PEER REVIEWED

A woman with diabetes and heart disease

VIVIENNE MILLER MB BS, FRACGP, DRACOG, DCH, MACPM, MWAME

This section is about the immediate management and investigation of an acute presentation in general practice. It is inspired by, but not based on, a real patient situation.

Christa is a 68-year-old woman well known to you. She weighs 72 kg and is tall, with a BMI of 26 kg/m². She has had well-controlled type 2 diabetes for 18 years and takes metformin extended-release 1 g at night and gliclazide sustained-released 60 mg in the morning. Occasionally, her self-monitored blood glucose levels before breakfast are 3.5 to 4.0 mmol/L. She had gestational diabetes and pregnancy-induced hypertension with her only child 24 years ago. Her menopause was at age 47 years.

Christa was diagnosed with systemic lupus erythematosus (SLE) 16 years ago but this is well controlled with 5 mg prednisone daily (she could not tolerate methotrexate). She also takes atorvastatin 20 mg daily. Her blood pressure has for some years been at or under 140/80 mmHg while taking perindopril 5 mg daily. She has never smoked and she drinks alcohol socially. She is a retired librarian and is fairly inactive apart from occasional gardening. She wants to see you today to discuss the results of some recent tests and is now particularly concerned about her risk of heart disease. Her brother, aged 72 years, has just had a coronary stent inserted for unstable angina. He did not have diabetes.

What risk factors does Christa have in her medical history for cardiovascular disease?

Answer: She has had longstanding diabetes without symptomatic hypoglycaemia, she is post-menopausal (the risk of cardiovascular disease in women rises significantly after menopause), she has SLE (this increases inflammatory proteins contributing to cardiovascular disease), she is taking prednisone (this will impair her blood glucose and cholesterol metabolism) and she has a family history of a first-degree relative, of a similar age, who has had ischaemic heart disease. It should be noted that Christa has a distant history of pregnancy-induced hypertension and so she is at increased risk of later hypertension and its complications.

You review Christa's recent results. Her total cholesterol level is 4.6 mmol/L (suggested under 4.0 mmol/L), her high-density lipoprotein cholesterol (HDL-C) level is 1.3 mmol/L (suggested over 1.0 mmol/L), her low-density lipoprotein cholesterol (LDL-C) level is 2.5 mmol/L (suggested normal at or under 2.5 mmol/L) and her triglyceride level is 1.6 mmol/L (suggested normal range under 1.7 mmol/L). Her creatine kinase level is normal at 120 µmol/L. Her fasting blood glucose level is 6.7 mmol/L (suggested under 5.5 mmol/L without hypoglycaemia) and her latest HbA_{1c} is 6.8% or 51 mmol/mol (generic target is under 7.0% or 53 mmol/mol). Her thyroid function, full blood count, liver function tests, and urea, creatinine and electrolytes levels are all normal. Her vitamin B_{12} is 200 nmol/L (normal range 150 to 600 nmol/L) and her antinuclear antibody is moderately positive at 1:750 (over 1:1250 is defined as 'high'). Her C-reactive protein level is 6.8 mg/L (normal under 5.0 mg/L).

What do you tell Christa about her results specifically relating to her concern about heart disease?

Answer: Her LDL-C level has been fairly well controlled at 2.5 mmol/L, but is not optimal as it should be under 2.0 mmol/L given she has diabetes. There is evidence that tight LDL-C control may even over time reverse atheromatous deposits. Her total cholesterol level is at 4.6 mmol/L but should be under 4.0 mmol/L. Her HDL-C level is not low. If she has already reduced her saturated fat intake appropriately (less than 15 g daily) it might be wise to increase her atorvastatin to 40 mg daily. There is no

ENDOCRINOLOGY TODAY 2015; 4(1): 47-48

Dr Miller is a GP in Sydney, medical journalist and author.

Practice points

- C-reactive protein test is better used as an aid to the investigation and management of acute or chronic inflammation or infection rather than as an aid to assessing the risk of ischaemic heart disease.
- It is unwise to simply reassure any patient who has specific and reasonable serious concerns about their health.
- There is no premenopausal protection from ischaemic heart disease if the patient has diabetes.
- Ischaemic heart disease can be silent or atypical in presentation, especially in women with diabetes.

contraindication to raising the atorvastatin dose as she has a normal creatine kinase level and no significant rise in her liver function tests. A quick review of her past cholesterol readings will give a more accurate assessment of her cholesterol control over time.

Her diabetes control is good and her medications need no change. You may still want to ask her if she would like to see a dietitian and diabetes educator. This is advised annually or at least every two years to ensure patients are up to date with current self-care advice. There is evidence that patient recall of dietary management and diabetes self-care may be improved with regular review.

She could complement office blood pressure readings with home readings and ambulatory blood pressure measures, aiming for less than 130/80 mmHg generally; there should be a low threshold for maximising the dose of perindopril to 10 mg daily.

What other general comments would you make about Christa's results?

Answer: Her vitamin B_{12} is at the lower end of normal and she may benefit from a check of her active vitamin B_{12} level and then, as indicated, a course of injections to replenish the levels. If Christa has low vitamin B_{12} levels then pernicious anaemia should be excluded (by antibody testing of antigastric parietal cell and anti-intrinsic factor). However, a low vitamin B_{12} level is probably due to malabsorption of the vitamin from the small bowel and is associated with taking metformin for years. Her full blood count, general kidney function and thyroid function are normal.

If she has not had an urinary albumin to creatinine ratio assessed in the past year this should be determined (from an early morning sample of urine, ideally midstream, after a shower). If this cannot be easily achieved by Christa the collection may be carried out later in the morning and the test repeated as instructed if abnormal. The urinary albumin to creatinine ratio is an important additional screening test for assessing kidney damage because both longstanding diabetes and SLE can cause albuminuria and proteinuria. Her SLE control is symptomatically good and this is the main reason for continued treatment with low-dose prednisone, despite her later development of diabetes. However, her antinuclear antibody level is still elevated and this suggests that even in the absence of symptoms she is not in complete remission. If she develops any unusual symptoms (especially aches, rashes, arthralgia, unusual fatigue or unexplained abnormalities on blood tests), a flare up of SLE should be considered.

Is measuring the C-reactive protein level of any use in the assessment of cardiovascular risk in the general population?

Answer: The routine measurement of the C-reactive protein to assist in the assessment of cardiovascular risk is controversial. In the case of Christa, it is of little value for this purpose due to the presence of chronic inflammatory disease. It is, however, of use as an aid to the investigation and management of acute or chronic inflammation or infection. Having active SLE already conveys an increased risk of cardiovascular disease for Christa, and the C-reactive protein measurements may be used in the monitoring of her disease activity.

Is it reasonable to reassure Christa regarding her concerns in light of her recent results and risk factors?

Answer: Christa has a number of risk factors for cardiovascular disease and these have been fairly well managed on the basis of recent test results. However, it is unwise to simply reassure any patient who has specific and reasonable concerns about their health, especially when they make direct requests for assessment. Modern medicine is turning more towards prevention, and Christa's case is a good example. There is an erroneous idea held by some that women tend not to develop heart disease to the same severity as men and hence risk factors in women may be overlooked. Ischaemic heart disease can be silent or atypical in presentation, especially in women with diabetes. There is also no premenopausal protection from ischaemic heart disease if the patient has diabetes.

What do you advise next?

Answer: It would be wise to order a resting ECG and to refer Christa to a cardiologist. If the ECG were normal, the cardiologist would likely arrange at least a stress echocardiography, plus further testing depending on the result. This is also a good opportunity to arrange a chronic diseases management plan for Christa's diabetes review and encourage her to have annual eye examinations, a bone density measurement and dental and podiatry care, in addition to seeing a dietitian and diabetes educator. If the cardiologist is happy with the results of the stress echocardiography, daily regular exercise should also be encouraged. This should be of moderate or greater intensity, commencing with at least 30 minutes three to four times per week and increasing as tolerated to ideally an hour daily.

Outcome: **Christa had a resting ECG performed and a cardiologist was consulted. The ECG showed a left anterior hemiblock and the cardiac echocardiogram suggested mild impairment of left ventricle contraction (with borderline normal ejection fraction). A stress echocardiography was not performed. Christa had an angiogram and this showed a 90% stenosis of her left anterior descending artery, which was successfully stented, in preference to a coronary artery bypass graft. She also had widespread but milder coronary atheromatous disease elsewhere. Her resting and stress cardiac echocardiograms were normal post-stenting. She is currently now also taking clopidogrel 75 mg and aspirin 100 mg daily. She elected to change her blood glucose therapy to a dipeptidyl peptidase-4 inhibitor (sitagliptin) rather than the gliclazide, to help minimise the risk of hypoglycaemia. Her statin therapy was intensified, aiming for a LDL-C level of below 1.8 mmol/L.** ET