Title
Vascular effects of cisplatin based chemotherapy for testicular cancer (VECTOR) study

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Introduction
Cisplatin-containing chemotherapy is an effective cure for the majority of men with testicular cancer. However, patients treated with cisplatin are at increased risk of thrombotic events. It is not clear whether this reflects primarily early direct vascular toxicity, or a latent pro-atherogenic state. We hypothesised that cisplatin-containing chemotherapy induces acute endothelial injury and a prothrombotic state that subsides with time.

Methods
We conducted a prospective study of patients attending the Beatson West of Scotland Cancer Centre with testicular cancer. Patients were recruited into 3 groups according to management: surveillance, 1-2 cycles of adjuvant cisplatin-containing chemotherapy or 3-4 cycles of curative cisplatin-containing chemotherapy. Patients attended 6 visits over 9 months, each visit including an assessment of endothelial function by % flow-mediated dilatation (FMD) and collection of venous blood. Visit 1 was <8 weeks following orchidectomy, visit 2 was <24 hours after initial cisplatin cycle and subsequent visits were at 6 weeks, 3 months, 6 months and 9 months.

Results
24 patients were recruited between January 2016 and March 2017. 8 patients were managed with surveillance, 6 received 1-2 cycles of cisplatin and 10 received 3-4 cycles of cisplatin. Amongst all patients receiving cisplatin, % FMD reduced from 15.3±1.3 to 10.8±0.7 within 24 hours (p<0.01; Figure 1.) On subsequent visits, % FMD was not significantly different from baseline.

Serum triglycerides increased from 1.9±0.5 to 3.4±0.9 mmol/L 3 months after receiving 3-4 cycles of cisplatin (p=0.03; Figure 2). There was a trend to increasing serum total cholesterol after cisplatin-containing chemotherapy (Figure 3).

Conclusion
Cisplatin-containing chemotherapy is associated with acute endothelial toxicity that recovers within 6 weeks, hypertriglyceridaemia and a trend to hypercholesterolaemia. Our observations may explain some of the early pro-thrombotic effects of cisplatin. Characterisation of longer-term endothelial and metabolic effects is in progress. These data should help define therapeutic strategies to prevent short- and long-term adverse vascular effects of cisplatin-containing chemotherapy.

Abstract character count
2000 characters (limit 2000)
Figures

Figure 1

![Graph showing % FMD by Study Visit for Surveillance and Cisplatin treatments.](image)

- Surveillance
- Cisplatin

* \( p < 0.01 \)

Figure 2

![Graph showing Triglycerides (mmol/L) by Study Visit for different Cisplatin doses.](image)

- Surveillance
- Low Dose Cisplatin
- High Dose Cisplatin

* \( p = 0.03 \)

Figure 3

![Graph showing Cholesterol (mmol/L) by Study Visit for different Cisplatin doses.](image)

- Surveillance
- Low Dose Cisplatin
- High Dose Cisplatin