Cancer Epidemiology xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Cancer Epidemiology

The International Journal of Cancer Epidemiology, Detection, and Prevention

journal homepage: www.cancerepidemiology.net

Trends in survival of multiple myeloma: A thirty-year population-based study in a single institution

Rafael Ríos-Tamayo[a,b,c,g,*], María José Sánchez[d,e,g], José Manuel Puerta[b], Juan Sáinz[a,b,c,g], Daysi-Yoe-Ling Chang[d,g], Teresa Rodríguez[h], Pilar López[b], José María de Pablos[b], Pilar Navarro[b], José Luís García de Veas[h], Antonio Romero[b], Pilar Garrido[b], Lucía Moratalla[b], Carolina Alarcón-Payer[i], Elisa López-Fernández[b], Pedro Antonio González[b], José Juan Jiménez-Moleón[e,f,g], Miguel Ángel Calleja-Hernández[g,i], Manuel Jurado[a,b,c,g]

[a] Monoclonal Gammopathies Unit, University Hospital Virgen de las Nieves, Granada, Spain
[b] Department of Hematology, University Hospital Virgen de las Nieves, Granada, Spain
[c] Genomic Oncology Area, GENYO, Centre for Genomics and Oncological Research: Pfizer/University of Granada/Andalusian Regional Government, PTS, Granada, Spain
[d] Granada Cancer Registry, Andalusian School of Public Health, Granada, Spain
[e] CIBER Epidemiology and Public Health, Granada, Spain
[f] Department of Preventive Medicine and Public Health, University of Granada, Granada, Spain
[g] Instituto de Investigación Biosanitaria de Granada (Ibs.GRANADA), Hospitales Universitarios de Granada/Universidad de Granada, Granada, Spain
[h] Department of Inmunology, University Hospital Virgen de las Nieves, Granada, Spain
[i] Pharmacy Department, University Hospital Virgen de las Nieves, Granada, Spain

ARTICLE INFO

Article history:
Received 4 May 2015
Received in revised form 2 August 2015
Accepted 6 August 2015
Available online xxx

Keywords:
Multiple myeloma
Population-based registry
Comorbidity
Survival

ABSTRACT

Background: Despite the progress made in recent years, multiple myeloma is still considered an incurable disease. Most survival data come from clinical trials. Little is known about the outcome in unselected real-life patients.
Methods: Overall survival was analyzed in a cohort of newly diagnosed symptomatic multiple myeloma patients, over the last three decades, in a single institution population-based study.
Results: 582 consecutive myeloma patients were included in the study. Survival increased over time in patients younger than 65 years but did not reach statistical significance in patients with 65 years or older. The prognostic factors associated with overall survival were the International Staging System, the serum lactate dehydrogenase level, the renal impairment, the realization of autologous stem cell transplantation, and the presence of concomitant amyloidosis. Overall survival shows a steady improvement over time.
Interpretation: The survival of myeloma is improving progressively in real-life patients, particularly after the widespread use of the novel agents. A comprehensive assessment of comorbidity can help to explain the huge heterogeneity of myeloma outcome. The optimization of current therapeutic resources as well as the incorporation of new drugs will allow further improvement of survival in the coming years.

1. Introduction

Multiple myeloma (MM) is a biologically complex and clinically heterogeneous disease [1,2] whose definition has been recently updated [3]. Symptomatic or active MM is characterized by a clonal expansion of plasma cells (PC) in the bone marrow (BM), the detection in most cases of a monoclonal immunoglobulin in serum and/or urine and the presence of end-organ damage. It accounts for approximately 1% of neoplastic diseases and 13% of hematologic cancers [4–6]. MM is always virtually preceded by a premalignant stage, termed monoclonal gammopathy of undetermined significance. Sometimes, a more advanced but still asymptomatic disease known as smoldering MM (SMM) may appear behaving as an

* Corresponding author at: Monoclonal Gammopathies Unit, University Hospital Virgen de las Nieves, Avda. Fuerzas Armadas, 2, 18014 Granada, Spain.
Fax: +34 958020655.
E-mail address: rriost33@gmail.com (R. Ríos-Tamayo).

http://dx.doi.org/10.1016/j.canep.2015.08.002
1877-7821/

intermediate entity between monoclonal gammopathy of undetermined significance and MM.

It has been shown that the course of MM is highly variable with both long-term and short-term surviving patients. At present, the prognosis of newly diagnosed MM (NDMM) is based on the International Staging System (ISS) as well as on the interphase fluorescence in situ hybridization (FISH) results [7]. These tools have represented a major advance in the prognostic evaluation of MM. However, many studies have identified other prognostic factors with additional capability to predict part of this heterogeneity in survival. Therefore, comorbidity should be taken into account to improve the prognostic assessment in MM [8].

There is no doubt that treatment has a major impact on the outcome. Overall survival (OS) has improved slightly over time with the use of conventional therapy (corticosteroids, anthracyclines and alkylating agents) whereas during the past decade, the widespread use of the novel agents has led to a marked improvement in OS. Fortunately, we can now face the future of MM as a chronic disease. In addition, the operational cure could be an achievable objective in a selected group of patients. Notwithstanding, the benefit in terms of survival varies between different studies and comorbidity could be responsible for part of this heterogeneity. The available information on OS studies is derived primarily from clinical trials, in which patients with common comorbidities are excluded. Little is known about OS in population-based series with real-life patients. The aim of this single institution population-based study is to report trends on OS over 30 years in a large population of unselected NDMM patients.

2. Materials and methods

2.1. Patients

The Granada Cancer Registry is a population-based cancer registry that works since 1985 and covers a population of 905.285 inhabitants, of which 442.523 belong to the reference area of our hospital. This Registry is integrated into the European Network of Cancer Registries, using internationally standardized work rules and procedures, ensuring the quality of the information. The main source of information is the electronic clinical record, but all other public and private available sources are continuously analyzed. In 2011, a comparison was made between the two available registries (hospital-based and population-based) [9] and a specific population-based monographic MM clinical registry (MMCR) was created. According to the International Classification of Diseases, only patients with C90.0 code were included, excluding patients with primary plasma cell leukemia (C90.1), extramedullary plasmacytoma (C90.2) or solitary plasmacytoma (C90.3). From January 1985 to January 2015, all NDMM patients who had their current residence at the time of diagnosis in Granada and met the diagnostic criteria of the International Myeloma Working Group (IMWG) [10], were included in the MMCR and are the basis of this study, which was performed according to the Declaration of Helsinki (Ethics Committee approval number C-14, CEI-Gr, 2014). Although our policy is to include those patients diagnosed post-mortem and by death certificate, provided they met the mentioned criteria, no case was incorporated by this method. Demographic and survival data are available for the whole cohort, but clinical data were incorporated in 1993.

2.2. Variables

All common baseline prognostic factors were recorded, such as age, subtype of myeloma, renal function, Eastern Cooperative Oncology Group (ECOG) performance status score, the presence of cytogenetic abnormalities by FISH and ISS. Renal function was assessed by serum creatinine (sCr, mg/dL) and the estimated glomerular filtration rate (eGFR). Other variables of increasing interest were also included in the study, such as the Body Mass Index (BMI), the occurrence of weight loss before diagnosis, the delay in diagnosis, the serum free light chain ratio (FLCr), lactate dehydrogenase (LDH), BMPC as measured by morphology and flow cytometry, the documentation of lytic lesions, the use of bortezomib in induction, the realization of autologous SCT (ASCT) and the calendar period. Comorbidity was divided in twenty

Table 1
Baseline patient characteristics according to calendar periods.

Characteristic	1985–1989	1990–1994	1995–1999	2000–2004	2005–2009	2010–2014	Total
No.(%)	63(10.8)	66(11.3)	107(18.4)	108(18.6)	109(18.7)	129(22.2)	582
Age, years							
Median	64	67	70	67	68	65	66
Range	28–83	35–85	31–91	39–87	21–88	12–91	12–91
Sex, *n*(%)							
Male sex	29(46)	32(48.5)	51(47.7)	53(49.1)	41(37.6)	74(57.4)	280(48.1)
Subtype, *n*(%)							
IgG	–	2(33.3)	28(58.3)	54(55.7)	61(57)	68(52.7)	213(55)
IgA	–	1(16.7)	11(22.9)	26(26.8)	26(24.3)	35(27.1)	99(25.6)
LC	–	3(50)	8(16.7)	9(9.3)	17(15.9)	22(17.1)	59(15.2)
NS	–	0	1(2.1)	7(7.2)	2(1.9)	3(2.3)	13(3.4)
IgD	–	0	0	1(1)	0	1(0.8)	2(0.5)
IgM	–	0	0	0	1(0.9)	0	1(0.3)
ISS, *n*(%)							
I	–	1(50)	1(8.3)	10(27.8)	20(22.2)	38(30.9)	70(26.6)
II	–	1(50)	4(33.3)	9(25)	23(25.6)	32(26)	69(26.2)
III	–	0	7(58.3)	17(42.2)	47(52.2)	53(43.1)	124(47.1)
eGFR < 60, %	–	50	72.8	53.2	54.9	45.4	52
%BMPC, mean	–	37	27.7	27.9	25	23.4	25.5
BMI ≥30, no.(%)	–	2(50)	4(26.7)	18(40)	26(32.9)	36(29.3)	86(32.3)

Abbreviations: Ig = immunoglobulin, LC = light chain only, NS = non-secretory, ISS = International Staging System, eGFR = estimated glomerular filtration rate (mL/min/1.73 m^2), BMPC = bone marrow plasma cells, BMI = Body Mass index (kg/m^2).

Please cite this article in press as: R. Ríos-Tamayo, et al., Trends in survival of multiple myeloma: A thirty-year population-based study in a single institution, Cancer Epidemiology (2015), http://dx.doi.org/10.1016/j.canep.2015.08.002