

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. © 2012 by the National Kidney Foundation, Inc.

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

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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 infarction²³ 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 hemodialy-

sis¹⁴⁻¹⁹ 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. National²⁹ and interna-

tional³⁰ hypertension guidelines describe the appropriate devices, cuff sizes, and technique of measurement of BP.

Devices

Although mercury sphygmomanometers are considered the most accurate, many hospitals and satellite hemodialysis units use automated devices. The most commonly used devices are oscillometric devices that derive systolic (SBP) and diastolic BP from an algorithm based on the measured oscillations in cuff pressure caused by arterial blood flow as the cuff is inflated to occlude blood flow, then deflated. Most,³¹⁻³³ but not all,³⁴ validation studies of patients receiving hemodialysis have demonstrated satisfactory performance of oscillometric devices compared with BP measured by auscultation using a mercury sphygmomanometer. Many hemodialysis units use dialysis machines that have these oscillometric BP measuring devices built into the machine.

Accurate measurement requires that all devices, including those that are part of the dialysis machine, are appropriately tested and regularly validated and serviced. Devices must be assessed according to evaluation protocols provided by the British Hypertension Society,³⁵ European Hypertension Society,³⁶ or Association for the Advancement of Medical Instrumentation.³⁷ The National Heart Foundation of Australia recommends validation of nonmercury sphygmomanometers against a mercury sphygmomanometer every 6 months and servicing of all sphygmomanometers at least annually.²⁹

Techniques

The hypertension guidelines make several practical recommendations for accurate BP measurement, including the appropriate patient position, cuff size, interpretation of Korotkoff sounds, and number of readings.^{29,30} However, many of the guideline recommendations are difficult to follow in the setting of routine hemodialysis (Table 2). The importance of BP measurement technique in the hemodialysis unit has been demonstrated by Rahman et al³⁸ in a study showing marked differences between the “usual method” of measuring pre- and posthemodialysis BP (a single measure) compared with a “standardized method” taking the mean of 3 BP measurements obtained by a specifically trained nurse.

RELIABILITY, AGREEMENT, AND VALIDITY OF BP MEASUREMENTS

The time that BP is measured in relation to the hemodialysis procedure may influence the clinical interpretation of the measurement because there is variability within individual hemodialysis patients

Table 2. Blood Pressure Measurement Recommendations Versus Usual Practice

Guideline Recommendation	Usual Practice in the Hemodialysis Unit
Avoid caffeine, cigarettes, or exercise before measurement	Not routinely avoided—hemodialysis fits into the patient's daily routine
Measure on both arms for first reading	Not usually possible due to AV access; sometimes measured on lower limbs if AV access on both arms
Rest in quiet room for a few minutes	Quiet room for this purpose not part of hemodialysis unit design
Patient relaxed	Ability to be relaxed prior to fistula needling and hemodialysis varies from person to person
Average of at least 2 readings	Duplication to average readings is rarely done because of time constraints (although multiple readings occur throughout a hemodialysis session)

Abbreviation: AV, arteriovenous.

and different clinical associations with different measurements and a lack of agreement between BPs measured within and outside the hemodialysis unit.

Reliability of Different BP Measurements

Overview

In clinical trials and in assessing response to therapy, it is critical that the measurement detects real change in BP rather than variation caused by other factors. This variation can be assessed by taking multiple measurements of BP in the same individual. In patients receiving hemodialysis, the variability of multiple BP measurements in the same individual during a 90-day period is as great as the variability in BP measurements between different individuals.¹² This variability in multiple BP measurements in the same individual is due to both biological variability and measurement error, and a measurement method with the smallest variability is the most reliable.

Biological Variability

Day-to-day variation in BP in patients undergoing hemodialysis differs from the general population because the normal diurnal variation is lost and patients experience extreme volume state fluctuations at their regular hemodialysis sessions. In the normotensive general population, SBP decreases by a median of ~15 mm Hg during sleep.³⁹ People for whom SBP fails to decrease by >10% during sleep are arbitrarily classified as “nondippers,” and these individuals could be at higher risk because nocturnal SBP may be a stronger predictor of outcome than daytime SBP.⁴⁰ In patients undergoing hemodialysis, this nocturnal dip

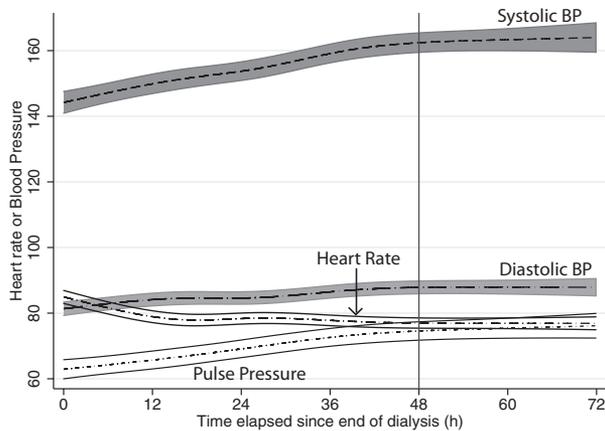


Figure 1. Changes in blood pressure (BP) and heart rate over time elapsed from the end of a hemodialysis session modelled using restricted cubic splines from multiple ambulatory measurements in 140 patients. Reproduced from Agarwal and Light⁴⁶ with permission of the National Kidney Foundation.

in SBP is attenuated,^{41,42} and nocturnal BPs are substantially higher compared with people with similar office BPs who do not have kidney disease.⁴³

Studies using ABPM have demonstrated that BP increases over time after a hemodialysis session.^{44,45} In one study, the average ambulatory BP in the first 15 hours after a hemodialysis session was found to be 147/82 mm Hg compared with 161/88 mm Hg in the third 15-hour period (Fig 1).⁴⁶ Increasing levels of weight gain and vascular stiffness both affect these diurnal BP changes in hemodialysis patients.⁴⁷ Nocturnal BP also may increase over time between hemodialysis sessions. In an article from Narita et al,⁴¹ the ratio of nocturnal SBP to daytime SBP increased significantly from 0.92 on the first night of ABPM after a hemodialysis session to 0.97 on the second night.

Measurement Error

Measurements at the hemodialysis unit. The reproducibility of hemodialysis unit BPs over 6 hemodialysis sessions is greatest when the average of all BP measurements for the session (prehemodialysis, during hemodialysis, and posthemodialysis) is calculated compared with single measurements or other combinations.⁴⁸ Thus, reproducibility of dialysis-unit BP measurements may be improved by averaging all measurements for the hemodialysis session.

Measurements at the hemodialysis unit versus ABPM. In 21 patients undergoing hemodialysis who had ABPM and routine hemodialysis unit BPs measured on 2 separate occasions, the prehemodialysis SBP demonstrated the highest variability of all methods, with a standard deviation of the difference (SDD) between the 2 measurements of 24.4 mm Hg.⁴⁹ The posthemodialysis SBP (SDD of 16.8 mm Hg) was more repro-

ducible, but 48-hour ABPM performed best (SDD of 10.6 mm Hg). The average of 5 hemodialysis-unit BP values was more reproducible than a single measurement, but less reproducible than ABPM in this study.

The variability of 44-hour ABPM has been reported as the change in classification of nocturnal dipping status, which changed in 43% of patients between the first and the second night after hemodialysis within the same ABPM study. In 38% of patients, dipping status differed on the corresponding night in separate 44-hour ABPM studies.⁴⁹

The reliability of a BP measurement method impacts on its ability to detect change over time. In a post hoc analysis of an RCT, ABPM, but not a single prehemodialysis BP measurement, could detect the change from baseline.⁵⁰ However, other hemodialysis unit measures detected this change, including the average of 6 prehemodialysis BP measurements, a single posthemodialysis measurement, the average of the previous 6 posthemodialysis BPs, and the median BP from a single hemodialysis session. Over- or underestimation of the ABPM results by all these measures was still present.

Hemodialysis unit versus home intermittent measurement. The reproducibility of intermittent home BP measurement has been shown to be superior to hemodialysis unit measurement, with a standard deviation of intraindividual changes of 12.4 mm Hg for home BP compared with 14.0 mm Hg for the mean of 3 prehemodialysis SBP measurements and 14.8 mm Hg for the corresponding posthemodialysis measurements.⁵¹ In this study, home BP was reported as more reproducible than ABPM (SDD of 12.6 mm Hg).

Agreement Between Different BP Measurements

Measurements at the Hemodialysis Unit

The study that compared “usual” measurements to a “standardized” method with a specifically trained nurse taking the mean of 3 BP measurements demonstrated that both the pre- and posthemodialysis SBP measured by the usual method were a mean of 14 mm Hg higher than by the standardized method, with >50% of usual readings >10 mm Hg higher than standardized ones.³⁸

Measurements at the Hemodialysis Unit Compared With ABPM

Hemodialysis unit measurements, especially the prehemodialysis measurement, typically are higher than the values obtained by ABPM. In one study, prehemodialysis SBP averaged over 6 sessions was a mean of 13.5 (95% CI, 9.3-17.7) mm Hg higher than the corresponding 44-hour average SBP by ABPM.⁵² A systematic review of similar studies demonstrated higher prehemodialysis BP than the ABPM-deter-

Table 3. International Guidelines for Measuring Blood Pressure in HD Patients

Guideline	Timing	Target Level	ABPM
CSN ⁵⁴ (2006)	Pre-HD	<140/90 mm Hg	Only if difficult to control
KDOQI ^{56,a} (2005)	Pre-HD, seated (advantage over post-HD not clear)	<140/90 mm Hg pre-HD; <130/80 mm Hg post-HD (provided no orthostatic symptoms or intradialytic hypotension)	May be better but there are practical and financial limitations
KDIGO Report ^{55,b} (2010)	Pre-HD and post-HD measurements to be used with caution	Further research recommended	Likely better than HD unit, but not feasible for many patients throughout the world
UK Renal Association ⁵⁷ (2011)	Pre-, intra-, & post-HD; interdialytic	<160/90 mm Hg; avoid SBP <120 mm Hg	If pre- & post-HD consistently elevated
CARI	No guideline	No guideline	No guideline
ERA-EDTA	No guideline	No guideline	No guideline

Abbreviations: ABPM, ambulatory blood pressure monitoring; CARI, Caring for Australasians With Renal Impairment; CSN, Canadian Society of Nephrology; ERA-EDTA, European Renal Association-European Dialysis and Transplant Association; HD, hemodialysis; KDIGO, Kidney Disease: Improving Global Outcomes; KDOQI, Kidney Disease Outcomes Quality Initiative; SBP, systolic blood pressure.

^aRecommendations from text; not a formal guideline statement.

^bOutcome of a meeting report; not a formal guideline statement.

mined BP, but the high level of heterogeneity did not allow a summary statistic to be reported.⁵³ In these studies, posthemodialysis BP measurements generally were much closer to the ABPM value. However, for both hemodialysis measurements in these studies, the Bland-Altman limits of agreement indicated that hemodialysis-unit measurements of BP frequently are very different than those obtained by ABPM. In the study that examined 5 methods of reporting hemodialysis-unit BP compared with 44-hour ABPM,⁴⁸ all 5 hemodialysis unit measures significantly overestimated the 44-hour ABPM value. The posthemodialysis measurement overestimated ABPM-derived BP by 4.0 mm Hg (95% CI, 1.1-6.9); the predialysis measurement, by 16.9 mm Hg (95% CI, 13.8-19.9); and the average of every hemodialysis unit measurement, by 6.4 mm Hg (95% CI, 3.9-8.9).

Home Intermittent BP Measurement Compared With ABPM

Home intermittent BP and hemodialysis-unit BP have not been directly compared, but the relationship of the former to ABPM has been examined. In an RCT, home BPs were measured 3 times daily for 1 week and compared with 44-hour ABPM measurements after the midweek hemodialysis session the following week.⁴⁶ The mean difference between the mean home SBP in different periods and the overall mean 44-hour ABPM value was calculated. This mean difference was 7.9 (95% CI, 5.3-10.5) mm Hg, 13.2 (95% CI, 11.0-15.4) mm Hg, and 21.6 (95% CI, 19.2-23.9) mm Hg higher for home intermittent SBP than ABPM in the first, second, and third 15-hour periods after a hemodialysis session, respectively. Because ABPM was performed in a different week

than the home measurements, this is not strictly an assessment of agreement.

Validity of Different BP Measurements: Outcome Associations

Guidelines for BP measurement have made various recommendations regarding which BP to use as a basis for therapeutic decisions in patients undergoing hemodialysis⁵⁴⁻⁵⁷ (Table 3). The most valid and therefore useful method of BP measurement should demonstrate an association with important clinical events, and ideally, therapy guided by that method should result in a change in practice that leads to a decrease in clinical events. The ability of different measures to predict mortality is summarized in Table 4.

Observational Studies of Different BP Measurements

A key feature of studies of clinical outcomes that use hemodialysis-unit BP measurements has been the failure to demonstrate an association of higher BP with outcome, as occurs in people without kidney disease. In studies that used ABPM, the expected association of higher BP with outcomes has been demonstrated.

In 326 patients receiving hemodialysis who were followed up for a mean of 32 months, mortality increased significantly with increasing quartiles of baseline SBP measured by ABPM.⁶⁰ An earlier report based on a median 24-month follow-up in 150 patients from this study demonstrated a significant increase in the hazard of death per standard deviation increase in 44-hour SBP by ABPM.⁵⁹ The association between mortality and home BP did not reach statistical significance, and there was no association between mortality and hemodialysis-unit BP (Table 4). In an

Table 4. Reliability, Agreement With ABPM, and Validity of SBP Measurements in HD Patients

Measurement	Study	Reliability (mm Hg)	ABPM Agreement (mm Hg) ^a	Mortality ^b
HD Unit				
Single pre-HD BP	Peixoto et al ⁴⁹ (2000)	24.4	NR	NR
	Agarwal et al ⁴⁸ (2008)	17.2	+16.9	NR
	Kalantar-Zadeh et al ⁸ (2005)	NR	NR	Greatest HR for SBP <110; no ↑ HR for SBP > 130-139 mm Hg
Single post-HD BP	Peixoto et al ⁴⁹ (2000)	16.8	NR	NR
	Agarwal et al ⁴⁸ (2008)	15.5	+4.0	NR
	Kalantar-Zadeh et al ⁸ (2005)	NR	NR	Greatest HR for SBP <110; no ↑ HR for SBP > 130-139 mm Hg
Median HD BP	Agarwal & Light ⁵⁰ (2010)	NR	0	NR
Average of all intradialytic BPs	Agarwal et al ⁴⁸ (2008)	12.2	+6.4	NR
Average of multiple pre-HD BPs	Peixoto et al ⁴⁹ (2000)	14.7	NR	NR
	Agarwal & Lewis ⁵² (2001)	NR	+13.5	NR
	Agarwal et al ⁵¹ (2009)	14.0	NR	NR
	Agarwal et al ⁵⁸ (2008)	NR	NR	HR per 10-mm Hg ↑: 1.05 (0.92-1.20), <i>P</i> = 0.5
	Alborzi et al ⁵⁹ (2007)	NR	NR	HR per SD ^c of SBP: 0.97 (0.72-1.30), <i>P</i> = 0.84
	Agarwal ⁶⁰ (2010)	NR	NR	Mortality model χ^2 : 4.97, <i>P</i> = 0.17
Average of multiple post-HD BPs	Peixoto et al ⁴⁹ (2000)	12.4	NR	NR
	Agarwal & Lewis ⁵² (2001)	NR	0	NR
	Agarwal et al ⁵¹ (2009)	14.8	NR	NR
	Agarwal et al ⁵⁸ (2008)	NR	NR	HR per 10-mm Hg ↑: 1.17 (1.00-1.37), <i>P</i> = 0.043
	Alborzi et al ⁵⁹ (2007)	NR	NR	HR per SD ^c of SBP: 1.19 (0.88-1.61), <i>P</i> = 0.26
	Agarwal ⁶⁰ (2010)	NR	NR	Mortality model χ^2 : 0.04, <i>P</i> = 0.997
Standardized pre-HD BP	Alborzi et al ⁵⁹ (2007)	NR	NR	HR per SD ^c of SBP: 1.16 (0.86-1.56), <i>P</i> = 0.32
	Agarwal et al ⁵⁸ (2008)	NR	NR	HR per 10-mm Hg ↑: 1.13 (0.99-1.30), <i>P</i> = 0.073
Standardized post-HD BP	Alborzi et al ⁵⁹ (2007)	NR	NR	HR per SD ^c of SBP: 1.18 (0.88-1.57), <i>P</i> = 0.27
HD BP	Agarwal et al ⁵⁸ (2008)	NR	NR	HR per 10-mm Hg ↑: 1.16 (1.01-1.33), <i>P</i> = 0.035
Home BP				
Average of 3×/d BPs for 1 wk	Agarwal et al ⁵¹ (2009)	12.4	NR	NR
	Agarwal & Light ⁴⁶ (2009)	NR	+14.1	NR
	Agarwal et al ⁵⁸ (2008)	NR	NR	HR per 10-mm Hg ↑: 1.17 (1.02-1.35), <i>P</i> = 0.026
	Alborzi et al ⁵⁹ (2007)	NR	NR	HR per SD ^c of SBP: 1.35 (0.99-1.84), <i>P</i> = 0.055
	Agarwal ⁶⁰ (2010)	NR	NR	Mortality model χ^2 : 49.52, <i>P</i> < 0.001
	Moriya et al ⁶¹ (2008)	NR	NR	Survival by 3 PP groups: log-rank <i>P</i> = 0.002
Average of 2×/d BPs, including in HD unit	Moriya et al ⁶¹ (2008)	NR	NR	Survival by 3 PP groups: log-rank <i>P</i> = 0.002
Middle 15 h after midwk HD (average of 3)	Agarwal & Light ⁴⁶ (2009)	NR	+13.2	NR
24-h ABPM	Amar et al ⁶² (2000)	NR	NR	HR per 10-mmHg ↑: 1.37 (0.95-1.96), <i>P</i> = 0.09; for PP: 2.05 (1.09-3.84), <i>P</i> = 0.03
44-h ABPM between HD sessions	Peixoto et al ⁴⁹ (2000)	10.6	Ref	NR
	Agarwal et al ⁵¹ (2009)	12.6	NR	NR
	Agarwal et al ⁵⁸ (2008)	NR	NR	HR per 10-mm Hg ↑: 1.22 (1.07-1.38), <i>P</i> = 0.002
	Alborzi et al ⁵⁹ (2007)	NR	NR	HR per SD ^c of SBP: 1.46 (1.09-1.94), <i>P</i> = 0.013
	Agarwal ⁶⁰ (2010)	NR	NR	Mortality model χ^2 : 59.50, <i>P</i> < 0.001
Sleep ABPM	Amar et al ⁶² (2010)	NR	NR	HR per 10-mm Hg ↑: 1.41 (1.08-1.84), <i>P</i> = 0.01

Note: Reliability is reported as the SD of the difference between measurements within individuals. Validity is the strength of association of BP with mortality, reported as an HR unless otherwise stated.

Abbreviations: ABPM, ambulatory blood pressure monitoring; BP, blood pressure; HD, hemodialysis; HR, hazard ratio; NR, not reported; PP, pulse pressure; Ref, reference; SBP, systolic blood pressure; SD, standard deviation.

^aIndicates how many millimeters of mercury higher the listed measurement was compared with the ABPM-derived measurement.

^bValues in parentheses are 95% confidence intervals.

^cThe SD of SBP in this study was 20-23 mm Hg for the different BP measures.

earlier study of 57 hypertensive hemodialysis patients followed up for a mean of 34 months, increased 24-hour pulse pressure and increased nocturnal SBP

measured by ABPM were associated with increased cardiovascular mortality.⁶² In 168 patients undergoing hemodialysis followed up for a mean of 38 months, a

higher ratio of nighttime SBP to daytime SBP by APBM was associated with increased mortality,⁶³ although this association was attenuated when left ventricular hypertrophy was included in a multivariate model.

The “weekly average” pulse pressure (SBP minus diastolic BP) from 20 measurements (twice-daily readings at home by the patients plus 2 readings from each hemodialysis session) was associated with mortality in 96 patients receiving hemodialysis who were followed up for a mean of 35 months.⁶¹ In an earlier study by the same group, this weekly average reading demonstrated a strong correlation with the first morning BP measured the day after the midweek hemodialysis session ($R^2=0.709$).⁶⁴

The location where BP is measured, rather than the number of measurements, may be more important with regard to the association with mortality.⁵⁸ In a study comparing ABPM, home, and hemodialysis-unit BP measurements, investigators took a random sample of each type of measurement so that the number of measurements included per patient was the same for each analysis. Home and ambulatory BP measurement were associated more strongly with mortality than hemodialysis-unit measurements. Use of a smaller number of home or ABPM readings did not reduce the ability to predict mortality compared with use of the full data set of BP measurements.⁵⁸

RCTs of Different BP Measurements

Although one study evaluated BP control as an outcome,⁶⁵ no study examining important clinical outcomes has randomly assigned hemodialysis patients to BP-lowering therapy based on ABPM or home measurements compared with therapy guided by hemodialysis-unit measurements.

Feasibility and Limitations of Obtaining Different BP Measurements

There is a spectrum of feasibility of BP measurements in hemodialysis patients. Hemodialysis-unit BP measurements are performed routinely for clinical management and thus are highly feasible. Standardized hemodialysis-unit BP measurement requires trained personnel to perform multiple measurements after the patient has had adequate rest and thus adds time and the cost of trained personnel to the process of having BP measured in the hemodialysis unit. Averaging hemodialysis-unit BP measurements requires recording these measurements in appropriate databases to enable calculations.

Having the patient measure BP at home adds the cost of the device and requires ongoing cooperation from the patient. Reliable automated devices for home BP measurement can be purchased relatively inexpen-

sively and patients can be taught to use them, even if they have a relatively low level of health literacy.⁶⁶ Although the patient’s reported BP can be checked against values stored in the memory of the device, adherence to the measurement schedule is not guaranteed. In one study of home BP adherence, 76% of patients deviated from their requested measurement schedule.⁶⁷

At the less feasible end of the spectrum, ABPM is limited by availability, cost, and patient acceptance. The first 2 factors vary greatly by institution. The first acceptability issue is whether to take measurement over the full 44-hour interdialytic period (including 2 nights), as performed in the study that demonstrated a strong mortality association with ABPM,⁶⁰ or over 24 hours, as is usual for nonhemodialysis patients. The latter requires a hospital visit on a nonhemodialysis day. Another potential limitation in applying ABPM data to practice is that most studies of ABPM were performed by the same investigators in a cohort of predominantly African American patients using 44-hour ABPM; thus, the generalizability of their conclusions to other populations may be limited. Second, ABPM may cause a decrease in sleep and level of activity, which may influence the recorded BP values.⁶⁸

SUMMARY

Which Type of BP Measurement Should Clinicians Use to Initiate and Monitor Treatment?

Accepting that there are limitations in the evidence for decreasing BP in patients receiving hemodialysis and that a target BP for any measure is yet to be defined, clinicians should consider a shift in practice away from assessment of routine hemodialysis-unit BPs, although these remain important for managing the dialysis procedure. In particular, the guideline recommendations to use a routine single prehemodialysis BP measurement to make clinical decisions should be reconsidered (Table 3). This shift would require increased effort on the part of the nephrologist to obtain a purposeful measurement of BP.

The choice of BP measurement is a balance between the feasibility, reliability, and validity for predicting clinical outcomes, and currently, no single measurement method can be recommended. Until further evidence is available regarding clinical associations, this shift in practice means using the most reliable measurement that can be performed given the resources available. The feasibility of purposeful measurement of BP in patients undergoing hemodialysis can be increased if it is undertaken in a directed manner and not used for every patient at every hemodialysis session.

Although there are strong advocates for routine use of ABPM,^{69,70} questions about its feasibility may limit its role to specific situations, such as persistently very high or very low BPs, or concerns about nocturnal BP. When 24-hour ABPM is used, it should be interpreted in light of whether it is the first or second 24-hour period after a hemodialysis session.

Which Type of BP Measurement Should Be Used in Clinical Trials?

As shown in Table 1, the RCTs of BP-lowering agents predominantly reported a prehemodialysis BP. This is the most poorly performing BP measurement with regard to reliability and agreement with other measures. Therefore, a suitable alternative with better reliability and ability to detect change is required for the optimal design of RCTs addressing aspects of management of BP. Again, no single recommendation can be made due to lack of evidence.

A small number of RCTs have reported measurement of BP outside the hemodialysis unit, suggesting that it is feasible. These include the average of thrice-daily home BP measurements over a 2-week period⁷¹; home BP measurement performed twice daily for 7 days, with 3 measurements obtained at each occasion⁶⁵; 24-hour ABPM with the device fitted immediately after the midweek hemodialysis treatment and removed 24 hours later⁶⁵; and ABPM measured for 44 hours after the midweek hemodialysis treatment.⁷²

Feasibility becomes increasingly important in larger trials. Before a large trial of BP therapy or targets is performed in hemodialysis patients, a BP measure balancing feasibility and reliability must be determined. Two RCTs are underway that may help inform the choice of BP measurement for clinical trials. The Blood Pressure in Dialysis Patients (BID; ClinicalTrials.gov identifier, NCT01421771) study of 2 different BP targets in hemodialysis patients will base therapy on a standardized prehemodialysis BP and also test the feasibility of home BP readings and 44 hour ABPM. The Beta-Blocker to Lower Cardiovascular Dialysis Events (BLOCADE; Australian New Zealand Clinical Trials Registry identifier, ACTRN12609000174280) Study comparing carvedilol to placebo will use the postdialysis SBP for decisions concerning titration of study drug and will record the median hemodialysis-unit BP because these are feasible measurements with greater reliability than the single prehemodialysis measurement. In a subgroup of participants, measurement of BP at home in the middle 15 hours between hemodialysis sessions and 24-hour ABPM is planned to assess the feasibility of obtaining out-of-hemodialysis-unit measurements.

CONCLUSION

Routine BP measurements performed in the hemodialysis unit are often used to inform clinical decisions, but have significant limitations. Increasing data indicate that BP measurements performed outside the hemodialysis unit or standardized BP measurements in the hemodialysis unit increase reliability. The former may have stronger clinical associations than routine hemodialysis-unit BPs. Although harder to obtain, these measurements should be considered in clinical management and clinical research so that improved measurement of this parameter will improve understanding of how to treat BP in this important group of patients.

ACKNOWLEDGEMENTS

The BLOCADE Feasibility Study Trial Management Committee consists of: Matthew Roberts and Frank Ierino (Austin Health and University of Melbourne); Nicole Isbel (Princess Alexandra Hospital and University of Queensland); Henry Krum (Monash University); Carmel Hawley (Princess Alexandra Hospital, Australasian Kidney Trials Network, and University of Queensland); Alan Cass (The George Institute for Global Health, and University of Sydney); Helen Pilmore (Auckland City Hospital); Andrew Tonkin (Monash University); Vlado Perkovic (The George Institute for Global Health and University of Sydney); Amit Garg (London Health Sciences Centre and Western University); Charles Thompson, Elaine Pascoe, and Liza Vergara (Australasian Kidney Trials Network and University of Queensland).

Support: Dr Roberts is supported by a National Health and Medical Research Council of Australia (NHMRC) Training Fellowship (628902). Dr Cass is supported by an NHMRC Principal Research Fellowship (1027204). The BLOCADE Feasibility Study has purchased Omron HEM7211 home BP measurement devices at a discounted price to use in the study; the authors attest that this arrangement had no effect on the decision to write this article or its content.

Financial Disclosure: The authors declare that they have no other relevant financial interests.

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