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NONINVASIVE METHODS IN CARDIOLOGY 2016

Edited by: **Kenner T., Cornélissen G., Siegelová J., Dobšák P.**

Brno 2016

Under the auspices of

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ISBN 978-80-210-8391-2

Lessons Learned from Worldwide Chronobiologically-Interpreted Blood Pressure Monitoring

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Dedicated to the memory of Franz Halberg who led the way on this journey.

Introduction

Only recently do guidelines [1] start considering the circadian variation in blood pressure (BP). For a long time, fixed limits of 140/90 mmHg (systolic/diastolic BP) were used to diagnose hypertension in all adults 18 years and older. The circadian rhythm in BP was thought to primarily reflect the rest-activity schedule rather than being in part endogenous [2]. While this is no longer the case, ambulatory BP monitoring is still restricted to "special cases", often limited to 24 hours. Evidence is presented herein for the need to routinely screen for BP and heart rate (HR) variability, and for continued monitoring in patients in need of treatment.

Self-measurements

Before the availability of devices for the automatic measurement of BP, chronobiologists relied on self-measurements taken a few times a day for two or more days to assess the circadian variation. Sampling requirements were specified [3] that include the need for at least one nightly measurement, preferably taken by another person in order not to disturb the subject's sleep, Figure 1. Despite the obvious shortcomings of self-measurements, usually taken with a mercury sphygmomanometer, important findings were made that laid the foundation for recognizing the importance of BP variability. Children with a positive family history of high BP and/or related cardiovascular diseases were found to have a larger circadian amplitude of BP than children with a negative such family history in several studies in schools in Italy, Portugal, and several states in the USA (Arkansas, Connecticut, and Minnesota) [4-13]. This result was later extended to neonates [14] once devices for the automatic around-the-clock monitoring of BP became available, in studies conducted in Minnesota, Italy, Japan, Russia, the Czech Republic, and Spain.

The Arteriosonde: an analog blood pressure monitor

In adults, the first automatic around-the-clock measurements of BP were obtained with the Arteriosonde, within the scope of the Minnesota-Kyushu study of breast cancer risk [15]. This analog device necessitated the manual taking off of data from graphic recordings. Despite this limitation, cardiovascular disease risk was related to the circannual amplitude of both BP and circulating aldosterone, Figure 2 [15, 16].

Portable Nippon-Colin BP monitor

With a portable – albeit not ambulatory – monitor from Masayuki Shinoda (Nippon Colin, Komaki, Japan), our first truly automatic BP measurements were collected. It was instrumental in demonstrating that BP increases toward mid-sleep, well before awakening, the latter associated with a larger and faster increase in BP [17], thus providing indirect evidence for the partly built-in nature of the circadian BP rhythm. Indirect evidence for the endogenous nature of the circadian variation in BP had been obtained much earlier by free-running: the circadian period of systolic BP of an afebrile boy with intermittent fever deviated statistically significantly from 24 hours, whereas it remained 24-hour synchronized for core temperature measured concomitantly around the clock [18].

The portable Nippon-Colin BP monitor also served to demonstrate the novelty effect and to assess the extent of day-to-day variability in circadian rhythm characteristics [19-21]. We showed that by extending the monitoring span from 24 to 48 hours, the uncertainty on the estimation of circadian parameters was reduced by 30%, with another 10% gain by prolonging the record to 7 days [7, 19].

Ambulatory BP monitoring

The next model from Nippon Colin was the ABPM-630, which operated on gas cartridges. It allowed us to collect around-the-clock data in several populations of clinically healthy individuals in 3 continents from neonates to centenarians, and during pregnancy [22-26]. These data were essential to derive time-specified reference values qualified by gender and age, on which our sphygmochron analysis is based [27-29]. They were critical for the assessment of outcomes from prospective as well as retrospective clinical trials [30].

The latter corroborated the risk associated with an excessive circadian amplitude of BP (CHAT, brief for Circadian Hyper-Amplitude-Tension). Outcome studies in Japan, Taiwan, Minnesota, the Czech Republic, and Germany further identified other abnormalities in the variability of BP and heart rate, which we named Vascular Variability Disorders (VVDs). Ongoing monitoring around the world by BIOCOS investigators and others, first with the ABPM-630, then with the TM-2421 and TM-2430 from A&D (Tokyo, Japan), continues to accumulate evidence for the need to routinely screen for VVDs and for the continued monitoring of patients in need of anti-hypertensive treatment [31].

Treatment is best optimized by timing (chronotherapy) on an individualized basis [32]. VVDs were found to occur in each cooperating center, Figure 3 [33]. Some VVDs were shown to be treatable. Indirect evidence documents that the elimination or reduction of CHAT reduces by more than a factor 2 the incidence of adverse cardiovascular events [34].

Discussion and Conclusion

As illustrated above, important lessons were learned from BP monitoring, which now await introduction into routine clinical care with focus on both primary and secondary prevention. Many more applications can benefit from a chronobiologic approach to BP monitoring, such as the determination of healthy lifestyle choices, in terms of tobacco use [35], alcohol consumption [36], salt intake [37], and prayer [38].

Longitudinal monitoring of BP also contributes invaluable information for health surveillance, for monitoring of the environment (e.g., pollution), and even for gaining a better understanding environmental and cosmic influences on physio-pathology [39, 40].

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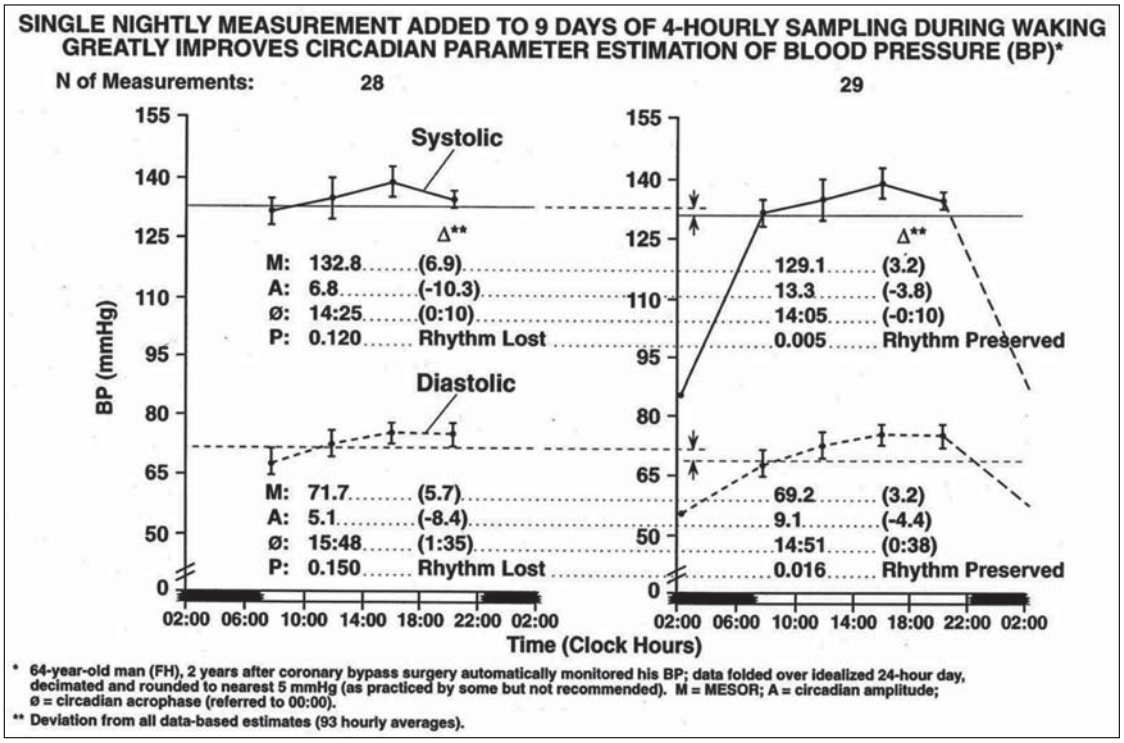

Figure 1: *Illustration of the need for nightly measurements of blood pressure to obtain a more reliable estimation of its circadian variation.* © Halberg Chronobiology Center.

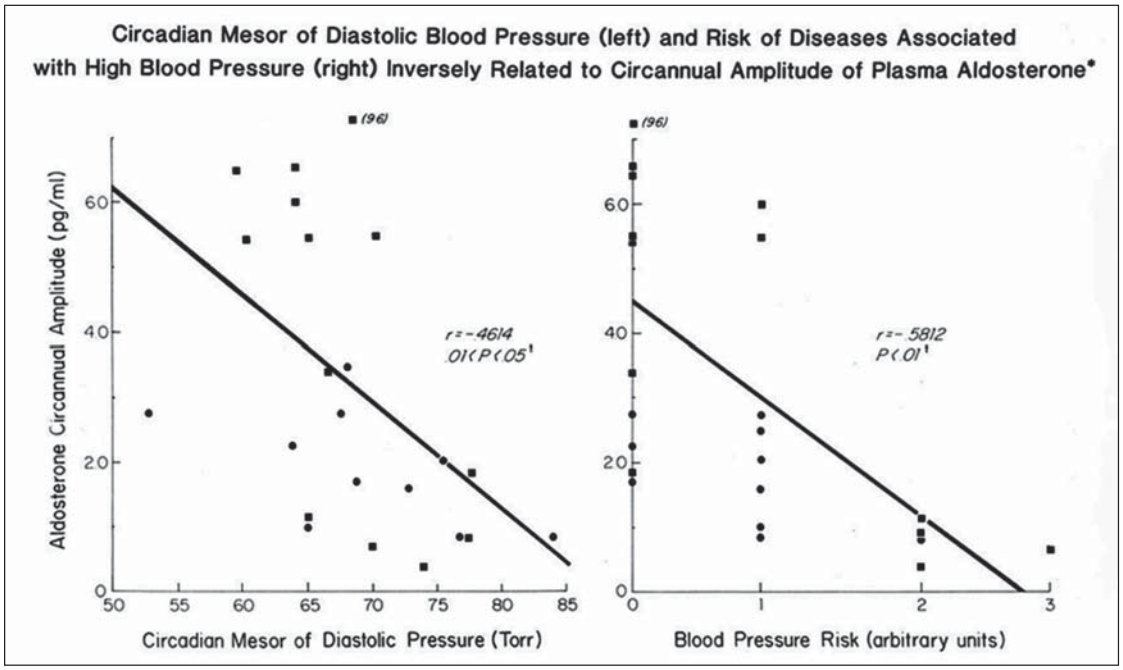

Figure 2: *Cardiovascular disease risk and diastolic BP are both related to the circannual amplitude of aldosterone [15].* © Halberg Chronobiology Center.

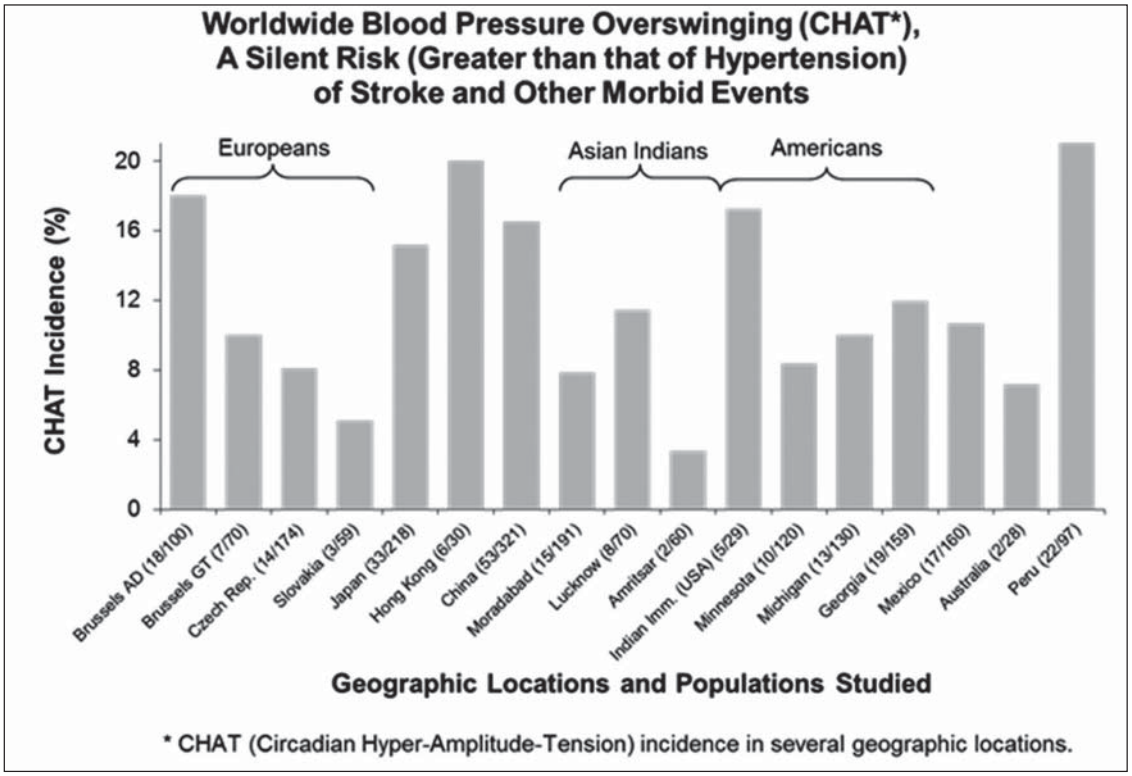

Figure 3: *Vascular Variability Disorders (VVDs) such as CHAT (Circadian Hyper-Amplitude-Tension) are detected in different geographic locations.* © Halberg Chronobiology Center.

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Support:
Halberg Chronobiology Fund
University of Minnesota Supercomputing Institute
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