

## REVIEW



# Arterial Hypertension in Women: State of the Art and Knowledge Gaps

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**ABSTRACT:** Hypertension is the leading risk factor for cardiovascular disease and premature death among women globally. However, there is a fundamental lack of knowledge regarding the sex-specific pathophysiology of the condition. In addition, risk factors for hypertension and cardiovascular disease unique to women or female sex are insufficiently acknowledged in clinical guidelines. This review summarizes the existing evidence on women and female-specific risk factors and clinical management of hypertension, to identify critical knowledge gaps relevant to research, clinical practice, and women's heart health awareness. Female-specific risk factors relate not only to reproduction, such as the association of gynecological conditions, adverse pregnancy outcomes or menopause with hypertension, but also to the specific roles of women in society and science, such as gender differences in received medical care and the underrepresentation of women in both the science workforce and as participants in research, which contribute to the limited evidence-based, gender- or sex-specific recommendations. A key point is that the development of hypertension starts in young, premenopausal women, often in association with disorders of reproductive organs, and therefore needs to be managed early in life to prevent future cardiovascular disease. Considering the lower blood pressure levels at which cardiovascular disease occurs, thresholds for diagnosis and treatment of hypertension may need to be lower for women.

**Key Words:** cardiometabolic risk factors ■ cardiovascular disease ■ gynecological disease ■ hypertension ■ menopause ■ pregnancy ■ women

Hypertension is a key risk factor for cardiovascular morbidity and mortality in women. An estimated 600 million women worldwide are hypertensive, including hypertension during pregnancy, a leading contributor to maternal death.<sup>1–11</sup> Globally, hypertension is underdiagnosed and undertreated, with control rates as low as 23% among women with hypertension.<sup>11</sup> Thus, better prevention, detection, and treatment of hypertension in women are critical health care challenges.<sup>4–11</sup> Established risk factors for hypertension including unhealthy diet and life style, obesity, and aging are common among both men and women and well-recognized in clinical guidelines.<sup>1–3</sup> However, women or female-specific risk factors are understudied in basic, clinical, and population research and underrepresented in hypertension guidelines. These risk factors are related not only

to menarche, reproduction, menopause, and (the pharmacological use of) sex hormones but also to variation in access to and intensity of health care.<sup>4–9,12–24</sup> Women are assumed to be protected from hypertension and associated increased cardiovascular risk until menopause. However, recent sex-specific analyses suggest that blood pressure increases more rapidly among premenopausal women compared with aged-matched men, whereas control declines with aging.<sup>7,17–19,21</sup> In addition, thresholds for treatment initiation and management targets for lowering blood pressure and cardiovascular disease (CVD) risk may differ between sexes (see Box 1).<sup>23,24</sup> This review elaborates on these specific risk factors for hypertension in women and identifies knowledge gaps relevant for research, clinical practice, and population health.

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## Nonstandard Abbreviations and Acronyms

<b>ACE</b>	angiotensin-converting enzyme
<b>CVD</b>	cardiovascular disease
<b>HMOD</b>	hypertension-mediated organ damage
<b>PCOS</b>	polycystic ovary syndrome

## HYPERTENSION IN WOMEN: KEY POINTS

### Box 1

- Blood pressure trajectories during the life course of women are steeper than in men.
- Hypertension increases and control declines with aging in women.
- The association of blood pressure with poor CVD outcomes is stronger in women than in men.
- Women and gender-specific aspects of hypertension are understudied and the existing evidence is poorly translated into clinical guidelines.

## SCOPE AND METHODS

This article is a condensed version of the full review including methods and definitions provided in the [Supplemental Material](#). We present a narrative review of the existing literature on female-specific risk factors for hypertension. The clinical management of hypertension during pregnancy is beyond the scope of this review. All experimental research cited had been performed with the approval of an appropriate ethics committee in compliance with the Helsinki Declaration.

## EPIDEMIOLOGY OF HYPERTENSION IN WOMEN

Hypertension prevalence, detection, and control differ by sex or gender, age, ancestry, and geographical region.<sup>11,18,19,25,26</sup> Younger men tend to have higher mean blood pressure than aged-matched women, but from age 30 years onwards, blood pressure rises more steeply over time among women compared with men.<sup>18,19</sup> As a consequence, the prevalence of hypertension in aging women is higher than among age-matched men, with >40% of postmenopausal women developing hypertension, which is often poorly controlled.<sup>7–9,21</sup> As summarized in a recent global overview, the prevalence of hypertension among women and men aged 30 to 79 years was 32% and 34%, respectively.<sup>11</sup> Diagnosis, treatment, and control rates were 59%, 47%, and 23% in hypertensive women, and 49%, 38%, and 18% in hypertensive men.<sup>11</sup> Hypertension prevalence is highest and control rates are lowest in women of African ancestry.<sup>11,25,26</sup>

## PATHOPHYSIOLOGY OF HYPERTENSION IN WOMEN

Women tend to live longer than men, but experience more frailty and ill-health upon aging than their male counterparts.<sup>27</sup> Clinical observations on sex and gender differences in blood pressure,<sup>7,9,11–15,18,19</sup> hypertension-related organ damage, and CVD across the life course,<sup>17,23,24,28,29</sup> indicate that the pathophysiology of hypertension and CVD differs fundamentally between men and women. Indeed, this difference is further evident by the strong association of hypertension and CVD with disorders of female reproductive organs (see Box 2).<sup>6,12–16,28</sup> However, these differences are understudied, incompletely understood, and insufficiently translated into clinical guidelines.

### Woman-Specific Aspect of Traditional Risk Factors for Hypertension

There is ample evidence that unhealthy diet, insufficient physical activity, and cardiometabolic risk factors for CVD (eg, [central] obesity, insulin resistance, glucose intolerance and diabetes, inflammation, dyslipidemia, metabolic-associated fatty liver disease, obstructive sleep apnea, and hypertension) tend to cluster in both men and women. However, associations between blood pressure and other cardiometabolic factors are reported to be stronger in women, with potential aggravation related to menarche, gynecological disorders, reproduction, and (peri-) menopause.<sup>4,6–9,12–17,28</sup> In addition, women are more likely to have several conditions that are associated with increased risk of hypertension and CVD, including migraine and chronic inflammatory diseases such as rheumatoid arthritis and systemic lupus erythematosus.<sup>2,4,6</sup>

### Woman-Specific Pathophysiology of Hypertension

Women generally have a shorter stature and arterial tree, with smaller hearts and coronary vessels. A higher heart rate, lower cardiovascular contractility, and earlier reflected arterial pulse waves with augmentation of central systolic rather than diastolic blood pressure are thought to result in lower brachial and central diastolic blood pressures and more microvascular damage than in men.<sup>9,17,29–31</sup> Sex differences in autonomic neuronal hemodynamic regulation are understudied.<sup>9,17,29,31</sup>

Estrogens are cardioprotective, reduce cardiomyocyte oxidative, ischemic, and hypertensive stress and promote vasodilation in the peripheral vasculature and coronary arteries while inhibiting the development of atherosclerosis.<sup>32,33</sup> However, in older women and pharmacological doses, estrogen might have adverse effects on the vessel wall.<sup>34</sup> Lowering estrogen levels in aging women has been linked to increased sodium sensitivity.<sup>35</sup>

Hypertension, gynecological disorders, (central) obesity, and a wide range of other risk factors for CVD tend to cluster in women, including perturbations in the regulation of sex hormones, leptin and insulin resistance, sodium sensitivity, chronic inflammation, metabolic-associated fatty liver disease, sympathetic nervous system activation, and endothelial and neuroendocrine dysfunction.<sup>12,14,15,20,36,37</sup>

The neuroendocrine hormone leptin is thought to have a key role in obesity, regulating food intake, metabolism, and fat distribution.<sup>38</sup> It may in some instances be the link between female sex and increased cardiovascular risk. Leptin has been implied in the high prevalence of obesity in women with uterine fibroids or polycystic ovary syndrome (PCOS).<sup>39–41</sup> Furthermore, progesterone is reported to promote leptin-mediated endothelial dysfunction in obese premenopausal women through aldosterone and endothelial mineralocorticoid receptors.<sup>36</sup> This may further enhance sodium sensitivity in these women.<sup>42</sup> It was also suggested that the greater salt sensitivity observed in women is related to greater sensitivity to the cardiovascular effects of endogenous marinobufagenin, a steroidal Na<sup>+</sup>/K<sup>+</sup>-ATPase inhibitor and sodium-sensitivity biomarker.<sup>43</sup>

The “classical” renin angiotensin system (RAS; ie, angiotensin II, ACE [angiotensin-converting enzyme], angiotensin AT<sub>1</sub> receptors) may contribute to sex differences in hypertension because it has a higher activity in males, with potentially adverse cardiovascular effects including sympathetic activation, vasoconstriction, aldosterone release, and sodium retention.<sup>33</sup> In females, components of the protective arm of the RAS (ACE2, angiotensin 1–7, angiotensin AT<sub>2</sub> receptor, and receptor MAS) are more strongly expressed,<sup>33,44</sup> which opposes the effects of the AT<sub>1</sub> receptor and mediates vasodilation and diuresis/natriuresis.<sup>44</sup> Sex-discrepant effects of RAS activation on sodium retention and hypertension have only recently been studied, and the modifying effects of body composition, gynecological disorders, and menopause on this hormonal system remain largely unclear.

## PATHOPHYSIOLOGY OF HYPERTENSION IN WOMEN: KEY POINTS

### Box 2

- Obesity is strongly associated with hypertension in women.
- Gynecological disorders and adverse pregnancy outcomes are associated with cardiometabolic risk and hypertension in women.
- Physiological levels of estrogen are cardioprotective and promote vasodilation.
- Pharmacological use of estrogen may increase blood pressure and CVD risk.
- Progesterone promotes leptin-mediated endothelial dysfunction in obese premenopausal women.
- Sodium sensitivity is more pronounced in women.

- Greater occurrence of inflammatory disorders associated with hypertension and CVD in women.
- Greater expression of the protective arm of the RAS in females.
- Sex differences in neuronal hemodynamic regulation are understudied.

## Risk Factors for Hypertension Across the Life Course of Women

Factors associated with hypertension across the life course of women are summarized under Box 3 and the Figure.

### Uterine Fibroids

Between 10% and 30% of women of reproductive age are reported to have uterine leiomyomas or fibroids, with greater risk in women of sub-Saharan African ancestry.<sup>12,39</sup> Uterine fibroids are generally unrecognized in woman-specific overviews or clinical cardiovascular guidelines,<sup>1–4,6–9</sup> despite an independent association with (gestational) hypertension, cardiometabolic risk factors including obesity, hypertension-mediated organ damage (HMOD), and CVD.<sup>12,13,39,45</sup> A higher risk of CVD is observed with uterine fibroids even in the absence of clinical hypertension.<sup>12</sup> In line with this, extensive ultrastructural endothelial and myocyte abnormalities were reported in resistance arterioles of both normotensive and hypertensive young, premenopausal women with fibroids.<sup>45</sup>

### Polycystic Ovary Syndrome

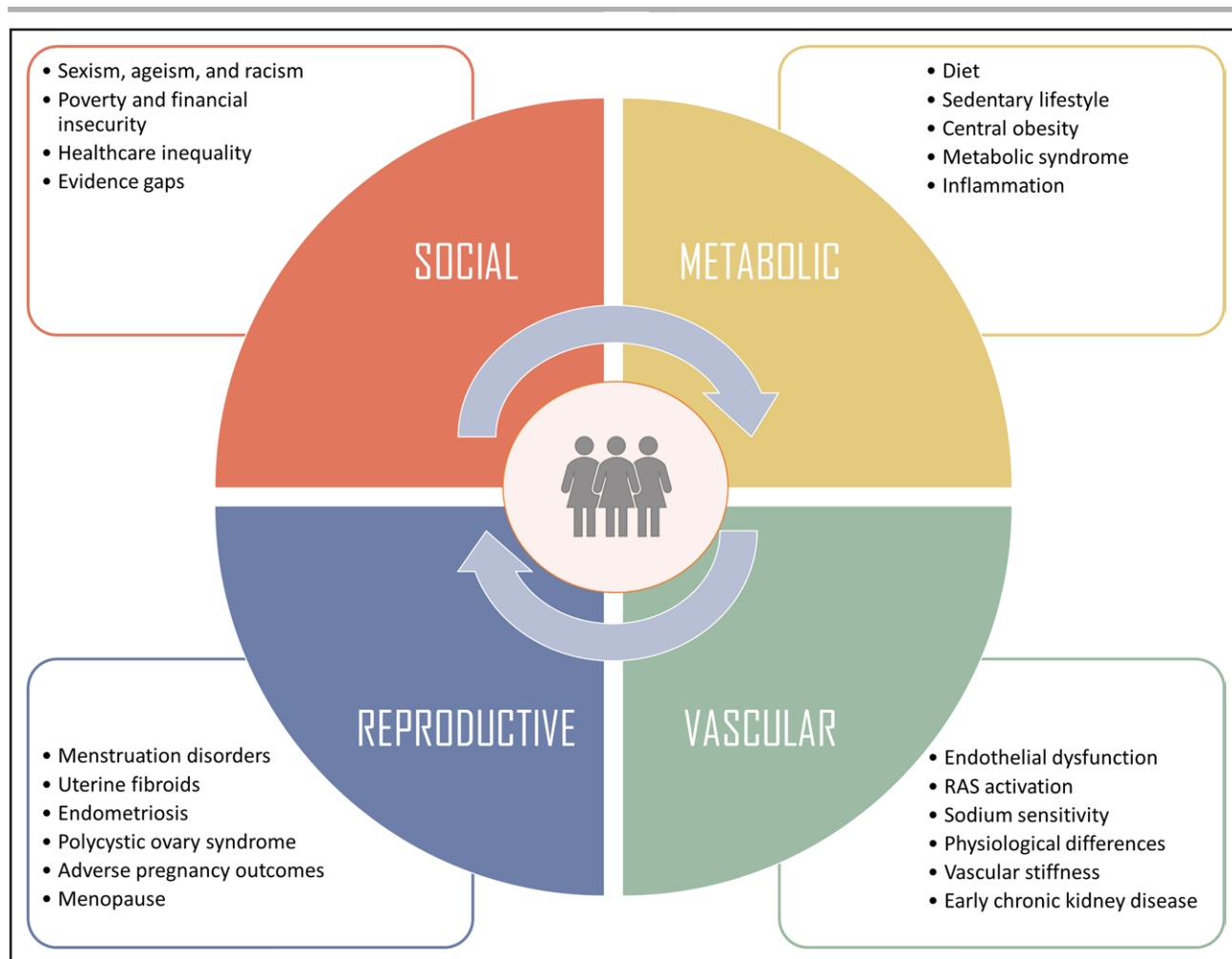
Hyperandrogenism is the clinical hallmark of PCOS, a complex syndrome with metabolic, reproductive, and psychological characteristics, with an estimated prevalence of 8% to 13%.<sup>14</sup> Women with PCOS may present with cardiometabolic disorders including obesity, insulin resistance, hyperglycemia, dyslipidemia, metabolic-associated fatty liver disease, hypertension, and gestational hypertension.<sup>14,15,41</sup>

### Endometriosis

Endometriosis is characterized by the presence of nonmalignant endometrium-like tissue (glands and/or stroma) outside the uterus that affects around 2% to 10% of women of childbearing age.<sup>46</sup> The condition induces chronic inflammation, chronic pelvic pain, dysmenorrhea, and reduced fertility and is associated with hypercholesterolemia, hypertension, hypertensive disorders of pregnancy, and increased CVD risk.<sup>46,47</sup>

### Fibromuscular Dysplasia

Diagnosed in 3% to 8% of women with hypertension, fibromuscular dysplasia is a female sex-predominant, non-atherosclerotic vascular disease characterized by abnormal



**Figure.** Hypertension among women has multiple sex-specific risk factors and management considerations.

RAS indicates renin angiotensin system.

cellular proliferation and distorted architecture of the tunica media or intima of medium-sized muscular arteries that may lead to renal artery stenosis with secondary hypertension, aneurysms, or other vascular abnormalities.<sup>48</sup>

### Menarche and Menstrual Disorders

Both early and late menarche have been associated with hypertension and other cardiometabolic risk factors leading to greater CVD risk.<sup>49</sup> Furthermore, women with menstrual disorders have a higher risk of developing hypertension. This includes heavy, painful, or irregular menstruations or premenstrual syndrome (somatic and psychological symptoms 1–2 weeks before menstruation).<sup>50,51</sup> Girls with Turner syndrome, the most common chromosomal abnormality in females, may present with menstrual disorders and hypertension at a young age.<sup>52</sup>

### Contraception, Reproduction, and Menopause

In pharmacological doses, estrogens may increase blood pressure and cardiometabolic risk, as well as the risk of

venous and arterial thromboembolic events, myocardial infarction, and stroke.<sup>2,28,34</sup>

Pregnancy is considered to be a cardiovascular stress test that might cause or reveal hypertension and CVD risk.<sup>13,16,28,53</sup> Importantly, adverse pregnancy outcomes (eg, complicated by gestational hypertension, preeclampsia, gestational diabetes, premature birth, low birth weight, and small for gestational-age newborns) may not only lead to increased maternal or child morbidity and mortality during the peri-pregnancy period but may also impact the future cardiovascular health of mother and child.<sup>16,28,53</sup> Indeed, family history of hypertension is associated with preeclampsia in women, whereas preeclampsia and gestational diabetes are associated with hypertension in the offspring.<sup>4,16</sup> Gynecological disorders such as uterine fibroids and PCOS are main risk factors for adverse pregnancy outcomes.<sup>13,14,46,47</sup> Greater prevalence of CVD has also been observed in other reproduction-related conditions, including nulliparous women, women with fertility problems, women who had never breastfed, and women experiencing early or premature menopause.<sup>16,54,55</sup> Cessation of ovarian function, whether through natural aging

or medical interventions, is known to be associated with increased cardiometabolic risk factor burden, including an increase in body mass, plasma glucose and cholesterol, and blood pressure, resulting in greater CVD risk.<sup>8,9,28,34,35,56</sup>

### Menopausal Hormone Therapy

Clinical guidelines agree on the (peri)-menopausal use of combined estrogen-progestin therapy (for women with an intact uterus, or estrogen use for women with a history of hysterectomy) with early menopause or premature ovarian insufficiency.<sup>28,56</sup> However, primary cardiovascular prevention with menopausal hormone therapy in healthy perimenopausal women is a matter of ongoing debate.<sup>28,34,56</sup> Current research is testing the so-called timing hypothesis, which suggests that menopausal hormone therapy has a beneficial effect on blood pressure and cardiovascular outcomes if initiated during a certain time window around menopause in women with risk factors, with a limited treatment duration of 5 to 10 years.<sup>28,56</sup>

### FEMALE-SPECIFIC RISK FACTORS FOR HYPERTENSION: KEY POINTS

#### Box 3

- Female-specific factors associated with hypertension and CVD later in life include timing of menarche, menstrual and fertility disorders, uterine fibroids, PCOS, endometriosis, adverse pregnancy outcomes, premature ovarian dysfunction, and menopause.
- Elevated risk during reproductive life could contribute to the perimenopausal or postmenopausal increase in CVD, with perhaps overlooked opportunities in younger women to prevent CVD.

### SEX DIFFERENCES IN HMOD

HMOD, the structural or functional changes in arteries or end organs in long-standing hypertension associated with increased CVD risk, include arterial stiffening, left ventricular hypertrophy, and chronic kidney disease.<sup>23</sup> A multitude of factors contribute to sex differences in HMOD and CVD, including hemodynamics, sodium sensitivity, sympathetic activity, classic vs protective RAS activation, and the decline of specific sex hormones with aging.<sup>7,9,17,18,20,28</sup> Earlier reflection of the propagated pressure wave along a generally shorter arterial tree in women is thought to promote arterial stiffening, a steeper rise in blood pressure with aging, and the development of concentric left ventricular hypertrophy.<sup>17,29</sup> The cardiovascular adaptation response to the increased afterload in women is associated with preserved ejection fraction.<sup>29</sup> Furthermore, the systolic amplification of the pressure wave in women is thought to lead to more advanced microvascular dysfunction,<sup>17,29,45</sup> implied as one

of the risk factors for chronic kidney disease<sup>29</sup> and cardiac disease (see Box 4).<sup>17</sup>

### HMOD AND CVD IN WOMEN: KEY POINTS

#### Box 4

- The cardiovascular adaptation response in women is associated with more advanced abnormalities of the microcirculation, and more chronic kidney disease, coronary microvascular dysfunction, and concentric left ventricular hypertrophy.
- Hypertension is a stronger risk factor for myocardial infarction, heart failure with preserved ejection fraction, stroke, cognitive decline, and lower extremity artery disease in women.
- Risk of CVD begins at  $\approx 10$  mmHg lower levels of brachial systolic blood pressure in women compared to men.

### CARDIOVASCULAR MORBIDITY AND MORTALITY IN WOMEN

Increased risk of myocardial infarction, heart failure, and stroke begins at around 10 mmHg lower brachial systolic blood pressure for women than for men.<sup>23,24</sup> Consequently, the proportion of potentially preventable cardiovascular events with proper risk management is higher for women than for men.<sup>57</sup> Hypertension is a major risk factor for coronary artery disease in women. Symptomatic ischemia but no obstructive coronary artery disease and myocardial infarction but no obstructive coronary artery disease are understudied manifestations of coronary microvascular dysfunction that occur more frequently in (younger) hypertensive women.<sup>6</sup>

Also, both heart failure with preserved ejection fraction (which occurs more frequently in women), and heart failure with reduced ejection fraction by current definitions are more strongly associated with hypertension as risk factor in women.<sup>6,58</sup>

Furthermore, migraine headaches with aura, the use of combined oral contraceptives, and preeclampsia are related to stroke risk,<sup>23,59</sup> and the association between hypertension and cognitive decline is stronger in women,<sup>60</sup> especially with a history of hypertensive disorders of pregnancy.<sup>61</sup> Finally, female sex is an independent risk factor for more severe lower extremity artery disease.<sup>62</sup>

### HEALTH SYSTEMS AND SOCIETY

The underrepresentation of (a diversity of) women in all aspects of biological research, as scientists and as participants, has hampered knowledge generation and translation in clinical guidelines.<sup>4,6,22,63,64</sup> Women also experience inequalities in healthcare access and delivery, as well as disregard of self-report symptoms.<sup>4,6,65,66</sup> Furthermore,



greater responsibilities as caregiver, lower literacy rates (in some settings), restricted mobility and finances, limited autonomy to act on health information, compounded with the consequences of sexism, racism, gendered ageism, abuse and violence, and general socioeconomic deprivation may create and sustain health disparities by sex and gender, with a greater impact on aging women and women of color.<sup>4,6,11,19,25,26,65</sup> Sex differences in environmental risk factors such as noise and air pollution have been incompletely studied,<sup>6</sup> but women of color more often live in a toxic environment, which might negatively impact blood pressure and reproductive and cardiovascular health.<sup>6,65,67</sup>

## MANAGEMENT OF HYPERTENSION IN WOMEN

### Clinical Practice Guidelines

There is a general paucity of data on specific antihypertensive drug therapy over the lifespan of women, regarding treatment thresholds, treatment goals, choice of drugs, and efficacy and adverse events.<sup>16,26,68–72</sup> Sex-neutral clinical practice guidelines<sup>1–3</sup> insufficiently acknowledge that clinical studies are often underpowered for women, such that “evidence creating” results could only be obtained for men or for both sexes together. Data particularly lack for specific subgroups, for example, pregnant women, women with gynecological disorders, women with a history of adverse pregnancy outcomes, women of color, and peri and postmenopausal women.<sup>16,26,69–71</sup> In addition, the higher cardiovascular risk with gynecological conditions and adverse pregnancy outcomes is absent from recommendations for history taking or currently used risk assessment tools, which tend to underestimate cardiovascular risk in women.<sup>1–3,16,23,68</sup> Moreover, women, especially women of color, less often receive the current, sex-neutral cardiovascular guideline-recommended care.<sup>4,6,9,65</sup> Finally, sex-specific blood pressure thresholds and treatment targets for hypertension have been suggested to improve CVD prevention in women,<sup>9,45</sup> but these are currently not incorporated in clinical practice guidelines. Below, we discuss women-specific aspects of hypertension management generally not specified in hypertension guidelines.<sup>1–3</sup>

### Women-Specific Aspects of Clinical Hypertension Management

#### History Taking

Aside general and cardiovascular history taking,<sup>1–3</sup> a history of gynecological disorders, fertility and childbirth history, and (adverse) pregnancy outcomes of the index person (and their mother and other family members) are relevant, as well as menopausal status and related symptoms and history of breast malignancy and treatment for these conditions.

### Clinical Examination

Blood pressure measurement and cardiovascular risk assessment should be offered to (peri-) menopausal as well as premenopausal women, particularly obese women, women with a history of gynecological disorders, women who wish to conceive, and women with a history of adverse pregnancy outcomes. Importantly, invasive intra-aortic systolic pressure was higher in women compared with men for the same noninvasive brachial systolic cuff blood pressure, suggesting that blood pressure–mediated CVD risk might be underestimated in women when brachial cuff blood pressure is measured.<sup>18,73,74</sup>

### Life Style Intervention

Exercise may be a less effective life style intervention to reduce obesity in women,<sup>75</sup> whereas the blood pressure–lowering effect of dietary sodium restriction is higher.<sup>20,42</sup> To control blood pressure, reduction of nonsteroidal anti-inflammatory drugs might be needed,<sup>2</sup> or replacement of oral contraceptives with other means of contraception,<sup>2</sup> especially in women with migraine.<sup>23,59</sup> Smoking should always be discouraged.

### Pharmacological Treatment

Lipid profile should be optimized, and abnormal glucose tolerance addressed.<sup>1–3</sup> Blood pressure lowering contributes most significantly to CVD reduction in women.<sup>6</sup> However, there are almost no specific treatment recommendations in clinical practice guidelines to manage hypertension in women,<sup>1–3</sup> including the greater hypertension and cardiovascular risk with uterine fibroids, PCOS, premenstrual syndrome, or adverse pregnancy outcomes.<sup>12,14–16,40,45,50,51</sup>

Earlier pharmacological therapy for women with stage 1 hypertension and a history of pregnancy-induced hypertension has been recently suggested.<sup>76</sup> Sparse data suggest that blood pressure lowering in women is greater with beta-adrenergic or calcium channel blockers,<sup>77</sup> but no consistent sex or gender differences in cardiovascular outcomes were observed.<sup>9,72,77</sup>

Furthermore, experimental evidence indicates that hypertensive women with obesity might benefit from aldosterone antagonists.<sup>36,42</sup> In women with PCOS, metformin or antiandrogens may be indicated, whereas spironolactone and RAS blockers are suggested antihypertensive drugs.<sup>71</sup> Metformin and RAS blockers have also been proposed for women with fibroids or a history of adverse pregnancy outcomes.<sup>16,70,78</sup> However, RAS blocker monotherapy might be less effective in women of African ancestry,<sup>69</sup> and these drugs are fetotoxic.<sup>1–3</sup> Finally, women tend to experience more adverse effects of antihypertensive drugs, probably due to understudied sex differences in pharmacokinetic or pharmacodynamic properties.<sup>77</sup> Data on sex differences in adherence are conflicting.<sup>21,77,79</sup>

### Other Interventions

Invasive procedures include surgery for cortisol-producing adrenal tumors, with unilateral primary aldosteronism occurring in younger women,<sup>2,80</sup> and renal denervation,

to which women with central obesity seem to respond better than other women or men.<sup>81</sup> Sex differences in the effect of baroreceptor pacing are understudied.<sup>82</sup> When uterine fibroids cause mechanical obstruction of pelvic ureters, removal of fibroids may improve blood pressure.<sup>83</sup> Hypertension with fibromuscular dysplasia and Turner syndrome requires multidisciplinary management.<sup>48,52</sup>

## SUMMARY AND IMPLICATIONS

This review provides a contemporary overview of the evidence on clinical, health system, and societal aspects of hypertension, the most deadly risk factor in women (see Box 5). The data indicate that women are characterized by a different, underrecognized, and understudied risk factor profile for hypertension and CVD.

Blood pressure increase and CVD risk accumulation start in young, premenopausal women and are closely linked to dysfunction of female reproductive organs. In addition, female sex-specific hemodynamic characteristics lead to early vascular stiffness, systolic hypertension, and microvascular damage with a different pattern of end-organ disease at lower brachial blood pressures than the current threshold for hypertension treatment. These aspects of the pathogenesis, diagnosis, and management of hypertension and hypertension-related CVD in women are insufficiently represented in science and hence in risk prediction models and hypertension guidelines.

## CARDIOVASCULAR HEALTH IN WOMEN: KEY POINTS

### Box 5

- Patient, provider, health system-level, and societal factors are implied in the blood pressure-related and cardiovascular outcomes in women.
- A healthy reproductive system is central to females' cardiovascular health, as well as that of their offspring.
- Earlier detection and better management of hypertension and cardiovascular risk factors in premenopausal women may not only increase their healthy life expectancy but also support women in having healthier pregnancies, thus reducing hypertension and CVD in future generations.

Gender-specific health system and societal factors such as women's position in society, their underrepresentation in the science workforce and clinical trials, and the compromised delivery of high-quality guideline-recommended healthcare add to suboptimal health outcomes among women.

There is sufficient evidence to propose a woman-specific research agenda that needs to assess how the interplay between biological, health system, socioeconomic, or other factors affects the risk of hypertension and CVD during the life course of women, not necessarily in

comparison with men or with men as the gold standard.<sup>4</sup> Major knowledge gaps include the nature of the association of gynecological disorders and adverse pregnancy outcomes with hypertension and CVD, woman-specific risk prediction models, optimal choice of antihypertensive drugs for women, and the thresholds for hypertension management, which should take the lower blood pressure level at which HMOD and CVD occur in women into account. Importantly, the timing of cardiovascular risk assessment during the life course of women should be addressed, as evidence indicates that interventions should not be delayed until the (peri)-menopause.

Furthermore, in a global effort, women should be empowered to govern their own cardiovascular health and made aware of the close link with reproductive health. A greater representation of women in medical education and the science workforce (including better access of women to leadership positions) and generous funding of women-specific research are needed to expand knowledge on and improve women's health.

Finally, awareness should be raised among physicians and healthcare providers that hypertension and CVD are leading causes of death in women, and are amplified by the intersection of age, ancestry, and socioeconomic vulnerability. Structural reforms, including multidisciplinary care by cardiovascular and obstetrics/gynecology specialists, are needed to reduce disparities in health by sex, gender, and ancestry and create equity and justice in health and health care for all women.

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