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Review Article

Impact of exaggerated blood pressure response in normotensive individuals on future hypertension and prognosis: Systematic review according to PRISMA guideline

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ABSTRACT

Purpose: Arterial hypertension (aHT) is the leading risk factor for morbidity and mortality worldwide. Blood pressure (BP) deviation at rest is well defined and accompanies risk for cardiovascular events and cardiovascular mortality. A growing body of evidence emphasises that an exaggerated blood pressure response (EBPR) in cardiopulmonary exercise testing (CPET) could help to identify seemingly cardiovascular healthy and normotensive subjects, who have an increased risk of developing aHT and cardiovascular events in the future.
Materials and methods: The PubMed online database was searched for published studies reporting exercise-related BP and both the risk of aHT and cardiovascular events in the future.
Results: We identified 18 original studies about EBPR in CPET, which included a total of 35,151 normotensive individuals for prediction of new onset of aHT in the future and 11 original studies with 43,012 enrolled subjects with the endpoint of cardiovascular events in the future.
Although an EBPR under CPET is not well defined, a large number of studies emphasise that EBPR in CPET is associated with both new-onset aHT and cardiovascular events in the future.
Conclusions: A growing number of studies support the hypothesis that EBPR in CPET may be a diagnostic tool to identify subjects with an elevated risk of developing aHT and cardiovascular events in the future.

Contents

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1. Introduction

Arterial hypertension (aHT) is the leading cardiovascular risk factor for morbidity and mortality worldwide [1–3].

In industrialised countries, the prevalence of aHT is growing with age and overweight [4]. In the United States, approximately 78 million adults suffer from aHT [5]. Prevalence of aHT in Germany was assessed as 10–35% in the 3 decades between 30th and 60th life-year and over 65% in people older than 60 years [6].

A large number of studies have emphasised that cardiovascular morbidity and mortality reveal a continuous relationship with both systolic and diastolic blood pressure (BP) [7–9]. The relationship between BP and cardiovascular events seems to be less strong for coronary artery disease (CAD) events than for stroke [7,8]. Therefore, stroke is the most important and a directly aHT-related complication [7,8]. It has been estimated that aHT is responsible for 7.6 million deaths per year worldwide [4].

Furthermore, both systolic and diastolic BP have shown an independent relationship with heart failure, atrial fibrillation, aortic dissection, atherosclerosis with peripheral artery disease, cognitive impairment, retinopathy and renal disease [2,4,7]. Therefore, aHT is a major risk factor for most of the cardiovascular and related diseases [2,7].

Diagnosis of aHT by resting BP is well defined, with systolic BP values of ≥140 mmHg and diastolic BP values of ≥90 mmHg [10]. A growing body of evidence indicates that aHT-related organ damage occurs beyond these boundaries [10,11]. Therefore, clinicians and scientists are searching for sensitive and specific diagnostic tools and methods to identify patients, who are at an increased risk of developing aHT and are at risk of the subsequent organ damage [10]. Although an increased exercise capacity was identified as a powerful predictor of mortality [12], several studies suggested that an exaggerated BP response (EBPR) in standard exercise testing could be one of these sensitive diagnostic tools [10].

1.1. Definition of arterial hypertension

BP is the product of cardiac output and vascular resistance [13,14]. Therefore, elevated BP is the result of changes of at least one of these factors [14].

According to the current ESC guidelines for the management of aHT [1] systolic BP values of ≥140 mmHg and diastolic BP values of ≥90 mmHg at rest were categorised as hypertensive BP values (Table 1) [1,7]. However, recent studies have suggested that organ damage occurs when individuals are progressing towards aHT and therefore are still in the normotensive BP range [10]. BP shows a continuous relationship with the risk of cardiovascular events starting at systolic and diastolic BP levels even as low as 115–110 mmHg and 75–70 mmHg, respectively [4,7,15]. Despite adverse events in cases of acute hypertensive BP deviation, such as bleeding in acute hypertensive crises, diseases from secondary causes develop mostly not in short term, but in longer follow-up periods (FU). These may occur approximately 10 years after the onset of aHT [4]. The SPRINT trial [16] emphasised the importance of a good BP management in aHT. Better BP adjustment towards a mean systolic BP value of 121 mmHg in patients with aHT was associated with a lower rate of cardiovascular events and better survival in comparison to those aHT patients with adjusted mean BP values of 136 mmHg [16].

For risk stratification of patients with aHT, the development of endorgan damage should also be taken into account, in addition to elevated systolic and diastolic BP values [2].

1.2. Prevalence of hypertension

aHT is the most prevalent cardiovascular disease in the industrialised world [10] and is a powerful risk factor for fatal and non-fatal cardiovascular events [15,17]. The World Health Organisation (WHO) estimated the worldwide overall prevalence of raised BP in adults ≥25 years as approximately 40% in the year 2008 [18]. It has been estimated that approximately 1 billion people suffer from uncontrolled aHT and 7.6 million deaths annually are BP related worldwide [18]. The reported regional prevalence of aHT varies around the world [18,19]. While a high prevalence has been reported in Africa for example, a lower prevalence was found in North America [18]. Men had a slightly higher prevalence than women worldwide [18].

Importantly, prevalence of aHT is growing with age and obesity in industrialised countries [4]. In the United States, approximately 78 million adults had an elevated BP [5]. In contrast to reports 20

Table 1
Definitions and classification of blood pressure levels (mmHg) and arterial hypertension categories according to the current ESC-Guideline for the management of arterial hypertension [1,7].

Categories	Systolic blood pressure		Diastolic blood pressure
Optimal	<120 mmHg	and	<80 mmHg
Normal	120–129 mmHg	and/or	80–84 mmHg
High-normal	130–139 mmHg	and/or	85–89 mmHg
Grade 1 hypertension	140–159 mmHg	and/or	90–99 mmHg
Grade 2 hypertension	160–179 mmHg	and/or	100–109 mmHg
Grade 3 hypertension	>180 mmHg	and/or	>110 mmHg
Isolated systolic hypertension	>140 mmHg	and	<90 mmHg