



Management of Cardiovascular Risk Factors After Stem Cell Transplant

These recommendations were developed by the Stem Cell Transplant Survivorship Community of Practice, under the direction of Cancer Care Ontario's Stem Cell Transplant Advisory Committee.

Introduction

Survivors of stem cell transplantation (SCT, also known as hematopoietic cell therapy [HCT]) have a life expectancy that is 30% lower than the general population at 5 years post-SCT (1) with cardiovascular disease (CVD) being one of the leading causes of non-relapse mortality (2,3). Compared to the general population, SCT survivors have two-times the risk of developing conventional CVD risk factors such as hypertension, diabetes and dyslipidemia (3,4), a higher incidence of the metabolic syndrome (5) and four-times the risk of developing CVD (3). Studies suggest that SCT survivors have an accelerated cardiovascular aging phenotype with a median age at first cardiovascular event of 53 years which is 14 years younger than the general population (6).

In recognition of the increased risks for both young and old SCT survivors of developing CVD, the major international transplant communities published consensus recommendations that all SCT survivors should undergo regular screening for conventional CVD risk-factors to ensure early diagnosis and aggressive management of these if present (7). In accordance with this, SCT Survivorship Community of Practice has developed this guidance document.

These recommendations are in line with National and US Recommendations for management of patients who are at high-risk of developing CVD and are adapted from the following sources:

- [NCCN Clinical Practice Guidelines in Oncology. Survivorship, Version 2.2017](#) (8)
- [2017 ACC/AHA Guidelines for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults](#) (9)
- [2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult](#) (10)
- Diabetes Canada Clinical Practice Guidelines Expert Committee. [Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada](#). Can J Diabetes. 2018;42(Suppl 1):S1-S325 (11)

Recommendations

1. Therapeutic Lifestyle Change

- Weight reduction with an aim for Ideal Body Weight (BMI 18.5-25 kg/m²) ([Center for Disease Control BMI Calculator](#));
- A healthy diet which is high in fruits, vegetables, whole grains, total fiber, nuts, and low in red and processed meats, sugars, saturated and total fat (for example the [DASH diet](#)). Reduce intake of dietary sodium (optimal goal of <1500mg/day);
- Regular exercise with an aim for a minimum of 20 to 30 minutes of moderate exercise (e.g. brisk walking) at least 5 days per week (target 150 minutes moderate activity per week);
- Avoid smoking/tobacco products. Smokers should commence a smoking cessation program that incorporates nicotine replacement therapy/pharmacotherapy;
- Moderation of alcohol intake with limits of 1 (one) drink/day for women and 2 drinks/day for men (where 1 drink refers to 14g of pure alcohol which is typically found in 12oz of regular beer, 5oz of wine and 1.5oz of distilled spirits).

2. Hypertension

2.1. Monitor BP every 3 to 6 months;

2.2. If BP > 130/80 mmHg on two measurements taken within one month, advise:

- Therapeutic Lifestyle Change as detailed above;
- Commence BP-lowering medication if no contraindication (consider ACEI +/- 2nd first-line class as per 2017 ACC/AHA Guidelines (9))
- Monitor electrolytes and renal profile closely;
- Re-assess in one month. If BP goal of <130/80 is achieved, re-assess every 3 months;
- Rule out secondary causes of hypertension as indicated;
- If hypertension persists, advise ambulatory BP monitoring and referral for cardiology consult.

3. Dyslipidemia

3.1. Check fasting lipid profile at least every 6 months;

3.2. Advise Therapeutic Lifestyle Change as above

- Additional advice about healthy eating in the context of dyslipidemia is available in 2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult (10)

3.3. Calculate the Framingham Risk Score (FRS) ([FRS Score Calculator](#));

3.4. Once AST/ALT are < 3 x ULN and if no contraindication, start statin* if any of the following exist:

- 40 years old with ≥ 1 CVD RF
- FRS $\geq 20\%$
- FRS $\geq 10\%$ and LDL-C ≥ 3.5 mmol/L or non-HDL-C ≥ 4.3 mmol/L

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- Clinical atherosclerosis
 - Abdominal aortic aneurysm
 - Diabetes mellitus
 - Chronic kidney disease: eGFR <60ml/min/1.73m² or ACR > 3mg/mmol
 - LDL-C >/=5.0mmol/L/Documented familial hypercholesterolemia
- 3.5. Repeat AST/ALT within 2 to 4 weeks of starting statin to ensure < 3 x ULN;
- 3.6. Repeat fasting lipids and AST/ALT every 6 to 8 weeks.
- Adjust statin dose +/-
 - Consider adding second line therapy such as ezetimibe to achieve target values of LDL-C < 2.0 mmol/L, non-HDL-C <2.6 mmol/L
- 3.7. Manage hyper-triglyceridemia as per 2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult (10).

*Choice of statin is important in SCT survivors (12) as some of the commonly used statins are metabolized by the same cytochrome CYP3A4 pathway which is used/inhibited by medications that SCT survivors may be taking such as calcineurin inhibitors,azole anti-fungals and macrolide antibiotics. These interactions can increase plasma statin levels and therefore the risk of toxicity. Pravastatin, rosuvastatin or fluvastatin are recommended as these drugs are not metabolized by this pathway.

1. Type 2 Diabetes

- Screen for fasting plasma glucose and A1C at least every 6 months;
- Adhere to [Canadian Diabetes Association Clinical Practice Guidelines for the Diagnosis and Management of Type 2 Diabetes](#);
- In post-SCT patients with a new diagnosis of Type 2 Diabetes, metformin should be started at the time of diagnosis (unless eGFR < 30ml/min (dose reduce if eGFR < 60ml/min), hepatic failure, or another contraindication), in conjunction with Therapeutic Lifestyle Change;
- Aim for A1C target of </= 6.5 within 2 to 3 months. This lower target is recommended (11) for increased risk populations as it is associated with a significantly lower incidence of nephropathy and retinopathy compared to standard glycemic control;
- Monitor A1C closely (at least every 3 months) and modify anti-hyperglycemic medication accordingly and in-line with the Canadian Diabetes Association Clinical Practice Guidelines ([Pharmacologic Glycemic Management of Type 2 Diabetes in Adults](#)).

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