

Cardiac Autonomic Nervous System and Risk of Arrhythmias in Cerebral Autosomal Dominant Arteriopathy With Subcortical Infarcts and Leukoencephalopathy (CADASIL)

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Background and Purpose—Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is an inherited systemic microangiopathy with prevalently cerebral manifestations. Among the causes of death, sudden unexpected death seems to occur in a significant number of CADASIL patients. Because potential causes of sudden unexpected death may include cardiac arrhythmias and myocardial infarction, we evaluated risk factors for life-threatening arrhythmias, such as reduced heart rate variability, sympathetic overactivity and QT interval (QTc) prolongation, in 23 CADASIL patients. The relationship of these changes with brain MRI pattern was also investigated.

Methods—Frequency domain measures of heart rate variability (10 minutes recordings) and QTc interval were recorded in 23 CADASIL patients (17 males, 6 females) and 22 healthy age- and sex-matched control subjects. The following heart rate variability spectral parameters were considered at rest during spontaneous and controlled breathing (Cb): total power, very-low-frequency component, low-frequency component, high-frequency component, low-frequency/high-frequency ratio, and Cb-total power, Cb-very-low-frequency component, Cb-low-frequency component, Cb-high-frequency component, Cb-low-frequency/high-frequency ratio. R-to-R wave and QTc interval were also analyzed. All data were statistically compared between CADASIL and control subjects. Conventional brain MRI was performed in patients with CADASIL and T1-weighted and T2-weighted lesion volumes, and were compared with each spectral component of the tachogram.

Results—During spontaneous and controlled breathing, total power spectrum and all spectral components (very low frequency component, high-frequency component, low-frequency component) of heart rate variability were significantly reduced in CADASIL patients with respect to controls ($P < 0.05$). The low-frequency/high-frequency component ratio was significantly higher in CADASIL patients than in controls. No significant correlation between heart rate variability spectral parameters and other variables including total brain T2-weighted and T1-weighted lesion volumes were observed in CADASIL subjects.

Conclusions—We found a statistically significant reduction in all frequency domain parameters of heart rate variability associated with a higher low frequency/high frequency ratio for CADASIL patients with respect to normal subjects. These data are consistent with autonomic derangement and suggests that CADASIL patients may be at risk for life-threatening arrhythmias. This could at least in part explain their higher recurrence of sudden unexpected death and should be taken into account in planning therapy. (*Stroke*. 2007;38:276-280.)

Key Words: arrhythmias ■ CADASIL ■ heart rate ■ sudden unexpected death

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is an inherited systemic microangiopathy, caused by mutations in the *Notch3* gene.^{1,2} The main clinical manifestations of CADASIL include recurrent strokes, migraine with aura, cognitive impairment and psychiatric disturbances.³ The clin-

ical course is highly variable and can lead to premature death.^{4,5} Among the causes of death, sudden unexpected death (SUD) seems to occur in a significant number of CADASIL patients.⁶

SUD may be caused by a number of factors, including cardiac arrhythmias and myocardial infarctions.⁷ It is well

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