

Original article

## Survival of Multiple Myeloma Patients Undergoing Dialysis or Plasma Exchange - A Single Centre's 25-Year Experience

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### Abstract

**Aim:** Multiple myeloma (MM) patients might require haemodialysis (HD) and/or plasma exchange (PE) in cases of acute kidney injury (AKI) and/or chronic kidney disease (CKD) and/or other indications. The study analysed the survival of MM patients who required HD and/or PE.

**Subjects and methods:** All 144 patients treated for MM at the University Hospital Centre Osijek between 1994 and 2018 (of whom 47.9 % were men) were included in the study. Data were collected from medical records. MedCalc Statistical Software version 17.8.2 was used for the statistical analysis, with significance set at  $\alpha = 0.05$ .

**Results:** Forty-three of 144 MM patients (29.9 %) were treated with HD and/or PE. Male patients required HD or PE more often than female patients (62.8 % vs 37.2 %,  $P = 0.02$ ). Patients who did not require HD or PE were significantly older at the time of their death than the patients treated with HD or PE [75 (interquartile range, IQR, 72 – 77) vs 72 (IQR 66 – 75) years;  $P = 0.009$ , Mann-Whitney test]. Among all patients who required acute or chronic HD, PE or a combination of the treatments, the longest life span was found in 17 patients who were treated with chronic HD (median 12 months, IQR 8 – 58).

**Conclusion:** Kidney failure requiring HD or PE in MM was associated with a significantly shorter life span in comparison with other MM patients. Chronic HD patients had the longest survival among patients who required acute or chronic HD, PE or a combination of the treatments. In general, MM patients in need for HD and/or PE had poor survival.

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## Introduction

Multiple myeloma (MM) represents malignant plasma cell proliferation. Tumours, their products and the reactions of the host that they produce lead to a number of dysfunctional organ conditions and symptoms, such as bone-related pain or fractures, kidney failure, susceptibility to infections, anaemia, hypercalcemia and sometimes clotting irregularities, neurological symptoms and symptoms of hyperviscosity (1).

Kidney failure occurs in nearly 25 % of the patients, while in more than half of MM patients, there is some kidney pathology. Hypercalcemia, deposition of amyloid in glomeruli, hyperuricemia, recurrent infections and kidney infiltration with tumour cells contribute to kidney disorders (1). In most cases, kidney damage is associated with immunoglobulin (Ig) and it includes the following conditions: light chain cast nephropathy (LCCN), also known as myeloma kidney, monoclonal immunoglobulin deposit disease and light chain amyloidosis (2). An increased quantity of light chains overloads tubular cells, which causes tubular damage, resulting in direct toxic effects of the light chain or indirect release of cell lysosomal enzymes. It can also cause Fanconi syndrome by the formation of crystalline inclusions in the proximal tubules, resulting in a high loss of glucose and amino acids as well as irregularities of acidification and urea concentration (1, 2). Plasma exchange (PE) has been suggested as a treatment option for LCCN in order to prevent kidney failure. Some retrospective studies have shown that PE can prevent acute kidney injury (AKI), which can verge into chronic kidney disease (CKD) and the need for dialysis (3), while other studies have considered PE as a treatment that does not have any effect on overall survival or need for haemodialysis (2, 4). Other treatment options for patients with MM and renal failure include bortezomib-based therapies or the use of high cut-off dialysis filters to remove free light chains (5). The administration of peritoneal dialysis and kidney transplant in MM patients with kidney failure are controversial treatment procedures because of their low rate of survival

and poor tolerance of therapy (6). At the University Hospital Centre Osijek, a proportion of MM patients were treated with acute or chronic HD, PE or a combination of the treatments. The focus of the study was to analyse the outcome in MM patients who required HD or PE.

## Subjects and methods

The retrospective study included all 144 patients treated at the University Hospital Centre Osijek for MM during the period between 1994 and 2018. Available patients' data were collected from medical records at the Department of Hematology, the Department of Nephrology and from the register of deaths at the Clinical Department of Pathology and Forensic Medicine of the University Hospital Centre Osijek. The study was conducted between June 2017 and February 2018. MM diagnosis was confirmed if the bone marrow analysis showed plasmacytosis (> 30 %) or if plasmacytosis > 10 % was accompanied by monoclonal paraprotein in serum and/or urine and osteolytic lesions or light chains in serum were present. Criteria for the start of HD treatment were AKI or clinical and laboratory signs of CKD that required substitution of renal function. PE was performed for hyperviscosity to remove the light chains.

### *Statistical methods*

Category data were represented by absolute and relative frequencies. The numerical data were described as median, minimum, maximum and interquartile range (IQR). Differences in nominal variables were tested by Fisher's exact test. Differences in numeric variables, due to deviations from normal distribution, were tested by Mann-Whitney's U Test. All P values were double-sided. The level of significance was set at  $\alpha = 0.05$ . MedCalc Statistical Software version 17.8.2 was used for the statistical analysis (MedCalc Software bvba, Ostend, Belgium; <http://www.medcalc.org>; 2017).

## Results

The study included 144 MM patients, 43 (29.9 %) of whom required HD or PE. Male patients needed HD or PE significantly more often (27 of 69, 62.8 %) than female patients (16 of 75, 37.2 %),  $P = 0.02$  (Fisher's exact test).

Up to the time of the study, 95 MM patients died (66 %), and at a significantly higher rate if a patient needed HD or PE (34 of 43, 79.1 %) than those who were not candidates for the treatments (61 of 101, 60.4 %),  $P = 0.03$  (Fisher's exact test) (Table 1).

**Table 1. Characteristics of patients (N = 144) with multiple myeloma (MM) with regard to haemodialysis (HD) or plasma exchange (PE) treatment and overall survival at the time of study**

	MM patients who required HD or PE treatment (n = 43, 29.9 %)	Number of (%) patients MM patients who did not require HD or PE treatment (n = 101, 70.1 %)	Total	<i>P</i> *
<b>Gender</b>				
<b>Male</b>	27 (62.8)	42 (41.6)	69 (47.9)	<b>0.02</b>
<b>Female</b>	16 (37.2)	59 (58.4)	75 (52.1)	
<b>Overall survival</b>				
<b>Alive</b>	9 (20.9)	40 (39.6)	49 (34)	<b>0.03</b>
<b>Deceased</b>	34 (79.1)	61 (60.4)	95 (66)	
<b>Total</b>	43 (100)	101 (100)	144 (100)	

\*Fisher's exact test

Among 43 MM patients who required HD or PE treatment, 12 (28 %) were treated only with acute HD, 11 (26 %) were treated only with chronic HD and 8 (19 %) only with PE. Seven (16 %) MM patients were treated with both acute HD and

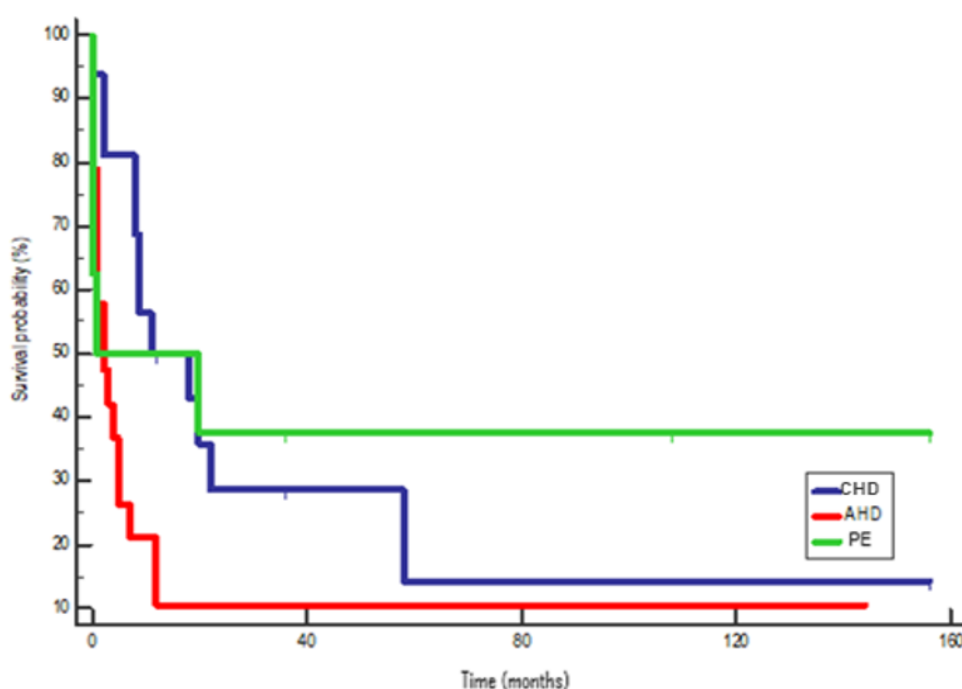
PE, 1 (2 %) MM patient was treated with both chronic HD and PE and 1 (2 %) with both acute and chronic HD. Finally, there were 3 (7 %) MM patients treated with acute HD, chronic HD and PE (Table 2).

**Table 2. Distribution of patients according to the type of treatment - acute or chronic haemodialysis (AHD or CHD) or plasma exchange (PE) (N = 43)**

Treatment	n	%
AHD	12	28
CHD	11	26
PE	8	19
AHD+PE	7	16
CHD+PE	1	2
AHD+CHD	1	2
AHD+CHD+PE	3	7
<b>Total</b>	43	100

Among 43 (29.9 %) MM patients who required HD or PE treatment, a total of 16 (37.2 %) patients were treated with chronic HD, including those treated with acute HD or PE in combination with chronic HD. Their median survival time was 11 months (IQR 8 – 58). A total of 19 (44.2 %) MM patients were treated with acute HD, including those treated with chronic HD or PE in

combination with acute HD and their median survival time was 2 months (IQR 1 – 5). Eight (18.6 %) MM patients were treated only with PE and their median survival time was 1 month (IQR 0 – 20). There was a significant difference in survival time among the examined groups ( $P = 0.04$ ) (Figure 1).

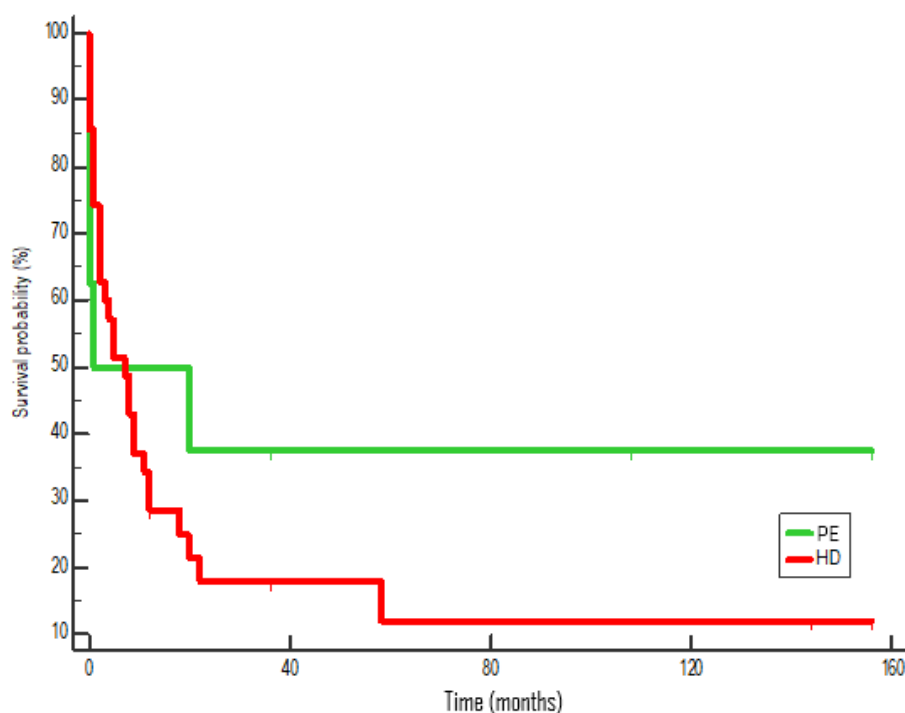


**Figure 1.** Kaplan- Meier plot of survival time (months) between the groups of patients who required haemodialysis (HD) or plasma exchange (PE) treatment. CHD includes multiple myeloma (MM) patients treated with chronic HD, including those treated with acute HD or PE in combination with chronic HD. Their median survival time was 11 months (IQR 8 – 58). AHD includes MM patients who were treated only with acute HD and those treated with a combination of acute HD and PE. Their median survival time was 2 months (IQR 1 – 5). PE encompasses MM patients who were treated only with PE and their median survival time was 1 month (IQR 0 – 20). There was a significant difference in survival time among the examined groups ( $P = 0.04$ ).

Survival time was calculated from the start of the treatment until the patient's death.

A total of 35 (81.4 %) MM patients were treated with HD, either only HD or in combination with PE, and their median survival time was 7 months (IQR 2 – 12). There were 8 (18.6 %) MM patients

treated only with PE and their median survival time was 1 month (IQR 0 – 20). There was no significant difference in survival time between those who were treated with HD (including patients treated only with HD or with a combination of HD and PE) and those treated only with PE ( $P = 0.39$ ) (Figure 2).



**Figure 2.** Kaplan-Meier plot of survival (months) between the groups of patients who were treated only with plasma exchange (PE) and those treated with haemodialysis (HD) (includes patients treated only with HD or with a combination of HD and PE). The median survival time of multiple myeloma (MM) patients treated with PE was 1 month (IQR 0 – 20). The median survival time of the other group was 7 months (IQR 2 – 12). There was no significant difference in survival time between these two groups ( $P = 0.39$ ).

## Discussion

Impairment of kidney function in MM patients requiring dialysis or PE was associated with a shorter life span than in MM patients without such treatments. Patients who had no need for treatment with HD or PE were older at the time of death than the patients who needed such treatment, as we had assumed. The need for dialysis or PE was accompanied by a poor outcome in terms of life span in general. At the moment of our research, the outcome of the treatment was negative (death of the patient) in 95 (66 %) cases; significantly, 34 (79.1 %) of these patients needed PE and/or HD.

CKD often appears in MM patients. Despite aggressive treatment, 65 % of MM patients with kidney damage will reach the end-stage renal disease within three months of their MM

diagnosis (7). Studies have shown that mortality and morbidity are more common among patients who need renal replacement therapy (RRT) than among those with regular kidney function (8). These findings correspond with our results.

Some research has demonstrated that patients with MM and impairment of kidney function can be treated either with HD or PE and that these procedures are equally effective (9). On the other hand, one retrospective study suggested that PE might be helpful in preventing the initiation or continuation of dialysis in patients with rapidly progressive renal failure which occurred due to MM (10). More recent studies have suggested that PE in combination with chemotherapy, especially bortezomib, leads to renal improvement (11, 12). In this research, among the patients who needed HD or PE, the

17 patients who were treated with chronic HD lived the longest. Studies conducted at different centres found contrasting results. Therefore, in the future, research on this issue should be conducted on a larger number of subjects to get the most accurate results.

Our research was a retrospective epidemiologic study. It should be noted that there were some limitations of this study due to data scarcity for the group without HD or PE treatment, which can account for some of the differences between our research and studies conducted by other researchers. There were missing facts about the time when the diagnoses of MM were confirmed, stage and type of MM, presence of kidney failure in those without non-conservative treatment, presence of other complications and methods of pharmacological treatment.

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## Conclusion

Our study has shown that the requirement of chronic HD is related to a better outcome than that of acute HD or PE when it comes to length of life.

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