



Androgen Deprivation Therapy: Adverse Events and How to Manage Them

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Androgen deprivation therapy (ADT)

- Plays an important role in the contemporary management of prostate cancer
- Is a highly effective treatment for prostate cancer across various stages of the disease
- Is associated with significant adverse events that span across multiple organ systems



Domains affected by ADT

- Cardiometabolic health
- Bone health
- Hot flashes
- Breast events
- Cognitive function
- Fatigue and anemia
- Sexual function
- Health-related quality of life



Goals of ADT

In partnership with a multidisciplinary team, the overall goal of the urologist is to optimize oncological outcomes while maintaining acceptable health-related quality of life



Cardiometabolic health

Cardiometabolic health refers to the effects of ADT on cardiovascular disease (CVD), body composition and metabolic parameters

ADT impacts multiple domains of cardiometabolic health

Medical optimization of risk factors is critical to mitigating ADT-related complications



Cardiometabolic health: Adverse events

- ADT may increase the risk of **cardiac complications**, especially in patients with pre-existing CVD or a history of major adverse cardiac events (MACE)
- ADT may increase the risk of **venous thromboembolism and stroke**
- ADT is associated with **changes in body composition**, including increased body weight and fat mass, decreased lean body mass and decreased muscle mass



Cardiometabolic health: Adverse events (cont'd)

- The **metabolic complications** of ADT include insulin resistance, glucose intolerance, and changes in lipid profile
- ADT is associated with increased risk of incident **diabetes** and may worsen glycemic control in men with a pre-existing diagnosis
- Men receiving ADT may be at risk for developing **metabolic syndrome**



Cardiometabolic health: Recommendations

- The patient's **primary care provider** should be informed that the patient has been initiated on ADT and that there may be adverse events associated with this therapy (*Expert opinion*)
- Providers should obtain a **comprehensive baseline physical examination** prior to ADT initiation that includes blood pressure, weight, waist circumference, and calculation of body mass index (BMI) (*Expert opinion*)



Cardiometabolic health: Recommendations (cont'd)

- Patients should have their blood pressure monitored and **hypertension should be treated** (*Expert opinion*)
- **Dyslipidemia should be treated** according to current best practice guidelines (*Expert opinion*)
- Metabolic assessments should be continued at 6–12-month intervals throughout treatment duration (*Expert opinion*)



Cardiometabolic health: Recommendations (cont'd)

- **Lifestyle modifications** (smoking cessation, dietary modifications, exercise) should be strongly encouraged (*Expert opinion*)
- Patients should be encouraged to attend **supervised exercise programs** using a combination of resistance and aerobic training (*Level of evidence [LE] 2, strong recommendation*)



Cardiometabolic health: Recommendations (cont'd)

- In patients with a history of myocardial infarction or stroke should be **referred to a cardiologist or cardio-oncologist** for assessment and medical optimization at the time of initiating ADT (*Expert opinion*)
- All patients receiving ADT should undergo a baseline cardiovascular risk assessment and be monitored for cardiovascular complications while receiving therapy (*Expert opinion*)



Bone health

Use of ADT in men with PCa has detrimental effects on bone health, including decreased bone mineral density (BMD), osteoporosis, and increased risk for clinical fractures



Bone health: Recommendations

- A comprehensive **history and physical examination** to include fall risk and height measurement should be performed prior to initiating ADT (*Expert opinion*)
- Providers should obtain baseline calcium and 25-hydroxyvitamin D levels at the start of ADT (*Expert opinion*)



Bone health:

Recommendations (cont'd)

- Patients should be counselled regarding **smoking and alcohol cessation** (*Expert opinion*)
- Patients should be encouraged to participate in **exercise therapy** using a combination of resistance and aerobic training, preferably in a supervised setting (*LE 2, strong recommendation*)



Bone health:

Recommendations (cont'd)

- Providers should screen men initiating long-term ADT for osteoporosis using **BMD testing** with dual energy x-ray absorptiometry (DXA) (as per the 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada) (*Expert opinion*)
- A 10-year major **osteoporotic fracture risk** using a validated tool should be calculated (*Expert opinion*)



Bone health:

Recommendations (cont'd)

- Men diagnosed with osteoporosis, those with history of fragility fractures in the hip or spine, those with a history of multiple fragility fractures, or those with a moderate or high 10-year fracture risk should be treated with a **bisphosphonate or denosumab at doses recommended for the general population** (*LE 1, strong recommendation*)
- DXA should be repeated every 2–3 years in men at low risk for fractures receiving ADT. In men with osteopenia or those at moderate or high risk for fractures, DXA should be repeated every 1–2 years until treatment cessation. Patients started on pharmacological therapy should have followup DXA to assess for treatment response (*Expert opinion*)



ADT - Other adverse events

Hot flashes

- Avoid triggers, use pharmacologic therapy, consider of intermittent ADT and acupuncture

Breast events

- Uncommon in men receiving GnRH agonists, antagonists or orchiectomy. Treatment with tamoxifen is most effective

Cognitive function

- Monitor for cognitive decline and depression

Fatigue and anemia

- Encourage exercise therapy

Sexual function

- Referral to sex therapists and medical management. Use of intermittent ADT may be considered

Health-related quality of life

- Encourage exercise therapy and consider intermittent ADT



Conclusions

- ADT improves survival in men with PC and is a mainstay of treatment
- ADT is associated with AEs that span multiple organ systems and should be reserved for those who are likely to derive an oncological benefit
- Patients require appropriate counselling regarding adverse events
- Multidisciplinary approach is needed to manage potential complications of ADT