Centenarians and their hearts: A prospective registry with comprehensive geriatric assessment, electrocardiogram, echocardiography, and follow-up

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Background Data on the cardiac characteristics of centenarians are scarce. Our aim was to describe electrocardiogram (ECG) and echocardiography in a cohort of centenarians and to correlate them with clinical data.

Methods We used prospective multicenter registry of 118 centenarians (28 men) with a mean age of 101.5 ± 1.7 years. Electrocardiogram was performed in 103 subjects (87.3%) and echocardiography in 100 (84.7%). All subjects underwent a follow-up for at least 6 months.

Results Centenarians with abnormal ECG were less frequently females (72% vs 93%), had higher rates of previous consumption of tobacco (14% vs 0) and alcohol (24% vs 12%), and scored lower in the perception of health status (6.8 ± 2.0 vs 8.3 ± 6.8). Centenarians with significant abnormalities in echocardiography were less frequently able to walk 6 m (33% vs 54%). Atrial fibrillation/flutter was found in 27 subjects (26%). Mean left ventricular (LV) ejection fraction was 60.0 ± 10.5%. Moderate or severe aortic valve stenosis was found in 16%, mitral valve regurgitation in 15%, and aortic valve regurgitation in 13%. Diastolic dysfunction was assessed in 79 subjects and was present in 55 (69.6%). Katz index and LV dilation were independently associated with the ability to walk 6 m. Age, Charlson and Katz indexes, and the presence of significant abnormalities in echocardiography were associated with mortality.

Conclusions Centenarians have frequent ECG alterations and abnormalities in echocardiography. More than one fifth has atrial fibrillation, and most have diastolic dysfunction. Left ventricular dilation was associated with the ability to walk 6 m. Significant abnormalities in echocardiography were associated with mortality. (Am Heart J 2015;169:798-805.e2.)

The centenarian population has been increasing rapidly in recent years,[1,2] and it is becoming more common to see centenarians in clinical practice.[3] Cardiovascular diseases are the leading cause of death in very old persons, although they are frequently underreported or unrecognized.[4-7] Moreover, data on cardiac anatomy, physiology, and pathophysiology in patients aged ≥100 years are lacking, not only because of the relative scarcity of such individuals, but also because they are often poorly studied. Some authors have suggested that centenarians could be healthier than the "younger" old, with a lower prevalence of atrial fibrillation,[8] diabetes mellitus, and other cardiovascular risk factors[9,10] probably because of demographic selection and the increased risk of death in patients with cardiovascular disease at earlier ages. Aging is associated with extensive changes in cardiovascular structure and function[11] that may result in detectable electrocardiographic and echocardiographic findings.

A recent study suggested that electrocardiogram (ECG) abnormalities are rare in centenarians,[3] whereas other

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studies have found frequent ischemic changes[4] or conduction anomalies.[12] However, previous ECG studies in centenarians are limited by low sample size and methodological biases.[3,4,12–19] The echocardiographic characteristics of centenarians have only been reported in a small retrospective group of 63 hospitalized subjects.[20]

The aim of this study was to describe ECG, echocardiography, and blood test results in a cohort of centenarians and to correlate them with survival and with clinical data obtained from the medical history and a comprehensive geriatric assessment.

Methods

The Cardiac and Clinical Characterization of Centenarians (4C) study is a prospective registry that recruited 118 centenarians in 9 Spanish centers over a 2-year period (April 2011 to March 2013). Hospitalization was the only exclusion criterion, although patients could be included on the day of their discharge from hospital.

The clinical history was obtained by direct interview with subjects and caregivers. Subjective perceived health status was recorded on a scale of 1 to 10. Cognitive status was assessed using the Short Portable Mental Status Questionnaire,[21] nutritional status using the Mini Nutritional Assessment–Short Form (MNA-SF),[22] activities of daily living using the Katz index,[23] and comorbidity using the Charlson index.[24] Physical performance was assessed by measuring the ability to walk 6 m and the time taken to walk 6 m at normal pace (gait speed).

Biochemical parameters were measured at baseline using standard methods in the routine clinical laboratory of each center. Electrocardiograms and echocardiograms were recorded according to the protocol shown in online Appendix Supplementary material. After baseline assessments, subjects were followed-up by telephone call for 6 to 34 months, and the time of death was recorded. All participants or their proxies signed a written informed consent. The study was approved by the ethics committee of the Hospital Universitario Gregorio Marañón, Madrid, Spain, and was supported in part by the *Proyecto de Registro Clínico de la Sección de Cardiología Clínica 2013*, Spanish Society of Cardiology, Madrid, Spain. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the manuscript, and its final contents.

Statistical analysis

Quantitative variables are reported as mean ± SD, and qualitative variables are reported as number and percentage. Continuous variables were compared using the *t* test or the Mann-Whitney *U* test if the variable had a non-normal distribution, and categorical variables were compared using the χ^2 test or Fisher exact test when the χ^2 test was not appropriate. To assess variables independently associated with the ability to walk 6 m, all variables with a significant association in the univariate analysis were included in the logistic regression modeling process, which involved forward and backward stepwise methods with a threshold for exit set at $P > .10$ and for enter at $P < .10$. The objective was to construct a parsimonious model, with the minimum number of variables per logit explaining the greater amount of variability. Cox regression modeling including potential confounders was performed to assess the association between ECG/echocardiography abnormalities and total mortality. We considered the following as potential confounders: age, gender, Charlson index, Katz index, mental index (Short Portable Mental Status Questionnaire), nutrition index (MNA-SF), ability to walk 6 m, and hospital admission. All statistical analyses were performed using SPSS software (V16, SPSS, Chicago, IL). All *P* values are 2-tailed, and $P < .05$ was regarded as statistically significant.

Results

A total of 118 centenarians were included (28 men and 90 women). Mean age was 101.5 ± 1.7 years (range, 100-110 years). On the day of inclusion, subjects were living at home (91, 77.1%) or in a nursing home (27, 22.9%). Seventy-three subjects (61.9%) were assessed at hospital discharge. Previously known cardiovascular diseases were frequently found, mainly heart failure in 40 subjects (33.9%), stroke/cerebrovascular disease in 18 (15.3%), and myocardial infarction in 15 (12.7%). A high rate of centenarians had low comorbidity (72% with Charlson index <3) and considered their health status to be very good (45% with score ≥8). By contrast, only 11% remained independent in all activities of daily living, and most (58%) were unable to walk 6 m. When the Katz index was divided into 3 groups,[25] 42%, 21%, and 37% were categorized, respectively, as minor or no dependency (A-C), moderate dependency (D, E, and H), and total dependency (F-G). A total of 31% maintained good nutritional status according to the MNA-SF, and 28% showed no cognitive impairment. Information on living first-degree relatives who lived beyond 90 years was available for 45 subjects, of whom 29 (64.4%) reported a first-degree relative older than 90 years.

Electrocardiogram was performed in 103 subjects (87.3%), and echocardiography was performed in 100 subjects (84.7%). Table I shows the main sociodemographic data, habits, and functional, cognitive, nutritional, and clinical status in centenarians with and without a normal ECG and with and without left ventricular ejection fraction (LVEF) depression or significant valve disease in echocardiography. Centenarians with abnormal ECG were less frequently females (72% vs 93%), had higher rates of previous consumption of tobacco (14% vs 0) and alcohol (24% vs 12%), and scored lower in the subjective perception of health status from 1 to 10 (6.8 ± 2.0 vs 8.3 ± 6.8). Centenarians with significant abnormalities in echocardiography were less frequently able to walk 6 m (33 vs 54%).

Table I. Sociodemographic and disease-related characteristics by ECG and echocardiography group

	Normal ECG (n = 27)	Abnormal ECG (n = 76)	*P*	LVEF >0.5 and no significant valve disease (n = 55)	Echo with significant abnormalities (n = 45)	*P*
Age (y)	101.5 ± 1.6	101.5 ± 1.8	.99	101.5 ± 1.6	101.4 ± 1.9	.81
Female sex (%)	25 (92.6)	55 (72.4)	.02	39 (70.9)	36 (80.0)	.30
Systolic blood pressure (mm Hg)	131 ± 23	130 ± 23	.86	135 ± 24	126 ± 22	.07
Heart rate (beat/min)	77 ± 13	78 ± 15	.72	13	13	.86
Body mass index (kg/m^2)	24.6 ± 6.4	25.1 ± 4.7	.69	25.1 ± 4.6	23.8 ± 6.3	.18
Previous tobacco consumption (%)	0	10 (13.9)	.004	7 (13.8)	3 (6.7)	.06
Previous alcohol consumption (%)	3 (12.0)	29 (24.3)	.03	16 (29.1)	14 (38.9)	.19
Myocardial infarction	2 (7.4)	8 (10.5)	.63	5 (9.1)	7 (15.6)	.33
Heart failure	6 (22.2)	28 (36.8)	.14	17 (30.9)	17 (37.8)	.48
Peripheral arterial disease	1 (3.7)	3 (4.0)	.96	2 (3.6)	2 (4.4)	.84
Stroke/cerebrovascular disease	3 (11.1)	13 (17.1)	.46	7 (12.7)	8 (17.8)	.49
Discharged from hospital admission	16 (59.2)	43 (56.6)	.52	33 (60.0)	30 (66.7)	.71
Charlson index score	1.6 ± 2.3	2.0 ± 1.9	.39	1.7 ± 2.2	2.4 ± 1.8	.12
Mental SPMSQ (Pfeiffer)	4.4 ± 3.7	5.3 ± 2.4	.34	4.6 ± 3.1	5.3 ± 3.1	.27
Nutritional MNA-SF assessment	9.2 ± 4.1	9.3 ± 3.3	.92	9.6 ± 3.6	8.5 ± 3.3	.14
Katz index (from A = 0 to G = 6)	2.8 ± 2.1	3.5 ± 2.2	.22	2.9 ± 2.1	3.7 ± 2.1	.07
Perceived health status from 1 to 10	8.3 ± 1.5	6.8 ± 2.0	.004	7.4 ± 1.7	6.7 ± 1.9	.16
Physical exercise before 65 y 3 or more times per wk (%)	20 (80.0)	9 (81.3)	.88	39 (72.2)	36 (81.8)	.27
Physical exercise after 65 y 3 or more times per wk (%)	19 (76.0)	55 (74.3)	.87	34 (64.2)	33 (75.0)	.25
Ability to walk 6 m (%)	11 (42.3)	31 (41.3)	.93	29 (53.7)	15 (33.3)	.04
Time to walk 6 m (s)	18 ± 10	22 ± 25	.58	21 ± 26	22 ± 13	.92
LVEF >0.5 and no significant valve disease	7 (31.8)	33 (49.3)	.15	–	–	–

Abbreviations: *Echo*, echocardiography; *SPMSQ*, Short Portable Mental Status Questionnaire.

Brain natriuretic peptide (BNP) was measured in 32 subjects and pro-BNP in 67. In both cases, levels tended to be higher in patients with a recent hospitalization (BNP 2,570 ± 7,831 vs 179 ± 102 ng/L, $P = .13$, and pro-BNP 6,624 ± 8,881 vs 2,673 ± 5,929 ng/L, $P = .03$). Mean C-reactive protein levels were also higher in recently hospitalized patients (20.3 ± 33.0 mg/L vs 7.5 ± 13.8 mg/L, $P = .01$). Laboratory data are shown in online Appendix Supplementary Table. Centenarians with abnormal ECG had higher levels of creatinine and pro-BNP, and those with significant abnormalities in the echocardiography had higher levels of hemoglobin A_{1c} and pro-BNP.

The main findings in ECG and echocardiography are shown in Tables II and III, respectively. Atrial fibrillation/flutter was found in 27 subjects (26%). Mean left ventricular (LV) dimensions were 4.0 ± 0.7 cm (1.73 ± 0.4 cm/m^2) (end diastolic) and 2.6 ± 0.7 cm (1.18 ± 0.2 cm/m^2) (end systolic), with a mean LVEF of 63.5% ± 10.6% and 60.0% ± 10.5%, as calculated using the Teichholz and Simpson methods, respectively. A total of 19 centenarians had LV systolic dysfunction. Mean ventricular thickness was 1.6 ± 0.3 cm (septal wall) and 1.1 ± 0.19 cm (LV posterior wall). Left ventricular hypertrophy was frequent (45%) and was poorly correlated with ECG: from 6 subjects with ECG criteria of LV hypertrophy and echocardiography, only 3 had echocardiographic criteria of hypertrophy. Mean aortic root diameter was 3.5 ± 0.4 cm (0.14 ± 0.1 cm/m^2), and mean left atrial dimension was 4.1 ± 0.6 cm (1.17 ± 0.2 cm/m^2); left atrial enlargement was found in most subjects (62%). Moderate or severe valve disease was common (aortic stenosis 16%, mitral regurgitation 15%, and aortic regurgitation 13%). The relation of the different valve diseases among them and with LVEF is shown in Figure 1. Overlap was very frequent, except in the case of aortic stenosis. No subject of the study had prior valve replacement. Moderate-severe pulmonary artery hypertension (≥45 mm Hg) was found in 35%. A total of 89 subjects had ECG and echocardiography, 74 (83.1%) had an abnormal ECG or low LVEF/significant valve disease, and 15 (16.9%) had a normal ECG and an echocardiography with normal LVEF/no significant valve disease. The relation of atrial fibrillation/flutter with significant valve disease is shown in Figure 2; again, there was a frequent overlap except in the case of aortic stenosis. Diastolic function was assessed in 79 subjects, and 55 (69.6%) had diastolic dysfunction, 45 (57.0%) had impaired relaxation, 6 (7.6%) had a pseudonormal pattern, and 4 (5.1%) had a restrictive diastolic pattern. The presence of significant aortic regurgitation was similar for subjects with and without diastolic dysfunction (6 [10.9%] vs 1 [4.2%], $P = .26$). Blood pressure was also similar for subjects with and without diastolic dysfunction (systolic 135 ± 22 vs 130 ± 23 mm Hg, $P = .35$, diastolic 72 ± 14 vs 68 ± 12 mm Hg, $P = .28$, respectively).

The only 2 variables that were independently associated with the ability to walk 6 m were the Katz index (which includes questions about mobility) and LV dilation (Table IV). All subjects had a complete follow-up of at least 6 months. Mean follow-up was 11.7 ± 9.1 months

Table II. Main electrocardiographic data in 103 centenarians

	N (%)
Abnormal ECG	76 (73.8)
Sinus bradycardia	8 (6.9)
Sinus tachycardia	4 (4.3)
Atrial fibrillation	24 (20.7)
Atrial flutter	3 (2.6)
Pacemaker rhythm	3 (2.6)
Premature atrial complexes	5 (5.0)
Premature ventricular complexes	4 (4.3)
Left ventricular hypertrophy	9 (7.6)
Left atrial enlargement	2 (2.4)
Right bundle branch block	11 (9.6)
Left bundle branch block	17 (14.8)
First-degree AV block	13 (11.2)
Pathologic Q wave	15 (15.0)
	Mean ± SD
QRS width (ms)	107 ± 37
PR interval (ms)	175 ± 42
Corrected QT interval (ms)	427 ± 44

Abbreviation: *AV*, atrioventricular.

Table III. Main echocardiographic data in 100 centenarians

LV dilation (end-diastolic dimension >60 mm)	13
LV hypertrophy (septal thickness or posterior wall thickness >12 mm)	45
Left atrial diameter >40 mm	62
LVEF (≥50/45-50/35-44/<35) (%)	81/13/1/5
Aortic stenosis (none/mild/moderate/severe) (%)	64/20/11/5
Aortic insufficiency (none/mild/moderate/severe) (%)	51/36/11/2
Mitral insufficiency (none/mild/moderate/severe) (%)	58/27/10/5
Pulmonary hypertension (artery systolic pressure <30/30-44/45-59/>59 mm Hg)	45/20/20/15
LV diastolic dysfunction (%)	55 (69.6)
Aortic valve calcification	79
Aortic valve thickening	50
Mitral annular calcification	48
Mitral valve annular calcification	48

Data reflect number and percentage except in diastolic dysfunction, evaluated only in 79 subjects.

(19.4 ± 7.7 months in survivors). Abnormal ECG was not related with mortality (univariate hazard ratio 1.2, 95% CI 0.7-2.2, $P = .46$), but the presence of systolic dysfunction or significant valve disease in echocardiography was associated with mortality, mainly at the expense of aortic regurgitation (Table V and Figures 3 and 4).

Discussion

The clinical characteristics of our cohort are similar to those published elsewhere for this age range,[25,26] namely, a high prevalence of dependency, malnutrition, and cognitive impairment. However, many of the centenarians considered their health status to be very good (45% with score ≥8/10), probably—at least in part—because of the relatively low comorbidity (72% with Charlson index <3). It is also remarkable that most centenarians had followed healthy lifestyles (ie, doing exercise before and after 65 years, no tobacco or alcohol consumption). As expected, age and the Charlson and Katz indexes were independent predictors of mortality. Interestingly, the presence of significant abnormalities in the echocardiography was also associated with mortality.

Electrocardiogram

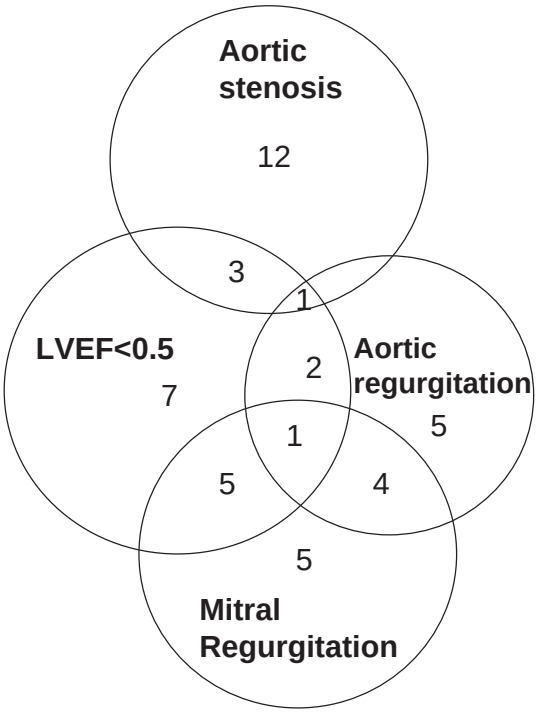
Few studies have assessed the electrocardiographic changes in centenarians, and the results found vary widely.[3,4,12-19] For example, the frequency of atrial fibrillation varies from 0% to 30%, and that of myocardial infarction ranges from 0% to 20% (Table VI). There are several reasons for these differences, including different enrollment criteria. All previous studies were single center, and most included fewer than 50 centenarians.[12,13,15,16,18] Some excluded centenarians with previous cardiac disease[12] and were performed retrospectively.[13,19] Our study was designed to avoid these biases and included a systematic approach to baseline health status, echocardiography, and follow-up. The data from the 4C registry together with information from studies with larger samples (Table VI) suggest that the prevalence of atrial fibrillation in centenarians is high, probably around 20%. It is well known that this prevalence increases with age, reaching 10% in those 85 years or older.[27] However, it has been suggested that, after that age, prevalence could decrease,[8] although this is most likely because of misdiagnosis and underreporting. Misdiagnosis and the frequent underreporting[4] are also probably the reason why we found no differences in the rate of cardiovascular diseases in patients with and without abnormalities in ECG. Many cardiovascular conditions such as myocardial infarction or atrial fibrillation may cause only subtle symptoms in centenarians and often go unrecognized.[5-7] However, subjects with abnormal ECG were less frequently females, had higher rates of previous tobacco and alcohol consumption, scored lower in the perception of health status, and had higher levels of creatinine and pro-BNP.

Echocardiography

The most frequent finding was LV diastolic dysfunction (69%); other very common anomalies included left atrial enlargement (62%), LV hypertrophy (45%), and moderate–severe pulmonary artery hypertension (35%). Mean interventricular septal thickness was 1.6 cm versus only 1.1 cm for the posterior wall, suggesting asymmetric septal hypertrophy. The correlation with ECG was poor for LV hypertrophy, and the rates of left atrial enlargement and moderate-severe pulmonary artery hypertension were more than 3 times higher than those of atrial fibrillation or right bundle branch block, respectively.

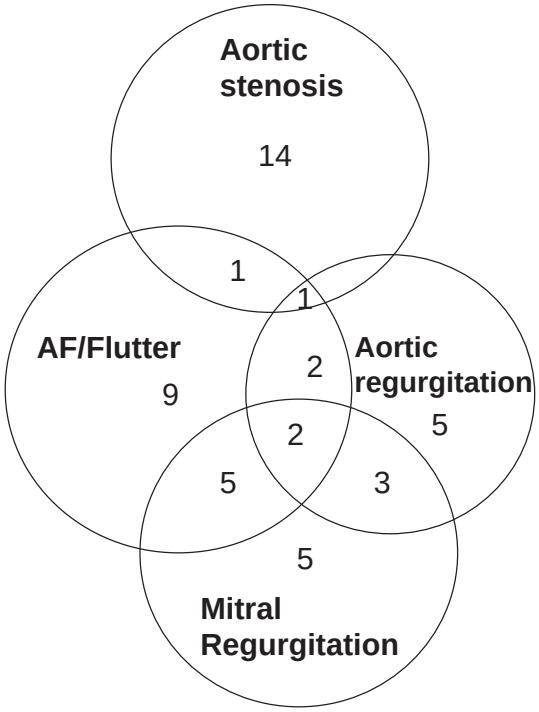
The only previous echocardiography study in centenarians was retrospective, performed in a small group of 63 hospitalized centenarians with local analysis, and had no ECG data or follow-up data.[20] The authors reported a similar

Figure 1



Venn diagram of the 45 subjects with LVEF <0.5 or significant heart valve disease.

Figure 2



Venn diagram of the 47 subjects with atrial fibrillation (AF)/flutter or significant heart valve disease.

mean LV end-diastolic dimension (4 cm) with a smaller mean LV end-systolic dimension (1.8 cm vs 2.6 in the 4C registry) and a resultant ejection fraction in the supernormal range (mean, 86%). We did not confirm this finding (mean LVEF in the 4C registry was 64% by the Teichholz method and 60% by the Simpson method). However, in our registry, roughly 4 of 5 centenarians had a normal ejection fraction. Mean LV posterior wall thickness was similar (1.1 cm) in both studies. In the 4C study, we also found frequent unsuspected moderate or severe valve disease with similar values for aortic stenosis, aortic insufficiency, and mitral insufficiency (between 13% and 16%). The overlap of these conditions among them and with LV systolic dysfunction was frequent, except for the case of aortic stenosis. Sadiq et al[20] found even higher rates of moderate or severe valve disease (aortic stenosis 27%, aortic regurgitation 17%, and mitral regurgitation 22%), probably because all of their centenarians were hospitalized, in many cases because of a heart condition. Carugo et al[28] studied 106 subjects aged 95.3 ± 3.7 years using echocardiography. Their sample included 17 centenarians, although they did not report the specific results for this low number of centenarians.

Centenarians with significant abnormalities in echocardiography were less frequently able to walk 6 m and had higher levels of hemoglobin A_{1c} and pro-BNP. Interestingly, LV dilation was 1 of the 2 variables independently associated with the ability to walk 6 m. Ability to walk is related to a wide range of factors, of which heart disease is one, although this finding is particularly relevant if we take into consideration that the other variable independently associated with this ability—the Katz index—includes questions about mobility.

About half of our centenarians died during the first year of follow-up. The Charlson and Katz indexes were independent predictors of mortality, and interestingly, an abnormal echocardiography was also associated with prognosis. This association was mainly related with the presence of aortic regurgitation. Severe or moderately severe aortic regurgitation has previously been associated with increased mortality, particularly in the elderly. However, given the low number of patients with moderate and severe aortic insufficiency, this finding must be interpreted with caution.

Blood tests

Mean BNP/pro-BNP was higher in our sample than in that of Nybo et al,[29] the authors of the only previous study that measured natriuretic peptides in centenarians. This finding could be related to the fact that some of our centenarians were being discharged from hospital and their levels were higher, although the difference was only significant in the case of pro-BNP, probably because of the low number of BNP determinations.

Table IV. Variables associated with the ability to walk 6 m

Univariate analysis	Unable to walk 6 m (n = 66)	Able to walk 6 m (n = 50)	*P*
Male sex (%)	11 (16.4%)	17 (34.0%)	.03
MNA-SF	8.1 ± 3.3	10.7 ± 2.9	<.0001
HDL (mg/dL)	41.8 ± 15.0	51.5 ± 22.7	.01
C-reactive protein (mg/L)	22.5 ± 35.0	6.8 ± 11.0	.002
LV dilation (%)	11 (20.0%)	2 (4.5%)	.01
Katz index (from A = 0 to G = 6)	0.5	0.4-0.7	<.0001
LV systolic dysfunction (LVEF <50%) (%)	17 (25.4%)	3 (6%)	.01
Multivariate analysis	**OR**	**95% CI**	***P***
Katz index (from A = 0 to G = 6)	0.5	0.4-0.7	<.0001
LV dilation (%)	0.15	0.02-0.90	.038

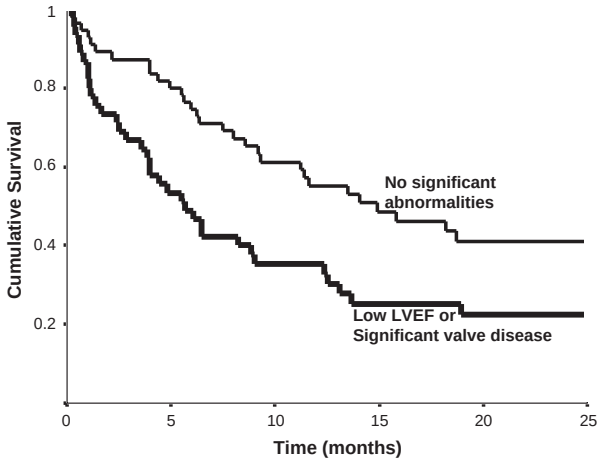
Abbreviations: *HDL*, high-density lipoprotein; *LV dilation*: end-diastolic dimension >60 mm; *OR*, odds ratio.

Table V. Predictors of mortality

Univariate analysis	HR	95% CI	*P*
Age (y)	1.2	1.03-1.34	.02
Charlson index	1.2	1.10-1.32	.0001
Katz index (from A = 0 to G = 6)	1.2	1.07-1.36	.002
Aortic regurgitation (from none = 0 to severe = 3)	1.8	1.34-2.51	.0001
Low LVEF or significant valve disease	1.9	1.1-3.1	.012
Atrial fibrillation/flutter	2.0	1.18-3.41	.009
SPMSQ	1.1	1.04-1.21	.005
MNA-SF	0.9	0.84-0.95	.002
Able to walk 6 m	0.5	0.28-0.77	.003
Multivariate analysis. Independent predictors			
Using low LVEF or significant valve disease			
Age (y)	1.2	1.1-1.4	.01
Charlson index	1.2	1.1-1.3	.03
Low LVEF or significant valve disease	1.9	1.1-3.1	.01
Using aortic regurgitation			
Age (y)	1.2	1.1-1.4	.01
Charlson index	1.1	1.01-1.3	.03
Katz index (from A = 0 to G = 6)	1.2	1.02-1.3	.02
Aortic regurgitation (from none = 0 to severe = 3)	1.8	1.3-2.5	.0004

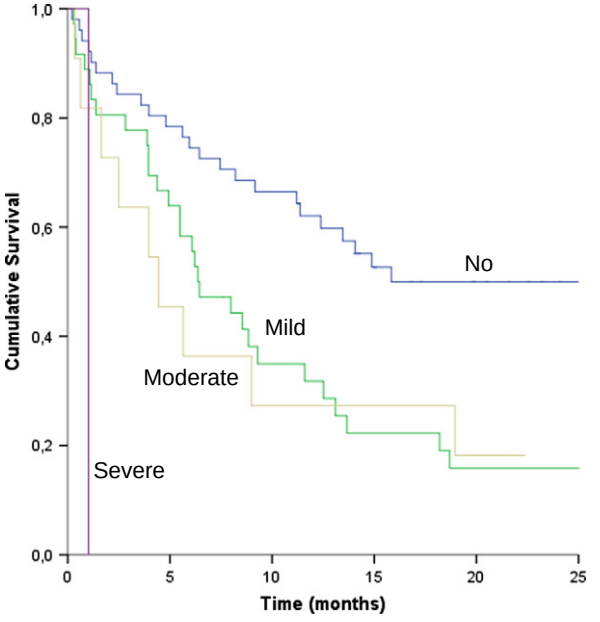
Abbreviation: HR, hazard ratio.

Figure 3



Cumulative survival in centenarians with LVEF <0.5 or significant heart valve disease (n = 45) versus those without these abnormalities (n = 55).

Figure 4



Cumulative survival of 100 centenarians who underwent echocardiography according to the degree of aortic regurgitation (none n = 51, mild n = 36, moderate n = 11, severe n = 2).

Limitations

The main limitation of our study is the representativeness of the sample. In addition to the nonrandom selection of the study population, the smaller number of males makes the analyses of gender differences difficult. Centenarians are a sparse population and therefore difficult to study properly,[25] mainly because of heterogeneity and the possibility of selection bias. The fact that about 60% of our centenarians were recruited at discharge after a period of presumed instability may have affected some of our findings. Thus, the results of our study may not be extrapolated to the entire population of centenarians. Nevertheless, the baseline characteristics of our sample are similar to those described in previous longevity studies in terms of comorbidity,[25] healthy habits, functional capacity,[9,26] cognitive impairment, and

Table VI. Principal electrocardiographic findings in centenarians of our study in comparison with previous studies

	Martínez-Sellés	Andersen-Ranberg[4]	Rabuñal[3]	Basile[12]	Lakkireddy[19]	Klich-Raczka[18]	Suzuki[17]	Chessari[16]	Wakida[15]	Cornu[13]
Year of Publication	2014	2013	2012	2011	2003	2003	2001	1996	1994	1979
Number of centenarians	118	134	80	42	132	35	234	49	32	25
Enrollment	Living at home/ nursing home/ hospital discharge	Community dwelling and institutionalized	Community dwelling	Healthy living independently	No evidence of cardiac disease	Community dwelling	Community dwelling	Living at home	Community dwelling	?
ECG findings (%)										
Normal ECG	26	–	7	17	7	6	–	–	–	20
Myocardial infarction	16	10	16	16	10	–	20	0	–	–
Atrial fibrillation	20	16	26	12	30	–	5	12	0	4
Pacemaker	3	3	0	10	0	–	1	0	0	0
First-degree AV block	14	–	10	24	17	17	?	10	25	40
Left ventricular hypertrophy	9	–	9	31	3	–	6	–	–	0
Left bundle branch block	16	–	10	0	17	–	1	6	–	12
Right bundle branch block	10	–	15	17	5	–	7	10	19	12

family environment.[9] Moreover, to our knowledge, this is the largest multicenter study using standardized echocardiography in centenarians and the largest to define the rate of normal ECG in these subjects.

In conclusion, our results add to our knowledge of cardiac anatomy and function in centenarians and, thus, help us to better understand the process of aging and exceptional longevity. Centenarians have frequent ECG alterations and abnormalities in echocardiography, but there is no clear pattern of age-related changes in this population. More than one fifth has atrial fibrillation, and most have diastolic dysfunction. Left ventricular dilation was present in 14% and was independently associated with the ability to walk 6 meters. The presence of significant abnormalities in echocardiography was associated with mortality.

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Appendix

A standard 12-lead ECG was recorded (unless the technique was unavailable on the day of clinical assessment) and analyzed by 2 researchers who were blind to clinical data according to the classification included in the Minnesota Code (Rose GA and Blackburn H, Cardiovascular Survey Methods. Geneva: World Health Organization, 1968). Discrepancies were resolved by a second joint review of the ECG. Electrocardiogram was considered normal if sinus rhythm was present, with heart rate between 60 and 100 beats per minute, normal repolarization, and absence of LV hypertrophy, left atrial enlargement, bundle branch block, atrioventricular block, and pathologic Q waves.

Echocardiography was performed to all patients, unless the technique was unavailable on the day of clinical assessment. Transthoracic echocardiography was performed, with image acquisition according to the guidelines of the American Society of Echocardiography (Lang et al, *J Am Soc Echocardiogr*. 2005;18(12):1440-63). The measurements were LV end-diastolic dimension, LV end-systolic dimension, ventricular septal thickness, LV posterior wall thickness, left atrial dimension, and right ventricular end-diastolic dimension. Doppler measurements included assessment of pulmonary artery systolic pressure and severity of valve stenosis and regurgitation. Aortic root diameter was measured from the parasternal long axis using a 2-dimensional guided M-mode recording. In recordings for which M-mode was not properly aligned, measurements were taken directly from 2-dimensional imaging. Left ventricular ejection fraction was calculated from LV dimensions using the Teichholz method and from the LV volumes using the Simpson method. We defined systolic dysfunction as the presence of an LVEF <50%. Left atrial end-systolic transverse dimension and mid-right ventricular transverse end-diastolic dimension were measured in the apical 4-chamber view. Pulmonary artery systolic pressure was determined from the highest tricuspid regurgitation velocity recorded in multiple views using the modified Bernoulli equation. Severity of valvular regurgitation was assessed based on standard color Doppler criteria. We followed the recommendations of the European Guidelines on Heart Valvular Disease to assess the severity of the valve disease (Vahanian et al, *Eur Heart J* 2012;33(19):2451-96). Aortic valve area was calculated using the continuity equation. Diastolic dysfunction was evaluated in patients with sinus rhythm by taking into account the mitral inflow E/A ratio, the tissue Doppler E′, and the deceleration time. A pulsed Doppler transmitral flow velocity profile was obtained from the apical 4-chamber view; peak transmitral velocities of early rapid filling (E) and late filling with atrial contraction (A) were recorded. The deceleration time of early filling was calculated at the time between peak E and the upper deceleration slope extrapolated to the baseline. E/A was calculated to reflect the LV relaxation. Real-time pulse-wave tissue Doppler imaging was performed to record longitudinal velocities at the mitral annulus. Early diastolic (E′) and late diastolic (A′) mitral annulus velocities were measured, and the averages of 3 consecutive cardiac cycles were reported. E/E′ ratios were calculated for the prediction of LV filling pressure. E/A was used for initial categorization of diastolic pattern, <1 reflects slowing of LV relaxation. Diastolic function was defined according to standard Doppler and tissue Doppler imaging parameters as following: normal ($E/A > 1$, $E'/A' > 1$), impaired relaxation ($E/A < 1$, $E'/A' < 1$), pseudonormal ($E/A > 1$, $E'/A' < 1$), or restrictive pattern ($E/A > 1$, $E'/A' < 1$, and $E' \leq 8$ cm/s). All studies were sent to a core laboratory (Instituto de Ciencias del Corazón, Hospital Clínico Universitario de Valladolid, Spain), where an experienced observer who was blind to clinical data analyzed the findings using the EchoPAC version 110.0.2 software (GE Healthcare, Horten, Norway).

Supplementary Table. Laboratory data of centenarians by ECG and echocardiography group

	Normal ECG (n = 27)	Abnormal ECG (n = 76)	*P*	LVEF >0.5 and no significant valve disease (n = 55)	Echo with significant abnormalities (n = 45)	*P*
Hemoglobin (g/dL)	11.9 ± 2.1	11.9 ± 1.6	.91	12.0 ± 1.7	11.5 ± 1.7	.48
Serum creatinine (mg/dL)	0.9 ± 0.4	1.2 ± 0.5	.01	1.1 ± 0.5	1.2 ± 0.5	.45
Blood glucose (mg/dL)	104.7 ± 31.0	113.0 ± 44.8	.36	105.6 ± 32.0	116.8 ± 52.8	.21
Hemoglobin A_{1c} (%)	6.0 ± 1.1	6.1 ± 1.1	.77	5.8 ± 0.9	6.4 ± 1.3	.01
Cholesterol (mg/dL)	164.3 ± 44.8	162.1 ± 40.6	.82	162.6 ± 42.2	157.2 ± 40.2	.53
LDL (mg/dL)	91.8 ± 29.8	96.3 ± 30.8	.54	91.6 ± 31.8	92.3 ± 29.3	.92
HDL (mg/dL)	50.8 ± 28.7	44.4 ± 15.1	.22	49.5 ± 21.9	42.6 ± 15.6	.08
Triglycerides (mg/dL)	100.0 ± 37.9	110.3 ± 54.4	.31	108.5 ± 58.3	107.1 ± 41.2	.89
C-reactive protein (mg/L)	10.5 ± 11.7	19.8 ± 33.8	.08	12.3 ± 24.7	19.6 ± 28.4	.22
Pro-BNP (ng/L) (n=67)	1836 ± 1884	6984 ± 9509	.006	2942 ± 3704	9016 ± 1164	.01
[median]	[1045]	[2936]		[1415]	[4062]	
BNP (ng/L) (n=32)	421 ± 595	1062 ± 3660	.48	482 ± 643	5066 ± 11496	.12
[median]	[198]	[236]		[236]	[255]	
Troponin T (ng/mL) (n=56)	26.9 ± 24.2	23.8 ± 31.3	.84	27.3 ± 34.3	13.7 ± 2.9	.20
[median]	[22]	[6.6]		[0.14]	[0.94]	
Troponin I (ng/mL) (n=39)	0.03 ± 0.04	0.09 ± 0.16	.18	0.08 ± 0.16	0.07 ± 0.10	.98
[median]	[0.02]	[0.02]		[0.02]	[0.03]	

Abbreviations: *Echo*, echocardiography; *LDL*, low-density lipoprotein; *HDL*, high-density lipoprotein.