# Importance of Cardiovascular Risk Profile for In-Hospital Mortality Due to Cerebral Infarction

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**Introduction and objectives.** To investigate cardiovascular risk profiles and their prognostic implications in patients with different subtypes of cerebral infarction.

**Methods.** The study involved the retrospective analysis of data from a hospital stroke registry on 2704 consecutive CI patients who were admitted between 1986 and 2004. Of the 2704 strokes recorded, 770 were classified as thrombotic, 763 as cardioembolic, 733 as lacunar, 324 as undetermined, and 114 as atypical. Multivariate analysis was used to compare cardiovascular risk profiles in each subtype and their influence on in-hospital mortality.

**Results.** Arterial hypertension (AH) was present in 55.5%, atrial fibrillation (AF) in 29.8%, and diabetes mellitus in 23.4%. The in-hospital mortality rate was 12.9%, and in-hospital mortality was independently associated with AF (odds ratio [OR]=2.33; 95% confidence interval [CI], 1.84-2.96), and heart failure (HF) (OR=1.96; 95% CI, 1.33-2.89). In patients with thrombotic stroke, the cardiovascular risk factors associated with in-hospital mortality were HF (OR=2.87; 95% CI, 1.45-5.71), AF (OR=1.80; 95% CI, 1.09-2.96) and age (OR=1.06; 95% CI, 1.04-1.08). In patients with cardioembolic stroke, they were peripheral vascular disease (OR=2.18; 95% CI, 1.17-4.05), previous cerebral infarction (OR=1.75; 95% CI, 1.16-2.63), HF (OR=1.71; 95% CI, 1.01-2.90), and age (OR=1.06; 95% CI, 1.04-1.08). In those with undetermined stroke, they were AH (OR=3.68; 95% CI, 1.78-7.62) and age (OR=1.05; 95% CI, 1.01-1.09).

**Conclusions.** Each cerebral infarction etiologic subtype was associated with its own cardiovascular risk profile. Consequently, the cardiovascular risk factors associated with mortality were also different for each ischemic stroke subtype.

**Key words:** *Cerebral ischemia. Risk factors. Mortality. Hypertension. Atrial fibrillation. Stroke registry.*

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## Importancia del perfil cardiovascular en la mortalidad hospitalaria de los infartos cerebrales

**Introducción y objetivos.** Analizar el perfil cardiovascular y su pronóstico en los infartos cerebrales y sus subtipos etiológicos.

**Métodos.** Se efectúa un análisis retrospectivo de una serie clínica de 2.704 pacientes con infartos cerebrales procedentes de un registro hospitalario de ictus ingresados entre 1986 y 2004 (770 trombóticos, 763 cardioembólicos, 733 lacunares, 324 indeterminados y 114 inhabituales). Se compara el perfil cardiovascular de cada subtipo etiológico y su influencia con la mortalidad hospitalaria mediante un análisis multivariable.

**Resultados.** La hipertensión arterial (HTA) se presentó en el 55,5%, seguida por la fibrilación auricular (FA) (29,8%) y la diabetes mellitus (23,4%). La mortalidad hospitalaria fue del 12,9% y estaba relacionada con la FA (*odds ratio* [OR] = 2,33; intervalo de confianza [IC] del 95%, 1,84-2,96) y la insuficiencia cardiaca (OR = 1,96; IC del 95%, 1,33-2,89). El perfil cardiovascular asociado a la mortalidad estaba formado en los trombóticos, por la insuficiencia cardiaca (OR = 2,87; IC del 95%, 1,45-5,71), la FA (OR = 1,80; IC del 95%, 1,09-2,96) y la edad (OR = 1,06; IC del 95%, 1,04-1,08); en los cardioembólicos, por la enfermedad vascular periférica (OR = 2,18; IC del 95%, 1,17-4,05), el infarto cerebral previo (OR = 1,75; IC del 95%, 1,16-2,63), la insuficiencia cardiaca (OR = 1,71; IC del 95%, 1,01-2,90) y la edad (OR = 1,06; IC del 95%, 1,04-1,08), y en los infartos indeterminados, por la HTA (OR = 3,68; IC del 95%, 1,78-7,62) y la edad (OR = 1,05; IC del 95%, 1,01-1,09).

**Conclusiones.** Cada subtipo etiológico de infarto cerebral presenta un perfil cardiovascular propio. El perfil cardiovascular asociado a la mortalidad también es diferente en cada subtipo de infarto cerebral.

**Palabras clave:** *Isquemia cerebral. Factores de riesgo. Mortalidad. Hipertensión arterial. Fibrilación auricular. Registros de ictus.*

ABBREVIATIONS

AF: atrial fibrillation
CInf: cerebral infarction
COPD: chronic obstructive pulmonary disease
HBP: high blood pressure
TIA: transitory ischemic attack

## INTRODUCTION

The link between cardiovascular risk factors and stroke is well established,[1,2] but less is known about the risk profiles associated with the different etiological types of stroke. Neither is the relationship between in-hospital mortality and the prognostic profile of the cardiovascular risks associated with different etiological types of stroke well known.[3] Recent therapeutic guidelines published by the American Heart Association[4] highlight this lack of knowledge and recommend studies be performed on the clinical status and risk profiles associated with different etiological types of stroke. The aim of the present study was to analyze these risk factor profiles and determine how they affect the prognosis of patients with strokes of different etiology. The study population was composed of 2704 consecutive patients with cerebral infarction (CInf) admitted to a hospital neurology department over a period of 19 years; all these patients were included in a previously validated stroke registry.

## METHODS

This clinical study involved an initial 3808 consecutive patients, all of whom were admitted with stroke to the Neurology Department of the Hospital Universitari del Sagrat Cor of Barcelona over a period of 19 years (1986-2004 inclusive), and all of whom were included in the center's cerebrovascular disease registry. This registry has been recently published and validated[5] and contains input on 161 items, including demographics, risk factors, and clinical data, neuroimaging data, the results of complementary examinations, the parenchymatous topographic diagnosis, cerebrovascular, nosological and etiological data, and information on the course of disease, prognosis, and neurological deficit at release. All information obtained during the hospital stay was recorded. The above-mentioned neurology department has 25 beds and a cerebrovascular disease unit.

The different types of stroke were classified according to the recommendations of the Grupo de Estudio de las Enfermedades Cerebrovasculares de la Sociedad Española de Neurología[6] (the Cerebrovascular Disease Study Group of the Spanish Neurological Society); these recommendations have been used in other studies by our group[5,7-9] and coincide with the definitions provided in a recent review[10] (Appendix). The definitions of cardiovascular risk factors used, of clinical features, and of the course of disease, were those referred to in other studies undertaken by our group.[7-10] Briefly, from 1999, high blood pressure (HBP) was defined as systolic/diastolic figures of >140/90 mm Hg or the use of anti-hypertension medication; before this time figures of >160/90 mm Hg were regarded as indicative of HBP. Diabetes mellitus was defined as a history of fasting glycemia of ≥7.7 mmol/L or the use of blood sugar lowering medication. Dyslipidemia was defined as a serum cholesterol concentration of >6.5 mmol/L or of triglycerides of >1.71 mmol/L, or the use of lipid lowering medication. Obesity was defined as an increase of >25% over the corresponding theoretical bodyweight for sex and age. Backgrounds of atrial fibrillation (AF), ischemic heart disease, valve disease, congestive heart failure, chronic obstructive pulmonary disease (COPD), peripheral vascular disease, smoking of >20 cigarettes/day, alcohol abuse (alcohol intake >80 g/day), CInf, cerebral hemorrhage or transient ischemic attack (TIA), the use of oral anticoagulants, and chronic hepatitis were recorded.

Those patients with hemorrhagic stroke (intracerebral hemorrhage, subarachnoid hemorrhage, subdural, and epidural hematomas) and TIA were excluded. The final study population was therefore composed of 2704 patients.

All patients were admitted within 48 h of the onset of symptoms. Their demographic characteristics, cerebrovascular risk factors, disease history, general clinical features, and neurological features were all noted, as were prognostic data and information regarding the course of disease.

All patients underwent the following complementary examinations: a hemogram, blood biochemical analysis, basic hemostasis analysis, an electrocardiogram, chest x-ray, and a cerebral computed tomography (CT) scan. Some 33.3% of patients also underwent cerebral magnetic resonance (MR) and/or MR angiography. In accordance with the study protocol, selected patients underwent Doppler echography, arterial DIVAS, transthoracic and transesophageal echocardiography, lumbar puncture, an immunological study, and an examination for occult thrombosis.

Functional limitation was quantified at release using the modified Rankin scale.[11] In-hospital mortality and cause of death were analyzed using the algorithm of Silver et al,[12] which classifies the causes of death as

neurological (cerebral herniation, cerebrovascular relapse), non-neurological (infections, respiratory, cardiac, vascular, and other), or unknown.

### Statistical Analysis

A descriptive analysis was made of the demographic and cardiovascular risk data, recording percentages, means (standard deviations), and the medians plus interquartile ranges. The risk factor profiles for each etiological type of stroke were compared (ie, atherothrombotic against non-atherothrombotic, lacunar against non-lacunar, undetermined against essential, and unusual against usual) via univariate analysis ($\chi^2$ test), using Yates correction as needed. Significance was set at $P$=.05. The studied variables were then subjected to multivariate analysis (stepwise logistic regression) when $P$=.10 in univariate analysis.[13] The different types of stroke were the dependent variable.

The effect of cardiovascular risk factors on in-hospital mortality were then analyzed, the predictive value of the sociodemographic variables and risk factors being calculated independently for each etiological type of stroke by univariate analysis and with respect to patient vital status (using the $\chi^2$ test plus Yates correction if required). Using the collected demographic and cardiovascular risk data, the predictive value of in-hospital mortality of each variable was analyzed employing four predictive models, the first involving the entire sample of patients, the second involving those with atherothrombotic stroke, the third involving those with cardioembolic stroke, and the fourth those with stroke of undertermined etiology. In-hospital mortality was the dependent variable in all these models.

The significance threshold for remaining in the model was set at $P$=.15. The tolerance threshold was set at 0.0001. Weighting estimates for the different variables in the models were based on the maximum likelihood method. The odds ratio (OR) and confidence intervals (CI) were calculated from the beta coefficients and standard deviations. The $\chi^2$ test was used to evaluate the goodness of fit of the models to logistic regression.[14] All calculations were performed using SPSS-PC+[15] and BMDP[16] software.

The study was approved by our institution's ethics committee.

## RESULTS

The Hospital del Sagrat Cor of Barcelona registry contains information on 3808 consecutive patients with stroke of the following presentations: TIA (n=611; 16%), CInf (n=2704; 71%), intracerebral hemorrhage (n=407; 10.5%), subarachnoid hemorrhage (n=47; 1.25%), spontaneous subdural hematoma (n=38; 1.20%), and spontaneous epidural hematoma (n=1; 0.05%).

The 2704 patients making up the study population represent 71% of the total. The different etiologies of stroke recorded included atherothrombotic (770; 28.5%), cardioembolic (763; 28.2%), lacunar (733; 27.1%), essential (324; 12%), and stroke of unusual etiology (114; 4.2%).

Some 49.4% of the patients were men. The mean age of the population was 75.5 (11.7) years. The main cardiovascular risk factors recorded were: HBP (55.5%), AF (29.8%), diabetes mellitus (23.4%), and dyslipidemia (17.8%). The cardiovascular risk profile of each etiological type of stroke was different (Table 1); differences were also seen according to patient age. The most common risk factors for patients ≥84 years and 75-84 years were HBP (48.4% and 58.4%, respectively) and AF (43.2% and 34.3% respectively). For those aged 65-74 or <65 years the most common risk factors were HBP (61% and 48.2% respectively) and diabetes mellitus (27.5% and 23.3% respectively) (Table 2). The frequency of the different types of stroke varied depending on age. Cardioembolic stroke was the most common among those aged ≥84 and 75-84 years (40.4% and 30.9% respectively), atherothrombotic stroke the most common among those aged 65-74 years (30.1%), and lacunar stroke the most common among those aged <65 years (31.9%). The latter group also had the highest frequency of stroke of unusual etiology (15.3%) (Table 2).

Multivariate analysis showed the independent risk factors directly associated with atherothrombotic stroke to be peripheral vascular disease (OR=2.28; 95% CI, 1.68-3.08), HBP (OR=1.84; 95% CI, 1.53-2.2), diabetes mellitus (OR=1.66; 95% CI, 1.36-2.03), TIA (OR=1.50; 95% CI, 1.16-1.95), COPD (OR=1.41; 95% CI, 1.04-1.93), prior CInf (OR=1.40; 95% CI, 1.12-1.76), and ischemic heart disease (OR=1.33; 95% CI, 1.06-1.68) (Table 3). The risk factors directly associated with lacunar infarctions were HBP (OR=2.64; 95% CI, 2.19-3.20), diabetes mellitus (OR=1.55; 95% CI, 1.23-1.90), and obesity (OR=1.50; 95% CI, 1.01-2.25). The risk factors directly associated with cardioembolic stroke were AF (OR=20.01; 95% CI, 15.98-25.05), valve disease (OR=5.60; 95% CI, 3.60-8.71), and ischemic heart disease (OR=2.09; 95% CI, 1.57-2.78) (Table 3).

In-hospital mortality was 12.9% (n=350). The immediate or specific causes of death were cerebral herniation (4.3%), pneumonia (2.3%), sepsis (1.8%), acute myocardial infarction (1.2%), pulmonary thromboembolism (0.7%), sudden death (2.1%), and unknown causes (0.5%). Table 4 shows the different risk factors and clinical characteristics associated with mortality. In order of decreasing frequency these were: congestive heart disease (30.4%), AF (22.8%), COPD (18.8%), prior CInf (17.1%), and prior cerebral hemorrhage (15.6%).

The cardiovascular risk profiles related to in-hospital mortality were different for each etiological type of stroke. Multivariate analysis (Table 5) showed atherothrombotic

TABLE 1. **Cardiovascular Risk Factors of 2704 Patients With Cerebral Infarction. Descriptive Analysis of Each Etiological Type of Stroke**

| | Total | Atherothrombotic | Lacunar | Cardioembolic | Undetermined | Unusual |
|---|---|---|---|---|---|---|
| Patients | | 770 (28.5) | 733 (27.1) | 763 (28.2) | 324 (12) | 114 (4.2) |
| High blood pressure | 1501 (55.5) | 509 (66.1)[a] | 525 (71.6)[a] | 377 (49.4)[a] | 59 (18.2)[a] | 31 (27.2)[a] |
| Atrial fibrillation | 807 (29.8) | 120 (15.6)[a] | 81 (11.1)[a] | 573 (75.1)[a] | 25 (7.7)[a] | 8 (7)[a] |
| Diabetes mellitus | 632 (23.4) | 242 (31.4)[a] | 218 (29.7)[a] | 142 (18.6)[b] | 24 (7.4)[a] | 6 (5.3)[a] |
| Dyslipidemia | 480 (17.8) | 164 (21.3)[a] | 166 (22.6)[a] | 88 (11.5)[a] | 52 (16)[a] | 10 (8.8) |
| Prior cerebral infarction | 468 (17.3) | 164 (21.3)[c] | 117 (16) | 146 (19.1) | 31 (9.6)[a] | 10 (8.8)[b] |
| Ischemic heart disease | 435 (16.1) | 150 (19.5)[c] | 104 (14.2) | 163 (21.4)[a] | 14 (4.3)[a] | 4 (3.5)[a] |
| TIA | 317 (11.7) | 116 (15.1)[b] | 80 (10.9) | 73 (9.6)[c] | 37 (11.4) | 11 (9.6) |
| Smoking (>20 cigarettes/day) | 260 (9.6) | 87 (11.3)[c] | 86 (11.7)[a] | 28 (3.7)[a] | 41 (12.7)[a] | 18 (6.9) |
| COPD | 223 (8.2) | 74 (9.6) | 61 (8.3) | 62 (8.1) | 20 (6.2) | 6 (5.3) |
| Peripheral vascular disease | 214 (7.9) | 100 (13)[b] | 57 (7.8) | 50 (6.6) | 3 (0.9)[b] | 4 (3.5)[c] |
| Valve disease | 174 (6.4) | 11 (1.4)[a] | 21 (2.9)[a] | 130 (17)[a] | 6 (1.9)[b] | 6 (5.3) |
| Congestive heart failure | 148 (5.5) | 43 (5.6) | 24 (3.3)[b] | 72 (9.4)[a] | 8 (2.5)[b] | 1 (0.9)[c] |
| Obesity | 118 (4.4) | 36 (4.7) | 47 (6.4)[a] | 17 (2.2)[b] | 13 (4) | 5 (4.4) |
| Oral anticoagulants | 94 (3.5) | 18 (2.3)[c] | 7 (1)[a] | 63 (8.3)[a] | 2 (0.6)[a] | 4 (3.5) |
| Alcohol abuse (>80 g/day) | 66 (2.4) | 26 (3.4)[c] | 21 (2.9) | 5 (0.7)[c] | 10 (3.1) | 4 (3.5) |
| Chronic liver disease | 57 (2.1) | 17 (2.2) | 15 (2.1) | 15 (2) | 10 (3.1) | 0 |
| Prior cerebral hemorrhage | 32 (1.2) | 9 (1.2) | 9 (1.2) | 7 (0.9) | 6 (1.9) | 1 (0.9) |

COPD indicates chronic obstructive pulmonary disease; TIA, transient ischemic attack.
[a]*P*<.001.
[b]*P*<.01.
[c]*P*<.05.
Data expressed as n (%).

infarctions to be associated with congestive heart failure (OR=2.87; 95% CI, 1.45-5.71), AF (OR=1.80; 95% CI, 1.09-2.96), and age (OR=1.03; 95% CI, 1.01-1.05). Cardioembolic infarctions were associated with peripheral vascular disease (OR=2.18; 95% CI, 1.17-4.05), prior CInf (OR=1.75; 95% CI, 1.16-2.63), congestive heart failure (OR=1.71; 95% CI, 1.01-2.90), and age (OR=1.06; 95% CI, 1.04-1.08). Infarctions of undetermined etiology were associated with HBP (OR=3.68; 95% CI, 1.78-7.62) and age (OR=1.05; 95% CI, 1.01-1.09).

Comparison of the periods 1986-1992, 1993-1998, and 1999-2004 showed a significant decline over time in terms of the number of days spent in hospital and in-hospital mortality (Table 6).

## DISCUSSION

In the present registry, CInf was responsible for some 71% of the total number of entries. The frequencies of the etiological types of stroke were as follows: atherothrombotic 28.5%, cardioembolic 28.2%, lacunar 27.1%, essential 12%, and unusual etiology 4.2%. This distribution is similar to those reported in other studies,[17-20] although differences are discernable among them. For example, atherothrombotic etiology is the most common in the Korean Hallym registry[17] (42%) and the Iranian Khorasan registry[20] (53.6%), while it occupies second place in the Athens[19] (15%) and Besançon registries[18] (30.5%) (cardioembolic etiology is the most common in these at 38% and 31% respectively). In all 4 of these registries (as in the present work), stroke of unusual etiology is the least common (1.9%, 2.9%, 3.3%, and 3.7% respectively).

Analysis of the population as a whole showed the main risk factors to be HBP (55.5%), AF (29.8%), diabetes mellitus (23.4%), and dyslipidemia (17.8%), similar to that reported in other studies.[17-20] In the Athens registry[19] the most common risk factors are HBP (68.1%) and AF (33.7%), in the Hallym[17] and Besançon registries[18] the most common are HBP (66% and 57.5% respectively) and smoking (34.5% and 33.7% respectively), while in the Khorasan registry[20] HBP (53.2%) and valve disease (17.7%) are the most common risk factors.

It should be noted, however, that in the present study each etiological type of stroke was associated with a particular cardiovascular risk profile. Atherothrombotic stroke was associated with a profile in which peripheral vascular disease stood out (OR=2.28) (peripheral vascular disease is a known indicator of generalized atherosclerosis),[21] along with HBP (OR=1.84) and diabetes mellitus (OR=1.66), risk factors classically linked to large artery cardiovascular and cerebrovascular morbidity.[18,19] Other risk factors included TIA (OR=1.50) (a neurological emergency given the associated early risk of definitive cerebral ischemia),[4,9] COPD (OR=1.40) (a disease related to smoking and repeated bronchiolar infections that can lead to a state of acquired subclinical hypercoagulability),[5,22] prior CInf (OR=1.40) (in itself a

TABLE 2. **Distribution by Age Group (≥85, 75-84, 65-74, and <65 Years) of Demographic Data, Cardiovascular Risk Factors, and Etiological Types of Cerebral Infarction in the 2704 Patientes With Cerebral Infarction of the Sample of Study**

| | ≥85 (n=570) | 75-84 (n=1068) | 65-74 (n=680) | <65 (n=386) | *P* |
|---|---|---|---|---|---|
| Demographic data | | | | | |
| Men | 186 (32.6) | 471 (44.1) | 409 (60.1) | 270 (69.9) | <.001 |
| Women | 384 (67.4) | 597 (55.9) | 271 (39.9) | 116 (30.1) | |
| Risk factors | | | | | |
| High blood pressure | 276 (48.4) | 624 (58.4) | 415 (61) | 186 (48.2) | <.001 |
| Atrial fibrillation | 246 (43.2) | 366 (34.3) | 157 (23.1) | 38 (9.8) | <.001 |
| Diabetes mellitus | 103 (18.1) | 252 (23.6) | 187 (27.5) | 90 (23.3) | .001 |
| Dyslipemia | 54 (9.5) | 161 (15.1) | 179 (26.3) | 86 (22.3) | <.001 |
| Prior cerebral infarction | 102 (17.9) | 194 (18.2) | 130 (19.1) | 42 (10.9) | .004 |
| Ischemic heart disease | 85 (14.9) | 185 (17.3) | 128 (18.8) | 37 (9.6) | .001 |
| TIA | 66 (11.6) | 132 (12.4) | 85 (12.5) | 34 (8.8) | .262 |
| Smoking (>20 cigarettes/day) | 10 (1.8) | 50 (4.7) | 88 (12.9) | 112 (29) | <.001 |
| COPD | 52 (9.1) | 103 (9.6) | 54 (7.9) | 14 (3.6) | .003 |
| Peripheral vascular disease | 27 (4.7) | 86 (8.1) | 79 (11.6) | 22 (5.7) | <.001 |
| Valve disease | 33 (5.8) | 69 (6.5) | 46 (6.8) | 26 (6.7) | .902 |
| Congestive heart failure | 71 (12.5) | 54 (5.1) | 16 (2.4) | 7 (1.8) | <.001 |
| Obesity | 12 (2.1) | 44 (4.1) | 42 (6.2) | 20 (5.2) | .004 |
| Oral anticoagulants | 18 (3.2) | 41 (3.8) | 25 (3.7) | 10 (2.6) | .665 |
| Alcohol abuse (>80 g/day) | 1 (0.2) | 7 (0.7) | 20 (2.9) | 38 (9.8) | <.000 |
| Prior cerebral hemorrhage | 4 (0.7) | 14 (1.3) | 10 (1.5) | 4 (1) | .608 |
| Types of cerebral infarction | | | | | <.001 |
| Cardioembolic | 230 (40.4) | 330 (30.9) | 147 (21.6) | 56 (14.5) | |
| Atherothrombotic | 159 (27.9) | 321 (30.1) | 208 (30.6) | 82 (21.2) | |
| Lacunar | 110 (19.3) | 277 (25.9) | 223 (32.8) | 123 (31.9) | |
| Essential | 65 (11.4) | 112 (10.5) | 81 (11.9) | 66 (17.1) | |
| Unusual | 6 (1.1) | 28 (2.6) | 21 (3.1) | 59 (15.3) | |

COPD indicates chronic obstructive pulmonary disease; TIA, transitory ischemic attack.

known risk of new CInf),[5] and ischemic heart disease (OR=1.33) (both an epiphenomenon of clinically defined atherosclerosis and a potential cause of repeat CInf).[1,4] In the Athens registry,[19] the most common risk factors associated with atherothrombotic stroke are HBP (73%), smoking (51%), and dyslipidemia (46%), while in the Turkish Ege registry[23] they are HBP (70%), diabetes mellitus (45%), and dyslipidemia (36%).

With respect to lacunar stroke, HBP (OR=2.64) and diabetes mellitus (OR=1.55) were the main factors in the cardiovascular risk profile. This agrees with the results of earlier anatomopathological studies[24] and observations made in other major studies.[25,26] Obesity (OR=1.50) was also a risk factor associated with lacunar stroke, as revealed by the German Stroke Data Bank, in which the maximum frequency of obesity is seen in the lacunar infarction subgroup (17.7%).[3] However, this is not seen in other registries[17-20]; further studies are therefore needed to confirm whether obesity is related to lipohyalinosis or microatheromatosis, the vessel pathologies of small vessel cerebrovascular disease.[27]

It is not surprising that the risk profile associated with cardioembolic stroke should include AF (OR=20.01), valve disease (OR=5.60), and ischemic heart disease (OR=2.09), the most common forms of heart disease.[28,29] The same is seen in the Athens regisrtry,[19] in which AF (80%), HBP (62%), and ischemic heart disease (24%) are the most common risk factors. The German Stroke Data Bank[3] also records HBP (62.5%), arrhythmia (61.1%), and ischemic heart disease (29.5%) to be the risk factors most strongly linked to stroke of cardiac origin.

It should be noted that, in stroke of undetermined and unusual etiology (ie, caused by hemopathies, infections, vasculitis, and many other problems), the classic cardiovascular risk factors are less strongly represented. This has also been noted by other authors.[30,31] The National Taiwan University Stroke Registry[32] records that for unusual stroke the frequency of HBP is just 38%, diabetes just 26%, and ischemic heart disease just 13%. The Ege Stroke Registry[23] records frequencies of 36% for HBP, 6% for diabetes, and 7% for AF and ischemic heart disease.

In the present work, which involved patients recruited over a period of 19 years (mean age, 75.5 years; women, 50.6%), in-hospital mortality was 12.9%—a figure similar to those observed in other studies, such as the 11% in the Scottish registry reported by Syme et al,[33] the 11.5%

TABLE 3. **Association of Cardiovascular Risk Factors With the Different Etiological Types of Stroke**

| Type of Stroke | β | $SE_β$ | OR (95% CI) | *P* |
|---|---|---|---|---|
| Atherothrombotic[a] | | | | |
| Peripheral vascular disease | .824 | 0.154 | 2.28 (1.68-3.08) | <.001 |
| High blood pressure | .608 | 0.093 | 1.84 (1.53-2.2) | <.001 |
| Diabetes mellitus | .509 | 0.101 | 1.66 (1.36-2.03) | <.000 |
| TIA | .408 | 0.133 | 1.50 (1.16-1.95) | .002 |
| COPD | .347 | 0.157 | 1.41 (1.04-1.93) | .028 |
| Prior cerebral infarction | .338 | 0.115 | 1.40 (1.12-1.76) | .003 |
| Ischemic heart disease | .287 | 0.119 | 1.33 (1.06-1.68) | .016 |
| Atrial fibrillation | –1.032 | 0.115 | 0.36 (0.28-0.45) | <.001 |
| Valve disease | –1.487 | 0.324 | 0.23 (0.12-0.43) | <.001 |
| Lacunar[b] | | | | |
| High blood pressure | .972 | 0.097 | 2.64 (2.19-3.20) | <.001 |
| Diabetes mellitus | .440 | 0.104 | 1.55 (1.23-1.90) | <.001 |
| Obesity | .408 | 0.207 | 1.50 (1.01-2.25) | .048 |
| Anticoagulants | –1.003 | 0.410 | 0.37 (0.16-0.82) | .014 |
| Atrial fibrillation | –1.510 | 0.130 | 0.22 (0.17-0.28) | <.001 |
| Cardioembolic[c] | | | | |
| Atrial fibrillation | 2.996 | 0.115 | 20.01 (15.98-25.05) | <.001 |
| Valve disease | 1.723 | 0.225 | 5.60 (3.60-8.71) | <.001 |
| Ischemic heart disease | .736 | 0.145 | 2.09 (1.57-2.78) | <.001 |
| Dyslipidemia | –.375 | 0.162 | 0.69 (0.50-0.94) | .021 |
| Diabetes mellitus | –.387 | 0.139 | 0.68 (0.52-0.89) | .005 |
| High blood pressure | –.390 | 0.114 | 0.67 (0.54-0.85) | .001 |
| TIA | –.420 | 0.186 | 0.66 (0.46-0.95) | .024 |
| Smoking (>20 cigarettes/day) | –.610 | 0.245 | 0.54 (0.34-0.88) | .013 |
| Obesity | –.959 | 0.330 | 0.38 (0.20-0.73) | .004 |
| Undetermined[d] | | | | |
| High blood pressure | –2.082 | 0.156 | 0.12 (0.09-0.17) | <.001 |
| Peripheral vascular disease | –2.051 | 0.597 | 0.13 (0.04-0.41) | .001 |
| Atrial fibrillation | –1.890 | 0.222 | 0.15 (0.10-0.23) | <.001 |
| Diabetes mellitus | –1.573 | 0.227 | 0.21 (0.13-0.32) | <.001 |
| Ischemic heart disease | –1.443 | 0.291 | 0.24 (0.13-0.42) | <.001 |
| Valve disease | –1.092 | 0.443 | 0.34 (0.14-0.80) | .014 |
| Prior cerebral infarction | –.494 | 0.213 | 0.61 (0.40-0.93) | .020 |
| Unusual[e] | | | | |
| Atrial fibrillation | –1.872 | 0.371 | 0.15 (0.07-0.32) | <.001 |
| Diabetes mellitus | –1.793 | 0.424 | 0.17 (0.07-0.38) | <.001 |
| Ischemic heart disease | –1.547 | 0.515 | 0.21 (0.08-0.58) | .003 |
| High blood pressure | –1.296 | 0.217 | 0.27 (0.18-0.42) | <.001 |

ABC indicates area under the ROC curve; CI, confidence interval; COPD, chronic obstructive pulmonary disease; OR, odds ratio; SE, standard error; TIA, transitory ischemic attack.
[a]β=–1.366; $SE_β$=0.089. ABC ROC=0.698.
[b]β=–1.356; $SE_β$=0.085. ABC ROC=0.715.
[c]β=–1.938; $SE_β$=0.109. ABC ROC=0.867.
[d]β=–0.302; $SE_β$=0.089. ABC ROC=0.735.
[e]β=–1.913; $SE_β$=0.125. ABC ROC=0.783.

of the Erlangen Stroke Project (Germany),[34] or the 12% of the Australian NEMESIS[35] registry. All these figures are higher, however, than the 5.3% of the Korean Yonsey Stroke Registry[36] or the 8.6% of the Indian registry reported by Kaul et al[37] (although in the latter mortality was recorded just 1 week after the onset of clinical symptoms). The present figure, however, is smaller than the 17% recorded in the Ege Stroke Registry.[23]

It should be noted that in-hospital mortality differs with respect to the risk factors present, showing the following descending order of frequency: congestive heart failure (30.4%), AF (22.8%), COPD (18.8%), prior CInf (17.1%), and prior cerebral hemorrhage (15.6%). This agrees with the Besançon registry,[18] in which the risk factors associated with mortality are heart failure (OR=4.2), AF (OR=3.3), ischemic heart disease (OR=2.3),

TABLE 4. **Association of In-Hospital Mortality With Cardiovascular Risk Factors and the Clinical Characteristics of the Different Etiological Types of Stroke: Descriptive and Comparative Analysis of Each Etiological Type**

| | Total | Atherothrombotic | Lacunar | Cardioembolic | Undetermined | Unusual |
|---|---|---|---|---|---|---|
| Patients | 350 (12.9) | 110 (14.3) | 4 (0.5) | 184 (24.1) | 39 (12) | 13 (11.4) |
| Congestive heart failure | 45 (30.4) | 15 (34.9)[a] | 1 (4.2) | 27 (37.5)[b] | 1 (12.5) | 1 (100) |
| Atrial fibrillation | 184 (22.8) | 27 (22.5)[b] | 1 (1.2) | 150 (26.2)[c] | 5 (20) | 1 (12.5) |
| COPD | 42 (18.8) | 16 (21.6)[c] | 0 | 184 (24.1) | 6 (30)d | 1 (16.7) |
| Prior cerebral infarction | 80 (17.1) | 24 (14.6) | 2 (1.7) | 48 (32.9)[b] | 4 (12.9) | 2 (20) |
| Prior cerebral hemorrhage | 5 (15.6) | 0 | 0 | 3 (42.9) | 2 (33.3) | 0 |
| Valve disease | 27 (15.5) | 1 (9.1) | 0 | 24 (18.5) | 1 (16.7) | 1 (16.7) |
| Peripheral vascular disease | 33 (15.4) | 13 (13) | 0 | 19 (38)d | 0 | 1 (25) |
| Ischemic heart disease | 66 (15.2) | 20 (13.3) | 0 | 43 (26.4) | 2 (14.3) | 1 (25) |
| Alcohol abuse (>80 g/day) | 10 (15.2) | 3 (11.5) | 0 | 3 (60) | 3 (30) | 1 (25) |
| TIA | 46 (14.5) | 22 (19) | 1 (1.3) | 16 (21.9) | 34 (11.8) | 11 (10.7) |
| High blood pressure | 190 (12.7) | 74 (14.5) | 2 (1) | 92 (24.4) | 16 (27.1)[a] | 6 (19.4) |
| Chronic liver disease | 7 (12.3) | 3 (17.6) | 0 | 3 (20) | 1 (10) | 0 |
| Diabetes mellitus | 69 (10.9) | 31 (12.8) | 0 | 32 (22.5) | 5 (20.8) | 1 (16.7) |
| Dyslipidemia | 32 (6.7) | 13 (7.9)[b] | 0 | 16 (18.2) | 2 (3.8)[c] | 1 (10) |
| Obesity | 118 (4.4) | 36 (4.7) | 47 (6.4) | 17 (2.2) | 13 (4) | 5 (4.4) |

[a]COPD indicates chronic obstructive pulmonary disease; TIA, transitory ischemic attack.
[b]*P*<.001.
[c]*P*=.005.
[d]*P*<.05.
The data express n (%).

TABLE 5. **Predictive Value of Cardiovascular Risk Factors With Respect to In-Hospital Mortality in the Different Etiological Types Stroke**

| Etiological Type | β | $SE_β$ | OR (95% CI) | *P* |
|---|---|---|---|---|
| Cerebral infarctions (whole sample)[a] | | | | |
| Atrial fibrillation | .846 | 0.122 | 2.33 (1.84-2.96) | <.001 |
| Heart failure | .673 | 0.199 | 1.96 (1.33-2.89) | .001 |
| COPD | .382 | 0.190 | 1.46 (1.01-1.89) | .044 |
| Prior cerebral infarction | .356 | 0.145 | 1.43 (1.07-1.89) | .014 |
| Age | .046 | 0.007 | 1.05 (1.03-1.06) | <.001 |
| Dyslipidemia | –.546 | 0.199 | 0.58 (0.39-0.85) | .006 |
| Atherothrombotic[b] | | | | |
| Heart failure | 1.055 | 0.350 | 2.87 (1.45-5.71) | .003 |
| Atrial fibrillation | .588 | 0.254 | 1.80 (1.09-2.96) | .021 |
| Age | .027 | 0.012 | 1.03 (1.01-1.05) | .033 |
| Dyslipidemia | –.640 | 0.319 | 0.53 (0.28-0.98) | .045 |
| Cardioembolic[c] | | | | |
| Peripheral vascular disease | .779 | 0.317 | 2.18 (1.17-4.05) | .014 |
| Prior cerebral infarction | .558 | 0.208 | 1.75 (1.16-2.63) | .007 |
| Heart failure | .536 | 0.270 | 1.71 (1.01-2.90) | .047 |
| Age | .060 | 0.011 | 1.06 (1.04-1.08) | <.001 |
| Undetermined[d] | | | | |
| High blood pressure | 1.303 | 0.372 | 3.68 (1.78-7.62) | <.001 |
| Age | .050 | 0.018 | 1.05 (1.01-1.09) | .005 |

[a]β=–5.942; $SE_β$=0.567. ABC=0.721; sensitivity=0.68; specificity=0.66; positive predictive power=0.23; negative predictive power=0.93; correctly classified=0.67.
[b]β=–3.949; $SE_β$=0.990. ABC=0.667; sensitivity=0.62; specificity=0.60; positive predictive power=0.21; negative predictive power=0.90; correctly classified=0.61.
[c]β=–6.207; $SE_β$=0.926. ABC=0.670; sensitivity=0.62; specificity=0.63; positive predictive power=0.34; negative predictive power=0.84; correctly classified=0.62.
[d]β=–6.179; $SE_β$=1.438. ABC=0.723; sensitivity=0.67; specificity. 0.67; positive predictive power=0.22; negative predictive power=0.94; correctly classified=0.67.

TABLE 6. **Comparative Analysis of Demographic Data, Length of Hospital Stay, and In-Hospital Mortality Associated With Cerebral Infarction Over 3 Periods of the Study**

| | Study Period | | | *P* |
|---|---|---|---|---|
| | 1986-1992 | 1993-1998 | 1999-2004 | |
| Total number of patients | 936 | 896 | 872 | |
| Age, mean (SD), y | 72 (12.9) | 75.8 (10.8) | 78.8 (10) | <.001 |
| Age group | | | | <.001 |
| <65 Years | 202 (21.6) | 108 (12.1) | 76 (8.7) | |
| 65-74 Years | 262 (28) | 249 (27.8) | 169 (19.4) | |
| 75-84 Years | 353 (37.7) | 362 (40.4) | 353 (40.5) | |
| ≥85 Years | 119 (12.7) | 177 (19.8) | 274 (31.4) | |
| Sex | | | | .102 |
| Men | 488 (52.1) | 424 (47.3) | 424 (48.6) | |
| Women | 448 (47.9) | 472 (52.7) | 448 (51.4) | |
| Hospital stay, median (interquartile range), d | 13 (8-22) | 13 (9-22) | 11 (8-18) | <.001 |
| In-hospital mortality | 140 (15) | 121 (13.5) | 89 (10.2) | .009 |

and diabetes mellitus (OR=1.5). This may explain why the presence of prior heart disease is a poor prognostic factor in patients with stroke.[28-30] Prior ischemic or hemorrhagic stroke, which are normally associated with significant functional limitation, are also poor prognostic markers associated with more dependence, immobility and death.[39] Chronic pneumopathy is also associated with poor progress in patients who suffer either ischemic or hemorrhagic stroke.[22]

However, it should be remembered that the present results show that each etiological type of stroke has its own cardiovascular risk profile, with a different influence on in-hospital mortality. In atherothrombotic stroke the presence of other heart disease is an independent risk factor (congestive heart failure: OR=2,87; AF: OR=1.80), in agreement with that reported by other authors.[30-32] Age is also a risk factor for mortality in patients with atherothrombotic stroke (OR=1.03), but also in cardioembolic (OR=1.06) and undetermined stroke (OR=1.05), as reported in other studies.[1,36]

It is noticeable that the risk profile associated with mortality in cardioembolic stroke should feature peripheral vascular disease above all else (OR=2.18), followed by prior CInf (OR=1.75), congestive heart failure (OR=1.71), and age. In the general population, peripheral vascular disease is a predictor of cardiovascular disease and death.[40] Finally, with respect to non-essential stroke, only HBP (OR=3.68) and age were independent risk factors associated with in-hospital mortality.

It is important to highlight the changes in disease progress, prognosis and the need for assistance detected in this study. Over time, in-hospital mortality fell (from 15% to 13.5% to 10.2%; *P*<.001), as did the median length of hospital stay (13 days to a final 11 days; *P*=.009). These results confirm the benefit obtained from appropriate therapeutic management and assistance, and coincide with the trends seen in the Laussane Stroke Registry[38] (which involved comparisons over a 25-year recruitment period).

Finally, it should be noted that the identification and treatment of the different risk factors and profiles associated with the different etiological types of stroke provide a rational basis for improving secondary prevention and reducing in-hospital mortality in patients with cerebral ischemia.

## CONCLUSIONS

Each etiological type of stroke has its own cardiovascular risk profile. The risk profile associated with in-hospital mortality is also different for each etiological type of stroke.

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## APPENDIX. **Definitions of the Different Etiological Types of Stroke**

*1*. Atherothrombotic stroke. Generally a medium or large infarction of cortical or subcortical topography and with a carotid or vertebrobasilar location. At least 1 of the following criteria must be met:

– Atherosclerosis with stenosis: stenosis ≥50% of the luminal diameter or occlusion of the corresponding extracranial large artery (middle cerebral artery, posterior cerebral artery, or basilar trunk) in the absence of other etiology
– Atherosclerosis without stenosis: presence of plaques or stenosis <50% in the middle cerebral artery, posterior cerebral artery, or basilar artery with no other etiology but in the presence of peripheral artery disease, ischemic heart disease or both

*2*. Cardioembolic stroke. Generally a medium or large infarction of habitually cortical topography in which (in the absence of other etiology) at least 1 of the following embologenic cardiopathies is seen: a thrombus or intracardiac tumor, rheumatic valve disease, a mitral or aortic prosthesis, endocarditis, atrial fibrillation or flutter, sinus node disease, left ventricular aneurysm after acute myocardial infarction, myocardial infarction in the acute phase (<3 months), or general cardiac hypokinesia.
*3*. Lacunar stroke. A small infarction (<1.5 cm maximum lesion diameter) in the area of distribution of a perforating cerebral artery that causes a classic lacunar syndrome (pure motor hemiparesis, pure sensory syndrome, sensory-motor syndrome, hemiparesis-ataxia, and dysarthria-clumsy hand syndrome) or atypical lacunar syndrome in patients with a history of HBP or other cardiovascular risk factors, in the absence of other etiology.
*4*. Stroke of unusual etiology. A small, medium, or large infarction, either cortical or subcortical in location, in the carotid or vertebrobasilar vascular areas of a patient in whom an atherothrombotic, cardioembolic and lacunar origin has been ruled out. Usually caused by systemic disease (connective tissue disease, infection, neoplasm, myeloproliferative syndrome, metabolic alterations, coagulation disorders, etc) or other problems such as arterial dissection, fibromuscular dysplasia, saccular aneurysm, arteriovenous malformation, thrombosis of the cerebral veins, angiitis, migraine, etc.
*5*. Stroke of undetermined etiology. A medium or large infarction, either cortical or subcortical in location, in the carotid or vertebrobasilar vascular areas of a patient in whom, after exhaustive analysis, atherothrombotic, cardioembolic lacunar, and unusual origins have been ruled out, or when more than 1 etiology is possible. Undetermined strokes are usually subdivided as: *a)* owing to incomplete examination; *b)* as having more than 1 etiology; and *c)* etiology unknown.