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ARTICLE ORIGINAL

EVALUATION OF PROGNOSTIC FACTORS IN AN ALGERIAN POPULATION WITH MULTIPLE MYELOMA : A SERIES OF 359 CASES

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MOTS CLÉS

Multiple myeloma;

prognostic factors;

free light chain assay;

ISS.

Abstract

INTRODUCTION. Multiple myeloma (MM) is a malignant intramedullary plasma cell proliferation characterized by the secretion of a complete monoclonal immunoglobulin (Ig) or a component of the Ig molecule. At present, it remains an incurable disease with a guarded prognosis. The objective of this study is to evaluate, within a prognostic framework, the factors involved in the pathophysiology of MM.

PATIENTS AND METHODS. We conducted a multicenter, descriptive and analytical, cross-sectional retro-prospective study based on the medical records of patients followed in the Immunology Unit of the Blida University Hospital Center.

A total of 359 patients were included from an initial cohort of 5,717 patients recruited over a period extending from 2012 to 2024. The study population comprised 194 men (54%) and 165 women (46%). Patients were referred from regional hematology departments, as well as rheumatology and nephrology units, met the International Myeloma Working Group (IMWG) diagnostic criteria, and had undergone regular follow-up at our center.

All 359 patients underwent both serum and urine investigations, including serum and urine protein electrophoresis and immunofixation using the Hydrasys automated system (HYDRAGEL B1–B2 kit), in order to detect and quantify the monoclonal component (MC) and to identify Bence Jones proteins (BJP). Quantitative measurements of proteins (immunoglobulins, free kappa and lambda light chains [FLCκ and FLCλ], β2-microglobulin, C-reactive protein [CRP], and lactate dehydrogenase [LDH]) were performed using Binding Site reagents on the SPA plus® immunoturbidimeter. Hemoglobin levels were measured using a SYSMEX® automated hematology analyzer.

Results. Our results demonstrated a reduction in median survival among patients presenting with increased levels of the studied parameters (serum calcium, CRP, LDH, β2-microglobulin, and involved free light chains), as well as decreased levels of other parameters such as hemoglobin and albumin.

The study confirmed the prognostic value of the International Staging System (ISS), as median survival decreased with advancing ISS stage.
CONCLUSION. This study aims to identify, on the one hand, the most effective prognostic factors and, on the other hand, the simplest parameters capable of accurately defining a patient's prognostic stage, thereby enabling a personalized approach. Such an approach may pave the way for more effective targeted therapies and an overall improvement in prognosis.

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INTRODUCTION

Multiple myeloma (MM), also known as Kahler disease, is a malignant proliferation of a clonal population of plasma cells within the bone marrow. MM is characterized by the production of a monoclonal immunoglobulin (Ig) detectable in serum and/or urine. At present, MM is still considered an incurable disease, with a highly variable prognosis ranging from prolonged survival to a high risk of disease relapse. Indeed, the median survival of affected patients varies from 19 to 72 months depending on ethnicity and the therapeutic regimens used [1–3].

In this context, it is essential to assess prognosis through the evaluation of factors involved in the diagnosis and follow-up of MM, in order to appropriately balance conventional therapeutic approaches with more innovative treatments while considering the risk of unfavorable disease progression [3,4].

Several prognostic classifications have been established. The earliest, the Durie–Salmon staging system, is based on the assessment of tumor cell mass. However, given its limitations [5], the identification of additional prognostic factors reflecting the intrinsic biological properties of the tumor clone and its interactions with the bone marrow microenvironment has been pursued. Consequently, other prognostic factors have been proposed and subsequently recognized as being associated with reduced survival in patients with MM, including age, β2-microglobulin, C-reactive protein (CRP), lactate dehydrogenase (LDH), albumin, the plasma cell labeling index, and cytogenetic abnormalities [6]. It is now widely accepted that the combination of these prognostic factors provides a more accurate prognostic assessment than the evaluation of each factor in isolation [7]. The development of combined prognostic systems has allowed a simpler and more effective stratification of patients into prognostic groups, exemplified by the International Staging System (ISS), which distinguishes three stages based on the combined assessment of β2-microglobulin and serum albumin levels [8].

For treatment decision-making, cytogenetic classification remains of major importance, as it enables the identification of the genetic profile of myeloma cells in individual patients. Certain specific chromosomal abnormalities, such as translocations t(4;14) and t(14;16), as well as numerical chromosomal abnormalities (hyperdiploidy, hypodiploidy, or deletion of the short arm of chromosome 17), have a significant impact on prognosis [9–13].

The Revised International Staging System (R-ISS) is currently considered a reference due to its high prognostic accuracy in patients with newly diagnosed MM. This system incorporates the ISS stage, serum LDH levels, and the presence of high-risk cytogenetic abnormalities (Del(17p), t(4;14), and t(14;16)). It classifies patients into favorable, intermediate, or unfavorable risk categories based on disease progression risk [14].

Furthermore, ongoing studies aim to identify novel prognostic markers that may enhance the predictive accuracy of MM prognosis. These include more comprehensive genetic profiling, gene expression analyses, and specific protein biomarkers. Within this framework, the objectives of our study include the identification and determination of prognostic factors capable of predicting survival in patients with MM, as well as the evaluation of the impact of combined prognostic factors on disease progression and overall survival in our patient population.

PATIENTS AND METHODS

We conducted a multicenter, retrospective-descriptive, and analytical cross-sectional study using the medical records of patients managed in the Immunology Unit of the Blida University Hospital Center. Out of an initial sample of 5717 patients recruited over a period from 2012 to 2024, 359 patients were included in this study. The cohort consisted of 194 men (54%) and 165 women (46%). These patients were referred from the regional Hematology, Rheumatology, and Nephrology departments. All included patients met the International Myeloma Working Group (IMWG) diagnostic criteria and had undergone regular

follow-up at our unit. The mean age of our patient population was 66 ± 14.77 years, with the most affected age group being between 60 and 80 years of age [60, 80[(Table 1 and Figure 1).

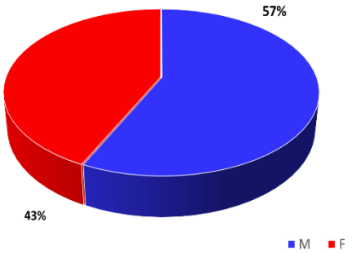

Figure 1. Distribution of patients by gender

Table 1. Distribution of patients by age group

Age group	Patient frequency (%)
<30	0,25%
[30, 40[	1,79%
[40, 50[	8,76%
[50, 60[	18,64%
[60, 70[	28,24%
[70, 80[	27,61%
>80	14,68%

Patients were excluded from our study if they presented with other malignant hemopathies or if their medical records were incomplete or unusable.

The 359 collected patients underwent serum and urinary exploration, involving serum and urinary protein electrophoresis and immunofixation performed on a Hydrasys analyzer (HYDRAGEL B1-B2 KIT) to detect and quantify the monoclonal component (MC), and to screen for Bence Jones proteins (BJP).

They also received a quantitative assay of proteins (Ig, free kappa and lambda light chains (FLCκ and FLCλ), β2-microglobulin, CRP, LDH) using Binding-Site reagents on the SPA plus® immunoturbidimeter, and hemoglobin detection via a SYSMEX®-type hematology analyzer.

RESULTS

1) Distribution of Patients According to the MC Isotype

In our series, the IgG isotype was the most represented MC, found in 233 patients (65%), with a clear predominance of IgG kappa (173 patients), followed by the IgA kappa light chain isotype. **(Table 2)**

Table 2. Distribution of patients according to CM isotype.

CM	Effectif (N/%)	Kappa	Lambda
IgG	234 (65%)	173	61
IgA	79 (22%)	63	15
IgD	2 (0,6%)	1	1
IgM	11 (3%)	8	3
Light chains	33 (9%)	23	10

2) Distribution of patients according to the level of polyclonal immunoglobulins

The serum protein electrophoresis performed on gel detected hypogammaglobulinemia in 288 patients, against 71 patients who had a normal quantification of polyclonal immunoglobulins. **(Table 3)**

SPE	Hypogammaglobulinemia	Normal Profile
Number of patients	209 (58%)	150 (42%)

3) Distribution of patients according to the results of the Bence-Jones proteinuria screening

The screening for Bence Jones proteins in 24-hour urine collected in a sterile jar was positive in 141 patients (i.e., 39%). It was of the same isotype as the serum MC light chain, with the exception of two patients: the first had negative serum electrophoresis and immunofixation, and the second had a light chain different from the one identified in the serum. **(Table 4)**

Table 4. Distribution according to the presence or absence of BJP.

BJP	Presence	Absence
Number of patients	140 (39%)	219 (61%)

4) Distribution of patients according to prognostic parameters

Our sample was composed of three prognostic groups, distributed according to the ISS classification : Stage I progressive, stage II, and stage III.

4.1- Distribution of patients according to age

The average age of our patients was 66 years, of whom 55% were aged over 65 years, with a mean survival of 23 months, statistically different from that of patients aged less than 65 years (27 months vs 23 months respectively, p=0.001).

4.2- Prognostic evaluation according to the immunoglobulin isotype

Two hundred and thirty-four patients, i.e., 63%, had an MC of the IgG isotype and a mean survival of 26 months; whereas for the 79 patients who presented an MC of the IgA isotype, their mean survival was 22 months; and finally, the mean survival of patients presenting an MC of the light chain isotype was 25 months, with a very significant difference between the three groups (p < 0.0001, HR = 0.33). (**Figure 1**)

For the IgD and monomeric IgM isotypes, the mean survival was 11 and 40 months, respectively.

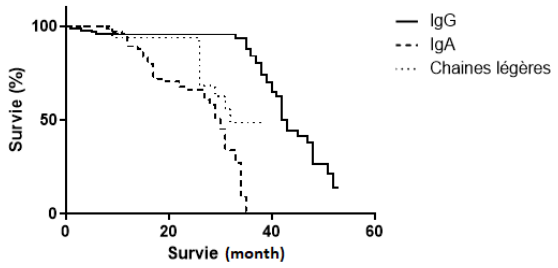

Figure 1. Prognostic evaluation according to the monoclonal immunoglobulin isotype.

4.3- Prognostic evaluation according to the level of the monoclonal component

In our series, the average level of the monoclonal component was 34 g/l. A better survival was noted in 153 patients (i.e., 63%) who had an MC level below 34 g/l compared to patients presenting with MC levels > 34 g/l. (26 months vs 22 months respectively, p < 0.0001, HR = 0.22). **(Figure 2)**

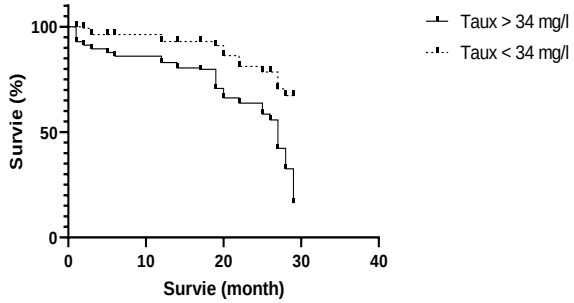

Figure 2. Prognostic evaluation according to the level of the monoclonal immunoglobulin isotype.

4.4- Prognostic evaluation according to the presence of Bence Jones proteins

In our series, 140 patients (i.e., 56%) presented positive BJP with a significantly higher mean survival compared to that of BJP-negative patients (25.40 vs 20.80 months, P = 0.0006; HR = 0.59). **(Figure 3)**

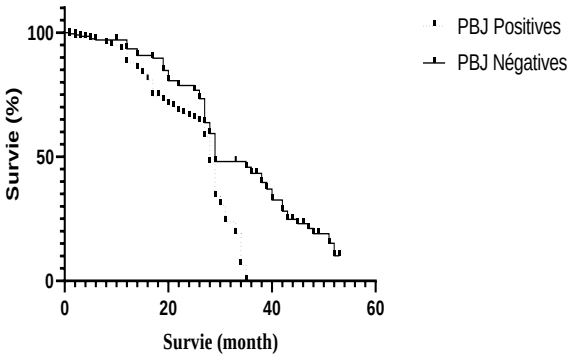

Figure 3. Prognostic evaluation according to the presence or absence of BJP.

4.5- Prognostic evaluation according to the ß2-microglobulin level

Our study noted a significant difference between the mean survival of the 94 patients (i.e., 26%) who had a β2m level < 3.5 mg/L, the 85 patients (i.e., 29%) who had a level between 3.5 and 5.5 mg/L, and the group of 180 patients (i.e., 45%) who had a level greater than 5.5 mg/L (26.52 months vs 24.03 months vs 22.73 months, respectively; p<0.0001). **(Figure 4)**

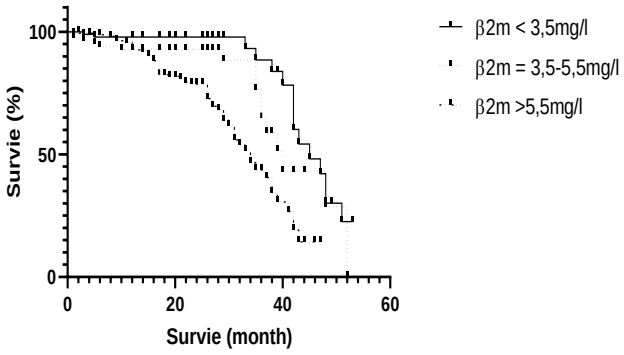

Figure 4. Prognostic evaluation according to the ß2m level.

4.6- Prognostic evaluation according to the albumin level

In our study, 135 patients, i.e., 37.6%, had a serum albumin level below 35 g/L and 62.4% had a serum

albumin level above 35 g/L, with a significant difference in the respective median survival between the two groups (28 months vs 29 months, P = 0.003, HR = 0.53). **(Figure 5)**

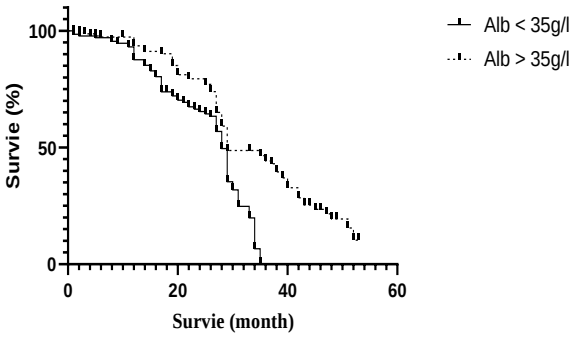

Figure 5. Prognostic evaluation according to the serum albumin level.

4.7- Prognostic evaluation according to the LDH level

In our series, the mean LDH was 270.5 IU/L, i.e., above the normal value between 30-200 IU/L. The 33 patients (9%) who had a level below 120 IU/L had a significantly better median survival compared to the groups who had an LDH level between 120 and 246 IU/L (13%), and the group of patients with an LDH level above 246 IU/L (78%), respectively (33 (9%) vs 45 (13%) vs 281 (78%), 34 months vs 29 months vs 27 months, p=0.008). **(Figure 6)**

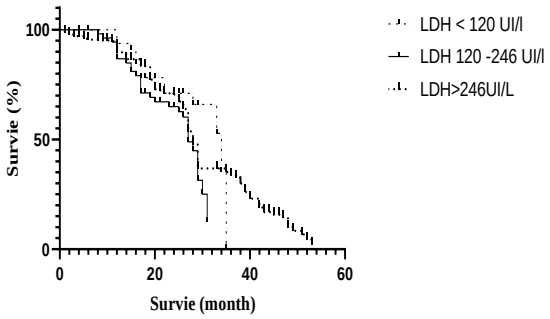

Figure 6. Prognostic evaluation according to the serum albumin level.

4.8- Prognostic evaluation according to the International Staging System (ISS)

In our sample, the patients were classified according to the ISS classification, which takes into account albumin and β2m, into three prognostic groups: Stage I progressive, stage II, and stage III. **(See Table 5)**

Table 5. Distribution of patients with MM according to the ISS classification.

Stage	Characteristics	Number of cases	Median survival
I	B2m < 3,5mg/L et Alb > 35g/L	84	32 months
II	B2m < 3,5mg/L et Alb < 35g/L **ou** 3,5 < B2m < 5,5 regardless of albuminemia	51	28 months
III	B2m > 5,5	224	26 months

A significant difference was noted between the three groups, with a better prognosis for patients classified as ISS stage I with an estimated median survival of 31 months, compared to patients in stages II and III (31 vs 28 vs 26 months respectively, p = 0.003). **(Figure 7)**

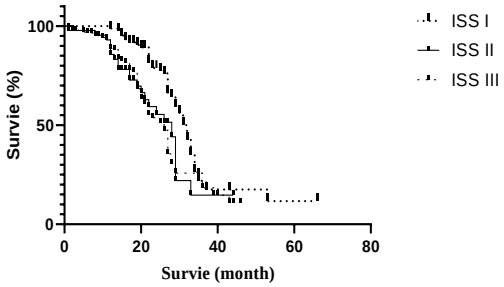

Figure 7. Prognostic evaluation according to the ISS classification.

4.9- Prognostic evaluation according to the free kappa/lambda light chain ratio

The measurement of free light chains (FLC) at diagnosis allowed us to distinguish two groups after calculating the κ/λ FLC ratio (rFLC): a group of 97 patients with a normal rFLC (between 0.26 – 1.65), and another group of 262 patients with an unbalanced rFLC (<0.26 or >1.65).

A significant difference was noted in our study between the two groups, with a better median survival for patients with a normal rFLC at diagnosis (31 years vs 26 years, respectively, p = 0.0002; HR = 0.55). **(Figure 7)**

It was highlighed that the text mentions "31 years vs 26 years" for median survival, which is highly unusual for multiple myeloma and likely a

typographical error from the original French "31 mois vs 26 mois" (months). I have translated it verbatim as requested. In an academic context, this discrepancy should be verified and corrected.

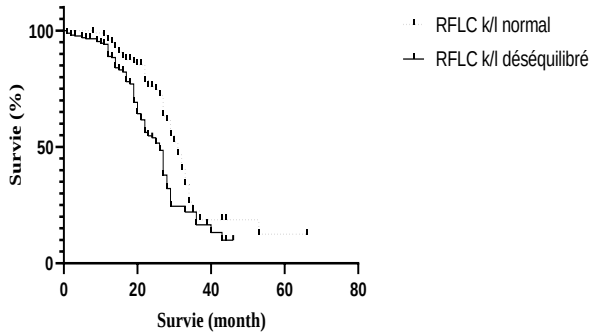

Figure 7. Prognostic evaluation according to the κ/λ FLC ratio.

In parallel, we calculated the ratio of involved to uninvolved free light chains (iFLC/uFLC ratio), which allowed us to distinguish two groups: a group of 156 patients with a ratio below 100, and a group of 203 patients with a ratio above 100. A significant difference was observed in our study between the two groups, with a better median survival for patients with an iFLC/uFLC ratio below 100 at diagnosis (29 years vs 26 years, respectively, p = 0.006; HR = 0.66). **(Figure 8)**

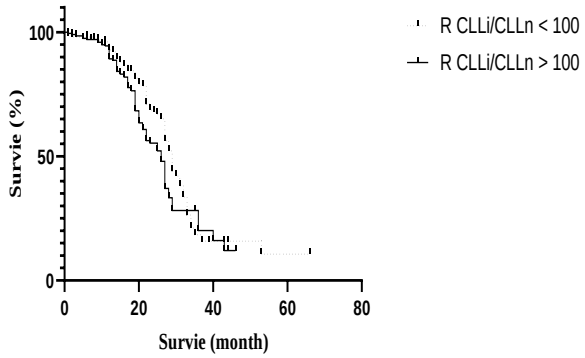

Figure 8. Prognostic evaluation according to the iFLC/uFLC ratio.

4.10- Prognostic evaluation according to the serum creatinine level

In our population of 359 patients, we distinguished two groups: a group of 76 patients (i.e., 21%) who had a normal creatinine level, and another group of 283 patients (i.e., 79%) who had creatinine above the normal level. The median survival was significantly better in patients with a normal creatinine level (32 years vs 26 years, respectively, p < 0.0001; HR = 0.56). **(Figure 9)**

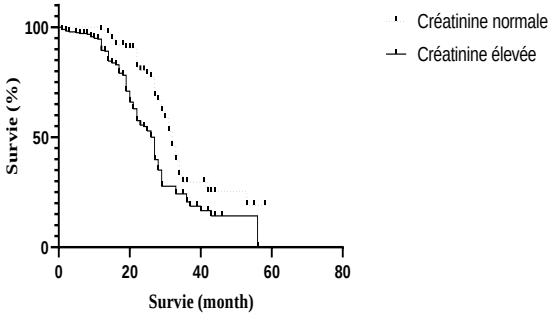

Figure 9. Prognostic evaluation according to the creatinine level.

4.11- Prognostic evaluation according to the calcium level

In our population, 251 patients (i.e., 70%) had a normal calcemia with a better median survival than the 108 patients (i.e., 30%) who had an elevated calcemia (28 years vs 27 years, respectively, p < 0.02; HR = 0.71). **(Figure 10)**

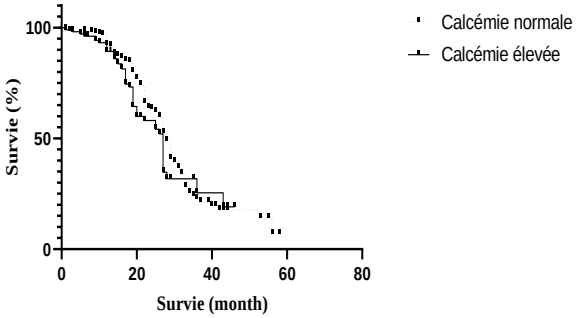

Figure 10. Prognostic evaluation according to the calcium level.

4.12- Prognostic evaluation according to the hemoglobin (Hb) level

In our series, the mean hemoglobin was 9.6 g/dL. A group of 116 patients, i.e., 32%, whose Hb was greater than 10 g/dL had a better median survival than the 93 patients (26%) with an Hb level between 8 and 10 g/dL and the 150 patients (42%) with an Hb level below 8 g/dL (30 years vs 25 years vs 23 years, respectively, p < 0.0001). **(Figure 11)**

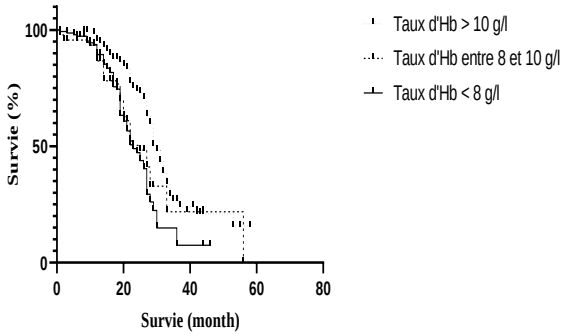

Figure 11. Prognostic evaluation according to the Hb level.

4.13- Prognostic evaluation according to the serum C-reactive protein (CRP) level

In our series, 233 patients, i.e., 65%, had a CRP level greater than 6 mg/L, and the remaining 126 patients, i.e., 35%, had a level below 6 mg/L. The median survival in patients with a level below 6 mg/L was significantly better than in patients with a CRP level greater than 6 mg/L (29 years vs 26 years, respectively; $p < 0.002$; HR = 0.63). **(Figure 12)**

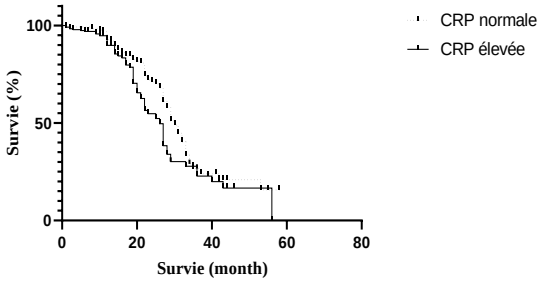

Figure 12. Prognostic evaluation according to the CRP level.

DISCUSSION

Over the past few decades, significant advances have been made in understanding the immunological aspects of MM, revealing the complexity of assessing the progression and prognosis of this disease. Several immunological parameters have been studied in this context, such as cellular subpopulations, markers of immune activation, cytokines, and growth factors.

In this study, we examined the correlation between several parameters (immunological and non-immunological) and survival in patients with MM, in order to identify potentially useful immunological markers in disease monitoring and to evaluate them in light of current knowledge.

Such an evaluation of immunological parameters can contribute to a better understanding of the mechanisms involved in MM and provide valuable information for predicting prognosis and making the best therapeutic choice. At this stage, it may be possible to identify patients at high risk of disease progression and direct them towards more aggressive therapeutic strategies.

The age of patients with MM is one of the prognostic elements; indeed, it is linked to the body's ability to tolerate intensive treatments (chemotherapy or stem cell transplants) and can also influence the speed of disease progression. Therapeutic strategies are therefore often adapted to the age and general condition of the patients. Advanced age constitutes a poor prognostic factor for the majority of authors such as Paule et al, Chombart et al, and Bauduer et al [15, 16, 17]. Our results are consistent with data from the literature, with a shorter mean survival in MM patients aged over 65 years.

Gender is not a major prognostic factor for MM, as survival is similar between the two sexes, although men are more frequently affected [17]. Several recent studies suggest fundamental genetic differences between the two sexes, without a significant influence on clinical expression and prognosis [16, 17, 18].

The assessment of the impact of gender in our study showed a slight male predominance of 57%, and the mean male survival was similar to that of female subjects with MM (24 months).

Hypogammaglobulinemia (or immunoparesis) is defined by a decrease in the serum level of one or two intact immunoglobulin isotypes not involved in the clonal process, a common situation in MM, and which constitutes one of the poor prognostic factors given the significant increase in the risk of severe infections, with increased morbidity and mortality, even with modern treatments. The worsening of prognosis is associated both with the risk of progression of the clonal disease and with the risk of infectious complications [19, 20].

The mechanisms of hypogammaglobulinemia are either related to MM itself (inhibitory effect of the malignant plasma cell clone), but also to associated AL amyloidosis, IgG hypercatabolism, inhibition of CD19+ B cells and plasma cells, abnormal expression of transcription factors by B cells, excessive production of TGFβ by myeloma cells,

and finally dysfunction of T helper lymphocytes [21, 22, 23].

In the literature, hypogammaglobulinemia is found in approximately 90% of newly diagnosed multiple myeloma cases [24], and 45 to 83% of patients followed for MM present with hypogammaglobulinemia at some point in the disease course, with a higher frequency in light chain MM, worsening the prognosis especially with the onset of renal lesions, and requiring rigorous management between prophylaxis and vaccination to reduce mortality [19].

In our study, 58% of our MM patients had hypogammaglobulinemia at varying levels, from a slight decrease to a collapse of the residual gamma globulin level. This measurement allowed the implementation of preventive measures in our patients to avoid the occurrence of infections that could complicate the management of these patients.

Bence-Jones proteins (urinary Free Light Chains) appear when the excess production of light chains exceeds the capacity of proximal tubular cells to catabolize them; they reach the distal tubule to bind with Tamm-Horsfall protein produced in the ascending part of the loop of Henle. This process leads to the formation of casts with obstruction of the distal tubule and ascending loop of Henle, and the elimination of excess light chains via urine [25].

The prognosis of MM with positive Bence-Jones protein is often considered less favorable, as it indicates that the disease is more aggressive, with significant renal involvement. Bence-Jones proteins are present in the majority of MM patients, with frequencies ranging from 50 to 80%. Several factors can influence their appearance in urine, including isotype, since the risk of their appearance is increased in patients with light chain MM (increases by 5 to 10%) [25].

In our work, 39% of our patients presented with positive Bence-Jones proteins, somewhat less than in the literature, especially since many of our patients were recruited at an early stage of the disease.

Several publications have highlighted the impact of isotype on the median survival of MM, such as free light chain isotypes, IgD and, in rare cases, IgE [26]. In our study, we found that patients with IgG MM had a better prognosis compared to patients with IgA MM and patients with light chain MM.

The characteristics and concentration of the monoclonal component is a key element of MM and can be used to assess tumor burden and disease progression. Several studies have reported a correlation between the concentration of the monoclonal component and the median survival of MM patients, such as the work conducted by Rajkumar where his patients who presented a high concentration of the monoclonal component had a less favorable prognosis and reduced survival compared to those with a lower concentration [27]. Furthermore, a meta-analysis conducted by Ludwig confirmed this association and concluded that higher levels of the monoclonal component were associated with an increased risk of rapid disease progression and shorter survival [28].

These results support the idea that the concentration of the monoclonal component is an important prognostic marker in MM and corroborate the results obtained in our study.

β2m is a first-line marker in malignant B lymphopathies and particularly in MM. Its measurement is also used in other pathologies. A correlation has been observed between the β2m level and survival in MM. It is an independent prognostic factor, confirmed by many authors [29, 30], and it was the most significant of all tumor mass-related parameters in our study (p=0.0001).

Serum albumin level is generally considered a biological marker and prognostic factor used for more than 30 years, reflecting nutritional status and systemic inflammatory response. Hypoalbuminemia is a common clinical feature in MM, and it comprises multiple etiologies, such as malnutrition, renal dysfunction, and hepatic insufficiency [31, 32]. It is reported as a poor prognostic factor in MM patients [33].

In our study, 37.6% had hypoalbuminemia (<35g/L), and they had a better median survival compared to patients with an albumin level >35 g/L. This correlates with the aforementioned studies.

LDH (Lactate Dehydrogenase) is an enzyme measured in the diagnosis and monitoring of MM patients, as a high level indicates a more aggressive form of the disease, a greater tumor burden, and consequently a poor prognosis. Several studies

have reported a significant correlation between LDH level and median survival in MM patients, such as the study conducted by Granell et al which showed that patients with a high LDH level had a significantly reduced median survival compared to those with a normal LDH level. These results were confirmed by Rajkumar et al [27, 34]. These results suggest that the LDH level can be an important prognostic marker for assessing the survival of MM patients. A high LDH level may reflect increased cellular metabolic activity, a greater tumor burden, or other underlying biological processes that can negatively influence patient survival. A finding well demonstrated by our present study.

The ISS classification is widely used to assess the stage and predict the prognosis of MM patients.

We observed concordance with several studies. We cite the study conducted by Greipp et al which was able to demonstrate the prognostic utility of the ISS classification by establishing a direct link between the stages of the ISS classification and the median survival of MM patients. This study also emphasized the predictive value of the ISS classification in terms of treatment response and overall survival [35]. The same results were concluded in a meta-analysis conducted by Kumar et al [36]. This confirms that the ISS classification is a valuable tool for predicting patient prognosis, with shorter survival observed in patients classified in higher stages.

In our study, patients classified in more advanced stages according to the ISS classification had a significantly reduced median survival compared to those classified in less advanced stages.

These results support the idea that the ISS classification is an important prognostic tool for assessing the survival of MM patients; it allows for the stratification of patients into risk groups and guides therapeutic decisions based on disease severity.

FLCs (Free Light Chains) are essential in the diagnosis and monitoring of MM, as they are produced in excess by the malignant clone plasma cells, and an abnormal κ/λ FLC ratio or a high iFLC/uFLC ratio can indicate rapid and aggressive disease progression. The calculation of the FLC ratio is crucial in light chain MM, especially if the classic monoclonal peak is not visible.

Several studies have reported high kappa/lambda light chain ratios in MM patients and correlated them with median survival [37, 38, 39]. Similarly, a meta-analysis conducted by confirmed the significant association between the FLC ratio and survival in MM patients and concluded that higher FLC ratios were associated with an increased risk of disease progression and shorter survival [40]. This confirms the importance of the FLC ratio as a diagnostic and prognostic marker in this disease.

The concordant results between our study and the literature support the idea that the FLC ratio is an important prognostic marker in MM. A high FLC ratio may reflect a greater tumor burden, increased disease activity, and a more unfavorable prognosis.

On the other hand, the calculation of the iFLC/uFLC ratio showed that the 57% of patients with a ratio > 100 had a less favorable prognosis than the 43% of patients with a ratio <100. This observation is in agreement with several MM studies [41, 42]. These results confirm the importance of this ratio as a diagnostic and prognostic marker in the disease. However, it is important to take into account other prognostic factors and clinical characteristics to fully assess the prognosis of an MM patient and their therapeutic monitoring. Variations in this ratio could indicate treatment efficacy and guide therapeutic decisions [42, 43].

However, it is essential to note that the involved to uninvolved free light chain ratio must be interpreted with caution, taking into account the particularities of each patient and other clinical parameters.

Regarding hypercalcemia, which is a common complication associated with MM and can be an indicator of disease progression. Several findings in previous studies have reported a correlation between calcium concentration and survival in MM patients; they have shown that patients with elevated calcium at diagnosis had a less favorable prognosis and reduced survival compared to those with normal calcium [44, 45]. These studies emphasize the association of high calcium with tumor burden, renal involvement, and deterioration of the patients' general condition.

These results are consistent with our study and support the interest of measuring calcium in MM patients as a prognostic marker.

Hemoglobin is often low (anemia) in MM due to a mechanism related to the invasion of the bone marrow by the malignant plasma cell clone, which results in anemia considered a major prognostic factor, included in the CRAB diagnostic criteria. It is accepted that a decreased Hb level in MM patients influences median survival and the prognosis is unfavorable [37]. An observation confirmed by our study.

Several other studies have also reported a significant correlation between CRP level and survival in MM patients [41, 46].

This study emphasized the presence of a chronic inflammatory environment in MM and that its measured intensity influences disease progression and prognosis.

Our study and the literature support the idea that the CRP level can be an important prognostic indicator in MM patients and that its increase correlates with more aggressive disease progression, which can negatively influence patient survival.

CONCLUSION

The prognosis of MM is determined by clinical, genetic, and molecular factors. Some of them are crucial and can independently reveal the aggressiveness of the disease, and others are included in scores such as ISS or R-ISS, allowing for a refined risk assessment. Although innovative treatments have transformed the disease into a chronic pathology, prolonging the survival of patients with an incurable disease.

Identifying and understanding factors with prognostic characteristics is important for optimizing patient management, after accurate risk stratification and proper guidance of therapeutic decision-making.

This study aims to identify the most effective factors on the one hand, and the simplest ones capable of specifying the precise prognostic stage of a patient for a personalized approach, which paves the way for more effective targeted therapies and an overall improvement in prognosis.

DECLARATION OF INTERESTS

No conflict of interest.

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