



Impact of Achieved Blood Pressures on Mortality Risk and End-Stage Renal Disease Among a Large, Diverse Hypertension Population

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ABSTRACT

BACKGROUND Medical data or clinical guidelines have not adequately addressed the ideal blood pressure (BP) treatment targets for survival and renal outcome.

OBJECTIVES This study sought to evaluate ranges of treated BP in a large hypertension population and compare risk of mortality and end-stage renal disease (ESRD).

METHODS A retrospective cohort study within the Kaiser Permanente Southern California health system was performed from January 1, 2006, to December 31, 2010. Treated hypertensive subjects ≥ 18 years of age were studied. Cox proportional hazards regression models were used to evaluate the risks (hazard ratios) for mortality and/or ESRD among different BP categories with and without stratification for diabetes mellitus and older age.

RESULTS Among 398,419 treated hypertensive subjects (30% with diabetes mellitus), mortality occurred in 25,182 (6.3%) and ESRD in 4,957 (1.2%). Adjusted hazard ratios (95% confidence intervals [CI]) for composite mortality/ESRD in systolic BP < 110 , 110 to 119, 120 to 129, 140 to 149, 150 to 159, 160 to 169, and ≥ 170 compared with 130 to 139 mm Hg were 4.1 (95% CI: 3.8 to 4.3), 1.8 (95% CI: 1.7 to 1.9), 1.1 (95% CI: 1.1 to 1.1), 1.4 (95% CI: 1.4 to 1.5), 2.3 (95% CI: 2.2 to 2.5), 3.3 (95% CI: 3.0 to 3.6), and 4.9 (95% CI: 4.4 to 5.5) respectively. Diastolic BP 60 to 79 mm Hg were associated with the lowest risk. The nadir systolic and diastolic BP for the lowest risk was 137 and 71 mm Hg, respectively. Stratified analyses revealed that the diabetes mellitus population had a similar hazard ratio curve but a lower nadir at 131 and 69 mm Hg but age ≥ 70 had a higher nadir (140 and 70 mm Hg).

CONCLUSIONS Both higher and lower treated BP compared with 130 to 139 mm Hg systolic and 60 to 79 mm Hg diastolic ranges had worsened outcomes. Our study adds to the growing uncertainty about BP treatment targets. (J Am Coll Cardiol 2014;64:588-97) © 2014 by the American College of Cardiology Foundation.

As treatment and control rates of hypertension (HTN) continue to improve (1,2), discussions have centered on the most appropriate target blood pressures (BP) in treated hypertensive patients, specifically related to how aggressively their HTN should be treated. Current treatment goals have been drafted with the assumption that there is a linear relationship between BP and risk for vascular

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and mortality outcomes. Lower observed BP across all age groups have been associated with the greatest morbidity and survival benefits (3). These observations have led to conclusions that lowering BP along that linear axis will correspond with a proportionate decrease in risk (4). The perception has been the same for the risk of renal failure (5). Indeed, significant risk reductions have been demonstrated in prospective interventional studies that have lowered BP in those with severe HTN (5-13). However, aggressive BP lowering has not convincingly shown benefit (14-19) and may actually predispose individuals to harm (20-24).

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In high-risk populations, such as those with diabetes mellitus (DM) and chronic kidney disease (CKD), interventions to lower BP below current target levels have not demonstrated outcome improvements (14,19,25). In fact, aggressive BP lowering has been associated with worsened outcomes (20-22), which is suggestive of a J-shaped curve. This nonlinear curve is similar to what has already been observed in other cardiovascular disease risk factors (24,26). Thus, for the treated general HTN population, the relationship between treated BP and outcomes is not well-defined. We used a large ethnically diverse population of subjects who were medically treated for HTN to evaluate discrete ranges of achieved BP and subsequent risk for mortality and end-stage renal disease (ESRD).

METHODS

A retrospective cohort study was performed among members of Kaiser Permanente Southern California (KPSC) during the period January 1, 2006, through December 31, 2010. KPSC is an integrated health system composed of 14 medical centers and >200 satellite medical offices, with a membership exceeding 3.5 million people. The membership population is ethnically and socioeconomically diverse, reflecting the population of the state of California (27). KPSC complete healthcare encounters are tracked using a common electronic health record and are collected as part of routine clinical care encounters. The KPSC Institutional Review Board approved the study protocol, which was exempt from informed consent.

The study population consisted of subjects ≥18 years of age who had a minimum of 6 months of continuous membership in the health plan. The HTN study cohort was identified in a 2-year window (January 1, 2006, to December 31, 2007) and followed up to December 31, 2010. HTN was identified as any member with 2 International Classifications of

Diseases-Ninth Revision (ICD-9) codes, specific to HTN (401.xx, 402.xx, 403.xx, 404.xx, 405.xx). The accuracy of ICD-9 coding for the diagnosis of HTN has been previously validated (28). Recorded BP values at baseline when the cohort was initially identified and all subsequent BP were retrieved. Inclusion criteria were hypertensive patients who had a minimum of 1 outpatient BP measurement and documented prescription(s) for antihypertensive medications. Patients were determined to be on an antihypertensive medication if it was prescribed and filled for ≥7 days within the observation period. Exclusion criteria were subjects <18 years of age, who were on dialysis, or who had received a renal transplant, with no documented diagnosis of HTN, no documented BP, or no documented prescription for antihypertensive medications. Patients with congestive heart failure also were excluded as their BP may not necessarily reflect treated BP values.

Comorbidities, including DM, ischemic heart disease, congestive heart failure, and cerebrovascular disease, were determined on the basis of inpatient and outpatient ICD-9 diagnoses codes. CKD

ABBREVIATIONS AND ACRONYMS

- BMI** = body mass index
- BP** = blood pressure
- CCI** = Charlson comorbidity index
- CI** = confidence interval
- CKD** = chronic kidney disease
- DBP** = diastolic blood pressure
- DM** = diabetes mellitus
- eGFR** = estimated glomerular filtration rate
- ESRD** = end-stage renal disease
- HR** = hazards ratio
- HTN** = hypertension
- ICD-9** = International Classifications of Diseases-Ninth Revision
- KPSC** = Kaiser Permanente Southern California
- SBP** = systolic blood pressure

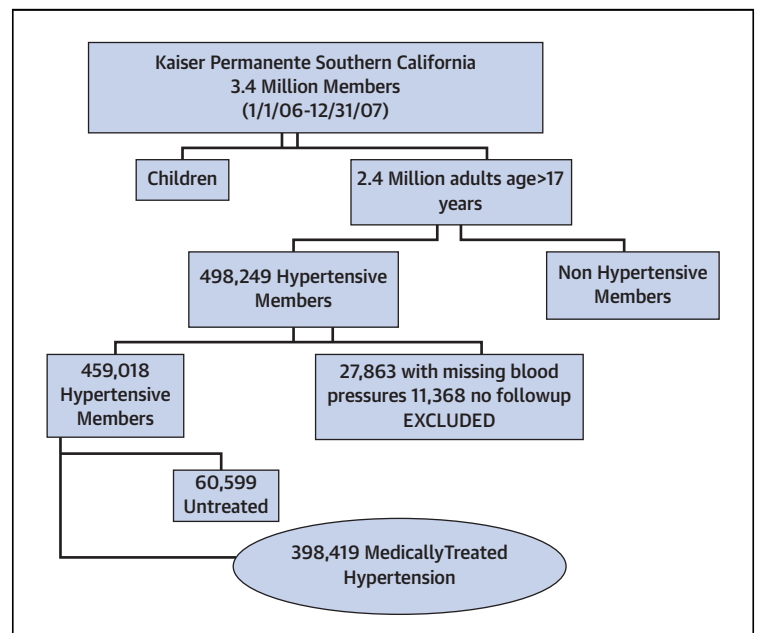


FIGURE 1 KPSC Treated Hypertension Study Cohort

A total of 398,419 hypertensive patients met inclusion criteria, meaning that they were treated with hypertensive medicines and had documented blood pressures during the period of follow-up to December 31, 2010. KPSC = Kaiser Permanente Southern California.

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