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A Clinical Prescription for Heart Health in Midlife Women

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Abstract

Cardiovascular disease is the leading cause of death in women throughout the United States and Europe. Despite efforts to raise awareness, the sex-specific risk factors are still poorly recognized in both regions, and many women do not identify cardiovascular disease as a primary threat. During midlife, the incidence of cardiovascular disease increases dramatically, and this unique time gives an opportunity to identify both traditional cardiovascular risk factors as well as emerging risk factors unique to women. This review will focus on the current guidelines for cardiovascular risk assessment in Europe and the United States, traditional and emerging cardiovascular risk factors, and preventive lifestyle recommendations for midlife women.

Keywords

Cardiovascular Disease; midlife; menopause; sex-based differences; risk assessment; prevention

Introduction

Heart disease remains the leading cause of death in women in Europe and the United States with the incidence increasing during midlife.¹ While one in thirty-one women will die from breast cancer, one in approximately two to three women will die from heart disease or stroke.¹² While most women are aware about traditional cardiovascular disease (CVD) risk

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Contributors

Chrisandra Shufelt was responsible for conceptualization of the review, funding acquisition, investigation, methodology, project administration and supervision, and produced the original draft of the review.

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factors, such as hypertension, dyslipidemia and diabetes, they are often unaware of sex specific risk factors that occur in midlife.³ Clinical risk factors can vary depending on the individual personal family history and can change as a woman ages. It is estimated that by midlife ninety percent of women have at least one risk factor for CVD; therefore, screening women during mid-life has substantial implications for primary CVD prevention.¹ This review will discuss CVD risk assessment tools, traditional and emerging CVD risk factors, diagnosis and screening guidelines, and lifestyle recommendations for midlife women.

CVD Risk Assessment in Midlife Women

In 2003, the European Society of Cardiology (ESC) published the Systematic Coronary Risk Evaluation (SCORE) system, a calculator that predicts the 10-year risk of both fatal and non-fatal coronary heart disease.⁴ This calculator was developed from 12 European cohort studies which included 88,080 women and 117,098 men examining the major CVD risk factors: gender, age, systolic blood pressure, total cholesterol and smoking status. Those at highest risk include men and women with documented CVD, diabetes mellitus, severe chronic kidney disease, and/or a SCORE greater than or equal to 10%. The differentiation between high, moderate and low-risk was predominantly dependent on SCORE results, highlighting traditional CVD risk factors in total CVD risk and mortality. The ESC guidelines recommend use of the risk estimator in asymptomatic individuals > 40 years of age without evidence of CVD, diabetes, chronic kidney disease, or familial hypercholesterolemia.⁴

In 2013, the American College of Cardiology (ACC) and American Heart Association (AHA) published guidelines on assessment of cardiovascular risk using the Atherosclerosis Cardiovascular Disease (ASCVD) risk calculator.⁵ This risk calculator considers age, gender, smoking status, total cholesterol, high-density lipoprotein, systolic blood pressure (SBP) and hypertension treatment to determine 10-year risk of CVD. The guidelines recommend assessing traditional risk factors in individuals that do not have CVD every 4–6 years in adults 20–79 years and to calculate the ASCVD risk calculator in those individuals every 4–6 years in adults ages 40–79 years.⁵

The SCORE system and the ASCVD risk calculator are validated and widely used. However, neither takes into account emerging risk factors seen in midlife women.⁶ ASCVD risk calculator is thought to often underestimate risk in women with novel risk factors such as inflammatory conditions. Such emerging risk factors must be taken into consideration when assessing a woman's cardiovascular risk.⁶ The ESC policy conference on CVD in women highlighted the underestimation of CVD risk in mid-life women and recommends tailoring risk assessment to risk factors relatively important for women, including diabetes and obesity.⁷

Traditional Risk Factors and Evaluation for Heart Health in Midlife women

Hypertension

Hypertension is the most frequent risk factor for CVD in women and studies have shown up to a 15% increase in CVD risk in women for every 10mm Hg increase in SBP.⁸ Prior to

menopause, women have lower blood pressure than age matched men, and by age 55 years, the prevalence is approximately equal with 54% of both men and women having hypertension.¹ After age 65, a relatively higher percentage of women have hypertension compared to men.¹

The increase in blood pressure in midlife women is multifactorial.^{9–11} Higher rates of comorbidities such as obesity, metabolic syndrome, and comorbid depression and anxiety play a role.⁹ However, the decline in estrogen is believed to play a key role in such age-related differences.¹² Estrogen promotes vasodilation via vascular smooth muscle cell relaxation and release of nitric oxide to lower blood pressure through the renin-angiotensin-aldosterone (RAAS) system.^{13,14} Animal studies have shown that estrogen directly regulates angiotensin I receptors by triggering binding proteins to bind cytosolic angiotensin I mRNA and inhibit expression.¹⁵ When there is a decrease or absence of estrogen, RAAS activity increases due to the lack of estrogen regulation.¹⁵ Estrogen has also been shown to reduce angiotensin converting enzyme mRNA concentrations in rats, thereby lowering ACE activity and subsequently blood pressure.¹⁶ There is evidence that estrogen/androgen ratios favoring higher levels of androgen activate RAAS as well as the sympathetic nervous system and vasoconstrictor eicosanoids.¹³

Salt sensitivity of blood pressure, referring to the response to dietary changes in salt intake, is an independent risk factor for CVD and may be attenuated by endogenous estrogen.¹⁷ Although menopausal women have higher rates of hypertension, the effects of exogenous estrogen use in the form combined oral contraceptive pills as well as oral hormone replacement therapy has found to increase risk of hypertension.¹⁸ Thus, the loss of estrogen alone may not explain higher prevalence of hypertension in the menopausal woman.

Recognizing and controlling high blood pressure is crucial for prevention of CVD. In August 2018, the European Society of Hypertension (ESH) and ESC jointly formulated new guidelines for treatment of hypertension.¹⁹ They define optimal blood pressure as systolic of less than 120 mm Hg and diastolic less than 80 mm Hg, normal blood pressure as systolic of 120–129 mm Hg and diastolic of 80–84 mm Hg. Other categories include high normal blood pressure as systolic of 130–139 mm Hg and/or diastolic of 85–89 mm Hg. Grade 1 hypertension is defined as systolic of 140–159 mm Hg and/or diastolic of 90–99 mm Hg. They recommend that all individuals above three years old should have their blood pressure measured at each office visit, with screening intervals depending on the blood pressure category. Women with optimal blood pressure should be screened every five years or less, and women with normal blood pressure should be screened at least every three years. Any woman with high normal blood pressure or worse should be screened annually. Both in-office and out-of-office measurements are recommended but diagnosis should be made after at least two in-office measurements on separate occasions. Once hypertension is diagnosed, women should undergo a thorough medical history that includes family history, lifestyle evaluation, and sex-specific risk factors such as history of pregnancy complications, oral contraceptive use, history of menopause and hormone replacement therapy use. Additional testing to evaluate for comorbidities: EKG, fasting metabolic panel with estimated GFR, fasting lipid panel, and urinalysis are recommended.¹⁹

In 2017, ACC and AHA released updated hypertension guidelines after the landmark Systolic Intervention Blood Pressure (SPRINT) trial.²⁰ Previously the Joint National Committee (JNC8) defined stage I hypertension as SBP >140 mm Hg and allowed for higher blood pressure in individuals <60 years.²¹ The SPRINT trial included 9,361 participants 50 years or older (mean age 69 years) with elevated CVD risk that were randomized to SBP target of <120 mm Hg or SBP target of <140 mm Hg. After a median follow-up of 3.3 years, the study found that the intensive blood pressure control to SBP <120 mm Hg lowered risk of myocardial infarction, acute coronary syndrome, stroke, congestive heart failure, or CVD death compared to standard treatment.²² Additional analysis of the SPRINT trial evaluated participants 75 years and older and found significantly lower rates of major CVD events and death with the intense treatment despite frailty status.²³ Consequently, the updated AHA guidelines redefined stage 1 hypertension as blood pressure >130/80 mmHg and does not have a separate category based on age.²⁰ The AHA recommends blood pressure checks at least each year if below 120/80 mm Hg, or more frequently if higher.²⁰

Dyslipidemia

Research demonstrates that as women transition to menopause, they develop adverse lipid profiles.^{24,25} In one cross-sectional study of 63,466 women evaluating CVD risk factors, total cholesterol and low-density lipoprotein cholesterol (LDL-C) levels were higher in women that entered menopause between age 46 and 55 years compared to premenopausal women in the same age range.²⁶ The Study of Women's Health Across the Nation, a longitudinal prospective study of 3,302 mid-life women, found LDL-C and triglyceride (TG) levels increase in the year prior to and year after the last menstrual cycle while high-density lipoprotein cholesterol (HDL-C) levels became stagnant.²⁷ Another review of 4,131 women found a worsening atherogenic profile with menopause to be independent of age, BMI, waist circumference and blood pressure.²⁸

Given the contribution of both age and menopause onset to lipid changes in midlife, ESC, in conjunction with the European Atherosclerosis Society, published updated guidelines in 2016 recommending lipid screening in women 50 years of age and older, or menopausal status.²⁹ Furthermore, all women with evidence of atherosclerosis or type 2 diabetes should be screened earlier. Women with a family history of premature CVD, hypertension, central obesity (defined as waist circumference > 80 cm), body mass index (BMI) > 25 kg/m², or autoimmune inflammatory conditions (such as rheumatoid arthritis, systemic lupus erythematosus, and psoriasis) and chronic kidney disease should also undergo early screening. No specific age recommendation is given. Screening lipid panel should include total cholesterol, LDL-C, TG, and HDL-C.²⁹

The ESC guidelines give Class IIa recommendations to screening for non-HDL-C and apolipoprotein B (Apo B), as well as lipoprotein(a) (Lp(a)).²⁹ Several studies have shown Apo B to be a strong predictor of CVD risk in midlife women and to correlate with non-HDL-C.^{30,31,32} Lp(a) serves as a marker of a prothrombotic state and has been found to be associated with increased CVD risk independent of LDL or non-HDL cholesterol levels.²⁹ Perhaps most importantly, elevated ApoB and Lp(a) are shown to have higher relative risk of CVD in women than men.²⁹

The 2013 AHA/ACC guidelines recommends a lipoprotein profile, measuring total cholesterol, HDL-C, and TG every 4–6 years in adults 20–79.³³ Non-fasting lipid measurements are considered sufficient to estimate initial risk for primary prevention. More frequent screening is recommended for those at elevated risk for CVD or stroke. The new guidelines no longer target cholesterol levels but focus on the 10-year ASCVD risk with the recommendations for treatment with statin therapy if ASCVD 10-year risk is ≥ 7.5% for primary prevention.³³ The AHA/ACC in 2013 states ApoB and LpA to be of uncertain benefit and no recommendation for or against it is made.³³

Diabetes

Diabetes mellitus type 2 causes nearly one in seven deaths in middle-aged women within Europe and in the United States.^{34,35} Diabetes prevalence increases in the midlife, yet the hormonal shifts that occur during menopause do not appear to be the main predictors of diabetes risk.^{36,37} Rather, the associated increase in visceral fat deposition and obesity adversely impacts insulin sensitivity and glucose metabolism.^{38,39} Increasing rates of depression and sleep disorders during midlife have also been found to contribute to poor glycemic control.³⁷

The most common cause of death for European women with diabetes is CVD.⁴⁰ Substantial evidence shows diabetes to pose a 45% higher CVD risk in women than men.^{41,42} In a meta-analysis of 37 prospective cohort studies the relative risk for fatal CVD associated with diabetes to be nearly doubled for women compared to men, independent of ethnicity.⁴³ This discordant CVD risk may be in part explained by the worse risk profile in women with diabetes although it remains largely unanswered.^{44,45} Importantly, the greater CVD burden in women from diabetes is seen during midlife with an average age of 54 years.⁴⁶

The ESC and European Association for the Study of Diabetes (EASD) use the American Diabetes Association (ADA) and World Health Organization glucometabolic classification.^{47–49} Diabetes is defined as hemoglobin A_{1c} ≥ 6.5%, fasting glucose ≥ 126 mg/dL or 2-hour glucose ≥ 200 mg/dL.⁴⁷ The EASD recommends the use of a diabetes risk score to determine which individuals need further screening, with the FiNish Diabetes Risk Score most frequently used in Europe.⁵⁰ This validated questionnaire predicts 10-year risk of Type 2 Diabetes with 85% accuracy and includes age, BMI, waist circumference, family history, level of fruit/vegetable intake and physical exercise.^{50,51} Guidelines recommend further screening with an oral glucose tolerance test or hemoglobin A_{1c} and fasting plasma glucose level in those individuals who have a high type 2 diabetes risk. However, women with known CVD should initially be screened with hemoglobin A_{1c} and fasting plasma glucose. If a woman is diagnosed with type 2 diabetes, screening for comorbid risk factors including high blood pressure, obesity, and dyslipidemia are recommended.⁴⁷

The 2013 ACC/AHA guidelines recommend screening adults ages 20–79 for traditional CVD risk factors, including diabetes. However, specific diagnostic criteria and screening methods are not discussed.⁵ In 2018, the ADA released updated standards of medical care for diabetes.⁴⁹ Evaluation of the general population should begin at age 45, at regular three-year intervals. Individuals at high risk should have early or more frequent screening, mainly those with family history of diabetes, overweight (BMI > 25 kg/m²), habitual physical

inactivity, of certain race/ethnicity (African-Americans, Hispanic-Americans, Native Americans, Asian-Americans, and Pacific Islanders), previously identified impaired fasting glucose or impaired glucose tolerance, hypertension, HDL-C ≤ 35 mg/dl (0.90 mmol/l) and/or a TG level ≥ 250 mg/dl (2.82 mmol/l), history of gestational diabetes, or polycystic ovary syndrome.⁴⁹

Family History of CVD

Both the ESC and AHA define family history of premature CVD as CVD in first-degree relatives, before age 65 years in a female relative and before the age of 55 years in a male relative.^{5,52} The ESC guidelines recommend consideration of family history when determining whether to screen for dyslipidemia as well as in determining CVD risk. The AHA guidelines for prevention of CVD in women emphasize consideration of family history of CVD in determining CVD risk.⁵ The Stockholm Heart Epidemiology Program constructed a validated genetic risk score including 28 genetic variants from a population of 24,124 participants from four Finnish cohorts.⁵³ The study found that family history of CVD is not only a risk factor for myocardial infarction but its effect is synergistic with traditional CVD risk factors. Results also found that adding genetic information and family history improved CVD risk prediction and resulted in 12% of subjects to be reclassified into high-risk category requiring treatment.⁵³

Tobacco/Nicotine Use

Europe has the highest global prevalence of tobacco consumption among adults and in 2017, the World Health Organization reported 15% of women above age 15 smoke tobacco in the European region.⁵⁴ Smoking poses a 25% greater CVD burden in females than in males, which may be in part due to the anti-estrogenic effects of tobacco.⁵⁵ Tobacco directly interferes with estrogen metabolism, and women who smoke begin menopause on average a year younger than non-smoking women.^{56,57} Both ESC and AHA consider tobacco use an established CVD risk factor and recommend counseling about tobacco use and tobacco cessation.^{5,52} Recently, electronic cigarettes also known as e-cigarettes have increased in popularity. These battery operated devices aerosolize the nicotine, flavors and other chemicals to be inhaled.⁵⁸ Research has suggested they are less harmful than traditional cigarettes, however they have been shown to increase oxidative stress and platelet aggregation, together leading to increased CVD risk.⁵⁹

Emerging Risk Factors and Evaluation for Heart Health in Midlife Women

Adverse Pregnancy Outcomes

Women with adverse health conditions during pregnancy, including gestational hypertension, preeclampsia, eclampsia, spontaneous preterm delivery and gestational diabetes have increased risk for CVD later in midlife and beyond.^{60–62} Pregnancy complications also increase risk of hypertension and diabetes, which are independent risk factor for CVD.^{63,64} While the underlying mechanism linking CVD to adverse pregnancy outcomes is unknown, it is believed that vascular dysfunction either preceding the pregnancy or at the time of placental implantation results in the subsequent increased CVD risk.⁶⁵ The ESC acknowledges the increased risk of CVD after obstetric complications and recommends

periodic monitoring for hypertension and diabetes in women with a history of eclampsia and/or pregnancy-induced hypertension.⁵² The risk has also been recognized by the AHA, which now recommends a pregnancy history in all women as initial evaluation of CVD risk.⁵

Inflammation / Autoimmune Disease

Inflammation play a key role in the progression of CVD directly contributing to plaque formation and plaque rupture.⁶⁶ T-cells, macrophages and mast cells contribute to development of an atheroma, and activation via inflammatory cytokines is shown to cause ischemia and infarction.⁶⁶ Research has examined the role of inflammatory biomarkers, such as C-reactive protein (CRP), tumor necrosis factor (TNF- α) and interleukin-6 (IL-6), as predictive tools for CVD.^{67,68} Compared to men, women have higher baseline CRP and in one study, after adjusting for CVD risk factors, BMI and estrogen use, a CRP level > 3 mg/l was more common in women.⁶⁹ The ESC Consensus statement on inflammation in atherosclerosis recognizes the connection between inflammation and CVD.²⁹ However, the ESC does not recommend routine assessment of circulating or urinary inflammatory biomarkers.²⁹ AHA recommends to consider checking CRP in those at intermediate risk defined as an ASCVD risk > 5%, although the benefits of such measurements remain unclear.⁵ Research demonstrates limited ability of additional inflammatory biomarkers to improve current risk classifications and the AHA does not recommend measuring them.⁵

Autoimmune diseases, more common in women, also contribute to the sex-specific risk factor consideration.⁷⁰ Conditions such as systemic lupus erythematosus, rheumatoid arthritis, psoriasis, and Sjogren's syndrome increase CVD risk as much as diabetes.⁷¹⁻⁷³ Furthermore, primary medications associated with the treatment for autoimmune diseases such as glucocorticoids and non-steroidal anti-inflammatory drugs can increase blood pressure, glucose and TG.⁷⁴ While traditional risk factors are more prevalent in patients with inflammatory autoimmune diseases, the greater CVD risk is attributed to the synergistic interaction between proinflammatory cytokines that accentuate CVD risk factors and contribute to accelerated atherosclerosis.⁷⁵ Therefore, traditional risk scores underestimate CVD risk in women with autoimmune conditions.⁷⁶ The European League against Rheumatism recommends an empirical multiplier of 1.5 to CVD risk scoring systems given the underestimated burden of CVD in such patients.⁷⁷ Neither the ESC nor AHA/ACC have established specific screening guidelines in this population.^{5,52}

Depression

Depressive disorders are more common in women and prevalence increases during the menopausal transition.⁷⁸ In midlife, a woman is four times more likely to display new onset depressive symptoms than when she was premenopausal.⁷⁹ Evidence suggests that a prior episode of depression is more predictive of a major depressive episode during perimenopause.⁸⁰ In previous decades, community based studies proposed that depressive symptoms during menopausal years were associated with physiological and psychosocial changes such as sleep disturbance and relationship or financial stress stress.^{81,82} The causative role of hormonal changes from menopausal transition on depressive symptoms is uncertain.^{83,84}

Screening for depression in midlife women is important due to the interplay between psychosocial and CVD health. Not only are patients with major depressive disorder at an increased risk for heart disease, but CVD patients with depression have more unfavorable outcomes including death, than patients without depression.^{85–87}

The 2016 ESC guidelines discuss depression in the larger context of psychosocial stress, and recommend two questions for those considered high risk for CVD: “do you feel down, depressed and hopeless?,” “have you lost interest and pleasure in life?”⁵² In 2008, the AHA published guidelines on Depression and Coronary Heart Disease recommending all patients with CVD should be screened with, at minimum, a 2-item patient health questionnaire (PHQ-2), which comprises two questions inquiring about mood and anhedonia. If a patient answers yes, a further screening instrument (PHQ-9) is used.⁸⁸

Cancer Treatments

Radiation and chemotherapy have been shown to directly increase risk of CVD.^{89–94} Radiation therapy leads to an increase in rate of ischemic heart disease that is proportional to the mean dose of radiation in gray units.^{93,94} Radiation-related heart disease also encompasses pericardial and myocardial fibrosis, and pericarditis.^{91,92} Anthracyclines, alkylating agents, such as cyclophosphamide, tyrosine kinase inhibitors, and monoclonal antibodies have variable effects on cardiac function.⁹⁰ For example, high rates of cardiotoxicity are associated with trastuzumab (Herceptin).⁸⁹ Specific recommendations were published in the UK regarding monitoring of cardiac function in patients treated with monoclonal antibodies.⁹⁵ Key recommendations include a baseline history and physical prior to initiation of chemotherapy and serial monitoring of left ventricular ejection fraction while on treatment.⁹⁵

The ESC developed a specific position statement for the cardiovascular side effects of cancer therapies which includes awareness of heart failure, close monitoring of cardiovascular function during treatment, along with the use simple biomarkers such as troponin and brain natriuretic peptides.⁹⁶ Recently, the AHA has developed a scientific statement to address the overlap of CVD and breast cancer.⁹⁷ This statement reviews common overlapping risk factors, chemotherapy agents that increase the risk for developing cardiac dysfunction, and recommendations for monitoring for CVD toxicity which includes imaging and the use of biomarkers.⁹⁷

Lifestyle Screening in Midlife

Lifestyle modification is considered the first-line therapy for reduction of all CVD risk factors. Such lifestyle practices encompass routine exercise, heart-healthy diet, maintaining a healthy weight and avoiding smoking as well as excessive alcohol consumption. In women, midlife provides a crucial period for healthcare providers to provide patient education and counseling about healthy lifestyle changes.

Exercise

Routine exercise is pivotal and recommended to reduce CVD and prolong life.⁹⁸ Exercise promotes weight loss, decreases plasma glucose concentration, raises insulin sensitivity,

lowers blood pressure, and enhances the lipid profile in women by increasing HDL-C and decreasing total cholesterol and LDL-C.⁹⁹ Furthermore, exercise promotes maintenance of muscle mass by increasing muscle strength and bone mass important for improving basal metabolic rate.¹⁰⁰ Exercise benefits not only physical but also mental health. Physical activity has proven beneficial in the management of depression in midlife women. While aerobic exercise is the cornerstone of cardiovascular prevention, other beneficial forms of exercise include deep breathing exercises, stretching activities, or yoga to manage stress and symptoms related to the onset of midlife.¹⁰⁰ Yoga specifically has been proven to reduce CVD risk by directly attenuating sympathetic response and lowering systolic and diastolic blood pressure, as well as improving lipid profiles and weight.¹⁰¹

Both the ESC and AHA recommend at least 150 minutes of moderate intensity exercise per week in women such as brisk walking, 75 minutes of vigorous exercise per week such as running as well as 2 days per week of muscle-strengthening activities¹⁰². Exercise strategy should be customized for each midlife woman, as it is important to develop a comprehensive exercise program suited to each woman's physical capabilities. For example, midlife women with orthopedic limitation may benefit from swimming as their form of aerobic exercise. Women should talk with their physicians before starting a new fitness program to plan the level of intensity of the program appropriate to suit their need.¹⁰³

Smoking Cessation

Smoking poses a greater CVD risk to women than men, and is the leading cause of CVD in women younger than 50 years old.^{104,105} In women, smoking also contributes to a range of malignancies, increases risk of fractures, and leads to hormonal dysregulation and chronic health conditions such lung disease, and diabetes.¹⁰⁶ The AHA and ESC advise using counseling, nicotine replacement, and/or other forms of smoking cessation therapy to help women quit smoking.^{52,102} In middle-aged women, smoking cessation immediately leads to a one-third decrease in excess risk of CVD.¹⁰⁷

While smoking cessation is a difficult task for many due to the nicotine addiction, fear of weight gain, or other psychosocial factors, it is imperative that midlife women refrain from smoking in order to benefit their overall health.¹⁰⁸ Vigorous exercise in combination with cognitive-behavioral programs is shown to improve smoking cessation.¹⁰⁹ If medication management is advised, it has been found that all commercially available forms of nicotine replacement therapy are effective in tobacco cessation.¹¹⁰ However, in women, varenicline is more effective than transdermal nicotine patches.¹¹¹ There is also strong evidence that use of bupropion in women results in smoking cessation.¹¹² E-cigarette use among midlife women is on the rise, yet varies according to smoking status.¹¹³

Alcohol Consumption

High levels of alcohol intake produce long term health risks including elevated blood pressure, heart disease, stroke, liver disease and increased risk for malignancies, as well as learning and memory problems.^{114–117} One-third of alcohol-attributable deaths are due to CVD events.¹⁰³ Alcohol consumption further impacts midlife women health by putting

women at risk for premature death, increasing the mortality rate. Moreover, alcoholics are more likely to be involved in accidents and also have a five-fold increased rate of suicide¹¹⁸.

Light-to-moderate drinking (1–2 drinks/day) at midlife is linked to successful aging, even reducing the risk of particular diseases including heart disease, diabetes, and cognitive decline when compared to heavy drinkers or abstainers.¹¹⁹ On the other hand, heavy drinking (≥ 3 drinks/day) or binge drinking, defined as four or more drinks at one time for women, harms health at midlife by causing liver damage, raising cancer risk, fractures, contributing to depression, and increasing fatal car accident risk.¹¹⁹ ESC recognizes the adverse CVD risk of more than three drinks per day and the AHA recommends no more than one drink of alcohol per day in women.^{52,102}

Weight Management

Menopause is responsible for increased visceral fat and may be responsible for increased rates of metabolic syndrome in midlife women. On average, the midlife woman gains 1.5 pounds (0.7 kg) per year regardless of race, ethnicity, and initial weight.¹²⁰ Obesity and metabolic syndrome have been shown to be associated with the incidence of coronary heart disease and heart failure in midlife women.¹²¹ Obesity contributes to CVD risk via negative impact on hemodynamics and cardiovascular structure as well as function through adipose tissue dysfunction and abnormal inflammatory pathways.¹²² The production of adipokines from abdominal fat leads to the development of metabolic abnormalities including resistance to insulin, hypertension, abnormal lipid profile, and abnormal fat distribution.¹²² Given the numerous health consequences of obesity, weight control and promotion of a healthy, balanced lifestyle should be promoted to prevent the prevalence of obesity.¹²³ ESC and AHA guidelines recommend BMI goal of 20–25 and waist circumference less than or equal to 80 cm in women.^{52,102} Proper diet and exercise are first-line treatment to lose weight.¹⁰² AHA recommends 60 minutes of aerobic exercise daily for weight loss.¹⁰²

Conclusion

Although strides have been made in women's heart health, CVD remains the leading cause of death in women in the United States and Europe.^{1,124} Incidence of CVD events rises dramatically during a woman's midlife, around 55 years, making menopause a unique time period during which preventative screening and measures can significantly reduce the risk of death.¹²⁵ Despite efforts to raise awareness, the differences in sex-based risk factors are still poorly recognized in both regions, and many women do not identify CVD as a primary threat. These mortality trends seem largely related to sex-based differences in diagnosis, prevention, and pathophysiology of traditional and emerging cardiovascular risk factors.¹⁰⁴ With the proper use of assessment tools, increased awareness of traditional and emerging risk factors, diligent screening and diagnoses, and tailored lifestyle modifications, risk of CVD in the midlife woman can be decreased.

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Highlights

- Cardiovascular disease is the leading cause of death in women throughout the United States and Europe.
- Midlife provides a crucial period for healthcare providers to provide patient education and counseling about healthy lifestyle changes.
- More recently identified risk factors for cardiovascular disease include adverse pregnancy outcomes, autoimmune disease, depression, and cancer treatments.

Table 1:

EU and US Screening Recommendations for Traditional CVD Risk Factors

Disease / Condition	EU Recommendation	US Recommendation
Hypertension	At every office visit in patients 3 years and older [*] (ESC)	Every 1–2 years in patients 20 years and older [*] (AHA)
Dyslipidemia	TC, LDL-C, TG, HDL-C, ApoB, Lp(a) in patients 50+ years or upon menopause [*] (ESC)	TC, HDL-C, TG every 4–6 years in patients 20–79 [*] (AHA/ACC)
Diabetes	Standardized questionnaire such as the (FiNnish) Diabetes Risk Score. Oral glucose tolerance or hemoglobin A1c and fasting glucose if at high risk for type 2 diabetes [*] (EASD)	Every 3 years in patients 45+years [*] (ADA)
Family History of CVD	Consider family history for dyslipidemia screening and CVD risk assessment (ESC)	Consider family history for CVD risk assessment (AHA)
Tobacco/Nicotine Consumption	Tobacco counseling and cessation therapy (ESC)	Tobacco counseling and cessation therapy (AHA)

^{*} More frequent screening is recommended if you have risk factors or family history

Table 2:

EU and US Hypertension Guidelines

	EU/ESC guidelines		US/AHA guidelines	
Category	Systolic (mmHg)	Diastolic (mm Hg)	Systolic (mm Hg)	Diastolic (mm Hg)
Normal	120–129	80–84	<120	<80
High Normal/Elevated	130–139	85–89	120–129	<80
Grade/Stage 1	140–159	90–99	130–139	80–89
Grade/Stage 2	160–179	100–109	140	90
Grade/Stage 3	>1180	>110		