

## Background

- Malignant hypertension (MH): a severe hypertension with end-organ injury [1,2] and high mortality [3].
- The residential Rice Diet Program (RDP) treated MH (1940-1992) using a very low sodium (5 meq/d), low protein (~5% kcal), low fat (~5% kcal), and high carbohydrate (~90% kcal) diet.
- Previous MH criteria included: 1) systolic BP (SBP) >170 mmHg, and 2) papilledema (P) and/or non-diabetic retinal hemorrhage (H) at any time during RDP [4].

## Objectives

- Identify MH patients meeting SBP criteria between Days -7 and +6, and meeting retinal criteria between Days -30 and +30.
- Examine differences in SBP and retinal changes between those with Class III (H+/P-) and Class-IV retinopathy (P+).
- Examine factors associated with SBP during the first 4 weeks of RDP.

## Methods

- Outcomes: SBP change at week 4 and weekly SBP.
- Univariable analysis selected variables with p<0.05.
- Multivariable regressions included gender, MH class (III v. IV), baseline SBP, blood non-protein nitrogen (NPN, a surrogate for renal function), and urine chloride (UCI, an adherence marker of sodium intake).
- Retinal findings compared between baseline and follow up (N=377).

## Results

Table 1 Baseline characteristics of MH patients

Mean (SD)	Class III (N=313)	Class IV (N=240)	Total (N=553)
Age, years	52.6 (9.8)	45.5 (10.5)	49.5 (10.7)
1 <sup>st</sup> episode, days	138 (166)	131 (174)	135 (169)
Gender/female, n (%)	114 (36.4%)	57 (23.8%)	171 (30.9%)
Systolic BP, mmHg	209 (26.9)	221 (24.2)	214 (26.5)
Diastolic BP, mmHg	121 (16.6)	135 (17.3)	127 (18.2)
BMI, kg/m <sup>2</sup> *	25.4 (6.4)	23.6 (3.5)	24.6 (5.4)
NPN, mg/dl*	44.9 (24.5)	63.8 (39.6)	53.7 (33.7)
UCI, mEq/L*	54.6 (35.3)	40.7 (26.4)	48.8 (32.6)

\*Missing counts: 224 BMI, 170 entry NPN, 238 entry UCI.

Table 2 Multivariable Regression on SBP change at week 4

(N=230)	Beta (95% CI)	P
Male gender	9.41 (2.6, 16.2)	0.007
Class IV (vs III)	7.56 (0.8, 14.3)	0.029
Baseline SBP	-0.33 (-0.4, -0.2)	<0.001
Baseline NPN	-0.02 (-0.1, 0.1)	0.758
Baseline UCI	-0.14 (-0.2, 0)	0.004

❖ Male gender and class IV had lower SBP reductions at week 4.

❖ Higher baseline SBP and UCI were associated with greater SBP reductions.

Table 3 Mixed model on weekly SBP averages during first 4 weeks

(N=319)	Beta (95% CI)	P
Male gender	6.40 (2.2, 10.6)	0.004
Class IV (vs III)	5.72 (1.6, 9.8)	0.007
Baseline SBP	0.77 (0.7, 0.8)	<0.001
Baseline NPN	0.01 (0, 0.1)	0.651
UCI weekly avg	-0.03 (-0.2, 0.1)	0.567
Week (1-4)	-7.02 (-7.8, -6.2)	<0.001
UCI x Week interaction	0.20 (0.1, 0.3)	<0.001

❖ Baseline NPN was not associated with SBP change or weekly SBP.

❖ Week affects SBP significantly. SBP reduction increased by 7.02 mmHg for each additional week.

❖ UCI lowered with time (week) and its effect on SBP increased with time (see also Figure 1).

Figure 1 Association of SBP and UCI by week

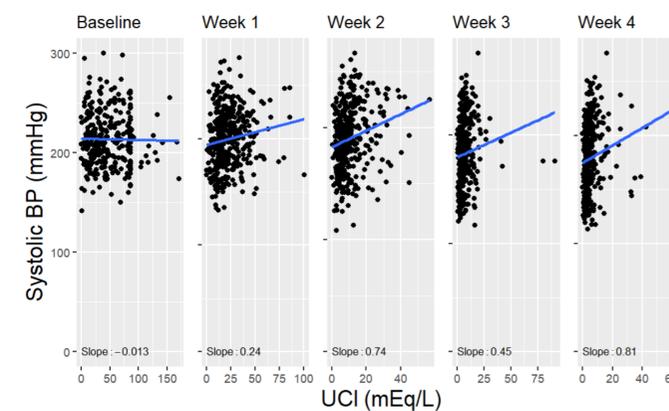


Figure 2 Weekly SBP by MH classes

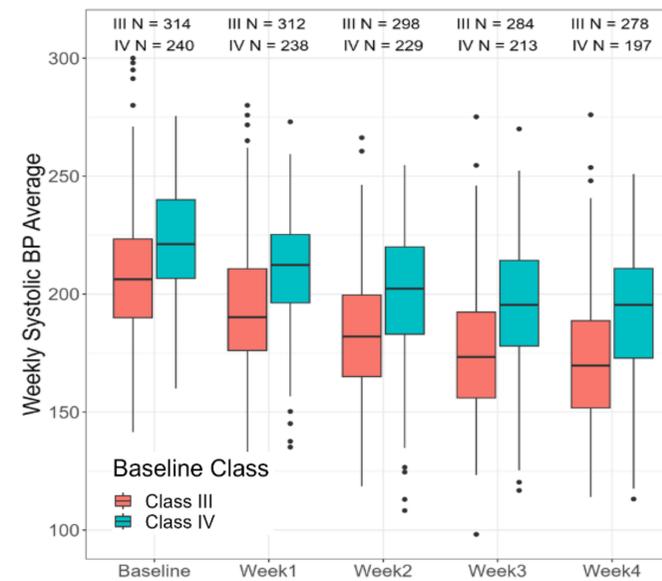
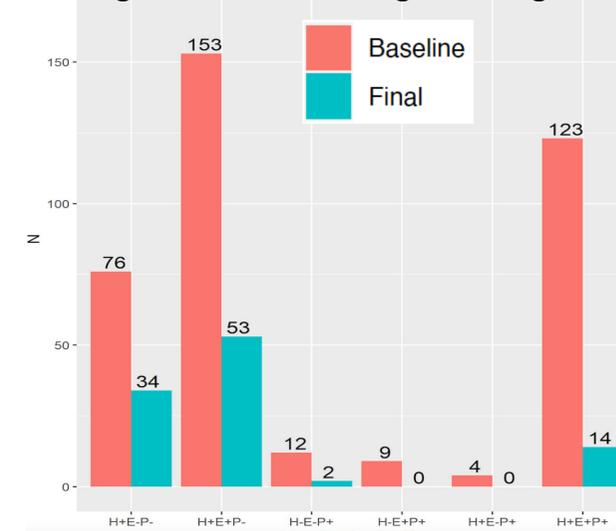


Figure 3 Retinal changes during RDP



- ❖ Class IV consistently had a higher SBP than class III (Figure 2).
- ❖ Number of patients with retinal hemorrhage dropped from 229 at baseline to 87 at end of follow up (~62% reduction) (Figure 3).
- ❖ Number of patients with retinal papilledema reduced from 148 at baseline to 16 at end of follow up (~89% reduction) (Figure 3).

## Conclusion

- ❑ SBP dropped within 1 week of starting a low-salt, low-protein, low-fat, high carbohydrate diet, and the drop continued weekly for the first 4 weeks.
- ❑ Retinal hemorrhage, exudates and papilledema improved in 60-90% of patients.
- ❑ Baseline papilledema predicted a lower SBP reduction than hemorrhage.
- ❑ A higher baseline SBP and UCI significantly predicted SBP reduction.

## References

1. Boulestreau et al. Malignant hypertension: Current perspectives and challenges. J Am Heart Assoc. 2022;11:e023397. DOI: 10.1161/JAHA.121.023397
2. Domek M, Gumprecht J, Lip G.Y.H. and Shantsila A. Malignant hypertension: does this still exist? J Hum Hypert 2020;34:1-4. DOI:10.1038/s41371-019-0267-y
3. Keith NM, Wagener HP, Barker NW. Some different types of essential hypertension: their course and prognosis. Am J Med Sci. 1974;268:336-45.
4. Lin et al. Blood pressure responses of Rice Diet Program patients with malignant hypertension. American Heart Association-Hypertension Annual meeting, September 2022, San Diego, CA.

## Disclosure

All data can be made available upon request.