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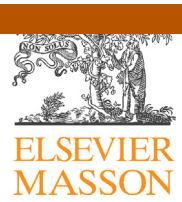

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CLINICAL RESEARCH

Management of outpatients in France with stable coronary artery disease. Findings from the prospeCtive observational LongitudinAl RegIstry oF patients with stable coronary arterY disease (CLARIFY) registry☆

Prise en charge des patients coronariens stables en France. Données du registre CLARIFY (ProspeCtive observational LongitudinAl RegIstry of patients with stable coronary arterY disease)

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KEYWORDS
Stable coronary artery disease;
Western Europe;
France;
Guidelines

Summary
Background. — Improvements in the treatment of coronary artery disease mean that an increasing number of patients survive acute cardiovascular events and live as outpatients with or without anginal symptoms.
Aim. — To determine the characteristics and management of contemporary outpatients with stable coronary artery disease in Western Europe, and to compare France with the other Western European countries.
Methods. — CLARIFY (prospeCtive observational LongitudinAl RegIstry oF patients with stable coronary arterY disease) is an international, prospective, observational, longitudinal study. Between November 2009 and July 2010, 32,954 adult outpatients with stable coronary artery disease (defined as a history of documented myocardial infarction [of > 3 months], prior coronary revascularization, chest pain with myocardial ischaemia, or coronary stenosis of > 50% proven by angiography) were enrolled in 45 countries. The demographics and management of CLARIFY patients enrolled in France were compared with those enrolled in other Western European countries (Austria, Belgium, Denmark, Germany, Greece, Ireland, Italy, Netherlands, Portugal, Spain, Switzerland and the UK).
Results. — Of the 14,726 patients enrolled in Western Europe (mean age 66.2 [10.2] years; 79.6% male), 2432 (16.5%) were from France. The use of aspirin was lower in France than in other Western European countries (74.5% vs. 86.9%, respectively), whereas use of thienopyridines (48.5% vs. 21.7%), oral anticoagulants (12.3% vs. 9.0%) and lipid-lowering drugs (95.8% vs. 92.5%) was higher. Beta-blockers were used in 73% of both groups. Angina was less prevalent in France (6.3% vs. 15.5%) and French patients showed higher levels of physical activity than their counterparts in Western Europe.
Conclusions. — The management of patients with stable CAD in France appears favourable, with good adherence to guideline-based therapies, but there remains room for improvement in terms of symptom and risk factor control.

MOTS CLÉS
Maladie coronaire stable ;
Europe de l'Ouest ;
France ;
Recommandations

Résumé
Contexte. — Les améliorations dans le traitement de la maladie coronaire impliquent qu'un nombre croissant de patients survivent après un événement coronaire aigu et deviennent des patients ambulatoires avec ou sans symptômes angineux.
Objectif. — Déterminer les caractéristiques et la prise en charge des patients ambulatoires porteurs d'une maladie coronaire stable en Europe de l'Ouest et comparer les patients français avec les patients des autres pays européens.
Méthodes. — CLARIFY (ProspeCtive observational LongitudinAl RegIstry oF patients with stable coronary arterY disease) est une étude internationale longitudinale prospective et observationnelle. Entre novembre 2009 et juillet 2010, 32 954 patients adultes porteurs d'une maladie coronaire stable (définie comme des patients ayant une histoire d'infarctus du myocarde documenté de plus de 3 mois, un antécédent de revascularisation coronaire, des douleurs thoraciques avec une ischémie myocardique ou une sténose coronaire de plus de 50 % démontrée par une coronarographie) ont été inclus dans 45 pays. Les caractéristiques démographiques et la prise en charge des patients CLARIFY inclus en France ont été comparés avec celles des patients inclus dans les autres pays d'Europe de l'Ouest (Autriche, Belgique, Danemark, Allemagne, Grèce, Irlande, Italie, Pays-Bas, Portugal, Espagne, Suisse et le Royaume-Uni).
Résultats. — Parmi les 14 726 patients inclus en Europe de l'Ouest (moyenne d'âge : 66,2 [10,2] ans ; 79,6 % d'hommes), 2432 (16,5 %) étaient des patients français. L'utilisation d'aspirine était

plus basse en France que dans les autres pays européens de l'Ouest (74,5 % vs 86,9 %, respectivement) tandis que l'utilisation des thiénopyridines (48,1 % vs 21,7 %), les anticoagulants oraux (12,3 % vs 9,0 %) et les traitements hypolipidémiants (95,8 % vs 92,5 %) étaient plus élevés. Les bêtabloqueurs étaient utilisés chez 73 % des patients des deux groupes. L'angine de poitrine était moins prévalente en France (6,3 % vs 15,5 %) et les patients français présentaient un plus haut niveau d'activité physique par rapport aux autres patients d'Europe de l'Ouest.
Conclusion. — La prise en charge des patients porteurs d'une maladie coronaire stable en France semble appropriée, avec une bonne adhésion aux thérapeutiques recommandées, mais il reste des améliorations à faire afin de contrôler les symptômes et les facteurs de risque.

Introduction

Despite substantial improvements in preventive cardiology, coronary artery disease (CAD) remains the leading cause of death and morbidity worldwide [1—3] and in Europe [4]. Secondary prevention of acute coronary syndromes has also advanced, with a series of large, randomized clinical trials establishing the value of antiplatelet therapy, statins, and angiotensin-converting enzyme inhibitors in this setting [5,6]. CAD places a major burden on public health [7—9], due not only to an ageing population, but also to the increasing numbers of patients who survive an initial acute cardiovascular event and live as outpatients, with or without anginal symptoms [5,6,10,11], and who are at high risk of myocardial infarction, heart failure, arrhythmia, and death. Important determinants of long-term CAD survival include risk factors and their management, including left ventricular function, extent of artery disease, heart rate [12—14], and treatment [15].

Important changes in the management and outcomes of patients with CAD mean that a need has arisen for current data in patients with stable CAD treated in everyday practice. It is important to have longitudinal observations of a large, representative cohort of patients, spanning several geographical regions, focusing on stable outpatients, and including both symptomatic and asymptomatic individuals. The prospeCtive observational LongitudinAl RegIstry oF patients with stable coronary arterY disease (CLARIFY) was initiated to improve our knowledge about the contemporary stable CAD population [16,17]. The aim of this analysis was to compare the characteristics and management of CLARIFY patients from France with those from patients in other Western European countries.

Methods

Study design

CLARIFY is an international, prospective, observational, longitudinal registry in outpatients with stable CAD, followed up for 5 years. The study rationale and methods have been published previously [16]. Patients were enrolled between November 2009 and July 2010 in 45 countries in Africa, Asia, Australia, Europe, the Middle East, and North, Central and South America.

The registry is being performed in accordance with the principles of the Declaration of Helsinki and has been approved by local institutional review boards. All patients gave written informed consent to participate in agreement with national and local guidelines. Patient confidentiality is ensured by the use of patient identification code numbers that correspond to computer files. As an observational study, the management and treatment of patients is conducted according to usual practices, with no specific tests or therapies defined in the study protocol.

Study population

Eligible subjects were outpatients with stable CAD demonstrated by a history of at least one of the following criteria: documented myocardial infarction (> 3 months previously); coronary stenosis > 50% proven by coronary angiography; chest pain with myocardial ischaemia proven by stress electrocardiogram, stress echocardiography, or myocardial imaging; or coronary artery bypass graft or percutaneous coronary intervention performed > 3 months previously.

Patients were excluded from participation if they had been hospitalized for cardiovascular disease within the previous 3 months (including for revascularization), were planned to undergo revascularization, or had a condition expected to hamper participation up to 5 years (e.g. limited cooperation or legal capacity, serious non-cardiovascular disease, a condition that could affect life expectancy [e.g. cancer, drug abuse], or severe cardiovascular disease [e.g. advanced heart failure, severe valve disease, history of valve repair/replacement]).

Evaluations

Baseline data were collected anonymously using electronic case report forms. Information documented included patient demographics, medical history, risk factors, employment status, the results of physical examination, heart rate (determined by both pulse palpation and 12-lead electrocardiography, using the most recent electrocardiogram within 6 months in clinically stable patients), laboratory values (if available), and current chronic medical treatments (i.e. taken regularly for ≥ 7 days before entry into the registry).

Study setting and site selection

To ensure that the population was representative of the real-life community of stable CAD outpatients, recruitment of sites and patients was based on the predefined selection of physician types and consecutive enrolment of eligible patients. In each country participating in CLARIFY, the types (office-based primary care physicians, internists, physicians based in hospitals with outpatient clinics, cardiologists, or other specialties) and practice settings (hospital-based as opposed to ambulatory practice) of physicians in charge of CAD patients was determined, using the best available epidemiological data and market research data. This allowed targeting of an appropriate proportion of each of these physician types and settings, and provided a distribution of physicians (and therefore of patient populations) across regions and locations (urban, suburban, or rural) that reflected the epidemiological patterns in each country. The national coordinator in each country also reviewed the site selection. Each physician recruited, over a brief period of time, 10—15 outpatients with stable CAD.

Data management and quality

Data were collected centrally using a standardized, international case report form (translated into the local language) and sent by each country to the data management centre (Robertson Centre for Biostatistics, University of Glasgow, UK) where checks for completeness, internal consistency, and accuracy were run. Data quality control is performed annually onsite in 1% of randomly selected sites up to 5 years. At these sites, 100% of case report forms for patients enrolled at that site were monitored for source documentation and accuracy. Data quality control was done at face-to-face quality control visits, and involved review of source documents supporting the adequacy and accuracy of data collected on the case report forms.

In this analysis, the data from patients enrolled in France were compared with those enrolled in the other Western European countries participating in CLARIFY (Austria, Belgium, Denmark, Germany, Greece, Ireland, Italy, Netherlands, Portugal, Spain, Switzerland, UK).

Statistical analysis

Data were analysed by an independent statistics centre at the Robertson Centre for Biostatistics. Baseline variables are summarized as mean (standard deviation) or median (interquartile range) for continuous data, depending on the distribution of the data, and as counts and percentages for categorical data, and were based on patients in whom data were available. Comparisons between patients in France and those in Western Europe were made using one-way ANOVA or the Kruskal-Wallis test for continuous variables, again depending on the distribution of the data, and Pearson's Chi^2 test or Fisher's exact test for categorical variables. All analyses were performed using SAS version 9.2. A significance level of 0.05 was used to test for statistical differences; all tests used were two-sided.

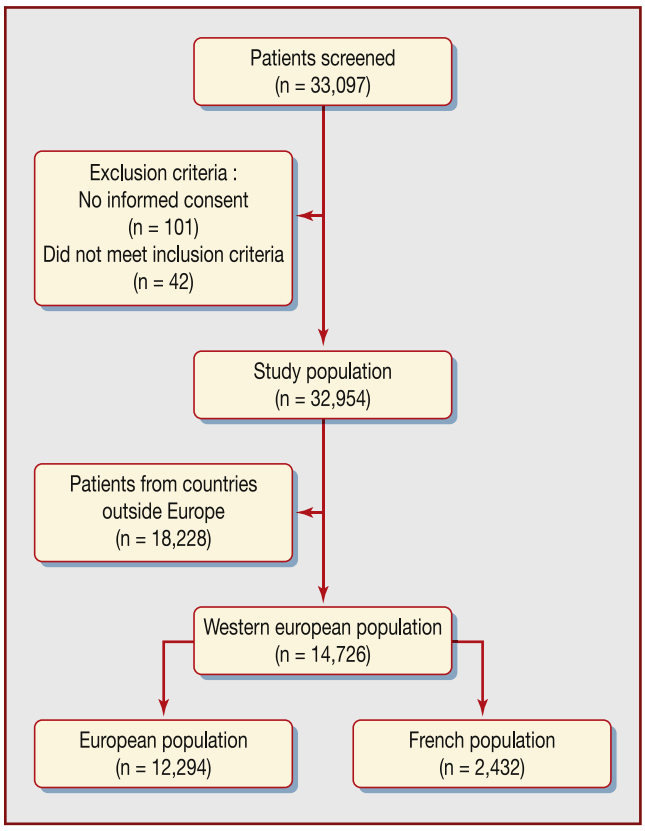

Figure 1. Patient flow chart.
Institutional review board (IRB).

Results

Study population

Of the 33,428 outpatients screened, 18,702 were excluded from the present analysis for one of the following reasons: 101 did not provide written informed consent, 42 did not meet the inclusion or exclusion criteria, in 331 patients informed consent or institutional review board approval was not ascertained or verifiable, and 18,228 patients were enrolled outside of Western Europe. Of the remaining 14,726 patients, 12,294 were from Western Europe (excluding France) and 2432 were from France (Fig. 1). Patient enrolment in France took place between May and July 2010.

The mean age of the Western European population was 66.2 (10.2) years and 79.6% were male. The baseline characteristics of the outpatients, classified according to enrolment in France or other Western European country, are detailed in Table 1. French patients were, on average, more frequently male (83.7% vs. 78.8%) and slightly older (66.7 vs. 66.1 years), and had a lower mean heart rate (64.6 vs. 66.5 beats per minute [bpm] on palpation) and higher left ventricular ejection fraction (59.3% vs. 56.9%) than patients in other Western European countries. French patients were less likely than those in other Western European countries to have treated hypertension (57.7% vs. 69.8%), to have a family history of premature CAD (24.7% vs. 29.6%) or to have congestive heart failure (2.9% vs. 7.9%), but were more likely to have dyslipidaemia (79.6% vs. 76.0%). A minority of

Table 1 Characteristics of the study population classified according to France vs. Europe.

Parameter	Patients with data	France ($n = 2432$)	Europe ($n = 12,294$)	*P*-value
Age (y), mean (SD)	14,701	66.7 (10.7)	66.1 (10.0)	0.0057
Men, *n* (%)	14,703	2031 (83.7)	9675 (78.8)	< 0.0001
BMI (kg/m^2), median (IQR)	14,691	26.8 (24.5, 29.7)	27.7 (25.4, 30.5)	< 0.0001
Risk factors				
Diabetes mellitus, *n* (%)	14,705	619 (25.5)	3272 (26.6)	0.25
Dyslipidaemia, *n* (%)	14,707	1930 (79.6)	9333 (76.0)	0.0001
Family history of CAD[a], *n* (%)	14,707	600 (24.7)	3634 (29.6)	< 0.0001
Treated hypertension, *n* (%)	14,707	1400 (57.7)	8578 (69.8)	< 0.0001
Presentation characteristics				
HR palpation (bpm), mean (SD)	14,679	64.6 (9.9)	66.5 (10.6)	< 0.0001
HR ECG (bpm), mean (SD)	11,564	63.5 (10.2)	65.9 (11.3)	< 0.0001
SBP (mmHg), mean (SD)	14,686	131.3 (14.1)	131.5 (16.4)	0.75
DBP (mmHg), mean (SD)	14,686	75.5 (8.4)	76.6 (9.5)	< 0.0001
Controlled blood pressure (SBP < 140/DBP < 90 mmHg)	14,686	1658 (68.9)	7903 (64.4)	< 0.0001
LVEF (%), mean (SD)	10,234	59.3 (10.1)	56.9 (10.8)	< 0.0001
Creatinine (mmol/L), median (IQR)	11,146	0.09 (0.08, 0.10)	0.09 (0.08, 0.10)	0.96
Total cholesterol (mmol/L), median (IQR)	11,678	4.3 (3.8, 4.9)	4.3 (3.7, 4.9)	0.21
LDL-cholesterol	10,005	2.3 (2.0, 2.8)	2.4 (1.9, 2.9)	0.08
LDL, *n* (%)	10,005			
< 70 mg/dL (< 1.82 mmol/L)		364 (18.4)	1611 (20.1)	< 0.0001
70—100 mg/dL (1.82—2.60 mmol/L)		925 (46.8)	3323 (41.4)	
> 100 mg/dL (> 2.60 mmol/L)		688 (34.8)	3094 (38.5)	
High-density lipoprotein cholesterol	10,884	1.2 (1.0, 1.5)	1.2 (1.0, 1.4)	<0.0001
CHF symptoms including NYHA class, *n* (%)	14,704			
No CHF		2352 (97.1)	11,313 (92.1)	< 0.0001
Class II		53 (2.2)	813 (6.6)	
Class III		18 (0.7)	155 (1.3)	
Current evidence of myocardial ischaemia, *n* (%)	14,692	300 (12.4)	2277 (18.6)	< 0.0001
Medical history				
Peripheral artery disease, *n* (%)	14,706	426 (17.6)	1408 (11.5)	< 0.0001
Myocardial infarction, *n* (%)	14,706	1304 (53.8)	7114 (57.9)	0.0002
Stroke, *n* (%)	14,706	59 (2.4)	428 (3.5)	0.0081
PCI, *n* (%)	14,707	1758 (72.5)	7322 (59.6)	< 0.0001
CABG, *n* (%)	14,707	547 (22.6)	3277 (26.7)	< 0.0001
Pacemaker, *n* (%)	14,707	94 (3.9)	365 (3.0)	0.019
Hospitalization for CHF, *n* (%)	14,707	111 (4.6)	464 (3.8)	0.06
Atrial fibrillation/flutter, *n* (%)	14,707	209 (8.6)	1041 (8.5)	0.82
Asthma/COPD, *n* (%)	14,707	217 (8.9)	1185 (9.6)	0.28
Reimbursement of cardiovascular agents, *n* (%)	14,665			
Fully reimbursed		2359 (97.8)	6684 (54.5)	< 0.0001
Partly reimbursed		51 (2.1)	4281 (34.9)	

Table 1 (*Continued*)

Parameter	Patients with data	France ($n = 2432$)	Europe ($n = 12,294$)	*P*-value
Not reimbursed		1 (0.04)	1289 (10.5)	
Lifestyle characteristics				
Smoking status, *n* (%)	14,708			
Current		250 (10.3)	1428 (11.6)	0.12
Former		1221 (50.4)	6207 (50.5)	
Never		954 (39.3)	4648 (37.8)	
Alcohol intake (number of drinks per week), *n* (%)	14,706			
0		836 (34.5)	4118 (33.5)	0.61
> 0 and < 20		1469 (60.6)	7528 (61.3)	
≥ 20		119 (4.9)	636 (5.2)	
Stimulant drinks consumed, *n* (%)	14,705			
Coffee		1550 (64.0)	7204 (58.7)	< 0.0001
Tea		187 (7.7)	2442 (19.9)	
Neither		686 (28.3)	2636 (21.5)	
Physical activity, *n* (%)	14,703			
None		353 (14.6)	2194 (17.9)	< 0.0001
Light physical activity most weeks		969 (40.0)	6126 (49.9)	
≥ 20 min vigorous physical activity 1–2 times/week		583 (24.1)	2116 (17.2)	
≥ 20 min vigorous physical activity ≥ 3 times/week		516 (21.3)	1846 (15.0)	

BMI: body mass index; CABG: coronary artery bypass graft; CAD: coronary artery disease; CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease; DBP: diastolic blood pressure; ECG: electrocardiogram; HR: heart rate; HRT: hormone replacement therapy; IQR: interquartile range; LDL: low-density lipoprotein; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; SBP: systolic blood pressure; SD: standard deviation; bpm: beats per minute; y: year.

[a] Myocardial infarction, sudden death, stable angina at age < 55 years (men) or < 65 years (women) in a first-degree relative.

patients achieved low-density lipoprotein cholesterol concentrations of < 1.8 mmol/L (< 70 mg/dL) (18.4% in France vs. 20.1% in other Western European countries). French patients also had a less frequent history of myocardial infarction (53.8% vs. 57.9%) and stroke (2.4% vs. 3.5%), but were more likely to have peripheral artery disease (17.6% vs. 11.5%). They were also more likely to have undergone a previous percutaneous coronary intervention (72.5% vs. 59.6%), whereas coronary artery bypass grafting was less frequently performed (22.6% vs. 26.7%). French patients showed higher levels of physical activity.

Angina was infrequent in French patients, and was more than twice as prevalent in the other Western European group (6.3% vs. 15.5%; Fig. 2). Of the patients with symptoms, 88.2% ($n = 135$) in France and 85.7% ($n = 1630$) in the other Western European countries reported no or slight limitation of ordinary physical activity (Canadian Cardiovascular Society [CCS] class I or II), 12% in both groups reported marked limitation (CCS class III), and a small percentage (1.8%) of those in Western Europe reported CCS class IV.

Chronic medication use

The use of selected chronic cardiovascular and non-cardiovascular medications at enrolment is detailed in Table 2. Overall use of antiplatelet therapy was high, with aspirin being the most frequently used drug (84.8% of patients); thienopyridines were used in 26.2% of the European patients, but with a much higher rate of use in France versus the other countries (48.5% vs. 21.7%). Dual antiplatelet therapy (DAPT) was used in 30.7% of French patients versus 22.4% of those in the other countries; corresponding data for patients with a history of PCI were 38.0% and 30.9%, respectively (Table 3). Similarly, oral anticoagulants were used more frequently in France (12.3% vs. 9.0%; Table 2). The use of lipid-lowering drugs was also high overall, with a significantly more frequent rate among the French group (95.8% vs. 92.5%), whereas angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers were used slightly less frequently in France (73.0% vs. 75.7%).

Almost three-quarters of the patients (72.5%) were taking beta-blockers, and 17.7% had symptoms indicative of intolerance or a contraindication to beta-blocker therapy (Table 2). The rates of use of beta-blockers in patients with or without a previous myocardial infarction did not differ between the two groups. The French group more commonly took calcium antagonists (29.6% vs. 24.6%), whereas use of ivabradine (10.6% vs. 13.2%) and long-acting nitrates was lower (10.2% vs. 20.0%).

Table 2 Selected cardiovascular and non-cardiovascular chronic medications: France vs. Europe.

Medication, *n* (%)	Patients with data	France (*n* = 2432)	Europe (*n* = 12,294)	*P*-value
Cardiovascular medications				
Aspirin	14,700	1804 (74.5)	10,667 (86.9)	< 0.0001
Thienopyridine	14,684	1175 (48.5)	2665 (21.7)	< 0.0001
Other antiplatelet	14,683	110 (4.6)	1031 (8.4)	< 0.0001
No or any antiplatelet	14,701			< 0.0001
No antiplatelet		94 (3.9)	701 (5.7)	
1 antiplatelet		1585 (65.4)	8827 (71.9)	
≥ 2 antiplatelets		744 (30.7)	2750 (22.4)	
Oral anticoagulant	14,699	299 (12.3)	1106 (9.0)	< 0.0001
Beta-blocker	14,700	1764 (72.8)	8900 (72.5)	0.76
In patients with previous MI	8414	1010 (77.6)	5383 (75.7)	0.14
In patients without previous MI	6284	754 (67.3)	3515 (68.1)	0.59
Intolerance or contraindication to beta-blocker therapy	14,696	499 (20.6)	2105 (17.2)	< 0.0001
Ivabradine	14,700	258 (10.6)	1625 (13.2)	0.0005
Calcium antagonist	14,698	717 (29.6)	3016 (24.6)	< 0.0001
Verapamil or diltiazem	14,698	246 (10.2)	692 (5.6)	< 0.0001
ACE or ARB	14,700	1769 (73.0)	9289 (75.7)	0.0064
Lipid-lowering drug[a]	14,700	2321 (95.8)	11,362 (92.5)	< 0.0001
Long-acting nitrate	14,698	247 (10.2)	2452 (20.0)	< 0.0001
Other antianginal agent	14,694	342 (14.1)	643 (5.24)	< 0.0001
Diuretic	14,697	640 (26.4)	3824 (31.2)	< 0.0001
Other antihypertensive agent[b]	14,695	120 (5.0)	903 (7.4)	< 0.0001
Digoxin and derivative	14,698	19 (0.8)	286 (2.3)	< 0.0001
Amiodarone or dronedarone	14,693	128 (5.3)	308 (2.5)	< 0.0001
Other antiarrhythmic drug	14,692	42 (1.7)	110 (0.9)	0.0002
Other medications				
NSAID	14,695	50 (2.1)	696 (5.7)	< 0.0001
Antidiabetic agent	14,699	579 (23.9)	2770 (22.6)	0.15
Thyroid HRT	14,698	93 (3.8)	748 (6.1)	< 0.0001
Proton pump inhibitor	14,698	746 (30.8)	4565 (37.2)	< 0.0001
HRT (postmenopausal women)	14,694	6 (0.2)	51 (0.4)	0.23
Erectile dysfunction	14,697	78 (3.2)	252 (2.1)	0.0004

ACE: angiotensin-converting enzyme; ARB: angiotensin II receptor blocker; CAD: coronary artery disease; CCS: Canadian Cardiovascular Society; HRT: hormone replacement therapy; NSAID: non-steroidal anti-inflammatory drug; MI: myocardial infarction.
[a] Statins, fibrates, niacin, ezetimibe.
[b] Alpha-blockers, central adrenergic stimulants.

Table 3 Use of antiplatelet therapies in patients with a history of percutaneous coronary intervention: France vs. Europe.

Medication, *n* (%)	Patients with data	France (*n* = 1758)	Europe (*n* = 7322)	*P*-value
Aspirin	9075	1318 (75.1)	6573 (89.8)	< 0.0001
Thienopyridine	9065	981 (55.9)	2063 (28.2)	< 0.0001
Other antiplatelet	9063	90 (5.1)	707 (9.7)	< 0.0001
No or any antiplatelet	9075			< 0.0001
No antiplatelet		47 (2.7)	266 (3.6)	
1 antiplatelet		1041 (59.3)	4791 (65.5)	
≥ 2 antiplatelets		668 (38.0)	2262 (30.9)	

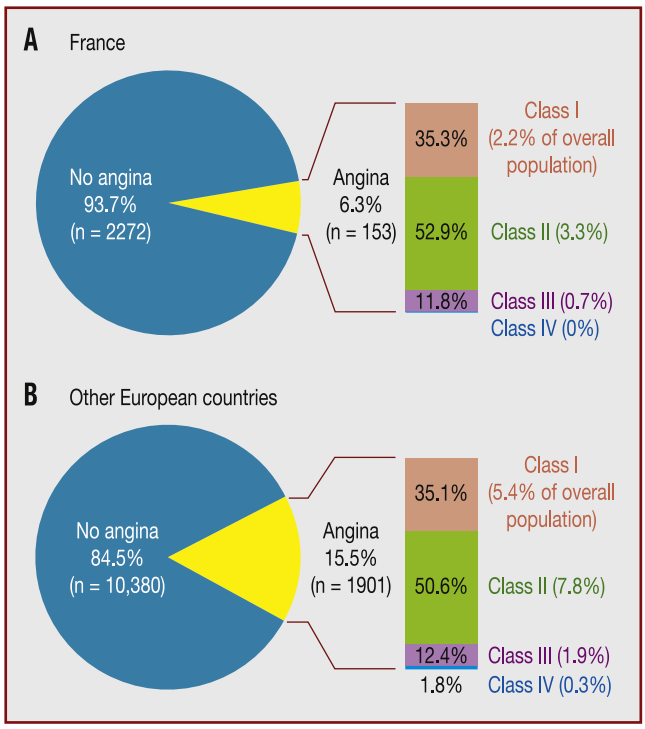

Figure 2. Angina status and Canadian Cardiovascular Society class.

Discussion

The results of the CLARIFY registry indicate that a large proportion of patients with stable CAD in France receive evidence-based therapies or treatments [15] for symptom control and for prevention of cardiovascular events; the findings are favourable in relation to CLARIFY patients in the other Western European countries. Patients in France are also more likely to go coronary intervention and are being treated with more aggressive antiplatelet therapy, which may reflect adherence to guidelines advocating treatment with dual antiplatelet therapy for 9—12 months following stent implantation [18]. Nevertheless, there remains room for improvement, illustrated by the fact that some patients still present angina episodes, albeit at a lower rate in France than in other Western European countries. Furthermore, while patients in France exhibit lower mean heart rates and higher rates of physical activity than their counterparts in other Western European countries, the mean heart rate of French patients is still somewhat high, and a substantial proportion of French patients report either no physical activity or only light levels of exercise.

The objective of managing stable CAD — through a combination of risk factor control, pharmacological therapy, lifestyle improvements, and patient education — is to reduce the patient's symptoms and improve their prognosis. Lifestyle modifications include smoking cessation, healthy diet, regular physical activity, maintaining a healthy weight, and achieving targets for lipids, blood pressure, and glucose [15]. Optimal medical therapy for patients with stable CAD involves at least one drug to manage symptoms of angina or ischaemia alongside drugs to prevent a coronary event [15]. Low-dose aspirin (or clopidogrel, in the case of aspirin intolerance) and statins are recommended in all patients with stable CAD, whereas angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers are recommended for stable CAD patients with another condition such as heart failure, hypertension, or diabetes. The CLARIFY registry data show that patients in France tend to have good blood pressure control, whereas low-density lipoprotein cholesterol is slightly higher than the recommended target of < 1.8 mmol/L [15]. About two-thirds of the patients achieved the LDL-cholesterol levels that were recommended at the time (< 2.60 mmol/L, 100 mg/dL) [19], and only approximately one-fifth the levels currently recommended in the European guidelines (< 1.8 mmol/L, 70 mg/dL) [15] despite the fact that 95.8% of patients were receiving some form of lipid-lowering therapy. Current recommendations on optimal management of lipids diverge between the European guidelines, recommending a target level < 1.8 mmol/L, and the American guidelines [20], suggesting to abandon any target altogether, but recommending to use the maximal tolerated dose of statins for any patient with documented coronary artery disease. The dose of statins was not recorded in CLARIFY, but the fact that the mean LDL-cholesterol level was 2.3 mmol/L suggests that only a minority of the patients received high-dose statins.

Of interest is the high rate of use of thienopyridines in France, which likely reflects the higher rate of percutaneous intervention and subsequent need for dual antiplatelet therapy. This finding is consistent with data from the World Health Organization MONICA (monitoring trends and determinants in cardiovascular disease) Project, from the late 1990s, which reported more intensive therapy in patients with a myocardial infarction in France when compared with other European regions [21,22]. The use of antiarrhythmic drugs and oral anticoagulants is also somewhat high in view of the slightly lower prevalence of a history of atrial fibrillation or flutter in the study and the fact that antiplatelets are preferred to oral anticoagulants for prevention of thrombotic events in patients without arrhythmias.

Contemporary data on the management and outcomes of patients with stable CAD are sparse. The Euro Heart Survey (EHS) of Newly Presenting Angina, conducted in 2002 and involving 3779 patients from Northern, Central, Western and Mediterranean Europe (20 from France) [23], identified a substantial gap between evidence-based therapies and implementation in practice [24]. These Western European data from CLARIFY indicate that progress has been made over the past decade, with much greater use of aspirin (52% in EHS vs. 84.8% in CLARIFY), beta-blockers (52% vs. 72.5%), calcium antagonists (18% vs. 25.4%), and lipid-lowering therapy (statin 30%, other lipid-lowering therapy 3% vs. 93.1%) [24]. The population profile has also changed over this period: in the CLARIFY Western European population, patients with stable CAD are on average older than those in the EHS (66.2 vs. 61 years), have a higher proportion of men (79.6% vs. 51%), are less likely to be current smokers (11.4% vs. 29%), but are much more likely to have diabetes (26.5% vs. 16%), dyslipidaemia (76.7% vs. 47%), and peripheral artery disease (12.5% vs. 7%) [23]. Our findings are in concert with the recent CORONOR (Suivi d'une cohorte de patients CORONariens stables en région NORd-pas-de-Calais) study, which involved 4184 patients with stable CAD (including those with serious, potentially life-threatening

cardiovascular or non-cardiovascular illnesses) in Northern France [25]. The CORONOR study reported an annual total mortality of 3.3%, the same as that expected for the general population, with only 41% of deaths being cardiovascular in origin. These findings are reassuring when taken in context with the high rates of use of secondary prevention strategies [25].

As expected from the distribution of alcohol consumption in the general population in European countries at the time the patients were included [26], there was no significant difference in the number of drinks per week between France and the rest of Europe. Unfortunately, the type of alcohol was not recorded in the study, so that possible differences in this regard (in particular, wine versus other alcoholic beverages) could not be studied.

The overall rate of peripheral artery disease in our Western European population is driven by the high prevalence in the French cohort. This rate is substantially higher than that in the global CLARIFY population (2825/30,493, 9.3%), but is also higher than the rates reported in other studies conducted in France. For example, in a study of 710 men (mean age 60.9 years) with stable CAD from Southwest France conducted between 2001 and 2004, the prevalence of peripheral artery disease was 11.7% compared with 17.6% in the CLARIFY French cohort [27]. In the more recent FAST-MI (French registries of Acute ST-elevation and non-ST-elevation Myocardial Infarction) 2010 study, involving 3079 patients with acute myocardial infarction enrolled from throughout the French territory, the prevalence of peripheral artery disease was 8% [28]. These differences in prevalence suggest the possibility of selection bias in the CLARIFY French cohort. Irrespective of this possibility, while the overall risk factor profile of the patients in France was slightly better than that in the other Western European countries in CLARIFY, the rise in prevalence of some risk factors over the past decade is of concern.

These contemporary Western European data demonstrate the impact of improvements in the diagnosis and management of acute coronary syndromes over the past 30 years, which have translated into reductions in associated acute and chronic mortality rates [10,21,22]. These improvements have not only changed the profile of patients with established CAD, but have led to an increasing population who would benefit from evidence-based management.

Limitations

As an observational registry, this study is subject to several limitations, including missing data and the potential for selection bias. Data on drug dosage and on adverse effects related to the use of medications were not collected; neither was information collected on the reasons for not using medications or undergoing cardiac interventions.

Conclusions

These observational data from the CLARIFY registry indicate good adherence to evidence-based guidelines in French outpatients with stable CAD. A minority of patients do, however, still have symptoms of angina. Furthermore, while the prevalence of some cardiovascular risk factors has declined over the past decade, others show an increase, revealing the need for better patient education regarding lifestyle improvements.

Contributors

All authors contributed to this work and approved the manuscript for submission.

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