CRASH score in the Older French patients with Non Hodgkin Lymphoma receiving chemotherapy

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Background

- Non Hodgkin Lymphoma are one of the most frequent hematological malignancies observed in elderly patients.
- Geriatric assessment objectives that old adults with NHL vary considerably in performance status, comorbidities and functional reserve.
- Comprehensive geriatric assessment is the best way to identify the functional risks and disabilities of aged patients with the aim of providing care and organizing long-term follow-up.
- The chemosensivity of NHL leads to prescription of a toxic anthracycline regimen with rituximab for fit patients and an adapted chemotherapy with rituximab for frail one.
- Patients have different levels of vulnerability to chemotherapy toxicity.
- CRASH score is known to be useful in older patients for screening risk of severe chemotoxicity in some variety of cancers.

Objective

- Validate CRASH score predictive value on adverse events in a geriatric population of Non Hodgkin Lymphoma patients.

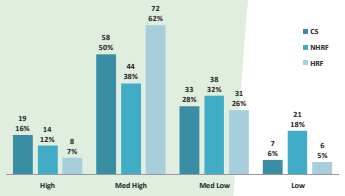
Methods

- We performed a prospective, multicentric study on consecutive NHL patients treated by chemotherapy from august 2013 to september 2015, conducted in the regional network HEMATOLIM.
- Inclusion criteria
  - 70 years old and over
  - Histologically proved B NHL according to the WHO guidelines
  - Geriatric assessment according to the SIOG recommendations for CGA
  - Available clinical and biological data
- CRASH score, Non Hematologic Risk Factor (NHRF) and Hematologic Risk Factor (HRF) are evaluated before chemotherapy.
- CRASH points for toxicity of chemotherapy regimens were established using the chemotox table values, regimens not listed were scored by analogy (1).
- Adverse events, grade 3 and 4, up to 1 month after chemotherapy are described according to the Common Terminology Criteria for Adverse Events version 3.0.(2).

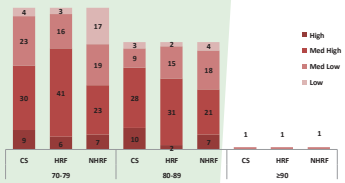
CRASH Score, NHRF and HRF results

CRASH Score	n (%)	70-79 n (%)	80-89 n (%)	≥ 90 n (%)
High	19 (16)	9 (14)	10 (20)	0
Med-High	58 (50)	30 (45)	28 (56)	0
Med-Low	33 (28)	23 (35)	9 (18)	1 (100)
Low	7 (6)	4 (6)	3 (6)	0
NHRF				
High	14 (12)	7 (10)	7 (14)	0
Med-High	44 (38)	23 (35)	21 (42)	0
Med-Low	38 (32)	19 (29)	18 (36)	1 (100)
Low	21 (21)	17 (26)	4 (8)	0
HRF				
High	8	6 (9)	2 (4)	0
Med-High	72	41 (62)	31 (62)	0
Med-Low	32	16 (24)	15 (30)	1 (100)
Low	5	3 (5)	2 (4)	0
Total	117	66	50	1

- CS, NHRF and HRF distribution



- CS, NHRF and HRF distribution by age group

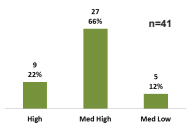


Toxicity results

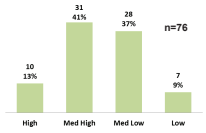
- Severe toxicity after treatment as been observed in 41/117 patients (35%)
  - 1 to 10 events per patient
  - Time of assesment:
    - post-c1: n=81
    - post-c4: n=7
    - post-c7: n=1
    - post-c2: n=10
    - post-c5: n=2
    - post-c9: n=1
    - post-c3: n=11
    - post-c6: n=1
    - post-c14: n=1
    - post-1month per os: n=2

Adverse events	n	%	70-79	80-89	≥ 90
Hospitalization	19	16	7	12	0
Hosp in emergency dept	10	9	3	7	0
Infection	4	3	2	2	0
Severe anemia	5	4	3	2	0
Severe neutropenia	26	22	17	9	0
Platelets <50000	10	9	4	6	0
AST(SGOT) or ALT(SGPT) x5	0	0	0	0	0
Creatinine x5	0	0	0	0	0
Fever	6	5	3	3	0
Asthenia	13	11	4	9	0
Falls	1	1	1	0	0
Confusion	1	1	0	1	0
Diarrhea	1	1	0	1	0
Loss of appetite	7	6	3	4	0
Weight loss	1	1	1	0	0
Total	104		48	56	0

- CS and adverse events



- CS and no adverse event



- CS group and adverse events

CS group	n	Adverse events	No adverse event	p
Low (Low+Med-Low)	40	5	35	
High (High+Med-High)	77	36	41	0.0002
Total	117	41	76	

Patients characteristics

- Included patients n=122
  - Evaluable patients: n=117/122
  - Exclusions for missing data: n=5

Characteristics	Value	%
Sex ratio	0.95	
Male	57	49
Female	60	51
Median age	79 [70-91]	
Age		
70-79	66	56
80-89	50	43
≥ 90	1	1
Histological subtypes		
DLBCL	53	46
Follicular	18	15
Mantle	18	15
Others	28	24

- Rituximab: 87% (n=102)
- Intravenous regimen: 97% (n=114)

Regimens	n	%	70-79	80-89	≥ 90
Anthracycline based CT	47	40	32	15	0
Alkylant agent based CT	19	16	8	10	1
Cytarabine based CT	17	15	8	9	0
Bendamustine	15	13	8	7	0
VP16-Holoxan	11	9	5	6	0
Others	8	7	5	3	0
Total	117	100	66	50	1

- Chemotoxicity classification

Level 0	Level 1	Level 2
Chloraminophene per os	Bendamustine	BAC
Endoxan per os	COP-Cytarabine	Bendamustine-Cytarabine
Rituximab	Endoxan IV	Bendamustine-Revlimid
	Ibrutinib	CHOP21/mini CHOP
	Idelalisib	Cytarabine -Torisel
	VP16-Holoxan	DHAC
	ZEM	GVD

Discussion

- Among patients with Low or Med-Low CRASH score, n=35/40 (87%), have no adverse event.
- Among patients with High or Med-HighCRASH score, n=36/77 (47%), have adverse events.
- The data collected confirm the preliminary results presented in 2014 (SIOG Lisbonne) and highlight the good predictive value of CRASH score for adverse events occurrence.
- **Occurrence of adverse events is significantly different between the High group and Low group, p=0.0002.** (Pearson's Chi-squared test)
- CRASH score objectives that quite half patients with High or Med-High risk have serious adverse events associated with chemotherapy.
- For most frail patients, management have to be adapted to their real health status.

Perspectives

- According to these results, we started a personalized management with a proactive care organization for all patients of the High group CRASH score eligible to chemoherapy.
- This personalised follow-up includes:
  - A close phone follow-up by the nurse care manager and a free direct oncall for patient.
  - Report to all the medical team when treatment starts:
    - Familly physician about hospitalization if necessary
    - Hospitals (refferal and peripheral hospitals)
    - Hematology and geriatrics departments
- We are considering to evaluate the impact of this managment, on the occurrence of long-term serious side effects.

References

(1) **Predicting the risk of chemotherapy toxicity in older patients: The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score. Cancer 2012**, M. Extermann and all.
(2) Cancer Therapy Evaluation Program, Common Terminology Criteria for Adverse Events, Version 3.0, DCTD, NCI, NIH, DHHS, March 31, 2003 (http://ctep.cancer.gov), Publish Date: August 9, 2006

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