Supplemental Digital Content

Figure 1: Distribution of MAP baseline measurement times in hours. The mean time was 2,261.6 hours ± 1,532.5 (standard deviation). Q1 (25th) is 719.8 hours, median (50th) is 2,500.8 hours and Q3 (75th) is 3,724.9 hours. Q1, median and Q3 are indicated in the graph below with the grey line.
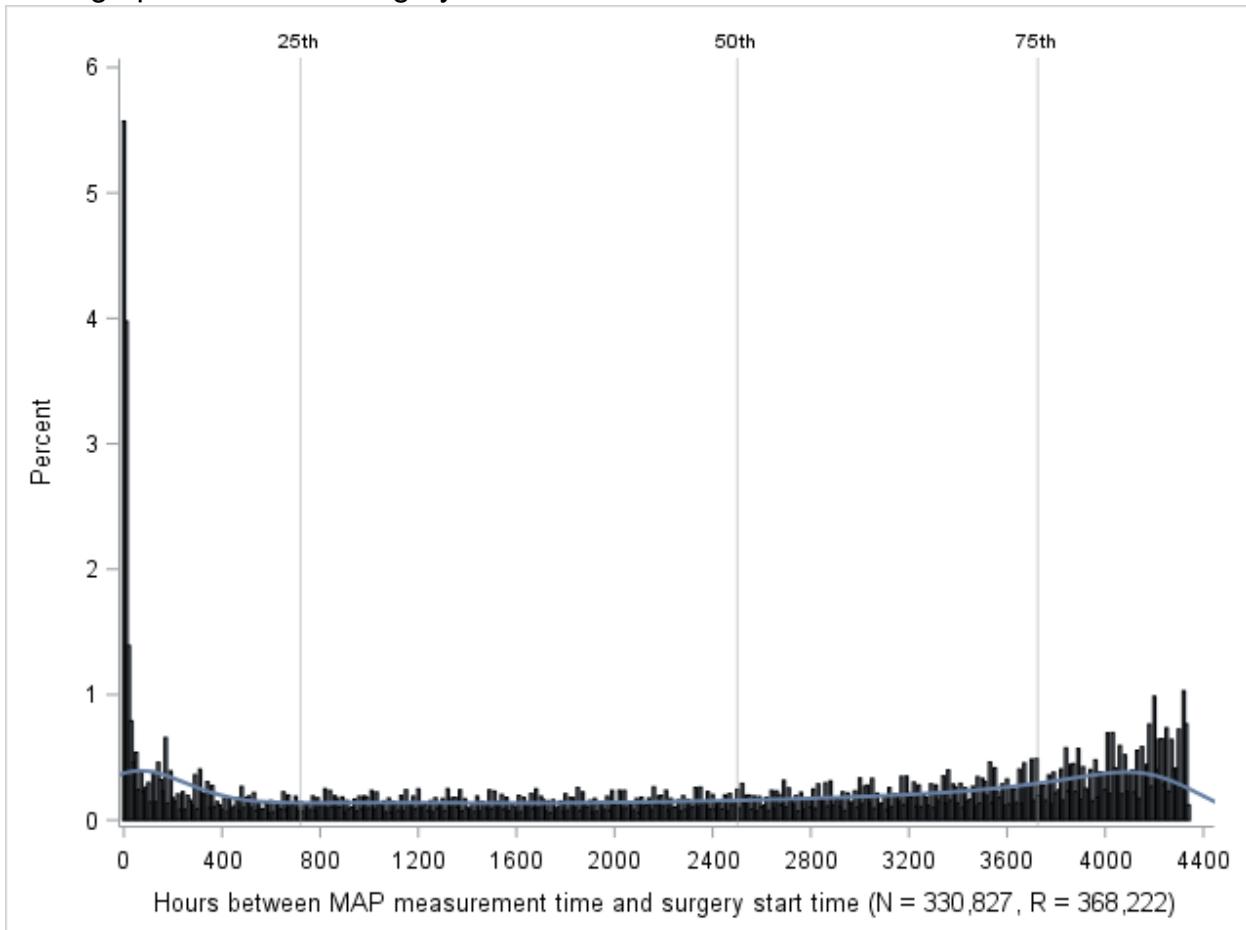
Figure 2: Methods for calculating exposures.
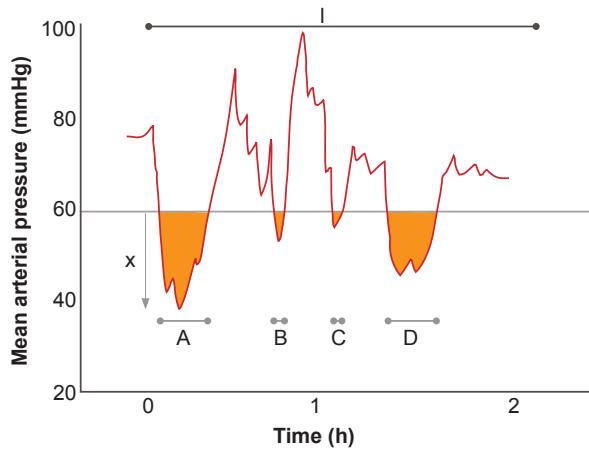
Methods

- Total duration of hypotensive episodes in minutes: A+B+C+D
- Absolute maximum decrease (AMD) in mmHg below specified MAP threshold: Lowest absolute value in ↓ (x)
- Total area under threshold (AUT): Sum of orange colored areas in mmHg/min
- Time weighted-MAP (TWA): Total AUT divided by the total OR time (I)

Footnote: The total duration of intraoperative hypotensive episodes (cumulative time) can apply to both absolute and relative intraoperative hypotensive thresholds. AUT: total area under the threshold; MAP: mean arterial pressure; OR: operating room; AMD: absolute maximum decrease (below specified MAP threshold); TWA: time-weighted average.

Figure 3. Cumulative incidence of intraoperative hypotension, by threshold, across the top 10 most common surgery types.
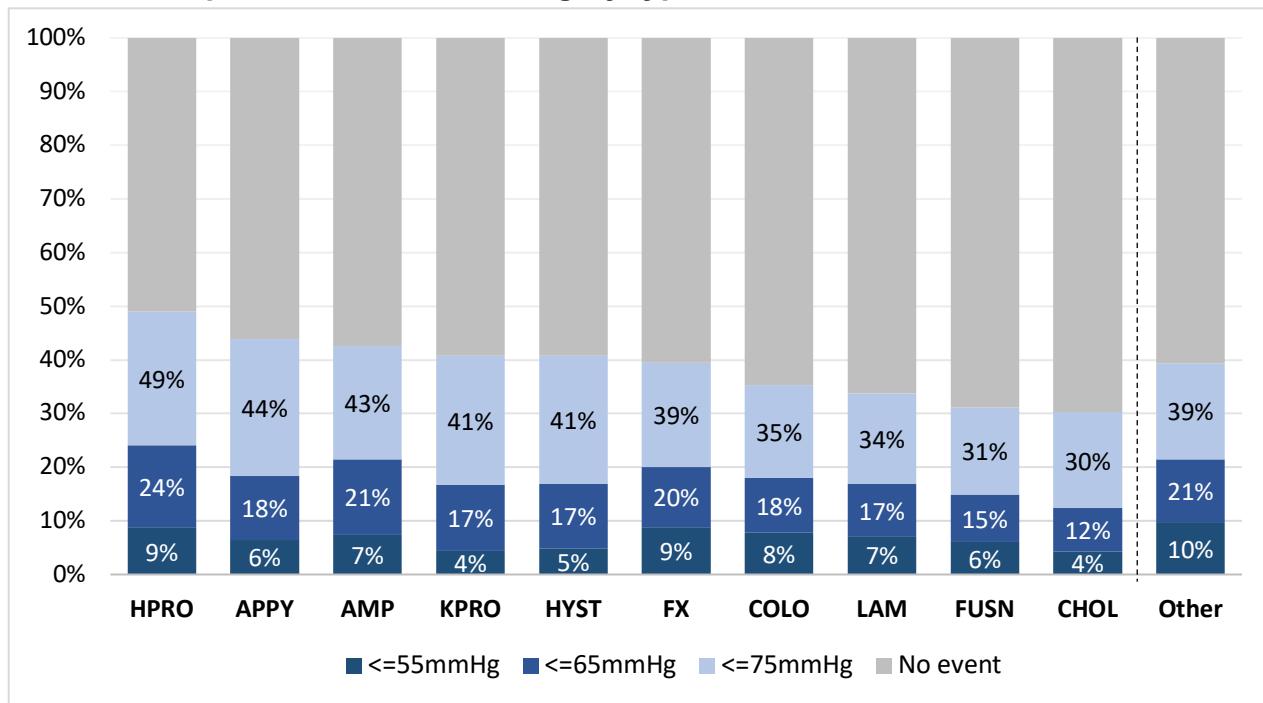
Percentages are cumulative with each threshold
**AMP: Limb amputation; APPY: Appendix; CHOL; Gallbladder; COLO: Colon; FUSN: Spinal fusion; FX: Open reduction of fracture; HPRO: Hip prosthesis; HYST: Hysterectomy; KPRO: Knee prosthesis; LAM: Laminectomy

Figure 4: Adjusted odds ratios for adverse clinical events (secondary outcomes) for all additional exposures evaluated: (A) each 5-mmHg of the time-weighted average-MAP under intraoperative hypotension MAP thresholds (B) each unit of area under intraoperative hypotension MAP thresholds (C) adverse clinical events for cumulative time (by 5-minute increments) under absolute intraoperative hypotension MAP thresholds (D) adverse clinical events for cumulative time (by 5-minute increments) under relative intraoperative hypotension MAP thresholds
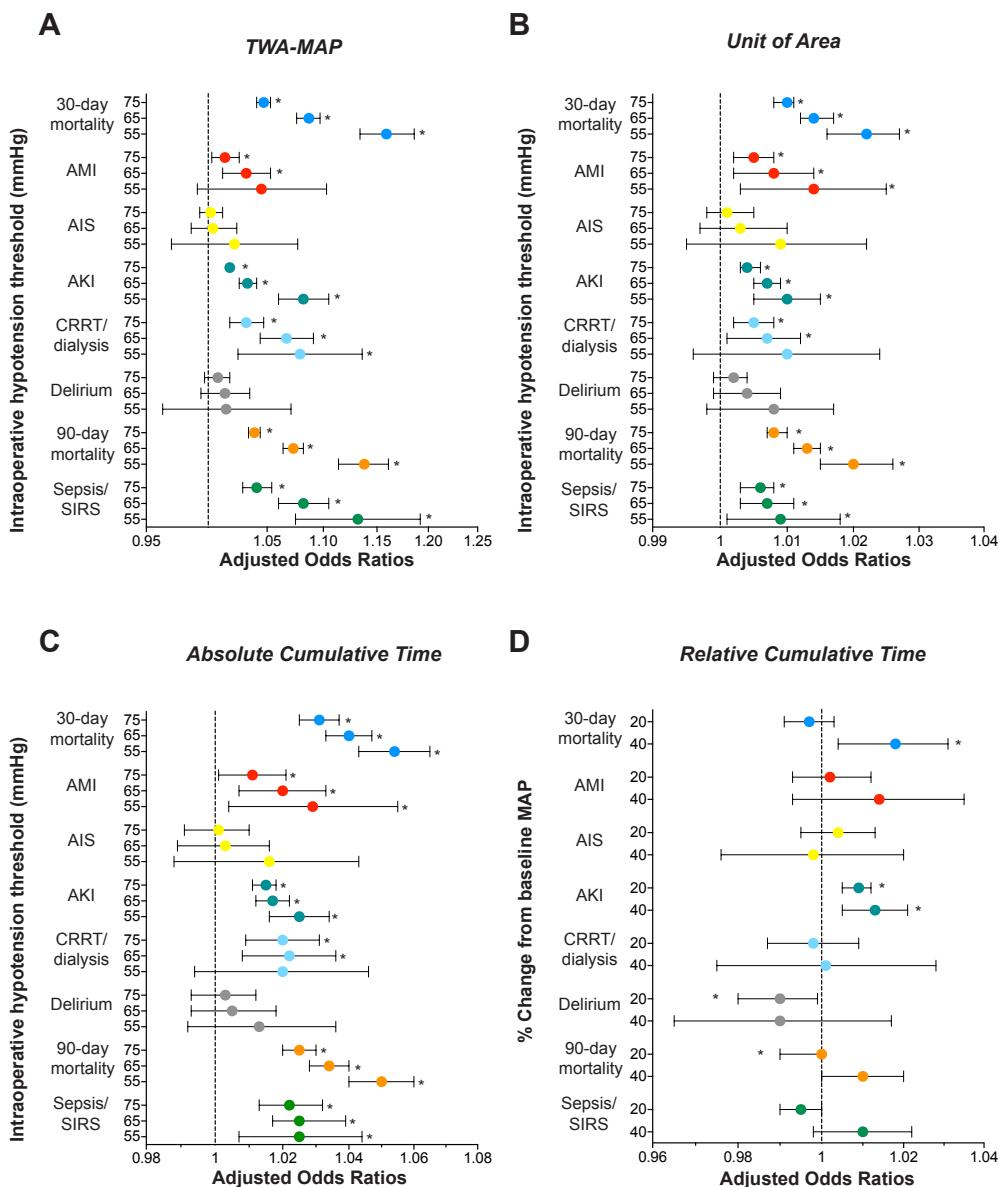
*Footnote: * denotes statistically significant findings with P≤0.05. IOH: intraoperative hypotension; TWA: time-weighted average; MAP: mean arterial pressure; AMI: acute myocardial infarction; AIS: acute ischemic stroke; AKI: acute kidney injury; CRRT: continuous renal replacement therapy; SIRS: systemic inflammatory response syndrome.*

Table 1: International Classification of Diseases (ICD) codes

Condition	ICD 9	ICD 10	CPT
Prior myocardial infarction	410, 412	I21, I22, I252	
Cerebrovascular accident	430, 431, 433, 434, 436-438	I60-I63, I6782, I69	
Chronic obstructive pulmonary disease	49, 500-505	I278, I279, J684, J701, J703, J40-J47, J60-J67	
Heart failure	428	I0981, I110, I130, I132, I50, I9713	
Valvar heart disease	424, 394-397	I34-I39, I05-I07	
Pulmonary circulatory disorder	416	I27	
Peripheral vascular disease	4439, 441, 7854, V434	I70, I71, I73, I771, I790, I792, K551, K558, K559, Z958, Z959	
Hypertension	401, 4160	I10-I13, I15, I16	
Paralysis	3441, 342	G041, G114, G801, G802, G81-G83	
Diabetes	249, 250	E08-E11, E13, E14	
Hypothyroidism	243, 244	E03, E890	
Renal disease	582, 583, 585, 586, 588	I12, I13, N03, N05, N17-N19, N25-N29, Z49, Z940, Z992	
Liver disease	570-573	K70-K77	
Lymphoma	200-202	C81-C86, C88	
Solid tumor (local + meta)	140-172, 174-198, 1990, 1991, 200-208	C0, C1, C20-C26, C30-C34, C37-C41, C43, C45-C58, C60-C85, C88, C90-C97	
Rheumatoid arthritis/collagen vascular disease	3571, 710, 714	M05, M06, M32, M34, M35	
Coagulopathy	286	D65-D68	
Obesity	278	E66	
Anemia	280-285	D50-D53, D55-D59, D61-D64	
Alcohol abuse	291, 303, 3050	F10, Z714 (excluding F1022)	
Drug abuse	292, 304, 305 (excluding 3051, 3050, 30500, 30501, 30502, 30503, 3059, 30590, 30591, 30592, 30593)	F11-F19 (excluding F1111, F1121, F1211, F1221, F1311, F1321, F1411, F1421, F1511, F1521, F1611, F1621, F17210, F17211, F17213, F17218, F17219, F17200, F17201, F17203, F17208, F17209, F17221, F17291, F1811, F1821, F1911, F1921)	
Smoking	3051, 3052	F1720, F1721	
Depression	296, 311	F32, F33, F34	
Sleep apnea	32721, 32723, 32727, 78057	G4730, G4731, G4733, G4737, R0681	
Dementia	290	F051, G311, F00, F01, F02, F03, G30	
Supplemental oxygen use	V462	Z9981	

Table 1: International Classification of Diseases (ICD) codes (continued)

Condition	ICD 9	ICD 10	CPT
Dialysis	39.95, 54.98	5A1D70Z, 5A1D80Z, 5A1D90Z, 5A1D00Z, 3E1M39Z	90935, 90937, 90945, 90947, 4054F, 4055F
Coronary artery bypass grafting	36.10-36.16, 36.2	0210093, 02100A3, 02100J3, 02100K3, 02100Z3, 210493, 02104A3, 02104J3, 02104K3, 02104Z3, 021008W, 021009W, 02100AW, 02100JW, 02100KW, 021048W, 021049W, 02104AW, 02104JW, 02104KW, 021108W, 021109W, 02110AW, 02110JW, 02110KW, 021148W, 021149W, 02114AW, 02114JW, 02114KW, 021208W, 021209W, 02120AW, 02120JW, 02120KW, 021248W, 021249W, 02124AW, 02124JW, 02124KW, 021308W, 021309W, 02130AW, 02130JW, 02130KW, 021348W, 021349W, 02134AW, 02134JW, 02134KW, 210088, 210089, 021008C, 210098, 210099, 021009C, 02100A8, 02100A9, 02100AC, 02100J8, 02100J9, 02100JC, 02100K8, 02100K9, 02100KC, 02100Z8, 02100Z9, 02100ZC, 210488, 210489, 021048C, 210498, 210499, 021049C, 02104A8, 02104A9, 02104AC, 02104J8, 02104J9, 02104JC, 02104K8, 02104K9, 02104KC, 02104Z8, 02104Z9, 02104ZC, 211088, 211089, 021108C, 211098, 211099, 021109C, 02110A8, 02110A9, 02110AC, 02110J8, 02110J9, 02110JC, 02110K8, 02110K9, 02110KC, 02110Z8, 02110Z9, 02110ZC, 211488, 211489, 021148C, 211498, 211499, 021149C, 02114A8, 02114A9, 02114AC, 02114J8, 02114J9, 02114JC, 02114K8, 02114K9, 02114KC, 02114Z8, 02114Z9, 02114ZC, 021208C, 021209C, 02120AC, 02120JC, 02120KC, 02120ZC, 021248C, 021249C, 02124AC, 02124JC, 02124KC, 02124ZC, 021308C, 021309C, 02130AC, 02130JC, 02130KC, 02130ZC, 021348C, 021349C, 02134AC, 02134JC, 02134KC, 02134ZC	33510, 33511, 33512, 33513, 33514, 33516, 33517, 33518, 33519, 33521, 33522, 33523, 33530, 33534, 33535, 33536
Percutaneous coronary intervention	00.66, 36.07	02703, 02704, 02713, 02714, 02723, 02724, 02733, 02734	92920, 92924, 92928, 92933, 92937, 92941, 92943
Continuous renal replacement therapy	39.95	5A1D90Z	90935, 90937, 4054F
Acute myocardial infarction	410	I21, I22	

Table 1: International Classification of Diseases (ICD) codes (continued)

Acute ischemic stroke	43301, 43311, 43321, 43331, 43381, 43391, 43401, 43411, 43491, 436, 4371	I63	
Acute kidney injury	584	N17	
Delirium	F05	29011, 2903, 2930, 2931, 30011, 308, 78009, 78039	
Electrolyte disorders	276	E87	
Sepsis/SIRS	028, 77181, 9959	A40, A41, P36, R65	

Table 2: E-values to assess the magnitude of an unobserved or unaccounted confounding effect for intraoperative hypotension using absolute maximum decrease. E-values were calculated for AMD exposure hazard ratios to determine unobserved or unaccounted confounding effects for IOH at three thresholds for primary and secondary endpoints. E-values represent the effect size required for an unmeasured confounding to reduce the observed effect to OR 1.0.

E-Values	MAP Threshold		
	≤55-mmHg	≤65-mmHg	≤75-mmHg
MACCE	1.83	1.62	1.49
30-day mortality	1.92	1.71	1.59
AMI	1.49	1.43	1.34
AIS	1.16	1.00	1.00
AKI	1.49	1.37	1.31
CRRT/dialysis	1.49	1.49	1.43
Delirium	1.34	1.28	1.24
90-day mortality	1.83	1.62	1.51
Sepsis/SIRS	1.88	1.71	1.57

Footnote: E-values were calculated as previously described by VanderWeele and Ding
(VanderWeele TJ, Ding P. Sensitivity Analysis in Observational Research: Introducing the E-Value. Annals of Internal Medicine. 2017;167(4):268.
*Specifically, following formula was used: **E-value=HR+sqrt{HR×(HR-1)}***
This formula applies to a risk ratio greater than 1; for a risk ratio less than 1, we first took the inverse of the observed risk ratio and then applied the same formula.

Table 3. Incidence of outcomes in total cohort.

Outcome	Incidence
MACCE (all-cause mortality, AMI, or AIS)	10,071 (2.73%)
30-day mortality	6,335 (1.72%)
90-day mortality	9,384 (2.54%)
AMI	1,674 (0.45%)
AKI	19,569 (5.66%)
AIS	2,482 (0.68%)
Delirium	1,872 (0.51%)
Dialysis/CRRT	1,115 (0.31%)
Sepsis/SIRS	1,370 (0.36%)

Footnote: Patients who had history of an event in the seven days prior to surgery were excluded from the corresponding outcome analysis. MACCE: major adverse cardiac and cerebrovascular event, comprised of a composite measure of all-cause mortality, acute myocardial infarction (AMI), or acute ischemic stroke (AIS). AMI: acute myocardial infarction; AKI: acute kidney injury; AIS: acute ischemic stroke; CRRT: continuous renal replacement therapy; SIRS: systemic inflammatory response syndrome

Table 4. Key stratification of odds ratios for the likelihood of MACCE and AKI by using absolute maximum decrease (AMD) and time-weighted average (TWA) of MAP below MAP threshold.

MACCE	≤55-mmHg		≤65-mmHg		≤75-mmHg	
	AMD OR (95% CI)	TWA OR (95% CI)	AMD OR (95% CI)	TWA OR (95% CI)	AMD OR (95% CI)	TWA OR (95% CI)
Sex						
Male	1.24 (1.19, 1.29)	1.14 (1.11, 1.18)	1.16 (1.13, 1.19)	1.08 (1.06, 1.09)	1.12 (1.10, 1.14)	1.03 (1.03, 1.04)
Female	1.28 (1.23, 1.33)	1.14 (1.11, 1.17)	1.18 (1.15, 1.21)	1.06 (1.05, 1.07)	1.12 (1.11, 1.14)	1.03 (1.03, 1.04)
Age						
< 65 years old	1.28 (1.22, 1.34)	1.15 (1.11, 1.19)	1.19 (1.15, 1.22)	1.08 (1.06, 1.09)	1.13 (1.11, 1.16)	1.03 (1.03, 1.04)
> 65 years old	1.25 (1.20, 1.29)	1.14 (1.11, 1.17)	1.17 (1.14, 1.19)	1.07 (1.06, 1.08)	1.12 (1.10, 1.13)	1.03 (1.03, 1.04)
CCI						
0	1.39 (1.28, 1.50)	1.22 (1.16, 1.29)	1.24 (1.17, 1.30)	1.08 (1.05, 1.11)	1.15 (1.10, 1.19)	1.03 (1.01, 1.04)
1	1.16 (1.07, 1.26)	1.06 (1.00, 1.13)	1.13 (1.07, 1.18)	1.06 (1.03, 1.08)	1.1 (1.07, 1.14)	1.03 (1.02, 1.04)
2	1.29 (1.19, 1.39)	1.19 (1.13, 1.26)	1.2 (1.14, 1.25)	1.07 (1.04, 1.09)	1.13 (1.10, 1.17)	1.03 (1.01, 1.04)
3	1.22 (1.13, 1.33)	1.15 (1.09, 1.22)	1.17 (1.11, 1.22)	1.08 (1.05, 1.10)	1.12 (1.08, 1.16)	1.04 (1.02, 1.05)
4+	1.24 (1.19, 1.30)	1.12 (1.09, 1.15)	1.15 (1.12, 1.18)	1.06 (1.05, 1.08)	1.11 (1.09, 1.13)	1.03 (1.03, 1.04)
Surgery length						
< 30min	1.38 (1.29, 1.48)	1.12 (1.09, 1.16)	1.24 (1.20, 1.29)	1.07 (1.06, 1.08)	1.16 (1.14, 1.19)	1.03 (1.03, 1.04)
30-60min	1.33 (1.25, 1.41)	1.14 (1.09, 1.18)	1.2 (1.16, 1.24)	1.06 (1.05, 1.08)	1.12 (1.10, 1.15)	1.03 (1.02, 1.04)
60-120min	1.23 (1.16, 1.29)	1.15 (1.10, 1.21)	1.14 (1.10, 1.18)	1.07 (1.05, 1.09)	1.09 (1.07, 1.12)	1.03 (1.02, 1.04)
120min+	1.18 (1.11, 1.26)	1.18 (1.11, 1.26)	1.12 (1.07, 1.16)	1.07 (1.04, 1.10)	1.09 (1.05, 1.13)	1.04 (1.02, 1.06)
Surgery type						
CHOL	1.38 (1.11, 1.71)	1.06 (0.89, 1.26)	1.22 (1.07, 1.38)	1.06 (1.00, 1.12)	1.16 (1.07, 1.26)	1.04 (1.01, 1.07)
FUSN	1.45 (1.20, 1.74)	1.32 (1.12, 1.54)	1.26 (1.11, 1.42)	1.08 (1.01, 1.15)	1.18 (1.09, 1.29)	1.03 (1.00, 1.07)
FX	1.22 (1.10, 1.35)	1.08 (1.01, 1.16)	1.14 (1.07, 1.21)	1.06 (1.03, 1.09)	1.12 (1.08, 1.17)	1.04 (1.02, 1.06)
HPRO	1.14 (1.01, 1.28)	1.05 (0.96, 1.15)	1.08 (1.01, 1.16)	1.04 (1.01, 1.07)	1.04 (0.99, 1.08)	1.00 (0.99, 1.02)
KRPO	1.41 (1.14, 1.73)	1.17 (1.00, 1.37)	1.14 (1.01, 1.28)	1.00 (0.95, 1.05)	1.03 (0.96, 1.11)	0.99 (0.97, 1.01)
Year						
2008-2014	1.27 (1.21, 1.33)	1.13 (1.10, 1.16)	1.17 (1.14, 1.21)	1.06 (1.05, 1.07)	1.12 (1.10, 1.14)	1.03 (1.02, 1.04)
2015-2017	1.26 (1.21, 1.31)	1.15 (1.12, 1.18)	1.17 (1.15, 1.2)	1.08 (1.07, 1.09)	1.12 (1.11, 1.14)	1.04 (1.03, 1.04)
Time of day						
Day	1.23 (1.19, 1.27)	1.14 (1.11, 1.17)	1.15 (1.13, 1.18)	1.06 (1.05, 1.07)	1.11 (1.09, 1.12)	1.03 (1.03, 1.04)
Night	1.42 (1.32, 1.52)	1.16 (1.11, 1.21)	1.27 (1.22, 1.32)	1.1 (1.08, 1.12)	1.19 (1.15, 1.22)	1.05 (1.03, 1.06)
Day of week						
Weekday	1.25 (1.21, 1.30)	1.15 (1.12, 1.17)	1.17 (1.15, 1.19)	1.07 (1.06, 1.08)	1.12 (1.10, 1.13)	1.03 (1.03, 1.04)
Weekend	1.29 (1.21, 1.36)	1.13 (1.09, 1.18)	1.18 (1.14, 1.22)	1.07 (1.05, 1.09)	1.13 (1.10, 1.16)	1.03 (1.02, 1.04)

(continued)

Table 4. Key stratification of odds ratios for the likelihood of MACCE and AKI by using absolute maximum decrease (AMD) and time-weighted average (TWA) of MAP below MAP threshold. (continued)

AKI	≤55-mmHg		≤65-mmHg		≤75-mmHg	
	AMD OR (95% CI)	TWA OR (95% CI)	AMD OR (95% CI)	TWA OR (95% CI)	AMD OR (95% CI)	TWA OR (95% CI)
Sex						
Male	1.14 (1.09, 1.19)	1.11 (1.08, 1.15)	1.09 (1.06, 1.11)	1.04 (1.03, 1.05)	1.07 (1.05, 1.08)	1.02 (1.02, 1.03)
Female	1.11 (1.07, 1.15)	1.07 (1.04, 1.10)	1.08 (1.06, 1.11)	1.03 (1.02, 1.04)	1.06 (1.04, 1.07)	1.02 (1.01, 1.02)
Age						
< 65 years old	1.16 (1.11, 1.20)	1.11 (1.08, 1.14)	1.11 (1.08, 1.14)	1.04 (1.03, 1.06)	1.08 (1.06, 1.10)	1.02 (1.01, 1.02)
> 65 years old	1.09 (1.05, 1.14)	1.06 (1.03, 1.09)	1.07 (1.04, 1.09)	1.03 (1.02, 1.04)	1.05 (1.03, 1.06)	1.02 (1.01, 1.02)
CCI						
0	1.21 (1.14, 1.28)	1.13 (1.08, 1.18)	1.13 (1.09, 1.17)	1.05 (1.03, 1.06)	1.08 (1.06, 1.11)	1.02 (1.01, 1.03)
1	1.15 (1.07, 1.23)	1.13 (1.07, 1.19)	1.11 (1.07, 1.16)	1.04 (1.02, 1.06)	1.08 (1.06, 1.11)	1.02 (1.01, 1.03)
2	1.04 (0.97, 1.12)	1.06 (1.01, 1.12)	1.05 (1.01, 1.09)	1.02 (1.00, 1.04)	1.04 (1.01, 1.07)	1.01 (1.00, 1.02)
3	1.07 (0.98, 1.16)	1.13 (1.07, 1.20)	1.06 (1.01, 1.11)	1.04 (1.02, 1.06)	1.05 (1.02, 1.08)	1.02 (1.01, 1.03)
4+	1.12 (1.07, 1.18)	1.05 (1.02, 1.09)	1.07 (1.04, 1.10)	1.03 (1.02, 1.04)	1.06 (1.04, 1.08)	1.02 (1.01, 1.02)
Surgery length						
< 30min	1.25 (1.16, 1.35)	1.09 (1.05, 1.13)	1.14 (1.10, 1.19)	1.03 (1.02, 1.04)	1.09 (1.07, 1.11)	1.02 (1.01, 1.02)
30-60min	1.13 (1.05, 1.21)	1.07 (1.03, 1.12)	1.09 (1.05, 1.13)	1.04 (1.02, 1.05)	1.07 (1.05, 1.09)	1.02 (1.01, 1.03)
60-120min	1.07 (1.02, 1.13)	1.09 (1.05, 1.14)	1.06 (1.02, 1.09)	1.04 (1.02, 1.06)	1.05 (1.03, 1.07)	1.03 (1.02, 1.04)
120min+	1.17 (1.11, 1.22)	1.14 (1.09, 1.20)	1.12 (1.08, 1.15)	1.05 (1.02, 1.07)	1.09 (1.06, 1.12)	1.02 (1.00, 1.03)
Surgery type						
CHOL	1.28 (1.03, 1.58)	1.08 (0.90, 1.29)	1.15 (1.02, 1.28)	1.03 (0.97, 1.09)	1.09 (1.02, 1.17)	1.02 (1.00, 1.05)
FUSN	1.12 (0.93, 1.36)	1.12 (0.97, 1.29)	1.14 (1.03, 1.26)	1.05 (1.00, 1.10)	1.16 (1.09, 1.24)	1.05 (1.03, 1.08)
FX	1.12 (1.00, 1.25)	1.07 (0.98, 1.16)	1.12 (1.05, 1.19)	1.04 (1.01, 1.07)	1.09 (1.05, 1.14)	1.03 (1.01, 1.04)
HPRO	1.13 (1.03, 1.23)	1.05 (0.98, 1.12)	1.08 (1.03, 1.13)	1.03 (1.01, 1.05)	1.05 (1.02, 1.08)	1.01 (1.00, 1.02)
KRPO	1.05 (0.91, 1.21)	1.04 (0.96, 1.14)	1.04 (0.98, 1.10)	1.00 (0.98, 1.03)	1.02 (0.98, 1.05)	1.00 (0.99, 1.01)
Year						
2008-2014	1.07 (1.02, 1.12)	1.08 (1.05, 1.11)	1.06 (1.03, 1.09)	1.03 (1.02, 1.04)	1.05 (1.03, 1.07)	1.01 (1.01, 1.02)
2015-2017	1.16 (1.12, 1.20)	1.10 (1.07, 1.13)	1.1 (1.08, 1.12)	1.04 (1.03, 1.05)	1.07 (1.06, 1.08)	1.02 (1.01, 1.02)
Time of day						
Day	1.12 (1.09, 1.15)	1.08 (1.06, 1.11)	1.08 (1.06, 1.10)	1.03 (1.02, 1.04)	1.06 (1.05, 1.07)	1.02 (1.01, 1.02)
Night	1.19 (1.09, 1.31)	1.15 (1.09, 1.21)	1.15 (1.09, 1.21)	1.07 (1.04, 1.09)	1.11 (1.07, 1.15)	1.04 (1.02, 1.05)
Day of week						
Weekday	1.14 (1.1, 1.17)	1.09 (1.07, 1.12)	1.09 (1.07, 1.11)	1.04 (1.03, 1.04)	1.06 (1.05, 1.08)	1.02 (1.01, 1.02)
Weekend	1.10 (1.03, 1.17)	1.09 (1.05, 1.14)	1.07 (1.03, 1.11)	1.03 (1.02, 1.05)	1.06 (1.03, 1.08)	1.02 (1.01, 1.03)

Footnote: MACCE: major adverse cardiac and cerebrovascular event; AKI: acute kidney injury; CHOL: Gallbladder; FUSN: Spinal fusion; FX: Open reduction of fracture; HPRO: Hip prosthesis; KPRO: Knee prosthesis; CCI: charlson comorbidity index; MAP: mean arterial pressure; AMD: absolute maximum decrease (below specified MAP threshold); TWA: time-weighted average OR: Odds ratio; CI: confidence interval.

Table 5: P-values (for key stratification [S] and interaction [I]) for MACCE and AKI outcomes for every 5-mmHg of absolute maximum decrease (AMD) and time-weighted average (TWA) below thresholds.

MACCE	≤55-mmHg				≤65-mmHg				≤75-mmHg			
	AMD		TWA		AMD		TWA		AMD		TWA	
	S p-value	I p-value	S p-value	I p-value	S p-value	I p-value	S p-value	I p-value	S p-value	I p-value	S p-value	I p-value
Sex												
Male	<0.001	0.1850	<0.001	0.941	<0.001	0.2186	<0.001	0.445	<0.001	0.2080	<0.001	0.359
Female	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Age												
< 65 years old	<0.001	0.4110	<0.001	0.442	<0.001	0.1926	<0.001	0.130	<0.001	0.1478	<0.001	0.890
> 65 years old	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
CCI												
0	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.003	<0.001	0.0001	<0.001	0.641
1	<0.001		0.059		<0.001		<0.001		<0.001		<0.001	
2	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
3	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
4+	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Surgery length												
< 30min	<0.001	<0.001	<0.001	0.542	<0.001	<0.001	<0.001	0.688	<0.001	<.0001	<0.001	0.449
30-60min	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
60-120min	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
120min+	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Surgery type												
CHOL	0.004	0.1075	0.510	0.017	0.003	0.0081	0.049	<0.001	<0.001	<0.001	0.005	<0.001
FUSN	<0.001		0.001		<0.001		0.024		<0.001		0.063	
FX	<0.001		0.034		<0.001		<0.001		<0.001		<0.001	
HPRO	0.038		0.256		0.027		0.007		0.135		0.595	
KRPO	0.001		0.050		0.033		0.858		0.446		0.322	
Year												
2008-2014	<0.001	0.1469	<0.001	0.743	<0.001	0.1372	<0.001	0.138	<0.001	0.2350	<0.001	0.977
2015-2017	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Time of day												
Day	<0.001	<0.001	<0.001	0.1918	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.002
Night	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Day of week												
Weekday	<0.001	0.6077	<0.001	0.2230	<0.001	0.8042	<0.001	0.576	<0.001	0.5842	<0.001	0.956
Weekend	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	

(continued)

Table 5: P-values (for key stratification [S] and interaction [I]) for MACCE and AKI outcomes for every 5-mmHg of absolute maximum decrease (AMD) and time-weighted average (TWA) below thresholds. (continued)

AKI	≤55-mmHg				≤65-mmHg				≤75-mmHg			
	AMD OR (95% CI)		TWA OR (95% CI)		AMD OR (95% CI)		TWA OR (95% CI)		AMD OR (95% CI)		TWA OR (95% CI)	
	S p-value	I p-value	S p-value	I p-value	S p-value	I p-value	S p-value	I p-value	S p-value	I p-value	S p-value	I p-value
Sex												
Male	<0.001	0.738	<0.001	0.443	<0.001	0.143	<0.001	0.442	<0.001	0.128	<0.001	0.332
Female	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Age												
< 65 years old	<0.001	0.007	<0.001	0.014	<0.001	0.001	<0.001	0.006	<0.001	<0.001	<0.001	0.260
> 65 years old	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
CCI												
0	<0.001	0.008	<0.001	0.004	<0.001	0.025	<0.001	0.262	<0.001	0.214	<0.001	0.388
1	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
2	0.301		0.028		0.018		0.019		0.0053		0.031	
3	0.116		<0.001		0.014		<0.001		0.0014		0.003	
4+	<0.001		0.005		<0.001		<0.001		<0.001		<0.001	
Surgery length												
< 30min	<0.001	0.002	<0.001	0.190	<0.001	<0.001	<0.001	0.370	<0.001	0.001	<0.001	0.362
30-60min	0.001		0.002		<0.001		<0.001		<0.001		<0.001	
60-120min	0.009		<0.001		0.001		<0.001		<0.001		<0.001	
120min+	<0.001		<0.001		<0.001		<0.001		<0.001		0.014	
Surgery type												
CHOL	0.024	0.554	0.400	0.216	0.018	0.044	0.317	0.001	0.0122	<0.001	0.043	<0.001
FUSN	0.240		0.137		0.015		0.061		<0.001		<0.001	
FX	0.049		0.112		0.001		0.009		<0.001		0.001	
HPRO	0.007		0.189		0.003		0.008		0.0035		0.042	
KRPO	0.496		0.335		0.256		0.786		0.3243		0.977	
Year												
2008-2014	0.004	<0.001	<0.001	0.088	<0.001	<0.001	<0.001	0.108	<0.001	0.001	<0.001	0.032
2015-2017	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Time of day												
Day	<0.001	0.042	<0.001	0.034	<0.001	0.008	<0.001	0.002	<0.001	0.005	<0.001	0.003
Night	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Day of week												
Weekday	<0.001	0.588	<0.001	0.900	<0.001	0.785	<0.001	0.888	<0.001	0.746	<0.001	0.356
Weekend	0.004		<0.001		<0.001		<0.001		<0.001		<0.001	

Footnote: S: Stratification; I: Interaction; MACCE: major adverse cardiac and cerebrovascular event; AKI: acute kidney injury; CHOL: Gallbladder; FUSN: Spinal fusion; FX: Open reduction of fracture; HPRO: Hip prosthesis; KPRO: Knee prosthesis; CCI: charlson comorbidity index; CI: confidence interval, MAP: mean arterial pressure; AMD: absolute maximum decrease (below specified MAP threshold); TWA: time-weighted average OR: Odds ratio; CI: confidence interval.

Table 6: Number of patients in each age category by MAP threshold and general MACCE and AKI outcomes stratified by age group.

	All patients (n = 363,439)	18-40 (n = 42,783)	41-50 (n = 47,504)	51-60 (n = 78,364)	61-70 (n = 94,454)	71-80 (n = 66,260)	> 80 (n = 34,074)
Number of patients in each age Category by MAP threshold							
≤55-mmHg	25,944 (7.1%)	2,931 (6.9%)	2,843 (6.0%)	5,217 (6.7%)	6,866 (7.3%)	5,093 (7.7%)	2,994 (8.8%)
>55-mmHg	337,495 (92.9%)	39,852 (93.2%)	44,661 (94.0%)	73,147 (93.3%)	87,588 (92.7%)	61,167 (92.3%)	31,080 (91.2)
≤65-mmHg	68,612 (18.9%)	7,466 (17.5%)	7,676 (16.2%)	13,783 (17.6%)	18,483 (19.6%)	13,651 (20.6%)	7,553 (22.2%)
>65-mmHg	294,827 (81.1%)	35,317 (82.6%)	39,828 (83.8%)	64,581 (82.4%)	75,971 (80.4%)	52,609 (79.4%)	26,521 (77.8%)
≤75-mmHg	142,387 (39.2%)	16,390 (38.3%)	16,757 (35.3%)	28,724 (36.7%)	38,108 (40.4%)	27,767 (41.9%)	14,641 (43.0%)
>75-mmHg	221,052 (60.8%)	26,393 (61.7%)	30,747 (64.7%)	49,640 (63.4%)	56,346 (59.7%)	38,493 (58.1%)	19,433 (57.0%)
General MACCE and AKI outcomes by age							
30-day MACCE	10,009 (2.8%)	273 (0.6%)	456 (1.0%)	1,374 (1.8%)	2,309 (2.4%)	2,686 (4.1%)	2.911 (8.5%)
AKI	19,444 (5.4%)	988 (2.3%)	1,690 (3.6%)	3,943 (5.0%)	5,541 (5.9%)	4,465 (6.7%)	2,817 (8.3%)

Table 7: Odds ratios for the likelihood of MACCE and AKI with hypotension, stratified by age groups, for both AMD and TWA of MAP exposures.

MACCE AMD and TWA ORs											
			≤55-mmHg			≤65-mmHg			≤75-mmHg		
Age Range	Overall No. Patients	patients with MACCE (%)	patients with MACCE (%)	AMD OR (99.72% CI)	TWA OR (99.72% CI)	patients with MACCE (%)	AMD OR (99.72% CI)	TWA OR (99.72% CI)	patients with MACCE (%)	AMD OR (99.72% CI)	TWA OR (99.72% CI)
18-40	42,783	273 (0.6%)	58 (2.0%)	1.42 * (1.12, 1.80)	1.33 * (1.14,1.54)	107 (1.4%)	1.37 * (1.18, 1.58)	1.15 * (1.09, 1.22)	141 (0.9%)	1.27 * (1.16, 1.39)	1.07 * (1.03, 1.10)
41-50	47,504	456 (1.0%)	76 (2.7%)	1.44 * (1.20, 1.72)	1.28 * (1.11, 1.49)	144 (1.9%)	1.27 * (1.13, 1.43)	1.12 * (1.06, 1.19)	226 (1.4%)	1.20 * (1.10, 1.32)	1.06 * (1.02, 1.09)
51-60	78,364	1,374 (1.8%)	208 (4.0%)	1.34 * (1.19, 1.51)	1.20 * (1.10, 1.32)	417 (3.0%)	1.20 * (1.13, 1.28)	1.07 * (1.04, 1.10)	659 (2.3%)	1.13 * (1.07, 1.20)	1.03 * (1.00, 1.06)
61-70	94,454	2,309 (2.4%)	413 (6.0%)	1.29 * (1.18, 1.41)	1.17 * (1.10, 1.24)	788 (4.3%)	1.21 * (1.14, 1.28)	1.09 * (1.06, 1.12)	1,246 (3.3%)	1.15 * (1.11, 1.18)	1.04 * (1.03, 1.06)
71-80	66,260	2,686 (4.1%)	502 (9.9%)	1.32 * (1.21, 1.44)	1.18 * (1.11, 1.25)	950 (7.0%)	1.22 * (1.15, 1.29)	1.08 * (1.05, 1.11)	1,458 (5.3%)	1.15 * (1.12, 1.18)	1.04 * (1.02, 1.05)
>80	34,074	2.911 (8.5%)	446 (14.9%)	1.22 * (1.11, 1.33)	1.12 * (1.06, 1.19)	921 (12.2%)	1.14 * (1.07, 1.21)	1.06 * (1.02, 1.09)	1,536 (10.5%)	1.10 * (1.07, 1.14)	1.03 * (1.02, 1.04)
AKI AMD and TWA ORs											
			≤55-mmHg			≤65-mmHg			≤75-mmHg		
Age Range	Overall No. Patients	patients with AKI (%)	patients with AKI (%)	AMD OR (99.72% CI)	TWA OR (99.72% CI)	patients with AKI (%)	AMD OR (99.72% CI)	TWA OR (99.72% CI)	patients with AKI (%)	AMD OR (99.72% CI)	TWA OR (99.72% CI)
18-40	42,783	988 (2.3%)	117 (4.0%)	1.23 * (1.03, 1.47)	1.21 * (1.08, 1.37)	208 (2.8%)	1.14 * (1.04, 1.25)	1.05 (0.99, 1.11)	386 (2.4%)	1.07 (1.01, 1.14)	1.01 (0.98, 1.04)
41-50	47,504	1,690 (3.6%)	170 (6.0%)	1.22 * (1.05, 1.42)	1.21 * (1.07, 1.36)	353 (4.6%)	1.13 * (1.03, 1.24)	1.07 * (1.03, 1.10)	638 (3.8%)	1.08 * (1.02, 1.14)	1.02 (0.99, 1.05)
51-60	78,364	3,943 (5.0%)	404 (7.7%)	1.22 * (1.12, 1.34)	1.17* (1.07, 1.28)	924 (6.7%)	1.15 * (1.08, 1.22)	1.06 * (1.02, 1.09)	1,678 (5.8%)	1.11 * (1.07, 1.14)	1.03 * (1.01, 1.04)
61-70	94,454	5,541 (5.9%)	519 (7.6%)	1.05 (0.96, 1.14)	1.03 (0.97, 1.09)	1,260 (6.8%)	1.04 (0.98, 1.11)	1.02 * (1.00, 1.05)	2,395 (6.3%)	1.04 * (1.01, 1.07)	1.01 * (1.00, 1.02)
71-80	66,260	4,465 (6.7%)	479 (9.4%)	1.15 * (1.05, 1.25)	1.11 * (1.05, 1.18)	1,122 (8.2%)	1.10 * (1.03, 1.16)	1.03 * (1.00, 1.06)	2,086 (7.5%)	1.07 * (1.04, 1.10)	1.03 * (1.01, 1.04)
>80	34,074	2,817 (8.3%)	304 (10.2%)	1.10 (0.98, 1.24)	1.06 (0.96, 1.15)	692 (9.2%)	1.07 * (1.01, 1.13)	1.02 (0.99, 1.05)	1,324 (9.0%)	1.05 * (1.01, 1.08)	1.01 (0.99, 1.02)

*Footnote: * Significant after applying Bonferroni adjustment (p-value of ≤0.05/18 (6 age groups x 3 MAP thresholds) or ≤0.0028)*