


Requirements and Pitfalls of Dialyzer Sieving Coefficients Comparisons

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Abstract: Sieving coefficients reported in dialyzer data sheets and instructions for use (IFUs) indicate the potential of different solutes to pass across a particular membrane. Despite being measured in vitro, sieving coefficient data are often used as a predictor of the clinical performance of dialyzers. Although standards for the measurement of sieving coefficients exist, the stated methodologies do not offer sufficient guidance to ensure comparability of test results between different dialyzers. The aim of this work was to investigate the relationship between sieving coefficients and published clinical performance indicators for two solutes, albumin loss and beta-2 microglobulin (β_2M) reduction ratio (RR), and to assess the impact of different in vitro test parameters on sieving coefficient values for albumin, β_2M , and myoglobin. Clinical albumin loss and β_2M RR for commercially available dialyzers used in hemodialysis (HD) and post-dilution hemodiafiltration (HDF) were extracted from the literature and plotted against sieving coefficients reported in data sheets and IFUs. Albumin, β_2M , and myoglobin

sieving coefficients of a selection of dialyzers were measured per the ISO 8637 standard. The impact of in vitro testing conditions was assessed by changing blood flow rate, ultrafiltration (UF) rate, sampling time, and origin of test plasma. Results showed variation in albumin loss and β_2M RR for the same sieving coefficient across different dialyzers in HD and HDF. Changes in blood flow rates, UF rates, sampling time, and test plasma (bovine vs. human) caused marked differences in sieving coefficient values for all investigated solutes. When identical testing conditions were used, sieving coefficient values for the same dialyzer were reproducible. Testing conditions have a marked impact on the measurement of sieving coefficients, and values should not be compared unless identical conditions are used. Further, variability in observed clinical data in part reflects the lack of definition of test conditions. **Key Words:** Albumin—Beta-2 microglobulin—Dialyzer—Hemodialysis—Membrane—Myoglobin—Renal replacement therapy—Sieving coefficient—Hemodiafiltration—In vitro testing.

Sieving coefficients indicate the *potential* of different solutes (e.g. albumin, beta-2 microglobulin [β_2M], or myoglobin) to pass across a particular dialyzer membrane (1). Two international standards (ISO 8637/EN 1283) (2,3) are commonly referenced for the measurement of in vitro sieving coefficients.

Sieving coefficients for different dialyzers are often compared with each other, as a result of the perception that citing the above standards is sufficient

to assure data comparability. Although referencing standards implies that clear and unambiguous guidance on test procedures is provided to achieve consistent testing across laboratories, they still allow for a certain variability of testing conditions. In the specific case of sieving coefficients, it is questionable whether the standards listed above provide sufficient guidance to enable comparability.

Furthermore, in vitro sieving coefficient values are often used as surrogates of solute removal performance, and to inform decisions that may impact clinical practice, despite not being measured using the same test conditions. In fact, a sieving coefficient is only one of many factors, including blood composition, dialyzer design, and treatment modality, that

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can impact solute loss and removal during dialysis (4–6).

The aims of this study were: (i) to assess the impact of different test parameters on sieving coefficient values within the framework provided and (ii) to investigate the relationship between sieving coefficient values and clinical albumin loss/ β_2 M reduction ratio (RR), as a predictor of solute removal performance.

METHODS

Literature review analysis of published solute removal and reported sieving coefficient values

Clinical data published between 2002 and April 2017 for albumin loss or β_2 M RR were identified using two searches: (i) OVID searches of Embase and MEDLINE databases and (ii) searches of abstract archives for ERA-EDTA, ASN, and ASAIO congresses. The search was limited to human, clinical data only. Publications were only included if an identifiable dialyzer was noted (and had publicly available sieving coefficient data, e.g., as mentioned in a data sheet, instructions for use [IFU], or manufacturer's brochure) and if the dialyzer was high-flux (high-cut-off dialyzers were excluded). Data on albumin loss (including both mean or median values per treatment) or β_2 M RR in patients during hemodialysis (HD) or hemodiafiltration (HDF) sessions were also required. For studies with the HDF treatment modality, only post-dilution was included, with convective volumes >15 L or infusion volumes >14 L (assuming weight loss of ≥ 1 kg per treatment session); publications with no HDF volumes reported were excluded. Duplicates of study data published in abstract form at different congresses and publications were removed.

Data on albumin loss and β_2 M RR during dialysis were extracted from the identified publications and plotted against sieving coefficients as reported on data sheets and IFUs for the dialyzers studied. For these analyses, sieving coefficient values listed as "less than" were considered equal to the stated value, but are clearly marked to aid comparison.

Analysis of the impact of test parameters on sieving coefficient values

Dialyzers used in these analyses were: Revaclear 400, Polyflux 170H (Baxter International Inc., Hechingen, Germany), Xevonta Hi18 (B. Braun Medical Ltd., Melsungen, Germany), Elisio 17H (Nipro Medical Corporation, Bridgewater, NJ,

USA), FX CorDiax 80, and FX 100 classix (Fresenius Medical Care, Bad Homburg, Germany).

For the first series of experiments, only the Revaclear dialyzer was used to assess the impact of testing conditions on the sieving coefficients of albumin, β_2 M, and myoglobin; tests were repeated six times to ensure robust data. For the second series of experiments, albumin, β_2 M, and myoglobin sieving coefficients of all the dialyzers listed above were determined.

For both sets of experiments, sieving coefficients were measured per the methodology stated in ISO 8637, with a recirculating fluid apparatus that provides a test setup comparable to hemofiltration mode (Supporting Information Fig. 1). Prior to testing, filters were primed with 0.9% NaCl solution. Both human plasma (Octapharma, Langenfeld, Germany) and bovine plasma (Kraeber & Co., Ellerbek, Germany) were used in separate experiments and had a specified total protein content of 60 ± 5 g/L. For the first series of experiments, blood flow rate (Q_B) and ultrafiltration rate (UF) were set according to predefined parameters (human plasma with Q_B of 300mL/min, UF 60mL/min; human plasma with Q_B /UF 500/100mL/min and bovine plasma with Q_B /UF 300/60mL/min). For the second series of experiments, sieving coefficients were measured using human plasma with Q_B /UF of 300/60mL/min. For both series of experiments, Q_B /UF were set (at the aforementioned levels) and kept at a constant and stable pressure; temperature and flow rates were verified. Samples were drawn 60 min after setting blood flow. Stability of test conditions was verified twice, 10 min after experimental setup and prior to drawing the samples.

To investigate the influence of the time of sampling on sieving coefficient, samples were taken after 15, 30, 45, and 60 min ($n=3$). Sieving coefficients were calculated as solute concentration on the filtrate side, divided by the average solute concentration as measured in the blood inlet and blood outlet sides. Concentrations of albumin, β_2 M, or myoglobin were analyzed using turbidimetric assays on a BN Prospec clinical analyzer (Siemens, Marburg, Germany) with the respective reagent kits used according to the manufacturer's instructions. Myoglobin concentration in bovine plasma was analyzed photometrically on a GE Ultrospec 8000 photometer (GE Healthcare, Frankfurt, Germany) via light absorbance at 405nm. Bovine serum albumin was quantified using a Cobas Mira clinical autoanalyzer (Roche Diagnostics, Penzberg, Germany), system with an albumin reagent kit (LT SYS, Berlin, Germany), based

on the bromocresol green method and using protein standards as a reference.

Statistical methodology

The relationship between published solute loss/RRs and the reported sieving coefficient values was analyzed by linear regression, and correlation coefficients were tested for statistical significance. Measured sieving coefficient data are displayed as mean values of six independent replicates plus/minus standard deviation. Normal distribution and equal variance of the data were verified using Shapiro–Wilk and equal variance tests. Data that were normally distributed with equal variance were analyzed using a *t*-test; *P* values less than 0.05 were considered significant. Data that were not normally distributed were analyzed with a Mann–Whitney rank sum test. Statistical calculations were conducted using SigmaPlot (Version 12.5, Systat Software Inc., San Jose, CA, USA).

RESULTS

Analysis of published solute loss and reported sieving coefficient values

For albumin loss, 31 publications were identified that met the search criteria, providing data from treatments in HD mode or post-dilution HDF mode. Albumin loss data were available for 24 dialyzers used in HDF mode and 13 dialyzers in HD mode. In HD mode, treatment times ranged from 199 to 295 min. In post-dilution HDF mode, treatment times ranged from 224 to 294 min, infusion volumes ranged from 14 to 27.9L, and UF volumes ranged from 15 to 29.9L. A significant correlation could be seen between albumin loss and reported sieving coefficients (as listed in data sheets and IFUs) for HD treatment modalities (Supporting Information

Table; $n=21$; $P=0.0316$; $R^2=0.2208$). For HDF treatment modalities, reported albumin sieving coefficients did not show a significant correlation with clinical data, that is, albumin loss as reported in the literature (Supporting Information Table; $n=63$; $P=0.2318$; $R^2=0.0234$). The majority of the reported sieving coefficient values in data sheets and IFUs were reported as “less than” values (e.g., “<0.01”), making comparison between dialyzers and their clinical performance more difficult as specific sieving coefficients were not provided.

For β_2 M removal, 12 publications were identified that met the search criteria (including treatments in HD mode or post-dilution HDF mode). In post-dilution HDF mode, treatment times ranged from 239 to 264 min, infusion volumes ranged from 14 to 28.7L, and UF volumes ranged from 15 to 30.6L. In HD mode, treatment times ranged from 180 to 264 min. Sieving coefficient data were available for eight dialyzers used in HDF mode and 11 dialyzers in HD mode. No correlation was identified between β_2 M RR and the reported sieving coefficient in HD mode ($n=21$; $P=0.3455$; $R^2=0.04693$), but a weak, statistically significant correlation was evident in HDF mode ($P=0.0002$; $R^2=0.42915$; Supporting Information Table).

Analysis of the impact of test parameters on sieving coefficient values

Changes in Q_B/UF flow rate and test plasma (human vs. bovine) had a marked impact on the sieving coefficient values for β_2 M, myoglobin, and albumin observed for the Revaclear dialyzer (Table 1). Human plasma at Q_B/UF 300/60mL/min resulted in the highest β_2 M and myoglobin sieving coefficient measurements of the three sets of testing conditions assessed. Human plasma with Q_B/UF of 500/100mL/min resulted in the lowest (0.16%) sieving coefficient for albumin, while bovine plasma with a $Q_B/$

TABLE 1. The impact of different testing conditions on Revaclear dialyzer sieving coefficients

| Testing conditions | Albumin | | β_2 M | | Myoglobin | |
|--|-----------------------|------|---------------------|----|---------------------|----|
| | Mean SC (%) | SD | Mean SC (%) | SD | Mean SC (%) | SD |
| Human plasma Q_B/UF 300/60mL/min | 0.27 ^[1,2] | 0.04 | 95 ^[3,4] | 4 | 68 ^[5,6] | 1 |
| Bovine plasma Q_B/UF 300/60mL/min | 0.69 ^[1] | 0.04 | 78 ^[3] | 4 | 58 ^[5] | 4 |
| Human plasma Q_B/UF 500/100mL/min | 0.16 ^[2] | 0.01 | 85 ^[4] | 3 | 54 ^[6] | 3 |

β_2 M, beta-2 microglobulin; Q_B , blood flow rate; SC, sieving coefficient; SD, standard deviation; UF, ultrafiltration rate. Superscript numbers indicate specific comparisons and statistical results.

^[1,3,4]*t*-test: significant difference; $P < 0.001$.

^[2,5,6]Mann–Whitney rank sum test; $P = 0.002$.

Sample number = 6.

UF of 300/60mL/min produced the highest (0.69%; Table 1).

The influence of sampling time on albumin, myoglobin, and β_2 M sieving coefficients was analyzed with Revaclear dialyzers using human plasma and testing conditions of Q_B /UF 300/60mL/min (sample $n=3$). Results are shown in Table 2. Sampling time had the most obvious impact on the albumin sieving coefficient; after 60 min, the sieving coefficient was only 46% of the measurement taken at 15 min. For myoglobin, the effect of sampling time was still visible but less pronounced than for albumin. No effect of sampling time was demonstrated for β_2 M, and the β_2 M sieving coefficient remained stable throughout the experiment (Table 2).

Comparison of published and measured sieving coefficient values

Albumin, β_2 M, and myoglobin sieving coefficients were measured for all dialyzers, using identical testing conditions (Q_B /UF 300/60mL/min; human plasma). Of the six dialyzers investigated, a specific

sieving coefficient for albumin was only available for one dialyzer, with the other five listed as having sieving coefficients less than a certain value, for example, <1%, which would allow the actual value to be as high as 0.99%. Specific sieving coefficients for albumin generated by measurements using human plasma were lower than the maximum values that comply with the “less than” values reported in data sheets and IFUs (Table 3).

Specific β_2 M sieving coefficients were available for four of the dialyzers, while a “greater than” value was provided for one dialyzer and no value was provided for one other. The β_2 M sieving coefficients reported here were higher than those listed in data sheets and IFUs, where provided, except for FX 100 classix, which was equivalent to that reported in the FX classix product brochure (7). Sieving coefficient values for β_2 M ranged from 70 to 96%, with Revaclear 400 and Elisio 17H showing the highest values (95% and 96%, respectively), despite Revaclear 400 having the lowest reported sieving coefficient in its data sheet/IFU (70%; Table 3).

TABLE 2. Revaclear sieving coefficients for albumin, myoglobin, and β_2 M after different times of sampling (human plasma, Q_B 300mL/min, UF 60mL/min)

| Time (min) | Albumin | | β_2 M | | Myoglobin | |
|------------|-------------|------|-------------|----|-------------|----|
| | Mean SC (%) | SD | Mean SC (%) | SD | Mean SC (%) | SD |
| 15 | 0.59 | 0.09 | 93 | 1 | 79 | 1 |
| 30 | 0.40 | 0.07 | 92 | 3 | 71 | 2 |
| 45 | 0.31 | 0.06 | 92 | 4 | 68 | 1 |
| 60 | 0.27 | 0.07 | 91 | 4 | 67 | 1 |

β_2 M, beta-2 microglobulin; Q_B , blood flow rate; SC, sieving coefficient; SD, standard deviation; UF, ultrafiltration rate. Sample number $n=3$.

TABLE 3. Sieving coefficients of commercial dialyzers generated using identical testing conditions (human plasma, Q_B 300mL/min, UF 60mL/min)

| Dialyzer | Albumin | | β_2 M | | Myoglobin | |
|---------------------------|------------------------------|------|---------------------------|----|--------------------------|-----|
| | Mean SC (%) | SD | Mean SC (%) | SD | Mean SC (%) | SD |
| Revaclear 400* | 0.27 (DS: <1) [†] | 0.04 | 95 (DS: 70) [†] | 4 | 68 (DS: NR) | 1 |
| Polyflux 170H* | 0.22 (DS: <1) [†] | 0.10 | 82 (DS: 70) [†] | 6 | 37 (DS: NR) | 7 |
| Xevonta Hi18 [‡] | 0.04 (DS: <0.1) [†] | 0.01 | 84 (DS: >80) [†] | 6 | 36 (DS: NR) | 3 |
| Elisio 17H [‡] | 0.16 (DS: 0.2) [†] | 0.03 | 96 (DS: NR) | 2 | 72 (DS: 22) [†] | 2 |
| FX CorDiax 80* | 0.04 (DS: <0.1) [†] | 0.01 | 92 (DS: 90) [†] | 4 | 50 (DS: 50) [†] | 4 |
| FX 100 classix* | 0.07 (DS: <0.1) [†] | 0.1 | 70 (DS: 70) [†] | 2 | 10 (DS: 10) [†] | 0.2 |

β_2 M, beta-2 microglobulin; DS, sieving coefficient value as displayed in the product data sheet; NR, not reported; Q_B , blood flow rate; SC, sieving coefficient; SD, standard deviation; UF, ultrafiltration rate. A value preceded by “<” indicates that a specific sieving coefficient value is not included on the data sheet; rather it is less than the value indicated. A value preceded by “>” indicates that a specific sieving coefficient value is not included on the data sheet; rather it is greater than the value indicated.

* Q_B /UF and test solution not identified in the data sheet.

[†]Data sheet values taken from product documentation (7–9, 16–19).

[‡] Q_B /UF listed as 300/60mL/min in the data sheet; test solution not identified. Sample number = 6.

Sieving coefficient data for myoglobin are not always listed in data sheets; therefore, no comparison with reported values can be made. Data ranged from 10 to 72%, with Revaclear 400 and Elisio 17H having the highest values (68% and 72%, respectively; Table 3).

Comparison of measured coefficient values vs. reported clinical albumin loss and β_2 M RR

For both treatment modalities, large differences were seen between many of the measured albumin sieving coefficient values and those reported in the IFUs/data sheets (Fig. 1). For example, in HD mode, two of the dialyzers with reported albumin sieving coefficient values of <1% had sieving coefficient values of 0.27% and 0.22%, respectively, when measured under identical conditions. The same was true for dialyzers tested in HDF mode. The differences were particularly evident for sieving coefficient values that were reported as “less than” figures (Supporting Information Table).

Comparison of the sieving coefficients with published albumin loss data showed significant correlations in HD mode, with an improvement in the correlation when sieving coefficients were measured with the same test parameters ($n=12$ published: $R^2=0.4216$, $P=0.032$ vs. measured $R^2=0.9655$, $P \leq 0.001$; Fig. 1). However, in HDF mode no significant correlation was seen ($n=35$ published: $R^2=0.0504$,

$P=0.195$ vs. measured $R^2=0.036$; $P=0.275$; Supporting Information Table).

When β_2 M sieving coefficients were compared with β_2 M RR in HD mode, the correlation was not significant, although it was close to the significance threshold when sieving coefficients were measured with the same test parameters ($n=16$, reported: $R^2=0.0011$, $P=0.905$ vs. measured: $R^2=0.2315$, $P=0.0592$; Fig. 2A). However, for β_2 M RR in HDF mode, a significant correlation could be seen, but only when sieving coefficients were measured with the same test parameters ($n=14$, reported: $R^2=0.1231$, $P=0.218$ vs. measured: $R^2=0.5318$, $P=0.0031$; Fig. 2B).

DISCUSSION

Sieving coefficients reported in dialyzer data sheets and IFUs, and hence those used in this analysis, indicate the *potential* of different solutes (e.g., albumin, β_2 M, or myoglobin) to pass across a particular membrane (1). Despite this definition and the fact that sieving coefficient data are generated in vitro, they are often used as a predictor of clinical solute removal performance. To our knowledge, there are no publications that have analyzed a possible correlation between sieving coefficient and clinical performance data, that is, highlighting the problem of extrapolating clinical performance from sieving coefficient data generated in vitro, given the

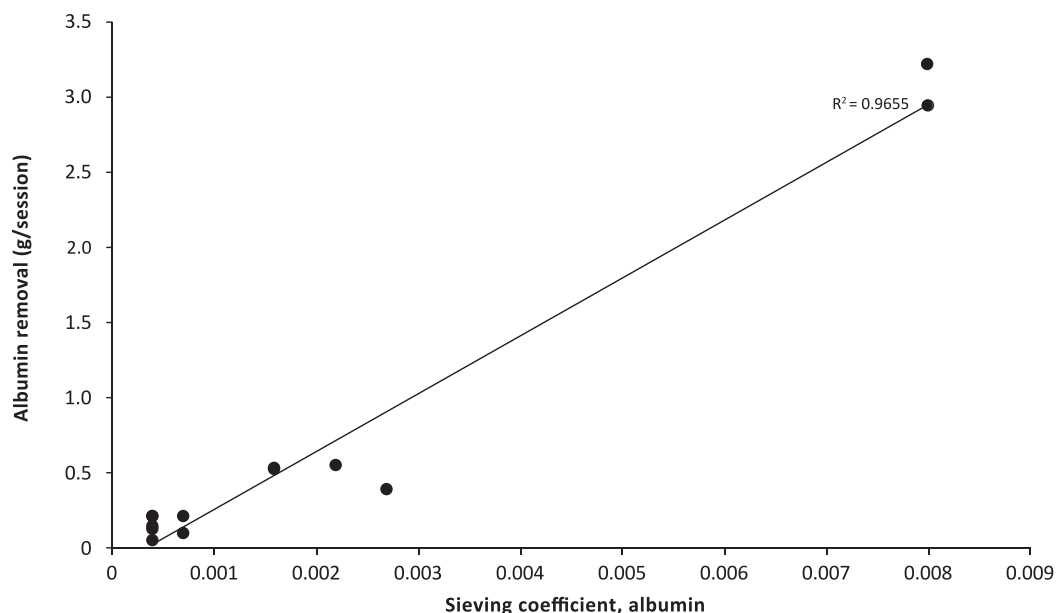


FIG. 1. Correlation of clinical albumin loss in hemodialysis (HD) mode and sieving coefficient, measured with human plasma (7–19). Albumin sieving coefficients are plotted for a range of dialyzers used in clinical studies that provided albumin removal data, as reported in the literature. Sieving coefficients were measured by Baxter using identical testing conditions, per the methodology stated in ISO 8637, and using human plasma with Q_B/UF of 300/60mL/min.

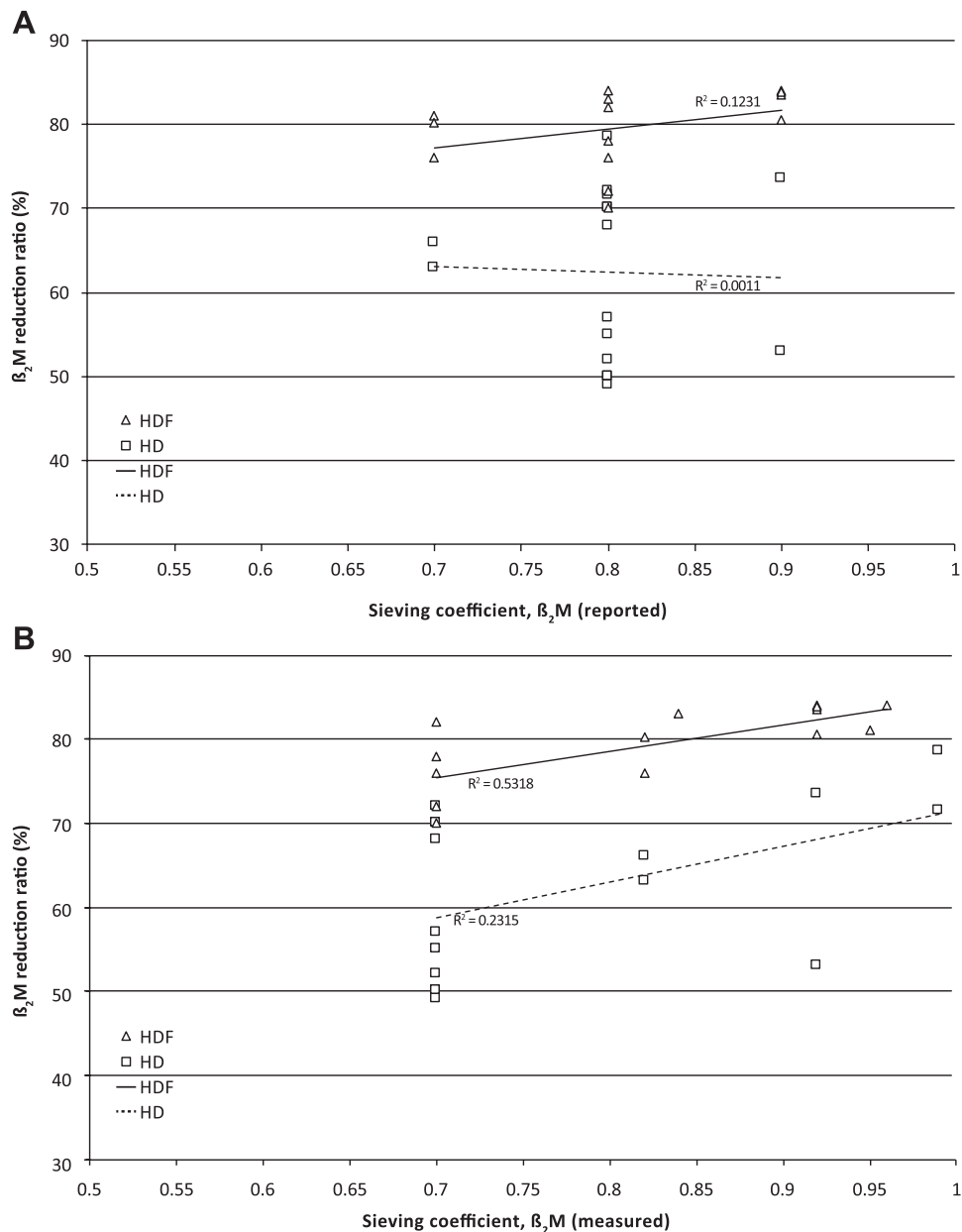


FIG. 2. Correlation of clinical beta-2 microglobulin reduction ratio (β_2M RR) data and sieving coefficient using (A) values reported in data sheets and instructions for use and (B) values measured under identical testing conditions (per the methodology stated in ISO 8637, using human plasma with Q_E/UF of 300/60mL/min) (7–12,15,19–26). HD, hemodialysis; HDF, hemodiafiltration.

weak relationship with clinical performance markers (i.e., albumin loss and β_2M RR).

Our analyses of the published literature on solute loss and the sieving coefficients reported in manufacturers' materials demonstrated that although correlations are sometimes identified, sieving coefficients do not always show a strong correlation to clinical performance indicators. Other factors such as the patient, treatment conditions, and the design of the dialyzer need to be considered as well (1,4,6,27-30). In

vitro sieving coefficients have limitations as parameters on which to base decisions in clinical practice and clinicians and other key decision makers should consider all available clinical information, which may provide a more accurate representation of clinical performance of a dialyzer than technical data generated in vitro alone.

Variation in reported sieving coefficients values may not be the sole reason for the discrepancies seen in the correlation with solute loss. For example, even

when measured using identical conditions, we did not observe any improvement in the correlation for albumin loss in HDF mode. This suggests that other parameters are likely to be more important for impacting the amount of albumin lost during treatment, such as treatment factors (e.g., UF volumes in relation to dialyzer surface area or blood flow rate), patient factors (e.g., blood viscosity), or the method used for assessing albumin loss. Furthermore, the borderline significance of the correlation between β_2 M RR in HDF mode and sieving coefficient values measured under the same conditions could be explained by factors relating to the patient. For example, based on the finding that β_2 M removal with HDF treatment was limited by the rate of intercompartmental transfer of β_2 M within the body, Ward et al. (31) recommended that altering the duration and frequency of treatment sessions, rather than increasing extracorporeal clearance in a given dialysis session, would be the most effective way of returning serum β_2 M levels to normal (31).

That there was no association between β_2 M sieving coefficient and RR in HD mode while there was a correlation in HDF mode that can be explained, in part, by the different mechanisms of transport across the membrane in these modalities. During HD mode, diffusion is the primary driving factor for mass transport and the other impacting factors, such as membrane permeability, will become less important, resulting in the lack of observed correlation. The opposite is true in HDF mode, where convection due to a transmembrane pressure gradient provides a strong driving force that makes the impact of other limiting factors, such as membrane permeability, more relevant; this results in a correlation between the β_2 M sieving coefficient and observed RR. However, it is important to note that—as observed here with albumin, a large molecule possessing a low sieving coefficient—multiple factors, such as membrane fouling over time, result in complex effects that limit the impact of small changes in sieving coefficient despite the strong driving force.

Our data also demonstrate the impact of different methodologies on generating *in vitro* sieving coefficient data and have important implications regarding the comparability of data from different sources. The recommended methods to measure sieving coefficients allow for variability in testing conditions in terms of plasma source (human vs. bovine), flow rates, and testing times. As we have observed, and building on the observations of other groups, all these factors can have a significant impact on the measured sieving coefficient, such that quite different values can be obtained for the same membrane

and solute if conditions are altered. As such, decision makers should be aware of the limitations of comparing sieving coefficients reported in product documentation that have been obtained using different methods. For example, a change in flow rate caused a marked difference in results; when flow rates (Q_B/UF) were lowered, sieving coefficient values increased. This finding is supported by work by Bresler et al. and Opong and Zydney, who reported that sieving coefficient values are filtrate flux and, therefore, flow dependent (32,33).

Our results also highlight the impact that the origin of plasma can have on sieving coefficient values. Given this knowledge, it could be argued that bovine plasma is not the most appropriate test medium to use for studies of devices intended for use in humans. The exception to this would be in situations where comparability studies have been conducted to ensure results generated using bovine plasma are equivalent to those generated using human plasma. Work by Windberger et al. supports this conclusion, in that the authors analyzed blood and plasma properties and found that differences in viscosity and shear rate were apparent between different species of animals (34). Although the data published by Windberger et al. were not generated in the context of sieving coefficients, it is known that both viscosity and shear rates can affect solute removal in dialysis (4,6). Besides this, it was also found that plasma protein composition can be different between human and bovine plasma. Human plasma tends to have higher concentrations of serum albumin and lower concentrations of globulins, particularly in the alpha 1-globulin and beta-globulin fractions, when compared with bovine plasma (35,36). Differences in plasma composition can be considered as an explanation for the observed differences in plasma viscosity. Beyond that, difference in plasma composition can also have a direct impact on sieving coefficients by creating different layers of adsorbed proteins upon contact with membrane material. This evidence also brings into question the comparability of data generated using plasma from different species.

In this work, an impact of sampling time on sieving coefficients was shown. Reduction of dextran sieving coefficients upon blood contact was also reported in work by Langsdorf and Zydney, in which sieving coefficients stabilized after 40 min of contact with blood (37). This effect can be explained by the formation of a protein layer which has an impact on sieving properties of the membrane (38). Sampling time is typically not mentioned in conjunction with published sieving coefficient data. This lack of information adds to the difficulty of sieving coefficient comparability.

Our analyses also highlight that sieving coefficients generated using identical testing methods stated here were similar for some dialyzers, despite reported values in data sheets and IFUs being markedly different. Based on results reported here, it can be presumed that such differences can be attributed to variations in testing methodology. There are inconsistencies between sieving coefficient values cited in product brochures and those reported in data sheets and IFUs (8,9); to the authors' knowledge, this is the first time that this finding has been formally reported specifically for commonly used dialyzers. Indeed, these findings reinforce the theory that sieving coefficients are subjected to variability (depending on testing conditions used) and should not be compared unless identical testing methods have been used.

There are limitations to the statistical analyses presented here. First, as with any analysis of data obtained from multiple studies, the differences in the trial methodologies will limit how comparable the data are, and this will in turn impact the statistical analyses that can be used. In addition, as these data were obtained from varying patient populations and treatment conditions (e.g., flow rates, treatment times, and substitution volumes in HDF mode), and as removal during dialysis does not have a linear correlation with many of these factors, it was not possible to normalize for these potential differences. This analysis is limited by which data are available, and an analysis of correlation can be skewed by limited data, especially at the extreme ends of the curve. Finally, in the case of albumin, exact sieving coefficient values are often not reported; instead, a range of values are provided in manufacturers' materials (e.g., <0.01). Therefore, although a positive correlation is formally indicated in some cases, the clinical relevance of this could be questioned due to the large spread of albumin loss reported for the same sieving coefficient values. Differences between the methods used to measure clinical albumin loss also make it difficult to draw comparisons and can add to the variation seen. For example, albumin loss reported for the FX 1000 dialyzer ranges from 1.2 to 3.611g per session (39–41). It is possible that differences in the methods used to measure albumin in spent dialysate may also contribute to the variation in results seen (13,39). Regardless of the potential limitations, there is a value to the statistical analyses; potential correlations were observed, which—in the absence of a direct comparative study—may help to support filter performance evaluations.

CONCLUSIONS

In summary, a lack of standardization of testing parameters makes it difficult to accurately compare sieving coefficients of different dialyzers; test parameters such as origin of plasma, Q_B/UF , and time will all impact the final measured sieving coefficient. The results presented here, using standardized conditions, allow comparability of sieving coefficients of some commonly used commercial dialyzers and highlight the need for stricter standardization of experimental conditions for the measurements of sieving coefficients. Unless measured under identical conditions, sieving coefficients should not be compared. The limitations and influencing factors shown here must be taken into consideration when considering the impact of sieving coefficients on clinical solute removal performance.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

FIG. S1. Setup for measuring sieving coefficients.

TABLE S1. Analyses of A) β_2 M reduction ratios and B) albumin loss vs. sieving coefficient values in HD and HDF treatment modes (sieving coefficient values reported in datasheets and IFUs vs. identical testing conditions).