Secondary Prevention of Coronary Heart Disease is Less Agressive in Patients Over 64 Years

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Introduction and objectives. Although elderly people has a higher incidence of coronary heart disease, this group is seldom included in clinical trials. Studies performed in Spain on elderly coronary heart disease patients have been conducted in hospital settings. The aim of our study was to analyse wether the management of coronary heart disease patients over 64 years of age cared by family physicians differed from that of the rest.

Patients and method. Cross-sectional multicentre study embedded in a clinical trial on 1,022 patients with stable coronary heart disease in which socio-demographic variables, comorbidity, treatment and cardiovascular risk- factor control were collected.

Results. Mean age was 64 ± 10, 74.0% were men and 53.8% of subjects were over 64 years. Patients over 64 years had a greater cardiovascular comorbidity (87.7 *vs* 82.6%; p = 0.002) and received lower number of drugs than the rest in the prevention of recurrences (60.4 *vs* 70.9%; p < 0.001). Probability to receive less than two drugs on secondary prevention by subjects over 64 years was 0.45 (95% CI, 0.30-0.68) despite comorbidity, sex and cardiovascular risk profile.

Conclusions. Coronary heart disease patients over 64 years receive less drugs for coronary event recurrence prevention than their younger counterparts despite their worse cardiovascular risk profile.

Key words: *Coronary disease. Aging. Prevention.*

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La prevención secundaria de la enfermedad coronaria es menos agresiva en los pacientes de más de 64 años

Introducción y objetivos. A pesar de que la población anciana presenta una mayor prevalencia de enfermedad coronaria, se encuentra escasamente representada en los ensayos clínicos. Los estudios realizados en España en ancianos con enfermedad coronaria se han llevado a cabo desde hospitales. El objetivo de este estudio fue analizar si los pacientes coronarios mayores de 64 años atendidos por los médicos de familia reciben un tratamiento diferente de los más jóvenes en la prevención de recurrencias coronarias.

Pacientes y método. Estudio transversal multicéntrico, anidado en un ensayo clínico en el que se recogen las variables sociodemográficas, la comorbilidad cardiovascular, el tratamiento (antiagregantes, bloqueadores beta, hipolipemiantes, inhibidores de la enzima conversiva de la angiotensina) y control de factores de riesgo de 1.022 pacientes con enfermedad coronaria estable, adscritos a 23 áreas básicas de salud.

Resultados. La edad media fue de 64 ± 10 años, el 74,0% eran varones y 53,8% eran mayores de 64 años. Los pacientes mayores de 64 años presentaron con mayor frecuencia comorbilidad cardiovascular (87,7 frente a 82,6%; p = 0,02) y recibieron menos fármacos en la prevención de recurrencias (60,4 frente a 70,9%; p < 0,001). La *odds ratio* de recibir menos de dos fármacos en los pacientes de más de 64 años fue de 0,45 (IC del 95%, 0,30-0,68), independientemente de la comorbilidad, el sexo y el perfil de riesgo cardiovascular.

Conclusiones. Los pacientes coronarios mayores de 64 años reciben menos fármacos que los más jóvenes en la prevención de recurrencias, a pesar de presentar un peor perfil de riesgo cardiovascular.

Palabras clave: *Enfermedad coronaria. Geriatría. Prevención.*

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ABBREVIATIONS

AMI: acute myocardial infarction.

INTRODUCTION

Cardiovascular disease is the main cause of death in Spain. Ischemic heart disease resulted in more than 30000 deaths during 2002.[1] The incidence of ischemic heart disease and associated mortality tends to increase with advancing age[2] and it is one of the most common diseases in persons over the age of 65 years. In this age group it accounts for 12.3% of deaths in men, 10.4% of deaths in women[3] and 17.4% of all visits to primary health care centers.[4] Fifteen percent of the population in Spain is already over 65 years old, and this percentage is expected to reach 20% by the year 2031.[5] Current life expectancy is 73.4 years in men and 81.3 years in women.[6]

Despite the fact that 30% of patients with acute myocardial infarction (AMI) are over 75 years of age, this population is very poorly represented in clinical trials aimed to improve the treatment and the secondary prevention of ischemic heart disease.[7,8] Although some studies suggest that aggressive secondary prevention in older patients is accompanied by reduced mortality from ischemic heart disease,[9] surveys undertaken in Spanish hospitals have shown that these patients in fact receive less intense therapy for recurrent coronary events.[10]

The aim of this study was to determine whether patients older than 64 years of age with stable coronary heart disease, seen in primary health care centers, receive different treatment for the prevention of recurrent coronary events compared to younger patients, and if so to elucidate the possible reasons.

PATIENTS AND METHODS

Study design

Cross-sectional multicenter study incorporated in a clinical trial within the community.

Patients

Inclusion criteria

Men and women 30 to 80 years of age were eligible for recruitment if they had survived a first or recurrent AMI or had documented angina (clinical charts or hospital report documenting electrocardiographic changes associated with pain or a positive exercise stress test or a coronary angiography showing more than 50% stenosis lesions) during the previous 6 months and who were clinically stable at the time. The study was undertaken during 1999 and 2000.

Exclusion criteria

Patients were excluded if they refused to participate in the study, if they had a severe physical, or mental disorder, or if their short-term life expectancy was unfavorable (terminal patients), or if they had had an AMI within the previous 28 days.

Study area. The population served by 23 basic health care areas in Catalonia, northeast Spain.

Sample size. The study was powered to 80% with an alpha error of 0.05 in a bilateral comparison, assuming a 10% difference in the probability of receiving multiple therapy in patients older than 64 years of age compared to the 50% probability for the younger patients.

Identification and selection of participants. Possible candidates for inclusion in the study were identified from hospital discharge reports and from the registries of the corresponding basic health care areas. All patients for whom sufficient information was available were included.

Study variables

The following data were obtained from the primary care charts: administrative and demographic characteristics, the most recent coronary event leading to eligibility (unstable angina or AMI within the previous 6 years), a history of diabetes, hypertension, hypercholesterolemia, peripheral arteriopathy, current smoking status, anthropometrical measurements, glycemia, total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides, blood pressure and the use of anti-aggregating agents, beta-blockers, angiotensin converting enzyme (ACE) inhibitors or lipid-lowering drugs for the prevention of recurrent coronary events. Multiple therapy was considered to be the use of two or more of these drugs. Use of nitrates and calcium antagonists was also recorded even though they were not considered essential for secondary prevention.[11]

Hypercholesterolemia was considered to be well controlled when total cholesterol was below 190 mg/dL and LDL cholesterol below 115 mg/dL.[12] Likewise, blood pressure was considered to be under control when the systolic pressure was lower than 140

mm Hg and the diastolic pressure lower than 90 mm Hg.[13]

The number of visits to the primary care physician during the previous year was recorded. Very frequent visitors were considered to be patients who made nine or more visits, as this was the 75th percentile of the overall number of visits.[14] The cut-off point for analysis according to age was 65 years because, in absolute terms, ageing refers to all persons of 65 or older.[15] Patients over 64 years were classified into four groups according to the 25th, 50th and 75th age percentiles to determine the possible trends in secondary prevention treatment received according to age. The SF-12 Health Survey, which evaluates quality of life and which has been previously validated for use in Spain,[16] was administered at baseline.

Statistical analysis

Comparison of proportions between the two groups was done with the χ^2 test and comparison of the means for continuous variables with Student's *t* test. Logistic regression analysis, adjusted for possible confounding variables, was used to determine the odds ratio (OR) of receiving multiple treatment for the prevention of recurrent coronary events in patients over 64 years of age. Variables were incorporated into the regression model if their *P* value was <.1 in bivariate analysis with the variables multiple treatment and age >64 years.

RESULTS

The charts of 1664 patients with ischemic heart disease were reviewed in the 23 basic health areas. Forty-seven patients refused to participate in the study; 148 were excluded because they had had their last coronary event before 1993, 191 were excluded for mistaken diagnosis, 71 were excluded because they were older than 80 years, 22 had died before recruitment, 100 had severe concomitant disease preventing inclusion, 40 were unknown in their basic health area, and 23 patients were excluded because their charts were duplicated. The study therefore included a total of 1022 patients; their mean age was 64 ± 10 years, 74.0% were

TABLE 1. **Medical history, characteristics, treatment received, degree of control and quality of life according to age**

	≤ 64 years (n=471)	>64 years (n=550)	*P*
Sex, female (%)	18.9	30.5	<.001
Comorbid cardiovascular disease (%)			
Diabetes	24.0	34.5	<.001
Hypertension	48.1	63.2	<.001
Hypercholesterolemia	65.3	60.1	NS
Peripheral arterial disease	8.6	13.6	.01
Stroke	5.3	13.1	<.001
Any of the above	82.6	87.7	.02
Smoker, %	27.8	9.1	<.001
Chronic obstructive pulmonary disease, %	15.0	20.9	.02
Inclusion event, % unstable angina	46.8	54.5	.01
Frequent visitor, >8 visits/year (%)	30.9	35.2	NS
Drug therapy, %			
Anti-patelet agents	80.6	72.7	.003
Beta blockers	40.9	30.0	<.001
ACE inhibitors	26.9	30.2	NS
Lipid lowering agents	59.8	47.5	<.001
Two or more of the above	70.9	60.4	<.001
Nitrates	41.3	59.5	<.001
Calcium antagonists	37.0	43.5	.05
Systolic BP, mm Hga	129.6±16.7	135.1±17.4	<.001
Diastolic BP, mm Hga	79.0±10.4	76.3±9.5	<.001
BP<140/90, mm Hg (%)	65.7	76.5	.001
Total cholesterol, mg/dLa	210.6±42.6	207.2±37.6	NS
HDL cholesterol, mg/dLa	47.8±14.9	51.3±13.3	.002
LDL cholesterol, mg/dLa	133.4±38.9	130.0±33.0	NS
Total cholesterol<190 and LDL<115 mg/dL, %	16.8	17.4	NS
Triglycerides, mg/dLb	125.5 (96.2-184.7)	112.0 (83.0-149.0)	<.001
Baseline glycemia, mg/dLa	119.1 (48.4)	120.5 (42.1)	NS
Perceived physical healtha	43.7 (5.3)	43.0 (6.2)	NS
Perceived mental healtha	46.1 (7.8)	46.1 (8.0)	NS

ACE indicates angiotensin converting enzyme. aMean ± SD. bMedian (25th-75th percentile).

TABLE 2. **Factors related with receiving two or more drugs considered essential for the prevention of recurrent coronary events**

	Fewer than two drugs (n=356)	Two or more drugs (n=356)	*P*
Sex, female (%)	22.9	26.3	NS
Age >64 years, %	61.2	49.7	.001
Comorbid conditions, %			
Diabetes	29.4	29.9	NS
Hypertension	50.8	58.9	.01
Hypercholesterolemia	45.7	70.7	<.001
Peripheral arterial disease	11.7	11.2	NS
Stroke	11.0	8.4	NS
Any of the above	74.8	91.0	<.001
Smoker, %	10.6	19.2	.006
Chronic obstructive pulmonary disease, %	21.3	16.6	NS
Inclusion event, % unstable angina	58.7	47.0	.001
Frequent visitor, >8 visits/year (%)	32.3	33.9	NS
Systolic BP, mm Hg[a]	133.1 ± 17.2	132.5 ± 17.4	NS
Diastolic BP, mm Hg[a]	77.7 ± 9.4	77.3 ± 10.2	NS
BP<140/90, mm Hg (%)	60.1	77.5	<.001
Total cholesterol, mg/dL	210.0 ± 34.1	208.2 ± 41.9	NS
HDL cholesterol, mg/dL	51.2 ± 15.6	49.1 ± 13.6	NS
LDL cholesterol, mg/dL	132.1 ± 29.0	131.4 ± 37.9	NS
Total cholesterol<190 and LDL<115, mg/dL %	8.7%	21.6%	<.001
Triglycerides, mg/dLb	112.0 (82.0-149.0)	120.0 (89.0-168.0)	.001
Baseline glycemia, mg/dL	121.7 (43.4)	119.1 (45.5)	NS
Perceived physical health	42.7 (6.1)	43.4 (5.8)	NS
Perceived mental health	47.2 (7.7)	45.9 (8.0)	NS

[a]Mean ± SE. [b]Median(25th-75th percentile).
NS indicates nonsignificant.

men and 53.8% were older than 64 years of age.

The proportion of women over 64 years of age was greater than in the younger patients (Table 1).

At least one drug shown to be of benefit for the prevention of recurrent coronary events was received by 60.4% of patients older than 64 years compared to 70.9% of patients younger than 64 years (*P*<.001). The drugs most frequently used for the prevention of these events in all the patients, regardless of age, were platelet anti-aggregating agents and lipid-lowering drugs.

The coronary event leading to inclusion in the study in the older group was mainly unstable angina. The patients older than 64 years also had a greater incidence of prior coexisting cardiovascular disease (diabetes mellitus, high blood pressure, hypercholesterolemia, stroke or peripheral arterial disease) (Table 1).

Calcium antagonists and nitrates were more frequently prescribed in the older group, independently of whether the patients had high blood pressure. Systolic blood pressure was significantly higher in the patients over 64 years and the diastolic blood pressure was significantly lower. High density lipoprotein cholesterol levels were greater in the patients over 64 years and triglyceride levels were lower. No significant differences were observed for total cholesterol or LDL cholesterol. The percentage of patients who smoked decreased with increasing age. No age-dependent relation was found between quality of life and taking two or more drugs (Table 1).

The probability of receiving therapy with more than two drugs for the prevention of recurrent coronary events was significantly greater in patients with hypertension or hypercholesterolemia, in patients younger than 65 years of age, in smokers and in patients whose reason for inclusion in the study was an AMI. Patients receiving multiple therapy had better control of their blood pressure (77.5% vs 60.1%; *P*<.001) and lipid profile (21.6% vs 8.7%; *P*<.001). No relation was detected between quality of life and multiple therapy (Table 2).

The group of patients over 64 years of age was divided into four ranges to determine any possible differences. As age increased, there was a growing proportion of women and an increasing number of visits to the primary care physician. Increasing age was also associated with a significantly reduced trend in the percentage of smokers and the number of patients who used beta blockers and lipid-lowering drugs. The older patients tended to use nitrates and calcium antagonists to a greater extent, although the differences were not

TABLE 3. **Analysis of the characteristics and treatment received in patients over 64 years of age, categorized by age group**

	65-68 years	69-71 years	72-75 years	>75 years	Linear association
Sex, female	26.8	26.5	33.6	36.1	.05
Comorbid conditions					
Diabetes	36.3	38.6	32.3	30.2	NS
Hypertension	63.7	63.4	65.7	59.5	NS
Hypercholesterolemia	63.4	55.3	62.4	58.6	NS
Peripheral arterial disease	13.7	15.5	12.7	12.3	NS
Stroke	10.3	14.5	11.9	16.4	NS
Any of the above	89.5	86.8	90.5	83.2	NS
Smoker	12.4	11.8	7.3	4.2	.01
BP<140/90, mm Hg	72.5	74.3	83.9	75.6	NS
Total cholesterol<190 and LDL cholesterol<115 mg/dL	20.3	15.4	20.4	12.6	NS
Inclusion event, % unstable angina	56.3	61.5	50.0	49.6	NS
Frequent visitor, >8 visits/year	30.1	33.1	35.8	43.7	.02
Drug therapy					
Anti-aggregating agents	73.2	69.9	73.7	73.9	NS
Beta-blockers	37.3	31.3	29.9	19.3	.002
ACE inhibitors	32.0	29.1	32.8	26.1	NS
Lipid lowering agents	54.9	49.3	48.9	34.5	.002
At least two of the above	67.3	57.4	62.8	52.1	.03
Calcium antagonists	37.3	44.9	44.4	48.6	.09
Nitrates	55.2	57.6	59.8	66.7	.07

Results expressed in percentages.
NS indicates nonsignificant.

statistically significant (Table 3).

Patients older than 64 years of age had an OR for receiving multiple therapy of 0.45 (95% CI, 0.30-0.68), after adjusting for sex, hypertension, hypercholesterolemia, triglyceride levels, smoking and coronary event leading to inclusion.

DISCUSSION

This study demonstrates a reduced use of drugs for the secondary prevention of ischemic heart disease in patients older than 64 years of age. These patients also visited their primary care physician more often and received more nitrates and calcium antagonists. These findings are important because they highlight clear differences in treatment received according to age. These differences are not justified by current recommendations based on available scientific evidence.[12,13]

The proportion of patients in our sample older than 64 years was higher than that of the general population. This is consistent with the fact that ischemic heart disease is more common in older people. The percentage of women was greater among the patients older than 64 years than among the younger patients. This has been noted by others,[17] although men still form the more numerous group of patients.

The systolic blood pressure was higher and the diastolic blood pressure lower in the patients older than 64 years of age. This agrees with several studies showing a relation between age and increased systolic pressure,[18,19] and which together indicate that the combination of a higher systolic pressure and a lower diastolic pressure constitute one of the main cardiovascular risk factors in older people.[20] Nevertheless, the percentage of patients with systolic pressure lower than 140 mm Hg and diastolic pressure lower than 90 mm Hg was greater in the patients over the age of 64 years.

The prevalence of smoking was lower in patients older than 65 years than in younger patients. This relation has also been seen in other similar studies, which show that this reduction is the consequence of a greater percentage of ex-smokers in the sample.[21] These percentages, however, are very similar to those of the general population of the same age,[22] which is cause for concern because it reveals that very few older persons cease smoking when they have ischemic heart disease.

The HDL cholesterol concentration was lower in patients with coronary heart disease who were younger than 64 years of age. This result is in agreement with the data from the REGICOR study performed among the general population.[21] This result differed from that of a study of the general population in North America, which showed a reduction in both total cholesterol and HDL cholesterol in older persons.[23]

Older patients made more visits to their primary care physician than the younger patients. This has been seen before in other studies undertaken in the general population,[24] and may be accounted for by the fact that these older patients generally have more coexisting morbid conditions.

The quality of life of the patients in our study was lower than the mean of the general population.[16] There were no differences according to age, even though other studies have demonstrated a greater impact on the quality of life of younger patients with coronary heart disease.[25] This impact was evident in their perception of physical health, possibly related to the fact that ischemic heart disease may affect their ability to work.

Two points worth noting are that older patients received fewer secondary prevention measures despite having a worse prognosis, and that rehabilitation programs are effective in older patients with ischemic heart disease.[26] This has also been reported in other stu dies.[10,27] One reason may be that the multiple comorbid conditions often seen in this age group necessitate the use of more drugs, and this is accompanied by more interactions and side effects.[28] The mean number of drugs used by older patients in the general population varies from 2-4 per person per day, and up to 58.1% of older persons routinely consume medication.[29]

The most frequently used drugs in the older patients were nitrates and calcium antagonists and the least frequent were beta-blockers, lipid lowering drugs, and anti-aggregating agents. This suggests that therapy in the older patient tends to be predominantly symptomatic. Indeed, studies exist demonstrating the underutilization of beta-blockers in older patients,[30] partly due to lack of representation of patients older than 70 years of age in clinical trials aimed at evaluating the effect of these drugs on increased survival. This may be because older patients generally show more contraindications to the use of beta-blockers, as for example patients with peripheral arterial disease, chronic obstructive pulmonary disease and diabetes mellitus. Nonetheless, in our study population these situations were not associated with the use of two or more drugs for the prevention of recurrent coronary events, as has been reported elsewhere.[31] Nor can we say that the patients in our study who were older than 64 years had more diseases with an unfavorable short-term prognosis for life expectancy or resulting in severe handicap, as these situations were both criteria for exclusion from the study.

Another explanation for the greater use of calcium antagonists, nitrates and ACE inhibitors among patients older than 64 years may be the prevalence of high blood pressure in this age group. These drugs can be used as adjuvant therapy or even as first-line therapy in certain situations, as is the case of ACE inhibitors in patients with diabetes mellitus.[32]

Study characteristics

Since the study was cross-sectional no causal associations can be established, although it does provide evidence of a situation that requires further examination. Answers are required as to whether more aggressive treatment of ischemic heart disease in older patients is accompanied by greater efficacy in the prevention of recurrent coronary events, and this can only be derived from studies with an experimental design. The age of the patients was limited to 80 years because the proportion of patients older than this was much lower than the proportion of patients in their seventies, and also because the same treatment may be taken for more than one disease.

The number of basic health areas included ensured that the population actually enrolled was sufficiently heterogeneous to guarantee external validity of the study.

CONCLUSIONS

Patients with coronary heart disease older than 64 years of age received fewer drugs for the prevention of recurrent coronary events despite having a worse cardiovascular risk profile, and independently of sex and coexisting morbid conditions. As the age of the patients increased the number of drugs used decreased, even though the number of visits to the primary care physician rose. These data demonstrate the need to insist on the application of recommendations based on scientific evidence, which should not discriminate against older people because of age. Although the older patient often has multiple diseases and certain pharmacokinetic peculiarities which may make more aggressive therapy necessary, adequate selection of drugs would benefit a wide group of patients who are currently under-treated.

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