

## Original article

## Attitude and Efficacy of Cardiologists With Respect to Smoking in Patients After Acute Coronary Syndromes

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## ABSTRACT

**Introduction and objectives:** Smoking is one of the most prevalent risk factors in acute coronary syndrome patients. The aim of this study was to assess the attitudes of cardiologists to the smoking habits of these patients**Methods:** A prospective multicenter registry of acute coronary syndrome patients. The primary endpoint was defined as smoking abstinence and the secondary endpoint as the incidence of all-cause mortality or nonfatal myocardial infarction.**Results:** The study population included 715 patients; 365 were current smokers. During follow-up (median, 375.0 days [interquartile range, 359.3-406.0 days]), 110 patients (30.6%) received smoking cessation support (19.7% at hospital discharge and 37.6% at month 3), specialized units and varenicline being the strategies most frequently used. No clinical differences were observed between patients who received smoking cessation support and those who did not, except for a higher prevalence of previous coronary heart disease in those who received support. In the multivariate analysis, the only variable independently associated with receiving smoking cessation support was previous coronary heart disease (odds ratio = 3.16; 95% confidence interval, 1.64-6.11;  $P < .01$ ). The abstinence rate was 72.3% at month 3 and 67.9% at 1 year; no differences were observed between the patients who received smoking cessation support and those who did not. During follow-up, a nonsignificant trend toward a lower incidence of the secondary endpoint was observed among the patients who were smokers at the time of acute coronary syndrome and who achieved abstinence ( $P = .07$ ).**Conclusions:** Use of smoking cessation support strategies is limited in acute coronary syndrome patients and is more widespread among those with previous coronary heart disease.

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## Actitud y eficacia de los cardiólogos frente al tabaquismo de los pacientes tras un síndrome coronario agudo

## RESUMEN

**Introducción y objetivos:** El tabaquismo es uno de los factores más prevalentes entre los pacientes con síndrome coronario agudo. El objetivo del estudio es analizar la actitud de los cardiólogos frente al tabaquismo de estos pacientes.**Métodos:** Registro prospectivo y multicéntrico de pacientes con síndrome coronario agudo. El objetivo primario se definió como abstinencia de tabaco y el secundario, incidencia de muerte o infarto no fatal.**Resultados:** Se incluyó a 715 pacientes, de los que 365 eran fumadores. Durante el seguimiento (mediana, 375,0 [amplitud intercuartílica, 359,3-406,0] días), 110 (30,6%) pacientes recibieron algún tipo de apoyo antitabáquico (el 19,7% al alta y el 37,6% en el tercer mes); las unidades antitabáquicas y la vareniclina fueron las estrategias más empleadas. No se observaron diferencias clínicas en función de recibir apoyo antitabáquico, salvo mayor prevalencia de cardiopatía isquémica previa entre los que sí lo recibieron. En el análisis multivariable, la única variable que se asoció independientemente con recibir apoyo antitabáquico fue el antecedente de cardiopatía isquémica (odds ratio = 3,16; intervalo de confianza del 95%, 1,64-6,11;  $p < 0,01$ ). La tasa de abstinencia de tabaco en la visita del tercer mes fue del 72,3% y al año, del 67,9%, sin diferencias en función de haber recibido algún apoyo antitabáquico. Durante el seguimiento hubo una tendencia no significativa a menor incidencia del objetivo secundario entre los fumadores que consiguieron abstenerse de tabaco ( $p = 0,07$ ).

## Palabras clave:

Síndrome coronario agudo

Tabaquismo

Medidas antitabáquicas

Abstinencia

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**Conclusiones:** La utilización de estrategias de apoyo para el abandono del tabaquismo es baja entre los pacientes tras un síndrome coronario agudo y es más frecuente entre los pacientes con cardiopatía isquémica previa.

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## Abbreviations

ACS: acute coronary syndrome

TABARCA: *TABA*quismo y *Riesgo de complicaciones cardiovasculares en pacientes con síndrome Coronario Agudo* (Smoking and Risk of Cardiovascular Complications in Patients with Acute Coronary Syndrome)

## INTRODUCTION

A personal history of smoking is a highly prevalent cardiovascular risk factor among patients with acute coronary syndrome (ACS), a finding corroborated by the fact that between 30% and 50% of these patients are smokers at the time of hospital admission and up to 20%-40% are ex-smokers.<sup>1-7</sup> Although the prognosis for survival of active smokers may be similar or even better during the hospital stay for ACS,<sup>8,9</sup> long-term follow-up demonstrates that the risk of recurrence of complications or of death is higher among smokers<sup>10-12</sup>; moreover, this risk is especially high among those who continue to smoke.<sup>6,13,14</sup>

The rate of smoking cessation following ACS is high, but up to 20% of patients return to the habit.<sup>6,14,15</sup> Indeed, the registries and studies involving patients with chronic coronary heart disease usually demonstrate that 10%-20% of the patients are active smokers<sup>16,17</sup>; moreover, specialists have been criticized for showing a lack of concern about smoking in these patients.<sup>18</sup> The Smoking and Risk of Cardiovascular Complications in Patients with Acute Coronary Syndrome (*TABA*quismo y *Riesgo de complicaciones cardiovasculares en pacientes con síndrome Coronario Agudo*, TABARCA) is a multicenter registry involving hospitals all over Spain, specifically designed to analyze patients with ACS in relation to their smoking habits. Based on the hypothesis that cardiologists do not usually employ smoking cessation strategies in patients who have had ACS, the objectives of the present study were to describe the therapeutic management of smoking in ACS patients by their cardiologists, and to analyze the rates of smoking cessation according to the strategies employed and their impact on prognosis during the first year after ACS.

## METHODS

### Study Design

The basis for and design of the study have been reported previously.<sup>19</sup> Briefly, TABARCA is a nationwide, multicenter, prospective cohort study of ACS patients, designed and coordinated by a committee of investigators from the Working Group on Hypertension of the Spanish Society of Cardiology and endorsed by the Research Agency of the Spanish Society of Cardiology. The protocol and informed consent form were approved by the Ethics Committee of *Hospital Universitario de San Juan*, in San Juan de Alicante, Spain. All patients signed the informed consent form

during the enrollment visit. The study protocol consisted of an enrollment phase, during the hospital stay for ACS, and 2 follow-up visits, 3 and 12 months after hospital discharge. As shown in [Figure 1](#), 35 of the 42 centers participating in the study agreed to carry out the follow-up phase and performed the complete follow-up of at least half of the recruited patients; consequently, the follow-up phase involved 83.3% of all the centers and 86.7% of the patients originally included in the study. There were no differences between the 825 patients originally included and the final sample.

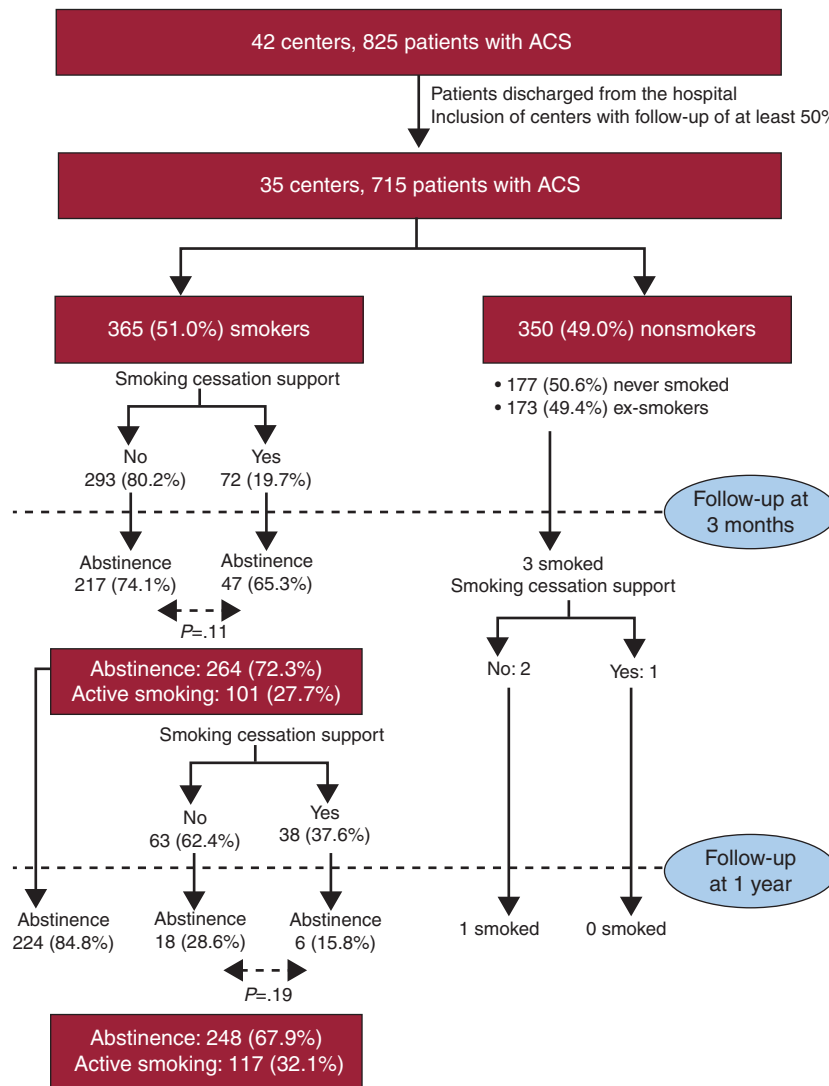
The inclusion criteria were age over 18 years and a diagnosis of ACS, defined as the presence of at least 2 of the following 3 diagnostic criteria: typical chest pain lasting 20 min or more, dynamic electrocardiographic changes compatible with myocardial ischemia, or an increase in serum markers of myocardial injury. The exclusion criteria were pregnancy, refusal to sign the informed consent form, or use of illegal substances or drugs (cocaine, amphetamines, heroin, etc.). The primary endpoint was abstinence from smoking at 1 year in those patients who were smokers at the time of ACS and the secondary endpoint was the incidence of all-cause mortality or nonfatal myocardial infarction.

The risk factors, clinical history, and treatments of all the patients were recorded in an electronic questionnaire, in addition to the clinical presentation of ACS, the treatments employed, and the major complications during the hospital stay. One section of the protocol consisted of specific questions about smoking habits; smokers and ex-smokers were asked about the number of years they had smoked, the number of cigarettes they smoked per day, their attempts to give up the habit, and the methods employed, etc. We recorded all the treatments prescribed for the patients at discharge and, in the case of smokers, whether their physicians had offered specific recommendations for smoking cessation such as specialized units, referral to specialists, drug therapies, standard advice, or any other type of support measure.

Smokers were defined as those patients who reported having smoked at least 1 cigarette a day up to the time of admission and ex-smokers as those who reported having smoked in the past; in the latter, the time elapsed since complete smoking cessation was recorded. The presence of chronic obstructive pulmonary disease (COPD) was included in the report if it had been diagnosed in previous medical records or if the patient continued to receive specific treatment. Blood samples were collected within the first 3 days after hospital admission. The glomerular filtration rate was estimated using the equation provided in the Modification of Diet in Renal Disease study<sup>20</sup> and, when lower than 60 mL/min/1.73 m<sup>2</sup>, it was considered to indicate renal dysfunction.

All the investigators received a CO-oximeter, as well as the necessary material and instructions for its use. Smoking abstinence was verified in all patients by measuring exhaled carbon monoxide.

The clinical complications recorded were defined in the protocol designed specifically for this study by the coordinators. Angina was defined as chest pain accompanied by dynamic changes in the electrocardiogram without an increase in serum markers of myocardial injury; when enzyme levels were higher than normal, the event was coded as a myocardial infarction. Heart failure was recorded when there were signs and symptoms of cardiac dysfunction accompanied by an imaging study



**Figure 1.** Flow chart representing the patients included in the in-hospital phase and follow-up, as well as the use of smoking cessation strategies during follow-up. ACS, acute coronary syndrome.

(radiological confirmation of pulmonary congestion or echocardiographic evidence of left ventricular systolic or diastolic dysfunction). In patients who underwent catheterization, the study protocol included assessment of the number and site of arteries with lesions involving more than 50% of the vessel, the performance of percutaneous coronary interventions, and the number and type of stents implanted. Stratification of ACS was carried out using the GRACE score (Global Registry of Acute Coronary Events)<sup>21</sup> in all patients.

### Statistical Analysis

The data obtained from the online questionnaire were sent to a centralized database by a company engaged for this purpose and were conveyed to the study coordinators. The statistical analysis was performed with the SPSS 15.0 statistical software package (SPSS Inc.; Chicago, Illinois, United States). Continuous variables are expressed as the mean (standard deviation) and the categorical variables as percentages. Student *t* test was utilized to compare the means of the continuous variables, and the  $\chi^2$  test was used for categorical variables. The variables independently associated with some type of smoking cessation support were analyzed by using

binary logistic regression, with the “enter” method; the variables that had shown statistical significance in the univariate comparison and those that could have a clinically relevant relationship were included in the model.<sup>22</sup> As the univariate analysis showed a significant difference in only 1 variable, the presence of possible confounding factors was ruled out by analyzing the possible interactions of a history of coronary heart disease and the remaining variables with having received smoking cessation support; finally, we included variables such as age, sex, hypertension, diabetes, dyslipidemia and a history of COPD, coronary heart disease, heart failure, stroke, or atrial fibrillation. The calibration of the model was performed with the Hosmer-Lemeshow statistic and the discriminatory power was determined using the area under the receiver operating characteristic curve of the model.

The analysis of survival during follow-up was performed with Cox proportional hazards regression, using the “enter” method, in which we included age, sex, all the risk factors, the presence of previous cardiovascular disease, treatments at hospital discharge, and coronary revascularization. The multivariate models were designed and assessed in accordance with current recommendations.<sup>22</sup> A *P*-value  $<.05$  was considered to indicate statistical significance.

**Table 1**  
General Characteristics of the Smokers According to Whether or not They Had Received Smoking Cessation Support at Some Time After Hospital Discharge

	Overall group	Without support	With support	P
Patients	365	255 (69.9)	110 (30.1)	
Age, years	56.0±10.5	56.4±10.8	55.2±9.8	.35
Men	308 (84.4)	215 (84.3)	93 (84.5)	.65
Smoker of over 20 cigarettes/day	56.6%	54.2%	61.8%	.19
Hypertension	47.4%	45.0%	52.7%	.18
Dyslipidemia	56.3%	54.2%	60.9%	.24
Diabetes	21.4%	21.7%	20.9%	.87
Previous CHD	16.4%	12.0%	26.4%	<.01
Previous HF	1.7%	0.8%	3.7%	.05
COPD	12.0%	11.2%	13.6%	.52
Previous stroke	4.2%	3.6%	5.5%	.42
Claudication	5.6%	6.0%	4.6%	.59
STEACS	61.3%	63.1%	57.3%	.52
GRACE score	131.2±30.1	131.3±30.0	131.0±3.5	.93
Primary angioplasty	39.0%	42.2%	31.8%	.06
Catheterization	92.2%	91.6%	93.6%	.58
Baseline blood glucose, mg/dL	114.8±38.1	115.0±36.8	114.3±41.0	.88
Total cholesterol, mg/dL	183.8±46.7	179.8±45.9	192.7±47.3	.02
LDL-C, mg/dL	112.2±38.7	108.8±38.2	119.9±39.1	.01
HDL-C, mg/dL	37.3±10.4	36.6±10.0	38.9±11.0	.06
Triglycerides, mg/dL	139.0 [106.0-190.4]	138.0 [135.8-183.0]	143 [106.0-198.5]	.35
Creatinine, mg/dL	0.96±0.29	0.96±0.30	0.98±0.30	.46
GFR, mL/min/1.72 m <sup>2</sup>	84.9±40.5	85.7±44.8	83.1±29.8	.61

CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; GRACE, Global Registry of Acute Coronary Events; HDL-C, high-density lipoprotein cholesterol; HF, heart failure; LDL-C, low-density lipoprotein cholesterol; STEACS, ST-elevated acute coronary syndrome. Unless otherwise indicated, the data are expressed as no. (%), mean±standard deviation, or median [interquartile range].

## RESULTS

As shown in Figure 1, 715 patients were included in the follow-up phase; only 72 (19.7%) of the 365 smokers were provided with some sort of smoking cessation strategy when discharged from hospital after ACS, and this percentage was higher in the follow-up visit at month 3. Throughout the entire follow-up period, 110 smokers (30.6%) received some type of smoking cessation support. No relevant differences were observed between the patients who received some kind of support and those who did not, except that, among those who did, there was a higher incidence of previous coronary heart disease and slightly higher cholesterol levels (Table 1). The presence of confounding factors was ruled out, given that we observed no significant interaction between a history of coronary heart disease and other variables on the one hand, and having received smoking cessation support on the other. In logistic regression analysis, the only variable independently

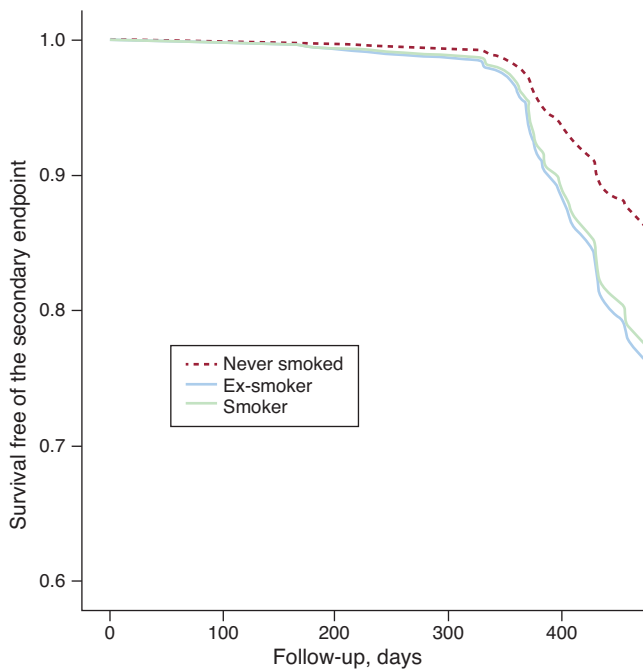
**Table 2**  
Smoking Cessation Support Strategies Recommended at Each Follow-up Visit, Taking Into Account the Fact That the Patients Could Have Access to Several of the Options

	At discharge	At 3 months of follow-up
None	293 (80.2)	63 (62.7)
Referred to specialized units	49 (13.6)	26 (24.8)
Varenicline	28 (7.8)	15 (14.3)
Nicotine patches	5 (1.4)	9 (8.6)
Nicotine gum	3 (0.8)	11 (10.5)
Bupropion	2 (0.6)	7 (6.3)

associated with receiving smoking cessation support was a history of coronary heart disease (odds ratio [OR] = 3.16; 95% confidence interval [95%CI], 1.64-6.11;  $P<.01$ ). The model displayed adequate calibration ( $\chi^2=10.4$ ;  $P=.23$ ) and discriminatory power (area under the receiver operating characteristic curve, 0.72; 95%CI, 0.61-0.79).

Table 2 shows the smoking cessation support strategies employed. In the follow-up visit at 1 year, 23.7% of the patients who had continued to smoke in month 3 had achieved abstinence; moreover, 40 (18.3%) of the ex-smokers who were not smoking at 3 months had returned to the habit at 1 year; that is, 84.8% of the abstinent patients continued to abstain in the follow-up visit at 1 year. The rate of smoking abstinence was 72.3% at the 3-month visit and 67.9% at 1 year. As shown in Figure 1, no difference was observed in the rate of abstinence among the patients who received some type of smoking cessation support. However, 5 patients who were ex-smokers at the time of ACS resumed the habit during follow-up (3 in the 3-month visit and 2 at 1 year).

The follow-up was completed by 94.3% of the patients, with a median duration of 375.0 days [interquartile range, 359.3-406.0 days]. The overall incidence of the secondary endpoint (all-cause mortality or nonfatal myocardial infarction) according to smoking habits at the time of hospital admission was 7.5% among nonsmokers, 12.4% among ex-smokers, and 9.5% among smokers ( $P=.30$ ). In Cox regression analysis adjusted for age, sex, risk factors, and previous coronary heart disease or heart failure, we observed no significantly increased risk for the secondary endpoint among smokers (hazard ratio=1.74; 95%CI, 0.75-4.05;  $P=.20$ ) or ex-smokers (hazard ratio=1.84; 95%CI, 0.77-4.38;  $P=.17$ ), although there was a trend toward a poorer prognosis (Fig. 2). We also observed a nonsignificant trend ( $P=.07$ ) toward a lower incidence of the secondary endpoint among smokers who had achieved complete abstinence at the end of follow-up (Fig. 3). The smoking

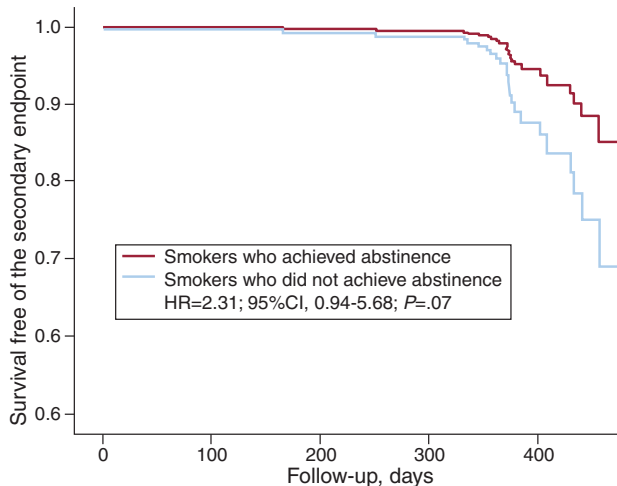


**Figure 2.** Results of Cox regression analysis for the evaluation of survival free of the secondary endpoint (all-cause mortality or nonfatal infarction) according to smoking habits at the time of acute coronary syndrome.

cessation measures appeared to be safe and there were no deaths among the patients who received some type of drug therapy.

## DISCUSSION

The major findings of the TABARCA registry are that most smokers admitted to the hospital for ACS receive no smoking cessation support of any type after discharge and that the success rate of these measures is low. In addition, this study reflects a trend toward a better prognosis in patients who have never smoked and in smokers who achieve abstinence during the first year after ACS.



**Figure 3.** Results of Cox regression analysis for the evaluation of survival free of the secondary endpoint (all-cause mortality or nonfatal infarction) according to smoking status after 1 year of follow-up in patients who were smokers at the time of acute coronary syndrome. 95%CI, 95% confidence interval; HR, hazard ratio.

Earlier data from this registry had shown that the mean age of smokers who have an ACS was 12 years younger and that the clinical presentation of the ACS was similar to that in patients who had never smoked or were ex-smokers<sup>19</sup>; the analysis of the follow-up at 1 year allows us to confirm that patients who are smokers at the time of ACS have a worse prognosis during the first year of follow-up, although this study lacks sufficient statistical power to demonstrate differences in clinical events. The TABARCA registry was designed specifically to analyze the characteristics and course of ACS patients according to smoking habits. Thus, the characteristics of patients in this registry could differ from those published in subanalyses of registries designed for other purposes, although the mean patient age and the prevalence of risk factors are similar to those of other previously published series.<sup>1–9,12,14</sup>

The low rate of the application of smoking cessation measures agrees with certain previously reported data.<sup>6,15,23</sup> Indeed, EUROASPIRE III (European Action on Secondary and Primary Prevention by Intervention to Reduce Events) demonstrated that 18.2% of the patients with chronic coronary heart disease reported that they continued to smoke<sup>17</sup>; moreover, this percentage was similar to the findings in previous registries (20.3% in 1995–1996 and 21.2% in 1999–2000). Importantly, this publication was accompanied by an editorial whose title encouraged cardiologists to be less passive with respect to smoking cessation<sup>18</sup>; in another publication, the measures employed by cardiologists as support for smoking cessation were analyzed in the EUROASPIRE III survey, which found that most patients only received standard advice.<sup>23</sup> The approach to the management of smoking cessation should differ from that employed with other cardiovascular risk factors, given that there is well-documented evidence of the existence of neuronal mechanisms that generate dependence on this habit.<sup>24</sup> Indeed, a 2009 meta-analysis demonstrated that, for patients with established cardiovascular disease, standard advice is significantly effective in achieving complete smoking cessation<sup>25</sup>; however, when behavioral support is provided through telephone calls, or individualized or group therapy, smoking cessation is significantly higher.

In addition, although there is no clear indication or definitive specifications in clinical practice guidelines, drug therapy is currently recommended for smoking cessation in patients with established cardiovascular disease or COPD and in pregnant women.<sup>26,27</sup> In their series, Mohiuddin et al.<sup>14</sup> employed nicotine replacement therapy and bupropion in patients who had had an ACS, and obtained an abstinence rate of 33% at 2 years. More recently, a randomized study that included only patients with stable cardiovascular disease demonstrated the superiority and efficacy of varenicline vs placebo, although with the active treatment, the abstinence achieved at 1 year was only 20%.<sup>28</sup> Our data also agree with the low success rate achieved with smoking cessation, a circumstance that could be partly explained by the limited experience of the physicians who recommend these measures and the patients' strong tobacco dependence, as well as by the rigorous verification of smoking abstinence by means of CO-oximetry.

Complete abstinence from smoking is a definitive recommendation in cardiovascular prevention, especially for patients at high risk or with established cardiovascular disease.<sup>29</sup> In one of the first reviews to analyze the effect of smoking cessation on patients with coronary heart disease, published in 1999, the authors observed a reduction in mortality associated with smoking cessation of 41% (OR=0.59; 95%CI, 0.53–0.66).<sup>30</sup> A meta-analysis published only 1 year later concluded that smoking cessation following myocardial infarction reduced the mortality rate by 56% (OR=0.54; 95%CI, 0.46–0.62).<sup>13</sup> More recently, in a series of myocardial infarction patients who underwent 2 years of follow-up, smoking cessation decreased mortality by 77% and reduced hospital



readmissions due to heart disease by 44%.<sup>14</sup> Moreover, a subanalysis of the OASIS-5 (Organization to Assess Strategies in Acute Ischemic Syndromes) study<sup>6</sup> demonstrated that smoking cessation following ACS is associated with a significant reduction in mortality during the first month after hospital discharge (OR=0.57; 95%CI, 0.36-0.89); in addition, smoking cessation had an additive beneficial effect, in terms of mortality and major cardiovascular complications, to that produced by increased physical exercise and improved diet. These studies serve to confirm, in contemporary series of patients with coronary heart disease, the benefits of smoking cessation observed in much earlier studies. Our study did not have sufficient statistical power to demonstrate differences in the secondary endpoint, although we were able to observe a clear trend toward lower rates of mortality and of the combination of death or reinfarction among patients who achieved smoking abstinence.

Although patients who received some type of supportive therapy for smoking cessation exhibited a higher prevalence of previous coronary heart disease, none of the patients who received these treatments died during follow-up; moreover, there was a trend toward a lower incidence of the secondary objective. The TABARCA study does not have the power to demonstrate the safety of these smoking cessation strategies, although its results provide an additional datum in this respect. In July 2011, the US Food and Drug Administration issued an alert on the slight increase in the incidence of nonfatal myocardial infarction observed in a randomized study comparing placebo and varenicline in patients with stable cardiovascular disease<sup>31</sup>; it is interesting to note the low rate of nonfatal infarction during the first year of follow-up, which was 2.0%, in the active treatment arm and 0.9% in the placebo arm. In our series, the patients who received varenicline exhibited a similar incidence of all-cause mortality and reinfarction, even though a history of coronary heart disease was more common in this group.

### Limitations

The major limitation of the TABARCA study could be the fact that the study design included equal numbers of smokers and nonsmokers, which could mean that the investigators did not recruit all the ACS patients treated consecutively in their centers; however, the characteristics of the sample and the rate of complications during follow-up were similar to those of other series.<sup>1-9</sup> Moreover, the study design did not allow us to avoid the existence of clear differences between centers or regions that would result in a considerable variability in the management of these patients. In this respect, some of the patients may have received smoking cessation support in the specialized units to which they had been referred; this aspect is not specifically recorded among the study data in the online electronic notebook and could constitute a limitation for the analysis of the smoking cessation strategies in different specialties. In addition, this was an observational study that did not allow us to clearly discern the superiority of active treatment for smoking cessation support vs placebo, but it did show the low rate of application of these measures in patients with ACS. Moreover, the study did not have sufficient statistical power to demonstrate differences in the secondary endpoint because of the small sample size, the low incidence of the endpoint events, and the relatively short follow-up period.

### CONCLUSIONS

The utilization of smoking cessation support strategies in patients who have had ACS is limited; the low rate of success associated with these measures could be due to the lack of

experience with their use and the patients' strong dependence. The rate of smoking cessation during the first year after ACS is close to two thirds, although it is noteworthy that nearly 15% of the patients who give up smoking during the first months after ACS resume the habit over the following months. These findings support the need for cardiologists to introduce strict measures to control smoking in their patients following ACS and to implement active strategies to achieve complete abstinence.

### ACKNOWLEDGMENTS

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### CONFLICTS OF INTEREST

None declared.

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