Should the Heart Rate of Hypertensive Patients Influence Clinical Decisions?

Thomas G. Pickering, MD, DPhil

Although heart rate (HR) is commonly recorded multiple times when blood pressure (BP) is measured, particularly when automatic devices are doing it in the clinic, at home, or during 24-hour ambulatory blood pressure monitoring (ABPM), many clinicians tend to ignore the HR unless it is extremely high or low. But perhaps this is inappropriate, because there is a great deal of information accumulating that indicates that HR is a significant predictor of cardiovascular risk.[1] There are at least 2 prognostic issues that might be predicted by a rapid HR that could in theory affect how aggressively we treat our patients. The first is that in younger persons with borderline hypertension, a high HR may predict the development of sustained hypertension, and the second is the prediction of cardiovascular events in older persons. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)[2] acknowledged this with the following statement: "Data from epidemiologic studies and clinical trials have demonstrated that elevations in resting HR and reduced HR variability are associated with higher cardiovascular risk. In the Framingham Heart Study, an average resting HR of 83 beats/min was associated with a substantially higher risk of death from a cardiovascular event than the risk associated with lower HR levels." This statement was based on a Framingham report[3] that used HRs taken during routine clinic visits in patients with less severe hypertension who were not originally on treatment and that concluded that a big difference in HR (40 beats/min) was associated with a doubling of mortality.

There has been much interest in the variability of HR, which reflects the degree of autonomic control, and as also mentioned in JNC 7, reduced HR variability has also been associated with increased cardiovascular morbidity. However, it is of course not part of any routine clinical examination, so it need not be further discussed here. One issue that is critical is how and when the HR should be measured for clinical use. This is discussed below.

HOW SHOULD INCREASED HR BE MEASURED?

HR assessment is supposed to be part of the routine clinical examination, but little attention is usually given to it. An important issue is how the studies that have shown HR to be of prognostic significance have recorded it. In the prospective studies that did predict mortality based on increased HR, the measures were mostly taken in the clinic setting. A number of techniques are possible and, just like BP measurements (with which HR measurements of course coincide), include measurements made during a clinic visit or outside it. The situation in which HR is measured may, not surprisingly, give different rates. Thus, in clinical practice it may be taken over 30 seconds or 1 minute while the patient is seated or taken for a few

From the Behavioral Cardiovascular Health and Hypertension Program, Columbia Presbyterian Medical Center, New York, NY
Address for correspondence: Thomas. G. Pickering, MD, DPhil, Behavioral Cardiovascular Health and Hypertension Program, Columbia Presbyterian Medical Center, PH 9-946, 622 West 168th Street, New York, NY 10032
E-mail: tp2114@columbia.edu

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seconds by electrocardiography while the patient is supine. As such, the latter HR values are likely to be consistently lower, although the effects of posture are probably not more than 2 beats/min.[4] While posture during clinic measurement has an effect on HR values, the patient's degree of anxiety during the visit does as well. The white-coat effect, which may result in higher BP measurements, may or may not raise HR as well.[5] In a large Italian study,[6] clinic HR correlated with clinic BP but not with 24-hour BP, and ambulatory HR was also not correlated with ambulatory BP, which is consistent with the idea that clinic HR is different than ambulatory HR.

Home BP monitors, which are increasingly used in hypertension practice, also routinely report HRs, so it is of interest to determine whether we should pay attention to them. The most powerful finding of the predictive value of home HR was obtained in the Ohasama study,[7] which prospectively followed 1780 patients for 10 years. There was a graded relationship between HR and the risk of cardiovascular mortality, where an increase of 5 beats/min in the morning HR (where the starting level was 61–64 beats/min) was associated with a 17% increase in the risk of cardiovascular mortality. This was independent of home BP readings. Thus, a home HR of >70 beats/min was associated with a doubling of cardiovascular risk as compared with a rate <70 beats/min. However, another analysis of this was the Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) study,[8] which found that clinic, home, and ambulatory BP values all predicted mortality, but none of the measures of HR obtained under the same circumstances did so. Thus, the amount of current information about the predictive value of home HR is rather small.

The third method is the evaluation of HR during ABPM. Although both HR and BP may be increased by the sympathetic nervous system, the correlation between the two over 24 hours is extremely weak,[9] so separate analysis is justified. The ambulatory HR may be affected by the degree of physical activity during the day: a person who sits on a couch and does not exercise may record a lower HR than one who is physically active and hence at lower risk, so readings performed under standardized conditions may be of more value. Thus, some of the ABPM studies that have found that BP predicted risk did not find the same for HR. Verdecchia and colleagues[9] found that neither clinic nor average ambulatory HR correlated with total mortality or cardiovascular morbidity, although a smaller day/night difference in HR was associated with all-cause mortality independent of BP changes. One of the best known clinical studies was the Systolic Hypertension in Europe Trial (Syst-Eur),[10] which used 24-hour BP monitoring in elderly patients with systolic hypertension and found that if the ambulatory HR was >79 beats/min, there was nearly a 2-fold increase in risk of all-cause death, but it did not predict cardiovascular mortality. Syst-Eur also found that the risk was the same in men and women. The Japanese Ohasama study,[7] which was one of the strongest in determining the predictive value of ambulatory and home BP, found that 24-hour recordings made via ABPM showed that neither daytime nor nighttime average HR predicted cardiovascular mortality. Nighttime HR and a small day/night difference, however, predicted general mortality. Thus, while clinic-measured HR seems to predict cardiovascular mortality, ABPM-measured HR does not.[6]

INCREASED HR AS A RISK FACTOR FOR FUTURE HYPERTENSION IN YOUNGER PATIENTS

The study that first made the observation that tachycardia in the young predicts future hypertension was published in 1945 by Levy and associates[11] in a follow-up of US army personnel. Since then, there have been several publications looking at whether HR in young persons predicts future hypertension, but the findings have been inconsistent.[12] This may be because HR is affected by other factors, such as exercise, that may not be adequately controlled for. The Framingham Offspring Study[13] of 20- to 49-year-olds found that increased HR was one of the predictors of future hypertension in both men and women, while another Framingham Study[14] in 40-year-olds found that increased HR predicted the onset of hypertension in men but not in women. The Coronary Artery Risk Development in Young Adults (CARDIA) study[12] also found that HR was an independent predictor of BP over a 10-year period in young white men and women and in black men but not in black women.

It has been suggested by Julius[15] that tachycardia is a manifestation of "hyperkinetic borderline hypertension" that is characterized by increased cardiac output resulting from increased sympathetic activity, which can be demonstrated by a number of measures such as increased catecholamine levels and sympathetic nerve activity.

An interesting population study that screened participants in the general population found that those who had previously undiagnosed hypertension also had relatively high resting HRs: they were nearly 5 times more likely to have a HR >85

beats/min than were those with normal BP values, even after controlling for multiple factors that were also associated with tachycardia (smoking, hypercholesterolemia, etc).[16]

INCREASED HR AS A RISK FACTOR FOR DEATH IN OLDER PATIENTS

Many studies have examined the effects of HR on prognosis. One example of a prospective study, in which nearly 20,000 French men and women were followed for up to 20 years, measured HR from baseline electrocardiography.[17] HRs were classified into 4 groups: <60, 60–80, 80–100, and >100 beats/min. The strongest predictive value was found in hypertensive men, in whom there was a large increase in mortality from coronary heart disease with higher HRs, but there was no increase in women. Not all studies have been positive, however. A study of 40,000 college students with a follow-up of 38 years found no prediction of subsequent coronary heart disease from the resting HR assessed at clinical examination.[18] A statement made by the European Society of Hypertension on the clinical significance of increased HR detected during clinical examination was published in 2006[1]; in it, they stated that there were 39 studies on the prognostic significance of increased HR and that almost all found significant relationships between a relatively fast HR measured in the clinic setting and all-cause mortality in men but that this finding was less consistent in women. Some of the studies (like the French one)[17] separated hypertensive and normotensive participants and in general found that the relationship was still present (in men but not in women). The majority of the studies did not find that there was a U-shaped relationship in which a very low HR was also associated with increased risk.

MECHANISMS BY WHICH INCREASED HR MIGHT ACCELERATE DISEASE

There are at least 3 mechanisms by which an increased HR may contribute to cardiovascular disease. First, the increased HR may itself cause vascular damage. An example of the possibility that a high HR might accelerate the development of atherosclerosis comes from an experimental study in monkeys that had bradycardia induced by sinoatrial node ablation and were fed an atherogenic diet.[4] This procedure reduced the HR by about 30% but did not affect the BP, and coronary artery atherosclerosis was substantially reduced. However, if the first possibility is true in humans, one might expect that ambulatory (24-hour) measures of HR would predict risk better than clinic-measured HR, whereas in fact the opposite seems to be true. The second possible mechanism is that the increased HR may just be a marker of increased sympathetic tone that leads to cardiovascular events by other sympathetically mediated effects. The third possible mechanism is arrhythmia, since tachycardia is a risk factor for sudden cardiac death (to which increased sympathetic and decreased vagal tone may both contribute).[19]

THERAPEUTIC IMPLICATIONS AND CONCLUSIONS

Even if it turns out that an increased HR is explained by other cardiovascular risk factors, such as anxiety or lack of regular exercise, it may still be of relevance since not all effects (eg, stress- and exercise-related effects on resting HR) are easy to quantify in clinical practice. For those of us whose patients monitor their home BP, we get to see their HR as well as their BP, and we might say that a rate of >70 beats/min might show increased risk, particularly in men, although the evidence is thin. It is thus possible that we might be a bit more aggressive in treating such patients. There is also the issue of whether we should choose antihypertensive treatment that slows the HR, such as β-blockers or some calcium channel blockers (eg, verapamil), while other calcium channel blockers (eg, nifedipine) might be avoided. A better recommendation might be more exercise, which paradoxically might increase the HR for parts of the day but slow it at other times. The European Consensus Report[1] concluded that "without evidence from prospective trials, the panel finds it difficult to make specific treatment recommendations" and also that "the practicing physician may use the HR for cardiovascular risk stratification." Exactly how we should change our patients' treatment recommendations remains unclear, but many of our treatment decisions are based on our personal judgement rather than on rigid recommendations.

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