Expert Interview

Aggressive Blood Pressure Lowering: Is It the Only Approach? An Expert Interview With Matthew R Weir, MD

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Editor's Note:
Matthew R. Weir, MD, is an attending physician and Director of the Division of Nephrology and Clinical Research Unit in the Department of Medicine at the University of Maryland Hospital in Baltimore. He is also a Professor of Medicine at the University of Maryland School of Medicine.

Dr. Weir's primary research interests include the use of antihypertensive therapy for the treatment of diabetic nephropathy, hypertensive renal injury in African Americans, and preventing chronic allograft nephropathy in transplant recipients. He has written more than 300 manuscripts and book chapters about these topics and has presented at numerous international scientific association meetings, hospitals, and medical schools.

Dr. Weir currently reviews manuscripts for 15 medical journals, including The American Journal of Kidney Disease, The Journal of the American Society of Nephrology, and The Archives of Internal Medicine. He is on the editorial board of 6 journals and is an Associate Editor of The American Journal of Kidney Diseases. In addition, he is a member of numerous associations, including the American Society of Nephrology, the National Kidney Foundation, the American Heart Association, and the American Society of Transplant Physicians.

Medscape: We hear these days that physicians should be pursuing "aggressive blood pressure [BP] lowering" for their hypertensive patients. But what do we mean by aggressive BP lowering? Assuming that it is indeed the goal, then how do we achieve it, and what type of patients most need it? Is aggressive BP lowering defined in any guidelines, or does it just mean giving as many drugs as needed to get the BP as low as possible?

Dr. Weir: Guidelines are based in part on the available information from clinical trials, but obviously also on the purview and perspective of the authors of the guidelines. Thus, the recommendations vary from guideline to guideline, because they are produced by different people with an array of opinions. The way I view guidelines is that they are, in general, aggregate information on clinical trials. They are generalizations. However, what we are really charged with doing in clinical practice is individualizing our approach.

Ultimately, physicians are charged with choosing what they feel are appropriate individual blood pressure goals. I do not know what the BP goal is, other than I fully appreciate that if I look at the epidemiologic data, there is a linear association between BP level and cardiovascular events, and that in general, lower is better. What we are lacking are clinical trials to test the hypothesis that if we purposely lower systolic blood pressure (SBP) to 130 mm Hg or lower, the patient will live longer than at 140 mm Hg, or that the patient will live even longer if we further lower it to 120 mm Hg.

The problem is that most of the available data we have are based on reductions in diastolic blood pressure (DBP) and the data on SBP reductions are inferential. We have data from a meta-analysis indicating that lower ambient SBP is associated with fewer events,[1] but this was just prevalent SBP, and in many cases it was not a purposeful reduction. So aggressive BP lowering just reflects the impression among healthcare providers that some people clearly need lower BP than others. However, I do not think that any of the current guidelines can truly define who
these people are who need the lower BP goals, other than that they are those with diabetes or chronic kidney disease.

Medscape: Does stressing the need for aggressive BP lowering reflect the fact that not enough people are getting their BP down far enough, even simply to as low as 140/90 mm Hg?

Dr. Weir: Aggressive means choosing the appropriate goal and getting there. Obviously, if general populations are not getting SBP below 140 mm Hg, that is a serious concern. That has to do with the medical healthcare providers not trying hard enough to get their patients to goal, or patient barriers to taking more medication, eg, cost, education, tolerability, simplicity, and compliance.

I think some of the problem is due to physician inertia. In the United Kingdom, there is recent evidence that now that physicians are being compensated according to the achievement of lower BP goals, BP control rates are improving. So it seems that tying compensation to achieving appropriate BP goals clearly is having an impact on the control of BP in the United Kingdom -- and I suspect that were this the reimbursement system elsewhere in the world, we would see a similar improvement in response rates.

I certainly would not want my BP to be at 140/90 mm Hg. The available literature suggests that lower is better, but how to evaluate the added value of lower BP in an individual is a much more difficult issue, because you have to justify the risk of pharmacotherapy relative to the risk reduction benefit of the lower BP. My suspicions are that people with more risk factors for cardiovascular disease -- be they family history, smoking, obesity, metabolic syndrome characteristics, etc -- likely do derive some advantage sufficient to justify more pharmacotherapy for getting their SBP below 130 mm Hg. So I am an advocate for achieving lower BP goals in patients at risk, perhaps a little more aggressive than what is currently listed in the guidelines, which predominantly stress this for people with chronic kidney disease or diabetes.

Medscape: Current US guidelines (the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [JNC 7]) recommend starting with one drug, a thiazide type diuretic, and then adding others. Is this what physicians in the United States should be doing?

Dr. Weir: No. The US guidelines indicate that thiazides are a preferred therapy unless there are compelling indications for other drugs. Thus, there are many other therapeutic choices. According to the guidelines, most of my patients have a compelling indication of one sort or another. Consequently, the most common therapy would be an angiotensin converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB) as an initial therapy, based on the list of compelling indication checkpoints for renin-angiotensin system (RAS) blockers. In the US guidelines, there is also the statement that if a patient is more than 20 mm Hg from goal, give them 2 drugs. So again, for many patients it is not what is the best first drug, but really what is the best regimen-based pharmacotherapeutic approach.

Medscape: So the first-choice drug in the patients that you usually see would be a RAS inhibitor?

Dr. Weir: Definitely. The real question here is, Do I give a RAS blocker with a thiazide or do I give a RAS blocker with a calcium channel blocker (CCB)? These drugs provide the most robust opportunity to reduce blood pressure with a RAS blocker.

Medscape: It is sometimes said that ARBs and ACE inhibitors don't lower BP quite as much as the other classes of antihypertensive drugs -- is that correct?

Dr. Weir: I think that is wrong. If people are dosed appropriately, within the full dosing range within the package insert, large population studies clearly show that they are all the same in their antihypertensive effects. When intermediate doses of individual drugs are chosen, often there is less BP reduction. Using the recommended doses in large populations, you will see very similar degrees of BP reduction whether you are using a thiazide-type diuretic, a beta-blocker, an ARB, an ACE inhibitor, an alpha-blocker, or a CCB.

Now, if you look in specific subsets of patients, like older patients or African Americans or people who eat a higher-salt diet, CCBs will have an advantage. They are a therapeutic class that provides robust opportunities to control BP regardless of age, gender, ethnicity, or even dietary sodium consumption. They maintain a better overall BP-lowering effect under those circumstances.
Medscape: Do you think that these subgroups require special treatments?

Dr. Weir: I really don't, because in general, if I am going to use an ACE inhibitor or an ARB in an African American, for example, or somebody eating a high-salt diet, I would likely give it with a thiazide-type diuretic, or with a CCB. Most of these people are going to need more than 1 drug anyway, so I do not get hung up on what is my best first choice.

Medscape: It sounds as though aggressive BP lowering is the only way to go. Is there really any other?

Dr. Weir: Like passive BP lowering? If you are going to do it, you do it. If you are going to make a decision that somebody needs lower BP, choose the appropriate goal and get to goal.

Medscape: But the goal varies with each individual patient and you said that it can be difficult to find out what that goal is.

Dr. Weir: It is not difficult to assess BP goals. It is based on known risk factors for cardiovascular disease and clinical intuition. So there is no mystery. If you think that an SBP of 130 mm Hg is the right goal, then you should go to that. If you think that 140 mm Hg is the right goal, then go to 140 mm Hg. Granted, it is not a perfect science, but we have to go on our clinical suspicions as to what we feel is best for an individual patient, and then we have to explain it to them!

Medscape: How will we get more information about this? Will physicians, going forward, have to rely on epidemiologic evidence only?

Dr. Weir: Healthcare providers will have data from epidemiologic studies and clinical trials that are under way. The good news is that the current clinical trials are finally testing the hypothesis that lower BP goals may be advantageous. The TRial Of Preventing Hypertension (TROPHY) study[3] and the Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension (ACCOMPLISH)[4] trial are both evaluating lower BP goals, so we are going to have information on SBP levels certainly going below 140 mm Hg, which will be a major advance from previously published clinical trials, which in large part have focused on achieving DBP levels below 90 mm Hg. Ultimately, though, there are still going to be questions about even lower BP goals for high-risk patients, and obviously we need to do those studies.

Medscape: Among the high-risk patients, are there any who should not achieve aggressive BP lowering, such as patients who have had a stroke or transient ischemic attack?

Dr. Weir: We haven't done large prospective studies in people who have had a recent stroke to test the hypothesis about lower BP goals. There is some debate in terms of optimal BP goals in patients with cerebrovascular disease, especially those with recent transient ischemic attack. There are studies being done looking at different pharmacologic agents to prevent recurrent stroke. Early data in clinical trials with ARBs are quite interesting (Losartan Intervention for Endpoint Reduction in hypertension [LIFE] and Mortality and Morbidity After Stroke - Eprosartan Compared with Nitrendipine in Secondary Prevention [MOSES]).[5,6]

I think the most exciting ones are the large trials being done with ARBs such as the ONGoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial (ONTARGET) and studies with different types of platelet antagonists. I think we do have evidence that lowering BP and blocking the RAS may be advantageous in people with a prior stroke.

Medscape: The BP-lowering therapy that patients start on, assuming we call it aggressive -- are they going to be on it all their lives? What about the side effects?

Dr. Weir: Everybody is different; medications can cause side effects in anybody. In general, we can treat people with high BP effectively, being mindful of potential side effects, with careful and judicious use of different medications. There are very, very few people whose BP cannot be controlled effectively with current medications. I think the biggest issue is how to wrestle with the amount of medication patients need as part of the global cardiovascular risk reduction strategy and ensure that they can pay for it and take it in a compliant fashion.

Medscape: In your experience, how many antihypertensive medications do your patients need to take, on
average?

**Dr. Weir:** I am a nephrologist, so I tend to take care of complicated patients with chronic kidney disease. In general, most of my patients need 2-5 medications to control their BP.

**Medscape:** These patients must be on a lot of other drugs.

**Dr. Weir:** Absolutely -- 2 to 5 medications is just for the BP. Then again, if you look at the Irbesartan Diabetic Nephropathy Trial (IDNT)[7] and Reduction in Endpoints in Non-insulin-dependent diabetes mellitus and nephropathy with the Angiotensin II Antagonist Losartan trial (RENAAL)[8] studies, the mean number of drugs used in those studies just for BP was 4, to get to SBP 140 mm Hg.

**Medscape:** So when the number reaches 5 -- obviously the first 2 are a diuretic and a RAS blocker, so what are the others most likely to be?

**Dr. Weir:** In many cases it could be a beta-blocker, CCB, minoxidil, an alpha-blocker -- whatever you need to get to goal.

**Medscape:** The cost of these multiple medications, even though many of them must be generic by now, must present difficulties.

**Dr. Weir:** It is a big issue. You have got to have samples. You have to be sensitive to what patients can afford, and in my practice I take care of patients with samples and schedule them back for follow-up visits based on their requirement for supplementary medications. It is key to know their pharmacy plan, if they have one!

**Medscape:** It sounds as though fixed-dose combination pills might be useful for these patients?

**Dr. Weir:** Absolutely. We are moving in that direction, for BP, cholesterol, and glucose -- and not just the two-fers; there will be three-fers on the market, I suspect, within a few years, if the regulatory authorities allow it.

**Medscape:** It's beginning to sound a bit like a polypill.

**Dr. Weir:** That has been suggested in the British press, and I don't disagree with it.

**Medscape:** So it seems that calling BP lowering "aggressive" is a given and that there isn't really anything else.

**Dr. Weir:** Of course there is dietary sodium restriction, regular exercise, limiting alcohol intake, losing weight, etc, but rarely are behavioral modifications entirely successful in curing or controlling high BP.

**Medscape:** These would be tried first in people with BP in the prehypertension category, presumably.

**Dr. Weir:** Maybe, but some prehypertensives I treat with medication.

**Medscape:** That sounds more like the recommendations recently proposed by the American Society of Hypertension writing group[9] than JNC 7.[2]

**Dr. Weir:** That is more in line with my general feeling as well. I tend to view people for global cardiovascular risk reduction. I try not to pigeonhole them based on just their BP. I try to look at the whole patient and then make appropriate decisions about treatment strategies.

**Medscape:** Then, in addition to the number of medications, there is also the issue that presumably they have to take them for life?

**Dr. Weir:** Yes, most patients will need medication for life. It is very, very unusual to go off medications because of lifestyle changes -- that was the old thinking; I haven't seen that in 25 years of practice. It may be possible to reduce
the dose, though not medications, with lifestyle modifications.

**Medscape:** How long do we have follow-up data for patients on 3 or more drugs?

**Dr. Weir:** That's a good question. Most of the clinical trials last 4 to 5 years at most, and yet what we do in practice is expose people to drugs for 20, 30, or 40 years. So we don't have a good long-term longitudinal follow-up.

**Medscape:** One of the remaining nagging issues that has been the subject of much discussion is the question of diuretics and beta-blockers and the increased risk of new-onset diabetes long term.

**Dr. Weir:** I am cautious about diuretics and beta-blockers with regard to metabolic issues. I prefer using lower doses; I would prefer to use them with a RAS inhibitor, which we know from the literature cuts the risk of new diabetes by anywhere from 23% to 35% with 5 years of follow-up.

**Medscape:** But at the end of the day, taking all these issues into consideration, I suppose that still leaves us with the challenge that statistics show that people are not getting their BP down, that it is not being controlled.

**Dr. Weir:** Yes, control rates are terrible. We do need to have means of educating patients about the need for controlling BP and monitoring it. Still, ultimately the best thing we can do for patients is to ensure that we have them educated and involved, and I think perhaps the best way to do that specifically is to have them monitor their pressure at home so that they get invested in it and ultimately are more willing to stay on treatment.

The bottom line is that hypertension is a common, lifelong disease process, it doesn't go away, and it is going to require treatment -- both lifestyle modifications and pharmacotherapy. We need to pay attention to it and deal with it, and the best opportunity we have for getting patients on board is obviously to provide sufficient education.

**References**


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Matthew Weir, MD, Professor of Medicine and Director, Division of Nephrology, University of Maryland School of Medicine, Baltimore, Maryland

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