ELECTROCARDIOGRAPHIC PREDICTORS OF SIX-MINUTE WALKING DISTANCE AMONG 63-76-YEAR-OLD WOMEN

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Master's Thesis in Sports and
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ABSTRACT

Anthropometric factors, physical activity, and chronic diseases are known to predict walking distance in the six-minute walking test, but the predictive value of electrocardiographic (ECG) variables in a non-clinical population is unknown. The aim of this study was to determine how different ECG variables predict walking distance in the six-minute walking test among 63-76-year-old Finnish female twins (n=434) and assess if ECG measurements give extra information for predicting walking distance in addition to measurements performed routinely by a physician in a normal clinical examination.

Main measurements performed were a standard 12-lead resting ECG and six-minute walking test. Age, heart rate, body mass index (BMI), chronic diseases, use of beta-blockers, physical activity, and resting blood pressure were regarded as information typically obtained by a physician in a clinical examination either through interviewing or observing and measuring the patient. These variables were used for the adjustment of results. Results were analyzed using linear regression analysis. Subjects with myocardial infarction, conduction abnormalities, and electronic pacing were excluded (n=48).

Mean distance walked during six minutes was 530 m. The best electrocardiographic predictors of a long walking distance were high TV_5, high TII, and high RV_5, but the explanation rates were small (0.04, 0.035, and 0.03, respectively). From clinical information low BMI, absence of chronic diseases, and high physical activity were the best predictors of distance walked, and explanation rates were larger than for the ECG variables (0.117, 0.084, and 0.07, respectively). When ECG variables were adjusted for age, heart rate, BMI, chronic diseases, beta-blockers, physical activity, and resting blood pressure, explanation rates remained small. The greatest explanation rate was for SV_3 (0.015), but only RV_5 reached statistical significance (R^2=0.008, P=0.049).

In conclusion, BMI, chronic diseases, and physical activity are good predictors of walking distance in relatively healthy older women, but the predictive value of ECG variables is smaller when cases with myocardial infarction are excluded. After including other variables in the models, additional information given by ECG variables is small.

Key Words: electrocardiography, six-minute walking test, the aged

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TIIVISTELMÄ

Tämän tutkimuksen tarkoituksena oli selvittää miten erilaiset elektrokardiografiset (EKG) muuttujat ennustavat käveltyä matkaa kuuden minuutin kävelytestissä 63-76-vuotiailla suomalaisilla kaksosnaisilla (n=434). Tämän lisäksi tarkoituksena oli selvittää antavatko EKG-muuttujat lisätietoa kävelymatkan ennustamiseen niiden muuttujien lisäksi, jotka lääkäri voi selvittää tavanomaisessa kliinisessä tutkimuksessa.

Koehenkilöille tehtiin standardi 12-kytkentäinen lepo-EKG-mittaus sekä kuuden minuutin kävelytesti. Ikä, syke, painoindeksi (BMI), krooniset sairaudet, beetasalpaajien käyttö, fyysinen aktiivisuus sekä lepoverenpaine katsottiin sellaisiksi muuttujiksi, jotka lääkäri voi kliinisessä tutkimuksessa selvittää. Nämä muuttujat kysyttiin ja selvitettiin koehenkilöiltä, ja niitä käytettiin tulosten vakiointiin. Tulokset analysoitiin lineaarisella regressioanalyysillä. Analyyseistä suljettiin pois koehenkilöt, joilla oli sydäninfarkti, haarakatkos tai sydämen tahdistin (n=48).

Koehenkilöt kävelivät keskimäärin 530 m kuuden minuutin aikana. Pitkän kävelymatkan parhaat elektrokardiografiset ennustajat olivat korkea TV_5 (R^2=0.04), korkea TII (R^2=0.035) ja korkea RV_5 (R^2=0.03). Kliinisistä muuttujista matala BMI (R^2=0.117), kroonisten sairauksien puuttuminen (R^2=0.084) sekä runsas fyysinen aktiivisuus (R^2=0.07) olivat pitkän kävelymatkan parhaat ennustajat. Kun EKG-muuttujat vakioitiin iällä, sykkeellä, BMI:llä, kroonisilla sairauksilla, beetasalpaajien käytöllä, fyysisellä aktiivisuudella sekä lepoverenpaineella, selitysosuudet pysyivät pieninä. Suurin selitysosuus oli SV_3:lla (0.015), mutta ainoastaan RV_5 oli tilastollisesti merkitsevä (R^2=0.008, P=0.049).

Johtopäätöksinä voidaan todeta, että BMI, krooniset sairaudet ja fyysinen aktiivisuus ennustavat hyvin kuuden minuutin kävelymatkaa suhteellisen terveillä ikääntyneillä naisilla, mutta EKG-muuttujien ennusteellinen arvo on näitä pienempi aineistossa, josta sydäninfarktitapaukset on poissuljettu. Kun EKG-muuttujat vakioidaan kliinisillä muuttujilla, niiden antama lisäinformaatio on myös pieni.

Avainsanat: elektrokardiografia, kuuden minuutin kävelytesti, ikääntyneet

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1 INTRODUCTION

Six-minute walking test is an easy and safe test to estimate functional exercise capacity of elderly persons (Enright et al 2003). Six-minute walking distance is known to be reduced by increasing age (Enright and Sherrill 1998, Troosters et al 1999, Lord and Menz 2002, Enright et al 2003), weight (Enright and Sherrill 1998, Troosters et al 1999, Enright et al 2003), and body mass index (Hulens et al 2003), female gender (Troosters et al 1999, Camarri et al 2006), and several chronic diseases, such as obstructive lung disease, heart failure, arthritis, and neuromuscular diseases (McGavin et al 1978, Bittner et al 1993). On the other hand, walking distance is known to be increased by greater height (Enright and Sherrill 1998, Troosters et al 1999, Camarri et al 2006) and lower-limb muscle strength (Lord and Menz 2002, Hulens et al 2003), and by physical activity (Harada et al 1999, Hulens et al 2003).

The role of electrocardiographic (ECG) measurements in predicting six-minute walking distance is unknown. ECG findings are known to be influenced by many factors, such as aging (Yasumura and Shibata 1989, Reardon and Malik 1996, Mangoni et al 2003), obesity (Frank et al 1986, El-Gamal et al 1995, Park and Swan 1997, Alpert et al 2000), and physical activity (Bjornstad et al 1993, Schuit et al 1998, Hannukainen et al 2005), which are for a large part the same factors as those predicting six-minute walking distance. Alterations in ECG have prognostic significance for future health, because some ECG abnormalities (e.g. T-wave inversions) are associated with increased risk of cardiovascular disease morbidity and mortality (Larsen et al 2002, Robbins et al 2003, Triola et al 2005, Yamazaki et al 2005, Rautaharju et al 2006a, Rautaharju et al 2006b).

Numerous ECG criteria, which are largely dependent on fixed voltage thresholds, have been proposed for the diagnosis of left ventricular hypertrophy (LVH), for example Cornell voltage ($RaVL + SV_3 > 2.8$ mV for men and > 2.0 mV for women) (Casale et al 1987) or Sokolow-Lyon voltage ($SV_1 + RV_5 > 3.5$ mV) (Sokolow and Lyon 1949). LVH has been shown to be associated with decreased exercise capacity (Olsen et al 2001, Pierson et al 2004) and this can negatively affect walking ability. T-wave flattenings and inversions are signs of myocardial ischaemia (Achar et al 2005), which can reduce walking ability. Other repolarization abnormalities, such as reduced velocity of repolarization (lengthened QT interval) may contribute to diastolic dysfunction, which through different mechanisms can lead to decreased exercise capacity (Gradman and Alfayoumi 2006) and walking ability.

The aim of this study was to determine how different resting ECG variables predict walking distance in the six-minute walking test in a group of relatively healthy older women. The aim was also to assess if ECG measurements give extra information for predicting walking distance in addition to measurements made by a physician in a normal clinical examination (e.g. chronic diseases, medication, physical activity).

2 METHODS

2.1 Participants

The present study is part of the Finnish Twin Study on Aging (FITSA) (Pajala et al 2004). The study sample was recruited from among the participants in the Finnish Twin Cohort Study (Kaprio and Koskenvuo 2002). The zygosity of the participating pairs was initially determined through a validated questionnaire (Sarna et al 1978).

An invitation to participate in FITSA was sent to 414 female pairs aged 63 to 76 years old surviving in 2000. To be included, both twin pair members had to agree to participate. The reasons for non-participation were that one or both sisters were unwilling to take part (106 pairs), had poor health status (85 pairs), or had died after vital status was last updated for all cohort members (6 pairs). As a result of the procedures, the study group consisted of 217 twin-sister pairs, including 102 monozygotic (MZ) pairs and 115 dizygotic (DZ) pairs.

Six-minute walking test was performed by 170 MZ and 189 DZ individuals. Reasons for not completing the test were no physician's permission to perform the test (n=54), lack of time (n=12), and the test was interrupted or participant was unwilling to perform the test (n=9).

Participants were informed about the study and written informed consent was obtained. The study was approved by the Ethics Committee of the Central Hospital of Central Finland.

2.2 Electrocardiographic Measurements

Using a Nihon Kohden Cardiofax Caps 12, a standard 12-lead resting ECG was recorded at 25 mm/s and 1 mV/cm standardization. ECG variables presented in Table 1 were measured. RaVL, SV_3, TV_1, TV_5, and TII were measured manually and the other variables were collected from the automatic listings of the ECG recorder. Conduction abnormalities were assessed by the specialist in internal medicine. All ECG measurements were carried out blind to other data.

2.3 Six-Minute Walking Test

Maximal walking distance was assessed using a validated six-minute walking test (ATS Statement 2002). The participants were requested to walk up and down a 50 m indoor straight track for six minutes and to complete as many laps as possible. The standardized protocol and security conditions followed the American Thoracic Society Statement (ATS Statement 2002). The distance covered by the end of the six minutes was recorded as the outcome.

2.4 Health Ascertainment and Assessment of Physical Activity

All participants underwent a 30-minute clinical examination by a physician. Self-reports of acute and chronic diseases and medication had been obtained earlier and were confirmed by the physician. Chronic diseases taken into account in this study were arthrosis of hip (n=45), knee (n=174), or ankle (n=19), rheumatoid arthritis (n=17), cerebral haemorrhage and stroke (n=23), and Parkinson´s disease (n=1), which may affect the results of the six-minute walking test. Diseases were dicothomized for yes or no, as was also the use of beta-blockers (n=111). Resting blood pressure (BP) was measured and classified into normal (diastolic BP < 100 mmHg, n=356) and abnormal (diastolic BP ≥ 100 mmHg, n=35). In the examination body height and weight of participants were measured and from these body mass index (BMI) was calculated (kg/m^2).

In the assessment of the present status of physical activity, a self-report scale designed by Grimby (1986) was used, with slight modifications. The highest category of the initial scale was divided into 2 categories, separating those participating in regular exercise fitness activities from those active in competitive sports. The 7-point scale ranged from 1 (hardly any activity) to 7 (participation in competitive sports). For this study participation in physical activity was dicothomized as follows. Participants were considered sedentary if they reported no other activity than light walking once or twice a week (n=126). In other cases participants were considered physically active (n=266).

2.5 Statistical analyses

Statistical analyses were run on SPSS, version 13.0. The predictive value of ECG and clinical variables for walking distance was analyzed using linear regression analysis, as was also the additional information given by ECG variables when clinical variables were taken into account. Because myocardial infarction has an effect on walking ability and specific conduction abnormalities make it impossible to interpret other ECG features in a meaningful way, participants with myocardial infarction (n=19), left bundle branch block (n=16), right bundle branch block (n=9), left anterior hemiblock (n=1), or electronic pacing (n=3) were excluded from statistical analyses investigating the predictive value of other ECG alterations/parameters for walking ability. Significance was set at P less than .05 (two-sided) for all tests.

3 RESULTS

Age, anthropometry, and results of the six-minute walking test and ECG measurements are shown in Table 1. Participants with myocardial infarction walked on average 488 m and the other participants 531 m during six minutes (P=0.048). The difference in walking distance between participants with conduction abnormalities and the others was not statistically significant (526 m vs. 530 m, P=0.810). Six-minute walking distance of all participants excluded from further statistical analyses did not differ statistically significantly from the distance covered by the included participants (511 m vs. 531 m, P=0.145).

Table 1 Age, anthropometry, and results of the six-minute walking test and ECG measurements

	Mean±SD	Range	n
Age (y)	68.6±3.4	63-76	434
Height (cm)	158.6±6.1	142.0-178.0	434
Weight (kg)	70.1±12.0	39.1-115.6	434
BMI (kg/m^2)	27.9±4.7	16.9-45.6	434
Six-minute walking test (m)	529.7±75.4	270.0-725.0	359
Heart rate (beats/min)	68.5±11.3	45-122	434
PR interval (ms)	165.2±25.8	100.0-260.0	386
QRS duration (ms)	86.6±8.5	64.0-144.0	390
QT duration (ms)	397.0±30.4	276.0-500.0	390
QTC (ms)	412.4±22.9	312.0-513.0	390
QRS axis (°)	29.2±26.9	-41.0-88.0	390
P axis (°)	47.3±21.4	-58.0-97.0	386
T axis (°)	44.4±32.6	-84.0-256.0	390
RaVL (mm)	4.6±3.0	0.0-15.5	390
SV_3 (mm)	6.9±3.8	0.0-19.5	388
Cornell voltage, RaVL + SV_3 (mm)	11.5±4.9	0.5-29.0	383
SV_1 (mV)	0.9±0.4	0.1-2.3	390
RV_5 (mV)	1.4±0.5	0.3-3.1	389
Sokolow-Lyon voltage, SV_1 + RV_5 (mV)	2.3±0.7	0.8-5.0	389
TV_1 (mm)	0.0±1.0	-3.0-4.0	390
TV_5 (mm)	1.8±1.5	-2.5-7.5	389
TII (mm)	1.6±1.1	-1.5-5.5	390

From all ECG measurements performed those presented in Table 2 reached statistical significance in explaining the variation in walking distance, with high TV_5, high TII, and high RV_5 being the best predictors of long walking distance. Cumulative explanation rate for statistically significant ECG variables was 0.116. When ECG variables were adjusted for age, the best predictors of distance walked remained same. After adjustment only SV_1 lost its statistical significance.

Table 2 Univariate and age-adjusted results of ECG measurements as predictors of the six-minute walking distance

	β	R^2	P	Cumulative R^2	*β	*R^2	*P
PR interval	-0.131	0.017	0.018	0.017	-0.107	0.010	0.050
QRS axis	0.136	0.019	0.013	0.029	0.113	0.013	0.038
RV_5	0.174	0.030	0.002	0.055	0.160	0.026	0.003
RaVL	-0.143	0.021	0.009	0.063	-0.128	0.017	0.019
SV_1	0.116	0.013	0.036	0.074	0.096	0.009	0.078
SV_3	-0.128	0.016	0.020	0.093	-0.116	0.016	0.033
TV_5	0.201	0.040	< 0.001	0.109	0.201	0.040	< 0.001
TII	0.186	0.035	0.001	0.116	0.190	0.036	< 0.001

*Age-adjusted results

Of the clinical variables, low BMI, absence of chronic diseases, and high physical activity were the best predictors of distance walked during six minutes (Table 3). β-coefficients and explanation rates of heart rate and resting blood pressure were small and they did not reach statistical significance. Cumulative explanation rate for all clinical variables was 0.294. After adjustment for age, the best predictors of walking distance were the same with small changes in β-coefficients and explanation rates.

Table 3 Univariate and age-adjusted results of clinical variables as predictors of the six-minute walking distance

	β	R^2	P	Cumulative R^2	*β	*R^2	*P
Age	-0.203	0.041	< 0.001	0.041			
Heart rate	-0.056	0.003	0.311	0.045	-0.059	0.004	0.276
BMI	-0.342	0.117	< 0.001	0.165	-0.349	0.122	< 0.001
Chronic diseases	-0.290	0.084	< 0.001	0.217	-0.295	0.087	< 0.001
Beta-blockers	-0.176	0.031	0.001	0.243	-0.163	0.027	0.003
Physical activity	0.264	0.070	< 0.001	0.286	0.248	0.061	< 0.001
Resting blood pressure	-0.093	0.009	0.091	0.294	-0.102	0.011	0.058

*Age-adjusted results

Multivariately adjusted results of ECG measurements as predictors of the six-minute walking distance are shown in Table 4. After adjustment for age, heart rate, BMI, chronic diseases, beta-blockers, physical activity, and resting blood pressure, β-coefficients and explanation rates were small. The greatest explanation rate was for SV_3, but only RV_5 reached statistical significance. Cumulative explanation rates for each ECG variable and clinical variables were from 0.294 (QRS axis and RaVL) to 0.309 (SV_3). Together all statistically significant ECG variables and clinical variables explained 34.2 % of the variation in walking distance.

Table 4 Multivariately adjusted results of ECG measurements as predictors of the six-minute walking distance

	*β	*R^2	*P	Cumulative R^2
PR interval	-0.048	0.007	0.317	0.301
QRS axis	-0.021	0.000	0.675	0.294
RV_5	0.096	0.008	0.049	0.302
RaVL	-0.006	0.000	0.900	0.294
SV_1	0.030	0.001	0.524	0.295
SV_3	-0.065	0.015	0.176	0.309
TV_5	0.074	0.004	0.140	0.298
TII	0.076	0.005	0.122	0.299

* Adjusted for age, heart rate, BMI, chronic diseases, beta-blockers, physical activity, and resting blood pressure

4 DISCUSSION

To our knowledge, this was the first study to investigate the role of ECG variables as predictors of the six-minute walking distance. Participants of this study walked on average 530 m during six minutes and the best electrocardiographic predictors of long walking distance were high TV_5, high TII, and high RV_5. Explanation rates were small. Low BMI, absence of chronic diseases, and high physical activity were the best clinical predictors of the six-minute walking distance and explanation rates were greater than for ECG variables. Clinical variables explained 29.4 % of the variance in walking distance. When ECG variables were adjusted for clinical variables, their explanation rates remained small. Together all statistically significant ECG variables and clinical variables were able to explain 34.2 % of the variance in walking distance.

The role of single ECG variable in explaining variance was small, but together eight statistically significant ECG variables explained 11.6 % of variance. One reason for small explanation rates and β-coefficients is that participants with serious heart diseases (myocardial infarction, conduction abnormalities, electronic pacing) were excluded from the analyses. In persons who have healthy heart, heart function does not limit exercise capacity and walking ability in the same way as in persons with known heart disease (e.g. myocardial infarction, heart failure). In this study, participants with myocardial infarction walked clearly shorter distance during six minutes than the other participants, and 7 participants with myocardial infarction were not able to perform the test at all.

TV_5, TII, and RV_5 were positively and the most strongly associated with six-minute walking distance in univariate analyses. Positive T-wave is usually a sign of normal ventricular repolarization (Yan et al 2003), while low or negative T-wave may be a sign of reduced heart function and thus limit exercise capacity and walking ability. The cause of a high-voltage QRS complex and thus also high RV_5 most often is increased muscle mass of the heart resulting from the cardiac hypertrophy (Guyton and Hall 2000). Cardiac hypertrophy is not always a pathological state because cardiac hypertrophy can also be caused by physical training and then the heart size is generally within the upper range of normal limits and is characterized by normal systolic and diastolic function (Gradman and Alfayoumi 2006). In this case exercise capacity and also six-minute walking distance can be enhanced through functional changes in the heart, such as greater stroke volume and cardiac output.

After adjustment for clinical variables, independent explanation rates of ECG variables were smaller than in univariate analyses and only one variable was statistically significant. One possible reason for smaller explanation rates is that among clinical variables there were factors which are known independently to cause changes in ECG findings (e.g. age, obesity) (Yasumura and Shibata 1989, Reardon and Malik 1996, Park and Swan 1997, Alpert et al 2000). Thus, ECG findings do not have great independent predictive value and this also show that six-minute walking distance is explained more by other factors than heart function in persons without known heart disease. According to this study, low BMI, absence of chronic diseases, and high physical activity were better predictors of six-minute walking distance than ECG variables. Low BMI, absence of chronic diseases, and high physical activity have shown to be good predictors of six-minute walking distance also in other studies (McGavin et al 1978, Bittner et al 1993, Harada et al 1999, Hulens et al 2003).

BMI predicted negatively the six-minute walking distance. Walking ability is often impaired as a direct consequence of obesity due to excess weight bearing and increased workload (Mattson et al 1996). Walking ability can also be reduced as an indirect consequence of mechanical complications such as osteoarthritis or pain in the feet or ankles (Messier et al 1994), the knees (Messier 1994), or the hips (Hart and Spector 1993, Oliveria et al 1999).

The presence of chronic diseases (other than heart diseases) was also a negative predictor of the six-minute walking distance. Chronic diseases such as arthrosis of hip or knee, or stroke may well reduce walking distance through increased pain and limited range of motion in the hip or knee, or inability to produce correct movement patterns needed in walking. Also other chronic diseases not taken into account in this study (e.g. multiple sclerosis) can reduce the six-minute walking distance.

Physical activity was a positive predictor of the six-minute walking distance. The greater walking distance of physically active participants can, for example, be explained by better exercise capacity (Asikainen et al 2002, Toraman et al 2004) and lower-limb muscle strength (Rogers and Evans 1993). On the other hand, the overall health status of physically active participants may have been better than in sedentary participants, and thus can partly explain the greater walking distance in physically active participants.

According to Ortega-Alonso et al (in press), 20 % of the variance in the six-minute walking distance accounted for by genetic influences in this material. With the studied factors it was possible to explain 34 % of the remaining 80 % of variance. Part of the remaining unexplained proportion of variance in this study can, for example, be explained by weight, height, lower-limb muscle strength, and peakVO_2, which have shown to be predictors of six-minute walking distance in other studies (Enright and Sherrill 1998, Troosters et al 1999, Lord and Menz 2002, Enright et al 2003, Hulens et al 2003, Camarri et al 2006). Other possible predictors could be such factors as decreased mental status (Enright et al 2003) or motivation. The role of spirometric measurements as predictors of six-minute walking distance was small in this study material. The best predictors were FEV_1 and FVC (R^2=0.039 and 0.038, respectively) (Alaoja 2005).

There are some limitations in this study. This study concerned only women with limited age range, which limits the generalizability of the results. Also, twin pairs with the poorest health status did not participate in the study and participants with serious heart diseases were excluded from the analyses, which further limit the generalizability and can affect the small predictive value of ECG variables. Thus, the results of this study are applicable only for relatively healthy older women without serious heart diseases. Although participants were twins, results were analyzed as if they would have been independent individuals. Taking into account clustering (twin pairs) in statistical analyses leads to small changes in some statistical parameters (distribution parameters, statistical significances) presented. However, this does not influence the mean values presented.

In conclusion, BMI, chronic diseases, and physical activity are good predictors of the six-minute walking distance in relatively healthy older women. The predictive value of ECG variables is smaller. After adjustment for age, heart rate, BMI, chronic diseases, use of beta-blockers, physical activity, and resting blood pressure, information given by ECG variables for predicting six-minute walking distance is small. Thus, the six-minute walking distance is explained more by other factors than heart function in older women without heart diseases.

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