INTERVENTIONAL CARDIOLOGY AND SURGERY

Use of secondary preventive drugs in patients with acute coronary syndromes treated medically or with coronary angioplasty: results from the nationwide French PREVENIR survey

N Danchin, O Grenier, J Ferrières, C Cantet, J-P Cambou

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See end of article for authors' affiliations

Correspondence to:
Dr Nicolas Danchin,
Hôpital Européen Georges
Pompidou, 20 rue Leblanc,
75015 Paris, France;
nicolas.danchin@
egp.ap-hop-paris.fr

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Background: There is evidence that several classes of drugs are beneficial for secondary prevention in patients with coronary artery disease.

Objective: To compare the use of secondary preventive drugs in patients with acute coronary syndromes given conservative treatment or percutaneous coronary interventions.

Design: The PREVENIR survey was designed to assess the management of patients with acute coronary syndromes admitted to hospital in France in January 1998. Drugs prescribed at hospital discharge were recorded retrospectively from the hospital records, and treatment at six months was assessed prospectively.

Setting: University hospitals, general hospitals, and private clinics throughout the country.

Results: Of 1394 patients participating in the survey, 668 underwent coronary angioplasty during the initial hospital stay and 706 had medical treatment only. At hospital discharge, aspirin, β blockers, and statins were prescribed significantly more often in patients undergoing angioplasty. Using multivariate logistic regression, coronary angioplasty was an independent predictor of treatment with aspirin (odds ratio 3.55), statins (1.92), and β blockers (1.41). Compared with treatment at discharge, only statin use differed at six months, with a significant increase both in patients treated medically and in those who had undergone angioplasty. Increased use of statins, aspirin, and β blockers was significantly correlated with coronary angioplasty during the initial hospital stay.

Conclusions: In this national French survey, patients treated with percutaneous coronary interventions were more likely to receive secondary preventive drugs than patients receiving medical treatment alone.

Percutaneous transluminal coronary angioplasty (PTCA) is often considered a "radical" treatment for coronary artery lesions. Coronary artery disease, however, is caused by a diffuse atherosclerotic process involving the whole coronary arterial tree. In recent years, evidence has accumulated that several classes of secondary preventive drugs are clinically effective.¹ These include aspirin,² β blocking agents,³ angiotensin converting enzyme (ACE) inhibitors,⁴⁻⁵ and statins,⁶⁻⁸ all of which can reduce morbidity and mortality in patients with coronary artery disease. Statin treatment, however, has been presented as an alternative to coronary angioplasty.⁹ Thus the question arises as to whether patients treated with PTCA receive less secondary prevention (that is, treatment of the atherosclerotic process itself) than patients managed medically.

Our aim in the present study was to document the use of secondary preventive drugs in patients treated with PTCA in the French nationwide PREVENIR registry in comparison with those treated medically. The PREVENIR study was designed to assess drugs prescribed at hospital discharge and at six months in patients admitted to an intensive care unit for an acute coronary syndrome (acute myocardial infarction or unstable angina).

METHODS

Study design

The PREVENIR-1 study included all patients admitted for an acute coronary syndrome in January 1998 at the participating centres. The participation of the centres was on a voluntary basis. Patient details (sex, age, height, and weight), the characteristics of their coronary artery disease (diagnosis, location

of myocardial infarction, left ventricular ejection fraction), the treatment procedures used in the acute stage (thrombolytic treatment, coronary artery bypass, PTCA), risk factors, and prescriptions at discharge were extracted from the medical records or discharge letters by a medical investigator. In addition, information on the outpatient treatment prescribed at six months was collected prospectively, either during an outpatient visit at the participating institution or by direct contact with the patients or their general practitioners.

Population

All subjects meeting the following criteria were included in the study:

- *Myocardial infarction* with at least two of the following characteristics: typical chest pain at rest of at least 30 minutes' duration and not relieved by glyceryl trinitrate; ST segment elevation of ≥ 0.1 mV in two adjacent frontal leads or ≥ 0.2 mV in two adjacent precordial leads of the ECG; the development of a new Q wave; significant elevation of creatine kinase MB isoenzyme (to more than twice the upper limit of normal).

Abbreviations: ACE, angiotensin converting enzyme; CI, confidence interval; ENACT, European network for acute coronary treatment; FRISC, Fragmin and fast revascularisation during instability in coronary artery disease; NRMI, national registry of myocardial infarction; OR, odds ratio; PTCA percutaneous transluminal coronary angioplasty; RR, relative risk

Table 1 Baseline characteristics and preadmission treatment in patients admitted to hospital for an acute coronary syndrome and receiving percutaneous transluminal coronary angioplasty or medical treatment alone

	PTCA (n=668)	Medical treatment (n=706)	p Value
Age <65 years	335 (50%)	255 (36%)	<0.001
Sex (male)	508 (76%)	471 (67%)	<0.001
History of MI	124 (19%)	180 (26%)	<0.003
PVD	55 (8%)	82 (12%)	<0.05
History of stroke	26 (4%)	47 (7%)	<0.05
Current smoking	293 (44%)	251 (36%)	<0.003
Diabetes mellitus	130 (19.5%)	154 (22%)	NS
Systemic hypertension	293 (44%)	364 (52%)	<0.005
Hyperlipidaemia	319 (48%)	304 (43%)	NS
Family history	216 (33%)	165 (24%)	<0.001
Admission for acute MI	390 (58%)	380 (54%)	NS
Treatment before admission			
Statins	104 (16%)	113 (16%)	NS
Fibrates	70 (10.5%)	61 (9%)	NS
Aspirin	245 (37%)	255 (36%)	NS
Oral anticoagulants	42 (6%)	50 (7%)	NS
β Blockers	190 (28%)	220 (31%)	NS
ACE inhibitors	107 (16%)	174 (25%)	<0.001
Calcium antagonists	156 (23%)	206 (29%)	<0.02
Oral antidiabetics	84 (13%)	96 (14%)	NS
Insulin	27 (4%)	32 (4.5%)	NS

ACE, angiotensin converting enzyme; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; PVD, peripheral vascular disease.

- *Unstable angina*, defined by one the following criteria: angina at rest; effort angina with crescendo pain, with sudden aggravation; severe de novo effort angina.

For the purposes of this study, the patients were categorised in two groups: those who had undergone PTCA during the initial hospital admission, either on an emergency or an elective basis, and those receiving medical treatment only during their entire hospital admission (that is, patients who had undergone neither PTCA nor coronary bypass grafting).

Statistical analysis

Variables were analysed as qualitative data. Univariate analyses were performed using the χ^2 test. Backward logistic regression analyses were done for multivariate analysis, using the prescription of secondary preventive drugs at discharge or at six months as the dependent variables. Analyses of treatment at discharge were performed on the whole population, and analyses of treatment at six months were done in the subset of patients alive and not lost to follow up at six months. For all statistical analyses, a probability value of $p < 0.05$ was considered significant.

RESULTS

Baseline characteristics

Among the 77 participating institutions, 76% had intervention facilities on site. Of the initial population of 1394 patients included in the study, 20 who had undergone coronary bypass surgery were excluded from the analyses; 668 (49%) underwent PTCA during the initial hospital stay; and 706 (51%) received only medical treatment. The baseline characteristics of the two populations and the drugs they received before hospital admission are detailed in table 1. Briefly, the PTCA patients were younger than their medically treated counterparts; and history of previous myocardial infarction, peripheral vascular disease, stroke, or systemic hypertension was less common. In contrast, there were more current smokers and more patients with a family history of coronary artery disease in the PTCA group.

Table 2 Treatment at hospital discharge

	PTCA (n=668)	Medical treatment (n=706)	p Value
Statins	281 (42%)	206 (29%)	<0.001
Fibrates	48 (7%)	43 (6%)	NS
Aspirin	638 (96%)	594 (84%)	<0.001
Other antiplatelet agents	451 (67.5%)	52 (7%)	<0.001
Oral anticoagulants	65 (10%)	122 (17%)	<0.001
Aspirin, other antiplatelet agents or oral anticoagulants	662 (99%)	664 (94%)	<0.01
β Blockers	493 (74%)	443 (63%)	<0.001
ACE inhibitors	267 (40%)	303 (43%)	NS
Calcium antagonists	158 (24%)	223 (32%)	<0.002
Any antianginal drugs	621 (93%)	656 (93%)	NS
Oral antidiabetics	71 (11%)	99 (14%)	NS
Insulin	35 (5%)	44 (6%)	NS

ACE, angiotensin converting enzyme; PTCA, percutaneous transluminal coronary angioplasty.

Drugs at hospital discharge

At hospital discharge, 90% of the patients were receiving aspirin, 35% statins, 68% β blockers, 41.5% ACE inhibitors, and 28% calcium antagonists. Aspirin, statins, and β blocking agents were prescribed more often in patients treated with PTCA (table 2). Using multivariate logistic regression (table 3), PTCA was an independent predictor of prescription of aspirin (odds ratio (OR) 2.87), statins (OR 1.70), and β blockers (OR 1.46), but not of ACE inhibitors. In addition, non-aspirin antiplatelet agents were prescribed more often in PTCA patients (67.5% v 7%), reflecting the use of thienopyridines in those undergoing stent placement. Patients treated medically were also less likely to receive any antithrombotic drugs (that is, aspirin, other antiplatelet agents, or oral anticoagulants) (table 2).

Drugs at six months

Data on drugs prescribed at six months were available in 1240 patients (table 4). For most classes of drugs little change was observed between hospital discharge and six months. As expected, however, the prescription of non-aspirin antiplatelet agents was much less likely at six months than immediately after the initial PTCA procedure. The most striking change was observed for statin treatment, with a significant increase from hospital discharge to the six month follow up in both the PTCA group and the medical treatment group. Of note was the absence of a catch up phenomenon in the medical treatment group (increase in use of statins 9%) compared with the PTCA group (increase in use of statins 10%). Here again, multivariate logistic regression showed that performance of a PTCA procedure during the index hospital admission was an independent predictor of the use of statins (relative risk (RR) 1.60, 95% confidence interval (CI) 1.24 to 2.07), aspirin (RR 2.47, 95% CI 1.73 to 3.53), and β blockers (RR 1.43, 95% CI 1.12 to 1.84) at six months.

DISCUSSION

Though numerous randomised trials and observational surveys have shown the efficacy of several classes of drugs in secondary prevention for coronary artery disease, little is known about the way current recommendations translate into real life clinical practice. In addition, very few data are available on the use of secondary preventive drugs according to the initial management of the patients (that is, coronary angioplasty v exclusively medical treatment).^{10 11} The French PREVENIR survey aimed to determine the way in which recommendations were implemented in the country as a whole, by assessing drugs prescribed at hospital discharge and six months later in patients admitted for an acute coronary syndrome. The participating centres represented more than 15%

Table 3 Multivariate analysis of secondary preventive drugs prescribed at the time of hospital discharge

	Relative risk	95% CI	p Value
<i>Statins</i>			
Age (years)			
65–74	0.79	0.57 to 1.08	0.14
75+	0.33	0.21 to 0.50	<0.001
Statins before admission	13.6	8.22 to 22.3	<0.001
Known hyperlipidaemia	3.01	2.24 to 4.04	<0.001
PTCA	1.70	1.28 to 2.27	<0.001
Admission to university hospital	1.72	1.30 to 2.28	<0.001
Current smoking	1.45	1.08 to 1.96	<0.02
Diabetes mellitus	0.68	0.47 to 0.98	<0.05
<i>Aspirin</i>			
PTCA	2.87	1.82 to 4.52	<0.001
Admission for MI	2.21	1.47 to 3.33	<0.001
Previous stroke	0.23	0.12 to 0.44	<0.001
Aspirin before admission	4.24	2.61 to 6.31	<0.001
Admission to university hospital	2.02	1.32 to 3.09	0.001
History of infarction	0.57	0.36 to 0.90	<0.02
History of angina	0.56	0.36 to 0.86	<0.01
Current smoking	1.54	1.00 to 2.39	0.05
<i>β Blockers</i>			
Age (years)			
65–74	0.90	0.65 to 1.24	NS
75+	0.39	0.27 to 0.55	<0.001
PVD	0.49	0.32 to 0.74	<0.001
PTCA	1.46	1.11 to 1.92	<0.01
Admission for MI	1.73	1.31 to 2.29	<0.001
β Blockers before admission	6.01	4.19 to 8.61	<0.001
LVEF			
36–50%	1.02	0.73 to 1.42	NS
≤35%	0.28	0.17 to 0.44	<0.001
Not measured	0.68	0.45 to 1.02	NS
Sex (female)	0.74	0.55 to 1.00	0.05
<i>ACE inhibitors</i>			
Admission for MI	3.30	2.47 to 4.39	<0.001
ACEI before admission	9.09	6.29 to 13.1	<0.001
Age (years)			
65–74	0.85	0.62 to 1.15	NS
75+	0.59	0.42 to 0.83	<0.005
Hypertension	1.35	1.09 to 2.52	<0.05
LVEF			
36–50%	3.23	2.37 to 4.41	<0.001
≤35%	7.27	4.36 to 12.1	<0.001
Not measured	1.66	1.09 to 2.52	<0.02

The model included sex, history of angina, myocardial infarction, stroke, or peripheral vascular disease, risk factors, type of institution, initial diagnosis, coronary angioplasty during the initial hospital stay, and for each class of drug, treatment with the same class before hospital admission; age and LVEF were also entered into the model as a categorical variables.

ACE, angiotensin converting enzyme; ACEI, angiotensin converting enzyme inhibitor; CI, confidence interval; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; PVD, peripheral vascular disease.

of all centres managing patients with acute myocardial infarction or unstable angina in France and were evenly distributed throughout the country. There was, however, an over representation of academic institutions and an under representation of private clinics, so we included the type of institution in our multivariate models.

One of the strengths of the survey was that the centres were recruited after the month of January 1998 (period of inclusion); drugs at the time of hospital discharge were recorded retrospectively from the clinical notes, so the participating centres could not have been influenced in their use of preventive drugs, which reflected the real life management of the patients at the participating institutions. In addition, the

Table 4 Drugs prescribed at six months

	PTCA (n=630)	Medical treatment (n=610)	p Value
Statins	329 (52%)	230 (38%)	<0.001
Fibrates	48 (8%)	41 (7%)	NS
Aspirin	579 (92%)	499 (82%)	<0.001
Other antiplatelet agents	64 (10%)	39 (6%)	<0.02
Oral anticoagulants	28 (6%)	77 (10%)	<0.01
β Blockers	456 (72%)	383 (63%)	<0.003
ACE inhibitors	257 (41%)	268 (44%)	NS
Calcium antagonists	148 (24%)	200 (33%)	<0.001
Oral antidiabetic agents	76 (12%)	95 (16%)	NS
Insulin	21 (3%)	36 (6%)	<0.05

ACE, angiotensin converting enzyme; PTCA, percutaneous transluminal coronary angioplasty.

survey provided prospective information on the use of secondary preventive drugs in the months following the acute coronary event.

As in the ENACT (European network for acute coronary treatment) study,¹¹ which was designed to assess the in-hospital management of patients with acute coronary syndromes throughout Europe, patients treated conservatively were less likely to receive aspirin, lipid lowering agents, and β blockers, while the percentage of patients treated with ACE inhibitors was similar. The increased use of aspirin in patients treated with PTCA was expected, as aspirin treatment is considered part of the PTCA procedure. In patients treated medically, however, only 84% were placed on aspirin at the time of hospital discharge, a figure which appears comparable or somewhat lower than previously noted in surveys of myocardial infarction carried out in France in recent years,^{12,13} but higher than that observed in a Veterans Affairs observational study of patients admitted for unstable angina in 1995 (74%).¹⁴

Overall, 91% of medically treated patients in the present survey received either aspirin or oral anticoagulants, and 94% received antithrombotic drugs. The use of coronary angioplasty was also independently correlated with the prescription of statins. The percentage of patients receiving statins was somewhat lower than that noted in the ENACT survey, which recruited patients during the year 1999, but the trend favouring patients treated with angioplasty procedures was similar in the two surveys. Interestingly, in the PREVENIR survey, a similar though small increase in the use of statins among the two populations was observed six months after the initial hospital admission, showing that there was no “catch up phenomenon” in patients treated conservatively: an additional 10% of patients were on statins at six months, both in those treated with coronary angioplasty and in those treated conservatively.

These results are concordant with the EUROASPIRE survey data,¹⁵ which showed that normalisation of cholesterol concentrations at six months was achieved slightly more often in the subset of patients included after coronary angioplasty than in the subset included after admission for an ischaemic syndrome treated medically. β Blocking agents were also prescribed more frequently, both at hospital discharge and at six months, in patients treated with coronary angioplasty. Although these data are in keeping with those in the ENACT survey, they are perhaps surprising, as it might have been expected that patients undergoing angioplasty would require fewer antianginal drugs than those given medical treatment only. In this regard, patients treated conservatively received more calcium antagonists (32% v 24%) and more nitrates (60% v 43%) than those treated with angioplasty, but the same percentage of patients in the two groups received at least one antianginal drug (β blocking agents, calcium antagonists, or

nitrates). In the FRISC-2 (Fragmin and fast revascularisation during instability in coronary artery disease) randomised trial,¹⁰ the level of prescription of β blocking agents at three months was high in both arms of the trial, though significantly higher in patients assigned to a conservative strategy.

Finally, there was no influence of the use of coronary angioplasty on the prescription of ACE inhibitors, which was essentially related to the type of coronary syndrome (acute myocardial infarction *v* unstable angina), or the presence of concomitant disease (hypertension). These observations are in keeping with those of the ENACT study, but differ from those of NRMI-2 (national registry of myocardial infarction) in the USA, which showed that patients undergoing PTCA after an acute myocardial infarct were less likely to receive ACE inhibitors than those treated conservatively.¹⁶ The data from the NRMI-2, however, corresponded to the 1994–96 period, where the use of ACE inhibitor treatment in secondary prevention may have been less universally accepted than in 1998.

In the non-invasive arm of the prospective randomised FRISC-2 trial,¹⁰ 94% of the patients were on aspirin three months after the initial episode of unstable angina, and there was no difference between the two arms of the trial. Similarly, the prescription of statins was high (56%), and equivalent in the two arms of the trial. It must be emphasised, however, that FRISC-2 was a prospective, randomised trial which therefore involved a selected population of patients; in addition, the overall management of patients included in the trial was likely to have been influenced by their very participation in the study, and may not reflect real life practice.

Conclusions

The implementation of recommendations on the use of secondary preventive drugs in patients admitted to hospital for acute coronary syndromes was more satisfactory in those treated with percutaneous coronary interventions than in those treated conservatively. In current clinical practice, patients treated with coronary angioplasty not only receive attention to a diseased coronary artery segment, but are also rightly considered to have diffuse vascular disease requiring secondary prevention.

Authors' affiliations

N Danchin, O Grenier, Cardiologie Hôpital Européen Georges Pompidou, Paris, France

J Ferrières, C Cantet, J-P Cambou, INSERM U 518, Toulouse, France

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