

## VIEWPOINT

## Diastolic blood pressure as a major determinant of tissue perfusion: Potential clinical consequences

Hulin I<sup>1</sup>, Kinova S<sup>2</sup>, Paulis L<sup>1,3</sup>, Slavkovsky P<sup>1</sup>, Duris I<sup>2</sup>, Mravec B<sup>1,4</sup>

*Institute of Pathophysiology, Faculty of Medicine, Comenius University, Bratislava, Slovakia.*  
ivan.hulin@fmed.uniba.sk

---

**Abstract:** Blood pressure measuring represents a routine investigation in general medicine. In the last decades large studies have determined average blood pressure values all around the world. Large clinical trials have shown that blood pressure reduction irrespective of the used type of therapeutic intervention reduces mortality. Based on the outcomes of these trials current guidelines for hypertension encourage more “aggressive” hypertension treatment compared to recommendations from the past. In clinical practice blood pressure is sometimes reduced even below normotensive values (at least in comparison with pre-treatment levels). However there is evidence that achieving too low levels of diastolic blood pressure during antihypertensive treatment has undesirable effects. Especially in the elderly a diastolic blood pressure reduction below 70 mm Hg should be avoided, because it is associated with increased mortality. A possible explanation of this phenomenon could be that antihypertensive treatment disequilibrates the balance between sufficient perfusion pressure and arteriolar vasodilation, both of which are required for adequate tissue perfusion. Impaired microcirculation, especially in the coronary bed may account for the increased mortality in hypertensive patients with low diastolic blood pressure levels. Thus we support the idea of cautious blood pressure reduction in the elderly. Furthermore, we suggest, that monitoring the level of tissue perfusion in treated hypertensive patients might help to provide individually tailored therapy (*Fig. 1, Ref. 9*). Full Text (Free, PDF) [www.bmj.sk](http://www.bmj.sk).  
Key words: diastolic blood pressure, elderly, microcirculation, mortality, arterial stiffness.

---

Blood pressure measuring has become a routine investigation in general medicine. In the last decades large clinical trials have determined average blood pressure values in different age and ethnical groups all around the world. Arbitrary intervals were set to distinguish physiological and pathological blood pressure values. Experimental and clinical studies investigating blood pressure regulation are however more descriptive than fundamental and more analytic than synthetic. Suzanne Oparil MD, current ASH president in her interview with Gorge D Lundberg, MD for Medscape mentioned that hypertension still remains an inhomogeneous syndrome which most prominent sign is the elevated blood pressure (1). However, the progression of the hypertensive syndrome and fixation of hypertension seem to be similar in cases with different etiology (2).

---

<sup>1</sup>Institute of Pathophysiology, School of Medicine, Comenius University, Bratislava, Slovakia, <sup>2</sup>First Department of Internal Medicine, Comenius University, Bratislava, Slovakia, <sup>3</sup>Institute of Normal and Pathological Physiology, Slovak Academy of Sciences, Bratislava, Slovakia, and <sup>4</sup>Institute of Experimental Endocrinology, Slovak Academy of Sciences, Bratislava, Slovakia

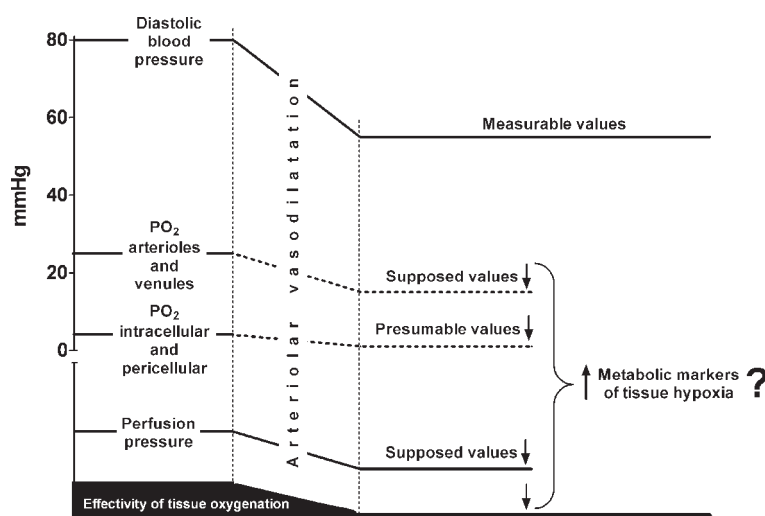
**Address for correspondence:** I. Hulin, MD, DSc, Inst of Pathophysiology, Faculty of Medicine, Comenius University, Spitalska 24, SK-813 72 Bratislava, Slovakia.  
Phone: +421.2.59357611, Fax: +421.2.59357601

**Acknowledgment:** This work was supported by VEGA grant No. 1/4251/07.

From the clinical point of view the mostly sought goal of antihypertensive treatment is the reduction of morbidity and mortality in patients with high blood pressure. Large clinical trials have shown that blood pressure reduction irrespective of the used type of therapeutic intervention reduces mortality (3, 4). The outcomes of these trials are reflected in the recent guidelines, which encourage more “aggressive” antihypertensive treatment compared to recommendations from the past (5).

Thus in clinical practice blood pressure is sometimes reduced almost to hypotensive values (at least in comparison with pre-treatment levels of blood pressure). Also experiments from our institute indicate that e.g. captopril may lower blood pressure in experimental hypertension even below normotensive values (6). Therefore the question emerges, whether an uncritical approach to hypertension treatment cannot generate potentially dangerous situations in everyday clinical conditions. Moreover, important clinical decisions in hypertensive (but in hypotensive as well) patients are made based upon measurement of arterial blood pressure, which does not reflect tissue perfusion.

The authors of a recently published article have for two years observed 331 patients with systolic hypertension aged over 70 and observed a J shaped relation between diastolic blood pressure and mortality (7). Diastolic blood pressure of 60 mmHg or less was associated with higher mortality. Although the conclusion clearly indicates an adverse effect of too low diastolic blood pressure values on cardiovascular mortality, the pathophysiologi-



**Fig. 1. Diagram of possible changes of oxygen pressure caused by arteriolar dilatation induced by antihypertensive drugs. Antihypertensive drug reduces systolic and diastolic blood pressure and their values are used to adjust the efficiency of the treatment. However, under conditions of low diastolic blood pressure, tissue hypoperfusion and cellular hypoxia might occur. These parameters can be estimated based on clinical and biochemical data, but are difficult to access directly.**

cal mechanisms of this phenomenon remain unclear. The authors of the study suggested 4 possible explanations: 1) low diastolic blood pressure is a marker of chronic disease; 2) low diastolic blood pressure is a marker of heart failure; 3) low diastolic blood pressure is a marker of increased arterial stiffness; 4) low diastolic blood pressure causes impaired coronary perfusion during the diastole. For the authors of the study the most plausible explanation was the reduced diastolic coronary flow (7). In fact, this study suggests that high systolic blood pressure in conditions of increased arterial stiffness might be insufficient to achieve an optimal tissue perfusion. On the contrary, in these conditions, the major determinant of mean arterial pressure, tissue perfusion and potentially mortality is the diastolic blood pressure.

Increased arterial stiffness is the most prominent cause of systolic hypertension in the elderly (1). Under conditions of increased arterial stiffness the diastolic blood pressure is the most responsible for the determination of mean arterial pressure and microcirculation, while the blood pressure during systole does not necessarily reflect the level of tissue perfusion. Nevertheless, it was shown, that low diastolic blood pressure and arterial stiffness are two independent predictors of cardiovascular risk (8, 7).

Very important question is the modulation of capillary flow and microcirculation by antihypertensive treatment (9). The whole capillary system is not perfused simultaneously. Capillaries are probably intermittently closed and opened and a continuous alternation between filtration and resorption in the same capillary occurs. This alternation might be predominantly determined by diastolic blood pressure values and disrupted perfusion pattern due to low diastolic blood pressure can be a key factor in the development of tissue hypoxia (10). Progressive hypoperfusion and hypoxia lead to deterioration of all organ functions. Although antihypertensive treatment decreases the undesired hemodynamic

overload, excessive reduction of diastolic blood pressure can even worsen tissue hypoperfusion which may possibly contribute to increased mortality in patients with diastolic blood pressure lower than 60 mm Hg. Resulting hypoxia not only decreases mitochondrial function and ATP production, but results in accumulation of metabolic products and reduction of pH leading to vasodilation, which should enhance tissue perfusion. However, under conditions of low blood pressure and generalized hypoxia, overall vasodilation further reduces perfusion pressure, decreases blood flow and promotes hypoxia. Such a situation should be opposed by sympathetic activation. Nevertheless antihypertensive treatment may disrupt these important regulatory mechanisms. Therefore in patients with low diastolic blood pressure, mortality and morbidity will not only be dependent on blood pressure values, but also on the fact, whether these values are constitutional, achieved by medicament treatment or resulting from a pathologic condition (e.g. aortic insufficiency) (11, 12). An experimental or clinical study revealing such differences is hard to design. Thus up-to-date none of these possibilities can be confirmed or disclosed.

The major problem of optimization of tissue perfusion is that both adequate vascular dilation and sufficient perfusion pressure are required. Antihypertensive treatment can disequilibrate this balance and impair microcirculation. We assume that **a decrease in diastolic pressure can bring about a decrease in intracellular and pericellular values of oxygen pressure** (Fig. 1). This fact could be responsible for the observed increase in mortality in patients with low diastolic blood pressure. Thus we support the idea of cautious blood pressure reduction in the elderly and especially to prevent reduction below 70 mm Hg. Furthermore, we suggest, that monitoring the level of tissue perfusion in treated hypertensive patients might help to provide individually tailored therapy.

## References

1. **Oparil S, Lundberg GD.** Hypertension: What It Is? What It Isn't? How to Think About It, to Prevent It, and to Manage It. Medscape General Medicine Webcast Video Interviews 12/12/2007 2007.
2. **Hulin I, Duris I, Paulis L, Sapakova E, Mravec B.** Dangerous versus useful hypertension (a holistic view of hypertension). *Eur J Intern Med* 2009; 20 (2): 226–230.
3. **Hansson L, Lindholm LH, Ekblom T, Dahlöf B, Lanke J, Schersten B, Wester PO, Hedner T, de Faire U.** Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity the Swedish Trial in Old Patients with Hypertension-2 study. *Lancet* 1999; 354 (9192): 1751–1756.
4. Major outcomes in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin vs usual care: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT). *J Amer Med Ass* 2002; 288 (23): 2998–3007.
5. **Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, Grassi G, Heagerty AM, Kjeldsen SE, Laurent S, Narkiewicz K, Ruilope L, Rynkiewicz A, Schmieder RE, Boudier HA, Zanchetti A, Vahanian A, Camm J, De Caterina R, Dean V, Dickstein K, Filippatos G, Funck-Brentano C, Hellems I, Kristensen SD, McGregor K, Sechtem U, Silber S, Tendera M, Widimsky P, Zamorano JL, Erdine S, Kiowski W, Agabiti-Rosei E, Ambrosioni E, Lindholm LH, Viigimaa M, Adamopoulos S, Bertomeu V, Clement D, Farsang C, Gaita D, Lip G, Mallion JM, Manolis AJ, Nilsson PM, O'Brien E, Ponikowski P, Redon J, Ruschitzka F, Tamargo J, van Zwieten P, Waeber B, Williams B.** 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2007; 25 (6): 1105–1187.
6. **Pechanova O, Matuskova J, Capikova D, Jendekova L, Paulis L, Simko F.** Effect of spironolactone and captopril on nitric oxide and S-nitrosothiol formation in kidney of L-NAME-treated rats. *Kidney Int* 2006; 70 (1): 170–176.
7. **Protogerou AD, Safar ME, Iaria P, Safar H, Le Dudal K, Filipovsky J, Henry O, Ducimetiere P, Blacher J.** Diastolic blood pressure and mortality in the elderly with cardiovascular disease. *Hypertension* 2007; 50 (1): 172–180.
8. **Blacher J, Guerin AP, Pannier B, Marchais SJ, Safar ME, London GM.** Impact of aortic stiffness on survival in end-stage renal disease. *Circulation* 1999; 99 (18): 2434–2439.
9. **Feihl F, Liaudet L, Waeber B, Levy BI.** Hypertension: a disease of the microcirculation? *Hypertension* 2006; 48 (6): 1012–1017.
10. **Goncalvesova E, Fabian J.** Graft dysfunction after heart transplantation. *Bratisl Lek Listy* 2000; 101 (9): 532–533.
11. **Goncalvesova E, Hnilica P, Motovska Z, Goncalves F, Kovac A.** Adrenal incidentalomas – Analysis of 23 cases discovered by ultrasound. *Neoplasma* 1997; 44 (2): 137–141.
12. **Goncalvesova E, Krizanova O, Micutkova L, Mravec B, Ksinantova L, Fabian J, Kvetnansky R.** Phenylethanolamine N-methyltransferase gene expression in transplanted human heart. *Transplant Proc* 2005; 37 (2): 1340–1342.

Received October 27, 2009  
Accepted November 2, 2009.