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REVIEW

Relationship Between Hypertension, Antihypertensive Drugs and Sexual Dysfunction in Men and Women: A Literature Review

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Abstract: Sexual dysfunction pertains to any issue that hinders an individual from attaining sexual contentment. This health issue can have a significant impact on the quality of life and psychological health of affected individuals. Sexual dysfunction can generate stress, anxiety, depression, and low self-esteem, which can lead to a reduction in overall life satisfaction and the quality of interpersonal relationships. Sexual dysfunction can manifest as erectile dysfunction in men or lack of sexual desire in women. Although both sexes can experience sexual problems, there are some significant differences in the manifestation of sexual dysfunction between men and women. In men, sexual dysfunction is usually physical and associated with problems such as erectile dysfunction, while in women, sexual dysfunction is usually related to psychological factors. Additionally, there was an association between hypertension and sexual dysfunction in both the sexes. In men, hypertension can cause erection problems, whereas in women, it can cause vaginal dryness and a decrease in sexual desire. Furthermore, antihypertensive drugs can negatively impact sexual function, which can decrease adherence to drug treatment. However, nebivolol, an antihypertensive drug, has beneficial effects on erectile dysfunction in men. This is believed to be because nebivolol improves blood flow to the penis by producing nitric oxide, which can help improve erections.

Keywords: sexual dysfunction, hypertension, antihypertensive drugs, erectile dysfunction, beta-blockers, nebivolol

Introduction

Sexual dysfunction refers to a diverse range of medical conditions that cause significant disruption to an individual's sexual response or pleasure.[1–3] Erectile dysfunction, for instance, was described in 1993 as a persistent incapacity to achieve and sustain an erection of the penis sufficient for satisfactory sexual activity.[4–6] In addition, sexual dysfunction may result in reduced libido or difficulties in ejaculation.[7] This can have various causes such as organic, psychological, and social factors.[8] At the pathophysiological level, erectile dysfunction may be associated with a lack of endothelial-derived nitric oxide and loss of parenchymal smooth muscle cells in the penis.[1] Erectile dysfunction is considered a phenomenon of psychological origin in the manifestation of an organic disease in which endothelial dysfunction predominates.[9] The ability to attain and sustain an erection arises from a delicate equilibrium between blood flow into the arteries and outflow from the cavernous tissues. Any imbalance that decreases arterial inflow and/or increases cavernous outflow can cause symptomatic erectile dysfunction. Current data suggest that vasculogenic erectile dysfunction originates from arterial issues and is primarily caused by systemic endothelial dysfunction. As systemic endothelial dysfunction is an early marker of cardiovascular disease, specifically atherosclerotic heart disease of the coronary arteries, it has been suggested that the onset of erectile dysfunction can be used as a marker of the presence or future

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development of atherosclerosis. Vasculogenic erectile dysfunction is not always due to vascular diseases, although most of these are. Physiologically, the progressive and genetically predetermined deterioration of the cavernous smooth muscle occurs through a metabolic process called apoptosis. From a physiological perspective, the penis is considered to be an extension of the vascular system. Therefore, it is deduced that any defect or disorder that affects the vascular system will also affect the penis and vice versa.[10] Compared with erectile dysfunction, female sexual dysfunction is a relatively poorly understood health problem. According to the WHO, it is defined as the inability to live a sexual relationship, understood, therefore, as a disorder that limits both the physical and emotional involvement between the woman and her partner, and should be understood as a basic human need, which in its absence can imply physical, psychological, cognitive, and/or social imbalance.[11]

In recent decades, the standards for quality of life have significantly increased. One of the factors that comprise it is sexual harmony, which has been observed to depend greatly on sexual desire and erectile function, particularly in men.[12] Sexual dysfunction is a common medical disorder associated with the pathology, psychological state, and social behavior of the general population. Additionally, it is considered a multifactorial condition that may include vascular, neurogenic, hormonal, muscular, and endothelial problems.[13] Although sexual dysfunction does not pose a threat to life, it can have a strong negative effect on the interpersonal relationships of patients and compromise their well-being and quality of life.[4,14] Sexual health is an integral part of overall health, and an active and healthy sexual life is an essential aspect of good quality of life. Erectile dysfunction has a significant psychological impact on affected patients, compromising their self-esteem, self-confidence, and mood, and may generate symptoms of anxiety and depression.[15] Sexual dysfunction also affects marital adjustment of married couples. One of the important factors affecting marital relationships is sexuality between partners. Satisfying the sexual needs of spouses and having a healthy sexual life also allow them to present positive attitudes in their marital adjustments. Although these are very common problems and can be successfully treated, the rate of requests to doctors or medical centers for sexual dysfunction is still low. Literature underscores that marriages in which sexual functioning is compromised tend to be unhappy and dissatisfied. Studies have shown that sexual satisfaction and frequency of sexual activity are closely linked to marital happiness.[16] Therefore, the objective of this literature review was to gather all available information on the relationship between hypertension, antihypertensive drugs, and sexual dysfunction.

Materials and Methods

From March 2023 to April 2023, a search was conducted across five databases (PubMed, Web of Science, Scopus, Cochrane Library and PsycINFO) to identify documents published within the past ten years (from 2013 to 2023). The search strategy employed was ("aliskiren" OR "Amlodipine" OR "Calcium antagonists" OR "Atenolol" OR "betanidine" OR "adrenergic blockers" OR "Bumetanide" OR "Captopril" OR "carvedilol" OR "Clonidine" OR "Chlorothiazide" OR "Chlorthalidone" OR "Dihydropyridines" OR "diltiazem" OR "diuretics" OR "Doxazosin" OR "Enalapril" OR "Spironolactone" OR "Antihypertensive drugs" OR "phenoxybenzamine" OR "phentolamine" OR "furosemide" OR "Guanabenzine" OR "Guanethidine" OR "Guanfacine" OR "haloperidol" OR "hydralazine" OR "hydrochlorothiazide" OR "Hypertension" OR "labetalol" OR "losartan" OR "methyldopa" OR "Metoprolol" OR "Nebivolol" OR "Nifedipine" OR "sodium nitroprusside" OR "Prazosin" OR "Propranolol" OR "reserpine" OR "triamterene" OR "Valsartan" OR "Verapamil") AND ("sexual desire" OR "Erectile dysfunction" OR "sexual dysfunction" OR "Erection" OR "Ejaculation" OR "sexual impotence" OR "Orgasm" OR "sexual pleasure" OR "erection problems" OR "vaginal dryness" OR "Sexuality"). As the present article was a literature review, we did not include any inclusion or exclusion criteria. We included all articles available in the scientific literature. A flow chart is shown in Figure 1. We were unable to conduct a systematic review and/or due to the limited number of studies available.

Results

Frequency of Sexual Dysfunction

The most prevalent sexual disorder affecting men is erectile dysfunction. It can affect individuals of all age groups and has a notable impact on their quality of life.[1] According to various studies, this condition occurs in approximately 10–52% of

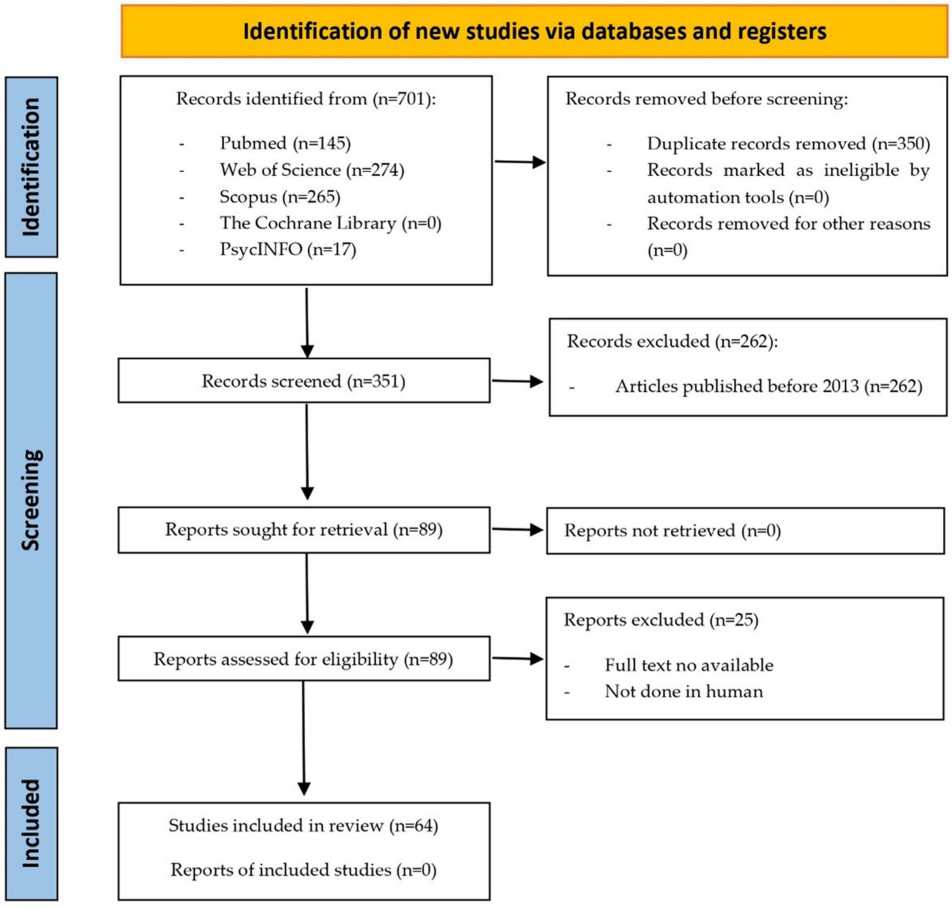

Figure 1 PRISMA flow chart.
Notes: PRISMA figure adapted from Liberati A, Altman D, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Journal of clinical epidemiology.* 2009;62(10):e1-34. Creative Commons.[17]

men.[2] Over 30 million men in the United States are affected by erectile dysfunction, with a worldwide estimate of approximately 100 million men affected by this condition.[6] Furthermore, this number is projected to increase to 322 million men by 2025.[18] The frequency rates vary according to age, although the frequency remains high. For example, more than 50% of men aged 40–70 have experienced some level of erectile dysfunction, and 10% have severe erectile dysfunction.[1] It is estimated that more than 75% of men aged 50–70 years have some degree of erectile dysfunction.[4] This rate seems to be similar in patients over 70 years of age, with frequencies of around 70%.[19] A survey of 1150 men aged 50–80 years from five Asian countries, including Hong Kong, Malaysia, the Philippines, Singapore, and Thailand, showed that the prevalence of erectile dysfunction was 63%.[18]

Prevalence studies have shown that erectile dysfunction occurs with higher incidence in men with hypertension,[6] which is approximately twice as common as in the normotensive population.[18] The scientific literature estimates that 30% of men with hypertension have erectile dysfunction.[20] Moreover, this sexual problem is present in approximately 58% of patients with hypertension.[9] Additionally, other pathological conditions associated with the cardiovascular system also increase erectile dysfunction, such as pelvic arterial insufficiency or stenosis of any segment of the iliac-pudendal-penile arterial system.[18] Sexual dysfunction in women has been poorly studied. However, it is estimated to be present in approximately 20–50% of women, which is also a high prevalence.[13]

Sexual Dysfunction in Men: Erectile Dysfunction

The prevalence of erectile dysfunction varies among studies. However, this problem is very common in men of any age. It is estimated that approximately 40% of men suffer from erectile dysfunction or impotence at least occasionally.[7,21] The older the

patient, the higher the rate of erectile dysfunction. The estimated prevalence is 1–10% in younger men (<40 years), 2–9% in middle-aged men (40–50 years), 20–40% in older individuals (60–69 years), and 50–100% in older individuals (>70 years).[7] There are various causes of erectile dysfunction are various, including testosterone deficiency, antidepressant drugs, aging, changes in cavernous molecules, and diseases such as hypertension. Hypertension is strongly associated with erectile dysfunction since arteriolar smooth muscle cells of the cavernous bodies are related to blood flow.[7,21–23]

Other authors have pointed out that erectile dysfunction is related to atherosclerotic changes that lead to reduced blood perfusion to the pelvis and penis gland, resulting in erectile dysfunction and overall deterioration of sexual function.[24] Erectile dysfunction can cause severe psychological distress and humiliation among most men, making it a health problem that needs to be considered clinically.[7,21–23]

Sexual Dysfunction in Women

Sexual desire and arousal were highly correlated in both men and women. Women are aroused under conditions of continuous physical stimulation, which further reinforces sexual desire. It is characterized by clitoral congestion, increased blood flow, and vaginal lubrication.[24] However, when this does not occur, it can lead to female sexual dysfunction. This term includes sexual disorders of desire, interest, arousal, orgasm, pain during genital-pelvic penetration, and satisfaction.[3,25]

At the physiological level, female sexual dysfunction is more complex than male erectile dysfunction.[26] Factors such as emotional stress, fatigue, or physical ailments such as hypertension can decrease female sexual desire. In women with hypertension, the blood supply to the pelvic area and genital organs is compromised. Constant elevation of blood pressure results in vessel wall transformation or remodeling, leading to reduced circulation in peripheral vascular tissues. Decreased genital blood flow secondary to atherosclerotic changes may result in vascular insufficiency of both the clitoris and the vagina. Since sexual arousal is affected, sexual desire is also compromised. Additionally, decreased pelvic blood flow may lead to fibrotic lesions in the smooth muscle of the clitoris and vaginal cylinder, reducing the efficacy of sexual stimulation. Hormonal changes associated with menopause can also contribute to sexual dysfunction in hypertensive women. Decreased estrogen levels in postmenopausal women can cause vaginal dryness, which is further aggravated by poor pelvic blood perfusion, negatively affecting female sexual functioning.[24]

Compared to erectile dysfunction in men, sexual dysfunction in women has been poorly studied. The main symptoms of female sexual dysfunction include pain during sexual intercourse or unpleasurable sex, lack of orgasm, low sexual desire, lack of arousal or decreased libido, and difficulty with vaginal lubrication.[16,24,27] Moreover, although it has been established that hypertension is associated with sexual dysfunction in men, this phenomenon has been poorly studied in women. However, the few available studies indicate that women with hypertension also experience sexual dysfunction, affecting all domains, such as sexual desire, arousal, lubrication, orgasm, satisfaction, and pain. In women, sexual dysfunction is associated with symptoms of anxiety and depression.[25] Female sexual dysfunction includes factors such as dissatisfaction, emotional frustration, mental impairment, and severe gynecological impairment.[13]

The prevalence of sexual dysfunction in women is debatable While some studies indicate that sexual dysfunction is more frequent in women than in men,[28] others indicate the opposite.[27] However, even with this controversy, the rates of female sexual dysfunction remain high, with most studies hovering at around 40%.[24] What seems to be common is that hypertension seems to affect men more than women in terms of sexual dysfunction.[28] Nevertheless, sexual dysfunction is significantly more frequent in women with hypertension than in those with normal blood pressure.[24]

Certain risk factors can increase the rate of sexual dysfunction among women. Among these, they are overweight, depressed, or hypertensive. In the case of hypertension, it is noted that the longer the duration of this cardiovascular disease, the worse the sexual function in women.[28] Aging decreases sexual activity in women. In fact, in women aged 57–64 years, sexual activity is 61.6%, while in women aged 65–74 years, it is 39.5%, and 16.7% in women aged 75–85 years. It is more frequent in middle-aged hypertensive women to observe disorders of desire, arousal, lubrication, orgasm, satisfaction, and pain during sexual intercourse.[11,27] Physiopathological risk factors are associated with changes in the vaginal and clitoral vasculature, decreased blood flow in the pelvic region, thinning of the vaginal wall and smooth muscles of the clitoris, and vaginal dryness.[16]

Although a clear relationship between hypertension and erectile dysfunction has been found in men, the relationship is not as clear in women with female sexual dysfunction.[29] However, some studies have suggested that sexual

dysfunction is more common in hypertensive women than in hypertensive men.[26] Compared with normotensive women, women with hypertension have a 2.7 times higher risk of developing sexual dysfunction.[24] Furthermore, the incidence of female sexual dysfunction is higher in untreated hypertensive women than in those who receive treatment or normotensive women with higher FSFI (Female Sexual Function Index) scores.[30] Although antihypertensive treatment may contribute to the development of sexual dysfunction in women with hypertension, no significant difference has been observed between hypertensive women taking antihypertensive medications and those not taking them.[24] It has been reported that 42.1% of women with hypertension experience sexual dysfunction compared with 19.4% of healthy women.[16] However, sexual function is rarely evaluated in clinical settings, despite being a common medical condition in women with resistant hypertension.[31] This lack of awareness can negatively affect the quality of life and sexual life of patients with resistant hypertension and their partners.[16]

Association Between Hypertension and Sexual Dysfunction

Association Between Hypertension and Sexual Dysfunction

High blood pressure is a known risk factor for erectile dysfunction, and untreated hypertension is associated with poor cardiac outcomes and erectile function.[32] Erectile dysfunction is a vascular disease that shares many risk factors with hypertension, and is considered a predictor of cardiovascular diseases.[33] In fact, erectile dysfunction shares a high prevalence, identical risk factors, age relationships, and very similar long-term outcomes with hypertension. Hypertension has been found to be the greatest risk factor for erectile dysfunction in some studies,[34,35] and male erectile dysfunction has been shown to be associated with an increased risk of cardiovascular disease, making hypertension a common and dangerous cardiovascular disease worldwide.[36]

Although there have been advances in pharmacological therapies for hypertension and the promulgation of treatment guidelines over the last two decades, only a small proportion of patients with documented hypertension have been controlled to target levels. Men with multiple cardiovascular risk factors and diseases are more likely to experience erectile dysfunction. Hypertension, in particular, is a significant risk factor and common comorbidity among men with this condition. However, research on this topic has not been profound, and often erectile dysfunction issues are often superficially treated.[37]

Although erectile dysfunction is almost twice as common in hypertensive patients as in normotensive patients, the presence of erectile dysfunction in the early stage of hypertension does not seem to have an unfavorable impact on established subclinical hypertensive sequelae, beyond mild impairment of diastolic function. The question has been raised as to whether erectile dysfunction starts in hypertension.[38] Sexual dysfunction is common in patients with systemic hypertension and may result from the natural progression of the disease or side effects of antihypertensive medication.[13]

Erectile dysfunction can occur due to high blood pressure or side effects of antihypertensive drugs. Endothelial dysfunction is a common mechanism underlying hypertension and erectile dysfunction, which can lead to increased contraction of vascular smooth muscle.[20] Although a clear association between hypertension and erectile dysfunction has been established, studies evaluating the relationship between masked hypertension and erectile dysfunction have not yet been conducted.[6,14] Patients with masked hypertension and sustained nocturnal hypertension patterns have been observed to have more severe erectile dysfunction.[14] Additionally, erectile dysfunction is particularly common among patients with resistant hypertension but unfortunately remains underdiagnosed in daily clinical practice.[39] The prevalence of erectile dysfunction varies by population group and affects approximately 50–60% of the general population. A U-shaped correlation between erectile dysfunction and diastolic blood pressure has been found,[1] and the incidence of erectile dysfunction increases in hypertensive patients, correlating with the duration and severity of the disease, as well as with polytherapy.[40]

Hypertension, Sexual Dysfunction, and Quality of Life

Hypertension is a chronic multifactorial degenerative disease that affects the blood vessels of the body, leading to changes in vasomotor tone, vasoconstriction, and increased blood pressure.[16] In addition, hypertensive patients present with anxiety and depressive symptoms as well as a high prevalence of sexual dysfunction. Patients with hypertension also experience medication side effects that can affect their quality of life, and the diagnosis of hypertension can alter

their modo.[25] Thus, hypertension is an important public health problem that not only increases cardiovascular risk but also significantly affects the quality of life of patients. Erectile dysfunction is one of the most important complications of hypertension and coronary artery disease.[41]

Prevalence of Sexual Dysfunction Associated with Hypertension

Erectile dysfunction is a common and troublesome problem in aging men, and it has been observed that patients with hypertension are at a higher risk of developing it.[9] In one study, it was found that up to one-third of patients with hypertension had mild erectile dysfunction, 8.3% had moderate erectile dysfunction, and 5.2% had severe erectile dysfunction.[42] Furthermore, the risk of erectile dysfunction has been reported to significantly increase with hypertension (OR=1.84, $p<0.000001$).[4] Erectile dysfunction may be an early sign of hypertension, and there is evidence that endothelial dysfunction is a common link between these two conditions. It is important to note that hypertension affects approximately 46% of the adult population in the United States, and although more than 80% of hypertensive patients are prescribed antihypertensive medication, less than 25% of them have the disease under control.[43] In a study conducted in a group of Nigerian participants, it was found that both erectile dysfunction and hypertension were positively correlated with age, and the prevalence of severe erectile dysfunction was higher among subjects with hypertension than among those with normal blood pressure.[44] As for sexual dysfunction in women, the prevalence of sexual dysfunction is higher in hypertensive women than in normotensive women, suggesting that arterial hypertension is a potential factor for female sexual dysfunction. In one study, sexual dysfunction was evaluated in hypertensive patients compared to normotensive patients, and it was found that 63% of hypertensive patients had sexual dysfunction compared with 39% of normotensive patients. Additionally, hypertensive women were found to have 1.67 times more chances of dysfunction than women with normal blood pressure.[3] It has been reported that 19.4% of healthy women and 42.1% of hypertensive women have sexual dysfunction.[13]

Hypertension, Associated Comorbidities, and Sexual Dysfunction

Pulmonary hypertension is a progressive and debilitating vascular disease characterized by a persistent increase in the mean arterial pressure in the pulmonary artery to >20 mmHg. Despite its prevalence, little is known regarding sexual dysfunction in this population. A clear impairment of self-reported sexual function has been observed in women with pulmonary hypertension.[11] Erectile dysfunction is associated with changes in the corpus cavernosum.[22] Nitric oxide is the main modulator of penile erection and relaxation of corporal smooth muscle.[5] In patients with newly diagnosed hypertension, the presence and severity of erectile dysfunction have been shown to be related to epicardial adipose tissue and carotid intima-media thickness, and left ventricular diastolic function is more affected in patients with erectile dysfunction.[45] Erectile dysfunction is more common in hypertensive patients with organic complications such as previous myocardial infarction, confirmed coronary artery disease, or stroke than in those without organic complications.[46] Hypertension and glucose dysregulation are common risk factors for vasculogenic erectile dysfunction, which is considered a clinical manifestation of generalized vascular disease.[47] In patients with heart failure, a relationship has been established between hypertension and heart disease; however, little is known about the relationship between hypertension and erectile dysfunction in these patients. One study showed that erectile dysfunction in patients with heart failure was negatively related to the number of years since the first diagnosis of hypertension. Sexual health is important in patients with heart failure, and more research is needed on the relationship between hypertension and erectile dysfunction in this population.[48]

Despite the prevalence of erectile dysfunction among hypertensive patients, erectile dysfunction is often not reported, recognized, or treated adequately. Lifestyle modification is the cornerstone of erectile dysfunction treatment in untreated hypertensive patients. In treated hypertensive patients, changing antihypertensive therapy should be considered unless the administered medications are absolutely indicated for the individual patient. Erectile dysfunction offers the opportunity to recognize asymptomatic cardiovascular diseases with evident benefits for the prevention of cardiovascular events. The main associated structural alterations include smooth muscle hypertrophy, stenotic lesions due to atherosclerosis, and altered blood flow, whereas functional abnormalities include endothelial dysfunction and defective nitric oxide-induced vasodilation.[49]

Hypertension as a Risk Factor for Erectile Dysfunction

Hypertension is a very common disorder that has been clinically correlated with a negative impact on sexual functioning in both men and women.[24] Specifically, hypertension has been closely linked to erectile dysfunction, with an OR of 1.74 and p-value <0.01. In addition, hypertension has also been identified as a risk factor for erectile dysfunction in different regions of the world, including Africa (OR = 3.35, p <0.01), America (OR = 1.97, p <0.01), Asia (OR = 1.46, p <0.01), and Europe (OR = 1.83, p <0.01). In fact, it is estimated that 67–68% of men with hypertension have some degree of erectile dysfunction. Therefore, it is important to perform a periodic and meticulous clinical evaluation of hypertension and personalized antihypertensive treatment to effectively treat patients with erectile dysfunction. Although hypertension is suggested to be a risk factor for erectile dysfunction, it is important to note that this association may be affected by different regions.[21]

Common Factors Between Hypertension and Sexual Dysfunction

Given that hypertension affects all vessels in the body, it is not surprising that it causes alterations in the structure and function of the penile vasculature. Erectile dysfunction and coronary artery disease have common risk factors such as aging, genetic susceptibility, hypertension, dyslipidemia, obesity, metabolic syndrome, and diabetes mellitus. Atherosclerosis is the most important structural anomaly that causes stenosis of blood flow. The penile arteries are smaller than the coronary arteries.[41]

Hypertension and erectile dysfunction are closely related physiopathologically, as they share common anomalies such as endothelial dysfunction and vessel stiffness. Vascular hardening, including penile vasculature, is probably the most important mechanism in erectile dysfunction and hypertension, especially during the aging process.[50] In recent decades, sexual dysfunction has emerged as an important predictor of cardiovascular risk. Patients with erectile dysfunction are more likely to have established coronary artery stenosis of >50%. Erectile dysfunction is related to the number of occluded vessels and occurs three years before coronary artery disease manifests. Hypertensive patients are twice as likely to experience erectile dysfunction than individuals with normal blood pressure levels. Unfortunately, erectile dysfunction often goes unreported, undetected, and untreated in this population. Nonetheless, erectile dysfunction can serve as an indicator of asymptomatic cardiovascular disease, offering the opportunity to identify relevant risk factors and potentially prevent the onset of cardiovascular disease.[15,49]

Physiopathology of Hypertension and Sexual Dysfunction

Within the penis, erection occurs through the relaxation of smooth muscle cells, facilitated by the release of neurotransmitters such as nitric oxide, which leads to vasodilation of the cavernous artery and helicine arterioles. This results in increased blood flow to the penis and compression of the venous plexus between the sinusoids and rigid tunica that covers the penis, trapping blood within the cavernous bodies. Endothelial nitric oxide release maintains erection, but smooth muscle dysfunction can disrupt venous outflow in later stages of erectile dysfunction.[1] Physiologically, cyclic guanosine monophosphate production leads to increased blood flow in penile tissue, resulting in erection. However, erection ends when the penile phosphodiesterase type 5 enzyme breaks down cyclic guanosine monophosphate into inactive guanosine monophosphate, stopping blood flow to the erectile tissue.[2]

Hypertension is associated with an increased risk of erectile dysfunction because the penis is a specialized vascular organ and an extension of the vascular system. These systems are similar in both embryonic development and physiology, so any disorder that affects the vascular system can also affect the penis and vice versa. Atherosclerosis can occur within the cavernous bodies of the penis, leading to a high vascular resistance and insufficient arterial flow. Long-term hypertension can also lead to endothelial dysfunction. Nitric oxide is crucial for arterial vasodilation and increased blood flow to the penis.[4] Therefore, erectile dysfunction in hypertensive patients may be an early sign of systemic vascular disease. Although little is known about the exact mechanisms of erectile dysfunction, it is known that the dysfunctional endothelium plays an important role in its development.[13,43]

The size of the arteries varies according to location, and the arteries of the penis are smaller than those of the coronary, carotid, and femoral arteries. Owing to the smaller size of the penile vasculature, the same burden of atherosclerotic plaque and endothelial dysfunction has a greater impact on blood flow. Erectile dysfunction in

hypertensive patients remains underestimated, under-recognized, and under-treated.[15] Chronic diseases such as systemic hypertension and hypertension drug therapy can contribute to sexual dysfunction. Heart disease can reduce libido and orgasm and increase complaints of vaginal dryness and dyspareunia in women. Hypertension can also affect the central modulation of sexual behavior and alter the autonomic nervous system. High blood pressure can worsen fibrosis in female genital tissue and cause damage to endothelial cells due to oxidation and inflammation related to hypertension.[11,27]

Symptoms of Sexual Dysfunction Associated with Hypertension in Women

It has been observed that hypertensive women frequently experience problems in achieving sexual satisfaction.[51] Furthermore, studies have shown that women with arterial hypertension have a lower frequency of orgasms and lower sexual satisfaction than normotensive women.[13] Arterial hypertension is associated with a high prevalence of sexual dysfunction in all aspects of the sexual function. In one study, the highest frequency was observed for desire and arousal (68.2%), followed by pain (56.1%), orgasm (55.4%), satisfaction (42%) and lubrication (41.4%). Women with arterial hypertension have a high prevalence of sexual dysfunction, especially in terms of difficulty with desire, arousal, and pain, although lower rates of problems with orgasm and sexual satisfaction have been reported. Additionally, according to a study conducted by Nascimento et al, women aged 18–29 with arterial hypertension experienced three times more pain during intercourse than women aged 50–59.[25]

Systemic arterial hypertension is harmful to health and can negatively affect female sexual responses owing to vascular changes caused by high blood pressure levels. Elevated blood pressure can cause a decrease in blood flow to the vagina and clitoris, leading to smooth muscle loss and development of fibrous tissue. Consequently, the clitoral cavernous arteries can harden and sclerose, which can interfere with the relaxation and dilation response during sexual stimulation, causing vaginal dryness and dyspareunia. Hypertensive women may experience fewer orgasms, more pain, and reduced vaginal lubrication than normotensive women.[3] Additionally, pulmonary hypertension can also affect various aspects of sexual dysfunction, such as lubrication, orgasm, sexual desire or interest, and pain.[11]

Association Between Antihypertensive Drugs and Sexual Dysfunction

Antihypertensive Treatment and Sexual Dysfunction

Erectile dysfunction is common in hypertensive patients, and its onset may be related to the intake of antihypertensive medications and other contributing factors.[2,52] Treated hypertensive patients are more likely to experience sexual dysfunction than untreated patients, suggesting a possible detrimental effect of antihypertensive treatment on erectile function.[15] Moreover, sexual dysfunction is considered secondary to the therapeutic efficacy of antihypertensive drugs.[9] A better understanding of the mechanisms and strategies for treating sexual dysfunction in patients is needed.[13] Medically induced erectile dysfunction can affect treatment adherence and negatively affect patient's long-term cardiovascular health.[25,38,49,50] It is important to consider the effects of different categories of antihypertensive drugs on sexual function when treating erectile dysfunction in hypertensive patients.[7,49] For example, beta-blockers can impair female sexual function, whereas angiotensin receptor blockers are beneficial for female sexual function. Blood pressure control is key when treating female sexual dysfunction in the presence of hypertension, and the administration of angiotensin receptor blockers is preferred.[27]

Although hypertension treatment can improve sexual function and overall quality of life, women receiving antihypertensive agents may experience sexual dysfunction as side effect of medication. In particular, first- and third-generation beta-blockers such as atenolol, metoprolol, or acebutolol may have adverse effects associated with sexual dysfunction. Available evidence is inconclusive on whether women taking different types of antihypertensive medications are more susceptible to sexual dysfunction.[24] Although the exact mechanism by which some antihypertensive drugs affect sexual function is unknown, some hypotheses include reduced libido due to sedation, decreased central sympathetic performance, disruption of vasodilation, and exacerbation of atherosclerosis due to hyperlipidemia and/or hyperglycemia.[27] Overall, it is important to select antihypertensive agents that are relatively safe for sexual function, especially in hypertensive patients with pre-existing sexual dysfunction.[7] Additionally, changing antihypertensive therapy

in treated hypertensive patients should be considered, unless the drugs administered are absolutely indicated for individual patients.[16]

Beta-Blockers and Erectile Dysfunction

High blood pressure and beta-blockers used to treat it can cause erectile dysfunction, according to a recent study.[53] Some antihypertensive medications include beta blockers, centrally acting alpha agonists, and thiazide diuretics.[4,34,41] Beta-blockers are widely used not only to treat hypertension but also to reduce mortality in patients with heart failure or a history of myocardial infarction. First-generation beta blockers are non-selective for beta receptors (eg, propranolol), whereas second-generation beta blockers are more selective for beta-1 receptors (eg, metoprolol and atenolol). Third-generation beta-blockers have beta-receptor blocking activity and additional vasodilating properties (eg, carvedilol, labetalol and nebivolol).[6] While there has been some debate regarding the relationship between beta-blockers and sexual dysfunction, current data indicate that older beta-blockers such as propranolol are more likely to cause sexual dysfunction,[7] while newer beta-blockers such as carvedilol and celiprolol have a lesser negative impact. However, nebivolol, a newer agent, significantly improves erectile dysfunction by increasing generation of nitric oxide.[49]

Beta blockers are commonly used in coronary artery bypass surgery. Although these medications have positive effects, they can also cause erectile dysfunction. The most commonly used drugs for ischemic heart disease are nebivolol and metoprolol. Third-generation beta-blocking agents, such as nebivolol, which have high selectivity for b1 adrenergic receptors, can help activate the nitric oxide system, leading to vasodilation and improved erection. Beta-blocking agents are particularly preferred for the treatment of hypertension and cardiovascular disease because of their antihypertensive, antiarrhythmic, and anti-ischemic properties.[5] However, metoprolol does not seem to have a significant effect on erectile dysfunction.[7] Although there are still no definitive studies on the effect of antihypertensive drugs on sexual dysfunction, diuretics and most beta-blockers have been shown to worsen erectile dysfunction.[26,52,54] Erectile dysfunction is an undesirable effect of antihypertensive treatment that is seldom discussed in consultation and can contribute to non-adherence to treatment.[54]

Nebivolol and Lower Erectile Dysfunction

Medications that promote NO release of nitric oxide can improve erectile function. Nebivolol is a third-generation beta-blocker that has recently been developed and is characterized by its high selectivity for adrenergic b1 receptors.[18] Beta-blockers, in general, have adverse effects on erectile dysfunction despite their antihypertensive, antiarrhythmic, and anti-ischemic properties.[5] However, nebivolol improves erectile function by increasing the bioavailability of nitric oxide.[41] This improvement is due to the ability of nebivolol to stimulate the endothelial release of nitric oxide, which leads to relaxation of the smooth muscle of the penile cavernous body, thereby allowing erection. Compared to other beta-blockers, nebivolol has an advantage in the treatment of hypertensive patients with erectile dysfunction owing to its unique mechanism of action. Limited studies have suggested that nebivolol does not worsen erectile dysfunction and may improve it in some cases.[6,54] Additionally, nebivolol does not appear to cause impotence, like other beta-blockers, because it does not decrease perfusion pressure, increases the expression of endothelial nitric oxide synthase, improves blood flow to the cavernous sinusoids, and decreases oxidative stress and collagen content in the penis.[15,50] Therefore, nebivolol may be advantageous in preserving sexual function in male patients with hypertension.[53] It is important to note that beta-blockers have additional disadvantages compared with other classes of antihypertensive medications, such as lower efficacy in preventing stroke, organ damage, and possible harmful effects on glucose metabolism when combined with diuretics. Nebivolol, the most cardioselective beta-blocker, exerts a synergistic effect with phosphodiesterase type 5 (PDE5-i) inhibitors in the treatment of erectile dysfunction, with reported beneficial effects on adherence.[50]

Other Antihypertensive Drugs and Sexual Dysfunction

Several studies have suggested that valsartan improves erectile dysfunction, orgasmic function, sexual desire, satisfaction, and frequency of sexual intercourse in patients with hypertension. In addition to its antihypertensive efficacy and organoprotective effects, the basic mechanism that leads to these effects is believed to be the inhibition of local angiotensin-converting enzyme, although other indirect mechanisms are also involved. Therefore, it can be concluded that valsartan is a good treatment option for patients with hypertension and erectile dysfunction, especially those with obesity and diabetes.[7,22,52] Other studies have shown that calcium channel blockers, angiotensin-converting enzyme

inhibitors, and angiotensin receptor blockers can also be good treatment options for hypertensive patients with erectile dysfunction.[4,34,41,51,52,54] However, some antihypertensive drugs, statins, diuretics, and antidiabetic drugs have also been found to cause erectile dysfunction.[5] With regard to combined therapy for overactive bladder and sexual dysfunction in young and middle-aged women, it has been demonstrated that both solifenacin monotherapy and combination therapy with solifenacin with doxazosin can improve severe symptoms, although the effects of solifenacin and doxazosin are superior to those of single use of solifenacin alone.[55] Furthermore, it has been discovered that herbal medicines, such as different species variants of ficus plants, can be a promising option in the management of numerous diseases, including hypertension and erectile dysfunction, owing their aphrodisiac and cardioprotective properties.[2]

Use of PDE5 Inhibitors to Improve Sexual Dysfunction

Since their introduction over a decade ago, PDE-5 inhibitors have revolutionized the treatment of sexual dysfunction. These drugs block the activity of the PDE-5 isoenzyme, which increases cyclic guanosine monophosphate levels, exerts vasodilatory properties, and facilitates penile erection. Sildenafil was the first drug of its kind to receive widespread acceptance due to its short half-life, food interactions, and associated visual disturbances, which has led to the development of new PDE-5 inhibitors, such as vardenafil, with a faster onset of action, and tadalafil, which has a longer half-life and no food interactions or side effects.[49] Although PDE-5 inhibitors are effective and safe in hypertensive patients with erectile dysfunction, they should be administered cautiously because of the risk of hypotension, especially with the co-administration of organic nitrates.[49] In addition, some PDE-5 inhibitors used to treat erectile dysfunction can affect blood pressure.[20] Sildenafil is an oral fast-absorbing drug for erectile dysfunction and pulmonary arterial hypertension that acts by inhibiting PDE5. Although the most important iatrogenic effect, it is very rare, it is associated with an increased risk of ischemic optic neuropathy and neurosensory hearing loss. The most common adverse effects of sildenafil are flushing and headache.[56] Tadalafil, a compound that selectively and reversibly inhibits cyclic guanosine monophosphate-specific phosphodiesterase type 5, can help prevent systolic hypertension and stroke, and is also used to treat erectile dysfunction and pulmonary arterial hypertension.[23] Phosphodiesterase-5 inhibitors (PDE5i), such as sildenafil, vardenafil, tadalafil, and avanafil, are considered the primary medical therapies for erectile dysfunction. Recently, sildenafil and tadalafil have been recommended as first-line therapies for patients with pulmonary hypertension. However, it is important to note that plasma concentrations of these drugs may increase when administered with cytochrome P (CYP) 3A inhibitors, which may increase the risk of side effects.[57,58]

Other Factors Associated with Sexual Dysfunction

Sexual function is constantly influenced by a series of factors that encompass both biological and psychological, social, economic, political, cultural, historical, legal, religious, and spiritual aspects.[11] The most relevant factors found in the scientific literature are described below.

Comorbidities

Sexual dysfunction in relation to hypertension and antihypertensive agents is complex because of the multiple interactive dynamics. Age, marital harmony, menopause, physical well-being, and other medical comorbidities such as dyslipidemia and diabetes mellitus may affect both female and male sexual functioning.[24,59] Additionally, hypertensive patients often have other comorbidities, such as depression, stress, anxiety, polypharmacy, smoking, obesity, and a sedentary lifestyle that can worsen aspects of their sexual health.[7,10] Erectile dysfunction is closely related to cardiovascular disease, obesity, diabetes mellitus, cirrhosis, and other chronic comorbidities.[27,60,61] Aging, obesity, metabolic syndrome, chronic comorbidities, and smoking are common risk factors for erectile dysfunction, hypertension, and cardiovascular diseases. Moreover, erectile dysfunction has been shown to cause the development of coronary artery disease and adverse cardiovascular events.[18]

Obesity in women increases sexual dysfunction,[3] whereas in men, there is a negative correlation between total testosterone levels and blood pressure.[12,62] Statistically significant links exist between the degree of obesity and arterial penile blood flow parameters as well as the severity of erectile dysfunction. The combination of overweight and obesity with hypertension suggests the presence of varying degrees of erectile dysfunction.[63] The combination of erectile

dysfunction with obesity and obstructive sleep apnea increases the risk of cardiovascular disease and their complications.[33,64] Additionally, there is a strong relationship between lower urinary tract symptoms and erectile dysfunction.[19] Microalbuminuria has been described as a marker of generalized vascular damage, and erectile dysfunction is more prevalent in hypertensive patients than in normotensive controls.[36] Sexual dysfunction is also found in populations with chronic diseases, such as chronic pain, fatigue, tremors, muscle rigidity, hormonal disorders, and sensory and motor changes. Women with hypertension who engage in physical exercise have better sexual dysfunction.[11] The sexual dysfunction is also observed in patients with gastrology-related diseases,[65] such as celiac disease.[66] It is also correlated with obstructive sleep apnea[67] or burning mouth syndrome.[68] The relationship between hypertension and heart failure has been previously reported, and heart failure is associated with a high prevalence of sexual dysfunction in both men and women.[29] Doxazosin or sildenafil as single drugs may be used to treat mild or mild-to-moderate symptoms, but more severe symptoms usually require a combination of both drugs to achieve patient satisfaction.[19]

Psychological Factors

Sexual satisfaction can be affected by different factors in people with chronic illnesses, such as anxiety, loss of self-esteem, sadness or depression. Additionally, some medications may generate side effects that negatively interfere with the sexual health of this population, especially in hypertensive women who also have sexual dysfunction, which is associated with significant levels of anxiety and depression.[25] Regarding the causes of sexual dysfunction, links have been found to be associated with anxiety, stress, and fear. It is common for people with these dysfunctions to present anxiety, and it has been shown that reducing anxiety can improve some aspects of these dysfunctions.[7]

Social Factors

Erectile dysfunction can be caused by various factors including age, lower education, unemployment, hypertension, diabetes, and depression.[7] Men with normal erectile function are usually younger, have higher education levels, lower blood pressure levels, and less frequently present depressive symptoms than men with erectile dysfunction. Additionally, men with higher education levels and socioeconomic status are less likely to develop erectile dysfunction because of their healthier behaviors and better economic income.[1] Worse socio-economic conditions are risk factors for the development of hypertension, and race, social class, and education level can influence its development. Aboriginal, Black, and Filipino people have a higher risk of hypertension than white people, and people with lower education levels have a higher risk of hypertension than those with higher education levels.[69] Hypertension is associated with a higher risk of erectile dysfunction after adjusting for obesity, unfavorable lipid levels, alcohol abuse, physical activity, smoking, education level, and other lifestyle-related factors.[4] Sexual dysfunction is more evident in hypertensive women who may experience a decrease in vaginal lubrication, reduction of orgasms, and increased pain during sexual intercourse.[13] Age, smoking, polypharmacy, and a long disease duration were significantly associated with erectile dysfunction. Other studies suggest that education does not seem to have a statistically significant association with erectile dysfunction,[42] although a low education level has been shown to be a risk factor associated with sexual pain.[25] In women with hypertension, sexual dysfunction and marital adjustment were negatively correlated. Hypertension can have a negative effect on sexual functioning problems and marital adjustment, but some women may accept this situation, for example if they are from an Islamic culture. People with sexual dysfunction often do not seek help because of shame or because it is considered a taboo topic.[16]

Lifestyle

Erectile dysfunction associated with hypertension can be treated with lifestyle modifications. Endothelial dysfunction is the main anomaly in erectile dysfunction, and risk factors such as obesity, decreased physical activity, smoking, hypertension, diabetes mellitus, and dyslipidemia have been associated with sexual dysfunction. Moderate physical activity can decrease the risk of erectile dysfunction by up to 30% compared to a sedentary lifestyle, whereas obesity increases the risk of erectile dysfunction by up to 30%.[41] Randomized clinical trials have shown that lifestyle modifications provide clinical benefits for improving erectile dysfunction. Adopting healthy lifestyle habits such as quitting smoking, maintaining a healthy weight, engaging in regular physical exercise, moderating alcohol consumption, and making dietary changes are effective ways to reduce hypertension, the risk of erectile dysfunction, and hypertension-related cardiovascular complications. The

Mediterranean diet is particularly useful for patients with erectile dysfunction and hypertension.[18] The combination of physical exercise and calorie restriction can result in weight loss, which in turn can reduce the risk of erectile dysfunction associated with obesity by up to 30%.[49] In addition, certain nutrients and foods may be beneficial for erectile dysfunction, such as folic acid, calcium, vitamins C and E, omega-3 fatty acids, chocolate, green tea, blueberries, and pomegranate. However, excessive alcohol consumption and obstructive sleep apnea syndrome are risk factors for erectile dysfunction.[36] Testosterone also plays an important role in erectile function, as sexual desire, arousal, and behavior are triggered by this hormone.[9] Studies in patients with erectile dysfunction show that people with decreasing levels of sexual desire have progressively lower hormone concentrations. Testosterone is also involved in the regulation of the expression and activity of endothelial and neuronal nitric oxide synthase enzyme expression and activity.[15] Therefore, lifestyle modification is an efficient and cost-effective treatment option for erectile dysfunction in patients with untreated hypertension. Lifestyle modification should be accompanied by pharmacological or psychological treatment in patients with erectile dysfunction associated with hypertension.[7]

Limitations

Studies on sexual dysfunction are scarce and could be related to the fact that it is a taboo topic. However, it is a health problem that affects both the society in general and the psychology of affected individuals. Although erectile dysfunction is not usually measured in research related to antihypertensive treatment, it is still unknown which antihypertensive drugs produce the most adverse effects on sexual dysfunction. Regarding women, no studies have measured the level or strength of decreased sexual function. There have also been no high-quality clinical trials studying the relationship between antihypertensive drugs and sexual dysfunction, and the studies available in the literature are observational studies with relatively small sample populations.

Although there is no consensus on the effect of antihypertensive drugs on sexual function and the available studies do not have optimal methodological quality and a lot of variability, it would be advisable to proactively evaluate erectile function before starting hypertension treatment and to periodically re-evaluate it. Erectile dysfunction may reveal ischemic heart disease or other atherosclerotic arteriopathies, degrade quality of life, and be responsible for poor compliance with antihypertensive treatments, which can affect the course of life of hypertensive patient. To the best of our knowledge, our study compiles all available information about the relationship between hypertension, antihypertensive drugs, and sexual dysfunction.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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References

1. Heikkila A, Kaipia A, Venermo M, Kautiainen H, Korhonen P. Relationship of blood pressure and erectile dysfunction in men without previously diagnosed hypertension. *J Sex Med*. 2017;14(11):1336–1341.
2. Ajeigbe OF, Oboh G, Ademosun AO. Ficus plants in the co-management of hypertension and erectile dysfunction. *Phytomedicine Plus*. 2021;1(3):100096. doi:10.1016/j.phyplu.2021.100096
3. Lunelli RP, Irigoyen MC, Goldmeier S. Hypertension as a risk factor for female sexual dysfunction: cross-sectional study. *Rev Bras Enferm*. 2018;71(5):2477–2482. doi:10.1590/0034-7167-2017-0259

4. Wang XY, Huang W, Zhang Y. Relation between hypertension and erectile dysfunction: a meta-analysis of cross-section studies. *Int J Impot Res*. 2018;30(3):141–146. doi:10.1038/s41443-018-0020-z
5. Gur O, Gurkan S, Yumun G, Turker P. The comparison of the effects of nebivolol and metoprolol on erectile dysfunction in the cases with coronary artery bypass surgery. *Anna Thorac Cardiovasc Surg*. 2017;23(2):91–95. doi:10.5761/atcs.oa.16-00242
6. Sharp RP, Gales BJ. Nebivolol versus other beta blockers in patients with hypertension and erectile dysfunction. *Ther Adv Urol*. 2017;9(2):59–63. doi:10.1177/1756287216685027
7. Salman M, Shehzadi N, Khan MT, et al. Erectile dysfunction: prevalence, risk factors and involvement of antihypertensive drugs intervention. *Trop J Pharm Res*. 2016;15(4):869–876. doi:10.4314/tjpr.v15i4.29
8. Ravikanth R. Diagnostic categorization of erectile dysfunction using duplex color Doppler ultrasonography and significance of phentolamine redosing in abolishing false diagnosis of venous leak impotence: a single center experience. *Indian J Radiol Imag*. 2020;30(3):344–353. doi:10.4103/ijri.IJRI_419_19
9. Altamar CMA, Torres OAC, Castillo CHM, Ramos SM, Barreto EI. Prevalence of comorbidities and risk factors associated with erectile dysfunction in hypertension patients in Cartagena HUC in 2013. *Urolog Colomb*. 2014;23(2):109–112. doi:10.1016/S0120-789X(14)50036-6
10. Rajfer J, Miner MM. Hypertension: the link between erectile dysfunction and coronary artery disease. *J Mens Health*. 2013;10(3):81–85. doi:10.1089/jomh.2013.1503
11. de Oliveira L, Chiavegato LD, Arakaki JSO, et al. Prevalence of sexual dysfunction in women with pulmonary hypertension and associated factors. *Heart Lung*. 2021;50(5):714–719. doi:10.1016/j.hrtlng.2021.04.018
12. Vintoniv OR, Popadynets IR, Hrodzinskyy VI, Melnyk SV, Herych PR, Halipchak IM. Algorithm of diagnostics of erectile dysfunction in patients with arterial hypertension and dynamics of arterial blood pressure against the background of androgenic deficiency. *Med Perspek*. 2021;26 (2):119–125. doi:10.26641/2307-0404.2021.2.234638
13. Santana LM, Perin L, Lunelli R, et al. Sexual dysfunction in women with hypertension: a systematic review and meta-analysis. *Curr Hypertens Rep*. 2019;21(3). doi:10.1007/s11906-019-0925-z
14. Ates I, Mutlu D, Kaya Z, Okutucu S, Sarier M, Cilingiroglu M. Relationship between masked arterial hypertension and erectile dysfunction. *J Mens Health*. 2020;16(SpecialIss):e4–12.
15. Viigimaa M, Vlachopoulos C, Doumas M, et al. Update of the position paper on arterial hypertension and erectile dysfunction. *J Hypertens*. 2020;38(7):1220–1234. doi:10.1097/HJH.0000000000002382
16. Ceyhan O, Ozen B, Simsek N, Dogan A. Sexuality and marital adjustment in women with hypertension in Turkey: how culture affects sex. *J Hum Hypertens*. 2019;33(5):378–384. doi:10.1038/s41371-019-0181-3
17. Liberati A, Altman DG and Tetzlaff J, et al. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol*, 62(10), e1–e34. doi:10.1016/j.jclinepi.2009.06.006
18. Wang TD, Lee CK, Chia YC, et al. Hypertension and erectile dysfunction: the role of endovascular therapy in Asia. *J Clin Hypertens*. 2021;23 (3):481–488. doi:10.1111/jch.14123
19. Abolyosr A, ElSagheer GA, Abdel-Kader MS, Hassan AM, Abou-Zeid AMM. Evaluation of the effect of sildenafil and/or doxazosin on Benign prostatic hyperplasia-related lower urinary tract symptoms and erectile dysfunction. *Urol Ann*. 2013;5(4):237–240. doi:10.4103/0974-7796.120293
20. Koroglu G, Kaya-Sezginer E, Yilmaz-Oral D, Gur S. Management of erectile dysfunction: an under-recognition of hypertension. *Curr Pharm Des*. 2018;24(30):3506–3519. doi:10.2174/1381612824666180828104350
21. Ning L, Yang L. Hypertension might be a risk factor for erectile dysfunction: a meta-analysis. *Andrologia*. 2017;49(4). doi:10.1111/and.12644
22. Babić Z. [The importance of valsartan in the treatment of hypertonic patients with erectile dysfunction]. Važnost valsartana u liječenju hipertoničara s erektilnom disfunkcijom. *Cardiol Croat*. 2015;10(11–12):290–294. doi:10.15836/ccar2015.290
23. Shin EY, Park JH, Shin ME, Song JE, Khang G. Formulation of double-layer tadalafil and amlodipine complex tablets to treat erectile dysfunction and hypertension. *Polymer-Korea*. 2019;43(2):274–281. doi:10.7317/pk.2019.43.2.274
24. Choy CL, Sidi H, Koon CS, et al. Systematic review and meta-analysis for sexual dysfunction in women with hypertension. *J Sex Med*. 2019;16 (7):1029–1048. doi:10.1016/j.jsxm.2019.04.007
25. Nascimento ER, Maia ACO, Nardi AE, Silva AC. Sexual dysfunction in arterial hypertension women: the role of depression and anxiety. *J Affect Disord*. 2015;181:96–100. doi:10.1016/j.jad.2015.03.050
26. Stavropoulos K, Imprialos K, Petidis K, et al. Female sexual dysfunction with diuretics in women with arterial hypertension. *J Hypertens*. 2018;36 (Supplement 1):e196. doi:10.1097/01.hjh.0000539543.01157.f5
27. Zhong Q, Anderson Y. Management of hypertension with female sexual dysfunction. *Medicina*. 2022;58:5.
28. Magfira N. 4-1 sexual dysfunction in women with hypertension: a cross-sectional study. *J Hypertens*. 2020;38(Supplement 1):e7. doi:10.1097/01.hjh.0000689184.98116.c2
29. Koutsampasopoulos K, Imprialos K, Stavropoulos K, et al. The relation of hypertension with female sexual dysfunction: the heart failure paradigm. *J Hypertens*. 2019;37(29). doi:10.1097/01.hjh.0000573072.90280.a7
30. De Franciscis P, Mainini G, Messalli EM, et al. Arterial hypertension and female sexual dysfunction in postmenopausal women. *Clin Exp Obstet Gynecol*. 2013;40:1.
31. Imprialos K, Stavropoulos K, Boutari C, et al. Prevalence of sexual dysfunction in females with resistant hypertension. *J Hypertens*. 2016;34:E174–E174. doi:10.1097/01.hjh.0000491819.57465.35
32. Yildirim U, Karakayali M, Uslu M, et al. Association between international index of erectile function-5 scores and circadian patterns of newly diagnosed hypertension in erectile dysfunction patients. *Andrologia*. 2022;54(11). doi:10.1111/and.14622
33. Alekseeva T, Mova EE, Starostin I, Gamidov S, Litvin A. Relationship between obstructive sleep apnoea and erectile dysfunction in patients with arterial hypertension. *J Hypertens*. 2018;36:28.
34. Arcila JFU. Prevalence of comorbidities and risk factors in hypertension patients associated with erectile dysfunction in Cartagena HUC in 2013 | prevalencia de comorbilidades y factores de riesgo asociados a disfuncion erectil en pacientes hipertensos del Hospital U. *Urolog Colomb*. 2014;23:2.
35. Kim SW, Jung J, Kim Y, et al. Efficacy and safety of fixed dose combination of amlodipine and tadalafil in both erectile dysfunction and hypertension patients being treated with amlodipine. *J Sex Med*. 2017;14(1):S29–30. doi:10.1016/j.jsxm.2016.11.065

36. Busari OA, Opadijo OG, Olarewaju TO, Oladosu YO. Male erectile dysfunction and microalbuminuria in adult Nigerians with essential hypertension. *N Am J Med Sci*. 2013;5(1):32–36. doi:10.4103/1947-2714.106191
37. Al Khaja KAJ, Sequeira RP, Alkhaja AK, Damanhori AHH. Antihypertensive drugs and male sexual dysfunction: a review of adult hypertension guideline recommendations. *J Cardiovasc Pharmacol Ther*. 2016;21(3):233–234. doi:10.1177/1074248415598321
38. Kakkavas A, Tsioufis C, Tsiachris D, et al. Erectile dysfunction and target organ damage in the early stages of hypertension. *J Clin Hypertens*. 2013;15(9):644–649. doi:10.1111/jch.12159
39. Boutari C, Imprialos KP, Stavropoulos K, et al. Prevalence and severity of erectile dysfunction in patients with resistant hypertension. *J Hypertens*. 2016;34:E259–E259. doi:10.1097/01.hjh.0000492091.81271.cf
40. Bouhanick B, Blacher J, Huyghe E, et al. Sexual dysfunction and antihypertensive treatment: involvement of the different therapeutic classes and what to do about the treatment of hypertension. *Pres Med*. 2019;48(11):1222–1228. doi:10.1016/j.lpm.2019.05.029
41. Boutari C, Doumas M, Manolis AJ. Approach to erectile dysfunction in patients with hypertension and coronary artery disease. *Hypert Cardiovasc Dis*. 2016;2016:309–327.
42. Satti RRUH, Rasheed SA, Gul R, Athar MH. Erectile dysfunction among patients with hypertension and associated socio-demographic factors. *Pakistan Armed Forces Med J*. 2022;72:S182–5.
43. De Oliveira AA, Nunes KP. Hypertension and erectile dysfunction: breaking down the challenges. *Am J Hypertens*. 2021;34(2):134–142. doi:10.1093/ajh/hpaa143
44. Ejike CECC, Eze KC, Okpan CE. Erectile dysfunction and hypertension among adult males in Umudike, Nigeria: a study of prevalence and relationships. *Asian J Sci Res*. 2015;8(3):315–323. doi:10.3923/ajsr.2015.315.323
45. Karakurt D, Ede H, Turan Y, Gurel A, Ardahanli I, Sarak T. Evaluation of the relationship between erectile dysfunction and epicardial fat tissue thickness and carotid intima-media thickness in patients with newly diagnosed hypertension. *Turk Kardiyol Dernegi Arsivi Archiv Turkish Soc Cardiol*. 2020;48:8.
46. Labudová M, Beňačka J, Zambojová I. Incidence and severity of erectile dysfunction in patients with hypertension. *Cardiology Letters*. 2021;30 (1):37–41. doi:10.4149/Cardiol_2021_1_7
47. Ioakeimidis N, Vlachopoulos C, Angelis A, et al. Arterial function and structure parameters are significantly impaired in pre-diabetic men with arterial hypertension and erectile dysfunction. *Eur Heart J*. 2018;39. doi:10.1093/eurheartj/ehy565.1158
48. Koutsampasopoulos K, Imprialos K, Stavropoulos K, et al. Hypertension and erectile dysfunction: new insights in heart failure patients. *J Hypertens*. 2019;37(29):e118. doi:10.1097/01.hjh.0000571536.94186.73
49. Viigimaa M, Vlachopoulos C, Lazaridis A, Doumas M. Management of erectile dysfunction in hypertension: tips and tricks. *World J Cardiol*. 2014;6(9):908–915. doi:10.4330/wjc.v6.i9.908
50. de Simone G, Mancusi C. Erectile dysfunction and arterial hypertension: still looking for a scapegoat. *Eur J Intern Med*. 2020;81:22–23. doi:10.1016/j.ejim.2020.09.004
51. Woznicka-Leskiewicz L, Posadzy-Malaczynska A. Sexual dysfunction in women with hypertension depending on the kind of antihypertensive therapy. *J Hypertens*. 2017;35:E60–1. doi:10.1097/01.hjh.0000523134.92900.53
52. Salobir B, Brguljan-Hitij J, Dolenc P, et al. Impact of valsartan and combination of valsartan and hydrochlorothiazide on erectile dysfunction in patients with mild to moderate hypertension. *J Hypertens*. 2016;34:E275–E275. doi:10.1097/01.hjh.0000492137.63346.75
53. Gungor G, Perk H, Soyupek S, Baykal B, Demir M, Sezer MT. Nebivolol protects erectile functions compared to Metoprolol in hypertensive men with atherogenic, venogenic, psychogenic erectile dysfunction: a prospective, randomized, cross-over, clinical trial. *Eur J Intern Med*. 2022;103:69–75. doi:10.1016/j.ejim.2022.06.013
54. Persu A. Sexuality and antihypertensive drugs. *Louv Med*. 2016;135(8):493–496.
55. Yangyun W, Xilong W, Guowei S, Jiayang H, Jun Z, Yanbin Z. Comparison of solifenacin monotherapy with solifenacin and doxazosin combination therapy for the treatment of severe overactive bladder with sexual dysfunction among youthful and middle-aged females. *Chin J Androl*. 2014;28(2):26–31.
56. Ala M, Mohammad Jafari R, Dehpour AR. Sildenafil beyond erectile dysfunction and pulmonary arterial hypertension: thinking about new indications. *Fundam Clin Pharmacol*. 2021;35(2):235–259. doi:10.1111/fcp.12633
57. Gur S, Kadowitz PJ, Gokce A, Sikka SC, Lokman U, Hellstrom WJG. Update on drug interactions with phosphodiesterase-5 inhibitors prescribed as first-line therapy for patients with erectile dysfunction or pulmonary hypertension. *Curr Drug Metab*. 2013;14(2):265–269.
58. Shkolyar E, Li SF, Tang J, Eisenberg ML. Risk of melanoma with phosphodiesterase type 5 inhibitor use among patients with erectile dysfunction, pulmonary hypertension, and lower urinary tract symptoms. *J Sex Med*. 2018;15(7):982–989. doi:10.1016/j.jsxm.2018.05.002
59. Diosdado-Figueiredo M, Balboa-Barreiro V, Pértega-Diaz S, Seoane-Pillado T, Pita-Fernández S, Chantada-Abal V. Erectile dysfunction in patients with arterial hypertension. Cardiovascular risk and impact on their quality of life. *Med Clin*. 2019;152(6):209–215. doi:10.1016/j.medcli.2018.05.022
60. Skeldon SC, Detsky AS, Goldenberg SL, Law MR. Erectile dysfunction and undiagnosed diabetes, hypertension, and hypercholesterolemia. *Ann Fam Med*. 2015;13(4):331–335. doi:10.1370/afm.1816
61. Paternostro R, Heinisch BB, Reiberger T, et al. Erectile dysfunction in cirrhosis is impacted by liver dysfunction, portal hypertension, diabetes and arterial hypertension. *Liver Internat*. 2018;38(8):1427–1436. doi:10.1111/liv.13704
62. Kratiras Z, Ioakeimidis N, Rokkas K, et al. Testosterone levels in erectile dysfunction patients with arterial hypertension and vascular organ damage. *J Sex Med*. 2016;13(5):S76–S76. doi:10.1016/j.jsxm.2016.03.007
63. Alekseeva TA, Shariya MA, Gamidov SI, et al. Interrelation of erectile dysfunction with obesity in patients with arterial hypertension. *Ter Arkh*. 2018;90(12):84–89. doi:10.26442/00403660.2018.12.000013
64. Alekseeva T, Litvin A, Gamidov S, Shariya M, Chazova I. Pericardial fat and erectile dysfunction in patients with obesity, obstructive sleep apnea and arterial hypertension. *J Hypertens*. 2019;37(29):e205–e206. doi:10.1097/01.hjh.0000572648.60915.37
65. Romano L, Zagari RM, Arcaniolo D, et al. Sexual dysfunction in gastroenterological patients: do gastroenterologists care enough? A nationwide survey from the Italian Society of Gastroenterology (SIGE). *Dig Liver Dis*. 2023;54(11):1494–1501. doi:10.1016/j.dld.2022.05.016
66. Romano L, Pellegrino R, Sciorio C, et al. Erectile and sexual dysfunction in male and female patients with celiac disease: a cross-sectional observational study. *Andrology*. 2023;10(5):910–918. doi:10.1111/andr.13186

67. Cantone E, Massanova M, Crocetto F, et al. The relationship between obstructive sleep apnoea and erectile dysfunction: an underdiagnosed link? A prospective cross-sectional study. *Andrologia*. 2023;54:9.
68. Leuci S, Coppola N, Adamo D, et al. Sexual desire, mood disorders and sleep disturbances in female BMS patients: a controlled study. *J Oral Pathol Med*. 2023;52(3):276–282. doi:10.1111/jop.13362
69. Veenstra G. Race, gender, class, sexuality (RGCS) and hypertension. *Soc Sci Med*. 2013;89:16–24. doi:10.1016/j.socscimed.2013.04.014