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Management of Hodgkin's Disease, Ino Experience 2014-2016

Mosse B. A. Wilfried*, Kietga Georges Gaël, Messouna Mohamed, Compaoré Bertrand, Seka Evrard Narcisse, Patricia Agbanglanon, Halima Ahmut, Bouhia Hasnae, Elmajjaoui Sana and Noureddine Benjaafar

Department of National Institute of Oncology/Rabat (Morocco), Department of Radiation Oncology. Mohamed V University, Rabat, Morocco

Abstract

Over the past century, Hodgkin's Lymphoma (HL) has gone from a uniformly fatal disease to a curable disease in approximately 75% of patients worldwide. The selection of therapy should balance the desire to maintain a high rate of cure with the need to minimize long-term complications. In this retrospective study, we propose to report the experience of the management of this pathology to the National Institute of Oncology (INO) in Rabat. We recorded and collected data from 152 patients admitted to the National Institute of Oncology for MDH, the average age is 36.2 +/-16.3 years with extremes of 17 and 81 years. Men made up 52%?? of the total population. The favourable localized stages (IA, IIA) represented 20.4%, we did not have enough data to classify 7 patients. ABVD (Doxorubicin, Bleomycin, Vinblastine, Dacarbazine) was the 1st line protocol in 66% of patients, BEACOPP standard 13.4% (Bleomycin, Etoposide, Doxorubicin, Cyclophosphamide, Vincristine, Procarbazine, Prednisone); some have BEACOPPP had the switcher protocol to the BEACOPP standard after 3 cures). 55.9% of patients received between 3 and 6 courses, 17.8% between 7 and 8 courses.

27.2% of patients had curative adjuvant radiotherapy using the irradiation technique (IFRT) Field concerned Radiotherapy with doses of 20 Gy and 30 Gy depending on the response to the initial medical treatment and the initial stage. The median overall survival for all stages was 72.9% after 84 months of follow-up. All-stage event-free survival was 69.3%. The over hall survival according to the favourable localized stages (IA and IIA) was 75.1% higher than that of the unfavourable stages of 71.5% (p=0.186). Patients who had adjuvant radio therapy had overall survival (72.4%) and those who had not been irradiated 72.1% (p=0.733). All-stage event-free survival was 65.1% after 84 months follow-up 95% CI (62.2%-67.9%). Hodgkin lymphoma is a curable malignant tumor in the early and late stages. The treatment should be refined on prognostic models.

Keywords: Hodgkin's Lymphoma • Oncology • Chemotherapy • BEACOPP

Introduction

Hodgkin's disease (MDH) represents in the USA and Europe about 10% of all lymphomas, 0.6% of all cancers, and 0.2% of all cancer deaths [1,2]. MDH represents 11.7% of malignant hemopathies according to the Rabat cancer registry in 2012 [3]. Over the past century, Hodgkin's Lymphoma (HL) has gone from a uniformly fatal disease to a curable disease in approximately 75% of patients worldwide. The selection of therapy must balance the desire to maintain a high cure rate and the need to minimize the long-term complications. Treatment has evolved so that patients with early-stage disease can achieve long-term remission with less intensive therapy, while more intensive therapy is reserved for patients with advanced disease.

The successful management of patients with HL requires careful attention to the details of the staging and treatment protocols to achieve these results while minimizing the potential serious toxicities of the therapy. The combination therapy is more effective than chemotherapy alone or radiotherapy alone in the treatment of lymphoma Hodgkin's at an early stage, it can reduce the risk of treatment failure [4]. The endpoint of many clinical trials is the absence of recurrence [5]. In this retrospective study, we propose to report the experience of the management of this pathology to the National Institute of Oncology (INO) in Rabat/Morocco.

Materials and Methods

This is a retrospective study in over 16 patients admitted at INO with a histological diagnosis of Hodgkin lymphoma (HL), 1st January 2014 to 31 December 2016. We exploited characteristics epidemiologic, the diagnostic method, classification, treatment received, and the s of data for patient monitoring.

Statistical analysis

The patient characteristics and therapy were analyzed descriptively. The survival without event (SSE) is the time between the date of diagnosis and disease progression, relapse, or death from any cause or censored at the date of the last information about the disease and overall survival (OS); the time between diagnosis and death or censored at the date of the latest information; in the event of an information delay of more than 12 months, information on the survival status was obtained by telephone contact with the patients (Figure 1).

Survival results were analyzed according to Kaplan-Meier and comparisons between treatment groups and prognosis groups using the log-Rank test. The results were statistically significant for p<0.05. Statistical calculations were performed with SPSS 20.0 (developed by IBM).

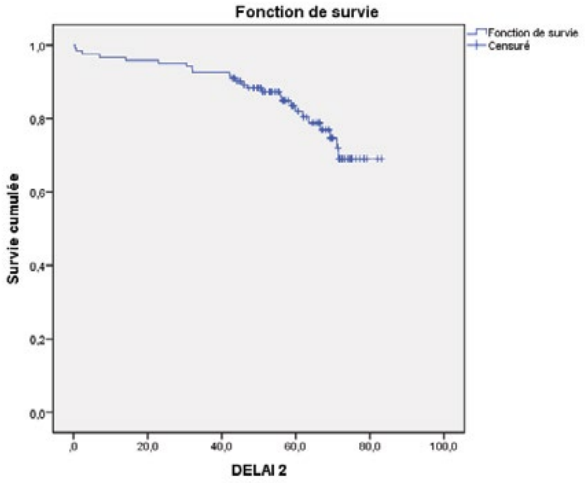

Figure 1. Overall survival.

***Address for Correspondence:** Wilfried Mosse B.A, Department of National Institute of Oncology/Rabat (Morocco), Department of Radiation Oncology, Mohamed V University, Rabat, Morocco, Tel:0698912749; E-mail: mossleboss2@gmail.com*

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Results

We recorded and collected data from 152 patients admitted to the National Oncology Institute for MDH, the average age is 36.2 +/-16.3 years with extremes of 17 and 81 years. Men made up 52% of the total population. The favourable localized stages (IA, IIA) represented 20.4%, we did not have enough data to classify 7 patients. Fifty-two percent (52%) patients had initially 2-3 sites invaded and 30.2% at least 4 sites invaded. The histological diagnosis was made on lymph node sampling in 94.1% of cases. Classical Hodgkin lymphoma accounted for 98% and the sub-type nodular sclerosis 78.9% of sub histological types. We found 3 cases of predominantly lymphocytic nodular Hodgkin lymphoma.

Only 5.9% (9 patients) underwent PET/CT for initial staging. The low-risk concerned 11.2% of patients and 17.8% were immediately metastatic. The treatment of first-line curative referred concerned 75.7% of patients and 19.7% or 30 patients were not treated with INO or exhibited u n bad state allowing no chemotherapy, so they have been excluded in the followed. ABVD (Doxorubicin, Bleomycin, Vinblastine, Dacarbazine) was the 1st line protocol in 66% of patients, BEACOPP standard 13.4% (Bleomycin, Etoposide, Doxorubicin, Cyclophosphamide, Vincristine, Procarbazine, Prednisone), BEACOPP escalated (note 17.3%) that some have had the protocol switcher to the standard BEACOPP after 3 cures). 55.9% of patients received between 3 and 6 courses, 17.8% between 7 and 8 courses (Figure 2).

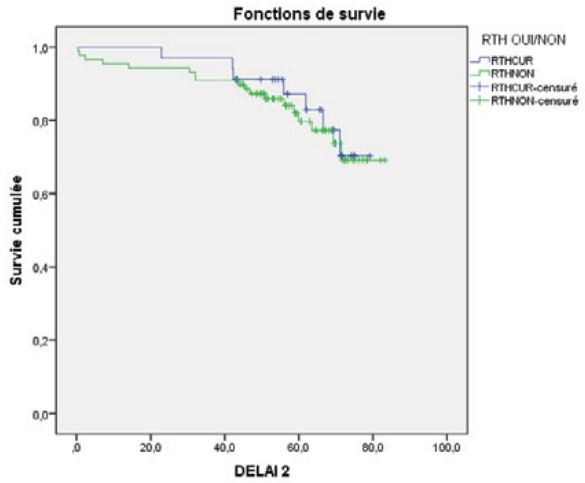

Figure 2. Survival curves for irradiated or non-irradiated patients.

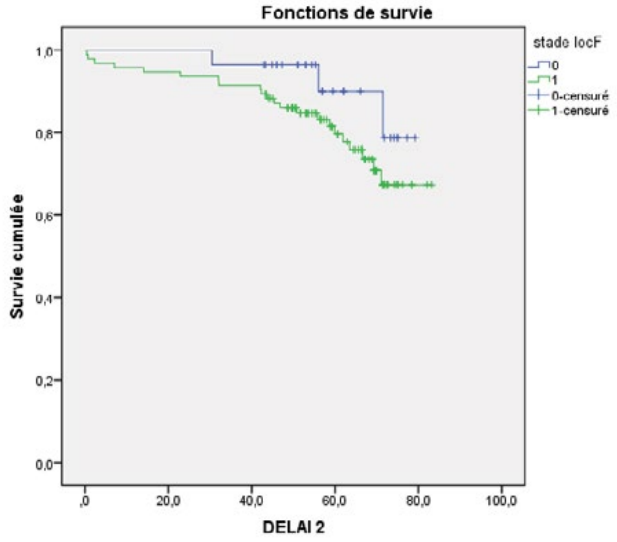

Figure 3. Survival curves for localized stages (blue) and advanced stages (green).

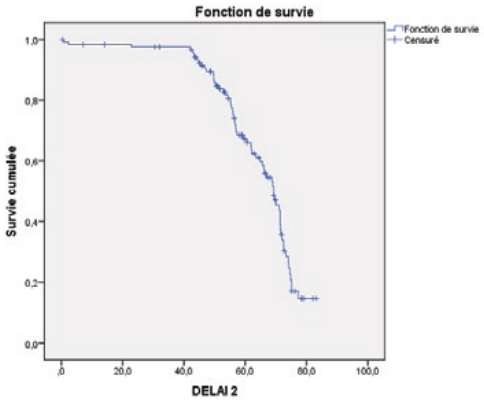

Figure 4. Event-free survival curve for all stages.

Table 1. Patient characteristics.

Variables		Number of patients (152)	Percentage %
Sex	Feminine	73	48
	Male	79	52
Age	Way	36.2 +/-16.3	
	Tidy	17-81	
Ann Arbor Stadium	Stage IA	8	5.3
	IB stage	5	3.3
	Stage IIA	23	15.1
	Stage IIB	33	21.7
	Stage IIIA	13	8.6
	Stage IIIB	35	23.1
	Stage IV	28	18.4
	NP	7	4.6
	Total	152	100
Number of sites	1	20	13.2
	02-Mar	79	52
	>3	46	30.2
	NP		4.6
Types of biopsy	Lymph node biopsy	143	94.1
	Organ Biopsy	9	5.9
Histological types			
Classic hodgkin lymphoma (clh)	Mixed Cellularity	18	11.8
	Lymphocytes+++	6	3.9
	Sclero-Nodular	120	78.9
	Not specified (LHc)	8	5.3
Lymphocyte-Predominantly Nodular Hodgkin Lymphoma (Lhnpl)	LHNPL	3	2
Initial Pet/Ct	No	143	94.1
	Yes	9	5.9
	Low risk	17	11.2
Risk Classification	Intermediate risk	65	42.8
	High risk	63	41.4
	NP	7	4.6
	Limited Unfavorable group	51	33.6
Prognostic Stage	Limited Favorable Group	17	11.2
	Locally Advanced unfavorable	25	16.4
	Locally Advanced Favorable	25	16.4
	Metastatic	27	17.8
	NP	7	4.6

Table 2. Treatment type.

Variables		Number of patients (122)	Percentage
Chemotherapy (CMT)	CMT Curative	115	75.7
	CMT Palliative	7	4.6
	Not done	30	19.7
	Total	122	100
1st line cmt type	ABVD	80	66
	BEACOPP ESCAL ADE	21	17.3
	BEACOPP STANDARD	16	13.4
	OEPA/COPDAC	1	0.8
	ABVD+COP/AVB	1	0.8
	Other palliatives (ICE/GNN/ENDOXAN	2	1.7
	EVD	1	0.8
Number of cures	"<3"	4	2.6
	">8"	6	3.9
	"3-4"	38	25
	"5-6"	47	30.9
	"7-8"	27	17.8
Cmt assessment	PET/CT	35	28.7
	TDM	76	62.3
	NP	11	8.1
Evaluation deadline	"2-4" cures	61	50
	"5-6" cures	37	30.3
	"8" cures	13	10.7
	NP	11	9
Cmt response	Complete Response (CR)	38	31.1
	RC uncertain	9	7.4
	Partial Response	33	27
	Stability	10	8.2
	Progression	21	17.2
	NP	11	9
Radio therapy	Curative RTH	34	27.9
	Palliative RTH	3	2.5
	Not done	85	69.7
Results/Follow-Up	Good Locoregional Control	56	45.9
	Progression	41	33.6
	Recidivism	4	3.3
	Stability	11	9
	NP	10	8.2

The results of chemotherapy were evaluated clinically in all patients and by CT scan in 62.3% and by PET/CT in 28.7%. This evaluation was done in 50% of patients between the 2nd and 4th treatment. We obtained a complete response in 31.1% of patients, an uncertain complete response in 7.4%, a partial response in 27%, stability in 8.2%, and progression on chemotherapy in 17.2%.

27.2% of patients underwent curative adjuvant radiotherapy using the irradiation technique (IFRT) Involved field Radiotherapy with doses of 20 Gy and 30 Gy depending on the response to initial medical treatment and the initial stage. At first inspection after treatment, 45.9% were in good control of their disease and 45.9% had been under treatment for 2nd line. The treatments received after the failure of treatment of 1st line were: ICE (The ifosfamide, carboplatin, and etoposide), DHAP (dexamethasone, cytarabine, and cisplatin), GNN (Gemcitabine, Navelbine, Natulan) and Cytoxan. Two patients benefited from autologous stem cell transplantation after progression under 2nd line chemotherapy.

The median overall survival for all stages was 72.9% after 84 months of follow-up. Event-free survival for all stages was 69.3%. The overall survival according to the favourable localized stages (IA and IIA) was 75.1% higher than that of the unfavourable stages of 71.5% (p=0.186). Patients with adjuvant radiation therapy had an overall survival (72.4%) and those who n ' have not been irradiated 72.1% (p=0.733). The event-free survival, all stages was 65.1% after 84 months follow-IC to 95% (62.2%-67.9%) (Tables 1 and 2).

Discussion

Hodgkin's disease is lymphoma that affects men and women with a comparable incidence. Scleronodular (SN) cLHc has a peak incidence between ages 15 and 35, while mixed cellularity (CM) cLHc has a bimodal distribution with a peak in young adults and the second pic in older adults. [6,7]. in our series the average of â age found was 36.2 years and the sex ratio of approximately 1. In the literature, the subtypes LHc represents: SN 70%, 20-25% CM, rich in cell 5% Lymphocyte depletion <1% [6]. We find a similar distribution in our series.

Cooperative research groups have used different definitions of the disease with favorable and unfavourable prognosis. The two most commonly used definitions of favorable disease are those offered by the European Organization for Research and Treatment of Cancer (EORTC) and the German Hodgkin Study Group (GHSG): EORTC defines the favourable prognostic group of limited-stage such as patients 50 years of age or younger; without large mediastinal lymphadenopathy; with erythrocyte sedimentation rate (ESR) less than 50 mm/h and no B symptoms (or with ESR less than 30 mm/h in those

with B symptoms); and disease limited to three or fewer regions of involvement [8]. The GHSG defines the limited stage, favourable prognostic group, as patients with no more than two disease sites; no extra-ganglionic extension; no mediastinal mass measuring one-third of the maximum chest diameter or more; and ESR less than 50 mm/h (less than 30 mm/h for symptoms B) [9]. The favourable localized stages (IA, IIA) without factors of poor prognosis represented only 20.4% of our patients according to the criteria of the EORTC), which suggests a late diagnosis in our patients.

The ABVD was the treatment of 1st line treatment in 66% of patients, the treatment of 1st intention proposed by the various cooperative research groups in localized disease followed by radiation to the affected areas [4,10-12]. Only 27.9% of our patients received adjuvant radiotherapy. Several randomized studies have investigated the place of radiotherapy in Hodgkin lymphoma [10,13]. So, patients with limited-stage Hodgkin lymphoma, Meyer et al. found no difference in overall survival between patients randomly assigned to receive treatment including radiotherapy or ABVD alone in the localized disease (Figure 3). Engers et al. on the other hand propose a de-escalation of treatment thus, they suggest that patients with Hodgkin lymphoma at an early stage and with a favourable prognosis, treatment with two cycles of ABVD followed by 20 Gy of field radiotherapy involved is as effective and less toxic than four cycles of ABVD followed by 30 Gy of field radiation therapy involved [9]. The role of RT for early-stage HL is still under debate and new combinations are emerging; an individualized approach should be recommended, taking into account all technical possibilities. Es of RT to minimize toxicity while maintaining efficacy [14].

In advanced stages, the intensified BEACOPP regimen improves the outcome of patients with advanced Hodgkin lymphoma (HL) but is associated with severe toxicity. Analysed the survival results of patients with high-risk and advanced HL treated with a response-sensitive therapy and concluded that escBEACOPP-ABVD combination therapy is well tolerated and effective in patients. HL patients who achieve negative interim PET results, while a positive PET result partially identifies those with poorer prognosis [15,16].

Radiation therapy has moved from wide-field radiation therapy (EFRT) to involved-field radiation therapy (IFRT), reducing toxicity while maintaining high cure rates. Recent publications recommend further reduction of involved lymph node radiotherapy (INRT) [17]. In our study, almost all of the patients had involved field radiation therapy (IFRT) (Figure 4).

To our overall survival patients after 84 months stay tracking 72.9% with an event-free survival confused any stage of 65.1%. Sasse analysed updated follow-up data from 4,276 patients treated in the HD7 and HD10 trials of the German Hodgkin study group for early-stage favourable HL and HD8 and HD11 for early-stage unfavourable LH between 1993 and 2003 and found a progression-free survival (PFS) at 15 years of 73% versus 52% in favour of the combined treatment [5].

Conclusion

Hodgkin lymphoma is a curable malignant tumour in the early and late stages. Most patients are diagnosed in adolescence or twenties, the toxicity of the treatment must be balanced with the goal of healing. Thus, the treatment has been refined over the years through prognostic models and directed therapy by positron emission tomography (PET-CT).

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