Systemic Blood Pressure Profile in Cerebral Autosomal Dominant Arteriopathy With Subcortical Infarcts and Leukoencephalopathy

Alessandra Rufa, MD; Maria Teresa Dotti, MD; Massimo Franchi, MD; Maria Laura Stromillo, MD; Gabriele Cevenini, PhD; Silvia Bianchi, PhD; Nicola De Stefano, MD; Antonio Federico, MD

Background and Purpose—Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a genetic form of subcortical ischemic vascular dementia (SIVD). The most common vascular risk factors are unremarkable in CADASIL; however, studies on systemic blood pressure (BP) changes over time are substantially lacking. Because BP instability is a relevant risk factor for developing or worsening white matter changes in sporadic SIVD, we aimed to study the BP profile of CADASIL to investigate its relationship with cognitive decline and white matter injury.

Methods—Twenty-four–hour ambulatory BP monitoring was performed in a group of 14 CADASIL patients (12 males and 2 females) and in a group of 15 healthy age-matched control subjects. The following BP variables were compared between the 2 groups: mean daytime and nighttime systolic, diastolic, and mean arterial BP ($SABP_{day}$, $DABP_{day}$, and $MABP_{day}$, and $SABP_{night}$, $DABP_{night}$, and $MABP_{night}$) and nocturnal percentage decline in arterial BP (%MABP reduction). Cognitive performances were tested by mini mental status examination (MMSE), and brain MRI was performed to extrapolate the T2-weighted lesion volume (LV) in each CADASIL patient. The 24-hour arterial BP variables were compared between CADASIL and controls. In addition, for CADASIL patients only, MMSE, LV, and age were compared with each pressure variable.

Results—Patients with CADASIL showed a significant reduction ($P<0.05$) of $SABP_{day}$, $DABP_{day}$, $MABP_{day}$ and %MABP decline with respect to controls. In addition, MMSE of CADASIL subjects correlated significantly ($P<0.0001$) with daytime MABP.

Conclusions—The low systemic BP profile observed in CADASIL patients was specifically attributable to reduced diurnal BP values. This may further affect cerebral hemodynamics and increase the risk of cognitive impairment in these patients. The pathogenesis of abnormal BP profile in CADASIL remains to be clarified. It is likely that central and peripheral mechanisms controlling BP variations are involved. **(*Stroke*. 2005;36:2554-2558.)**

Key Words: blood pressure ■ CADASIL ■ dementia ■ magnetic resonance imaging

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a generalized small- and medium-sized arteriopathy attributable to mutations in the *Notch3* gene,[1] which causes repeated strokes, MRI evidence of diffuse white matter (WM) changes, and progressive cognitive impairment.[2] Although the nature of *Notch3* mutations is highly stereotyped, the phenotypic expression of the disease is extremely variable,[3] suggesting a possible modulating role of other genetic or acquired factors, including cardiovascular risk factors.[4,5] Vascular smooth muscle cells are thought to be targeted by the disease.[6] Their degeneration presumably leads to loss of systemic arteriolar wall tone and failure of cerebral autoregulation with chronic hypoperfusion or abrupt lack of perfusion.[7] Unlike in other forms of sporadic subcortical ischemic vascular dementia (SIVD), arteriolar occlusions were rarely observed in autopsied cases.[8] However, the exact mechanism of how the alterations of the deep small penetrating arteries cause WM changes and lacunar infarcts characteristic of CADASIL are still debated.[9,10] Cerebral WM abnormalities similar to those observed in CADASIL patients, are frequently seen on MRI of elderly individuals, particularly in those with vascular risk factors and with cognitive impairment.[11] Blood pressure (BP) instability is a serious risk factor for developing or worsening WM changes in sporadic SIVD because prolonged hypertensive or conversely hypotensive

Received April 19, 2005; final revision received September 19, 2005; accepted September 30, 2005.

From the Dipartimento di Scienze Neurologiche e del Comportamento (A.R., M.T.D., M.L.S., S.B., N.D., A.F.), Università di Siena, Italy; Dipartimento di Medicina Clinica e Scienze Immunologiche Applicate (M.F.), Università di Siena, Italy; and Dipartimento di Chirurgia e Bioingegneria (G.C.), Università di Siena, Italy.

Correspondence to Maria Teresa Dotti, MD, Dipartimento di Scienze Neurologiche e del Comportamento, Università di Siena, Viale Bracci, 53100 Siena, Italy. E-mail dotti@unisi.it

Stroke **is available at http://www.strokeaha.org** **DOI: 10.1161/01.STR.0000190832.17620.25**