

Supplemental Digital Content, Table 1. Occurrence intraoperative hypotension (IOH) using four different thresholds of the mean arterial pressure (MAP) to define IOH, stratified for different categories of the mean intraoperative heart rate.

	Mean intraoperative heart rate (beats per minute)				
	<60	60-69	70-79	80-89	>90
	N=248	N=296	N=203	N=84	N=59
Number of patients with IOH* (%)					
MAP [†] <60 mmHg	126 (51)	147 (50)	104 (51)	44 (52)	29 (49)
MAP [†] <50 mmHg	28 (11)	30 (10)	28 (14)	12 (14)	5 (8)
≥30% decrease from pre-induction MAP [‡]	192 (83)	221 (82)	149 (81)	57 (70)	33 (70)
≥40% decrease from pre-induction MAP [‡]	133 (58)	134 (50)	99 (54)	39 (50)	18 (38)

* Intraoperative Hypotension; † Mean Arterial Pressure; ‡ The total number of patients in each category is N=231, N=269, N=185, N=78 and N=47 patients, respectively, because in 80 patients the pre-induction MAP was not available, hence the relative decrease of MAP could not be calculated.

Supplemental Digital Content, table 2. Association between the duration of intraoperative hypotension (IOH) defined as a 40% decrease in mean arterial blood pressure, and myocardial injury, adjusted for age, sex, comorbidities, preoperative medication use, heart rate, intraoperative blood loss and duration of surgery.

	RR [†]	98.8% CI [‡]	p-value
Duration of IOH [§] (minutes)			
≤1	<i>Ref</i>		
2-5	1.3	0.7 – 2.2	0.27
6-10	0.8	0.4 – 1.6	0.34
11-20	1.3	0.8 – 2.4	0.21
21-30	0.8	0.4 – 1.7	0.46
>30	1.7	1.1 – 2.5	0.002
Female	1.1	0.8 – 1.6	0.34
Age (per year)	1.3	1.1 – 1.5	0.001
Diabetes	0.9	0.5 – 1.5	0.58
History of myocardial infarction	1.8	1.3 – 2.5	<0.001
History of heart failure	1.3	0.8 – 2.1	0.16
History of cerebrovascular disease	1.0	0.7 – 1.6	0.83
Preoperative renal failure	1.7	1.1 – 2.7	<0.01
Preoperative medication use			
Beta blocker	1.6	1.2 – 2.3	<0.001
Calcium channel blocker	0.9	0.6 – 1.3	0.45
Renin angiotensin system inhibitor	0.8	0.6 – 1.1	0.07
Diuretics	1.3	0.9 – 1.8	0.05
High risk surgery	1.0	0.7 – 1.4	0.87
Emergency surgery	1.6	1.1 – 2.2	0.001
Mean heart rate (per 10 beats per minute)	1.3	1.2 – 1.5	<0.001
Intraoperative blood loss			
<500 mL	<i>Ref</i>		
500-1000 mL	1.5	0.9 – 2.3	0.05
1000-2000 mL	1.5	0.7 – 3.1	0.19
>2000 mL	1.1	0.5 – 2.4	0.72
Center: UHNT [¶]	0.6	0.4 – 0.9	0.001
Duration of surgery (per 10 minutes)	1.01	1.00 – 1.02	0.03

[†] Relative risk; [‡] Confidence interval; [§] Intraoperative hypotension; [¶] University Health Network Toronto.

Supplemental Digital Content, table 3. Association between the duration of intraoperative hypotension (IOH) and myocardial injury for four different definitions of hypotension. The results are adjusted for age, sex, comorbidities, preoperative medication use, heart rate, intraoperative blood loss and duration of surgery.

Definition of IOH*	Duration of IOH* (minutes)	RR [†]	98.8% CI [‡]	p-value
MAP[§] < 50 mmHg	≤1	<i>Ref</i>		
	2-5	1.3	0.7 – 2.1	0.28
	6-10	2.0	1.2 – 3.6	0.002
	11-20	0.7	0.3 – 2.0	0.41
	21-30	2.4	0.8 – 6.9	0.04
	>30	1.6	0.4 – 6.0	0.38
MAP[§] < 60 mmHg	≤1	<i>Ref</i>		
	2-5	1.1	0.7 – 1.7	0.56
	6-10	0.8	0.5 – 1.5	0.49
	11-20	1.5	1.0 – 2.3	0.01
	21-30	1.4	0.9 – 2.3	0.06
	>30	1.5	0.9 – 2.3	0.03
30% decrease from pre-induction MAP[§]	≤1	<i>Ref</i>		
	2-5	1.6	0.8 – 3.6	0.11
	6-10	2.8	1.5 – 5.0	<0.001
	11-20	1.8	0.9 – 3.3	0.03
	21-30	0.9	0.4 – 2.2	0.79
	>30	1.7	1.0 – 2.8	0.02
40% decrease from pre-induction MAP[§]	≤1	<i>Ref</i>		
	2-5	1.3	0.7 – 2.2	0.27
	6-10	0.8	0.4 – 1.6	0.34
	11-20	1.3	0.8 – 2.4	0.21
	21-30	0.8	0.4 – 1.7	0.46
	>30	1.7	1.1 – 2.5	0.002

* Intraoperative hypotension; † Relative Risk; ‡ Confidence interval; § Mean arterial pressure.

Supplemental Digital Content, table 4. Association between the severity of intraoperative hypotension (IOH), defined as the area under the curve (duration times depth) below the threshold of a 40% decrease in mean arterial blood pressure, and myocardial injury, adjusted for age, sex, comorbidities, preoperative medication use, heart rate and intraoperative blood loss.

	RR [†]	98.8% CI [‡]	p-value
AUC [§] of IOH [¶] (minutes*mmHg)			
≤10	<i>Ref</i>		
11-50	1.1	0.7 – 1.9	0.49
51-101	0.7	0.3 – 1.5	0.21
101-200	1.3	0.7 – 2.2	0.25
201-300	1.2	0.5 – 2.8	0.57
>300	1.8	1.2 – 2.7	<0.001
Female	1.1	0.8 – 1.6	0.39
Age (per year)	1.3	1.0 – 1.5	0.002
Diabetes	0.9	0.5 – 1.6	0.62
History of myocardial infarction	1.8	1.3 – 2.5	<0.001
History of heart failure	1.2	0.8 – 2.0	0.27
History of cerebrovascular disease	1.0	0.6 – 1.5	0.85
Preoperative renal failure	1.7	1.1 – 2.6	0.002
Preoperative medication use			
Beta blocker	1.7	1.2 – 2.3	<0.001
Calcium channel blocker	0.9	0.7 – 1.3	0.63
Renin angiotensin system inhibitor	0.8	0.6 – 1.1	0.08
Diuretics	1.3	0.9 – 1.7	0.06
High risk surgery	1.1	0.8 – 1.5	0.52
Emergency surgery	1.5	1.1 – 2.1	0.001
Mean heart rate (per 10 beats per minute)	1.3	1.2 – 1.5	<0.001
Intraoperative blood loss			
<500 mL	<i>Ref</i>		
500-1000 mL	1.5	0.9 – 2.4	0.03
1000-2000 mL	1.9	1.0 – 3.7	0.01
>2000 mL	1.4	0.7 – 2.7	0.20
Center: UHNT ^{¶¶}	0.6	0.4 – 0.9	<0.001

[†] Relative risk; [‡] Confidence interval; [§] Area Under the Curve; [¶] Intraoperative hypotension; ^{¶¶} University Health Network Toronto.

Supplemental Digital Content, table 5. Association between the severity of intraoperative hypotension (IOH), defined as the area under the curve (duration times depth) below the threshold of a 40% decrease in mean arterial blood pressure) for four different definitions of hypotension. The results are adjusted for age, sex, comorbidities, preoperative medication use, heart rate and intraoperative blood loss.

Definition of IOH [†]	AUC [‡] of IOH [†] (minutes*mmHg)	RR [§]	98.8% CI [¶]	p-value
MAP < 50 mmHg	≤10	<i>Ref</i>		
	11-50	2.0	1.3 – 3.1	<0.001
	51-101	0.9	0.4 – 2.0	0.86
	101-200	1.0	0.2 – 3.9	0.93
	201-300	1.5	0.1 – 18.6	0.68
	>300	3.4	1.3 – 9.2	0.002
MAP < 60 mmHg	≤10	<i>Ref</i>		
	11-50	0.8	0.5 – 1.2	0.20
	51-101	1.0	0.6 – 1.7	0.82
	101-200	1.4	0.9 – 2.2	0.03
	201-300	1.6	1.0 – 2.7	0.02
	>300	1.5	0.9 – 2.5	0.06
30% decrease from pre-induction MAP	≤10	<i>Ref</i>		
	11-50	2.1	1.2 – 3.7	0.001
	51-101	2.0	1.1 – 3.8	0.005
	101-200	1.0	0.5 – 2.0	0.90
	201-300	1.5	0.6 – 3.3	0.24
	>300	1.7	1.0 – 2.8	0.007
40% decrease from pre-induction MAP	≤10	<i>Ref</i>		
	11-50	1.1	0.7 – 1.9	0.49
	51-101	0.7	0.3 – 1.5	0.21
	101-200	1.3	0.7 – 2.2	0.25
	201-300	1.2	0.5 – 2.8	0.57
	>300	1.8	1.2 – 2.7	<0.001

[†] Intraoperative hypotension; [‡] Area Under the Curve; [§] Relative risk; [¶] Confidence interval; ^{||} Mean arterial pressure.

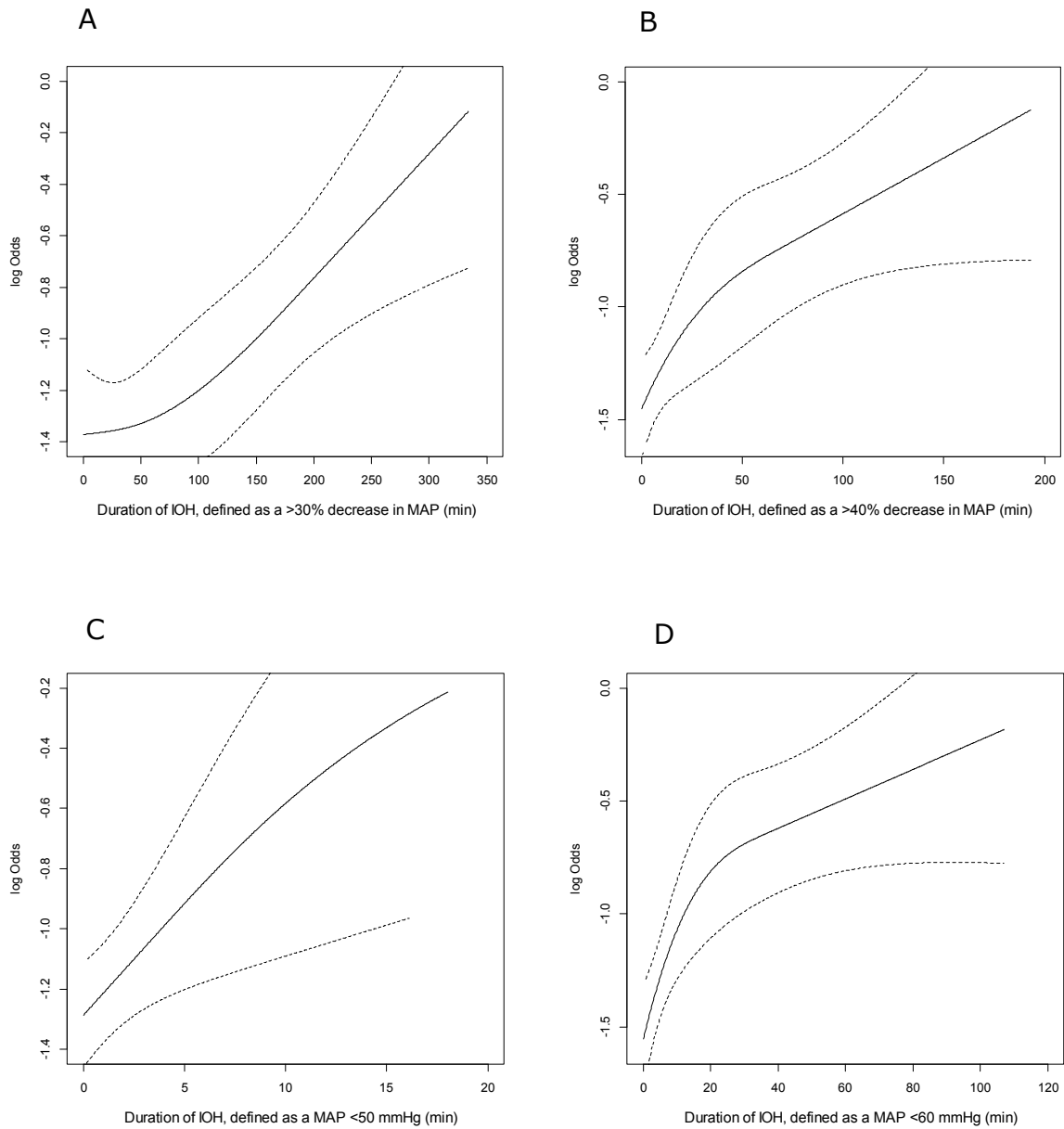
Supplemental Digital Content, table 6. Comparison of two hypotension study populations.

	POISE-2 trial*	UHN [†] Toronto UMC [‡] Utrecht
Mean age (years)	69	73
Male	53%	70%
History of coronary artery disease	23%	21%
History of cerebrovascular disease	5%	20%
History of chronic heart failure	3%	6%
Emergency surgery	7%	30%
Chronic medication use		
Beta-blockers	29%	53%
Calcium channel blockers	5%	30%
Renin angiotensin system inhibitors	N.R. §	38%
Statins	46%	57%
Myocardial infarction within 30 days	6.4%	4.0%
30-day mortality	1.3%	3.4%
Perioperative hypotension (all)	42%	N.R. ‡
Intraoperative hypotension	35%	MAP [¶] <60 mmHg: 51%
		MAP [¶] <50 mmHg: 12%
		≥30% decrease in MAP [¶] : 81%
		≥40% decrease in MAP [¶] : 51%

*Perioperative Ischemic Evaluation 2 trial; [†]University Health Network Toronto; [‡]University Medical Center Utrecht; § Not reported; [¶] Mean arterial pressure.

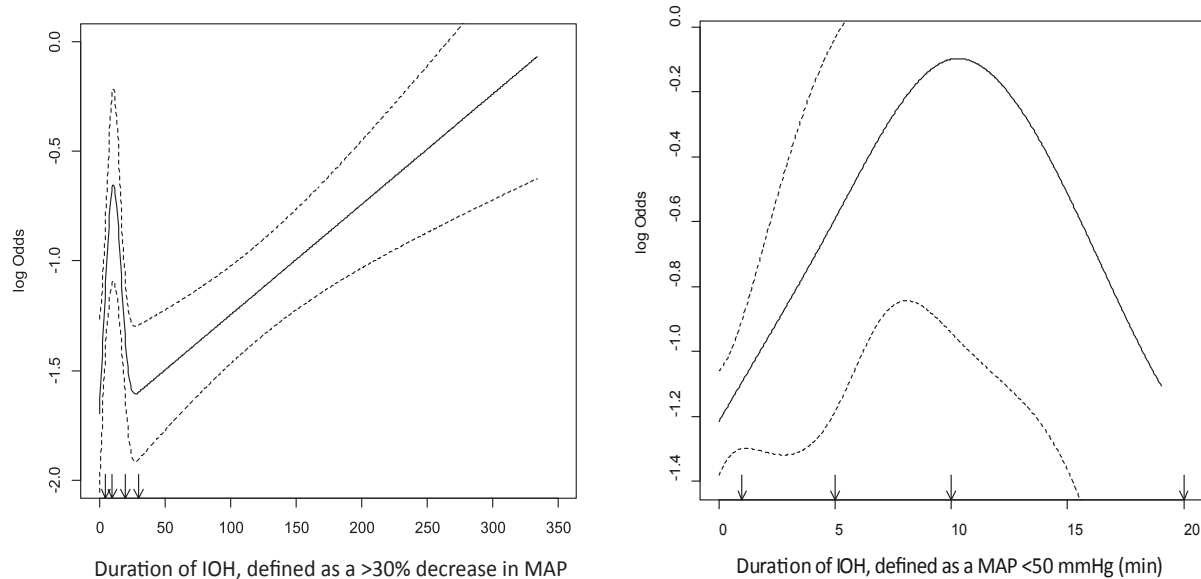
Supplemental Digital Content, Figure 1.

Restricted cubic spline of the association between the duration of intraoperative hypotension (IOH), defined by four different thresholds of the mean arterial pressure (MAP), and postoperative myocardial injury. The log Odds on the Y-axis represents the beta-coefficient of the logistic regression model used in the restricted cubic spline analysis. A) IOH defined as $\geq 30\%$ decrease in MAP; B) IOH defined as $\geq 40\%$ decrease in MAP; C) IOH defined as a MAP < 60 mmHg; D) IOH defined as a MAP < 50 mmHg.



Supplemental Digital Content, figure 2.

Restricted cubic spline analysis of the association between the duration of intraoperative hypotension (IOH) as defined by a 30% decrease in mean arterial pressure (MAP) or a MAP <50 mmHg, and postoperative myocardial injury, using predefined categories for the duration of hypotension.



The duration of hypotension was analyzed as a categorical variable instead of a continuous variable because the association between hypotension and myocardial injury was expected to be nonlinear. The categories of the duration of hypotension (<1, 2-5, 6-10, 11-20, 21-30 and >30 minutes) were arbitrarily chosen in advance, aiming at more or less equally sized groups for each of the four definitions of hypotension. As is shown in Table 4, there appears to be a significant association between hypotension defined as a $\geq 30\%$ decrease in MAP and a MAP <50 mmHg with a duration of 6-10 minutes. However, then we would expect that this would be consistent for longer durations of hypotension, i.e. for durations >10 minutes, but that is not the case. We further explored this by studying the restricted cubic splines in which the chosen cut-off points were used to define the knot locations. From these splines, we concluded that the association seen at the 6-10 minute interval was rather due to overfitting by the chosen cut-off points, hence we did not consider this to be a true association.