Presse Med. 2017; 46: e259–e267
en ligne sur / *on line on*
www.em-consulte.com/revue/lpm
www.sciencedirect.com

Original article

Temporal trends in the premorbid use of preventive treatments in patients with acute ischemic cerebrovascular events and a history of vascular disease: The Dijon Stroke Registry (1985–2010)

Catia Khoumri [1], Henri Bailly [1], Benoit Delpont [1], Benoit Daubail [1], Christelle Blanc [1], Cécile Chazalon [1], Jérôme Durier [1], Marie Hervieu-Bègue [1], Guy-Victor Osseby [1], Olivier Rouaud [1], Maurice Giroud [1], Catherine Vergely [2], Yannick Béjot [1]

Received 20 August 2016
Accepted 5 January 2017
Available online: 22 November 2017

1. Dijon Stroke Registry, EA7460 Pathophysiology and Epidemiology of Cerebro-Cardio-vascular diseases (PEC2), Department of Neurology, University Hospital of Dijon, University of Burgundy, France
2. EA7460 Pathophysiology and Epidemiology of Cerebro-Cardio-vascular diseases (PEC2), University of Burgundy, France

Correspondence:
Yannick Béjot, University Hospital, Department of Neurology, Dijon Stroke Registry, Bocage central, 14, rue Gaffarel, BP 77908, 21079 Dijon cedex, France.
ybejot@yahoo.fr

Summary

Introduction > Although secondary prevention in patients with arterial vascular diseases has improved, a gap between recommendations and clinical practice may exist.
Objectives > We aimed to evaluate temporal trends in the premorbid use of preventive treatments in patients with ischemic cerebrovascular events (ICVE) and prior vascular disease.
Methods > Patients with acute ICVE (ischemic stroke/TIA) were identified through the population-based stroke registry of Dijon, France (1985–2010). Only those with history of arterial vascular disease were included and were classified into four groups: patients with previous coronary artery disease only (CAD), previous peripheral artery disease only (PAD), previous ICVE only, and patients with at least two different past vascular diseases (polyvascular group). We assessed trends in the proportion of patients who were treated with antihypertensive treatments and antithrombotics at the time of their ICVE using multivariable logistic regression models.
Results > Among the 5309 patients with acute ICVE, 2128 had a history of vascular disease (mean age 77.3 ± 11.9, 51% men; 25.1% CAD 7.5% PAD, 39.8% ICVE, and 27.5% poylvascular). A total of 45.8% of them were on antithrombotics, 64.1% on antihypertensive treatment, and 34.4% on both. Compared with period 1985–1993, periods 1994–2002 and 2003–2010 were associated with a greater frequency of prior-to-ICVE use of antithrombotics (adjusted OR = 5.94; 95% CI: 4.61–7.65, $P < 0.01$, and adjusted OR = 6.92; 95% CI: 5.33–8.98, $P < 0.01$, respectively) but not of antihypertensive drugs. Consistent results were found when analyses were stratified according to the type of history of arterial vascular disease.

http://dx.doi.org/10.1016/j.lpm.2017.01.025

Conclusion > Patients with ICVE and previous vascular disease were still undertreated with recommended preventive therapies.

Résumé

Évolution temporelle de l'utilisation des traitements de prévention secondaire chez les patients aux anté?cédents de maladie vasculaire et victimes d'un évènement cérébrovasculaire ischémique : registre dijonnais des AVC (1985–2010)

Introduction > *Bien que la prévention secondaire des maladies vasculaires ischémiques se soit améliorée, un écart entre les recommandations et la pratique clinique pourrait exister.*
Objectifs > *Évaluer l'évolution temporelle de l'utilisation des traitements de prévention chez les patients aux antécédents de maladie vasculaire ischémique et victimes d'un évènement ischémique cérébrovasculaire (EICV).*
Méthodes > *Les patients victimes d'un EICV (infarctus cérébral ou AIT) furent identifiés à partir du Registre de population des AVC de Dijon (1985–2010). Seuls les patients aux antécédents de maladie vasculaire ischémique furent analysés et classés en 4 groupes : antécédent de coronaropathie seul (Co), antécédent d'artérite des membres inférieurs seul (AOMI), antécédent d'EICV seul, et patients avec au moins 2 atteintes différentes (groupe polyvasculaire). L'évolution temporelle de la proportion des patients recevant antérieurement un antihypertenseur et/ou un antithrombotique au moment de l'EICV fut analysée à l'aide de modèles multivariés de régression logistique.*
Résultats > *Parmi les 5309 patients victimes d'un EICV, 2118 avaient un antécédent de maladie vasculaire ischémique (âge moyen 77,3 ± 11,9 : 51 % d'hommes ; 25,1 % Co, 7,5 % AOMI, 39,8 % EICV, et 27,5 % poylvasculaire). Parmi eux, 45,8 % étaient sous antithrombotique, 64,1 % sous antihypertenseur et 34,4 % sous ces deux traitements. Comparées à la période 1985–1993, les périodes 1994–2002 et 2003–2010 étaient associées à une plus grande fréquence d'utilisation pré-morbide d'antithrombotiques (respectivement OR ajusté = 5,94 ; IC 95 % : 4,61–7,65,* p *< 0,01, et OR ajusté = 6,92 ; IC 95 % : 5,33–8,98,* p *< 0,01) mais pas d'antihypertenseurs. Des résultats similaires furent observés en analyses stratifiées selon la nature de l'antécédent de maladie vasculaire ischémique.*
Conclusion > *Une sous-utilisation des traitements de prévention secondaire persiste chez les patients aux antécédents de maladie vasculaire ischémique victimes d'un EICV.*

Introduction

The incidence of arterial vascular diseases is decreasing in high-income countries thanks to major improvements in primary prevention that took place over the last two decades [1,2]. The global burden of these conditions remains high. Ischemic heart disease and stroke account for the first and second cause of years of life lost [3], and their prevalence is rising [1,2]. These trends reflect both population growth and aging, and are expected to go on in coming years. Patients with a history of vascular disease are at risk of recurrent events in either the same or another vascular bed [4,5]. There has been considerable progress in secondary prevention of coronary artery disease (CAD), ischemic cerebrovascular events (ICVE), and peripheral arterial disease (PAD), thanks to randomized clinical trials that highlighted the efficacy of therapies in reducing the risk of ischemic recurrence and mortality. As a result, guideline recommendations for secondary prevention of arterial vascular diseases have been established. Several studies have pointed out that a gap may exist between current evidence-based recommendations and clinical practice [6–17].

This study aimed to determine whether medical practices have changed over the last three decades, with regard to the use of medications indicated in secondary prevention of arterial vascular diseases so as to identify potential targets to reduce recurrences.

Methods

Case-ascertainment procedures

Patients were identified from the Dijon Stroke Registry, a population-based study that has evaluated the epidemiology of stroke and transient ischemic attack (TIA) among the residents of the city of Dijon, France (2007 census: 151,543 inhabitants)

since 1985 [18], and complies with the defined criteria for conducting stroke incidence studies [19,20]. The exhaustiveness of case-ascertainment is based on multiple overlapping sources of information so as to identify fatal and non-fatal stroke and TIA in hospitalized and non-hospitalized patients:

- review of medical records prospectively undertaken by a stroke neurologist involved in the Registry, of all patients referred to the emergency rooms, and all the clinical and radiological departments of Dijon University Hospital, where the only stroke unit is located;
- review of medical records from the emergency rooms and all of the clinical departments of the three private hospitals of the city and its suburbs;
- review of computerised hospital diagnostic codes of the Dijon University Hospital. The International Classification of Diseases, tenth revision (ICD-10) is used, and the following codes are initially searched for: I61 (intracerebral haemorrhage), I62 (non-traumatic intracranial haemorrhage), I63 (ischemic stroke), I64 (non-determined stroke), G45 (vascular syndromes), G46 (transient ischemic attack) G81 (hemiplegia). Study investigators then consult the medical records of identified patients to confirm or not the reported diagnosis or to reclassify the patients if a misclassification is noted;
- collaboration with the general practitioners to identify stroke patients from home or nursing homes, with diagnosis assessed by public or private neurologists from outpatient clinics, or Dijon residents who had their stroke when outside the city;
- review of the medical records of patients identified from a computer-generated list of all requests for imaging to the private radiological and Doppler ultrasound centres of the city and its suburbs;
- and regular checking of the death certificates obtained from the local authorities that are responsible for the registration of deaths in the community particularly fatal strokes outside hospital.

For this study, we considered patients with ischemic cerebrovascular events (ICVE) including both ischemic stroke and TIA [21].

Data collected

Prior-to-event vascular risk factors were systematically collected at the time of the inclusion of patients thanks to patients' self-report, and hospital and general practitioners' records: hypertension (high blood pressure noted in a patient's medical history or patients under antihypertensive treatment), diabetes mellitus (glucose level $\geq$ 7.8 mmol/L reported in the medical record or patients under insulin or oral hypoglycaemic agents), hypercholesterolemia (total cholesterol level $\geq$ 5.7 mmol/L reported in the medical history or patients treated with lipid-lowering therapy), atrial fibrillation, and smoking. For each patient, vascular history was collected including past ICVE, coronary heart disease (CAD) (myocardial infarction, unstable angina, coronary artery bypass graft, or percutaneous coronary intervention), and peripheral arterial disease (PAD) (prior intermittent claudication, critical lower limb ischemia, or vascular surgery).

Prestroke use of medications was also recorded: antithrombotic therapy (either aspirin, clopidogrel, dipyridamole, ticlopidine, or vitamin K antagonists), and blood pressure lowering therapy (beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonist, calcium antagonists, or diuretics). The use of statins was recorded in our files only from 2005 onwards, and thus was not considered in this study. In addition, guidelines for the use of statins after stroke were published in 2007, which did not allow sufficient time to evaluate temporal trends in their use. Therefore, "optimal" therapy was defined by the association of at least one antithrombotic drug and one blood pressure lowering drug.

Classification of patients

Overall ICVE patients were classified into four groups: patients with past ICVE only (either TIA and/or ischemic stroke), patients with a history of CAD without ICVE or PAD, patients with a history of PAD without CAD or ICVE, and patients with at least two different past vascular diseases (polyvascular group).

Statistical analysis

Proportions and mean values of baseline characteristics were compared between groups using the Chi^2 test and analysis of variance, when appropriate. Multivariable logistic regression models were generated to identify factors associated with the premorbid use of antithrombotic therapy, antihypertensive drugs, and optimal therapy. In the models, we introduced age categories, sex, prior atrial fibrillation, diabetes, type of previous vascular disease, and treatments. We used a dummy indicator for smoking status to prevent the deletion of data for patients with missing values. The proportion of missing values for other variables was less than 1%. As the definition of hypertension included the use of antihypertensive treatments, we did not introduce this factor in the analyses. Stratified analyses were performed according to the type of the arterial vascular disease history. *P*-values < 0.05 were considered statistically significant. The statistical analysis was performed with STATA 10.0 software.

Ethics

The Dijon Stroke Registry was approved by the Comité d'évaluation des registres (French National Committee of Registers).

Results

Over the 28-year study period, 5,309 patients with an ICVE were recorded (53.1% women, mean age $\pm$ SD: 74.8 $\pm$ 14.1). Among these patients, 2128 had a history of arterial vascular disease (mean age 77.3 $\pm$ 11.9, 51% men), including 535 (25.1%) patients with CAD only, 160 (7.5%) with PAD only, 847 (39.8%) with ICVE only and 586 (27.5%) with poylvascular disease. Baseline characteristics of patients according to the type of their past arterial vascular disease are shown in *table*

Table I
Characteristics of ICVE patients according to the nature of their past arterial vascular disease

	CAD only (*n* = 535)		PAD only (*n* = 160)		ICVE only (*n* = 847)		Polyvascular (*n* = 586)		*P*	Overall (*n* = 2128)	
	n	%	*n*	%	*n*	%	*n*	%		*n*	%
Age, mean ± SD	79.0 ± 10.2		74.4 ± 12.0		76.3 ± 12.5		77.9 ± 9.9		< 0.001	77.3 ± 11.3	
Age categories									< 0.001		
< 60	30	5.6	23	14.3	84	9.9	35	5.9	< 0.001	172	8.1
60–79	232	43.4	79	49.4	368	43.5	274	46.8	0.343	953	44.8
≥ 80	273	51.0	58	36.3	395	46.6	277	47.3	0.012	1003	47.1
Male gender	256	47.9	106	66.3	391	46.2	337	57.5	< 0.001	1090	51.2
ICVE type									0.022		
TIA	91	17.0	26	16.3	175	20.7	85	14.5		377	17.7
Ischemic stroke	444	83.0	134	83.7	672	79.3	501	85.5		1751	82.3
Vascular risk factors											
Hypertension	451	84.3	110	68.8	631	74.4	525	89.6	< 0.001	1717	80.7
Diabetes	105	19.6	32	20.0	121	14.3	175	29.9	< 0.001	433	20.4
Hypercholesterolemia	148	27.7	47	29.4	240	28.3	225	38.4	< 0.001	600	31.0
Atrial fibrillation	166	31.0	42	26.3	245	28.9	215	36.7	0.007	668	31.4
Smoking											
Yes	151	28.2	80	50.0	284	33.5	276	47.1	< 0.001	791	37.2
No	295	55.2	67	41.9	473	55.9	249	42.5	< 0.001	1084	50.9
Unknown	89	16.6	13	8.1	90	10.6	61	10.4	0.001	253	11.9
Medication											
Antithrombotic agents	228	42.6	77	48.1	374	44.2	296	50.5	0.034	975	45.8
Antiplatelet agents	177	33.1	63	39.4	298	35.2	242	41.3	0.022	780	36.7
Anticoagulants	44	8.2	13	8.1	64	7.6	41	7.0	0.882	162	7.6
Both	7	1.3	1	0.6	12	1.4	13	2.2	0.405	33	1.6
Antihypertensive therapy	383	71.6	79	49.4	465	54.9	437	74.6	< 0.001	1364	64.1
Optimal therapy	193	36.1	48	30.0	247	29.2	245	41.8	< 0.001	733	34.4

I. Globally, 45.8% of patients were on antithrombotic agents, 64.1% received an antihypertensive treatment and 34.4% were on optimal therapy prior to the qualifying event. Great differences in these proportions were found according to the nature of the past arterial vascular disease. Preventive treatments were most frequently used in patients with polyvascular disease. In contrast, a less frequent use of antithrombotics was observed in patients with CAD only, and of antihypertensive treatment in patients with ICVE only.

Temporal trends in the prevalence of the premorbid use of preventive treatments are shown in *figures 1 and 2*. When considering overall patients, the prevalence of the use of antithrombotics progressively increased between 1985 and 1998 from 10% to 60% before reaching a plateau thereafter. In contrast, the use of antihypertensive therapy slightly increased between 1985 and 1998 (from 53% to 72%) and then decreased to 58% in 2009–2010 with yearly fluctuations. Trends according to the nature of the history of arterial vascular disease are shown in *figure 2*. The highest prevalence of the use of preventive treatments was found in patients with CAD only and in those with polyvascular disease.

In multivariable analyses, compared with the period 1985–1993, periods 1994–2002 and 2003–2010 were associated with a greater frequency of prior-to-ICVE use of antithrombotics

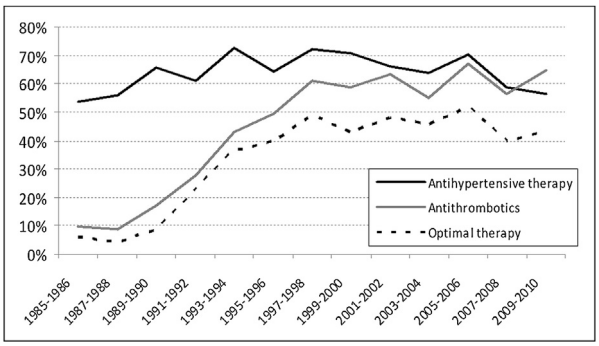

FIGURE 1

Temporal trends in the prevalence of premorbid use of preventive treatments in overall ICVE patients

(OR = 5.94; 95% CI: 4.61–7.65, $P < 0.01$, and OR = 6.92; 95% CI: 5.33–8.98, $P < 0.01$, respectively) but not of antihypertensive drugs (*table II*). In stratified analyses, the increase in the use of antithrombotics with time was observed whatever the type of arterial vascular disease history (*table III*). In contrast, a greater use of antihypertensive therapy was noted during the period 1994–2002 in patients with a history of CAD only. A higher frequency of prior-to-ICVE use of optimal therapy was noted with time in each group except for the period 1994–2002 in patients with PAD only.

Discussion

This study points out that patients with acute ICVE and a history of arterial vascular disease were undertreated by recommended preventive therapies, including during the most recent study periods: less than two-thirds were treated with either antithrombotics or antihypertensive drugs, and less than half were on optimal therapy when the acute ICVE occurred. Although the premorbid use of antithrombotics has increased over the last 26 years, that of antihypertensive treatment did not really improve.

Our results are consistent with previous studies that highlighted the gap between published guidelines for the management of secondary prevention in patients with arterial vascular disease, and their application in clinical practice. The reasons for the observed underutilisation of recommended treatments are

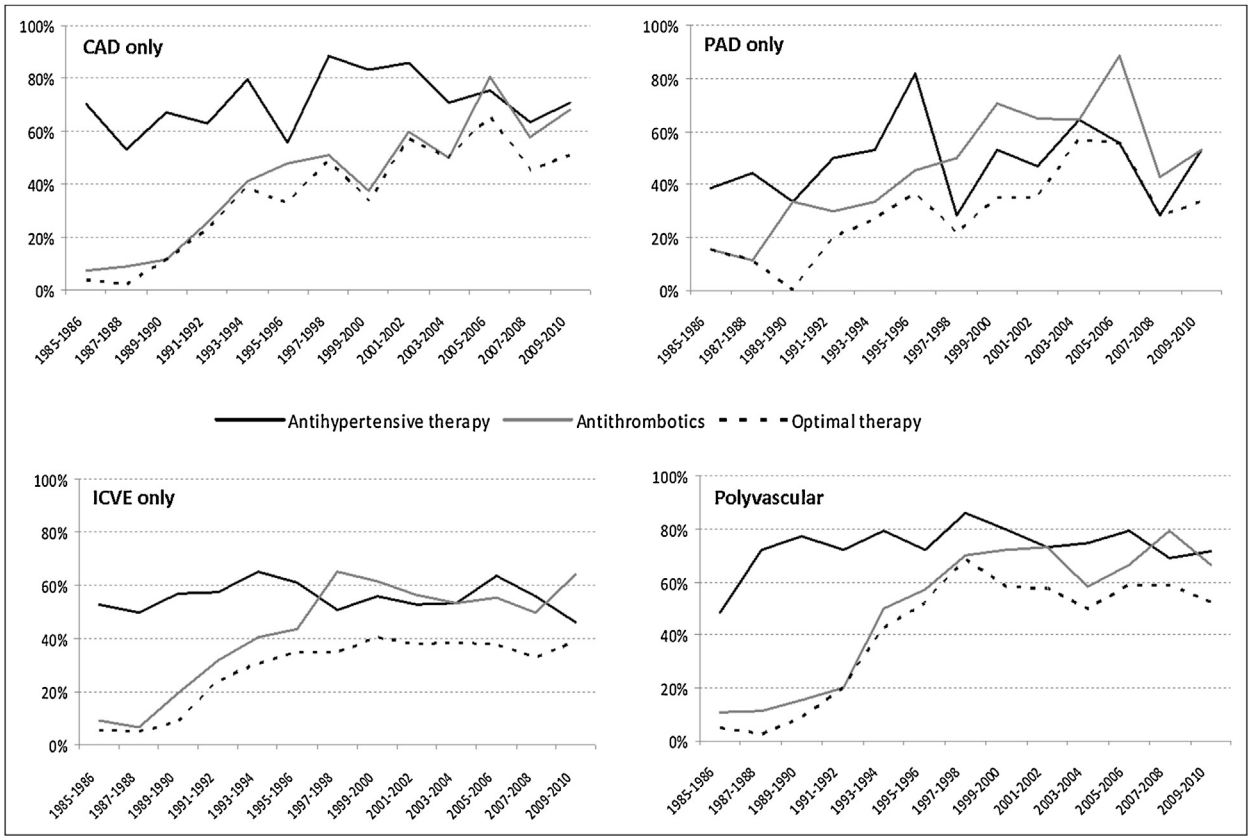

FIGURE 2

Temporal trends in the prevalence of premorbid use of preventive treatments in overall ICVE patients according to the type of arterial vascular history

Table II
Factors associated with the use of preventive treatments in multivariable analyses

	Antithrombotics			Antihypertensive therapy			Optimal therapy		
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Age categories									
< 60	Ref	–	–	Ref	–	–	Ref	–	–
60–79	1.15	0.79–1.65	0.47	1.31	0.92–1.84	0.13	1.32	0.89–1.94	0.17
≥ 80	1.13	0.78–1.64	0.52	1.45	1.01–2.06	0.04	1.33	0.89–1.98	0.17
Male gender	1.36	1.09–1.70	< 0.01	0.82	0.66–1.02	0.07	1.21	0.97–1.53	0.10
Diabetes	1.19	0.93–1.52	0.17	1.42	1.10–1.83	< 0.01	1.33	1.04–1.69	0.02
Hypercholesterolemia	1.43	1.15–1.77	< 0.01	1.31	1.05–1.64	0.02	1.35	1.09–1.68	< 0.01
Atrial fibrillation	1.75	1.42–2.16	< 0.01	1.01	0.88–1.53	0.04	1.45	1.17–1.79	< 0.01
Smoking									
No	Ref	–	–	Ref	–	–	Ref	–	–
Yes	1.00	0.78–1.28	0.99	1.34	1.05–1.70	0.02	1.00	0.78–1.29	0.99
Unknown	0.91	0.67–1.23	0.56	1.26	0.92–1.72	0.15	0.95	0.69–1.28	0.74
Time periods									
1985–1993	Ref	–	–	Ref	–	–	Ref	–	–
1994–2002	5.94	4.61–7.65	< 0.01	1.21	0.96–1.53	0.10	5.42	4.10–7.16	< 0.01
2003–2010	6.92	5.33–8.98	< 0.01	1.01	0.80–1.27	0.96	5.81	4.37–7.73	< 0.01
Prior arterial vascular disease									
CAD only	Ref	–	–	Ref	–	–	Ref	–	–
PAD only	1.27	0.86–1.88	0.24	0.39	0.27–0.57	< 0.01	0.73	0.48–1.09	0.13
ICVE only	1.07	0.84–1.37	0.57	0.50	0.40–0.64	< 0.01	0.71	0.56–0.91	< 0.01
Polyvascular disease	1.34	1.03–1.74	0.03	1.06	0.81–1.39	0.66	1.22	0.94–1.59	0.14

multiple. First, it could be assumed that an insufficient prescription of treatments after an initial vascular event may partly account for our findings. Although recent studies reported a high rate of prescription of antithrombotic agents in patients with either recent CAD or ICVE, ranging from 81 to 98% [9,12,13,22–25], the frequency of prescription of this therapy remained low in patients with PAD: less than 50% of patients were treated with antiplatelet agents after PAD diagnosis in Danish nationwide administrative registries [26], and a previous systematic review of the literature indicated that only 63% of PAD patients were prescribed antithrombotics [10]. The underutilization of recommended treatments was even more pronounced for antihypertensive therapy. In a French nationwide hospital discharge database, 82% of patients were prescribed angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers after acute CAD [22], but the Swedish Stroke Register reported that only 33% of patients suffering an ischemic stroke were treated with angiotensin-converting enzyme inhibitors at discharge [9], and a systematic review concluded that only 46% of PAD patients received antihypertensive therapy [10]. Another reason that could explain the low rate of use of preventive treatments is the poor adherence of patients to the prescribed regimen [6–8,12,14,27]. This point is of a major importance and efforts to improve the lack of compliance in secondary preventive therapies have to been made given its association with poor outcomes in terms of vascular recurrence, re-hospitalization and mortality [14,28,29].

In our study, the observed rates of the use of preventive treatments must be interpreted with caution as they were much lower than most of those observed in cohort studies. This was because of methodological differences, since we only included patients with an acute ICVE and a history of vascular disease, in other terms patients who were more likely to have missed the opportunity of secondary prevention, and not those with a

Table III

Multivariable analyses of the association between time periods and the use of preventive treatments stratified by type of arterial vascular history

	Antithrombotics			Antihypertensive therapy			Optimal therapy		
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Patients with CAD only									
1985–1993	Ref	–	–	Ref	–	–	Ref	–	–
1994–2002	5.68	3.37–9.58	< 0.01	1.75	1.08–2.81	0.02	5.82	3.35–10.12	< 0.01
2003–2010	10.16	5.78–17.84	< 0.01	1.27	0.77–2.08	0.35	8.46	4.73–15.13	< 0.01
Patients with PAD only									
1985–1993	Ref	–	–	Ref	–	–	Ref	–	–
1994–2002	3.68	1.51–9.01	< 0.01	1.05	0.47–2.33	0.91	1.85	0.69–4.99	0.22
2003–2010	4.55	1.57–11.50	< 0.01	1.30	0.53–3.17	0.57	3.20	1.11–9.20	0.03
Patients with ICVE only									
1985–1993	Ref	–	–	Ref	–	–	Ref	–	–
1994–2002	5.03	3.31–7.65	< 0.01	0.98	0.67–1.41	0.90	3.50	2.19–5.59	< 0.01
2003–2010	5.02	3.38–7.48	< 0.01	0.90	0.64–1.27	0.55	3.48	2.23–5.44	< 0.01
Patients with polyvascular disease									
1985–1993	Ref	–	–	Ref	–	–	Ref	–	–
1994–2002	8.99	5.60–14.42	< 0.01	1.35	0.85–2.12	0.20	10.64	6.28–18.03	< 0.01
2003–2010	9.74	5.77–16.44	< 0.01	1.01	0.61–1.65	0.98	9.53	5.41–16.78	< 0.01

Models adjusted for age categories, gender, diabetes, hypercholesterolemia, atrial fibrillation, and smoking status.

history of vascular disease who had a vascular recurrence. However, our findings are of interest because they clearly identified actions that can be implemented by clinicians so as to reduce recurrences in patients with arterial vascular diseases.

The observed increase in the frequency of use of antithrombotics over time is encouraging, but it contrasts with the disappointing stable use of antihypertensive treatments, irrespective of the type of history of the arterial vascular disease. This finding is not in agreement with other studies, which demonstrated an improvement in the use of both antihypertensive treatments and antithrombotics in patients with CAD, PAD, or ischemic stroke [15,26]. To explain these divergent findings, we must again consider the methodology of our study. Since hypertension is a major contributor to ICVE, it is not surprising that patients who were included in the present study were those who were the least likely to be correctly treated for hypertension. Hence, this result reinforces the need to target hypertension in patients with arterial vascular disease so as to reduce the burden of subsequent stroke.

The major strength of our study is the continuous prospective ascertainment over 26 years based on a population-based registry to ensure exhaustiveness. Several limitations must be acknowledged. The reasons for not using preventive therapy were not collected, which prevented us from distinguishing between prescription failure and poor adherence of patients, or contra-indications of the treatments. No data about the indication of antihypertensive drugs in patients with CAD were available. Therefore, it was not possible to distinguish between users for hypertension, arrhythmia, or prevention of heart failure. In addition, the time between the first arterial vascular disease and the qualifying ICVE was unknown. This is unfortunate since it has been suggested that a patient's adherence to treatment may decrease with time [6]. All patients with a reported history of TIA (based on report from the patient or medical files, or collected as an event in the registry if it occurred during the study period covered by the registry) were included in our study, and we cannot exclude that some of them were in fact TIA-mimics because the diagnosis of TIA is sometime a difficult challenge. Since we did not determine whether the prevention target was achieved or not, the included patients may have suffered the recurrent vascular event because of uncontrolled risk factors, especially blood pressure, despite supposedly adequate treatment. Moreover, the trial of ORG

10,172 in acute stroke treatment (TOAST) classification to determine causes of ICVE was introduced in the Dijon Stroke Registry in 2005 only. Therefore, it was not possible to stratify analyses based on the mechanisms for the whole study period. Since some patients with specific causes of ICVE, especially those with dissection, may be not eligible for long-term prevention therapy, they may have been considered as undertreated patients. Nevertheless, these patients represented only 2% of overall ICVE in our registry over the period 2006–2011 and were at low risk of recurrence [30]. Consequently, it could be assumed that this limitation did not alter the global results of the study.

To conclude, despite some improvements, patients with ICVE and previous vascular disease remain undertreated with recommended preventive therapies. Efforts are still needed to optimize secondary prevention strategies in patients with arterial vascular disease so as to reduce the burden of stroke.

Funding: the Dijon Stroke Registry is supported by the Institut de veille sanitaire – Santé publique France, and INSERM.

Disclosure of interest: Yannick Béjot received honoraria for participation to advisory boards or as a symposium speaker for AstraZeneca France, Daiichi-Sankyo, MSD France, Pfizer, Bayer, and Covidiem. The other authors declare that they have no competing interest.

References

[1] Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990–2010: findings from the global burden of disease study 2010. Lancet 2014;383:245–54.

[2] Moran AE, Forouzanfar MH, Roth GA, Mensah GA, Ezzati M, Flaxman A, et al. The global burden of ischemic heart disease in 1990 and 2010: the global burden of disease 2010 study. Circulation 2014;129:1493–501.

[3] GBD 2013 mortality and causes of death collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the global burden of disease study 2013. Lancet 2015;385:117–71.

[4] Witt BJ, Brown Jr RD, Jacobsen SJ, Weston SA, Yawn BP, Roger VL. A community-based study of stroke incidence after myocardial infarction. Ann Intern Med 2005;143:785–92.

[5] Touzé E, Varenne O, Chatellier G, Peyrard S, Rothwell PM, Mas JL. Risk of myocardial infarction and vascular death after transient ischemic attack and ischemic stroke: a systematic review and meta-analysis. Stroke 2005;36:2748–55.

[6] Glader EL, Sjölander M, Eriksson M, Lundberg M. Persistent use of secondary preventive drugs declines rapidly during the first 2 years after stroke. Stroke 2010;41:397–401.

[7] Bushnell CD, Olson DM, Zhao X, Pan W, Zimmer LO, Goldstein LB, et al. Secondary preventive medication persistence and adherence 1 year after stroke. Neurology 2011;77:1182–90.

[8] De Schryver EL, van Gijn J, Kappelle LJ, Koudstaal PJ, Algra A, Dutch TIA trial and SPIRIT study groups. Non-adherence to aspirin or oral anticoagulants in secondary prevention after ischaemic stroke. J Neurol 2005;252:1316–21.

[9] Asberg S, Henriksson KM, Farahmand B, Asplund K, Norrving B, Appelros P, et al. Ischemic stroke and secondary prevention in clinical practice: a cohort study of 14,529 patients in the Swedish stroke register. Stroke 2010;41:1338–42.

[10] Flu HC, Tamsma JT, Lindeman JH, Hamming JF, Lardenoye JH. A systematic review of implementation of established recommended secondary prevention measures in patients with PAOD. Eur J Vasc Endovasc Surg 2010;39:70–86.

[11] Kotseva K, Wood D, De Backer G, De Bacquer D, Pyörälä K, Keil U, et al. EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries. Eur J Cardiovasc Prev Rehabil 2009;16:121–37.

[12] Husted S. Evidence-based prescribing and adherence to antiplatelet therapy – how much difference do they make to patients with atherothrombosis? Int J Cardiol 2009;134:150–9.

[13] Saposnik G, Goodman SG, Leiter LA, Yan RT, Fitchett DH, Bayer NH, et al. Applying the evidence: do patients with stroke, coronary artery disease, or both achieve similar treatment goals? Stroke 2009;40:1417–24.

[14] Newby LK, LaPointe NM, Chen AY, Kramer JM, Hammill BG, DeLong ER, et al. Long-term adherence to evidence-based secondary prevention therapies in coronary artery disease. Circulation 2006;113:203–12.

[15] Girot M, Mackowiak-Cordoliani MA, Deplanque D, Hénon H, Lucas C, Leys D. Secondary prevention after ischemic stroke. Evolution over time in practice. J Neurol 2005;252:14–20.

[16] Cacoub PP, Zeymer U, Limbourg T, Baumgartner I, Poldermans D, Röther J, et al. Effects of adherence to guidelines for the control of major cardiovascular risk factors on outcomes in the REduction of Atherothrombosis for Continued Health (REACH) registry Europe. Heart 2011;97:660–7.

[17] Béjot Y, Zeller M, Lorgis L, Troisgros O, Aboa-Eboulé C, Osseby GV, et al. Secondary prevention in patients with vascular disease. A population based study on the underuse of recommended medications. J Neurol Neurosurg Psychiatry 2013;84:348–53.

[18] Béjot Y, Rouaud O, Jacquin A, Osseby GV, Durier J, Manckoundia P, et al. Stroke in the very old: incidence, risk factors, clinical features, outcomes and access to resources – a 22-year population-based study. Cerebrovasc Dis 2010;29:111–21.

[19] Malmgren R, Warlow C, Bamford J, Sandercock P. Geographical and secular trends in stroke incidence. Lancet 1987;2:1196–200.

[20] Sudlow CL, Warlow CP. Comparing stroke incidence worldwide: what makes studies comparable? Stroke 1996;27:550–8.

[21] WHO. The world health report 2000: Health Systems improving performance. Geneva: WHO; 2000.

[22] Tuppin P, Neumann A, Danchin N, Weill A, Ricordeau P, de Peretti C, et al. Combined secondary prevention after hospitalization for myocardial infarction in France: analysis from a large administrative database. Arch Cardiovasc Dis 2009;102:279–92.

[23] 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.

[24] Mehta RH, Roe MT, Chen AY, Lytle BL, Pollack Jr CV, Brindis RG, et al. Recent trends in the care of patients with non-ST-segment elevation acute coronary syndromes: insights from the CRUSADE initiative. Arch Intern Med 2006;9(166):2027–34.

[25] Wei JW, Wang JG, Huang Y, Liu M, Wu Y, Wong LK, et al. Secondary prevention of ischemic stroke in urban China. Stroke 2010;41:967–74.

[26] Subherwal S, Patel MR, Kober L, Peterson ED, Jones WS, Gislason GH, et al. Missed opportunities: despite improvement in use of cardioprotective medications among patients

with lower-extremity peripheral artery disease, underuse remains. Circulation 2012;126:1345–54.
[27] Wang Y, Wu D, Wang Y, Ma R, Wang C, Zhao W. A survey on adherence to secondary ischemic stroke prevention. Neurol Res 2006;28:16–20.
[28] Tuppin P, Neumann A, Danchin N, de Peretti C, Weill A, Ricordeau P, et al. Evidence-based pharmacotherapy after myocardial infarction in France: adherence-associated factors and relationship with 30 month mortality and rehospitalization. Arch Cardiovasc Dis 2010;103:363–75.
[29] Park JH, Ovbiagele B. Optimal combination secondary prevention drug treatment and stroke outcomes. Neurology 2015;84:50–6.
[30] Béjot Y, Daubail B, Debette S, Durier J, Giroud M. Incidence and outcome of cerebrovascular events related to cervical artery dissection: the Dijon Stroke Registry. Int J Stroke 2014;9:879–82.