Online Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Lehman[*] LH, Saeed[*] M, Talmor D, Mark RG, and Malhotra A. Methods of Blood Pressure Measurement in the Intensive Care Unit. ([*]co- first authors)

Appendix A. Filters for Blood Pressure Measurements

In all analyses, blood pressure values beyond reasonable physiological bounds were removed. Both invasive and non-invasive blood pressure measurements were filtered with the following bounds: systolic blood pressure (SBP) [40, 250] mmHg, mean blood pressure (MAP) [20, 200] mmHg, and diastolic blood pressure (DBP) [10, 150] mmHg. Further, measurements with a MAP measurement greater than SBP or less than DBP were removed. These bounds were applied to once-per-minute trends as well as the hourly nurse-verified measurements.

For pair-wise analysis, the following filters were applied to the once-per-minute invasive blood pressure measurements. First, a pulse pressure check was performed to eliminate artifacts due to damping of the arterial line. Specifically, pressure measurements where pulse pressures were less than 30% of recorded MAPs were rejected. Secondly, to ensure that the recorded MAP did not deviate from the estimated MAP (based on SBP and DBP) significantly, blood pressure measurements were excluded if the absolute difference between the estimated and recorded MAPs was greater than 30% of measured MAP, where estimated MAP was defined with the formula MAP = (2 * DBP + SBP) / 3.

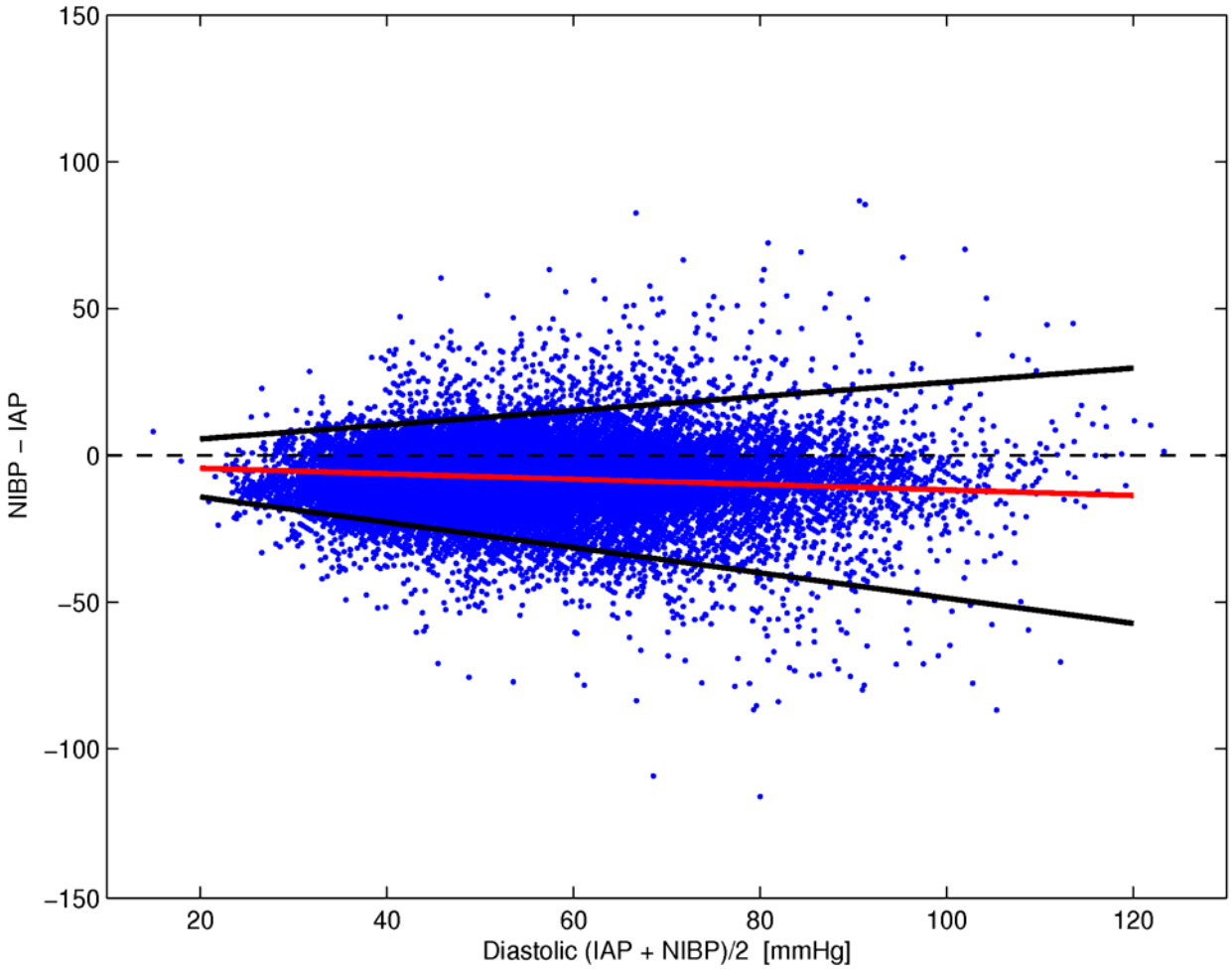
Finally, patients who had pair-wise systolic IAP/NIBP discrepancies >= 50mmHg with documented a-line problems (from nursing notes) were excluded from the regression analysis.

Appendix B. Bias and 95% Limits of Agreement from Regression-Based Bland-Altman Analysis

This appendix contains tabulated results for Figures 1A and1B in the main text, and the Bland-Altman plot that compares the diastolic NIBP and IAP measurements. Pair-wise comparison was performed using a regression-based Bland-Altman technique, which models the mean and standard deviation of the blood pressure differences as a function of the averaged measurements. The bias and the 95% limits of agreement of the pair-wise differences were assessed using a regression-based Bland-Altman technique.

Regression slopes and intercepts for the Bland Altman plots in Figures 1A, 1B, and Appendix Figure 1 are reported in Appendix Table 1. Regression of differences on averages (of IAP and NIBP) yielded significant relationships ($P < 0.05$) for *systolic, mean*, and *diastolic* blood pressures. All data analyses were performed using Matlab 7.10 and supporting statistical toolboxes.

Bland-Altman Plot for Diastolic IAP/NIBP Measurements



Appendix Figure 1. Bias and 95% limits of agreement between concurrently measured invasive and non-invasive diastolic blood pressure.

Regression Coefficients for the Bland-Altman Analysis

	Intercept (95% CI)	Slope (95% CI)	P value
Systolic	28.11 (22.70,33.35)	-0.30(-0.35,-0.25)	<0.05
MAP	16.34 (11.36,21.62)	-0.31(-0.38,-0.24)	<0.05
Diastolic	-2.42 (-6.85,2.23)	-0.09(-0.18,-0.01)	<0.05

Appendix Table 1. **Regression coefficients for the Bland-Altman plots (Figures 1A and 1B and Appendix Figure 1). Bootstrapped mean and 95% confidence intervals are reported. Regression of differences on averages (of IAP and NIBP) yielded significant relationships (P < 0.05) for *systolic, mean*, and *diastolic* blood pressures. The p values are determined based on the bootstrapped 95% confidence intervals.**

Appendix Table 2A. Tabulated results for Figure 1 A in the main text.

Systolic (mmHg)	Lower Limit of Agreement	Bias	Upper Limit of Agreement
50	-11.26	13.06	37.38
60	-15.32	10.05	35.42
70	-19.37	7.04	33.46
80	-23.43	4.03	31.49
90	-27.48	1.02	29.53
100	-31.54	-1.99	27.56
110	-35.59	-5.00	25.60
120	-39.65	-8.01	23.63
130	-43.71	-11.02	21.67
140	-47.76	-14.03	19.71
150	-51.82	-17.04	17.74
160	-55.87	-20.05	15.78
170	-59.93	-23.06	13.81
180	-63.98	-26.07	11.85
190	-68.04	-29.08	9.89
200	-72.09	-32.09	7.92
210	-76.15	-35.10	5.96
220	-80.21	-38.11	3.99
230	-84.26	-41.12	2.03

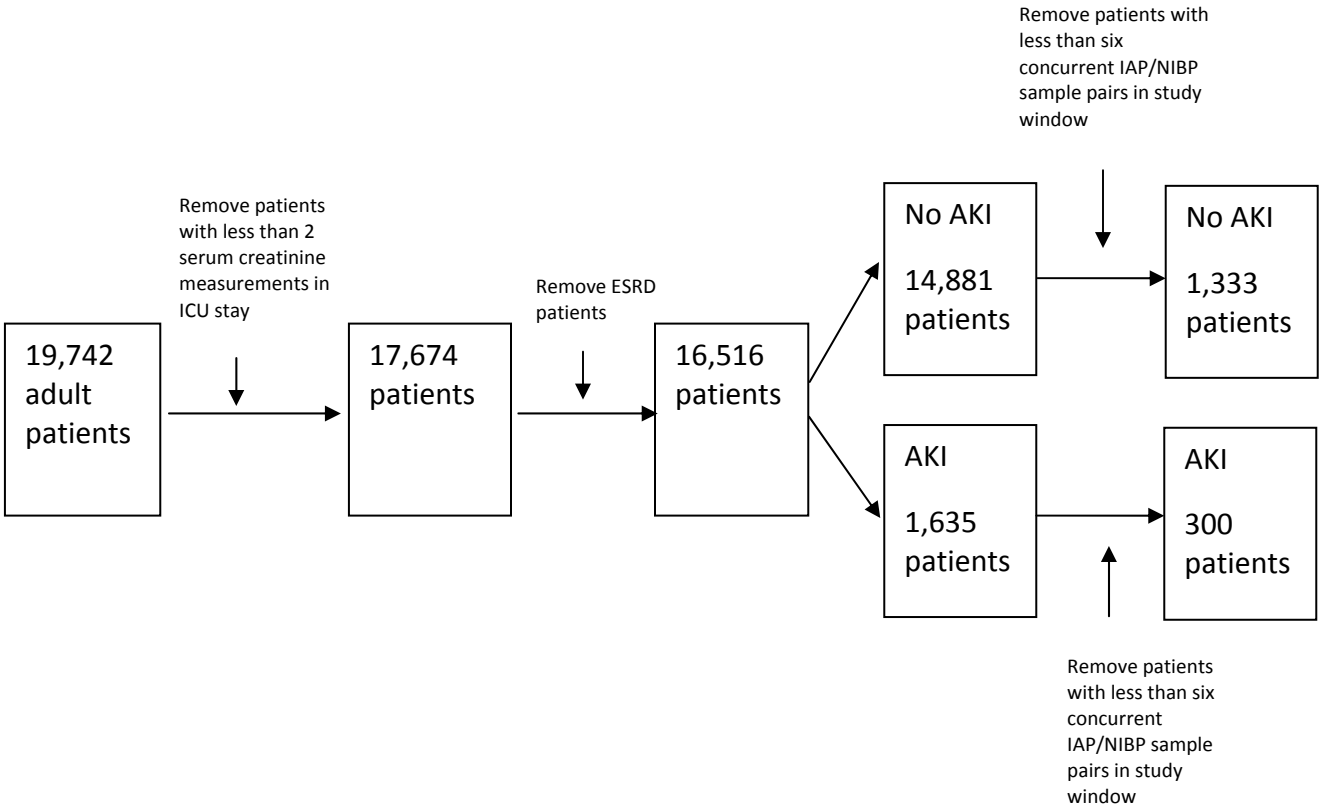
Appendix Table 2B. Tabulated results for Figure 1 B in the main text.

MAP (mmHg)	Lower Limit of Agreement	Bias	Upper Limit of Agreement
40	-9.72	3.90	17.52
50	-15.06	0.79	16.64
60	-20.41	-2.32	15.76
70	-25.75	-5.43	14.88
80	-31.09	-8.54	14.01
90	-36.43	-11.65	13.13
100	-41.78	-14.76	12.25
110	-47.12	-17.87	11.37
120	-52.46	-20.98	10.50
130	-57.81	-24.09	9.62
140	-63.15	-27.21	8.74
150	-68.49	-30.32	7.86

Appendix Table 2C. Tabulated results for Figure 1in the Appendix.

Diastolic (mmHg)	Lower Limit of Agreement	Bias	Upper Limit of Agreement
20	-14.26	-4.31	5.65
30	-18.56	-5.25	8.05
40	-22.86	-6.20	10.46
50	-27.15	-7.14	12.87
60	-31.45	-8.09	15.27
70	-35.75	-9.03	17.68
80	-40.04	-9.98	20.09
90	-44.34	-10.92	22.50
100	-48.63	-11.87	24.90
110	-52.93	-12.81	27.31
120	-57.23	-13.76	29.72

Appendix C. Derivation of the Patient Population in the Blood Pressure and AKI Study



Appendix Figure 2. Patient selection diagram for the AKI study (N = 1633).

Appendix D. Derivation of the Patient Population in the Blood Pressure and ICU Mortality Study

For the ICU mortality study, we included only patients who had at least six concurrently time-stamped IAP/NIBP sample pairs regardless of pressor treatment or resuscitation. 4,957 of the 19,742 adult patients in MIMIC II clinical database met the criterion. These patients were included to study the association between blood pressure and ICU mortality.

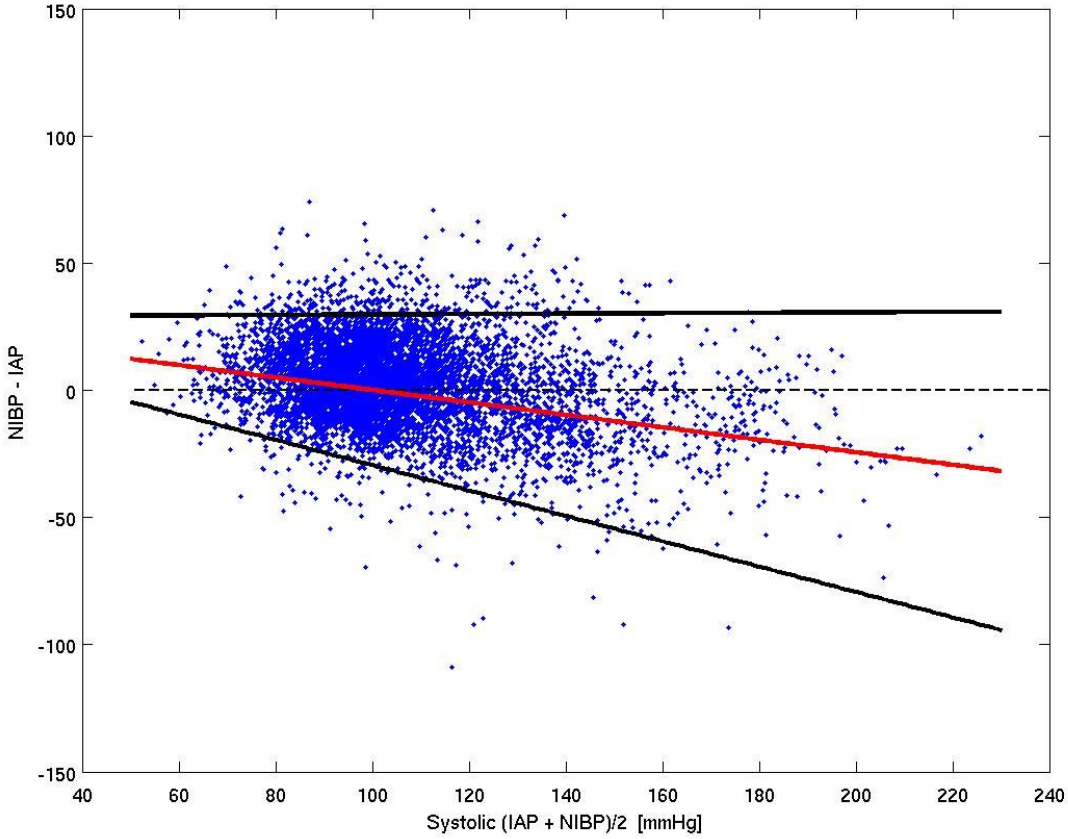
Appendix E. Further Pair-wise Analysis: Effect of Vasopressor Medications

To investigate whether our results were dependent on the use of vasopressor medications, we analyzed the differences between NIBP and IAP for 20,399 (of the 27,022) pair-wise IAP/NIBP measurements with available clinical information (from 609 unique patients). A total of 7,490 IAP/NIBP measurement pairs (from 258 patients) obtained during pressor treatment formed the pressor group. The rest of the pair-wise measurements formed the no pressor group. The differences between NIBP and IAP were analyzed for the pressor and no-pressor groups respectively using the same regression-based Bland-Altman techniques as in Figure 1 in the main text. The biases and 95% limits of agreement for NIBP/IAP discrepancies for the pressor and the no pressor groups are plotted in the figures below.

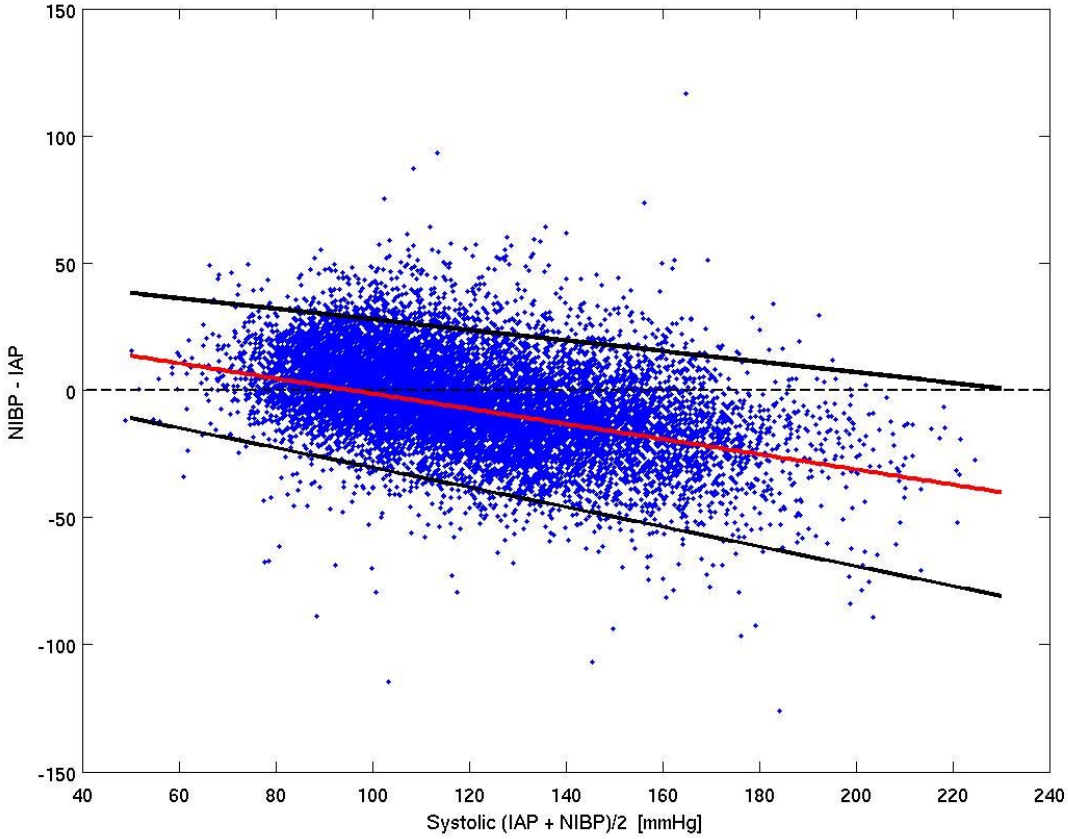
Systolic Blood Pressure: Pressor vs. No-Pressor Groups

For the pressor group, the biases (with the 95% limits of agreement in parentheses) between non-invasive and invasive *systolic* blood pressure measurements in the hypotensive range from 60 to 90 mmHg were 9.86 (-9.70, 29.42), 7.41(-14.69, 29.51), 4.96(-19.67, 29.59), 2.51(-24.65, 29.68) mmHg respectively in each of the 10-mmHg intervals.

For the no pressor group, the biases (with the 95% limits of agreement in parentheses) between non-invasive and invasive *systolic* blood pressure measurements in the hypotensive range from 60 to 90 mmHg were 10.64(-14.91, 36.19), 7.65(-18.79, 34.10), 4.67(-22.67, 32.02), 1.69(-26.55, 29.93) mmHg respectively in each of the 10-mmHg intervals.



Appendix Figure 3A. Pressor Group -- Biases and the 95% limits of agreement between concurrently measured systolic IAP/NIBP during pressor treatment.

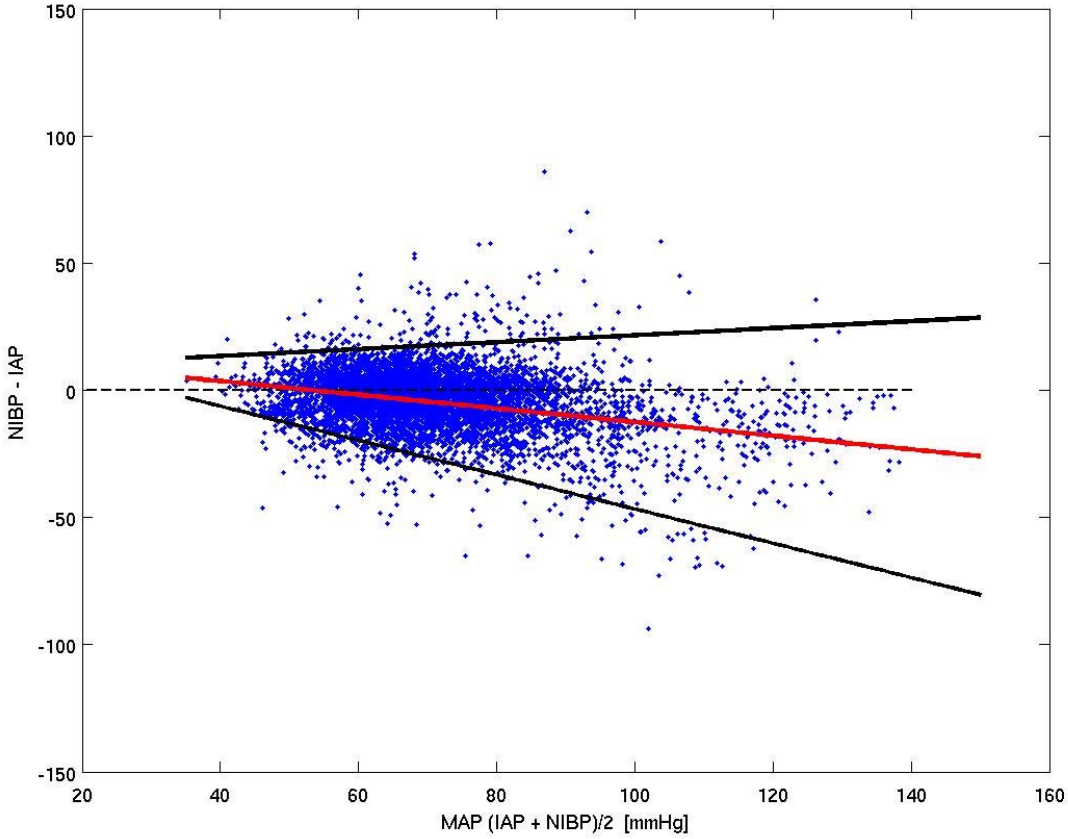


Appendix Figure 3B. No Pressor Group -- Biases and the 95% limits of agreement between concurrently measured systolic IAP/NIBP outside of the pressor treatment.

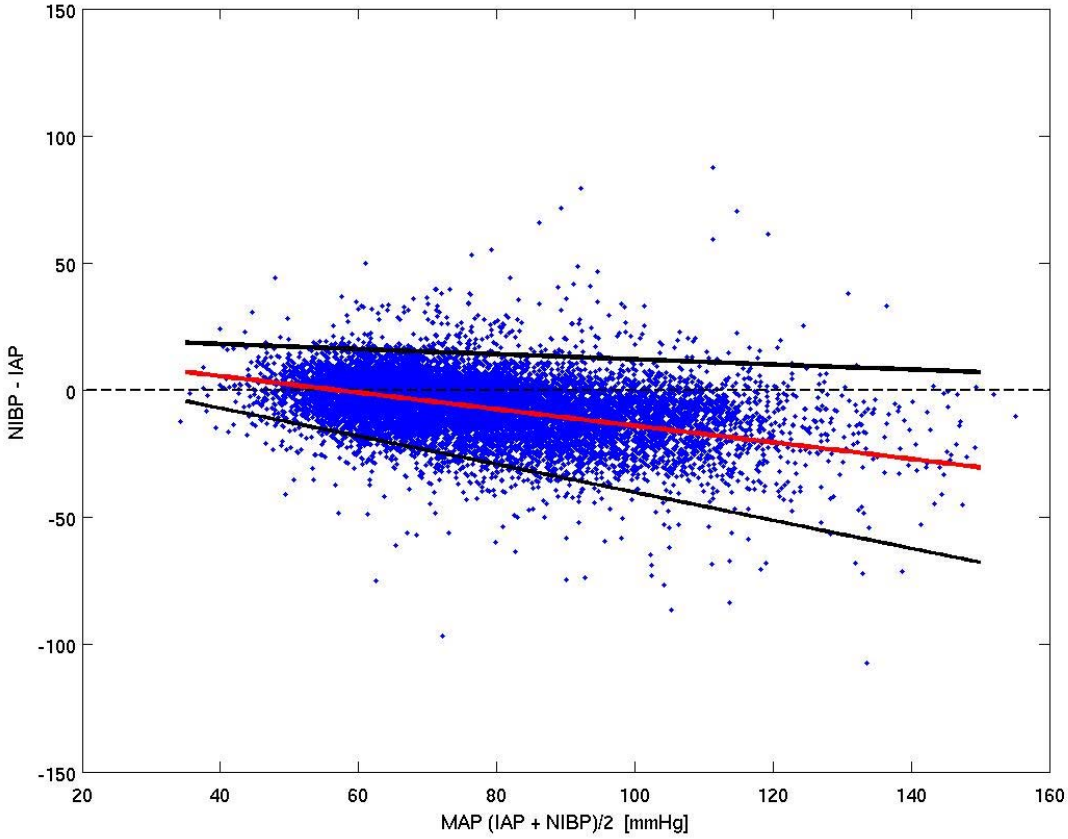
Mean Blood Pressure: Pressor vs. No-Pressor Groups

For the pressor group, the biases (with the 95% limits of agreement in parentheses) between non-invasive and invasive *mean* blood pressure measurements in the hypotensive range from 40 to 60 mmHg were 3.54 (-6.30, 13.39), 0.86 (-13.04, 14.76), -1.83 (-19.78, 16.13) mmHg respectively in each of the 10-mmHg intervals.

For the no pressor group, the biases (with the 95% limits of agreement in parentheses) between non-invasive and invasive *mean* blood pressure measurements in the hypotensive range from 40 to 60 mmHg were 5.53 (-7.10, 18.16), 2.27 (-12.61, 17.15), -0.99 (-18.12, 16.15) mmHg respectively in each of the 10-mmHg intervals.



Appendix Figure 4A. Pressor Group -- Biases and the 95% limits of agreement between concurrently measured mean IAP/NIBP during pressor treatment.

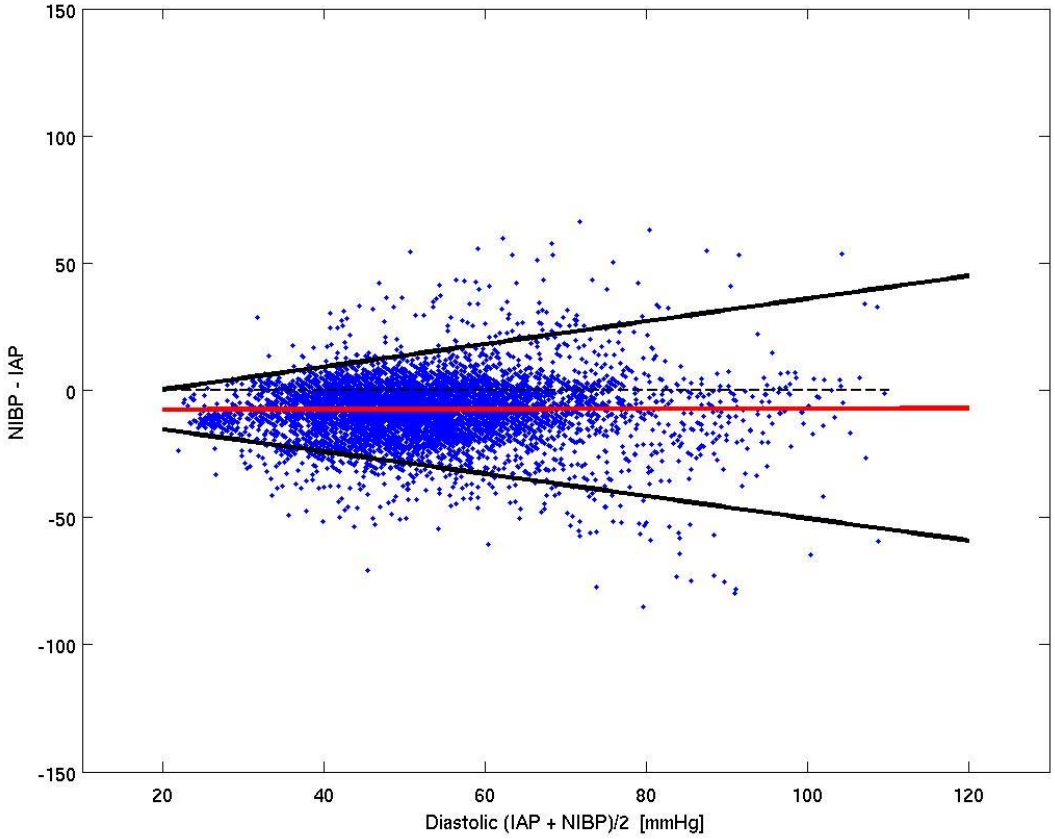


Appendix Figure 4B. No Pressor Group -- Biases and the 95% limits of agreement between concurrently measured mean IAP/NIBP outside of the pressor treatment.

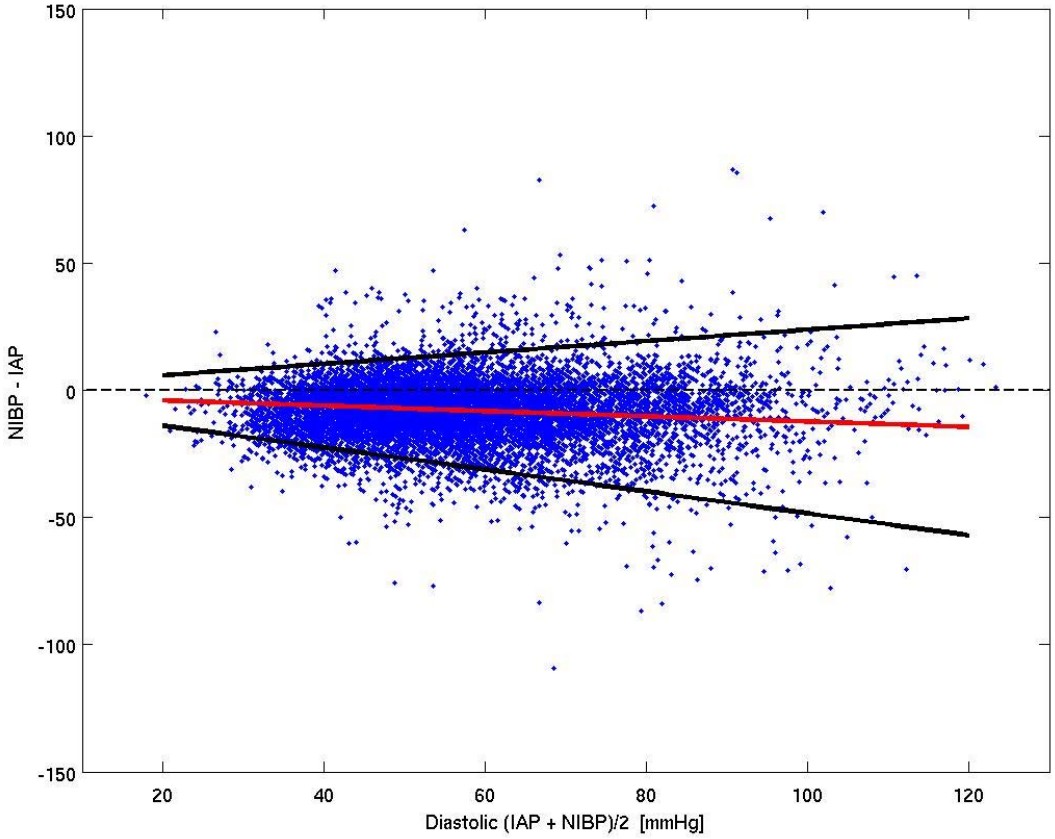
Diastolic Blood Pressure: Pressor vs. No-Pressor Groups

For the pressor group, the biases (with the 95% limits of agreement in parentheses) between non-invasive and invasive *diastolic* blood pressure measurements in the hypotensive range from 20 to 40 mmHg were -7.60 (-15.45, 0.25), -7.55 (-19.82, 4.72), -7.50 (-24.19, 9.18) mmHg respectively in each of the 10-mmHg intervals.

For the no pressor group, the biases (with the 95% limits of agreement in parentheses) between non-invasive and invasive *diastolic* blood pressure measurements in the hypotensive range from 20 to 40 mmHg were -4.05 (-13.95, 5.85), -5.09 (-18.27, 8.09), -6.13 (-22.58, 10.33) mmHg respectively in each of the 10-mmHg intervals.



Appendix Figure 5A. Pressor Group -- Biases and the 95% limits of agreement between concurrently measured diastolic IAP/NIBP during pressor treatment.



Appendix Figure 5B. No Pressor Group -- Biases and the 95% limits of agreement between concurrently measured diastolic IAP/NIBP outside of the pressor treatment.

Appendix F. Sensitivity/Specificity of IAP and NIBP in Assessing Patients' Risk for Developing AKI

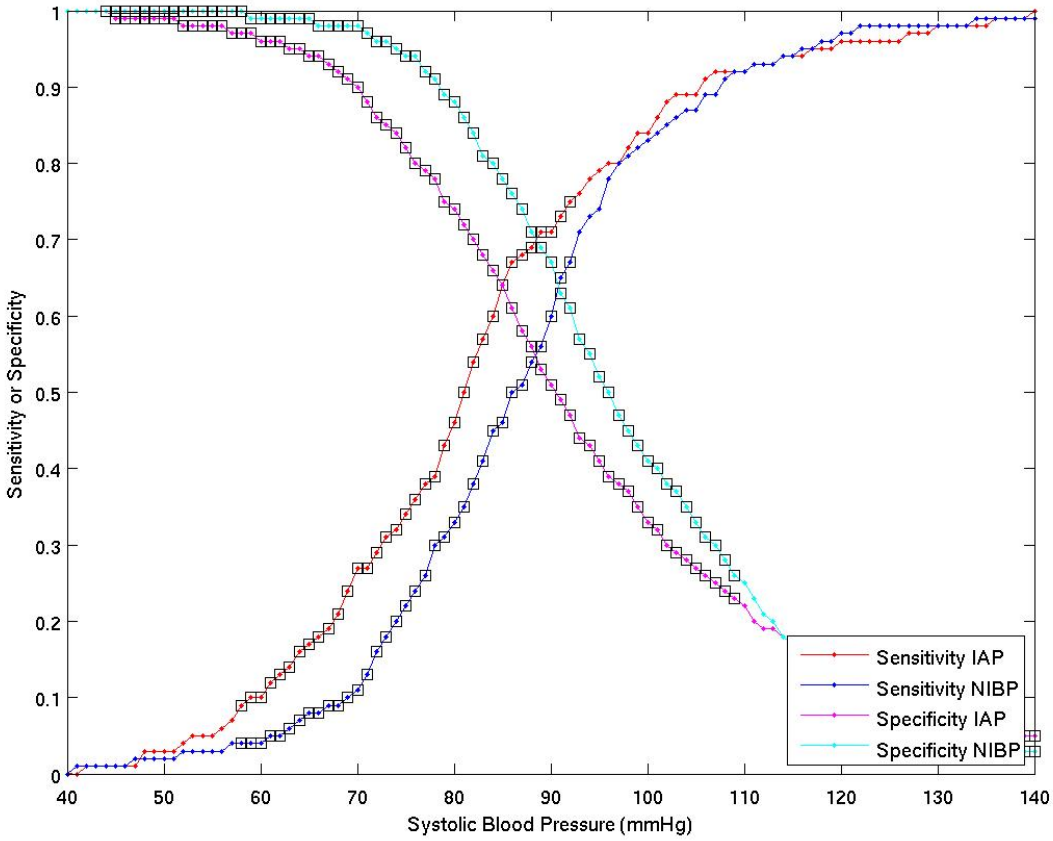
	Sensitivity Systolic <= 90 or MAP <= 60mmHg	Specificity Systolic <= 90 or MAP <= 60mmHg	AUC
Systolic IAP	0.71[§]	0.51[§]	0.66
Systolic NIBP	0.60[§]	0.67[§]	0.69
MAP IAP	0.63[¶]	0.62[§]	0.65
MAP NIBP	0.69[¶]	0.51[§]	0.66

¶ Not significantly different between invasive and non-invasive measurements. IAP vs. NIBP MAP (<=60mmHg) sensitivity P=0.10. IAP vs NIBP MAP<=65 mmHg (not shown in table) IAP sensitivity 0.76, NIBP sensitivity 0.82, P= 0.07.

§ Significantly different between invasive and non-invasive measurements (P<0.05). IAP vs NIBP *systolic* (<=90mmHg) sensitivity P=0.004, specificity P<0.001. IAP vs. NIBP MAP (<=60mmHg) specificity P<0.001.

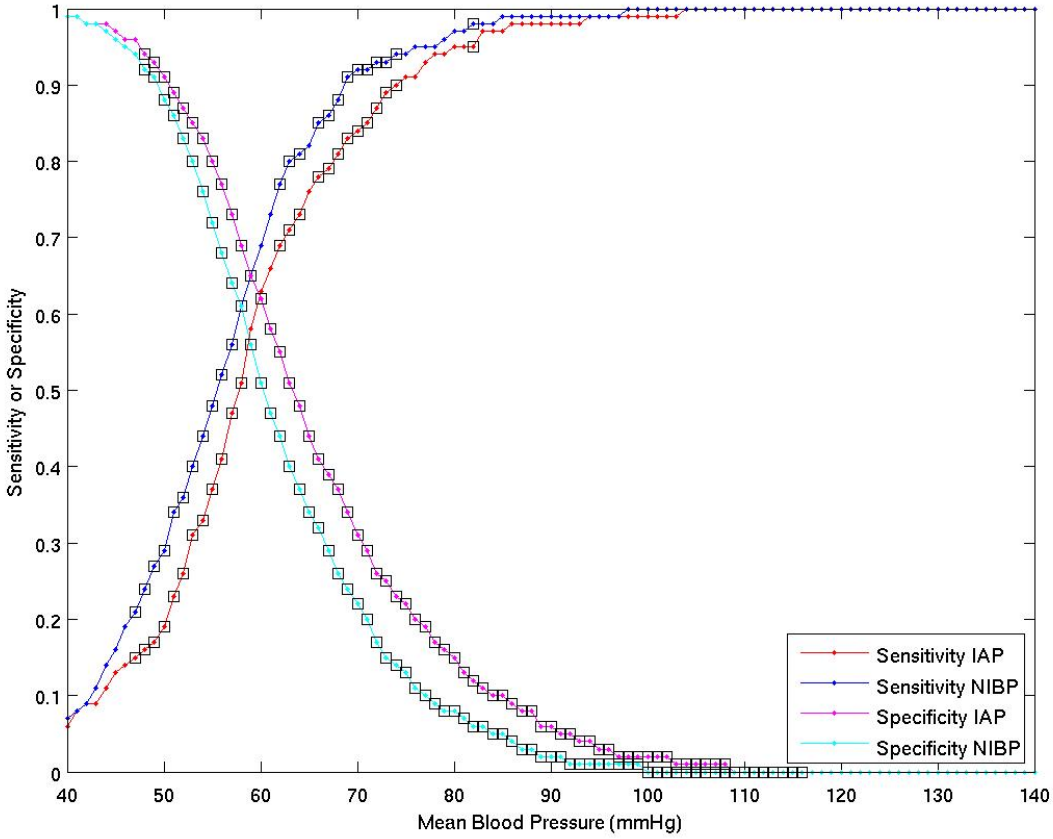
Appendix Table 3. Table shows sensitivity/specificity performance of IAP and NIBP using minimum blood pressure values (sampled from the study window described in the Materials and Methods section in the main text) for assessing patients' risk of developing AKI. Table shows sensitivity and specificity for AKI risk assessment when applying commonly used hypotension thresholds (<=90 mmHg for Systolic, or <=60 mmHg for MAP) on minimum blood pressure values in the target window. Significance of performance differences in sensitivity or specificity between invasive and non-invasive measurements was determined with the Chi-square test (significant if P<0.05).

Systolic Blood Pressure: Sensitivity/Specificity for AKI Development



Appendix Figure 6A. Sensitivity and specificity in AKI risk assessment using the minimum *systolic* blood pressure values. Subjects with at least six concurrently time-stamped IAP and NIBP blood pressure measurements in the target window were used to generate the statistics. Data points with small square black boxes indicate that the differences between invasive and non-invasive measurements are significant (p-value < 0.05). Using <=90 mmHg as a threshold, systolic IAP has a sensitivity of 0.71, which is significantly higher than systolic NIBP (p value 0.0035) using the same threshold (systolic NIBP sensitivity 0.60). The discrepancy between the sensitivity performance of *systolic* IAP and NIBP widens at lower pressures, such as 85 mmHg (IAP 0.64, NIBP 0.46, P<0.001) and 80 mmHg (IAP 0.46, NIBP 0.33, P=0.002). A higher threshold needs to be used for systolic NIBP to achieve the same sensitivity as the invasive measurement.

Mean Blood Pressure: Sensitivity/Specificity for AKI Development



Appendix Figure 6B. Sensitivity and specificity in AKI risk assessment using the minimum *mean* blood pressure values. Data points with small square black boxes indicate that the differences between invasive and non-invasive measurements were significant (p-value < 0.05). Using <=60 mmHg as a threshold, invasive and non-invasive *mean* blood pressure have a sensitivity of 0.63 and 0.69 respectively, which are not statistically significantly different (p-value 0.1019).