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Longitudinal Clinical and Hemodynamic Observations During Sequential Use of Three β2-Microglobulin Adsorption Column Sizes in Dialysis-Related Amyloidosis: A Case Report and Literature Review

Takayuki Matsuo

tmatsuo@kaishou.or.jp

Toshima Central Hospital, Kaishokai Medical Corporation

Ren Takahashi

Kaikoukai Josai Hospital

Takashi Hibino

Kaikoukai Josai Hospital

Hiroki Yabe

Seirei Christopher University

Tetsuya Yamada

Kaikoukai Healthcare Group

Naomichi Hayashi

Toshima Central Hospital, Kaishokai Medical Corporation

Miwa Nezu

Toshima Central Hospital, Kaishokai Medical Corporation

Noriko Yamanaka

Toshima Central Hospital, Kaishokai Medical Corporation

Case Report

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Title page

Longitudinal Clinical and Hemodynamic Observations During Sequential Use of Three β2-Microglobulin Adsorption Column Sizes in Dialysis-Related Amyloidosis: A Case Report and Literature Review

The names of the authors

Takayuki Matsuo[1], Ren Takahashi[2], Takashi Hibino[2], Hiroki Yabe[3], Tetsuya Yamada[4], Naomichi Hayashi[1], Miwa Nezu[1], Noriko Yamanaka[5]

The affiliations and addresses of the authors

1) Department of Dialysis, Toshima Central Hospital, Kaishokai Medical Corporation, Toshima-ku, Tokyo, Japan.

2) Department of Rehabilitation, Kaikoukai Josai Hospital, Nagoya, Aichi, Japan.

3) Department of Physical Therapy, School of Rehabilitation Sciences, Seirei Christopher University, Hamamatsu, Shizuoka, Japan.

4) Corporate Headquarters, Kaikoukai Healthcare Group, Nagoya, Aichi, Japan.

5) Department of Clinical Medicine, Toshima Central Hospital, Kaishokai Medical Corporation, Toshima-ku, Tokyo, Japan.

Correspondence:

Takayuki Matsuo

Department of Clinical Engineering, Toshima Central Hospital, Kaishokai Medical Corporation, Tokyo, Japan, 2-42-21 Kami-Ikebukuro, Toshima-ku, Tokyo 170-0012, Japan

TEL:03-3916-7211

E-mail: tmatsuo@kaishou.or.jp

Abstract

Background: Dialysis-related amyloidosis (DRA) is a complication of long-term dialysis associated with accumulation of β2-microglobulin (β2-MG) and can manifest as arthralgia, carpal tunnel syndrome, and bone cysts. Lixelle is a β2-MG adsorption column designed to selectively remove β2-MG. Reports describing within-patient clinical and hemodynamic trajectories during sequential use of different Lixelle column sizes are limited. We report longitudinal observations in a patient with DRA during sequential use of low-capacity (S-15), medium-capacity (S-25), and high-capacity (S-35) columns.

Case presentation: A man in his 50s with type 1 diabetes mellitus, a long history of maintenance hemodialysis, and histologically confirmed β2-MG amyloid deposition was observed during sequential use of S-15, S-25, and S-35, each for 90 days. Pain assessed using the Numerical Rating Scale (NRS), pinch strength, serum β2-MG, interleukin-6 (IL-6), high-sensitivity IL-1β, tumor necrosis factor-α (TNF-α), blood pressure, and heart rate were evaluated longitudinally. Mean NRS decreased from 8.29±1.7 before introduction to 7.1±0.6, 4.7±0.2, and 4.1±0.4 in the low-, medium-, and high-capacity phases, respectively. Right-hand pinch strength changed from 4.2 to 5.6±0.4 kg and left-hand pinch strength from 3.4 to 4.0±0.2 kg. Serum β2-MG transiently increased in the low-capacity phase and subsequently decreased, without a monotonic change with increasing column size. IL-6 changed from 4.8 pg/mL before introduction to 4.2 pg/mL at the end of the high-capacity phase. High-sensitivity IL-1β was 1.1 pg/mL at day 30 and below the detection limit (<0.2 pg/mL) at subsequent

measurements. Mean intradialytic SBP, DBP, and heart rate were lowest during the medium-capacity phase and did not show a further unidirectional decrease after transition to the high-capacity phase.

Conclusions: This case provides a longitudinal description of changes in pain, physical function, inflammatory markers, and intradialytic hemodynamic parameters during sequential use of three β2-MG adsorption column sizes. The observed trajectories differed among clinical, biochemical, and hemodynamic measures and provide descriptive information for future investigation of column-size selection in DRA.

Keywords

Dialysis-related amyloidosis; β2-microglobulin; Lixelle; hemodialysis; adsorption column; hemodynamics; case report

Background

Dialysis-related amyloidosis (DRA) is a refractory complication of long-term dialysis in which β2-microglobulin (β2-MG) accumulates in the circulation and deposits as amyloid fibrils in bones, joints, tendons, and ligaments, resulting in manifestations such as arthralgia, carpal tunnel syndrome, and bone cysts [1,2]. Online hemodiafiltration (Online HDF) is used in patients with DRA because of its enhanced removal of middle-molecular-weight solutes; however, symptoms may persist despite Online HDF alone [2,3]. β2-MG adsorption columns have therefore been developed as blood purification devices for DRA and are used in series with the dialyzer in the extracorporeal circuit [4-9]. These columns contain porous cellulose beads with immobilized hexadecyl ligands and selectively adsorb β2-MG through a combination of molecular sieving and hydrophobic interactions [4-9]. Previous studies have reported

reductions in serum β2-MG and improvements in pain, pinch strength, peripheral motor nerve conduction, and activities of daily living (ADL) during β2-MG adsorption therapy [4-8,10,11]. Adsorption of cytokines such as IL-6 and IL-1β has also been reported [1,2,4-6,8,9].

Three Lixelle column sizes are available: S-15, S-25, and S-35, which are referred to in this report as low-, medium-, and high-capacity columns, respectively. Larger column sizes contain more adsorbent but also increase extracorporeal blood volume, raising concern regarding hemodynamic effects such as hypotension [4-8,10]. Previous studies have reported adverse events including transient hypotension and anemia, and cautious use has been suggested in patients with heart failure, older age, low body weight, or a tendency toward intradialytic hypotension [2-6,8,10,11]. Column size is therefore selected according to individual clinical background and hemodynamic status, although objective criteria for changing column size have not been established [4-8].

Reports describing longitudinal changes in pain, physical function, β2-MG, inflammatory markers, and hemodynamic parameters within the same patient during sequential use of low-, medium-, and high-capacity columns are limited [4-8,10,11]. We therefore report a patient with DRA associated with long-term dialysis in whom Lixelle was used sequentially as S-15, S-25, and S-35, each for 90 days, and describe the longitudinal trajectories of NRS, pinch strength, serum β2-MG, inflammatory markers, blood pressure, and heart rate during this clinical course.

Case presentation

Clinical course

The patient was a man in his 50s with a native arteriovenous fistula in the left forearm. Type 1 diabetes mellitus was diagnosed at 10 years of age, and insulin therapy

was initiated. Hemodialysis was started at 23 years of age because of progressive chronic kidney disease. At 30 years of age, pain and numbness developed in the first through third digits of the left hand, and left carpal tunnel syndrome was diagnosed. At 50 years of age, he underwent endoscopic carpal tunnel release, and postoperative histopathology confirmed β2-MG amyloid deposition. He subsequently transferred to our institution for outpatient maintenance dialysis. Pain in the first and second digits of the right hand was present at transfer, and DRA was diagnosed on the basis of his long dialysis history and imaging findings, after which β2-MG adsorption therapy was initiated. Because the increase in extracorporeal blood volume associated with larger column sizes was considered a potential hemodynamic concern in the context of type 1 diabetes and long-term dialysis, sequential use beginning with the low-capacity column was selected. Baseline laboratory findings are shown in Table 1.

Observation periods and assessments

The 30 days before initiation of the β2-MG adsorption column (Lixelle; Kaneka Medix Corporation) were defined as the pre-introduction period. After initiation, S-15 was used during the low-capacity phase, S-25 during the medium-capacity phase, and S-35 during the high-capacity phase; each column size was used for 90 days. Dialysis conditions were kept constant throughout the observation period using Online HDF for 4 hours, a blood flow rate of 200 mL/min, a substitution fluid flow rate of 400 mL/min, and an ABH-22PA dialyzer. The β2-MG adsorption column was connected in series downstream of the dialyzer.

Pre- and post-dialysis body weight, cardiothoracic ratio (CTR), and dry weight (DW) were measured monthly during the pre-introduction, low-capacity, medium-capacity, and high-capacity phases. Blood pressure (systolic blood pressure [SBP] and

diastolic blood pressure [DBP]) and heart rate were recorded immediately before dialysis (Pre-HD), at dialysis initiation (0 minutes), and every 30 minutes thereafter through 240 minutes. Pain was assessed using the NRS at the shoulder, elbow, finger joints, lower back, hip, knee, and ankle before initiation and every 30 days thereafter, for a total of 10 assessments. At each assessment, the mean and standard deviation of NRS scores across the seven sites were calculated and plotted over time; site-specific NRS data are provided in the supplementary data. Bilateral pinch strength was measured before initiation and every 30 days thereafter, for a total of 10 assessments. A BASELINE® Electronic Pinch Gauge (Fabrication Enterprises Inc., Elmsford, NY, USA; 60-lb/27-kg capacity) was used to measure lateral pinch strength between the thumb and index finger.; two to three maximal efforts were performed, and the highest value was recorded. Predialysis serum β2-MG was measured before initiation and every 30 days thereafter. Predialysis IL-6 and TNF-α were measured before initiation and at days 30, 90, 180, and 270, while CRP and high-sensitivity IL-1β were measured at days 30, 90, 180, and 270.

Assessment and descriptive analysis

This was a longitudinal observation of a single case, and no inferential statistical comparisons were performed. Descriptive statistics (mean±standard deviation) were calculated for the pre-introduction, low-capacity, medium-capacity, and high-capacity phases. The low-, medium-, and high-capacity phases were defined as the 90-day periods during which S-15, S-25, and S-35, respectively, were used. Longitudinal changes were illustrated using line graphs and evaluated visually in terms of level, trend, and variability. Individual NRS and pinch-strength measurements were shown

together with linear fitted curves. Percentage change for each capacity phase was calculated relative to the representative value during the pre-introduction period.

Percentage change (Δ%) = (representative value for each capacity phase − representative value for the pre-introduction period) / representative value for the pre-introduction period × 100

SBP, DBP, and heart rate were recorded immediately before dialysis (Pre-HD), at dialysis initiation (0 minutes), and every 30 minutes thereafter through 240 minutes. Pre-HD values were displayed in Figure 2 to characterize predialysis hemodynamic status but were not included in the phase-specific representative values. For each phase, the mean at each of the nine intradialytic time points (0, 30, 60, 90, 120, 150, 180, 210, and 240 minutes) was calculated across all dialysis sessions in that phase. The arithmetic mean of these nine time-point means was used as the phase-specific representative mean. The sample standard deviation across the nine time-point means was reported as the SD and represents intradialytic time-point variability rather than between-session variability. Percentage changes in SBP, DBP, and heart rate were calculated relative to the representative value from the pre-introduction period, which was derived from dialysis sessions within the 30 days before initiation using the same method. During manuscript preparation, ChatGPT (OpenAI) was used for English-language editing and assistance with manuscript organization and formatting. All generated content was reviewed, verified, and revised by the authors, who take full responsibility for the final manuscript.

Longitudinal observations

Both pre- and post-dialysis body weight tended to increase from the low- to the high-capacity phase. DW showed a similar pattern. CTR varied within phases, but the overall change during the observation period was relatively small (Figure 1).

The phase-specific mean intradialytic SBP was 168.89±3.27 mmHg during the pre-introduction period, 138.05±8.78 mmHg in the low-capacity phase (Δ% −18.3%), 129.84±8.32 mmHg in the medium-capacity phase (Δ% −23.1%), and 135.47±9.11 mmHg in the high-capacity phase (Δ% −19.8%). Mean intradialytic SBP was lowest in the medium-capacity phase and increased modestly in the high-capacity phase. The phase-specific mean intradialytic DBP was 97.42±2.27, 82.74±6.39 (Δ% −15.1%), 74.28±5.44 (Δ% −23.8%), and 76.86±4.72 mmHg (Δ% −21.1%), respectively, showing the same pattern (Figure 2a,b). The phase-specific mean intradialytic heart rate was 60.41±2.06 bpm during the pre-introduction period, 58.47±1.98 bpm in the low-capacity phase (Δ% −3.2%), 52.66±1.33 bpm in the medium-capacity phase (Δ% −12.8%), and 53.19±2.04 bpm in the high-capacity phase (Δ% −12.0%). Mean intradialytic heart rate decreased by 5.81 bpm from the low- to the medium-capacity phase and then increased slightly by 0.53 bpm in the high-capacity phase (Figure 2c). Thus, mean intradialytic SBP, DBP, and heart rate were lowest in the medium-capacity phase, but none showed a unidirectional decrease with increasing column size.

Longitudinal changes in inflammatory markers are shown in Table 2. IL-6 was 4.8 pg/mL before introduction and 7.8, 9.0, 6.8, and 4.2 pg/mL at days 30, 90, 180, and 270, respectively; the value at day 270 was 12.5% lower than the pre-introduction value. High-sensitivity IL-1β was 1.1 pg/mL at day 30 and below the detection limit (<0.2 pg/mL) at days 90, 180, and 270. TNF-α (HS) was 1.2 pg/mL before introduction and 2.7, 4.4, 2.8, and 3.7 pg/mL at days 30, 90, 180, and 270, respectively. CRP was 0.10, 0.40, 0.11, and 0.53 mg/dL at days 30, 90, 180, and 270, respectively.

Mean NRS across the seven sites was 8.29±1.7 before introduction, 7.1±0.6 in the low-capacity phase (Δ% −14.9%), 4.7±0.2 in the medium-capacity phase (Δ% −43.7%), and 4.1±0.4 in the high-capacity phase (Δ% −50.6%), showing a downward trend over the observation period (Figure 3, Table 3). Site-specific NRS data are shown in the supplementary figure.

Right-hand pinch strength was 4.2 kg before introduction, 4.8±0.2 kg in the low-capacity phase (Δ% 13.5%), 5.1±0.4 kg in the medium-capacity phase (Δ% 22.2%), and 5.6±0.4 kg in the high-capacity phase (Δ% 32.5%). Left-hand pinch strength was 3.4, 3.7±0.1 (Δ% 9.8%), 4.1±0.2 (Δ% 19.6%), and 4.0±0.2 kg (Δ% 17.7%), respectively (Table 3). Both hands showed an overall upward trend during the observation period (Figure 4).

Serum β2-MG was 32.2 mg/L before introduction, 34.5±1.6 mg/L in the low-capacity phase (Δ% +7.3%), 31.7±0.9 mg/L in the medium-capacity phase (Δ% −1.7%), and 30.9±1.3 mg/L in the high-capacity phase (Δ% −3.9%) (Table 3). After a transient increase in the low-capacity phase, lower values were observed in the medium- and high-capacity phases; however, the pattern was not a monotonic decrease with increasing column size (Figure 5).

Discussion and Conclusions

This report documents longitudinal clinical, biochemical, and hemodynamic observations during sequential 90-day use of low-, medium-, and high-capacity β2-MG adsorption columns in a patient with DRA associated with long-term dialysis. NRS tended to decrease and pinch strength tended to increase across the observation period, while selected inflammatory markers also changed over time. Mean intradialytic SBP, DBP, and heart rate were lowest during the medium-capacity phase and did not show a

225 further unidirectional decrease after transition to the high-capacity phase. The differing
226 temporal patterns across these measures provide descriptive information on the clinical
227 course during sequential use of three Lixelle column sizes.

228 To our knowledge, the major clinical studies evaluating symptoms and biochemical
229 markers during β2-MG adsorption therapy for DRA are summarized in Table 4. In these
230 reports, a direct hemoperfusion column containing porous cellulose beads with
231 immobilized hexadecyl ligands was connected in series upstream of the dialyzer and
232 used during thrice-weekly dialysis [8,10,12-14]. The principal outcomes included serum
233 β2-MG, joint pain, pinch or grip strength, activities of daily living (ADL), and
234 radiographic bone cysts, and the treatment periods in interventional studies were
235 generally approximately 1-2 years. The columns used included the large-capacity S-35
236 (350 mL) [8], the small-capacity S-15 (150 mL) [10], or selection between S-15 and S-
237 35 according to patient characteristics or tolerance [13]; some reports did not specify the
238 column size [12]. However, none of these previous studies used a design in which
239 column capacity was deliberately escalated over the clinical course, and studies
240 evaluating responses to sequential increases in adsorption capacity within the same
241 patient are lacking. In the present case, clinical indices (pain NRS and pinch strength)
242 and biochemical indices (serum β2-MG, IL-6, high-sensitivity IL-1β, and TNF-α) were
243 observed longitudinally within the same patient during sequential use of three column
244 sizes. In addition, the concurrent longitudinal measurement of multiple inflammatory
245 cytokines together with β2-MG may provide insight into biological changes
246 accompanying β2-MG adsorption therapy that cannot be obtained from fixed-capacity
247 designs.

248 Previous studies of β2-MG adsorption therapy have reported reductions in serum
249 β2-MG and improvements in joint pain, pinch strength, activities of daily living, and

peripheral nerve conduction [3-8,10,11]. The decreases in NRS and increases in pinch strength observed in this case were directionally consistent with those reports. Serum β2-MG increased transiently during the low-capacity phase and was lower during the medium- and high-capacity phases, although a monotonic capacity-related decline was not observed. IL-6 and high-sensitivity IL-1β decreased at later assessments, whereas TNF-α and CRP fluctuated over time. These observations show that clinical and biochemical measures did not follow a uniform temporal pattern during the observation period and support longitudinal assessment of multiple complementary markers.

Regarding hemodynamic parameters, the phase-specific mean intradialytic SBP and DBP were already lower in the low-capacity phase than during the pre-introduction period (SBP, 168.89 to 138.05 mmHg; DBP, 97.42 to 82.74 mmHg), decreased further in the medium-capacity phase (129.84 and 74.28 mmHg, respectively), and then increased modestly in the high-capacity phase (135.47 and 76.86 mmHg, respectively). Mean intradialytic heart rate changed from 60.41 bpm during the pre-introduction period to 58.47 bpm in the low-capacity phase, decreased to 52.66 bpm in the medium-capacity phase, and was 53.19 bpm in the high-capacity phase. Accordingly, the largest reductions in mean intradialytic SBP and DBP from the pre-introduction period were already apparent by the low-capacity phase, whereas the most notable phase-to-phase decrease in mean intradialytic heart rate occurred between the low- and medium-capacity phases. None of these parameters showed progressive lowering after transition to the high-capacity phase. Thus, the hemodynamic observations did not show a simple monotonic relationship with increasing column size and underscore the value of continued hemodynamic observation during sequential changes in column size.

This report has several limitations. First, it is a longitudinal observation of a single patient without a control group; therefore, inferential statistical testing and causal

inference are not possible. Second, the low-, medium-, and high-capacity columns were used in a fixed chronological sequence, so column size was inseparable from the passage of time. Consequently, capacity-specific effects cannot be distinguished from cumulative treatment effects, natural history, or other time-dependent factors. Third, NRS is subjective and may be influenced by expectation, placebo effects, and recall bias, and neither the patient nor the evaluator was blinded. Fourth, adverse events were not predefined or systematically collected and assessed; therefore, the safety of sequential use cannot be determined, nor can this approach be considered safer than initiating treatment with a high-capacity column. Fifth, autonomic nervous activity and baroreflex function were not measured, so mechanisms underlying the observed hemodynamic trajectory could not be evaluated. Accordingly, these findings should be interpreted as exploratory and hypothesis-generating. Larger prospective studies with standardized criteria for column-size selection, predefined monitoring variables, and systematic adverse-event assessment are needed to confirm these observations.

In this patient with DRA, sequential 90-day use of low-, medium-, and high-capacity β2-MG adsorption columns was accompanied by decreases in NRS, increases in pinch strength, changes in inflammatory markers, and changes in mean intradialytic SBP, DBP, and heart rate. The clinical, biochemical, and hemodynamic measures showed different temporal trajectories, and mean intradialytic SBP, DBP, and heart rate did not continue to decrease after transition to the high-capacity phase. This case provides descriptive longitudinal information on the clinical course during sequential use of three Lixelle column sizes in DRA.

List of abbreviations

ADL, activities of daily living; AVF, arteriovenous fistula; CRP, C-reactive protein; CTR, cardiothoracic ratio; DBP, diastolic blood pressure; DRA, dialysis-related amyloidosis; DW, dry weight; HDF, hemodiafiltration; IL, interleukin; NRS, Numerical Rating Scale; SBP, systolic blood pressure; TNF-α, tumor necrosis factor-α; β2-MG, β2-microglobulin.

Declarations

Ethics approval and consent to participate

The Ethics Committee of Kaishokai confirmed that formal ethical approval was not required for this study because it was a single case report (Approval No. 26006_01TO). Written informed consent was obtained from the patient for participation and publication.

Consent for publication

Informed consent for publication of this case report and the accompanying clinical data was obtained from the patient.

Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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None

Authors' contributions

TM conceived the study. TM, MN and NH collected the data. TM, MN and NH developed the methodology and performed the formal analysis. TM drafted the manuscript. RT, TH, TY, HY and NY contributed to data interpretation and critically reviewed the manuscript. RT supervised the study. All authors participated in the review and editing of the manuscript. All authors read and approved the final manuscript.

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Figure legends

Figure 1. Longitudinal changes in body weight, dry weight, and cardiothoracic ratio

(a) Pre-hemodialysis body weight, post-hemodialysis body weight, and dry weight during the pre-introduction, low-capacity (S-15), medium-capacity (S-25), and high-capacity (S-35) phases. (b) Cardiothoracic ratio during the same observation periods. CTR, cardiothoracic ratio; DW, dry weight; HD, hemodialysis.

Figure 2. Mean intradialytic SBP, DBP, and heart rate across column-size phases

(a) Systolic blood pressure, (b) diastolic blood pressure, and (c) heart rate. Pre-HD values indicate measurements obtained immediately before dialysis; 0 min indicates

dialysis initiation. Subsequent measurements were obtained every 30 minutes through 240 minutes. Baseline, pre-introduction period; Low, S-15; Medium, S-25; High, S-35; DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure.

Figure 3. Longitudinal changes in pain assessed using the Numerical Rating Scale

Mean NRS scores across seven anatomical sites (shoulder, elbow, finger joints, lower back, hip, knee, and ankle) are shown before initiation and every 30 days thereafter. Error bars indicate the standard deviation across the seven sites at each assessment. The fitted line illustrates the overall longitudinal trend. NRS, Numerical Rating Scale.

Figure 4. Longitudinal changes in bilateral pinch strength

Right- and left-hand pinch strength were measured before initiation and every 30 days thereafter. At each assessment, the highest value from two to three maximal lateral-pinch efforts was recorded. Linear fitted lines illustrate the longitudinal trends.

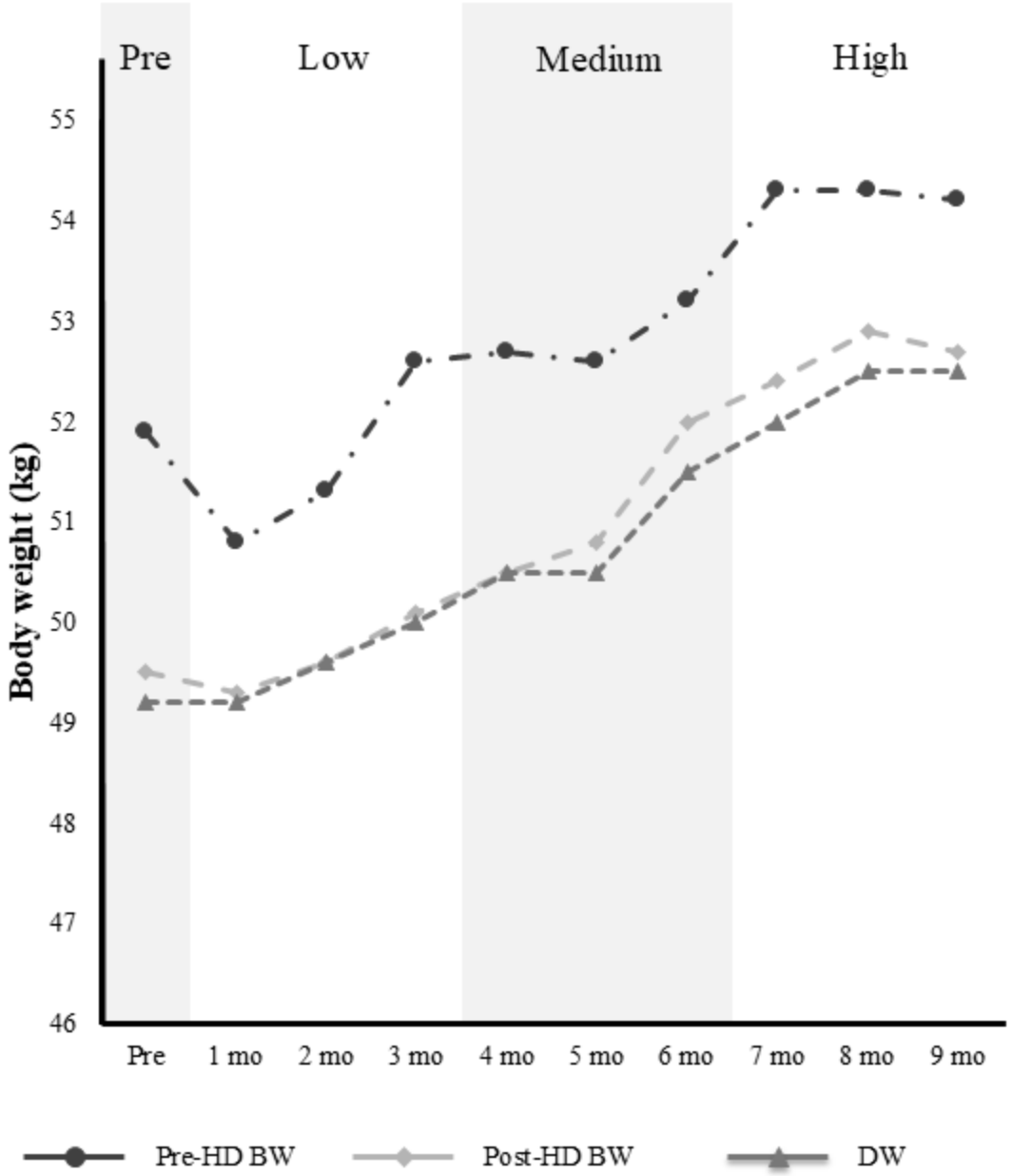
Figure 5. Longitudinal changes in predialysis serum β2-microglobulin

Predialysis serum β2-microglobulin was measured before initiation and every 30 days thereafter during sequential use of S-15, S-25, and S-35. The fitted line illustrates the overall longitudinal trend. β2-MG, β2-microglobulin.

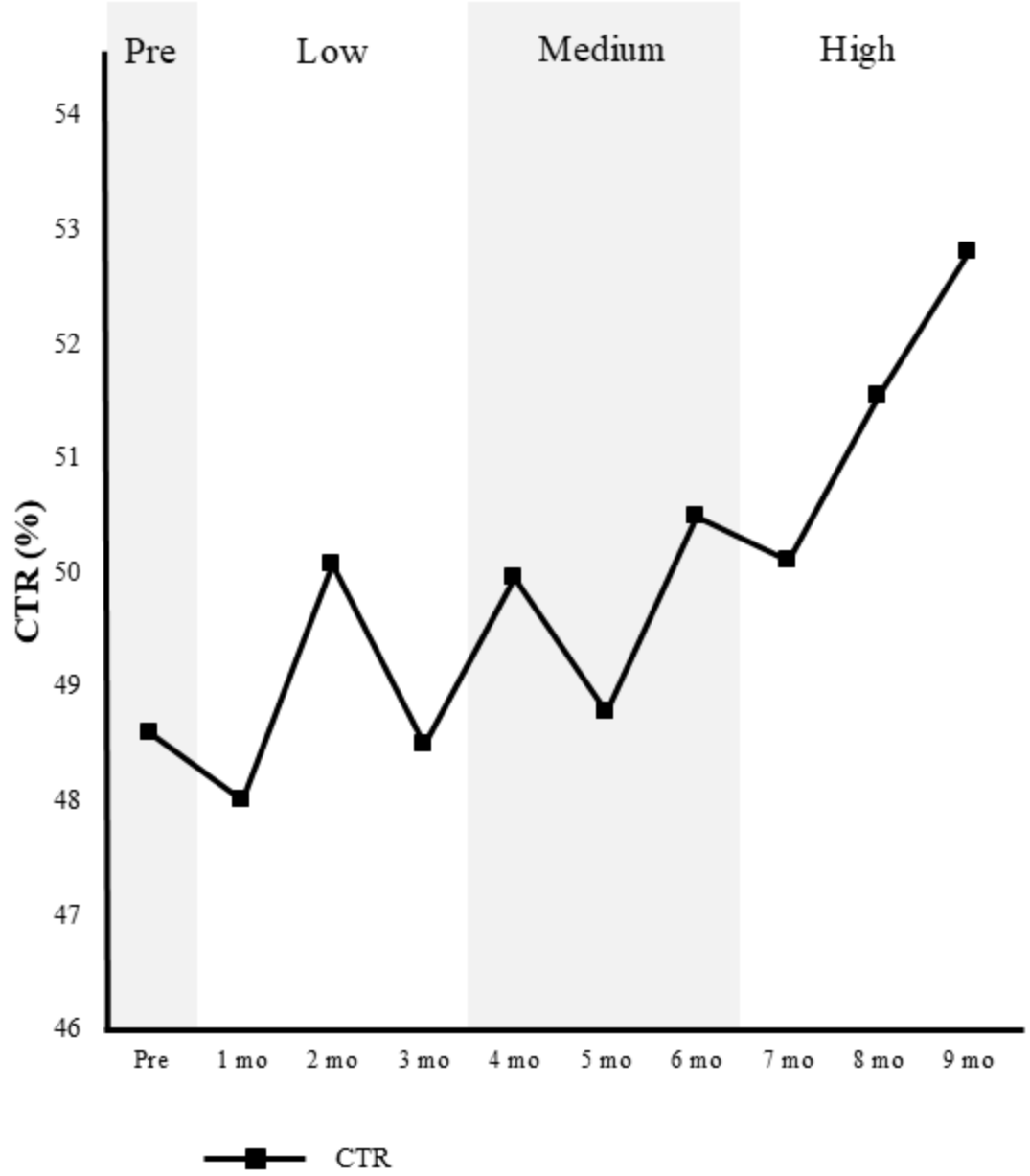
Supplementary Figure S1. Site-specific longitudinal changes in pain

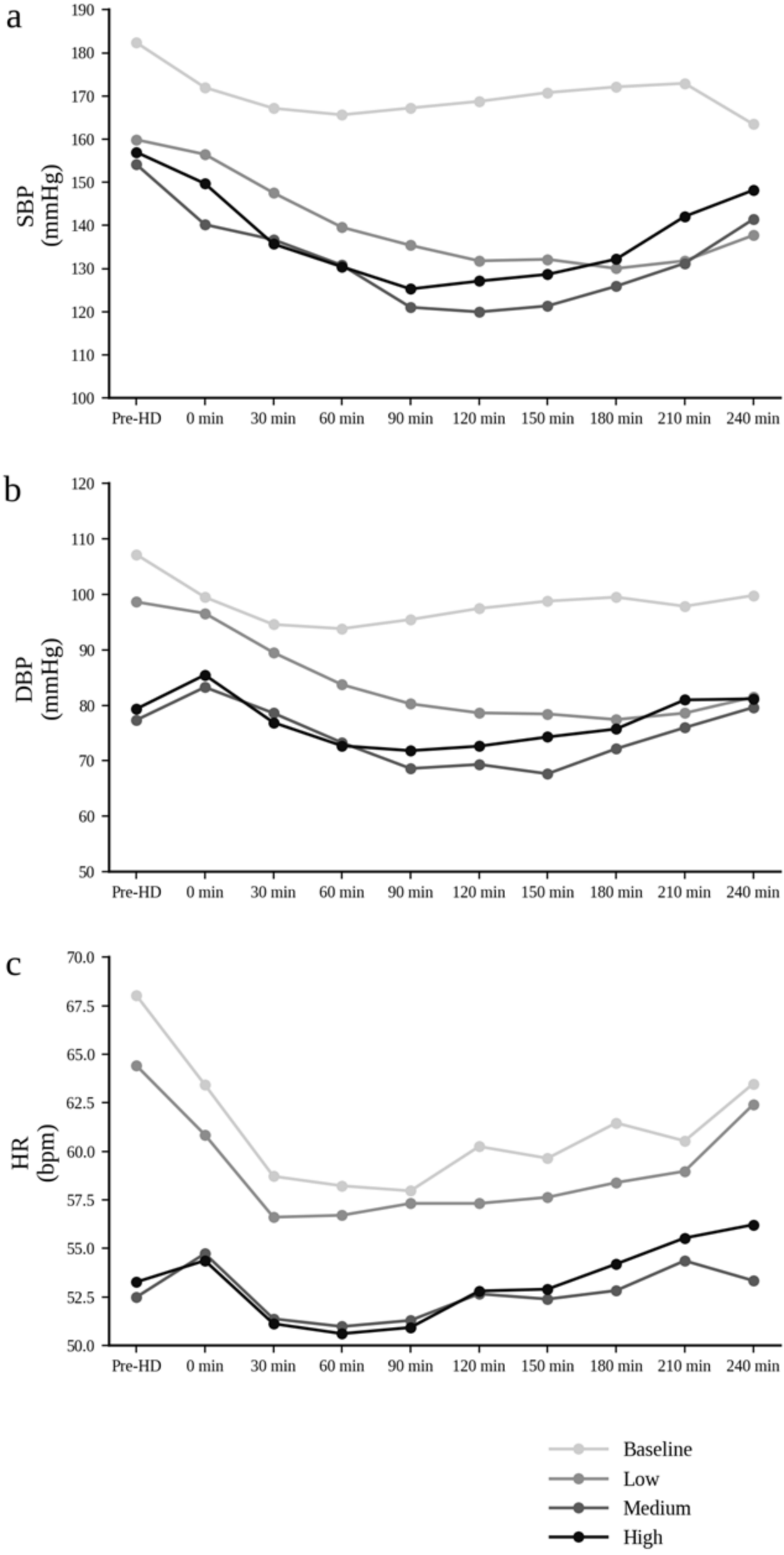
Longitudinal NRS scores for the shoulder, elbow, finger joints, lower back, hip, knee, and ankle are shown before initiation and every 30 days thereafter. NRS, Numerical Rating Scale.

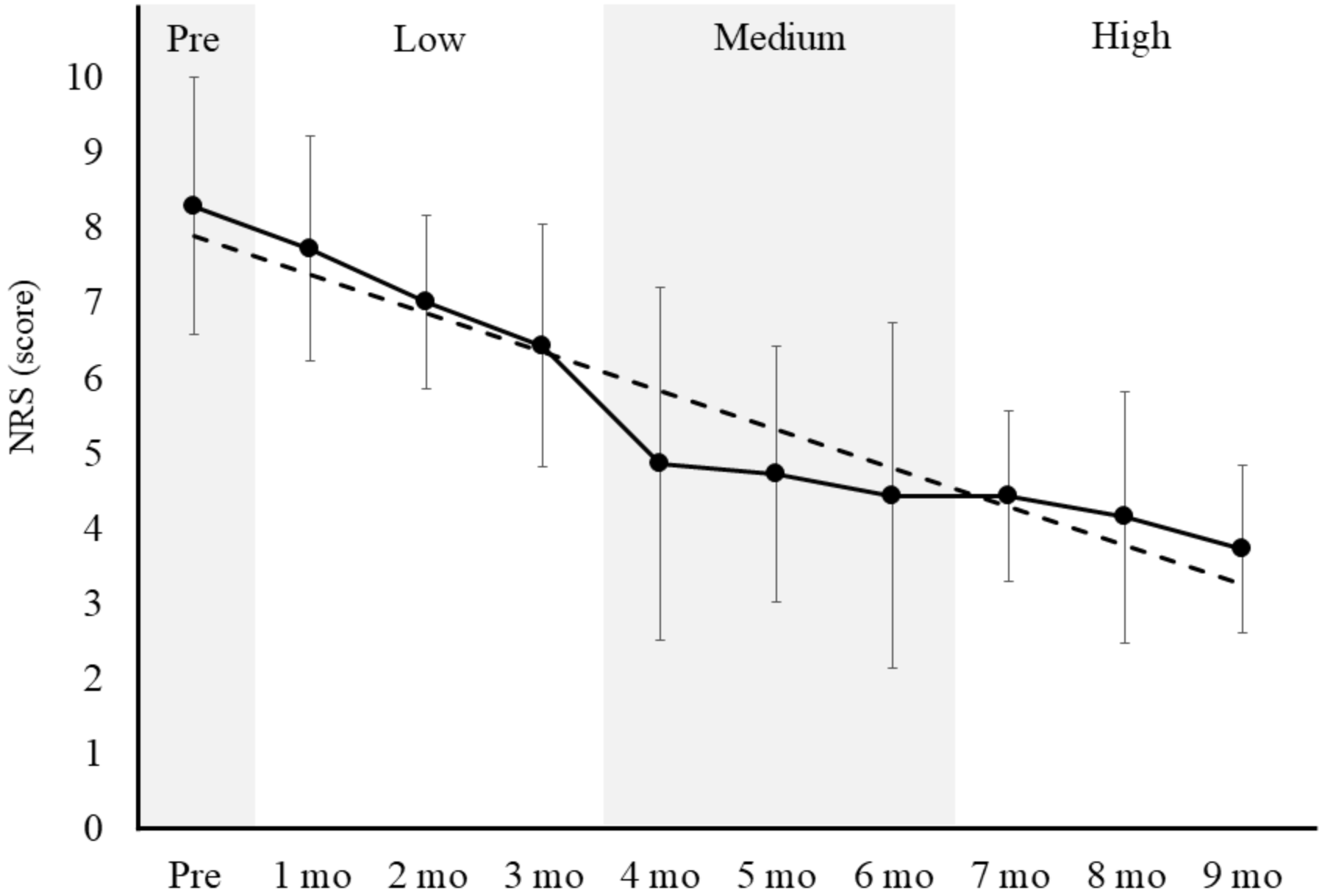
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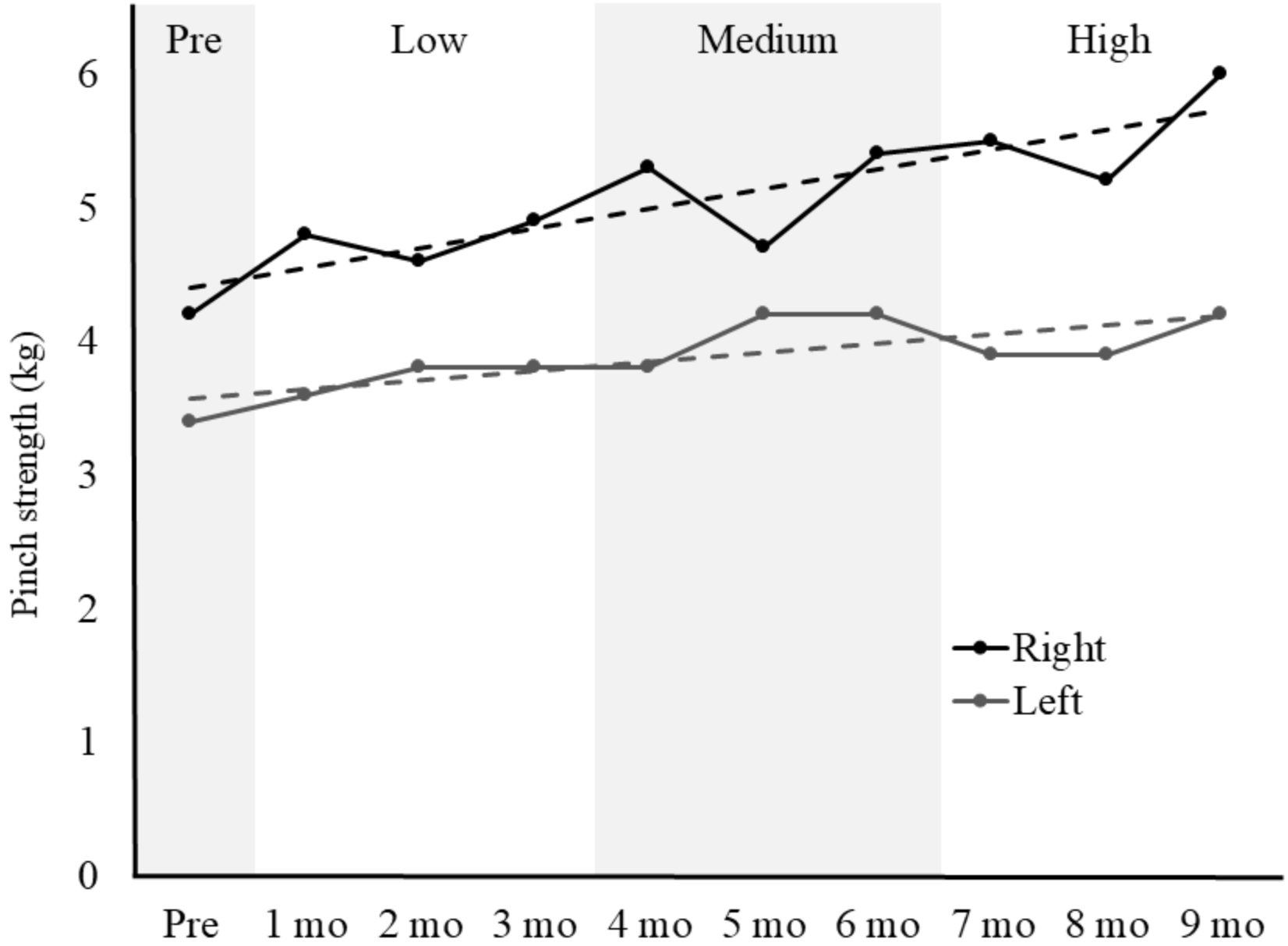

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Pre
1 mo
2 mo
3 mo
4 mo
5 mo
6 mo
7 mo
8 mo
9 mo
Pre-HD BW
Post-HD BW
DW

b


Pre
Low
Medium
High
CTR (%)
54
53
52
51
50
49
48
47
46
Pre
1 mo
2 mo
3 mo
4 mo
5 mo
6 mo
7 mo
8 mo
9 mo
CTR


a
SBP (mmHg)
190
180
170
160
150
140
130
120
110
100
Pre-HD
0 min
30 min
60 min
90 min
120 min
150 min
180 min
210 min
240 min
b
DBP (mmHg)
120
110
100
90
80
70
60
50
Pre-HD
0 min
30 min
60 min
90 min
120 min
150 min
180 min
210 min
240 min
c
HR (bpm)
70.0
67.5
65.0
62.5
60.0
57.5
55.0
52.5
50.0
Pre-HD
0 min
30 min
60 min
90 min
120 min
150 min
180 min
210 min
240 min
Baseline
Low
Medium
High


Pre
Low
Medium
High
NRS (score)
10
9
8
7
6
5
4
3
2
1
0
Pre
1 mo
2 mo
3 mo
4 mo
5 mo
6 mo
7 mo
8 mo
9 mo


Pre
Low
Medium
High
Pinch strength (kg)
0
1
2
3
4
5
6
Pre
1 mo
2 mo
3 mo
4 mo
5 mo
6 mo
7 mo
8 mo
9 mo
Right
Left

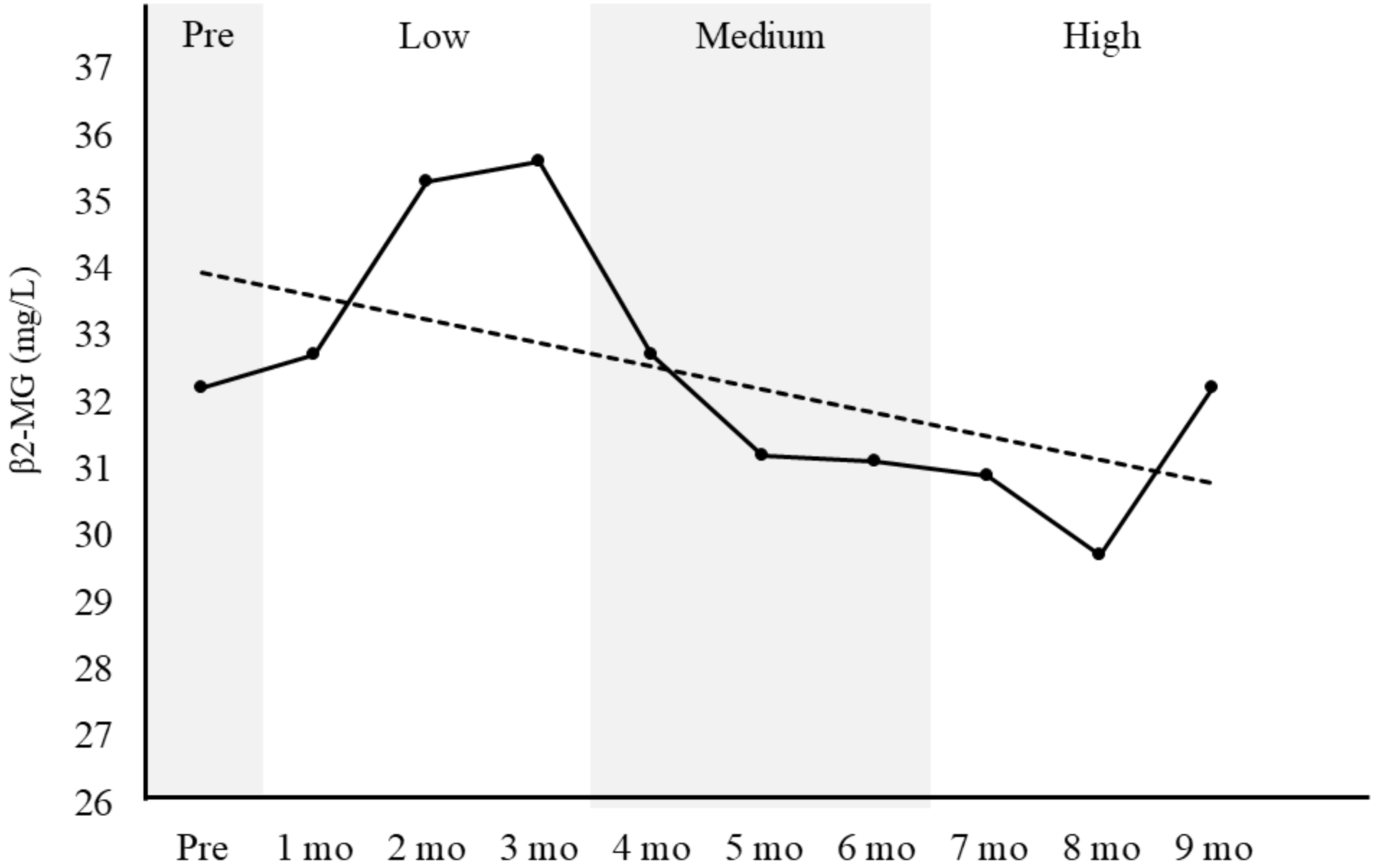

Pre
Low
Medium
High
β2-MG (mg/L)
37
36
35
34
33
32
31
30
29
28
27
26
Pre
1 mo
2 mo
3 mo
4 mo
5 mo
6 mo
7 mo
8 mo
9 mo

Table 1. Baseline laboratory data

Laboratory parameter (unit)	Value
Blood urea nitrogen (mg/dL)	55.1
Creatinine (mg/dL)	8.76
Albumin (g/dL)	3.2
Sodium (mEq/L)	139
Potassium (mEq/L)	4.3
Chloride (mEq/L)	104
Calcium (mg/dL)	8.7
Phosphorus (mg/dL)	3.7
Total cholesterol (mg/dL)	118
Triglycerides (mg/dL)	24
HDL cholesterol (mg/dL)	66
TC/HDL ratio	1.8
LDL cholesterol (mg/dL)	33
Glycated albumin (%)	34.2
Fasting blood glucose (mg/dL)	132
CRP (mg/dL)	0.1
White blood cell count (/μL)	2500
Red blood cell count ($\times 10^4$/μL)	370
Hemoglobin (g/dL)	10.6
Hematocrit (%)	34.2
MCV (fL)	92
MCH (pg)	28.6
MCHC (%)	31
Platelet count ($\times 10^4$/μL)	8.3
β2-microglobulin (mg/L)	32.2

Abbreviations: TC, total cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein; CRP, C-reactive protein; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; β2-MG, β2-microglobulin.

Table 2. Inflammatory markers

	Pre	Low (S-15)		Medium (S-25)	High (S-35)
	Baseline	Day 30	Day 90	Day 180	Day 270
CRP (mg/dL)	—	0.10	0.40	0.11	0.53
IL-6 (pg/mL)	4.8	7.8	9.0	6.8	4.2
High-sensitivity IL-1β (pg/mL)	—	1.1	<0.2	<0.2	<0.2
TNF-α (HS, pg/mL)	1.2	2.7	4.4	2.8	3.7

Abbreviations: CRP, C-reactive protein; IL, interleukin; TNF, tumor necrosis factor; HS, high-sensitivity assay. —, not measured.

Table 3. Phase-specific values and percentage changes from baseline

Outcome	Baseline	Low (S-15)		Medium (S-25)		High (S-35)	
	Value	Mean	Change (%)	Mean	Change (%)	Mean	Change (%)
Systolic blood pressure (mmHg)	168.89±3.27	138.05±8.78	-18.3	129.84±8.32	-23.1	135.47±9.11	-19.8
Diastolic blood pressure (mmHg)	97.42±2.27	82.74±6.39	-15.1	74.28±5.44	-23.8	76.86±4.72	-21.1
Heart rate (bpm)	60.41±2.06	58.47±1.98	-3.2	52.66±1.33	-12.8	53.19±2.04	-12.0
NRS (score)	8.29±1.7	7.1±0.6	-14.9	4.7±0.2	-43.7	4.1±0.4	-50.6
β2-MG (mg/L)	32.2	34.5±1.6	7.3	31.7±0.9	-1.7	30.9±1.3	-3.9
Pinch strength							
Right (kg)	4.2	4.8±0.2	13.5	5.1±0.4	22.2	5.6±0.4	32.5
Left (kg)	3.4	3.7±0.1	9.8	4.1±0.2	19.6	4.0±0.2	17.7

For SBP, DBP, and heart rate, values represent the mean ± SD of the nine intradialytic time-point means (0–240 min); Pre-HD values shown in Figure 2 were excluded. SD represents variability across the nine time-point means, not between-session variability. Percentage change is relative to the baseline representative value.

Table 4. Major clinical studies evaluating β2-microglobulin adsorption therapy (Lixelle) in dialysis-related amyloidosis

Author (year)	Study design	Population	Column	Treatment protocol
Abe et al. (2003) [8]	Prospective single-arm before-and-after study with a 1-year high-flux dialysis lead-in	Patients with DRA on HD: 22 enrolled; 17 completed and were analyzed	Lixelle 350-mL column	Three times weekly for 1 year after of unchanged high-flux dialysis
Gejyo et al. (2004) [12]	Prospective multicenter controlled trial	10 centers; 22 patients enrolled in each group; 18 patients per group included in the main analysis	Lixelle (model/column volume not explicitly stated; priming volume reported as 177 mL)	Lixelle placed upstream of the dialy used at each dialysis session for up years
Kuragano et al. (2011) [13]	Multicenter comparative study with a retrospective HD control group	Lixelle group: 39 patients; HD control group: 28 patients in the reported analyses	Lixelle S-15 (150-mL column) or S-35 (350-mL column); S-15 used when S-35 was not tolerated	Three times weekly for 1 year

Yamamoto et al. (2011) [10]	Prospective single-arm before-and-after study	Patients with DRA on HD: 20 enrolled; 17 completed (mean dialysis vintage, 24.3 years; mean BMI, 19.7 kg/m²)	Lixelle S-15 (column volume 150 mL; priming volume 65 mL)	Three times weekly for 1 year; clini outcomes assessed every 3 months blood tests every 6 months
Gejyo et al. (2013) [14]	Nationwide questionnaire survey	345 patients at 138 institutions; Lixelle treatment ≥9 months (mean, 3.5 years) and mean dialysis vintage 25.9 years	Lixelle; available column volumes were 350, 250, and 150 mL, but patient-level column-size use was not reported	Treatment duration and prescription by patient and institution

Abbreviations: ADL, activities of daily living; BMI, body mass index; DRA, dialysis-related amyloidosis; HAQ, Health Assessment Questionnaire; HD, hemodialysis; hs-CRP, high-sensitivity C-reactive protein; m-HAQ,

Supplementary Files

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- Suppfigure4.png