
Corrado (16)	No	No			
Le (29)	No	?			
Malhotra (93)	Yes	?	?		
Papadakis (30)	Yes	?	?	22 (0.8)	Excluded, >140 or 90
Magalski (80)	Yes	?	?	♂(5)/♀(0.6)	>140 or >90 repeated
Wilson (33)	Yes	?	Supine	10 (0.8)	
Gademan (82)	No	?			
Schmied (94)	Yes	?	?	2 (1.9)	?
Kervio (78)	No	?			
Schmied (32)	Yes	?	Supine	4 (1.9)	>140 or >90
Zaidi (81)	Yes	?	?	?	Excluded, ≥120/80
Riding (76)	Yes	?	Supine	17 (1.5)	>140, referred to ABP
Brosnan (28)	No	?			
Zaidi (95)	Yes	?	?	?	Excluded, ≥140/90
Riding (96)	Yes	?	?	16 (1.2)	Referred to ABP
Gati (97)	Yes	?	?	12 (0.5)	Excluded, ≥140/90

they tried to avoid physical activity for 24 hours prior to the investigations. We might even argue that since professional soccer players are training almost every day, some degree of post exercise hypotension is probably representative for their resting BP.

Figure 21. Example from BP recordings in the Nick of Time Foundation's heart screening at Snohomish Highschool in 2012. BP is recorded by emergency staff at the first station for physical examinations, and repeated later if high.

The IOC Consensus Statement recommends that bilateral brachial BP should be measured, on more than one reading (1). In a systematic review of BP in athletes, preliminary results from 40 studies revealed that only one study included BP in both arms (112). In a study among 401 general practitioners in the UK, three quarters were aware of similar recommendations, but only 30% agreed to it and 13% adhered to it (113). The main reasons for these recommendations in the general population are that different BP between arms could stem from abnormalities (co-arctation, stenosis, dissection, etc.) (114). In young trained people, differences could also be caused by muscles compressing an artery.

Ambulatory blood pressure

The ambulatory BP recordings were done in a standardized way. To include as many as possible (93%), the project leader (HMB) travelled around Norway to meet players. Since we also included a 5 minutes' heart rhythm variability test, the players were not allowed to eat or drink in the morning, or to use any snuff. Afterwards they were allowed to use snuff so it mimicked their ordinary days. Some players were distressed because of the fasting, but overall, they tolerated the procedures very well.

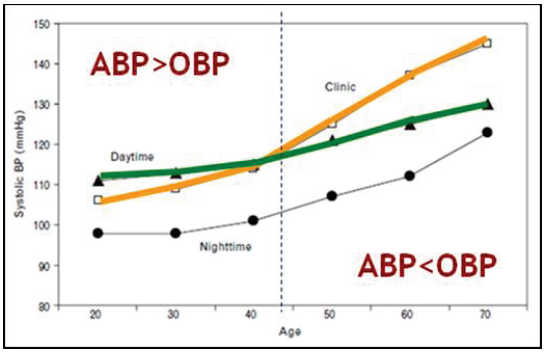

Figure 22. The common opinion has been that office BP is higher than ambulatory BP, and that is true for people aged 40-50 years of age, but not in the younger population. Adapted from Pickering,TG. 2008 J Hypertens.

That ambulatory BP is superior to office BP in predicting cardiovascular outcome was first shown in 1983 (115), and was the reason why we wanted to perform ambulatory BP recordings in the follow up of players with high office BP. This was not part of the original project protocol, but was added when we discovered that only six of the 39 players with high office BP at La Manga had been recommended to repeat office BP recordings at home. This is in accordance with other screening studies which also pay little attention to BP results. Among the 26 studies reported in table 6, BP recordings were mentioned in 16, prevalence of hypertension/high office BP reported in twelve, and reference values for high office BP defined only in nine. The prevalence varied between 0.2% and 5%, and definitions from ≥120/80 mm Hg to >160/100 mm Hg. Only two studies (reporting from almost the same population) referred athletes with high office BP to ambulatory BP recordings, and none had recorded ambulatory BP in athletes with normal office BP. Four studies excluded participants with elevated BP.

We designed the study as a case (high office BP) – control (optimal office BP) study.Players with optimal office BP were used as controls, because we wanted to test if players with high office BP have less heart rate variability than players with normal BP, and also if there are other differences between the two groups of otherwise healthy athletes,. Results from these tests are not published, but we found no significant differences between the groups, but a trend toward increased sympathetic activity in players with high office BP, but not with high ambulatory BP. This might indicate different influence of sympathetic activity in high ambulatory BP versus high office BP, as previously suggested by Fagard *et al* (116).

The most striking results after ambulatory BP was recorded in the first 20 players was a high mean ambulatory BP and lack of nocturnal dip (figure 23). This was a surprising finding, and we sought for errors by checking the devices and measuring the players' upper arm circumference to make sure that we had used correct cuffs.

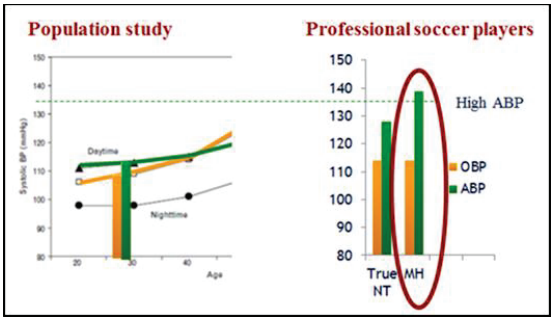

Figure 23. Compared to the small difference (<5 mm Hg) between systolic office BP and systolic ambulatory BP in a population study of adults <40 years of age, the difference is >15 mm Hg in professional soccer players with masked hypertension.

The term "masked HT" was first defined by Thomas G. Pickering in 2002. The prevalence of masked HT has varied in studies published after 2002, especially owing to methodological reasons (as discussed in **paper II)**. A recent Pubmed search with MESH term "masked hypertension" retrieved 22 studies in 2013, and 16, 14 and one in the preceding years, and zero before 2010. In studies published during the last two years the study participants are younger (in their 40s) compared to earlier studies (117-119). In one study of white-collar workers split in different age groups, the prevalence of masked HT in participants <40 years (n=240) was 14.6% (117). For comparison, the prevalence of normotension is 71.7%, white coat HT 2.9% and sustained HT 10.9%. These figures confirm our findings that masked HT probably is a bigger problem than white coat HT (figure 24).

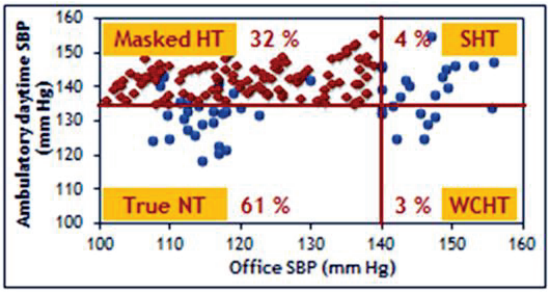

Figure 24. Estimated prevalence of soccer players in the four different BP subgroups. HT; hypertension, NT; normotension, SHT; sustained HT, WCHT; white coat HT.

We discussed possible factors associated with high ambulatory BP in **paper II**. In a recent study of 246 healthy young students (mean age 15.7 years), shorter sleep duration was related to higher ambulatory BP during 24 h, and during the night in white, but not in black adolescents (120). These data are consistent with the hypothesis that the cardiovascular consequences of short sleep may begin early (121). Yet another study from 2013 showed that most metabolic risk

factors were higher in patients with masked and sustained HT compared to normotensives and patients with white coat HT (122). This study also showed that significantly more patients with masked HT had LV hypertrophy on ECG, decreased transmitral peak early/atrial (E/A) velocity ratio by pulsed Doppler, compared to patients with normotension and white coat HT. Patients with masked and sustained HT in another study showed significantly lower early diastolic velocity (E') by tissue Doppler imaging, indicating impaired LV relaxation and significantly higher transmitral peak early velocity to early diastolic velocity by tissue Doppler imaging (E/E') ratios, reflecting higher LV filling pressures compared to normotensives (123). We could not demonstrate any differences, but these findings were not likely to be found in these professional young athletes, and the number of participants in each BP subgroup was also low. Nevertheless, in the total cohort we demonstrated a significant linear association between increased BP and LV $mass_{BSA}$. Similar associations have been seen in three other studies in athletes (76;124;125). Most recently in a study of 132 professional American-style football participants who had BP and LV remodeling assessed before and after season (125). Both systolic and diastolic BP increased significantly, and 47% met the criteria for prehypertension and 14% hypertension grade I postseason (110). The strongest predictors for postseason BP were lineman field position, intraseason weight gain, and family history of HT. There was a significant increase in the prevalence of concentric LV hypertrophy (2 of 64 [3%] versus 20 of 64 [31%]; $P<0.001$) among linemen, and change in left ventricular mass correlated with intraseason change in systolic BP ($R=0.46$, $P<0.001$). A high prevalence of HT was also shown among male collegiate football athletes in the US (126). Although American-style football is difficult to compare to European soccer, we agree with the authors that better strategies for awareness, prevention, and treatment are needed.

We speculated in **Paper I** whether athletes with elevated BP have an increased risk of developing future atrial fibrillation as result of the combination of pressure and volume overload (43). We demonstrated 11% increase in left atrial end systolic $volume_{BSA}$ from players with optimal to high BP. The soccer players had significantly lower heart rate than controls, and 12.1% had first-degree AV block with PR interval >200 ms (**Paper III**), both factors associated with increased prevalence of lone atrial fibrillation in "the Birkopp study" (43). Low heart rate also predicted lone atrial fibrillation in another study of healthy middle-aged men in Norway (127). In a systematic review and meta-analysis, the calculated increased risk of atrial fibrillation in endurance athletes is five-fold (128). Masked HT might be yet another risk factor for "lone" atrial fibrillation, since HT is the most important risk factor for atrial fibrillation (129). But if HT also is a risk factor for cardiovascular disease in healthy athletes is unknown, since all studies are

conducted in the general population. Maybe the reference values for HT should be adjusted in physically active people: without any end organ damage and BP <160/100 mm Hg, a diagnosis of HT is without consequences for sports participation (12).

In international guidelines for HT published from 2000 to 2012, seven of 13 recommend ambulatory BP recordings for suspected masked HT, and nine for assessing nocturnal dipping status (130). Different algorithms are proposed for assessment and management of masked HT in the general population (131;132). Results from the Masked Hypertension Study, a worksite-based population study, indicate that ambulatory BP recordings are unnecessary if the office BP is optimal (118). This is in contrast to our study where we unmasked high ambulatory BP in players with optimal BP. Until new prospectively designed studies of high ambulatory BP in athletes are performed, we do not know how to best tackle the possible increased health risk in players with masked HT.

Electrocardiography

Four cardiologists reviewed most of the ECGs recorded at La Manga (figure 14), but had no common protocol describing how to perform the measurements or exactly which criteria to use. This reflects common practice in screening studies as shown in table 7. This table presents an informal review of screening studies involving ≥100 athletes with a mean/median age ≥18 years. Looking just at papers published during the last five years (2009-2013), only half of the eighteen studies made any descriptions at all of measurement methods, and ten different criteria for abnormal ECG findings were applied. In addition to different athlete-related variables (table 4), prior screening examinations influence the prevalence of abnormal findings. In the much cited Italian study of 1 005 national team members (from 9 to 55 years and 38 sporting disciplines), many were screened and found eligible for sports before, as Italy has had mandatory screening since 1982 (133). This reduces the prevalence of new abnormal findings in the largest subgroup. But they also included 220 athletes referred from other screening centers due to miscellaneous findings, which increased the prevalence of abnormal fidnings in this subgroup (31). Abnormal findings also increase when athletes are screened for the first time, as in our study. The overall prevalence of abnormal ECGs in studies during the last five years varied from 4.5% to 23% (table 7).

In **paper III** we discuss how different criteria, factors related to technical specifications of the ECG device, and the recording situation influence the results. In **paper IV** we discuss how different measurement methods affect the prevalence of abnormal ECGs.

ECG device and technical specifications

The type of ECG devices that had been used in the different screening studies, were specified in thirteen of eighteen papers from the last five years, and seven different types were used. But none of the studies mentioned type or version of software, filter settings or lead placements (table 7). The technical specifications vary between software. Our ECG device detected waveforms with amplitudes of at least 25 μV and durations of at least 6 ms and compressed the signals 4:1, with expressed noise measured as root mean square errors of only 0.16%. Some years ago the compression ratio had to be higher because of limited storage capacity (50). This results in more noise (low- and high-frequency), and affects the high-frequency components of the ECG most, with the potential to alter measurements of Q-wave duration and R-wave amplitude within the QRS complexes. How this might influence measurements of findings in athlete's ECG is not investigated, but in the general population it can influence the criteria for myocardial infarction, among other diagnoses (134). Noise can be reduced to below 5 μV by incorporating more complexes into the representative complex (135). This will allow <10% estimated error in deflections of 20 μV. In our program, all digital samples were displayed on screen during the measurements, because the pixel-to-sample ratio ≥1.0 (52), and the on-screen callipers marked as small differences as 2 ms and 50 μV. Compared to measurements with ruler on ECG paper, where the smallest detectable differences are to the nearest 10 ms and 100 μV (figure 25 and 26).

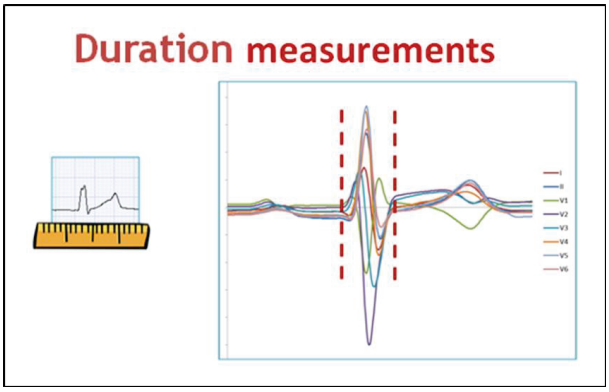

Figure 25. This figure illustrates two different ways to measure durations: with ruler on ECG paper (left), and with on screen callipers on the superimposed global complex(right).

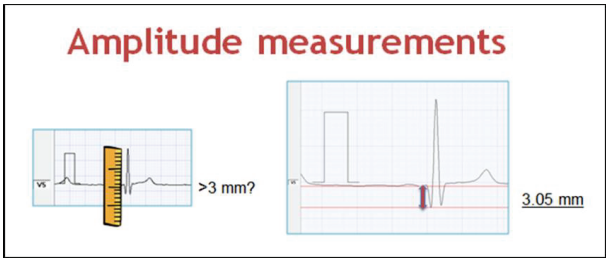

Figure 26. This figure illustrates two different ways to measure amplitudes: with ruler on ECG paper (left), and with on-screen callipers in each lead (right).

Hence, detection of small deflections as ST depressions >0.5 mm, TWI ≥1.0 mm and Q waves ≥3.0 mm were made easier and can partly explain the higher prevalence of abnormal TWI and pathologic Q waves in our study. In our ECG program, first onset – latest offset of the global PQRST complex was demarcated in all leads, but the SGC were not visible simultaneously. More modern software which makes manual adjustment of the demarcation lines in the SGC possible in all leads synchronously will further increase accuracy of duration measurements (figure 27). The correlation between visual measurement in the averaged PQRST complex in lead II and the first onset – latest offset of the SGC was moderate, r=0.432, with mean difference 6.4 ms.

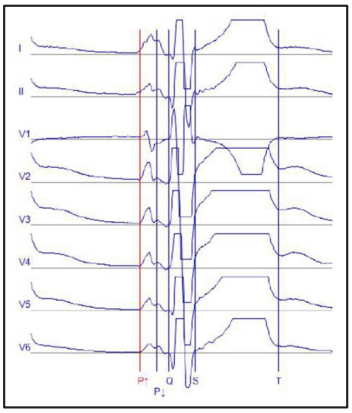

Figure 27. This figure illustrates how measurements of first onset - latest offset are displayed in all leads simultaneously. This ECG is recorded with CardeaScreen, Cardea Associates Inc, Seattle, WA, USA.

Three different filter settings which is meant for improving the ECG signal quality while real-time sampling and recording are conducted should be described (136): 1) Power line/AC filter which remove a very narrow band of signal frequency, centered at the power frequency 50 Hz or 60 Hz, dependent on country. This filter affects the S wave area of the QRS complex. 2) Baseline filter which should always be on to stabilize the isoelectrical line, but that does not affect the accuracy of the ECG signal because of the systems algorithm for removal of internal drifting. 3) Muscle tremor filter with selected frequencies between 25 Hz and 50 Hz, which is usually activated during exercise ECG tests. Unfortunately, the muscular filter was turned on during ECG recordings in the resting position at La Manga, possibly because the investigators relied on settings from the company, and were unaware of the implications. But when this filter filters out all high frequency signals above the selected frequency, this can reduce the sharp corners of the QRS complexes and widen it, and reduce the R wave amplitude by more than 20%. In most modern ECG devices

the muscular filters only affects the display of the ECG on the screen, while the unfiltered signals are stored. Unfortunately, our device only stored the filtered signals.

Athlete's position and placement of leads during recording

Five of the latest 18 screening studies described the athlete's position during ECG recording, and they were in a supine position. Previous studies have shown that the body position during ECG recording is important for the axis, QRS voltage, and depth of the Q wave and length of the QT interval (137;138).

Only one study in table 7 paid attention to the lead placements in their papers (28). In this study from Australia they also write that abnormal ECGs or groups of ECGs with unusual pattern were repeated with careful lead placement, if possible. We agree that this reflects "real world" practice. In our project a meeting was arranged ahead of the screening where correct placements were demonstrated. All six nurses responsible for lead placements were trained in cardiology departments, while one assistant without prior experience also put on the leads. The importance of correct lead placements was illustrated in a study where they deliberately misplaced the electrodes 2 cm upward and downward in 15 patients and found significant ECG interpretation changes in all patients (139). In half of the patients a >25% change in R wave amplitude was produced by only 2 cm vertical displacement and this lead to altered R wave progression in 20% of the patients. This can have important implications for diagnosis of ventricular hypertrophy. Another experimental study showed important changes in diagnostic classification in 6% of the cases when interpreted by the computer, and in 3% when interpreted by an expert cardiologist (140).

ECGs are usually recorded in a resting situation. The Seattle criteria recommend physical activity to check whether long PR interval duration or atrioventricular block is reversible (59;60). Corrado *et al* and Wilson *et al* defined long PR interval duration as respectively ≥210 ms or >200 ms following exercise or hyperventilation (15;33). Some of the soccer players were also recommended to move around before repeating an ECG, but this was random and not noted on the report. The player with bradycardia (31 bpm) had only one ECG recording. Another player with second degree atrioventricular block type II on the first recorded ECG had first degree atrioventricular block four minutes later. If we want to prospectively study long PR interval and bradycardia as risk factors for atrial fibrillation in athletes, the recordings should be categorized according to activity.

Table 7. Description of factors related to recording, measurement and interpretation of ECG in studies of preparticipation cardiac screening in athletes

1st author (Ref)	ECG device	Soft-ware	Paperspeed mm/sec & mm/mV	Position
Maron (87)	Burdick ek-5A	?	?	Supine
Bjørnstad (88)	Siemens Mingograph	?	25	Supine
Pellicia (31)	?	?	?	Supine
Choo (89)	?	?	?	?
Corrado (15)	?	?	50	?
Pellicia (72)	?	?	25	Supine
Magalski (79)	?	?	25	Supine
Basavarajaiah (90)	Marquette Hellige	?	25	Supine
Thunenkotter (91)	?	?	?	?
Baggish (92)	MAC 5500	?	?	?
Corrado (16)	?	?	?	Supine
Le (29)	Schiller	?	?	?
Malhotra (93)	?	?	?	?
Papadakis (30)	Marquette/ Philips	?	25 & 10	?
Magalski (80)	?	?	25	Supine
Wilson (33)	COSMED Quark	?	?	?
Gademan (82)	Schiller	?	?	?
Schmied (94)	Schiller AT-101	?	?	?
Kervio (78)	Mac 1200	?	?	?
Schmied (32)	Schiller AT-101	?	25	Supine
Zaidi (81)	MAC 5000/5500	?	?	Supine
Riding (76)	COSMED Quark	?	?	?
Brosnan (28)	?	?	25 & 10	?
Zaidi (95)	MAC 5000/5500	?	?	?
Riding (96)	MAC 5500	?	?	Supine
Gati (97)	Marquette /Philips	?	25 & 10	?

Table 7 continues

Lead placements	ECG measurements	ECG Criteria	Abnormal ECGs (%)	Echo*
?	?	Maron 1987	14.2	FU
?	?	Bjørnstad 1991	4.8	None
?	?	Pellicia 2000	14.4	All
?	?	Chou/ Knilans	55.0	None
?	?	Corrado 1979	9.0	FU
?	?	Pellicia 2000	11.8	FU
?	?	Pellicia 2000	4.5	FU
?	Callipers and millimetre ruler	Bazett/Sokolow	?	All
?	?	ESC 2005	?	All
?	?	ESC 2005	23.1	All
?	?	ESC 2010	11.0	All
?	Digital measurements	Stanford	10.0	FU
?	?	ESC 2005	18.7	FU
?	Each lead with callipers	Papadakis 2011	?	All
?	?	Pellicia 2000	10.0	All
?	Measured in each lead	ESC 2010+	9.9	FU
?	Digital measurements	?	?	FU
?	?	ESC 2010	?	FU
?	Tracer table	Pellicia 2000/ESC 2010	12.1	All
?	?	ESC/Seattle	12.4	All
?	Callipers	Zaidi 2013	?	All
?	Measured in each lead	ESC 2010+	?	All
Careful	?	ESC 2010 & Seattle	17.3 & 4.5	FU
?	Callipers	ESC 2010/2011/Seattle	?	All
?	?	Drezner 2012	4.7	All
?	Measured in each lead	ESC 2010	13.0	All

*Echocardiography for all or none participants, or only as recommended follow up (FU) of other abnormal screening results.

Measurement methods

In the description of methodology of all the papers in table 7, 23 of 26 papers use the words "standard", "12-lead" or "standard 12-lead" ECG. Only two authors (81;90) have a reference to this standard: "the variables were measured in each lead using callipers and a millimeter ruler as described elsewhere", that goes back to a book by Friedmann from 1971 (141). This "standard" is probably not standard any longer, but how it has changed and how this influences the results of measurements is impossible to say.

We chose to relate all measurements of amplitudes to the PR line. A different baseline could have influenced the results in both directions (figure 28-30).

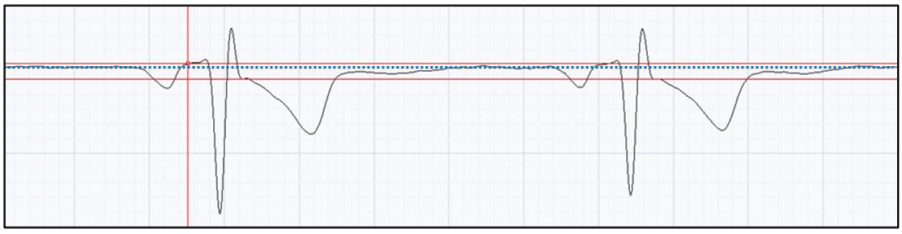

Figure 28. This figure illustrates that the ST segments are depressed >1.0 mm in lead aVR when the PR line (upper red line) is referred to as the isoelectrical line, and not if the TP segment (blue dotted line) is referred to.

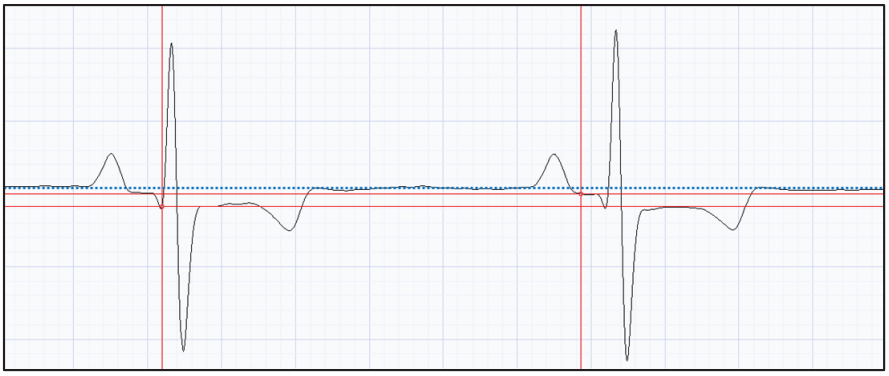

Figure 29. This figure illustrates that the ST segments are depressed >0.5 mm in lead II whether the PR line (upper red line) or the TP segment (blue dotted line) is referred to as the isoelectrical line. But the maximum P wave amplitude indicates right atrial enlargement only when the PR line is referred to.

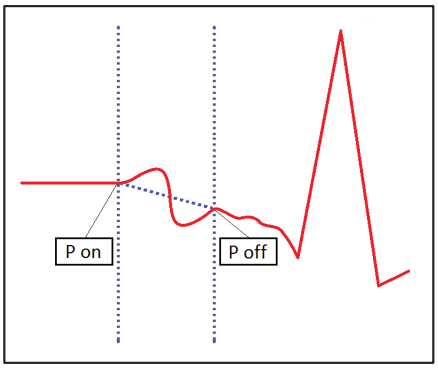

Figure 30. This figure illustrates yet another baseline for measurement of P wave amplitudes. It refers to the interpoloated line between P on and P off.

These figures illustrate how important it is to describe how measurements of amplitudes are performed in a study. The same is true for measurements of durations (figure 25, 27, 31). Computer-based measurements of P waves and PR interval durations were missing from 42 players because of irregular rhythm. In a recent study of 5 757 men and women aged 40 years and older, Soliman *et al* evaluated PR interval dependence on heart rate and found a statistically significant interaction between PR and heart rate with age (142). They produced a formula to make the PR interval independent of heart rate: PRa = PR+0.26 (heart rate-70). In the age group 40-60 years, they found that a reasonable threshold for defining first degree atrioventricular block would be 220 ms (98th percentile), with 205 ms as borderline reference value (95th percentile). This formula has to be tested in younger populations where the factor for adjustment (0.26) probably will be smaller. It's also worth mentioning that the PR interval might vary with 10 ms when heart rate is < 45 or >90 bpm, and that differences between softwares might be up to 20 and 25 ms (142).

The most challenging with measurements of duration was to decide where to end the QRS complex. In a comment to where to draw the line, professor Frölicher wrote: "Early repolarization redux: the devil is in the methods". The QRS end is also the beginning of the ST segment, where early repolarization is measured as the height at this point (143). To make this even more confusing, early repolarization changes are described as either elevation of the QRS ST junction, ST elevation, J point elevation, J waves, or increase from baseline (PR-line). Not to wonder that the prevalence range from 14.3% in Pellicia *et al*, to 79% in black athletes in Wilson *et al* (supplemental table 9, **Paper III**) (31;33). ST elevations above 2 mm is mentioned as

uncommon by Uberoi et al, but not included as an abnormal finding.(57) In the professional soccer players, 30% had ST elevation ≥2 mm, but this was regarded as a normal finding. The association with higher median HR in these players, 57 bpm versus 54 bpm (unpublished data), might indicate though that this is not a training-related alteration.

In a study of QTc time related to positions, Pressler *et al* used computer-derived measurements (137). To make diagnostic statements on reference values down to <10 ms was not possible before. In our study we found very good correlation (r=0.934 to 0.971) between QT interval duration measured in lead II, V_3 or V_5 respectively, with median QT interval duration two ms longer in lead II. This fits well with the recommendations to measure the longest QT interval, with a preference for lead II (144). We used a semi automated method and adjusted the fiducial points placed by an automated algorithm (52). Improved algorithms offered now by several manufacturers actually allow them to be used as the primary measurement tool (144).

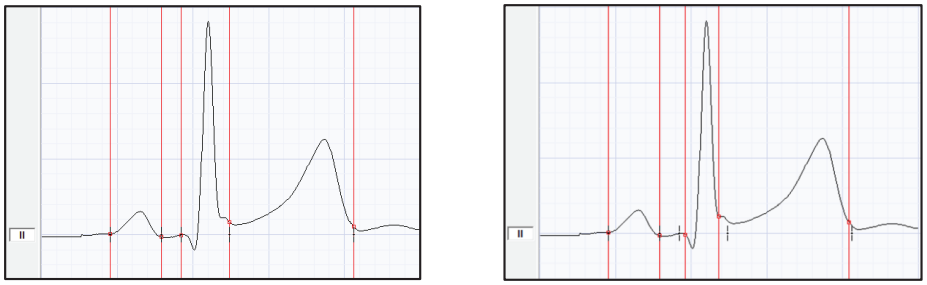

Figure 31. The left figure illustrate that QRS interval is 128 ms when the computer has placed the callipers to measure durations in the superimposed global PQRST complex in lead II. With manually adjusted callipers in the right figure, the QRS duration is 96 ms. For comparison, the measurement table for this player is displayed in figure 5, showing that medium QRS duration in lead II is 112 ms .

Criteria

The ESC recommendations lack the necessary details, and we therefore applied Uberoi *et al's* definitions of abnormality, which are based on the ESC's recommendations. In a study that compared these two sets of criteria (145), the authors found 19.7% abnormal ECGs applying strictly the ESC 2010 recommendations, and 3.9% applying Uberoi *et al's* criteria. Compared to these findings we have probably not underreported abnormal findings when we chose Uberoi *et*

als' specifications which reduced abnormal ECGs with 80% compared to the ESC 2010 recommendations (145). Based on echocardiographic evaluations this reduction increased the specificity of the Seattle criteria, without increasing the number of false negative ECGs.

The need for different criteria related to black and white athletes is already described, but Riding *et al* found no difference in the frequency of uncommon and training-unrelated ECGs between Arabic and Caucasian athletes, and concluded that the ESC guidelines are clinically relevant and acceptable for use within Arabic athletes (76).

How to define the different abnormalities is described in many ways (supplemental online table 10, **paper III**). The criteria for pathologic T wave inversions are described as; ≥-0.1 mV to ≥-0.2 mV in two, or in two contiguous leads, or in all leads (or in predefined groups of leads), or in all leads except in leads V_1, V_2, aVR or III. Pathologic Q waves are described as either ≥2 mm in depth in ≥2 leads, or ≥4 mm in depth in one, or ≥4 mm in ≥2 contiguous leads, or ≥25% of the height of the ensuing R wave, or ≥40 ms duration, or the latter in combination with QS pattern in ≥2 leads. The prevalence of abnormal ECG findings changes accordingly, as presented in supplemental online table 9, **paper III**. What impact these disparities would have had on the prevalence of abnormal ECG findings in our study is presented in supplemental online table 8, **paper III**.

There are reasons to believe that the ESC criteria can be simplified without loss of accuracy. Zaidi *et al* compared right ventricular hypertrophy on ECG between healthy athletes, healthy controls, patients with established arrhythmogenic right ventricular hypertrophy and patients with pulmonary hypertension (95), and found that the Sokolow Lyon voltage criteria for right ventricular hypertrophy are frequently fulfilled in healthy athletes without underlying RV pathology (on echocardiography or magnetic resonance imaging). They concluded that such findings should not prompt further evaluation if observed in isolation, because all patients had additional ECG abnormalities. In another study, Gati *et al*, compared isolated axis deviation and atrial enlargement in 2 533 athletes compared to 9 997 asymptomatic controls (97) and demonstrated that these two abnormalities comprised 5.5% of the abnormal findings in athletes, compared to 4.4% in the controls (p=0.023). No major structural or functional abnormalities were identified in any of them on echocardiography. As a consequence they suggested that these abnormalities should be excluded by the ESC guidelines. This was supported in an editorial by Corrado *et al* (146).

The Seattle criteria represent yet another set of recommendations for interpretation of athletes' ECGs. It is unfortunate to have different recommendations, and several members of the expert

panels are common to all three panels, so one possibility would be to improve the Seattle criteria, which were based on international consensus. The Seattle criteria have also been presented as three free learning modules in the British Journal of Medicine (147), and by the end of February 2014, over 7,300 modules have been completed by physicians from 93 countries around the world. Drezner *et al* recently showed that application of a standardized ECG criteria tool significantly improved the ability to interpret athlete's ECG across physician specialties (148).

ECG results versus echocardiography

Hypertrophic cardiomyopathy is the most common cause of SCD in athletes in the US (4). In the general young population the prevalence of hypertrophic cardiomyopathy is 0.2% (149). With similar prevalence in athletes we would expect to discover two athletes per 1 000 athletes screened. However, the observed number of cases is lower. Possibly reasons for this observation can be that adolescents with symptoms have withdrawn from sports at an earlier age, athletes with disease have been excluded during earlier screening situations, or because of failure to detect those with disease, e.g. due to atypical hypertrophic cardiomyopathy. There were for instance no athletes with hypertrophic cardiomyopathy after screening 1 078 athletes in Australia, 4 450 young athletes in Italy, 3 500 elite athletes in the UK or 1 473 college athletes in the US (28;90;93;150). Only one fifth of the college athletes had echocardiography, but since ECG in an early study by Corrado *et al* was found to be highly sensitive for hypertrophic cardiomyopathy, no false negative findings were suspected (5). But since the mean age of the college athletes was 19 years, the prevalence could have increased with age, since phenotypic hypertrophic cardiomyopathy can be unmasked with age (151). In our study, one player had concentric hypertrophy discovered only on echocardiography. He kept his medical clearance, but was recommended follow-up with magnetic resonance imaging. In a recent study, patients with hypertrophic cardiomyopathy, who had normal ECG or only LV hypertrophy on ECG, had less serious phenotype and no events during follow up (152). These observations support the presumptions that isolated QRS voltage criteria can be viewed as normal (152).

T wave inversions were the most common abnormal ECG finding in our study. Marked ventricular repolarization abnormalities can disappear after a detraining period, but case reports indicate that these changes are not only training related, but can be a marker of an underlying disease resulting in cardiomyopathies, SCA or SCD (30;153-155). Therefore, soccer players with T wave inversions should be recommended repeated investigations to detect changes suggestive of cardiomyopathy.

Conclusions

- Although the prevalence of high blood pressure in professional soccer players was low, our data indicates that there is an association between elevated blood pressure and reduced arterial compliance, increased left ventricle mass and left atrium volume even in young athletes. This emphasizes the importance of blood pressure measurements and standardized follow-up after preparticipation screening of athletes.

- More than one third of players with optimal OBP had high ambulatory BP, which is a novel finding in athletes. High PP and nighttime ambulatory BP, and lack of nocturnal dip suggest that professional soccer players have an increased sympathetic activity. These players might have an increased risk for CV disease. Follow-up of high OBP after preparticipation screening is often random and should be organized.

- The new Seattle criteria reduced the number of athletes with abnormal ECGs considerably compared to the specified European Society of Cardiology's (ESC) recommendations. Based on echocardiographic evaluations this reduction increased the specificity of the Seattle criteria, without increasing the number of false negative ECGs. Echocardiography in isolation seemed to be of limited value. To compare prevalences between studies, proper standardization of methods is still needed.

- Abnormal ECGs were more than twice as common after computer-based versus visual measurements. Agreement between visual versus computer-based findings was better for the Seattle criteria than for the ESC' recommendations. Reference values for abnormality might be adjusted depending on measurement methods. Computer-based interpretations of abnormality according to the Seattle criteria might be reliable without further assessment by a physician.

Perspectives

The main aim of this project was to describe the Norwegian athlete's heart. Secondarily, we wanted to get experience with preparticipation cardiac screening, and ultimately we hoped to prevent sudden cardiac arrest (SCA) and sudden cardiac death (SCD) in professional soccer players. In a recent review of evidence for cardiac screening in young athletes, Stokstad *et al* found that recommendations in favor of screening are based on studies of limited quality and on the personal opinion of experts (156). In a retrospective study of sports-related SCDs in Norway, myocardial infarction was reported as cause in 11 of 22 cases (157). If the coronary atherosclerotic process is asymptomatic, this will not be detected on routine screening, with or without resting ECG. Exercise ECG, with the potential to indicate coronary disease, was included in preparticipation cardiac screening before the FIFA World Cup in Germany in 2006, but the diagnostic value was limited, because the majority of tests were terminated before the athletes reached their maximum exercise capacity (91). Multidetector computer tomography is currently the best non-invasive diagnostic tool to detect coronary disease, but is not an option in routine screening owing to availability, costs, and radiation (158). Echocardiography in isolation has failed to identify additional cardiomyopathies in many screening studies, but is still mandatory. If modern ECG devices use the algorithms for interpretation of abnormal ECG findings according to the Seattle criteria, echocardiography seems unnecessary in athletes with normal findings. ECG algorithms that are specific for athlete characteristics, such as age, ethnicity and sporting disciplines, will increase the usefulness of ECG by avoiding misclassifications of normal training-related findings as abnormal. The ECG device CardeaScreen (Cardea Associates Inc, Seattle, WA, USA) is developed for interpretation of ECG in athletes. Data can be stored anonymously online and by pooling databases it might be possible to make new reference values for abnormal ECG findings depending on age, ethnicity and sporting disciplines. Abnormal T wave inversions were the most common finding in our study, and players with marked repolarization changes should be followed, even if the initial examinations are normal. Such changes might be an early marker of cardiomyopathy. To be able to compare results from different studies, we need proper descriptions of methodology, definitions of ethnicity, and new "standards".

Follow up of high office BP after cardiac screening was not systematic in our study, as in most other studies. The associations between elevated office BP and reduced arterial compliance, increased left ventricle mass and left atrium volume revealed that high office BP is probably not an innocent condition even in young athletes, and should be followed up according to the

standards of best clinical care. If office BP remains high after standard recordings, ambulatory BP should be measured. To learn more about the prevalence of masked hypertension and its potential role as cardiovascular risk factor in athletes, we need large prospective studies.

The highest incidence of SCA/SCD has recently been demonstrated in black African elite basketball players (1/3100 athletes per year) in a high quality study among National Collegiate Athletic Association student athletes in the US (159). This in contrast to a study of high school athletes in Minnesota, where the incidence based on various sources was 0.7/100 000 person years, but still highest in basketball players (160). From the last study, the authors calculated that only 2 of 1 000 000 athletes/year could be reliably detected by screening. We know from public media reports that some of the Norwegian soccer players have had cardiac disease or suffered SCA after the cardiac screening at La Manga, and it therefore seems that screening did not prevent SCA. However, SCD was prevented because the players were aware of symptoms and sought medical attendance in time, and because cardiopulmonary resuscitation was started immediately and automated external defibrillators were available. The importance of first-responder treatment on the field was also demonstrated in a study from the National Registry for use of automated external defibrillators in sports, where 16 (89%) of 18 students athletes who had cardiac arrest during physical activity survived (161). SCA during activity has just been included in the National Registry for Cardiac Arrest in Norway (162), and this is fundamental for quantification of these incidents, and for learning if they are preventable. Currently, the best strategy is "hands-on" education in cardiopulmonary resuscitation, and increased availability of automated external defibrillators. That children in Norway inhibit the Guinness World record in CPR is promising for the future!

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I

II

III

Prevalence of abnormal ECGs in male soccer players is still high, but decreases with the Seattle criteria

Seattle criteria and abnormal athletes' ECGs

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Abstract

Background

Abnormal ECG findings are important reasons for follow-up investigations after preparticipation cardiac screening in athletes. The main aim of this study was to compare the prevalence of abnormal ECG findings in athletes according to European Society of Cardiology's (ESC) recommendations and the Seattle criteria.

Methods and Results

A Norwegian preparticipation cardiac screening of male professional soccer players in 2008 enrolled BP, ECGs and echocardiography from 587 of 595 (99%) players (mean age 25 years, range 18-38). ECG was recorded with ClickECG, and measurements were derived with visually adjusted on-screen callipers on the computer-based averaged PQRST complex. The echocardiographic recordings were performed with Vivid 7 and Vivid i and categorised according to reference values for athlete's heart. Three cardiologists recommended follow-up after the initial screening. All ECGs were later interpreted according to both the ESC's recommendations and the Seattle criteria. In total 32 (5.5%) players were initially recommended follow-up. The prevalence of abnormal ECGs was 29.3% versus 11.2% according to the ESC's recommendations and the Seattle criteria, respectively. Echocardiography alone detected one player with abnormalities. None of the players with abnormal ECGs according to the ESC's recommendations only, had abnormal echocardiograms.

Conclusions

The Seattle criteria reduced the number of athletes with abnormal ECGs considerably compared to the ESC recommendations. Based on echocardiographic evaluations this reduction increased the specificity of the Seattle criteria, without increasing the number of false negative ECGs.

Keywords: ECG criteria; screening; electrocardiography; echocardiography, sudden cardiac death

ECG has a low sensitivity and specificity to detect potentially lethal cardiac disorders in athletes, speaking against its inclusion in preparticipation cardiac screening.[1] Application of the recently published Seattle criteria for interpreting ECG in athletes will lead to a reduction in abnormal ECG findings by categorizing more commonly found alterations as normal.[2]

The prevalence of abnormal ECG findings relates to age, gender, ethnicity, level of activity and sporting discipline.[3-8] Prior participation in screening will also influence the prevalence. However, many studies compile all results despite a heterogeneous population.[9;10] In order to identify ECG findings that may discriminate normal from pathological remodeling, we need standards comprising all phases of the ECG recording, processing and interpretation. The ECG devices' technical specifications, lead placements and methods for measurement can all result in significant differences in the reported amplitudes, intervals and diagnostic statements.[11;12] However, such information is rarely presented.[12]

During the last decade, ECG devices with built-in algorithms for measuring intervals from earliest wave onset to latest offset in all leads have become more utilized, and must be accounted for in comparative studies.[12]

Hence, the main aim of this study was to compare the prevalence of abnormal ECG findings between the European Society of Cardiology's (ESC) recommendations as specified by Uberoi et al, with the new Seattle criteria for interpreting ECG, in professional soccer players in Norway.[2;13] The performance of the ECG procedure is described in detail to facilitate meaningful comparison with other studies.

Methods

Participants

595 male professional soccer players in Norway underwent mandatory preparticipation cardiac screening during a preseason training camp in 2008.[14] Players aged 18 to 40 years responded to a questionnaire regarding their height, weight, ethnicity (Caucasian (white), Afro-American (black) or other), whether they had experienced symptoms during or in close proximity to exercise (table 1), and about cardiovascular disease in first-degree relatives <55 years (table 1). All participants gave informed written consent, and the study was approved by the Regional Ethical Committee.

Physical examination

Sitting blood pressure (BP) was registered after at least one hour rest as the mean of two consecutive BP measurements from a validated automatic BP monitor (Dinamap ProCare DPC300N, GE, Milwaukee, USA), and categorised as high BP when systolic BP (SBP) ≥ 140 mm Hg or diastolic BP (DBP) ≥ 90 mm Hg.

Electrocardiography

With the player in a supine position, the precordial ECG electrodes were placed according to recommendations,[12] and the four limb lead electrodes were placed on the arms and legs just distal to the shoulders and hips . ClickECG (Cardiette Cardioline, Milan, Italy) with Real Click software version 3.2.10 collected the simultaneous ten seconds digital recordings with a front-end sampling rate of 2000 per second and compression ratio 4:1. Paper speed was 25 mm/s with 10 mV gain. The frequency response was 0.05 Hz - 150 Hz, the baseline filter was always on, network filter was set at 50 Hz and muscular filter at 40 Hz. The software recognized waveforms with amplitudes of at least 25 μV and durations of at least 6 ms. The average PQRST complex in each lead was calculated by the trimmed mean, discarding the first and last quartile of the data. The superimposed global complex (SGC) was composed of 12 representative beats superimposed from 12 leads (figure 1), and the duration of the QRS interval was measured from the earliest wave onset to the latest offset in the SGC. According to the Seattle criteria, intraventricular conduction was categorised as

abnormal if the computer-derived QRS interval duration was ≥140ms after visual assessment of first onset and latest offset in all leads in the SGC.

The visual analysis was performed on 100- 400% magnified signals on a 24" screen with 1680x1050 MPixel resolution, using on-screen callipers (Real Click, software version 3.5.4.): The P wave, PR interval and QRS durations were measured to the nearest 2 ms from the averaged PQRST complex in lead II. If the PR interval was <120 ms in lead II, all leads were measured, and the PR interval was categorised as short if <120 ms in all leads. The R and S wave amplitudes were measured to the nearest 1 μV as the mean of the highest amplitudes in the QRS complexes, and the maximum P wave amplitude was measured in lead II. The offset of the QT interval was adjusted visually using the intersection between a tangent drawn from the descending part of the T wave to the horizontal line drawn from the PR interval in lead II. QTc was defined according to Bazett's formula and categorised as long if ≥470 ms in any lead. The QT duration was visually assessed in all leads if ≤330 ms or QTc <340 ms (ESC criteria), or QTc ≤320 ms (Seattle criteria), and only regarded as short if these criteria were fulfilled in all leads. The following amplitudes were visually assessed on-screen in the precordial leads and limb leads, and measured with on-screen calipers in the separate leads if borderline: ST segment depression was categorised as >0.5 to 1.0 mm or >1.0 mm in any lateral leads (I, aVL, V_5 or V_6) and >1.0 mm in any other lead, ST segment elevation was categorised as >1.0 mm to 2.0 mm or >2.0 mm, pathological T wave inversion as >1.0 mm or >2.0 mm (or negative part of biphasic T wave >1 mm) and pathological Q wave amplitudes as ≥3.0 mm and/or 40 ms in duration. All amplitudes were related to the PR line.

Heart rate in beats per minute (bpm) and QRS axis in degrees were derived from the computer and visually confirmed.

For detailed differences between the specified ESC recommendations and the Seattle criteria, see table 1-3 in supplemental data online.

Echocardiography

All echocardiographic recordings were performed with a 2.5-MHz transducer (Vivid 7 and Vivid i; GE Vingmed Ultrasound AS, Horten, Norway) as described previously.[11]

Interpretations and follow-up

On site, experienced cardiologists decided if the players were eligible for professional soccer based on history, BP, ECG and echocardiographic evaluation. After consensus, three cardiologists recommended additional follow-up based on best clinical judgment at that time. For the present study, all ECGs were assessed and measured by one investigator (HMB), who also developed separate syntaxes adjusted to the different criteria, and possible rhythm or conduction disturbances were discussed with a cardiac electrophysiologist (KG). The ECGs were categorised as normal, including common and training-related ECG changes, or as abnormal.

Statistical analyses

Since most of the ECG measurements had non-Gaussian distribution, data are presented as medians and interquartile ranges (IQR). The Mann-Whitney U test was used to test for significant differences between two groups. Correlation between QRS duration from the SGC and visual analysis from the average PQRST complex in lead II was tested using Pearson's bivariate correlation analysis. Differences between two subgroups were analyzed using t-tests for continuous variables, and χ^2 or Fisher's exact tests for categorical variables. $P<0.05$ was considered statistically significant, and all tests were two-tailed. All statistical analyses were conducted using SPSS (PASW Statistics 18; IBM Corporation 2010, New York, USA).

Results

ECG of good quality was available from 587 players (99%) of 595 players. Their median age was 25.0 years (21.0-28.0), height 183.0 cm (179-187) and weight 79.0 kg (74.0-84.0). The skin color was white in 497 (85%), black in 48 (8%), mixed for 13 (2%) and other for 29 (5%). History of symptoms during sports activity and cardiovascular disease in first-degree relatives are presented in table 1 and there were no significant differences in these between players with abnormal versus normal ECGs. Median office BP was 121/69 mm Hg (115.0-128.5/64.0-74.5) and 39 (7%) players had high BPs.

ECG findings according to the ESC and Seattle criteria

Abnormal findings were present in 172 (29.3%) players' ECG according to the specified ESC recommendations,[13] including all the 66 (11.2%) players with abnormal ECGs according to the Seattle criteria (figure 2) (see online-only Data Supplement).[2] The main differences were accounted for by the reduction in T-wave inversion (-7.1%), right atrial enlargement (-5.6%), right ventricular hypertrophy (-4.5%) and intraventricular conduction abnormalities (-3.9%) (figure 2). Common and training-related findings were found in 382 (65.1%) and 512 (87.2%) players according to the specified ESC recommendations and Seattle criteria, respectively. The increased prevalence was mainly driven by more incomplete right bundle branch block (+7.5%) and first-degree AV block (+7.0%) (see online-only Data Supplement).

The median QRS axis was 78.5° (64.0-88.8). The median QRS duration of the SGC and the average PQRST complex in lead II was 110 ms (100-120) and 104 ms (98-108), respectively, and they correlated moderately, r=0.43 (p<0.0001). For visually analyzed intervals and amplitudes, see table 7 in supplemental data online. After visual assessment, four out of seven ECGs with computer derived QRS duration of ≥140ms in the SCG were categorised as showing abnormal non-specific intraventricular conduction delay. One of twelve ECGs with short PR interval in lead II had short PR interval in all leads.

Recommended follow-up

After the initial assessment 593 (99.7%) players were found eligible for competitive soccer while two were temporarily excluded due to hypertension grade II (≥160/95 mmHg) and left ventricle hypertrophy (LVH) on

echocardiography. One of them had abnormal ECG findings according to both criteria, while the other had a normal ECG. Two players were already under medical attention when the screening was performed (Wolff-Parkinson-White (n=1) and idioventricular escape rhythm (n=1)). After the second assessment, another 28 players received letters with recommendations for follow-up due to: abnormal ECG findings (n=13), high BP (n=4), valve insufficiencies (n=9), concentric hypertrophy (n=2), atrium septum aneurism (n=1), or combinations of these. One of the players with concentric hypertrophy was detected through echocardiography only, though his heart rate was borderline; 31 bpm. Six of the 28 players were recommended follow-up due to causes later considered normal and training-related (Mobitz type I second degree AV block (n=2), ectopic atrial rhythm (n=2), junctional escape rhythm (n=1) and moderate eccentric hypertrophy (n=1)).

If recommendations for follow-up should be based solely on abnormal ECG findings and high BP, 194 (33%) versus 88 (15%) of the players would have been recommended follow-up according to the specified ESC recommendations and Seattle criteria, respectively (figure 3). Echocardiograms in all players with abnormal ECG findings according to the ESC recommendations only, were normal. Nine players with normal ECGs and valve insufficiencies grade I-II (n=8), atrium septum aneurism (n=1) and the one with concentric hypertrophy would have been missed without echocardiography of all players.

Other findings

Table 8 online relates the present prevalence of abnormal findings to other studies: T-wave inversions and ST elevations ≥1 or 2 mm divided in different groups, Q waves categorised as 25% of the ensuing R wave or ≥4 mm in ≥two leads, and LVH with associated nonvoltage criteria.

Discussion

The prevalence of abnormal ECGs in professional soccer players in Norway was reduced from 29.3% to 11.2% when the specified ESC recommendations were substituted by the new Seattle criteria. The main differences were accounted for by the reduction in T-wave inversion, right atrial enlargement, right ventricular hypertrophy and intraventricular conduction abnormalities (figure 2). Using the Seattle criteria, common and training-related ECG changes increased from 65.1% to 83.8%, mainly driven by an increased prevalence of incomplete right bundle branch block and first-degree AV block. Only one case of concentric hypertrophy was diagnosed by echocardiography alone, and all players with abnormal ECGs according to the ESC's recommendations only, were normal.

ECG findings according to the ESC and Seattle criteria

The great benefit of the new Seattle criteria is their detailed description of each ECG finding with corresponding reference value for abnormality and recommended follow-up.[2] Hence, comparison with other studies is simplified. In a recent study applying the new Seattle criteria on 16-35 years old Australian elite athletes of both sexes, recruited from >15 sporting disciplines**,** Brosnan et al. found 4.5% with abnormal ECGs.[15] We found more than twice as many abnormal ECGs using the same criteria. There are several explanations for this. First, our athletic population consisted only of men playing soccer, both factors associated with more abnormal ECG findings.[10] Second, body position or exact placement of ECG electrodes are not reported by Brosnan et al., nor are specifications of their ECG device. The ECG device's technical specifications, software, printed paper output and screen resolutions are all factors that influence the final result.[11;12] The muscular filter setting to 40 Hz in our study may have broadened the QRS complexes**.** Manual ECG ruler without magnifier measures only to the nearest 10 ms and 0.1 mV. In our study all digital samples were displayed, and the on-screen callipers measured durations and amplitudes down to 2 ms and 0.05 mV, respectively. Hence, small deflections as T-wave inversions ≥1.0 mm and Q waves ≥3.0 mm were easier to detect.[11] Third, the visual assessment both on paper and on-screen has subjective components: where to start and end a measurement and in choice of lead. The correlation between visual analyses of the QRS duration in the average PQRST complex in lead II and computerized measurements in the superimposed global complex

was moderate. According to the principle of first wave onset and latest offset, intervals derived from the SGC will always be greater than in individual leads, explaining the higher prevalence of intraventricular conduction delay in our study.[12] Consequently, redefinitions are required for SGC measurements.[12] Still, computer derived pathological measurements should always be visually assessed to check for technical errors. Forth, choice of reference values: In lack of detailed descriptions and reference values in the ESC recommendations,[16] we chose to add the specifications from Uberoi et al., while Brosnan et al. chose other reference values. These differences had special impact on the prevalence of long and short QT interval, 0.5% versus 2.3% and 0.7% versus 4.3%, respectively, and on the prevalence of common and training-related ECG findings as first-degree AV block (see online-only Data Supplement). Moreover, the huge difference in prevalence of early repolarization might be explained by the confusing definition of J point (see online-only Data Supplement) in addition to different reference values.[17] Earlier participation in screening will also influence the results: the prevalence of abnormal findings will be lower in Italy where many athletes already are excluded owing to mandatory cardiac screening since 1982, and higher in Norway after the very first cardiac screening.

The prevalence of abnormal ECGs in other studies varies from 1.8% to 35%.[3;4;6-10;15;18] Pathologic T-wave inversions and Q waves, which account for the majority of abnormal ECG findings in our study, vary from 0% to 22.8% and 0% to 3.0%, respectively due to different reference values in other studies.[3;4;6-10;15;18] Different reference values in our study could have reduced the prevalence of pathologic T-wave inversions to 0.9% and Q waves to 0% (see online-only Data Supplement).

Recommended follow-up

Mandatory echocardiography revealed one player with concentric hypertrophy and a normal ECG. If the lower limit for heart rate had been increased from 30 to 35 bpm, he would have been referred to follow up. The other two players with heart rate <35 bpm had type II second degree AV block. Riding et al found no athletes with hypertrophic cardiomyopathy by echocardiography alone .[19] The two players with left ventricle hypertrophy due to hypertension would have been detected if players with repeated BP ≥160/100 mm Hg were referred for follow-up. Hypertension as the only manifested reason for restricted activity and treatment after screening, underscores the need for proper follow-up of young athletes with high BP.[20] This increased the need for follow up with 22 players compared to the initial assessments (figure 3). Since all players underwent

echocardiography, auscultation was not performed. It might, however, have detected some among the nine players with grade I-II valve insufficiencies. No abnormal echocardiograms in any of the 106 players with abnormal ECGs according to the ESC's recommendations only, indicate that the Seattle criteria increase the specificity without increasing the number of false negative findings.

Differences related to ethnicity and sporting discipline

We have presented all abnormal ECG findings related to ethnicity, but because of a small number of black players, we do not want to draw any conclusions. Anyway, the results are difficult to compare with other investigations, because some studies lack definition of ethnicity,[3;4] while other studies use self-definition through questionnaires.[6;21;22] Interestingly, none of these studies describe how they define athletes descending from parents with different ethnicity. Bhopal recommended that researchers should explain their understanding of the concepts of race or ethnicity and the classification they use.[23] The prevalence of LVH in black athletes is usually reported to be high.[7;18] Variations in cardiovascular diseases between African-born and Caribbean-born black people in New York exceed those between black and white people.[24] Hence, environmental factors as birthplace and migration might also influence development of LVH**.**

Professional American football players who play at positions that require sprinting and similar bursts of physical activity associated with abrupt elevations in heart rate, like our outfield players, showed more abnormal ECGs than players at positions with lower levels of activity.[3] This might contribute to higher prevalence of abnormal ECG findings in our athletes, compared to studies of athletes from other sporting disciplines (see online-only Data Supplement).

Family history, symptoms and ECG findings

There were no significant differences in family history of cardiovascular disease or symptoms during sports activity between players with abnormal versus normal ECGs. To assess retrospectively if the players "yes" or "no" should have warranted further follow up was not possible. It has previously been reported that 13.0% of the anonymous responders had been afraid of losing their license to play soccer.[25] This might have led to underreporting in the present as well as other studies.[7;22] Papadakis et al. describe no serious cardiac symptoms among 904 black athletes.[6] On the other side, Wilson et al refer the highest prevalence of positive

family history of heart disease in 29.9% of junior athletes, even though cut-off for young age in family members was <35 years, in contrast to usually 50-55 years.[26] This high score is probably owing to that participants were encouraged to ask their first and second degree relatives if the family cardiac disease history was unknown to them initially.

Limitations

Our results are representative for professional male soccer players in Norway, but not necessarily for athletes in other sporting disciplines and with different age and sex. Our application of on-screen measurements of superimposed global complex and averaged PQRST complexes cannot be compared with results from traditional measurements on paper; however, the method used in the present study gives significantly less variability.[12]

In ClickECG first wave onset and latest offset of the SGC were indicated in all averaged PQRST complexes, but only one averaged lead was visible each time. Accuracy of interval measurements would have increased further with newer software, which permits manual adjustment of the demarcation lines in the SGC in all leads synchronously.

The Regional Ethical Committee did not permit results of recommended follow-up examinations to be part of the study, consequently leaving the exact number of players with false positive or negative ECGs unknown. Lack of long-term follow-up data make it difficult to say whether or not the players who had abnormal ECG according to the ESC-based screening, but passed the ECG-test based on the Seattle criteria, safely could continue athletic activity, or belong to a group at higher than normal cardiovascular risk.

Clinical impact and conclusions

We have shown a marked reduction in ECG findings classified as abnormal when applying the Seattle criteria instead of the specified ESC recommendations in professional male soccer players. Echocardiographic screening alone only revealed one additional player with concentric hypertrophy, but he might have been detected anyway because of borderline bradycardia. None of the players with abnormal ECGs only according to the ESC's recommendations had abnormal echocardiograms. We therefore consider the new Seattle criteria as an important step to reduce the burdens and costs of the follow-up that is required in athletes' screening

programs.[4;5;27] However, to make comparisons between studies meaningful, factors related to participants, the ECG recordings and technical specifications have to be thoroughly described.

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Disclosures

None.

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Table 1. Symptoms related to exercise and family history of cardiovascular disease reported by 587 professional male soccer players in Norway

Symptoms related to exercise	
Chest pain	22 (3.7)
Palpitations	25 (4.3)
Syncope/ near syncope	17 (2.9)
Breathlessness	35 (6.0)
Family history in relatives <55 years	
Sudden cardiac death	24 (4.1)
Cardiovascular disease	45 (7.7)
Hypertension	83 (14.1)
Diabetes	50 (8.5)

Values are presented as n (%).

Figure legend

Figure 1.

Superimposed global PQRST-complex (SGC) computed from eight leads' raw data in ECG recording of a 20 years old professional white male Norwegian soccer player. The player had first-degree atrioventricular block with PR interval duration=230 ms, rSR' pattern in V_1 with QRS interval duration=120 ms and maximum P wave amplitude=0.252 mV in lead II.

Figure 2.

Flow-chart showing abnormal ECG findings according to the specified ESC recommendations and Seattle criteria.

Figure 3.

Flow chart showing the estimated need for follow up after BP recordings and abnormal ECG findings according to the ESC versus Seattle criteria. Abnormal echocardiographic results are displayed.

Figure 1.

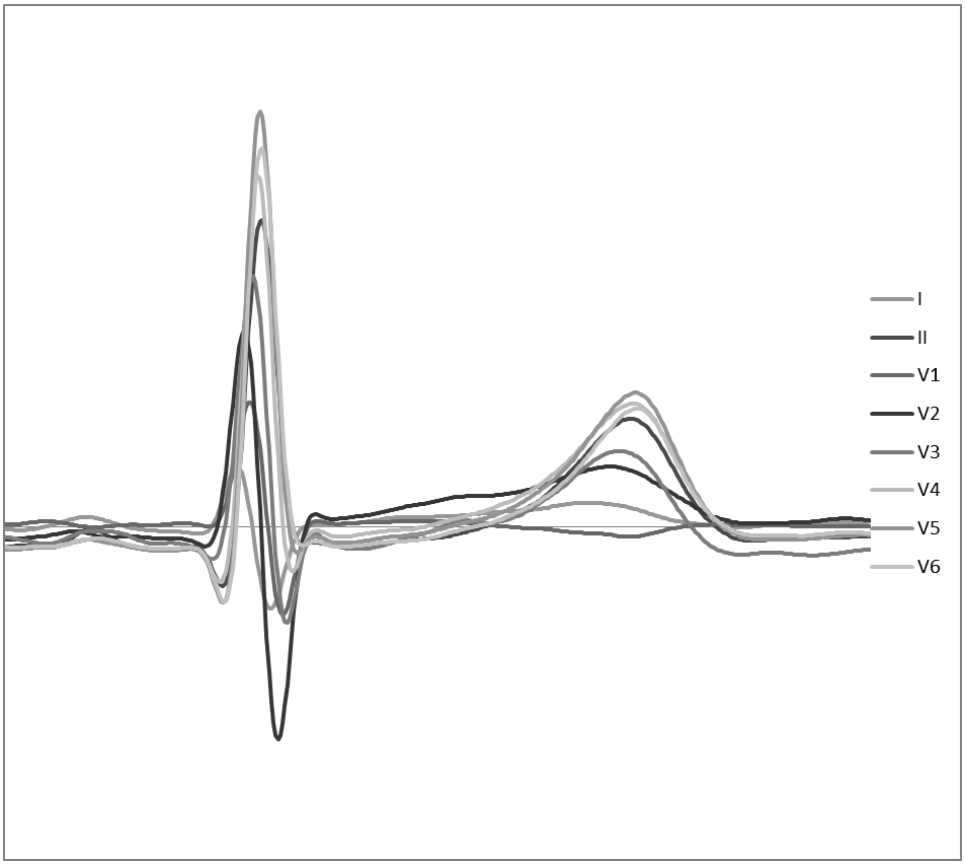


Figure 2.

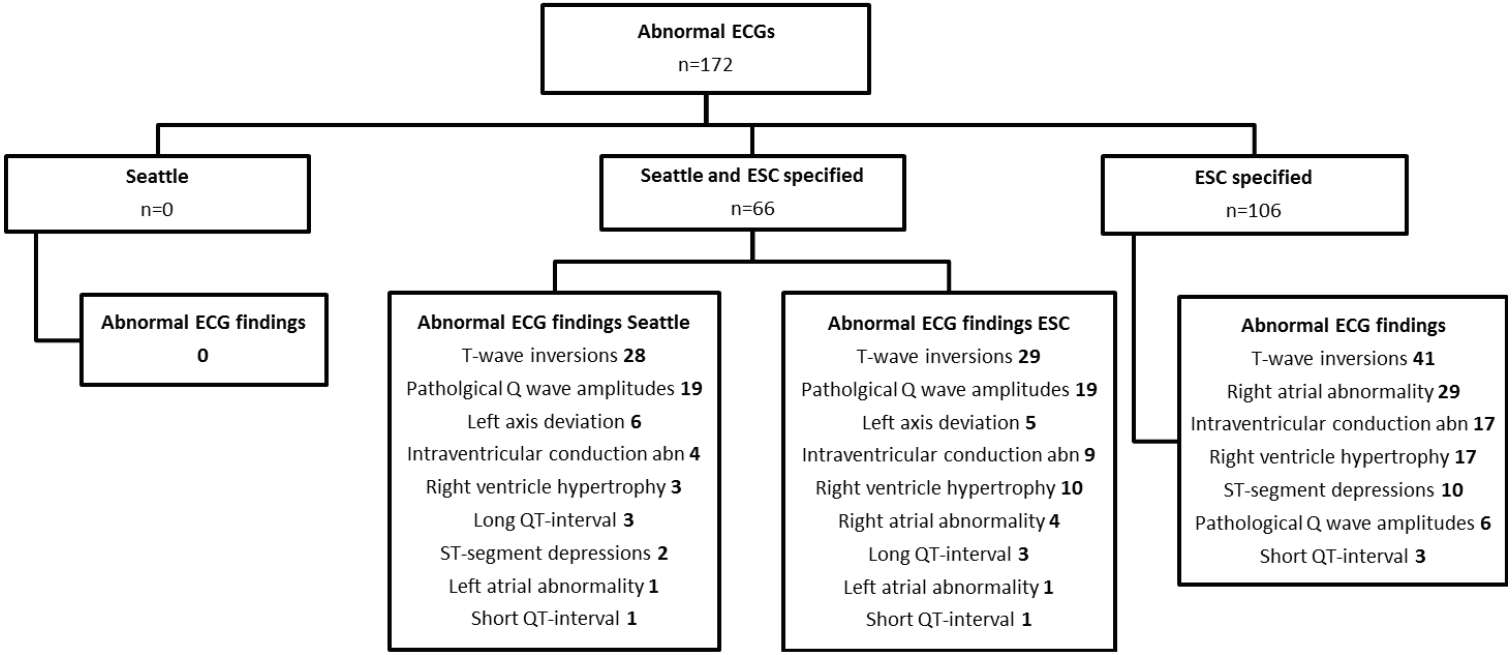
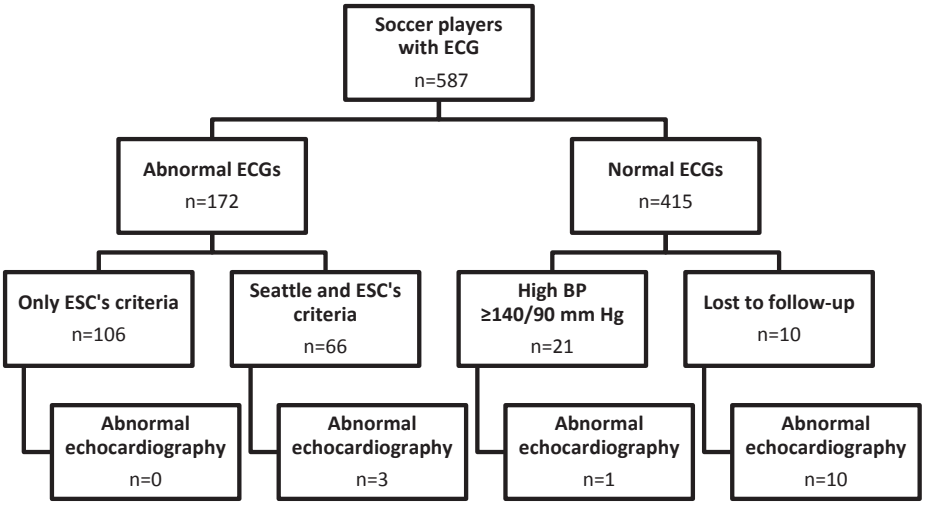

Abnormal ECGs
n=172
Seattle
n=0
Seattle and ESC specified
n=66
ESC specified
n=106
Abnormal ECG findings
0
Abnormal ECG findings Seattle
T-wave inversions 28
Patholgical Q wave amplitudes 19
Left axis deviation 6
Intraventricular conduction abn 4
Right ventricle hypertrophy 3
Long QT-interval 3
ST-segment depressions 2
Left atrial abnormality 1
Short QT-interval 1
Abnormal ECG findings ESC
T-wave inversions 29
Patholgical Q wave amplitudes 19
Left axis deviation 5
Intraventricular conduction abn 9
Right ventricle hypertrophy 10
Right atrial abnormality 4
Long QT-interval 3
Left atrial abnormality 1
Short QT-interval 1
Abnormal ECG findings
T-wave inversions 41
Right atrial abnormality 29
Intraventricular conduction abn 17
Right ventricle hypertrophy 17
ST-segment depressions 10
Pathological Q wave amplitudes 6
Short QT-interval 3

Figure 3.


Soccer players with ECG
n=587
Abnormal ECGs
n=172
Normal ECGs
n=415
Only ESC's criteria
n=106
Seattle and ESC's criteria
n=66
High BP ≥140/90 mm Hg
n=21
Lost to follow-up
n=10
Abnormal echocardiography
n=0
Abnormal echocardiography
n=3
Abnormal echocardiography
n=1
Abnormal echocardiography
n=10

Supplemental Material

Table 1. Reference values for patterns suggestive of cardiomyopathy according to the European Society of Cardiology's (ESC) classification of 12-lead ECG pattern with specifications from Uberoi et al., compared to the new Seattle criteria for ECG interpretations in athletes

	ESC with specifications	Seattle criteria
Abnormal ECG findings		
T-wave inversions	≥1.0 mm in leads other than III, aVR and V_1-V_2, except common ST-T changes in leads V_1-V_4 in black/Africans	>1 mm in depth in two or more leads V_2-V_6, II and aVF or I and aVL (excludes III, aVR and V1, and common ST-T changes in leads V_1-V_4 in black/Africans)
ST-segment depressions	>0.5 mm in any lateral leads (I, aVL, V_5 or V_6) or > 1 mm in any other lead	≥0.5 mm in depth in two or more leads
Pathological Q waves	>3 mm and/or >40 ms in any leads except III, aVR and V_1	>3 mm and/or >40 ms in two or more contiguous leads (except III and aVR)
Complete left bundle branch block	QRS ≥120 ms, predominantly negative QRS complex in lead V_1 (QS or rS), and upright monophasic R wave in I and V_6	QRS ≥120 ms, predominantly negative QRS complex in lead V_1 (QS or rS), and upright monophasic R wave in I and V_6
Intraventricular conduction abnormalities	Any QRS duration >120 ms visually measured in lead II	Any QRS duration ≥140 ms from the superimposed global complex, visually adjusted
Left-axis deviation	≤-31° to -90°	≤-30° to -90°
Left atrial enlargement	1) a negative component of the P wave in lead V_1 or V_2 of 40 ms duration and 1 mm amplitude, and 2) total P wave duration of >120 ms	Prolonged P wave duration of >120 ms in lead I or II with negative portion of the P wave ≥1 mm in depth and ≥40 ms in duration in lead V1
Right atrial enlargement	Max P-wave amplitude in lead II ≥2.5 mm	NA
Right-axis deviation	>115° to 180°	>120° to 180°
Left posterior hemiblock	Right-axis deviation and QRS duration <120 ms	Right-axis deviation and QRS duration in lead II <120 ms
Extreme axis deviation	≥-91° to -180°	≥-91° to -180°
Right ventricular hypertrophy (RVH) in athletes ≥ 30 years old	RV_1 >7 mm, RV_1/SV_1 ratio >1 or sum of R wave in lead V_1 and S wave in lead V_5 or V_6 >10.5 mm	Sum of R wave in lead V_1 and S wave in lead V_5 >10.5 mm and right-axis deviation >120°
Right ventricular hypertrophy in athletes < 30 years old	Above criteria for RVH plus right atrial enlargement, T wave inversions in V_2, V_3 or right axis deviation >115°	sum of R wave in lead V_1 and S wave in lead V_5 >10.5 mm and right-axis deviation >120°
Premature ventricular contractions	One per 10 seconds tracing	≥2 per 10 seconds tracing
Ventricular arrhythmias	Couplets, triplets and non-sustained ventricular tachycardia, and idioventricular escape rhythm	Couplets, triplets and non-sustained ventricular tachycardia, and idioventricular escape rhythm

NA, not applicable.

Table 2. Reference values for patterns suggestive of primary electrical disease according to the European Society of Cardiology's (ESC) classification of 12-lead ECG pattern with specifications from Uberoi et al., compared to the new Seattle criteria for ECG interpretations in athletes

	ESC with specifications	Seattle criteria
Abnormal ECG findings		
Ventricular pre-excitation	PR interval <120 ms with a delta wave (slurred upstroke in the QRS complex) and wide QRS (>120 ms)	PR interval <120 ms with a delta wave (slurred upstroke in the QRS complex) and wide QRS (>120 ms)
Long QT-interval	QTc >470 ms in men	QTc ≥470 ms/ QTc ≥500 ms (marked QT prolongation) in men
Short QT-interval	Short QT ≤330 ms or short QTc <340 ms	Short QTc ≤320 ms
Brugada-like ECG pattern	High take-off and downsloping ST segment elevation followed by a negative T wave in ≥2 leads in V_1-V_3	High take-off and downsloping ST segment elevation followed by a negative T wave in ≥2 leads in V_1-V_3
Profound sinus bradycardia	<30 beats per minute or sinus pauses ≥3 seconds	<30 beats per minute or sinus pauses ≥3 seconds
Atrial tachyarrhythmias	Supraventricular tachycardia, atrial-fibrillation, atrial-flutter	Supraventricular tachycardia, atrial-fibrillation, atrial-flutter
Premature ventricular contractions	One per 10 seconds tracing	≥2 per 10 seconds tracing
Ventricular arrhythmias	Couplets, triplets and non-sustained ventricular tachycardia, and idioventricular escape rhythm	Couplets, triplets and non-sustained ventricular tachycardia, and idioventricular escape rhythm
Mobitz type II second-degree AV block	Abrupt loss of P wave conduction (P wave with no ensuing QRS complex), without prior PR prolongation	Abrupt loss of P wave conduction (P wave with no ensuing QRS complex), without prior PR prolongation

Table 3. Reference values for patterns suggestive of normal training-related ECG findings according to the European Society of Cardiology's (ESC) classification of 12-lead ECG pattern with specifications from Uberoi et al., compared to the new Seattle criteria for ECG interpretations in athletes

	ESC with specifications	Seattle criteria
Normal ECG findings		
Sinus bradycardia	≥30 and <60 beats per minute	≥30 and <60 beats per minute
Sinus arrhythmia	Quite irregular heart rhythm with normal P wave axis in the frontal plane	Quite irregular heart rhythm with normal P wave axis in the frontal plane
Ectopic atrial rhythm	P waves are present, but are a different morphology compared to the sinus P wave	P waves are present, but are a different morphology compared to the sinus P wave
Junctional escape rhythm	The QRS rate is faster than the resting P wave or sinus rate	The QRS rate is faster than the resting P wave or sinus rate
First-degree atrioventricular block	Prolonged PR interval >220 ms, but the same duration on every beat	Prolonged PR interval >200 ms, but the same duration on every beat
Mobitz type I (Wenckebach) second-degree AV block	Progressive lengthening of the PR interval from beat to beat, until there is a non-conducted P wave with no QRS complex. The first PR interval after the dropped beat is shorter than the last conducted PR interval before the dropped beat.	Progressive lengthening of the PR interval from beat to beat, until there is a non-conducted P wave with no QRS complex. The first PR interval after the dropped beat is shorter than the last conducted PR interval before the dropped beat.
Incomplete right bundle branch block	rSr' pattern with QRS duration >110 ms to 119 ms	rSr' pattern with QRS duration >110 ms to 119 ms
Isolated QRS voltage criteria for left ventricle hypertrophy	Sokolow-Lyon (sum of S-wave voltage in lead V_1 and R-wave voltage in lead V_5 or V_6 ≥35 mm) or Cornell voltage score (sum of S-wave in lead V_3 and R wave in lead aVL ≥28 mm for male subjects)	Sokolow-Lyon (sum of S-wave voltage in lead V_1 and R-wave voltage in lead V_5 or V_6 ≥35 mm) or Cornell voltage score (sum of S-wave in lead V_3 and R wave in lead aVL ≥28 mm for male subjects)
Early repolarization	ST elevation of 1 mm from baseline (PR-line)	≥two contiguous ST elevations >1 mm in any group; V_5-V_6-I-aVL, II-III-aVF or V_2-V_3-V_4
Common ST-T wave changes in black/African athletes	Convex ('domed') ST segment elevation combined with T wave inversion in leads V1-V4 in black/ other athletes	Convex ('domed') ST segment elevation combined with T wave inversion in leads V1-V4 in black/ other athletes

Table 4. ECG findings from pre-participation screening of 587 athletes: numbers and percentages (%) of patterns suggestive of cardiomyopathy according to the European Society of Cardiology's (ESC) classification of 12-lead ECG pattern with specifications from Uberoi et al., compared to the new Seattle criteria for ECG interpretations in athletes

	ESC with specifications				Seattle criteria			
Total number of players	Total n=587 (%)	White n=497 (%)	Black n=48 (%)	Other n=42 (%)	Total n=587 (%)	White n=497 (%)	Black n=48 (%)	Other n=42 (%)
Abnormal ECG findings								
T-wave inversions	70 (11.9)	60 (12.1)	7 (14.6)	3 (7.1)	28 (4.8)	24 (4.8)	3 (6.3)	1 (2.4)
ST-segment depression	10 (1.7)	7 (1.4)	2 (4.2)	1 (2.4)	2 (0.3)	1 (0.2)	1 (2.1)	0
Pathologic Q waves	25 (4.3)	23 (4.6)	2 (4.2)	0	19 (3.2)	18 (3.6)	1 (2.1)	0
Complete left bundle branch block	0	0	0	0	0	0	0	0
Intraventricular conduction abnormality	27 (4.5)	26 (5.2)	0	1 (2.4)	4 (0.7)	4 (0.8)	0	0
Left-axis deviation	5 (0.9)	3 (0.6)	0	2 (4.8)	6 (1.0)	4 (0.8)	0	2 (4.8)
Left atrial enlargement	1 (0.2)	1 (0.2)	0	0	1 (0.2)	1 (0.2)	0	0
Right atrial enlargement	33 (5.6)	21 (4.2)	8 (16.7)	4 (9.5)	NA	NA	NA	NA
Right-axis deviation	5 (0.9)	4 (0.8)	0	1 (2.4)	5 (0.9)	4 (0.8)	0	1 (2.4)
Left posterior hemiblock	4 (0.7)	3 (0.6)	0	1 (2.4)	4 (0.7)	3 (0.6)	0	1 (2.4)
Extreme axis deviation	1 (0.2)	1 (0.2)	0	0	1 (0.2)	1 (0.2)	0	0
Right ventricular hypertrophy (RVH) in athletes ≥ 30 years old	13 (2.2)	12 (2.4)	0	1 (2.4)	1 (0.2)	0	0	1 (2.4)
Right ventricular hypertrophy in athletes < 30 years old	14 (2.4)	10 (2.0)	3 (6.3)	1 (2.4)	2 (0.3)	2 (0.4)	0	0
Premature ventricular contractions	1 (0.2)	1 (0.2)	0	0	1 (0.2)	1 (0.2)	0	0
Ventricular arrhythmias	1 (0.2)	1 (0.2)	0	0	1 (0.2)	1 (0.2)	0	0

For reference values, see table 1. NA, not applicable.

Table 5. ECG findings from pre-participation screening of 587 athletes: numbers and percentages (%) of patterns suggestive of primary electrical disease according to the European Society of Cardiology's (ESC) classification of 12-lead ECG pattern with specifications from Uberoi et al., compared to the new Seattle criteria for ECG interpretations in athletes

	ESC with specifications				Seattle criteria			
Total number of players	Total n=587 (%)	White n=497 (%)	Black n=48 (%)	Other n=42 (%)	Total n=587 (%)	White n=497 (%)	Black n=48 (%)	Other n=42 (%)
Abnormal ECG findings								
Ventricular pre-excitation	1 (0.2)	1 (0.2)	0	0	1 (0.2)	1 (0.2)	0	0
Long QT-interval	3 (0.5)	2 (0.4)	0	1 (2.4)	3 (0.5)	2 (0.4)	0	1 (2.4)
Short QT-interval	4 (0.7)	3 (0.6)	1 (2.1)	0	1 (0.2)	1 (0.2)	0	0
Brugada-like ECG pattern	0	0	0	0	0	0	0	0
Profound sinus bradycardia	0	0	0	0	0	0	0	0
Atrial tachyarrhythmias	0	0	0	0	0	0	0	0
Premature ventricular contractions	1 (0.2)	1 (0.2)	0	0	1 (0.2)	1 (0.2)	0	0
Ventricular arrhythmias	1 (0.2)	1 (0.2)	0	0	1 (0.2)	1 (0.2)	0	0
Mobitz type II second-degree AV block	3 (0.5)	2 (0.4)	0	1 (2.4)	3 (0.5)	2 (0.4)	0	1 (2.4)

For reference values, see table 2.

Table 6. ECG findings from pre-participation screening of 587 athletes: numbers and percentages (%) of common and training-related changes according to the European Society of Cardiology's (ESC) classification of 12-lead ECG pattern with specifications from Uberoi et al., compared to the new Seattle criteria for ECG interpretations in athletes

	ESC with specifications				Seattle criteria			
Total number of players	Total n=587 (%)	White n=497 (%)	Black n=48 (%)	Other n=42 (%)	Total n=587 (%)	White n=497 (%)	Black n=48 (%)	Other n=42 (%)
Normal ECG findings								
Sinus bradycardia	402 (68.5)	148 (29.8)	7 (14.6)	8 (19.0)	402 (68.5)	148 (29.8)	7 (14.6)	8 (19.0)
Sinus arrhythmia	223 (38.0)	192 (38.6)	15 (31.1)	16 (38.1)	209 (35.6)	181 (36.4)	13 (27.1)	15 (35.7)
Ectopic atrial rhythm	8 (1.4)	8 (1.6)	0	0	8 (1.4)	8 (1.6)	0	0
Junctional escape rhythm	12 (2.0)	11 (2.2)	0	1 (2.4)	12 (2.0)	11 (2.2)	0	1 (2.4)
First-degree atrioventricular block	30 (5.1)	23 (4.6)	5 (10.4)	2 (4.8)	71 (12.1)	57 (11.5)	11 (22.9)	3 (7.1)
Mobitz type I (Wenckebach) second-degree AV block	3 (0.5)	2 (0.4)	0	1 (2.4)	3 (0.5)	2 (0.4)	0	1 (2.4)
Incomplete right bundle branch block	24 (4.1)	22 (4.4)	0	2 (4.8)	68 (11.6)	63 (12.7)	2 (4.2)	3 (7.1)
Isolated QRS voltage criteria for left ventricle hypertrophy	104 (17.7)	86 (17.3)	10 (20.8)	8 (19.0)	117 (19.9)	96 (19.3)	12 (25.0)	9 (21.4)
Early repolarization	537 (91.5)	452 (90.9)	45 (93.8)	40 (95.2)	402 (68.5)	330 (66.4)	36 (75.0)	36 (85.7)
Common ST-T wave changes in black/African athletes*	22 (24.4)	0	15 (31.3)	7 (16.7)	22 (24.4)	0	15 (31.3)	7 (16.7)

For reference values, see table 3. *N=48 black/African and 42 other athletes, mostly black.

Table 7. Median ECG measurements in 587 professional male soccer players in Norway

Total number of players	Total N=587	White players n=497	Black players n=48	P value
Computer derived measurements				
Heart rate, beats per minute	55.0 (49.0 – 61.0)	55.0 (48.0-61.0)	57.5 (52.0-61.0)	0.049
QRS axis, °	78.5 (64.0 - 88.8)	80 (65-89)	69 (60-80)	0.001
QRS duration, ms*	110 (100-120)	110 (100-120)	112 (100-118)	0.599
Visually measured durations†				
P wave in lead II, ms	114 (104-124)	114 (102-122)	120 (113-131)	<0.001
PR interval in lead II, ms	164 (148-178)	164 (146-178)	176 (158-196)	<0.001
QRS duration in lead II, ms	102 (98-108)	104 (98-108)	100 (94-104)	<0.001
QT interval in lead II, ms‡	416 (398-440)	418 (400-442)	400 (386-414)	<0.001
Visually measured amplitudes§				
P wave in lead II, µV	143 (105-180)	138 (103-175)	163 (121-232)	0.001
R wave in lead V_1, µV	263 (180-398)	263 (185-388)	320 (155-444)	0.459
S wave in lead V_1, µV	-852 (-1178-(-559))	-832 (-1153-(-561))	-1033 (-1501-(-678))	0.011
S wave in lead V_3, µV	-850 (-1235-(-513))	-875 (-1253-(-556))	-562 (-1141-(-309))	0.004
R wave in lead V_5, µV	1868 (1515-2308)	1879 (1549-2307)	1734 (1403-2217)	0.151
S wave in lead V_5, µV	-218 (-353-(-115))	-220 (-355-(-120))	-140 (-332-(-35))	0.013
R wave in lead V_6, µV	1415 (1153-1788)	1446 (1181-1788)	1304 (947-1793)	0.083
S wave in lead V_6, µV	-138 (-245-(-58))	-141 (-243-(-64))	-100 (-239-(0))	0.163
R wave in lead aVL, µV	109 (73-173)	108 (70-170)	123 (85-197)	0.259

Values are presented as medians (interquartile range).

*QRS duration derived from the superimposed global complex. †Durations measured from the average PQRST complex. ‡QT durations from the average PQRST complex with computer derived first onset and visually adjusted offset with a tangent drawn from the descending part of the T line to the PR line. §Amplitudes measured as the mean of the highest amplitudes

Table 8. Other ECG findings in 587 male professional male football players in Norway and showing how slightly different reference values would have altered the number of normal and abnormal ECG findings

	Total n=587 (%)	White n=497 (%)	Black n=48 (%)	Other n=42 (%)
Epsilon waves	0	0	0	0
Long PR interval >300 ms	0	0	0	0
Nonvoltage criteria for LVH* according to				
ESC with specifications	31 (5.3)	26 (5.2)	4 (8.3)	1 (2.4)
Seattle	18 (3.1)	16 (3.2)	2 (4.2)	0
Q waves 25% of the ensuing R wave	0	0	0	0
Q waves ≥4 mm in ≥2 leads	2	2	0	0
TWI ≥1 mm in groups in leads†	28 (4.8)	24 (4.8)	3 (6.3)	1 (2.4)
II-aVF	6 (1.0)	3 (0.6)	2 (4.2)	1 (2.4)
I-aVL	0	0	0	0
V_2-V_6	26 (4.4)	23 (4.6)	2 (4.2)	1 (2.4)
Deep TWI-wave inversions‡	5 (0.9)	3 (0.6)	1 (2.1)	1 (2.4)
ST elevations ≥1 mm in groups in leads	402 (68.5)	330 (66.4)	36 (75.0)	36 (85.7)
II-III-aVF	25 (4.3)	20 (4.0)	3 (6.3)	2 (4.8)
V_5-V_6-I-aVL	16 (2.7)	14 (2.8)	1 (2.1)	1 (2.4)
V_2-V_3	386 (65.8)	316 (63.6)	35 (72.9)	35 (83.3)
V_3-V_4	115 (19.6)	94 (18.9)	12 (25.0)	9 (21.4)
V_2-V_3-V_4	397 (67.6)	327 (65.8)	35 (72.9)	35 (83.3)
ST elevation ≥2 mm in lead§	176 (30.0)	156 (31.4)	10 (20.8)	10 (23.8)
V_1	3 (0.5)	2 (0.4)	0	1 (2.4)
V_2	143 (24.4)	115 (81.5)	17 (35.4)	11 (26.2)
V_3	96 (16.4)	85 (17.1)	8 (16.7)	3 (7.1)
V_4	10 (1.7)	9 (1.8)	1 (2.1)	0
ST-T changes in leads V_1-V_4 in black/Africans‖			15 (31.3)	7 (16.7)
V_1			3 (6.3)	2 (4.8)
V_2			11 (22.9)	6 (14.3)
V_3			9 (18.8)	4 (9.5)
V_4			2 (4.2)	0

Values are presented as n (%). *LVH (left ventricle hypertrophy) with associated left atrial enlargement, left-axis deviation, ST segment depression, T wave inversion or pathological Q waves. †≥1 mm in depth in two or more leads V_2-V_6, II and aVF or I and aVL (excludes III, aVR and V_1, and common ST-T changes in leads V_1-V_4 in black/Africans). ‡≥2 mm in ≥2 adjacent leads, except common ST-T changes in leads V_1-V_4 in black/Africans. §ST elevations >=2 mm in either V_1, V_2, V_3 or V_4, except when common ST- T changes in black/Africans. ‖ST-T changes in either V_1, V_2, V_3 or V_4 in black/Africans, or others (two from Northern Africa, two from Asia, two with mixed ethnicity and one from South/Middle America; all with dark skin color).

Table 9. Prevalence of variables in other studies with greatest discrepancy to prevalence of the same variables in our preparticipation screening study of 587 professional male football players in Norway

Ref.no	Participants*	Abnormal ECGs	TWI	Q waves	PR interval	LVH	Early repolarization
[1]	1005 athletes, Italy Male 54% Age 9-55 years Sporting disciplines 38 White 99.8%	Distinctly abnormal 14.4% Males 17.0% (Mildly abnormal 25.6%) Males 28.0%	2.7%	1.7%	7.5%	23.2%	14.3%
[2]	42386 athletes, Italy Age 12-35 years	9.0%, included 7% false positive findings	?	?	?	?	?
[3]	1959 collegiate football players Male 100% Mean age 23.0±0.9 years (20-29) White 31%, black 67%	Distinctly abnormal 4.5% (Mildly abnormal 20%) White 1.8% Black 5.8%	White 0.2% Black 2.6%	White 0% Black 0.2%	?	White 0.2% Black 2.0%	?
[4]	658 Stanford University students Male 54% Mean age 20 years Sporting disciplines 20 White 39%, African American 7%	Three sets of criteria: Pellicia 2000; 15% ESC 2005; 35% Stanford 10%	3.0%	3.0%	?	Up to 66%	53.0%
[5]	904 athletes Mean age 22.5±5.0 years (14-35) Sporting disciplines 25 Black 100%	?	Up to 22.8%?	0.9%	11.2%	23.2%	63.2%
[6]	118 professional football players Mean age 24.3±4.2 years (17-35) White European 100%	6.0%	0%	0%	4.2%	Isolated 4.2%	9.3%
[7]	420 athletes Mean age Caucasian 26.6±4.5 vs black 23.7±5.0 years, (12-35) Sporting disciplines 17 Caucasian 29%, black 71%	Caucasian 5.8% Black 18.0%, *using ESC criteria, but included RAA in addition*	?	?	Caucasian 4.2% Black 13.0%	Caucasian 23.3% Black 26.8%	Caucasian 66.7% Black 79.9%
[8]	210 soccer players, Gabon Male 100% Mean age 18.6 years (18-22) Black 100%	12.4%	4.8%, and common ST-T changes in 16.2%	1.4%	11.4%	Isolated 55.2%	71.4%

Ref.no	Participants*	Prevalence					
[9]	1005 athletes, Italy Male 54% Age 9-55 years Sporting disciplines 38 White 99.8%	11%	?	?	?	Isolated 23.2%	5.9%
[10]	1078 elite athletes, Australia Male 82% Median age 19 years (16-35) Sporting disciplines >15 Caucasian 86% African 1%, other 13%	ESC 17.3% Seattle 4.5%	ESC 6.4% Seattle 2.3%	ESC 0.2% Seattle 0.2%	ESC 7.5% Seattle 7.5%	ESC 28.2%, using voltage criteria 12.4%, using Romhilt-Estes score	ESC 38.4%
Our study	587 professional football players, Norway Male 100% Median age 25.0 years (18-38) White 84.7%, black 8.2%	ESC† 29.5% Seattle 11.1%	ESC† 11.9% Seattle 4.8%	ESC† 4.3% Seattle 3.2%	ESC† 5.1% Seattle 12.1%	ESC† Isolated 19.8% LVH with nonvoltage criteria 5.3% Seattle Isolated 19.9% LVH with nonvoltage criteria 3.1%	ESC† 91.5% Seattle 68.5%

Ref.no; reference number in the following reference list.

*Participants are presented as total number of athletes, male sex (%), median or mean (±SD) age (range), sporting disciplines and ethnicity if reported in the papers.

†Interpreted according to the European Society of Cardiology's recommendations from 2009,[9] with specifications from Uberoi et al in 2011.[11]

Table 10. Reference values for abnormality of variables with greatest discrepancies in prevalence to variables in our preparticipation screening study of 587 professional male football players in Norway

Ref.no	ECG device	TWI	Q waves	PR interval	LVH	Early repolarization
[1]	?	>2 mm in ≥2 leads	≥4 mm in depth in ≥2 contiguous leads	>200 ms	Striking increase in R or S wave voltage (≥35 mm) in any lead	≥2 mm in >2 leads
[2]	?	Flattening or inversion in ≥2 leads	≥40 ms duration or ≥25% of the height of the ensuing R wave. QS pattern in ≥2 leads	≥210 ms, not shortening with hyperventilation	R or S wave in a standard lead ≥2 mm OR S wave in lead V_1 or V_2 ≥3 mm OR R wave in lead V_5 or V_6 ≥3 mm	
[3]	?	>2 mm in ≥2 leads, except aVR		?		
[4]	Schiller	≥2 leads, except V_1 and V_2	≥40 ms duration or ≥25% of the height of the ensuing R wave QS pattern in ≥2 leads	?	SV_1RV_5/V_6 ≥35 mm OR Romhilt-Estes LVH probable score ≥4 and the ESC voltage criteria	
[5]	GE Marquette Hellige OR Philips pagewriter Trim III	≥1 mm in ≥2 leads, except V_1, aVR and III OR deep ≥2 mm OR biphasic TWI	≥40 ms duration or ≥25% of the height of the ensuing R wave QS pattern in ≥2 leads		SV_1RV_5 ≥35 mm	
[6]	Mac 1200	>2 mm in ≥2 leads	≥4 mm in depth	>200 ms	SV_1RV_5 ≥35 mm	≥2 mm in >2 leads
[7]	COSMED Quark	≥2 mm in ≥2 contiguous leads, except V_1, aVR and III	≥40 ms duration or ≥25% of the height of the ensuing R wave QS pattern in ≥2 leads	>200 ms following exercise or hyperventilation	SV_1RV_5/V_6 ≥35 mm OR Romhilt-Estes LVH probable score ≥4	≥1 mm in ≥2 peripheral or precordial leads
[8]	Schiller AT-101	≥2 mm in ≥2 contiguous leads, except V_1, aVR and III	≥2 mm in ≥2 leads	>200 ms		≥1 mm in ≥2 contiguous leads
[9]	?	ESC >2 mm in ≥2 leads	ESC ?	ESC ?	ESC Sokolow-Lyon or Cornell criteria	ESC QRS-ST junction >1 mm from baseline
[10]	?	ESC	ESC	ESC	ESC	ESC

		Deep: ≥2 mm, ≥2 leads OR 'minor' in ≥2 leads	>4 mm deep in any lead escept III, aVR	>200 ms	SV_1RV_5 ≥35 mm. SV_1RV_6 ≥35 mm. Romhilt-Estes score ≥5	Elevation of the J point of at least 1 mm in ≥2 leads
		Seattle	Seattle	Seattle	Seattle	Seattle
		>1 mm deep, ≥2 leads in V_2-V_6, II, aVF, I and aVL	>3 mm deep and/or >40 ms duration in ≥2 leads except III and aVR	?	?	?
Our study	ClickECG with RealClick software v. 3.2.10	ESC*	ESC*	ESC*	ESC*	ESC*
		≥1 mm, except in III, aVR and V_1-V_2†	>3 mm deep and/or >40 ms duration in any leads, except III, aVR and V_1	>220 ms	SV_1RV_5/V_6 ≥35 mm OR Cornell voltage score (SV_3RaVL≥28 mm) Nonvoltage criteria†	≥1 mm from PR-line
		Seattle	Seattle	Seattle	Seattle	Seattle
		≥1 mm in ≥2 leads V_2-V_6, II and aVF, or I and aVL‡	>3 mm deep and/or >40 ms duration in ≥2 contiguous leads, except III and aVR	>200 ms	SV_1RV_5/V_6 ≥35 mm OR Cornell voltage score (SV_3RaVL≥28 mm) Nonvoltage criteria†	≥1 mm in ≥2 contiguous leads; V_5-V_6-I-aVL, II-III-aVF or V_2-V_3-V_4

Ref.no; reference number in the following reference list. *Interpreted according to the European Society of Cardiology's recommendations from 2009,[9] with specifications from Uberoi et al in 2011.[11] †Nonvoltage criteria; left atrial enlargement, left-axis deviation, ST segment depression, T wave inversion or pathological Q waves. ‡Except common ST-T changes in leads V_1-V_4 in black/Africans.

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