INTRODUCTION

This year, we are devoting our Update section to the subject, “Non-coronary arterial disease.” Through nine carefully selected review articles, entrusted to internationally recognized experts, we hope to cover, in their entirety and in sufficient depth, the most important aspects of this disease, which is currently a burning issue (Table). The idea is to provide a critical, rigorous update of this fascinating facet of cardiovascular disease, often pushed to the background, or even forgotten.

Atherosclerosis is a progressive systemic disease that affects different vascular beds.\(^1,2\) In fact, the coexistence of coronary, cerebral and peripheral involvement is very common.\(^2,3\) Aside from certain peculiarities, the risk factors associated with the different sites are similar, the clinical signs depend on the most severely affected territory, and medical treatment (antiplatelet agents, statins, and angiotensin-converting enzyme [ACE] inhibitors) has common beneficial effects in these patients.\(^1-3\)

Vascular disease is a chronic condition that represents a serious public health problem; however, in view of the foreseen aging of the population, its importance will undoubtedly grow in the immediate future.\(^1-3\) Consequently, prevention emerges as a strategy of top priority. Recent data concerning the situation in Spain reveal the tremendous amount of work that remains to be done in order to achieve adequate control of the classical risk factors.\(^4,5\) In this respect, equations for the prediction of cardiovascular risk can help to guide prophylactic treatment.\(^5\) Moreover, unprecedented advances have recently been made in our ability to directly and noninvasively “visualize” the presence of the disease in multiple vascular beds (global atherosclerotic burden), even in the silent phase. The measurement of the calcium score or the visualization of the atheromatous plaque and the residual lumen in different arterial territories, either by computed tomography or by magnetic resonance, has revolutionized the diagnosis of this disease.\(^7-9\) The precision in the anatomical characterization that these techniques now provide in medium-sized and large vessels is simply spectacular. All this information should enable us to optimize our therapeutic efforts in selected patients.

Cerebral Vascular Disease

The aging of the population is having a decisive impact on the incidence and prevalence of cerebrovascular diseases (CVD).\(^10-13\) We know that the consequences of stroke, both for the patient and society, are usually devastating. Some systematic reviews reveal truly disturbing data.\(^11\) A recent study points out that the incidence of CVD in Europe will increase dramatically in the coming years (from 1 000 000/year in 2000 to 1 500 000/year in 2025), merely as an expression of demographic changes.\(^11\) The reduction in age-adjusted rates of cerebrovascular mortality observed over the last four decades will thus be amply surpassed by the net increase in mortality because of the aging of the population.\(^10-13\) The incidence of CVD in Spain has been

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estimated to be between 218 and 364 per 100,000 population among men and between 127 and 169 among women. In patients over 70 years of age, the estimates are 10-fold higher, while the prevalence in individuals over the age of 65 is 7% in men and 6% in women. We must remember that in the brain, aside from the general atherosclerotic process, there is a specific substrate for vascular degeneration. With the deposition of a beta-amyloid substance, known as “cerebral amyloid angiopathy”, which can cause recurrent cerebral hemorrhages.

The most recent data (2004) on mortality due to CVD in Spain from the Centro Nacional de Epidemiología (National Center for Epidemiology) are shown in Figure. These data only reflect in-hospital mortality, and it has recently been pointed out that up to two thirds of the deaths due to CVD occur outside the hospital setting. Thus, the overall mortality due to CVD is as high as 36%. Stroke is the leading cause of adult disability, the second leading cause of dementia and the third leading cause of death in industrialized countries. In Spain, CVD are the leading cause of death in women.

All patients with CVD should receive extensive information on the modification of risk factors, as well as proper medical treatment. A number of studies have demonstrated that treatment with statins reduces the incidence of stroke in high cardiovascular risk patients. There has also been speculation concerning the “stroke paradox,” according to which, despite the fact that epidemiological studies have found no clear relationship between cholesterol concentrations and stroke risk, there are data that clearly show that statin therapy prevents stroke in patients with ischemic heart disease. Moreover, very recent studies have also demonstrated that, in patients with no known coronary heart disease who have had a stroke or a transient ischemic attack, intensive statin therapy reduces the rate of recurrence. This treatment, however, might not be effective, or may even be harmful in patients who have had a hemorrhagic stroke.

Carotid Disease

The easy access to this artery has made it a highly attractive target for the study of atherosclerosis in general. Thus, incipient carotid atherosclerosis can be analyzed with precision using ultrasound to measure the intima-media thickness of posterior wall of the common carotid artery. Values over 1.1 mm not only are associated with the presence of atherosclerosis at other sites, but are also predictive of cardiovascular risk.

In 1951, Fisher reported the pathological relationship between the carotid atheromatous plaque and ipsilateral stroke. Since then, carotid endarterectomy has been the surgical intervention most widely performed for stroke prevention. In contrast to what we have learned...
in ischemic heart disease, where the demonstration of the presence of ischemia is universally considered to be an indispensable requirement for the indication for revascularization, in carotid disease, the mere presence of an angiographically severe lesion—even “asymptomatic”—justifies the intervention. Its status as a mature technique, acquired over more than 5 decades, supports the results of carotid endarterectomy. However, in recent years, percutaneous interventional procedures have aroused a great amount of expectation. In this respect, carotid stent implantation has been shown to be a feasible alternative in selected high-risk patients. However, the U.S. Food and Drug Administration has approved stent placement only in symptomatic patients, with over 70% internal carotid artery stenosis and at risk for developing complications following endarterectomy. At the present time, there is an intense debate concerning the real value of this technique in patients who do not present high surgical risk. A recent Cochrane systematic review concluded that carotid endarterectomy should continue to be considered the treatment of choice in this disease. More recently, two extensive randomized studies have had to be suspended prematurely, sowing new doubts about the efficacy of percutaneous treatment as an alternative to surgery. Nevertheless, we should remember that, in some of these studies, the interventional procedure was performed by personnel with limited previous experience and that the systems for preventing distal embolization were not systematically employed. Recent data suggest that the morphological features of the plaque (identified by noninvasive means) could help predict the risk of embolization after the intervention and efforts are presently being made to improve the selection of the patients who might benefit from this technique. The continuing technological advances, together with new ongoing randomized studies, demonstrate that, with regard to revascularization in carotid artery stenosis, the swords remain drawn.

Peripheral Arterial Disease

Peripheral arterial disease (PAD) is generally understood to be the obstruction of the blood flow in any arterial territory, with the exception of the coronary and cerebral territories. The area of interest extends to the abdominal aorta, the renal and mesenteric arteries, or, more specifically, to the lower extremities. Peripheral arterial disease usually coexists with coronary and cerebrovascular disease. Thus, the risk of myocardial infarction, stroke and death in patients with PAD is between two and four times higher, while approximately one third of the patients with coronary or cerebrovascular disease also have PAD. The early diagnosis and treatment of PAD reduces the incidence of renal insufficiency, mesenteric ischemia, aortic aneurysm rupture and amputations. Although atherosclerosis is the major cause of PAD, we should take into consideration other degenerative diseases (Marfan syndrome, Ehlers-Danlos syndrome), fibromuscular dysplasia, vasculitis (large vessels [Takayasu’s disease and Behçet’s syndrome], medium-sized vessels [Kawasaki disease and Churg-Strauss syndrome] and small vessels [lupus and rheumatoid arthritis], and the prothrombotic and vasospastic diseases as possible etiologies.

The prevalence of PAD is elevated and it has been estimated to affect up to 20% of the patients over 65 years of age, in whom it is usually asymptomatic. Although the cardinal symptom is intermittent claudication, the ankle-brachial index, at baseline and following exercise, is much more sensitive and thus provides a clearly cost-effective measure for the detection of PAD. This index is calculated as the highest pressure in each lower limb (dorsal pedal or posterior tibial artery), divided by the highest pressure in either of the two arms (normal: between 1 and 1.29). The ankle-brachial index not only is useful for the diagnosis of PAD, but for the prediction of overall cardiovascular risk, as well. In turn, stress testing or, better still, the six-minute walk test enables the objective measurement of the functional limitation of patients with PAD.

Aortic Disease

The role of the cardiologist in the study of thoracic aortic disease has never been questioned, and this subject will be reviewed in two specific sections of this Update. Here, we will only mention the interest aroused recently by the new “endovascular” treatments, aided by modern imaging techniques and by the creation of multidisciplinary teams, which make it possible to optimize the diagnosis and treatment of thoracic aortic diseases.

However, until now, the involvement of the cardiologist in abdominal aortic disease has been very limited. Thus, we should remember that the prevalence of abdominal aortic aneurysms (AAA) (anteroposterior diameter greater than 3 cm) also depends on age (1.3% in men aged 45 to 55 years; 12.5% in men over 75). The systematic performance of ultrasonographic evaluation in all male smokers over the age of 65 years has recently been recommended. Atherosclerosis in the thoracic aorta and an abnormal intima-media thickening of the carotid artery are common findings in patients with AAA, a circumstance that again reflects a generalized atherosclerotic process. In their natural history, AAA undergo gradual dilation (the larger the aneurysm, the faster this process) and thrombosis. The most feared complications are rupture, ischemic events and compression or erosion of adjacent structures. The cumulative risk of rupture depends on the size (20% when the aneurysm is greater than 5 cm and 40% when it measures over 6 cm) and the consequences are...
catastrófico, con una tasa de mortalidad de más del 90%.\(^2\) Por lo tanto, la recomendación I es para pacientes con aneurisma de la aorta abdominal infrarrenal o juxtarrenal de 5,5 mm o más que requieran reparación, mientras que la recomendación IIa es para aquellos con aneurismas de la aorta abdominal infrarrenal o juxtarrenal de 5 cm.\(^2\) Además, los bloqueadores beta son recomendados para reducir la mortalidad a largo plazo, la duración de los efectos de este tratamiento ha de ser establecida.\(^3\) Por otro lado, el tratamiento quirúrgico para pacientes con enfermedad arterial coronaria es la principal causa de mortalidad en pacientes con aneurisma, por lo que su correcta identificación y tratamiento es de vital importancia. No obstante, el simple optimización del tratamiento quirúrgico es el aspecto más importante.\(^3\) En un estudio aleatorio que involucró a pacientes con aneurisma de la aorta abdominal con enfermedad coronaria, se consideró que el tratamiento con alta presión,\(^3\) tratamiento médico intensivo (bloqueadores beta, antiplaquetarios, estatinas y inhibidores ACE) demostró ser efectivo como una estrategia de revascularización sistémica en el tratamiento de eventos isquémicos adversos (AAA en 33% y PAD en 67%).\(^2\)

Otras problemas relacionados con la enfermedad arterial del abdomen son menos conocidos. La enfermedad mesentérica se debe a la enfermedad arterial sistémica (generalmente múltiple debido a la abundante circulación colateral en esta zona) o a condiciones asociadas con hemodinámica severa.\(^1\) La enfermedad mesentérica generalmente conduce a necrosis intestinal, que es fatal a pesar del tratamiento agresivo.\(^2\) Los lineamientos de práctica clínica insisten en la información controlada de estudios en esta zona del cuerpo para incentivar la realización de estudios de alta calidad.\(^2\)

### Renal Vascular Disease

La enfermedad arterial renal es attributable a la enfermedad arterial en 90% de los casos (proximal) e incluye enfermedad arterial en el 10% (distal).\(^2\) En algunos países, muchas enfermedades son de tipo Takayasu. La prevalencia de la enfermedad arterial renal está entre 7% de los pacientes mayores de 65 años. Es frecuentemente asociada con hipertensión y renal insuficiencia.\(^2\) Debemos mantener en cuenta que la enfermedad renal es la más común de las enfermedades isquémicas. En pacientes seleccionados, la colocación de esténose es superior a la angioplastia, tanto en el control del sangrado y en la reducción del riesgo de reestenosis.\(^3\) Sin embargo, este tratamiento requiere una indicación clínica clara: enfermedad renal crónica, insuficiencia renal, edema pulmonar agudo, etc. Además, el grado de recuperación de la función renal después de la revascularización es limitado y altamente variable.

### CONCLUSIONS

El tiempo de discusión sobre qué especialista es el mejor preparado para tratar las diferentes áreas de enfermedad arterial no coronaria es ahora. Multidisciplinarias equipos de profesionales cualificados en diferentes áreas de la enfermedad arterial no coronaria son el nuevo reto. No obstante, como veremos en esta actualización, la evidencia muestra que el cardiólogo debe jugar un papel fundamental en la prevención, diagnóstico y tratamiento en estos pacientes.

En este nuevo sistema de enfermedad, que está caracterizado por la presencia de enfermedades y sus tratamientos que a menudo se olvidan, una mejor comprensión de ciertas áreas del sistema cardiovascular puede despertar nuevo interés científico que facilitará la investigación en el futuro. Respecto a la enfermedad arterial coronaria, la enfermedad arterial no coronaria ya no es una preocupación. Equipos multidisciplinarios están preparados para abordar la variedad de enfermedades no coronarias.

### REFERENCES

28. Alfonso F et al. Introducción. Non-Coronary Arterial Disease: of Interest to Cardiologists?