System of integrating biosignals during hemodialysis: the CONTINUAL (Continuous mOnitoriNg viTal slgN dUring hemodiALysis) registry

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**Background:** Appropriate monitoring of intradialytic biosignals is essential to minimize adverse outcomes because intradialytic hypotension and arrhythmia are associated with cardiovascular risk in hemodialysis patients. However, a continuous monitoring system for intradialytic biosignals has not yet been developed.

**Methods:** This study investigated a cloud system that hosted a prospective, open-source registry to monitor and collect intradialytic biosignals, which was named the CONTINUAL (Continuous mOnitoriNg viTal slgN dUring hemodiALysis) registry. This registry was based on real-time multimodal data acquisition, such as blood pressure, heart rate, electrocardiogram, and photoplethysmogram results.

**Results:** We analyzed session information from this system for the initial 8 months, including data for some cases with hemodynamic complications such as intradialytic hypotension and arrhythmia.

**Conclusion:** This biosignal registry provides valuable data that can be applied to conduct epidemiological surveys on hemodynamic complications during hemodialysis and develop artificial intelligence models that predict biosignal changes which can improve patient outcomes.

**Keywords:** Biosignal, Cardiac arrhythmias, Hypertension, Hypotension, Renal dialysis

**Introduction**

End-stage kidney disease is an increasing burden for global health care, such that approximately 2.6 million patients are receiving dialysis worldwide and this number is expected to more than double in 2030 [1]. Approximately
80% to 90% of end-stage kidney disease patients receive hemodialysis and the rest undergo peritoneal dialysis or transplantation [2,3]. Hemodialysis frequently leads to hemodynamic instability and autonomic imbalances, which predispose patients to intradialytic complications, such as hypotension, hypertension, and arrhythmia [4]. These hemodynamic events ultimately lead to cardiovascular death, which is the most common cause of death after starting hemodialysis, and accounts for more than 40% of deaths [5,6]. According to the United States Renal Data System database, among hemodialysis patients, arrhythmia is responsible for up to 60% and 20% of cardiovascular and all-cause deaths, respectively [7,8]. Accordingly, appropriate monitoring of hemodynamic complications during hemodialysis is essential to prevent adverse outcomes.

A biosignal is a physiological sign, such as blood pressure (BP), heart rate (HR), electrocardiogram (ECG) results, cardiac output, central venous pressure, heart rhythm, electroencephalogram, electrolytes, sympathetic nerve activity, and respiratory rhythms [9,10]. Monitoring biosignals increases the awareness of their clinical importance because they can serve as indicators for unpredictable events during routine or urgent practice. Hemodialysis per se changes the biosignals of patients with or sometimes without symptoms, and thus monitoring changes in biosignals may allow for tracing or predicting hemodynamic complications during hemodialysis [11–13]. Some studies have traced intradialytic biosignals such as BP and ECG, and the risk of hemodynamic complications and relevant outcomes could be identified in detail by monitoring these signals [8,14–16]. Nevertheless, intradialytic biosignals other than BP have been underutilized because systems that coordinate detection and storage have not been established in most centers.

To improve care quality and patient outcomes during hemodialysis, a system that integrates and utilizes biosignals should be incorporated into clinical practice. Regarding ECG, devices such as implantable loop recorders [8,14,15], Holter ECGs [16], and adhesive single-lead patches [17] could be applied during hemodialysis, but the clinical accessibility and applicability have not been validated. Herein, we developed system that integrated conventional monitoring of BP, HR, ECG, and photoplethysmogram with peripheral oxygen saturation (SpO₂), which was used to provide information to the cloud-based CONTINUAL (Continuous mOnitoriNg viTal slgN dUring hemodiALysis) registry. This registry can be utilized in future studies to apply intradialytic biosignals in epidemiological surveys on hemodynamic complications and to develop artificial intelligence models with biosignals to predict relevant cardiovascular risks.

**Methods**

**Ethical considerations**

This study protocol was approved by the Institutional Review Board (IRB) of the Seoul National University Hospital in Seoul, Republic of Korea (No. 2005-018-1121) and was conducted in accordance with the principles of the Declaration of Helsinki. The registry did not include personal information such as name and unique identification information. The requirement to obtain informed consent from the patients was waived by the IRB.

**Aim and study design**

The system was established in the hemodialysis facility of the Seoul National University Hospital, which has maintained the biosignal registry since September 2020. Two categories of datasets were collected and could be merged, including hemodialysis-setting data from electronic medical records and real-time biosignal data from bedside monitoring. The former data included hemodialysis dates, times to start and end, the target value of the blood filtration rate and ultrafiltration, and the components and temperature of the dialysates and anticoagulants. The information was stored in Microsoft Excel format (Fig. 1A).

**Study population**

The registry consisted of adult patients (aged ≥18 years) who received vital sign monitoring with the developed system regardless of the reason for hemodialysis.

**Data collection**

Bedside monitors (Solar 8000i; GE Healthcare, Waukesha, WI, USA) produced the biosignals, including BP, HR, ECG, and SpO₂ by photoplethysmogram. For three-lead values
for all patients, two electrodes were placed below the right and left clavicles, and the other electrode was placed on the left lower chest. The bandpass filter for ECG ranged from 0.05 to 40 Hz. Values of changes in the ST segment, either elevation or depression, were also measured. Waveform biosignals such as ECG and photoplethysmogram were sampled at 500 Hz and updated every 2 seconds. Fig. 1A shows the overall system integration and delivery of intradialytic biosignals to the cloud, wherein the Vital Recorder program was applied [18]. Fig. 1B shows a repre-

**Figure 1. System and registry.** (A) Schematic representation of the system platform from monitoring to storage. (B) Representative image of the bedside equipment.

AC, anticoagulants; BFR, blood flow rate; CONTINUAL, Continuous mOni torsNG vi Tal slgN dUring hemodiALysis; ECG, electrocardiogram; HD, hemodialysis; HIS, hospital information system; HR, heart rate; SpO₂, peripheral oxygen saturation; Temp, temperature; UF, ultrafiltration.
sentative image of the bedside system equipment which provided time-synchronized data to facilitate integrated biosignal analysis. Data recording was initiated once the connection between the monitors and the Vital Recorder was established. The connection started to work when the HR and SpO\textsubscript{2} input values were recorded more than 5 times within 1 minute. The data were continuously backed up to the intranet-attached storage. The recordings and transfers automatically ended after 10 minutes if the biosignal inputs stopped. Subsequently, clinicians could monitor the real-time biosignals via the screen of any accessible computer. After acquiring the hemodialysis and biosignal data, these were merged based on unique identifiers such as date, time, and the bed number for the hemodialysis session.

Safety issue

The research team regularly inspects the system and the registry every month.

Statistical analysis

All statistical analyses were performed using IBM SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Data are presented as percentages for categorical parameters. Means ± standard deviations or medians (interquartile ranges) were used for continuous parameters according to the normal distribution.

Results

Baseline characteristics during the initial 8-month period

Data were collected for cases during an initial 8-month period and data for approximately 300 sessions per month continue to be collected. A total of 2,243 hemodialysis sessions were collected from 612 patients between September 2020 and April 2021. The mean age was 64 ± 15 years old, and 1,279 (57.0%) were male. Comorbidities of permanent and paroxysmal atrial fibrillation were noted in 11.4% and 5.8% of cases, respectively. The hemodialysis time per session was 3.7 ± 0.9 hours. The initial blood flow rate and target ultrafiltration were 220 ± 38 mL/min and 1.7 ± 1.0 L, respectively. More than 60% of patients used nafamostat mesylate as an anticoagulant. Additional information is presented in Table 1.

| Table 1. Baseline characteristics of the hemodialysis sessions |
|-----------------|-----------------|
| Variable            | Total            |
| No. of patients     | 2,243            |
| Age (yr)            | 64.1 ± 14.6      |
| Male sex            | 1,279 (57.0)     |
| Body mass index (kg/m\textsuperscript{2}) | 23.7 ± 6.2 |
| Comorbidity         |                  |
| Hypertension        | 2,166 (96.6)     |
| Diabetes mellitus   | 1,770 (78.9)     |
| Heart failure       | 361 (16.1)       |
| Coronary artery disease | 599 (26.7) |
| Stroke              | 354 (15.8)       |
| Permanent atrial fibrillation | 256 (11.4) |
| Paroxysmal atrial fibrillation | 130 (5.8) |
| Hemodialysis time (hr) | 4.0 (3.5–4.0)   |
| Blood flow rate (mL/min) | 219.9 ± 37.6     |
| Ultrafiltration (L) | 1.7 ± 1.0        |
| Dialysate findings  |                  |
| Dialysate sodium (mmol/L) | 137.8 ± 1.6     |
| Dialysate potassium (mmol/L) | 2.3 ± 0.6      |
| Dialysate bicarbonate (mmol/L) | 33.7 ± 1.4     |
| Dialysate temperature (°C) | 36.5 ± 0.6     |
| Use of anticoagulant|                  |
| Heparin             | 713 (31.8)       |
| Nafamostat mesilate | 1,357 (60.5)     |
| None                | 173 (7.7)        |
| Access              |                  |
| Arteriovenous fistula| 1,072 (47.8)    |
| Arteriovenous graft  | 128 (5.7)        |
| Catheter            | 1,043 (46.5)     |

Data are expressed as number only, mean ± standard deviation, or number (%).
topenia, and two-vessel coronary artery disease. The initial systolic and diastolic BPs were 175 mmHg and 72 mmHg, respectively, with an HR of 81 per minute. He had a normal sinus ECG rhythm. After starting hemodialysis, his BP gradually decreased to 130/56 mmHg at 34 minutes and 98/54 mmHg at 97 minutes. The patient reported no symptoms, and BP then increased up to 176/72 mmHg at 130 minutes without prompting any medical action (Fig. 2). The National Kidney Foundation’s Kidney Disease Outcomes Quality Initiative guidelines define intradialytic hypotension as a decrease in either systolic BP of ≥20 mmHg or mean arterial pressure of ≥10 mmHg [19]. This case is a clear example of intradialytic hypotension, but physicians were not notified because his BP recovered. Nevertheless, recurrent hypotensive events, even without symptoms and with recovery, could be associated with a high risk of cardiovascular death and thus should be continuously monitored.

The second case was a 52-year-old male patient who received a kidney transplant because of progressive immunoglobulin A nephropathy and underwent radical nephrectomy of the graft 10 years later because of kidney cancer. Accordingly, the patient underwent hemodialysis thrice weekly for 7 years. His comorbidities included hypertension, hypothyroidism, and left ventricular hypertrophy. On initiation of hemodialysis, sinus tachycardia was noted, and the systolic and diastolic BPs were 156 mmHg and 120 mmHg, respectively. Forty-six minutes after starting hemodialysis, the ratio of R to S on ECG was ≥1 [20], followed by depression of the ST segment and high amplitude of the R wave (Fig. 3). His BP increased over time, but he did not have any symptoms, such as chest pain or dyspnea. This case indicates that the system could be used to identify subclinical cardiac ischemia.

The third case was a 66-year-old female patient who had been on hemodialysis for 9 years because of drug-induced nephrotoxicity. Her comorbidities included hypertension and paroxysmal atrial fibrillation. She was admitted to the ward because of fungal pneumonia. Before hemodialysis, she had a normal sinus ECG rhythm, and HR was 98 beats per minute. The initial systolic and diastolic BP values were 140 mmHg and 82 mmHg, respectively. Paroxysmal atrial fibrillation occurred at 60 minutes, followed by a drop in systolic and diastolic BPs to 90 mmHg and 63 mmHg, respectively (Fig. 4). This case indicates that a preceding arrhythmia during hemodialysis can affect the risk of hypotension.

The fourth case was a 68-year-old female patient. She was on hemodialysis for 7 years due to diabetic nephropathy. Her comorbidities included hypertension, paroxysmal atrial fibrillation, and three-vessel coronary artery disease. She

Figure 2. Case with subclinical intradialytic hypotension (IDH). (A) Biosignal changes with time of dialysis as monitored through the system. Sweep rate = 25 mm/sec. Voltage (vertical axis) against time (horizontal axis) = –1.5 to 2.5 mV. (B) Blood pressure (BP) and heart rate (HR) during hemodialysis. DBP, diastolic BP; SBP, systolic BP.
had received a percutaneous coronary artery intervention procedure on the proximal, middle left anterior descending, and right coronary arteries 3 years before. She was admitted due to left foot necrosis and underwent an amputation below the knee. At 60 minutes after starting hemodialysis, she had nonsustained ventricular tachycardia (Fig. 5) for her ECG rhythm, and this arrhythmia was repeated in subsequent hemodialysis sessions. Currently, limited data for the prognostic significance of incidentally detected arrhythmias in hemodialysis patients are limited. Therefore, monitoring intradialytic arrhythmia may be helpful for identifying patients at risk of sudden complications.

Figure 3. Case with intradialytic hypertension. (A) Biosignal changes with time of dialysis as monitored through the system. Sweep rate = 25 mm/sec. Voltage (vertical axis) against time (horizontal axis) = –2.5 to 2.5 mV. (B) Blood pressure (BP) and heart rate (HR) during hemodialysis. An R/S ratio equal to or greater than 1 suggests the presence of potential pathology in heart. DBP, diastolic BP; SBP, systolic BP.

Figure 4. Case with paroxysmal atrial fibrillation (Af), followed by intradialytic hypotension (IDH). (A) Biosignal changes with time of dialysis as monitored through the system. Sweep rate = 25 mm/sec. Voltage (vertical axis) against time (horizontal axis) = –0.5 to 1.5 mV. (B) Blood pressure (BP) and heart rate (HR) during hemodialysis. DBP, diastolic BP; SBP, systolic BP.
Discussion

Biosignal monitoring may be essential for detecting and preventing intradialytic complications. We developed an intradialytic biosignal-integrating system, which continuously updated the CONTINUAL registry. This approach can overcome some inherent limitations of current technology, such as providing real-time monitoring and storage of data. In this report, we also provided representative cases with hemodynamic complications, all of which required prompt prediction, prevention, and treatment. This CONTINUAL registry will be used in the future for predicting patient risks and preventive hemodialysis services based on both handcrafted and artificial intelligence models.

An approach that supports continuous and real-time monitoring of biosignals during hemodialysis is needed, and it will be more feasible if the system is noninvasive. This will allow clinicians to dynamically track changes in the patient statuses during hemodialysis more closely than with sporadic measurements conducted at most centers [21]. As shown in previous cases, a threshold number of sessions could provide sufficient data to predict hemodynamic complications during hemodialysis, some of which can have asymptomatic features. Hemodialysis can induce significant alterations in the hemodynamics of the circulatory system, which imposes a cardiac burden [22]. The burden will manifest as arrhythmias, silent or evident myocardial ischemia, and reversible or irreversible cardiac dysfunction [23]. Currently, hemodialysis machines do not collect biosignal datasets, and thus, some biosignals are missed. This missing data may reflect the cardiovascular risk of hemodialysis patients.

The practical goal of using this system is to utilize the biosignal registry for developing predictive models and to enhance decisions for complication risks. The large quantity of biosignals necessitates advanced or novel analytics that range from collection to interpretation [24]. Machine learning, including deep learning, is a rapidly developing branch of artificial intelligence that has shown promise for use in clinics [13,25]. A major limitation in utilizing biosignals for artificial intelligence-based clinical purposes is the lack of data storage [26]. This system supports intranet-attached storage to facilitate future utilization. The availability of a large, readily accessible registry with biosignals can shorten the time of model training [26]. We are currently conducting several projects with the help of machine learning using this CONTINUAL system.

Some limitations should be considered before fully utilizing this system and registry. The connection with the bedside monitor could be momentarily lost because of vio-
lent movement or arbitrary removal of the connector. This may result in loss of the significant biosignals and relevant intradialytic events and thus provide insufficient information to medical doctors or in developing models. The registry currently consists of data from hemodialysis patients hospitalized in a tertiary hospital, whose characteristics and risks of hemodynamic complications could differ from those admitted to general hospitals.

In summary, we developed an integrated system of intradialytic biosignals that included BP, HR, ECG, and photoplethysmogram with SpO$_2$. This system-derived biosignal registry will facilitate epidemiological surveys on hemodynamic complications, enhance artificial intelligence models for predicting risks, and thus improve patient outcomes.

**Conflicts of interest**

All authors have no conflicts of interest to declare.

**Authors’ contributions**

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