

Control of Risk Factors in and Treatment of Patients With Coronary Heart Disease: The TRECE Study

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The aim of the TRECE study was to describe treatment in patients with coronary heart disease (CHD). It was an observational, cross-sectional, multicenter study of patients who were treated in either an internal medicine (n=50) or cardiology (n=50) department, or in primary care (n=100) during 2006. The patients' history, risk factors, and treatment were recorded, and noncardiac disease was evaluated using the Charlson index. Optimal medical treatment (OMT) was regarded as comprising combined administration of antiplatelet agents, statins, beta-blockers, and renin-angiotensin-aldosterone system blockers. In total, data on 2897 patients were analyzed; their mean age was 67.4 years and 71.5% were male. Overall, 25.9% (95% confidence interval, 25.6-26.2) received OMT. Multivariate analysis showed that prescription of OMT was independently associated with hypertension, diabetes, current smoking, myocardial infarction, and angina. In contrast, nonprescription of OMT was associated with atrial fibrillation, chronic obstructive pulmonary disease and a Charlson index =4. The main findings were that few CHD patients were prescribed OMT and that its prescription was determined by the presence of symptoms and comorbid conditions.

Key words: *Optimal medical treatment. Limitations. Coronary heart disease*

Control de los factores de riesgo y tratamiento de los pacientes con cardiopatía isquémica: registro TRECE

El registro TRECE describe el tratamiento de pacientes con cardiopatía isquémica (CI). Estudio transversal, observacional y multicéntrico de pacientes atendidos en medicina interna (n = 50), cardiología (n = 50) y atención primaria (n = 100) en 2006. Se registraron antecedentes, factores de riesgo y tratamientos; la afección extracardiaca se evaluó mediante el índice de Charlson. Se consideró tratamiento médico óptimo (TMO) la prescripción conjunta de antiagregación, bloqueadores beta, estatinas y bloqueo del sistema renina-angiotensina-aldosterona. Se analizó a 2.897 pacientes, con una media de edad de 67,4 años; el 71,5% eran varones. El TMO se realizó en el 25,9% (intervalo de confianza del 95%, 25,6-26,2) de los pacientes. El análisis multivariable mostró que la hipertensión arterial, la diabetes, el tabaquismo, el infarto previo y la angina conllevaron mayor prescripción de TMO; la fibrilación auricular, la enfermedad pulmonar obstructiva crónica y el índice de Charlson = 4 se relacionaron con menor prescripción. La principal conclusión es que la prescripción del TMO de pacientes con CI es baja y se ve determinada por los síntomas y comorbilidades.

Palabras clave: *Tratamiento médico óptimo. Limitaciones. Cardiopatía isquémica.*

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The co-ordinators of the TRECE Study are listed at the end of the article.

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INTRODUCTION

The number of patients with coronary heart disease (CHD) is increasing^{1,2} and the medical treatment and management of associated risk factors can result in important prognostic improvements for these patients.³⁻⁵ Combined treatment with antiplatelet aggregators, beta-blockers, statins and renin-angiotensin-aldosterone system block with angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor antagonists (ARA-II) is considered to be the optimal medical treatment (OMT).³⁻⁵

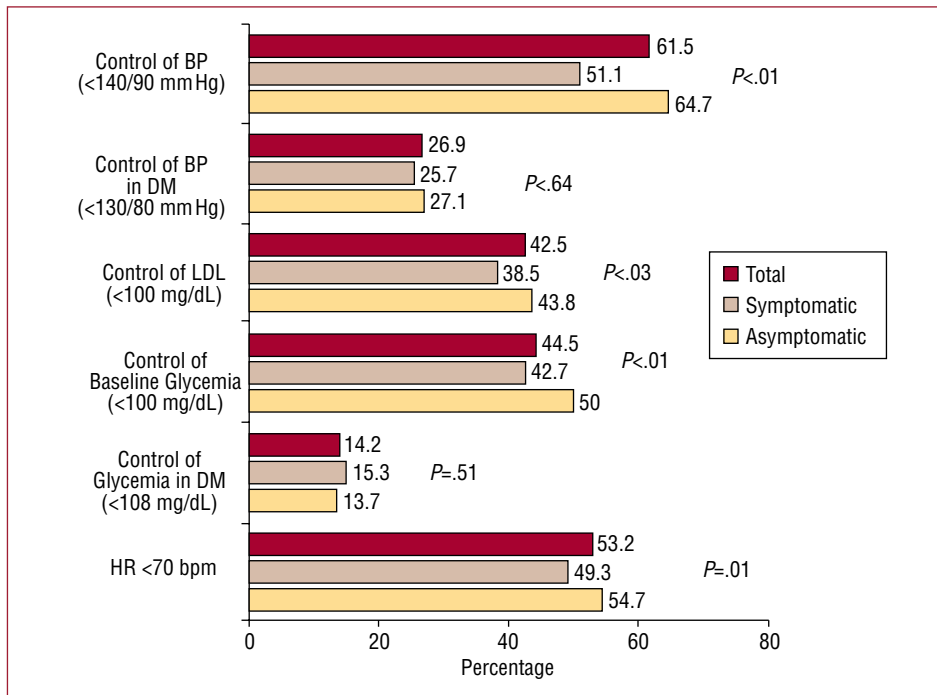


Figure 1. Control of cardiovascular risk factors according to the presence or absence of angina crisis. DM, diabetes mellitus; HR, heart rate; LDL, low-density lipoproteins; BP, blood pressure. *P* values for the comparison between the 4 groups.

The Spanish Society of Cardiology sections on Arterial Hypertension, Ischemic Heart Disease and Clinical and Extrahospital Cardiology undertook the TRECE Study (TRatamiento de la Enfermedad Coronaria en España—Treatment of Coronary Heart Disease in Spain) in order to describe the control and prescription of the OMT of patients with CHD.

METHODS

Study Design

We undertook a descriptive, cross-sectional multicenter study involving specialists from 20 randomly selected health care areas. A total of 200 physicians took part (50 specialists in cardiology, 50 in internal medicine, and 100 primary care physicians) and 3000 consecutive patients during the first quarter of 2006; 103 patients were excluded as their data were either incomplete or contradictory. The protocol was approved by the Ethics Committee of the Hospital Universitario de San Juan, Alicante. The inclusion criteria were: a confirmed clinical diagnosis of stable chronic angina, chest pain with a positive stress test, a prior diagnosis of acute coronary syndrome, myocardial infarction, or unstable angina. The patients could have more than one of the inclusion criteria, which were obtained from the clinical history or medical records provided by the patients.

Optimal medical treatment was considered to be the joint prescription of antiplatelet aggregators, beta-blockers, statins and ACE inhibitors or ARA-II.³⁻⁵ Hypertension was considered to be controlled if it was <140/90 mm Hg or <130/80 mm Hg in diabetics.⁶ The resting heart rate (HR) was considered to be controlled if it was <70 bpm during the physical examination or on the electrocardiogram (ECG) during the office visit.⁷ Low-density lipoprotein (LDL) concentrations <100 mg/dL were accepted to represent controlled dyslipidemia.⁸ The control of diabetes mellitus was only done by glycemia levels <108 mg/dL; a baseline glycemia <100 mg/dL was considered to be controlled.⁹ The diagnosis of atrial fibrillation (AF) was only done by ECG. Chronic obstructive pulmonary disease (COPD) was recorded if a diagnosis of COPD existed on the clinical history or the patient was taking specific medication. The joint analysis of the comorbid conditions was done using the Charlson index, adapted to patients with CHD. A high comorbidity rate was considered to be a Charlson score of ≥ 4 .¹⁰

The data were analyzed using the SPSS 15.0 statistical program (SPSS Inc, Chicago, IL). Comparisons between means were analyzed using the Student *t* test. The multivariate analysis was done using logistic regression and the results are presented, after adjustment for age and sex, in the form of the odds ratio (OR) with the 95% confidence interval (CI). Statistical significance was set at $P \leq .05$.

TABLE 1. General Characteristics and Risk Factors of the Study Patients According to Whether or Not They Had Angina

	Total	Asymptomatic	Symptomatic	P
Patients, n (%)	2767	2055 (74.3)	712 (25.7)	
Age (years), mean (SD)	67.5 (11.4)	67.2 (11.4)	68.4 (11.4)	.02
Men, %	71.5	72.9	67.4	<.01
Years of evolution, mean (SD)	5.9 (6)	5.9 (5.9)	5.8 (6.3)	.62
Percutaneous revascularization, n (%)	1144 (41.3)	840 (40.9)	304 (42.7)	.36
Surgical revascularization, n (%)	438 (15.8)	325 (15.8)	113 (15.9)	.91
Heart failure, %	18.4	16.9	22.6	<.01
Atrial fibrillation, %	10.1	9.5	11.8	.08
Hypertension, %	68.5	66.9	73.1	<.01
Diabetes mellitus, %	38.8	37.1	43.8	.37
Dyslipidemia, %	67.1	67.0	67.3	.87
Ex-smokers, %	51.4	51	52.7	.44
Current smokers, %	10.9	9.3	15.6	<.01
Obesity, %	53.7	52.5	57.2	.06
Abdominal obesity, %	29.3	29.4	29.1	.87
Charlson score, mean (interval)	2 (1-3)	2 (1-3)	3 (1-4)	.01
Charlson score ≥ 4 , %	26.3	23.5	34.2	<.01
History of coronary heart disease, %				
Stable angina	29.3	28.1	32.7	.02
AMI	42	43.3	38.1	.01
Non-Q wave AMI	18.3	18.1	18.8	.65
Unstable angina	35.1	29.4	51.7	<.01

AMI indicates acute myocardial infarction; SD, standard deviation.
P values for comparison between groups.

TABLE 2. Pharmacologic Treatment of the Patients Before and After Their Inclusion Visit According to the Presence or Absence of Angina

	Total	Asymptomatic	Symptomatic	P
Antiplatelets, before	80.7%	82.2%	76.5%	<.01
Antiplatelets, after	84%	82.1%	89.5%	<.01
Beta-blockers, before	58.3%	60.5%	51.8%	<.01
Beta-blockers, after	64.5%	62.1%	71.6%	<.01
Statins, before	68.1%	70.8%	60.4%	<.01
Statins, after	75%	74.3%	77.1%	.30
ACE inhibitors, before	43.7%	43.9%	43.1%	.70
ACE inhibitors, after	32%	30.7%	35.8%	.01
ARA II, before	18.7%	18.7%	18.8%	.9
ARA II, after	19.5%	18.9%	21.1%	.2
Nitrates, before	40.3%	37.6%	42.3%	<.01
Nitrates, after	42.4%	34.2%	66.1%	<.01
Calcium antagonists, before	35.4%	33.4%	40.5%	<.01
Calcium antagonists, after	38.1%	35%	46.3%	<.01
OMT*, before	27.2%	29%	21.9%	<.01
OMT*, after	25.9%	24.3%	30.5%	<.01

ACE indicates angiotensin converting enzyme; ARA II, angiotensin II receptor antagonists; OMT, optimal medical treatment.

*Combination of 4 drugs: antiplatelet, beta-blocker, statin, and ACE inhibitor or ARA II.

P values for the comparison between the 2 groups.

RESULTS

The characteristics of the sample are shown in Table 1. The control of the risk factors was generally poor and significantly worse in those patients who reported having angina (Figure). The patients who were receiving treatment with beta-

blockers had a lower resting HR than those who were not receiving this treatment (67.3 bpm vs 72.8 bpm; $P<.01$), although only 61.4% (95% CI, 60.8-70) had a HR<70 bpm; no differences were found in the HR of the patients who were being treated with calcium antagonists.

TABLE 3. Relation Between Various Clinical Characteristics and the Prescription of Optimal Medical Treatment

Clinical Variable	OR	95% CI	P
Hypertension	1.95	1.55-2.45	<.01
Diabetes mellitus	1.4	1.14-1.72	.01
Dyslipidemia	1.23	1-1.53	.05
Current smoker	1.5	1.08-2.07	.01
Stroke	1.19	0.86-1.65	.3
Peripheral arterial disease	0.87	0.66-1.16	.37
Heart failure	1.81	1.39-2.37	<.01
COPD	0.65	0.48-0.87	<.01
Atrial fibrillation	0.23	0.14-0.36	<.01
Renal failure*	1.03	0.81-1.32	.81
Angina pectoris	1.6	1.27-2.04	.01
Stable angina	1.09	0.86-1.38	.46
Prior myocardial infarction	1.6	1.26-2.02	<.01
Non-Q wave myocardial infarction	1.27	0.95-1.7	.10
Unstable angina	1.07	0.86-1.34	.53

CI indicates confidence interval; COPD, chronic obstructive pulmonary disease; OR, odds ratio.

*Glomerular filtration rate <60 mL/min.

Table 2 shows the treatments being received by the patients before and after the inclusion visit. The OMT was only being given in 25.9% (95% CI, 25.6-26.2) of the patients. The multivariate analysis, adjusted for age and sex, showed that hypertension, diabetes, heart failure, smoking, acute myocardial infarction, and angina were associated with the prescription of OMT (Table 3). AF or COPD were the main clinical limitations to the prescription of OMT; no association was found with the other clinical characteristics. The joint analysis of all the comorbid conditions showed that a Charlson score of ≥ 4 was related with less prescription of optimal treatment (OR=0.77; 95% CI, 0.61-0.98; $P=.03$). Of the patients with AF, 53% were receiving a beta-blocker, 50.2% antiplatelet aggregators and 60% anticoagulants; and of the patients with COPD, 78.2% were receiving antiplatelet aggregators, 72.7% statins and just 39.3% were receiving beta-blockers.

DISCUSSION

The TRECE Study shows that the control of risk factors in patients with CHD is generally poor, especially in those who have symptoms of angina pectoris; and furthermore, the prescription of the OMT was low and determined by the accompanying disorders. The sample of patients included in the TRECE Study was very similar to that of other international^{3,11,12} and national^{1,13} surveys.

The low percentage of patients who were controlled is a constant finding in the many studies available.¹⁰⁻¹³ Our results also show that only half the

patients with CHD had their resting HR controlled and that, in general clinical practice, beta-blockers achieve a poor control. The presence of noncardiac involvement is an important predictor of mortality in patients with CHD; the Charlson index is useful to identify those patients with a worse prognosis¹⁰ and our data demonstrate that the index identifies patients with a lower prescription of OMT.

Various reasons may explain the low compliance of OMT in the patients with CHD. A low degree of awareness of the aims of control of risk factors has been reported in Spain.¹³ The data from the TRECE Study have enabled us to identify that AF, COPD and comorbid conditions are the main limiting factors for the therapeutic implementation of OMT. Concerning AF, the underuse of antiplatelet aggregators seems to be related with the 60% anticoagulation, although the poor use of beta-blockers was also notable. Severe forms of COPD are a relative contraindication to the use of beta-blockers, though these drugs reduce the number of readmissions; the use of cardioselective beta-blockers,¹⁴ calcium antagonists⁵ or selective inhibitors of the sinus node If current, such as ivabradine,¹⁵ are effective alternatives.

Study Limitations

As this was a multicenter study, the collection of data was simplified and did not include the measurement of glycohemoglobin; this measurement has been used in previous studies¹³ and may have underestimated the awareness of control of diabetes.

Coordinators of the TRECE Study (in alphabetical order of surnames)

Eduardo Alegría (Navarra), Joaquín Alonso (Madrid), Manuel Anguita (Cordoba), Alfredo Bardají (Tarragona), Javier García-Moll (Barcelona), Isidoro González (Madrid), Joseph Guindo (Barcelona), Víctor López (Seville), Félix Malpartida (Malaga), Manuel Martínez (Madrid), J. Ignacio Martínez (Gijón), Nekane Murga (Bilbao), Marco A. Paz (Gerona), Juan Quiles (Alicante), José Antonio Romero (Granada), Antonio Salvador (Valencia), Milagros Pedreira (Santiago de Compostela), Justo Torres (Valladolid), Mariano Valdés (Murcia), and Ruperto Vargas (Canary Isles).

REFERENCES

1. Heras M, Marrugat J, Aros F, Bosch X, Enero J, Suarez MA, et al. Reducción de la mortalidad por infarto agudo de miocardio en un periodo de 5 años. *Rev Esp Cardiol.* 2006;59:200-8.

2. Rosamond W, Flegal K, Furie K, Go A, Greenlund K, Haase N, et al. Heart disease and stroke statistics—2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2008;117:e25-146.
3. Daly C, Clemens F, Lopez-Sendon JL, Tavazzi L, Boersma E, Danchin N, et al. The impact of guideline compliant medical therapy on clinical outcome in patients with stable angina: findings from the Euro Heart Survey of stable angina. *Eur Heart J*. 2006;27:1298-304.
4. Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med*. 2007;356:1503-16.
5. Fraker TD Jr, Fihn SD, Gibbons RJ, Abrams J, Chatterjee K, Daley J, et al. 2007 Chronic Angina Focused Update of the ACC/AHA 2002 Guidelines for the Management of Patients With Chronic Stable Angina: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Writing Group to Develop the Focused Update of the 2002 Guidelines for the Management of Patients With Chronic Stable Angina. *Circulation*. 2007;116:2762-72.
6. 2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. *J Hypertens*. 2003;21:1011-53.
7. Diaz A, Bourassa MG, Guertin MC, Tardif JC. Long-term prognostic value of resting heart rate in patients with suspected or proven coronary artery disease. *Eur Heart J*. 2005;26:967-74.
8. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA*. 2001;285:2486-97.
9. Ryden L, Standl E, Bartnik M, Van den BG, Betteridge J, de Boer MJ, et al. Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary. The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). *Eur Heart J*. 2007;28:88-136.
10. Sachdev M, Sun JL, Tsiatis AA, Nelson CL, Mark DB, Jollis JG. The prognostic importance of comorbidity for mortality in patients with stable coronary artery disease. *J Am Coll Cardiol*. 2004;43:576-82.
11. Bhatt DL, Steg PG, Ohman EM, Hirsch AT, Ikeda Y, Mas JL, et al. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. *JAMA*. 2006;295:180-9.
12. Clinical reality of coronary prevention guidelines: a comparison of EUROASPIRE I and II in nine countries. EUROASPIRE I and II Group. *European Action on Secondary Prevention by Intervention to Reduce Events*. *Lancet*. 2001;357:995-1001.
13. Gonzalez-Juanatey JR, Alegria-Ezquerro E, Aznar-Costa J, Bertomeu-Martinez V, Franch-Nadal J, Palma-Gamiz JL. Conocimiento y aplicación de las guías de práctica clínica sobre riesgo cardiovascular en las consultas generales y especializadas. *Rev Esp Cardiol*. 2006;59:801-6.
14. Lopez-Sendon J, Swedberg K, McMurray J, Tamargo J, Maggioni AP, Dargie H, et al. Documento de Consenso de Expertos sobre bloqueadores de los receptores b-adrenérgicos. *Rev Esp Cardiol*. 2005;58:65-90.
15. Lopez-Bescos L, Filipova S, Martos R. Long-term safety and efficacy of ivabradine in patients with chronic stable angina. *Cardiology*. 2007;108:387-96.