AJKD
Narrative Review

Challenges in Blood Pressure Measurement in Patients Treated With Maintenance Hemodialysis

*Matthew A. Roberts, FRACP, PhD,[1,2] Helen L. Pilmore, FRACP, MD,[3] Andrew M. Tonkin, FRACP, MD,[4] Amit X. Garg, MD, PhD,[5,6,7] Elaine M. Pascoe, MBiostat,[8] Sunil V. Badve, FRACP, MD,[8,9] Alan Cass, FRACP, PhD,[10,11] Francesco L. Ierino, FRACP, PhD,[1,2] and Carmel M. Hawley, FRACP, MMedSci,[8,9] on behalf of the Beta-Blocker to Lower Cardiovascular Dialysis Events (BLOCADE) Feasibility Study Trial Management Committee**

The association between blood pressure and cardiovascular outcomes in patients undergoing hemodialysis remains controversial. This may relate in part to the technique and device used and the timing of the blood pressure measurement in relation to the hemodialysis procedure. Emerging evidence indicates that standardized hemodialysis unit blood pressure measurements or measurements obtained at home, either by the patient or using an ambulatory blood pressure monitor, may offer advantages over routine hemodialysis unit blood pressure measurements for determining cardiovascular risk and treatment. This review discusses the available evidence and implications for clinicians and clinical trials.
Am J Kidney Dis. 60(3):463-472.

INDEX WORDS: Renal dialysis; hemodialysis; blood pressure; measurement; cardiovascular disease.

Higher systolic and diastolic blood pressures (BPs) are each associated in a continuous fashion with stroke, coronary artery disease,[1] and cardiac failure.[2] Many large randomized controlled trials (RCTs) have demonstrated the benefits of lowering BP with various agents in the general population.[3] In these trials, BP typically was measured in a standardized way before randomization and at each visit to assess response.

In contrast, the improvement in clinical outcomes achieved by lowering BP in patients requiring dialysis, who are at high absolute risk of cardiovascular disease and have a high prevalence of elevated BP,[4] has not been proven unequivocally. The association of BP and clinical outcomes in patients undergoing hemodialysis has been studied in observational studies of BP levels, observational studies addressing the effect of BP-lowering agents, and RCTs of BP-lowering agents. An RCT studying BP targets and clinical outcomes in this population has never been reported.

In an observational study of BP levels of hemodialysis patients in whom BP was measured just prior to a hemodialysis session, increased mean arterial pressure was associated significantly with increased left ventricular mass index and de novo cardiac failure.[5] However, a 10–mm Hg decrease in mean arterial pressure was associated with a 37% increase in mortality ($P = 0.004$). This paradoxical finding has been demonstrated consistently in observational studies, and even patients with very high BP appear to have no or minimal increase in mortality.[6-8] Possible explanations for this observation include the influence of comorbid conditions such as age, diabetes,[9] reverse causation by heart failure in patients with low BP, and survival bias due to the relatively short follow-up in observational studies. For example, the association of low BP with mortality is attenuated when only patients who survive beyond 3 years are analyzed.[10] These studies predominantly used BP measured in the hemodialysis unit (Table 1).

Most observational studies demonstrate better outcomes in patients receiving BP-lowering agents. The Japanese Renal Data Registry, which includes 163,668

From the [1]Department of Nephrology, Austin Health, Melbourne, Australia; [2]Department of Medicine, University of Melbourne, Melbourne, Australia; [3]Department of Renal Medicine, Auckland Hospital, Auckland, New Zealand; [4]Cardiovascular Research Unit, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia; [5]Division of Nephrology, Department of Medicine, and [6]Department of Epidemiology and Biostatistics, Western University, London; [7]The Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada; [8]Australasian Kidney Trials Network, The University of Queensland; [9]Department of Nephrology and Transplantation Services, Princess Alexandra Hospital, Brisbane, Australia; [10]The George Institute for Global Health; and [11]Sydney Medical School, University of Sydney, Sydney, Australia.

** A list of the members of the BLOCADE Feasibility Study Trial Management Committee appears in the Acknowledgements.*

Received December 24, 2011. Accepted in revised form April 10, 2012. Originally published online June 12, 2012.

Address correspondence to Matthew A. Roberts, FRACP, PhD, Department of Nephrology, Austin Health, PO Box 5555, Heidelberg 3084, Australia. E-mail: matthew.roberts@austin.org.au

0272-6386/$36.00
http://dx.doi.org/10.1053/j.ajkd.2012.04.026

Table 1. Blood Pressure Measurement Reported in Observational Studies and Randomized Controlled Trials of HD Patients

Study	Blood Pressure	Time in Relation to HD
	Observational Studies	
Foley et al[5] (1996)	MAP	Pre-HD
Zager et al[6] (1998)	SBP, DBP, MAP	Pre- and post- HD (average over 90 d)
Port et al[7] (1999)	SBP, DBP	Pre- and post-HD (average of 3 sessions)
Foley et al[11] (2002)	SBP, DBP (PP by inference)	Pre- and post-HD (average of last 3)
Kalantar-Zadeh et al[8] (2005)	SBP, DBP	Pre- and post-HD
Stidley et al[10] (2006)	SBP, DBP, PP	Pre- and post-HD (average over 90 d)
Rohrscheib et al[12] (2008)	SBP, DBP, MAP, PP	Pre- and post-HD (average over 90 d)
Myers et al[9] (2010)	SBP, DBP	Pre-HD
	Randomized Controlled Trials	
Cice et al[13] (2003)	SBP, DBP	Not stated
Takahashi et al[14] (2006)	SBP, DBP	Not stated
Zannad et al[15] (2006)	SBP, DBP, PP	Immediately pre-HD
Nakao et al[16] (2007)	SBP, DBP	Not clear, possibly pre-HD
Suzuki et al[17] (2008)	SBP, DBP	Pre- and post-HD
Tepel et al[18] (2008)	SBP, DBP	Pre-HD after 10 min recumbent
Cice et al[19] (2010)	SBP, DBP	Pre-HD

Abbreviations: HD, hemodialysis; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; SBP, systolic blood pressure.

patients, reported an adjusted odds ratio of 0.72 (95% confidence interval [CI], 0.68-0.77) for mortality at 1 year in long-term hemodialysis patients who were receiving antihypertensive agents versus counterparts who were not receiving this treatment.[20] Data from 11,142 prevalent hemodialysis patients reported to the US Renal Data System (USRDS) demonstrated a 16% decrease in mortality for patients receiving β-blockers compared with those not given this therapy ($P = 0.001$).[11] In a separate USRDS cohort of incident patients receiving dialysis (n = 3,716, including peritoneal dialysis), the adjusted risk of death was 21% lower for patients receiving a calcium antagonist than for patients not receiving a calcium antagonist ($P = 0.001$).[21] In contrast, a post hoc analysis of an RCT of dialysis prescription demonstrated that participants receiving angiotensin-converting enzyme inhibitors had no decrease in mortality compared with those who did not.[22] In other reports that included patients with a history of myocardial infarction[23] or patients stratified by the presence of heart failure,[24] BP-lowering agents were associated with decreased mortality. However, actions of these drugs other than lowering BP may have influenced this result. For example, β-blockers substantially decrease mortality in patients with heart failure,[25] including patients with chronic kidney disease.[26] Heart failure is a common comorbid condition in patients receiving dialysis, but there is only one RCT addressing this condition.[13]

The 2 meta-analyses[27,28] that identified 7 RCTs of BP-lowering agents in patients undergoing hemodialysis[14-19] suggested that BP-lowering treatment decreases cardiovascular events and all-cause mortality. One analysis demonstrated a significantly greater benefit of therapy in studies that included only hypertensive participants,[28] whereas the other did not.[27] Again, there may be mechanisms other than BP lowering by which these agents decrease clinically important events. For inclusion criteria and reporting of BP measurements, the studies in these meta-analyses used either a single or an average of several previous hemodialysis-unit BP measurements (Table 1). Substantial heterogeneity across the primary studies was attributed to differing patient characteristics, different classes of agents investigated, and differences in study design. Heterogeneity due to the method of BP measurement was not assessed.

In this review, we consider how the technique and timing of BP measurement in patients treated with hemodialysis might affect clinical decision making regarding treatment of BP as a cardiovascular risk factor and the reporting of BP values in clinical trials. In particular, we examine the reliability, validity, and feasibility of measurements obtained at the hemodialysis center, at home intermittently, or at home in a continuous fashion using ambulatory BP monitoring (ABPM).

DEVICES AND TECHNIQUES FOR MEASURING BP

BP measurements in the hemodialysis unit are performed on multiple occasions for the purpose of volume assessment and safety. National[29] and interna-