cancer survivors impacts negatively upon somatic health. The primary aim of the present study was to examine mortality and causes of death in HLSs included in a questionnaire survey in 1994 which explored the presence of CF after a mean observation time since diagnosis of 12 years [1], and to compare their survival to that of controls (Ctrs) from the general population. Secondarily we explored the mortality in HLSs with or without CF and in the non-responders, using HLSs without CF as reference group in the survival analysis.
Methods: In 1994, 557 disease-free HLSs were included. In 2008 the HLSs were allocated to three groups: 1) responders without CF (n = 329), 2) responders with CF (n = 113), and 3) non-responders (n = 98). A control group was drawn from the general population using five Ctrs per patient, matched on age and sex (n = 2785). Dates and causes of death for all subjects were retrieved from the National Statistics for Causes of Deaths. Observation time was calculated from January 1st 1994 until date of death or a cut-off of January 1st 2007. Kaplan-Meier plots were used for univariate analyses and Cox models were fitted to adjust for multiple covariates.
Results: By January1st 2007, 149 (27%) of the HLSs had died compared to 197 (7%) of the Ctrs. HLSs had almost five times higher mortality compared to Ctrs (HR = 4.93; 95% CI: 3.91−6.21). Responders with CF had an increased risk of mortality by 4.85 (95% CI: 3.02−7.77), responders without CF had a mortality risk of 4.35 (95% CI: 3.16−6.00), whereas non-responders had the highest mortality risk of 9.45 (95% CI: 5.44−16.41), all groups compared to Ctrs. The non-responders had a two-fold increased mortality compared to HLSs without CF (HR:2.05, 95% CI:1.37−3.07), whereas there was no significant difference in mortality in HLSs with CF compared to those without CF. Among HLSs, 83/149 of deaths were caused by malignant diseases (21/149 due to recurrent Hodgkin lymphoma) and 36/149 by cardiovascular diseases.
Conclusions: After a median of 23 years since diagnosis HLSs had a near five-fold increased mortality risk compared to Ctrs. The highest mortality risk was found among the non-responders from the 1994-survey, whereas there was not found increased mortality risk in HLSs with CF compared to those without CF. The former findings indicate that health problems probably are underestimated among non-responders in cross-sectional questionnaire surveys.

References

[1] Loge et al.J Clin Oncol 1999;17(1):253−61.

9227 POSTER

Involved node radiotherapy (INRT) and modern radiation treatment techniques in patients with Hodgkin lymphoma

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Background: To assess the clinical outcome of the involved node radiotherapy (INRT) concept and the use of modern radiation treatments (intensity modulated radiotherapy (IMRT) or deep-inspiration breath-hold radiotherapy (DIBH)) in patients with localized supra diaphragmatic Hodgkin lymphoma.
Material and Methods: All but two were early stage Hodgkin lymphoma patients and were treated with chemotherapy prior to irradiation. Radiation treatments were delivered using INRT concept according to the EORTC guidelines. IMRT planning was performed using CadPlan® v.6.3.6, (Varian Oncology Systems, Palo Alto, CA) with dose constraints assigned to a virtual volume located behind the PTV and/or the origin of the coronary arteries. For breath-adapted technique, a dedicated spirometer to DIBH radiotherapy (Spiro Dyn'RX system®, Dyn'R, Muret, France) was used with video-glasses that allow a visual monitoring of the patient. The DIBH technique was implemented with a 3-dimensions conformal radiotherapy.
Results: 50 patients with Hodgkin lymphoma (48 patients with primary Hodgkin lymphoma, 1 patient with recurrent and 1 with refractory disease) entered the study from January 2003 to August 2008. 32 were treated with IMRT and 18 with DIBH. The median age was 28 years (range 17 to 62). 34 (68%) patients had stage I-IIA and 16 (32%) had a stage I-IIB. All but 3 patients received 3 to 6 cycles of adriamycin, bleomycin, vinblastine and dacarbazine (ABVD). The median radiation dose to patients treated with IMRT and DIBH technique was respectively 40 Gy (range: 21.6−40 Gy) and 30.6 Gy (range: 19.8−40 Gy). The median mean dose delivered to coronary artery origin, the median heart V30 and the median lung V20 were respectively with IMRT and DIBH 34.5 Gy and 27.4 Gy, 15.5% and 2%, 28.6% and 21%. The median follow-up was 38 months (range: 9−74 months). The 3-year progression-free survival and overall survival were 92% and 98% respectively. Recurrences were observed in 4 patients, 2 were in-field recurrences and 2 were at a distance from radiation fields with visceral recurrences. There was one grade 3 lung acute toxicity (transient pneumonitis).
Conclusion: Our results suggest that patients with localized Hodgkin lymphoma can be safely and efficiently treated using the INRT concept and modern radiation treatment techniques such as IMRT and DIBH.

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Involved-Field Radiotherapy (IFRT) after induction chemotherapy with 4−6 cycles of ABVD in early stage (I/IIA) Hodgkin Lymphoma: long term results of a single institution

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Background: Combined-modality treatment with induction chemotherapy, followed by IFRT in early stage Hodgkin's disease, appears to be beneficiary for the patients in terms of survival rates and quality of life in general.
Materials and Methods: We analyzed the data of 150 patients, with early Hodgkin's disease (stage IA/IIB) who underwent adjuvant IFRT after 4−6 cycles of ABVD, during the period 1996 to 2000, in our department. All patients were retrospectively analyzed for acute, chronic side effects and clinical results.
Results: The 5 year disease free survival rate (DFS) was 87.5%. Of the 19 (12.5%) patients who relapsed, 7 (5%) relapsed in the irradiated field (infield relapse). Five year overall survival rate was 93%. Only 1 patient presented with Acute Myelogenous Leukemia (AML). The clinicaly recorded acute side effects (fatigue, dermatitis, esophagitis, nausea, diarrhea, neutropenia) were mild and acceptable.
Conclusions: Our findings indicate that, IFRT after chemotherapy with ABVD, presents as a highly effective and safe treatment for early stage Hogkin's disease, though a larger number of patients has to be studied in order to achieve results of higher statistical significance.

9229 POSTER

Polymorphisms of glutathione S-transferase mu 1(GSTM1), theta 1 (GSTT1) and pi 1 (GSTP1) in outcome of Hodgkin's lymphoma patients

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Background: The chemotherapic regiments for Hodgkin's lymphoma (HL) patients include alkylating agents, anthracyclines and cyclophosphamide; that are metabolized by enzymes of the glutathione S-transferase system. The *GSTM1*, *GSTT1* and *GSTP1* genes are polymorphic in humans. The *GSTM1* and *GSTT1* may be homozygous null in 10−60% of individuals of distinct populations, which result in a lack of the proteins. The variant allele Val of the *GSTP1* Ile105Val polymorphism, found in 10% of healthy individuals, was associated with a decreased enzyme activity. In a unique study, HL patients with at least one *GSTM1* or *GSTT1* null had a significant better disease-free survival compared to those with undeleted genes. In another study, the variant Val allele of the *GSTP1* Ile105Val polymorphism was associated with an improved free survival in HL patients. In this report, we studied the impact of genetic polymorphisms of the *GSTM1*, *GSTT1* and *GSTP1* genes in outcome of Brazilian HL patients.
Material and Methods: Our analysis included 110 consecutive patients (median age: 27 years, range: 17−63; 58 males, 52 females; 67 at stages I / II, 42 at stages III / IV) treated with ABVD or BEACOPP. Genomic DNA was analysed by the multiplex-PCR or PCR-RFLP for identification of the *GSTM1*, *GSTT1* and *GSTP1* genotypes. Disease free survival (DFS) and overall survival (OS) were calculated using the Kaplan-Meier estimate probabilities. Differences between survival curves were analysed by the log-rank test.
Results: At 120 months of follow-up, the DFS in patients with the *GSTM1* null genotype was higher than in those with undeleted gene (95% *vs* 68%, P = 0.03). The DFS was not influenced by the *GSTT1* (P = 0.30) and *GSTP1* (P = 0.38) genotypes. The OS was higher in patients with the *GSTT1* gene than in those with the null genotype (80% *vs* 72%, P = 0.006) and in patients with the Val allele (Ile/Val plus Val/Val) than in those with the Ile/Ile genotype (93% *vs* 78%, P = 0.04) at 120 months of follow-up, but was not influenced by the *GSTM1* genotype (P = 0.80). Similar results were found when patients were stratified by the age and stage of the tumour.
Conclusions: Our results suggest that the *GSTs* polymorphisms interfere in outcome of HL patients treated with ABVD or BEACOPP. However, ongoing studies of toxicity, pharmacokinetics and proteins should clarify whether carriers of the distinct genotypes should receive distinct doses of chemotherapic agents. Financial support: FAPESP and CNPq