Non-invasive Continuous Intradialytic Blood Pressure Monitoring: The Key to Improving Haemodynamic Stability

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Abstract

Purpose of Review

Intradialytic hypotension (IDH) occurs in 20% of haemodialysis treatments, leading to end-organ ischaemia, increased morbidity and mortality; and contributing to poor quality of life for patients. Treatment of IDH is reactive since brachial blood pressure (BP) is recorded only intermittently during haemodialysis, making early detection and prediction of hypotension impossible. Non-invasive continuous BP monitoring would allow earlier detection of IDH and thus support development of methods for its prediction and consequently prevention.

Recent Findings

Non-invasive continuous BP monitoring is not yet part of routine practice in renal dialysis units, with a small number of devices (e.g. finger cuffs) having occasionally been used in research settings. In use, patients frequently report pain or discomfort at measurement sites. Additionally, these devices can be unreliable in patients with reduced blood flow to the digits, often manifest in dialysis patients. All existing methods are sensitive to patient movement.

A new method for continuously estimating BP has been developed by monitoring arterial pressure near the arteriovenous fistula which can be achieved without any extraneous monitoring equipment attached to the patient. Additionally, Artificial Intelligence (AI)-based methods for real-time prediction of intradialytic hypotension are currently emerging.

Summary

Key monitoring technologies and computational methods are emerging to support the development of real-time intradialytic hypotension prediction.

Keywords: *Non-Invasive; Intradialytic Monitoring; Hypotension Prediction; Continuous BP Measurement.*

Introduction

Intradialytic haemodynamic instability is a significant clinical problem, often leading to end-organ ischaemia and contributing to morbidity and mortality in haemodialysis patients. Currently, non-invasive continuous blood pressure monitoring is not part of routine practice but may aid detection, prediction, and prevention of hypotension during dialysis. Current methods of continuous non-invasive blood pressure monitoring tend to restrict movement, can be sensitive to external disturbances and patient movement, and can compromise wearer comfort and hence, patient experience. Additionally, poor patient blood circulation often exhibited by haemodialysis patients, can lead to unreliable measurements. Recently developed novel methodologies and associated technologies to continuously estimate blood pressure address these shortcomings by using, for example, pressure sensors in the extra-corporeal dialysis circuit, which do not require any direct contact with the person receiving dialysis treatment

BP monitoring is normally conducted in a clinical setting via the use of an occluding arm cuff that provides a robust, but irregular and intermittent measurement methodology that disrupts the normal blood flow, and consequently requires a significant settling time between measurements [1,2]. A ward monitoring regime of 30 minutes between BP measurements is a sampling rate many orders of magnitude larger than fundamental Baroreflex BP control [3] and intradialytic physiological time-constants [4,5], and hence a 30-min sampling rate is unsuitable for real-time BP prediction.

Continuous monitoring of BP during dialysis [1] has the potential to improve patient outcomes [6,7,8] and could ultimately inform a personalised treatment regime or close a therapeutic intervention loop via modulation of dialysis time and/or duration, dialysate sodium concentration and/or temperature on a per patient basis. Of particular interest is intradialytic hypotension (IDH), generally a relatively sudden event with associated symptoms include dizziness or fainting, muscle cramps, abdominal discomfort, nausea and vomiting. IDH often results in truncated dialysis treatments and is associated with increased risk of cerebral ischemic incidents.

Continuous non-Invasive BP monitoring

Arterial cannulation is widely regarded as the gold standard reference for continuous measurement of BP. While a common procedure during high-risk surgery, it is not considered appropriate for haemodialysis patients where non-invasive monitoring is indicated. There are currently three principal methods for non-invasive monitoring of BP which have generally been used in research settings.

1. In arterial applanation tonometry [9], a transducer is positioned above a superficial artery compressing it against an underlying bone [10]. This method has been used in cardiology and anaesthetised procedures to avoid the insertion of an arterial cannula [11,12], but as these devices are hand-held and are operator-dependent, they are unsuitable for continuous monitoring.
2. Pulse Transition Time (PTT) [13] is based on measured photoplestimography (PPG) and electrocardiogram (ECG) signals during several cardiac cycles. PTT is then calculated as the time difference between the ‘R’ peak in the ECG signal and the corresponding time instance of the inflection point on the maximum slope of the PPG signal. PTT is the time delay for the pressure wave to travel between two arterial sites. PTT is often inversely linearly related to BP and can be estimated simply from the relative timing between proximal and distal waveforms indicative of the arterial pulse. However, this may not be accurate due in part to

the unaccounted physiological factors in the blood pressure regulation mechanism and reliance on accurate ECG triggering [14].

3. The volume clamp (or vascular unloading) method [2] utilises an inflatable finger-cuff combined with an embedded photodiode to measure the diameter of finger artery. Cuff pressure is adjusted to maintain a constant artery diameter, and the changes in cuff pressure are used to calculate a BP curve in the brachial artery. In use, patients frequently report pain or discomfort at the fingertips where volume clamp cuffs are placed, and this device can be unreliable in patients with reduced blood flow to the digits, often manifest in dialysis patients [13].

All three non-invasive methods described are sensitive to patient movement (especially ECG signals) [10], therefore, their use would result in an unacceptable and uncomfortable restriction placed on patients during a four-hour dialysis treatment.

New Methodologies

Based upon the problems associated with existing technologies, an ideal paradigm-shift methodology would fulfil the following constraints:

- Reliable, continuous monitoring is achieved irrespective of patient movement and/or compromised blood flow in the extremities
- A method which is completely non-invasive (including wearable sensors) and does not compromise comfort or the patient experience
- A method which can operate continuously for the entire duration of treatment sessions

The state-of-the-art fulfilling these requirements is relatively sparse. In previously published methods [15], analysis of finger pulse waves, obtained from O2 sensors, estimates a beat-to-beat systolic pressure value. However, described above, it is noted that the accuracy of estimation is significantly compromised by patient movement. The use of pressure signals from the arterial and venous blood lines of a dialysis machine have been shown in principle to enable continuous online monitoring of a patient's heart rate, even for patients with low cardiac signal amplitude [16,17]. The method has been extended to monitor ventricular premature beats [18]. Performance was, however, studied for only one dialysis flow rate (400 ml/min), and results lacked fidelity where patient heart and haemodialysis pump oscillatory rates came close to coinciding. While promising, the method generated several false positive and false negative predictions of IDH.

A feasibility study of a novel method for continuously monitoring BP has been conducted, which introduces the placement of pressure sensors on the dialysis venous blood line at the bubble trap and the arterial blood line close to the arteriovenous fistula [19], in which relationships between static and dynamic pressures in these extra-corporeal blood lines and brachial BP were derived. Pressure sensors were attached to the blood lines (rather than making use of the pressure sensors present within the dialysis machines) and utilised the existing ports and connection points which are common and standardised on most dialysis blood line sets. The paper describes [19] the development of the measurement system and subsequent *in vivo* patient feasibility study with concurrent measurement validation by *Finapres Nova* physiological measurement and data acquisition device. Real-time physiological data is collected over the entire period of (typically 4-hour) dialysis treatments. A quasi-linear mathematical function to describe the relationship between arterial line pressure and brachial artery BP was derived and confirmed by patient study. The results suggest that it is feasible to derive a continuous measurement of brachial pressure from continuous measurements of arterial and venous line pressures via an empirically based and updated mathematical model. The methodology presented requires no interfacing to proprietary dialysis machine systems, no sensors to be attached to the patient directly, and is robust to patient movement during treatment and also to the effects of the cyclical pressure waveforms induced by the haemodialysis peristaltic blood pump. This new technique represents a key enabling factor to the development of a practical continuous blood pressure monitoring device for dialysis

Unmodelled non-linearities, dynamics and time-varying parameters present challenges to the development of an accurate BP estimation system. In a further paper [20], the authors start to address the problem of physiological parameter time variance during treatment by novel application of an iterative learning run-to-run modelling methodology (originally developed for process control engineering applications) to a parameterised BP model. The learning methodology was applied to the real-time data measured during an observational study [20], supporting subsequent development of an adaptive real-time BP estimator. Tracking of patient BP is analysed for all the subjects in the patient study, supported only by intermittent calibration updates from BP cuff measurements.

Machine learning AI has been applied to ICU data in order to predict hypotensive events [22]. Although the technique is applied to data sets rather than real-time measured patient data, the algorithm predicts hypotension up to 30 minutes *a priori* based upon a 5-minute moving window of physiological data, demonstrating the potential of machine learning algorithms. In another study [23], machine learning algorithms are applied to high-fidelity arterial pressure waveforms which can predict intraoperative hypotensive events 15 minutes prior to their occurrence with sensitivity 88% and specificity 87%, concluding that hypotension prediction is possible but that the approach still requires significant further study. These studies have been supported by the availability of high quality continuous physiological measurement data streams which have been acquired at sufficiently high sample rates. Development of this kind have been problematic in the analysis and modelling of IDH due to the difficulty of obtaining reliable, continuous data streams from non-invasive devices running for the duration of treatment.

Papers associated with dialysis treatment and AI analysis techniques have, however, recently started to appear. A deep learning neural network (AI) model has recently been developed [21] to predict the risk of intradialytic hypotension within a timestamped dataset of patients with 1-hourly brachial cuff measurement and demonstrates ability to calculate the risk of hypotension within 1-hour predictive windows. The addition of continuous BP monitoring at individual patient level should further refine the predictive ability of neural network (and other machine learning AI) methodologies to the point that their predictive capability is sufficiently accurate to provide reliable decision support regarding treatment modification to avoid IDH. In recent paper [24], the authors describe the development of AI models to guide management of BP, fluid volume and dialysis dose based upon hemodynamic responses, historic characteristics and dialysis related prescriptions via proof of concept and first clinical assessments. The conclusion is made that AI modelling may help in the development of personalised dialysis treatment prescriptions which affect patients' intradialytic hemodynamics.

Conclusion

A new methodology and associated technology implementation has been shown to be capable of tracking patient BP non-invasively via arterial line pressure measurement during complete 4-hour treatment sessions. A robust and tractable method has been demonstrated, and future refinements to the approach have been defined. Direct measurement of fluid pressure waveforms in the dialysis lines are suitable for continuous measurement during dialysis treatment due to the non-invasive nature of the sensors, data insensitivity to patient movement, and lack of sensitivity to compromised blood flow in the patient's extremities. Continuous BP monitoring over the entire 4-hour treatment time would, if combined with an accurate hypotension onset predictor via machine learning supported AI, create the means to implement decision support and eventually closed loop control to achieve pro-active treatment regimes.

Key Points

• Non-invasive continuous intradialytic BP monitoring will support methods to predict and prevent intradialytic hypotension

• Previously described methods are limited by patient discomfort and sensitivity to patient movement

• A novel method for non-invasive continuous intradialytic BP monitoring has been developed that does not require additional monitoring equipment to be attached to patients

• Application of artificial intelligence techniques to continuous blood pressure data shows promise in predicting intradialytic hypotension

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Conflicts of Interest

None

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Although this study is based on discrete rather than continuous methods, it is an early indicator of the potential benefits of the application of new AI pattern recognition methods to BP prediction and hence management in the long term.

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Further demonstration of the potential scope of AI methodology when applied to the BP prediction problem

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Very interesting first steps examining the potential for intradialytic hemodynamic management based upon AI models to inform treatment modification.