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OBSERVATION

# Arterial hypertension, cerebrovascular diseases and dementia

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## Abstract

Arterial hypertension (AH) is the most relevant risk factor for acute cerebrovascular disease in general. However, the prevalence of AH is not the same for the different stroke subtypes and is particularly high in lacunar infarcts and atherothrombotic stroke, low in infarcts of unusual cause and undetermined origin, and intermediate in cardioembolic stroke. This risk factor has also been related to vascular dementia and Alzheimer's disease and their pathological manifestations (senile plaques, neurofibrillary tangles, hippocampal atrophy). The mechanisms linking AH to Alzheimer's disease remain to be elucidated but some recent studies showed that white matter lesions seen on cerebral magnetic resonance imaging appear to be a good marker of this association. Hypertension-associated pathological changes in the brain and its vasculature include vascular remodelling and impaired cerebral autoregulation like hypoperfusion, ischemia and hypoxia, which may initiate the pathological process of Alzheimer's disease and the expression of dementia. Therefore, prompt diagnosis and adequate control of hypertension and different vascular risk factors are the rational basis for a more effective strategy in the secondary prevention of cerebrovascular disease and dementia.



## INTRODUCTION

Stroke after heart disease and cancer is the third commonest cause of death in industrialized countries and accounts for more than 50% of all neurological hospital admissions to adult wards. Hypertension was found in 52% of patients with ischemic stroke included in The Sagrat Cor Hospital of Barcelona Stroke registry and constituted, as in other stroke registries, the most relevant risk factor for acute cerebrovascular disease in general as well as when acute cerebrovascular events are divided into ischemic stroke and hemorrhagic stroke[1].

## HYPERTENSION IN DIFFERENT STROKE SUBTYPES

Although hypertension is extensively recognised as a major cardiovascular risk factor, the prevalence of hypertension is not the same for the different stroke subtypes[1-3]. In our experience, the prevalence of hypertension is particularly high in lacunar infarcts (71.6%) and atherothrombotic stroke (66.1%), low in infarcts of unusual cause (27.2%) and undetermined origin (18.2%), and intermediate in cardioembolic stroke (49.4%) (Table 1)[1]. In the Athens Stroke registry, the most frequent risk factors in atherothrombotic stroke were hypertension (73%),

**Table 1 Arterial hypertension and other cardiovascular risk factors according to the ischemic stroke subtype in the Sagrat Cor Hospital of Barcelona Stroke Registry *n* (%)**

| Variable | Atherothrombotic (*n* = 770) | Lacunar (*n* = 733) | Cardioembolic (*n* = 763) | Undetermined etiology (*n* = 324) | Unusual cause (*n* = 114) |
|---|---|---|---|---|---|
| Hypertension | 509 (66.1)[d] | 525 (71.6)[d] | 377 (49.4)[d] | 59 (18.2)[d] | 31 (27.2)[d] |
| Atrial fibrillation | 120 (15.6)[d] | 81 (11.1)[d] | 573 (75.1)[d] | 25 (7.7)[d] | 8 (7.0)[d] |
| Diabetes mellitus | 242 (31.4)[d] | 218 (29.7)[d] | 142 (18.6)[b] | 24 (7.4)[d] | 6 (5.3)[d] |
| Hyperlipidemia | 164 (21.3)[d] | 166 (22.6)[d] | 88 (11.5)[d] | 52 (16.0)[d] | 10 (8.8) |
| Previous cerebral infarction | 164 (21.3)[a] | 117 (16.0) | 146 (19.1) | 31 (9.6)[d] | 10 (8.8)[b] |
| Ischemic heart disease | 150 (19.5)[a] | 104 (14.2) | 163 (21.4)[d] | 14 (4.3)[d] | 4 (3.5)[d] |
| Transient ischemic attack | 116 (15.1)[b] | 80 (10.9) | 73 (9.6)[a] | 37 (11.4) | 11 (9.6) |
| Smoking (> 20 cigarettes/d) | 87 (11.3)[a] | 86 (11.7)[d] | 28 (3.7)[d] | 41 (12.7)[d] | 18 (6.9) |
| COPD | 74 (9.6) | 61 (8.3) | 62 (8.1) | 20 (6.2) | 6 (5.3) |
| Peripheral arterial disease | 100 (13.0)[b] | 57 (7.8) | 50 (6.6) | 3 (0.9)[b] | 4 (3.5)[b] |
| Valve heart disease | 11 (1.4)[d] | 21 (2.9)[d] | 130 (17.0)[d] | 6 (1.9)[b] | 6 (5.3) |
| Congestive heart failure | 43 (5.6) | 24 (3.3)[b] | 72 (9.4)[d] | 8 (2.5)[b] | 1 (0.9)[a] |
| Obesity | 36 (4.7) | 47 (6.4)[d] | 17 (2.2)[b] | 13 (4.0) | 5 (4.4) |
| Oral anticoagulants | 18 (2.3)[a] | 7 (1)[d] | 63 (8.3)[d] | 2 (0.6)[d] | 4 (3.5) |
| Alcohol abuse (> 80 g/d) | 26 (3.4)[a] | 21 (2.9) | 5 (0.7)[a] | 10 (3.1) | 4 (3.5) |
| Chronic liver disease | 17 (2.2) | 15 (2.1) | 15 (2.0) | 10 (3.1) | 0 |
| Previous cerebral hemorrhage | 9 (1.2) | 9 (1.2) | 7 (0.9) | 6 (1.9) | 1 (0.9) |

[a]$P < 0.05$, [b]$P < 0.01$, [d]$P < 0.001$. COPD: Chronic obstructive pulmonary disease.

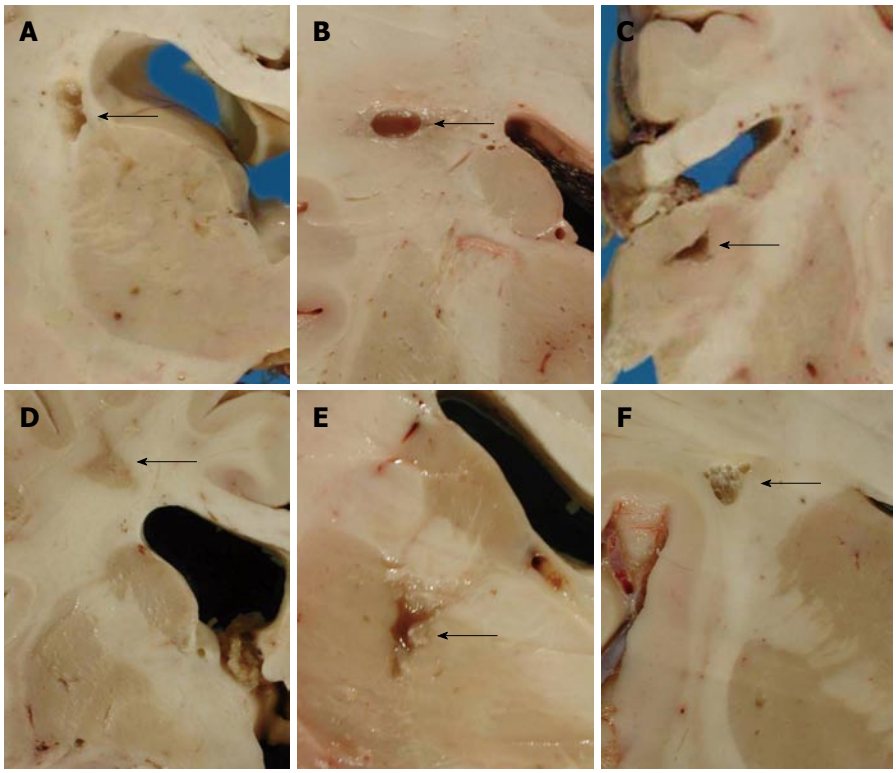


**Figure 1 Lacunar infarcts (arrows) in semi oval centre (A, B, D, F), thalamus (C) and putamen (E).** Figure provided courtesy of Isidre Ferrer (University of Barcelona, Catalonia, Spain).

smoking (51%) and dyslipidemia (46%)[4], whereas in the Ege Stroke registry, hypertension (70%), diabetes mellitus (45%) and dyslipidemia (35%) were the most common[5]. These findings reveal that hypertension does not constitute the main risk factor for all ischemic stroke subtypes. Hypertension is simultaneously a risk factor (for atherosclerosis) and a cause of lipohyalinosis associated with lacunar infarct (Figure 1).

On the other hand, high blood pressure may aggravate atherosclerosis and induce complex pathological changes in arteries and arterioles. As a consequence, hypertension is a precursor of large-artery disease and hypertensive small-vessel disease, such as lipohyalinosis, which is one of the most common causes of lacunar infarction[1,6-8]. In a recent clinical study, hypertensive patients with ischemic stroke have different clinical features than non-hyper-

tensive patients[1]. Lacunar syndrome, female gender and previous cerebral infarction were independent variables associated with hypertensive ischemic stroke[1].

## HYPERTENSION IN DEMENTIA

Hypertension is also a risk factor for ischemic white matter lesions, microbleeds, general atherosclerosis, myocardial infarction and cardiovascular diseases, and often clusters with other vascular risk factors, including diabetes mellitus, obesity and hypercholesterolemia. These risk factors have also been related to Alzheimer's disease[9] and their pathological manifestations (senile plaques, neurofibrillary tangles, hippocampal atrophy)[10]. The mechanisms linking hypertension to Alzheimer's disease remain to be elucidated but some recent studies showed that white matter lesions seen on cerebral magnetic resonance imaging appear to be a good marker of this association[11]. In terms of the pathophysiology of hypertensive brain damage, several hypothesis have been developed, such as hypertension may promote a pre-existing subclinical Alzheimer's disease, hypertension could determine neurobiological alterations (such as β-amyloid accumulation) resulting in neuropathological damage and, finally, age and cerebrovascular risk factors may act together to cause cerebral vascular degeneration, mitochondrial disruption, reduced glucose oxidation and reduced ATP synthesis. The consequences of these alterations are neuronal death and dementia[10-12]. Hypertension-associated pathological changes in the brain and its vasculature include vascular remodelling and impaired cerebral autoregulation like hypoperfusion, ischemia and hypoxia, which may initiate the pathological process of Alzheimer's disease and the expression of dementia[9].

## CONCLUSION

Management of hypertension is equally effective in reducing the risk of stroke in women and men. In addition, recurrent stroke has been shown to be more frequent among hypertensive patients than among non-hypertensive patients[13-16]. Therefore, prompt diagnosis and adequate control of hypertension and different vascular risk factors are the rational basis for a more effective strategy in the secondary prevention of cerebrovascular disease and dementia.

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