Association Between Visit-to-Visit Variability of Systolic Blood Pressure and All-Cause Mortality

BRIAN A. CLEMENTS, NATHAN ALLRED, ERIK RIESSEN, BENJAMIN D. HORNE, RAYMOND O. MCCUBREY, HEIDI T. MAY, JOSEPH B. MUHLESTEIN.

Intermountain Medical Center Heart Institute, Salt Lake City, UT, USA

Intermountain® Heart Institute
Intermountain Medical Center

Intermountain Healthcare
Healing for life®

BACKGROUND

- Visit-to-visit blood pressure variability (VVV) is a proposed risk predictor of CV events, but a more complete understanding of this association is desired.
- We analyzed >10 years of data from electronic health records of Intermountain Healthcare to investigate the potential relation between systolic blood pressure (SBP) VVV and all-cause mortality in a large real-world outpatient population.

METHODS

- This study was modeled after a *post hoc* analysis of VVV in the ALLHAT Trial, including assignment of VVV thresholds of <6.5, 6.5-14.4, and >14.4 mmHg.
- Patients (N=10,903) were included if they had at least 7 SBP measurements between January 1, 2007 and December 31, 2011.
- VVV was calculated as the standard deviation of those 7 SBPs.
- After the 7th SBP (baseline), patients were followed for >5 years to June, 2016, for all-cause mortality (3,013 [27.6%] died).
- Cox regression was used to adjust for demographics, mean SBP (VVV models only), and 20 comorbidities and 29 medications recorded at the 7th SBP measurement.

CONCLUSIONS

- **SBP CoV (VVV divided by mean SBP), but not VVV alone, was associated with a higher risk of mortality after multivariable adjustment in a real-world patient population.**
- **Further analyses of the influence of common SBP medications on the association of VVV/CoV with mortality and optimal actual-practice thresholds of VVV are necessary.**

RESULTS

TABLE 1. BASELINE CHARACTERISTICS OF THE STUDY POPULATION.

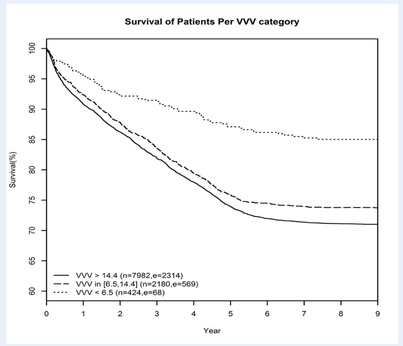
	Overall	VVV <6.5	VVV 6.5-14.4	VVV >14.4	p-value
Characteristic	10586	443 (4.2%)	2204 (20.8%)	7939 (75.0%)	
Demographics and Cardiac Risk Factors					
Age (Years)	71.57±10.14	68.3±9.06	71.09±10.07	71.89±10.18	<0.001
Male	4101 (38.7%)	249 (56.21%)	841 (38.16%)	3011 (37.93%)	<0.001
Female	6485 (61.3%)	194 (43.79%)	1363 (61.84%)	4928 (62.07%)	<0.001
Mean SBP	136.86+/-14.34	126.49+/-11.77	133.54+/-12.84	138.36+/-14.47	<0.001
BMI (kg/m2)	30.13±7.32	30.94±5.92	30.6±.62	29.96±7.29	0.0021
Total:HDL ratio (first)	4.15±1.43	4.11±1.29	4.1±1.4	4.17±1.45	0.42
Total cholesterol (first)	179.42±43.44	172.8±38.26	177.45±42.84	180.49±43.91	0.0049
HDL-C (first)	46.43±14.67	44.93±14.56	46.43±14.59	46.53±14.7	0.24
LDL-C (first)	101.4±35.97	97.1±30.79	99.94±34.82	102.15±36.63	0.031
Triglycerides (first)	160.76±103.46	157.11±87.54	157.33±105.62	162.08±103.81	0.34
VLDL (first)	30.01±13.94	29.39±13.18	29.42±13.38	30.24±14.16	0.18
Morbidities at baseline (defined as visit of 7th SBP measurement)					
A-fib history	2309 (21.81%)	63 (14.22%)	505 (22.91%)	1741 (21.93%)	<0.001
Anxiety history	3202 (30.25%)	88 (19.86%)	757 (34.35%)	2357 (29.69%)	<0.001
Aortic plaque history	914 (8.63%)	23 (5.19%)	217 (9.85%)	674 (8.49%)	0.0042
CAD history	4759 (44.96%)	169 (38.15%)	1011 (45.87%)	3579 (45.08%)	0.011
HF history (any)	2967 (28.03%)	90 (20.32%)	674 (30.58%)	2203 (27.75%)	<0.001
HF history (diastolic)	521 (4.92%)	11 (2.48%)	110 (4.99%)	400 (5.04%)	0.053
HF history (systolic)	367 (3.47%)	13 (2.93%)	77 (3.49%)	277 (3.49%)	0.82
COPD history	1808 (17.08%)	49 (11.06%)	408 (18.51%)	1351 (17.02%)	<0.001
CVA history	711 (6.72%)	16 (3.61%)	141 (6.4%)	554 (6.98%)	0.018
Depression history	3838 (36.26%)	127 (28.67%)	919 (41.7%)	2792 (35.17%)	<0.001
Diabetes history	4605 (43.5%)	172 (38.83%)	1052 (47.73%)	3381 (42.59%)	<0.001
Hyperlipidemia history	9062 (85.6%)	386 (87.13%)	1964 (89.11%)	6712 (84.54%)	<0.001
Hypertension history	10586 (100%)	443 (100%)	2204 (100%)	7939 (100%)	<0.001
MI history	755 (7.13%)	34 (7.67%)	129 (5.85%)	592 (7.46%)	0.032
PVD history	2917 (27.56%)	86 (19.41%)	652 (29.58%)	2179 (27.45%)	<0.001
Renal failure history	1511 (14.27%)	37 (8.35%)	358 (16.24%)	1116 (14.06%)	<0.001
Revascularization history	646 (6.1%)	21 (4.74%)	121 (5.49%)	504 (6.35%)	0.16
Sleep apnea history	2988 (28.23%)	111 (25.06%)	710 (32.21%)	2167 (27.3%)	<0.001
TIA history	1241 (11.72%)	32 (7.22%)	280 (12.7%)	929 (11.7%)	0.0047
Tobacco history	2754 (26.02%)	101 (22.8%)	575 (26.09%)	2078 (26.17%)	0.29

TABLE 2. BASELINE MEDICATIONS OF THE STUDY POPULATION.

	Overall	VVV <6.5	VVV 6.5-14.4	VVV >14.4	p-value
ACE inhibitor	5018 (47.4%)	239 (53.95%)	986 (44.74%)	3793 (47.78%)	<0.001
Aldosterone Blocker	464 (4.38%)	16 (3.61%)	96 (4.36%)	352 (4.43%)	0.71
Alpha-2 Agonist	282 (2.66%)	2 (0.45%)	38 (1.72%)	242 (3.05%)	<0.001
Alpha and Beta Blocker	1268 (11.98%)	37 (8.35%)	250 (11.34%)	981 (12.36%)	0.024
Alpha Blocker	294 (2.78%)	20 (4.51%)	67 (3.04%)	207 (2.61%)	0.042
Antianxiety	1343 (12.69%)	35 (7.9%)	303 (13.75%)	1005 (12.66%)	0.0033
Antidepressant	2508 (23.69%)	89 (20.09%)	591 (26.81%)	1828 (23.03%)	<0.001
Antidiabetic	2715 (25.65%)	122 (27.54%)	571 (25.91%)	2022 (25.47%)	0.59
ARB	2754 (26.02%)	92 (20.77%)	603 (27.36%)	2059 (25.94%)	0.015
Aspirin	2181 (20.6%)	83 (18.74%)	403 (18.28%)	1695 (21.35%)	0.0043
BB: cardio-selective	2986 (28.21%)	112 (25.28%)	606 (27.5%)	2268 (28.57%)	0.23
BB: non-cardio selective	1583 (14.95%)	47 (10.61%)	307 (13.93%)	1229 (15.48%)	0.0063
CCB: dihydro	1967 (18.58%)	65 (14.67%)	376 (17.06%)	1526 (19.22%)	0.0067
CCB: non-dihydro	764 (7.22%)	43 (9.71%)	157 (7.12%)	564 (7.1%)	0.12
Diuretic: carbonic	25 (0.24%)	2 (0.45%)	5 (0.23%)	18 (0.23%)	0.63
Diuretic: K-sparing	862 (8.14%)	37 (8.35%)	180 (8.17%)	645 (8.12%)	0.98
Diuretic: loop	1609 (15.2%)	44 (9.93%)	356 (16.15%)	1209 (15.23%)	0.0039
Diuretic: misc	43 (0.41%)	2 (0.45%)	12 (0.54%)	29 (0.37%)	0.50
Diuretic: thiazide	4381 (41.38%)	180 (40.63%)	875 (39.7%)	3326 (41.89%)	0.17
DOAC	87 (0.82%)	1 (0.23%)	20 (0.91%)	66 (0.83%)	0.34
Lipid lowering	4943 (46.69%)	252 (56.88%)	1023 (46.42%)	3668 (46.2%)	<0.001
Narcotic	3635 (34.34%)	114 (25.73%)	742 (33.67%)	2779 (35%)	<0.001
NSAID	3268 (30.87%)	130 (29.35%)	635 (28.81%)	2503 (31.53%)	0.039
P2Y12 inhibitor	1058 (9.99%)	38 (8.58%)	203 (9.21%)	817 (10.29%)	0.20
Plavix	989 (9.34%)	35 (7.9%)	188 (8.53%)	766 (9.65%)	0.16
Statin	4542 (42.91%)	234 (52.82%)	939 (42.6%)	3369 (42.44%)	<0.001
Vasodilator	729 (6.89%)	15 (3.39%)	122 (5.54%)	592 (7.46%)	<0.001
Warfarin	982 (9.28%)	29 (6.55%)	226 (10.25%)	727 (9.16%)	0.038

FIGURE 1. KAPLAN-MEIER SURVIVAL CURVES DURING UP TO 9 YEARS OF FOLLOW-UP FOR: A) VISIT-TO-VISIT VARIABILITY (VVV) CATEGORIES (BASED ON THE ALLHAT THRESHOLDS) AND B) COEFFICIENT OF VARIATION (COV) QUARTILES.

A)



B)

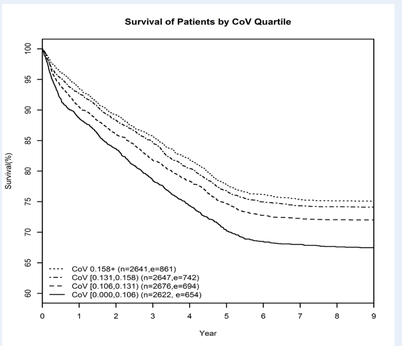
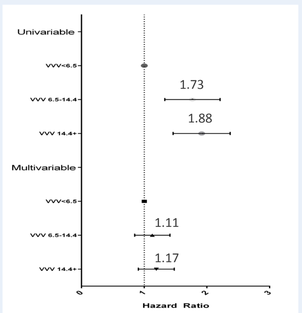
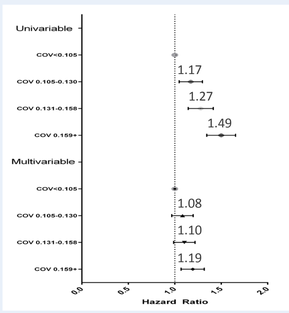


FIGURE 2. FOREST PLOTS OF A) VVV CATEGORIES (ALLHAT THRESHOLDS) AND B) COEFFICIENT OF VARIATION (COV) QUARTILES IN UNIVARIABLE AND MULTIVARIABLE COX REGRESSION MODELING.

A)



B)



No Conflicts of interest to disclose