

Cause of Death in Hodgking Lymphoma. A Real-World Analysis in A Single Center

Aviles A*¹ and Cleto S²

¹Oncology Research Unit, Mexico

²Department of Hematology, Oncology Hospital, National Medical Center, IMSS, Mexico Ciity, Mexico

*Corresponding author:

Agustin Aviles,
Oncology Research Unit, Mexico

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1. Abstract

1.1. Background: Hodgkin lymphoma (HL) is one of the hematological malignancies that is most frequent in younger population, and excellent survival, thus the presence of other morbidities are common and has been suggested that this condition, could be the cause of death, and diminished the survival of HL and increases costs. We performed a real analysis in a single center.

1.2. Patients and Methods: From 1975 to 2023, 9916 patients, were diagnosed and treated in our Institution, this population was not different in relationship with other studies. All the patients have a longer follow-up, at least 5 years.

1.3. Results: The most common comorbidities were cardiac, neurological diseases and diabetes, but, the same number of cases were diagnosed before and after the diagnosis and treatment of HL. Only 789 cases (7.8 %) and 66 (0.2%) could be associated to tumor progression, relapse or infection were directly related to tumor and related. At a median of 10-years, 91% of patients remain alive.

1.4. Conclusion: The presence of comorbidities in the course of HL, will be considered a natural presence, because the most common diseases are in same during after and before the diagnosis of HL. We conclude that it is very difficult to treat to associate HL and comorbidities could be cause of excess mortality.

2. Introduction

Hodgkin lymphoma is a hematological malignancy that accounts for about 10 % of newly diagnosed malignant lymphoma; in our institution, from 1975 to 2023, 9916 patients were diagnosed (annual

media: 218). Greater advances have been achieved in the treatment of this disease, and prolonged survival has been observed; more than 85 % of patients have survival and 20 years, and probably could be considered cured.

Thus, with prolonged survival in a younger population, the possibility of development of some morbidities, that have been considered that could be associated with the neoplasm or treatment, and in most cases were considered cause not related (CNR) of an increase in mortality in patients with HL. Multiple analyses have been published about these possibilities, but, more were retrospective, SEER analysis, and they analyzed that the treatment in this setting of patients it is the cause of excessive mortality in HL; with more emphasis on statistical analysis, and did not mention: that all human beings have death as a natural conduct; too much of the mentioned associated, not had any scientific bases. In our country, diabetes and cardiovascular problems are the principal cause of death and those cases did not have any association with any type of cancer (1-5). We did not find reports that examined in a real bases, and shown a specific reason to demonstrate the association, thus, we performed a real world analysis in a homogeneous group of HL, treated according to clinical trials, with a longer follow-up.

3. Patients and Methods

We review the data of 9916 patients that have followed criteria entry: confirmed pathological diagnosis of HL, a minimal follow-up of 5 years, the cause of death will be confirmed, if the patient die in a hospital of our institution, signed for a member

of the team that treated the patient , autopsies was non-mandatory. It is an retrospective analysis, but , we given an signed consent for the familiar.

4. Results

From January 1985 to December 2018, 9916 cases were collected. (Table 1), show the clinical characteristics at the time of diagnosis. Female, age, 60 years, early stage (I-II) , pathological nodular sclerosis, good performance (< 2), with no differences with most reports of this disease. The most frequent treatment was combined

chemotherapy and radiotherapy. The median follow-up was 28.9 (range 7 to 33) years .(Table 2) show related cause of death (RCD) : 789 (7.8%) patients were found, and 717 (7.2%) death was considered directly : refractory, relapse,, 66 (0.6), die secondary to infection related to hematological cause during treatment of , 3 months after any treatment. From Not-COD were 215 patients, diabetes, cardiological and neurological disease were the cause. (Table 3) show the time (before of after) the treatment for HL, no differences were observed between the initial diagnosis of No-COD.

Table 1: Chararacteristics

	Total (No, %)	Stage I & II (No, %)	Stage III-IV (No, %)
Total	9916 (100)	6004 (60.5)	3912 (39.4)
Gender			
Male	4017 (40.5)	2911 (48.4)	2126 (54.3)
Female	5899 (59.4)	3093 (50.5)	1780 (45.5)
Age			
< 60 years	7819 (78.8)	4840 (80.7)	2779 (71.0)
> 60 years	2097 (21.3)	1158 (19.2)	1133 (25.9)
Pathology			
Nodular Sclerosis	7622 (76.8)	469 (78.1)	2928 (74.9)
Mixed Cellularity	1601 (17.9)	922 (15.3)	679 (17.3)
Lymphocyte Depletion	693 (0.6)	388 (0.4)	305 (7.7)
Performance Status (PS)			
0	5827 (63.6)	4001 (66.6)	1826 (46.6)
1	2045 (22.3)	1690 (28.4)	1255 (32.0)
2	1209 (12.1)	314 (5.6)	835 (21.3)
Treatment			
Radiotherapy alone	825 (8.3)	609 (10.4)	221 (5.6)
- Limited field	189 (1.9)	104 (1.7)	88 (2.2)
- Mantle	536 (3.9)	423 (7.4)	114 (2.9)
- Subtotal nodal	99 (0.9)	80 (0.3)	19 (2.0)
Chemotherapy alone	793 (7.9)	609 (10.4)	221 (5.6)
- MOPP	88 (0.8)	43 (0.7)	45 (1.1)
- ABVD	532 (5.3)	306 (5.0)	226 (5.7)
- Stanford V	173 (1.7)	88 (2.1)	85 (2.0)
Chemotherapy/Radiotherapy	8298 (83.6)	4438 (73.9)	3917 (47.8)

Abbreviations: PS: performed status. ABVD (adriamycine, bleomycin, vinblastine, dacarbazine)

Category	No. (%)
RELATED	783 (100)
- Hodgkin lymphoma	717 (78.0)
- Infections	66 (7.2)
NON-RELATED	215 (7.2)
- Second neoplasms	27 (0.2)
- Cardiac diseases	48 (0.2)
- Diabetes	46 (0.4)
- Lung	4 (0.04)
- Hepatic	27 (0.2)
- Renal	3 (0.3)
- Neurological	48 (0.8)
- Accident	16 (0.8)
- Suicide	6 (0.6)

Table 2: Cause related and non-related

Table 3: Relations between diagnosis of Hodgkin lymphoma and apparition of non related cause of death

Condition	BEFORE (No., Years Range)	AFTER (No., Years Range)
Second neoplasms	27 (11-34)	27 (11-34)
Cardiac disease	26 (1-6)	22 (13-31)
Diabetes	24 (21-23)	24 (6-23)
Lung disease	0	4 (11-22)
Hepatic	9 (6-9)	20 (11-24)
Renal	0	3 (14-18)
Neurological	11 (3-21)	37 (13-23)
Accident	—	1 (3.4)
Suicide	0	6 (19-36)

5. Discussion

Greater advances in the understanding of HL, an achieved, and improve in outcome, actually, > 85 % ate alive at > 10 years, and probably most of these could be considered cure. Taking in consideration, that HL is most frequent in patients < 50 years, logically the presence of any disease during an normal life. However, some studies suggested that the no-malignant disease present after diagnosis of treatment of HL, will be considered to be associated to the treatment of HL, this disease will consider as secondary late toxicities and diminished the survival, and also increase the cost during the years that are alive the patient.

However most of these studies, are based in SEER analysis, statistical methods, retrospective analysis, without any scientific basis. We did not find an real world analysis that can confirmed these possibility. We has been performed analysis of mortality associated tohematological malignancies and the treatment administered, first, the presence of a minor number of cases was evident, second we did no show any specific cause-effect in relation second neoplasms and cardiac toxicity (7,8), and a real analysis of cause of death in patients wit diffuse large cell-lymphoma, with the same results (9)We show an real analysis of this mentioned associated, and we observed that No-COD , are the most common cause of death in our country, also, the age of presentation is the same with a general population. In our study the patients who were treated in our Institute can be followed closely in our Hospital during the first 5 years of follow-w, subsequently are followed in the Familiar Unit, but, the physicians that attending the patients had instruction to the care of these patients , if they have suspicious of any medical disease, they had to resend the patients at the Oncology Hospital. We considered that the presence of any disease after treatment of HL, will not be automatically considered as late toxicities and possible RCD. Some bias could be observed, it is retrospective study and performed in an single center, but, for this reasons for these results it are a real in this type of patients. Thus we confirmed that longer survival is real in this patients , and real survival is > 90 %

6. Conflict of Interest

The work did not receive any economic support and was performed with owner resources of the Instituto Mexicano del Seguro Social

7. Authors Contribution

Both authors performed the design, acquisition of dates, critically revised the work and write the work.

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