Determining Blood Pressure Threshold for Intervention in Hemodialysis Patients: A Stratified Treatment Intention Analysis

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Introduction

- Hypertension is highly prevalent among patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD).[1,2]
- While hypertension in almost all other human populations increases risk of poor patient outcomes, higher blood pressure (BP) appears paradoxically associated with better health outcomes in ESRD patients receiving hemodialysis (HD). This observation likely stems from residual confounding from overall health status.[3]
- There are no randomized clinical trials that have studied various BP targets among ESRD patients. Thus clinical decisions must be made based on observational data.
- One means to minimize confounding in observational studies is to study *treatment intention*. Specifically, to evaluate: 1) for any given BP, do patients do better if steps are taken to further reduce BP versus if such steps are not taken? and 2) what is the lowest value of BP at which intervention is beneficial?
- Therefore, we conducted a stratified treatment intention analysis of BP intervention in ESRD patients.
  - Patients were segregated into narrow strata with similar BP to reduce the opportunity for substantial patient differences.
  - Within each stratum, outcomes were compared between patients who received BP intervention versus those who did not.
  - We sought the lowest BP stratum in which outcomes were better among patients who received intervention.

Objectives

We conducted a stratified treatment intention analysis to estimate (among patients with 30-day mean pre-dialysis sitting blood pressure within defined strata) the association between subsequent blood pressure intervention (versus no intervention) and all-cause mortality and missed treatment rate.

Methods

- *Study Population*. Received in-center HD 01-Jan-2012 through at least 01-Apr-2014 at a large dialysis organization; >18 years old; mean pre-HD systolic BP 120-179 mmHg; receiving ≥1 antihypertensive drug via a pharmacy service; and had a defined exposure status.
- *Systolic Blood Pressure Strata*. For the primary analysis, mean pre-HD, systolic BP recoded in Jan-2012 were classified into the following strata: 120-129, 130-134, 135-139, 140-149, 150-159, 160-169, and 170-179 mmHg.
  - In a secondary analysis, 2 strata were considered: 120-149 and 150-179 mmHg

Methods

- *Exposure Status*. Within each BP stratum, exposure status was attributed as follows:

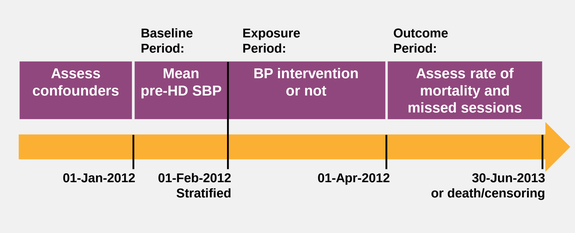
	Δ in no. of BP medications over the exposure period	Δ in target weight over the exposure period
Intervention	↑	↓
Intervention	↔	↓
Intervention	↑	↔
Control	↔	↔
Excluded [a]	↓	Any
Excluded [a]	Any	↑

Abbreviations: BP, blood pressure; no., number.

[a] Patients were excluded because no inference could be make regarding the intent to treat BP.

- *Propensity Score Matching*. In each BP stratum, intervention and control patients were matched 1:1 (without replacement; to nearest neighbor, max caliper width ± 0.005) based on the following parameters:
  - Age
  - Sex
  - Race
  - Incident/prevalent (≤12 m, >12 m)
  - Etiology ESRD
  - Access type
  - Schedule (MWF, TTS)
  - Post-dialysis weight
  - Difference post-target weight
  - Inter-dialytic weight gain
  - Charlson Comorbidity Index
  - Diabetes
  - Coronary disease
  - Heart failure
  - Albumin
  - Phosphate
  - Hemoglobin
  - ESA dose
- *Outcomes of Interest*.
  - Mortality rate (number of deaths/time at-risk) analyzed within each BP stratum and intervention/control status associations were estimated by proportional hazards model.
  - Missed treatment rate (number of missed treatments/time at-risk) analyzed within each BP stratum and intervention/control status associations were estimated by negative binomial regression.

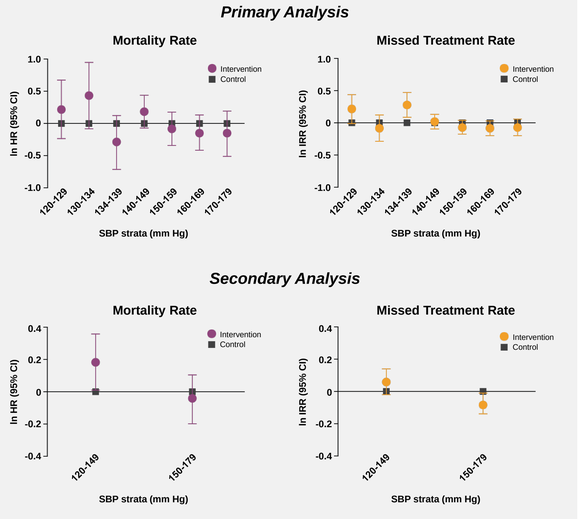
Figure 1. Study Design



Abbreviations: BP, blood pressure; HD, hemodialysis; SBP, systolic blood pressure.

Results

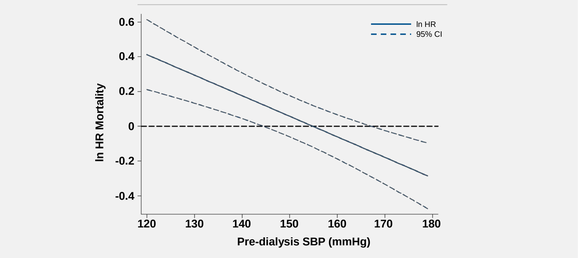
Figure 2. Natural Log Plots of Hazard Ratios and Incident Rate Ratios for Mortality and Missed Treatment Rates



Control group = no intervention
Point estimates for intervention > 0 (data points above line) favor no intervention.
Point estimates for intervention < 0 (data points below line) favor intervention.

Abbreviations: CI, confidence interval; HR, hazard ratio; IRR, incidence rate ratio; ln, natural log; SBP, systolic blood pressure.

Figure 3. Natural Log Plot of Hazard Ratio for Mortality Rate



p-interaction = 0.003 indicates that the effect of intervention is significantly different based on level of pre-dialysis systolic BP.

Abbreviations: CI, confidence interval; HR, hazard ratio; ln, natural log; SBP, systolic blood pressure.

- In the primary analysis, BP intervention was associated with:
  - Numerically greater adjusted risk of death and missed treatment rates in the setting of pre-dialysis systolic BPs 120-129 through 140-149 mmHg
  - Numerically lower adjusted risk of death and missed treatment rates in the setting of pre-dialysis systolic BPs 150-159 through 170-179 mmHg
  - Estimates were not statistically significant
- In the secondary analysis, BP intervention was associated with:
  - Statistically significantly greater adjusted risk of death and numerically greater adjusted rate of missed treatments in the setting of pre-dialysis systolic BP 120-149 mmHg
  - Statistically significantly lower adjusted rate of missed treatment and no difference in adjusted risk of mortality in the setting of pre-dialysis systolic BP 150-179 mmHg
- When pre-dialysis systolic BP was considered as a continuous variable, intervention was associated with:
  - Statistically significantly greater adjusted risk of death for BP < 145 mmHg
  - Statistically significantly lower adjusted risk of death for BP > 170 mmHg

Conclusions

- Among HD patients, these data:
  - Do not support institution of BP-lowering interventions for pre-dialysis BP < 150 mmHg
  - Support institution of BP-lowering interventions for pre-dialysis BP > 150 mmHg
- Stratified treatment intention analyses may prove useful when randomized clinical trial evidence is lacking and robust databases are available.

References

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