

Exercise Hypertension – A Review

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Abstract

The actual significance and definition of hypertensive response to exercise (HRE) is still debated. Up to now, there is consensus in defining it as a systolic blood pressure value of either ≥ 210 mmHg in men and ≥ 190 mmHg in women or a diastolic blood pressure ≥ 110 mmHg during maximal exercise stress test.

The mechanisms underlying an exaggerated blood pressure response to exercise are poorly understood; however, there are studies suggesting that HRE may represent a pre-clinical stadium of essential hypertension, which shares several common pathological mechanisms mostly related to an endothelial dysfunction and vascular stiffness.

In this article we review the present knowledge with particular respect to prognostic significance and diagnostic and therapeutic strategies in different populations. A separate section is dedicated to athletes with HRE.

Keywords: Exercise hypertension, arterial hypertension, clinical recommendation, cardiovascular risk

Zusammenfassung

Die tatsächliche Bedeutung und Definition der Belastungshypertonie ist noch umstritten. Es herrscht jedoch weitgehend Konsens bei der Definition: systolischer Blutdruckwert von entweder ≥ 210 mmHg bei Männern und ≥ 190 mmHg bei Frauen oder ein diastolischer Blutdruckwert von ≥ 110 mmHg, jeweils bei maximaler Belastung während einer Ergometrie. Die Mechanismen, die einer Belastungshypertonie zugrunde liegen, sind nur ungenügend verstanden. In Studien konnte jedoch gezeigt werden, dass die Belastungshypertonie möglicherweise eine präklinische Manifestation der arteriellen Hypertonie (in Ruhe) darstellen könnte. Dies insbesondere, weil mehrere pathophysiologische Mechanismen, meist im Zusammenhang mit endothelialer Dysfunktion und Gefäßsteifheit, bei beiden Erkrankungen nachgewiesen wurden.

In diesem Artikel fassen wir den aktuellen Wissensstand zur Belastungshypertonie mit besonderem Augenmerk auf prognostische, diagnostische und therapeutische Überlegungen in verschiedenen Patientenpopulationen zusammen. Ein separater Abschnitt widmet sich Athleten mit Belastungshypertonie.

Schlüsselwörter: Übungshypertonie, arterielle Hypertonie, klinische Empfehlung, kardiovaskuläres Risiko



Exercise Hypertension: Definition

A stress test with a cycle ergometer or on a treadmill is routinely performed in daily practice to evaluate patients with known coronary artery disease, heart failure, or as a general screening to evaluate the cardiovascular risk. Beside monitoring heart rhythm and repolarization changes with electrocardiography, blood pressure is usually measured repetitively manually or automatically with an arm cuff.

A pathological blood pressure response to exercise may include an impaired response or even in a decrease during incremental exercise, conditions that are mostly associated with ischemic heart disease. However, recently also an exaggerated increase in blood pressure has been investigated. Although there is no official consensus yet, an hypertensive response to exercise (HRE) is defined according to epidemiological studies as either a systolic blood pressure value of ≥ 210 mmHg in men and ≥ 190 mmHg in women or a diastolic blood pressure ≥ 110 in both during maximal exercise stress test. [1] A systolic blood pressure ≥ 175 mmHg under light-intensity stress test has been proposed as further cut-off, as well. [2] (see Table 1). A normal response to exercise is defined as a mean increase of 10mmHg per metabolic equivalent. [3]

		Systolic Blood Pressure	Diastolic Blood Pressure
High-intensity exercise	Men	≥ 210 mmHg	≥ 100 mmHg
	Women	≥ 190 mmHg	≥ 95 mmHg
Light-intensity exercise	Men	≥ 175 mmHg	
	Women	≥ 175 mmHg	
Athletes	Men	≥ 220 mmHg	≥ 85 mmHg
	Women	≥ 200 mmHg	≥ 80 mmHg

Table 1: Proposed cut-off for the diagnosis of Hypertensive Response to Exercise (HRE) in different populations. Adapted from [14,18,21].

Pathophysiology of Exercise Hypertension

The mechanisms underlying an HRE are poorly understood. Several mechanisms have been proposed with respect to different population groups.

In an epidemiological study, young (mean age < 30 years) normotensive subjects with no known cardiovascular risk factors were compared to subjects with a positive familiar history for hypertension or with high-normal resting blood pressure: The latter were more likely to present HRE during maximal exercise effort. A blunted decline in peripheral resistance was proposed as underlying mechanisms. [4] As such, in young patients with no manifest cardiovascular risk factors, an endothelial dysfunction with insufficient nitroxide-oxide (NO)-production has been postulated as primary mechanism leading to HRE. [5]

In older patients, the pathophysiological mechanism is more likely to be linked to an increased subclinical arterial stiffness with reduced vascular compliance, as well, which becomes firstly evident during exercise. [5] In an observational study analyzing subjects aged between 55–75 years with untreated high-normal resting blood pressure, an im-

paired endothelial function as measured by flow-mediated dilation independently correlated with an increased pulse pressure under physical stress both in men and in women. [6] Furthermore, subjects with HRE were found to have an impaired response to acetylcholine, as a sign of imbalanced production of endothelial NO and an exaggerated response to vasoconstrictors. [7] Although data are sparse, there is evidence that HRE may represent a preclinical stadium of essential hypertension, which shares several common pathological mechanisms mostly related to a endothelial dysfunction and vascular stiffness.

Furthermore HRE, similarly to manifest hypertension, has been observed to be associated with both structural and functional anomalies of left ventricle such as diastolic dysfunction. [8,9]

Both HRE and manifest hypertension seems to share common risk factors, as well: they both have been positively associated with parameters denoting an underlying metabolic syndrome such as increased levels of serum cholesterol and insulin resistance. [2,10]

Prognostic Value and possible Treatment Strategies

Exercise hypertension has been associated to an increased risk of developing manifest clinical hypertension in several studies and meta-analyses. Although these studies were performed using different test protocols and used different cut-off values of HRE, their conclusions are quite homogeneous. As such, a 1.19 to 1.90-times higher risk of developing clinical manifest hypertension has been observed for HRE measured at the peak of moderate or maximal exercise, independently from values of resting blood pressure. In this study, each 10 mmHg increase in systolic BP during exercise resulted in a 4% increase in cardiovascular adverse events and mortality even after correction for resting office blood pressure, age or other known cardiovascular risk factors. [11] In another meta-analysis including 12 longitudinal studies involving subjects with no known coronary artery disease, systolic blood pressure at moderate, but not maximal, workload was associated with an increase in adverse cardiovascular outcomes after a mean follow-up of 15 years. [12] However, the authors recognize there was a substantial heterogeneity in populations between studies which make comparisons difficult. Furthermore, no out-of-office blood pressures were recorded, so that masked hypertension was not considered.

It has been observed, that exercise could reveal cases of inadequate resting blood pressure control in the so-called masked hypertension. In such patients, HRE is the clinical manifestation of a pre-existent hypertension and, thus, these subjects should be considered at higher cardiovascular risk and might be treated consequentially. [13,14] The prescription of a 24-hours-blood pressure measurement may be thus evaluated in order to make a definitive diagnosis and classify the real grade of resting hypertension.

Treatment strategies for HRE still need to be developed. A diagnostic and therapeutic algorithm is proposed in Figure 1. As discussed above, HRE shares many pathophysiological pathways with resting hypertension, of which possibly represents a precursor. As such, life-style modifications should be implemented and encouraged in these subjects as well, independently from other classical cardiovascular risk factors. Pharmacological treatment of HRE is still debated and is not

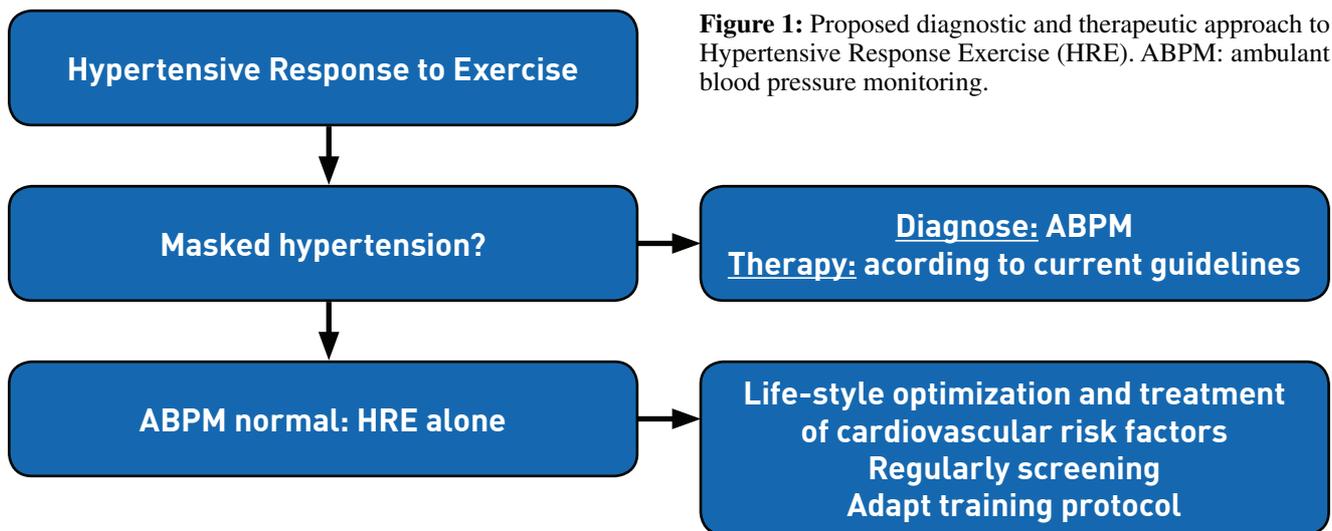


Figure 1: Proposed diagnostic and therapeutic approach to Hypertensive Response Exercise (HRE). ABPM: ambulant blood pressure monitoring.

taken into account in the current guidelines for hypertension, yet. Angiotensin-II seems to play an important role in the onset of HRE, so a therapy with ACE-inhibitors or renin-angiotensin-aldosterone system antagonists could be considered. [9] Similarly, the use of beta-blockers could reduce the adrenergic tone during physical effort, although could limit exercise capacity.

Exercise Hypertension in Athletes: Special Considerations

As athletes usually undergo regular exercise tests to check their fitness level, these tests provide a unique opportunity to also check for HRE. Fitness level, as expressed by maximal oxygen uptake, independently influence blood pressure response under stress. [15] In athletes, a hypertensive response during exercise is considered as a systolic blood pressure > 220 mmHg in male and > 200 mmHg in female and > 85 mmHg in male or > 80 mmHg in female for diastolic blood pressure during cycle ergometry. [16,17] Blood pressure should be routinely assessed during exercise testing in all athletes in order to rule out exercise-induced hypertension and the exercise effort should be pushed to their maximal limit. According to the new position statement on athletes with arterial hypertension, subjects with borderline resting hypertension or with suspected masked hypertension should undergo ambulatory BP monitoring also during training sessions. [18,19]

Although a masked or not yet clinical manifest essential hypertension is possible in athletes as well, specific causes of secondary hypertension such as abuse of antirheumatic drugs, adrenergic stimulants, androgenic-anabolic steroids, growth hormone, erythropoietin or other doping substances should be considered and appropriately investigated.

Athletes diagnosed with arterial hypertension should be treated according to general guidelines and only those with associated clinical conditions or target organ damage should be restricted from sports, in particular from those with isometric components. [20] It should be paid particular attention to prescribing antihypertensive in athletes, since some drugs are considered doping substances and are banned by many sports associations. A list of pharmacological therapies for different disciplines is provided in Table 2.

Athletes with suspected arterial hypertension should undergo regular evaluation to assess the need for the adequacy of pharmacological therapy and should be regularly screened for secondary organ damage such as left ventricular hypertrophy. This represents a diagnostic challenge as other cardiomyopathies of interest for athletes such as hypertrophic cardiomyopathy may initially present identically, therefore an adequate follow-up over time is particularly important. A period of detraining may be considered in this case to help differentiating a primary hypertrophic cardiomyopathy from exercise-related left-ventricular hypertrophy.

Antihypertensive drugs in athletes	Is it doping?	Adverse effects on performance	Indications
Diuretics	Rapid weight loss: Boxe, Judo, Wrestling	Hypovolemia, orthostatic hypotension, electrolyte imbalance	2° line therapy
B-blockers	Precision and concentration sports: Shooters, Diving, Archery, Ski Jumping	Reduction in isotropism, heart rate and cardiac output, bronchospasm, hypoglycaemia	Only if there is an underlying condition
RAAS-blockers	no	Relative vasodilation with no impairment of VO ₂ max.	1° line therapy
Ca-antagonists	no	Potential diffuse vasodilation and early onset of anaerobic-threshold	1° line therapy, mainly in black athletes

Table 2: Antihypertensive therapy in athletes and effects on sportive performance.

Conclusion

HRE is an underdiagnosed and under-investigated clinical condition. Cut-off values relevant to all-day practice and with prognostic relevance need to be better explored in big population studies. HRE shares many pathophysiological mechanisms with essential hypertension, of which could be considered a precursor. As such, particular attention should be given on those patients with normal resting blood pressure values but who develop inappropriate high blood pressure values independently from the stage of physical effort. Particular attention should be given to athletes, in whom HRE may be further enhanced by isometric training protocols and who could, thus, be at higher risk of developing secondary organ damage.

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