# Cardiovascular diseases in testicular germ cell tumors survivors

Testicular germ cell tumors (GCT) often occur in adolescence and youth. Due to advances in treatment, especially cisplatin-based chemotherapy, GCT has become a curable disease.[1,2] Cisplatin-based chemotherapy is essential in treating metastatic testicular cancer, but it can cause long-term cardiovascular complications. Cisplatin can be detected in plasma and urine decades after treatment, raising concerns about its subsequent late side-effects. This successful treatment increases the number of long-term survivors, and patients can have a normal life expectancy. This has led to more attention being paid to the long-term side-effects of treatments.[1,2]

Survivors may experience complications such as secondary malignancies, cardiovascular disease, neuropathy, pulmonary toxicity, renal toxicity, ototoxicity, thromboembolism, hypogonadism, and infertility several years later.[3]

Meinardi *et al*. evaluated 87 patients with metastatic testicular cancer, who were treated with cisplatin-containing chemotherapy; patients were followed for 9 to 16 years.[4] This study reported that cardiac events occurred in 5 (6%), hypercholesterolemia in 49 (79%), hypertension in 24 (39%), Raynaud's phenomenon in 22 (25%), and microalbuminuria in 11 (22%) patients. The combination of various risk factors (overweight, microalbuminuria, hypertension, insulin resistance, elevated total serum cholesterol, decreased high-density lipoprotein, and high triglyceride level) can create a syndrome-X-like state for patients treated with cisplatin-containing chemotherapy. Electrocardiogram (ECG) and left ventricular (LV) systolic function on echocardiography were normal in most patients. LV diastolic dysfunction was noted in 19 (33%) patients on echocardiography. Due to the delayed occurrence of cardiac complications in this study, the role of long-term follow-up becomes more important.[4]

Another study analyzed a cohort of 2,512 patients and evaluated cardiovascular disease in 5-year testicular cancer survivors.[3] This study showed that treatment with PVB (bleomycin, vinblastine, cisplatin) and BEP (bleomycin, etoposide, cisplatin) was associated with a 1.9-fold (95% CI, 1.7-2.0) and 1.5-fold increase (95% CI, 1.0-2.2), respectively, in the risk of cardiovascular disease compared to the general population, and 694 (18%) patients developed cardiovascular disease within 20 years of cancer treatment.[3,5]

Lauritsen *et al*. evaluated 5,185 patients with GCT who were treated with BEP.[6] The authors reported that the risk of cardiovascular disease began to increase one year after treatment and gradually increased over time. In these patients, the development of metabolic syndrome could cause cardiovascular disease, especially hypertension and hypercholesterolemia. The pathophysiology of cardiovascular disease has not yet been determined, but it may be explained by direct vascular and endothelial damage and increased levels of inflammatory markers (vWF, t-PA, PAI-1,

fibrinogen, and hs-CRP). All of these can cause premature atherosclerosis.[6,7]

Frequent follow-up visits of these patients and accurate screening for cardiac risk factors and cardiovascular disease are very important. Evaluation and treatment of cardiovascular risk factors (such as insufficient exercise, hypertension, obesity, dyslipidemia, and smoking) should be performed lifelong for these patients.[3,6]

Finally, patients with a history of testicular GCT who were treated with cisplatin-based chemotherapy in childhood, adolescence, or youth must have a lifelong follow-up for screening for cardiovascular risk factors and evaluation for cardiovascular diseases. These patients need more care, surveillance, and close observation in terms of cardiovascular disease and screening for cardiovascular risk factors than the general population.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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| **Website:** https://journals.lww.com/crst | Quick Response Code |
| **DOI:** 10.4103/crst.crst_31_23 | |

**How to cite this article:** Alizadehasl A, Mohseni M, Ahmadi R. Cardiovascular diseases in testicular germ cell tumors survivors. Cancer Res Stat Treat 2023;6:352-3.

**Submitted:** 14-Feb-2023 **Revised:** 07-Jun-2023
**Accepted:** 08-Jun-2023 **Published:** 02-Aug-2023