

# MIDDLE MOLECULE REMOVAL IN HDF COMPARISON OF MID- versus POST-DILUTION (MIDEMM STUDY)

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## OBJECTIVES

Online Haemodiafiltration (HDF) with high-volume substitution fluid is an optimal way to remove uremic substances ranging from small to high molecular weight (MW) molecules. Post-dilution HDF is the most efficient infusion mode to obtain maximum clearance of both small and larger solutes. Mid-dilution infusion is an interesting alternative that represents simultaneous pre- and postdilution infusion modes and could be a highly effective technique to remove uremic toxins, avoiding the disadvantages of pre- and post-dilutional modes. The aim of this prospective, randomized, multicentric study was to compare mid-dilution (MID) with post-dilution HDF (POST) efficiency in removing different middle MW and protein bound uremic toxins.

## METHODS

We performed a cross-over study including 158 Patients from 11 Belgian and 10 French centres. All patients gave their informed consent and were randomized in two different groups for three months (Fig 2). 64 patients were excluded from the final analysis because of incomplete data. The reduction rate (RR) of middle and protein bound molecules were centrally determined as well as the Kt/Vd and Albumin loss. Unpaired t student test was performed using GraphPad prism version 4.00 for Windows.

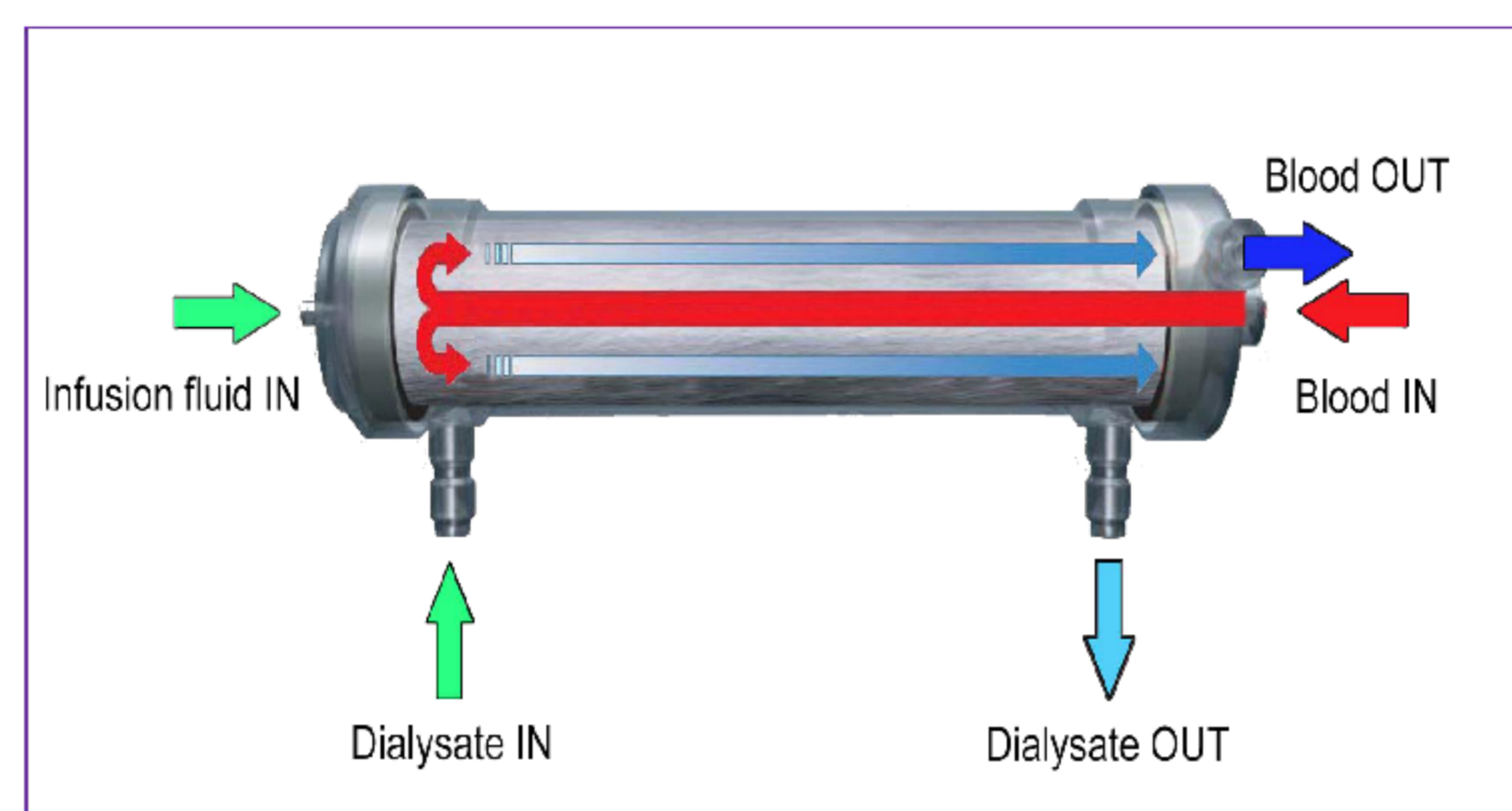


Fig. 1: MID Dilution revers configuration

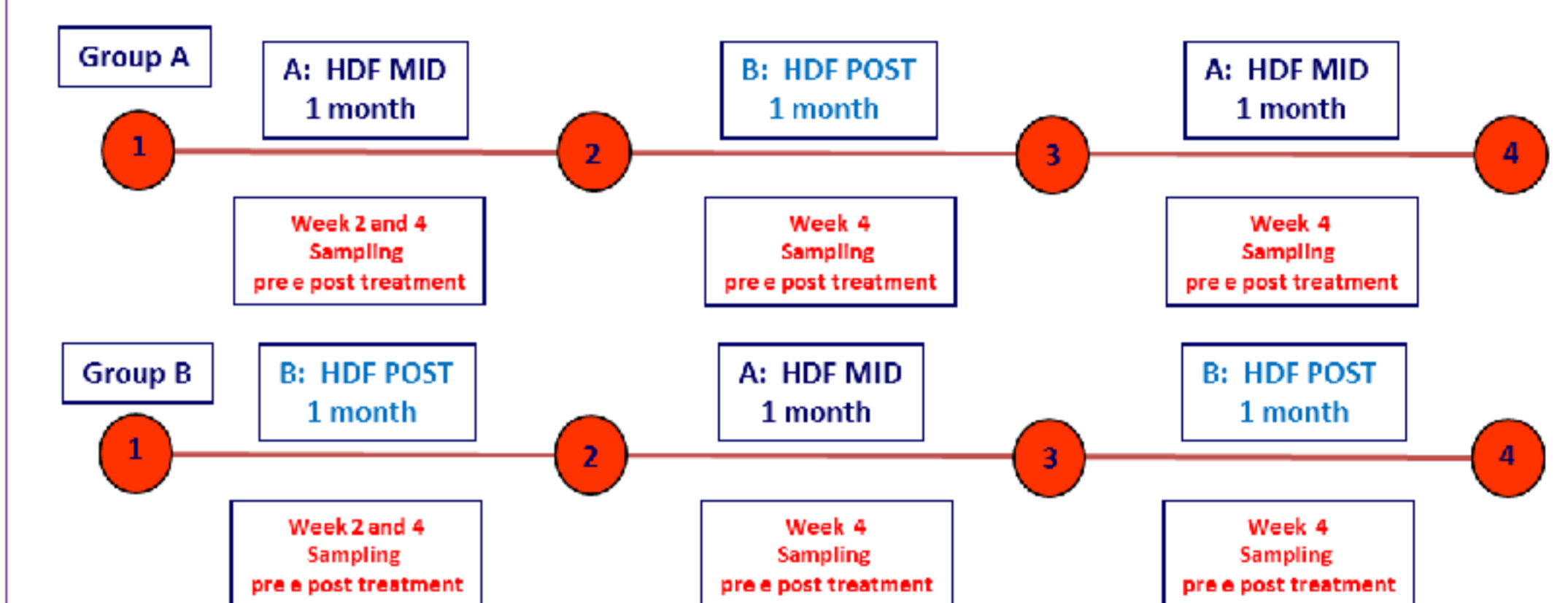


Fig. 2: MIDEMM Study design

## RESULTS

Molecule	Post HDF	MID HDF	P
Homocysteine	54,4±0,8	55,4±0,7	0,337
ADMA	51,6± 0,8	52,8± 0,9	0,341
β2 m	80,1±0,4	81,6±0,4	0,0103 (*)
Leptine	58,3±1,5	60,8±1,7	0,286
Myoglobin	70,5±0,9	72,5± 0,7	0,092
RBP	24,1± 0,9	30,0±0,8	0,0025 (*)
Compl. Fact D	72,8± 0,8	76,4± 0,6	0,0003 (*)

Table 1: Main results; significant difference in RR (%) was found for three middle MW molecules, β2M, RBP and Complement Factor D

The data of 94 (48 from group A and 46 from group B) patients (53M and 41F) were analyzed corresponding to 164 MID sessions and 161 POST sessions. The median age was 70 (27-92) years and dialysis vintage was 47 (7-454) months. No difference was found in the demographic characteristics and treatment parameters. A significant difference in RR (%) was found for three middle MW molecules: **β-2 Microglobulin (β2M), Complement Factor D (CFD) and Retinol Binding protein (RBP) (Table 1)**. The RR of the other investigated molecules (ADMA, Homocystein, Leptin and Myoglobin) were not significantly different. The reinfused volume was significantly higher in MID than in POST (average total volume of 43,63 L vs 20,96 L respectively) (Table 2). In the MID group, the amount of reinfused volume in its post-dilution stage (estimated around the 2/3 as shown by Maduell et al. (1)) is significantly higher than in POST (28,8 L vs 20,96 L respectively). This difference could explain the better depuration of middle MW molecules in MID compared to POST. Indeed, was found a linear correlation (R2 0.83) between the delta in RR (D = RR MID – RR POST) and the MW of studied molecules (Figure 3). No significant difference between MID and POST was observed for small MW molecules depuration (second generation Daugirdas Kt/Vd), neither for Albumin loss.

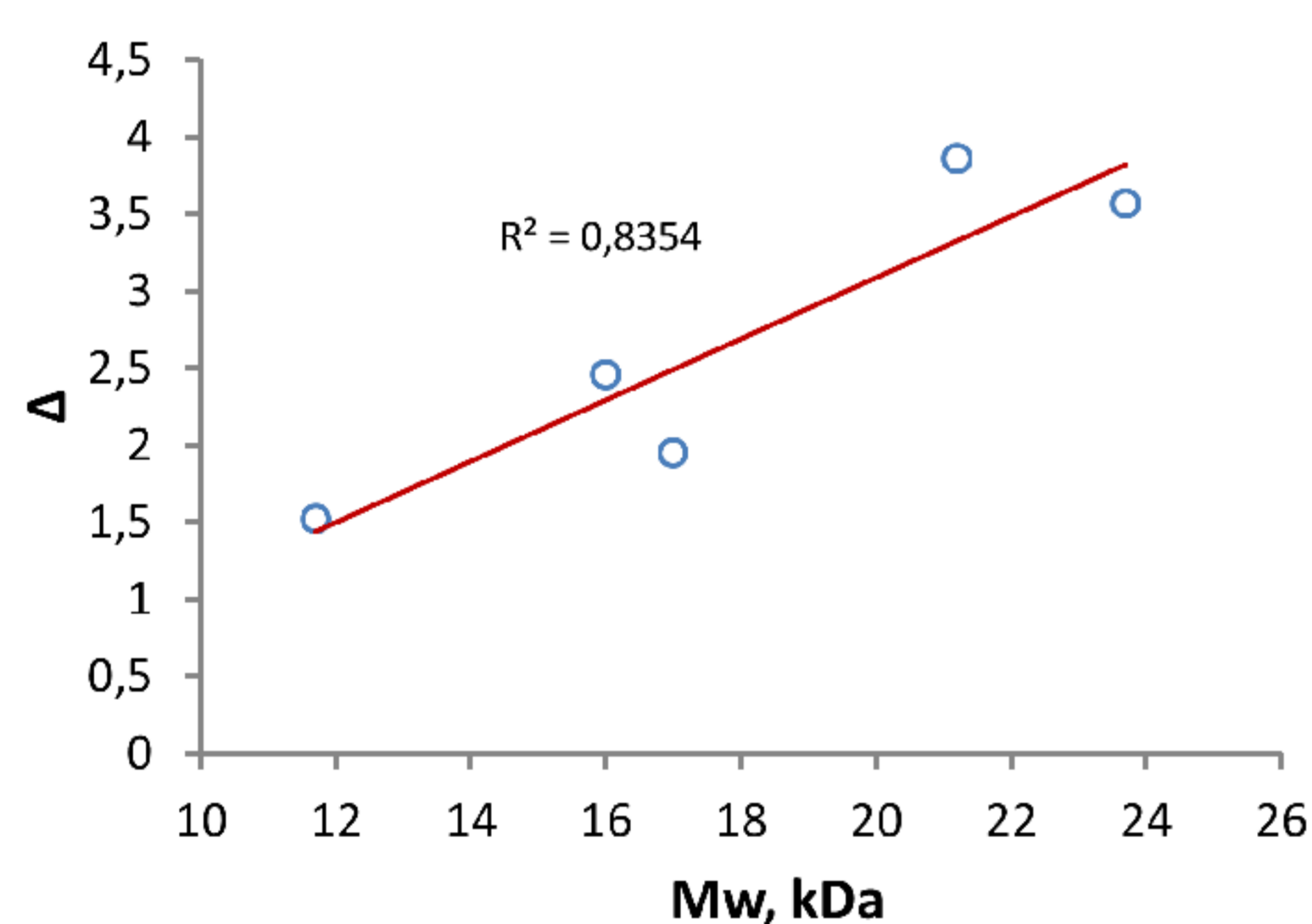


Fig. 3: Effect of MW on removal of middle molecules between MID and post HDF; Linear correlation between the delta in RR (Δ = RR Mid – RR Post) and the MW of the middle molecules tested (β2-m (1.52,11.8), Leptine (2.46,16), Myoglobine (1.95,17), RBP (3.86,21.2) and CFD (3.57,23.7)).

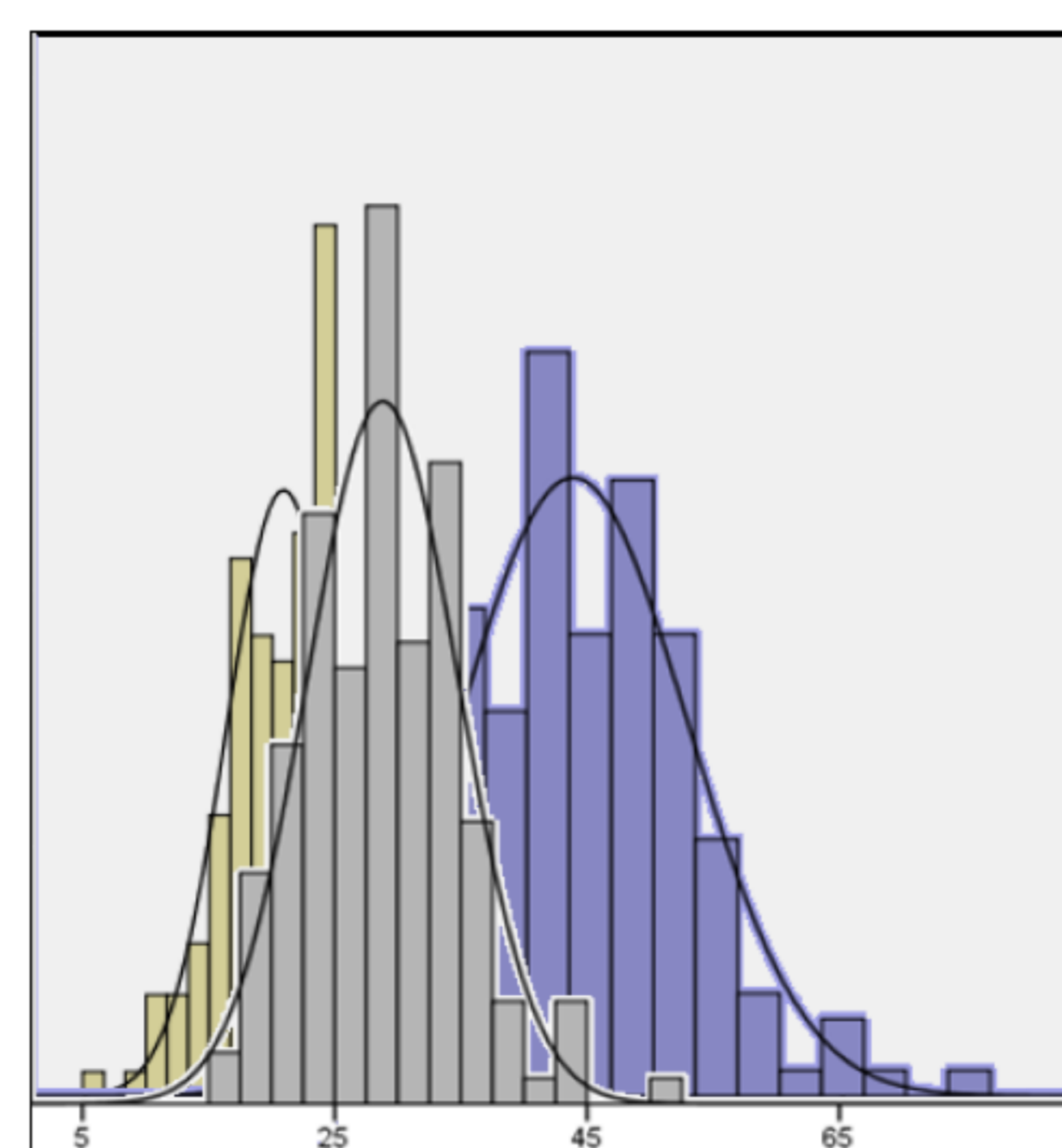


Fig. 4: Gaussian behaviour of convective and MID total infused volume

	Total Vol Post L	Total Vol MID L	Post Inf Vol MID L
N. sessions	161	164	164
Mean	20,96	43,63	28,80
SEM	0,35	0,70	0,46
Min	10,0	24,9	16,4
Max	29,70	76,50	50,5

Table 2: Mean convective volume for HDF post and MID dilution; The convective post infusion for MID HDF it has been calculated as 2/3 of the total convective volume

## CONCLUSIONS

MID Dilution seems to better remove some middle molecular weight molecules compared to HDF POST. This might be related to a higher total and equivalent post substituted volume obtained in MID Dilution compared to HDF POST group.

## REFERENCES:

Francisco Maduell et al.; *Blood Purif* 2010;30:25–33  
Francisco Maduell et al.; *J Am Soc Nephrol*, 2013; 24: 487–497

