Electrocardiographic Abnormalities in Centenarians and Octogenarians: A Case-Matched Study

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Background: Centenarians have been proposed as a model of successful aging but recent studies suggest a high prevalence of cardiovascular diseases. Some findings on their electrocardiograms (ECGs) are simply age-related and others mirror underlying diseases. We aimed to identify ECG features truly associated with extreme age.

Methods: Retrospective analysis of 55 centenarians hospitalized between January 2000 and June 2010. Each centenarian was matched with three octogenarians according to gender, presence of hypertension, aortic stenosis, heart failure, and ischemic heart disease.

Results: A history of hypertension was present in 32 (58%) centenarians, aortic stenosis in 6 (11%), heart failure in 8 (15%), and ischemic heart disease in 6 (11%). Centenarians had a higher heart rate than octogenarians (81 ± 15 bpm vs. 72 ± 15 bpm, respectively, $P < 0.001$) but were less frequently on beta-blockers (7% vs. 36%, respectively, $P < 0.001$). Centenarians displayed more frequently atrial premature beats than octogenarians (18% vs. 3%, respectively, $P < 0.001$) but tended to have less atrial fibrillation (15% vs. 22% respectively, $P = 0.21$). Centenarians had more frequently left QRS axis deviation (48% vs. 28%, $P = 0.009$) and Q waves (14% vs. 1%, $P = 0.02$). QT interval was more prolonged in centenarians (446 ± 42 ms vs. 429 ± 39 ms, $P = 0.008$). Two centenarians (4%) and 24 (15%) octogenarians had a strictly normal ECG ($P = 0.02$).

Conclusions: Abnormal ECG is a common finding in centenarians, with different characteristics than in younger elderly individuals. These differences are unrelated to the presence of cardiac diseases.

Ann Noninvasive Electrocardiol 2012;17(4):372–377

centenarians; elderly; electrocardiogram; atrial fibrillation; case-matched study

Aging is accompanied by an increase in cardiovascular diseases and overall mortality. Centenarians have been proposed as a model of successful aging¹ but population-based and autopsy studies challenged this concept by suggesting a

high prevalence of cardiovascular morbidity in this population.^{2,3} Few studies described the electrocardiograms (ECG) of centenarians^{4–8} and their findings most probably combine features simply age-related and others mirroring underlying

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Sources of funding: None.

Conflict of interest: None.

illnesses. In a study comparing ECGs and Holter recordings in unselected centenarians and healthy younger elderly individuals,⁸ it cannot be determined which differences between groups were due to age progression rather than to the presence of cardiac diseases in the centenarian group. In order to identify features associated with extreme age alone, we compared ECGs of centenarians and octogenarians matched for major cardiac diseases (hypertension, aortic valve stenosis, heart failure, and ischemic heart disease).

METHODS

Study Design

Fifty-five centenarians were hospitalized 93 times between January 2000 and June 2010 in the cardiology, rheumatology, internal medicine, and gerontology departments of Lariboisière university hospital (Paris, France). Medical history and standard 12-lead ECG on admission were retrospectively retrieved from hospital records. In case of multiple admissions, only the first one was considered. The patients' medical diagnoses were coded in the French national hospital discharge database (*Programme de médicalisation du système d'information* [PMSI]) according to the International Classification of Diseases (10th revision; [ICD-10]).

For each centenarian, three octogenarians matched for gender, presence of essential hypertension (ICD-10 code I10), aortic valve stenosis (I35.0), heart failure or dilated cardiomyopathy (I50 or I42.0), and chronic ischemic heart disease (I25) were identified through the database. Their medical history and admission ECG were collected and analyzed. The study was approved by the local research ethics committee.

ECG Analysis

Two experienced electrophysiologists (GM and VA) blinded to patient age independently analyzed the ECGs. Differences between the two readers were resolved by consensus. Left atrial abnormality was defined as a P-wave duration ≥ 120 ms with a widely notched P wave. Pathological Q waves were defined according to the 2007 ESC/ACCF/AHA/WHF Universal Definition of Myocardial Infarction,⁹ as (a) any Q wave in V2-V3 ≥ 0.02 seconds or QS complex in V2 and V3, or (b) Q wave ≥ 0.03 seconds and ≥ 0.1 mV deep or QS complex in leads I, II, aVL, aVF, or V₄-V₆ in

any two leads of a contiguous lead grouping. Intra-ventricular conduction disturbances were defined according to the 2009 AHA/ACCF/HRS Recommendations for the Standardization and Interpretation of the ECG.¹⁰ Left ventricular hypertrophy was defined using the Sokolow-Lyon criteria (SV1 + RV5 or RV6 > 35 mm).¹¹ ST-segment depression and T-wave abnormality were considered lone if unrelated to bundle branch block or left ventricular hypertrophy. T-wave abnormality was defined as a flat, negative, or biphasic T wave except in lead V₁. QT interval was manually measured from the onset of the QRS complex to the end of the T wave in lead II, using the baseline method (visual return of the T wave to baseline level) for the determination of the end of the T wave. When the end of T wave was difficult to determine (e.g., in case of very low T-wave amplitude or trouble distinguishing between T waves and U waves), either lead III or V₅ were used. QTc interval was calculated according to Bazett's formula and considered prolonged if ≥ 440 ms.¹² Strictly normal ECG was defined by sinus rhythm without pacing or premature beats, and normal P wave, PR interval, QRS axis, voltage and width, ST segment, T wave morphology, and QTc interval.

In patients implanted with a pacemaker, due to the retrospective nature of our study, we were not able to turn down the rate and some ECG parameters unfortunately could not be obtained. Heart rate, P wave, and PR interval could not be analyzed if atrial stimulation was present. PR interval, QRS complex, T wave, and QTc interval could not be analyzed if ventricular stimulation was present.

Statistical Analysis

Continuous variables are expressed as mean $\pm$ standard deviation and were compared with Student's *t*-test or Mann-Whitney U-test as appropriate. Categorical variables are expressed as number of patients in each category and corresponding percentage and were compared by chi-square analysis or Fisher's exact test, as appropriate. A P-value < 0.05 indicated statistical significance. Statistical analysis was performed with Statview software version 5.0 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Study Population

The centenarians group comprised 10 men (18%) and 45 women (82%) with a mean age of

Table 1. Electrocardiographic Findings in Centenarians and Octogenarians

		Centenarians N (%)	Octogenarians N (%)	P
Rhythm ^a	Sinus rhythm	44 (80%)	123 (75%)	0.41
	Atrial fibrillation	8 (15%)	37 (22%)	0.21
	Heart rate (bpm)	81 ± 15	72 ± 15	<0.001
	Premature beat	11 (20%)	15 (9%)	0.09
	Atrial premature beat	10 (18%)	5 (3%)	<0.001
	Ventricular premature beat	2 (4%)	10 (6%)	0.74
P wave	Normal P wave	38 (83%)	107 (86%)	0.55
	Left atrial abnormality	8 (17%)	17 (14%)	0.55
PR interval	Normal PR interval	30 (70%)	97 (82%)	0.11
	First degree AV block	13 (30%)	22 (19%)	0.11
	Second or third degree AV block	2 (4%)	0 (0%)	0.27
QRS	Normal axis	24 (48%)	104 (68%)	0.01
	Left-axis deviation	24 (48%)	43 (28%)	0.009
	Right-axis deviation	2 (4%)	6 (4%)	1.00
	Normal QRS duration	30 (60%)	101 (73%)	0.08
	Complete BBB	14 (28%)	36 (26%)	0.79
	Complete left BBB	9 (18%)	14 (10%)	0.15
	Complete right BBB	5 (10%)	21 (15%)	0.36
	Incomplete left BBB	2 (4%)	1 (0.7%)	0.17
	Incomplete right BBB	2 (4%)	0 (0%)	0.07
	Q wave	7 (14%)	2 (1%)	0.02
	Left ventricular hypertrophy	4 (8%)	6 (4%)	0.27
	Lone ST depression ^b	3 (6%)	8 (5%)	0.7
	T = wave abnormality ^c	35 (70%)	89 (58%)	0.14
T wave	Lone T = wave abnormality ^b	21 (42%)	77 (50%)	0.55
	Lone T = wave abnormality other than negative in D3 ^b	13 (26%)	46 (30%)	0.58
	QTc (Bazett's formula)	446 ± 42 ms	429 ± 39 ms	0.008
QTc interval	QTc ≥ 440ms	25 (49%)	48 (32%)	0.03

AV = atrioventricular; BBB = bundle branch block.

^a4 centenarians and 15 octogenarians were paced in the atrium and/or ventricle (see text); ^bUnrelated to bundle branch block or left ventricular hypertrophy; ^cFlat, negative or biphasic, except in V1.

102 ± 2 years. Thirty-two centenarians (58%) were admitted to the internal medicine department, 18 (33%) to gerontology, 3 (6%) to cardiology, and 2 (4%) to rheumatology. The most frequent causes of admission were respiratory tract infections (n = 13), heart failure (n = 7), both of the aforementioned (n = 7), falls (n = 5), and dehydration (n = 4). Thirty-two centenarians (58%) had hypertension, 6 (11%) aortic stenosis, 8 (15%) heart failure, and 6 (11%) ischemic heart disease. The matched group comprised 165 octogenarians including 30 men and 135 women, with a mean age of 84 ± 3 years. A history of atrial fibrillation (AF) tended to be less frequent in centenarians than octogenarians (22% vs. 33%, respectively, P = 0.13). Ten centenarians (18%) and 19 octogenarians (12%) had a pacemaker (P = 0.25).

On admission, octogenarians were more frequently on beta-blockers than centenarians (36%

vs. 7%, respectively, P < 0.001), despite similar prevalence of hypertension, heart failure, and ischemic heart disease. Rates of prescription of digoxin and amiodarone were similar between centenarians and octogenarians (7% and 5%, respectively for digoxin, P = 0.74; 13% and 10% respectively for amiodarone, P = 0.61).

ECG Analysis

Among centenarians implanted with a pacemaker, 3 were paced in the ventricle alone and 1 in the atrium and ventricle. Among octogenarians implanted with a pacemaker, 10 were paced in the ventricle alone, 2 in the atrium alone, and 3 in the atrium and ventricle. Centenarians had a higher heart rate and more frequent atrial premature beats than octogenarians (Table 1). AF on admission tended to be less frequent in centenarians

than octogenarians (15% vs. 22%, respectively, $P = 0.21$). Prevalence of atrioventricular block and left bundle branch block were similar between the two groups. Left QRS axis deviation was more frequent in centenarians, as were Q waves (Table 1). Q waves were present in 7 centenarians: 5 in inferior leads (2 contiguous leads in 3 patients and 3 contiguous leads in 2 patients) and 2 in V_2 - V_3 . Two octogenarians had Q waves, both in leads V_2 - V_4 . QTc was more often prolonged (≥ 440 ms) in centenarians than octogenarians (49% vs. 32%, respectively, $P = 0.03$). Only 2 (4%) centenarians and 24 (15%) octogenarians had a strictly normal ECG ($P = 0.02$).

DISCUSSION

While many data exist on the electrocardiographic features of elderly individuals, few studies have examined the oldest old, the centenarians.⁴⁻⁸ In our series of centenarians compared with octogenarians matched for gender and presence of hypertension, aortic valve stenosis, heart failure, and ischemic heart disease, we observed that centenarians had a higher heart rate, more frequent atrial premature beats but less AF, more frequent left QRS axis deviation, Q waves, and prolonged QTc interval.

Aging of the heart is characterized by anatomical and electrophysiological changes favoring arrhythmias and conduction disturbances.^{13,14} It is also associated with a marked increase in the prevalence of concentric left ventricular remodeling and ischemic heart disease.^{15,16} Therefore, it is not surprising that ECGs of centenarians were rarely strictly normal. Only 4% of them in our study did not exhibit any abnormality, in line with the 7% in two recent studies.^{6,7}

It is important however to distinguish between abnormalities related to age itself and major abnormalities potentially related to cardiovascular diseases which might be associated with worse outcome. Previous studies were not aimed to address this question either because there was no control group⁴⁻⁶ or because the control group was not matched for cardiovascular profile.⁸ Lakireddy et al.⁷ attempted to describe the ECG of centenarians without cardiac disease, but this condition was determined only by the information quoted in the indication for the ECG. We overcame this limitation by matching each centenarian with three oc-

togenarians for major cardiac diseases. We found that ECG characteristics observed more frequently in centenarians were those usually considered benign. As in the study of Wakida et al.,⁸ atrial premature beats and QTc prolongation were more frequent in centenarians than in octogenarians. We also noted that centenarians exhibited left QRS axis deviation more frequently. None of these findings has been reported to be related to mortality.^{12,17-19} In the study by Tervahauta et al.²⁰ of men aged 65-84 years, the association between Q-waves and the risk of coronary events and mortality was not significant when adjusted for the history of coronary heart disease. The only exception is the higher heart rate we observed in centenarians. Raised heart rate has been shown to be associated with mortality even in elderly subjects²¹ but this finding could be simply explained by the much lower beta-blocker prescription rate in centenarians than octogenarians, despite similar prevalence of hypertension, heart failure, and ischemic heart disease.

On the other hand, the prevalence of ECG findings traditionally associated with bad prognosis did not increase with extreme age. Several studies in the elderly have demonstrated that ST-T patterns suggestive of ischemia predicted mortality.^{20,22,23} In our study, ST-segment depression and T-wave abnormalities were not more frequent in centenarians than octogenarians. First-degree atrioventricular block and complete bundle branch block are also associated with all-cause mortality in the general and elderly population.²²⁻²⁵ The prevalence of these findings was similar in centenarians and octogenarians in our study. Even more remarkable, the nonsignificant trend of less AF with extreme age is to be highlighted. Prevalence of AF ranges from 0 to 12% in centenarians,^{4,5,8} with the exception of the study by Lakkireddy et al.⁷ in which it was reported to be 30%. AF is accompanied by an increased risk of mortality at younger ages and it is possible that the population of centenarians may be biased by the selection of relatively healthy survivors. Another explanation is that centenarians have a more favorable biological and cardiovascular risk profiles,¹ which may prevent development of AF.

Our study has several limitations. It is possible that the observed differences between centenarians and octogenarians may be due to the progression of known cardiac diseases or incidence of

under-diagnosed illnesses. All patients were hospitalized and these results may not apply to patients in the community; however they were recruited in various departments and presented a broad range of diseases on admission. Some other limitations pertain to the choice of ECG criteria itself. For identification of left ventricular hypertrophy, we chose to focus on the Sokolow-Lyon criteria because of its widespread use and to the absence of studies reporting the accuracy of any other particular criterion in centenarians. Moreover, we would not have been able to compare the validity of different ECG criteria in our study because the echocardiographic (or other imaging technique) data necessary to diagnose hypertrophy was missing for many patients. Several factors may cause P-wave abnormality such as left atrial dilatation/hypertrophy and delayed interatrial conduction; their individual effects may not be distinguishable. Finally, in patients implanted with a pacemaker the percentage of pacing was not available, not allowing accurate assessment of the role of cardiac memory in T-wave inversions in nonpaced ventricular beats. However, only 13 of the 29 patients with pacemakers in this study were not paced in the ventricle and lone (unrelated to bundle branch block or left ventricular hypertrophy) T-wave inversions were observed in only 2 of these patients (one diffuse and one limited to inferior leads), indicating probably limited cardiac memory-related changes in this subset of patients.

In summary, an abnormal ECG is a common finding in the elderly. Centenarians exhibit specific electrocardiographic characteristics compared with younger elderly individuals, independently of the presence of clinically evident major cardiac diseases. Abnormalities whose prevalence increased with age are usually not considered to be associated with a bad prognosis. People with truly pathological findings probably do not reach such an extreme age.

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