Between the two 5-year periods (1988–92 vs. 1993–97), 5-year OS rates increased by 10% (p = 0.05). (Males were 2.0 times more likely to die than females (95% CI: 1.5–2.7), with OS respectively at 67.4% (95% CI: 62.4–72.4) and 82.4% (95% CI: 78.0–86.8) at 5 years (p < 0.001).
Conclusion: Compared with pediatric series, poor results in acute lymphoblastic leukemia and malignant bone tumors have to be highlighted, and deserve further studies concerning the type of regimens used for these patients

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Ifosfamide vs cyclophosphamide: long term gonadal effects in 116 male survivors of childhood cancer

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Purpose: to compare the effects of ifosfamide vs cyclophosphamide in infertility and long term gonadal damage in male survivors of childhood cancer.
Patients: 116 males were evaluated after treatment of a Soft tissue sarcoma (51), Osteoasarcoma (27), Ewing (7), Lymphoma (28), other (3). 57patients received ifosfamide as unique alkylating agent and the other 59 received cyclophosphamide as the other unique alkylating agent between 1984 and 2000. Median age at treatment was 10 years (0–18yrs). Median interval after the end of the treatment was 9.5 years (4.1–19.6 yrs), median age at evaluation was 20.5 years (17.5–31.3 yrs). Median dose of ifosfamide was 51g/m2 (18–114), median dose of cycle was 8.3 g/m^2 (4.6–22). Age at treatment and at evaluation were similar in both groups.
Methods: Evaluation was based on basal FSH measurement known for its correlation with spermatogenesis. LH and testosterone were also measured in most of the patients.
Results: All males but two (17.5 and 22.7 yrs) had normal testosterone levels. FSH was above laboratory upper limit in 28 of the 59 males (47.5%) treated with cyclophosphamide and was within the normal range in 56 of 57 patients (98%) treated with ifosfamide. One patient who received 54 g/m2 of ifosamide fathered two children, another patient who received 51 g/m^2 had a boy.
The risk of abnormal FSH increased with the cumulative dose of cyclophosphamide: only 2/16 boys (12%) who received more than 12 g/m^2 had a normal dosage of FSH, while 29/43 (67%) of the boys who received lower doses of cyclo did so.
Conclusions: These results show a low risk of gonadal dysfunction in men exposed to ifosfamide (median dose 51 g/m^2) compared to the results for males treated with cyclophosphamide. Additional patients are under evaluation.

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Longitudinal cardiac follow-up in doxorubicin-treated bone tumour survivors

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Background: Previously we performed cardiac assessments (CA) in anthracycline-treated long-term bone tumour (BT) survivors at median 8.9 (CA-1) and 14.1 (CA-2) years post-treatment. Between CA-1 and CA-2 systolic function did not deteriorate. At CA-2 heart rate variability (HRV) was progressively impaired compared to CA-1 (Med Pediatr Oncol 2002;39:86). The aim of the current study (CA-3) was to re-assess the cardiac status up to 27 years post-treatment.
Patients and methods: The original cohort consisted of 31 patients. 22 of them participated in CA-1, CA-2 and CA-3. Causes for non-participation in CA-2 or 3: death from congestive heart failure (n = 1); death from second malignancy (SMT; n = 1); thoracic irradiation for SMT, hence exclusion (n = 2); terminal neurodegenerative disease (n = 1); refusal (n = 4). Median age at diagnosis was 17.8 (10–45.8) years. At CA-3 median age was 39 (27–59) years, follow-up 22 (15–27.5) years. All patients were treated with Rosen's T5 or T10 protocol between 1977–1990; they received a median cumulative dose of doxorubicin of 360 (225–550) mg/m^2. Cardiac function was assessed by history, physical examination, 24-hrs ambulatory ECG and 2D-colour Doppler echocardiography. Shortening fraction (SF) < 0.29 and/or wall motion score index (WMSI; only performed in CA-3) >1.0 represented systolic dysfunction. E/A ratio (E/A; performed in CA-2 and CA-3) < 1.0 represented diastolic dysfunction. Statistical analyses were done by non-parametric tests.
Results: None of the 22 patients had signs of clinical heart failure. At CA-3 6/22 (27%) had a decreased SF versus 2/22 (9%) at CA-2 (p = 0.02). All 6 patients with a decreased SF in CA-3 also had an abnormal WMSI: 2/6 had a diffuse wall motion abnormality and 4/6 had a regional wall motion abnormality. A decreased E/A was more frequently found in CA-3 compared to CA-2: 10/22 (45%) versus 4/22 (18%; p = 0.02). We found no correlation between SF, WMSI or E/A ratio and cumulative dose of doxorubicin, age at diagnosis, current age or duration of follow-up. Although not significant, compared to an age-matched control group, all HRV variables shifted towards sympathetic domination.
Conclusions: During a prolonged follow-up period up to 27 years doxorubicin-treated BT-survivors developed progressive systolic and diastolic cardiac dysfunction. The finding of regional wall motion abnormalities in 4 patients suggests ischemic infarction. In addition, all patients showed progressive deterioration of HRV variables.

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Cardiovascular morbidity in long-term survivors of Hodgkin lymphoma (HL)

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Background: Cardiovascular disease (CVD) causes excess morbidity and mortality in survivors of HL. The objective of the study was to assess the incidence of CVD in long-term survivors of HL after primary treatment stratified by treatment and age at treatment.
Material and methods: We assessed the incidence of CVD in 899 5-year survivors of HL treated before the age of 41 years in the Netherlands Cancer Institute, Amsterdam or the Erasmus MC-Daniel den Hoed Cancer Center, Rotterdam between 1960 and 1995. Median age at diagnosis of HL was 24.7 years. 30% of the patients were treated with radiotherapy (RT) alone, 4% with chemotherapy (CT) alone, 23% with initial combined modality treatment without treatment for relapses and 43% with initial therapy including maintenance CT or initial therapy followed by salvage therapy.15% of all patients received anthracycline-containing therapy. Information on medical status was complete for 95% of the cohort. In the Netherlands, population-based incidence rates are available for several CVDs, i.e. acute myocardial infarction (MI), angina pectoris (AP), congestive heart failure (CHF), and cerebrovascular disease (CD). We compared the observed numbers of these CVDs in our HL cohort with the numbers expected based on age- and gender-specific incidence rates of CVDs in the Dutch population.
Results: After a median follow-up of 19.5 years, 159 out of 899 patients developed one or more CVDs, while only 35 were expected [RR = 4.6; 95%-CI: 3.9–5.3]. Seventy-two patients had a MI [RR = 7.9; 95%-CI: 6.1–9.9], 38 CHF [RR = 8.1; 95%-CI: 5.8–11.2] and 25 CD [RR = 3.6; 95%-CI: 2.3–5.3] The RR of all CVDs remained increased with longer follow-up. The RR of CVD was significantly lower for patients who received primary RT+CT than for patients who received maintenance therapy or salvage therapy (RRs 3.4 respectively 6.4; p = 0.01). No significant influence of anthracyclines could be demonstrated; however, the number of patients treated with anthracycline containing therapy was rather small and the median follow up only 13 years.
Conclusion: The incidence of several types of CVDs was strongly increased after treatment for HL. This risk of CVD remained elevated even after prolonged follow-up. The RR of CVD was significantly higher in patients who were treated with maintenance therapy or salvage therapy as compared to the RR in those treated with primary CT+RT only. The effect of anthracycline-containing therapy remains to be determined.