

Impact of High Cut-Off Dialysis on Renal Recovery in Dialysis-dependent Multiple Myeloma Patients – Results from a Nested Case-Control Study

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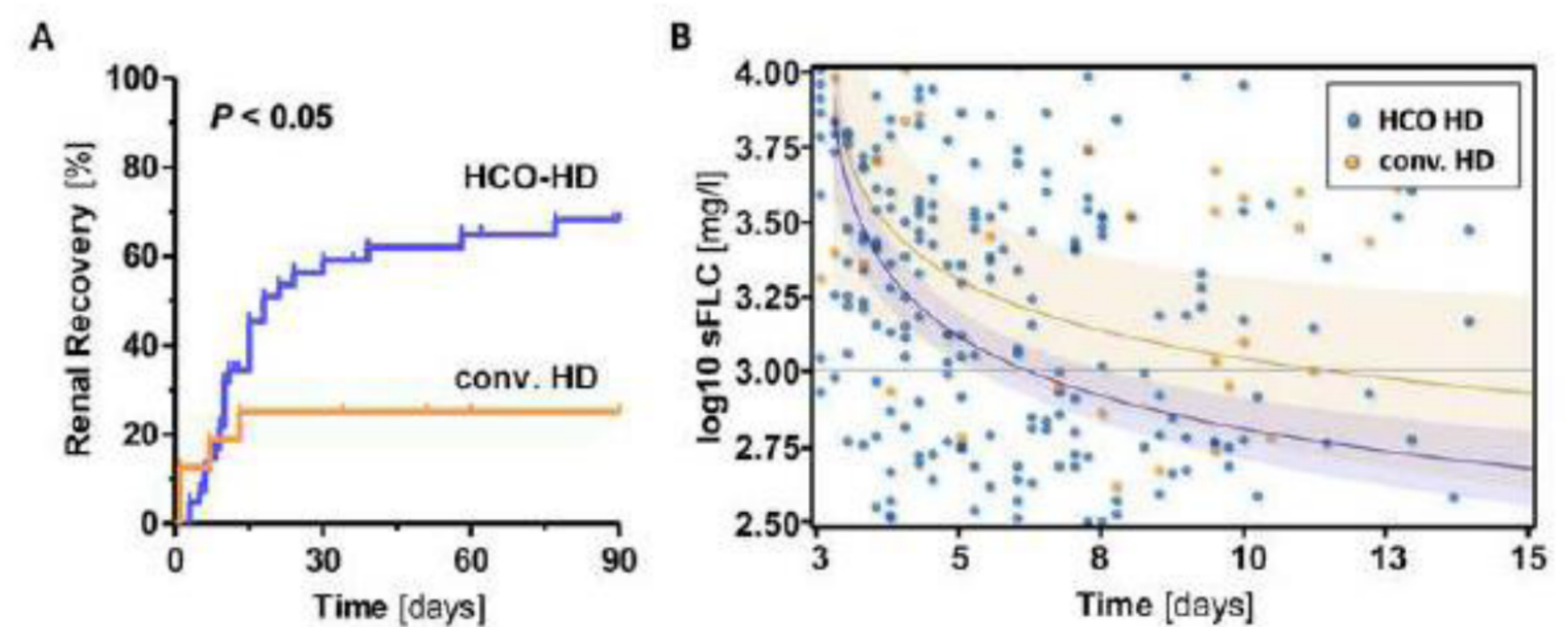
Background:

High cut-off hemodialysis (HCO-HD) can effectively reduce high concentrations of circulating serum free light chains (sFLC) in patients with dialysis-dependent acute kidney injury (AKI) due to multiple myeloma (MM). Therefore the aim of this study was to analyze renal recovery in a retrospective nested single-center cohort of dialysis-dependent MM patients treated with either conventional HD (conv. HD) or HCO-HD.

Methods and Results:

The cohort consisted of 59 patients treated with HCO-HD (n=42) or conv. HD (n=17), respectively. Sustained sFLC response was detected in a significantly higher proportion of HCO-HD patients (83.3%) compared to 29.4% of conv. HD patients (p=0.007). The median duration of sFLC to reach values <1000 mg/l was 14.5 days in the HCO-HD group, compared to 36 days in the conv. HD group. The corresponding rate of renal recovery was 64.3% and 29.4%, respectively (Chi-Square-test, p=0.014). Multivariate regression as well as decision tree analysis (recursive partitioning) revealed HCO-HD (adjusted OR 6.1 [95%CI 1.5-24.5], p=0.011) and low initial uric acid values (adjusted OR 1.3 [95%CI 1.0-1.7], p=0.045) as independent and paramount variables for favorable renal outcome.

Figure 1: Renal recovery rate and sFLC values

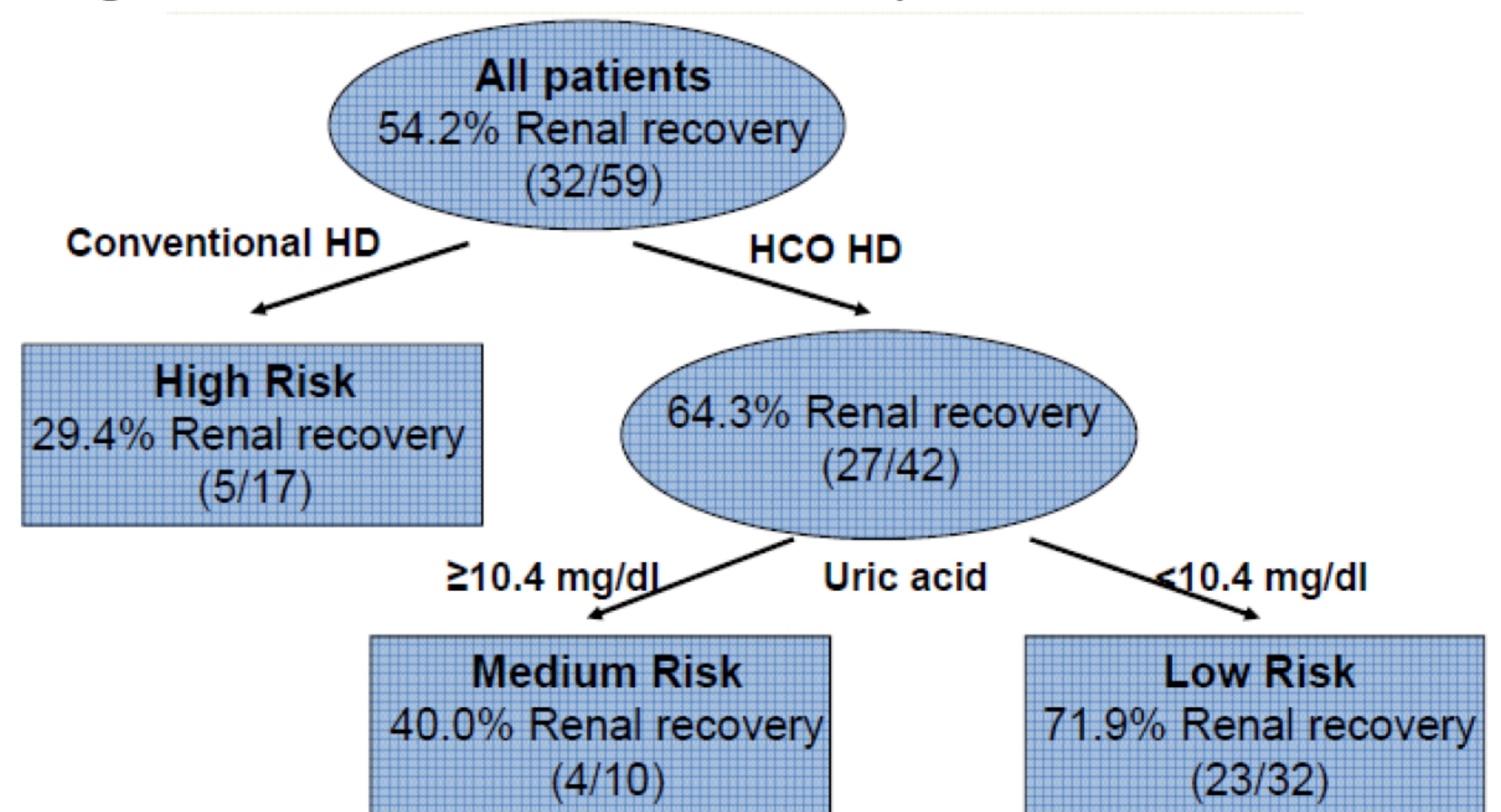


	All pat. (n=59)	HCO-HD (n=42)	Conv. HD (n=17)	P-value ^a	
Renal recovery at day 90	32 (54.2)	27 (64.3)	5 (29.4)	0.014	
Serum creatinine d90	1.1 (0.8 - 1.9)	1.4 (0.9 - 1.9)	0.8 (0.6 - 1.0)	0.022	
eGFR d90 [ml/min]	≥60	13 (40.6)	4 (80)	0.128	
	30-59	10 (31.3)	1 (20)		
	15-29	6 (18.8)	-		
	<15 (without HD)	-	-		
	Missing data	3 (9.4)	-		
Sust. sFLC response	30 (50.8)	26 (61.9)	4 (23.5)	0.007	
Mortality					
	day 90	12 (20.3)	9 (21.4)	3 (17.6)	0.741
	one year	22 (37.3)	13 (31.0)	9 (52.9)	0.117
Myeloma response (IMWG)					
	sCR/CR	5 (8.5)	5 (11.9)	-	0.224
	VGPR	8 (13.6)	7 (16.7)	1 (5.9)	
	PR	9 (15.3)	8 (19)	1 (5.9)	
	SD	6 (10.2)	3 (7.1)	3 (17.6)	
	PD	15 (25.4)	12 (28.9)	3 (17.6)	

	All patients (n=59)	HCO-HD (n=42)	Conv. HD (n=17)	P-value		
Age	63.1 (56.3 - 69.2)	64.4 (56.7 - 69.8)	58.4 (53.7 - 66.4)	0.132		
>60 years	31 (52.5)	25 (59.5)	6 (35.3)	0.090		
Gender, m/f	30/29 (50.8/49.2)	20/22 (47.6/52.4)	10/7 (58.8/41.2)	0.435		
Status				0.652		
	Primary diagnosis	32 (54.2)	22 (52.4)		10 (58.8)	
	Relapse/refractory	27 (45.8)	20 (47.6)	7 (41.2)		
sFLC type				0.826		
	Kappa	36 (61)	26 (61.9)		10 (58.8)	
	lambda	23 (39)	16 (38.1)		7 (41.2)	
	kappa [mg/l]	8450 (3170 - 16100)	8545 (3500 - 16600)		5130 (1955 - 19650)	
	lambda [mg/l]	6100 (3310 - 12400)	5250 (3037 - 9677)	12400 (3310 - 15900)	0.109	
MM type				0.352		
	IgG kappa	15 (25.4)	12 (28.6)		3 (17.6)	
	IgG lambda	10 (16.9)	8 (19.0)		2 (11.8)	
	IgA kappa	3 (5.1)	3 (7.1)		-	
	IgA lambda	3 (5.1)	1 (2.4)		2 (11.8)	
	sFLC kappa only	19 (32.2)	12 (28.6)		7 (41.2)	
	sFLC lambda only	9 (15.3)	6 (14.3)	3 (17.6)		
ISS stage				0.500		
	I	1 (1.7)	1 (2.4)		-	
	II	1 (1.7)	1 (2.4)		-	
	III	57 (96.6)	40 (95.2)	17 (100)		
Previous renal status				0.376		
	pre-existing CKD (≥3)	16 (27.1)	10 (23.8)		6 (35.3)	
	Prev. creatinine [mg/dl]	1.0 (0.8 - 1.2)	1.0 (0.8 - 1.1)	1.0 (0.8 - 1.6)	0.489	
	previous eGFR [ml/min]	74.5 (50.9 - 80.7)	75.6 (61.7 - 80.9)	73.7 (42.5 - 79.3)	0.384	
Renal status at presentation				0.315		
	Serum creatinine [mg/dl]	4.5 (2.9 - 6.9)	4.4 (2.8 - 6.1)		5.0 (3.8 - 7.8)	
	BUN [mg/dl]	63 (44 - 81)	60.5 (39.0 - 75.5)	76 (51 - 122)	0.064	
	AKI I	7 (11.9)	4 (9.5)	3 (17.6)	0.679	
	AKI II	10 (16.9)	7 (16.7)	3 (17.6)		
	AKI III	42 (71.2)	31 (73.8)	11 (64.7)		
Renal biopsy				0.214		
	Cast Nephropathy	16 (27.1)	14 (33.3)		2 (11.8)	
	Others	1 (1.7)	-		1 (5.9)	
	Declined / contraind.	42 (71.2)	28 (66.7)	14 (82.4)		
Laboratory data				0.782		
	Haemoglobin [g/dl]	9.1 (8.3 - 10.2)	9.0 (8.3 - 10.3)		9.2 (8.0 - 9.8)	
	Platelet counts [x10 ⁹ /l]	160 (83 - 216)	158 (86 - 216)		175 (74 - 217)	0.770
	LDH [U/l]	278 (209 - 427)	285 (219 - 492)		272 (198 - 378)	0.407
	Uric acid [mg/dl]	8.4 (6.2 - 10.2)	8.6 (6.8 - 10.3)		8.0 (5.7 - 10.2)	0.574
	Beta2-MG [mg/l]	13.25 (7 - 31.5)	11.3 (7 - 17.6)	26.4 (8.5 - 36.7)	0.124	
Chemotherapy regimen				0.033		
	Days from admission to chemotherapy initiation	2 (0 - 6)	2 (0 - 6)		4 (2 - 11)	
	Novel agents	36 (61)	32 (76.2)		4 (23.5)	<0.0001
	Cyclophosphamide	10 (17)	8 (19)		2 (11.8)	
	Dexamethasone	5 (8.5)	1 (2.4)		4 (23.5)	
	Anthracycline-based	5 (8.5)	-	5 (29.4)		
	Melphalan/Bendamustin	3 (5.1)	1 (2.4)	2 (11.8)		
Extracorporeal treatment				0.004		
	Days from admission to first treatment	1 (0 - 3)	2 (1 - 3)		0 (0 - 2.5)	
	Treatment period (days) ^c	14 (7 - 24)	10.5 (6.7 - 22.2)		19 (6 - 40.5)	
	No. of HCO / HD (n)	8 (5 - 16)	8 (5 - 14.5)	9 (3.5 - 18.5)	0.782	

	Univariate		Multivariate	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Primary diagnosis vs. Relapse/refractory	0.91 (0.32 - 2.54)	0.852		
Male gender	0.40 (0.14 - 1.15)	0.090	0.46 (0.13 - 1.62)	0.226
Age	0.99 (0.94 - 1.05)	0.861		
Previous eGFR [ml/min; CKD-EPI]	1.00 (0.98 - 1.02)	0.740		
Serum Creatinine ^a [mg/dl]	1.27 (1.01 - 1.58)	0.038	1.14 (0.86 - 1.51)	0.369
BUN ^a [mg/dl]	1.03 (1.01 - 1.05)	0.010		
AKI III ^b [KDIGO] vs. others	1.08 (0.35 - 3.33)	0.899		
sFLC ^a [mg/dl]	1.00 (1.00 - 1.00)	0.410		
Haemoglobin ^a [g/dl]	0.84 (0.59 - 1.20)	0.341		
Uric acid ^a [mg/dl]	1.22 (0.97 - 1.52)	0.089	1.30 (1.01 - 1.70)	0.045
Novel agents vs. others	2.75 (0.94 - 8.09)	0.066	2.17 (0.58 - 8.18)	0.249
HCO-HD vs. conv. HD	4.32 (1.28 - 14.62)	0.019	6.08 (1.51 - 24.55)	0.011

Figure 2: Prediction of Renal Recovery



Conclusions:

In summary, results from this retrospective case-control study suggest an additional benefit of HCO-HD on sFLC removal and renal outcome in dialysis-dependent AKI secondary to MM. This accounted especially to patients with low initial uric acid values, resulting in a promising renal recovery rate of 71.9%. Further prospective studies are warranted.