ATCOR

June 2022

The Role of Central Aortic Pressure Monitoring in the Management of Patients with Chronic Kidney Disease

Executive Summary

- Chronic kidney disease (CKD) is common and effects approximately 15% of adults in the USA (37 million people). Kidney disease is the ninth leading cause of death. CKD increases the risk for cardiac disease, stroke, and death, and leads to multiple significant additional diseases.
- Hypertension and diabetes are the leading causes of CKD in adults and also represent the most treatable targets to prevent CKD and to reduce CKD progression. Hypertension is responsible for continued morbidity, mortality and high socioeconomic costs despite the widespread availability and use of cuff brachial artery measurements for diagnosis and monitoring.
- Elevated central aortic pressure is predictive of impaired renal function. Brachial and central aortic pressures provide complimentary information for risk prediction and management decisions.
- The risk of adverse cardiovascular outcomes with elevated central pressure is at least as high and possibly higher than with brachial pressure.
- Prescription of anti-hypertension medications has the potential of significant benefit but as with all medications, may be associated with adverse consequences (hypotension and drug specific adverse effects) and should always be judicious and carefully considered, particularly in patients with CKD.
- Measurements of central arterial pressures can be incorporated into the current approaches to hypertension management as the dual arterial pressure SphygmoCor XCEL device can provide both brachial and central aortic pressures in the same clinic setting.
- Incorporation of central aortic pressure monitoring should be considered for all patients with chronic kidney disease.

Background

Chronic Kidney Disease

Chronic kidney disease (CKD) encompasses mild through severe impairment of renal function. The definition of CKD is kidney damage or a decreased glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m2 for at least 3 months.[1]

CKD is classified according to GFR as follows:[1]

Stage 1: Kidney damage with normal or increased GFR (>90 mL/min/1.73 m2)

Stage 2: Mild reduction in GFR (60-89 mL/min/1.73 m2)

Stage 3a: Moderate reduction in GFR (45-59 mL/min/1.73 m2)

Stage 3b: Moderate reduction in GFR (30-44 mL/min/1.73 m2)

Stage 4: Severe reduction in GFR (15-29 mL/min/1.73 m2)

Stage 5: Kidney failure (GFR < 15 mL/min/1.73 m2 or dialysis)

Stage 5 CKD is most often referred to as end-stage renal disease (ESRD).

Chronic kidney disease (CKD) is common and effects approximately 15% of adults in the USA (37 million people).2 Most adults (90%) are unaware that they have CKD as it is generally slowly progressive. According to the Centers for Disease Control and Prevention (CDC), CKD occurs in 38% of adults at least 65 years old, 12% of those between 45 and 64 years, and 6% of people between 18 and 44 years. The following statistics are from the USA.[2]

- Kidney disease is the ninth leading cause of death
- 350 people begin dialysis each day due to ESRD
- 131,600 people start treatment for ESRD in a year
- 786,000 people are living with ESRD with 71% receiving dialysis and 29% with a kidney transplant.

The cost of treating CKD in Medicare recipients has been estimated to be $82 billion (2018), with an additional $36.6 billion of cost for treating those with ESRD.2 A 2017 study included 106,050 patients with CKD and 56,761 controls without CKD.3 Average all-cause annual costs increased exponentially with increase CKD stage [(a) commercial group – from $7,537 (no CKD) to $76,969 (CKD stages 4-5), (b) Medicare group – $8,091 (no CKD) to $46,178 (CKD stages 4-5)]. Average annual costs for ESRD patients were $121,948 (commercial group) and $87,339 (Medicare group).[3]

Approximately 15% of US adults (37 million people) have CKD. The cost for treating CKD in Medicare recipients has been estimated to be $82 billion, with an additional $36.6 billion for treating ESRD.

CKD increases the risk for cardiac disease, stroke, and death. A substantial list of symptoms and diseases are a consequence of CKD and include anemia, anorexia, cardiac dysfunction (including arrhythmias), diminished immune responses, electrolyte alteration, encephalopathy, erectile dysfunction, fatigue, fluid retention (peripheral and pulmonary edema), hypertension, impaired cognition, metabolic bone disease, nausea, pericarditis, peripheral neuropathy, platelet dysfunction (bleeding, ecchymosis), and sleep disorders (restless leg syndrome).

Hypertension and diabetes are the leading causes of CKD in adults. Other etiologic factors include cardiovascular disease, family history of CKD including inherited kidney disorders, immune mediated diseases, past damage to the kidneys, and older age. It is readily apparent therefore that hypertension and diabetes

represent the most treatable targets to prevent CKD. The objective of this document is to describe the role of central aortic blood pressure monitoring as an important part of hypertension management with the goal of reducing the adverse downstream consequences on renal function.

Hypertension and diabetes are the leading causes of CKD in adults and represent the most treatable targets to prevent CKD and CKD progression.

Central Aortic Pressure as a Predictive Measure of Renal Impairment

Hypertension leading to end-organ damage results from elevated central aortic pressures as this is what is directly transmitted to organs such as the kidney, heart, and brain. Central systolic pressures are correlated to peripheral systolic pressures and threshold values can be defined for treatment decisions; however, central pressures cannot reliably be predicted within an individual based on their brachial pressures.[4-8]

Central aortic pressure is predictive of end-organ damage including impaired renal function. Wang et al in a study of 1,272 subjects found that adjustment for demographics and relevant comorbidities, cSBP was the variable that consistently was independently predictive of deaths categorized as cardiovascular with a hazard ratio of 1.30 (per 10 mmHg increase).[9]

Glomerular filtration rate and carotid intima-media were more strongly related to central pressures than peripheral pressures.9

A separate published report examined the relationship of organ damage to blood pressure and showed that that central pressure provided additional information regarding the likelihood of renal damage (using estimated glomerular filtration rate) and cardiac damage (using left ventricular mass index) related to hypertension.[10]

Central pressure provided additional information regarding the propensity to end-organ damage (including renal damage) related to hypertension.[10]

The report by Yu and colleagues in 1,983 elderly subjects, demonstrated that groups can be distinguished based on concordance and discordance of brachial and central elevated pressures using a brachial target of 140/90 mm Hg and a central pressure target of 130/90 mmHg. The clinically relevant implication is that both pressures are valuable for deciding on management approaches and for the evaluation of risk.[11]

Incorporating Central Aortic Pressure Monitoring into the Care of Patients with Impaired Renal Function: Optimization of Pharmacotherapy for Hypertension

Numerous peer-reviewed publications have documented that non-invasive central aortic pressure assessment can provide independent and additional information (relative to brachial pressures) for determining risk of end-organ damage and cardiovascular morbidity and mortality.[12-24] As well, controlled studies have indicated that pharmacotherapy may have different effects on brachial compared to central blood pressure, which has implications for management decisions.[12]

Hypertension management through the addition of non-invasive measurements of central aortic pressures has the potential to improve care through: (a) refining requirements for BP monitoring, (b) decreasing over-treatment, (c) early identification for earlier or more aggressive treatment, and (d) decreasing the overall cost of care (e.g., use of tools such as ambulatory blood pressure monitoring (ABPM), drug costs).

Identifying the requirements and amount of medication is critical to controlling gestational hypertension.

The following table provides examples where central aortic blood pressure monitoring may positively impact the treatment of gestational hypertension:

Table 1: Examples of clinical utility of measuring both brachial and central aortic blood pressure.

CLINICAL USE	BRACHIAL BP	CENTRAL BP
Confirming hypertension (drug prescription is optimized)	Elevated	Elevated
Suspicion of white coat hypertension	Elevated	Normal or Low
Avoidance of increased drug prescription	Borderline high	Normal or Low
Consideration of reducing drug prescription (patients receiving at least one anti-hypertensive medication	Normal (particularly when there is suspected medication adverse effects)	Low (or extended period of normal)

The measurement of central aortic pressures in addition to brachial pressures provides clinically important patient care information.

Reduced Morbidity Association with Overtreatment of Hypertension

Overtreatment of hypertension may readily occur if office-based cuff measurements are misleadingly high. All medications are associated with side effects specific to the medication (e.g., cough in angiotensin converting enzyme inhibitors, constipation in calcium channel blockers); however, all anti-hypertensive medications have the potential for hypotension and consequences thereof. Elderly patients are more susceptible to hypotension and adverse consequences from hypotension. Furthermore, the association of blood pressure with cardiovascular events appears to be bimodal with higher rates at both low and high blood pressures.[25] In a study of 10,001 patients followed for approximately 5 years, patients with a pre-existing history of coronary artery disease and a low blood pressure (110–120/60–70 mmHg) had an increased risk of cardiovascular events other than stroke.[25] Several studies have noted an increased mortality in elderly patients related to lower treated blood pressure.[26,27] Older hypertensive patient have an increased risk of postural hypotension, balance and gait impairment, confusion, and dizziness.[28] Finally, an increased risk for injuries related to falls may result from overly aggressive treatment of hypertension.[28]

Cushman et al performed a randomized trial of intensive BP control (systolic BP <120 mm Hg) compared to standard therapy (systolic BO < 140 mm Hg) in 4,733 subjects with type 2 diabetes. The mean follow-up was 4.7 years.[29] Intensive therapy did not reduce the rate of the composite of fatal and non-fatal cardiovascular

events. However, intensive therapy vs. standard therapy was associated with a higher proportion of subjects with serious adverse events (3.3% vs. 1.3%, p<0.001), elevated creatinine (23.8% vs. 15.5%, p<0.001), and reduced eGFR (4.2% vs. 2.2%, p<0.001). The study highlights the need to ensure that decisions for hypertension management consider any propensity to medication induced episodes of hypotension, which may impact renal function. The addition of central pressure monitoring can assist in this objective (e.g., normal to high normal brachial pressure and low-normal to low central aortic pressure).

A study examining 651,749 US veterans with CKD sought to assess the association of blood pressure with mortality in CKD patients.26 The lowest mortality was observed with blood pressure of 130–159/70–89 mmHg. Patients with systolic and diastolic BP concomitantly very high or very low had the highest mortality. Results were consistent in subgroups of patients with normal and elevated levels of urine microalbumin-creatinine ratio. Depending on the model used, the hazard ratio for mortality with systolic BP < 120 mm Hg and diastolic BP < 80 mm Hg ranged from 1.42 to 1.62 (i.e., 42% to 62% increased risk). As with the previous study, avoiding hypotension should have a significant clinical impact. Again, the addition of central pressure monitoring in patients with CKD can assist in this objective.

The addition of central aortic pressure monitoring can assist in hypertension management decisions that consider any propensity towards medication induced episodes of hypotension, which may negatively impact renal function.

In summary, prescription of anti-hypertension medications has the potential of significant benefit but as with all medications, may be associated with adverse consequences such as reduced renal function and should always be judicious and carefully considered, particularly in patients with CKD. Assessment of central pressures provides relevant information that informs prescription medication needs.

Summary and Conclusions

The following is a summary of the key discussion points:

- Chronic kidney disease (CKD) is common and effects approximately 15% of adults in the USA (37 million people). Kidney disease is the ninth leading cause of death. CKD increases the risk for cardiac disease, stroke, and death, and leads to multiple significant additional diseases.
- Hypertension and diabetes are the leading causes of CKD in adults and also represent the most treatable targets to prevent CKD and to reduce CKD progression. Hypertension is responsible for continued morbidity, mortality and high socioeconomic costs despite the widespread availability and use of cuff brachial artery measurements for diagnosis and monitoring.
- Elevated central aortic pressure is predictive of end-organ damage including impaired renal function. Brachial and central aortic pressures provide complimentary information for risk prediction and management decisions.
- The risk of adverse CV outcomes with elevated central pressure is at least as high and possibly higher than with brachial pressure.
- Assessment of central pressures provides relevant information that informs prescription medication needs.

- Measurements of central arterial pressures can be incorporated into the current approaches to hypertension management as the dual arterial pressure SphygmoCor XCEL device can provide both brachial and central aortic pressures in the same clinic setting.

In conclusion, incorporation of central aortic pressure monitoring should be considered for all patients with chronic kidney disease.

REFERENCES

1. Levey AS, Eckardt KW, Tsukamoto Q, Levin A, Coresh J, Rossert J, de Zeeuw D, Hostette TH, Lameire N, Eknoyan G. Definition and classification of chronic kidney disease: A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney International 2005;67:2089-100.
2. Centers for Disease Control and Prevention. Chronic Kidney Disease Initiative. https://www.cdc.gov/kidneydisease/basics.html. Accessed July 21, 2021.
3. Golestanhe L, Alvarex PJ, Reaven MA, Funk SE, McGaughey KJ, Romero A, Breener MS, Macaulay O. All-cause costs increase exponentially with increased chronic kidney disease stage. Am J Manag Care. 2017;23:S0.
4. Cheng HM, Chuang SY Sung SH, Yu WC, Pearson A, Lakatta EG, Pan WH, Chen CH. Derivation and validation of diagnostic threshold for central blood pressure measurements based on long-term cardiovascular risks. J Am Coll Cardiol. 2013;62:1780-7.
5. McEniery CM, Yasmin BM, Munnery M, Wallace SM, Rowe CV, Cockcroft JR, Wilkinson IB. Central pressure: variability and impact of cardiovascular risk factors. The Anglo-Cardiff Collaborative Trial II. Hypertension. 2008;51:1476-1482.
6. Izzo JL. Brachial vs. central systolic pressure and pulse wave transmission indicators: a critical analysis. Am J Hypertension 2014;27:1433-42.
7. Takase H, Dohi Y, Kimura G. Distribution of central blood pressure values estimated by Omron HEM-9000AI in the Japanese general population. Hypertension Research 2013;36:50-57.
8. McEniery CM, Cockcroft JR, Roman MJ, Franklin SS, Wilkinson IB. Central blood pressure: current evidence and clinical importance. Eur Heart J. 2014. Doi:10.1093/eurheart/eht565.
9. Wang KL, Cheng HM, Chuang SY, Spurgeon HA, Ting CT, Lakatta EG, Yin FCP, Chou P, Chan CH. Central or peripheral systolic or pulse pressure: which best relates to target organs and future mortality? J Hypertens. 2009;27:461-67.
10. Booysen HL, Norton GR, Maseko MJ, Libhaber CD, Majane OHI, Sareli P, Woodiwiss AJ. Aortic, but not brachial blood pressure category enhances the ability to identify target organ changes in normotensives. J Hypertension 2013;31:1124-30.
11. Yu S, Xiong J, Lu Y, Chi C, Teliewubai J, Bai B, Ji H, Zhou Y, Fan X, Blacher J, Li J, Zhang Y, Xu Y. The prevalence of central hypertension defined by a central blood pressure type I device and its association with target organ damage in the community-dwelling elderly Chinese: The Northern Shanghai Study. J Am Soc Hypertens. 2018 Mar;12(3):211-219. doi: 10.1016/j.jash.2017.12.013.
12. Williams B, Lacy PS, Thom SM, Cruickshank K, Stanton A, Collier D, Hughes AD, Thurston H, O'Rourke M. CAFE Investigators; Anglo-Scandinavian Cardiac Outcomes Trial Investigators; CAFE Steering Committee and Writing Committee. Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes: principal results of the Conduit Artery Function Evaluation (CAFE) study. Circulation 2006; 113: 1213–1225.
13. Agabiti-Rosei E, Mancia G, O'Rourke MF, Roman MJ, Safar ME, Smulyan H, Wang JG, Wilkinson IB, Williams B, Vlachopoulos C. Central blood pressure measurements and antihypertensive therapy: a consensus document. Hypertension 2007; 50: 154–160.
14. Roman MJ, Devereux RB, Kizer JR, Lee ET, Galloway JM, Ali T, Umans JG, Howard BV. Central pressure more strongly relates to vascular disease and outcome than does brachial pressure: the Strong Heart Study. Hypertension 2007; 50: 197–203.
15. Vlachopoulos C, Aznaouridis K, O'Rourke MF, Safar ME, Baou K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with central haemodynamics: a systematic review and meta-analysis. Eur Heart J 2010; 31: 1865–1871.
16. Williams B, Lacy PS. Central aortic pressure and clinical outcomes. J Hypertens 2009; 27: 1123–1125.
17. Wang KL, Cheng HM, Chuang SY, Spurgeon HA, Ting CT, Lakatta EG, Yin FC, Chou P, Chen CH. Central or peripheral systolic or pulse pressure: which best relates to target organs and future mortality? J Hypertension 2009; 27: 461–467.
18. Vlachopoulos C, Axnaouridis K, O'Rourke MF, Safar ME, Baou K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with central haemodynamics: a systemic review and meta-analysis. Eur Heart J 2010;31:1865-71.
19. Li WF, Huang Y, Feng Y. Association between central haemodynamics and risk of all-cause mortality and cardiovascular disease: a systematic review and meta-analysis. J Human Hypertension 2019;33:531-541.
20. Lamarche F, Agharazii M, Madore F, Goupil R. Prediction of cardiovascular events by type I central systolic blood pressure. A prospective study. Hypertension 2021;77:319-327.
21. McEneiry CM, Ben-Shlomo Y, May MT, Spears M, Brumback L, Chen CH, Chirinos JA, et al. Central haemodynamics and cardiovascular risk prediction: an individual participant meta-analysis of prospective observational data from 22,433 subjects. (unpublished report)

22. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, et al. 2017 ACC/AHA/AAPA/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults. A report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. Circulation 2018;138:e484-e594. doi: 10.1.1161/CIR.0000000000000596

23. Townsend RR, Black HR, Chirinos JA, Feig PU, Ferdinand KC, Germain M, Rosendorff C, Steigerwalt SP, Stepanek JA. Clinical use of pulse wave analysis: proceedings from a symposium sponsored by North American Artery. J Clin Hyper 2015;17:503-13.

24. Sharman JE, Marwick RH, Gilroy D, Otahal P, Abhayaratna WP, Stowasser M. Randomized trial of guiding hypertension management using central aortic blood pressure compared with best-practice care. Principal findings of the BP Guide Study. Hypertension 2013;62:1138-45.

25. Bangalore S, Messerli FH, Wun CC, et al. J-curve revisited: An analysis of blood pressure and cardiovascular events in the Treating to New Targets (TNT) Trial. Eur Heart J. 2010; 31(23): 2897–2908.

26. Kovesdy CP, Bleyer AJ, Molnar MZ, et al. Blood pressure and mortality in U.S. veterans with chronic kidney disease. A cohort study. Annals Intern Med. 2013; 159(4):233–242.

27. Sim JJ, Shi J, Kovesdy CP, Kalantar-Zadeh K, Jacobsen SJ. Impact of achieved blood pressures on mortality risk and end-stage renal disease among a large, diverse hypertension population. JACC. 2014; 64(6):588–597.

28. Aronow WS, Fleg JL, Pepine CJ, et al. ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus documents developed in collaboration with the American Academy of Neurology, American Geriatrics Society, American Society for Preventive Curr Hypertens Rep. Cardiology, American Society of Hypertension, American Society of Nephrology, Association of Black Cardiologists, and European Society of Hypertension. JACC. 2011; 57(20):2037–2114.

29. Cushman WC, Evans GW, Byington RP, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med. 2010; 362(17):1575–1585.

Contact us at: info@atcormedical.com
www.atcormedical.com

ATCOR

"The Gold Standard" in
Central Blood Pressure Analysis

DCN 102240
ATCOR
2020-01-20