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Comment on 'Chemotherapy for testicular cancer induces acute alterations in diastolic heart function'

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Sir,

The cardiovascular toxicity of cisplatin-based chemotherapy of testicular cancer (TC) patients has been well recognised since the late eighties (Doll *et al*, 1986), but the underlying pathogenetic pathways are still poorly understood.

van Schinkel *et al* (2013) addressed the question of cardiac toxicity of cisplatin-based chemotherapy with a quite novel method. By performing cardiac magnetic resonance imaging (MRI) before and again after chemotherapy, the authors found a significant deterioration of diastolic heart function secondary to cisplatin-based therapy. This result is in line with previous findings in echocardiographic examinations (Altena *et al*, 2009).

The authors rightly discuss that cardiac dysfunction after chemotherapy may be caused either by direct impact of chemotherapy on cardiomyocytes or by endothelial damage. Unfortunately, the authors solely point to select experimental data to support the endothelial damage caused by systemic therapy (Nuver *et al*, 2010). In fact, there is an ever growing body of clinical evidence of acute cardiovascular toxicity of chemotherapy in TC patients that is probably based on vascular wall damage. Clearly, the readers should be informed accordingly. In a survey performed in German treatment centres, we found a calculated incidence 0.3% of major cardiovascular events during chemotherapy of testicular cancer (Dieckmann *et al*, 2010). Noteworthy, the clinical features of those cases were strongly suggestive of (acute) thrombo-embolic origin rather than (chronic) atherosclerotic origin of the events. Further cases have been reported since the publication of that survey. As a consequence, it appears quite rational to suggest endothelial apoptosis as one probable pathogenetic pathway of cardiac toxicity of chemotherapy. As pointed out by van Schinkel *et al* (2013), cardiomyocytic damage may be another one.

The authors suggested to determine troponine I levels in TC patients during chemotherapy to evaluate cardiac toxicity early. Accordingly, such serum levels have been found to be completely unchanged in a longitudinal study on 33 TC patients. Yet, von Willebrand factor antigen increased significantly, thus lending support to the endothelial damage hypothesis (Dieckmann *et al*, 2011).

Caution should be used to interpret the increase of serum levels of low-density lipoprotein and total cholesterol. These results are based on just 14 patients and they are clearly conflicting with several other reports involving much more patients (Fenton *et al*, 2002; Hisamatsu *et al*, 2005; Dieckmann *et al*, 2011; Koc *et al*, 2011).

In all, the results of the cardiac MRI examinations appear quite promising. However, owing to the small number of patients ($n = 14$), the results certainly need confirmation in further studies, and this is particularly true with respect to the serum lipid profile measurements.

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Reply: Comment on 'Chemotherapy for testicular cancer induces acute alterations in diastolic heart function'

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Sir,

We thank you for the response and valuable comments (Dieckmann, 2014). We appreciate your contribution by pointing out that, besides experimental data (Nuver *et al*, 2010), there is growing clinical evidence of acute cardiovascular toxicity of chemotherapy in TC patients, which is most likely based on vascular wall damage. Previous studies have suggested not only chronic atherosclerotic effects of chemotherapy for TC, but also more acute effects of thrombo-embolic origin (Dieckmann *et al*, 2010). The increased von Willebrand factor found in patients directly after chemotherapy contributes to the idea of acute vascular toxicity of chemotherapy (Dieckmann *et al*, 2011). It is indeed important for clinicians treating patients with TC, to appreciate the acute as well as the more chronic vascular effects of cisplatin-based chemotherapy.

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