

# Erectile dysfunction in arterial hypertension

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## Summary

Erectile dysfunction, the inability to attain, respectively maintain a penile erection sufficient for sexual intercourse, is a frequent finding in the general population. It is a multi-factorial syndrome that may arise from chronic disease such as arterial hypertension, but also from psychosocial problems, as a side effect of certain medications, alcohol or drugs, or from impaired nerve function. Erectile dysfunction is associated with an increased risk of cardiovascular morbidity and mortality. The approach to the patient should include a thorough cardiovascular, endocrine, neurological, urological and psychological evaluation. In patients with arterial hypertension, diuretics and beta-blockers may impair erectile function while beneficial effects of angiotensin receptor blockers, ACE inhibitors, and nebivolol have been demonstrated. PDE-5-inhibitors may be considered in stable patients with controlled arterial hypertension but refractory erectile dysfunction.

*Key words: sexual dysfunction; erectile dysfunction; arterial hypertension; anti-hypertensive treatment*

## Take home messages

- Erectile dysfunction is a frequent finding in the population.
- Erectile dysfunction is associated with chronic disease (e.g., arterial hypertension), certain medications, alcohol, drugs, nerve or psychosocial disorders.
- Erectile dysfunction is associated with increased cardiovascular morbidity and mortality.
- Treatment of arterial hypertension with diuretics or beta-blockers may impair erectile function, while treatment with angiotensin receptor blockers, ACE inhibitors, calcium antagonists, and nebivolol appears to have less affect and may even be beneficial in patients with hypertension and erectile dysfunction.

## Introduction

Erectile dysfunction, characterised by the inability to develop or maintain an erection of the penis during sexual performance, is a frequent

finding in men with arterial hypertension. As arterial hypertension is a major risk factor for the formation of atherosclerosis, it is not amazing that erectile dysfunction is associated with increased cardiovascular morbidity and mortality.

On the other hand it is well known that erectile dysfunction may be a direct consequence of anti-hypertensive treatment. The goal of this article is to summarise the current knowledge on causes and consequences of sexual dysfunction in men with arterial hypertension.

## Definition, causes, and epidemiology of erectile dysfunction

Erectile dysfunction is seen as the hallmark of sexual dysfunction in men and defined as the persistent inability to attain, respectively maintain a penile erection sufficient for sexual intercourse [1]. While sexual and erectile dysfunction may be used synonymously in men, defining this syndrome in women is far more difficult and includes the persistent or recurrent decrease in sexual desire/arousal or the difficulty to achieve orgasm or the feeling of pain during sexual intercourse [2]. It is estimated that the prevalence of sexual dysfunction in the population is in the range of 15–20%. Erectile dysfunction affects between 5% of men at the age of 20–39 years and up to 70% of men at the age of 70 years or older [3]. Erectile dysfunction is a multi-factorial syndrome and may be arise as a consequence of

- Chronic disease (e.g., arterial hypertension, diabetes mellitus, obesity, chronic renal failure)
- Interference with medication, alcohol, and drugs (e.g., anti-hypertensive medication, anti-depressants, medication for the treatment of dyslipidemias)

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- Psychosocial problems (e.g., performance anxiety, relationship problems, depression and other psychiatric disorders)
- Interference with nerve function (e.g., Parkinson's disease, Alzheimer's disease, multiple sclerosis, diabetic neuropathy)
- Urological problems (e.g., Peyronie's disease, pelvic trauma).

Vascular diseases account for nearly half of all cases of erectile dysfunction in men older than 50 years. Vascular diseases include atherosclerosis, peripheral vascular disease, myocardial infarction, and arterial hypertension. In particular, arterial hypertension is associated with a 1.3–6.9x increased risk for erectile dysfunction [3].

### Pathophysiology of erectile dysfunction

#### Overview

Penile erection is evoked by both reflex and psychogenic erection, achieved by mechanical, and erotic or emotional stimulation. Via parasympathetic nerve fibres from the central nervous system, the release of acetylcholine triggers production of nitric oxide (NO) in endothelial cells, leading to activation of guanylate cyclase in vascular smooth muscle cells, an increase of cyclic GMP, reduction of intracellular calcium and ultimately to relaxation of vascular smooth muscle cells. As a consequence, arterial blood flow to the penis is increased and the corpora cavernosa dilate reducing the venous return by compressing the penile venous system and finally leading to erection. After ejaculation, a strong sympathetic stimulus decreases arterial blood flow via activation of phospholipase C and a phosphatidylinositol biphosphate- and inositol triphosphate-triggered increase of intracellular calcium. Thus, besides an intact endocrine system, both an intact neural as well as an intact vascular system is required for a successful and complete erection [4].

#### Endothelial and erectile dysfunction

Regular endothelial function is characterised by a sensitive balance of vasodilating (e.g., prostacyclin, adenosine) and vasoconstrictive factors (e.g., thromboxane, endothelin, angiotensin II) [5]. Cardiovascular risk factors such as arterial hypertension lead to increased oxidative stress in the vascular system triggering vascular inflammation, endothelial cell injury, and finally to endothelial dysfunction and atherosclerosis [4, 6]. Given the relatively small diameter of the penile artery [1–2 mm, compared to the coronary (3–4 mm) or femoral artery (6–8 mm)] and the fact that increase in arterial blood flow required for erection is comparable to that required by the heart for vigorous exercise [7], it becomes evident that endothelial dysfunction may lead to erectile dysfunction as a very early clinical sign of impaired (penile) arterial blood flow due to vascular

disease. In fact, erectile dysfunction is significantly associated with an increased risk of myocardial infarction, cardiovascular, and all-cause death in patients at high cardiovascular risk [8].

#### Hypertension, anti-hypertensive therapy and endothelial dysfunction

Both in experimental and human studies, the link between arterial hypertension and impaired endothelial function has been well established [9]. Reduction of cardiovascular morbidity and mortality has been demonstrated for all major anti-hypertensive drug classes (diuretics, calcium channel blockers, beta-blockers, angiotensin converting enzyme inhibitors, and angiotensin receptor blockers). However, these drug classes affect endothelial dysfunction to different extents. A recent meta-analysis demonstrated an improvement of endothelial function for ACE inhibitors and angiotensin receptor blockers while improvement of endothelial function was less prominent or even absent for diuretics, beta-blockers (with the exception of nebivolol), and calcium channel blockers [10].

#### Hypertension, anti-hypertensive therapy, and erectile dysfunction

The approach to the patient with arterial hypertension and erectile dysfunction should include the search for psychological, urological, neurological, endocrine and vascular causes as well as the search for pharmacological causes of this syndrome. In a recent trial, Doumas and colleagues were able to demonstrate a significant relationship between increasing stages of arterial hypertension and decreasing erectile function scoring, indicating higher prevalences of erectile dysfunction in more severe stages of arterial hypertension [11]. Among other factors like hypertension duration and age, anti-hypertensive medication – namely diuretics and beta-blockers – was positively correlated with erectile dysfunction while erectile dysfunction was less frequent when calcium channel blockers, ACE inhibitors, or angiotensin receptor blockers were used.

As in patients without sexual dysfunction, the therapy of arterial hypertension in patients with sexual dysfunction is based on life style modifications. Potential beneficial effects of angiotensin receptor blockers and ACE inhibitors on erectile dysfunction have been demonstrated in a comprehensive analysis of trials investigating the effects of antihypertensive therapy. Beneficial effects have also been described for the beta-blocker nebivolol which may improve sexual dysfunction by an increase of the bioavailability of NO [12]. However, there may be an important exception. In patients with high cardiovascular risk, the addition of inhibitors of the renin-angiotensin-aldosterone system to a broad spectrum of anti-hypertensive medication did not appear to result in an improvement of erectile dysfunction [8].

In refractory cases, the use of PDE-5-inhibitors such as sildenafil or tadalafil, may be the only option to improve erectile dysfunction. It is certainly important to emphasise that PDE-5-inhibitors should only be initiated in stable patients with controlled arterial hypertension. In addition, administration of PDE-5-inhibitors together with nitrates or  $\alpha$ -blockers (e.g., prazosin, doxazosin, terazosin) is contraindicated since this may lead to severe hypotension. Taking into account these restrictions, the administration of PDE-5-inhibitors in hypertensive patients with erectile dysfunction may even be beneficial as sexual dysfunction is a major contributor to malcompliance with anti-hypertensive therapy. Moreover, administration of PDE-5-inhibitors may even be associated with initiation and addition of anti-hypertensive therapy [13].

### Summary and conclusion

Sexual dysfunction is a highly prevalent condition in the general population, with higher risk in hypertensive patients. Erectile dysfunction is strongly linked to age, psychological reasons and, most frequently and importantly, to vascular disease. In addition, erectile dysfunction is associated with increased cardiovascular morbidity and mortality. However, erectile dysfunction may also occur as a consequence of treatment of cardiovascular disease, in particular arterial hypertension. The evaluation of erectile dysfunction should include the search for psychological, urological, neurological, endocrine and vascular causes as well as the search for pharmacological causes. A higher prevalence of erectile dysfunction is found with anti-hypertensive treatment with beta-blockers (with the exception of nebivolol which is known to increase the bioavailability of NO), diuretics, and calcium channel blockers compared to ACE inhibitors and angiotensin receptor blockers. On the other hand, anti-hypertensive therapy may improve erectile dysfunction in hypertensive patients which was particularly demonstrated for angiotensin receptor blockers as well as for the beta-blocker nebivolol.

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