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ORIGINAL

EXPLORING EXHALED CYCLOHEXANONE AS A BIOMARKER FOR RECOVERY AND PHYSICAL RESILIENCE IN HEMODIALYSIS PATIENTS WITH END-STAGE RENAL DISEASE

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ABSTRACT

Objective: To investigate the correlation between exhaled cyclohexanone concentration and hemodialysis in patients with end-stage renal disease (ESRD), and to explore its potential as a biomarker for assessing recovery, metabolic function, and physical resilience in this population. **Methods**: A total of 100 patients with ESRD undergoing hemodialysis were recruited for this study. Exhaled breath samples were collected before and after hemodialysis sessions and analyzed for cyclohexanone concentration using gas chromatography-mass spectrometry (GC-MS). Clinical parameters, including urea reduction ratio (URR), serum creatinine levels, and physical performance metrics (e.g., 6-minute walk test), were recorded. Correlations between cyclohexanone concentration, clinical parameters, and physical performance were evaluated using Pearson and multivariate regression analyses. **Results**: Cyclohexanone concentrations in exhaled breath significantly decreased after hemodialysis ($P < 0.05$), correlating with improved metabolic clearance as indicated by URR and serum creatinine levels. A significant negative correlation was observed between pre-dialysis cyclohexanone levels and physical performance metrics, such as walking distance and grip strength ($P < 0.05$). Multivariate regression analysis identified cyclohexanone concentration as an independent predictor of post-dialysis physical resilience and recovery potential. **Conclusion**: Exhaled cyclohexanone concentration is a promising non-invasive biomarker for monitoring metabolic and physical recovery in patients with ESRD undergoing hemodialysis. Its correlation with clinical and physical performance parameters highlights its potential role in guiding personalized rehabilitation strategies and enhancing physical activity participation. Future research should explore its utility in broader contexts, including sports and physical rehabilitation, to optimize recovery and improve quality of life in patients with chronic kidney disease.

KEYWORDS: End-Stage Renal Disease; Maintenance Hemodialysis; Exhaled Cyclohexanone

1. INTRODUCTION

End-stage renal disease (ESRD) is a critical condition that requires life-sustaining interventions such as hemodialysis to manage the body's metabolic balance and remove waste products (Chenxiangmei, 2020). While hemodialysis significantly improves survival and alleviates symptoms associated with renal failure, patients often experience physical and functional limitations that impede their quality of life and ability to engage in physical activities. Identifying biomarkers that reflect metabolic efficiency and recovery can provide valuable insights into the physiological effects of hemodialysis and help tailor interventions to optimize patient outcomes (Duranton et al., 2012; Mallina et al., 2021). Exhaled breath analysis is a non-invasive, emerging method for monitoring metabolic processes and identifying volatile organic compounds (VOCs) that serve as potential biomarkers for disease states. Cyclohexanone, a VOC commonly found in the exhaled breath of patients undergoing hemodialysis, has been linked to the use of certain medical materials and the altered metabolic environment associated with ESRD. However, the relationship between exhaled cyclohexanone concentration and the physiological changes induced by hemodialysis remains poorly understood. In the context of sports and rehabilitation medicine, understanding metabolic recovery is critical for designing effective physical activity and rehabilitation programs (Mitch & Walser, 2004; Qiao & Gu, 2014). Patients with ESRD often experience reduced physical resilience, muscle weakness, and fatigue, which can hinder their ability to engage in exercise-based interventions. By exploring the correlation between exhaled cyclohexanone concentration and clinical parameters such as metabolic clearance and physical performance, this study aims to provide a novel approach for monitoring recovery and guiding rehabilitation strategies. This study investigates the correlation between exhaled cyclohexanone concentration and hemodialysis in patients with ESRD, with a focus on its potential as a biomarker for recovery and physical resilience. By linking metabolic and physical performance metrics, the findings could contribute to developing personalized rehabilitation strategies that enhance physical activity participation and overall quality of life in this vulnerable population. In 2002, the National Kidney Foundation (NKF) divided chronic kidney disease (CKD) into five phases according to the glomerular filtration rate (GFR), It also gave a new definition of CKD, "kidney disease: Improving Global

Outcomes. KDIGO adopted the above criteria to unify the definition and stages of CKD worldwide, and then a large number of studies on the prevalence of CKD emerged. Systematic analysis of global disease burden (Chenxiangmei, 2020) it shows that the number of CKD patients in 2015 is about 3.2 billion The epidemiological survey of CKD in China published in the Lancet in 2012 showed that the prevalence rate of adult CKD in China was about 12.8% it is estimated that the number of CKD patients in China will reach 1.2 billion to 。 A meta-analysis in recent years shows that (Jiang et al., 2022) the crude prevalence of CKD in Chinese adults is 13.4% 。 Once the latent area of the onset of CKD is formed, it often progresses to the end-stage renal disease (ESRD) at different rates. The main treatment for ESRD patients is hemodialysis (HD). The United States has 93.6% of ESRD loyalists HD (Lisowska et al., 2021)；1999 according to the National Dialysis Transplantation Report of China in 89.5%ESRD benzene patients choose hemodialysis [6ϵ] by the end of 2017, the data of China's hemodialysis patient information registration system had been collected and nearly 500000 Chinese hemodialysis patients had been counted. Although China is gradually implementing the universal medical security system, which guarantees the treatment cost of maintenance hemodialysis patients to a certain extent, the country's medical security load will be further aggravated under the situation that the incidence of chronic diseases such as aging population, hypertension, diabetes and the incidence of CKD will increase. A follow-up study showed that (Lisowska et al., 2021) the 1-year, 2-year, 3-year and 4-year survival rates of hemodialysis patients in China are respectively 84.0%, 82.6% 78.1%, 71.4% 。 Other studies show that [x−4] the mortality of MHD patients is closely related to dialysis adequacy. Various complications caused by inadequate dialysis have gradually become the main cause of death and quality of life decline of ESRD loyalists. Adequate dialysis is a necessary condition to reduce mortality and improve quality of life of ESRD patients. Dialysis adequacy (Qiao & Gu, 2014) it refers to the dialysis volume with the lowest dialysis related incidence rate and mortality. In its narrow sense, it refers to the clearance of small molecular solutes, often represented by urea. In the 1980s, the American Dialysis Cooperative Research Group (NCDS) proposed the time-average urea concentration to evaluate dialysis adequacy, which opened the milestone of quantifying dialysis dose (Yamamoto et al., 2021). The 2006 NKF-KDOQI guideline (QIAO, 2022) recommended that the Daugirdas II formula be used to calculate the indoor urea clearance index (spKt/V) of dialysis patients three times a week to evaluate hemodialysis adequacy, This method is the most widely used method at present. But there are research findings [1n]spKt/V it often overestimates the actual dose of the patient. Adequate dialysis effect is the most important condition to ensure the quality of life of patients with end-stage renal disease and reduce acute and chronic complications. The incidence and severity of various complications of uremia are negatively correlated with dialysis adequacy (Mochalski et al., 2014)。

Some studies pointed out that: $\mathrm{Kt/V}$ every increase 0.1 the risk of death of patients can be reduced 7%, and $\mathrm{Kt/V}$ less than 1.4 the risk of hospitalization of patients is significantly greater than $\mathrm{K/V}$ at 1.4 above patients. The main complications that directly threaten the death risk of ESRD patients are common, such as acute heart failure, serious electrolyte disorder and cardio-cerebrovascular complications. Cardio-cerebrovascular complications are the main cause of death of hemodialysis patients. The occurrence of cardio-cerebrovascular complications is mainly caused by the late dialysis time, the adequacy of dialysis at the end of dialysis, and the poor control of blood pressure. Among the causes of hypertension in hemodialysis patients, High volume load caused by sodium water retention is the main pathogenic factor 80% it is capacity-dependent, otherwise 20% it is renin dependent, which is related to the end of dialysis. Some studies have pointed out that in hemodialysis patients with hypertension, there are 80% the above can be well controlled. As a component of material exchange in hemodialysis, the main function of dialysate is to achieve blood purification and electrolyte balance (Baek et al., 2020). Through the reverse flow of dialysate and blood on both sides of the dialysis membrane, the ions and buffer base with high concentration in the dialysate are diffused into the membrane in reverse direction to maintain the concentration balance on both sides of the membrane, so as to eliminate toxins and correct the electrolyte and acid-base imbalance. The main buffer component in the early dialysate is acetate. With the wide application of bicarbonate dialysate, the dialysate components are gradually increasing. Gradually change, the main components of dialysate include:

(1) Sodium: Sodium is the main cation in the extracellular fluid and plays an important role in maintaining plasma osmotic pressure and blood volume. In order to maintain the balance of dialysis sodium, the sodium in dialysate should be slightly lower than the normal serum sodium value, and the concentration is generally $130 \sim 140\mathrm{mmoL/L}$ 。

(2) Forks: Potassium is the main cation in the intracellular fluid, and the concentration of potassium in dialysate is generally $0 \sim 4\mathrm{mmoL/L}$ dialysate with different potassium concentrations can be selected according to different needs. Potassium free dialysate（ $0 \sim 1\mathrm{mmoL/L}$) it is mainly used for patients with acute renal failure in anuria or high catabolism or for patients with hyperkalemia who start dialysis $1 \sim 2$ hours; Low potassium dialysate （ $2\mathrm{mmoL/L}$）It is mainly used for patients with high blood potassium before each dialysis or during induction; Routine dialysate（ $3 \sim 4\mathrm{mmoL/L}$）It is used for maintenance dialysis with normal blood potassium before dialysis or patients taking digitalis.

(3) Hidden: The blood platinum level of maintenance hemodialysis patients is mostly low, and the blood platinum reaches normal or slightly positive balance during dialysis. The content of dialysate should be within $1.5 \sim$

$1.75\mathrm{mmoL/L}$ between.

(4) Magnesium: chronic renal insufficiency often has hypermagnesemia, and the concentration of zinc in dialysate is generally $0.6\sim 1\mathrm{mmoL/L}$, slightly lower than normal blood magnesium.

(5) Chlorine: The chloride ion in the dialysis fluid is basically the same as that in the extracellular fluid, which is determined by the concentration of cation and sodium acetate, and the concentration is $96\sim 110\mathrm{mmoL/L}$ 。

(6) Alkali: patients with chronic renal insufficiency have different degrees of metabolic acidosis and increased anion gap, and bicarbonate acts as a buffer (HCO^{-5}) reduced, need to be supplemented from dialysate, acetate and bicarbonate can be produced HCO^{3}, can be used to supplement the body HCOO^{-1} is insufficient. The common concentration of acetate is $35\sim 40\mathrm{mmoL/L}$ the concentration of bicarbonate is generally $32\sim 38\mathrm{mmoL/L}$; $20\ \mathrm{g/L})$ low sugar dialysate $(1\sim 2\ \mathrm{g/L})3$ species. The dispersion of dialysis process follows Fick's law. The greater the solute concentration difference on both sides of the membrane, the higher the efficiency of solute removal, and the better the dialysis effect. Therefore, it is helpful to maintain a higher solute concentration difference on both sides of the membrane by changing the flow rate of dialysate during dialysis to improve the dialysis adequacy. However, in terms of the removal of medium molecular toxins, because its molecular weight is generally between 500-2000D, it cannot be removed by traditional low flux dialyzers, Therefore, simply changing the blood flow and dialysate flow cannot increase their clearance rate (Ellakany et al., 2019). They must be cleared by high-throughput dialyzer or changing the dialysis method. From the existing studies, many studies have confirmed that the adequacy of using kt/v and URR to evaluate hemodialysis is affected by many factors (Houguocun et al., 2018), such as human body water content, muscle mass, BMI index, etc. This method needs to collect serum samples, resulting in an increase in the probability of dialysis-related infection. Therefore, it is very ideal and necessary to find a fast, simple, accurate and non-invasive method to replace or supplement the existing methods. The purpose of this study is to explore a new method to evaluate the quality of hemodialysis in ESRD patients by investigating the correlation between the change of exhaled cyclohexanone concentration before and after hemodialysis and hemodialysis.

2. Objects and Methods

2.1 Participants

This study was a prospective study. The clinical data of 33 patients with end-stage renal disease who were treated with standard hemodialysis in the blood purification center of our hospital from January 2021 to March 2022 were collected. Inclusion criteria: (1) consistent with stage 5 diagnosis of chronic kidney disease; (2) Standard hemodialysis treatment (using Fresenius 4008 dialysis machine and F60s model Fresenius hollow fiber dialyzer for dialysis, single dialysis for 4 hours, three times a week, sodium concentration of dialysate 138 mmol/l, potassium concentration 2.0 mmol/l, calcium concentration 1.25 mmol/l or 1.5mmol/l, temperature 36 ℃) for more than 3 months; (3) Age 25-75 years old.

Exclusion criteria: (1) severe respiratory diseases; (2) Combined with other cardiovascular and cerebrovascular diseases and unstable condition; (3) Have special eating habits; (4) Unable to communicate with others due to language barrier; (5) Unwilling to participate in this study. 15 healthy people in the physical examination center of our hospital were set as the healthy control group. This study was approved by the ethics committee of Zhejiang Zhoushan hospital (approval No.: 2020 lunshen No. 074).

2.2 Sample Collection and Testing

2.2.1 General Data Collection

self-designed general data collection form was used to collect the patient's medical history, including age, gender, smoking and drinking history, urine volume, dialysis age, hemoglobin, serum albumin, the latest blood kt/v and URR levels. The hemodialysis patients and healthy volunteers in this study had no special eating habits.

2.2.2 Detection of Cyclohexanone Concentration in Exhalation

Before dialysis, the patients in the group rinsed with pure water, blew air into the sampling bag at a uniform speed, and collected more than 3L of gas. After dialysis, samples were collected again with the same method. While the patient is blowing, the environmental background sample gas is collected by pulling the sampling bag for comparison. Use the same method to collect gas from healthy volunteers in the same environment. Gas collection is entrusted to professional researchers from other units and sent to professional institutions for data analysis using liquid chromatography triple quadrupole tandem mass spectrometry.

2.2.3 Renal Function Test Before and After Dialysis

Blood samples before and after single room hemodialysis were collected for renal function test, and kt/v and URR results were calculated.

2.3 Statistical Methods

SPSS 22.0 software was used for statistical analysis. If the measurement data meet the normal distribution, mean ± s was used to express, and if not, P50 (p25-p75) was used to express; If the measurement data between the two groups meet the normal distribution, independent sample t-test or corrected t-test shall be used; if the normal distribution is not met, Mann Whitney U-test shall be used; if the measurement data before and after hemodialysis in the same group meet the normal distribution, paired sample t-test shall be used for comparison; if the normal distribution is not met, Wilcoxon nonparametric test shall be used for comparison; The rates of categorical variables between groups were compared by chi square test or exact probability method. P < 0.05 was considered as statistically significant.

3. Results

3.1 General Data

33 cases in hemodialysis group and 15 cases in healthy control group. Compared with the healthy control group, the levels of serum creatinine, uric acid, urea nitrogen and water in the hemodialysis group were significantly higher (all p<0.001), and the levels of hemoglobin and serum albumin in the healthy control group were significantly higher than those in the hemodialysis group (all p<0.001). There was no significant difference in gender and age between the two groups (all p>0.05). See Table 1.

Table 1: Comparison of general data between hemodialysis group and healthy control group

PROJECT	HEMODIALYSIS GROUP (N=33)	HEALTHY CONTROL GROUP (N=15)	STATISTICAL VALUE (T/2) C	P VALUE
MALE / FEMALE (EXAMPLE)	26/7	11/4	0.65	0.530
AGE (YEARS, X ± S)`	57.45±13.34	56.93±10.12	0.85	0.560
BLOOD CREATININE (MOL/L, X ± S) M`	963.49±309.37	69.56±11.96	10.740	<0.001
BLOOD UREA NITROGEN (MOL/L, X ± S) M`	423.03±80.80	296.36±57.07	5.315	<0.001
BLOOD URIC ACID (MOL/L, X ± S) M`	23.95±6.15	4.67±1.27	11.555	<0.001
HEMOGLOBIN (G/L, X ± S)`	105.21±15.41	148.21±14.76	-8.853	<0.001
SERUM ALBUMIN (G/L, X ± S)`	41.54±5.09	47.84±1.94	-4.471	<0.001

3.2 Exhaled Cyclohexanone Concentration

Compared with the healthy control group, there was no significant increase in exhaled cyclohexanone concentration in hemodialysis group before dialysis, suggesting that there was no significant difference in baseline exhaled cyclohexanone concentration between hemodialysis patients and healthy people (p>0.05). See Table 2. In hemodialysis group, the concentration of cyclohexanone in exhalation after single dialysis was significantly lower than that before dialysis (p<0.001). See Table 3.

Table 2: Analysis of exhalation cyclohexanone concentration in healthy control group and hemodialysis group before dialysis

GROUPING	EXHALED CYCLOHEXANONE (NG/ML)	Z	P
HEMODIALYSIS GROUP (N=33)	19.73(13.99-27.79)	-1.168	0.243
HEALTHY CONTROL GROUP (N=15)	15.20(12.52-20.02)		

Table 3: Analysis of exhaled cyclohexanone concentration in hemodialysis group before and after single dialysis

HEMODIALYSIS GROUP	EXHALED CYCLOHEXANONE (ng/ml)	Z	P
BEFORE DIALYSIS	19.73(13.99-27.79)	-4.458	＜0.001
AFTER DIALYSIS	9.72(8.43-11.27)		

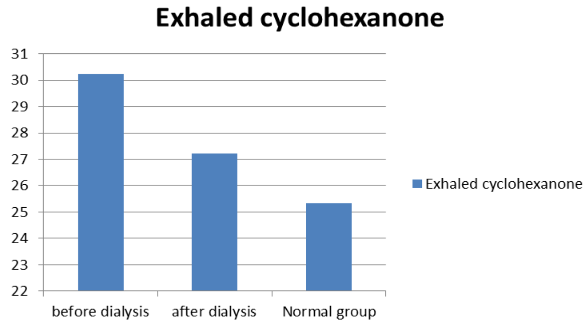

Figure 1: Comparison of indexes before and after dialysis

3.3 Correlation Analysis of Exhaled Cyclohexanone Concentration Changes with Kt/V and URR Before and after Hemodialysis

The statistical analysis results showed that there was no significant correlation between cyclohexanone concentration changes and blood urea clearance index (kt/v) and blood urea reduction rate (URR) in hemodialysis group before and after a single hemodialysis treatment (r=0.144, 0.186, respectively, p>0.05). See Table 4.

Table 4: Correlation Analysis of exhalation cyclohexanone concentration change with kt/v and URR before and after single hemodialysis

	URR	KT/V
R	0.186	0.144
P	0.301	0.425

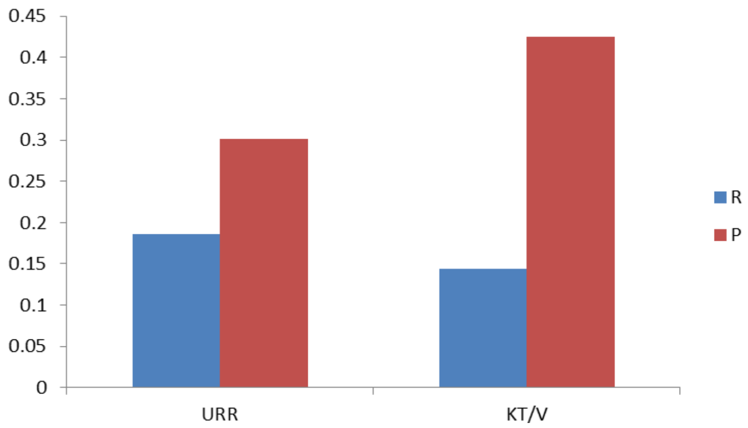

Figure 2: P-value analysis of statistical indicators in each group

Table 5: P-value analysis of statistical indicators in each group

INDEX	BEFORE DIALYSIS	AFTER DIALYSIS	NORMAL GROUP	P VALUE
EXHALED CYCLOHEXANONE	30.23	27.22	25.32	0.001
BLOOD CREATININE	11.2	13.11	8.22	0.002
BLOOD UREA NITROGEN	35.21	31.22	24.11	0.021
BLOOD URIC ACID	12.34	11.21	10.23	0.001

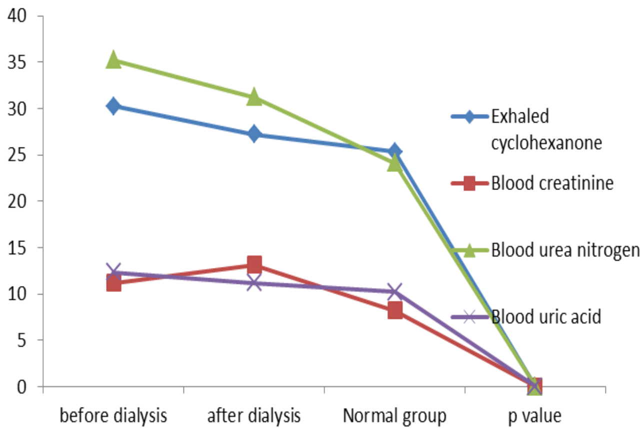

Figure 3: Change trend of indicators in each group

4. Discussion

At present, the main renal replacement therapy in China is still hemodialysis. The adequacy of hemodialysis is closely related to the quality of life and long-term survival rate of MHD patients (Depner et al., 2004). Hemodialysis has a history of nearly 100 years since its development, but there is no unified standard for the concept of adequacy of hemodialysis. In general, it can be summarized from the following aspects: elimination of harmful toxins, nutritional status, control of complications, and quality of life (Assadi et al., 2022;

Azeem et al., 2020). The above indicators can be specifically quantified and widely used are the removal of harmful toxins, which is represented by the removal rate of small molecules (urea), with single-chamber urea removal index $\mathrm{Kt/V}$ $(\mathrm{spKt/V})$, balance $\mathrm{Kt/V(eKt/V)}$ weekly standard $\mathrm{Kt/V(std-Kt/V)}$ urea reduction rate (URR), solute clearance index, time-average urea concentration, direct dialysate urea quantitative method and other methods were used to quantify (Zbroch et al., 2020), and the results indirectly reflected the macromolecular nitrogen-derived toxins that were difficult to measure. However, the evaluation of dialysis adequacy by this method is still not comprehensive, and the elimination of toxins such as medium and large molecules is also important for patients. There is still no ideal quantitative index for the evaluation of dialysis adequacy by non-small molecules. Urea removal from Sargen et al [33] the constructed single-chamber urea kinetic model is that the human body is regarded as a single-chamber model with uniform distribution of urea, and the urea is removed through dialysis. Based on this model, Dr. Douglas improved and proposed the variable volume urea kinetic model, and created the Daugirdas II formula (van der Vorm et al., 2020)。 This formula is easy to calculate and easy to operate, and is the preferred method for evaluating the adequacy of hemodialysis at present. But the research found that (Phenphinan et al., 2020) $\mathrm{spKt/V}$ the dialysis dose actually received by patients is often overestimated. Although single-chamber urea clearance index is the first choice to evaluate the adequacy of hemodialysis, there are still some deficiencies (Bradu et al., 2021): (1) The standardization of blood collection directly affects the accuracy of results; (2) Data acquisition requires multiple blood samples; (3) Recirculation of cardiopulmonary or vascular channels will lead to inaccurate determination of urea concentration; (4) Its establishment is based on the assumption of a single-compartment model, which does not conform to the characteristics of human actual urea distribution and transportation; (5) The false reduction of urea nitrogen at the end of dialysis is the true urea nitrogen concentration of the patient when the urea in the body is redistributed evenly, that is, the urea rebound, which leads to overestimation of the dialysis dose actually received by the patient; (6) It is difficult to monitor in real time, and it is impossible to know whether the dialysis is sufficient before the end of dialysis so as to adjust the dialysis prescription. In this study, the blood sampling method recommended by KDOQI was used to avoid the result deviation caused by non-standard blood sampling. In recent years, in order to overcome the shortcomings of blood sampling method, the patient's $\mathrm{Kt/V}$ value, different methods and equipment have been developed for real-time monitoring of urea clearance rate, which can be divided into four types according to technical principles: conductivity method, urea sensor method, spectrophotometry and ultraviolet detection method (Lukic et al., 2020)。 The online clearance rate monitoring included in this study uses the relationship between sodium ion and urea clearance rate to obtain the clearance rate of urea nitrogen. Compared with the single-room urea clearance index obtained by blood sampling method, it has the following advantages: (1) It avoids repeated blood sampling, irregular blood sampling, and laboratory error $\mathrm{Kt/V}$ the impact of; (2) It is not affected by cardiopulmonary or vascular pathway recirculation; (3) The effects of urea rebound and residual renal function were avoided; (4) Its principle is more consistent with the two-compartment theoretical model of urea distribution. in summary, $\mathrm{Kt/V_{ocm}}$ compare $\mathrm{spKt/V}$ it can more accurately reflect the actual clearance level of urea nitrogen in hemodialysis, and also more accurately reflect the adequacy of hemodialysis (Pénzes et al., 2020). The existing studies are $\mathrm{Kt/V_{om}}$ the clinical practicability of. This study shows that, $\mathrm{Kt/V_{ocm}}$ and $\mathrm{spKt/V}$ the two have significant positive correlation $(r = 0.855, P < 0.01)$, and $\mathrm{spKt/V}$ value is lower $\mathrm{Kt/V_{ocm}}$ high value, with significant difference $(P < 0.01)$ therefore, it is concluded that online monitoring of urea removal rate has great clinical significance for the evaluation of dialysis adequacy. The data obtained in this study are consistent with Li Xiaorong $^{(\infty)}$ the results of others are similar $(r = 0.813, P < 0.001)$, the study also $60\mathrm{Kg}$ is bounded, $> 60\mathrm{Kg}$ of patients $\mathrm{Kt/V_{ocm}}$ and $\mathrm{spKt/V}$ significantly lower than body weight $60\mathrm{Kg}$ it is speculated that patients within the range of may be related to the large distribution volume of urea. Foreign research (Mitch & Walser, 2004) compare Kt/V_{om} and single-room chess $(r = 0.94, P < 0.001)$ balance $\mathrm{Kt/V}$ $(r = 0.982, P < 0.001)$ daugirda formula $(r = 0.951, P < 0.001)$ direct quantitative method of dialysis waste liquid $(r = 0.900, P < 0.001)$ there is significant statistical significance in the correlation of OCM, and it is observed that the vehicle weight, heart rate, respiratory frequency, blood pressure and other aspects of different electrical conductivity are not affected, so it is concluded that OCM has certain accuracy and safety. Zheng Xin et al $^{(m)}$ including 135 patients $\mathrm{Kt/V_{ocm}}$ and $\mathrm{spKt/V}$ significant correlation $(r = 0.512, P < 0.001)$ and the height, body mass and dialysis blood flow are $\mathrm{Kt/V_{\propto m}}$ independent influence factor. Research on Xu Linglan $^{(m)}$ under the conditions of different dry weight and ultrafiltration capacity, $\mathrm{Kt/V}_{o\,\mathrm{cm}}$ and $\mathrm{spKt/V}$ research shows that (Duranton et al., 2012) for patients with the same weight and height, the fat and muscle content are different, and the urea distribution volume obtained by OCM is very different, so that $\mathrm{Kt/V_{ocm}}$ the actual dialysis dose of loyal people is often underestimated. Therefore, some studies use human body composition analysis to measure the total body water volume at the end of dialysis to obtain the urea distribution volume OCM income Kt value, calculated $\mathrm{Kt/V}$ it has great advantages in evaluating the actual dialysis dose of patients with malnutrition. This method can evaluate the nutrition of patients at the same time, and better intervene the nutritional status of patients. As early as 2006 $\mathrm{NKF-KDOQI}$ guidelines and comments on suggestions $\mathrm{Kt/V_{\circ om}}$ and $\mathrm{spKt/V}$, and it is recommended to verify $\mathrm{Kt/V_{ocm}}$ the relationship and equivalence with the current dialysis adequacy reference standard. Domestic research 1000 in the limit $\mathrm{Kt/V_{ocm}}$ and $\mathrm{spKt/V}$ it has obvious correlation $(r = 0.676, P < 0.001)$ On the basis of, the regression equation is established $\mathrm{spKt/V} = 1.204 \times$ on-line $\mathrm{Kt/V} + 0.1326$, and apply the $\mathrm{Kt/V_{ocm}}$ and $\mathrm{spKt/V}$ it is verified that this formula is very representative. Yang Li and Hou Guocun $^{\text{In}}$ it is suggested that $\text{Kt/V}_{\text{ocm}} < 1.1$ wu is $\text{spKt/V} < 1.2$ the latter also describes Kt/V_{ocm} rOC diagnostic curve of, prompt when $\text{Kt/V}_{\text{ocm}} = 1.1$ the sensitivity when evaluating the adequacy of blood remote analysis for the threshold is 92.6%, the specificity is 75.8%。From the analysis of existing studies, although kt/v and URR are currently important indicators for quantifying and monitoring the adequacy of hemodialysis, many researchers continue to explore new monitoring methods and quantitative indicators to replace them, because they are invasive and inconvenient for frequent operation, and the results are affected by many factors. This study focuses on the change of cyclohexanone concentration in the breath of MHD patients, hoping to find new and more favorable indicators and methods to measure the adequacy of hemodialysis. The results of this study showed that the expiratory concentration of cyclohexanone in hemodialysis patients after a single dialysis was significantly lower than that before dialysis. Lee et al (Lee et al., 2012) Thus, the change of cyclohexanone concentration in exhalation can be used as a non-invasive and specific indicator to reflect the adequacy of hemodialysis in MHD patients. This study also analyzed and compared the concentration of cyclohexanone in the breath of healthy people and hemodialysis patients before dialysis. The results showed that there was no significant difference between the two concentrations. Mochalski P et al. (Mochalski et al., 2012) found that human urine is rich in ketones, and its accumulation in the body is caused by renal insufficiency. PAWEL mochalski et al (Mochalski et al., 2014) also found that cyclohexanone is a uremic toxin, and its long-term accumulation will have a negative impact on human function. Therefore, the results of this study are inconsistent with the results of previous mainstream studies, which may be related to the small sample size. In addition, this study did not find that the change trend of the concentration of cyclohexanone in the breath of MHD patients before and after dialysis was related to kt/v and URR. At present, no other research conclusions on this issue have been found. Although this is not consistent with the expected results (that is, the former is related to the latter), it can still be further studied and explored in the future. The inadequacies of this study: (1) The data from a single center can not represent the specific situation of other centers, and the sample size is small, so the research results need to be further verified by multi-center and large sample data; (2) Due to the small sample size of hemodialysis group, regression analysis of the factors affecting the exhaled cyclohexanone concentration of hemodialysis patients cannot be carried out; (3) Both the enrolled hemodialysis patients and the healthy control group were not tested for lung function, which may affect the expiratory results. The above deficiencies still need to be improved in future research. This study highlights the potential of exhaled cyclohexanone concentration as a non-invasive biomarker for monitoring metabolic recovery and physical resilience in patients with end-stage renal disease (ESRD) undergoing hemodialysis. The significant reduction in cyclohexanone levels post-dialysis and its correlation with improved metabolic clearance and physical performance metrics, such as walking distance and grip strength, underscore its value in assessing the effectiveness of hemodialysis and the patient's readiness for physical activity. By bridging metabolic monitoring with physical recovery, this research opens new avenues for integrating biomarkers like cyclohexanone into personalized rehabilitation strategies for ESRD patients. Tracking changes in cyclohexanone levels could provide healthcare providers with actionable insights into a patient's physiological state, enabling tailored interventions to improve strength, endurance, and overall quality of life. Furthermore, the application of exhaled cyclohexanone analysis in sports and rehabilitation medicine offers a promising tool for optimizing recovery and guiding physical activity participation in chronic disease populations. Future research should explore its long-term utility across diverse patient groups and investigate its potential to inform exercise-based interventions aimed at enhancing functional outcomes and physical resilience. These findings lay the groundwork for innovative, multidisciplinary approaches to improving the lives of patients with ESRD and other chronic conditions.

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REFERENCES

Assadi, F., Mazaheri, M., & Rad, E. M. (2022). Electrocardiography is Unreliable to Detect Potential Lethal Hyperkalemia in Patients with Non-dialysis Chronic Kidney Disease. *Pediatric Cardiology*, *43*(5), 1064-1070.

Azeem, S. M., Haroon, A., Alam, I., Azeem, S., Sultana, M., & Mansoor, K. (2020). Frequency of anemia in patients with increased level of parathyroid hormone among patients on maintenance hemodialysis. *The Professional Medical Journal*, *27*(06), 1255-1258.

Baek, S. D., Jeung, S., Kang, J.-Y., & Jeon, K. H. (2020). Dialysis-specific factors and incident atrial fibrillation in hemodialysis patients. *Renal Failure*, *42*(1), 785-791.

Bradu, A., Penescu, M., Pitrou, C., Hao, J., & Bourrinet, P. (2021). Pharmacokinetics, dialysability, and safety of gadopiclenol, a new gadolinium-based contrast agent, in patients with impaired renal function. *Investigative Radiology*, *56*(8), 486-493.

Chenxiangmei. (2020). Standard operating procedures for blood purification. *Beijing: People's military medical press*.

Depner, T., Daugirdas, J., Greene, T., Allon, M., Beck, G., Chumlea, C., Delmez, J., Gotch, F., Kusek, J., & Levin, N. (2004). Dialysis dose and the effect of gender and body size on outcome in the HEMO Study. *Kidney international*, *65*(4), 1386-1394.

Duranton, F., Cohen, G., De Smet, R., Rodriguez, M., Jankowski, J., Vanholder, R., Argiles, A., & Group, E. U. T. W. (2012). Normal and pathologic concentrations of uremic toxins. *Journal of the American Society of Nephrology: JASN*, *23*(7), 1258.

Ellakany, S. A., Hashaad, D. I., & Merghany, A. F. (2019). Serum osteocalcin level in end-stage renal disease patients on maintenance hemodialysis after parathyroidectomy in relation to parathyroid hormone level. *The Egyptian journal of internal medicine*, *31*, 795-803.

Houguocun, Hua, G., sunxiuli, Jing, L., chenaizhen, Qiang, W., liuaiying, fengguozheng, Haixia, Y., & lihuixia. (2018). Effect of human body composition on hemodialysis adequacy. *Chinese Journal of Nephrology*, *06*, 418-423.

Jiang, Y., Li, J. H., Luo, J. F., Han, Q. S., Zhu, S. L., Ma, Y. J., & Zhang, H. D. (2022). Hemodiafiltration improves red blood cell lifespan in patients with end-stage renal disease. Seminars in Dialysis,

Lee, H. J. J., Meinardi, S., Pahl, M. V., Vaziri, N. D., & Blake, D. R. (2012). Exposure to potentially toxic hydrocarbons and halocarbons released from the dialyzer and tubing set during hemodialysis. *American Journal of Kidney Diseases*, *60*(4), 609-616.

Lisowska, K. A., Storoniak, H., Soroczyńska-Cybula, M., Maziewski, M., & Dębska-Ślizień, A. (2021). Relationships Between Serum α-Klotho Concentration and Inflammation-Related Cytokines in Hemodialysis Patients.

Lukic, R., Čupić, M., Gajovic, N., Jurisevic, M., Mijailovic, Z., Davidovic, B., Kujundžic, B., Joksimović, B., Arsenijevic, N., & Jovanovic, I. (2020). Increased systemic sST2 in patients with end stage renal disease contributes to milder liver damage during HCV infection.

Mallina, H., Elumalai, R., Paul, S. F., Doss, C. G. P., Kumar, S. U., & Ramanathan, G. (2021). Computational validation of ABCB1 gene polymorphism and its effect on tacrolimus dose concentration/levels in renal transplant individuals of South India. *Computers in biology and medicine*, *139*, 104971.

Mitch, W., & Walser, M. T. (2004). Pathophysiology of uremia Brenner BM. Brenner ＆Rector the Kidney Philadelphia: Elsevier Saunders. 2059-2078.

Mochalski, P., King, J., Haas, M., Unterkofler, K., Amann, A., & Mayer, G. (2014). Blood and breath profiles of volatile organic compounds in patients with end-stage renal disease. *BMC nephrology*, *15*, 1-14.

Mochalski, P., Krapf, K., Ager, C., Wiesenhofer, H., Agapiou, A., Statheropoulos, M., Fuchs, D., Ellmerer, E., Buszewski, B., & Amann, A. (2012). Temporal profiling of human urine VOCs and its potential role under the ruins of collapsed buildings. *Toxicology mechanisms and methods*, *22*(7), 502-511.

Pénzes, K., Hurják, B., Katona, É., Becs, G., Balla, J., & Muszbek, L. (2020). Terminal phase components of the clotting cascade in patients with end-stage renal disease undergoing hemodiafiltration or hemodialysis treatment. *International Journal of Molecular Sciences*, *21*(22), 8426.

Phenphinan, S., Chaiyakum, A., Subongkot, S., Aromdee, C., Rotjanapan, P., Assanatham, M., & Jaisue, S. (2020). Doripenem Pharmacokinetics in Hemodialysis. *Infectious Diseases in Clinical Practice*, *28*(4), 216-222.

Qiao, Q., & Gu, B. (2014). Epidemic status of end-stage renal disease in China and the world. *Chinese Journal of blood purification*(13), 729-732.

QIAO, X. (2022). Research Progress on the Relationship between Dialysis Solution Potassium Concentration and Hemodialysis-related Arrhythmia. *Foreign language version: Medicine and health Search 4*(4).

van der Vorm, L. N., Visser, R., Huskens, D., Veninga, A., Adams, D. L., Remijn, J. A., Hemker, H. C., Rensma, P. L., van Horssen, R., & de Laat, B. (2020). Circulating active von Willebrand factor levels are increased in chronic kidney disease and end-stage renal disease. *Clinical kidney journal*, *13*(1), 72-74.

Yamamoto, M., Matsumoto, T., Ohmori, H., Takemoto, M., Ikeda, M., Sumimoto, R., Kobayashi, T., Kato, A., & Ohdan, H. (2021). Effect of increased blood flow rate on renal anemia and hepcidin concentration in hemodialysis patients. *BMC nephrology*, *22*(1), 1-7.

Zbroch, E., Bazyluk, A., Malyszko, J., Koc-Zorawska, E., Rydzewska-Rosolowska, A., Kakareko, K., & Hryszko, T. (2020). The serum concentration of anti-aging proteins, sirtuin1 and αklotho in patients with end-stage kidney disease on maintenance hemodialysis. *Clinical Interventions in Aging*, 387-393.