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Incidence and outcome of patients starting renal replacement therapy for end-stage renal disease due to multiple myeloma or light-chain deposit disease: an ERA-EDTA Registry study

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Abstract

Background. Information on demographics and survival of patients starting renal replacement therapy (RRT) for end-stage renal disease (ESRD) due to multiple myeloma (MM) or light-chain deposit disease (LCDD) is scarce. The aim of this study was to describe the incidence, characteristics, causes of death and survival rates of RRT for ESRD due to MM or LCDD in the ERA-EDTA Registry.

Methods. Thirteen national registries providing data on patients who started RRT from 1986–2005 to the ERA-EDTA Registry participated. Incidence per million population (pmp) of RRT for ESRD due to MM or LCDD and other causes (non-MM) was observed overtime. Patient survival on RRT was examined, unadjusted and adjusted for age and gender.

Results. Of the 159 637 patients on RRT, 2453 (1.54%) had MM or LCDD. The incidence of RRT for ESRD due to MM or LCDD, adjusted for age and gender, increased from 0.70 pmp in 1986–1990 to 2.52 pmp in 2001–2005. MM and LCDD patients compared to non-MM patients were older and a higher percentage was on haemodialysis at day 91 after the start of RRT. The most common causes of death in MM and LCDD patients were malignancy (36.1%), cardiovascular causes (17.2%) and infection (14.7%). MM and LCDD patients had a 2.77 (95% CI, 2.65–2.90) higher risk of death compared to non-MM patients. The unadjusted median survival on RRT was 0.91 years in MM and LCDD patients and 4.46 years in non-MM patients. During follow-up, 35 patients were transplanted and their mean survival was 9.6 years.

Conclusion. The incidence of RRT for ESRD due to MM or LCDD has increased over the past 20 years in Europe. The median patient survival on RRT for MM and LCDD patients was 0.91 years, compared to 4.46 years for non-MM patients. These results suggest that dialysis, and in selected cases even transplantation, should be offered to MM and LCDD patients.

Keywords: haemodialysis; incidence; multiple myeloma; light-chain deposit disease; peritoneal dialysis; survival; transplantation

Introduction

Multiple myeloma (MM) is a clonal B cell dyscrasia associated with monoclonal protein production and lytic bone lesions due to slowly proliferating plasma cells. The annual incidence of MM in the USA is 4.3 per 100 000 people, but there is a wide range from 1 per 100 000 for people aged 40–49 to 49 per 100 000 for people aged over 80 years [1,2]. MM in Europe accounts for 1% of all malignant diseases with an annual incidence of 3 to 4 per 100 000 people [3–5], and this incidence rate per 100 000 age-adjusted to the USA and Europe population has not changed significantly during the last decades [2,4,5].

However, despite its relative rarity, MM is suggested to be the most common neoplastic disorder causing end-stage renal disease (ESRD) [6] and the first malignancy to be recommended for dialysis treatment [6,7]. Early reports in the 1970s and 1980s, most of them limited case series, suggested that dialysis was a vain option of treatment in MM patients who had developed renal failure [7,8]. In recent years, this opinion has been reversed, as, although MM is a highly malignant disease which is rarely cured with conventional chemotherapy, there is evidence suggesting that survival rates of MM patients on dialysis were

found to be similar to that of MM patients not reaching uraemia [9].

The measure to justify any treatment should be based on meaningful survival data. There are numerous publications on the outcome of MM patients without or with a degree of renal impairment. Mild renal insufficiency (serum creatinine >1.3 mg/dl) is a presenting feature in nearly 50% of patients, and severe renal insufficiency (serum creatinine >2.0 to 2.5 mg/dl) is found in 15–20% of cases (reviewed in [6]). In the majority of patients, renal function improves after correction of precipitating factors causing renal failure, namely dehydration, hypercalcaemia and discontinuation of nephrotoxic drugs. However, 1% of those who do not regain normal renal function and are left with some degree of chronic kidney disease will require long-term renal replacement therapy (RRT) [6,10,11]. Most of the information on characteristics and survival of MM patients receiving long-term RRT is limited to case series or reports with a small number of patients. The only report that described characteristics and survival of MM patients in a national sample of patients with ESRD comes from the United States Renal Data System (USRDS) [12]. The aim of our study was to describe the incidence, characteristics, causes of death and survival rates in patients starting RRT for ESRD due to MM in the ERA-EDTA Registry.

Materials and methods

Patients

At an annual basis, the ERA-EDTA Registry collects data on patients who start RRT from national and regional renal registries in Europe. Renal registries sending individual data to the ERA-EDTA Registry for at least 12 years between 1986 and 2005 participated, including Austria, Belgium (French speaking), Catalonia (Spain), Finland, Greece, The Netherlands, Norway, Scotland (UK), Denmark (1990–2005), Sweden (1991–2005), Basque Country, Spain (1992–2005), Valencian Region, Spain (1992–2005) and Belgium (Dutch speaking) (1994–2005).

Methods

The analyses in this study were based on patients starting RRT for ESRD whose primary renal disease (PRD) was reported to be MM including light-chain deposit disease (LCDD) (ERA-EDTA PRD code 82) [13]. The inclusion of these two entities under one PRD code constitutes the main limitation of this study. The registry does not provide any information on histological types of MM, and there is no information on haematology criteria for the diagnosis of MM, LCDD and AL amyloidosis. Ideally, one would expect to have used the broader term of 'plasma cell disorders', but unfortunately there is no EDTA PRD code to cover all entities clustered under this term, while there are separate PRD codes for amyloid (code 83) and Waldestrom's disease (code 78), which are listed under the term and were not included in this study. Therefore, the diagnosis of MM and LCDD, provided by contributing centres, is accepted on the understanding that there may be limitations in the diagnoses of PRDs.

In this manuscript, patients with ERA-EDTA PRD code 82 will be further indicated as MM patients. All others will be indicated as non-MM patients. The following subjects were excluded from the analyses: patients who were not residing in the area covered by the contributing registry and patients younger than 20 years of age. The details of methods of data collection and data processing are described elsewhere [13]. The number of missing values of PRDs in this cohort was 0.10%, and in 16.8% of the cases, PRD was uncertain (the doctor could not identify PRD).

MM patients were described by age (group) at the start of RRT, gender, treatment modality and country and compared with non-MM patients. First treatment modality was defined as treatment at day 91 after the start of RRT, as some patients received haemodialysis (HD) for a short period, while preparations were made for peritoneal dialysis (PD). In addition, the number of transplants during the course of RRT was examined. Causes of death were studied for MM patients and non-MM patients, separately for those who died within and after 90 days since the start of RRT. The cause of death was defined according to the ERA-EDTA coding systems and categorized according to the ERA-EDTA categories [13].

Table 1. Incidence of RRT for ESRD due to MM, by country

Country	Number of patients at start RRT		
	Total	MM	% of MM
Austria	17 849	302	1.69
Basque Country (Spain)	2841	20	0.70
Belgium (Dutch speaking)	10 632	170	1.60
Belgium (French speaking)	10 037	157	1.56
Catalonia (Spain)	14 388	155	1.08
Denmark	8793	158	1.80
Finland	7315	73	1.00
Greece	23 480	230	0.98
The Netherlands	25 662	397	1.55
Norway	6531	165	2.53
Scotland (UK)	8603	183	2.13
Sweden	15 599	358	2.30
Valencian Region (Spain)	7907	85	1.07
All countries	159 637	2453	1.54

Statistical analysis

Time trends in the incidence of RRT per million population (pmp) were studied by dividing the study population into four 5-year cohorts according to the start date of RRT. Incidence rates were standardized for age and gender using the European standard population of 1995 as a reference. To compare the characteristics of the MM patients with those of the non-MM patients, the Mann–Whitney test was used for the continuous variable age having a skewed distribution, and the chi-square test was used for categorical variables. A two-tailed P value of <0.05 was considered as statistically significant.

Kaplan–Meier and Cox regression analyses, the latter adjusted for age and gender were performed to examine patient survival on RRT as well as patient survival on dialysis separately for MM patients and non-MM patients. Survival analyses were compared for those who started between 1986–1995 and 1996–2005, and in order to delineate the possible effect of modern therapy for MM, we performed analyses also for the periods 1986–1990 vs 2001–2005. The first day on RRT or on dialysis was taken as the starting point for the analysis. The death of the patient was the event studied. Follow-up time was censored at recovery of renal function, loss to follow-up and the end of the follow-up time at 31 December 2005. In the patient survival on dialysis, follow-up time was additionally censored at transplantation. To compare the results of the current study with those from the USRDS [12], patient survival was also performed since day 91. All analyses were performed using SAS 9.1.

Results

Of all 159 637 patients starting RRT from 1986 to 2005, 2453 were MM patients (1.54%; ranging from 0.70 to 2.53% between registries) (Table 1). The incidence of RRT for ESRD due to MM, adjusted for age and gender, increased from 0.70 pmp in 1986–1990 to 2.52 pmp in 2001–2005 (Figure 1, upper panel) representing a more than 3-fold increase. There was an increase in new cases of RRT for ESRD due to MM by 0.95, 1.41, 1.50 and 1.82% in the periods 1986–1990, 1991–1995, 1996–2000 and 2001–2005, respectively (Figure 1, lower panel).

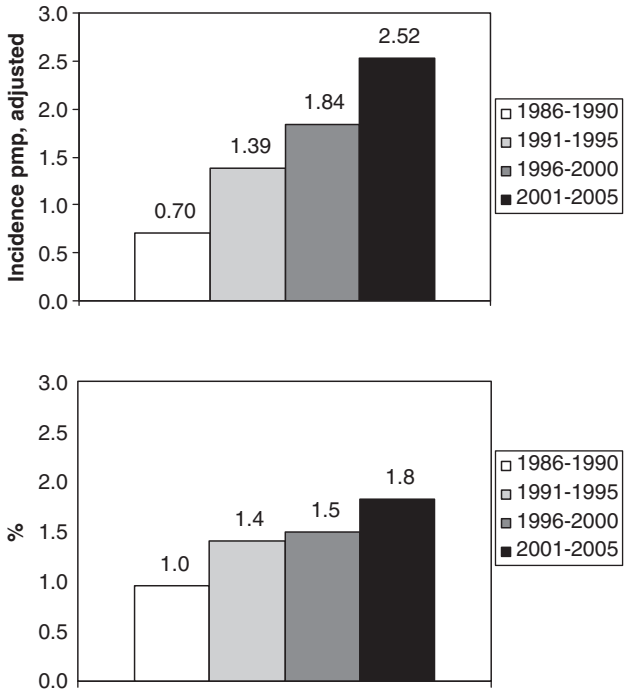

Fig. 1. Incidence of RRT for ESRD due to MM per million population, by cohort, standardized for age and gender using the European standard population of 1995 as reference (upper panel) and the percentage of new patients on RRT for ESRD due to MM, by cohort (lower panel).

These trends shown in Figure 1 were similar across contributing registries.

The characteristics of patients and treatment modality of MM patients and non-MM patients are shown in Table 2. MM patients were significantly older at the start of RRT compared to non-MM patients (mean age 67.9 vs 61.4 years, $P < 0.001$). The median age of MM patients and non-MM patients at the start of RRT increased from 64.7 and 58.0 years in 1986–1990 to 70.9 and 67.6 years in 2001–2005, respectively (Table 3), and this trend was evident in most registries.

Within 90 days from commencing RRT, 500 (20.4%) MM patients and 9868 (6.3%) non-MM patients died ($P < 0.001$), whereas renal function recovered in 75 (3.1%) of the MM patients and in 1975 (1.3%) of the non-MM patients ($P < 0.001$) within this period (Table 2). At day 91 after the start of RRT, 88.2 and 11.6% received HD and PD in the MM patients compared to 77.2 and 19.8% in the non-MM patients, respectively ($P < 0.001$).

Thirty-five MM patients (1.4%) received a renal transplantation during RRT follow-up at a mean age of 52.8 years. Of these, 11 patients received their first transplants from a living donor (31.4%) and 24 patients from a deceased donor. These transplants were performed in 9 of the 13 countries [not in Greece, Denmark, Spain (Basque Country and Valencian Region)]. In the non-MM patients, 37 048 (23.6%) received a renal transplant, and 6834 patients (18.5%) received their first graft from a living donor.

Table 4 shows that more than one-third of the MM patients died from malignancy compared to 6.2% in the non-MM patients, whereas almost 40% of the non-MM patients died from cardiovascular causes compared to 17.2% in those with MM. These differences were similar in the subgroups of patients dying within and after 90 days from the start of RRT. In patients dying within the first 90 days after the start of RRT, deaths due to infection were higher in the MM patients (18.4%) than in non-MM patients (14.1%) ($P < 0.001$), and this difference did not exist in those who died after 90 days from the start of RRT. Causes of death due to withdrawal of treatment, suicide and cachexia were not different between MM and non-MM patients.

The unadjusted median patient survival from day 1 of RRT was 0.91 years in MM patients compared to 4.46 years in non-MM patients as can be seen from Figure 2 (upper panel). Adjusted for age and gender, MM patients had a 2.77 (95% CI, 2.65–2.90) higher risk of death compared to non-MM patients. The unadjusted median survival from day 1 on dialysis was 0.90 years in MM patients compared to 3.57 years for non-MM patients (Figure 2, lower figure). Adjusted for age and gender, MM patients had a 2.72 (95% CI, 2.60–2.84) higher risk of death compared to non-MM patients.

Furthermore, patient survival on RRT from day 1 did not improve significantly from 1986–1990 to 2001–2005 in MM patients (HR = 0.91; 95% CI, 0.76–1.09), whereas this did improve in non-MM patients by 19% (HR = 0.81;

Table 2. Characteristics for MM and non-MM patients starting RRT and outcome over the first 90 days of RRT

	MM	Non-MM	*P* value
Number of patients at day 1	2453	157 184	
Male (%)	57.0	60.7	<0.001
Age (years), mean (standard deviation)	67.9 (10.3)	61.4 (15.1)	<0.001
Age (years), median [25th–75th percentile]	69.4 [61.4–75.4]	63.4 [51.8–73.0]	
Number of patients dying within 90 days from starting RRT	500 (20.4%)	9868 (6.3%)	<0.001
Renal function recovered within 90 days from starting RRT	75 (3.1%)	1975 (1.3%)	<0.001
Loss to follow-up	14 (0.6%)	381 (0.2%)	<0.001
Stopped treatment/limited care	0	47 (0.03%)	NA
Number of patients at day 91 (% of number of patients at day 1)	1864 (76.0%)	144 913 (92.2%)	
Treatment modality at day 91			<0.001
HD (%)	88.2	77.2	
PD (%)	11.6	19.8	
Pre-emptive transplantation (%)	0.2	3.0	

NA,not applicable.

Table 3. Mean age (standard deviation) and median age [25th–75th percentile] for MM patients and non-MM patients at the start of RRT, by cohort

	MM		Non-MM	
Cohort	Mean age (SD)	Median age [25th–75th percentile]	Mean age (SD)	Median age [25th–75th percentile]
1986–1990	55.6 (14.7)	58.0 [45.4–66.8]	64.2 (11.6)	64.7 [58.4–73.1]
1991–1995	59.0 (15.1)	62.0 [49.0–70.5]	67.2 (10.5)	68.3 [52.5–73.2]
1996–2000	61.9 (14.9)	65.1 [52.5–73.2]	67.1 (10.4)	69.1 [60.7–74.5]
2001–2005	64.3 (14.8)	67.6 [55.3–75.7]	69.3 (9.8)	70.9 [62.7–76.7]

SD, standard deviation.

Table 4. Causes of death in patients starting RRT during follow-up and in subgroups of patients dying within and after 90 days from the start of RRT

	Died during follow-up period				Died within first 90 days since start RRT				Died after 90 days since start RRT			
	MM $n = 2059$		Non-MM $n = 92\ 905$		MM $n = 500$		Non-MM $n = 9865$		MM $n = 1559$		Non-MM $n = 83\ 040$	
	n	%	n	%	n	%	n	%	n	%	n	%
Cardiovascular causes	354	17.2	36 992	39.9	74	14.8	4090	41.5	280	18.0	32 902	39.6
Myocardial ischaemia/infarction	85	4.1	11 314	12.2	17	3.4	1282	13.0	68	4.4	10 032	12.1
Heart failure	95	4.6	7573	8.2	21	4.2	1025	10.4	74	4.7	6548	7.9
Cardiac arrest; other cause/unknown	111	5.4	11 196	12.1	23	4.6	1219	12.4	88	5.6	9977	12.0
Cerebrovascular accident	63	3.1	6909	7.4	13	2.6	564	5.7	50	3.2	6345	7.6
Infection	303	14.7	13 419	14.4	92	18.4	1396	14.1	211	13.5	12 023	14.5
Suicide/refusal treatment	78	3.8	2829	3.0	27	5.4	344	3.5	51	3.3	2485	3.0
Withdrawal of treatment	88	4.3	3811	4.1	21	4.2	501	5.1	67	4.3	3310	4.0
Cachexia	49	2.4	3043	3.3	4	0.8	249	2.5	45	2.9	2794	3.4
Malignancy	744	36.1	5788	6.2	189	37.8	476	4.8	555	35.6	5312	6.4
Miscellaneous	177	8.6	11 175	12.0	37	7.4	1102	11.2	140	9.0	10 073	12.1
Unknown/unavailable/missing	266	12.9	15 848	17.1	56	11.2	1707	17.3	210	13.5	14 141	17.0

Percentages may not add up to 100% because of rounding.

95% CI, 0.79–0.83) (Figure 3). The patient survival on dialysis also improved significantly between these two periods only in the non-MM patients (HR = 0.85; 95% CI, 0.83–0.87). Patient survival analysis comparing period cohorts between 1986–95 and 1996–2005 showed a non-significant improvement in both MM and non-MM patients (data not shown). The unadjusted median survival for patients who were alive and on RRT at day 90 was 1.29 years in MM patients and 4.98 years in non-MM patients. The survival at 2 years since day 91 was 34.6% in MM patients and 74.9% in non-MM patients.

The unadjusted median survival of the 35 MM patients who received a renal transplant during follow-up was 9.6 years since the first day on RRT. Of these 35 patients, 17 patients died during follow-up, and their causes of death were cardiac ($n = 5$), infections ($n = 3$), malignancy ($n = 3$) and miscellaneous/unknown ($n = 6$). The unadjusted median survival of the 37 048 non-MM patients who received a renal transplant during follow-up was 19.6 years since the first day on RRT.

Discussion

In the literature, there are several reports on characteristics and the clinical course of patients presenting with MM, but information on those who progress to ESRD and RRT is mostly limited to case series and reports with a small number of patients. It is estimated that in the general population, the incidence of MM is around 3 to 4 per 100 000 people, and half of them, will present with some degree of renal insufficiency [1–6]. However, only 1% will require long-term RRT [10,11]. Therefore, meaningful results for these patients should be based on large studies, and until now, there is only one such study from the USRDS [12]. This latter study reported that in 375 152 dialysis patients, 0.88% had MM as PRD. In our registry, there was a variation in incidence among the 13 participating countries and regions ranging from 0.70 to 2.53%, probably due to differences in acceptance and diagnosis criteria and this could also apply to the difference in incidence between the national USRDS and the multinational ERA-EDTA Registries. In both registries, MM was more common in older patients and males, and the majority of them were more likely to start on HD than PD, despite evidence suggesting that both modalities of RRT are equally effective [14,15].

In our study, we found that the adjusted incidence of RRT for ESRD due to MM increased step-wise up to 3-fold from 1986 to 2005. This partly reflects the overall increased incidence of RRT by 87% during that period, as incidence of RRT for ESRD due to MM has increased

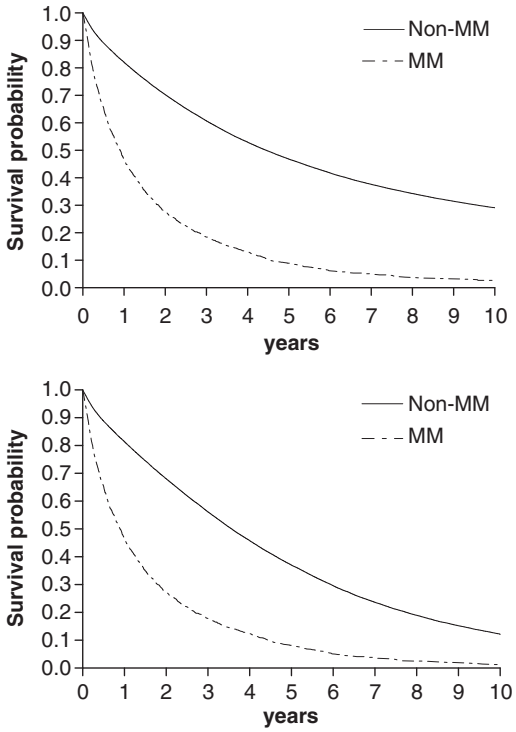

Fig. 2. Unadjusted patient survival on RRT (upper panel) and on dialysis (lower panel) since day 1 in MM and non-MM patients. The median survival on RRT was 0.91 years in MM patients compared to 4.46 years in non-MM patients, whereas the median survival on dialysis was 0.90 years in MM patients compared to 3.57 years for non-MM patients.

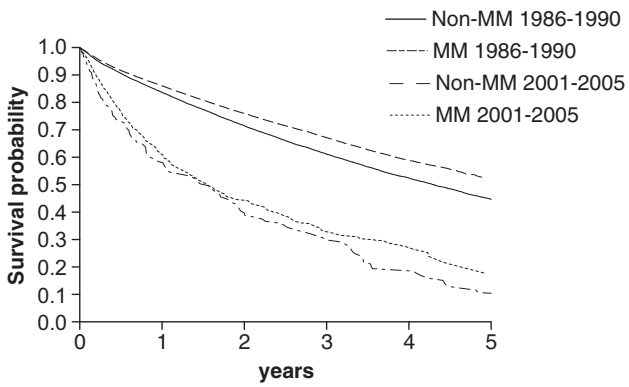

Fig. 3. Patient survival RRT since day 1 in MM and non-MM patients, adjusted for age and gender, by cohort (1986–90 vs 2001–05). The median survival on RRT did not improve significantly from 1986–90 to 2001–05 in MM patients (HR = 0.91; 95% CI, 0.76–1.09), whereas there was a statistical improvement by 19% in non-MM patients (HR = 0.81; 95% CI, 0.79–0.83).

more than due to other PRDs. The explanation for this cannot be attributed to increased incidence rate of MM in the general population, as evidence suggests that this has not changed significantly in USA and Europe during the last decades [3,5,6]. In the Olmsted County study, the overall incidence of MM was 4.1 per 100 000 population, and there was no significant change from 1945 to 1990 [3]. In Europe, the UK Cancer Statistics registered an incidence of diagnosed MM just over 4 per 100 000 population that was basically similar from 1986 to 2004 [5] and that was also the case for another study in Malmö, Sweden during an earlier period from 1950 to 1979 [6].

It is well known that in recent years we have been receiving in RRT older patients, more diabetics and generally 'sicker' patients in terms of other morbid conditions. This is shown in our results as both the incidence of RRT for ESRD due to MM and non-MM has increased but more so for the former group. In the ERA-EDTA Registry, as there are no data on comorbidity other than age and PRDs (i.e. diabetes), we could not delineate which criteria of selection may have vary over time to account for this finding. However, apart from the most likely explanation of a more liberal take-on policy for patients with high comorbidity, it is probable that the higher increase in incidence of RRT for ESRD due to MM could be due to improved treatment with chemotherapy regimens and the introduction of autologous stem cell transplantation (ASCT), resulting in improvement of MM patient survival allowing more of them to progress to ESRD [6,10,16,17]. This is in agreement with the finding in our study that age increased more in patients with MM than in patients with non-MM from 1986 to 2005.

In a recent review, dialysis was recommended as a mode of treatment in all four histological subtypes of MM [6], but Montseny *et al.* argued that tumour cell mass is a poor predictor for dialysis patients and dialysis is warranted particularly in non-elderly patients if renal biopsy discloses LCDD or AL amyloidosis but not cast nephropathy [18]. Early reports also suggested that dialysis should not be offered in MM patients with high tumour cell mass [8]. Other markers that have been implicated in the prognosis of MM dialysis patients, besides the severity and histology of disease, were age, lower serum haemoglobin, the degree of renal failure at presentation and mainly response to chemotherapy [6,9,12,18]. Pozzi *et al.* found that serum creatinine at presentation was predictive of worse renal survival, but patient survival of MM patients undergoing dialysis was similar to those patients not reaching uraemia [9]. In accordance with this finding was the report of Sharland *et al.* who did not find any correlation between age, clinical stage, labelling index, response to treatment and difference in outcome between patients with and without renal failure [19]. The contradiction in findings between these studies could be due to the small number of patients and lack of adjustment for several confounders that interfere with patient survival. Furthermore, there is evidence suggesting that MM patients on dialysis are variably undertreated and they do not receive all optimal chemotherapy for the fear of side effects, and usually they are not considered and they do not benefit from ASCT [10,16,17,20]. The ERA-EDTA Registry did not collect histological data, clinical or biochemical information and therefore cannot present results on the association between such possible prognostic factors and the clinical outcome.

An interesting finding in our study was that 1.4% of the MM patients had renal transplantation during RRT follow-up, and more interestingly, one-third of them were from a living donor. The question of whether MM patients should be transplanted or not is controversial, and most reports based on a very small number of transplants

suggest careful assessment and caution in selecting candidates, particularly for those suffering from AL amyloidosis [6,12,17,21,22]. The reason for this scepticism is the increased risk of sepsis in MM patients and the fear that immunosuppression may exacerbate the course of MM. Van Bommel reviewed the literature and reported nine transplanted patients with a survival that ranged from 14 to 114 months; six of these died from progressive myeloma and sepsis [21]. In a recent review, Penfield suggested that transplantation could be performed in young patients if they have a complete remission [17], which is in accordance with a small report by Leung *et al.* [22] in which seven patients with LCDD received a functioning graft. They have clearly demonstrated that complete remission has to be achieved before renal transplantation, otherwise recurrence of LCDD will be observed within the first 40 months following transplantation. In our study, the median survival of the transplanted MM patients was 9.6 years. Although we do not have information on the type and severity of MM in these patients, it is most probable that there was a selection of healthier MM patients for transplantation, especially as one-third of them received a graft from a living donor. The long-term survival of the MM patients indicates that transplantation should not be ruled out as a therapeutic option in steady MM patients with complete remission.

The most common causes of death in our study were from malignancy, infection and cardiovascular causes that were in line with other reports [18,23].

In the registry, there are no codes of death due to specific cancers, and therefore it is not possible to clarify whether the 36.1% of deaths caused by malignancy were in fact related to the underlying myeloma. However, since in the non-MM patients only one-sixth died from all types of malignancies compared to those in the MM patients (Table 4), it is reasonable to assume that this large difference most likely is due to deaths from MM in the latter group. In our patients, deaths within 90 days from the start of RRT were recorded in one-quarter of MM patients, and one-third of them probably died from the severity of myeloma. Deaths due to infection were higher in the MM patients, and this difference did not exist in those who died after 90 days from the start of RRT. Causes of death due to withdrawal of treatment, suicide and cachexia were not different between MM and non-MM patients, probably because significantly more MM patients died within 90 days from the start of RRT leaving on RRT thereafter the 'healthier' ones. Furthermore, recovery of renal function within 90 days from the start of RRT was observed twice as often in MM patients compared to non-MM patients.

In our study, MM patients had an almost 3-fold risk of death compared to non-MM patients, and the median survival from day 1 of RRT was 0.91 and 4.46 years in the two groups, respectively, results similar to those reported by USRDS. Comparison of survival adjusted for age and gender in MM patients did not show any statistical difference comparing the period cohorts 1986 vs 2001–2005, which may be partially due to lack of statistical power. In contrast, in non-MM patients the survival on RRT improved significantly over time by 19% and the survival on dialysis by 15%. This finding does not coincide with the acknowledged improved quality in treatment of RRT and better treatment of MM in recent years. One would expect that patients who started therapy in the 2001–2005 period would have benefited more. Results from trials showing a beneficial effect of thalidomide [24], bortezomib [25] and lenalidomide [26] on patients with MM were reported recently, and most likely the majority of our MM patients were not treated with these agents. The effect of plasma exchange in patients with MM has shown little difference in outcome compared to controls [27,28], and the use of extended HD with a protein-leaking dialyser was found to remove effectively up to 90% of monoclonal free light chains in a small number of MM patients with acute renal failure [29]. However, these trials did not include patients with MM on RRT, and although use of these drugs and techniques in the early stages of MM may improve survival allowing more patients to reach ESRD, their effect on MM patient survival receiving RRT has not been tested as yet.

In the literature, there are several smaller studies comparing outcome of patients with MM with renal insufficiency dependent on dialysis or not [14,16,18–20,23]. In these reports, median survival on dialysis ranged from 2 months to 47 months, and this wide variation contains contradictory findings. In the study by Montseny *et al.* of 118 patients with MM, 46 required HD, and their median survival according to tumour mass, classified as stage 1, 2 or 3 by Durie and Salmon criteria, was 18, 6 and 2 months [18]. Korzets *et al.* reported a median survival of 24.6 months in 10 patients with MM on CAPD, but patients who responded to chemotherapy had a better median survival of 47 months compared to 17 months in those not responding to treatment [14]. In contrast, Sharland *et al.* reported an identical median 22 months survival irrespective of clinical stage and response to treatment [19]. Some studies reported that 25–30% of the patients might survive more than 3 years [23], and furthermore Lee *et al.* reported a 5-year event-free survival in 25% of 59 MM patients on dialysis treated with high dose melphalan and ASCT [16]. These findings indicate that satisfactory quality of life and survival with both dialysis and transplantation may be achieved if patients are treated early and optimally with adequate chemotherapy and if ASCT is not withheld.

There are certain limitations in this study mainly related to a single PRD code for both entities of MM and LCDD and the lack of information regarding the histology and severity of the disease. Unfortunately in the registry, there is no broad PRD code covering all plasma cell disorders and the contributing centres did not use this broad diagnosis in reporting their data. However, we believe that our study provides useful feedback information on patients reported to have MM or LCDD for the last 20 years by contributing centres. It has been reported that these two entities may represent 60–89% of plasma cell disorders [18,30]. Other studies have defined monoclonal Ig deposition disease in approximately one-quarter of MM patients, and LCDD constituted the most frequent form (up to 70%) of these monoclonal gammopathies [31,32].

In conclusion, the incidence of RRT for ESRD due to MM has increased over the past 20 years in Europe, partly because of increased acceptance. Although patient survival

is unfavourable compared with patients starting RRT without MM as PRD, it appears long enough to justify dialysis and in selected patients even kidney transplantation.

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