Available online at www.sciencedirect.com

ScienceDirect

Journal of Electrocardiology 47 (2014) 914–921

JOURNAL OF Electrocardiology

www.jecgonline.com

Normal values of the electrocardiogram for ages 16–90 years

Peter R. Rijnbeek, PhD,[a,*] Gerard van Herpen, MD, PhD,[a] Michiel L. Bots, MD, PhD,[b] Sumche Man, MD,[c] Niek Verweij, MD,[d] Albert Hofman, MD, PhD,[e] Hans Hillege, MD, PhD,[d] Matthijs E. Numans, MD, PhD,[b,f] Cees A. Swenne, PhD,[c] Jacqueline C.M. Witteman, PhD,[e] Jan A. Kors, PhD[a]

[a] *Department of Medical Informatics, Erasmus University Medical Center, Rotterdam, The Netherlands*
[b] *Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands*
[c] *Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands*
[d] *Department of Cardiology, University Medical Center Groningen, Groningen, The Netherlands*
[e] *Department of Epidemiology, Erasmus University Medical Center, Rotterdam, The Netherlands*
[f] *Department of General Practice, Free University Medical Center, Amsterdam, The Netherlands*

Abstract

Introduction: To establish an up-to-date and comprehensive set of normal values for the clinically current measurements in the adult ECG, covering all ages for both sexes.

Methods: The study population included 13,354 individuals, taken from four population studies in The Netherlands, ranging in age from 16 to 90 years (55% men) and cardiologically healthy by commonly accepted criteria. Standard 12-lead ECGs were available for all participants. The ECGs were processed by a well-validated computer program. Normal limits were taken as the 2nd and 98th percentiles of the measurement distribution per age group.

Results: Our study corroborates many findings of previous studies, but also provides more differentiated results, in particular for the older age groups. Age trends were apparent for the QTc interval, QRS axis, and indices of left ventricular hypertrophy. Amplitudes in the left precordial leads showed a substantial increase in the older age groups for women, but not for men. Sex-dependent differences were apparent for most ECG parameters. All results are available on the Website www.normalecg.org, both in tabular and in graphical format.

Conclusions: We determined age- and sex-dependent normal values of the adult ECG. Our study distinguishes itself from other studies by the large size of the study population, comprising both sexes, the broad range of ages, and the exhaustive set of measurements. Our results emphasize that most diagnostic ECG criteria should be age- and sex-specific.

Keywords: Electrocardiogram; Adult; Elderly; Normal limits; Normal values

Introduction

Normal values of the electrocardiogram (ECG) are the basis for establishing and refining diagnostic criteria. Normal values for the adult ECG have been determined in a number of studies [1–11]. However, they all carry their imperfections. Firstly, in the early studies the measurements had to be done by hand and lead by lead, i.e., without the timing information offered by simultaneously recorded leads [1–3]. Today, computer-assisted analysis of digitized multi-channel ECGs allows more accurate and greatly faster measurement. A second weakness of the older studies is that the ECG recording equipment was generally not up to modern standards in terms of bandwidth or sampling frequency, as a consequence of which ECG amplitudes are liable to have been underestimated. In the third place, anthropometric factors change over time and may render normal values that were established long ago less applicable. A fourth limitation is that many studies, among them the most recent ones, focus on a limited set of parameters [7,8], or even on only one single specific measurement, e.g. QT-interval duration [6] or QRS-T angle [9]. A fifth objection is that ECGs, although taken from normal subjects, were sometimes excluded on the sole ground that they were deemed to be abnormal by the investigators [7]. Lastly, the study population is often small, may contain subjects of only one sex, may not include all

* Corresponding author at: Department of Medical Informatics, Erasmus University Medical Center, P.O. Box 2040, 3000 CA Rotterdam, The Netherlands.
E-mail address: p.rijnbeek@erasmusmc.nl

http://dx.doi.org/10.1016/j.jelectrocard.2014.07.022
0022-0736/

age groups and in particular suffers from a scarcity of subjects of advanced age.

An extensive overview of normal limits was published by Macfarlane in 1989 (republished in 2010 [11]) based on 1338 apparently healthy individuals from Scotland. However, the number of participants older than 50 years is small, as is the number of female participants older than 30 years, and parameters that have come into vogue more recently are missing, such as several voltage criteria for left ventricular hypertrophy (LVH) and their QRS duration products, or T-loop morphology parameters. In 2003, Wu et al. published a comprehensive study of a Chinese population of 5360 men and women [5]. Ages ranged from 18 to 84, divided into five age groups, the group >60 years not being further broken down because of its limited size. A study by Mason et al. from 2007 comprises a much larger population of 46,129 subjects, enrolled in clinical trials and expected to be free of disease-associated ECG effects, but was restricted to heart rate, interval durations, and axes [8]. Reference ranges were found to differ significantly from those previously reported and in general use. Rautaharju, in his treatise of 2007 on the application of the ECG in epidemiological studies and clinical trials [12], provides very detailed tables from 11,707 individuals on intervals, amplitudes and axes, but only for the age groups 40–59 years and 60+ years. In our present study, we establish an up-to-date and comprehensive set of normal values for clinically common measurements in the adult ECG, based on a large and diverse study population of – as far as possible – established normality, covering all ages and with a proper balance between the sexes. The measurements have been made by a validated ECG computer program. Normal values are not only available by age and sex in tabular form, as in previous studies, but also in graphical form as continuous functions of age. This avoids the jumps between age groups that occur when a fixed value is employed per age group of, typically, 10 years. All results of our study are available on the Website www.normalecg.org.

Methods

Study population

The ECGs included in our study were selected from four studies performed in The Netherlands:

(1) The Rotterdam Study. This project, started in 1990, is an ongoing population-based prospective cohort study of the occurrence of cardiovascular, locomotor, neurologic, and ophthalmologic disease in the elderly [13]. All inhabitants of Ommoord, a suburb of Rotterdam, aged 55 years or older were invited to take part in the study, of whom 10,994 agreed to participate. Participants were visited at home for a standardized questionnaire and were subsequently examined at the research center, where a 12-lead ECG was digitally recorded and stored on an ACTA electrocardiograph (ESAOTE, Florence, Italy). Detailed information was collected on health status, medical history, and medication.

(2) The Prevention of Renal and Vascular ENdstage Disease (PREVEND) Study. PREVEND is a population-based prospective cohort study to investigate the natural course of microalbuminuria and its relation to renal and cardiovascular disease in the general population [14]. The study, started in 1997, comprised 8592 men and women, aged 28–75 years, from the city of Groningen, The Netherlands. Medical records were available for all participants including medication use. ECGs were recorded with Cardio Perfect equipment (Welch Allyn Cardio Control, USA).

(3) The Utrecht Health Project (UHP). The UHP, which started in 2000, is an ongoing longitudinal population-based study among all inhabitants of Leidsche Rijn, a newly developed residential area of Utrecht [15]. The study cohort consisted of 6542 participants. Baseline assessments included physical examination, ECG, blood tests, and interview-assisted questionnaires. Pharmacy records were used to obtain medication use. ECGs were recorded with Cardio Perfect equipment (Welch Allyn Cardio Control, USA).

(4) The Leiden University Einthoven Science Project dataset was collected between 2005 and 2007. In the course of their education, standard 10-second 12-lead ECGs were obtained from 787 medical students of Leiden University (Leiden, The Netherlands), who attested to be in good health [9]. Age varied between 17 and 29 years. All ECGs were recorded with Megacart electrocardiographs (Siemens, Erlangen, Germany).

The electrocardiographs that were used in these studies recorded all ECG leads simultaneously at a sampling rate of at least 500 Hz, and complied with AHA recommendations of a bandwidth from 0.05 to 150 Hz. All studies have been approved by the medical ethics committees of the respective institutes and all participants have given written informed consent. The great majority of the participants were Caucasian. We could not separate between “white” and “African”, as is often done in studies from the USA, because Dutch anti-discrimination regulations prohibit the registration of ethnicity information.

From the four populations, to all intents and purposes, a cardiologically healthy subgroup was selected. Those with a history of myocardial infarction, heart failure, coronary bypass surgery, coronary angioplasty, or pacemaker implantation were excluded. Other exclusion criteria were hypertension and diabetes mellitus. Hypertension was defined as use of antihypertensive medication, or as a systolic blood pressure of ≥160 mmHg and/or a diastolic blood pressure of ≥100 mmHg. Diabetes mellitus was defined as the use of anti-diabetic medication, or as a non-fasting serum glucose level higher than 11.0 mmol/l. We only considered ECGs of subjects for whom none of these parameters were missing. This reduced the initial set of 26,915 ECGs to 21,800 ECGs, of which another 7656 had to be discarded because of non-ECG exclusion criteria, leaving 14,144 ECGs. In such a

cardiologically normal population no ECG should be excluded because of its unusual appearance, but, as is usually done, we made an exception for complete right- or left bundle-branch block (n = 220), Wolf–Parkinson–White pattern (n = 12), atrial fibrillation or atrial flutter (n = 52), and second or higher degree A-V block (n = 15). All ECGs were also visually checked for correct waveform recognition by the ECG computer program. Those with bad signal quality or waveform recognition errors (mainly due to excessive noise) were also removed from the dataset (n = 440). Electrode interchanges were detected by a special feature in the computer program [16]. After visual confirmation these ECGs were also discarded (n = 51). This left a total of 13,354 ECGs for analysis (see Table 1).

ECG measurements

All ECGs were processed by the Modular ECG Analysis System (MEANS) [17]. MEANS has extensively been evaluated both by its developers [17] and by others [18,19]. In the latter studies, the MEANS measurements were gauged against those obtained from a panel of cardiologists, proving their accuracy and stability. Also in comparison to other programs MEANS scored among the best. The interval measurements are lead-independent, i.e., they make use of the common wave onsets and offsets of the 12 simultaneous leads together. The morphological measurements are lead-dependent, i.e., they are taken per lead from one averaged representative complex. A wave within a complex is counted as present if it has both an amplitude of at least 0.025 mV and a duration of at least 8 ms.

Frontal plane P, QRS and T axes are estimated, in daily practice, from peak amplitudes in the extremity leads. The mathematically founded method, which we applied, is to calculate the vector components of an axis from the net areas under the waves of the contributing leads. For the frontal P, QRS and T axes we used the quasi-orthogonal leads I and aVF (after correcting the weaker lead strength of aVF by a factor $\frac{2}{3}\sqrt{3}$). The spatial axes were calculated from the vectorcardiographic X, Y and Z leads. The vectorcardiographic leads can, in good approximation, be reconstructed from the standard ECG leads. One can choose between a model-based [20] and a regression-based [21] method. In this article, we used the regression method, which has previously been shown to yield superior performance [21–23]. Normal values for the various axis-calculation techniques are given on the website.

Table 1
Age and sex distribution of the study population.

Age group (years)	Male	Female	Total
16–19	149	385	534 (4.0%)
20–29	538	868	1406 (10.5%)
30–39	2017	1435	3452 (25.8%)
40–49	1546	597	2143 (16.0%)
50–59	1385	1077	2462 (18.4%)
60–69	1291	1124	2415 (18.1%)
70–79	354	443	797 (6.0%)
80–89	46	99	145 (1.1%)
Total	7326	6028	13,354 (100%)

Estimation of normal values

For each ECG parameter the median and the 2nd and 98th percentiles of the measurement distribution per age group and gender were determined. The 2nd percentile was taken as the lower limit of normal (LLN), the 98th percentile as the upper limit of normal (ULN). The statistical treatment of interval durations (heart rate, QRS duration, etc.) is straightforward since they are measured in every single case of the study population. The various wave components within the QRS complexes, however, are of varying occurrence. For example, in the present material of 13,354 normal cases a Q in lead V2 is an uncommon finding. It was observed 113 times (0.8%). The median duration of these Q waves is 20 ms and the 98th percentile 65 ms. Clearly, this does not imply that in the normal lead V2 a Q wave is to be expected of such duration. Rather, if all 13,241 cases in which a Q wave is missing, i.e., where the Q duration is 0, are included in the calculation, the median Q duration will certainly be 0, as will be the ULN since the Q occurs in less than 2% of the population. This means that a Q wave should be considered to be absent in the normal lead V2. If the proportion of Q's in the total population is high, like it is in lead III, the ULN will move toward the one calculated separately for the Q, but the median value, by definition, will remain 0 as long as this proportion stays $<50\%$. There is no ground why this reasoning should not be generalized to other leads and waves, which is what we did.

An alternative solution, followed in other studies, is to present "normal values" drawn from the subset of cases in which the feature is present, with mention of the number of cases in this subset. However, normal values are commonly understood to pertain to the whole group of normal ECGs and should not apply to the subgroup only. We thought it better to avoid such ambivalence.

Results

Table 2 is concerned with the overall, lead-independent measurements. The heart rate in men sinks after adolescence to a median value of 65 beats per minute (bpm), to reach the adolescent level of 73 bpm again in advanced age. It fluctuates between a ULN of ~95, or ~100 in those over 70, and an LLN of ~50 bpm. A woman's heart seems to beat slightly faster.

P durations are a trifle longer for men than for women, as are PQ durations. Both these measurements increase slightly with age up to a median value of 120 ms for P duration and 170 ms for PQ duration, with corresponding upper limits of ~150 ms and ~230 ms, respectively.

The QRS duration remains steady for all ages at 100 ms for men and 92 ms for women. The ULN is 124 ms in men and 114 ms in women.

QT duration has a median value close to 400 ms and a ULN not higher than 460 for all ages and both sexes. The QTc interval has been calculated according to five different correction formulas and is consistently longer than the QT interval, which follows from the median heart rate being higher than the standard 60 bpm. Three of the formulae

Table 2
Lead-independent ECG parameters in various age groups: median (2nd percentile, 98th percentile).

Parameter	Sex	16–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89
Heart rate (bpm)	Male	73 (49, 107)	65 (45, 94)	65 (46, 95)	66 (47, 95)	67 (48, 94)	67 (48, 95)	67 (50, 99)	74 (40, 97)
	Female	72 (47, 105)	67 (48, 98)	66 (47, 95)	67 (47, 90)	69 (52, 94)	71 (53, 94)	72 (55, 98)	72 (50, 102)
P duration (ms)	Male	106 (90, 136)	110 (90, 128)	110 (90, 134)	110 (90, 134)	116 (94, 140)	120 (94, 146)	120 (94, 144)	121 (92, 152)
	Female	104 (89, 124)	104 (88, 122)	106 (89, 128)	108 (90, 128)	112 (92, 134)	114 (92, 138)	116 (90, 144)	118 (90, 146)
PQ duration (ms)	Male	148 (118, 200)	150 (118, 196)	152 (118, 198)	152 (115, 200)	160 (124, 206)	164 (126, 220)	164 (129, 228)	172 (122, 290)
	Female	144 (112, 190)	144 (110, 190)	146 (114, 196)	148 (112, 200)	156 (120, 206)	158 (120, 206)	162 (121, 210)	170 (125, 235)
QRS duration	Male	100 (82, 126)	100 (80, 126)	100 (78, 124)	100 (78, 122)	100 (80, 124)	100 (80, 124)	101 (80, 131)	98 (70, 136)
(ms)	Female	92 (74, 112)	90 (76, 110)	92 (74, 114)	90 (76, 114)	92 (76, 114)	92 (76, 115)	92 (74, 114)	92 (72, 118)
QT interval	Male	378 (332, 452)	394 (342, 454)	396 (344, 454)	394 (342, 458)	396 (342, 458)	398 (346, 454)	398 (336, 458)	395 (334, 476)
(ms)	Female	390 (337, 455)	394 (340, 456)	400 (346, 460)	396 (350, 458)	398 (349, 458)	396 (351, 454)	394 (342, 454)	394 (332, 461)
QTc, Bazett	Male	416 (379, 460)	409 (364, 453)	413 (365, 458)	416 (372, 462)	418 (375, 463)	419 (379, 463)	421 (379, 478)	430 (388, 500)
(ms)	Female	429 (382, 473)	418 (374, 458)	419 (377, 464)	421 (379, 468)	427 (391, 472)	429 (391, 473)	432 (396, 476)	432 (393, 480)
QTc, Frederica	Male	403 (375, 452)	404 (366, 440)	408 (372, 445)	408 (374, 446)	411 (376, 449)	412 (380, 451)	414 (378, 464)	417 (375, 487)
(ms)	Female	415 (377, 452)	409 (375, 446)	413 (378, 452)	414 (377, 449)	417 (385, 456)	419 (386, 460)	419 (387, 464)	419 (377, 453)
QTc, Framingham	Male	403 (375, 452)	404 (367, 439)	408 (368, 443)	408 (373, 444)	411 (376, 448)	412 (378, 450)	413 (379, 463)	417 (379, 484)
(ms)	Female	415 (377, 451)	409 (375, 445)	413 (377, 450)	414 (378, 448)	417 (388, 456)	418 (388, 459)	419 (388, 459)	420 (381, 451)
QTc, Hodges	Male	405 (374, 450)	405 (369, 440)	408 (374, 445)	408 (376, 448)	410 (377, 447)	412 (381, 450)	413 (379, 462)	418 (378, 479)
(ms)	Female	414 (379, 452)	409 (376, 448)	412 (379, 453)	412 (379, 450)	416 (385, 453)	416 (386, 456)	417 (385, 461)	419 (377, 447)
QTc, Rautaharju	Male	409 (377, 454)	408 (369, 442)	411 (372, 447)	412 (376, 448)	415 (378, 451)	416 (382, 453)	417 (381, 464)	423 (389, 486)
(ms)	Female	422 (380, 456)	414 (379, 449)	416 (379, 454)	418 (381, 453)	421 (391, 458)	423 (390, 461)	425 (392, 465)	425 (386, 458)
Frontal P axis (°)	Male	59 (−22, 81)	53 (−8, 79)	57 (−13, 81)	61 (−1, 82)	61 (3, 81)	61 (−1, 82)	63 (−4, 82)	63 (−79, 105)
	Female	51 (−7, 78)	46 (−21, 75)	50 (−20, 79)	58 (−8, 80)	56 (−1, 80)	56 (−2, 81)	57 (−9, 80)	56 (−19, 80)
Frontal QRS	Male	74 (−15, 111)	66 (−25, 98)	69 (−29, 100)	69 (−40, 97)	56 (−49, 92)	42 (−62, 90)	33 (−66, 83)	15 (−60, 83)
axis (°)	Female	65 (−11, 103)	57 (−18, 93)	57 (−25, 95)	58 (−20, 94)	40 (−36, 88)	28 (−46, 81)	13 (−54, 77)	6 (−52, 82)
Frontal T axis (°)	Male	51 (−3, 73)	45 (0, 77)	50 (0, 78)	54 (−2, 81)	51 (−4, 84)	54 (−14, 86)	56 (0, 90)	57 (−142, 93)
	Female	43 (4, 68)	38 (−10, 66)	40 (−5, 74)	48 (−4, 80)	44 (0, 81)	48 (−13, 88)	54 (−2, 104)	56 (−52, 159)
QRS-T angle (°)	Male	51 (9, 111)	46 (9, 97)	44 (9, 101)	49 (11, 107)	50 (13, 117)	57 (16, 125)	61 (10, 129)	61 (13, 142)
	Female	43 (11, 107)	34 (7, 87)	37 (9, 95)	43 (11, 96)	44 (11, 105)	52 (13, 114)	60 (11, 128)	71 (20, 154)

(Frederica, Framingham, and Hodges) are in close range and yield median values for the young male of 405 ms, that slowly approach 420 ms in the very old. The upper limits remain in the 440–450 ms range until they climb to 460 ms in the 70–79 years age group, and even higher in those over 80. By Rautaharju's formula the ULN values are overall some 5 ms higher, for Bazett's correction 10–15 ms. Varying with the correction method, women have 5–10 ms longer durations, except in the highest age group.

The median frontal P axis is stable over the various age groups at about 60° for both sexes, in the direction of lead II.

The median QRS axis remains at about 70° for men, 60° for women, up to age 50 and then starts to rotate to the left, both in men and women, until it is almost horizontal in the highest age groups. The extreme of leftward deviation is in the order of −60°.

The median frontal T axis in men is at around 50° until age 60 and rotates somewhat more rightward in old age. In women it is initially 5–10° more to the left than in men but ends in the same direction as in men. The ULN initially is around 80° but tends to become larger with advancing age.

The spatial QRS-T angle is greater in men than in women for the younger age groups, but this difference disappears in latter years. In both sexes, the QRS-T angle becomes larger in the aged.

The lead-dependent measurements are arranged in supplemental tables, except for Table 3 where the normal limits of LVH indices are presented (see below). Lead aVR is left out of consideration. Due to its polarity the deflections in this lead are inverted with respect to those in most other leads. This confounds the interpretation of lead aVR and vitiates its clinical usefulness. Presentation of the extremity leads in the arrangement proposed by Cabrera (aVL, I, −aVR, II, aVF, III) makes lead aVR behave like its companion leads and clarifies its logical connection to the other extremity leads [24]. Normal

Table 3
Sokolow and Cornell voltages (mV) and products (mV · ms) in various age groups: median (98th percentile).

Index	Sex	16–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89
Sokolow–Lyon voltage	Male	2.99 (4.63)	2.68 (4.28)	2.35 (3.92)	2.25 (3.77)	2.27 (3.93)	2.20 (3.82)	2.16 (3.85)	1.91 (3.48)
(SV1 + max [RV5, RV6])	Female	2.25 (3.78)	2.05 (3.28)	1.98 (3.19)	1.94 (3.39)	2.09 (3.49)	2.09 (3.60)	2.14 (3.80)	2.27 (4.46)
Cornell voltage (RaVL + SV3)	Male	1.40 (2.85)	1.21 (2.78)	1.05 (2.28)	1.09 (2.29)	1.17 (2.39)	1.24 (2.47)	1.29 (2.54)	1.27 (2.87)
	Female	0.98 (2.22)	0.73 (1.73)	0.76 (1.78)	0.82 (1.64)	1.04 (1.98)	1.18 (2.22)	1.32 (2.46)	1.60 (3.14)
Sokolow–Lyon product	Male	299 (459)	267 (439)	230 (412)	220 (373)	225 (399)	219 (389)	216 (398)	191 (315)
([SV1 + max (RV5, RV6)] · QRS)	Female	206 (361)	184 (307)	182 (305)	176 (319)	194 (332)	192 (328)	196 (362)	205 (434)
Cornell product ([RaVL + SV3] · QRS)	Male	139 (321)	121 (273)	103 (237)	108 (248)	117 (256)	123 (256)	128 (273)	120 (294)
	Female	90 (216)	67 (162)	70 (174)	74 (165)	97 (198)	108 (218)	121 (249)	144 (309)

values for the extremity leads in the Cabrera sequence are provided on the Website.

We will here summarize the contents of the supplemental tables.

(1) P waves (Supplemental Tables 1 and 2): P-wave amplitude hardly varies with age and sex. The highest amplitude is encountered in lead II, as is commonly acknowledged, with a ULN of 0.25 mV. In the precordial leads the positive P waves do not show much difference in amplitude across the leads, with a ULN of 0.15 mV. A small negative P deflection may be present in V1 (ULN 0.11 mV in absolute value), and a still smaller one in V2, aVL and III. In the other leads a negative P is virtually absent.

(2) Q waves (Supplemental Tables 3 and 4) and QS patterns (Supplemental Table 5): We chose to treat QS patterns as an independent entity because Q waves and QS waves have a different clinical significance. QS patterns are relatively common in lead aVL (7.7% of all cases), with a predominance of males (5.3%), perhaps corresponding with their somewhat more rightward QRS axis. That these QS patterns become uncommon in the highest age groups can be explained by rotation of the QRS axis to the left in later age. Lead V1 also has a fair number of QS (3.2%), followed by lead III (1.8%) and lead V2 (0.6%). In the other leads QS patterns are rare to absent.

In the precordial leads, the distribution of 0-values for Q-wave amplitudes and durations confirms that, for all practical purposes, Q waves are absent in leads V1–V2. They appear in V5–V6, as the mirror image of the initial R wave in V1, their ULNs being ~30 ms (at amplitudes ~0.3 mV). These ULNs are in agreement with the threshold of ≥ 30 ms that is generally adopted for an infarct Q. In the extremity leads Q waves in aVL and I appear in the majority of men and women after age 60, corresponding with the tendency to develop left axis deviation. Their median values are ≤ 20 ms (at amplitudes ≤ 0.05 mV), with ULNs reaching 35 ms (at 0.2 mV). Q waves in aVF, present in the younger years, disappear with age. The ULN of Q-wave duration might be generally a little shorter in women than in men, whereas Q-wave amplitude is almost the same.

(3) R- and S-waves (Supplemental Tables 6 and 7): Differences in amplitudes between men and women are prominent in the younger age groups, but tend to diminish with increasing age. In the inferior leads II, III, and aVF the R amplitudes decrease with age, and the S amplitudes increase, as do the R waves in I and aVL, in parallel to the age-dependent leftward rotation of the QRS axis. In the precordial leads, there is a definite drop in R amplitudes on entering the 30–39 and 40–49 age groups, especially in men. Hereafter the median amplitudes rise somewhat again to remain relatively stable with age. The S wave follows the same pattern. In the younger age groups the S in V2 is conspicuously larger than that in the neighboring leads, but this difference vanishes in the course of life.

Table 3 gives the normal values for the Sokolow–Lyon index (SV1 + max [RV5, RV6]), the Cornell voltage index (RaVL + SV3), and their QRS duration products. The Sokolow–Lyon index shows highest values in the younger age groups, on account of their deep SV1, and stabilizes with age in men after age 40. In women there is an increase again after this age to reach the male level at age 70, corresponding to a gain in amplitude of the R in V5 or V6. The Cornell index increases with age from 30 years onwards, both for men and women but more prominently in the latter. This reflects the age-dependent leftward rotation of the QRS axis, expressed in a taller R in aVL.

(4) ST segments (Supplemental Tables 8 and 9): J-point amplitude in the extremity leads shows hardly an effect of sex or age. In the precordial leads, sex differences are prominent in leads V2–V4, with ULNs being 30–50% lower in women than in men, with a tendency to decrease with age in both sexes. Normal values of the ST amplitude (J + 60 ms) follow a similar pattern as those of the J amplitude.

(5) T waves (Supplemental Tables 10 and 11): T waves are generally larger in men than in women, but the differences decrease in the course of life, because T-wave amplitude declines at a greater rate in men than in women. Negative T waves deeper than 0.1 mV may be present in III, aVL and V1, with amplitudes that decrease with increasing age. The median values are 0 mV in all standard leads except for women in V1 where they may reach 0.1 mV in absolute value.

Discussion

We determined normal values for the adult ECG based on computerized analysis of a large set of ECGs. Because of the much larger number of ECGs per age and sex group (allowing more reliable estimates), the range of the ages (from young adulthood to very old), and the number of parameters (covering all diagnostically current measurements), our study is able to furnish more differentiated and detailed data, in particular for the older age groups, than the studies of Macfarlane et al. [11], Wu et al. [5], Mason et al. [8], and Rautaharju [12]. In the population of Macfarlane et al., persons aged 50 years and older were relatively few and were assembled in one age group. Wu et al. did the same for those over 60 years of age. This makes it impossible to trace trends in normal values for the elderly. The same applies to the extensive study of Rautaharju in which, remarkably, the age group under 40 is entirely missing. Our data clearly show age trends over the full range of ages for many parameters. A very large population of all ages, going as far as an age category of 90–99, was collected by Mason et al., but they measured only a few parameters, viz. heart rate, PQ, QRS and QTc intervals, and QRS axis, while we provide figures for all standard measurements.

Why the ECG should change over the years is a largely unanswered question. The mechanisms behind these changes are likely to be sought in the changing topography of the heart in relation to thorax and diaphragm, perhaps in still other modifications in the constituents of the volume conductor (skin, subcutaneous fat, lung parenchyma), or, lastly, in alterations of cardiac configuration and intracardiac conduction. The same holds for the differences between the sexes. They are sufficiently strong to predict the male or female provenance of an ECG with reasonable accuracy [25]. In our material sex-dependent differences were

apparent for most parameters, and may have clinical consequences. For example, Q duration is shorter in women than in men, which might be a cause of underdiagnosis of infarction in women.

In the following, we will go over our results and compare them to those of the other studies. The median heart rates in our population varied around ~65 bpm, with a ULN of 95 bpm and an LLN of 50 bpm, values that agree with those found by Mason et al., Wu et al. and Rautaharju, but are 5 bpm lower for men and 10 bpm for women than given by Macfarlane et al.

The median QRS duration is 100 ms for men and 92 ms for women. Mason et al. gives 94 ms and 88 ms, respectively, almost identical with Rautaharju, but the former does not see a difference in ULN between sexes, where we and also Rautaharju, Macfarlane et al. and Wu et al. found that the ULN was consistently some 10 ms higher in males than in females.

QT duration is a hot topic today and deserves special consideration. Its measurement is not unambiguous. Determination of the end of the T wave may be incommoded by inconvenient U waves and one may even propound that the U wave is an integral part of repolarization, which, therefore, is only finished at the "end of U", the "end of T" being a mere inflectional point in the total repolarization curve [26]. Moreover, QT duration is usually normalized for heart rate. The Bazett correction, although under criticism, is still the most widely used. The median of the Bazett QTc interval for men in our study is about 420 ms with an ULN of 460 ms, which is 10–15 ms longer than the value given by Mason et al., and around 10 ms shorter than that reported by Macfarlane et al. The lower ULN values from Mason et al. may, at least partially, be explained by the exclusion in that study of a substantial group of subjects with intra-ventricular conduction delay other than right- or left-bundle branch block. The higher values in Macfarlane et al. may be attributed to their higher heart rates. It is well-known that Bazett's formula overcorrects for heart rates above 60 bpm [6,27]. Indeed, for Hodges' QT correction, which has very low residual correlation with heart rate [6], our results are similar to those reported by Macfarlane et al. [11]. On the other hand, the QTc values in Wu's male Chinese population were some 10 ms shorter than in ours at similar heart rates and measured by the same computer program. In this case the difference might be an intrinsic one between populations. We observe a slight increase with time for the QTc interval, which is also reported by Wu et al. and Mason et al. All studies agree that in women QTc is longer than in men: by ~10 ms in our study and in that of Mason et al., and by a good 15 ms in that of Wu et al. and of Macfarlane et al.

The frontal plane axes and the spatial QRS-T angle were calculated from the net areas under the waves of the contributing leads I and aVF, respectively the vectorial X, Y and Z components. Other studies may follow their own calculation methods. Although age trends in normal values across methods are the same, the medians and ULNs may differ, sometimes markedly. This underlines that normal values for axes and angles should be specified for the computation method that was used. The superior rotation of the QRS axis, which already starts in young adulthood, accelerates in the elderly. As a corollary of this, the R amplitudes in lead I and aVL show a clear positive trend for those aged 50 years and older, with decreasing R amplitude in aVF.

We established a notable increase of left-precordial R-wave amplitudes with increasing age in women, which confirms the findings of Wu et al. A similar trend, although less marked, had also been noted in a smaller sample of Chinese subjects [28]. In white and black women, an increase of R amplitudes in V5 with age was also reported before [29]. Conversely, left-precordial R waves tend to decrease in males.

The Sokolow–Lyon index turned out to be substantially higher in men than in women except for the higher age groups, consistent with the age-related decrease of left-precordial amplitudes in men and their increase in women. If LVH is defined according to the conventional Sokolow–Lyon criterion (SV1 + max (RV5, RV6) > 3.5 mV), the prevalence of "LVH" in our normal population varied between 3.8% and 20.1% for the different age groups of men (overall 6.0%) and between 0.7% and 4.4% (overall 1.6%) for women. Contrarily, the Cornell criterion for men (RaVL + SV3 > 2.8 mV) is very specific (ranging from 0.0% to 1.3% for different age groups, overall 0.2%) thanks to its high threshold value which counterpoises the age-dependent progression of R amplitude in aVL. The Cornell criterion for women (RaVL + SV3 > 2.0 mV) is less specific overall (2.4%), varying between 0.7% and 10.8% over the age groups. The latter high figure follows from the steep rise in R amplitudes in aVL after age 50 and a threshold value that is much lower than in men. These results suggest that these indices should be applied with age- and sex-specific cut-offs.

The normal values in the tables apply to the median age in the age groups. One should be aware that an age effect within age groups may still be present. For those with ages close to the boundary of an age group, it is sensible to interpolate normal values between adjacent age groups. No such complication is encountered when the data are represented in graphical form. As an example, Fig. 1 shows the continuous age-dependent percentile curves of the QRS duration for ages from 0 to 80 years (after age 80 curves could not reliably be estimated because of data sparseness). For the curves of other parameters the reader is referred to our Website. The data for the ages from 0 to 16 have been furnished by our previous study of normal limits for the pediatric ECG [30] and have been integrated with the adult data for measurements that were common to both studies.

Our study has its limitations and constraints. Our subjects were selected from population studies, applying strict inclusion criteria to ascertain their cardiological health. Nevertheless, cases may have crept in that were pathological but clinically silent (infarct, ischemia), or were exhibiting ECG changes (left anterior fascicular block, low atrial rhythm) without a pathological substrate. This is probably the cause of the scatter in the measurements in the highest

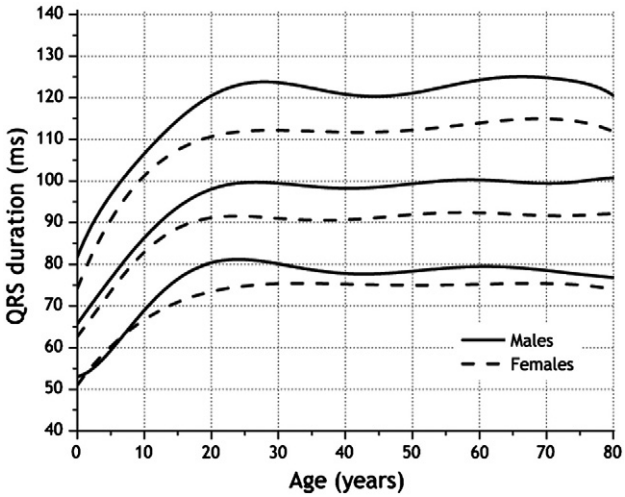

Fig. 1. Continuous age-dependent percentile curves of the QRS duration for normal male and female pediatric and adult populations. The upper, middle, and lower curves denote the upper limit of normal (ULN), median, and lower limit of normal (LLN), respectively.

age group where such changes are more likely to occur and where the number of cases is still too small. One may even wonder whether perfect health and high age are not contradictory: "senectus ipsa morbus" (senescence is a disease in itself) is an ancient saying. The inclusion of some pathological cases in the total material, for that matter, will hardly change the result of the measurements. Finally, technical problems may have been of influence. Waveform recognition errors by the computer program and electrode interchanges were eliminated as far as possible, but systematic variations in electrode positioning are practically impossible to detect.

In summary, this study presents a comprehensive overview of normal ECG values. Our results show that the normal limits of most ECG parameters vary with age and sex, and strongly suggest that diagnostic ECG criteria should be age- and sex-specific. The Website (www.normalecg.org) that accompanies this article allows for easy inspection of the normal values, both in tabular and graphical format, and provides some additional parameters. The Website also contains the results of our earlier study on normal values in children, so that the whole range of ages from the very young to the very old is being covered. It also allows for future updates and expansion. In that respect, we will be happy to consider requests for supplying normal values of new or not yet covered ECG parameters.

Acknowledgments

N. Verweij is supported by the Netherlands Heart Foundation (grant NHS2010B280).

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jelectrocard.2014.07.022.

References

[1] Hiss RG, Lamb LE, Allen MF. Electrocardiographic findings in 67,375 asymptomatic subjects. X. Normal values. Am J Cardiol 1960;6:200–31 [Epub 1960/07/01].
[2] Simonson E. Differentiation between normal and abnormal electrocardiography. St. Louis, Missouri: Mosby; 1961.
[3] Blackburn H, Vasquez C, Keys A. The aging electrocardiogram. Am J Cardiol 1967;20:618–27.
[4] Gambill CL, Wilkins ML, Haisty Jr WK, Anderson ST, Maynard C, Wagner NB, et al. T wave amplitudes in normal populations. Variation with ECG lead, sex, and age. J Electrocardiol 1995;28(3):191–7.
[5] Wu J, Kors JA, Rijnbeek PR, van Herpen G, Lu Z, Xu C. Normal limits of the electrocardiogram in Chinese subjects. Int J Cardiol 2003;87(1):37–51 [Epub 2002/12/07].
[6] Luo S, Michler K, Johnston P, Macfarlane PW. A comparison of commonly used QT correction formulae: the effect of heart rate on the QTc of normal ECGs. J Electrocardiol 2004(37 Suppl):81–90.
[7] Dmitrienko AA, Sides GD, Winters KJ, Kovacs RJ, Rebhun DM, Bloom JC, et al. Electrocardiogram reference ranges derived from a standardized clinical trial population. Drug Inf J 2005;39(4):395–405.
[8] Mason JW, Ramseth DJ, Chanter DO, Moon TE, Goodman DB, Mendzelevski B. Electrocardiographic reference ranges derived from 79,743 ambulatory subjects. J Electrocardiol 2007;40(3):228–34 [Epub 2007/02/06].
[9] Scherptong RW, Henkens IR, Man SC, Le Cessie S, Vliegen HW, Draisma HH, et al. Normal limits of the spatial QRS-T angle and ventricular gradient in 12-lead electrocardiograms of young adults: dependence on sex and heart rate. J Electrocardiol 2008;41(6):648–55 [Epub 2008/09/27].
[10] Stead LG, Vaidyanathan L, Schears RM, Gilmore RM, Vedula KC, Behera SR, et al. Electrocardiographic intervals in the healthy geriatric population—what are the "normals"? Am J Geriatr Cardiol 2008;17(2):87–91.
[11] Macfarlane PW, van Oosterom A, Pahlm O, Kligfield P, Janse M, Camm J. Comprehensive electrocardiology. New York: Springer; 2010.
[12] Rautaharju P. Investigative electrocardiography in epidemiological studies and clinical trials. London: Springer; 2007.
[13] Hofman A, van Duijn CM, Franco OH, Ikram MA, Janssen HL, Klaver CC, et al. The Rotterdam Study: 2012 objectives and design update. Eur J Epidemiol 2011;26(8):657–86 [Epub 2011/08/31].
[14] de Jong PE, Hillege HL, Pinto-Sietsma SJ, de Zeeuw D. Screening for microalbuminuria in the general population: a tool to detect subjects at risk for progressive renal failure in an early phase? Nephrol Dial Transplant 2003;18(1):10–3 [Epub 2002/12/14].
[15] Grobbee DE, Hoes AW, Verheij TJ, Schrijvers AJ, van Ameijden EJ, Numans ME. The Utrecht Health Project: optimization of routine healthcare data for research. Eur J Epidemiol 2005;20(3):285–7 [Epub 2005/06/01].
[16] Kors JA, van Herpen G. Accurate automatic detection of electrode interchange in the electrocardiogram. Am J Cardiol 2001;88(4):396–9 [Epub 2001/09/08].
[17] van Bemmel JH, Kors JA, van Herpen G. Methodology of the modular ECG analysis system MEANS. Methods Inf Med 1990;29(4):346–53.
[18] Willems JL, Arnaud P, van Bemmel JH, Bourdillon PJ, Degani R, Denis B, et al. A reference data base for multilead electrocardiographic computer measurement programs. J Am Coll Cardiol 1987;10(6):1313–21.
[19] Zywietz C, Willems JL, Arnaud P, van Bemmel JH, Degani R, Macfarlane PW, et al. Stability of computer ECG amplitude measurements in the presence of noise. Comput Biomed Res 1990;23(1):10–31.
[20] Edenbrandt L, Pahlm O. Vectorcardiogram synthesized from a 12-lead ECG: superiority of the inverse Dower matrix. J Electrocardiol 1988;21(4):361–7.
[21] Kors JA, van Herpen G, Sittig AC, van Bemmel JH. Reconstruction of the Frank vectorcardiogram from standard electrocardiographic leads: diagnostic comparison of different methods. Eur Heart J 1990;11(12):1083–92.
[22] Cortez DL, Schlegel TT. When deriving the spatial QRS-T angle from the 12-lead electrocardiogram, which transform is more Frank: regression or inverse Dower? J Electrocardiol 2010;43(4):302–9 [Epub 2010/05/15].

[23] Schreurs CA, Algra AM, Man SC, Cannegieter SC, van der Wall EE, Schalij MJ, et al. The spatial QRS-T angle in the Frank vectorcardiogram: accuracy of estimates derived from the 12-lead electrocardiogram. J Electrocardiol 2010;43(4):294–301 [Epub 2010/04/27].
[24] Dower GE, Nazzal SB, Pahlm O, Haistey Jr WK, Marriott HL, Bullington RH, et al. Limb leads of the electrocardiogram: sequencing revisited. Clin Cardiol 1990;13(5):346–8 [Epub 1990/05/01].
[25] Bourdillon PJ, Dawson D, Ritsema van Eck HJ, Gorter S. Classification of the sex of healthy and abnormal subjects using the electrocardiogram. Computers in cardiology. Long Beach: IEEE Computer Society; 197555–7.
[26] Ritsema van Eck HJ, Kors JA, van Herpen G. The U wave in the electrocardiogram: a solution for a 100-year-old riddle. Cardiovasc Res 2005;67(2):256–62 [Epub 2005/05/26].
[27] Rautaharju PM, Zhang ZM. Linearly scaled, rate-invariant normal limits for QT interval: eight decades of incorrect application of power functions. J Cardiovasc Electrophysiol 2002;13(12):1211–8 [Epub 2003/01/11].
[28] Chen CY, Chiang BN, Macfarlane PW. Normal limits of the electrocardiogram in a Chinese population. J Electrocardiol 1989;22 (1):1–15.
[29] Rautaharju PM, Zhou SH, Calhoun HP. Ethnic differences in ECG amplitudes in North American white, black, and Hispanic men and women. Effect of obesity and age. J Electrocardiol 1994 (27 Suppl):20–31.
[30] Rijnbeek PR, Witsenburg M, Schrama E, Hess J, Kors JA. New normal limits for the paediatric electrocardiogram. Eur Heart J 2001;22(8):702–11.

Articles Appearing in the Next Issue

Left Ventricular Electrical Activation During Right Ventricular Pacing in Heart Failure patients with LBBB: Visualization by Electrocardiographic Imaging and Implications for Cardiac Resynchronization Therapy - Niraj Varma

The Availability of Prior ECGs Improves Paramedic Accuracy in Recognizing ST-Segment Elevation Myocardial Infarction - Daniel O'Donnell, Mike Mancera, Eric Savory, Shawn Christopher, Jason Schaffer, and Steve Roumpf

Surface 12 Lead Electrocardiogram Recordings using Smart Phone Technology – Giselle Baquero, Javier Banchs, Shameer Ahmed, Gerald Naccarelli, and Jerry Luck

Low QRS voltage and attenuation of the amplitude of QRS complexes in takotsubo cardiomyopathy - Masami Kosuge and Kazuo Kimura