Roundtable Discussion

Out-of-Office Blood Pressures—Are They Helpful in Guiding the Treatment of Hypertension Patients?

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Following a hypertension symposium in Philadelphia in September 2005, a roundtable was convened to discuss the significance of out-of-office blood pressure. Dr. Marvin Moser of the Yale School of Medicine, New Haven, CT, moderated the panel discussion. Participants included Dr. Raymond Townsend of the University of Pennsylvania School of Medicine, Philadelphia, PA, and Dr. Norman Kaplan of the University of Texas Health Science Center in Dallas, Dallas, TX. (J Clin Hypertens. 2006;8:202–206)

DR. MOSER: Norm, I know that you're an advocate of out-of-office blood pressures (BPs). You have been for quite a long time. Tell me why. It seems to me that all of the estimates of cardiovascular risk from Framingham and other epidemiologic studies are based on casual BPs taken in the clinic or office and all of the BPs that are used to determine benefits of treatment are casual BPs. In most of the long-term trials, as you know, people would come in just three times a year to have their pressures taken. If it was low, their outcome was better; if it was high, their risk was greater. Have we missed something?

DR. KAPLAN: Well, two answers. First of all, if you look at data like Framingham, which are based on a few office readings, people with a BP of 160/100 mm Hg will have a 35% chance of a heart attack, but the other 65% won't develop a heart attack. I think that many people who don't develop a heart attack probably have office or white coat hypertension. Nobody has ever proved that; they never did ambulatory tracings on the people in Framingham until recently. The risk, therefore, may be much greater in those who have more sustained hypertension than those who have the white coat effect.

Actually, in the September 2005 issue of *The Journal of Clinical Hypertension* (*JCH*), Dr. Pickering wrote an editorial suggesting that there should be a therapeutic trial with white coat hypertensives. There is still a question about how much risk these patients have and whether they should be treated or not. Clearly they don't respond to treatment nearly as well as people with similar BPs in the office and at home.

The other answer to the question is that there are now a fair number of large trials that have looked at office, home, and ambulatory BPs and the results suggest that the closest prognosticator is ambulatory BP, followed closely by home BPs, which are better than office recordings. The office pressures tend not to be as prognostically useful or accurate as those that are taken out of the office.

First, I think that out-of-office readings are better at diagnosing white coat hypertension and, second, are better at getting an idea of the prognosis of a specific BP level. I also want to be sure about the response to therapy. If people are only seen in the office and have a white coat effect which may, by the way, persist for many years, we may not recognize the levels of pressure that are actually present during usual activities and that may be lower than office readings.

DR. MOSER: So, what you're saying is that although the present data are based on casual

pressures, using home BPs might assess risk and outcome better. Well, Ray, are there any good studies showing that people with normal BPs at home and higher pressures in the office have the same risk as normotensives? Are they different? Or, do they have an intermediate risk between a true hypertensive and a normotensive at home and in the office? If, for example, someone has a BP of 150/90 mm Hg in your office three or four times and doesn't wish to go on medication because their BP at home is always about 130/80 mm Hg, what are you going to do? Are you going to just continue to follow them or decide that the office BP should be treated?

DR. TOWNSEND: There are several answers. There have been some attempts to follow these people to see what happens with them, but we certainly do not have definitive data on outcome. When you follow people with white coat hypertension who experience the stress of a BP visit, they also experience the stress of stopping at a stop sign or just the stress of choosing options in daily life and these play some role in affecting their BP. About 40% of those whose BP is normal at home and high, i.e., above 140/90 mm Hg in the physician's office, will actually develop persistent high BP.

DR. MOSER: So, you don't think that white coat hypertension is a totally benign event.

DR. TOWNSEND: I don't think it's totally benign, but depending on whose BP you read, you can come away with different conclusions. If you measure heart wall thickness, the amount of albumin in the urine, or response to sodium restriction, you'll find literature that says that these individuals are no different than those who are normal at home and in the office. On the other hand, you'll find literature that says they're somewhere in between those who are clearly normal at home and in the office and those who are hypertensive at home and in the office. My gut feeling is that they do fall somewhere between the two.

DR. KAPLAN: Let me quote from Dr. Pickering's Reflections in Hypertension column in the September 2005 issue of *JCH*. He says that one of the reasons for expressing doubt on the view that white coat hypertension is benign comes from a recent analysis of an international database that pooled prospective data from four individual studies in the United States, Italy, and Japan. They analyzed the incidence of stroke during a 10-year follow-up. The point is that there was no increase in stroke until about 5 to 6 years later and then it went up virtually to the level equal to patients who had initial persistent hypertension.

So, I think that particular analysis has changed a lot of our minds from saying that white coat hypertension in itself is benign unless it evolves into progressive hypertension. I think now we have to at least keep an open mind. White coat hypertension may not be so benign and, therefore, may need to be treated earlier than what we have assumed in the past.

DR. MOSER: A follow-up, Norm. The patient has 150/90 mm Hg repeatedly in the office of one of your colleagues and 130/80 mm Hg repeatedly at home, with no particular BP surge in the morning. He checked his pressure at seven o'clock in the morning; he's thin and exercises, has one drink of vodka every night, doesn't smoke, and his blood glucose level is normal. His lipid levels are borderline but certainly not high. What should be done?

DR. KAPLAN: Facetiously, I would tell him not to go back to his doctor because the doctor is obviously provoking an elevated BP. It is an interesting problem. I think we all appreciate that white coat hypertension should be carefully defined—high pressures repeatedly in the office, normal BPs repeatedly out of the office. I've seen a lot of people who have been called white coat hypertensives who have a lower pressure just on occasion but, when they are properly evaluated, do have high pressure. So, we ought to be careful about making that diagnosis. Really, it's hard to define it unless you perform a 24-hour ambulatory BP. In this way, you get BPs with different activities. It's hard to take BP on yourself while you're driving a car in traffic, when you might get a hypertensive response. Unless you have an ambulatory monitor, you're not going to identify those kinds of stress-related BP readings.

DR. MOSER: We'll get back to that in a minute, but you didn't give me an answer to this patient's problem.

DR. KAPLAN: I would tell him that he did not need specific treatment. I would watch and monitor him and have him self-monitor his pressures. If they begin to go up then, of course, we'd have to consider him as a hypertensive. But at the moment, I would not treat him.

DR. MOSER: Okay. Now Ray, I believe that you are aware of the data on subtle changes in endothelial cell function, on subtle changes in left ventricular mass, and on microalbuminuria in people who may have high normal BP or, as we now label it, prehypertension. In other words, BPs are not at a predefined level of >140/90 mm Hg where they should be treated, but are in the range of 130–135/85–90 mm Hg. Would you worry that if you waited a year or two for the time when this person developed elevated BPs at home, that you already have allowed some vascular and target organ changes? Or do you

treat these patients with therapy other than lifestyle measures? And, do people with white coat hypertension fit in the same category?

DR. TOWNSEND: I wouldn't treat at an early stage, but there is one thing I do, especially when I get called with this exact situation, i.e., someone is measuring their BP 100 times a week and is a compulsive worrier. The thing I do, dare I say it, is perform an echocardiogram. I measure left ventricular mass and the ability of the left ventricle to relax in diastole, their E-to-A ratio (diastolic function). If they have normal diastolic cardiac function and left ventricular walls that are <10- to 11-mm thick, then I'm happier to follow them over time, even given the fact that I anticipate a certain percentage of them will note some progression.

On the other hand, some of the people will show subtle but definite evidence of cardiac involvement; they are at higher risk and I wouldn't wait as long to treat them. The thing that bothers me is the issue of the so-called residual risk phenomenon. If you treat someone's BP and lower it to 120/80 mm Hg on medication, the cardiovascular risk will not be the same as an originally normotensive individual—even though BP is now the same. There is something about having hypertension, even when you treat it adequately, that may allow for a different outcome.

DR. MOSER: Is this conclusion based on solid data? Would this be in patients who may have had an elevated BP for months or years?

DR. TOWNSEND: We published a small editorial entitled "Residual Risk in Questions & Answers" about that a few months ago in the *JCH*. This is a real, but small, phenomenon. However, it's the sort of thing that becomes an issue because, if you wait, some structural change in vessels may occur and other changes might be a prelude to a stroke or heart failure or some other pressure-related consequence.

DR. MOSER: So perhaps we shouldn't wait despite all of the caveats. You know, this discussion reminds me of a paper published by George Perera in 1955 on the benign nature of hypertension. For the first 10 or 12 years of follow-up, there were no more cardiovascular events in the hypertension patients than in the normotensives. But after about 10 or 12 years, the curves began to separate; strokes, heart attacks, heart failure, and kidney failure all were increased in the hypertensive groups. The study was quoted widely to point out the benign nature of hypertension. Most of these patients, however, began to be followed when they were about 40 years of age. At about 50, 55, they were experiencing events. We treat elevated lipid levels before someone gets in trouble, because we believe that there are changes in blood vessel structure and the beginnings of atherosclerosis long before we can detect it clinically. Why shouldn't we treat high normal, prehypertensive, or white coat hypertensives early on?

DR. KAPLAN: There is a study underway called TROPHY (Trial of Preventing Hypertension), which will probably be published in early 2006. About 1000 people with what we call high normal BP, 130–140 and 85–89 mm Hg, are being studied. Half of them have been put on an angiotensin-II receptor blocker and the other half on a placebo. It is a randomized controlled trial. The objective is to see whether progression of hypertension can be delayed or stopped. There are not enough people in the trial to look for end points of cardiovascular disease, but the data should be of interest.

This trial is what is referred to as a proof of principle—whether you can give antihypertensive therapy over a short period and prevent further progression of hypertension, which would occur naturally. This can be done in animals. We don't know whether it can occur in people, but if we could treat individuals with any degree of elevated BP (anything above 120/80 mm Hg) and give them a year or two of antihypertensive therapy, stop the therapy, and prevent progression of BP, that would obviously be a phenomenal observation. There will have to be more studies after TROPHY because this is only the first look, but I think it certainly is something that should have been done a long time ago.

DR. MOSER: To summarize, you believe that if someone who is hypertensive in the office and normotensive at home, based on self-administered home BP recordings, you probably would encourage lifestyle changes but, at this point with our knowledge base, not use antihypertensive drugs? I am not sure that I agree with this approach.

I could understand this approach 20 or 30 years ago when we used reserpine, α methyldopa, and hydralazine to treat hypertension. These drugs caused either sleepiness, depression, tachycardia, or any number of other symptoms—the benefit-to-risk had to be carefully considered. But in an era when we use low-dose diuretics, angiotensin receptor blockers, or angiotensin-converting enzyme inhibitors where the risk of treatment is minimal, shouldn't the possible benefit of treatment, even though we do not have outcome data to prove benefit, seem to overwhelm the possible risk of even white coat hypertension and move us toward treating more of these people a little earlier?

DR. TOWNSEND: There are two things I would say in response to this approach. The first is: what

are you going to treat? If the home BPs are normal, what is going to be your end point for the therapy?

DR. MOSER: I still believe that you should treat the casual BP in your office.

DR. TOWNSEND: Okay, now the second point then is that when you look at the casual BP in your office even in patients on therapy, there are many white coat hypertensives who continue to display the white coat effect despite antihypertensive drugs. Moreover, no class of antihypertensive drug, at least as far as I can determine, can abolish the white coat effect. Consequently, you will not obliterate the effect by virtue of treating it preemptively.

We do approximately 20 to 30 ambulatory BP monitors every month and, consistently, once a month I have a 20-something-year-old person, often a woman, with BPs in the office that are high and an ambulatory monitor absolutely normal, i.e., a daytime average of 110/70 mm Hg. Am I going to take a 24-year-old woman and treat her for an unknown period of time with BP medicine without any evidence that I can really make a difference in the likelihood that she's going to turn hypertensive or develop a cardiovascular event.

DR. MOSER: Do these people have office pressures of 150 mm Hg or thereabouts?

DR. TOWNSEND: Mostly 140s, not usually 150s.

DR. MOSER: I would answer that in the following way. There is no question that antihypertensive drugs are not going to control every white coat hypertensive at normal office BPs, but they're going to lower the pressure somewhat. I liken this to the argument in the 1950s and 1960s about treating so-called mild hypertension, which was then defined as diastolic BPs of 90–104 mm Hg. Many people said that we had no data on outcomes, and we didn't. We had a lot of data on the risk of elevated pressures but even with the limited data on treatment instincts told us to lower the BP if we didn't produce any adverse effects. I think everyone would agree today that you should treat someone with BPs of 140/90 mm Hg or higher.

I'm not going to make any predictions, but I would guess that some of the ongoing studies will show that we should probably be a little more aggressive in treating white coat hypertension with medications that do not cause too many side effects or lower the home BPs too much. I know that if I had definite white coat hypertension, I would want to be on specific medication. If I had a low-density lipoprotein cholesterol level of 160 mg/dL or higher, even without any other risk factors, I think I'd like it reduced. But there are differences of opinion.

Now Norm, what about another debate—ambulatory BP compared with home readings? You could make the argument that ambulatory monitoring gives you a BP snapshot of 24 to 48 hours, but if you've ever worn one of the monitors, and I'm sure you have, you know that when it starts recording you tend to stop doing whatever you're doing. If you're sleeping, you turn over; if you're running or playing tennis, you stop; and if you're driving and moving your arm around, you stop. So, you're getting a snapshot but sometimes it's not a true reading during activity. On the other hand, home BPs give you numerous readings over time at different hours of the day and over weeks. I have a hunch that maybe home pressures are more useful in the long term, without the expense and annoyance of ambulatory recording.

DR. KAPLAN: Well, I think that in the best of all worlds, ambulatory BP monitoring should be more available and more widely used, only because it's quicker. I think the data pretty well confirm that home and ambulatory pressures give you the same overall levels of pressure. Now it is important that we use only the daytime ambulatory BPs when we're comparing home readings with ambulatory readings. If you take the 24-hour readings, you're going to include nighttime levels which, for 85% of people who dip during the night, are obviously going to be lower than what they get during the day. Therefore, that would be an unfair comparison.

But when daytime ambulatory readings are compared with daytime readings taken at home, the two are virtually the same. And I think they're the same prognostically as well as diagnostically. Therefore, I agree, for $30–$40, buy a semi-automatic, battery-operated home BP monitor with an adequate size cuff. I think this is something every home in the United States ought to have. I think that it would be just as important, even more so, than a thermometer, and I'll bet that everybody has a thermometer.

DR. MOSER: Ray, what do you think about that?

DR. TOWNSEND: We recommend home monitoring. Our biggest worry is the accuracy of the monitor.

DR. MOSER: Aren't they pretty well calibrated?

DR. TOWNSEND: They are reasonably so, but there are occasional monitors, and I've seen them read typically lower than my office readings. We are very careful to make sure that patients take their BPs correctly. I prefer to observe their techniques in the office and watch them apply the cuff and take the reading.

DR. KAPLAN: Let me make another small point about using home monitoring. I don't know what

percentage of people in the United States are doing that for hypertension; I would imagine no more than 5%, maybe 10%. But let's look at type 1 diabetes. I think that every type 1 diabetic is told to have home monitoring of blood sugar and adjust their insulin dose according to what glucose levels they record.

Type 1 diabetes is a terrible problem for a lot of people, much more obvious a problem than hypertension. But as far as the dangers are concerned, hypertensives get into almost as much trouble as diabetics. I believe that we've been too lackadaisical in having people come back to the office every 6 months to get a clinic BP and basing all of our judgments regarding treatment on that alone. People are now doing their own prothrombin times at home and calling in with results so that the doses of anticoagulant can be adjusted. So, I think the whole idea of hypertension being easy to manage with an occasional office visit is part of the reason we've not done any better in reducing risk even among presumably well-treated hypertensives. I'm not so sure that they've been that well treated. I think we need a lot more BPs to ensure adequacy of therapy.

DR. MOSER: One last question for both of you. If you have someone who is hypertensive and you treat them and their office BPs are consistently normal, would you still want them to perform home BPs even if there were no symptoms? Obviously, if they're getting dizzy at home or getting headaches you would.

DR. TOWNSEND: I may recommend that they do home pressures, perhaps about twice a month for the following reason: it keeps them engaged.

DR. MOSER: Reinforcement.

DR. TOWNSEND: Reinforcement, right. When you deal with a basically asymptomatic disorder like high BP, every once in awhile it's a bit of positive feedback for the patient to see numbers at home that are consistent or even slightly better than what you see in the office. And it keeps them thinking. They may say "I may not feel this, but I know the medicine is working because I can see the numbers on the display."

DR. MOSER: Fair enough.

DR. KAPLAN: We mentioned masked hypertension, and I would just like to reiterate that there are now data that say that as much as 10% of the general population have a normal clinic BP but a high BP out of the office. I'm a little surprised that it's anywhere near 10%, but I'm sure it occurs, and there are data now that say that they get into trouble. That is, their prognosis is just as bad as someone who has high pressures both in the clinic and at home.

DR. MOSER: So, you would like to see home pressures?

DR. KAPLAN: On everybody. I think so.

DR. MOSER: One caveat: Ray alluded to this in his patient who's taking his pressure a thousand times a week; I believe that we have to tell people they don't have to take BPs more than once or twice a week except initially when medication is being adjusted.

DR. TOWNSEND: I have some engineers who bring spreadsheets and multicolored graphs with all the standard deviations when they do home BPs.

DR. MOSER: I believe that the gist of our discussion is that home BPs have a place; they're not being used as often as they should. White coat hypertension ought to be treated before any specific observable findings of target organ involvement develop, although there is difference of opinion here. Drs. Kaplan and Townsend believe that specific therapy can be delayed in these patients; that they should be observed carefully; and, if the pressures tend to go up at home, then they should be treated with specific antihypertensive drugs. Thank you.