

Diabetes and menopause: a special population and growing

As the number of menopausal women with diabetes increases, Ob/Gyns face new challenges in managing the risk of cardiovascular disease. Here, the author outlines options to treat this potentially dangerous duo.

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Females in the menopause are more vulnerable to developing diabetes, as it is well known that the incidence of the disease increases with age. Nowadays, diabetes is nearing epidemic proportions, due to an increased number of older Americans, and a greater prevalence of obesity and sedentary lifestyles. In fact, the number of women over the age of 45 with diabetes has increased 10-

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fold in the past century.^{1,2,3} As a result, more and more menopausal women with diabetes are presenting to their Ob/Gyn to help them manage this potentially dangerous duo.

It is difficult enough for a woman to weather the symptoms associated with menopause. Add diabetes to the list and she faces other, more pressing problems. While diabetic management and glycemic swings add to the difficulties of living with—and beyond—the menopause,

the combination presents a more important concern: cardiovascular disease (CVD). Lower levels of estrogen during and after menopause are thought to increase a woman's risk for CVD. This risk is increased 2- to 4-fold in women with diabetes. In fact,

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studies have shown that a menopausal woman with diabetes has a 75% chance of death from CVD, whereas a menopausal woman without diabetes has a 45% risk. In addition, patients with diabetes also may have other complications, including dyslipidemia, hypertension, and atherothrombotic changes, that can exacerbate coronary health risks.³

The good news is that there are preventive measures. Here, I will focus on 4 medical interventions that the Ob/Gyn can employ to lessen the chance of myocardial events in the menopausal woman with diabetes.

Determining risk factors

A menopausal woman with diabetes should be screened twice a year to assess her risk for cardiovascular disease (fixed and modifiable factors). Fixed risk factors include family history, age, and race. Evidence suggests that diabetes is more common in African-Americans, Latinos, Native Americans, Asian-Americans, and Pacific-Islanders, as well as the aged population. In addition, a woman's chance of a coronary event is more than doubled from age 40 to 50.⁴

The presence of fixed risk factors should alert physicians to check for modifiable risk factors such as high cholesterol, high blood pressure, smoking, and obesity (*Table 1*). In doing so, the clinician can then determine effective management strategies and/or proper chemoprophylaxis interventions.

It is clear that lifestyle changes offer considerable benefits to reducing the risk of CVD. Therefore, it is vital that the patient be counseled to quit smoking, incorporate a nutri-

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Prevalence of cardiovascular risk factors: women older than 40 with and without diabetes

TABLE 1

PERCENT REPORTING	DIABETES		NO DIABETES	
	40-59	≥60	40-59	≥60
High blood pressure	14.1	6.2	6.4	7.8
High cholesterol	16.1	14.2	9.8	9.9
Smoking	22.2	9.2	21.4	10.7

tious, low-fat diet into her daily routine and exercise for at least 30 minutes on most days. Unfortunately, complying with these directives can be difficult. Some women fear that if they quit smoking, they will gain weight. However, the benefits of not smoking are much greater than the risks associated with the expected weight gain.⁵ In fact, smoking cessation accounts for a 50% decrease in coronary heart disease-related events.

To increase compliance, it is important for Ob/Gyns to set goals with their patients, i.e., stop smoking within 3 months and exercise twice a week and build up to 4 days per week. These simple measures will go a long way toward minimizing the incidence of CVD.

Prophylaxis intervention

Hormone fluctuations during menopause may significantly alter blood glucose levels. With less progesterone, a woman with diabetes may have greater insulin sensitivity, but

with less estrogen, there is the chance of increased insulin resistance. Either way, this hormonal imbalance can lead to serious cardiovascular events.

Most prospective randomized controlled trials have studied the effects cardiovascular intervention has on men. However, some research confirming its benefits on women exists.⁶ In trials studying women, researchers noted the positive effects hormone replacement therapy (HRT), low-dose aspirin, angiotensin converting enzyme (ACE) inhibitors, and thiazolidinediones (TZDs) have in preventing CVD. The following is an assessment of the risks and benefits of each: **HRT.** Typically, menopausal women without diabetes take HRT for the treatment of vasomotor symptoms, urogenital maintenance, and the prevention of osteoporosis. For some women, HRT also may offer some cardiac protection and may help in the prevention of Alzheimer's disease. HRT confers a similar or

Health issues at menopause: additional effects of diabetes and cardiovascular disease

TABLE 2

REASONS FOR HRT IN WOMEN WITHOUT DIABETES	ADDITIONAL REASONS FOR HRT IN WOMEN WITH DIABETES
Cardiovascular protection	Greater benefit
Urogenital maintenance	Greater benefit
Cosmetic	Slightly more benefit
Osteoporosis prevention	Individual benefits
Symptom relief	Similar benefit
Prevention or delay of Alzheimers's disease	Possible greater benefit
REASONS AGAINST HRT IN WOMEN WITHOUT DIABETES	ADDITIONAL REASONS AGAINST HRT IN WOMEN WITH DIABETES
Breast cancer concern	Similar
Hassle and expense of pill	Similar or slightly greater
Worsening of hypertriglyceridemia	Greater

greater benefit to menopausal women with diabetes (*Table 2*).^{7,8,9} Why? Research indicates that HRT has a direct action on the vascular wall and improves lipid profiles, thereby maximizing cardiovascular protection in the menopausal patient with diabetes. Two caveats: Studies have shown that HRT use in women with diabetes may worsen hypertriglyceridemia, and women who have had a prior cardiac event are at a higher risk of a second after starting HRT.¹⁰ Also, women in general may have a greater chance of breast cancer when taking HRT.

More studies are needed to definitively answer whether or not HRT can play a primary or secondary role in the prevention of CVD. In the meantime, physicians may consider its use in patients with diabetes, but should not start HRT in women who have had a myocardial event in the past 6 to 12 months.

Low-dose aspirin. The American Diabetes Association (ADA) recommends 81 to 325 mg of aspirin a day for the prevention of adverse cardiovascular events associated with diabetes. In the past, there has been concern

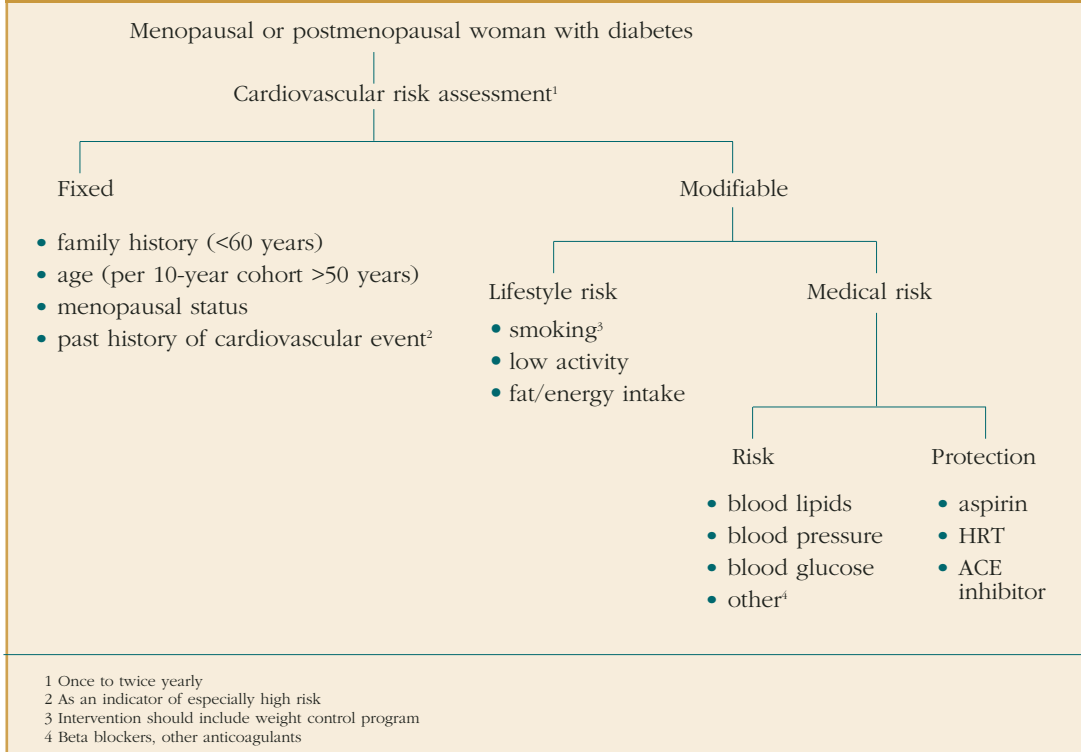
that low-dose aspirin increases the risk of retinal hemorrhage and interferes with the actions of oral hyperglycemic medications. Neither is true.

Studies on the prevention of diabetic retinopathy with aspirin have shown neither risk nor benefit with regard to retinal bleeding.¹¹ Further, only high-dose aspirin—more than 1,000 mg per day—increases the risk of hypoglycemia. Additionally, studies have shown that taking low-dose aspirin decreases the chance of myocardial events by 30%.¹² Therefore, menopausal women with or without diabetes may benefit from taking low-dose aspirin.

ACE inhibitors. The role of this agent is evolving. The Heart Outcomes Prevention Study (HOPE) examined whether the addition of an ACE inhibitor in 9,000 patients with vascular disease or diabetes could lower the risk of CVD. It showed that 10 mg of this agent administered over a 5-year period reduced the risk of myocardial infarction, stroke, or cardiovascular death.¹³ While women and their doctors may not wish to add yet another medication to a list that may include ther-

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Minimizing CVD in women with diabetes



apy for hyperglycemia, hypertension, dyslipidemia, and osteoporosis, ACE inhibitors are worth considering given their beneficial effects on the microvascular complications of diabetes including nephropathy, retinopathy, and neuropathy.

Thiazolidinediones. In addition to reducing insulin resistance, TZDs may have a direct effect on CVD risk factors. Studies have shown that TZDs reduce vascular intima-media thickness and promote vascular relaxation. Further, the use of this medication has been known to improve lipid profiles,

decrease triglycerides, and reduce the progression of atherogenesis.¹⁴ On the other hand, studies also have shown that TZD users may experience fluid retention, edema, and weight gain. In addition, physicians should observe patients for signs and symptoms of heart failure and discontinue if any deterioration in cardiac status occurs. Monitoring of liver function also is advised.

Conclusion

There are many opportunities to decrease the risk of CVD in menopausal women with diabetes who have no family history of CVD and a range of modifiable risk factors. On the other hand, options are limited for women with a strong family history of premature CVD with low-risk blood pressure and lipid profiles who cannot take HRT and who bleed with prophylactic anticoagulants. Women who fall under this category should still be advised to follow a low-fat, nutritious diet and exercise regularly.

Clearly, each woman will have varying risk factor profiles and priorities. Therefore, it is important that she be routinely screened during her menopausal years, and, if possible,

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Key points

- HRT use in women with diabetes may worsen hypertriglyceridemia.
- The American Diabetes Association (ADA) recommends 81 to 325 mg of aspirin a day for the prevention of adverse cardiovascular events associated with diabetes.
- A menopausal woman with diabetes has a 75% chance of death from cardiovascular disease, whereas a menopausal woman without diabetes has a 45% risk.

Cardiovascular interventions in menopause

FALLACIES	FACTS
HRT	
HRT makes you fat HRT causes high blood pressure HRT worsens insulin resistance	If anything, HRT is associated with a small decrease in weight, blood pressure, and insulin resistance and with a healthier gynecoid (“pear”) fat distribution
HRT increases the risk of cardiovascular events	HRT halves the cardiovascular event rate
Alternative therapies (e.g., plant phytoestrogens, evening primrose oil) are effective and safe substitutes for HRT	There is no evidence of the benefit of alternative therapies in the menopause; in fact, placebo therapy reduces symptoms in 30% to 50% of postmenopausal women. Further, the formulations of most preparations are not regulated, and the unopposed estrogen activity of phytoestrogens may increase the risk of endometrial cancer
SMOKING CESSATION	
Weight gain feared	The benefits of cardiovascular risk reduction greatly exceed the risks associated with weight gain, which is common but not inevitable
LOW-DOSE ASPIRIN	
Increased risk of retinal hemorrhage	No increased risk found in clinical trials
Interference with oral hyperglycemic agents (sulfonylureas)	No adverse interactions found in clinical trials

when she is perimenopausal.

While there are no definitive studies that compare cardiovascular risk factor intervention in women with diabetes to those without, at the very least, patients should be advised to quit smoking, follow a low-fat diet with exercise, and take HRT and low-dose aspirin. This strategy will go a long way toward reducing the impact of serious heart conditions in menopausal women with diabetes. ■

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