Wieviel Blutdruck braucht der Mensch ?

Past, present, future of BP management

Patrick Wanner
Herbstsymposium Anästhesiologie
Universitätsspital Basel
25. Oktober 2025

Conflicts of interest

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Co-Investigator of the
BBB Study (Biomarkers, Blood pressure, BIS)

Principal Investigator of the
AUTOREGULATE-NONCARDIAC Study

Collaboration with Covidien/Medtronic
Planned subanalysis of AUTOREGULATE-NONCARDIAC to independently evalute Covidien/Medtronic Cotrending algorithm in major noncardiac surgery

Key messages

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We know less than we think about hemodynamics.

Key messages

We know less than we think about hemodynamics.

Both pressure and flow matter.

Key messages

We know less than we think about hemodynamics.

Both pressure and flow matter.

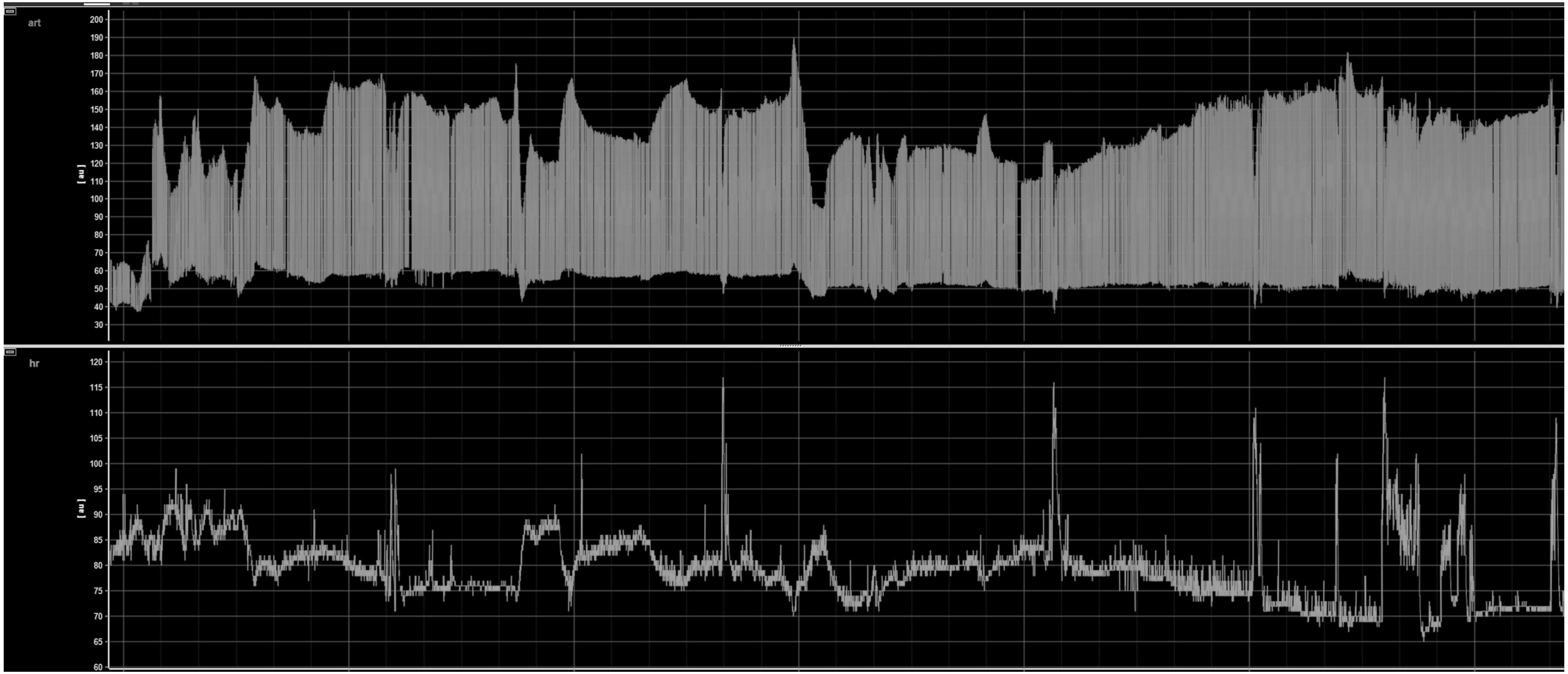
Postop matters too.

MAP $>$ 65 mmHg

MAP > 65 mmHg

What does this actually mean ?

MAP - a case study in a postop. patient



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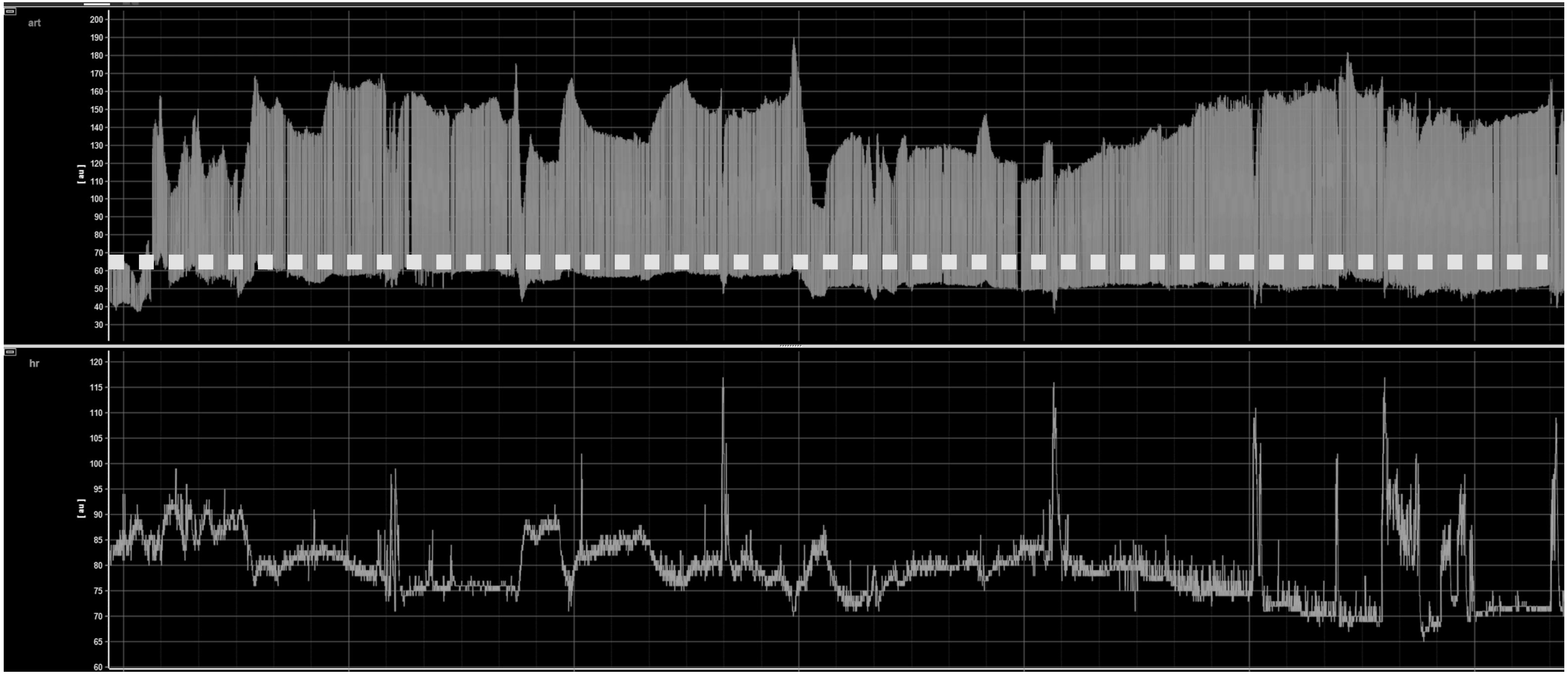

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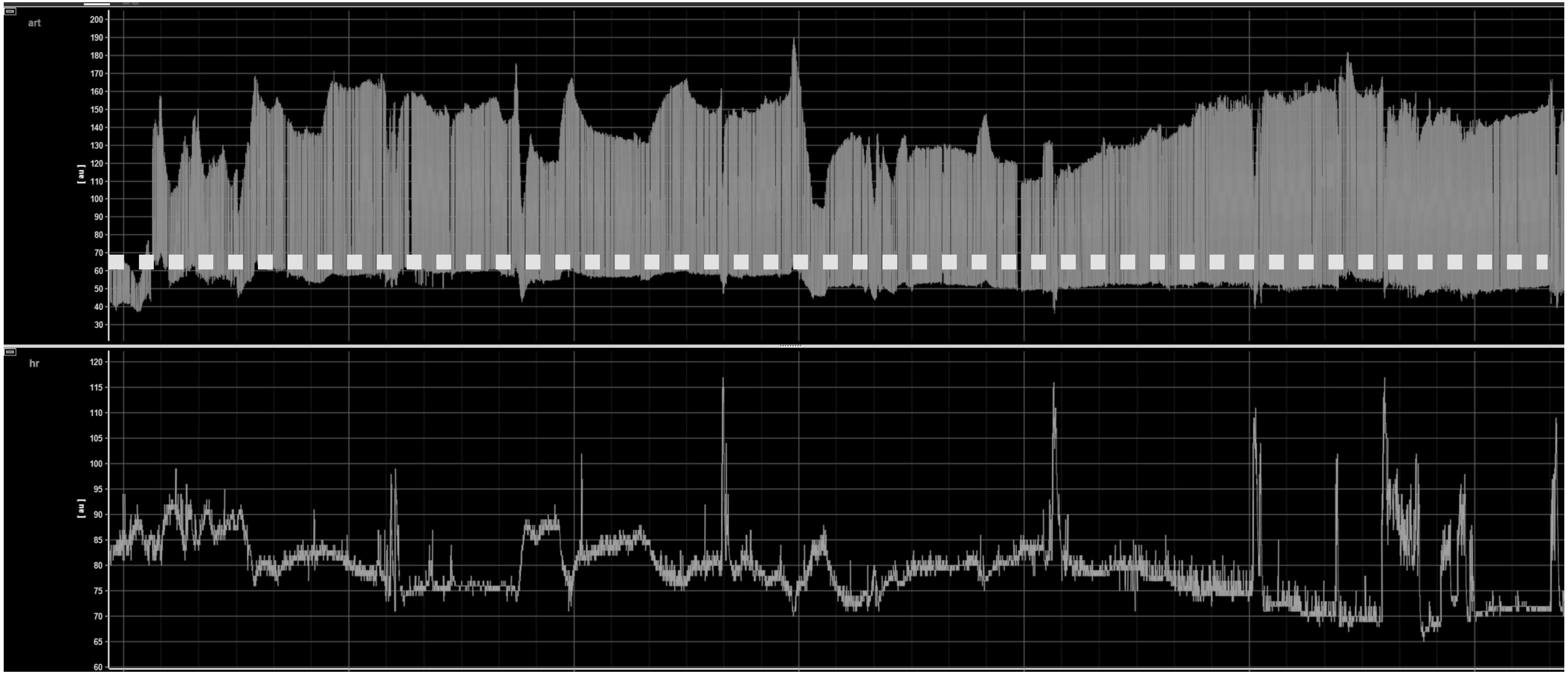
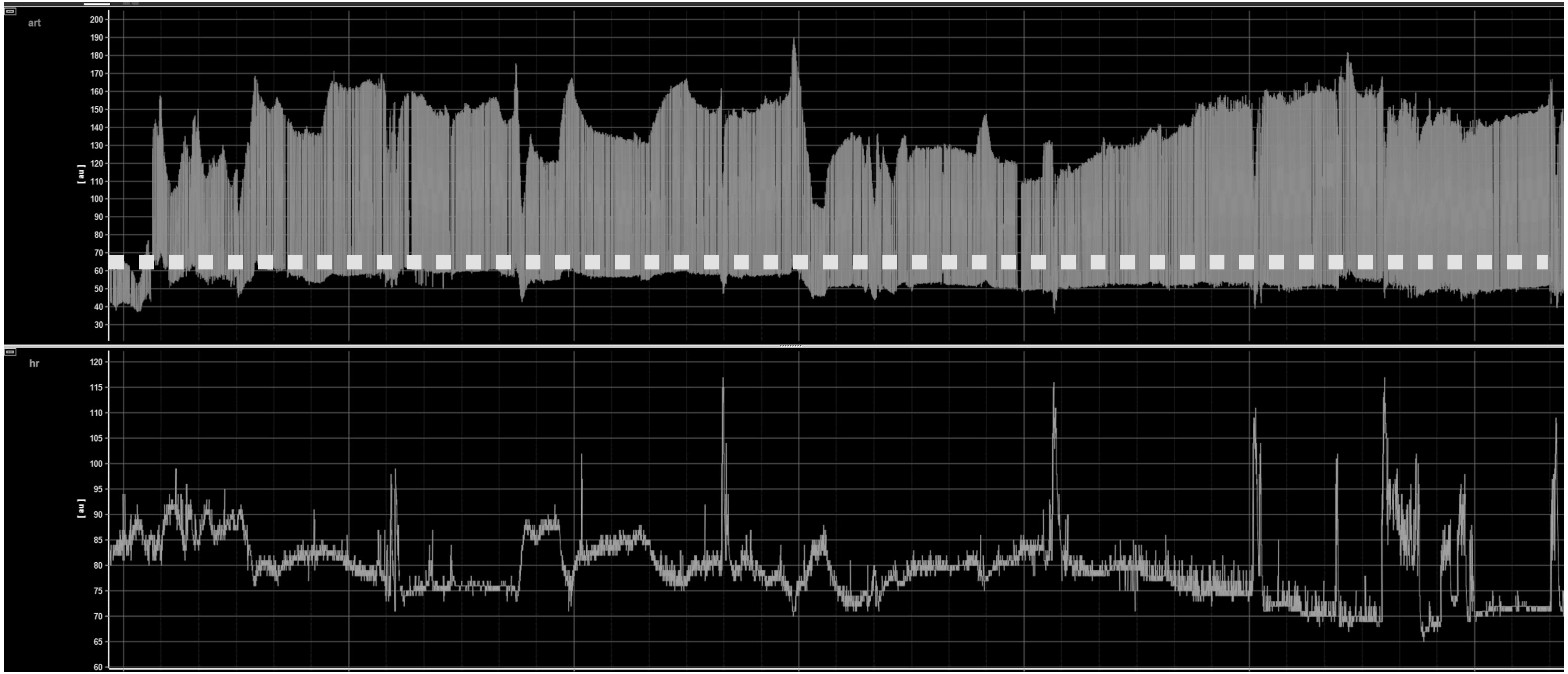


ARE WE HAPPY ?

MAP - a case study in a postop. patient



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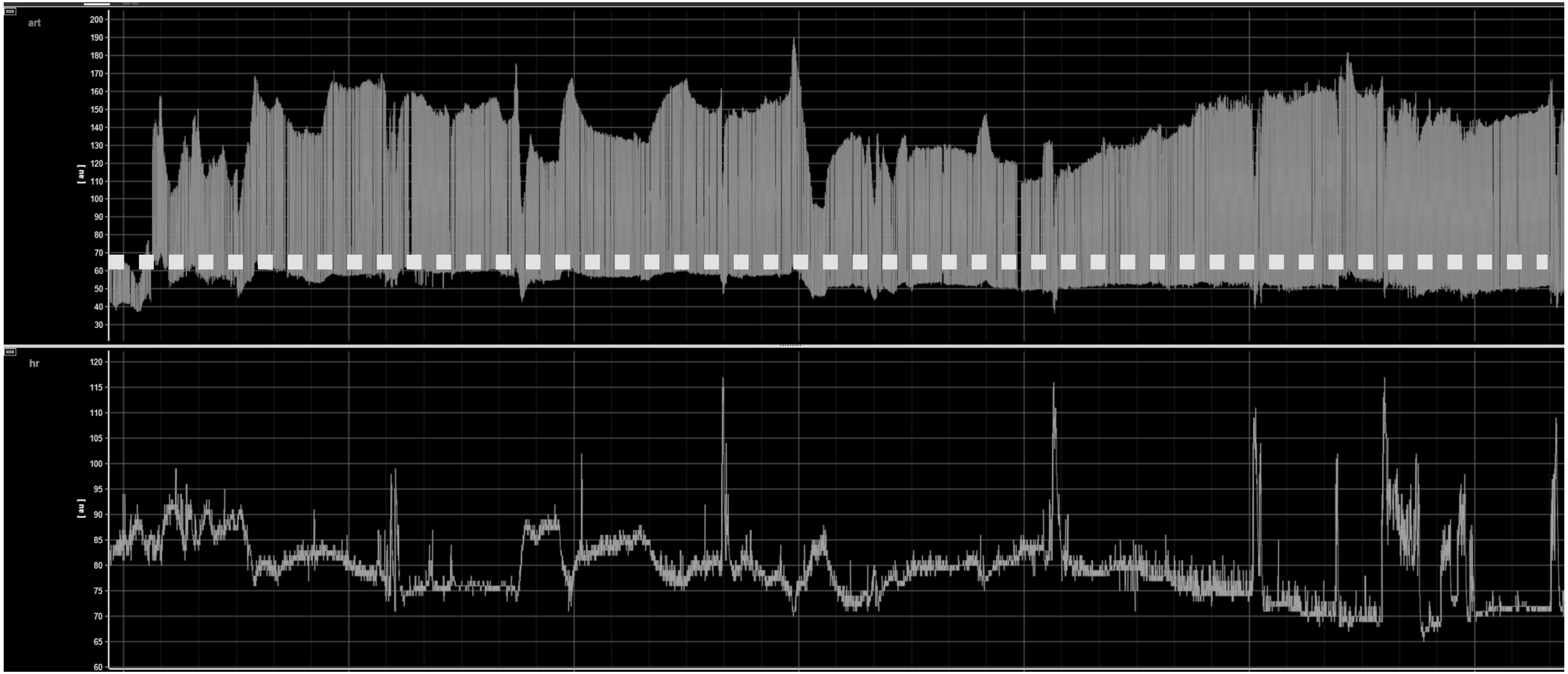
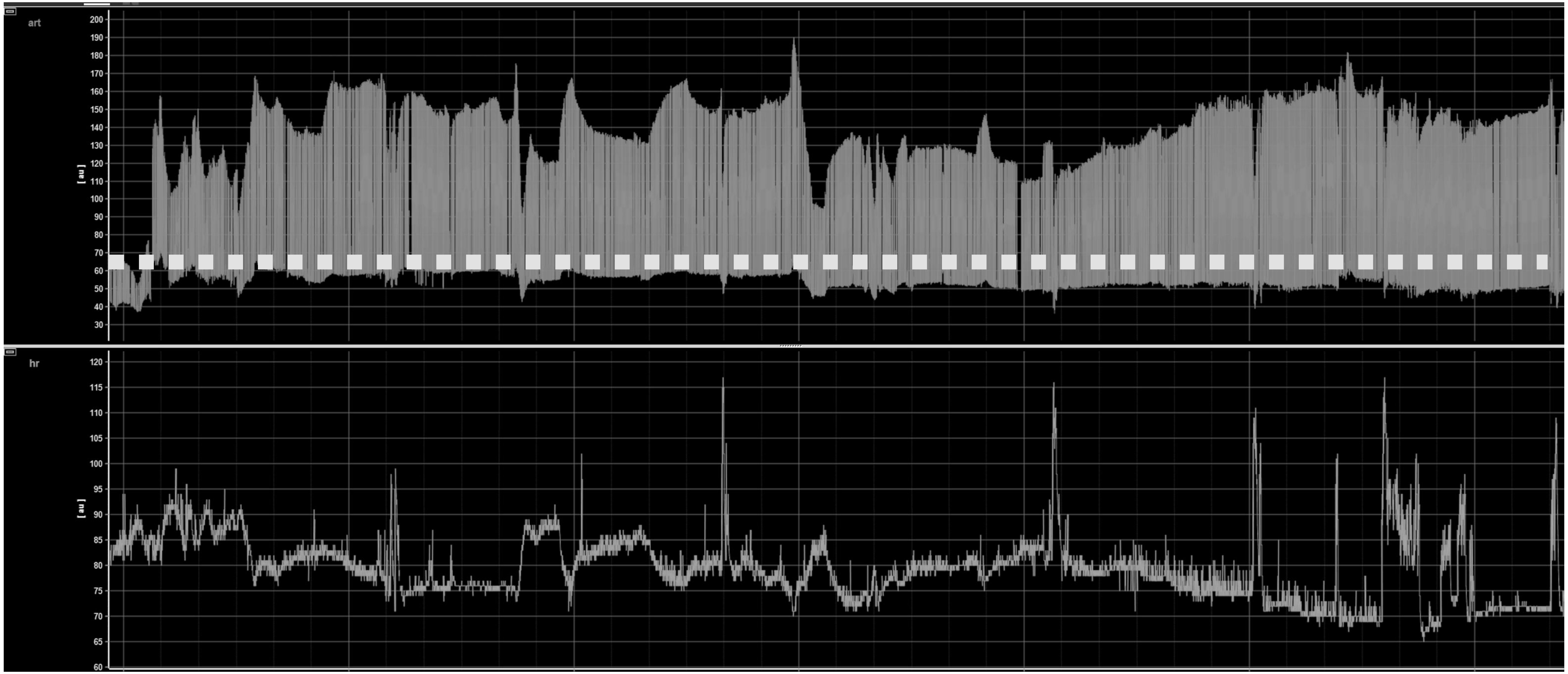


NORADRENALINE 30 MCG/MIN
VASOPRESSIN 0.03 E/MIN
DOBUTAMINE 300 MCG/MIN

MAP - a case study in a postop. patient



NORADRENALINE 30 MCG/MIN
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ARE WE STILL HAPPY ?

MAP > 65 mmHg

What does this actually mean ?

MAP > 65 mmHg

What does this actually mean ?

And where does it come from ?

MAP vs. outcomes

MAP vs. outcomes

Intraoperative hypotension and the risk of postoperative adverse outcomes: a systematic review

E. M. Wesselink[1,*], T. H. Kappen[1], H. M. Torn[1], A. J. C. Slooter[2] and W. A. van Klei[1]

[1]Department of Anesthesiology, Utrecht, The Netherlands and [2]Department of Intensive Care Medicine, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

depth	duration	mortality		acute kidney injury		myocardial injury		stroke		delirium		overall organ injury	
MAPMAP	Minutes	based on quality score ≥ 80%	based on quality score ≥ 80% and significant result	based on quality score ≥ 80%	based on quality score ≥ 80% and significant result	based on quality score ≥ 80%	based on quality score ≥ 80% and significant result	based on quality score ≥ 80%	based on quality score ≥ 80% and significant result	based on quality score ≥ 80%	based on quality score ≥ 80% and significant result	based on quality score ≥ 80%	based on quality score ≥ 80% and significant result
< 80 mmHg	≥ 1												
	≥ 5												
	≥ 10	1.02	1.02									Low	Low
	≥ 20	1.04	1.04									Low	Low
< 75 mmHg	≥ 1												
	≥ 5												
	≥ 10	1.02	1.02									Low	Low
	≥ 20	1.09	1.09									Low	Low
< 70 mmHg	≥ 1	1.002 *						1.003*				Low	
	≥ 5	1.01 *						1.015*				Low	
	≥ 10	1.04	1.04					1.030*				Low	Low
	≥ 20	1.09	1.09					1.062*				Low	Low
< 65 mmHg	≥ 1	1.002 *		1.3 *		1.01 *		1.003*				Low	
	≥ 5	1.01 *		1.6 *		1.2 *		1.015*				Moderate	
	≥ 10	1.04	1.04	1.6 *		1.3	1.3	1.030*				Moderate	Low
	≥ 20	1.09	1.09	2.3 *		1.8	1.8	1.062*				High	Moderate
< 60 mmHg	≥ 1	1.1 *		1.3 *		1.1 *		1.003*				Low	
	≥ 5	1.1 *		1.6 *		1.2 *		1.015*				Moderate	
	≥ 10	1.1 *	1.09	1.8	1.8	1.5	1.5	1.030*				Moderate	Moderate
	≥ 20	1.2	1.2	2.3	2.3	2.5	1.8	1.062*				High	High
< 55 mmHg	≥ 1	1.2 *	1.04	1.4*	1.2	1.3	1.3	1.003*				Moderate	Low
	≥ 5	1.2	1.2	1.6 *	1.2	1.5	1.5	1.015*				Moderate	Moderate
	≥ 10	1.4	1.4	2.3	2.3	1.8	1.8	1.030*				High	High
	≥ 20	2.0	2.0	3.5	3.5	2.5	2.5	1.062*				High	High
< 50 mmHg	≥ 1	1.2 *	1.04	1.6 *	1.2	1.3	1.3	1.004*		● p = 0.409 *		Moderate	Low
	≥ 5	2.4	2.4	1.6 *	1.2	4.4	4.4	1.020*		● p = 0.409 *		High	High
	≥ 10	2.4	2.4	2.3	2.3	4.4	4.4	1.041*		● p = 0.409 *		High	High
	≥ 20	2.4	2.4	3.5	3.5	4.4	4.4	1.083*		● p = 0.409 *		High	High
< 45 mmHg	≥ 1	1.2 *	1.04	1.6 *	1.2	1.3	1.3	1.013*		● p = 0.409 *		Moderate	Low
	≥ 5	2.4	2.4	1.6 *	1.2	4.4	4.4	1.067*		● p = 0.409 *		High	High
	≥ 10	2.4	2.4	2.3	2.3	4.4	4.4	1.138*		● p = 0.409 *		High	High
	≥ 20	2.4	2.4	3.5	3.5	4.4	4.4	1.295*		● p = 0.409 *		High	High
< 40 mmHg	≥ 1	1.2 *	1.04	3.8	3.8	1.3	1.3	1.013*		● p = 0.409 *		High	High
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Low	1.0 < OR, RR or HR < 1.4
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Intraoperative hypotension and the risk of postoperative adverse outcomes: a systematic review

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< 60 mmHg	≥ 1	1.1 *		1.3 *		1.1 *		1.003*				Low	
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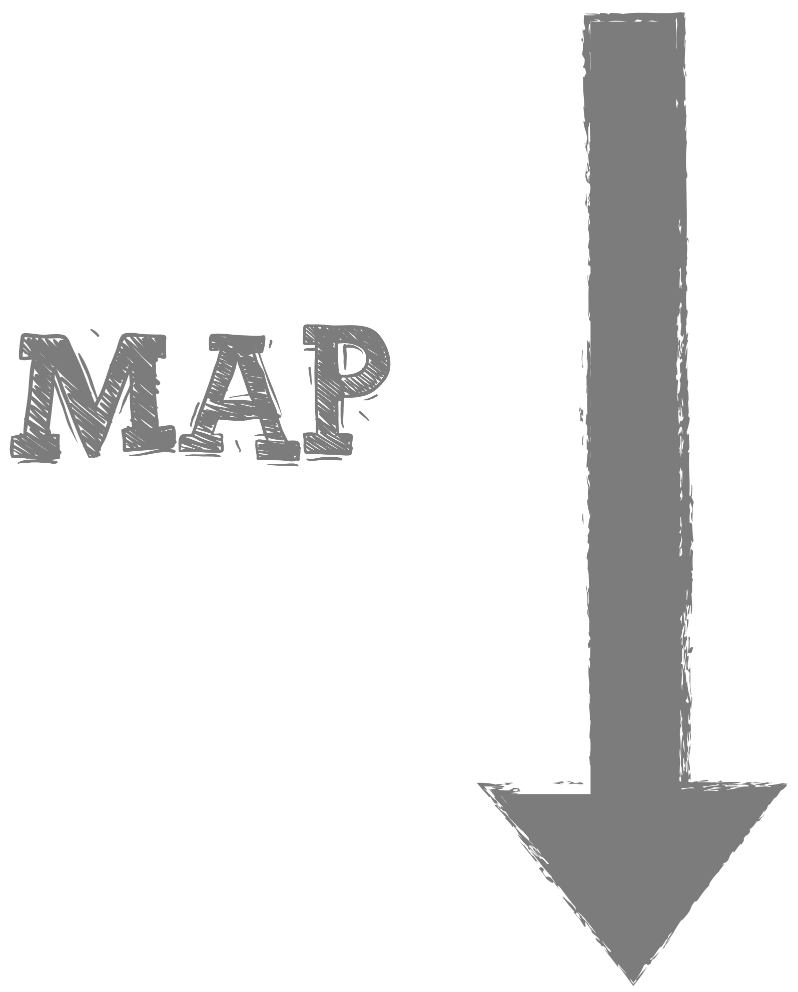

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	≥ 20	1.09	1.09	2.3 *		[illegible]	[illegible]	[illegible]				High	Moderate
< 60 mmHg	≥ 1	1.1 *		1.3 *		1.1 *		1.003*				Low	
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Current guidelines and consensus statements

ESC European Society of Cardiology
European Heart Journal (2022) 00, 1–99
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Developed by the task force for cardiovascular assessment and management of patients undergoing non-cardiac surgery of the European Society of Cardiology (ESC)

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Recommendation Table 33 — Recommendations for peri-operative monitoring and anaesthesia

Recommendations	Class[a]	Level[b]
In order to preserve optimal CV stability, it is recommended to apply goal-directed haemodynamic therapy in patients undergoing high-risk NCS.[614–618]	I	A
It is recommended to avoid post-operative acute pain.[614]	I	B
In order to minimize the risk of post-operative organ dysfunction, it is recommended to avoid an intra-operative mean arterial pressure decrease of >20% from baseline values or <60–70 mmHg for ≥10 min.[214,600–602,634]	I	B
Non-aspirin NSAIDs are not recommended as first-line analgesics in patients with established or high risk of CVD.[633,635]	III	B

CV, cardiovascular; CVD, cardiovascular disease; NCS, non-cardiac surgery; NSAID, non-steroidal anti-inflammatory drug.
[a]Class of recommendation.
[b]Level of evidence.

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REVIEW ARTICLE

PeriOperative Quality Initiative (POQI) international consensus statement on perioperative arterial pressure management

Bernd Saugel[1,2,*], Nick Fletcher[3], Tong J. Gan[4], Michael P. W. Grocott[5], Paul S. Myles[6], Daniel I. Sessler[7], on behalf of the PeriOperative Quality Initiative XI (POQI XI) Workgroup Members[†]

Consensus statements and recommendations

Consensus statement 1: Intraoperative mean arterial pressures <60–70 mm Hg or systolic arterial pressures <90–100 mm Hg are associated with acute kidney injury, myocardial injury, myocardial infarction, and death. Injury is a function of hypotension severity and duration (high-quality evidence).

Consensus recommendation 1: We recommend keeping intraoperative mean arterial pressure ≥60 mm Hg in at-risk patients (strong recommendation, moderate-quality evidence).

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CV, cardiovascular; CVD, cardiovascular disease; NCS, non-cardiac surgery; NSAID, non-steroidal anti-inflammatory drug.
[a]Class of recommendation.
[b]Level of evidence.

REVIEW ARTICLE

PeriOperative Quality Initiative (POQI) international consensus statement on perioperative arterial pressure management

Bernd Saugel[1,2,*], Nick Fletcher[3], Tong J. Gan[4], Michael P. W. Grocott[5], Paul S. Myles[6], Daniel I. Sessler[7], on behalf of the PeriOperative Quality Initiative XI (POQI XI) Workgroup Members[†]

Consensus statements and recommendations

Consensus statement 1: Intraoperative mean arterial pressures <60–70 mm Hg or systolic arterial pressures <90–100 mm Hg are associated with acute kidney injury, myocardial injury, myocardial infarction, and death. Injury is a function of hypotension severity and duration (high-quality evidence).

Consensus recommendation 1: We recommend keeping intraoperative mean arterial pressure ≥60 mm Hg in at-risk patients (strong recommendation, moderate-quality evidence).

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CLINICAL PRACTICE GUIDELINE

2024 AHA/ACC/ACS/ASNC/HRS/SCA/SCCT/SCMR/SVM Guideline for Perioperative Cardiovascular Management for Noncardiac Surgery

A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Intraoperative Blood Pressure Management

1	B-NR	3. In patients undergoing NCS, maintaining an intraoperative mean arterial pressure (MAP) ≥60 to 65 mm Hg or SBP ≥90 mm Hg is recommended to reduce the risk of myocardial injury.[3-9]

Current guidelines and consensus statements

ESC European Society of Cardiology European Heart Journal (2022) 00, 1–99 https://doi.org/10.1093/eurheartj/ehac270 ESC GUIDELINES

2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery

Developed by the task force for cardiovascular assessment and management of patients undergoing non-cardiac surgery of the European Society of Cardiology (ESC)

Endorsed by the European Society of Anaesthesiology and Intensive Care (ESAIC)

Recommendation Table 33 — Recommendations for peri-operative monitoring and anaesthesia

Recommendations	Class[a]	Level[b]
In order to preserve optimal CV stability, it is recommended to apply goal-directed haemodynamic therapy in patients undergoing high-risk NCS.[614–618]	I	A
It is recommended to avoid post-operative acute pain.[614]	I	B
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MAP > 60-70 OR 80% BASELINE

4 trials on perioperative BP management in noncardiac surgery

4 major BP trials in noncardiac surgery

4 major BP trials in noncardiac surgery

MAP > 80% “baseline”

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery
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INPRESS

Potentially improved renal and neurological outcomes

4 major BP trials in noncardiac surgery

MAP > 80% “baseline”

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INPRESS

Potentially improved renal and neurological outcomes

MAP > 75

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 78, NO. 18, 2021

ORIGINAL INVESTIGATIONS

Targeting Higher Intraoperative Blood Pressures Does Not Reduce Adverse Cardiovascular Events Following Noncardiac Surgery

Patrick M. Wanner, MD,[a,*] Dirk U. Wulff, PhD,[b] Mirjana Djurdjevic,[a] Wolfgang Korte, MD,[c] Thomas W. Schnider, MD,[a] Miodrag Filipovic, MD[a]

BBB

No differences in cardiovasc. or renal outcomes

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BBB

No differences in cardiovasc. or renal outcomes

MAP > 80

Annals of Internal Medicine ORIGINAL RESEARCH

Hypotension-Avoidance Versus Hypertension-Avoidance Strategies in Noncardiac Surgery

An International Randomized Controlled Trial

Maura Marcucci, MD; Thomas W. Painter, MBChB; David Conen, MD; Vladimir Lomivorotov, MD; Daniel I. Sessler, MD; Matthew T.V. Chan, MBBS; Flavia K. Borges, MD; Kate Leslie, MD; Emmanuelle Duceppe, MD; María José Martínez-Zapata, MD; Chew Yin Wang, MBChB; Denis Xavier, MD; Sandra N. Ofori, MBBS; Michael Ke Wang, MD; Sergey Efremov, MD; Giovanni Landoni, MD; Ydo V. Kleinlugtenbelt, MD; Wojciech Szczeklik, MD; Denis Schmartz, MD; Amit X. Garg, MD; Timothy G. Short, MD; Maria Wittmann, MD; Christian S. Meyhoff, MD; Mohammed Amir, MBBS; David Torres, MD; Ameen Patel, MD; Kurt Ruetzler, MD; Joel L. Parlow, MD; Vikas Tandon, MD; Edith Fleischmann, MD; Carisi A. Polanczyk, MD; Andre Lamy, MD; Raja Jayaram, MD; Sergey V. Astrakov, MD; William Ka Kei Wu, PhD; Chao Chia Cheong, MD; Sabry Ayad, MD; Mikhail Kirov, MD; Miriam de Nadal, MD; Valery V. Likhvantsev, MD; Pilar Paniagua, MD; Hector J. Aguado, MD; Kamal Maheshwari, MD; Richard P. Whitlock, MD; Michael H. McGillion, RN; Jessica Vincent, MSc; Ingrid Copland; Kumar Balasubramanian, MSc; Bruce M. Biccard, MBChB; Sadeesh Srinathan, MD; Samandar Ismoilov, MD; Shirley Pettit, RN; David Stillo, MASc; Andrea Kurz, MD; Emilie P. Belley-Côté, MD; Jessica Spence, MD; William F. McIntyre, MD; Shrikant I. Bangdiwala, PhD; Gordon Guyatt, MD; Salim Yusuf, MD; and P.J. Devereaux, MD, PhD; on behalf of the POISE-3 Trial Investigators and Study Groups*

POISE-3

No differences in cardiovasc. or renal outcomes

4 major BP trials in noncardiac surgery

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INPRESS

Potentially improved renal and neurological outcomes

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POISE-3

No differences in cardiovasc. or renal outcomes

MAP > nighttime BP

JAMA | Original Investigation

Individualized Perioperative Blood Pressure Management in Patients Undergoing Major Abdominal Surgery

The IMPROVE-multi Randomized Clinical Trial

Bernd Saugel, MD; Agnes S. Meidert, MD; Frank M. Brunkhorst, MD; Robert Bischoff, MD; Joseph Esser, MD; Minca Mattis, MD; Pauline Naue; Katharina Vogel, BSc; Alina Bergholz, MD; Moritz Flick, MD; Alina Kröker, MD; Dominik X. Müller, MD; Kristen K. Thomsen, MD; Christina Vokuhl, MD; Mirja Wegge, MD; Sebastian Bratke, MD; Martin Graeßner, MD; Bettina Jungwirth, MD; Sebastian Schmid, MD; Carla D. Grundmann, MD; Jan M. Wischermann, MD; Patrick Kellner, MD; Moritz Steinhaus, MD; Linda Grüßer, MD; Sina M. Coldewey, MD, PhD; Kai Zacharowski, MD, PhD; Patrick Meybohm, MD; Marit Habicher, MD; Alexander Zarbock, MD; Amelie Zitzmann, MD; Svenja Letz, MD; Claudia Neumann, MD; Jan Larmann, MD, PhD; Thomas Renné, MD, PhD; Linda Krause, PhD; Eik Vettorazzi, MSc; Antonia Zapf, PhD; Annemarie Carlstedt, PhD; Daniel I. Sessler, MD; Karim Kouz, MD; for the IMPROVE-multi Trial Group

IMPROVE-MULTI

No differences in cardiovasc. or renal outcomes

4 major trials, no treatment effects.

4 major trials, no treatment effects.

Why ?

3 Questions.


Are all patients alike ?


Are all patients alike ?
Of course not!

Precision hemodynamic management

Precision hemodynamic management

How ?

Precision approach 1:

Precision approach 1:

Baseline BP as guide

Baseline BPs as a therapeutic target

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

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IMPROVE-MULTI

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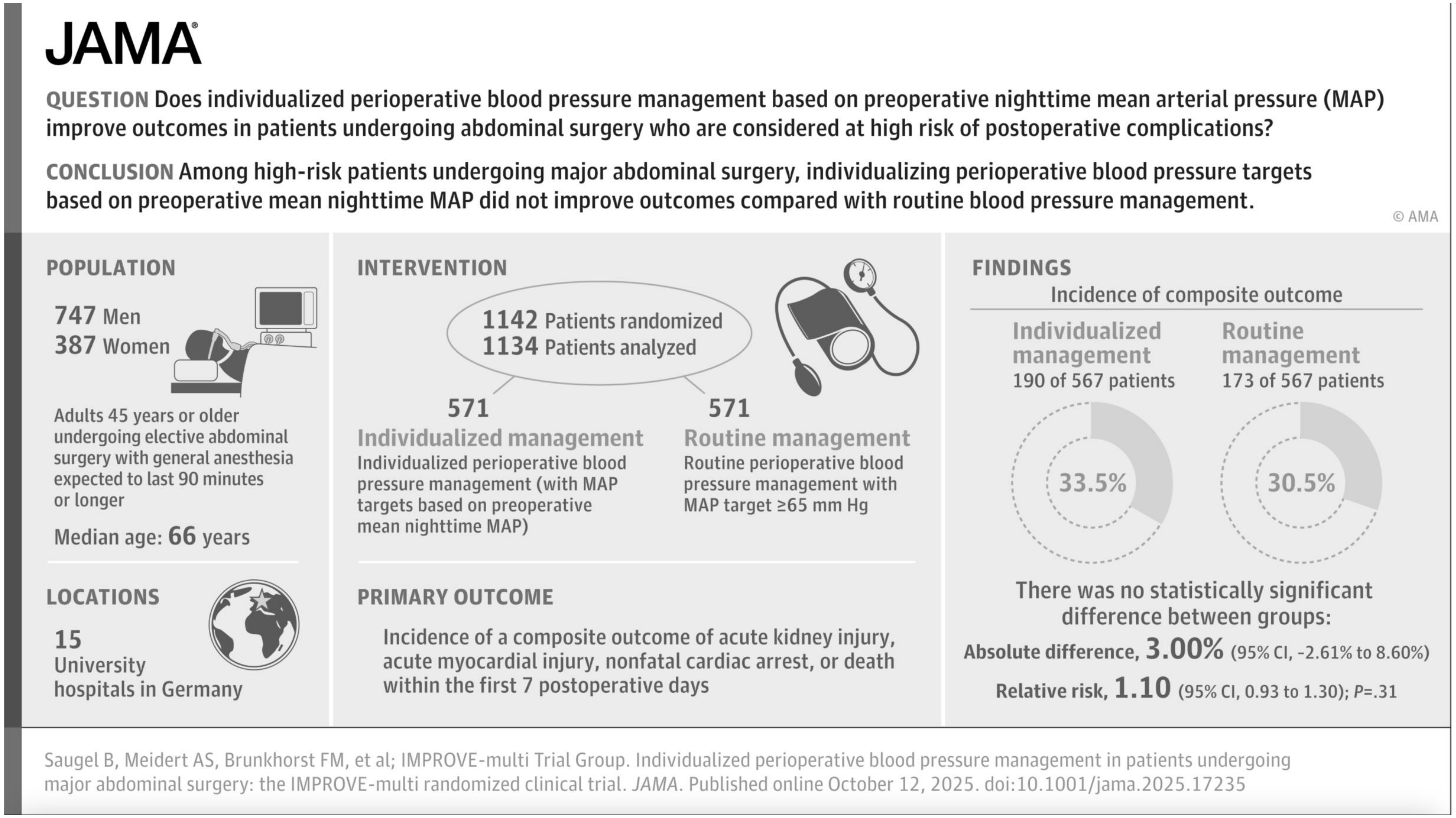
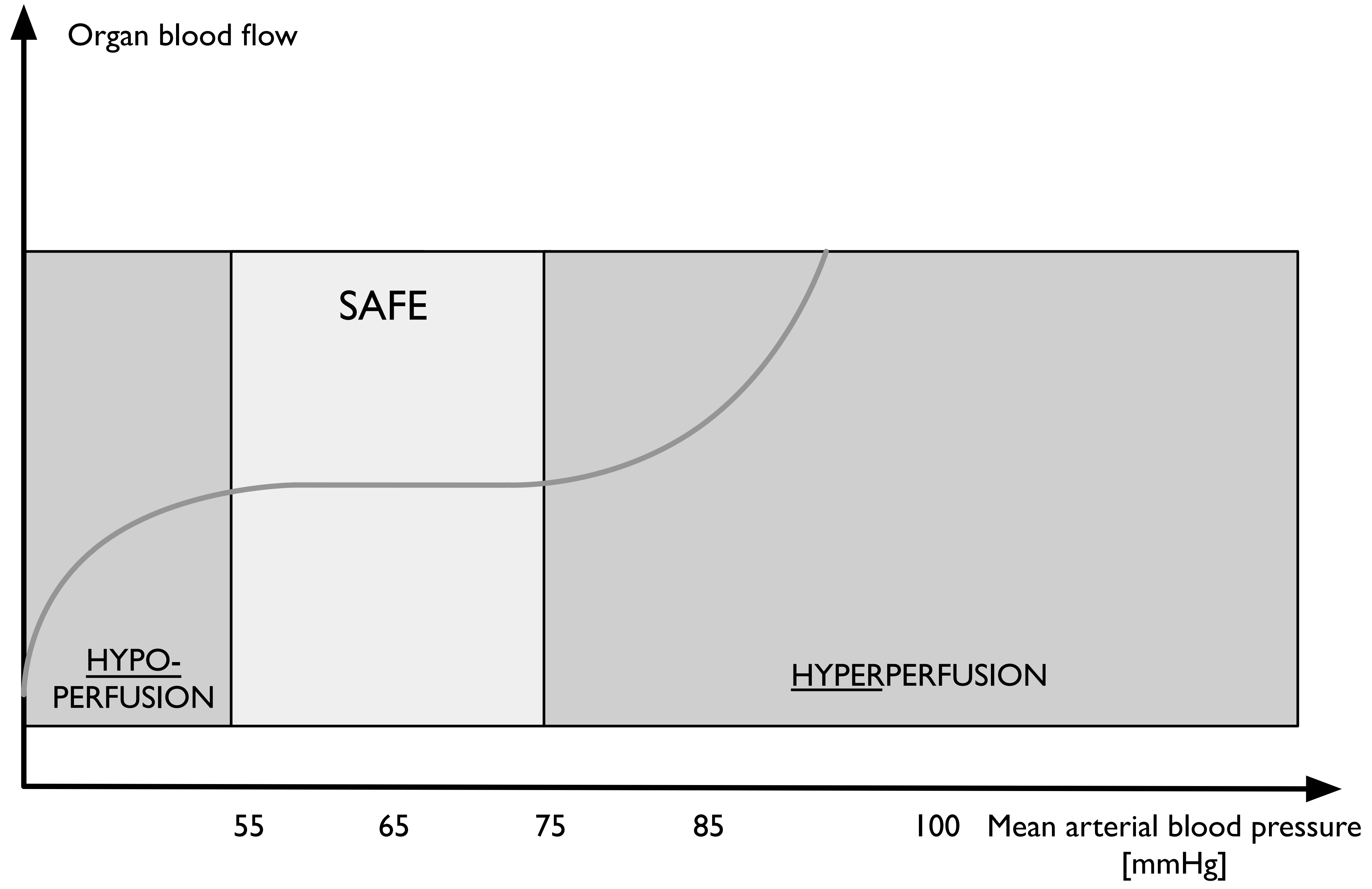


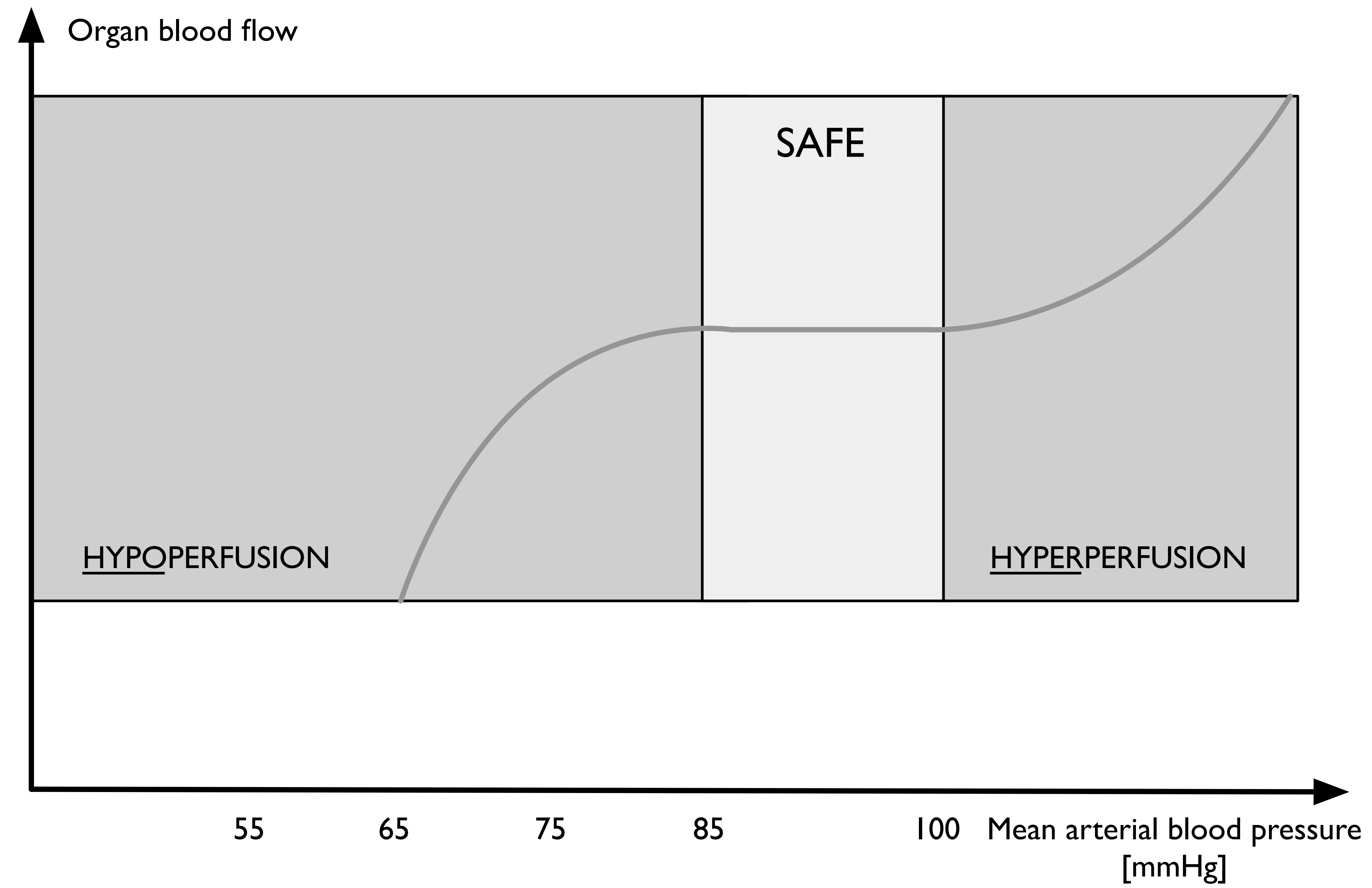
Precision approach 2:

Precision approach 2:

Monitor organ perfusion

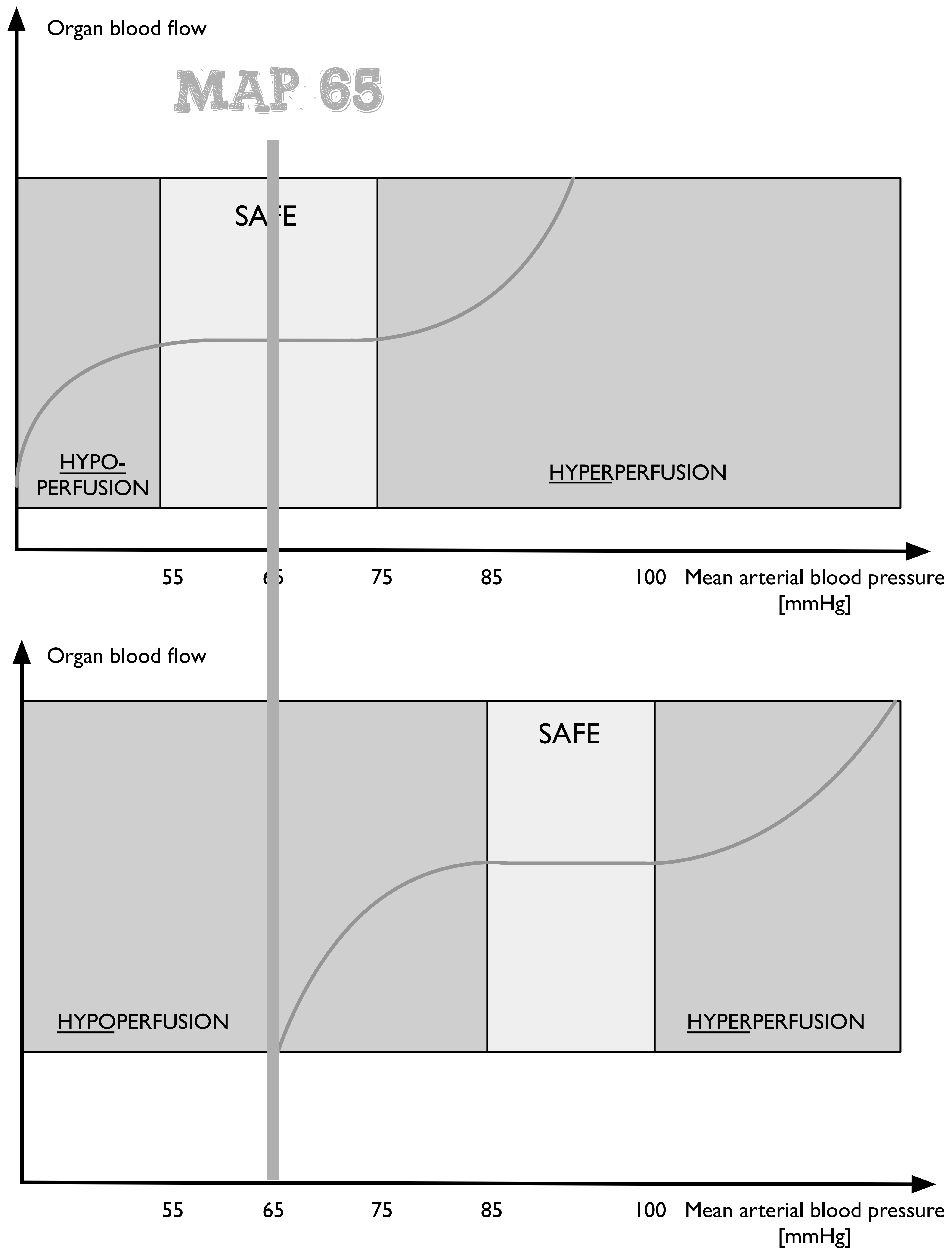
Autoregulation





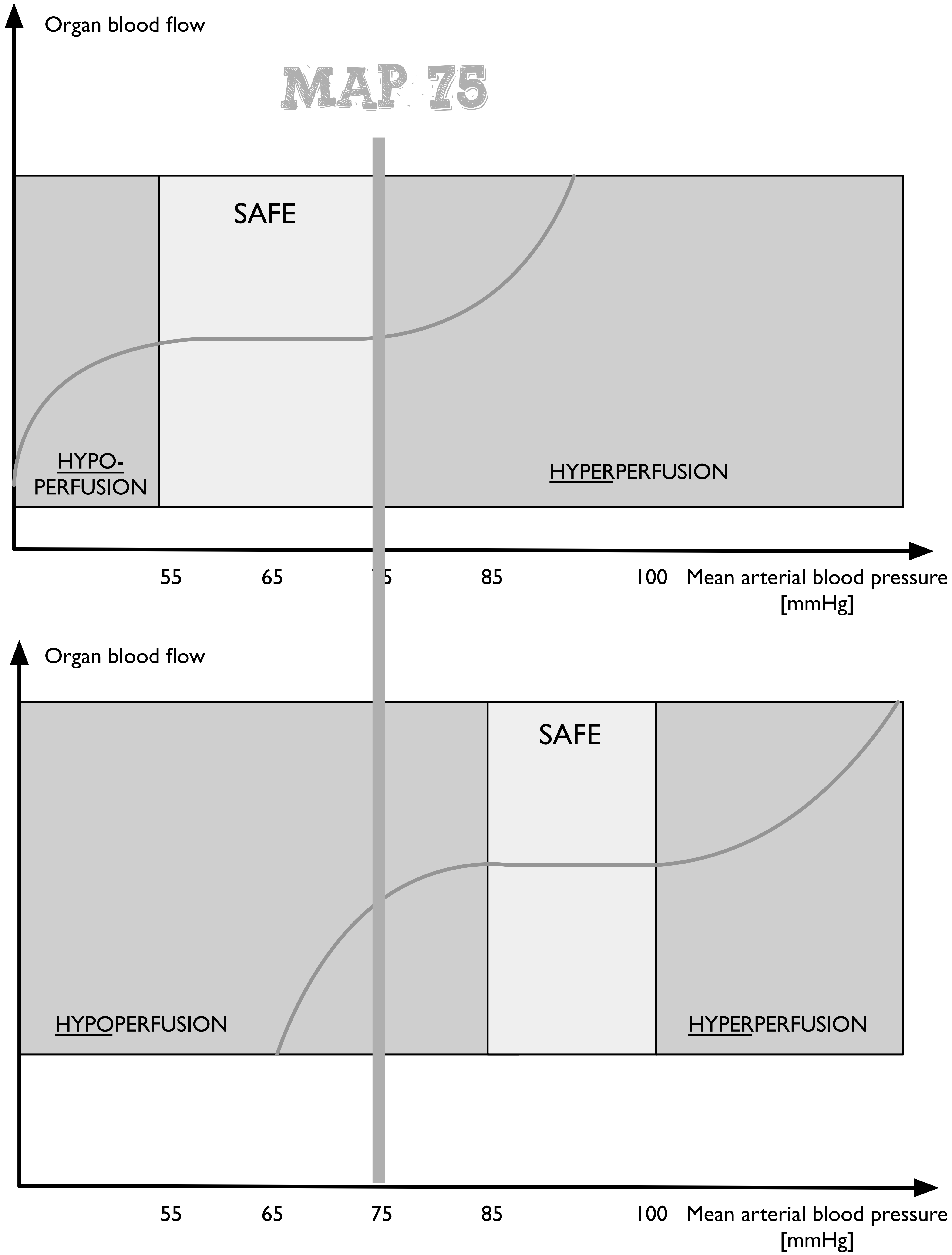
CONCEPT

Autoregulation



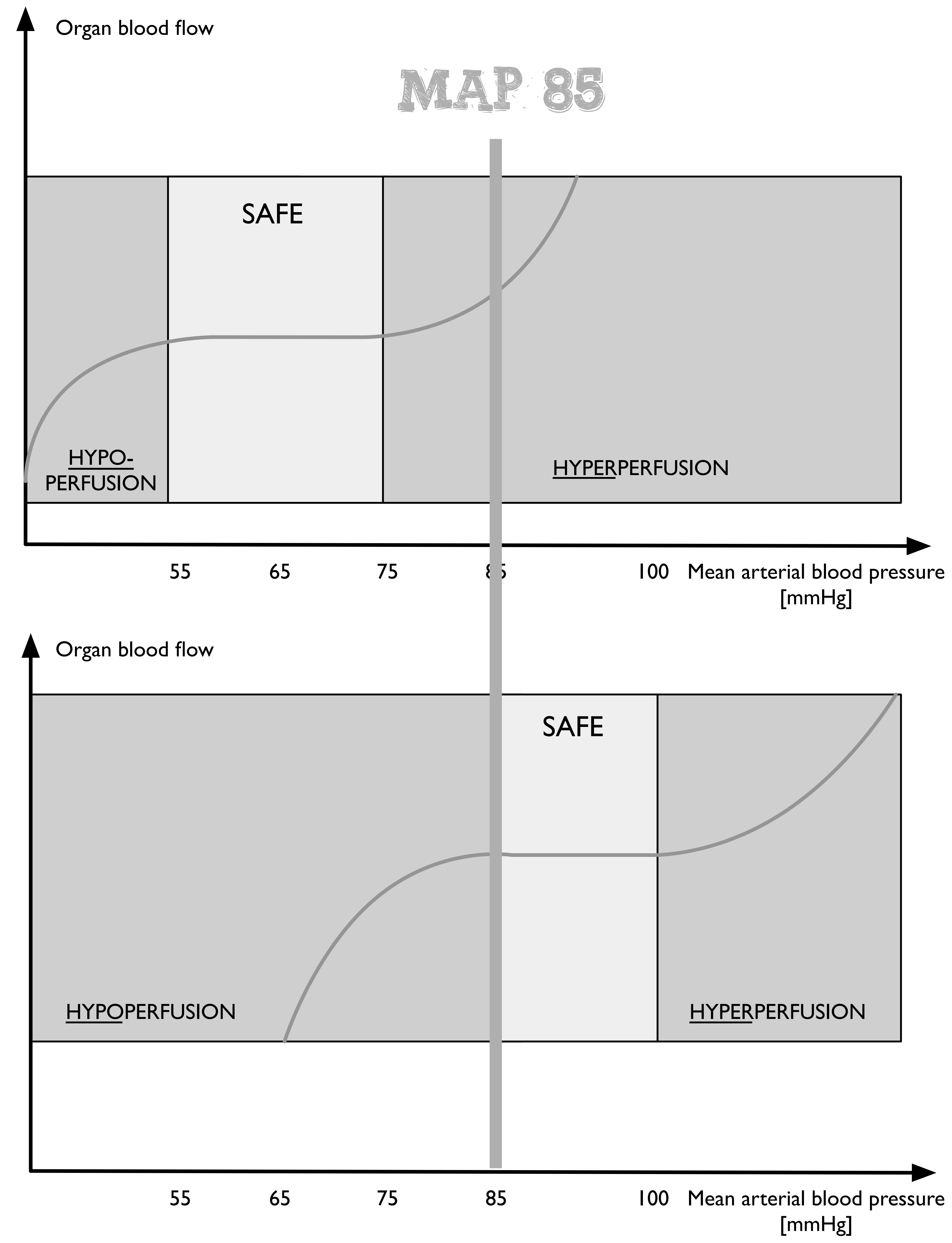
CONCEPT

Autoregulation



CONCEPT

Autoregulation



CONCEPT

Precision approach 2:

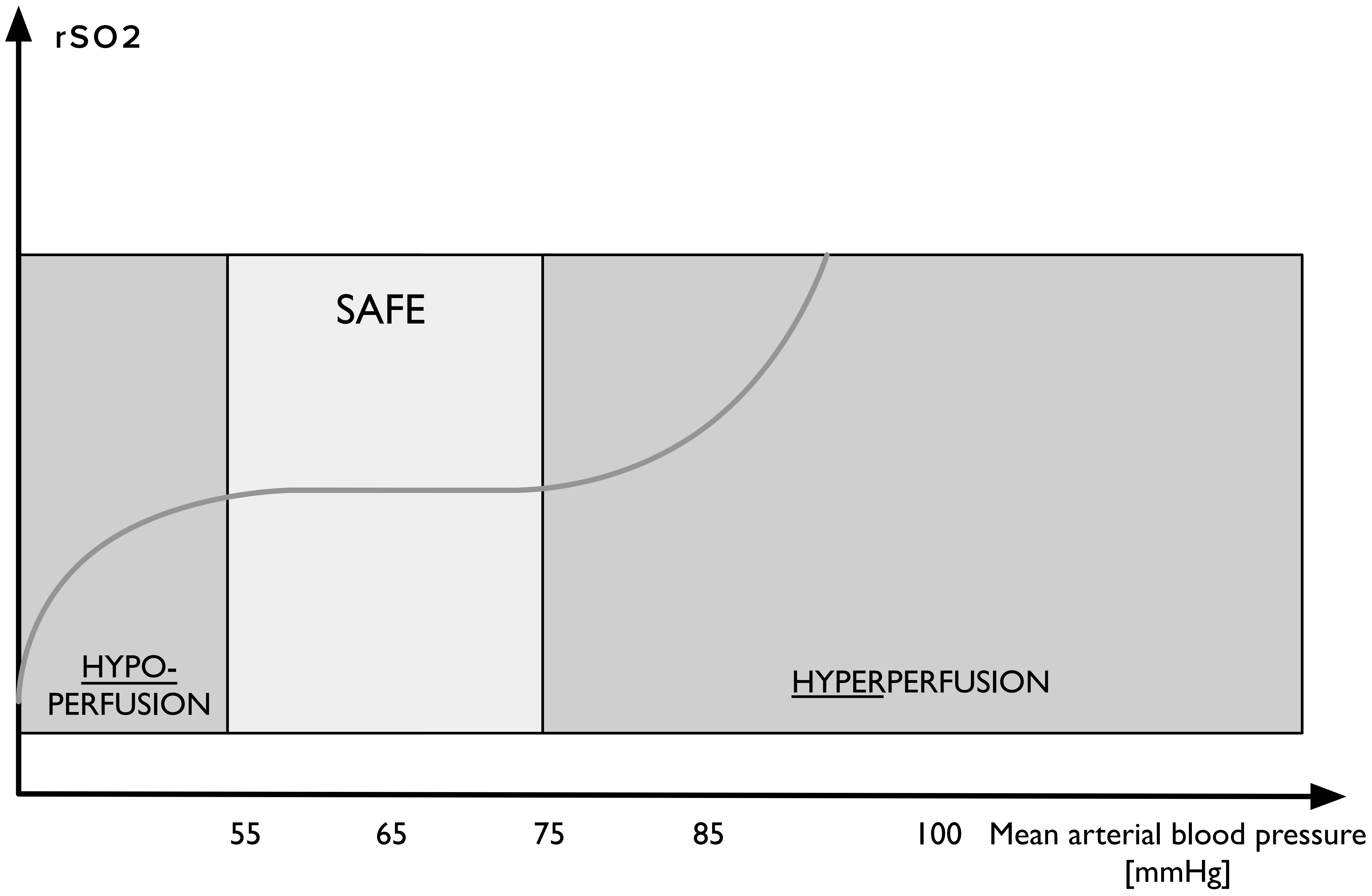
Monitor organ perfusion

Precision approach 2:

Monitor organ perfusion

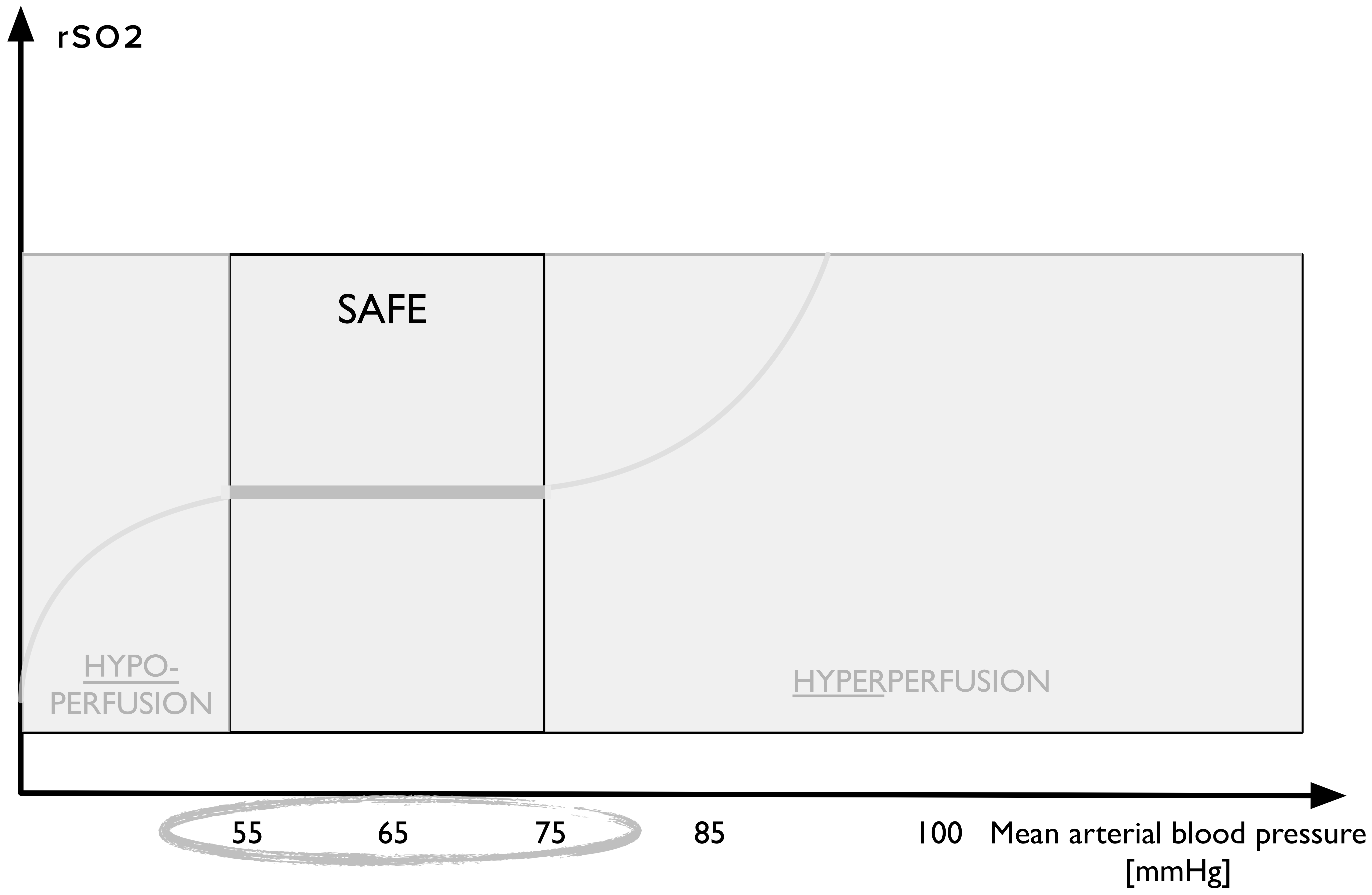
rSO2 (NIRS) as surrogate of CBF

Autoregulation



CONCEPT

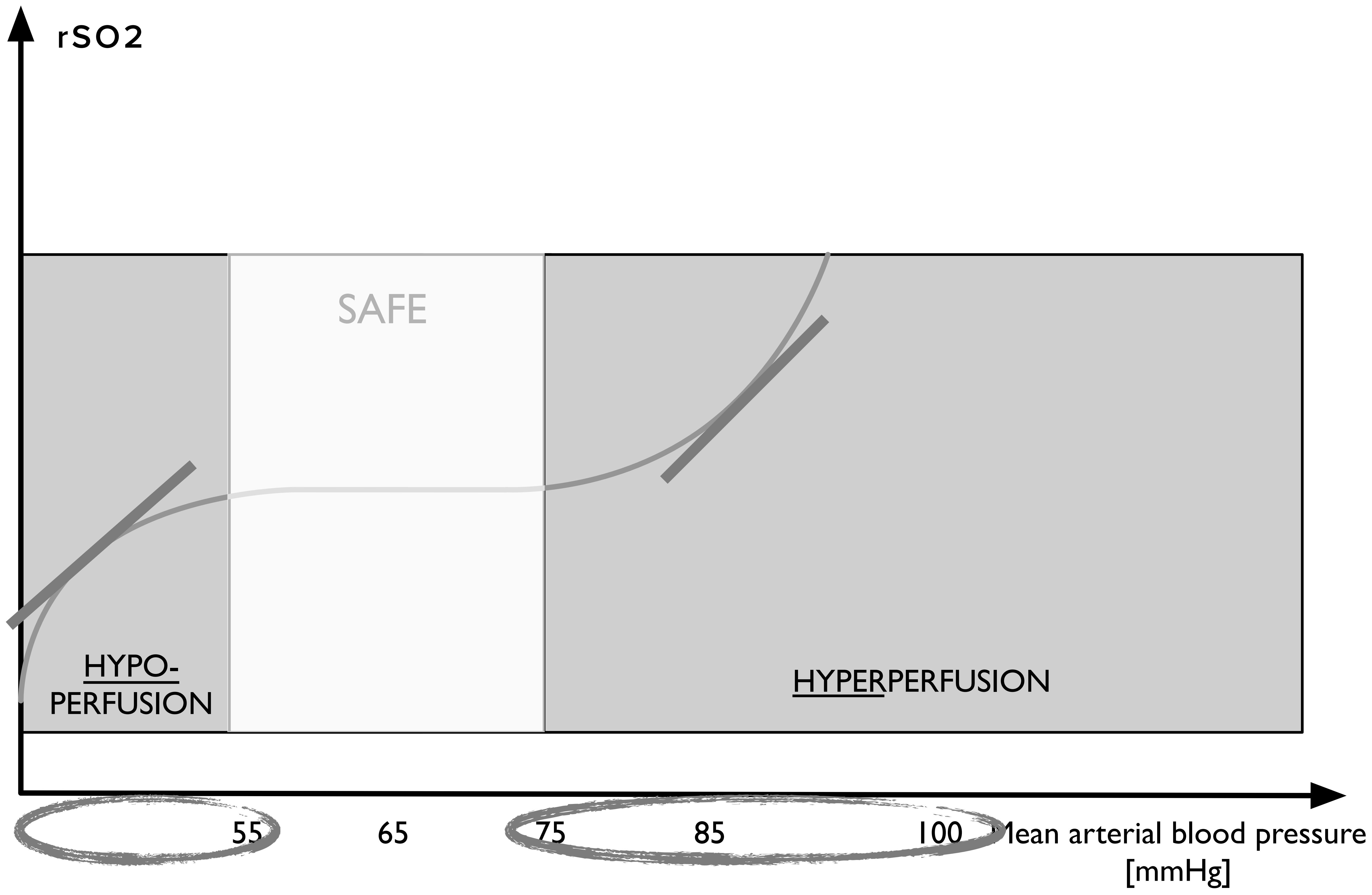
Autoregulation



Preserved cAR: Flow ≠ f(Pressure)

CONCEPT

Autoregulation



Disturbed cAR: Flow = f(Pressure)

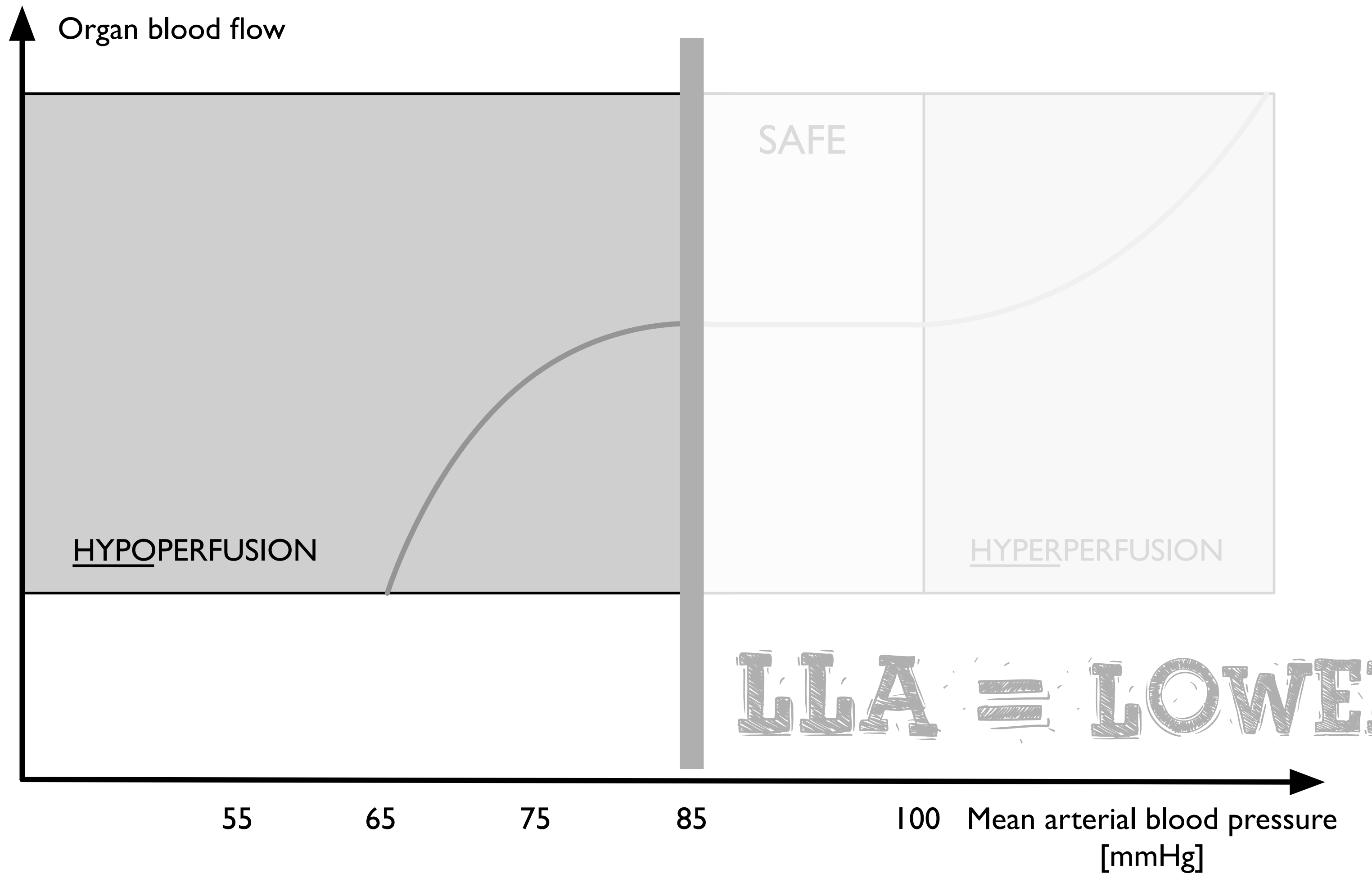
Cerebral autoregulation (cAR) in noncardiac surgery

Monitoring of cerebral blood flow autoregulation in adults undergoing sevoflurane anesthesia: a prospective cohort study of two age groups

Nicolai Goettel[1,2] · Camille Patet[3] · Ariane Rossi[3] · Christoph S. Burkhart[1,5] · Marek Czosnyka[4] · Stephan P. Strebel[1] · Luzius A. Steiner[1,2]

Table 4 Limits and range of cerebral blood flow autoregulation

	Group 1 (18–40 year)	Group 2 (≥65 year)	*P* value
Lower limit of autoregulation (mmHg)	66 ± 12	73 ± 14	0.08
Upper limit of autoregulation (mmHg)	73 ± 19	70 ± 14	0.30
Autoregulatory range (mmHg)	13.8 ± 9.8	10.2 ± 8.6	0.08



LLA = LOWER LIMIT OF AUTOREGULATION

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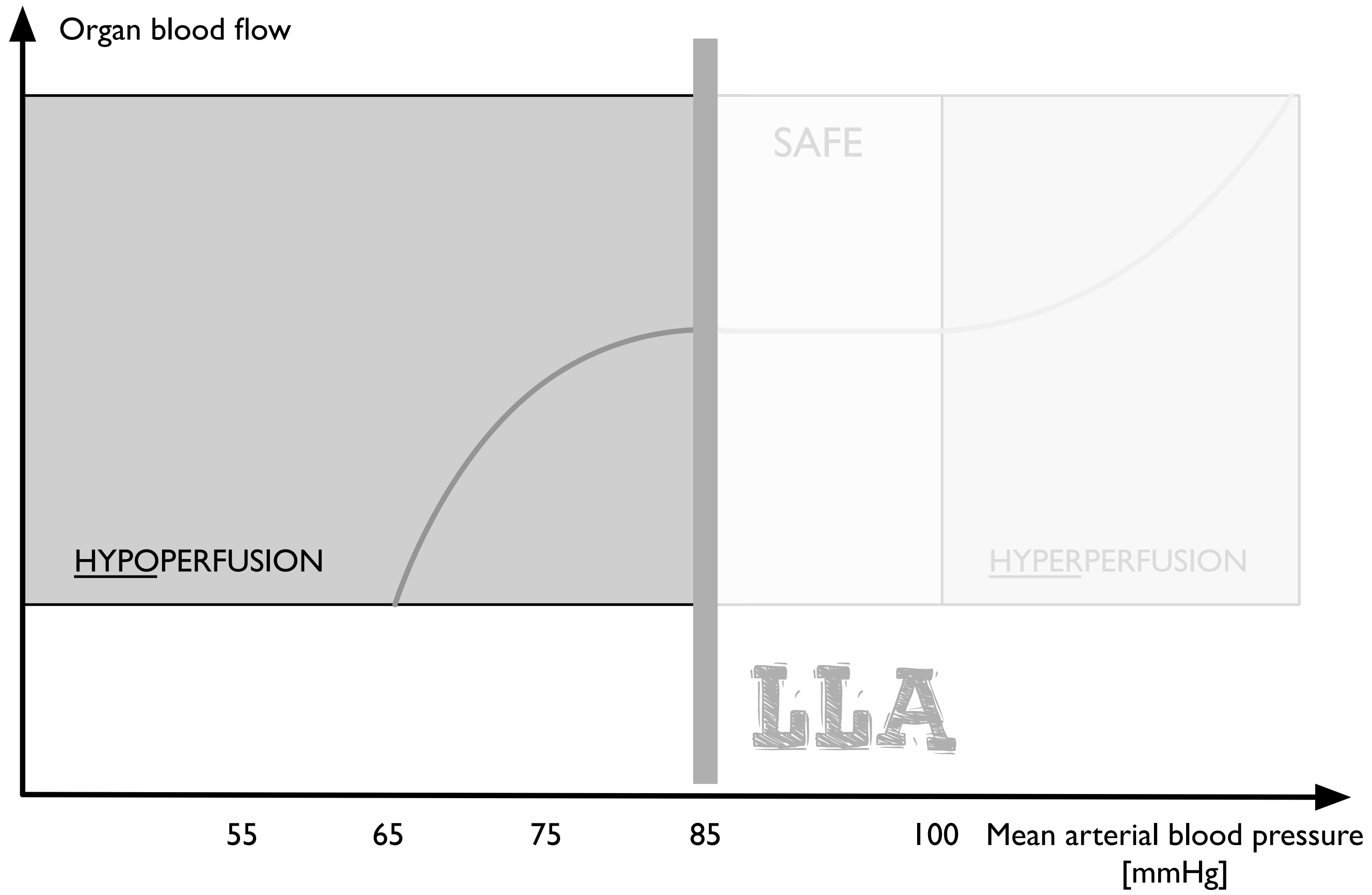
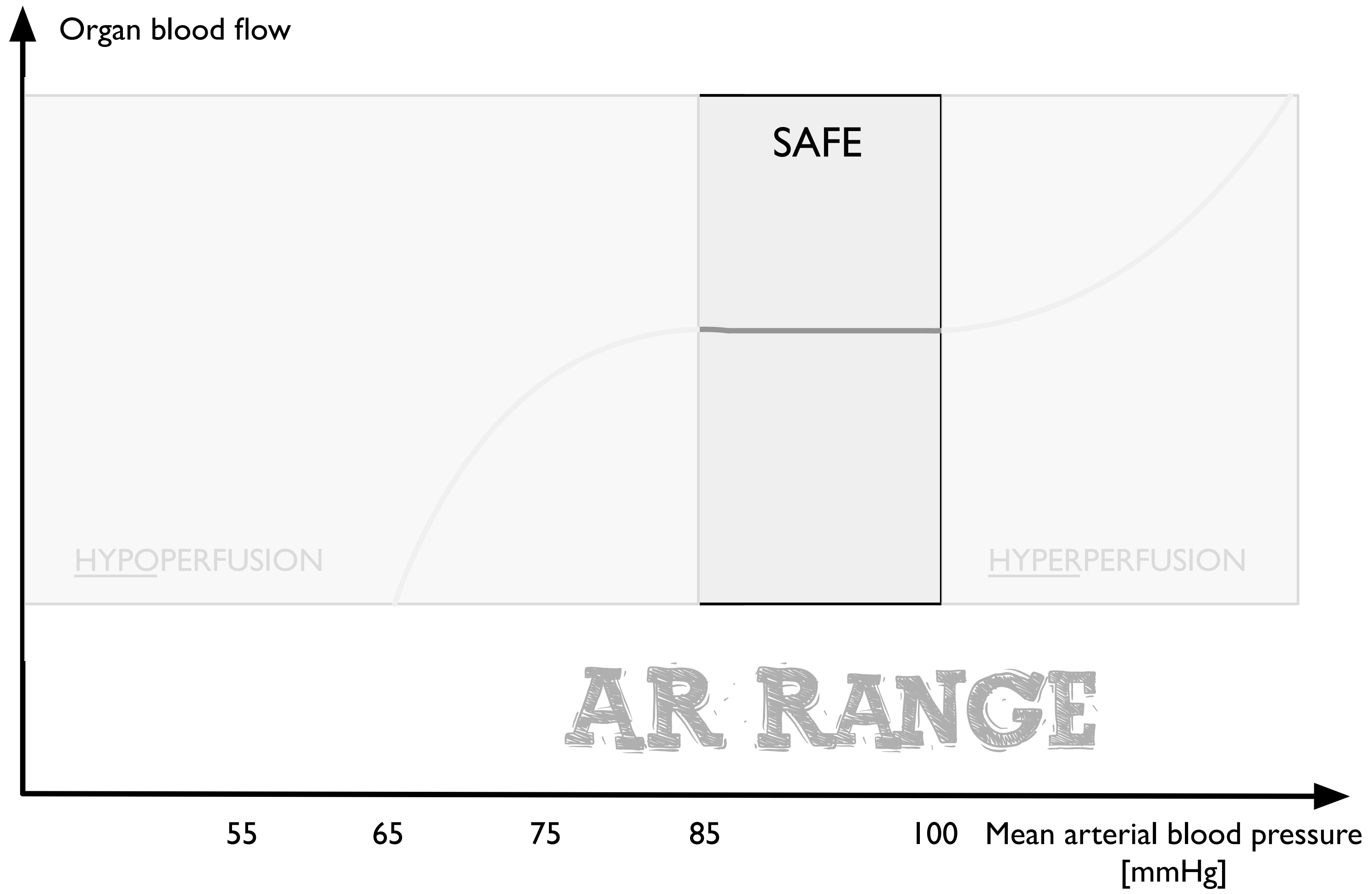
Lower limit of autoregulation (mmHg)	66 ± 12	73 ± 14	0.08
Upper limit of autoregulation (mmHg)	73 ± 19	70 ± 14	0.30
Autoregulatory range (mmHg)	13.8 ± 9.8	10.2 ± 8.6	0.08





Cerebral autoregulation (cAR) in noncardiac surgery

Shoulder Surgery in the Beach Chair Position Is Associated with Diminished Cerebral Autoregulation but No Differences in Postoperative Cognition or Brain Injury Biomarker Levels Compared with Supine Positioning: The Anesthesia Patient Safety Foundation Beach Chair Study

Andrew Laflam, BS,* Brijen Joshi, MD,† Kenneth Brady, MD,‡ Gayane Yenokyan, PhD,§ Charles Brown, MD,* Allen Everett, MD,|| Ola Selnes, PhD,¶ Edward McFarland, MD,# and Charles W. Hogue, MD*

Table 3. Comparison of Mean Arterial Blood Pressure (MAP), Bispectral Index (BIS), and Cerebral Oximetry Index (Cox Autoregulation Data for Patients Who Underwent Surgery in the Lateral Decubitus and Beach Chair Position)

Characteristic	Lateral decubitus (*n* = 109)	Beach chair (*n* = 109)	β coefficient (95% confidence interval)	*P* value[a]
MAP (mm Hg)	73 ± 14	79 ± 13	6.6 (2.2, 11.0)	0.003
Estimated average MAP (mm Hg) at tragus	76 ± 13	50 ± 16	−28.0 (−32.7, −23.3)	<0.0001
BIS	41 ± 11	46 ± 10	1.6 (−1.3, 4.5)	0.276
Mean left $rSco_2$ (%)	75 ± 13	64 ± 14	−7.7 (−11.8, −3.5)	<0.0001
Mean right $rSco_2$ (%)	74 ± 14	63 ± 14	−8.3 (−12.4, −4.2)	<0.0001
Mean Cox (left and right)	0.09 ± 0.12	0.15 ± 0.13	0.04 (0.00, 0.08)	0.035
Patients achieving LLA	65%	75%	−0.3 (−1.0, 0.4)	0.367
MAP at LLA (mm Hg)[b]	65 (55–75)	70 (55–80)	1.3 (−3.9, 6.5)	0. 620

Data are given as mean ± SD unless otherwise indicated. The *P* values were adjusted for age and hypertension status at baseline.
$rSco_2$ = regional cerebral O_2 saturation; LLA = lower limit of autoregulation.
[a]Wald test from the generalized linear regression model with robust variance. The model is fitted using fractional polynomial approach in Stata (Reference: Royston and Altman.[29]
[b]Median (25th–75th percentile).

Large variability of AR boundaries in noncardiac Surgery

cAR boundaries cannot be predicted

Predicting the Limits of Cerebral Autoregulation During Cardiopulmonary Bypass

Brijen Joshi, MD,* Masahiro Ono, MD,† Charles Brown, MD,* Kenneth Brady, MD,‡
R. Blaine Easley, MD,§ Gayane Yenokyan, PhD,‖ Rebecca F. Gottesman, MD, PhD,¶
and Charles W. Hogue, MD*

Table 4. Sensitivity, Specificity, and Area Under the Receiver Operator Characteristic (ROC) Curve for Various Cut-Offs of Mean Arterial Blood Pressure (MAP) from Preoperative Baseline Measurement for Predicting the Lower Limit of Cerebral Blood Flow Autoregulation

MAP decrement from baseline	Sensitivity	95% CI	Specificity	95% CI	Area under ROC
>15%	91%	87% to 93%	37%	32% to 41%	0.7354
>25%	71%	66% to 76%	66%	61% to 70%	
>35%	42%	37% to 47%	88%	85% to 91%	

CI = confidence interval; MAP = mean arterial blood pressure.

Not just the brain, other organs too

BJA

British Journal of Anaesthesia, 129 (1): 22–32 (2022)

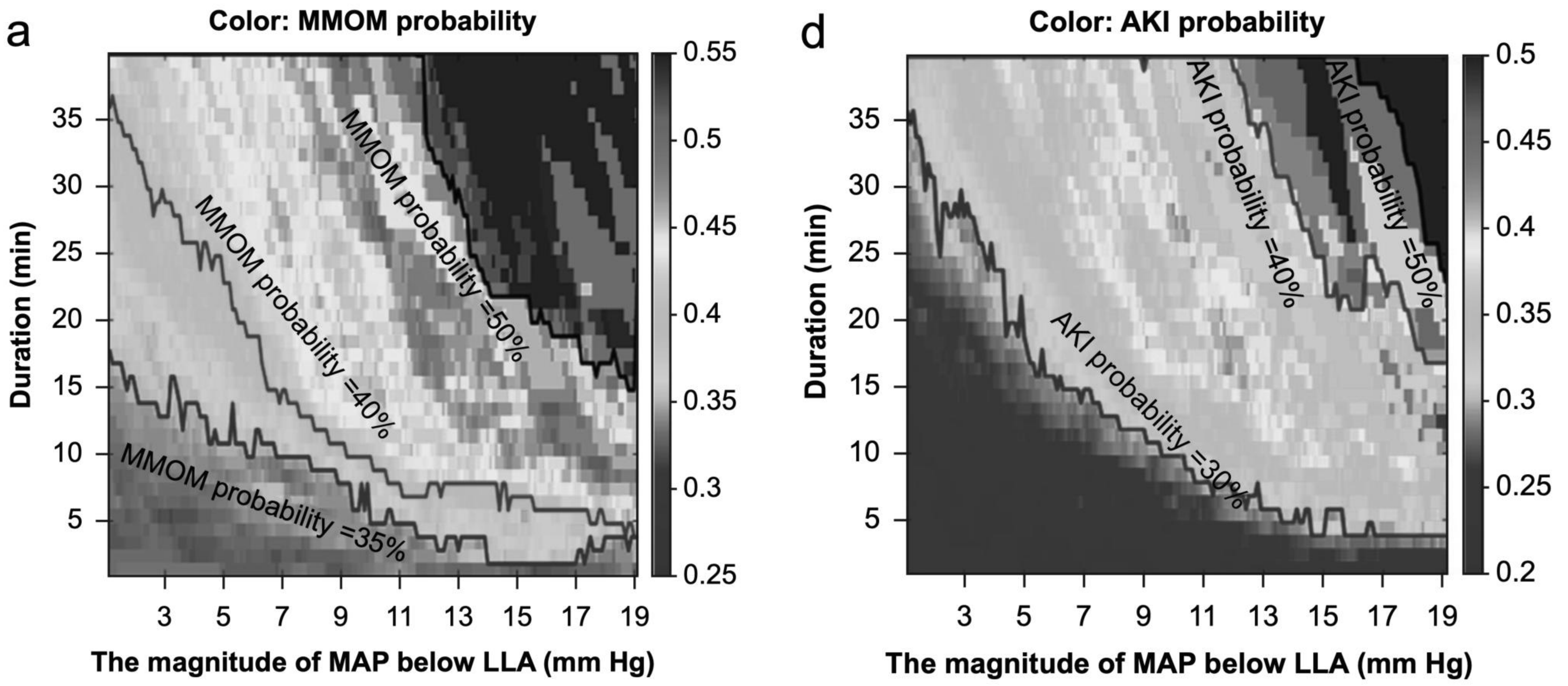
doi: 10.1016/j.bja.2022.03.029
Advance Access Publication Date: 18 May 2022
Cardiovascular

Comparison of different metrics of cerebral autoregulation in association with major morbidity and mortality after cardiac surgery

Xiuyun Liu[1,2,*], Joseph Donnelly[3], Ken M. Brady[4], Kei Akiyoshi[1], Brian Bush[1], Raymond C. Koehler[1], Jennifer K. Lee[1], Charles W. Hogue[5], Marek Czosnyka[6,7], Peter Smielewski[6] and Charles H. Brown IV [1,*]

[1]Department of Anesthesiology and Critical Care Medicine, School of Medicine, Johns Hopkins University, Baltimore, MD, USA, [2]Academy of Medical Engineering and Translational Medicine, Tianjin University, Tianjin, China, [3]Department of Anaesthesiology, University of Auckland, Auckland, New Zealand, [4]Department of Anesthesiology, Northwestern University, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA, [5]Department of Anesthesiology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA, [6]Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK and [7]Institute of Electronic Systems, Warsaw University of Technology, Warsaw, Poland

*Corresponding authors. E-mails: liuxiuyun1@gmail.com, cbrownv@jhmi.edu



CARDIAC SURGERY

Not just the brain, other organs too

BJA

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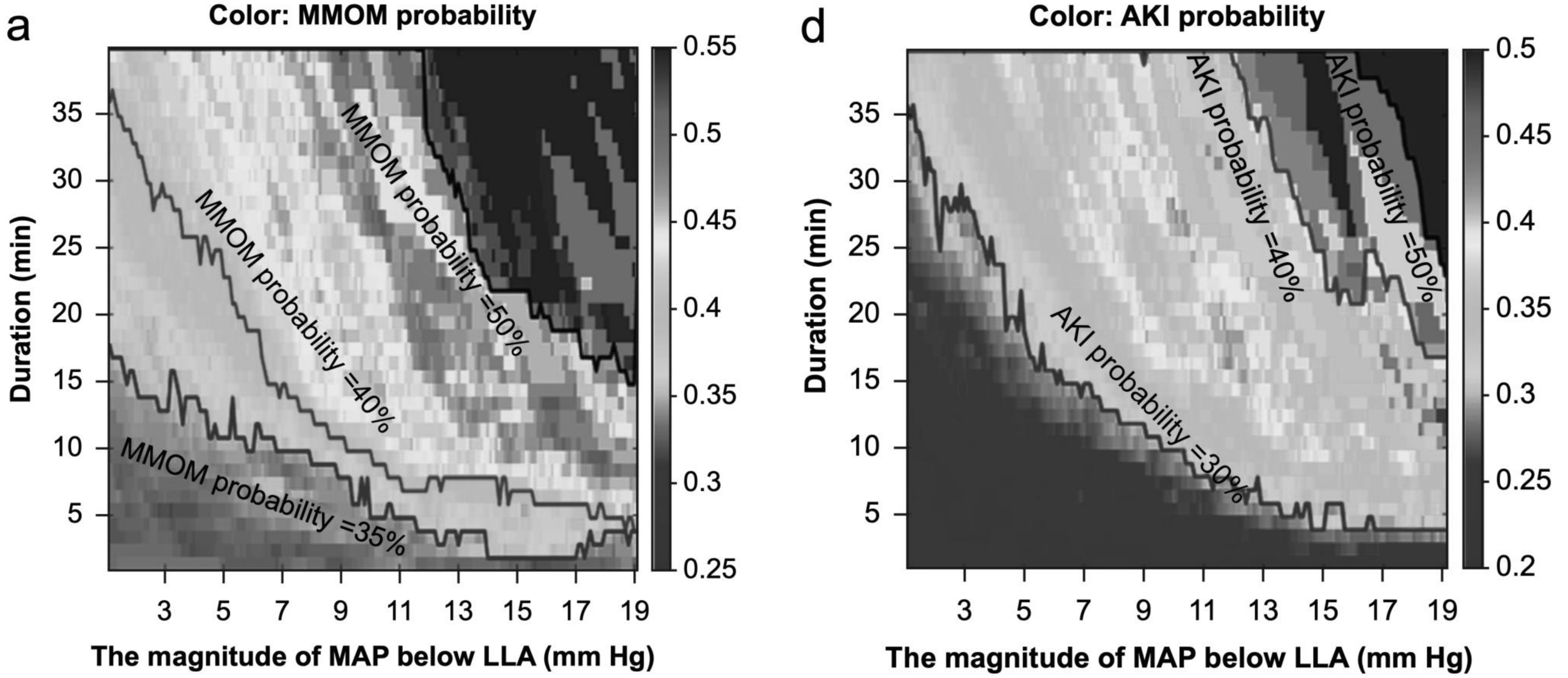
*Corresponding authors. E-mails: liuxiuyun1@gmail.com, cbrownv@jhmi.edu



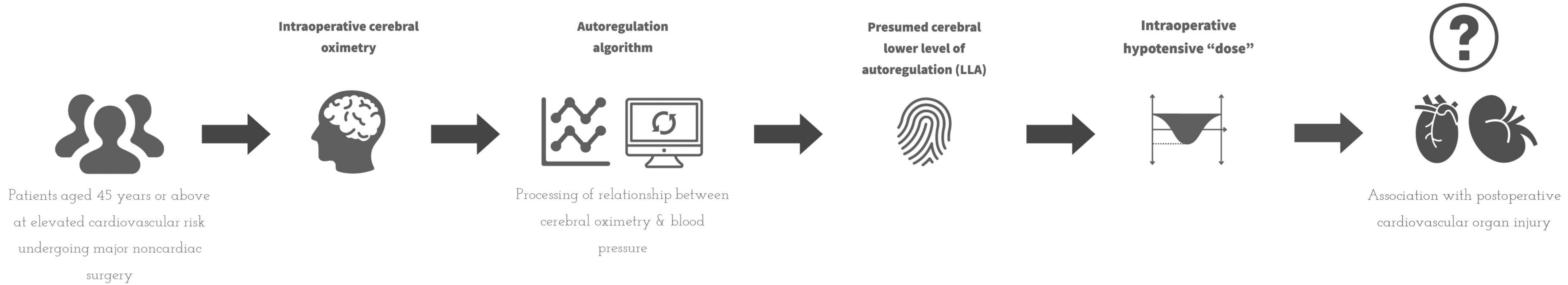
MAGNITUDE & DURATION OF
MAP < CEREBRAL LLA ASSOCIATED WITH
CARDIOVASCULAR AND RENAL MORBIDITY FOLLOWING
CARDIAC SURGERY

What Does this Mean for Noncardiac Surgery ?

WHAT DOES THIS MEAN FOR NONCARDIAC SURGERY ?

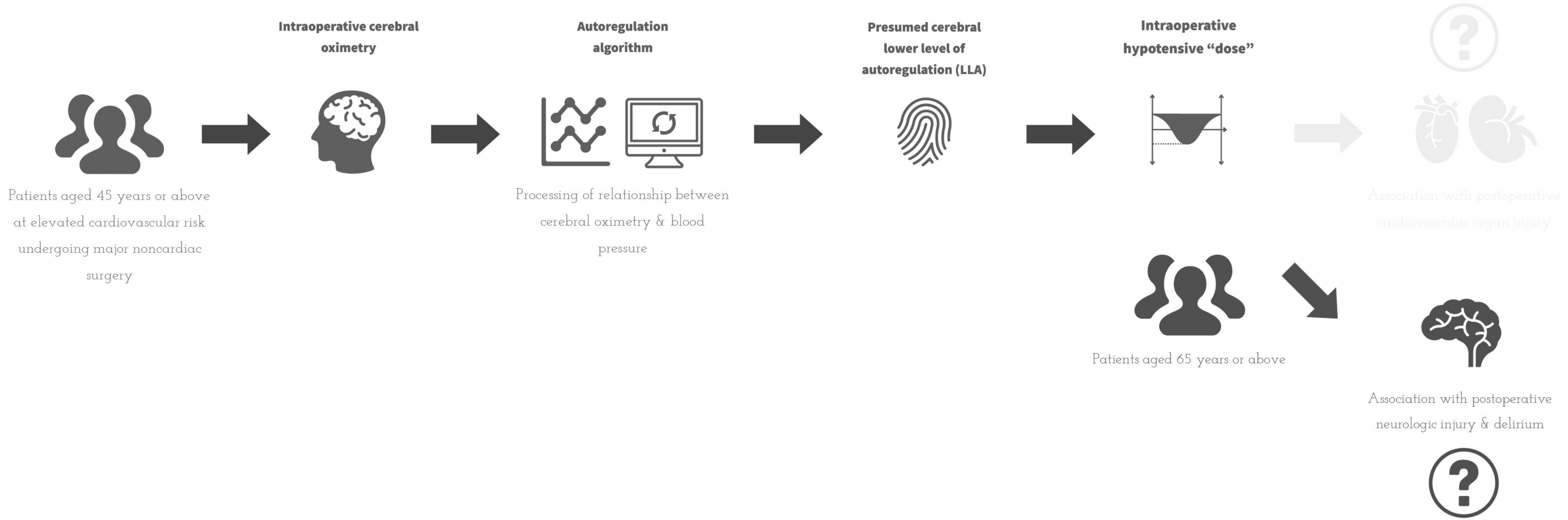
WE DO NOT KNOW, YET.

AUTOREGULATE-NONCARDIAC



CONFLICT OF INTEREST

AUTOREGULATE-NONCARDIAC



CONFLICT OF INTEREST

AUTOREGULATE-NONCARDIAC

CONFLICT OF INTEREST

Cerebral autoregulation in real life: Individual patients

cAR monitoring in real life

Intraoperative hypotension and postoperative outcomes: just the tip of the iceberg. Comment on *Br J Anaesth* 2023; 131: 823–31

Patrick M. Wanner[1,*], Andreas P. Vogt[2], Miodrag Filipovic[3], Luzius A. Steiner[1] on behalf of the Personalising Acute Care Network

[1]Clinic for Anaesthesia, Intermediate Care, Prehospital Emergency Medicine and Pain Therapy, University Hospital Basel, Basel, Switzerland, [2]Department of Anaesthesiology and Pain Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland and [3]Division of Perioperative Intensive Care Medicine, Kantonsspital St.Gallen, St. Gallen, Switzerland

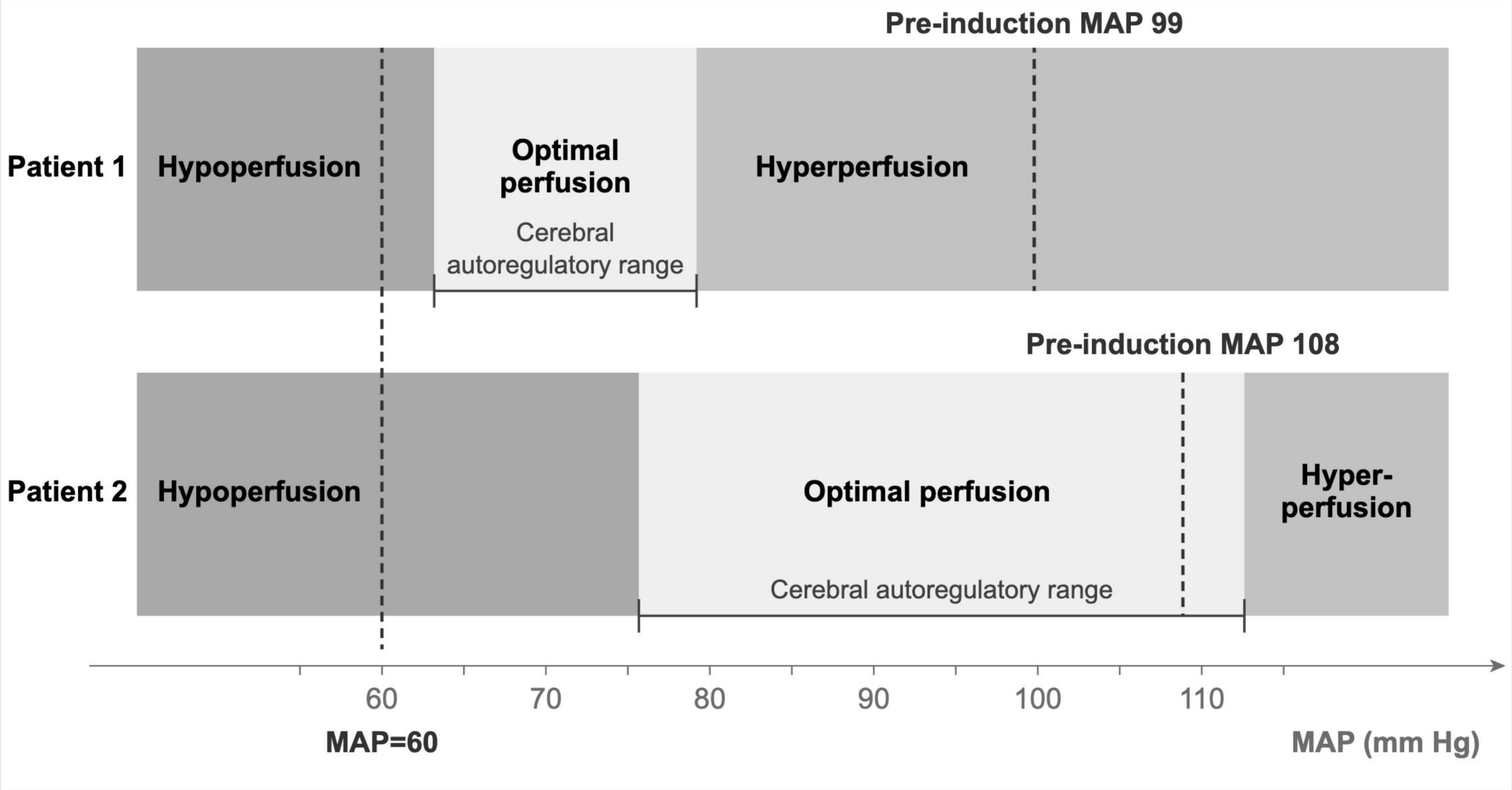


Fig 1. The cerebral autoregulatory range under general anaesthesia varies markedly between patients. Unpublished data from the AUTOREGULATE-NONCARDIAC study: patient 1 has an optimal perfusion range of 63–79 mm Hg and patient 2 of 76–113 mm Hg. An MAP ≤60 mm Hg would likely cause cerebral hypoperfusion in both patients, but even preoperatively tolerated arterial pressures might be unsafe under general anaesthesia. MAP, mean arterial pressure.

cAR monitoring in real life

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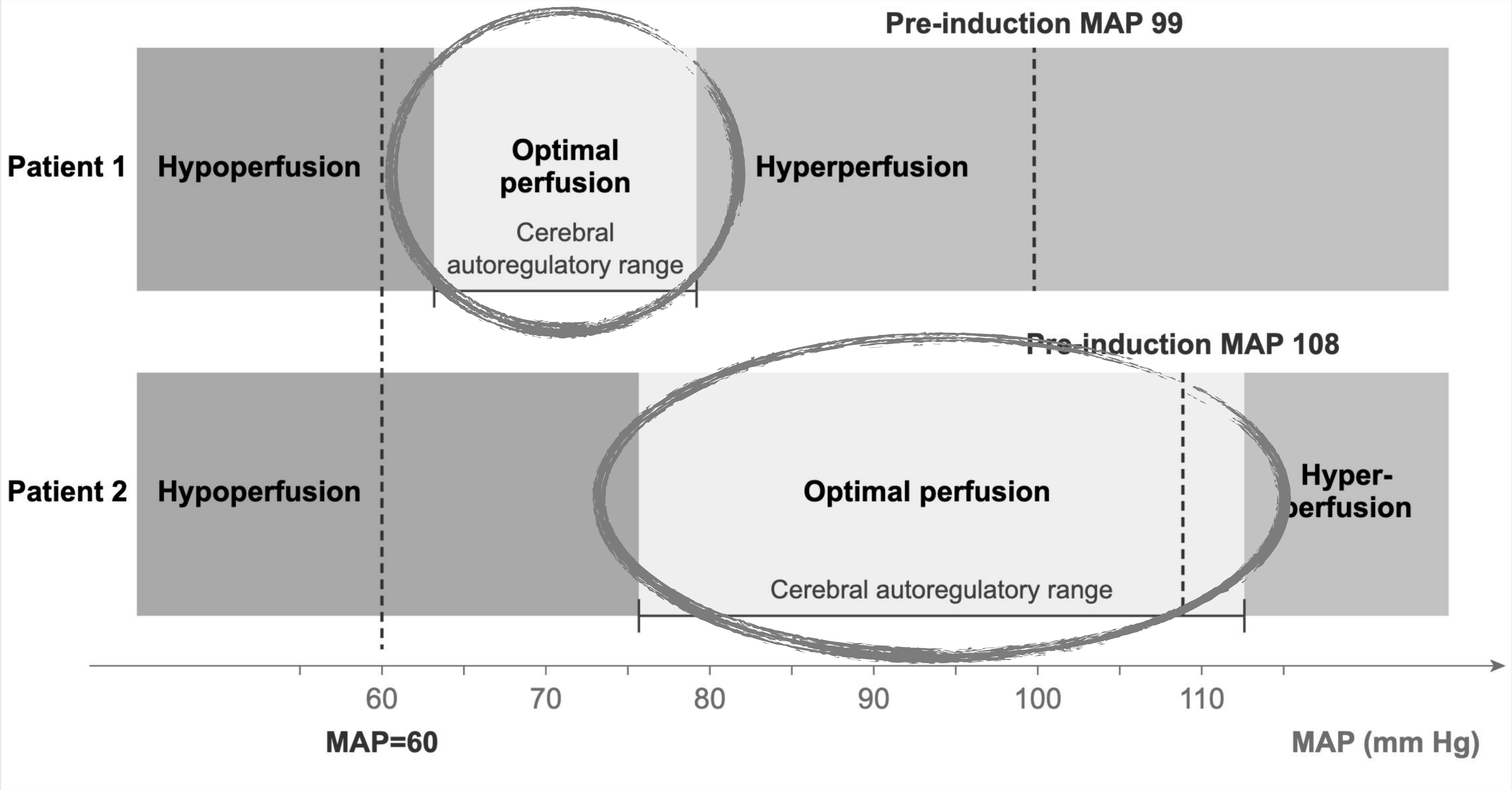

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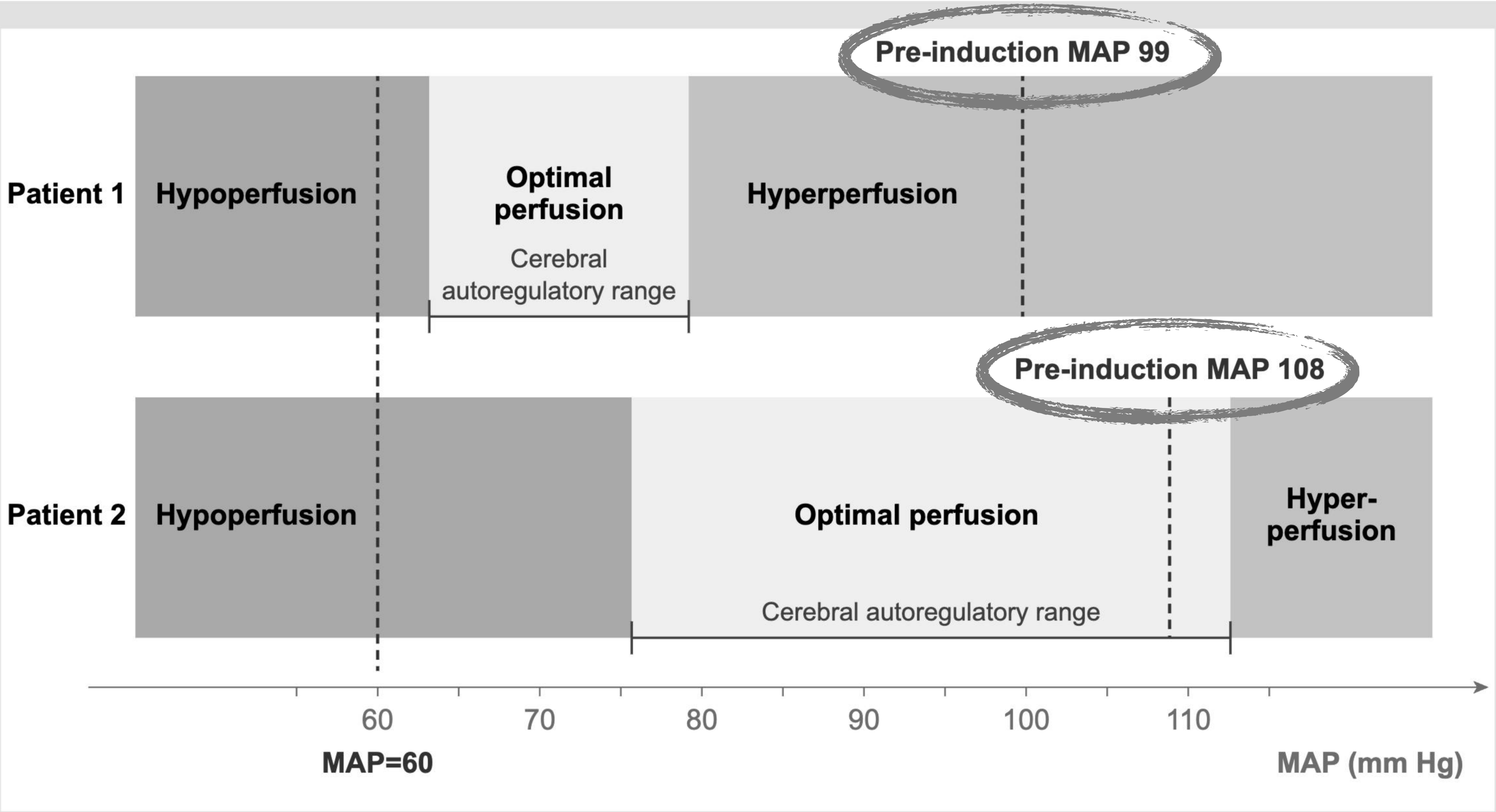

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Cerebral autoregulation in real life: Individual patients

Patients differ and
even preop BPs may be unsafe.

Cerebral autoregulation in real life: Whole populations

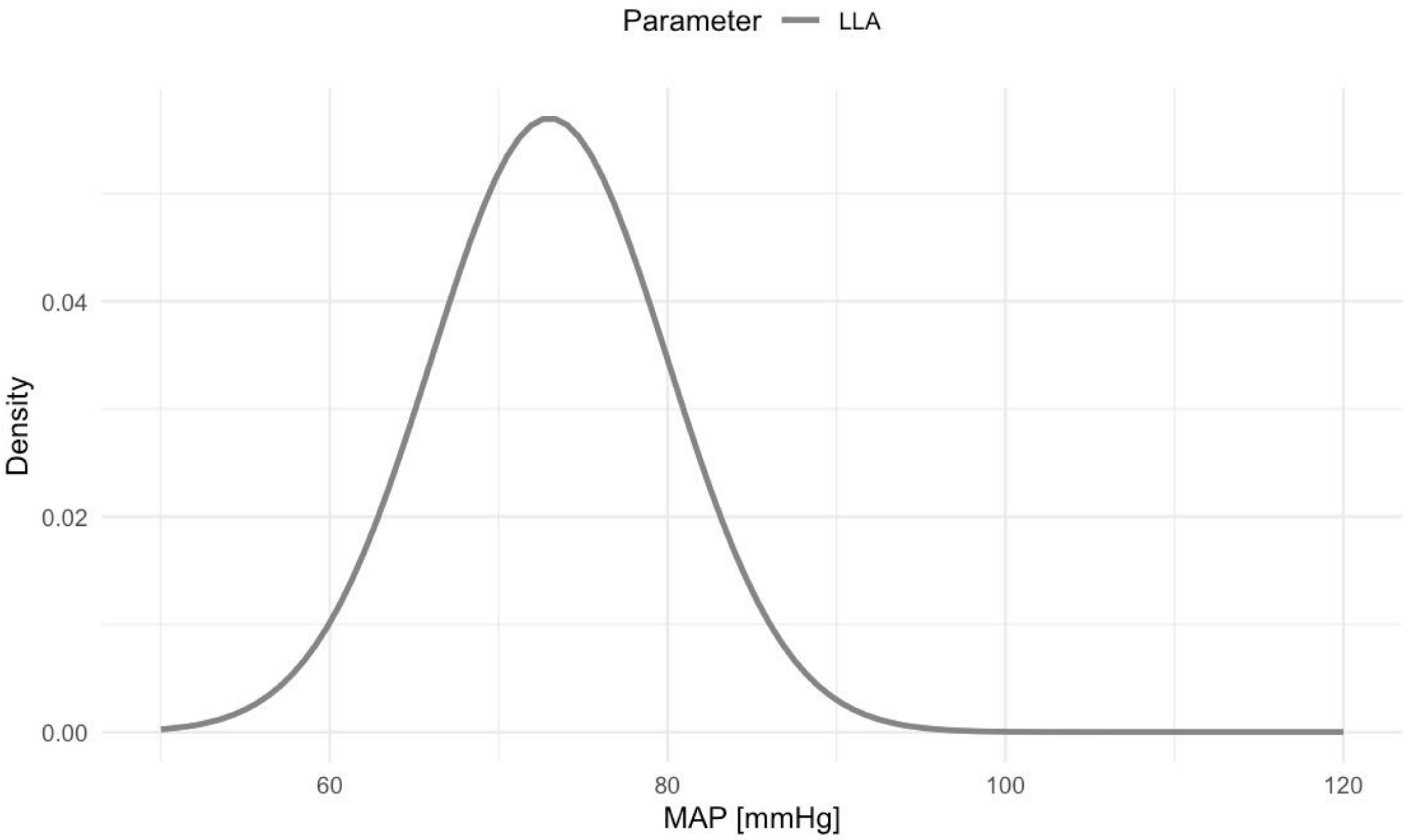
Prelim findings in a high-risk population

AUTOREGULATE-NONCARDIAC

Cave: preliminary, not peer-reviewed.

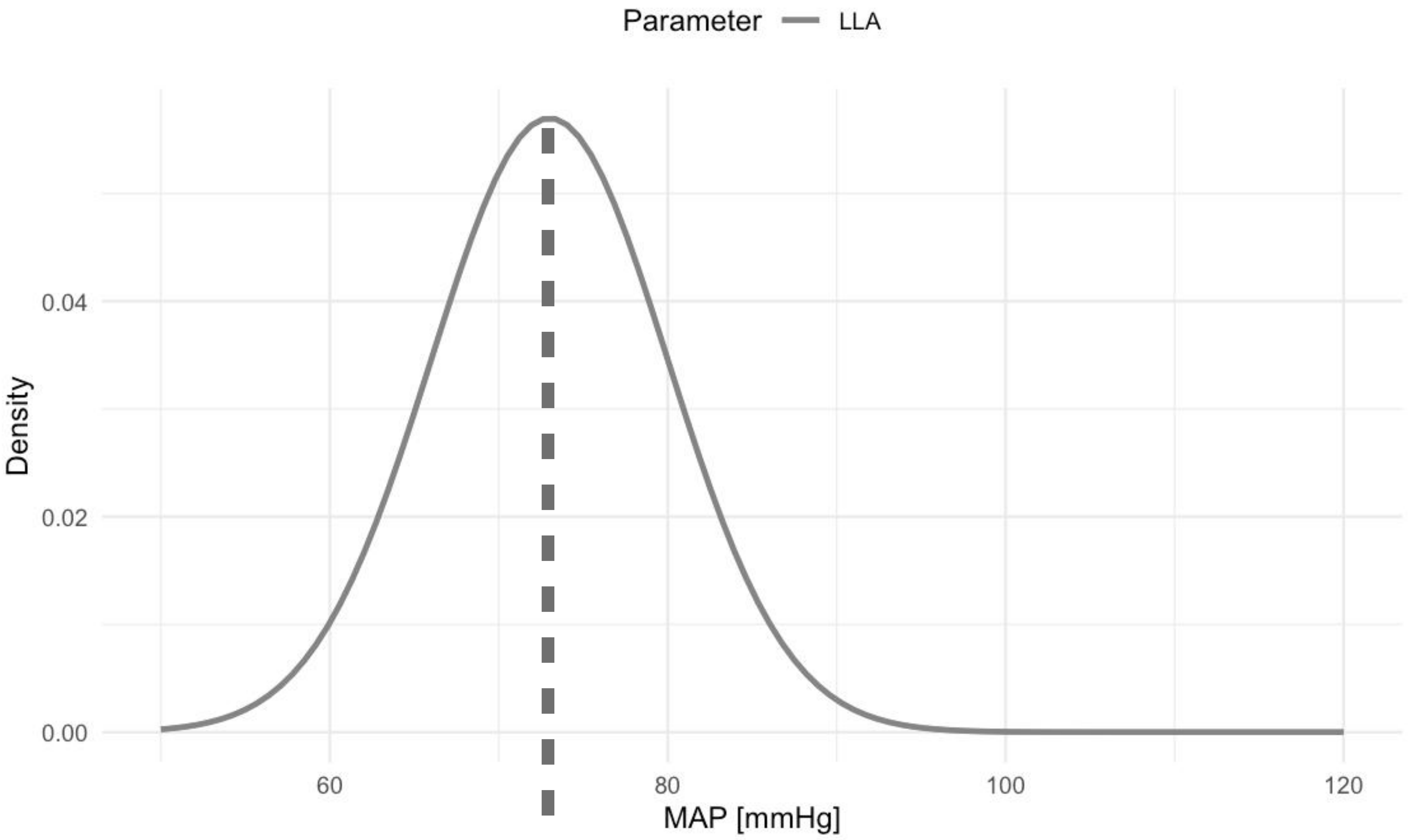
Preliminary findings on a population level

LLA = LOWEST SAFE BP



Preliminary findings on a population level

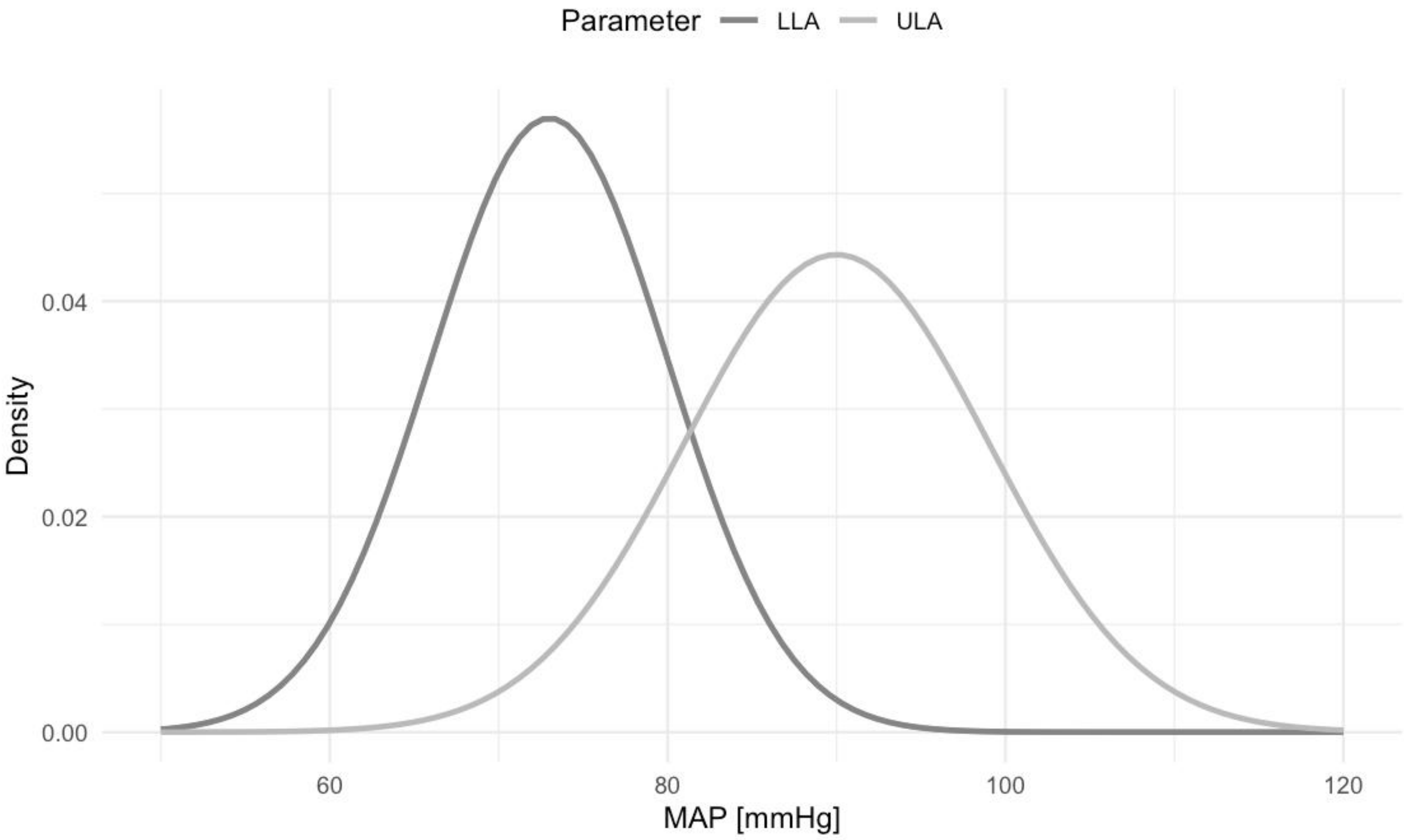
LLA = LOWEST SAFE BP



MEDIAN LLA 73 (95% CI 70-75)
IQR 68-77

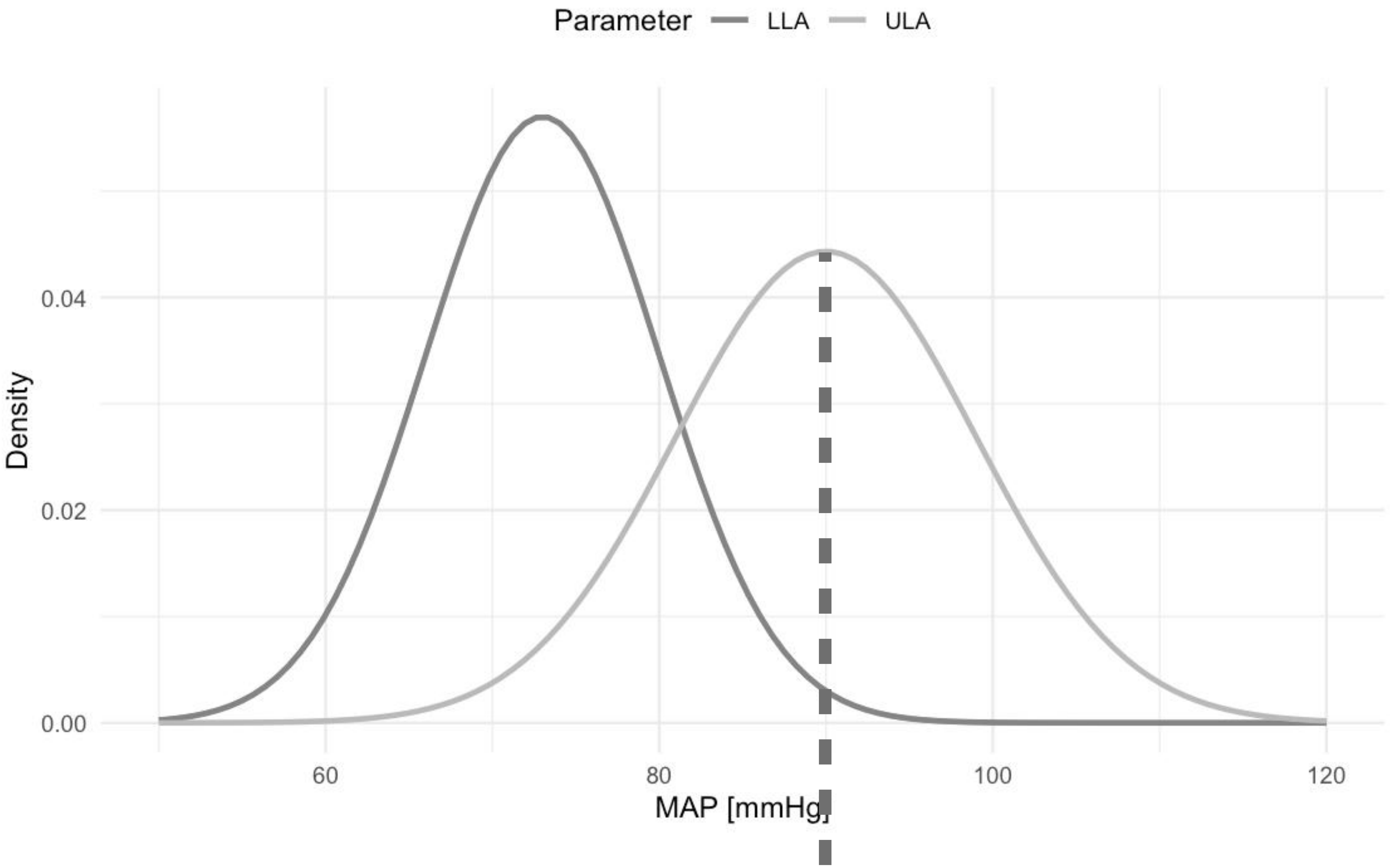
Preliminary findings on a population level

ULA = Highest safe BP



Preliminary findings on a population level

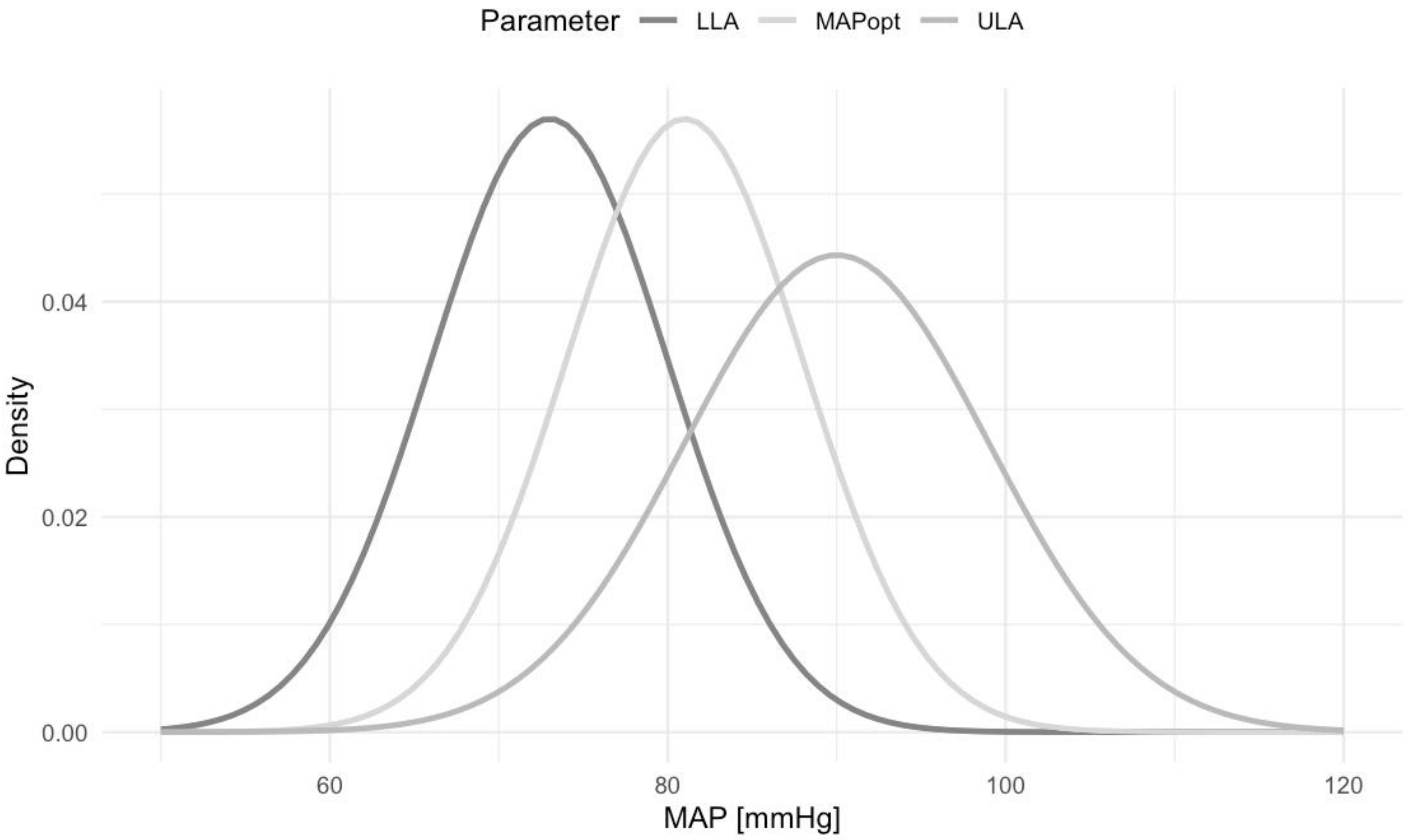
ULA = HIGHEST SAFE BP



MEDIAN ULA 89 (95% CI 85-92)
IQR 81-94

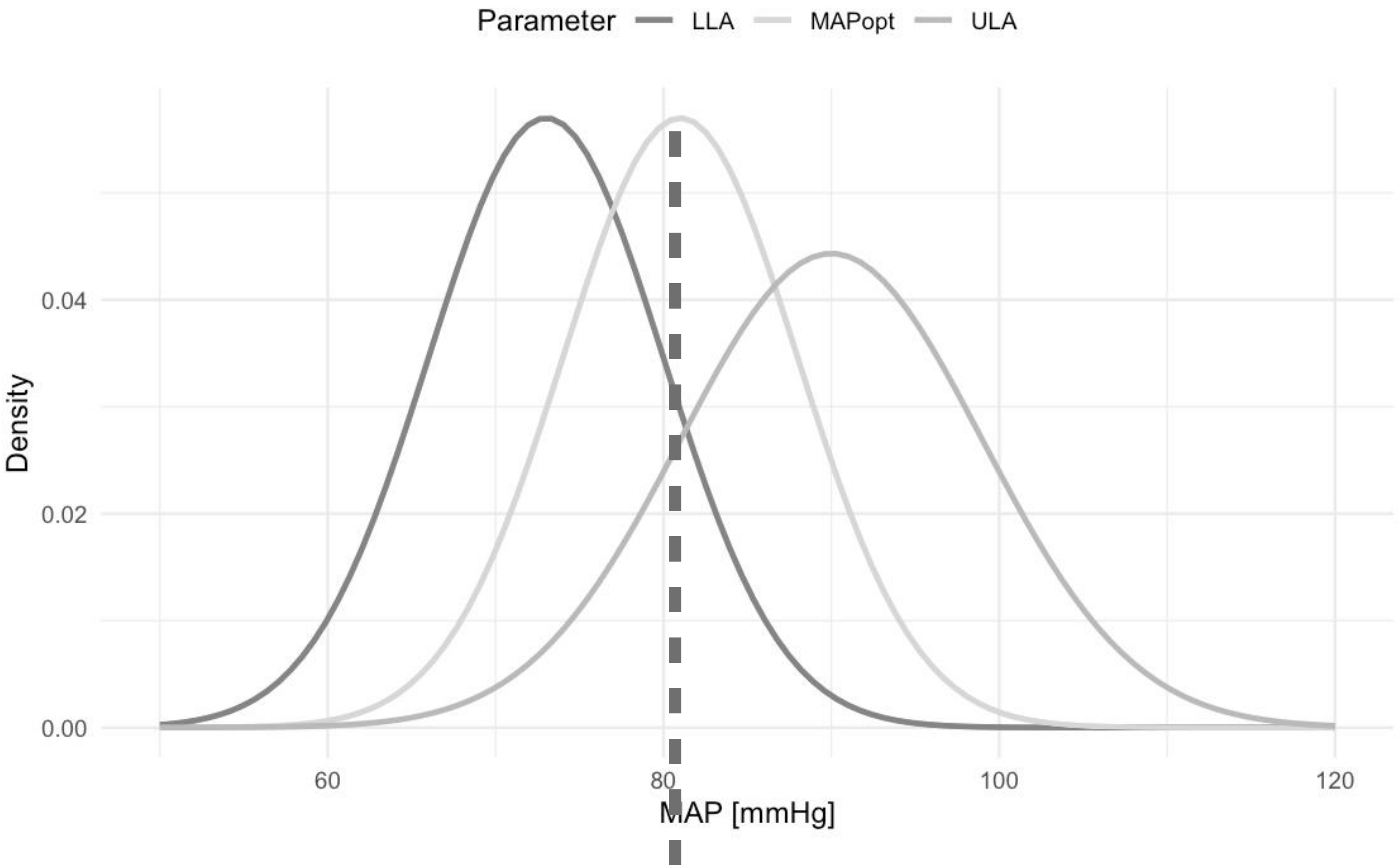
Preliminary findings on a population level

MAPopt = Optimal BP



Preliminary findings on a population level

MAPopt = Optimal BP



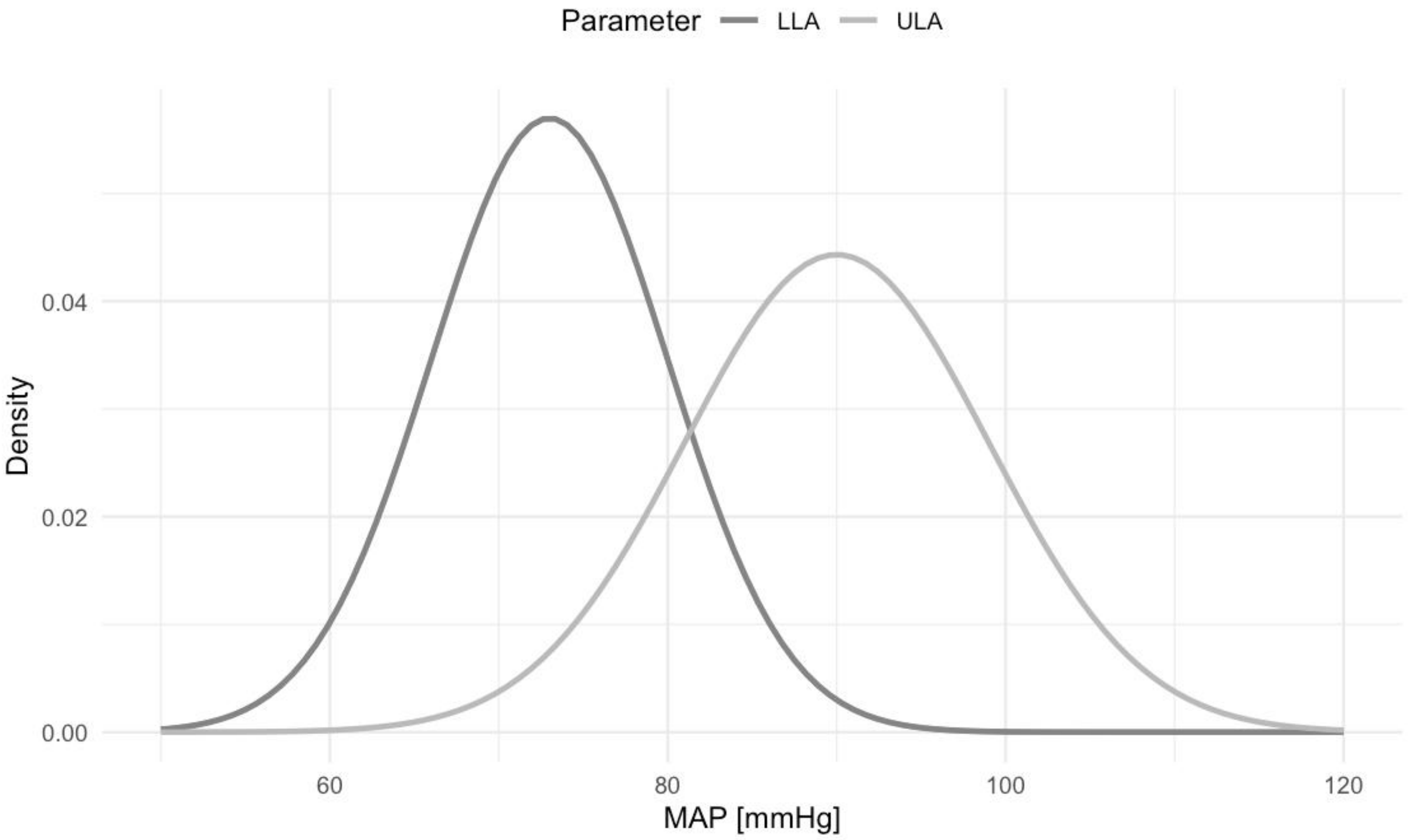
Median MAPopt 80 (95% CI 79-83)
IQR 75-85

AUTOREGULATE-NONCARDIAC

Preliminary

But what does this mean for us
in the OR ?

Preliminary findings on a population level

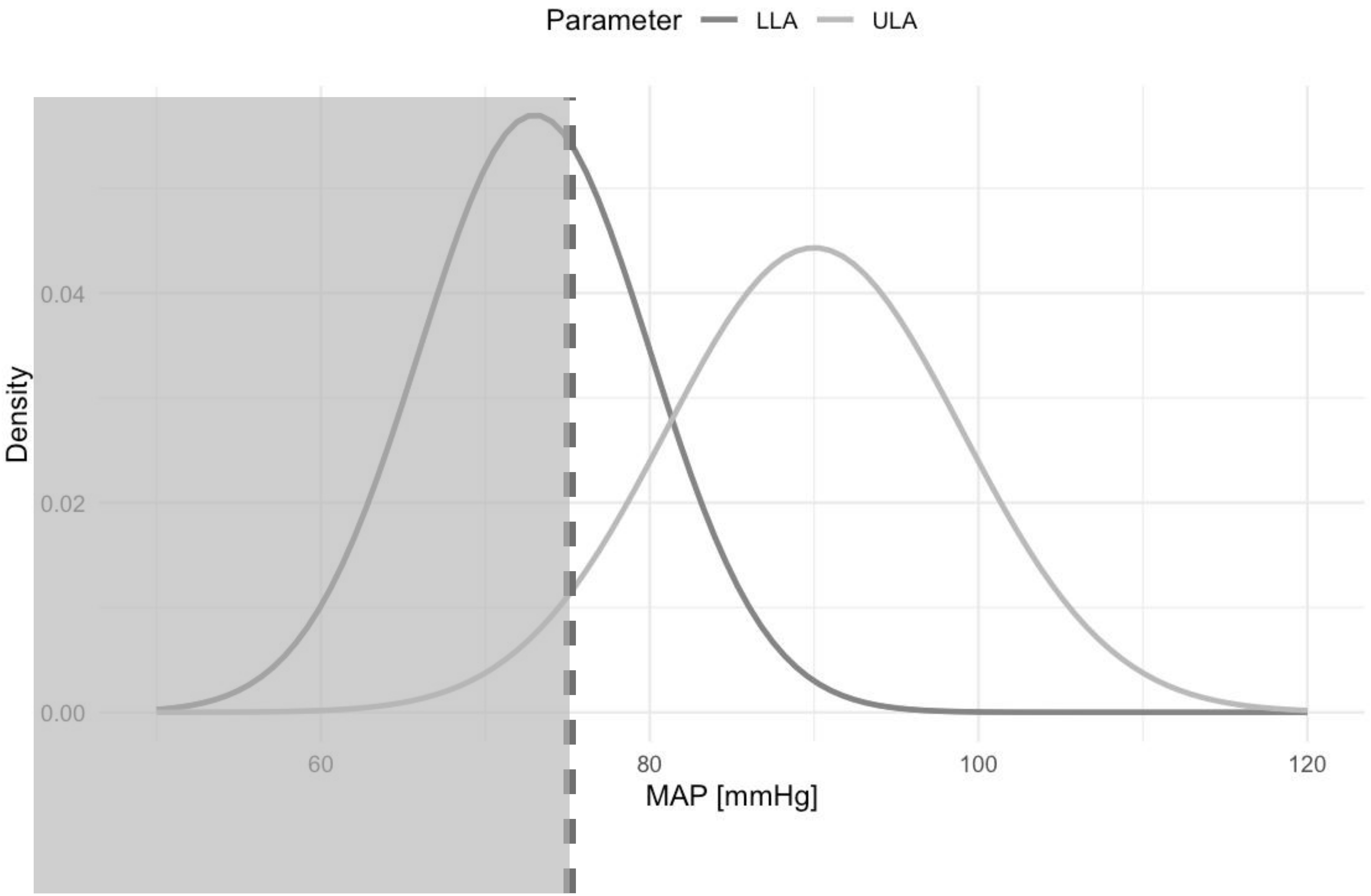


AUTOREGULATE-NONCARDIAC

PRELIMINARY

Preliminary findings on a population level

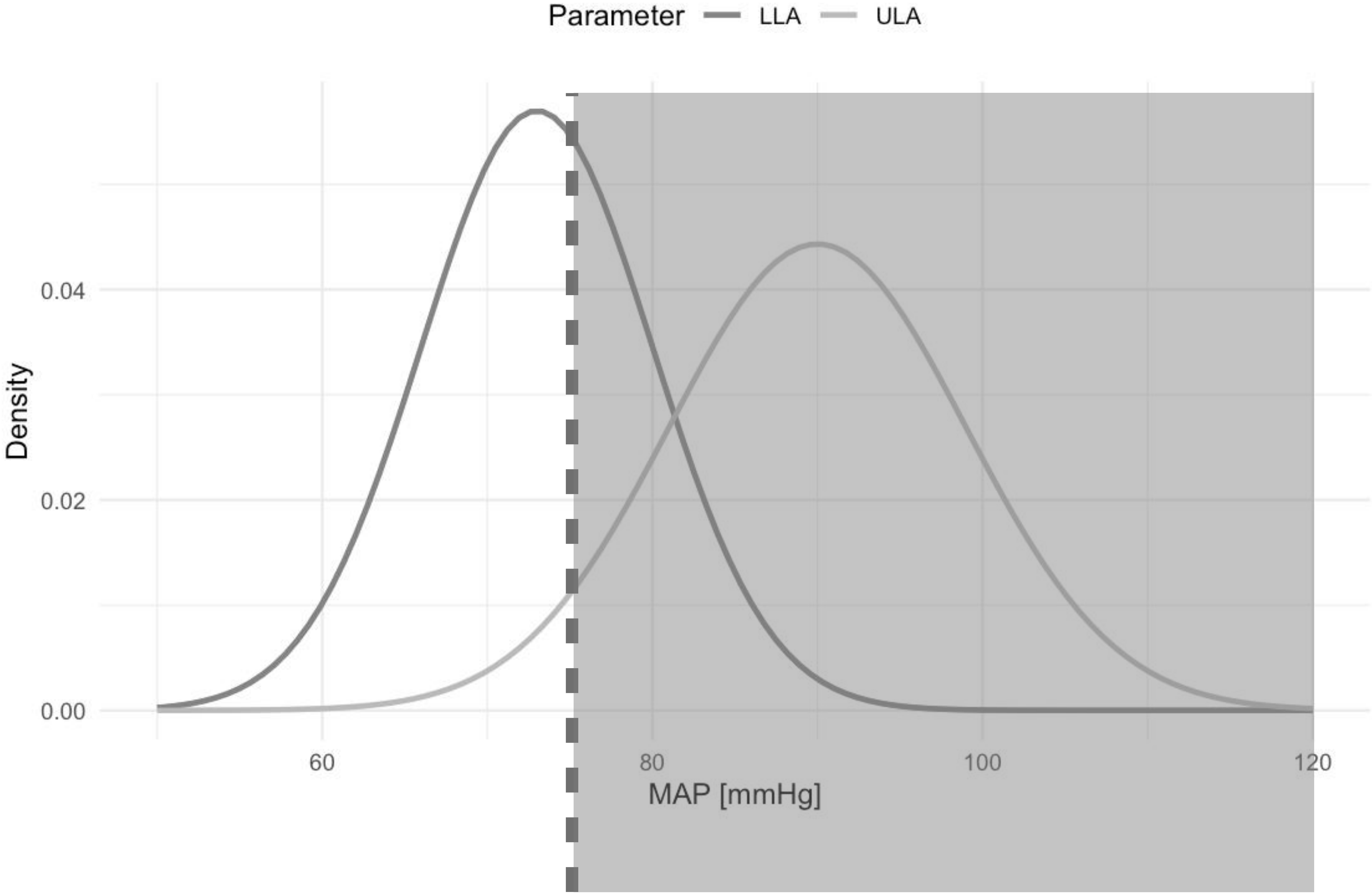
Excessive BP, fluids & vasopressors



High MAP targets = overtreatment

Preliminary findings on a population level

Insufficient BP for organ perfusion



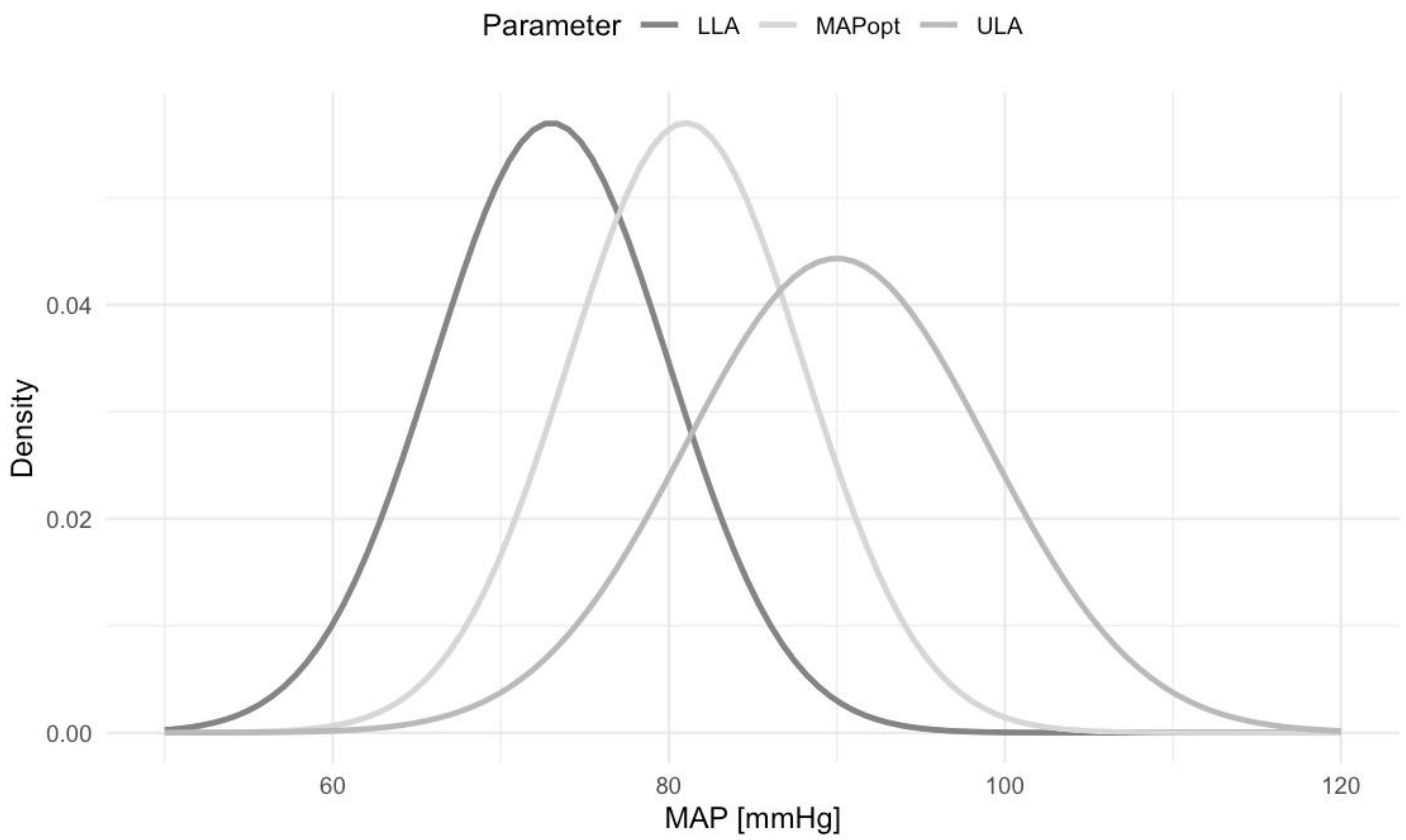
High MAP targets ≠ no guarantee for safety

AUTOREGULATE-NONCARDIAC

Preliminary

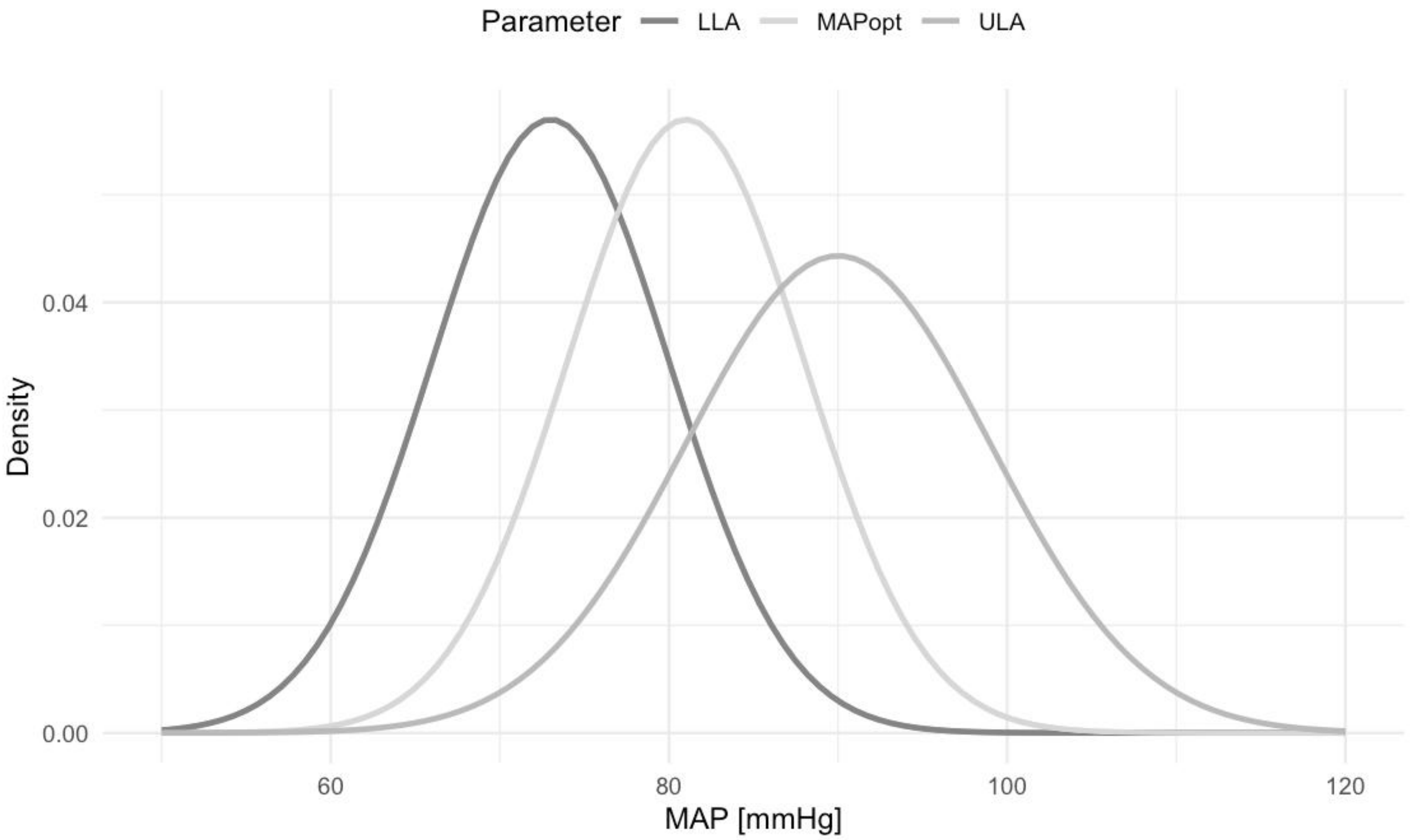
Preliminary findings on a population level

MAPopt as a potential BP target ?



Balancing risks of over- & undertreatment

Preliminary findings on a population level



Time for a paradigm shift ?

Monitor target organs.

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery
A Randomized Clinical Trial

Emmanuel Futier, MD, PhD; Jean-Yves Lefrant, MD, PhD; Pierre-Gregoire Guinot, MD, PhD; Thomas Godet, MD, PhD; Emmanuel Lorne, MD; Philippe Cuvillon, MD, PhD; Sebastien Bertran, MD; Marc Leone, MD, PhD; Bruno Pastene, MD; Vincent Piriou, MD, PhD; Serge Molliex, MD, PhD; Jacques Albanese, MD, PhD; Jean-Michel Julia, MD; Benoit Tavernier, MD, PhD; Etienne Imhoff, MD; Jean-Etienne Bazin, MD, PhD; Jean-Michel Constantin, MD, PhD; Bruno Pereira, PhD; Samir Jaber, MD, PhD; for the INPRESS Study Group

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 78, NO. 18, 2021

ORIGINAL INVESTIGATIONS

Targeting Higher Intraoperative Blood Pressures Does Not Reduce Adverse Cardiovascular Events Following Noncardiac Surgery

Patrick M. Wanner, MD,[a,*] Dirk U. Wulff, PhD,[b] Mirjana Djurdjevic,[a] Wolfgang Korte, MD,[c] Thomas W. Schnider, MD,[a] Miodrag Filipovic, MD[a]

Annals of Internal Medicine ORIGINAL RESEARCH

Hypotension-Avoidance Versus Hypertension-Avoidance Strategies in Noncardiac Surgery
An International Randomized Controlled Trial

Maura Marcucci, MD; Thomas W. Painter, MBChB; David Conen, MD; Vladimir Lomivorotov, MD; Daniel I. Sessler, MD; Matthew T.V. Chan, MBBS; Flavia K. Borges, MD; Kate Leslie, MD; Emmanuelle Duceppe, MD; María José Martínez-Zapata, MD; Chew Yin Wang, MBChB; Denis Xavier, MD; Sandra N. Ofori, MBBS; Michael Ke Wang, MD; Sergey Efremov, MD; Giovanni Landoni, MD; Ydo V. Kleinlugtenbelt, MD; Wojciech Szczeklik, MD; Denis Schmartz, MD; Amit X. Garg, MD; Timothy G. Short, MD; Maria Wittmann, MD; Christian S. Meyhoff, MD; Mohammed Amir, MBBS; David Torres, MD; Ameen Patel, MD; Kurt Ruetzler, MD; Joel L. Parlow, MD; Vikas Tandon, MD; Edith Fleischmann, MD; Carisi A. Polanczyk, MD; Andre Lamy, MD; Raja Jayaram, MD; Sergey V. Astrakov, MD; William Ka Kei Wu, PhD; Chao Chia Cheong, MD; Sabry Ayad, MD; Mikhail Kirov, MD; Miriam de Nadal, MD; Valery V. Likhvantsev, MD; Pilar Paniagua, MD; Hector J. Aguado, MD; Kamal Maheshwari, MD; Richard P. Whitlock, MD; Michael H. McGillion, RN; Jessica Vincent, MSc; Ingrid Copland; Kumar Balasubramanian, MSc; Bruce M. Biccard, MBChB; Sadeesh Srinathan, MD; Samandar Ismoilov, MD; Shirley Pettit, RN; David Stillo, MASc; Andrea Kurz, MD; Emilie P. Belley-Côté, MD; Jessica Spence, MD; William F. McIntyre, MD; Shrikant I. Bangdiwala, PhD; Gordon Guyatt, MD; Salim Yusuf, MD; and P.J. Devereaux, MD, PhD; on behalf of the POISE-3 Trial Investigators and Study Groups*

JAMA | Original Investigation

Individualized Perioperative Blood Pressure Management in Patients Undergoing Major Abdominal Surgery
The IMPROVE-multi Randomized Clinical Trial

Bernd Saugel, MD; Agnes S. Meidert, MD; Frank M. Brunkhorst, MD; Robert Bischoff, MD; Joseph Esser, MD; Minca Mattis, MD; Pauline Naue; Katharina Vogel, BSc; Alina Bergholz, MD; Moritz Flick, MD; Alina Kröker, MD; Dominik X. Müller, MD; Kristen K. Thomsen, MD; Christina Vokuhl, MD; Mirja Wegge, MD; Sebastian Bratke, MD; Martin Graeßner, MD; Bettina Jungwirth, MD; Sebastian Schmid, MD; Carla D. Grundmann, MD; Jan M. Wischermann, MD; Patrick Kellner, MD; Moritz Steinhaus, MD; Linda Grüßer, MD; Sina M. Coldewey, MD, PhD; Kai Zacharowski, MD, PhD; Patrick Meybohm, MD; Marit Habicher, MD; Alexander Zarbock, MD; Amelie Zitzmann, MD; Svenja Letz, MD; Claudia Neumann, MD; Jan Larmann, MD, PhD; Thomas Renné, MD, PhD; Linda Krause, PhD; Eik Vettorazzi, MSc; Antonia Zapf, PhD; Annemarie Carlstedt, PhD; Daniel I. Sessler, MD; Karim Kouz, MD; for the IMPROVE-multi Trial Group

Why have BP trials fallen short ?

Question 2

IS PRESSURE EVERYTHING?

Pressure vs. Flow

BJA

British Journal of Anaesthesia, 127 (6): 845–861 (2021)

doi: 10.1016/j.bja.2021.06.048
Advance Access Publication Date: 12 August 2021
Review Article

CARDIOVASCULAR

Heterogeneous impact of hypotension on organ perfusion and outcomes: a narrative review

Lingzhong Meng*

Department of Anesthesiology, Yale University School of Medicine, New Haven, CT, USA

E-mail: lingzhong.meng@yale.edu

Pressure vs. Flow

BJA

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Review Article

CARDIOVASCULAR

Heterogeneous impact of hypotension on organ perfusion and outcomes: a narrative review

Lingzhong Meng*

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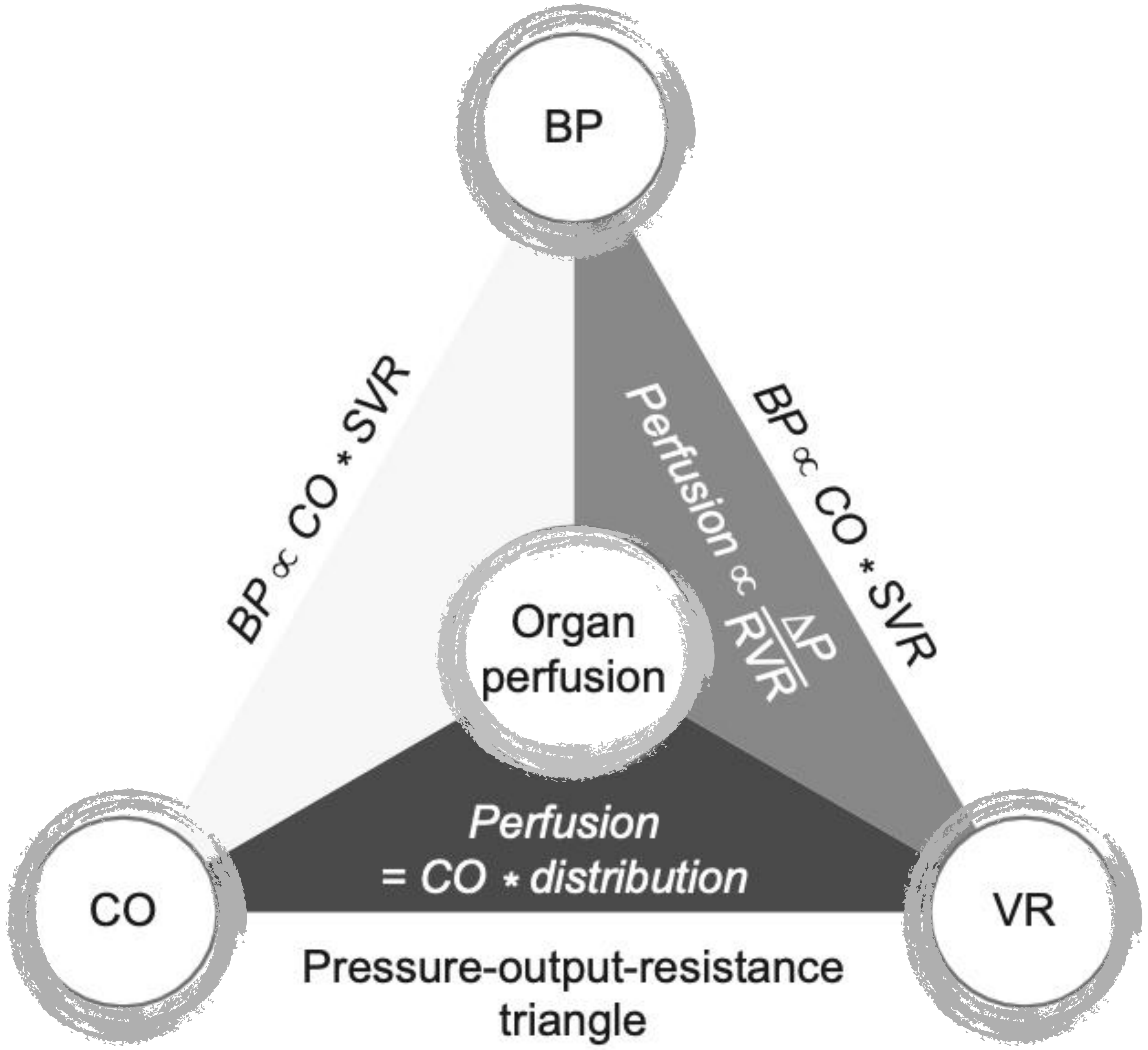


JUST THEORY ?

Pressure vs. Flow

J Appl Physiol 113: 307–314, 2012.
First published May 24, 2012; doi:10.1152/japplphysiol.00024.2012.
Innovative Methodology

Renovascular reactivity measured by near-infrared spectroscopy

Christopher J. Rhee,[1] Kathleen K. Kibler,[2] R. Blaine Easley,[2] Dean B. Andropoulos,[2] Marek Czosnyka,[3] Peter Smielewski,[3] and Ken M. Brady[2]

[1]*Department of Pediatrics, Section of Neonatology, Texas Children's Hospital/Baylor College of Medicine, Houston, Texas;* [2]*Departments of Anesthesiology, Critical Care Medicine, and Pediatrics, Texas Children's Hospital/Baylor College of Medicine, Houston, Texas;* [3]*Department of Academic Neurosurgery, Addenbrooke's Hospital, University of Cambridge, Cambridge, United Kingdom*

Submitted 11 January 2012; accepted in final form 22 May 2012

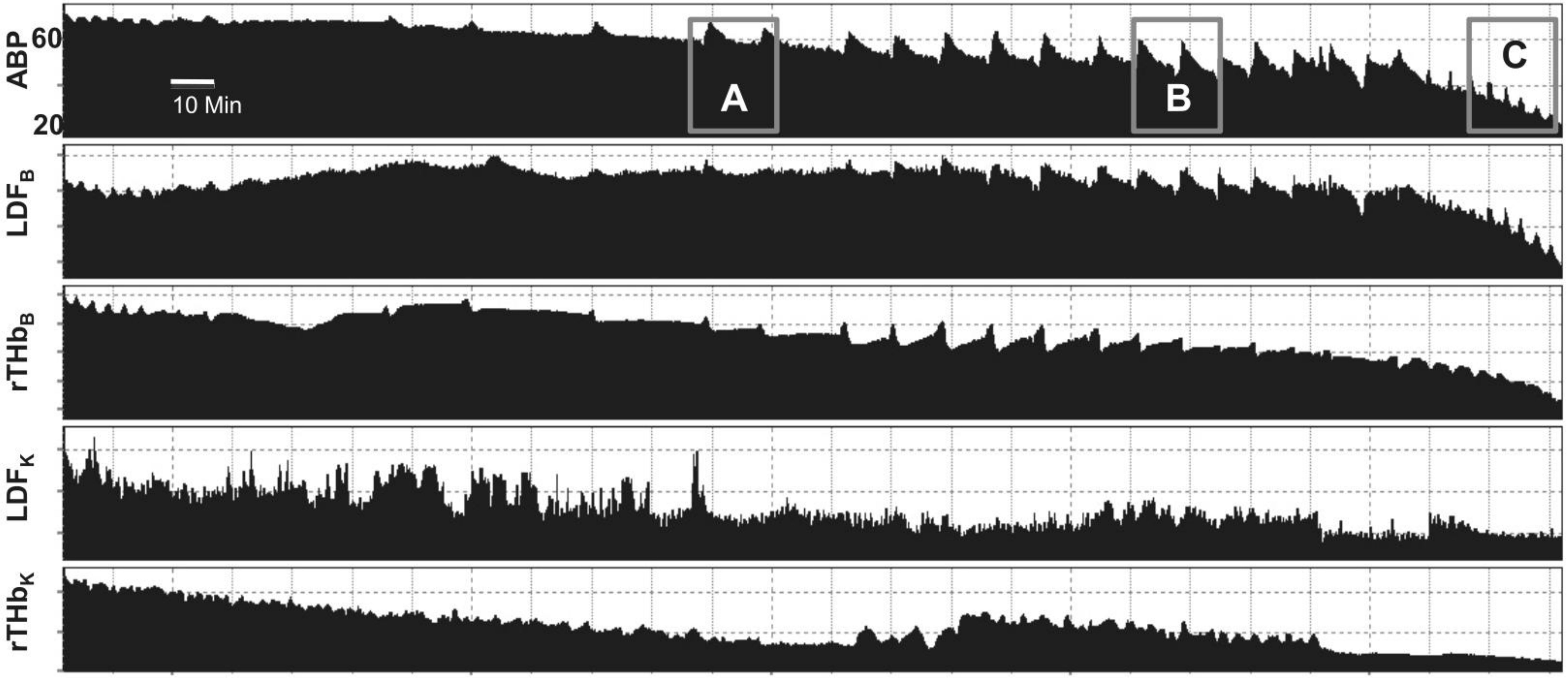

Fig. 1. Physiological recordings during induced hypotension. Arterial blood pressure (ABP, mmHg), cerebral cortical laser-Doppler flux (LDF_B, AU), cerebral relative total hemoglobin ($rTHb_B$, AU), renal cortical laser-Doppler flux (LDF_K, AU), and renal relative total hemoglobin ($rTHb_K$, AU) were recorded in a piglet during exsanguination over 4.5 h. Laser-Doppler recordings were used to define quartile reductions in renal and cerebral blood flow. Highlighted sections *A*, *B*, and *C* are shown in higher detail in Fig. 2.

ANIMAL MODEL

PIGLET HEMORRHAGIC SHOCK MODEL

Pressure vs. Flow

J Appl Physiol 113: 307–314, 2012.
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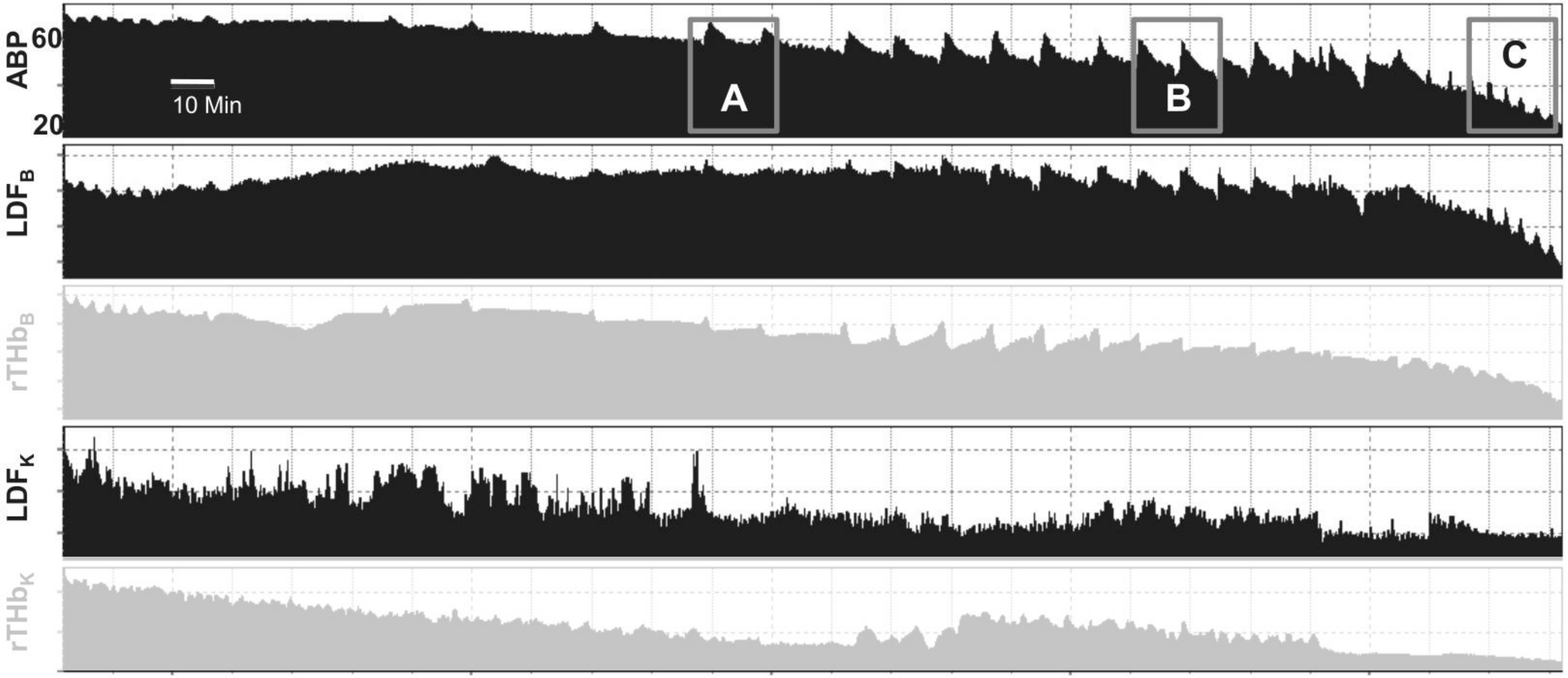
Innovative Methodology

Renovascular reactivity measured by near-infrared spectroscopy

Christopher J. Rhee,[1] Kathleen K. Kibler,[2] R. Blaine Easley,[2] Dean B. Andropoulos,[2] Marek Czosnyka,[3] Peter Smielewski,[3] and Ken M. Brady[2]

[1]*Department of Pediatrics, Section of Neonatology, Texas Children's Hospital/Baylor College of Medicine, Houston, Texas;* [2]*Departments of Anesthesiology, Critical Care Medicine, and Pediatrics, Texas Children's Hospital/Baylor College of Medicine, Houston, Texas;* [3]*Department of Academic Neurosurgery, Addenbrooke's Hospital, University of Cambridge, Cambridge, United Kingdom*

Submitted 11 January 2012; accepted in final form 22 May 2012



MAP

CEREBRAL BLOOD FLOW

RENAL BLOOD FLOW

Fig. 1. Physiological recordings during induced hypotension. Arterial blood pressure (ABP, mmHg), cerebral cortical laser-Doppler flux (LDF_B, AU), cerebral relative total hemoglobin ($rTHb_B$, AU), renal cortical laser-Doppler flux (LDF_K, AU), and renal relative total hemoglobin ($rTHb_K$, AU) were recorded in a piglet during exsanguination over 4.5 h. Laser-Doppler recordings were used to define quartile reductions in renal and cerebral blood flow. Highlighted sections *A*, *B*, and *C* are shown in higher detail in Fig. 2.

ANIMAL MODEL

PIGLET HEMORRHAGIC SHOCK MODEL

Pressure vs. Flow

J Appl Physiol 113: 307–314, 2012.
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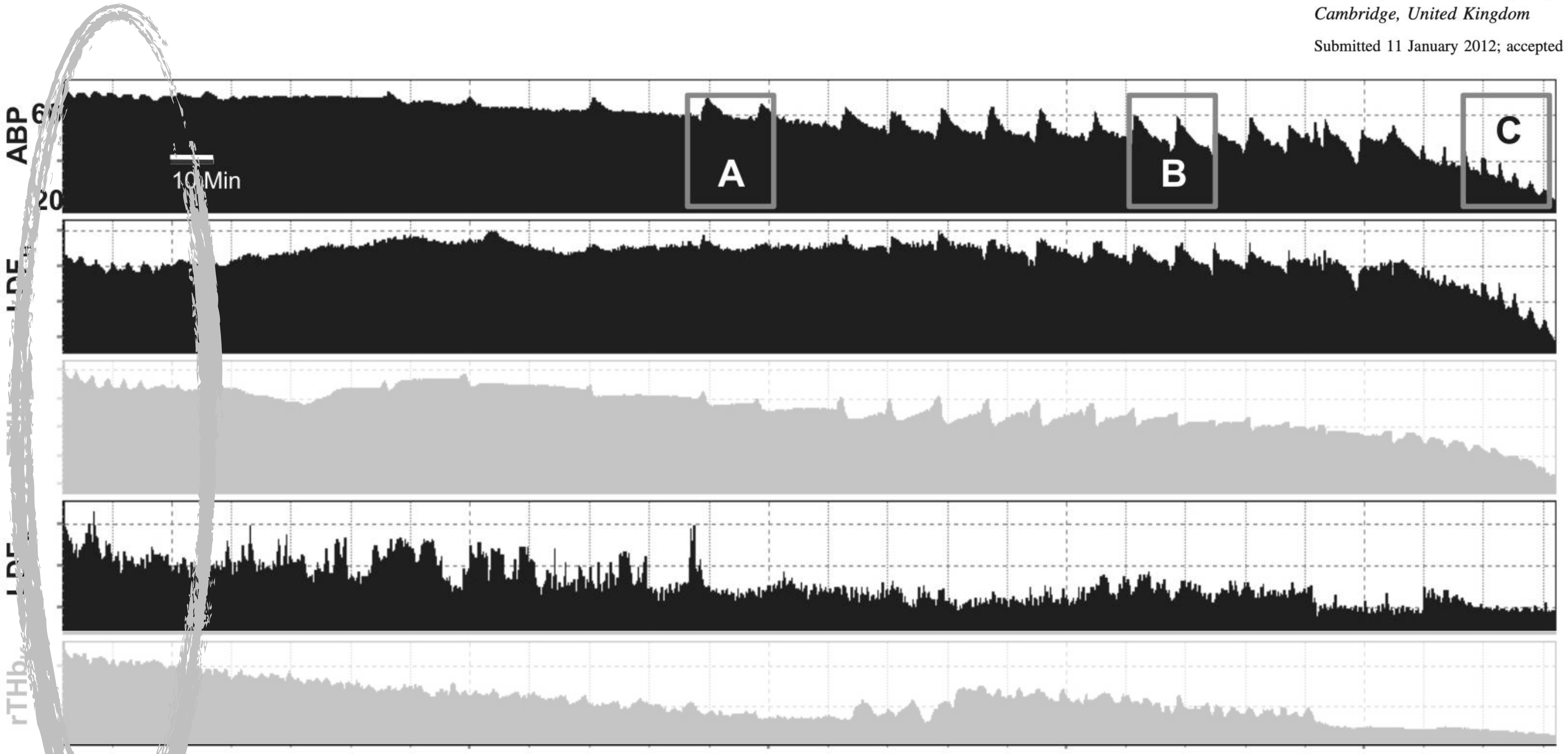
Innovative Methodology

Renovascular reactivity measured by near-infrared spectroscopy

Christopher J. Rhee,[1] Kathleen K. Kibler,[2] R. Blaine Easley,[2] Dean B. Andropoulos,[2] Marek Czosnyka,[3] Peter Smielewski,[3] and Ken M. Brady[2]

[1]*Department of Pediatrics, Section of Neonatology, Texas Children's Hospital/Baylor College of Medicine, Houston, Texas;* [2]*Departments of Anesthesiology, Critical Care Medicine, and Pediatrics, Texas Children's Hospital/Baylor College of Medicine, Houston, Texas;* [3]*Department of Academic Neurosurgery, Addenbrooke's Hospital, University of Cambridge, Cambridge, United Kingdom*

Submitted 11 January 2012; accepted in final form 22 May 2012



MAP

CEREBRAL BLOOD FLOW

RENAL BLOOD FLOW

Fig. 1. Physiological recordings during induced hypotension. Arterial blood pressure (ABP, mmHg), cerebral cortical laser-Doppler flux (LDF_B, AU), cerebral relative total hemoglobin ($rTHb_B$, AU), renal cortical laser-Doppler flux (LDF_K, AU), and renal relative total hemoglobin ($rTHb_K$, AU) were recorded in a piglet during exsanguination over 4.5 h. Laser-Doppler recordings were used to define quartile reductions in renal and cerebral blood flow. Highlighted sections *A*, *B*, and *C* are shown in higher detail in Fig. 2.

ANIMAL MODEL

PIGLET HEMORRHAGIC SHOCK MODEL

Pressure vs. Flow

J Appl Physiol 113: 307–314, 2012.
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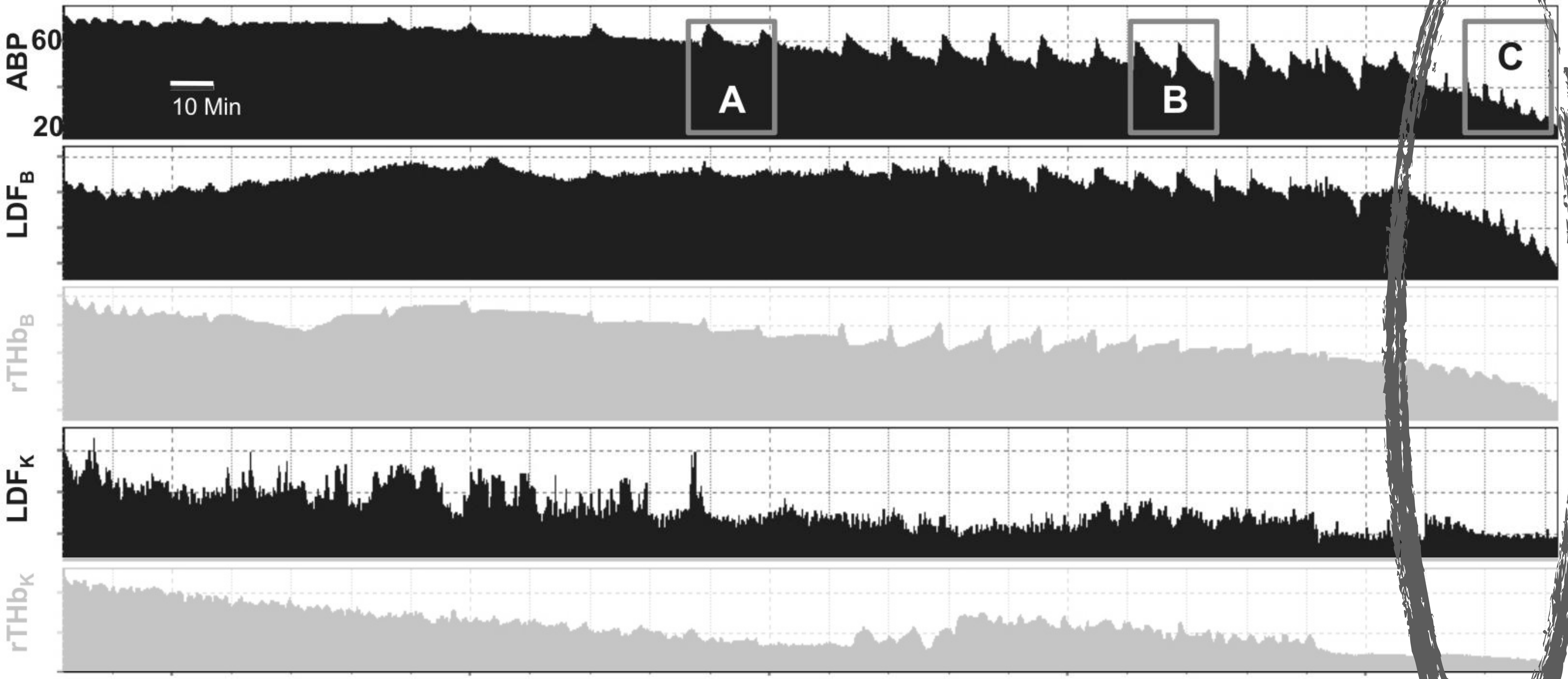

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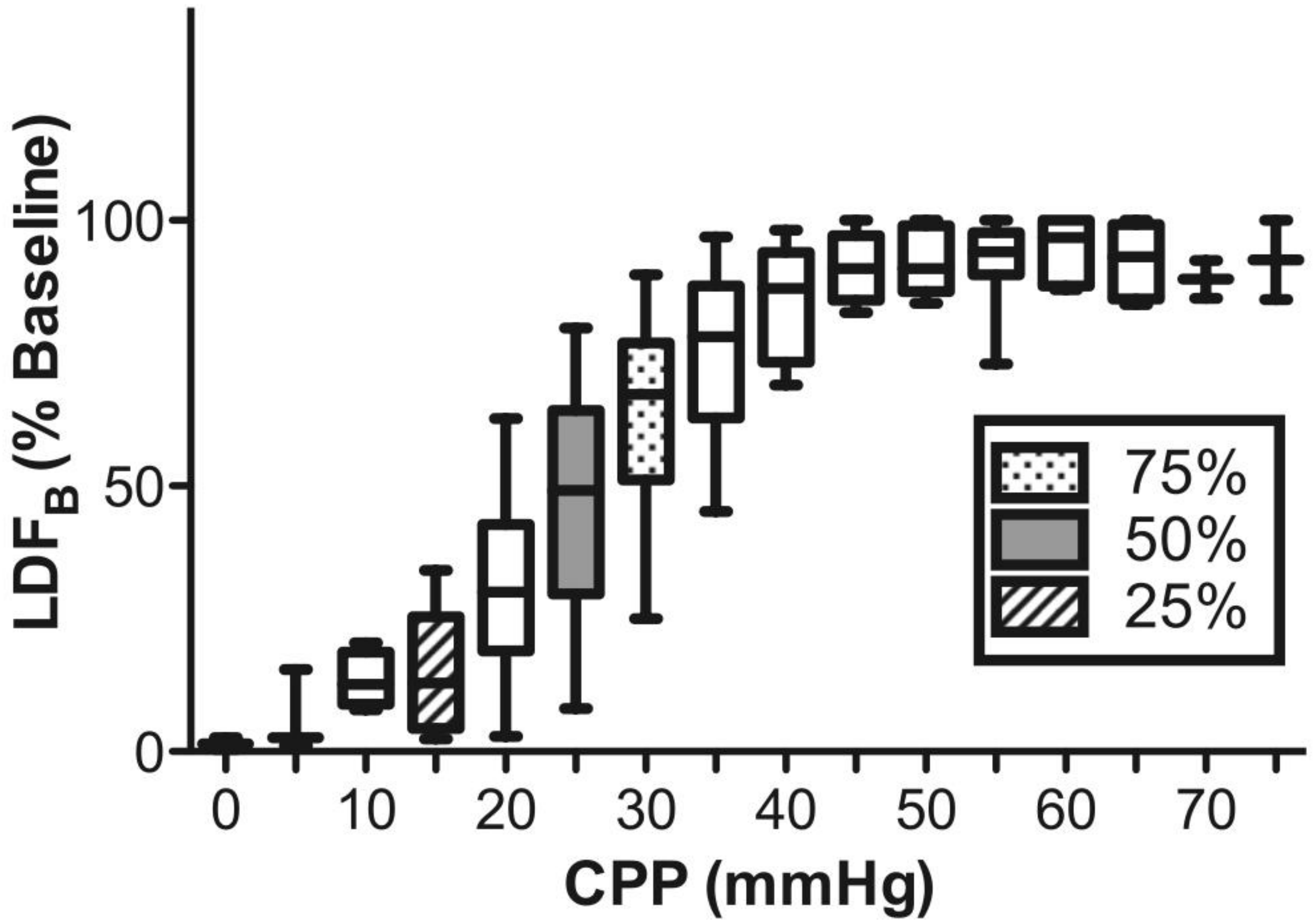

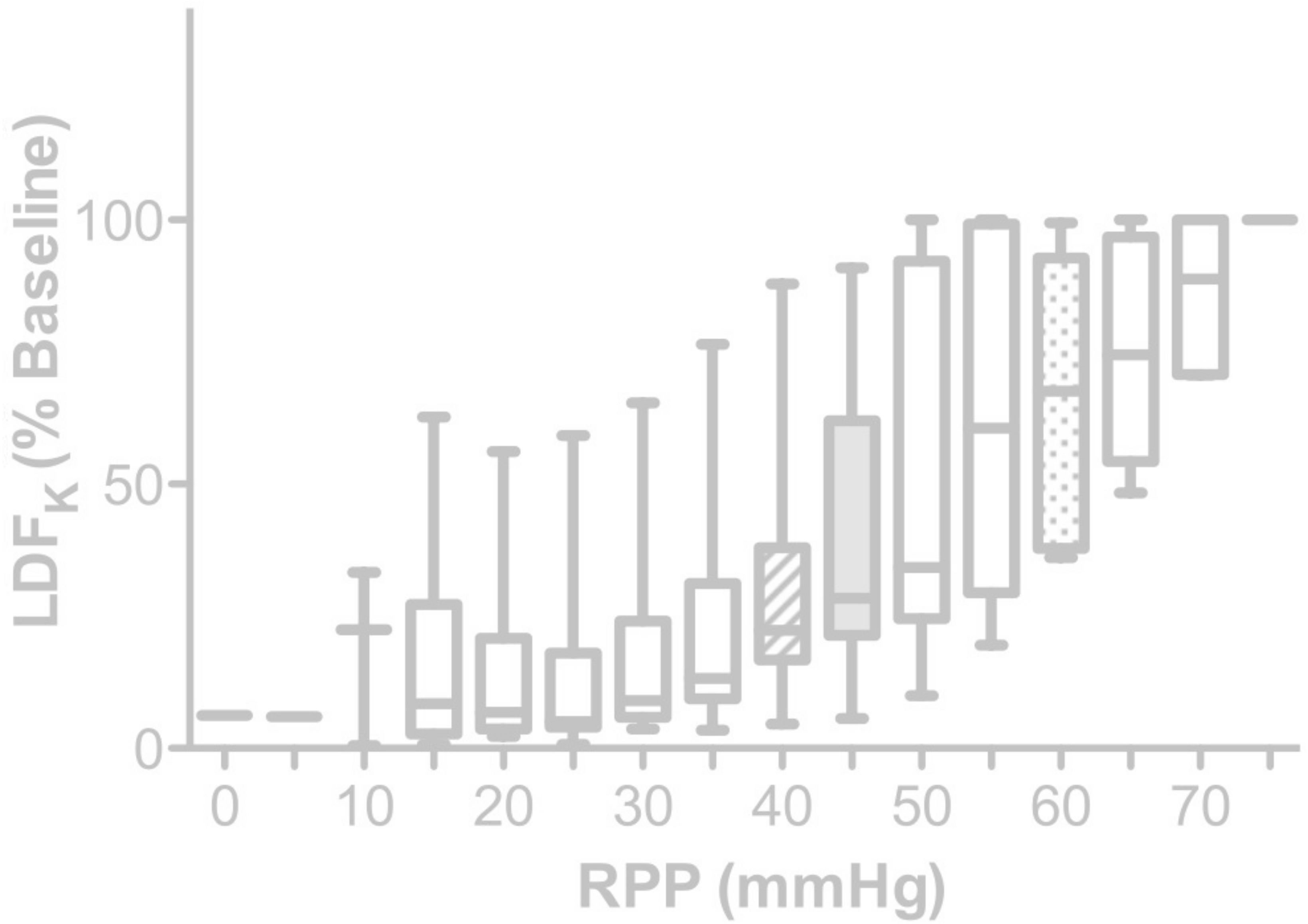

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ANIMAL MODEL

Pressure vs. Flow

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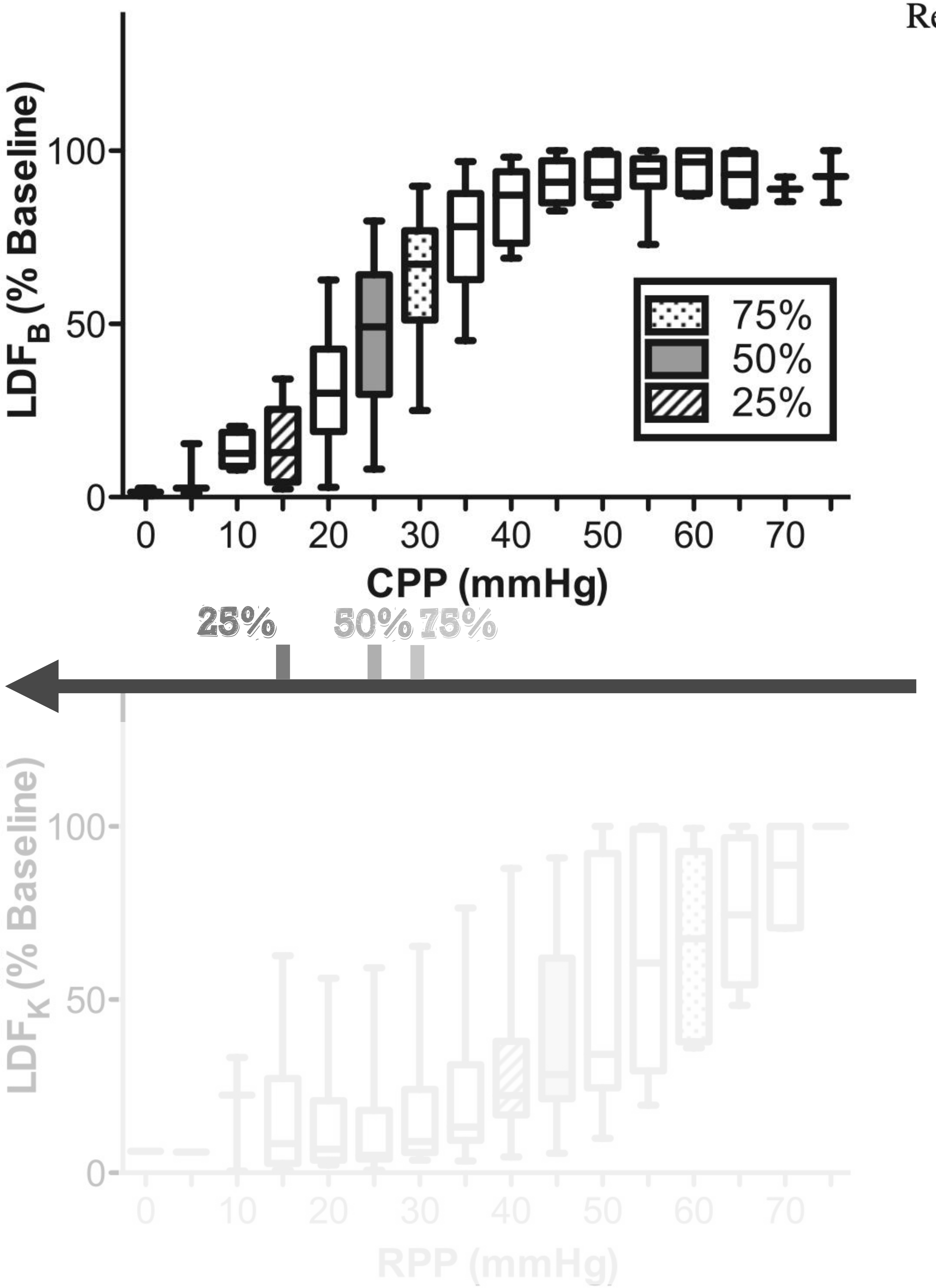

ORGAN BLOOD FLOW VS. PERFUSION PRESSURE

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CEREBRAL BLOOD FLOW

ORGAN BLOOD FLOW VS. PERFUSION PRESSURE

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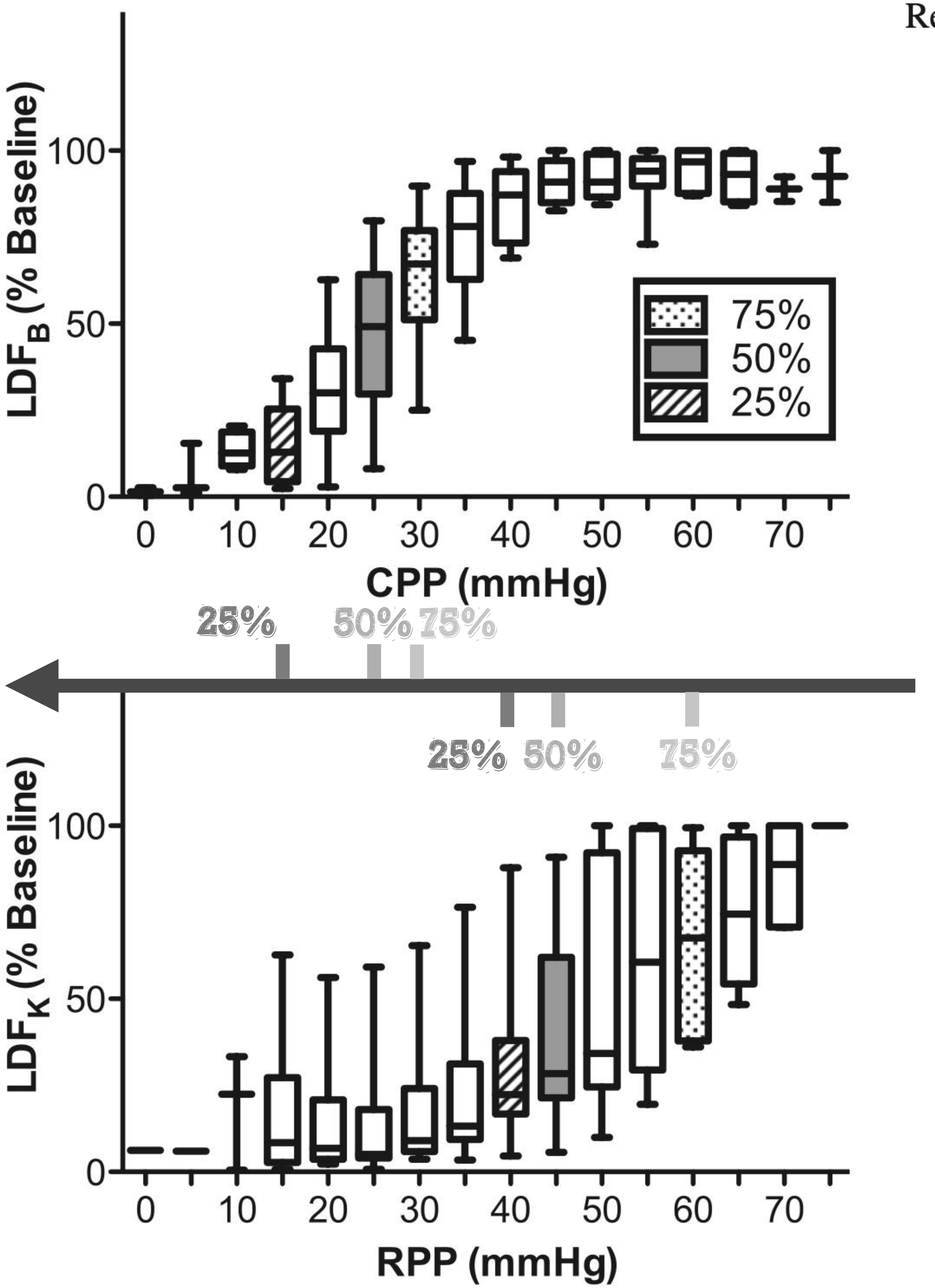

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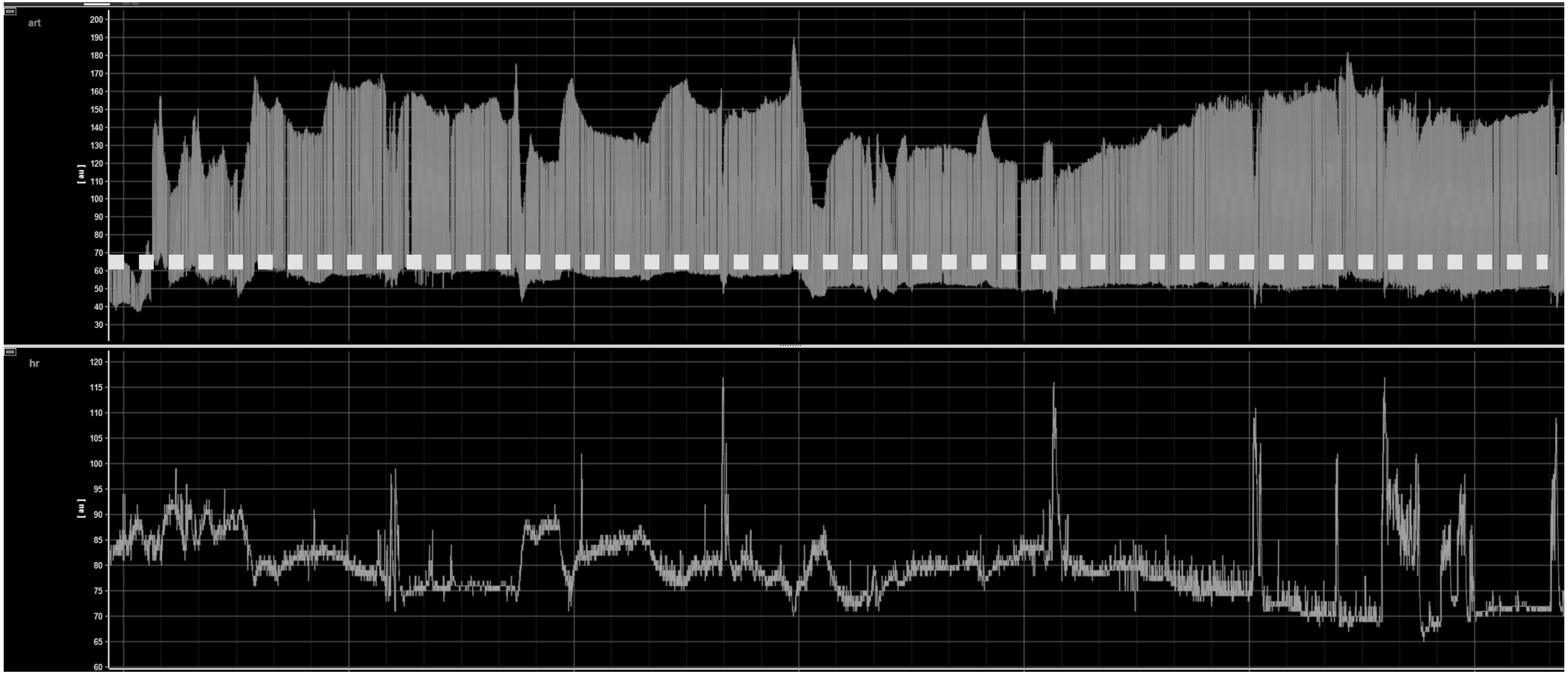
KIDNEY IS SENSITIVE NOT JUST TO HYPOTENSION, BUT ALSO TO REDUCED CARDIAC OUTPUT!

Pressure is not everything

Pressure is not everything

Flow matters too.
And so does how we get there.

MAP - a case study in a postop. patient



Noradrenaline 30 mcg/min

Vasopressin 0.03 E/min

Dobutamine 300 mcg/min

Pressure vs. FLOW

Why have BP trials fallen short ?

Question 3

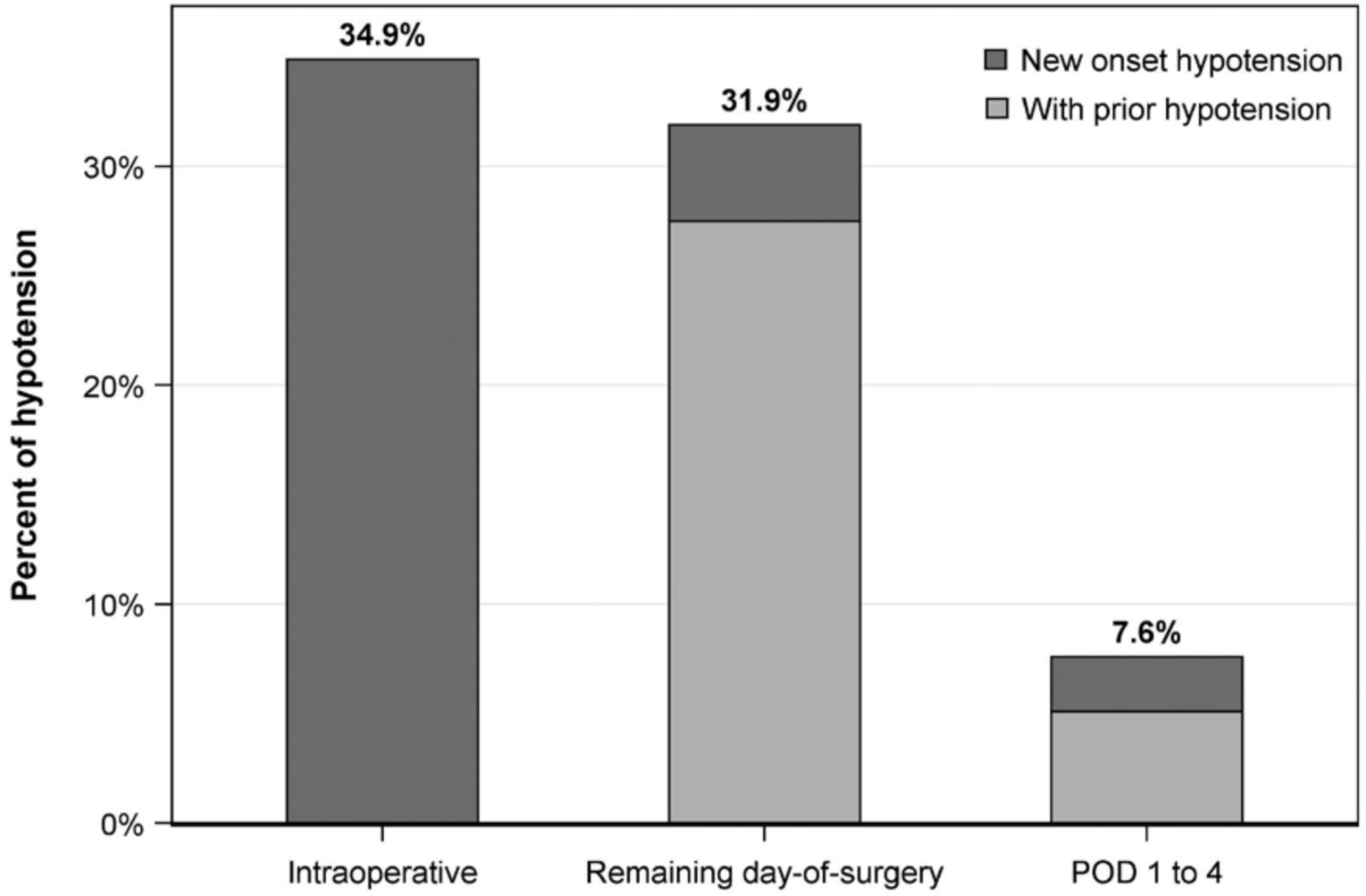
WHAT HAPPENS POSTOP ?

Postoperative hypotension

Period-dependent Associations between Hypotension during and for Four Days after Noncardiac Surgery and a Composite of Myocardial Infarction and Death

A Substudy of the POISE-2 Trial

Daniel I. Sessler, M.D., Christian S. Meyhoff, M.D., Ph.D., Nicole M. Zimmerman, M.S., Guangmei Mao, M.P.H., Kate Leslie, M.B.B.S., Skarlet M. Vásquez, M.Sc., Packianathaswamy Balaji, M.D., Jesús Alvarez-Garcia, M.D., Ph.D., Alexandre B. Cavalcanti, M.D., Ph.D., Joel L. Parlow, M.D., Prashant V. Rahate, M.D., Manfred D. Seeberger, M.D., Bruno Gossetti, M.D., S. A. Walker, M.B.Ch.B., Rajendra K. Premchand, M.D., Rikke M. Dahl, M.D., Emmanuelle Duceppe, M.D., Reitze Rodseth, M.B.Ch.B., Fernando Botto, M.D., P. J. Devereaux, M.D., Ph.D.



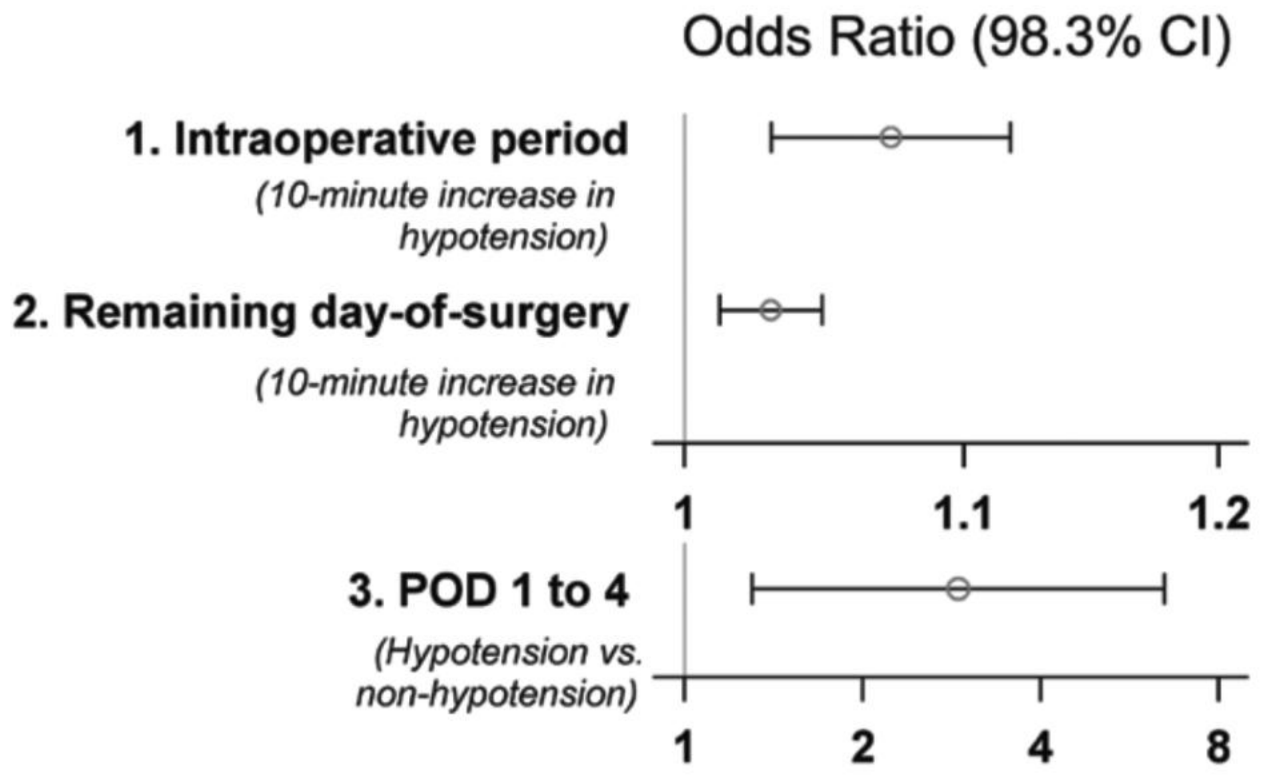


Fig. 4. Odds ratios of average relative effect on the primary composite of 30-day myocardial infarction and mortality for three perioperative periods: intraoperative, remaining day of surgery, and the initial four PODs of hospitalization. CIs for multiple comparisons were adjusted by Bonferroni correction. Correspondingly, $P < 0.017$ (0.05/3) was considered to be significant for the average relative effect. The *circles* present the odds ratios, and the *bars* present the CIs. POD = postoperative day.

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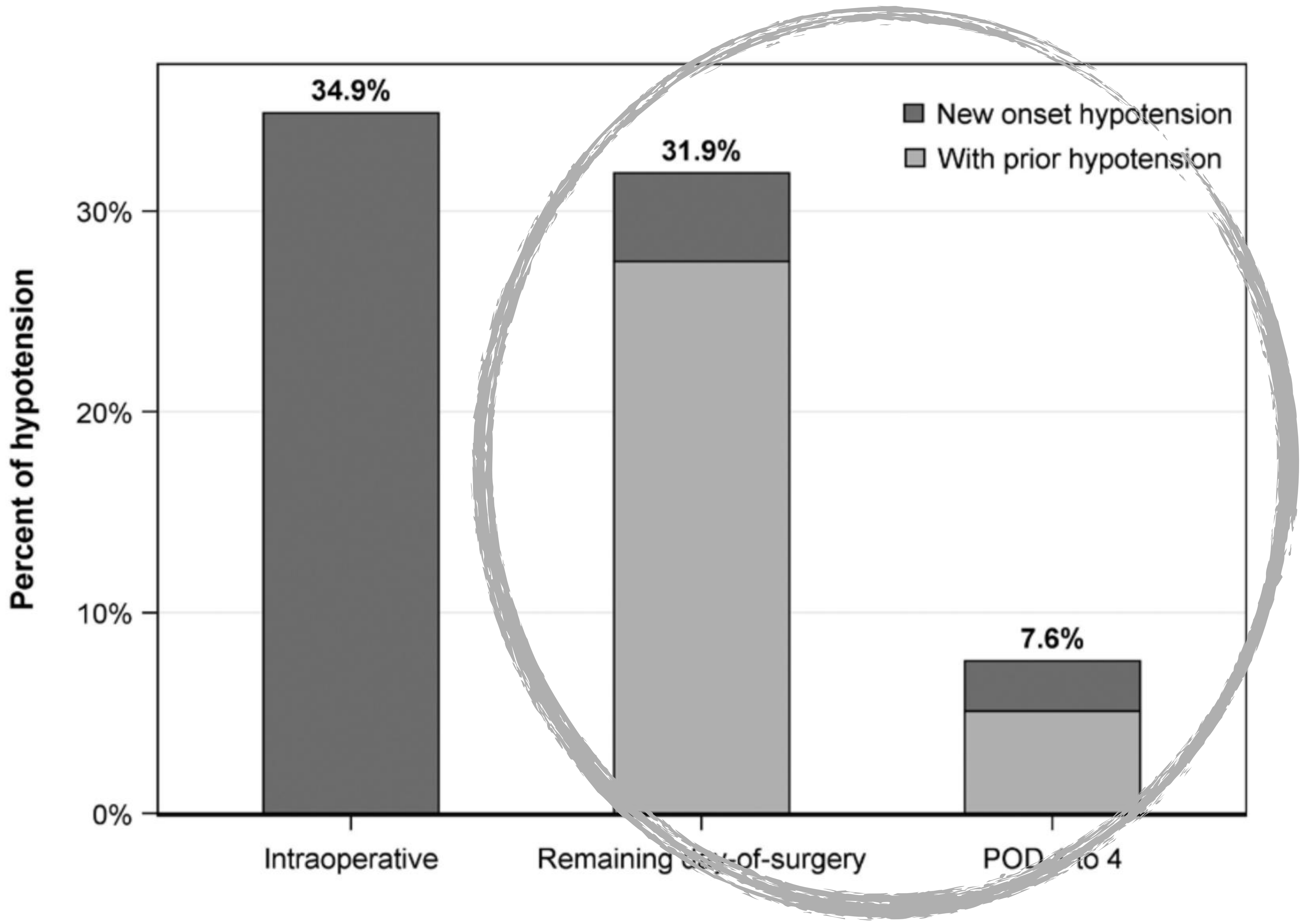

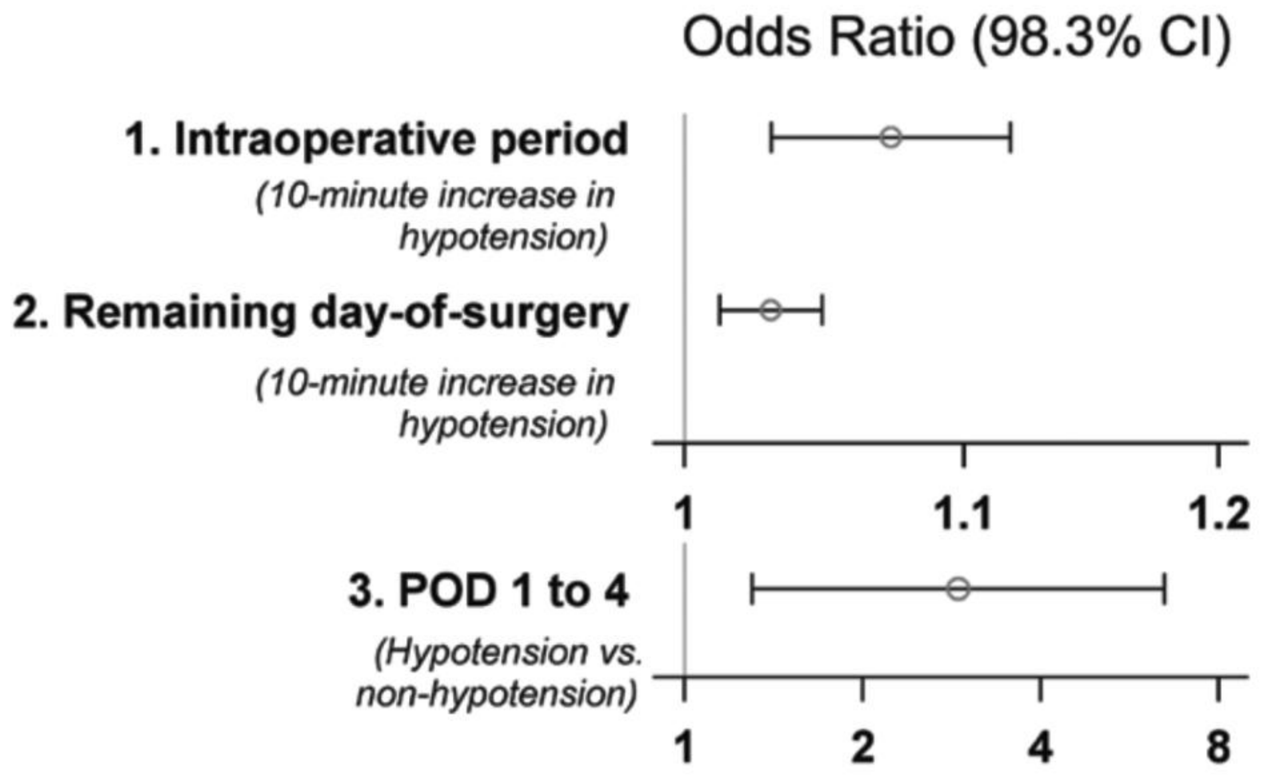

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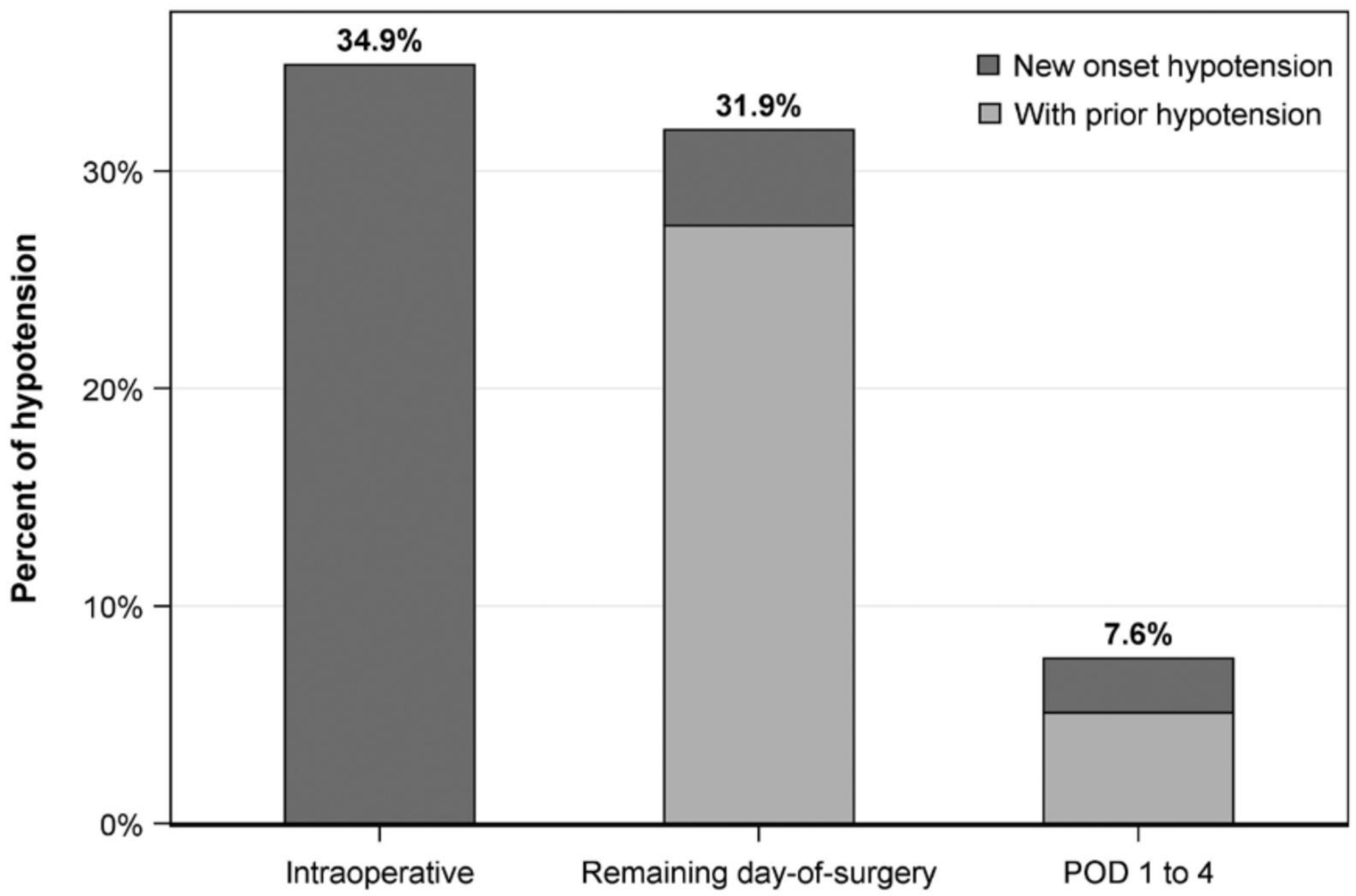

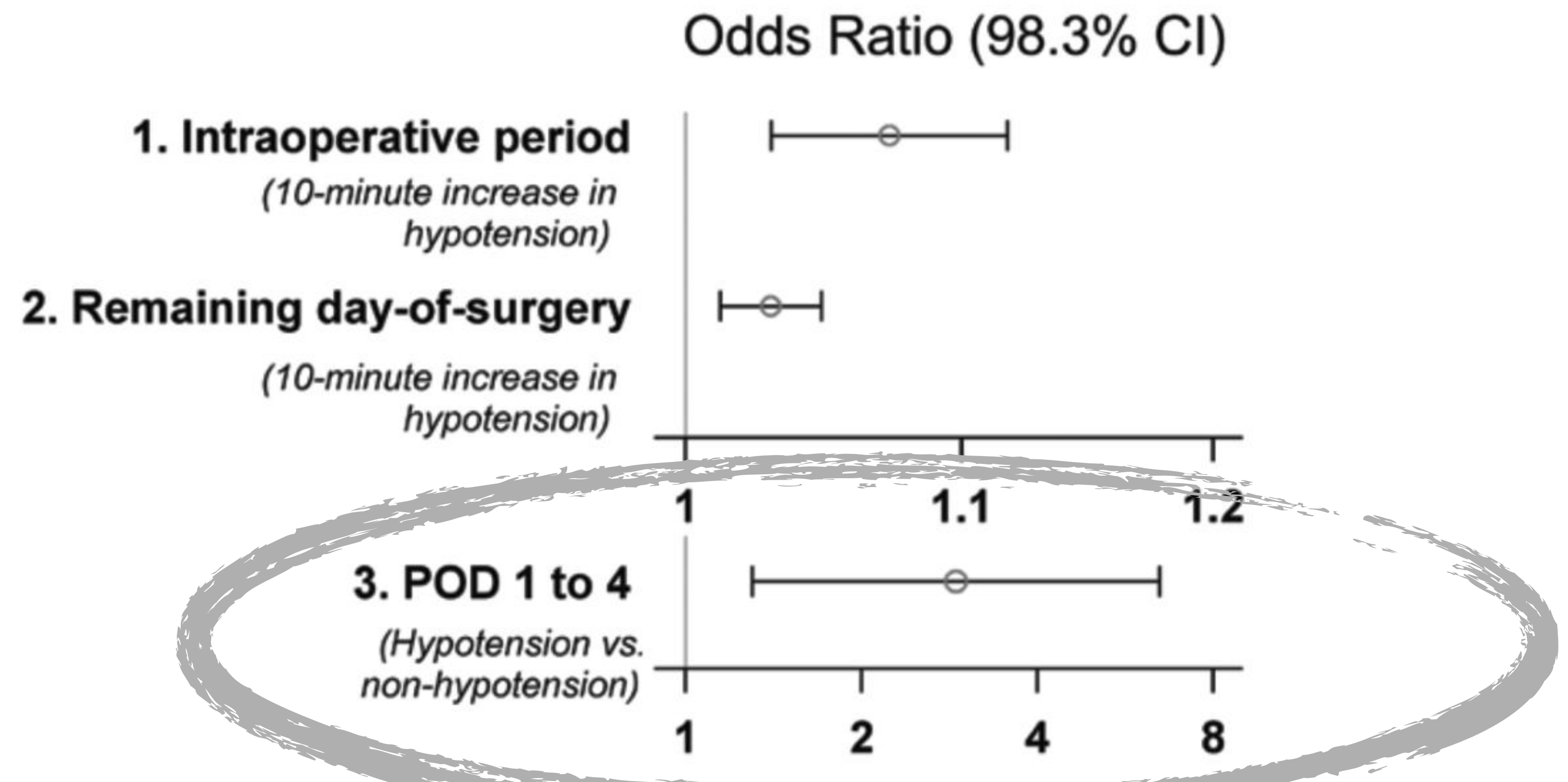

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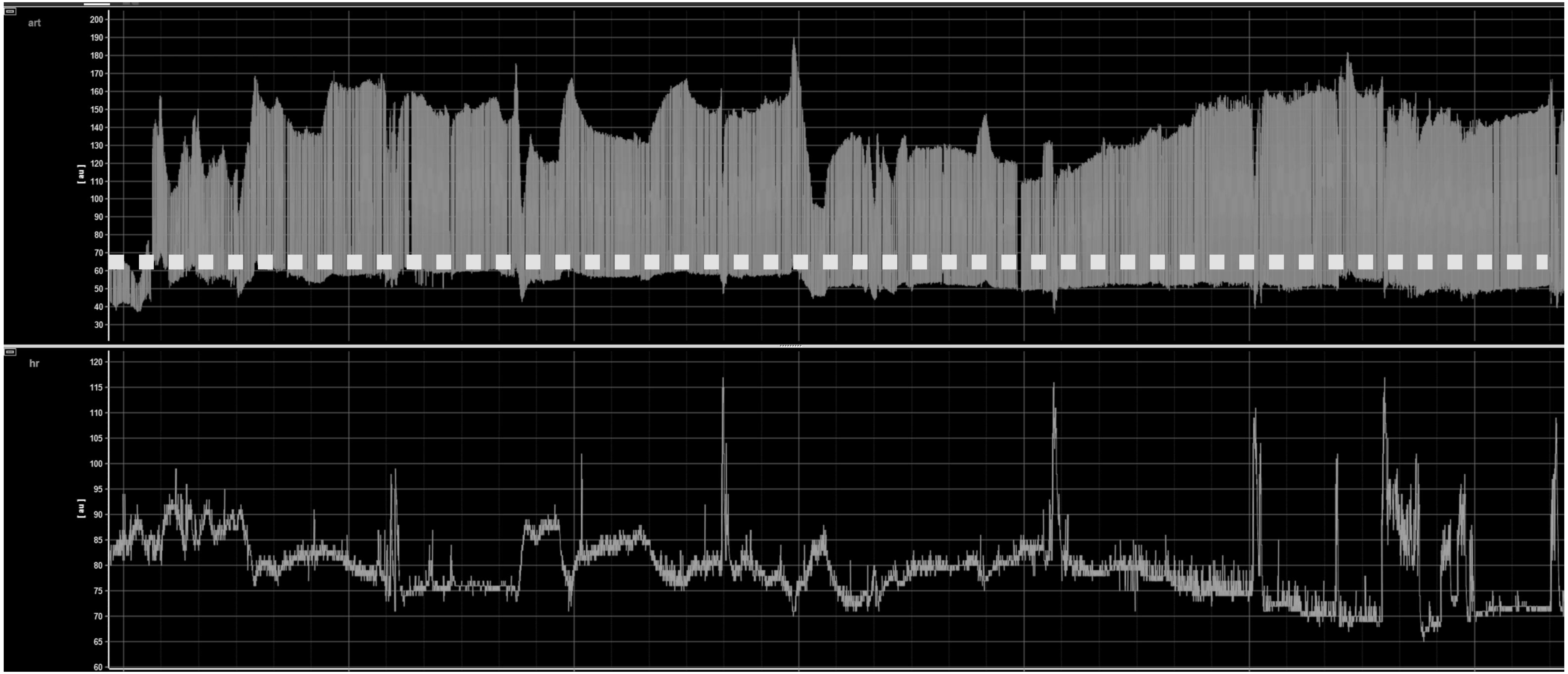
MAP - a case study in a postop. patient



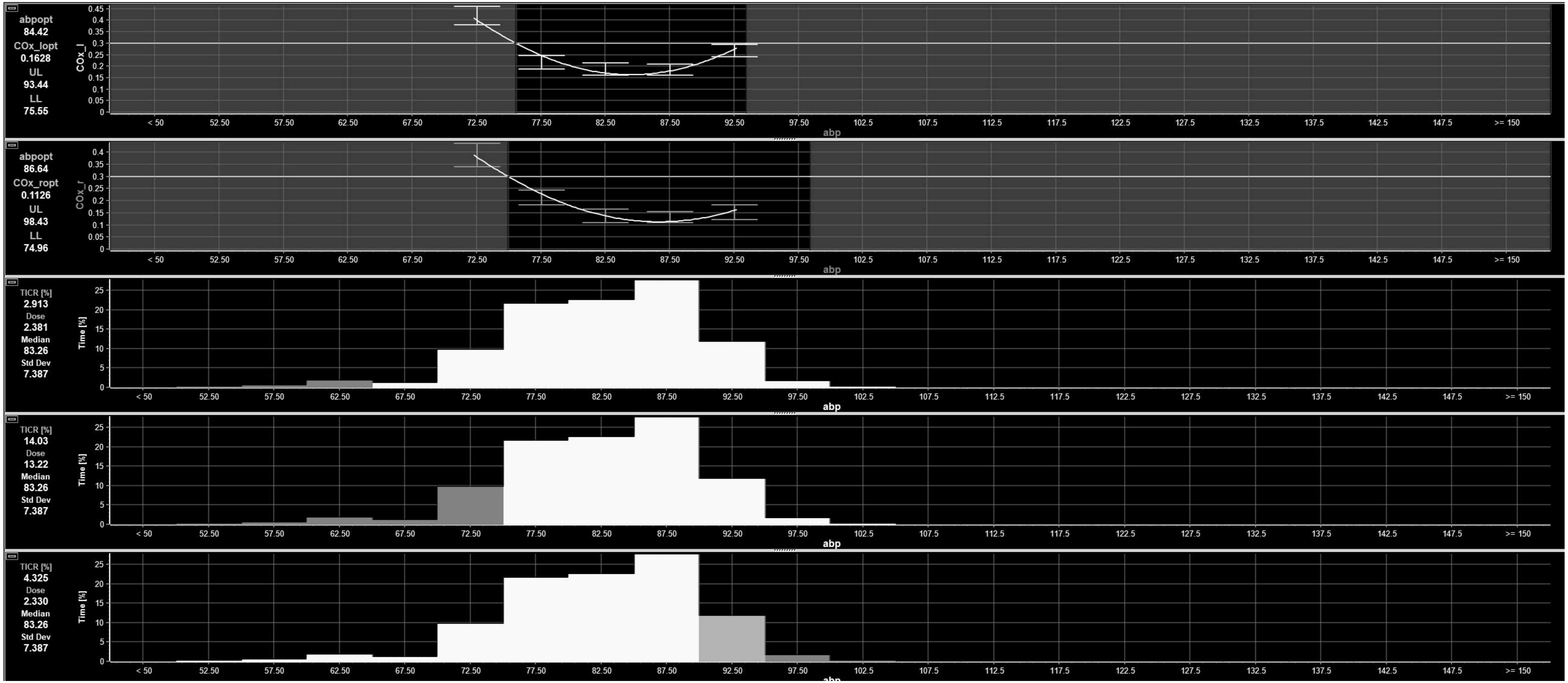
Noradrenaline 30 mcg/min

Vasopressin 0.03 E/min

Dobutamine 300 mcg/min

Are we still happy ?

MAP - a case study in a postop. patient, continued



SEPTIC SHOCK, CAROTID STENOSIS

Key messages & future directions

We know less than we think about hemodynamics.

Key messages & future directions

We know less than we think about hemodynamics.

Focus on <u>understanding</u> & <u>precision</u>

Key messages & future directions

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Both pressure and flow matter.

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Postop matters too.

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Postop matters too.

Precision care pathways

Thank you.

Study participants & their families
Study team
Clinical staff
My mentors

Thank you.

Study participants & their families
Study team
Clinical staff
My mentors

Summary of 3 trials: Management & population

	BP_lo	BP_hi	Intervention duration	ACE-I & ARB	Surgical population	Surgical duration [min]	Epidural analgesia BP_hi vs. BP_lo	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Blood loss BP_hi vs. BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	ICU postop. BP_hi vs. BP_lo [%]
BBB	MAP ≥ 60 mmHg	MAP ≥ 75 mmHg	Intraop.	Continued	67% vascular, 12% abdominal, 10% urological	316 (249-428) vs. 322 (256-419) *Mean 350 (134)* #	39% vs. 37% #	Noradrenaline: 98% vs. 97% Ephedrine: 84% vs. 68% #	2800 (2000-4000) vs. 3000 (2000-4225) #	0 (0-0) vs. 0 (0-0) (15% vs. 17%) #	400 (150-1000) vs. 500 (150-1160) #	3.6% vs. 3.5% #	50% vs. 51% #
INPRESS	SBP > 80 mmHg, within 40% resting BP + ephedrine (Standard)	SBP within 10% resting BP + noradrenaline (Individualized)	Intraop. + 4h postop.	Withheld	95% abdominal	260 (170-365) vs. 280 (200-375)	45% vs. 45%	Noradrenaline: 95% vs. 26% Ephedrine 0.7% vs. 84%	1500 (1000-2000) vs. 2000 (1500-2500)	875 (500-1500) vs. 1000 (500-1500)	500 (200-925) vs. 500 (200-837)	26.5% vs. 23.4%	12% vs. 14% (planned)
POISE-3	MAP ≥ 60 mmHg (Hypertension avoidance)	MAP ≥ 80 mmHg (Hypotension avoidance)	Intraop.	Hypotension-avoidance: withheld Hypertension-avoidance: continued	36% general, 24% orthopedic, 14% vascular	mean 170	n/a	n/a	n/a	n/a	n/a	n/a	n/a

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INPRESS	SBP > 80 mmHg, within 40% resting BP + ephedrine (Standard)	SBP within 10% resting BP + noradrenaline (Individualized)	Intraop. + 4h postop.	Withheld	95% abdominal	260 (170-365) vs. 280 (200-375)	45% vs. 45%
POISE-3	MAP ≥ 60 mmHg (Hypertension avoidance)	MAP ≥ 80 mmHg (Hypotension avoidance)	Intraop.	Hypotension-avoidance: withheld Hypertension-avoidance: continued	36% general, 24% orthopedic, 14% vascular	mean 170	n/a

	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Blood loss BP_hi vs. BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	ICU postop. BP_hi vs. BP_lo [%]
BBB	Noradrenaline: 98% vs. 97% Ephedrine: 84% vs. 68% #	2800 (2000-4000) vs. 3000 (2000-4225) #	0 (0-0) vs. 0 (0-0) (15% vs. 17%) #	400 (150-1000) vs. 500 (150-1160) #	3.6% vs. 3.5% #	50% vs. 51% #
INPRESS	Noradrenaline: 95% vs. 26% Ephedrine 0.7% vs. 84%	1500 (1000-2000) vs. 2000 (1500-2500)	875 (500-1500) vs. 1000 (500-1500)	500 (200-925) vs. 500 (200-837)	26.5% vs. 23.4%	12% vs. 14% (planned)
POISE-3	n/a	n/a	n/a	n/a	n/a	n/a

UNPUBLISHED DATA - CALCULATED FOR PURPOSES OF PRESENTATION

Summary of 3 trials: Management & population

	BP_lo	BP_hi	Intervention duration	ACE-I & ARB	Surgical population	Surgical duration [min]	Epidural analgesia BP_hi vs. BP_lo	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Blood loss BP_hi vs. BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	ICU postop. BP_hi vs. BP_lo [%]
BBB	MAP ≥ 60 mmHg	MAP ≥ 75 mmHg	Intraop.	Continued	67% vascular, 12% abdominal, 10% urological	316 (249-428) vs. 322 (256-419) *Mean 350 (134)* #	39% vs. 37% #	Noradrenaline: 98% vs. 97% Ephedrine: 84% vs. 68% #	2800 (2000-4000) vs. 3000 (2000-4225) #	0 (0-0) vs. 0 (0-0) (15% vs. 17%) #	400 (150-1000) vs. 500 (150-1160) #	3.6% vs. 3.5% #	50% vs. 51% #
INPRESS	SBP > 80 mmHg, within 40% resting BP + ephedrine (Standard)	SBP within 10% resting BP + noradrenaline (Individualized)	Intraop. + 4h postop.	Withheld	9[illegible]% abdominal	260 (170-365) vs. 280 (200-375)	45% vs. 45%	Noradrenaline: 95% vs. 26% Ephedrine 0.7% vs. 84%	1500 (1000-2000) vs. 2000 (1500-2500)	875 (500-1500) vs. 1000 (500-1500)	500 (200-925) vs. 500 (200-837)	26.5% vs. 23.4%	12% vs. 14% (planned)
POISE-3	MAP ≥ 60 mmHg (Hypertension avoidance)	MAP ≥ 80 mmHg (Hypotension avoidance)	Intraop.	Hypotension-avoidance: withheld Hypertension-avoidance: continued	36% general, 24% orthopedic, 14% vascular	mean 170	n/a	n/a	n/a	n/a	n/a	n/a	n/a

UNPUBLISHED DATA - CALCULATED FOR PURPOSES OF PRESENTATION

Summary of 3 trials: Management & population

	BP_lo	BP_hi	Intervention duration	ACE-I & ARB	Surgical population	Surgical duration [min]	Epidural analgesia BP_hi vs. BP_lo	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Blood loss BP_hi vs. BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	ICU postop. BP_hi vs. BP_lo [%]
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POISE-3	MAP ≥ 60 mmHg (Hypertension avoidance)	MAP ≥ 80 mmHg (Hypotension avoidance)	Intraop.	Hypotension-avoidance: withheld Hypertension-avoidance: continued	36% general, 4% orthopedic, 14% vascular	mean 170	n/a	n/a	n/a	n/a	n/a	n/a	n/a

UNPUBLISHED DATA - CALCULATED FOR PURPOSES OF PRESENTATION

Summary of 3 trials: Management & population

	BP_lo	BP_hi	Intervention duration	ACE-I & ARB	Surgical population	Surgical duration [min]	Epidural analgesia BP_hi vs. BP_lo	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Blood loss BP_hi vs. BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	ICU postop. BP_hi vs. BP_lo [%]
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UNPUBLISHED DATA - CALCULATED FOR PURPOSES OF PRESENTATION

Summary of 3 trials: Management & population

	BP_lo	BP_hi	Intervention duration	ACE-I & ARB	Surgical population	Surgical duration [min]	Epidural analgesia BP_hi vs. BP_lo	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Blood loss BP_hi vs. BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	ICU postop. BP_hi vs. BP_lo [%]
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UNPUBLISHED DATA - CALCULATED FOR PURPOSES OF PRESENTATION

Summary of 3 trials: Management & population

	BP_lo	BP_hi	Intervention duration	ACE-I & ARB	Surgical population	Surgical duration [min]	Epidural analgesia BP_hi vs. BP_lo	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Blood loss BP_hi vs. BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	ICU postop. BP_hi vs. BP_lo [%]
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UNPUBLISHED DATA - CALCULATED FOR PURPOSES OF PRESENTATION

Summary of 3 trials: Management & population

	BP_lo	BP_hi	Intervention duration	ACE-I & ARB	Surgical population	Surgical duration [min]	Epidural analgesia BP_hi vs. BP_lo	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Blood loss BP_hi vs. BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	ICU postop. BP_hi vs. BP_lo [%]
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Summary of 3 trials: Management & population

	BP_lo	BP_hi	Intervention duration	ACE-I & ARB	Surgical population	Surgical duration [min]	Epidural analgesia BP_hi vs. BP_lo	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Blood loss BP_hi vs. BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	ICU postop. BP_hi vs. BP_lo [%]
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Summary of 3 trials: Management & population

	BP_lo	BP_hi	Intervention duration	ACE-I & ARB	Surgical population	Surgical duration [min]
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	Epidural analgesia BP_hi vs. BP_lo	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Blood loss BP_hi vs. BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	ICU postop. BP_hi vs. BP_lo [%]
BBB	39% vs. 37% #	Noradrenaline: 98% vs. 97% Ephedrine: 84% vs. 68% #	2800 (2000-4000) vs. 3000 (2000-4225) #	0 (0-0) vs. 0 (0-0) (15% vs. 17%) #	400 (150-1000) vs. 500 (150-1160) #	3.6% vs. 3.5% #	50% vs. 51% #
INPRESS	4[illegible]% vs. 45%	Noradrenaline: 95% vs. 26% Ephedrine 0.7% vs. 84%	1500 (1000-2000) vs. 2000 (1500-2500)	875 (500-1500) vs. 1000 (500-1500)	500 (200-925) vs. 500 (200-837)	26.5% vs. 23.4%	12% vs. 14% (planned)
POISE-3	n/a	n/a	n/a	n/a	n/a	n/a	n/a

UNPUBLISHED DATA - CALCULATED FOR PURPOSES OF PRESENTATION

Summary of 3 trials: Management & population

	BP_lo	BP_hi	Intervention duration	ACE-I & ARB	Surgical population	Surgical duration [min]	Epidural analgesia BP_hi vs. BP_lo	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Blood loss BP_hi vs. BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	ICU postop. BP_hi vs. BP_lo [%]
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Summary of 3 trials: Management & population

	BP_lo	BP_hi	Intervention duration	ACE-I & ARB	Surgical population	Surgical duration [min]	Epidural analgesia BP_hi vs. BP_lo	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Blood loss BP_hi vs. BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	ICU postop. BP_hi vs. BP_lo [%]
BBB	MAP ≥ 60 mmHg	MAP ≥ 75 mmHg	Intraop.	Continued	67% vascular, 12% abdominal, 10% urological	316 (249-428) vs. 322 (256-419) *Mean 35[illegible] (134)* #	39% vs. 37% #	[illegible]oradrenaline: 9[illegible]% vs. 97% [illegible]phedrine: 8[illegible]% vs. 68% #	2800 (2000-4000) vs. 3000 (2000-4225) #	0 (0-0) vs. 0 (0-0) (15% vs. 17%) #	400 (150-1000) vs. 500 (150-1160) #	3.6% vs. 3.5% #	50% vs. 51% #
INPRESS	SBP > 80 mmHg, within 40% resting BP + ephedrine (Standard)	SBP within 10% resting BP + noradrenaline (Individualized)	Intraop. + 4h postop.	Withheld	95% abdominal	260 (170-3[illegible]5) vs. 280 (200-37[illegible])	45% vs. 45%	No[illegible]adrenaline: 9[illegible]% vs. 26% [illegible]Ephedrine [illegible].7% vs. 84%	1500 (1000-2000) vs. 2000 (1500-2500)	875 (500-1500) vs. 1000 (500-1500)	500 (200-925) vs. 500 (200-837)	26.5% vs. 23.4%	12% vs. 14% (planned)
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	BP_lo	BP_hi	Intervention duration	ACE-I & ARB	Surgical population	Surgical duration [min]	Epidural analgesia BP_hi vs. BP_lo	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Blood loss BP_hi vs. BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	ICU postop. BP_hi vs. BP_lo [%]
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INPRESS	SBP > 80 mmHg, within 40% resting BP + ephedrine (Standard)	SBP within 10% resting BP + noradrenaline (Individualized)	Intraop. + 4h postop.	Withheld	95% abdominal	260 (170-365) vs. 280 (200-375)	45% vs. 45%	Noradrenaline: 95% vs. 26% Ephedrine 0.7% vs. 84%	1500 (1000-2000) vs. 2000 (1500-2500)	875 (500-1500) vs. 1000 (500-1500)	500 (200-925) vs. 500 (200-837)	26.5% vs. 23.4%	12% vs. 14% (planned)
POISE-3	MAP ≥ 60 mmHg (Hypertension avoidance)	MAP ≥ 80 mmHg (Hypotension avoidance)	Intraop.	Hypotension-avoidance: withheld Hypertension-avoidance: continued	36% general, 24% orthopedic, 14% vascular	mean 170	n/a	n/a	n/a	n/a	n/a	n/a	n/a

UNPUBLISHED DATA - CALCULATED FOR PURPOSES OF PRESENTATION

Summary of 3 trials: Management & population

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Summary of 3 trials: Primary outcomes

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BBB	MAP ≥ 60 mmHg	MAP ≥ 75 mmHg	Intraop.	67% vascular, 12% abdominal, 10% urological	**Acute myocardial injury and/or 30-day MACE/AKI** (MACE = ACS, CHF, coronary revasc., stroke, death)	451	RR 0.92 (0.76 to 1.11) MAP 75 vs 60
INPRESS	SBP > 80 mmHg, within 40% resting BP + ephedrine (Standard)	SBP within 10% resting BP + noradrenaline (Individualized)	Intraop. + 4h postop.	95% abdominal	**Postoperative organ dysfunction** (SIRS + 1 organ dysfunction: renal, CV, resp, neuro, coagulation)	292	RR 0.74 (0.57 to 0.95) Individualized vs. Standard
POISE-3	MAP ≥ 60 mmHg (Hypertension avoidance)	MAP ≥ 80 mmHg (Hypotension avoidance)	Intraop.	36% general, 24% orthopedic, 14% vascular	**Major vascular complication** (Vascular death, non-fatal MINS, stroke, cardiac arrest at 30 days)	7490	HR 0.99 (0.88 to 1.12) Hypotension vs. Hypertension avoidance

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INPRESS	SBP > 80 mmHg, within 40% resting BP + ephedrine (Standard)	SBP within 10% resting BP + noradrenaline (Individualized)	Intraop. + 4h postop.	95% abdominal	**Postoperative organ dysfunction** (SIRS + 1 organ dysfunction: renal, CV, resp, neuro, coagulation)	292	RR 0.74 (0.57 to 0.95) Individualized vs. Standard
POISE-3	MAP ≥ 60 mmHg (Hypertension avoidance)	MAP ≥ 80 mmHg (Hypotension avoidance)	Intraop.	36% general, 24% orthopedic, 14% vascular	**Major vascular complication** (Vascular death, non-fatal MINS, stroke, cardiac arrest at 30 days)	7490	HR 0.99 (0.88 to 1.12) Hypotension vs. Hypertension avoidance

Summary of 3 trials: Primary outcomes

	BP_lo	BP_hi	Intervention duration	Surgical population	Primary outcome	Patients in ITT population	RR resp. HR (95% CI) for primary outcome
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Summary of 3 trials: Cardiovascular outcomes

	BP_lo	BP_hi	Intervention duration	Surgical population	Cardiovascular outcome	Patients in ITT population	Events BP target 1	Events BP target 2	RR resp. HR (95% CI) for CV outcome
BBB	MAP ≥ 60 mmHg	MAP ≥ 75 mmHg	Intraop.	67% vascular, 12% abdominal, 10% urological	**Acute myocardial injury and/or 30-day MACE** (ACS, CHF, coronary revasc., stroke, death)	451	45 (20%)	35 (16%)	RR 0.78 (0.52 to 1.17) MAP 75 vs 60 \#
INPRESS	SBP > 80 mmHg, within 40% resting BP + ephedrine (Standard)	SBP within 10% resting BP + noradrenaline (Individualized)	Intraop. + 4h postop.	95% abdominal	Acute heart failure, myocardial ischemia/infarction	292	1 (0.7%)	1 (0.7%)	n/a
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Summary of 3 trials: Renal outcomes

	BP_lo	BP_hi	Intervention duration	ACE-I & ARB	Surgical population	Vasoactive Medications BP_hi vs. BP_lo [%]	Crystalloids Intraop. BP_hi vs. BP_lo [ml]	Colloids Intraop. BP_hi vs BP_lo [ml]	Transfusion Intraop. BP_hi vs. BP_lo [%]	Renal outcome	Patients in ITT population	Events BP_lo	Events BP_hi	RR (95% CI) for renal outcome
BBB	MAP ≥ 60 mmHg	MAP ≥ 75 mmHg	Intraop.	**Continued**	**67% vascular,** 12% abdominal, 10% urological	Noradrenaline: 98% vs. 97% Ephedrine: 84% vs. 68% #	2800 (2000-4000) vs. 3000 (2000-4225) p=0.3 #	0 (0-0) vs. 0 (0-0) (15% vs. 17%) #	3.6% vs. 3.5% #	**AKI** (AKIN I or higher)	451	104 (46%)	96 (43%)	**RR 0.93 (0.75 to 1.14)** MAP 75 vs 60 #
INPRESS	SBP > 80 mmHg, within 40% resting BP + ephedrine (Standard)	SBP within 10% resting BP + noradrenaline (Individualized)	Intraop. + 4h postop.	**Withheld**	**95% abdominal**	**Noradrenaline: 95% vs. 26%** **Ephedrine 0.7% vs. 84%**	**1500 (1000-2000) vs. 2000 (1500-2500** **p<0.001**	875 (500-1500) vs. 1000 (500-1500)	26.5% vs. 23.4%	**Renal dysfunction** (RIFLE RISK or higher)	292	71 (49%)	48 (33%)	**RR 0.67 (0.50 to 0.89)** Individualized vs. Standard
POISE-3	MAP ≥ 60 mmHg (Hypertension avoidance)	MAP ≥ 80 mmHg (Hypotension avoidance)	Intraop.	Hypotension-avoidance: withheld Hypertension avoidance: continued	36% general, 24% orthopedic, 14% vascular	-	-	-	-	-	-	-	-	-

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BBB	MAP ≥ 60 mmHg	MAP ≥ 75 mmHg	Intraop.	**Continued**	**67% vascular,** 12% abdominal, 10% urological	Noradrenaline: 98% vs. 97% Ephedrine: 84% vs. 68% #	2800 (2000-4000) vs. 3000 (2000-4225) p=0.3 #	0 (0-0) vs. 0 (0-0) (15% vs. 17%) #	3.6% vs. 3.5% #	**AKI** (AKIN I or higher)	451	104 (46%)	96 (43%)	**RR 0.93 (0.75 to 1.14)** MAP 75 vs 60 #
INPRESS	SBP > 80 mmHg, within 40% resting BP + ephedrine (Standard)	SBP within 10% resting BP + noradrenaline (Individualized)	Intraop. + 4h postop.	**Withheld**	**95% abdominal**	**Noradrenaline: 95% vs. 26%** **Ephedrine 0.7% vs. 84%**	**1500 (1000-2000) vs. 2000 (1500-2500** **p<0.001**	875 (500-1500) vs. 1000 (500-1500)	26.5% vs. 23.4%	**Renal dysfunction** (RIFLE RISK or higher)	292	71 (49%)	48 (33%)	**RR 0.67 (0.50 to 0.89)** Individualized vs. Standard
POISE-3	MAP ≥ 60 mmHg (Hypertension avoidance)	MAP ≥ 80 mmHg (Hypotension avoidance)	Intraop.	Hypotension-avoidance: withheld Hypertension avoidance: continued	36% general, 24% orthopedic, 14% vascular	-	-	-	-	**AKI** (within 2 -7 days)	7307	505 (14%)	530 (15%)	-

UNPUBLISHED DATA - CALCULATED FOR PURPOSES OF PRESENTATION

Summary of 3 trials: Renal outcomes

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UNPUBLISHED DATA - CALCULATED FOR PURPOSES OF PRESENTATION

3 trials on BP management in noncardiac surgery

MAP > 80% "baseline"

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery

A Randomized Clinical Trial

Emmanuel Futier, MD, PhD; Jean-Yves Lefrant, MD, PhD; Pierre-Gregoire Guinot, MD, PhD; Thomas Godet, MD, PhD; Emmanuel Lorne, MD; Philippe Cuvillon, MD, PhD; Sebastien Bertran, MD; Marc Leone, MD, PhD; Bruno Pastene, MD; Vincent Piriou, MD, PhD; Serge Molliex, MD, PhD; Jacques Albanese, MD, PhD; Jean-Michel Julia, MD; Benoit Tavernier, MD, PhD; Etienne Imhoff, MD; Jean-Etienne Bazin, MD, PhD; Jean-Michel Constantin, MD, PhD; Bruno Pereira, PhD; Samir Jaber, MD, PhD; for the INPRESS Study Group

INPRESS

Potentially improved renal and neurological outcomes

MAP > 75

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 78, NO. 18, 2021

ORIGINAL INVESTIGATIONS

Targeting Higher Intraoperative Blood Pressures Does Not Reduce Adverse Cardiovascular Events Following Noncardiac Surgery

Patrick M. Wanner, MD,[a,*] Dirk U. Wulff, PhD,[b] Mirjana Djurdjevic,[a] Wolfgang Korte, MD,[c] Thomas W. Schnider, MD,[a] Miodrag Filipovic, MD[a]

BBB

No differences in cardiovasc. or renal outcomes

MAP > 80

Annals of Internal Medicine

ORIGINAL RESEARCH

Hypotension-Avoidance Versus Hypertension-Avoidance Strategies in Noncardiac Surgery

An International Randomized Controlled Trial

Maura Marcucci, MD; Thomas W. Painter, MBChB; David Conen, MD; Vladimir Lomivorotov, MD; Daniel I. Sessler, MD; Matthew T.V. Chan, MBBS; Flavia K. Borges, MD; Kate Leslie, MD; Emmanuelle Duceppe, MD; María José Martínez-Zapata, MD; Chew Yin Wang, MBChB; Denis Xavier, MD; Sandra N. Ofori, MBBS; Michael Ke Wang, MD; Sergey Efremov, MD; Giovanni Landoni, MD; Ydo V. Kleinlugtenbelt, MD; Wojciech Szczeklik, MD; Denis Schmartz, MD; Amit X. Garg, MD; Timothy G. Short, MD; Maria Wittmann, MD; Christian S. Meyhoff, MD; Mohammed Amir, MBBS; David Torres, MD; Ameen Patel, MD; Kurt Ruetzler, MD; Joel L. Parlow, MD; Vikas Tandon, MD; Edith Fleischmann, MD; Carisi A. Polanczyk, MD; Andre Lamy, MD; Raja Jayaram, MD; Sergey V. Astrakov, MD; William Ka Kei Wu, PhD; Chao Chia Cheong, MD; Sabry Ayad, MD; Mikhail Kirov, MD; Miriam de Nadal, MD; Valery V. Likhvantsev, MD; Pilar Paniagua, MD; Hector J. Aguado, MD; Kamal Maheshwari, MD; Richard P. Whitlock, MD; Michael H. McGillion, RN; Jessica Vincent, MSc; Ingrid Copland; Kumar Balasubramanian, MSc; Bruce M. Biccard, MBChB; Sadeesh Srinathan, MD; Samandar Ismoilov, MD; Shirley Pettit, RN; David Stillo, MASc; Andrea Kurz, MD; Emilie P. Belley-Côté, MD; Jessica Spence, MD; William F. McIntyre, MD; Shrikant I. Bangdiwala, PhD; Gordon Guyatt, MD; Salim Yusuf, MD; and P.J. Devereaux, MD, PhD; on behalf of the POISE-3 Trial Investigators and Study Groups*

POISE-3

No differences in cardiovasc. or renal outcomes

Pressure vs. Flow

BJA

British Journal of Anaesthesia, xxx (xxx): xxx (xxxx)

doi: 10.1016/j.bja.2022.07.056
Advance Access Publication Date: xxx
Clinical Investigation

CLINICAL INVESTIGATION

Endotypes of intraoperative hypotension during major abdominal surgery: a retrospective machine learning analysis of an observational cohort study

Karim Kouz[1], Lennart Brockmann[1], Lea Malin Timmermann[1], Alina Bergholz[1], Moritz Flick[1], Kamal Maheshwari[2,3], Daniel I. Sessler[2], Linda Krause[4,†] and Bernd Saugel[1,5,*,†]

[1]Department of Anesthesiology, Center of Anesthesiology and Intensive Care Medicine, University Medical Center Hamburg–Eppendorf, Hamburg, Germany, [2]Department of Outcomes Research, Cleveland Clinic, Cleveland, OH, USA, [3]Department of General Anesthesiology, Anesthesiology Institute, Cleveland Clinic, Cleveland, OH, USA, [4]Institute of Medical Biometry and Epidemiology, University Medical Center Hamburg–Eppendorf, Hamburg, Germany and [5]Outcomes Research Consortium, Cleveland, OH, USA

*Corresponding author. E-mail: bernd.saugel@gmx.de
†Contributed equally to this work.

⋆Prior presentation of preliminary results: International Symposium on Intensive Care & Emergency Medicine, Brussels, Belgium, March 22–25, 2022.

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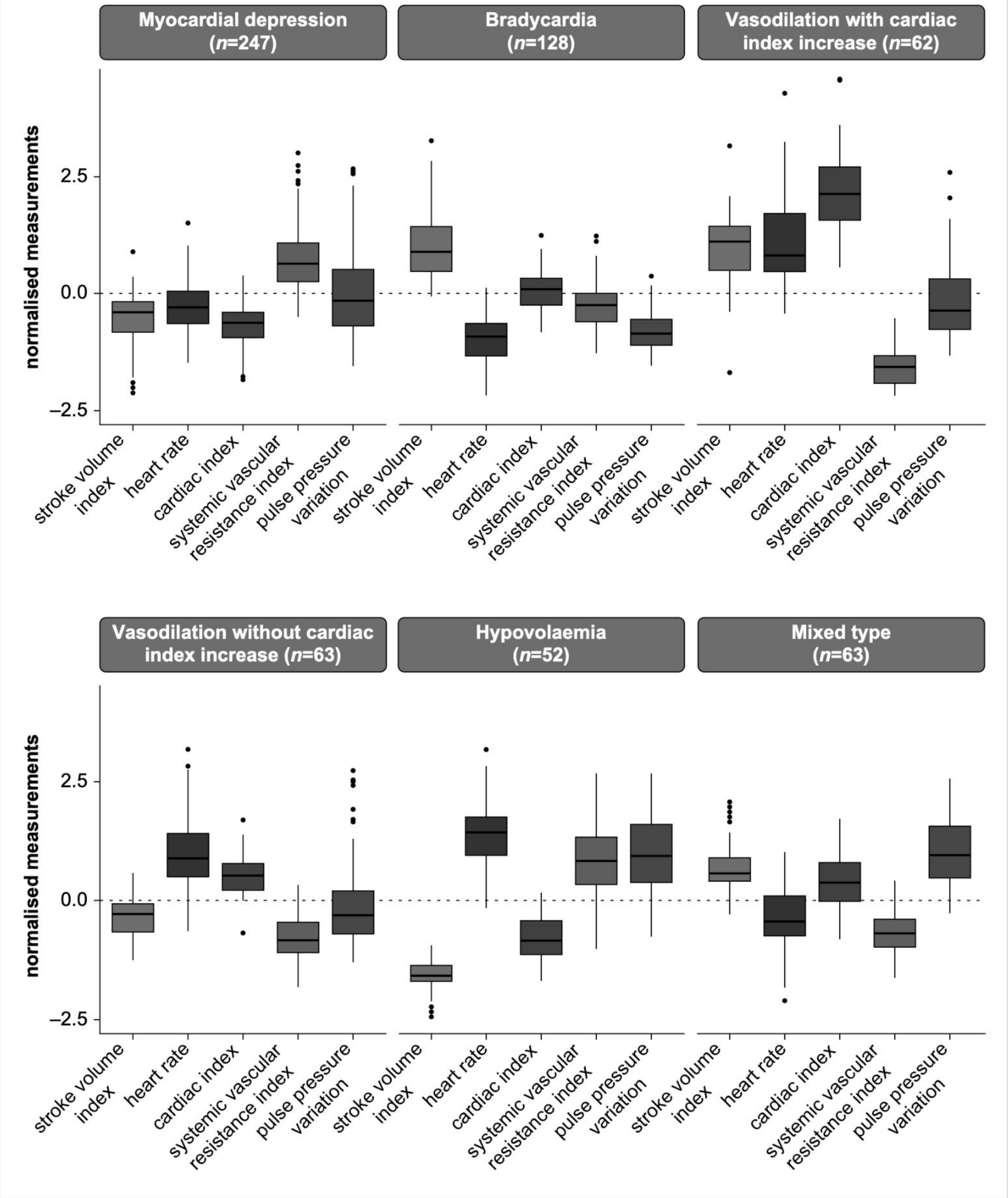

Fig 3. Boxplots showing normalised values of stroke volume index (blue boxes), heart rate (purple boxes), cardiac index (green boxes), systemic vascular resistance index (orange boxes), and pulse pressure variation (red boxes) for each intraoperative hypotension endotype. Data are normalised to a mean of zero (dashed horizontal line) and a standard deviation of 1.

Pressure vs. Flow

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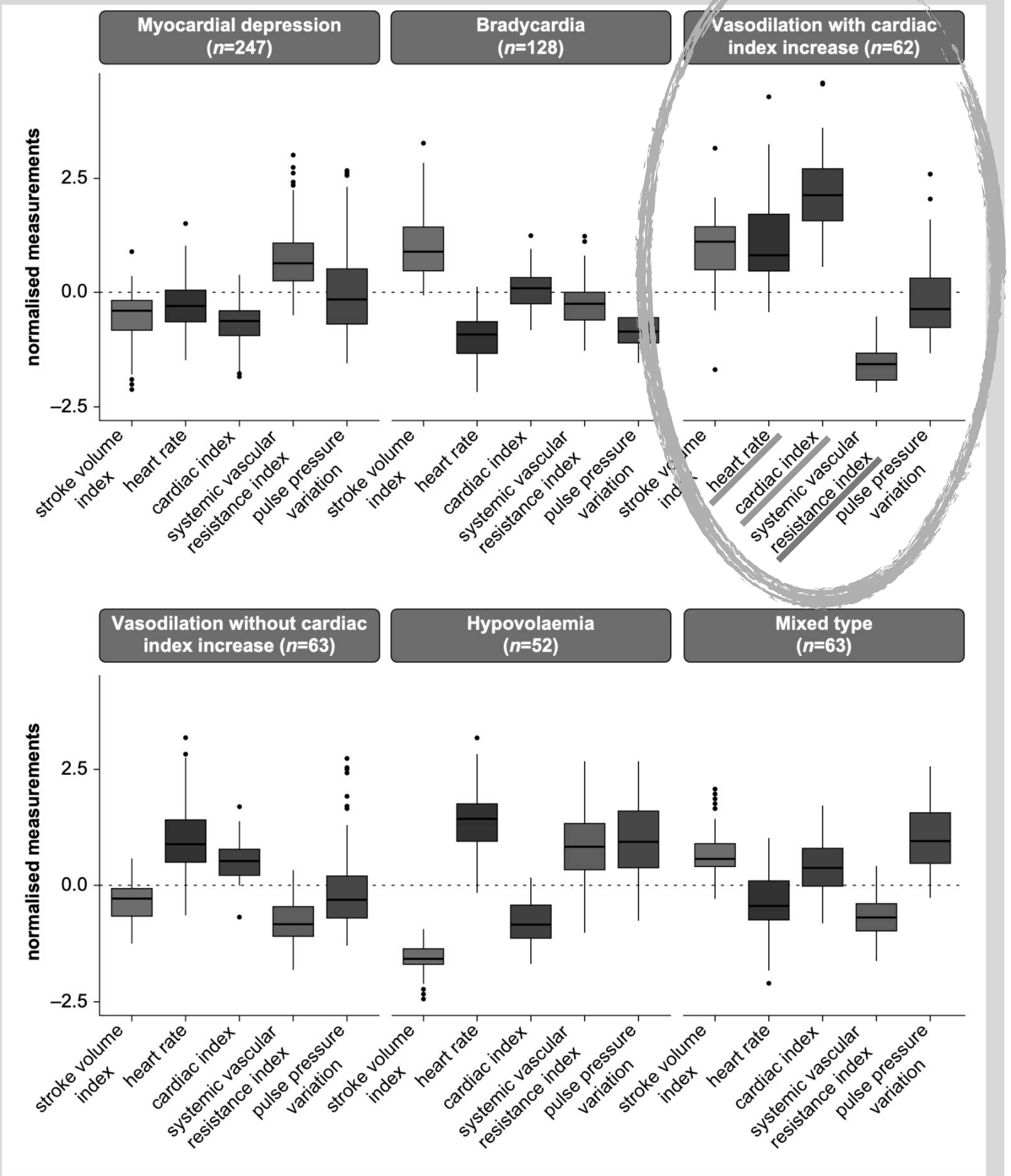

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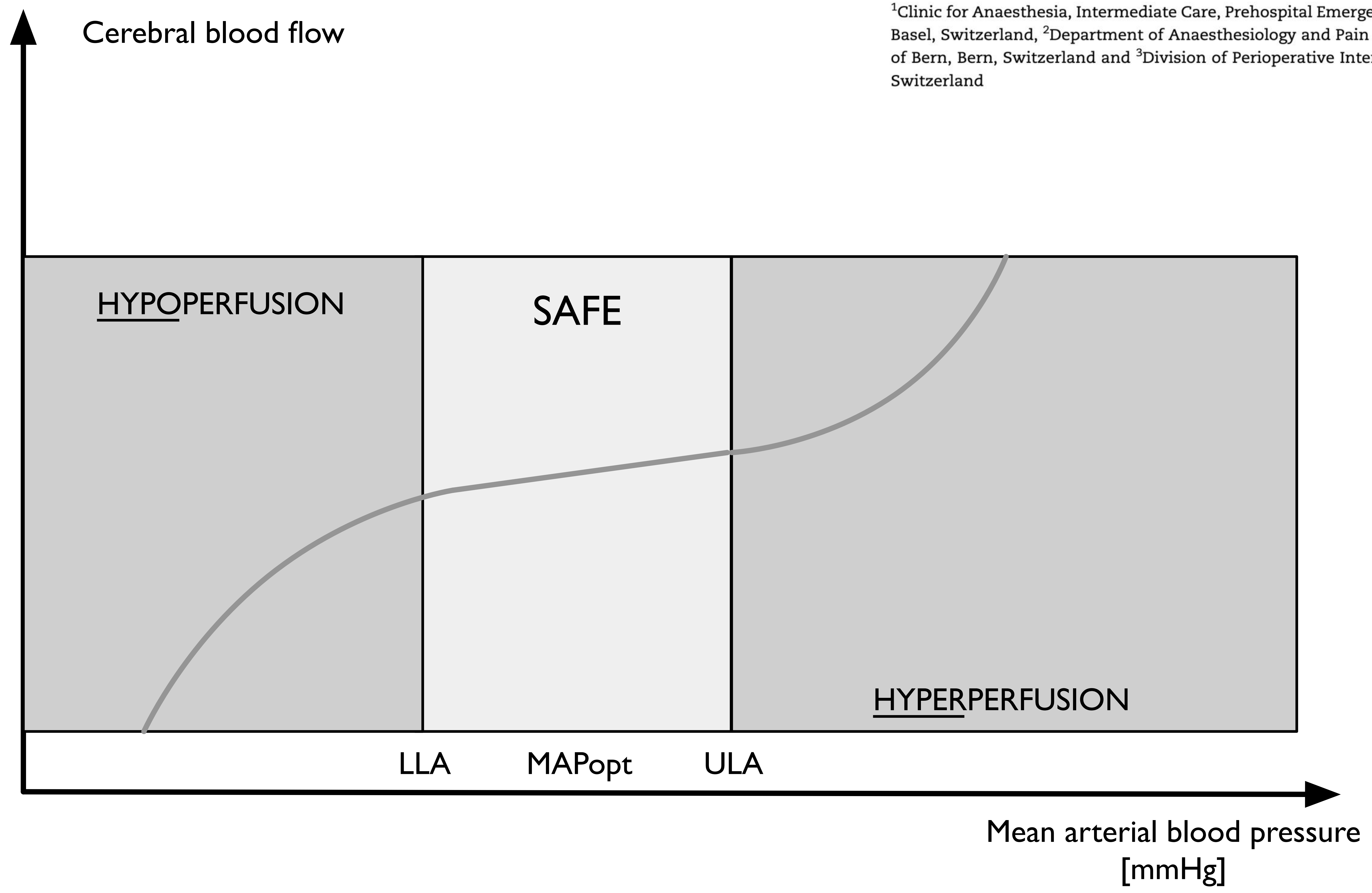
cAR monitoring in real life

CORRESPONDENCE

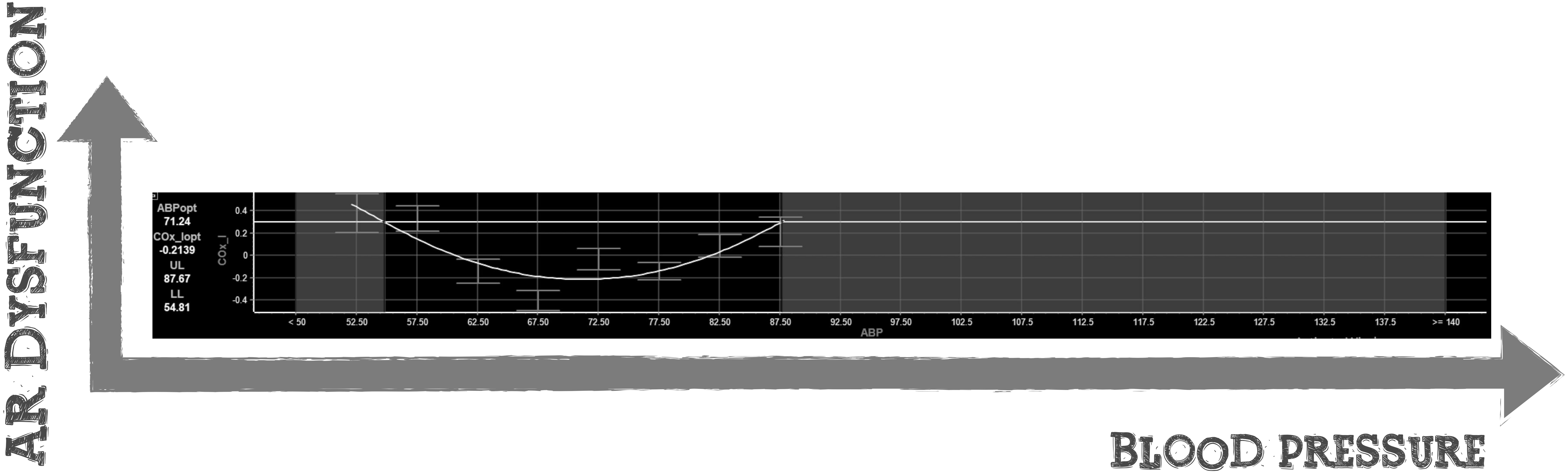
Intraoperative hypotension and postoperative outcomes: just the tip of the iceberg. Comment on *Br J Anaesth* 2023; 131: 823–31

Patrick M. Wanner[1,*], Andreas P. Vogt[2], Miodrag Filipovic[3], Luzius A. Steiner[1] on behalf of the Personalising Acute Care Network

[1]Clinic for Anaesthesia, Intermediate Care, Prehospital Emergency Medicine and Pain Therapy, University Hospital Basel, Basel, Switzerland, [2]Department of Anaesthesiology and Pain Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland and [3]Division of Perioperative Intensive Care Medicine, Kantonsspital St.Gallen, St. Gallen, Switzerland



cAR monitoring in real life



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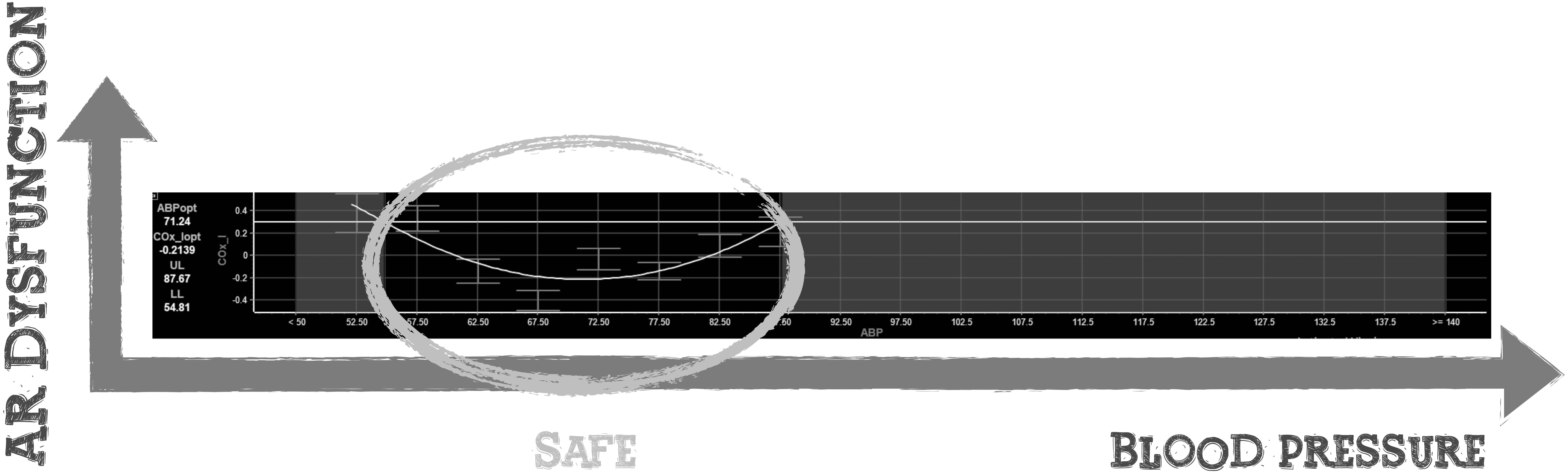
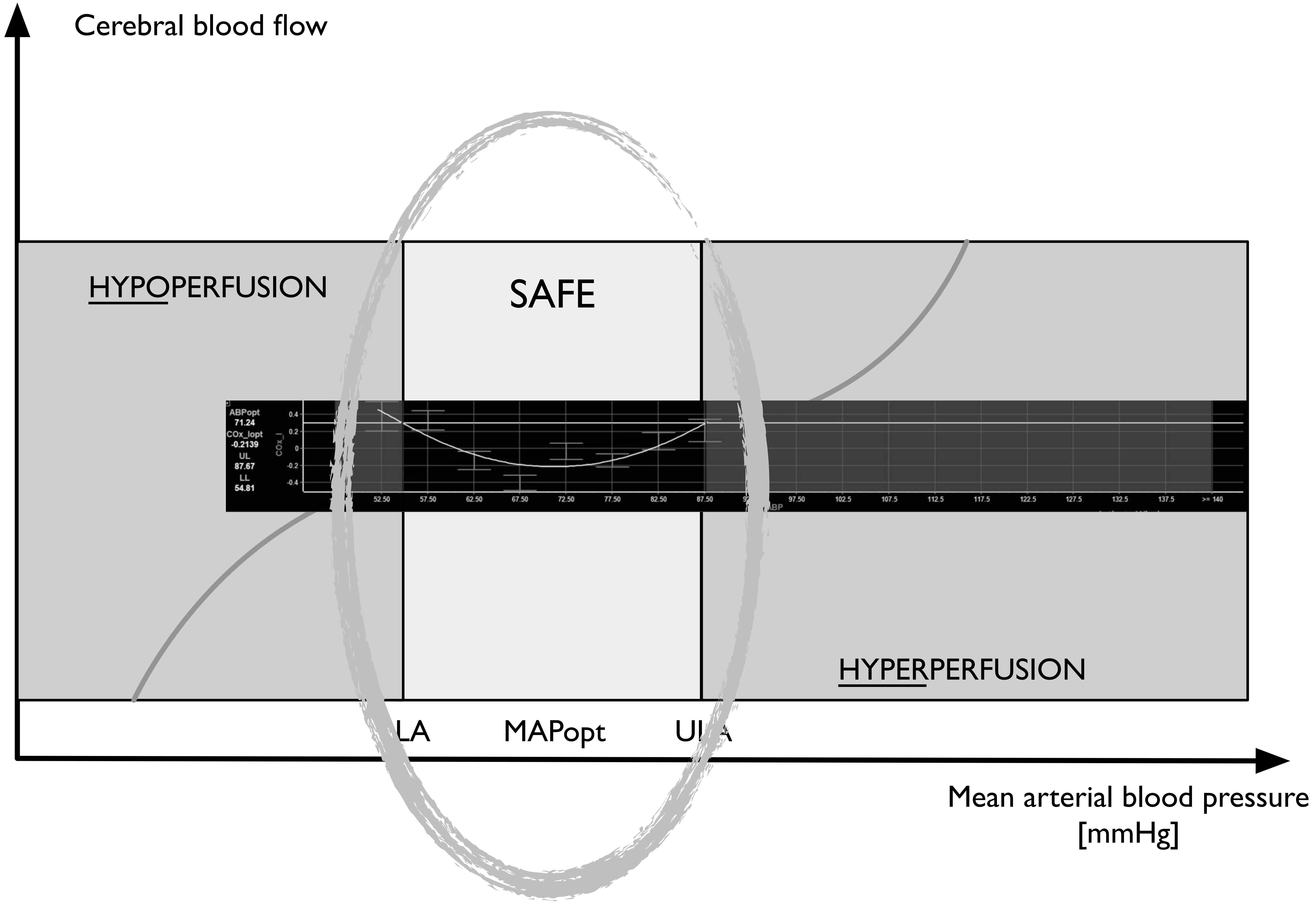


cAR monitoring in real life



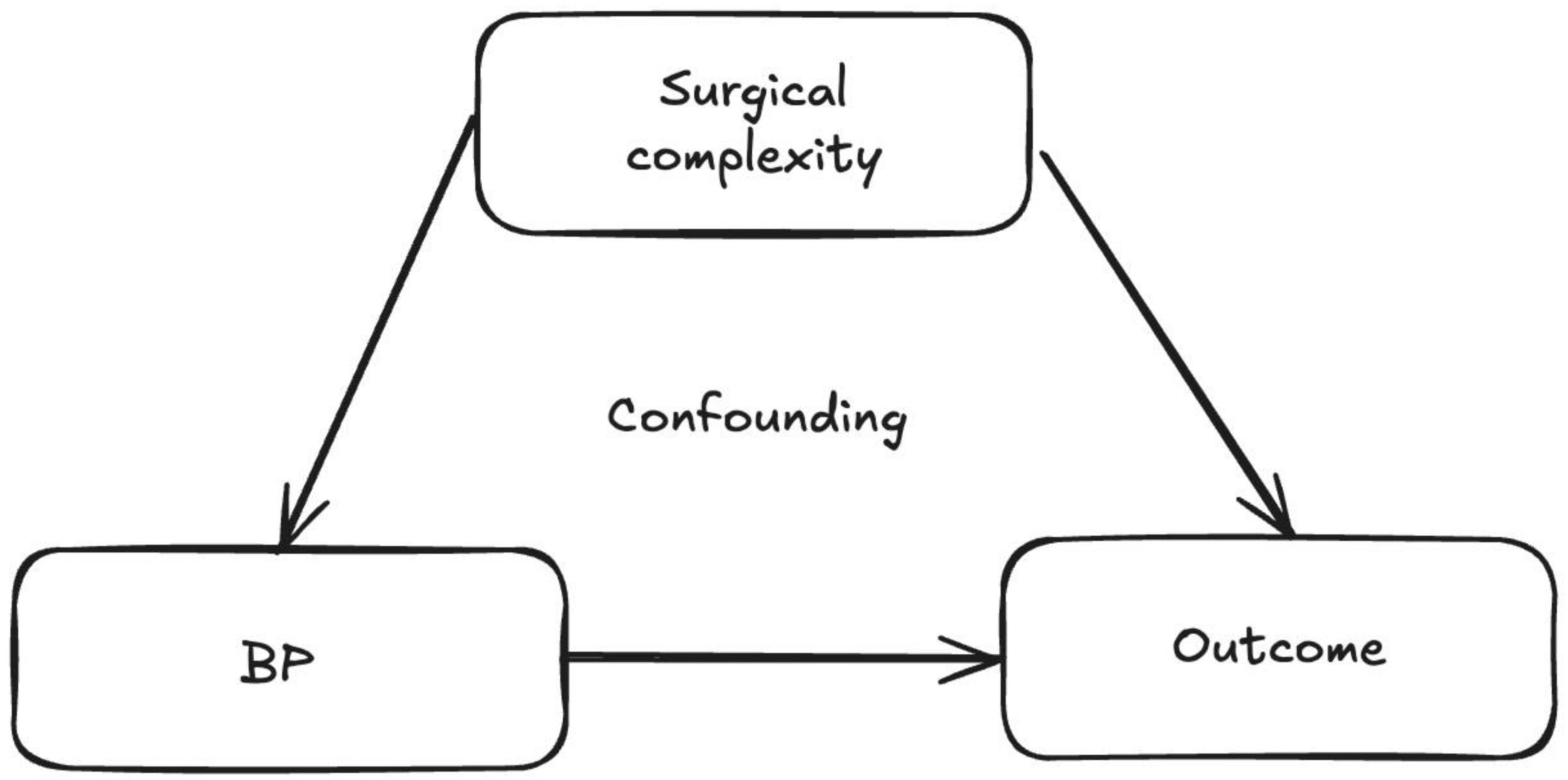
Pitfalls: Reductionism

Possible explanations for RCTs without relevant Tx effects ?

Pitfalls: Reductionism

Possible explanations for RCTs without relevant Tx effects ?

Residual confounding in observational studies



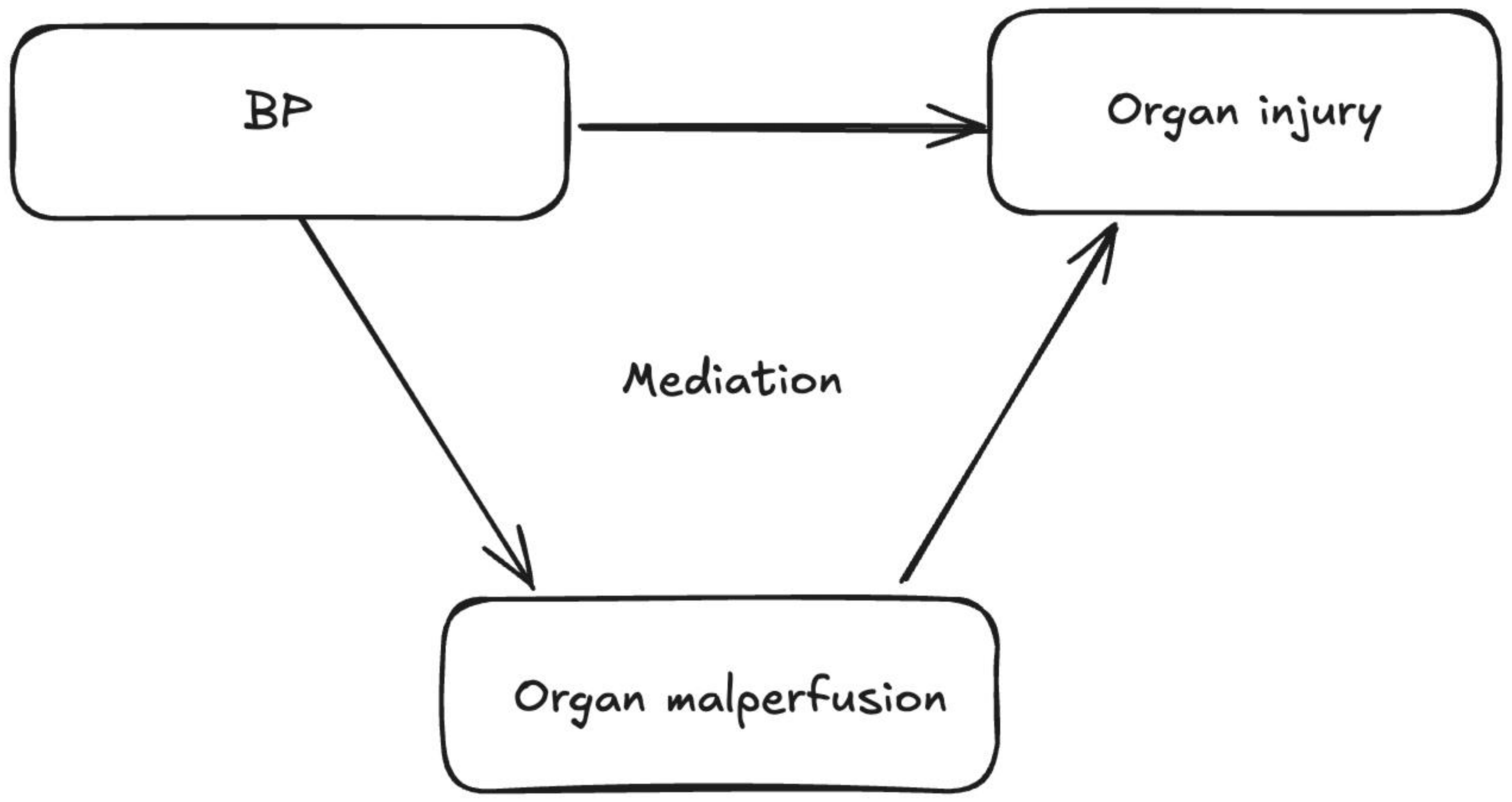
Association does not imply causation!

Pitfalls: Reductionism

Possible explanations for RCTs without relevant Tx effects ?

Residual confounding in observational studies

Complex causal networks



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Possible explanations for RCTs without relevant Tx effects ?

Residual confounding in observational studies

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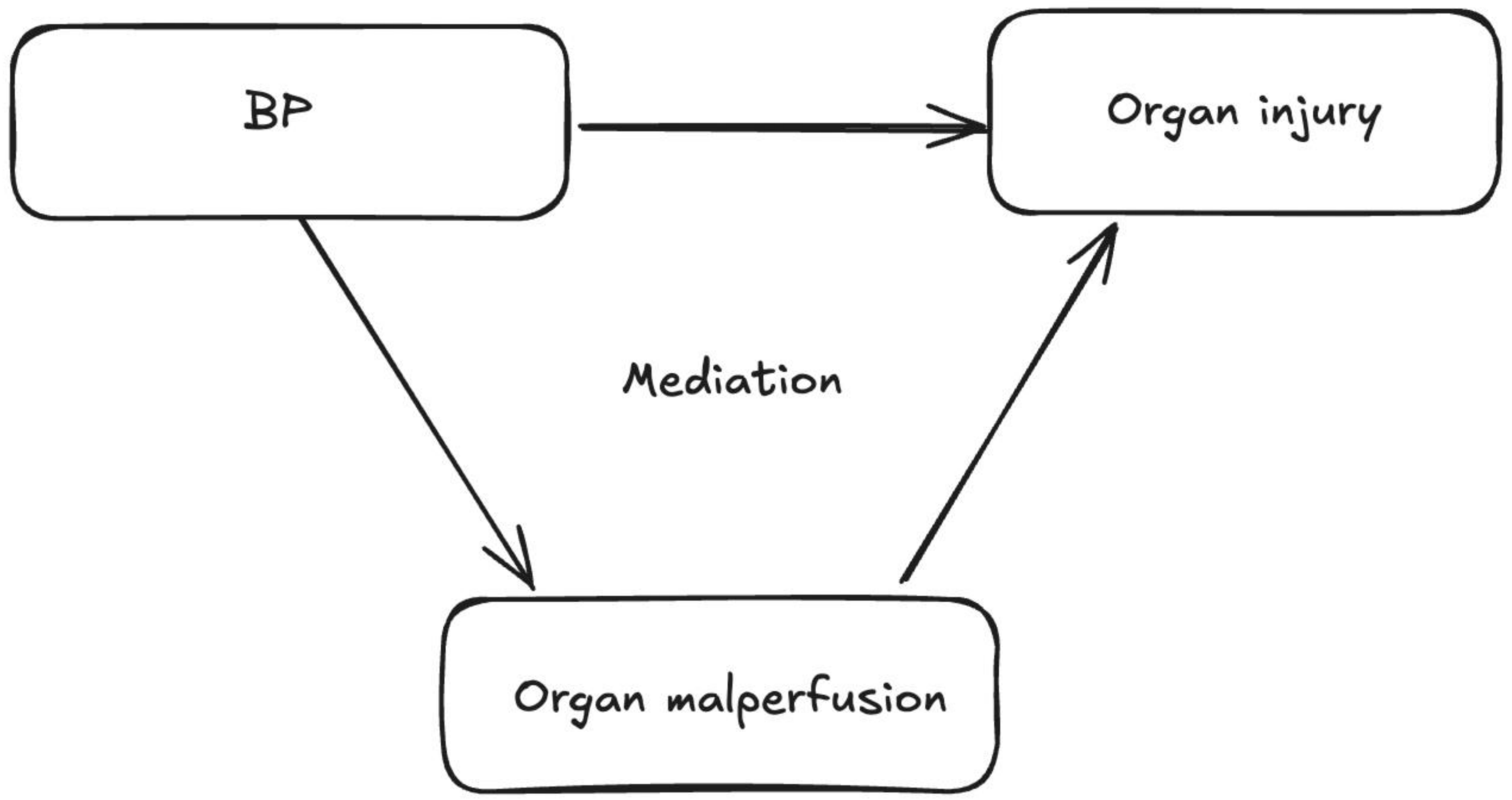

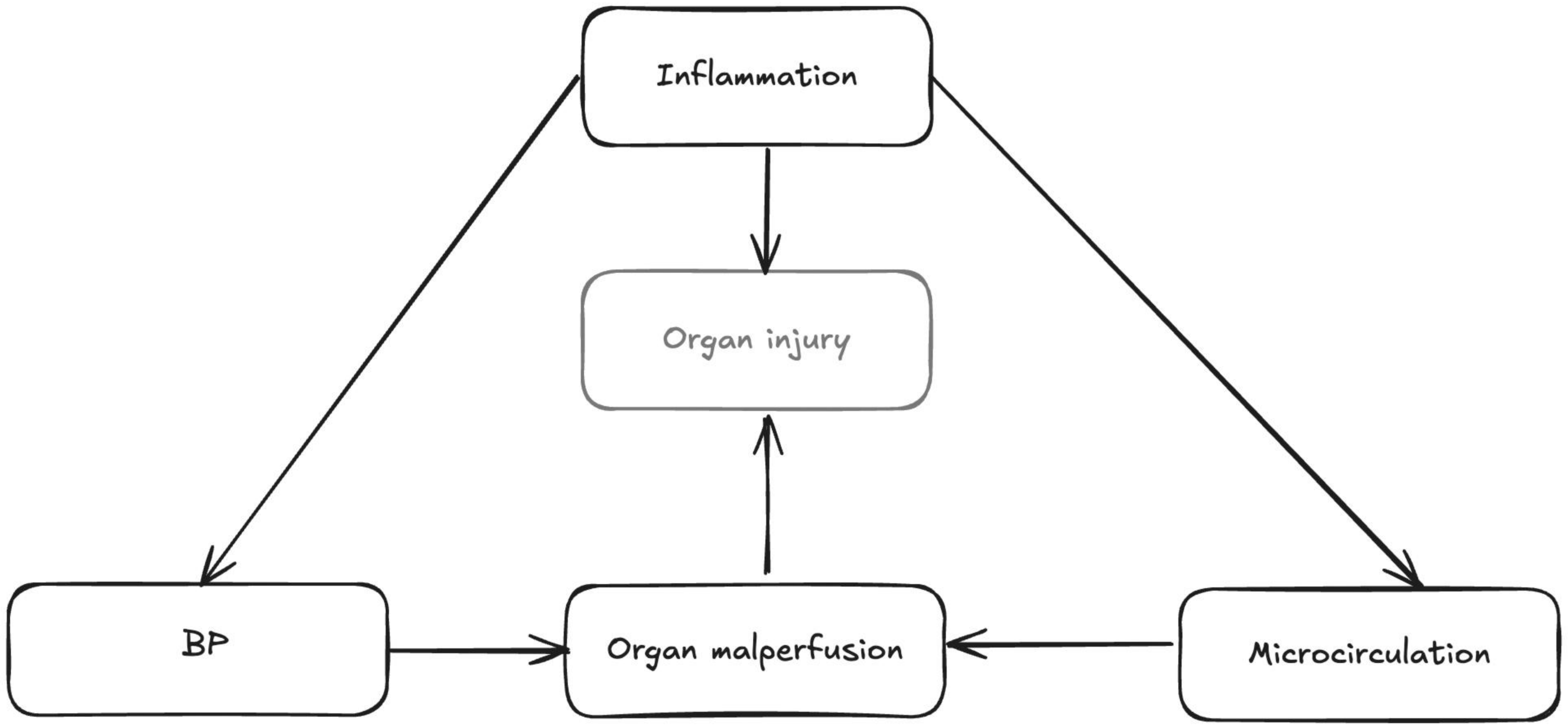

And many more factors...

Pitfalls: Reductionism

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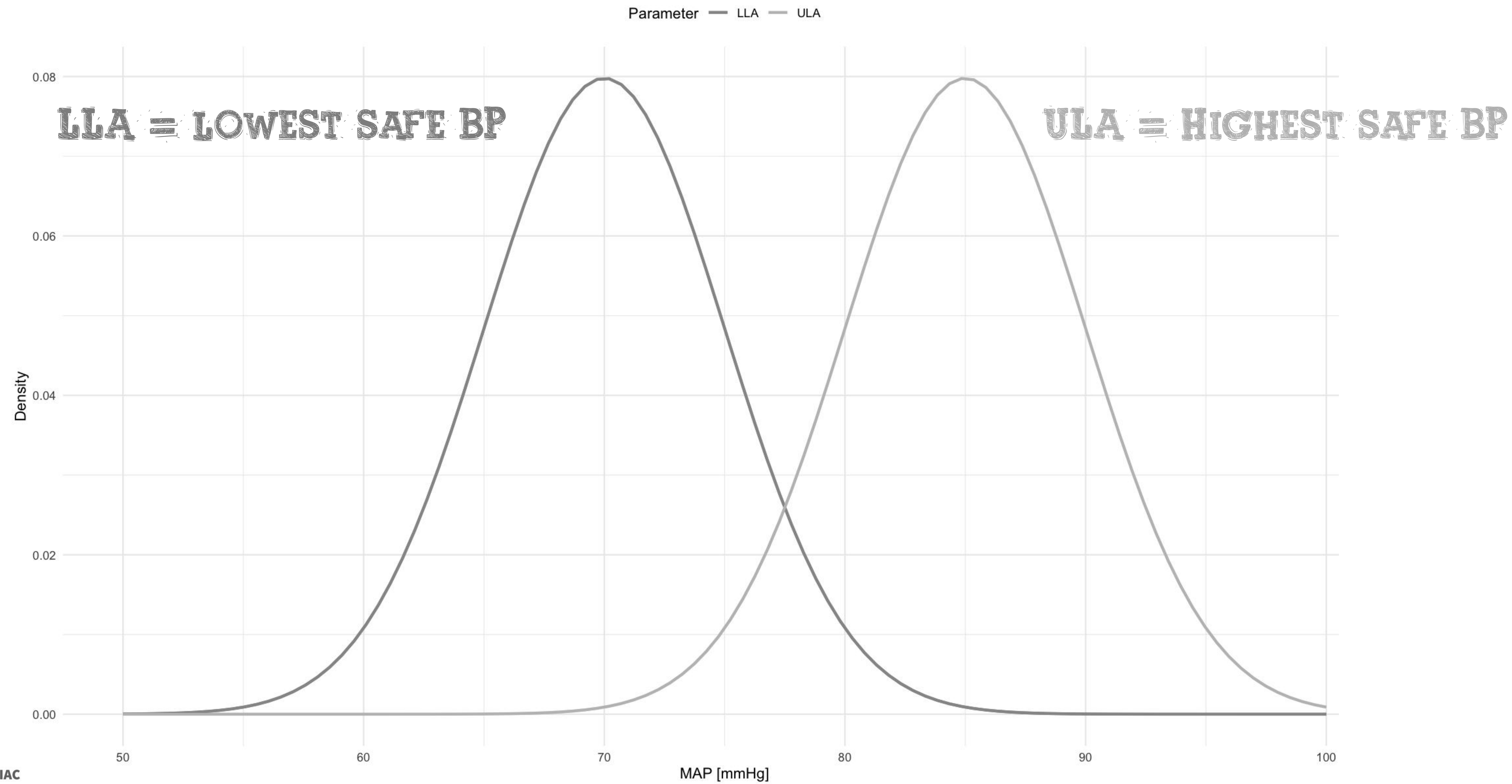
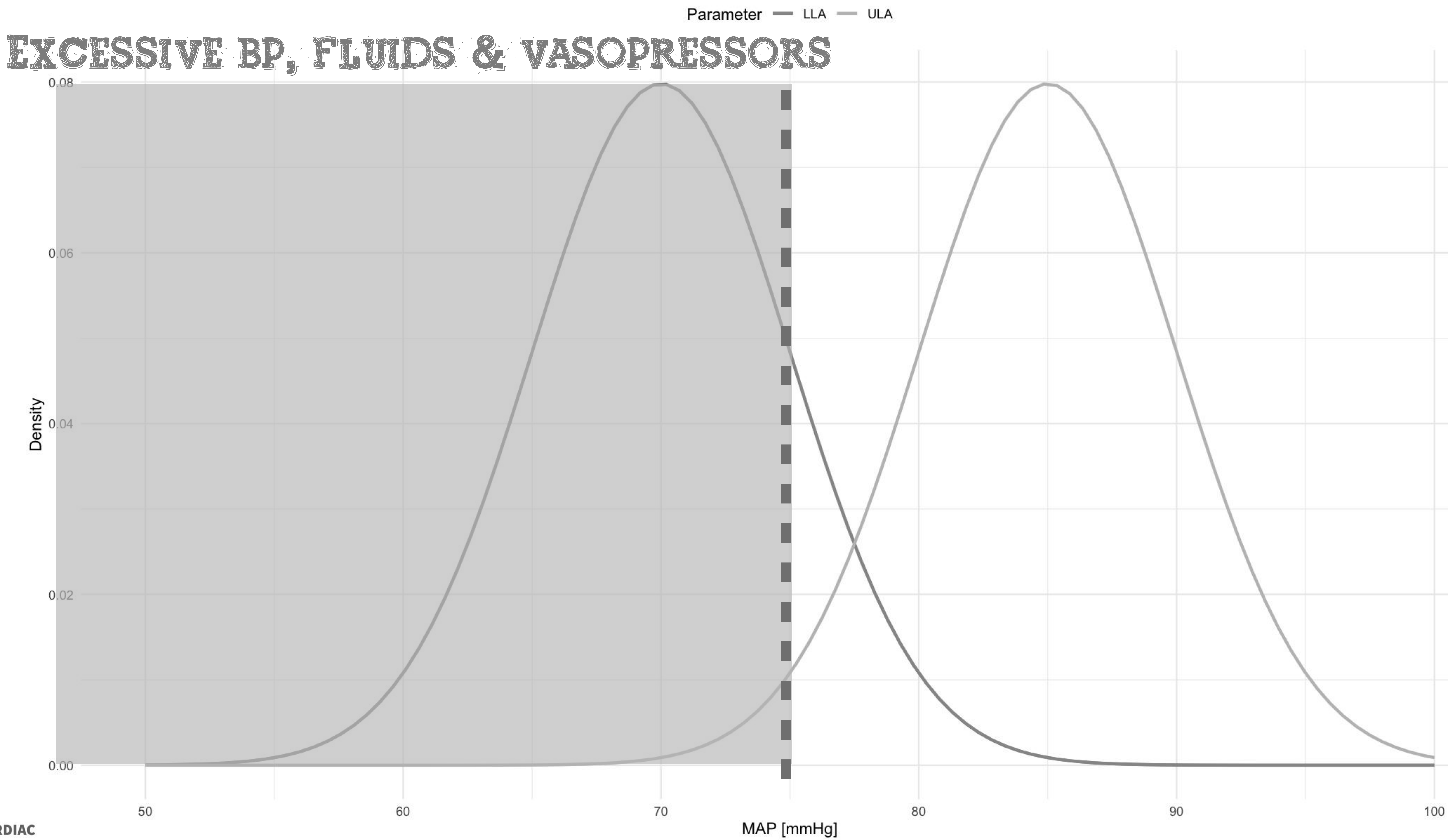
Heterogeneity of populations and treatment effect

Heterogeneity in hemodynamic needs



Heterogeneity in hemodynamic needs

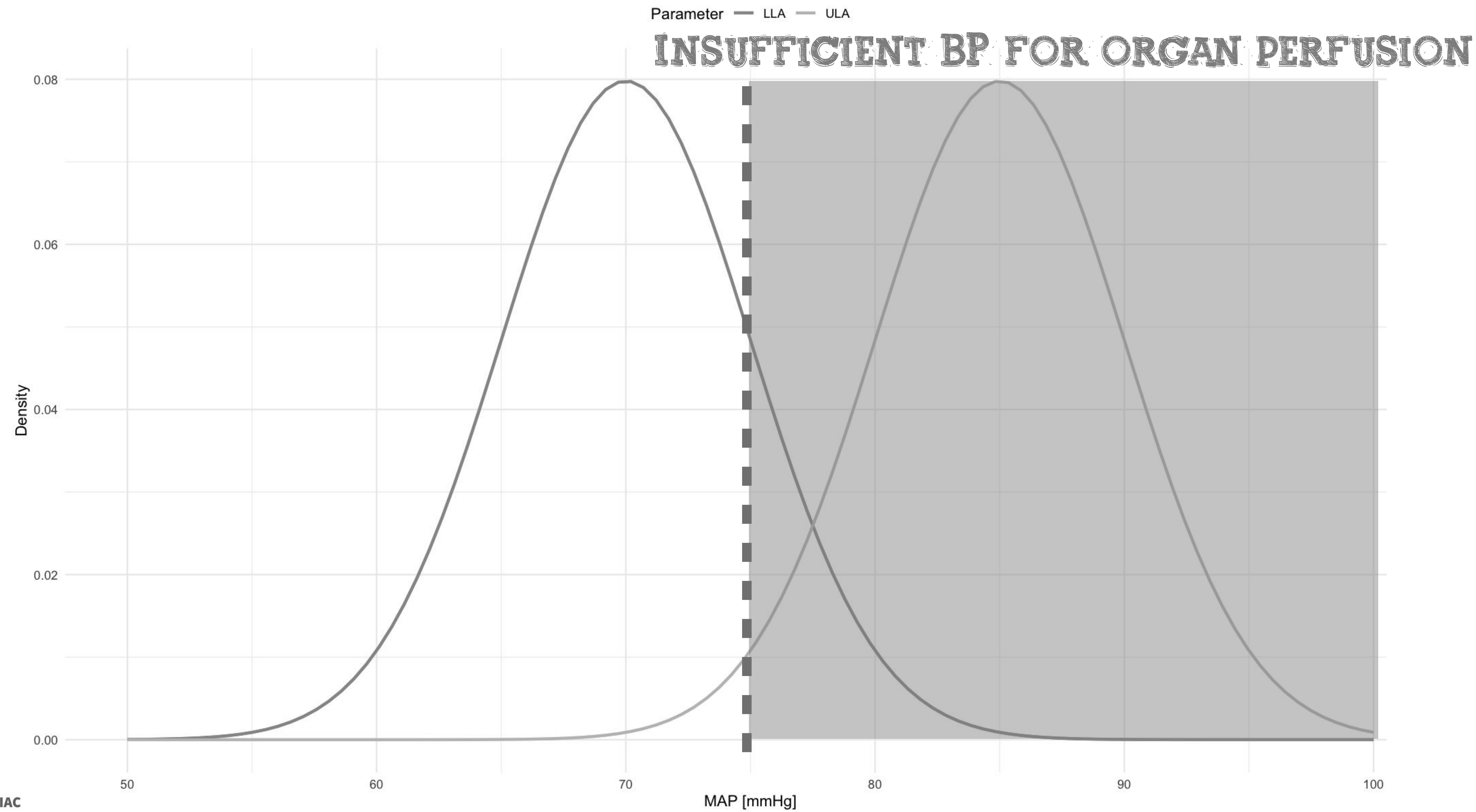


High MAP targets = overtreatment

AUTOREGULATE-NONCARDIAC

Preliminary

Heterogeneity in hemodynamic needs



AUTOREGULATE-NONCARDIAC

Preliminary

High MAP targets ≠ no guarantee for safety

Pitfalls: Reductionism

Possible explanations for RCTs without relevant Tx effects ?

Residual confounding in observational studies

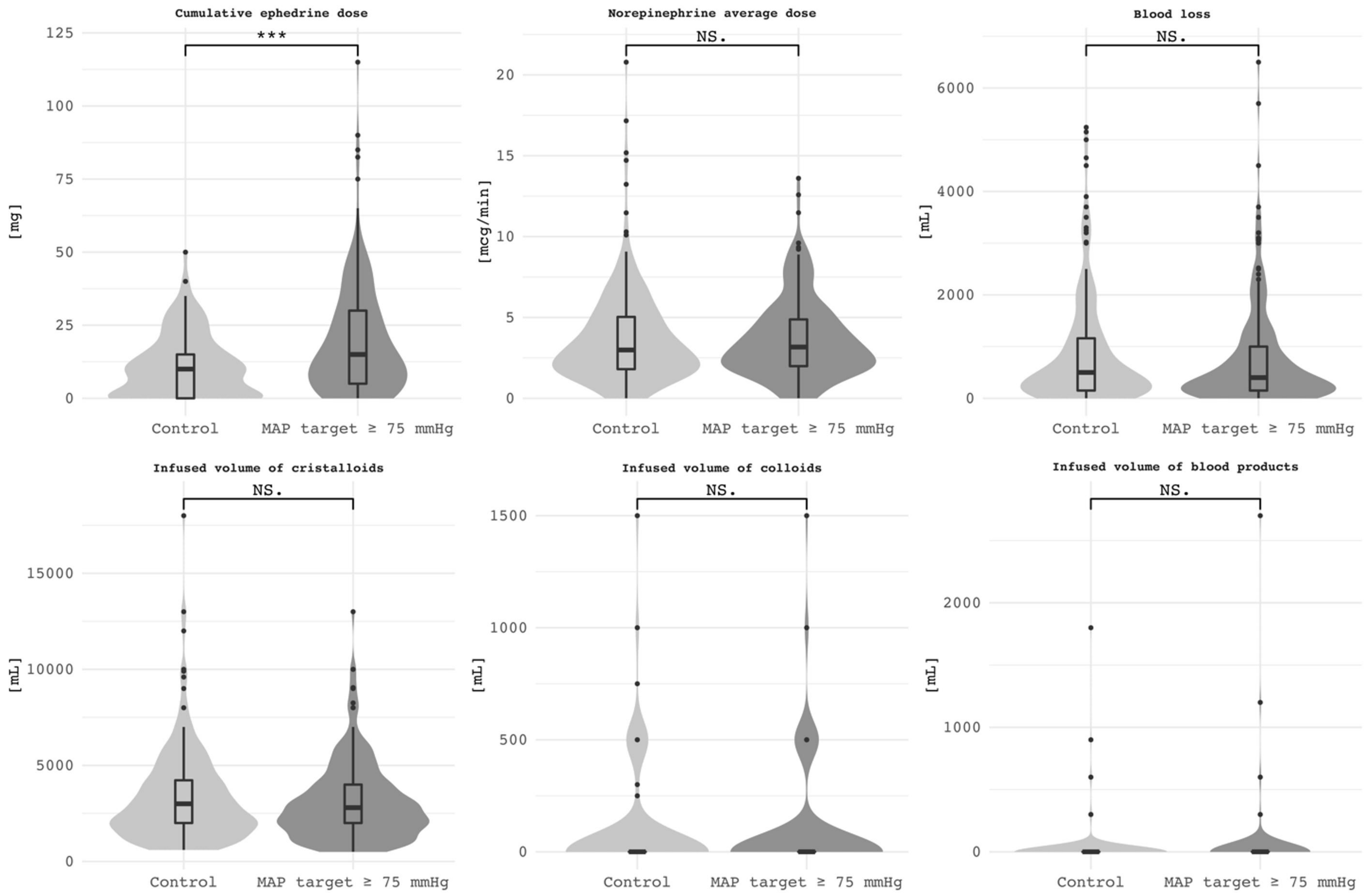
Complex causal networks

Heterogeneity of populations and treatment effect

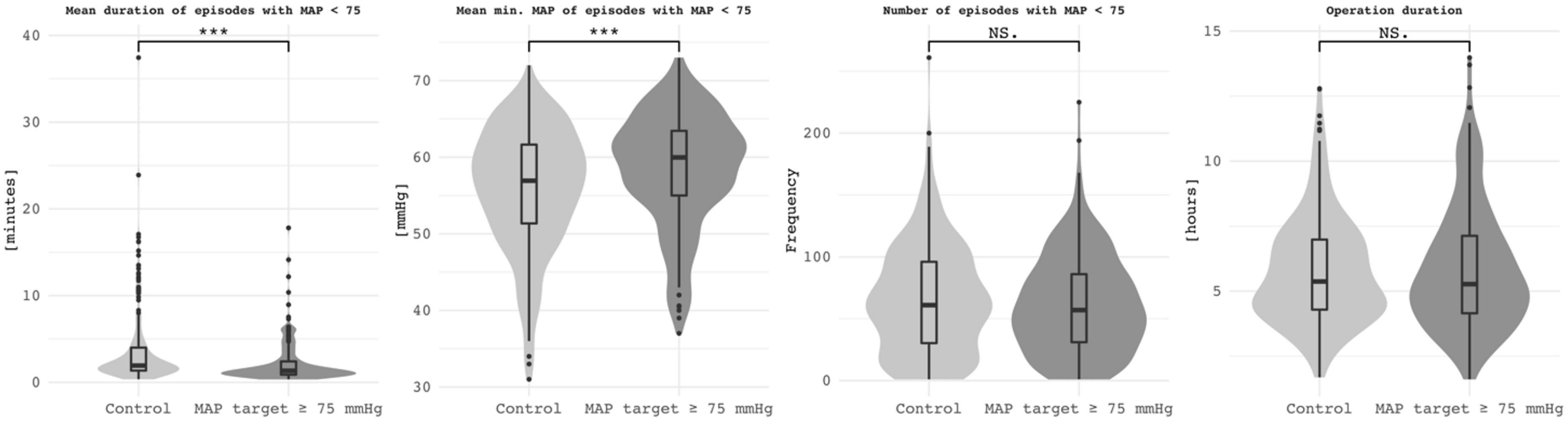
Multifactorial / syndrome outcomes

BBB Suppl.

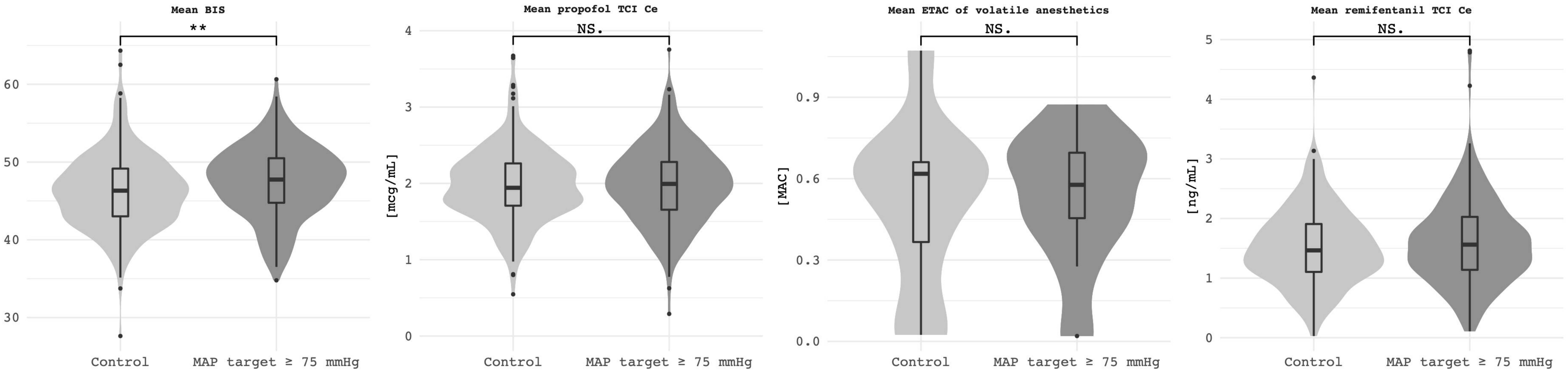
Limitations



Cumulative ephedrine dose
***
[mg]
125
100
75
50
25
0
Control
MAP target ≥ 75 mmHg
Norepinephrine average dose
NS.
[mcg/min]
20
15
10
5
0
Control
MAP target ≥ 75 mmHg
Blood loss
NS.
[mL]
6000
4000
2000
0
Control
MAP target ≥ 75 mmHg
Infused volume of cristalloids
NS.
[mL]
15000
10000
5000
0
Control
MAP target ≥ 75 mmHg
Infused volume of colloids
NS.
[mL]
1500
1000
500
0
Control
MAP target ≥ 75 mmHg
Infused volume of blood products
NS.
[mL]
2000
1000
0
Control
MAP target ≥ 75 mmHg



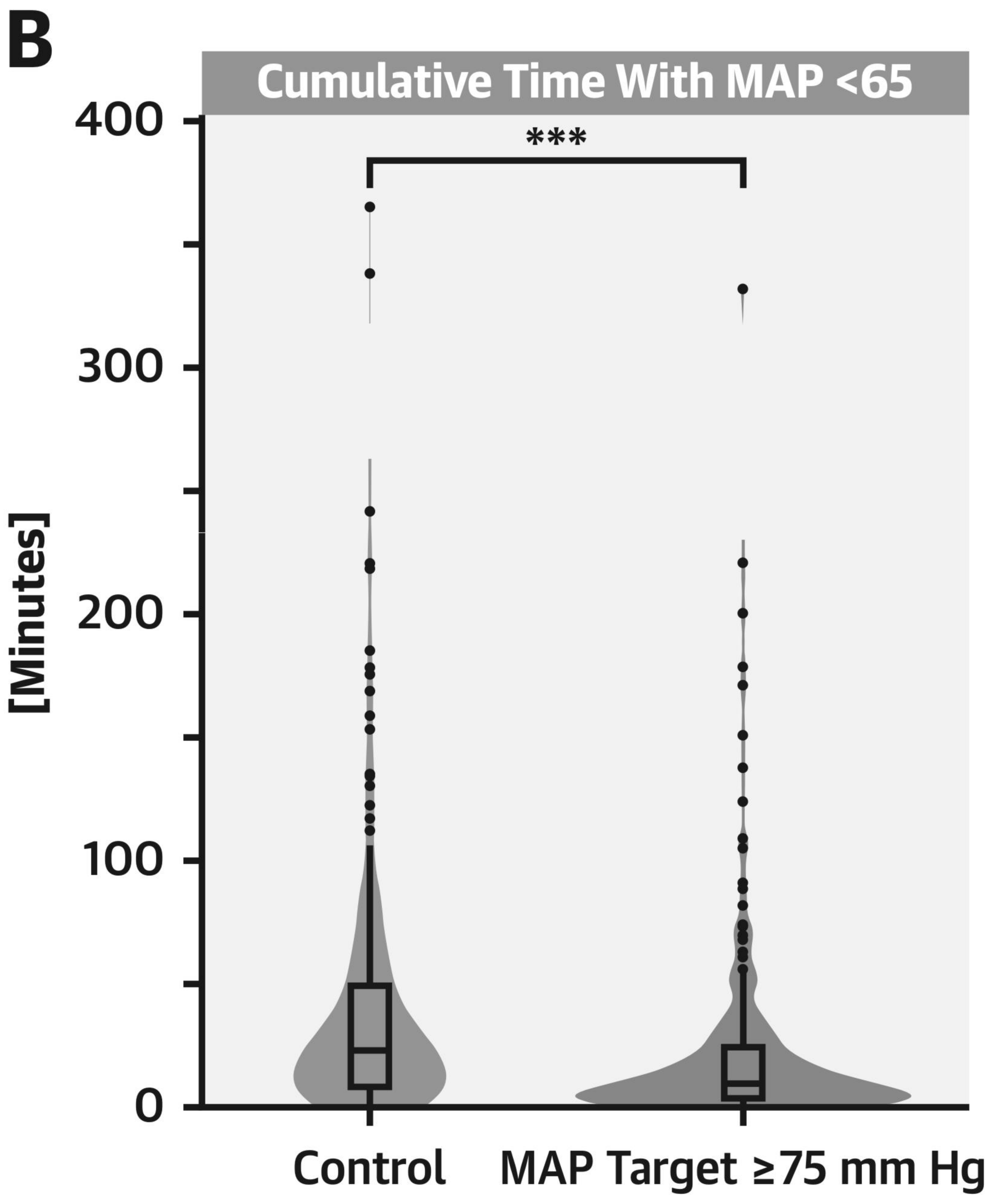
Mean duration of episodes with MAP < 75
***
[minutes]
0
10
20
30
40
Control
MAP target ≥ 75 mmHg
Mean min. MAP of episodes with MAP < 75
***
[mmHg]
30
40
50
60
70
Control
MAP target ≥ 75 mmHg
Number of episodes with MAP < 75
NS.
Frequency
0
100
200
Control
MAP target ≥ 75 mmHg
Operation duration
NS.
[hours]
5
10
15
Control
MAP target ≥ 75 mmHg



Mean BIS
**
60
50
40
30
Control
MAP target ≥ 75 mmHg
Mean propofol TCI Ce
NS.
[mcg/mL]
4
3
2
1
0
Control
MAP target ≥ 75 mmHg
Mean ETAC of volatile anesthetics
NS.
[MAC]
0.9
0.6
0.3
0.0
Control
MAP target ≥ 75 mmHg
Mean remifentanil TCI Ce
NS.
[ng/mL]
5
4
3
2
1
0
Control
MAP target ≥ 75 mmHg

NOT PUBLISHED

	Control	Intervention
Duration MAP < 65 mmHg [min]	23 [8-50]	9 [3-24]
Percentage time MAP < 65 mmHg	8% [3-14%]	3% [1-7%]
TWA MAP < 65 mmHg	0.35 [0.128-0.765]	0.153 [0.049-0.41]



AKI

AKI as an endpoint

Acute Kidney Injury in Critically Ill Patients After Noncardiac Major Surgery: Early Versus Late Onset

Shengnan Li, MD[1,2]; Shu Wang, MS[1,3]; Priyanka Priyanka, BAMS, MPH[1]; John A. Kellum, MD, MCCM[1]

TABLE 4. Multivariable Logistic Models for Comparing Mortality Among Acute Kidney Injury Diagnosed at Different Time Windows

Model	Outcomes	Variable	Adjusted OR (95% CI)	*p*
1	90-d mortality[a]	AKI		< 0.001
		Early AKI vs no AKI	2.24 (1.72–2.92)	< 0.001
		Late AKI vs no AKI	1.68 (1.19–2.36)	0.003
2	365-d mortality[b]	AKI		< 0.001
		Early AKI vs no AKI	1.84 (1.50–2.27)	< 0.001
		Late AKI vs no AKI	1.42 (1.09–1.85)	0.01
3	90-d mortality[c]	AKI		0.12
		Early AKI vs no AKI	1.32 (0.99–1.77)	0.06
		Late AKI vs no AKI	1.04 (0.72–1.50)	0.83
4	365-d mortality[d]	AKI		0.01
		Early AKI vs no AKI	1.39 (1.12–1.73)	0.003
		Late AKI vs no AKI	1.09 (0.82–1.43)	0.56

AKI = acute kidney injury, OR = odds ratio.
[a,b]Models were adjusted by age, body mass index (BMI), estimated glomerular filtration rate (eGFR), comorbidities, surgery type.
[c,d]Models were adjusted by age, BMI, eGFR, comorbidities, surgery type, and postoperative complications.

TABLE 3. Outcomes of Patients Undergoing Noncardiac Major Surgery by Postoperative Acute Kidney Injury

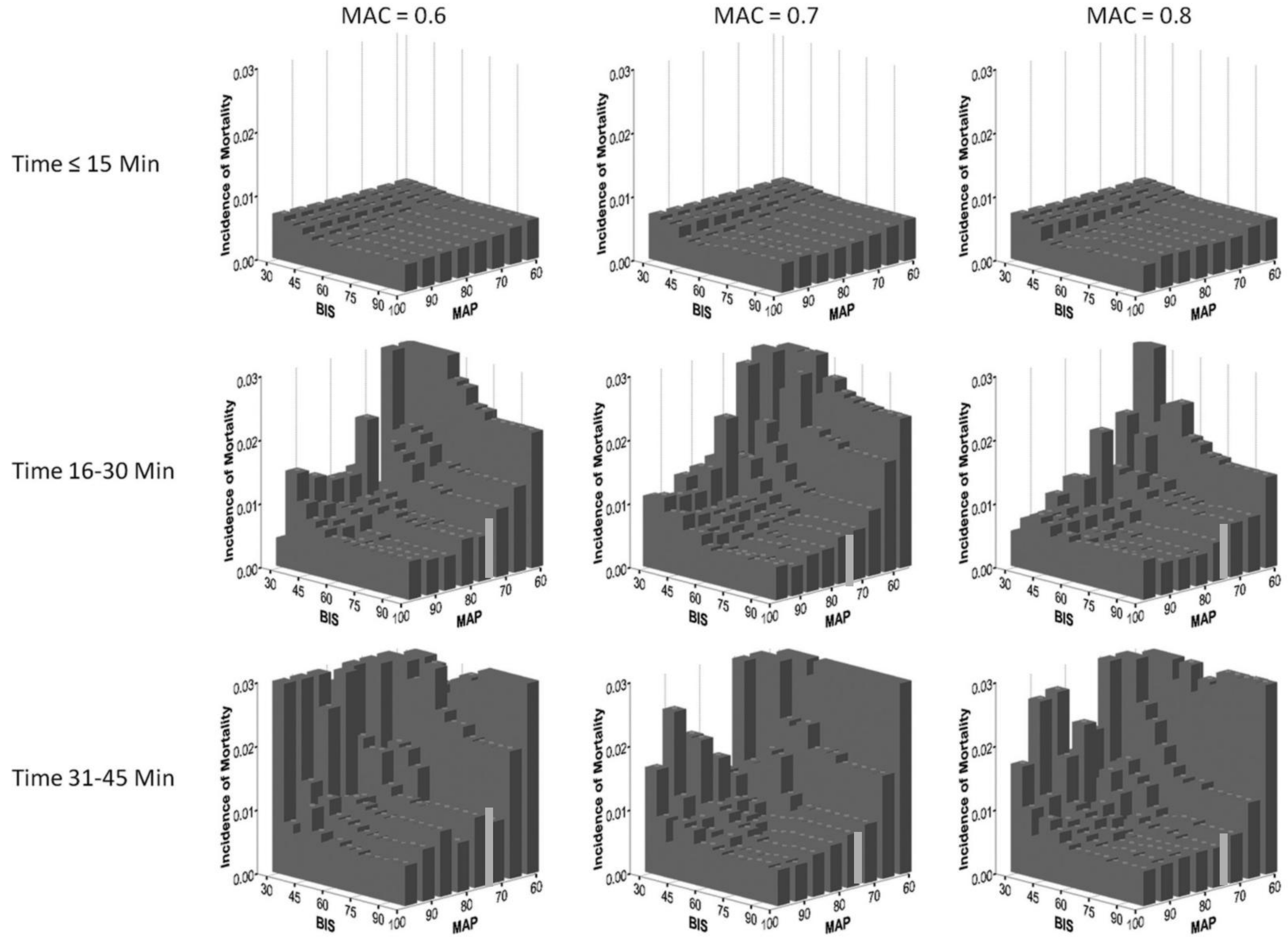
Variable (*n* = 3,499)	No AKI (*n* = 1,536)	Early AKI (*n* = 1,459)	Late AKI (*n* = 504)	*p*[a]	*p*[b]
LOS in ICU, median (IQR)	3.00 (2.00–4.00)	4.00 (3.00–9.00)	6.00 (3.00–12.00)	< 0.001	< 0.001
LOS in hospital, median (IQR)	10.00 (7.00–17.00)	14.0 (9.00–23.00)	17.50 (10.75–29.00)	< 0.001	< 0.001
Hospital mortality, *n* (%)	67 (4.4)	155 (10.6)	38 (7.5)	< 0.001	0.06
90-d mortality, *n* (%)	123 (8.0)	229 (15.7)	61 (12.1)	< 0.001	0.06
365-d mortality, *n* (%)	260 (16.9)	387 (26.5)	108 (21.4)	< 0.001	0.03
Death or dialysis at day 90, *n* (%)	123 (8.0)	233 (16.0)	61 (12.1)	< 0.001	0.04
Death or dialysis at day 365, *n* (%)	260 (16.9)	391 (26.8)	109 (21.6)	< 0.001	0.03

BP TARGETS

Rationale for BP targets I

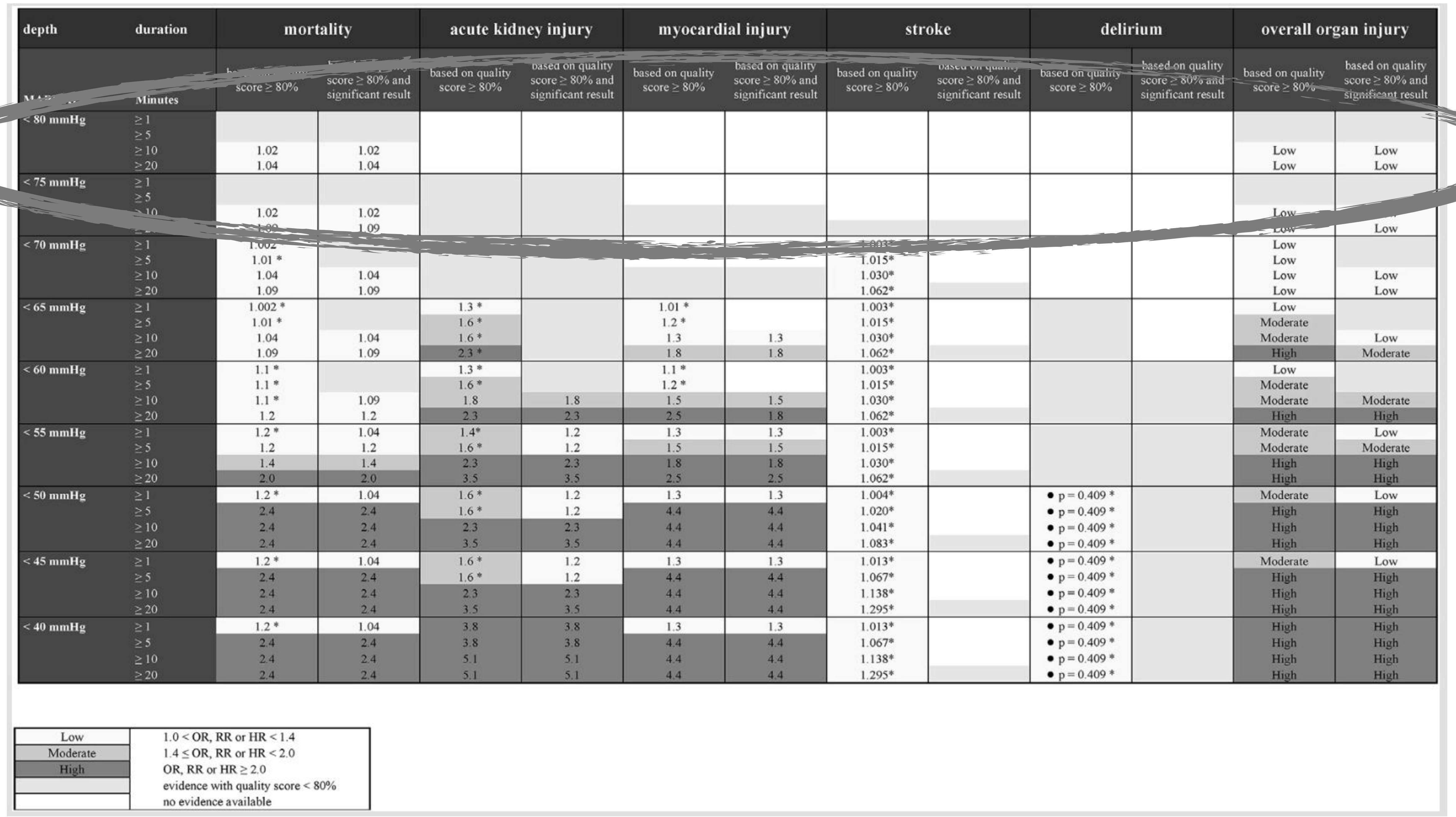
MAP > 75 - WHY ?

2015



Sessler DI et al. Hospital stay and mortality are increased in patients having a "triple low" of low blood pressure, low bispectral index, and low minimum alveolar concentration of volatile anesthesia. Anesthesiology 2012;116(6):1195-203.

2022



depth	duration	mortality		acute kidney injury		myocardial injury		stroke		delirium		overall organ injury	
MAP	Minutes	based on quality score ≥ 80%	based on quality score ≥ 80% and significant result	based on quality score ≥ 80%	based on quality score ≥ 80% and significant result	based on quality score ≥ 80%	based on quality score ≥ 80% and significant result	based on quality score ≥ 80%	based on quality score ≥ 80% and significant result	based on quality score ≥ 80%	based on quality score ≥ 80% and significant result	based on quality score ≥ 80%	based on quality score ≥ 80% and significant result
< 80 mmHg	≥ 1												
	≥ 5												
	≥ 10	1.02	1.02									Low	Low
	≥ 20	1.04	1.04									Low	Low
< 75 mmHg	≥ 1												
	≥ 5												
	≥ 10	1.02	1.02									Low	[illegible]
	≥ 20	1.09	1.09									Low	Low
< 70 mmHg	≥ 1	1.002						1.003*				Low	
	≥ 5	1.01 *						1.015*				Low	
	≥ 10	1.04	1.04					1.030*				Low	Low
	≥ 20	1.09	1.09					1.062*				Low	Low
< 65 mmHg	≥ 1	1.002 *		1.3 *		1.01 *		1.003*				Low	
	≥ 5	1.01 *		1.6 *		1.2 *		1.015*				Moderate	
	≥ 10	1.04	1.04	1.6 *		1.3	1.3	1.030*				Moderate	Low
	≥ 20	1.09	1.09	2.3 *		1.8	1.8	1.062*				High	Moderate
< 60 mmHg	≥ 1	1.1 *		1.3 *		1.1 *		1.003*				Low	
	≥ 5	1.1 *		1.6 *		1.2 *		1.015*				Moderate	
	≥ 10	1.1 *	1.09	1.8	1.8	1.5	1.5	1.030*				Moderate	Moderate
	≥ 20	1.2	1.2	2.3	2.3	2.5	1.8	1.062*				High	High
< 55 mmHg	≥ 1	1.2 *	1.04	1.4*	1.2	1.3	1.3	1.003*				Moderate	Low
	≥ 5	1.2	1.2	1.6 *	1.2	1.5	1.5	1.015*				Moderate	Moderate
	≥ 10	1.4	1.4	2.3	2.3	1.8	1.8	1.030*				High	High
	≥ 20	2.0	2.0	3.5	3.5	2.5	2.5	1.062*				High	High
< 50 mmHg	≥ 1	1.2 *	1.04	1.6 *	1.2	1.3	1.3	1.004*		• p = 0.409 *		Moderate	Low
	≥ 5	2.4	2.4	1.6 *	1.2	4.4	4.4	1.020*		• p = 0.409 *		High	High
	≥ 10	2.4	2.4	2.3	2.3	4.4	4.4	1.041*		• p = 0.409 *		High	High
	≥ 20	2.4	2.4	3.5	3.5	4.4	4.4	1.083*		• p = 0.409 *		High	High
< 45 mmHg	≥ 1	1.2 *	1.04	1.6 *	1.2	1.3	1.3	1.013*		• p = 0.409 *		Moderate	Low
	≥ 5	2.4	2.4	1.6 *	1.2	4.4	4.4	1.067*		• p = 0.409 *		High	High
	≥ 10	2.4	2.4	2.3	2.3	4.4	4.4	1.138*		• p = 0.409 *		High	High
	≥ 20	2.4	2.4	3.5	3.5	4.4	4.4	1.295*		• p = 0.409 *		High	High
< 40 mmHg	≥ 1	1.2 *	1.04	3.8	3.8	1.3	1.3	1.013*		• p = 0.409 *		High	High
	≥ 5	2.4	2.4	3.8	3.8	4.4	4.4	1.067*		• p = 0.409 *		High	High
	≥ 10	2.4	2.4	5.1	5.1	4.4	4.4	1.138*		• p = 0.409 *		High	High
	≥ 20	2.4	2.4	5.1	5.1	4.4	4.4	1.295*		• p = 0.409 *		High	High

Low	1.0 < OR, RR or HR < 1.4
Moderate	1.4 ≤ OR, RR or HR < 2.0
High	OR, RR or HR ≥ 2.0
	evidence with quality score < 80%
	no evidence available

Wesselink EM et al. Intraoperative hypotension and the risk of postoperative adverse outcomes: a systematic review. Br J Anaesth 2018;121(4):706-721.

Rationale for BP targets II

MAP > 60 - WHY ?

2015

Recommendations on anaesthesia

Recommendations	Class[a]	Level[b]	Ref.[c]
Patients with high cardiac and surgical risk should be considered for goal-directed therapy.	IIa	B	261–264
The measurement of natriuretic peptides and high-sensitivity troponin after surgery may be considered in high-risk patients to improve risk stratification.	IIb	B	3,55,266, 268,272
Neuraxial anaesthesia (alone), in the absence of contra-indications and after estimation of the risk–benefit ratio, reduces the risk of peri-operative mortality and morbidity compared with general anaesthesia and may be considered.	IIb	B	10,252–257
Avoiding arterial hypotension (mean arterial pressure <60 mm Hg) for prolonged cumulative periods (>30 minutes) may be considered.	IIb	B	104,245,246
Neuraxial analgesia, in the absence of contra-indications, may be considered to provide post-operative analgesia.	IIb	B	272
Avoiding non-steroidal anti-inflammatory drugs (especially cyclo-oxygenase-2 inhibitors) as the first-line analgesics in patients with IHD or stroke may be considered.	IIb	B	279

Kristensen SD et al. 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). Eur Heart J 2014;35(35):2383-431.

2022

Recommendation Table 33 — Recommendations for peri-operative monitoring and anaesthesia

Recommendations	Class[a]	Level[b]
In order to preserve optimal CV stability, it is recommended to apply goal-directed haemodynamic therapy in patients undergoing high-risk NCS.[614–618]	I	A
It is recommended to avoid post-operative acute pain.[614]	I	B
In order to minimize the risk of post-operative organ dysfunction, it is recommended to avoid an intra-operative mean arterial pressure decrease of >20% from baseline values or <60–70 mmHg for ≥10 min.[214,600–602,634]	I	B
Non-aspirin NSAIDs are not recommended as first-line analgesics in patients with established or high risk of CVD.[633,635]	III	B

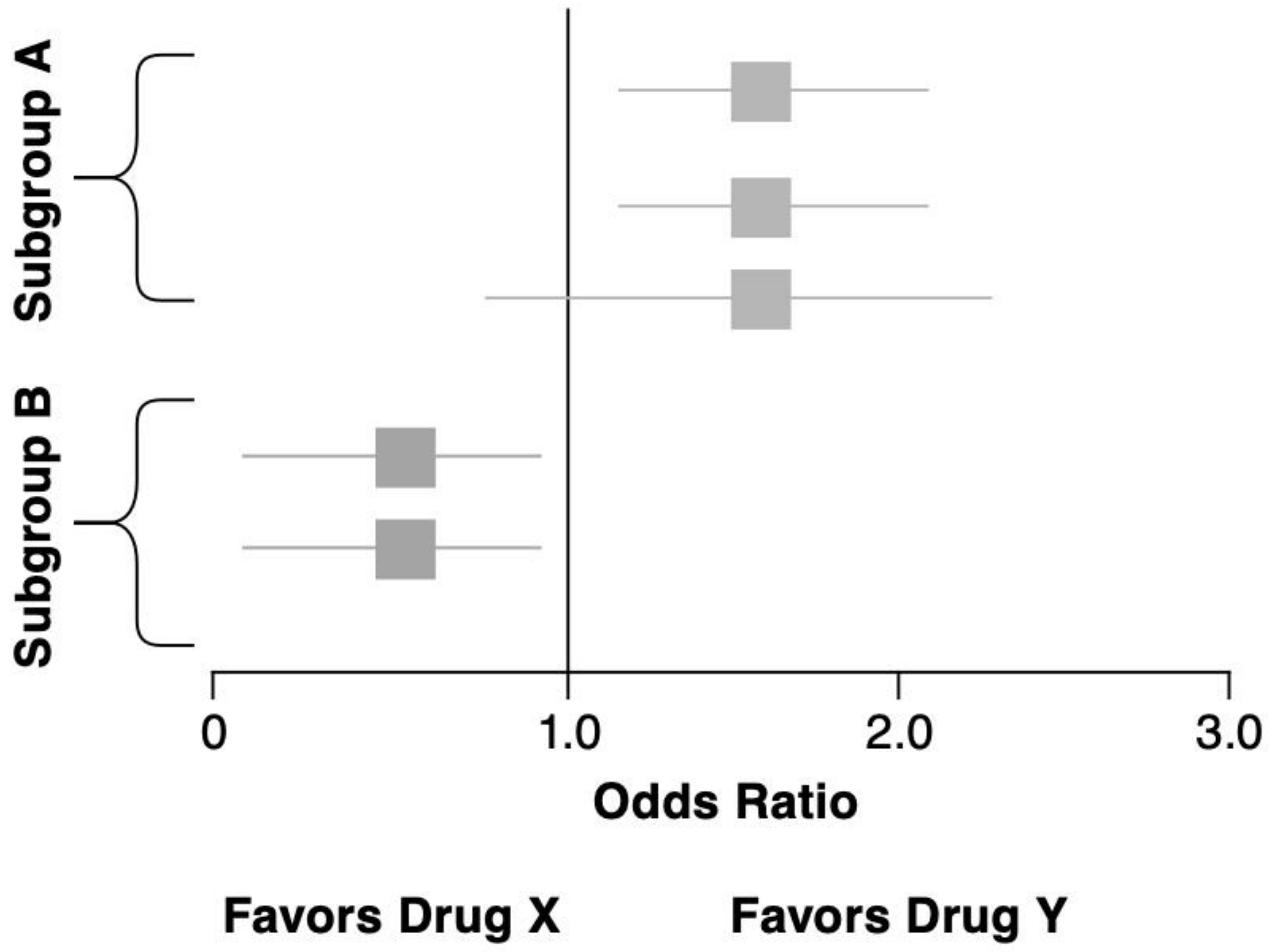
CV, cardiovascular; CVD, cardiovascular disease; NCS, non-cardiac surgery; NSAID, non-steroidal anti-inflammatory drug.
[a]Class of recommendation.
[b]Level of evidence.

Halvorsen S, Mehilli J, Cassese S, et al. 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery. Eur Heart J 2022.

Heterogeneity in treatment effects

Heterogeneity in autoregulatory ranges = heterogeneity in treatment effects ?

C. Clinical heterogeneity is present and leads to a relevant impact on the treatment effect because subgroup B has an effect that is opposite subgroup A, lying to the left of the odds ratio value of 1.0.



Source: West SL, Gartlehner G, Mansfield AJ, et al. Comparative effectiveness review methods: clinical heterogeneity.[13]

AUTOREGULATION

AR-Guided BP management is viable

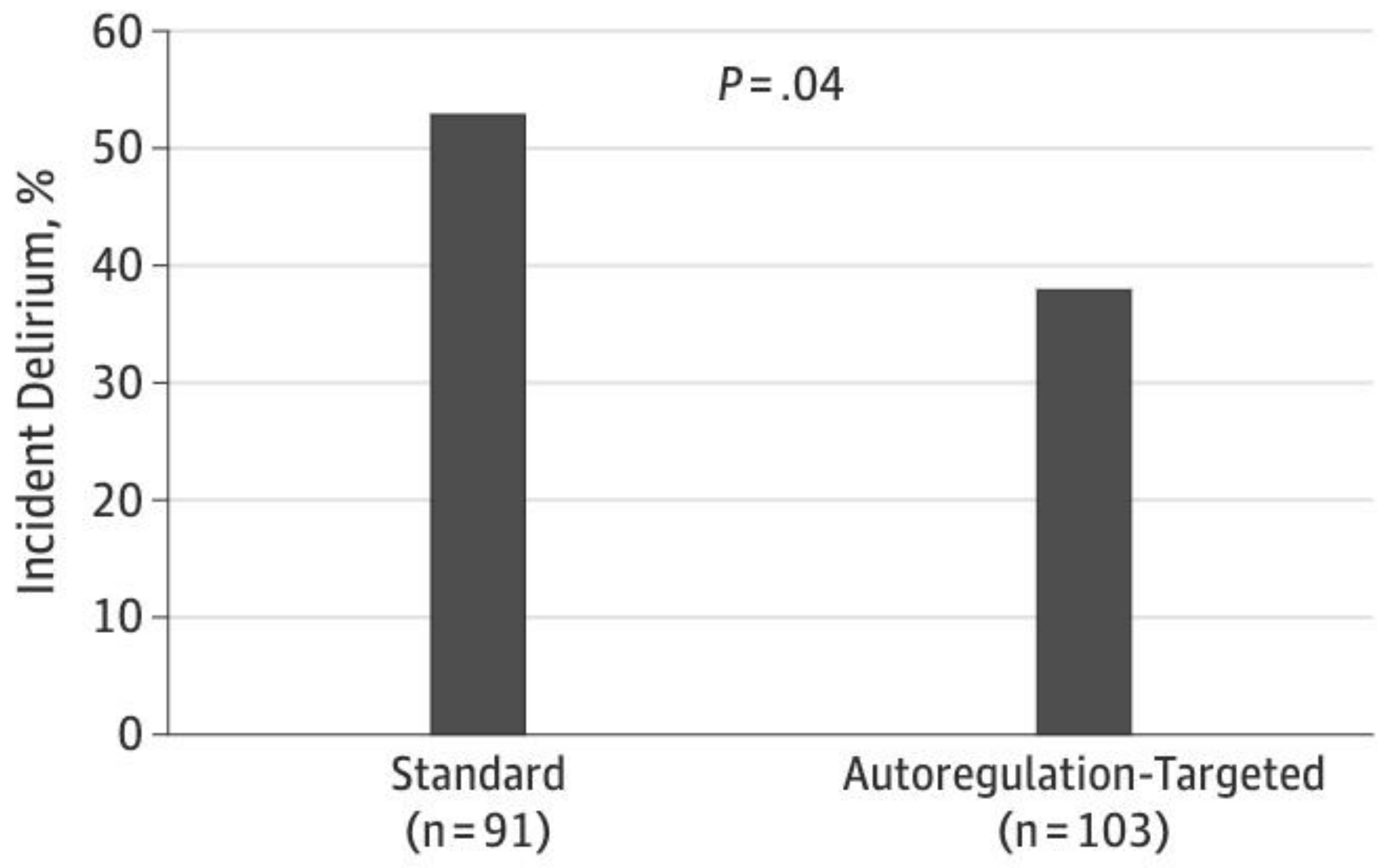
JAMA Surgery | Original Investigation

Effect of Targeting Mean Arterial Pressure During Cardiopulmonary Bypass by Monitoring Cerebral Autoregulation on Postsurgical Delirium Among Older Patients

A Nested Randomized Clinical Trial

Charles H. Brown IV, MD, MHS; Karin J. Neufeld, MD, MPH; Jing Tian, MS; Julia Probert, BA; Andrew LaFlam, BA; Laura Max, MHS, PA-C; Daijiro Hori, MD; Yohei Nomura, MD; Kaushik Mandal, MD; Ken Brady, MD; Charles W. Hogue, MD; and the Cerebral Autoregulation Study Group

Figure 2. Delirium Incidence by Randomization Group



Mean arterial pressure during cardiopulmonary bypass was managed according to standard care or autoregulation-targeted goals. Delirium incidence by randomization group is shown.

Need for autoregulation monitoring: safe BP ranges variable I

Monitoring of cerebral blood flow autoregulation in adults undergoing sevoflurane anesthesia: a prospective cohort study of two age groups

Nicolai Goettel[1,2] · Camille Patet[3] · Ariane Rossi[3] · Christoph S. Burkhart[1,5] · Marek Czosnyka[4] · Stephan P. Strebel[1] · Luzius A. Steiner[1,2]

Table 4 Limits and range of cerebral blood flow autoregulation

	Group 1 (18–40 year)	Group 2 (≥65 year)	*P* value
Lower limit of autoregulation (mmHg)	66 ± 12	73 ± 14	0.08
Upper limit of autoregulation (mmHg)	73 ± 19	70 ± 14	0.30
Autoregulatory range (mmHg)	13.8 ± 9.8	10.2 ± 8.6	0.08

Need for autoregulation monitoring: safe BP ranges variable II

Shoulder Surgery in the Beach Chair Position Is Associated with Diminished Cerebral Autoregulation but No Differences in Postoperative Cognition or Brain Injury Biomarker Levels Compared with Supine Positioning: The Anesthesia Patient Safety Foundation Beach Chair Study

Andrew Laflam, BS,* Brijen Joshi, MD,† Kenneth Brady, MD,‡ Gayane Yenokyan, PhD,§ Charles Brown, MD,* Allen Everett, MD,|| Ola Selnes, PhD,¶ Edward McFarland, MD,# and Charles W. Hogue, MD*

Table 3. Comparison of Mean Arterial Blood Pressure (MAP), Bispectral Index (BIS), and Cerebral Oximetry Index (Cox Autoregulation Data for Patients Who Underwent Surgery in the Lateral Decubitus and Beach Chair Position)

Characteristic	Lateral decubitus (n = 109)	Beach chair (n = 109)	β coefficient (95% confidence interval)	P value[a]
MAP (mm Hg)	73 ± 14	79 ± 13	6.6 (2.2, 11.0)	0.003
Estimated average MAP (mm Hg) at tragus	76 ± 13	50 ± 16	−28.0 (−32.7, −23.3)	<0.0001
BIS	41 ± 11	46 ± 10	1.6 (−1.3, 4.5)	0.276
Mean left $rSco_2$ (%)	75 ± 13	64 ± 14	−7.7 (−11.8, −3.5)	<0.0001
Mean right $rSco_2$ (%)	74 ± 14	63 ± 14	−8.3 (−12.4, −4.2)	<0.0001
Mean Cox (left and right)	0.09 ± 0.12	0.15 ± 0.13	0.04 (0.00, 0.08)	0.035
Patients achieving LLA	65%	75%	−0.3 (−1.0, 0.4)	0.367
MAP at LLA (mm Hg)[b]	65 (55–75)	70 (55–80)	1.3 (−3.9, 6.5)	0. 620

Data are given as mean ± SD unless otherwise indicated. The P values were adjusted for age and hypertension status at baseline.
$rSco_2$ = regional cerebral O_2 saturation; LLA = lower limit of autoregulation.
[a]Wald test from the generalized linear regression model with robust variance. The model is fitted using fractional polynomial approach in Stata (Reference: Royston and Altman.[29]
[b]Median (25th–75th percentile).

Need for autoregulation: safe BP ranges not predictable

Predicting the Limits of Cerebral Autoregulation During Cardiopulmonary Bypass

Brijen Joshi, MD,* Masahiro Ono, MD,† Charles Brown, MD,* Kenneth Brady, MD,‡
R. Blaine Easley, MD,§ Gayane Yenokyan, PhD,‖ Rebecca F. Gottesman, MD, PhD,¶
and Charles W. Hogue, MD*

Table 4. Sensitivity, Specificity, and Area Under the Receiver Operator Characteristic (ROC) Curve for Various Cut-Offs of Mean Arterial Blood Pressure (MAP) from Preoperative Baseline Measurement for Predicting the Lower Limit of Cerebral Blood Flow Autoregulation

MAP decrement from baseline	Sensitivity	95% CI	Specificity	95% CI	Area under ROC
>15%	91%	87% to 93%	37%	32% to 41%	0.7354
>25%	71%	66% to 76%	66%	61% to 70%	
>35%	42%	37% to 47%	88%	85% to 91%	

CI = confidence interval; MAP = mean arterial blood pressure.

Phenotypes

Hypotension is not hypotension - towards phenotypes ?

The association of hypotension during non-cardiac surgery, before and after skin incision, with postoperative acute kidney injury: a retrospective cohort analysis

K. Maheshwari,[1] **A. Turan,**[1] **G. Mao,**[2] **D. Yang,**[2] **A. K. Niazi,**[3] **D. Agarwal,**[4] **D. I. Sessler**[5] and **A. Kurz**[6]

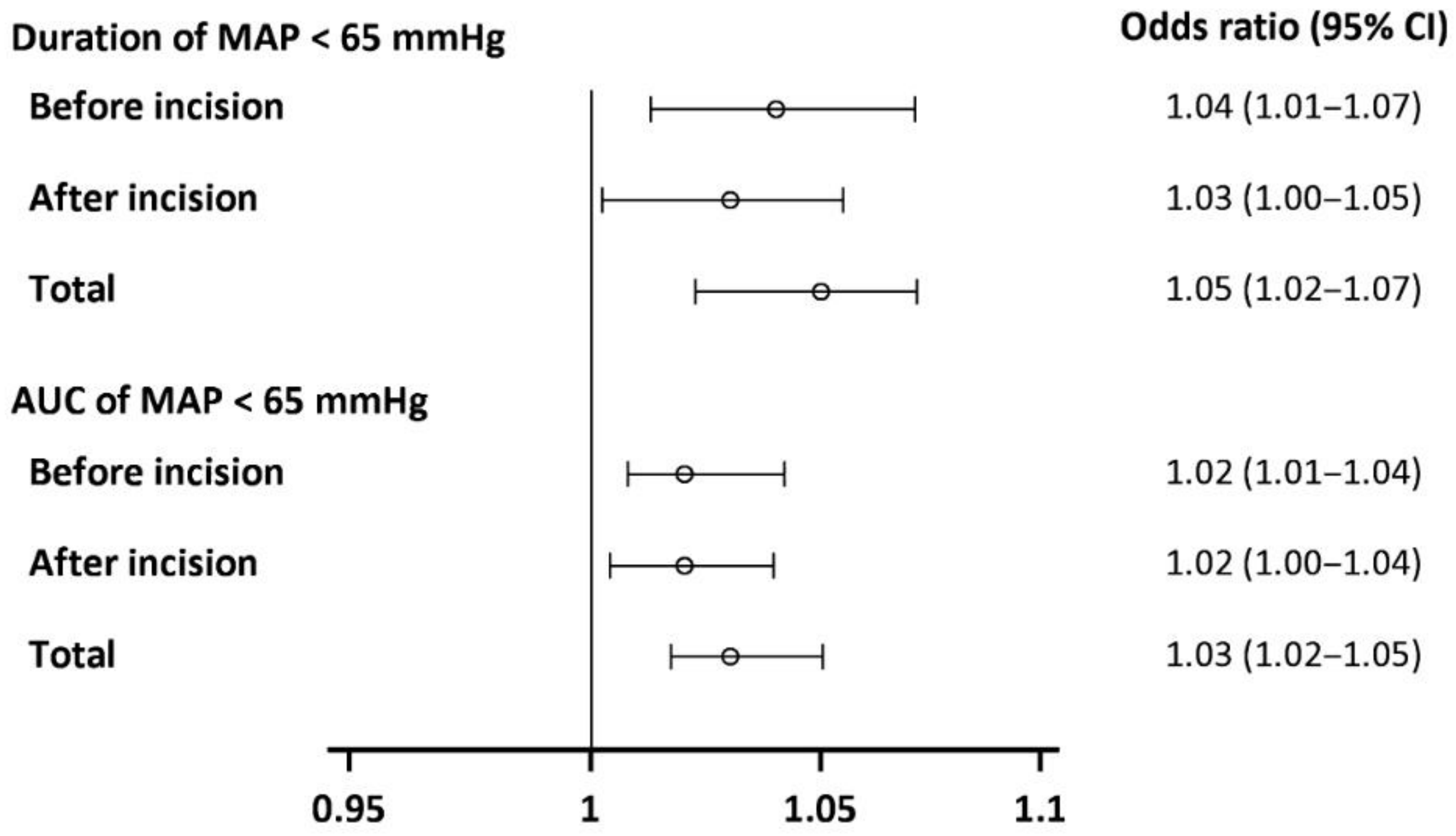


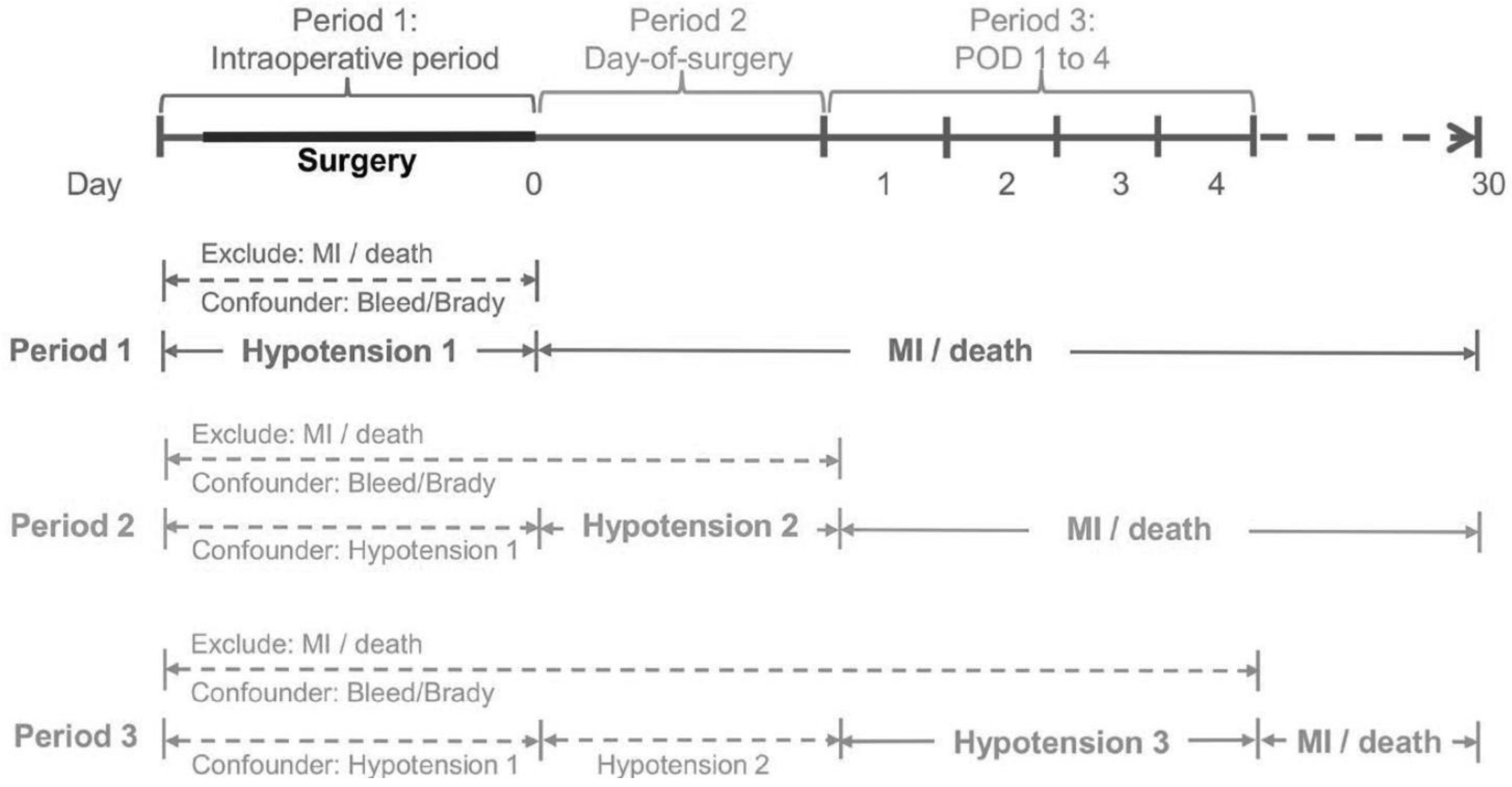
Figure 3 The OR (95% CI) for the associations between doubling of the duration of hypotension (MAP < 65 mmHg) during anaesthesia and postoperative acute kidney injury, diagnosed in 2328 out of 42,825 patients after elective non-cardiac surgery. Circles (bars) are the OR (95%CI). AUC, area under the curve; MAP, mean arterial pressure.

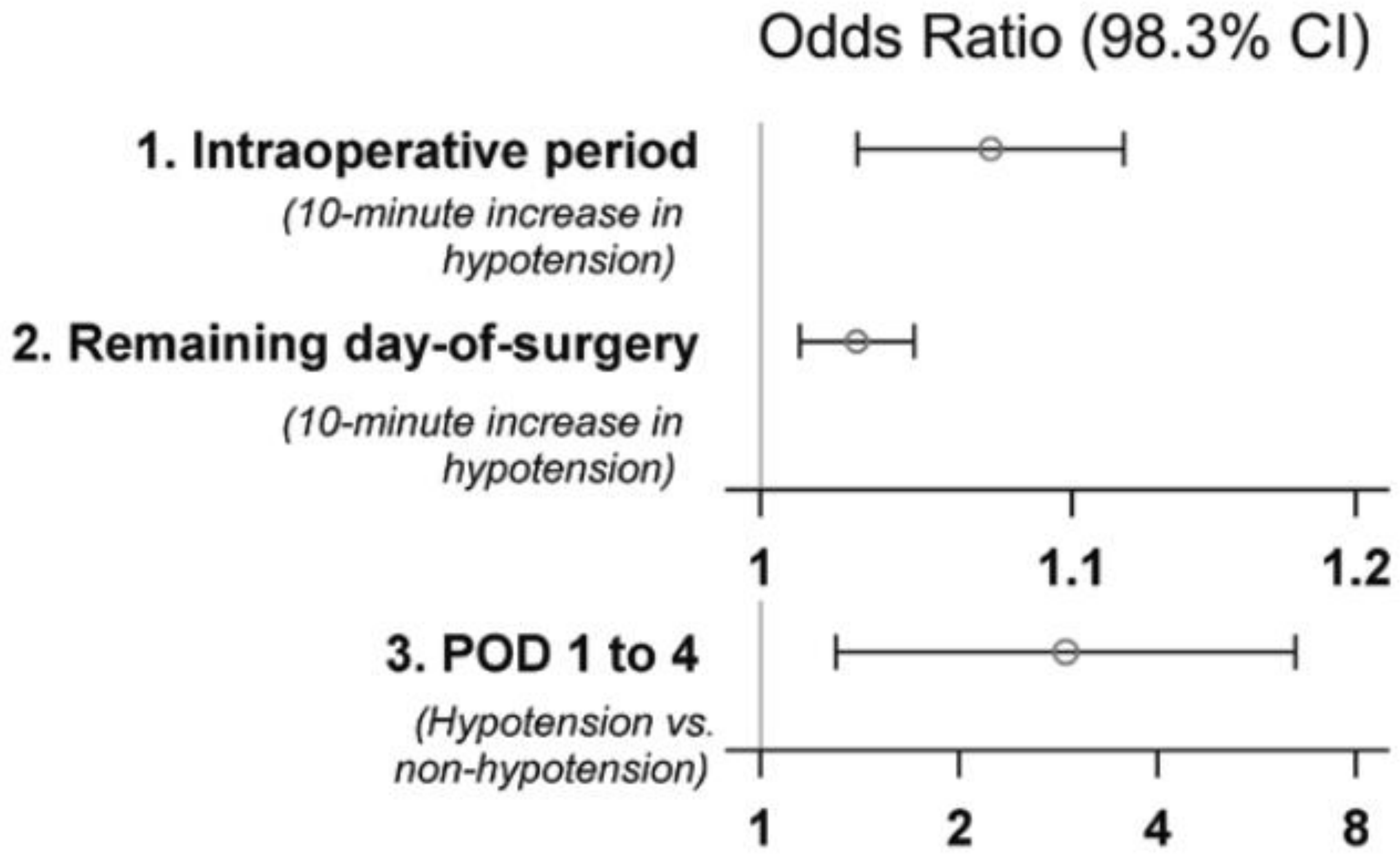
Prognostic relevance of postoperative hypotension

Period-dependent Associations between Hypotension during and for Four Days after Noncardiac Surgery and a Composite of Myocardial Infarction and Death

A Substudy of the POISE-2 Trial

Daniel I. Sessler, M.D., Christian S. Meyhoff, M.D., Ph.D., Nicole M. Zimmerman, M.S., Guangmei Mao, M.P.H., Kate Leslie, M.B.B.S., Skarlet M. Vásquez, M.Sc., Packianathaswamy Balaji, M.D., Jesús Alvarez-Garcia, M.D., Ph.D., Alexandre B. Cavalcanti, M.D., Ph.D., Joel L. Parlow, M.D., Prashant V. Rahate, M.D., Manfred D. Seeberger, M.D., Bruno Gossetti, M.D., S. A. Walker, M.B.Ch.B., Rajendra K. Premchand, M.D., Rikke M. Dahl, M.D., Emmanuelle Duceppe, M.D., Reitze Rodseth, M.B.Ch.B., Fernando Botto, M.D., P. J. Devereaux, M.D., Ph.D.





CONSENSUS STATEMENTS

Consensus statements - intraoperative management

Perioperative Quality Initiative consensus statement on intraoperative blood pressure, risk and outcomes for elective surgery

Daniel I. Sessler[1,*,†], Joshua A. Bloomstone[2,3,4,9,†], Solomon Aronson[5], Colin Berry[6], Tong J. Gan[7], John A. Kellum[8], James Plumb[11,12,13], Monty G. Mythen[9,10], Michael P. W. Grocott[9,11,12,13], Mark R. Edwards[11,12,13], Timothy E. Miller[5,9], the Perioperative Quality Initiative-3 workgroup[‡]

Consensus statement 1: *Intraoperative mean arterial blood pressures below 60–70 mm Hg are associated with myocardial injury, acute kidney injury, and death. Systolic arterial pressures below 100 mm Hg are associated with myocardial injury and death. Injury is a function of hypotension severity and duration.*

Consensus statements - postoperative management

Perioperative Quality Initiative consensus statement on intraoperative blood pressure, risk and outcomes for elective surgery

Daniel I. Sessler[1,*,†], Joshua A. Bloomstone[2,3,4,9,†], Solomon Aronson[5], Colin Berry[6], Tong J. Gan[7], John A. Kellum[8], James Plumb[11,12,13], Monty G. Mythen[9,10], Michael P. W. Grocott[9,11,12,13], Mark R. Edwards[11,12,13], Timothy E. Miller[5,9], the Perioperative Quality Initiative-3 workgroup[‡]

Consensus statement 1: *Intraoperative mean arterial blood pressures below 60–70 mm Hg are associated with myocardial injury, acute kidney injury, and death*. *Systolic arterial pressures below 100 mm Hg are associated with myocardial injury and death*. *Injury is a function of hypotension severity and duration.*

Consensus statement 2: *For adults having non-cardiac surgery, there is insufficient evidence to recommend a general upper limit of blood pressure at which therapy should be initiated.*

WESSELINK

Limitations of observational evidence - populations I

Table 2 Summary of the patient, surgery and hypotension characteristics of each study. Continuous variables are expressed as mean (SD) or x (x~x) = mean (range) or x (x-x) = median (interquartile range). Categorical variables are expressed as xx% body mass index or weight (W) is expressed as kg m^{-2} or kg. Any definition of history of arrhythmia or renal dysfunction was included. If available, renal dysfunction was expressed as serum creatinine in μmol l^{-1}. –, not available; *, values are the weighted mean values of the study groups; †, median (10^{th}–90^{th} percentile). a-, absolute threshold expressed as mm Hg; AR, achievement rate; AUT, area under the threshold; BP blood pressure; CAD, coronary artery disease; Cr, creatinine; CVD, cerebrovascular disease; DBP, diastolic blood pressure; Di, dichotomous; DM, diabetes mellitus; Du, duration under a blood pressure threshold; eGFR, estimated glomerular filtration rate; Gen. anaesth., general anaesthesia; GI, gastro-intestinal; HT, hypertension; LiverTX, liver transplantation; Low, lowest blood pressure; MAP, mean blood pressure; MI, myocardial injury; r-, relative threshold expressed as percentage decrease from baseline BP; RCRI, Revised Cardiac Risk Index; SAS, blood pressure as part of Surgical Apgar Score; SBP, systolic blood pressure; TIA, transient ischaemic attack; TL, triple low; TWA, time-weighted average; V, blood pressure variance; Var, variability or variance

Studies		Patient characteristics		Comorbidity (%)									Procedure characteristics (%)				Intraoperative hypotension		
First author	Total	Age	Sex	ASA				Stroke	HT	DM	CAD	Renal disease	Gen. anaesth.	Length of surgery	Emergency surgery	Type of surgery	BP threshold type	Threshold	Analysis
(yr)	n	(yr)	F, %	1	2	3	4					any		min		most frequent			
Hirsch (2015)[5]	594	74 (6)	51	48		–	–	4	–	–	–	–	71	300 (144)	0	Orthopaedic 53	rSBP, rMAP, aMAP	↓ >10–40%, <50 mm Hg	Du, Var
Monk (2015)[6]	18 756	60 (13)	7	3	26	58	13	–	–	–	–	19	–	120 (72–186)	8	General 32	aSBP	<80 mm Hg	Du
Willingham (2015)[7]	13 198	56 (44–66)	47	9	39	35	16	any: 3	48	17	20	–	100	178 (115–259)	–	–	aMAP, TL	<75mm Hg	Du
Bijker (2012)*,[8]	48 241 (42/252)	66 (57–76)	40	68		32		38	69	–	–	–	–	163 (130–232)	–	Vascular 48	aSBP, aMAP, rSBP, rMAP	<100–70 mm Hg, <70–40 mm Hg, ↓ >10–40%	Du
Mizota (2017)*,[9]	231	54 (44–60)	51	–	–	–	–	–	–	19	–	22	100	838 (752–960)	–	LiverTX 100	aMAP	<40,<50 mm Hg	Du, Di
Sun (2015)*,[3]	5127	61 (14)	53	–	–	–	–	any: 2	48	15	11	16	–	>120: 79	0	General 26	aMAP	<65, <60, <55 mm Hg	Du
Schmid (2016)*,[10]	180	66 (12)	23	–	–	–	–	–	–	56	20	6	100	–	100	Abdominal 100	aMAP	>70 mm Hg	AR
Roshanov (2017)[11]	14 687	65 (12)	52	–	–	–	–	7	47	19	12	eGFR: 79 (23)	–	–	14	Orthopaedic 20	aSBP	<90 mm Hg	Di
Salmasi (2017)*,[12]	57 315	56 (15)	56	2	38	54	7	3	49	17	–	1	–	225(121)	4	Abdominal 23	aMAP, rMAP	<80–40 mm Hg, ↓>10–60%	Du, TWA
Babazade (2016)[13]	2521	56 (15)	45	45		50	5	–	42	14	–	4	100	199 (142–265)	1	Colorectal 100	aSBP, aMAP	<80mm Hg, <55mm Hg	Du
Hallqvist (2016)[14]	300	67 (57–74)	53	10	46	43	0.3	–	43	8	–	–	39	–	0	Abdominal 40	rSBP	↓ >50%, >5 min	Di
van Waes (2016)*,[15]	890	74 (8)	31	1	14	36	49	21	–	10	–	8	100	191 (108)	30	(T)EVAR 24	aMAP	<50, <60 mm Hg, ↓>30%, ↓ >40%	Du, (AUT)
Mascha (2015)*,[16]	104 401	57 (18)	53	5	40	47	8	1	48	17	14	6	–	174 (114–252)	5	–	aMAP	<80–50 mm Hg	Du, TWA, Var

Continued

Limitations of observational evidence - populations II

Table 2 Summary of the patient, surgery and hypotension characteristics of each study. Continuous variables are expressed as mean (SD) or x (x–x) = mean (range) or x (x-x) = median

Studies		Patient characteristics		Comorbidity (%)									Procedure characteristics (%)				Intraoperative hypotension		
First author	Total	Age	Sex	ASA				Stroke	HT	DM	CAD	Renal disease	Gen. anaesth.	Length of surgery	Emergency surgery	Type of surgery	BP threshold type	Threshold	Analysis
(yr)	n	(yr)	F, %	1	2	3	4					any		min		most frequent			
Pipanmekaporn (2014)*,[17]	719	49 (16)	29	14	58	28	–	–	18	10	2	10	100	142 (65)	46	Thoracic 100	aSBP, aMAP	<80 or <60 mm Hg, >15 min	Di
Walsh (2013)*,[4]	33 330	56 (16)	50	2	40	50	8	5	–	13	–	eGFR: 93 (27)	–	–	7	–	aMAP	<75–55 mm Hg	Du
Bijker (2009)[18]	1705	52 (16)	48	38	51	11		7	22	8	any: 15	–	88	112 (73–163)	0	General 88	aSBP, rSBP, aMAP, rMAP	<100–70 mm Hg, ↓ >10–40%, <70-40 mm Hg, ↓ >10–40%	Du
Kheterpal (2009)*,[19]	7740	≥68: 23	49	–	–	–	–	any: 5	40	13	–	3	88	–	12	–	aSBP, aMAP, rSBP, rMAP	<80–70 mm Hg, <60–50 mm Hg, ↓ >30–40%	Di?
Monk (2005)[2]	1064	51 (37–65)	64	13	52	35		4	33	4	6	–	100	186 (138–258)	–	Orthopaedic 26	aSBP	<80 mm Hg	Du
White (2016)[20]	11 085	83 (24–104)	72	3	30	55	12	11	55	7	–	14	54	–	–	Hip surgery 100	aSBP, aMAP	Lowest BP	Low
Brinkman (2015)*,[21]	40	69 (9)	35	–	–	–	–	–	68	13	–	–	100	228 (84)	0	Aorta 100	aMAP	<65 mm Hg	AUT
Petsiti (2015)[22]	248	64 (11)	48	–	–	32		1	47	13	8	3	100	232 (55)	0	Abdominal 100	aMAP, rMAP	<60 or <70 mm Hg + ↓ >30%	Di
Marcantonio (1998)[23]	1341	67 (9)	55	–	–	–	–	–	–	–	–	–	–	–	–	Orthopaedic 43	aSBP or rSBP	<90 mm Hg or ↓ >33%	Di
Tallgren (2007)*,[24]	69	67 (60–74)	22	–	–	–	–	–	66	7	43	–	100		0	Aorta 100	aMAP	<65 mm Hg, >15 min	Di
House (2016)*,[25]	46 799	54 (13)	47			41		3	43	16	–	4	–	162 (108)	4	–	aMAP	<40 mm Hg	Di/SAS
Sessler (2012)[26]	24 120	–	–	–	–	–	–	–	–	–	–	–	100	–	–	–	aMAP, TL	<70 mm Hg	Du
Sabaté (2011)[27]	3387	67 (47–81)†	52	8	55	33	4	–	–	–	RCRI ≥3: 7	–	61	120 (60–248)†	7	Orthopaedic 34	aSBP or aMAP/rMAP	<100 mm Hg or ↓ >20 mm Hg/20%, >60 min	Di
Taffé (2009)*,[28]	147 573	55 (18)	56	27	48	22	3	–	–	–	–	–	67	104 (?–?)	20	–	rMAP	↓ >30%, >10 min	Di
Sirivatanauksorn (2014)*,[29]	81	53 (23–70)	31	–	–	–	–	–	–	–	–	Cr: 90 (38–168)	100	276 (168–438)	–	LiverTX 100	aMAP	<70 mm Hg, >30 min	Di
Tassoudis (2011)[30]	100	62 (14)	47	–	32	–	–	1	46	12	8	3	100	195 (71)	0	Abdominal 100	aMAP, rMAP	<60 or <70mm Hg + ↓ >30%	Di

Continued

Limitations of observational evidence - populations III

Table 2 Continued

Studies		Patient characteristics		Comorbidity (%)									Procedure characteristics (%)				Intraoperative hypotension		
First author	Total	Age	Sex	ASA				Stroke	HT	DM	CAD	Renal disease	Gen. anaesth.	Length of surgery	Emergency surgery	Type of surgery	BP threshold type	Threshold	Analysis
(yr)	n	(yr)	F, %	1	2	3	4					any		min		most frequent			
Stapelfeldt (2017)[31]	152 445	–	–	–	–	–	–	–	–	–	–	–	–	179 (118–259)	90	–	aMAP	<75–45 mm Hg	Du
Jiang (2016)*[32]	451	65 (18)	50	–	–	–	–	–	14	6	–	1	100	164 (62)	–	Spine 100	aSBP	<80 mm Hg	Di
Yang (2016)*[33]	480	81 (6)	51	–	71	29	–	–	43	30	43	–	100	188 (32)	0	–	r?BP	↓ >30%	Di
Yue (2013)*[34]	71	>70: 37	21	–	–	–	–	–	–	11	–	23	100	–	38	Aorta 100	aSBP/aMAP	<↓ 30/<65 mm Hg	Di
Franck (2011)*[35]	2350	53 (41–65)	50	50		50		–	–	–	–	–	100	98 (63–148)	–	–	aSBP, rSBP	<100 or ↓>30%, <92 mm Hg, <80 mm Hg, ↓ >20%	Di
Patti (2011)*[36]	100	70 (3)	60	9	41	29	21	–	–	–	–	–	100	121 (24)	0	Abdominal 100	aMAP	≤60mm Hg	Di
Vasivej (2016)*[37]	55 648 (42/168)	58 (14)	52	–	–	–	–	6	43	27	23	39	59	153 (78–244)	7	–	aMAP	<65 mm Hg	Di
Thakar (2007)*[38]	504	43 (10)	83	–	–	–	–	–	57	26	–	4	100	–	0	Abdominal 100	aMAP	<60 mm Hg	Di
Barone (2002)*[39]	25 501	74 (11)	45	Mean ASA: 2.9				–	40	19	any: 30	–	–	124 (55)	27	–	aSBP	<100 mm Hg, >10 min	Di
Lima (2003)*[40]	92	44 (14)	48	–	–	–	–	–	–	–	–	Cr: 88 (35)	100	–	–	LiverTX 100	aMAP	<60 mm Hg	Di
Nakamura (2009)*[41]	72	71 (10)	29	–	–	–	–	any: 15	88	7	any: 19	11	–	–	15	Aorta 100	aSBP	<70 mm Hg	Di
Davidovic (2017)[42]	450	66 (7)	12	–	–	–	–	–	70	–	26	11	100	–	0%	Aorta 100%	aSBP	<100 mm Hg	Di
Sharma (2006)*[43]	1800	43 (9)	80	–	–	–	–	–	57	22	–	2	100	223 (63)	0%	Abdominal 100%	aSBP	<100 mm Hg, >5 min	Di

Limitations of observational evidence - definitions of hypotension I

Table 2 Summary of the patient, surgery and hypotension characteristics of each study. Continuous variables are expressed as mean (SD) or x (x–x) = mean (range) or x (x-x) = median (interquartile range). Categorical variables are expressed as xx% body mass index or weight (W) is expressed as kg m^{-2} or kg. Any definition of history of arrhythmia or renal dysfunction was included. If available, renal dysfunction was expressed as serum creatinine in µmol l^{-1}. –, not available; *, values are the weighted mean values of the study groups; †, median (10^{th}–90^{th} percentile). a-, absolute threshold expressed as mm Hg; AR, achievement rate; AUT, area under the threshold; BP blood pressure; CAD, coronary artery disease; Cr, creatinine; CVD, cerebrovascular disease; DBP, diastolic blood pressure; Di, dichotomous; DM, diabetes mellitus; Du, duration under a blood pressure threshold; eGFR, estimated glomerular filtration rate; Gen. anaesth., general anaesthesia; GI, gastro-intestinal; HT, hypertension; LiverTX, liver transplantation; Low, lowest blood pressure; MAP, mean blood pressure; MI, myocardial injury; r-, relative threshold expressed as percentage decrease from baseline BP; RCRI, Revised Cardiac Risk Index; SAS, blood pressure as part of Surgical Apgar Score; SBP, systolic blood pressure; TIA, transient ischaemic attack; TL, triple low; TWA, time-weighted average; V, blood pressure variance; Var, variability or variance

Studies		Patient characteristics		Comorbidity (%)									Procedure characteristics (%)				Intraoperative hypotension		
First author	Total	Age	Sex	ASA				Stroke	HT	DM	CAD	Renal disease	Gen. anaesth.	Length of surgery	Emergency surgery	Type of surgery	BP threshold type	Threshold	Analysis
(yr)	n	(yr)	F, %	1	2	3	4					any		min		most frequent			
Hirsch (2015)[5]	594	74 (6)	51	48		–	–	4	–	–	–	–	71	300 (144)	0	Orthopaedic 53	rSBP, rMAP, aMAP	↓ >10–40%, <50 mm Hg	Du, Var
Monk (2015)[6]	18 756	60 (13)	7	3	26	58	13	–	–	–	–	19	–	120 (72–186)	8	General 32	aSBP	<80 mm Hg	Du
Willingham (2015)[7]	13 198	56 (44–66)	47	9	39	35	16	any: 3	48	17	20	–	100	178 (115–259)	–	–	aMAP, TL	<75mm Hg	Du
Bijker (2012)*,[8]	48 241 (42/252)	66 (57–76)	40	68		32		38	69	–	–	–	–	163 (130–232)	–	Vascular 48	aSBP, aMAP, rSBP, rMAP	<100–70 mm Hg, <70–40 mm Hg, ↓ >10–40%	Du
Mizota (2017)*,[9]	231	54 (44–60)	51	–	–	–	–	–	–	19	–	22	100	838 (752–960)	–	LiverTX 100	aMAP	<40,<50 mm Hg	Du, Di
Sun (2015)*,[3]	5127	61 (14)	53	–	–	–	–	any: 2	48	15	11	16	–	>120: 79	0	General 26	aMAP	<65, <60, <55 mm Hg	Du
Schmid (2016)*,[10]	180	66 (12)	23	–	–	–	–	–	–	56	20	6	100	–	100	Abdominal 100	aMAP	>70 mm Hg	AR
Roshanov (2017)[11]	14 687	65 (12)	52	–	–	–	–	7	47	19	12	eGFR: 79 (23)	–	–	14	Orthopaedic 20	aSBP	<90 mm Hg	Di
Salmasi (2017)*,[12]	57 315	56 (15)	56	2	38	54	7	3	49	17	–	1	–	225(121)	4	Abdominal 23	aMAP, rMAP	<80–40 mm Hg, ↓>10–60%	Du, TWA
Babazade (2016)[13]	2521	56 (15)	45	45		50	5	–	42	14	–	4	100	199 (142–265)	1	Colorectal 100	aSBP, aMAP	<80mm Hg, <55mm Hg	Du
Hallqvist (2016)[14]	300	67 (57–74)	53	10	46	43	0.3	–	43	8	–	–	39	–	0	Abdominal 40	rSBP	↓ >50%, >5 min	Di
van Waes (2016)*,[15]	890	74 (8)	31	1	14	36	49	21	–	10	–	8	100	191 (108)	30	(T)EVAR 24	aMAP	<50, <60 mm Hg, ↓>30%, ↓ >40%	Du, (AUT)
Mascha (2015)*,[16]	104 401	57 (18)	53	5	40	47	8	1	48	17	14	6	–	174 (114–252)	5	–	aMAP	<80–50 mm Hg	Du, TWA, Var

Continued

Limitations of observational evidence - definitions of hypotension II

Studies		Patient characteristics		Comorbidity (%)									Procedure characteristics (%)				Intraoperative hypotension		
First author	Total	Age	Sex	ASA				Stroke	HT	DM	CAD	Renal disease	Gen. anaesth.	Length of surgery	Emergency surgery	Type of surgery	BP threshold type	Threshold	Analysis
(yr)	n	(yr)	F, %	1	2	3	4					any		min		most frequent			
Pipanmekaporn (2014)*,[17]	719	49 (16)	29	14	58	28	–	–	18	10	2	10	100	142 (65)	46	Thoracic 100	aSBP, aMAP	<80 or <60 mm Hg, >15 min	Di
Walsh (2013)*,[4]	33 330	56 (16)	50	2	40	50	8	5	–	13	–	eGFR: 93 (27)	–	–	7	–	aMAP	<75–55 mm Hg	Du
Bijker (2009)[18]	1705	52 (16)	48	38	51	11		7	22	8	any: 15	–	88	112 (73–163)	0	General 88	aSBP, rSBP, aMAP, rMAP	<100–70 mm Hg, ↓ >10–40%, <70-40 mm Hg, ↓ >10–40%	Du
Kheterpal (2009)*,[19]	7740	≥68: 23	49	–	–	–	–	any: 5	40	13	–	3	88	–	12	–	aSBP, aMAP, rSBP, rMAP	<80–70 mm Hg, <60–50 mm Hg, ↓ >30–40%	Di?
Monk (2005)[2]	1064	51 (37–65)	64	13	52	35		4	33	4	6	–	100	186 (138–258)	–	Orthopaedic 26	aSBP	<80 mm Hg	Du
White (2016)[20]	11 085	83 (24–104)	72	3	30	55	12	11	55	7	–	14	54	–	–	Hip surgery 100	aSBP, aMAP	Lowest BP	Low
Brinkman (2015)*,[21]	40	69 (9)	35	–	–	–	–	–	68	13	–	–	100	228 (84)	0	Aorta 100	aMAP	<65 mm Hg	AUT
Petsiti (2015)[22]	248	64 (11)	48	–	–	32		1	47	13	8	3	100	232 (55)	0	Abdominal 100	aMAP, rMAP	<60 or <70 mm Hg + ↓ >30%	Di
Marcantonio (1998)[23]	1341	67 (9)	55	–	–	–	–	–	–	–	–	–	–	–	–	Orthopaedic 43	aSBP or rSBP	<90 mm Hg or ↓ >33%	Di
Tallgren (2007)*,[24]	69	67 (60–74)	22	–	–	–	–	–	66	7	43	–	100		0	Aorta 100	aMAP	<65 mm Hg, >15 min	Di
House (2016)*,[25]	46 799	54 (13)	47			41		3	43	16	–	4	–	162 (108)	4	–	aMAP	<40 mm Hg	Di/SAS
Sessler (2012)[26]	24 120	–	–	–	–	–	–	–	–	–	–	–	100	–	–	–	aMAP, TL	<70 mm Hg	Du
Sabaté (2011)[27]	3387	67 (47–81)†	52	8	55	33	4	–	–	–	RCRI ≥3: 7	–	61	120 (60–248)†	7	Orthopaedic 24	aSBP or aMAP/rMAP	<100 mm Hg or ↓ >20 mm Hg/20%, >60 min	Di
Taffé (2009)*,[28]	147 573	55 (18)	56	27	48	22	3	–	–	–	–	–	67	104 (?–?)	20	–	rMAP	↓ >30%, >10 min	Di
Sirivatanauksorn (2014)*,[29]	81	53 (23–70)	31	–	–	–	–	–	–	–	–	Cr: 90 (38–168)	100	276 (168–438)	–	Liver TX 100	aMAP	<70 mm Hg, >30 min	Di
Tassoudis (2011)[30]	100	62 (14)	47	–	32	–	–	1	46	12	8	3	100	195 (71)	0	Abdominal 100	aMAP, rMAP	<60 or <70mm Hg + ↓ >30%	Di

Continued

Limitations of observational evidence - definitions of hypotension III

Table 2 Continued

Studies		Patient characteristics		Comorbidity (%)									Procedure characteristics (%)				Intraoperative hypotension		
First author	Total	Age	Sex	ASA				Stroke	HT	DM	CAD	Renal disease	Gen. anaesth.	Length of surgery	Emergency surgery	Type of surgery	BP threshold type	Threshold	Analysis
(yr)	n	(yr)	F, %	1	2	3	4					any		min		most frequent			
Stapelfeldt (2017)[31]	152 445	–	–	–	–	–	–	–	–	–	–	–	–	179 (118–259)	90	–	aMAP	<75–45 mm Hg	Du
Jiang (2016)[*,32]	451	65 (18)	50	–	–	–	–	–	14	6	–	1	100	164 (62)	–	Spine 100	aSBP	<80 mm Hg	Di
Yang (2016)[*,33]	480	81 (6)	51	–	71	29	–	–	43	30	43	–	100	188 (32)	0	–	r?BP	↓ >30%	Di
Yue (2013)[*,34]	71	>70: 37	21	–	–	–	–	–	–	11	–	23	100	–	38	Aorta 100	aSBP/aMAP	<↓ 30/<65 mm Hg	Di
Franck (2011)[*,35]	2350	53 (41–65)	50	50		50		–	–	–	–	–	100	98 (63–148)	–	–	aSBP, rSBP	<100 or ↓>30%, <92 mm Hg, <80 mm Hg, ↓ >20%	Di
Patti (2011)[*,36]	100	70 (3)	60	9	41	29	21	–	–	–	–	–	100	121 (24)	0	Abdominal 100	aMAP	≤60mm Hg	Di
Vasivej (2016)[*,37]	55 648 (42/168)	58 (14)	52	–	–	–	–	6	43	27	23	39	59	153 (78–244)	7	–	aMAP	<65 mm Hg	Di
Thakar (2007)[*,38]	504	43 (10)	83	–	–	–	–	–	57	26	–	4	100	–	0	Abdominal 100	aMAP	<60 mm Hg	Di
Barone (2002)[*,39]	25 501	74 (11)	45	Mean ASA: 2.9				–	40	19	any: 30	–	–	124 (55)	27	–	aSBP	<100 mm Hg, >10 min	Di
Lima (2003)[*,40]	92	44 (14)	48	–	–	–	–	–	–	–	–	Cr: 88 (35)	100	–	–	LiverTX 100	aMAP	<60 mm Hg	Di
Nakamura (2009)[*,41]	72	71 (10)	29	–	–	–	–	any: 15	88	7	any: 19	11	–	–	15	Aorta 100	aSBP	<70 mm Hg	Di
Davidovic (2017)[42]	450	66 (7)	12	–	–	–	–	–	70	–	26	11	100	–	0%	Aorta 100%	aSBP	<100 mm Hg	Di
Sharma (2006)[*,43]	1800	43 (9)	80	–	–	–	–	–	57	22	–	2	100	223 (63)	0%	Abdominal 100%	aSBP	<100 mm Hg, >5 min	Di

INPRESS

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery

A Randomized Clinical Trial

Emmanuel Futier, MD, PhD; Jean-Yves Lefrant, MD, PhD; Pierre-Gregoire Guinot, MD, PhD; Thomas Godet, MD, PhD; Emmanuel Lorne, MD; Philippe Cuvillon, MD, PhD; Sebastien Bertran, MD; Marc Leone, MD, PhD; Bruno Pastene, MD; Vincent Piriou, MD, PhD; Serge Molliex, MD, PhD; Jacques Albanese, MD, PhD; Jean-Michel Julia, MD; Benoit Tavernier, MD, PhD; Etienne Imhoff, MD; Jean-Etienne Bazin, MD, PhD; Jean-Michel Constantin, MD, PhD; Bruno Pereira, PhD; Samir Jaber, MD, PhD; for the INPRESS Study Group

Study population

- **Inclusion criteria**
  1. Adult patients older than 50 years
  2. Scheduled for major abdominal or non-abdominal surgery
  3. Expected surgical duration of at least 2 hours
  4. American Society of Anesthesiologists (ASA) physical status (ASA class II or higher)
  5. Acute Kidney Injury (AKI) risk index[9] (4 or more of the following):
     a. Age ≥56 years
     b. Male sex
     c. Congestive heart failure
     d. Chronic hypertension
     e. Emergency surgery
     f. Abdominal surgery
     g. Ascites
     h. Renal insufficiency-mild or moderate (preoperative serum creatinine value >1.2 mg/dl or >105.6 µmol/l)
     i. Diabetes mellitus-oral or insulin therapy

- **Exclusion criteria**
  1. Severe untreated or uncontrolled hypertension despite medications
  2. Chronic kidney disease with glomerular filtration rate <30 ml/min/1.73 m2 or requiring renal-replacement therapy for end-stage renal disease
  3. Acute cardiovascular event, including acute or decompensated heart failure and acute coronary syndrome
  4. Renal vascular surgery
  5. Preoperative sepsis
  6. Circulatory shock
  7. Preoperative norepinephrine infusion before study entry
  8. Surgical procedure under regional anesthesia (both epidural and spinal anesthesia)
  9. No affiliation with the French healthcare system
  10. Participation in another competing interventional study
  11. Refusal to participate
  12. Pregnant or breastfeeding women

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Study design

The Intraoperative Norepinephrine to control arterial PRESSure (INPRESS) trial is a multicenter, prospective, randomized, stratified, parallel-group clinical trial with concealed allocation of patients at high-risk of postoperative complications after abdominal surgery in a 1:1 ratio to a standard or an individualized treatment strategy:

- Control group = standard (curative) treatment strategy
  In the standard treatment group, patients will receive intravenous boluses of ephedrine to treat any drop in SBP below 80 mmHg or lower than 40% from the patient resting blood pressure (used as the reference value)

- Intervention group = individualized (preventive) treatment strategy
  In the individualized treatment group, patients will receive continuous infusion of norepinephrine to maintain SBP within ±10% of the patient resting blood pressure (used as the reference value)

In the two treatment groups, the patient resting blood pressure will be used as the reference value. If not available, the blood pressure value obtained in the surgical ward the day before surgery (after a 5-min rest while lying supine) will be used as reference value.

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Study design

The Intraoperative Norepinephrine to control arterial PRESSure (INPRESS) trial is a multicenter, prospective, randomized, stratified, parallel-group clinical trial with concealed allocation of patients at high-risk of postoperative complications after abdominal surgery in a 1:1 ratio to a standard or an individualized treatment strategy:

- Control group = standard (curative) treatment strategy
  In the standard treatment group, patients will receive intravenous boluses of ephedrine to treat any drop in SBP below 80 mmHg or lower than 40% from the patient resting blood pressure (used as the reference value)

- Intervention group = individualized (preventive) treatment strategy
  In the individualized treatment group, patients will receive continuous infusion of norepinephrine to maintain SBP within ±10% of the patient resting blood pressure (used as the reference value)

In the two treatment groups, the patient resting blood pressure will be used as the reference value. If not available, the blood pressure value obtained in the surgical ward the day before surgery (after a 5-min rest while lying supine) will be used as reference value.

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- Mechanical ventilation with the use of a tidal volume between 8 and 10 ml/kg predicted body weight, with a positive end-expiratory pressure between 5 and 10 cmH2O, an inspired oxygen fraction (FIO2) to maintain oxygen saturation ≥95% and the respiratory rate adjusted to maintain end-tidal carbon dioxide concentration between 30-35 mmHg.
- Blood transfusion to maintain hemoglobin level at greater than 10 g/dl.
- Core temperature maintained at 37°C.
- Epidural analgesia is authorized for use postoperatively, but not during surgery.
- The following treatments will be prohibited:
    a. Ketamine
    b. Nonsteroidal inflammatory drugs
    c. Benzodiazepine

Angiotensin-converting enzyme inhibitor (ACEI) and angiotensin II receptor antagonist (AIIRA) are routinely withhold the day before surgery. The continuing of ACEI or AIIRA before surgery will be recorded in the case report form.

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- **Primary outcome**

The primary outcome measure will be a composite of systemic inflammatory response syndrome (SIRS) and at least one major organ dysfunction for renal, cardiovascular, respiratory, neurologic and coagulation systems by day 7 after surgery.

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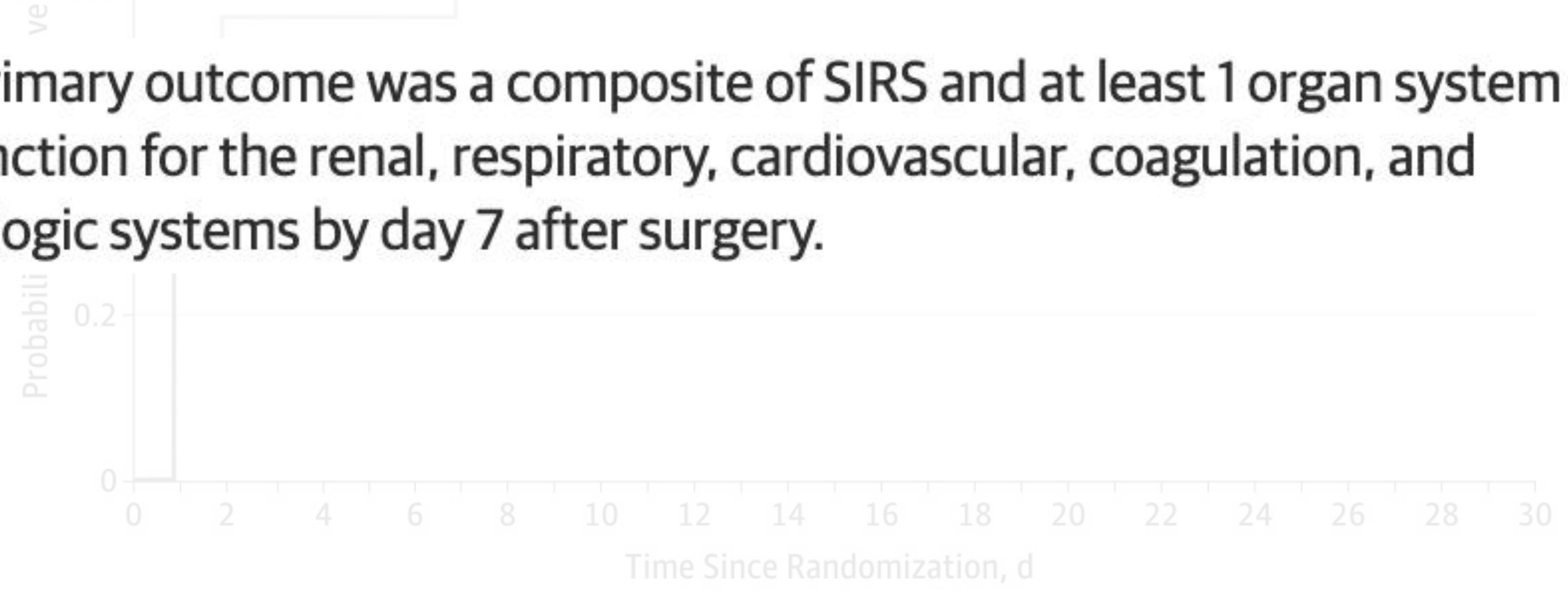
Figure 3. Kaplan-Meier Estimates of the Probability of Postoperative Organ Dysfunction by Day 30 After Surgery

Table 3. Primary and Secondary Outcomes and Adverse Events

Variable	Individualized Treatment (n = 147)	Standard Treatment (n = 145)	Between-Group Absolute Difference, % (95% CI)	Unadjusted Relative Risk (95% CI)	*P* Value	Adjusted Relative Risk (95% CI)[a]	*P* Value
Primary Outcome							
Primary composite outcome, No. (%)[b]	56 (38.1)	75 (51.7)	−14 (−25 to −2)	0.74 (0.57 to 0.95)	.02	0.73 (0.56 to 0.94)	.02

[b] The primary outcome was a composite of SIRS and at least 1 organ system dysfunction for the renal, respiratory, cardiovascular, coagulation, and neurologic systems by day 7 after surgery.



No. at risk						
Standard treatment	145	78	65	58	54	53
Individualized treatment	147	99	91	82	80	79

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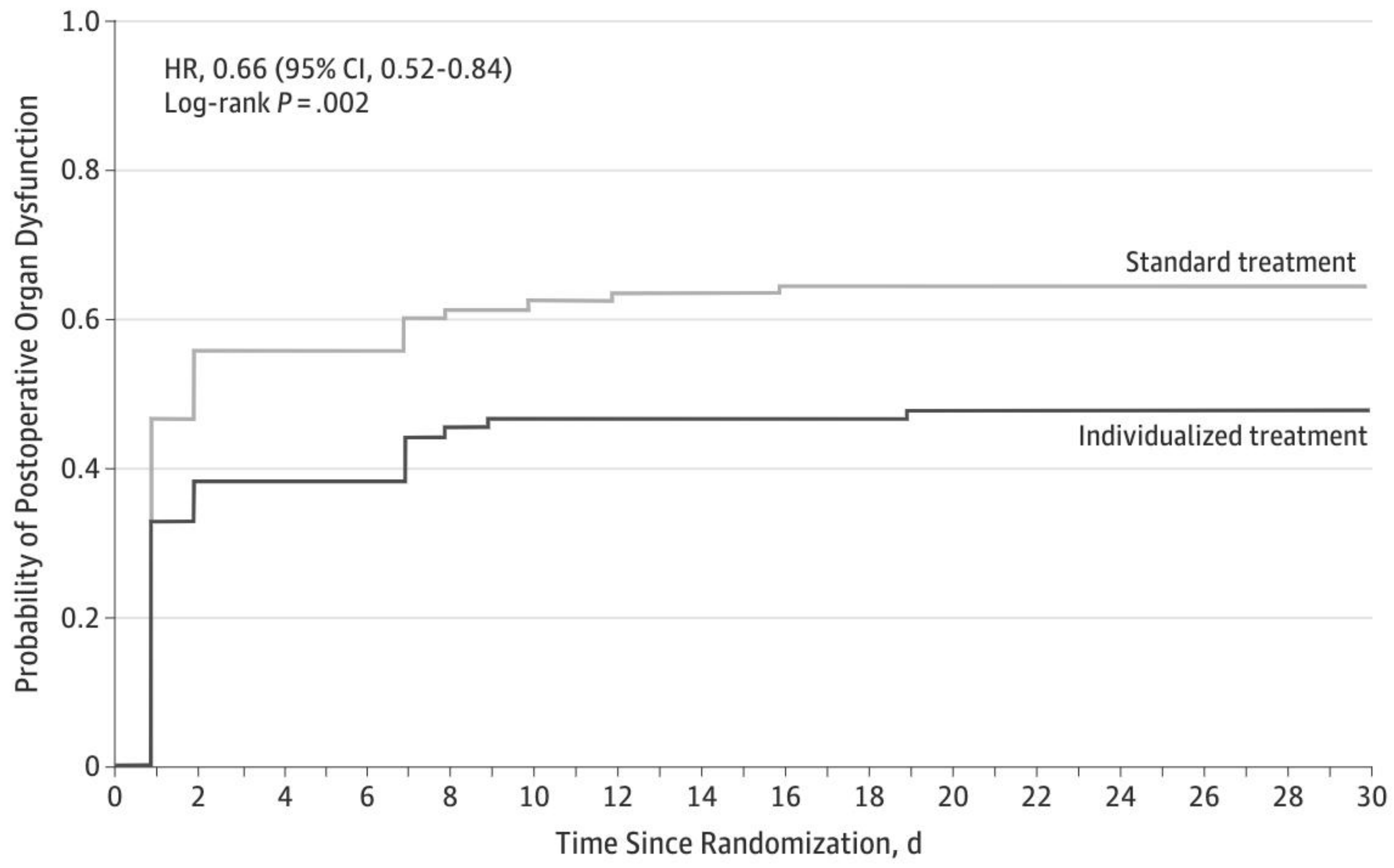

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Table 2. Clinical Management of Patients During the Intervention Period, Including During Surgery and for 4 Hours Following Surgery[a]

Variable	Individualized Treatment (n = 147)	Standard Treatment (n = 145)	P Value
Cumulative volume of crystalloid, median (IQR), mL	2275 (1600-3000)	2500 (1825-3225)	.09
During surgery	1500 (1000-2000)	2000 (1500-2500)	<.001
During 4 h following surgery	750 (500-1000)	600 (500-1000)	.54
Cumulative volume of colloid, median (IQR), mL	1000 (500-1500)	1000 (500-1750)	.25
During surgery	875 (500-1500)	1000 (500-1500)	.12
During 4 h following surgery	500 (300-500)	500 (400-1500)	.43
Use of blood products			
Patients, No. (%)	39 (26.5)	34 (23.4)	.54
No. of units/patient, mean (SD)	2.5 (1.4)	2.8 (1.7)	.28
Blood loss, median (IQR), mL	500 (200-925)	500 (200-837)	.63
Blood pressure, mean (SD), mm Hg			

Sepsis, No. (%)	13 (8.8)	23 (15.9)	−7 (−15 to 0)	0.56 (0.29 to 1.06)	.07	0.55 (0.29 to 1.04)	.07
Severe sepsis or septic shock, No. (%)	13 (8.8)	13 (9.0)	0 (−6 to 7)	0.99 (0.47 to 2.05)	.97	1.01 (0.49 to 2.11)	.97

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Secondary Outcomes							
Complications within 7 d							
SIRS							
No. (%)	108 (73.5)	105 (72.4)	1 (−9 to 11)	0.84 (0.65 to 1.10)	.20	1.01 (0.92 to 1.12)	.78
SIRS score, No. (%)[c]							
2	49 (33.3)	36 (24.8)	9 (−2 to 19)	1.18 (0.90 to 1.59)	.29	1.19 (0.89 to 1.59)	.25
≥3	59 (40.1)	69 (47.6)	−8 (−19 to 4)	0.84 (0.65 to 1.10)	.20	0.81 (0.64 to 1.02)	.07
Daily SIRS score, mean (95% CI)[c]	1.5 (1.3 to 1.7)	1.6 (1.4 to 1.7)			.62		.61
Acute kidney injury according to RIFLE criteria, No. (%)[d]							
Risk	23 (15.7)	36 (24.8)	−9 (−18 to 0)	0.63 (0.39 to 1.00)	.05	0.73 (0.47 to 1.14)	.17
Injury	16 (10.9)	26 (17.9)	−7 (−15 to 1)	0.61 (0.34 to 1.08)	.09	0.61 (0.34 to 1.08)	.09
Failure	9 (6.1)	9 (6.2)	0 (−6 to 5)	0.99 (0.40 to 2.41)	.98	0.97 (0.40 to 2.34)	.95
Use of renal replacement therapy, No. (%)	4 (2.7)	5 (3.5)	0 (−5 to 3)	0.79 (0.22 to 2.88)	.72	0.81 (0.22 to 2.97)	.76
Acute heart failure, No. (%)	1 (0.7)	0	1 (−1 to 2)				
Myocardial ischemia or infarction, No. (%)	0	1 (0.7)	−1 (−2 to 1)				
Altered consciousness, No. (%)[e]	8 (5.4)	23 (15.9)	−10 (−17 to −3)	0.34 (0.16 to 0.74)	.007	0.34 (0.16 to 0.75)	.007
Stroke, No. (%)	0	0					
Coagulation SOFA score ≥2, No. (%)	16 (11.0)	11 (7.6)	3 (−3 to 10)	1.44 (0.69 to 3.01)	.33	1.47 (0.07 to 2.23)	.07
Hypoxemia, No. (%)	21 (14.3)	33 (22.8)	−8 (−17 to 0)	0.63 (0.38 to 1.03)	.07	0.64 (0.40 to 1.03)	.07
Pneumonia, No. (%)	4 (2.7)	11 (7.6)	−5 (−10 to 0)	0.36 (0.12 to 1.10)	.07	0.36 (0.12 to 1.10)	.07
ARDS, No. (%)	7 (4.8)	7 (4.8)	0 (−5 to 5)	0.99 (0.35 to 2.74)	.98	0.98 (0.35 to 2.67)	.95
Reintubation, No. (%)	10 (6.8)	15 (10.3)	−4 (−10 to 3)	0.66 (0.31 to 1.42)	.28	0.66 (0.31 to 1.42)	.28
Need for noninvasive or invasive ventilation, No. (%)	25 (17.0)	36 (24.8)	−8 (−17 to 1)	0.68 (0.43 to 1.08)	.10	0.71 (0.45 to 1.11)	.13
SOFA score, median (IQR)[f]							
Day 1	1 (0-3)	1 (0-3)			.31		.36
Day 2	1 (0-2)	2 (0-3)			.19		.21
Day 7	0 (0-1)	0 (0-1)			.66		.68
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Acute kidney injury according to RIFLE criteria, No. (%)[d]							
Risk	23 (15.7)	36 (24.8)	−9 (−18 to 0)	0.63 (0.39 to 1.00)	.05	0.73 (0.47 to 1.14)	.17
Injury	16 (10.9)	26 (17.9)	−7 (−15 to 1)	0.61 (0.34 to 1.08)	.09	0.61 (0.34 to 1.08)	.09
Failure	9 (6.1)	9 (6.2)	0 (−6 to 5)	0.99 (0.40 to 2.41)	.98	0.97 (0.40 to 2.34)	.95
Use of renal replacement therapy, No. (%)	4 (2.7)	5 (3.5)	0 (−5 to 3)	0.79 (0.22 to 2.88)	.72	0.81 (0.22 to 2.97)	.76
Acute heart failure, No. (%)	1 (0.7)	0	1 (−1 to 2)				
Myocardial ischemia or infarction, No. (%)	0	1 (0.7)	−1 (−2 to 1)				
Altered consciousness, No. (%)[e]	8 (5.4)	23 (15.9)	−10 (−17 to −3)	0.34 (0.16 to 0.74)	.007	0.34 (0.16 to 0.75)	.007
Stroke, No. (%)	0	0					
Coagulation SOFA score ≥2, No. (%)	16 (11.0)	11 (7.6)	3 (−3 to 10)	1.44 (0.69 to 3.01)	.33	1.47 (0.07 to 2.23)	.07
Hypoxemia, No. (%)	21 (14.3)	33 (22.8)	−8 (−17 to 0)	0.63 (0.38 to 1.03)	.07	0.64 (0.40 to 1.03)	.07
Pneumonia, No. (%)	4 (2.7)	11 (7.6)	−5 (−10 to 0)	0.36 (0.12 to 1.10)	.07	0.36 (0.12 to 1.10)	.07
ARDS, No. (%)	7 (4.8)	7 (4.8)	0 (−5 to 5)	0.99 (0.35 to 2.74)	.98	0.98 (0.35 to 2.67)	.95
Reintubation, No. (%)	10 (6.8)	15 (10.3)	−4 (−10 to 3)	0.66 (0.31 to 1.42)	.28	0.66 (0.31 to 1.42)	.28
Need for noninvasive or invasive ventilation, No. (%)	25 (17.0)	36 (24.8)	−8 (−17 to 1)	0.68 (0.43 to 1.08)	.10	0.71 (0.45 to 1.11)	.13
SOFA score, median (IQR)[f]							
Day 1	1 (0-3)	1 (0-3)			.31		.36
Day 2	1 (0-2)	2 (0-3)			.19		.21
Day 7	0 (0-1)	0 (0-1)			.66		.68
Sepsis, No. (%)	13 (8.8)	23 (15.9)	−7 (−15 to 0)	0.56 (0.29 to 1.06)	.07	0.55 (0.29 to 1.04)	.07
Severe sepsis or septic shock, No. (%)	13 (8.8)	13 (9.0)	0 (−6 to 7)	0.99 (0.47 to 2.05)	.97	1.01 (0.49 to 2.11)	.97

THE BBB-STUDY

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 78, NO. 18, 2021

ORIGINAL INVESTIGATIONS

Targeting Higher Intraoperative Blood Pressures Does Not Reduce Adverse Cardiovascular Events Following Noncardiac Surgery

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FNSNF SWISS NATIONAL SCIENCE FOUNDATION

Kantonsspital St.Gallen

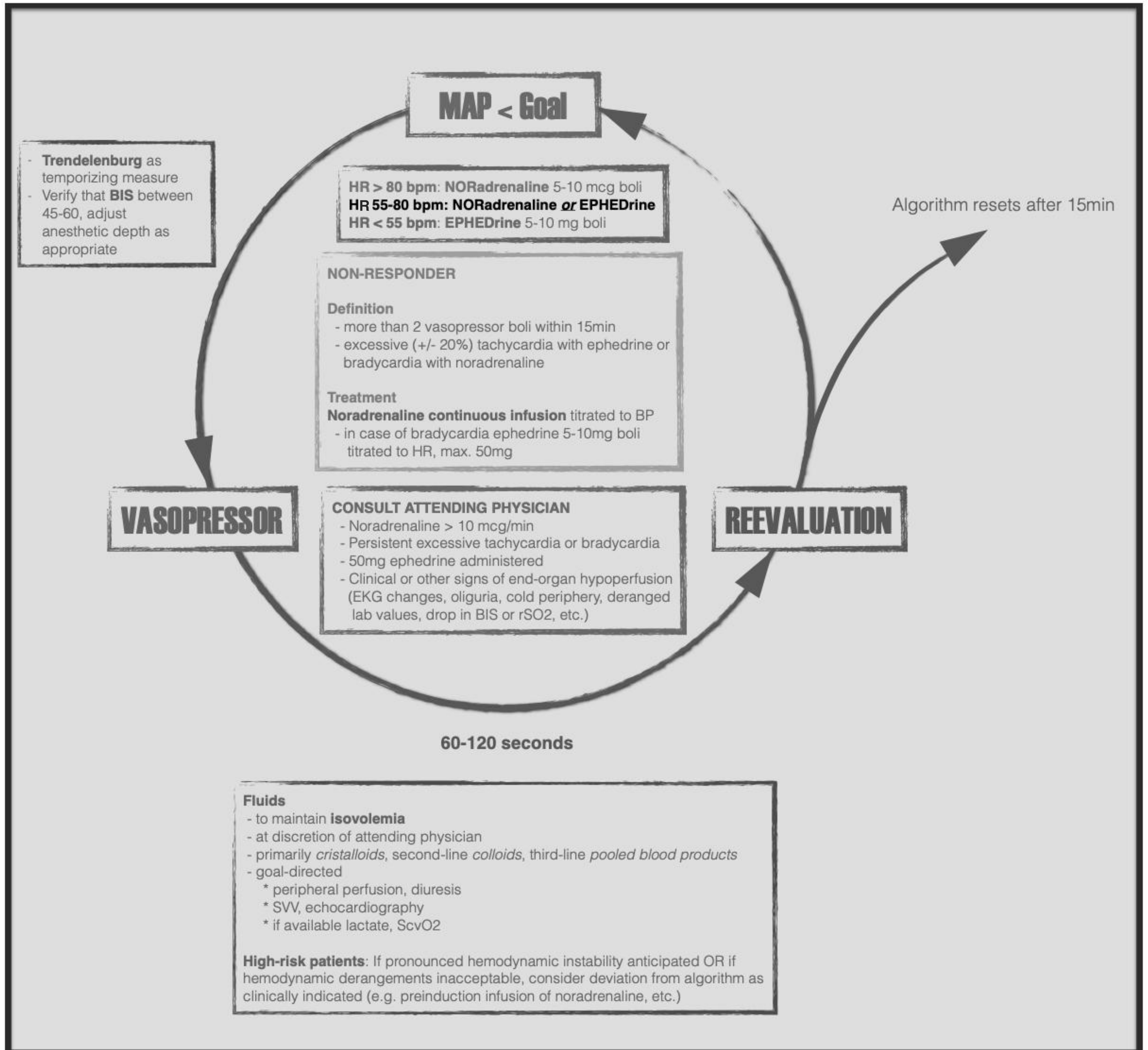
Schweizerische Herzstiftung
Fondation Suisse de Cardiologie
Fondazione Svizzera di Cardiologia

RESEARCH QUESTION

Population	≥ 45 years, cardiovascular risk, major noncardiac surgery
Intervention	Targeting intraoperative MAP ≥ 75 mmHg
Comparator	Targeting intraoperative MAP ≥ 60 mmHg (2014 ESC/ESA Guidelines)[1]
Outcome	Composite acute myocardial injury POD0-3 and/or 30-day major adverse cardiovascular events (MACE) / acute kidney injury (AKI)

1: 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA)

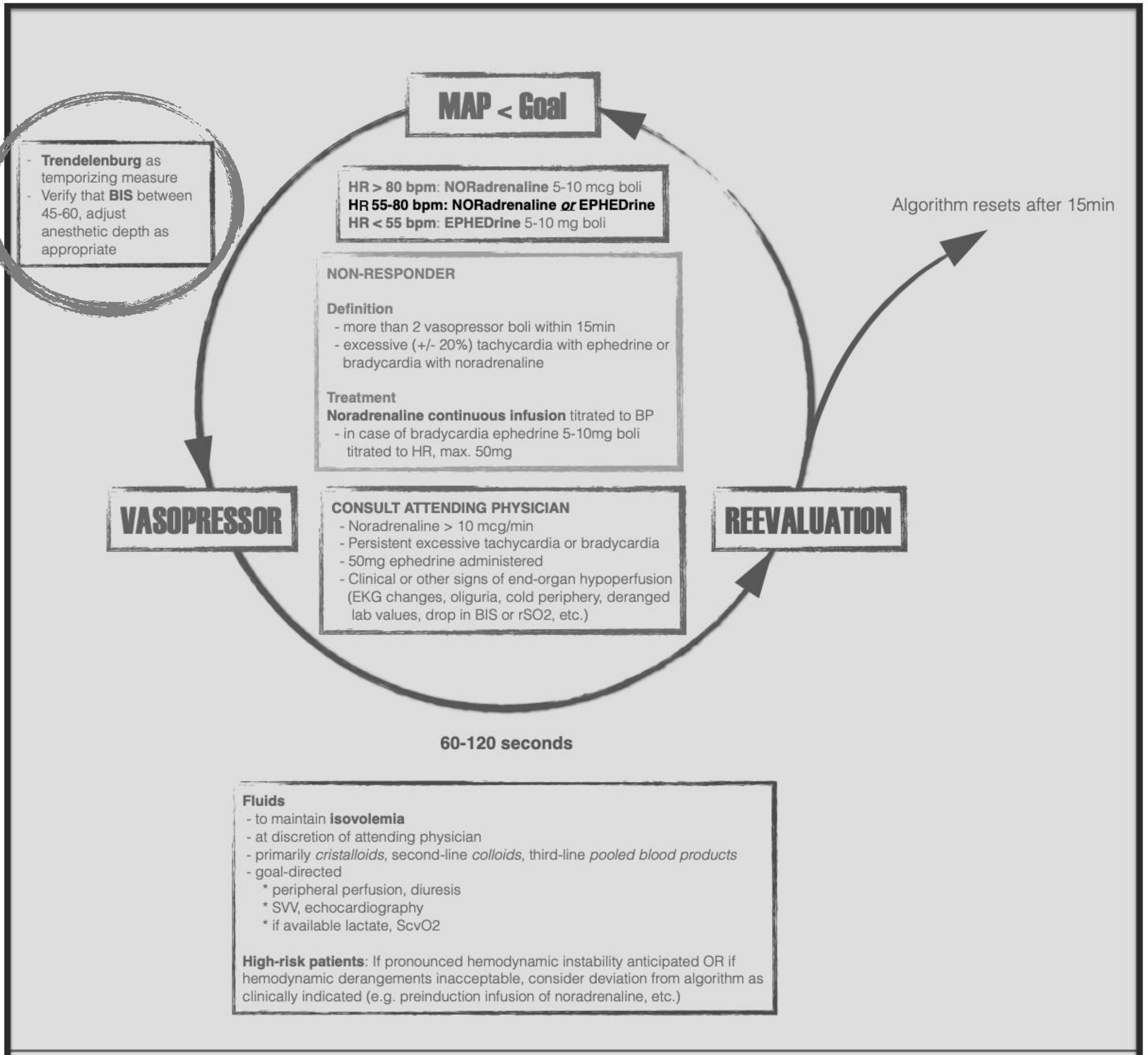
INTERVENTION



Intraoperative hemodynamic management algorithm, ***Division of Anaesthesiology, Intensive Care, Rescue and Pain Medicine, Kantonsspital St. Gallen***

Abbreviations: MAP, *mean arterial pressure*; HR, *heart rate*; BIS, *bispectral index*, rSO2, *cerebral oxygen saturation*; SVV, *stroke volume variability*; ScvO2, *central venous oxygen saturation*

Intervention



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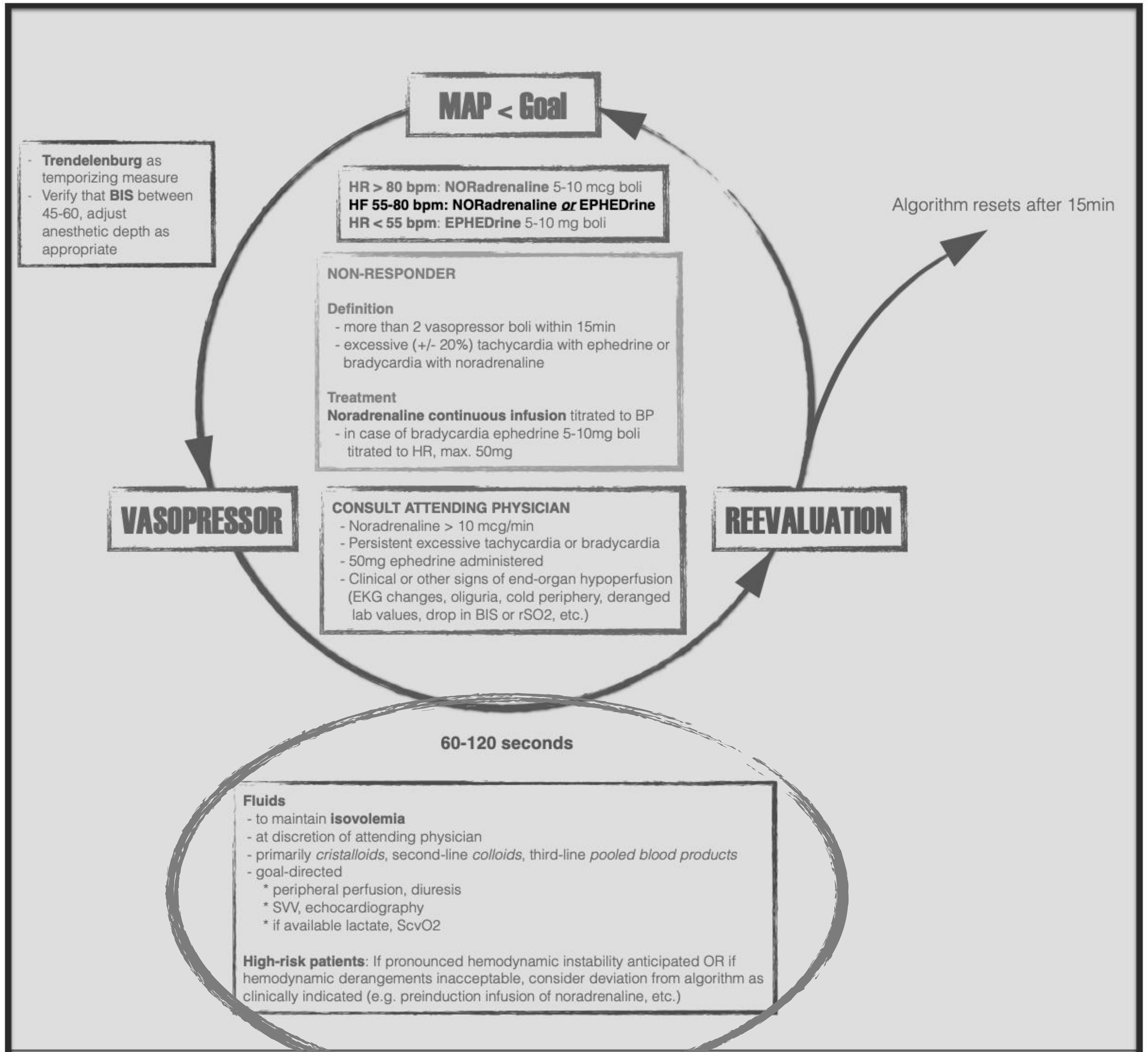
Non-pharmacologic Interventions

Intervention



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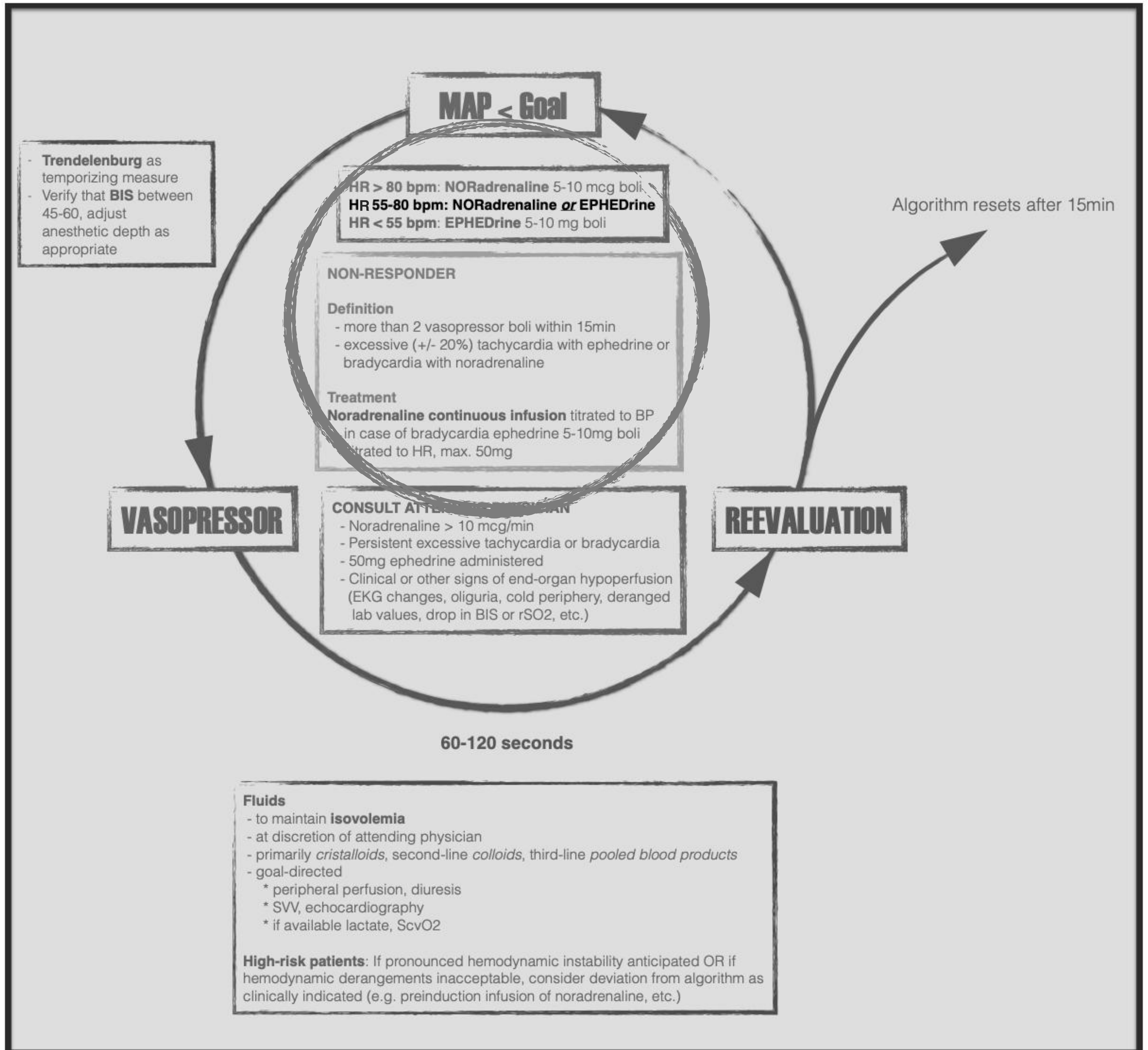
Abbreviations: MAP, *mean arterial pressure*; HR, *heart rate*; BIS, *bispectral index*, rSO2, *cerebral oxygen saturation*; SVV, *stroke volume variability*; ScvO2, *central venous oxygen saturation*

Fluids

Intervention



Intraoperative hemodynamic management algorithm, ***Division of Anaesthesiology, Intensive Care, Rescue and Pain Medicine, Kantonsspital St. Gallen***

Abbreviations: MAP, *mean arterial pressure*; HR, *heart rate*; BIS, *bispectral index*, rSO2, *cerebral oxygen saturation*; SVV, *stroke volume variability*; ScvO2, *central venous oxygen saturation*

Vasopressors

Outcomes

Primary

Acute myocardial injury postoperative days 0-3 (hs-cTnI > 40 ng/L [99th percentile of the upper reference limit] and relative increase ≥ 35% compared with the preoperative value)

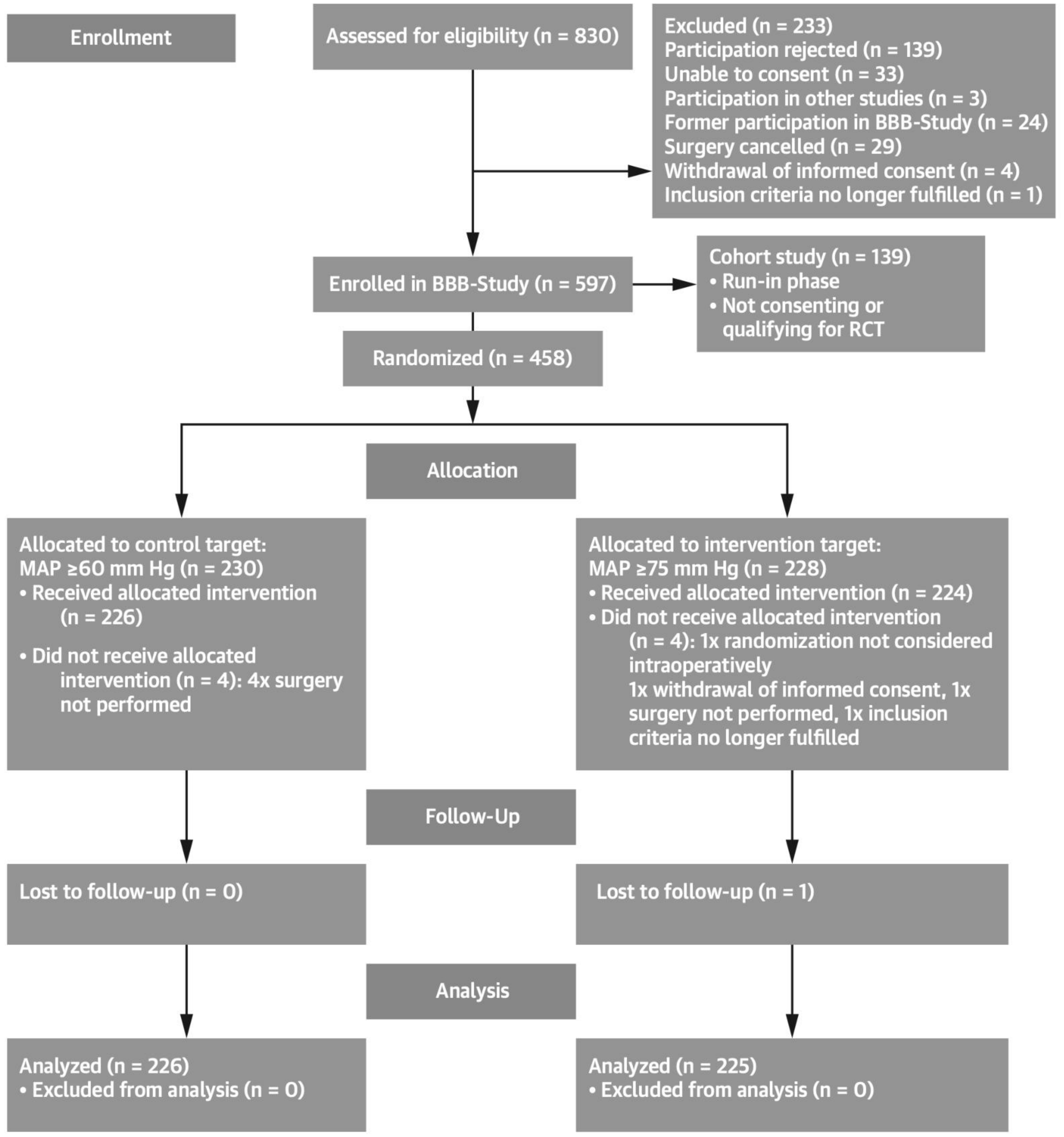
and/or

30-day MACE/AKI (acute coronary syndrome, new or worsening congestive heart failure, coronary revascularization, stroke, AKI, all-cause mortality)

RESULTS

Results - Enrolment

FIGURE 1 Enrollment Flow Diagram



Results - Baseline characteristics

TABLE 1 Characteristics of Patients at Baseline

	Control (n = 226)	MAP Target ≥75 mm Hg (n = 225)
Age, y	69 ± 10	70 ± 8
Sex		
Male	182 (81)	186 (83)
Female	44 (19)	39 (17)
ASA physical status		
2	81 (36)	76 (34)
3	142 (63)	144 (64)
4	3 (1)	5 (2)
Charlson comorbidity index		
0	44 (19)	37 (16)
1	52 (23)	33 (15)
2	40 (18)	62 (28)
3	40 (18)	44 (20)
4	32 (14)	31 (14)
5	12 (5)	6 (3)
6	1 (0)	6 (3)
7	2 (1)	2 (1)
8	0 (0)	2 (1)
9	2 (1)	2 (1)
10	1 (0)	0 (0)
Revised cardiac risk index		
0	2 (1)	2 (1)
1	109 (48)	95 (42)
2	81 (36)	94 (42)
3	29 (13)	29 (13)
4	4 (2)	5 (2)
5	1 (0)	0 (0)
Fulfilment of ≥3 Lee criteria	38 (17)	34 (15)
History of coronary artery disease	84 (37)	111 (49)
History of peripheral artery disease	94 (42)	110 (49)
History of congestive heart failure	1 (0)	2 (1)
History of stroke	23 (10)	11 (5)
History of transient ischemic attack	7 (3)	9 (4)
Preoperative serum creatinine >175 µmol/L	33 (15)	34 (15)
Insulin-dependent diabetes mellitus	24 (11)	19 (8)
Preoperative brain-type natriuretic peptide	52 (29-102)	54 (28-108)
Preoperative high-sensitivity cardiac troponin I	10 (10-11)	10 (10-10)
ACE inhibitor		
None	160 (71)	147 (65)
Continued perioperatively	66 (29)	78 (35)
Stopped perioperatively	0 (0)	0 (0)
Angiotensin receptor blocker		
None	154 (68)	165 (73)
Continued perioperatively	71 (31)	59 (26)
Stopped perioperatively	1 (0)	1 (0)
Beta-blocker		
None	114 (50)	116 (52)
Continued perioperatively	112 (50)	108 (48)
Stopped perioperatively	0 (0)	1 (0)
Calcium-channel blocker		
None	169 (75)	163 (72)
Continued perioperatively	57 (25)	60 (27)
Stopped perioperatively	0 (0)	2 (1)
Operations		
Gynecological surgery	4 (2)	1 (0)
Orthopedic surgery	6 (3)	7 (3)
Thoracic surgery	11 (5)	18 (8)
Urological surgery	15 (7)	31 (14)
Vascular surgery	161 (71)	142 (63)
Visceral surgery	29 (13)	26 (12)

Continued on the next page

TABLE 1 Continued

Values are mean ± SD, n (%), or median (interquartile range).
ACE = angiotensin-converting enzyme; ASA = American Society of Anesthesiologists.

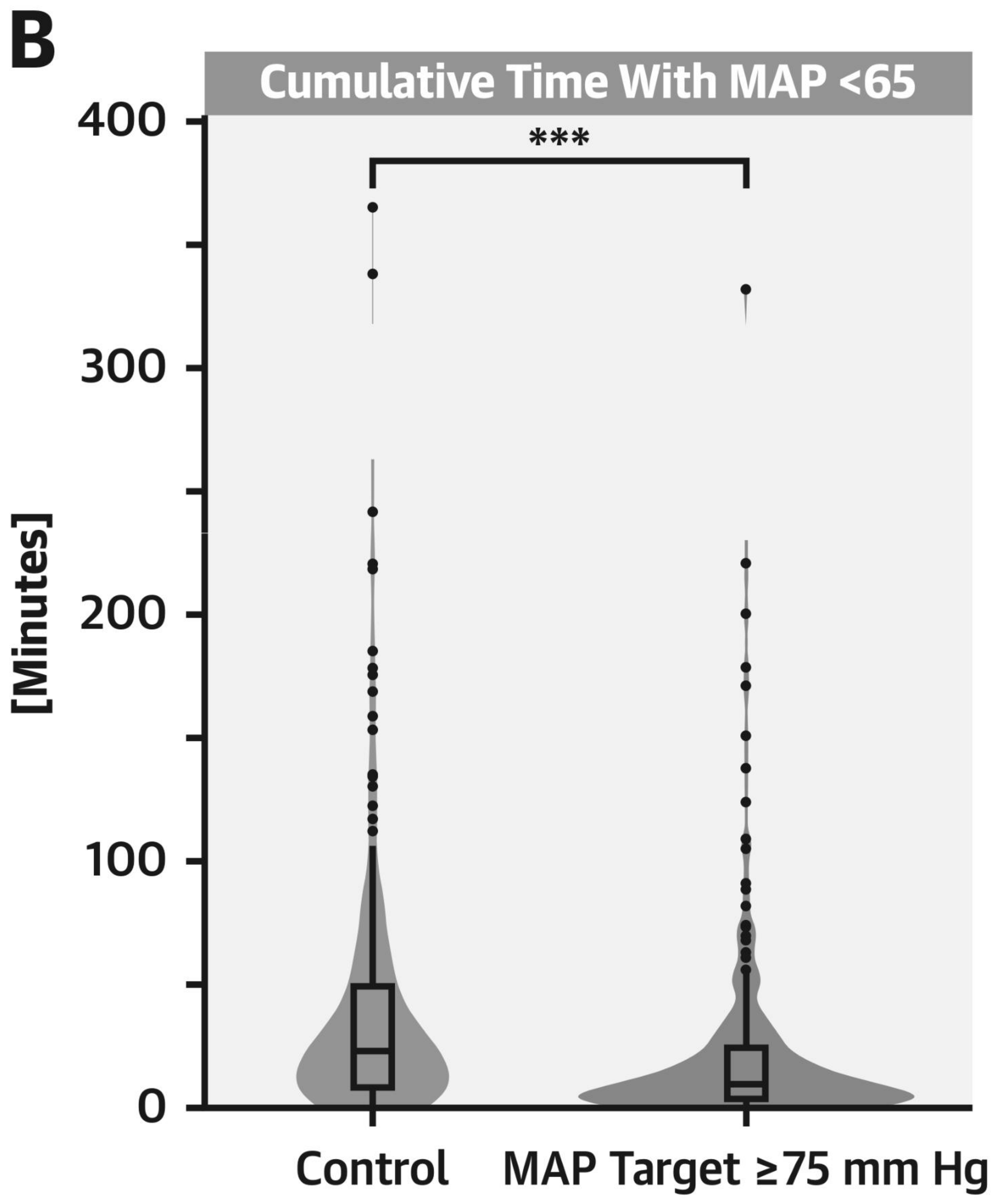
67% Vascular Surgery

12% Abdominal Surgery

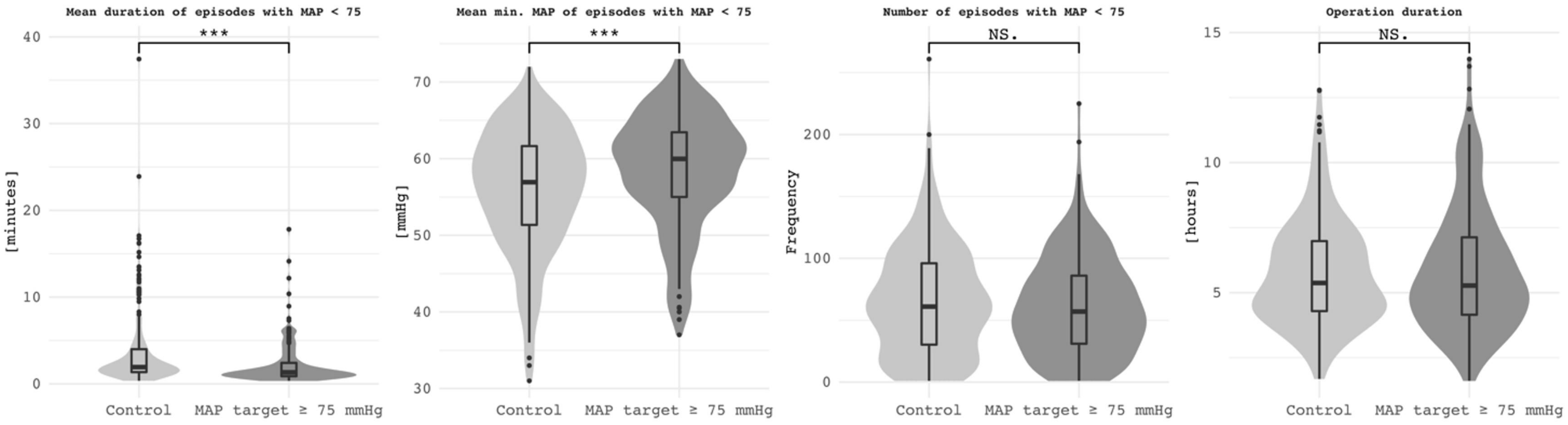
10% Urological Surgery

Results - Hemodynamic intervention I

60% reduction of duration with MAP < 65



Results - Hemodynamic intervention II

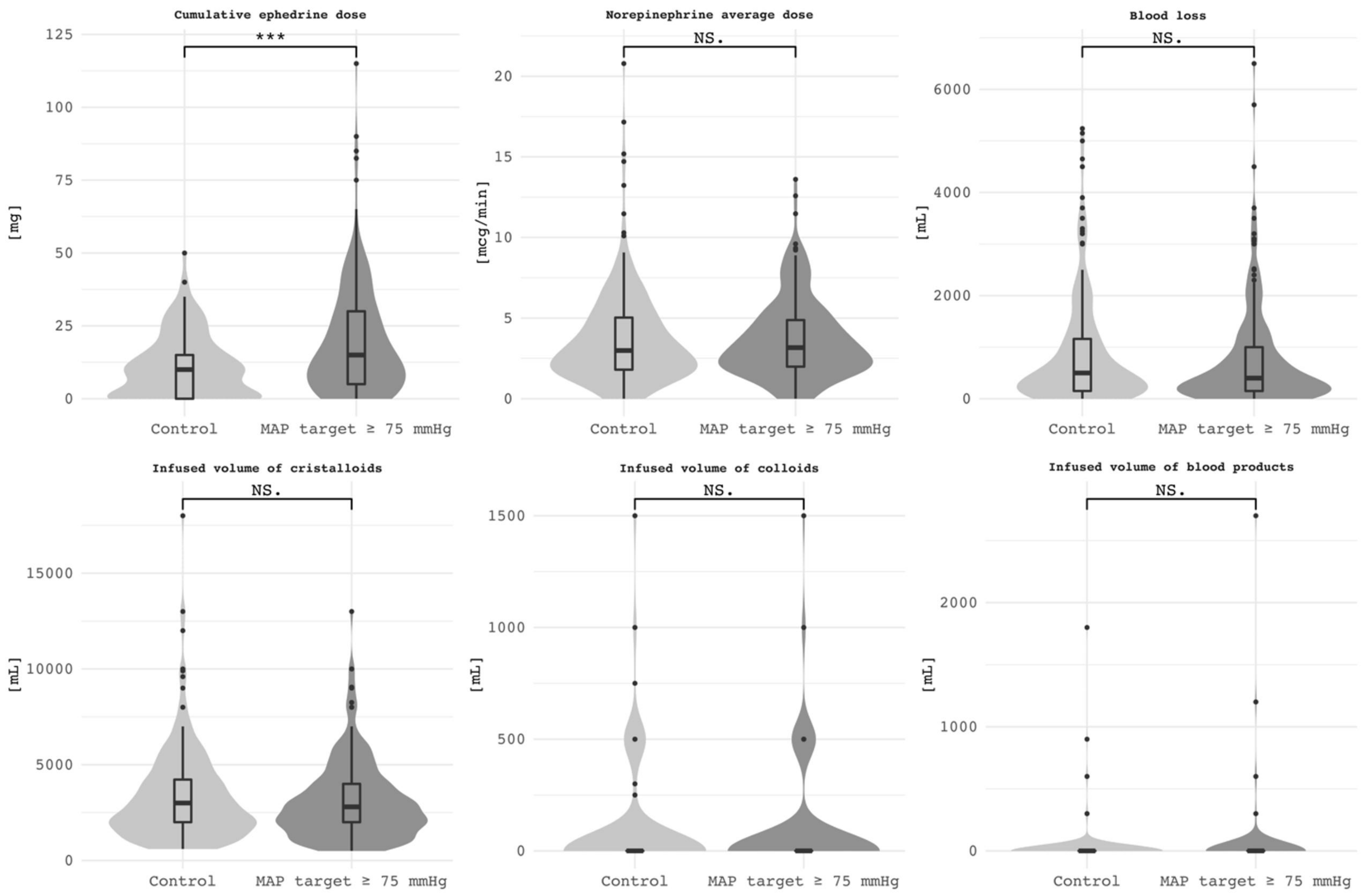


Episodes shorter & less pronounced

Results - Hemodynamic Management

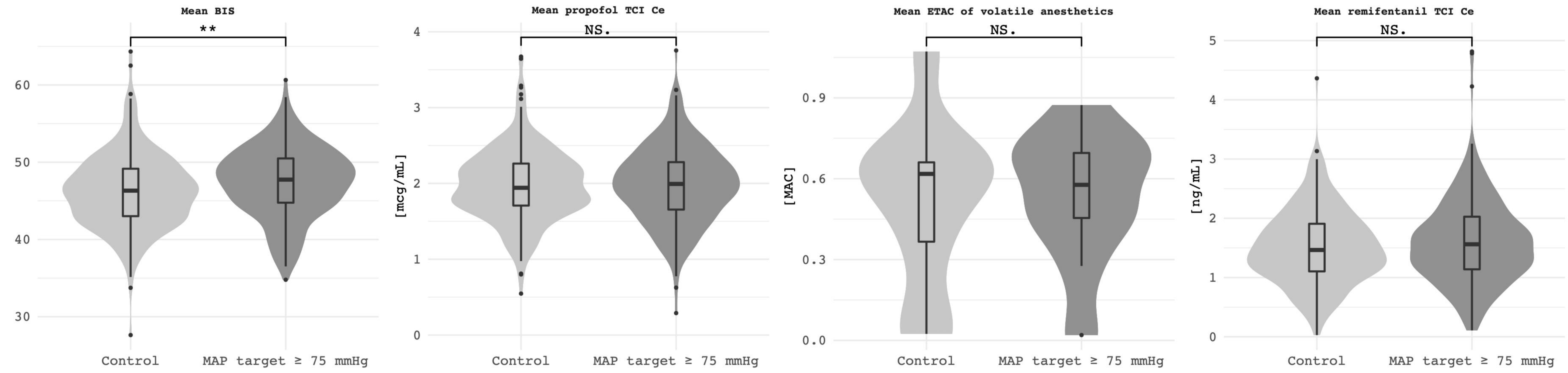
More Ephedrine in intervention Group

Few Colloids/ Blood prod.



Results - Anesthetic Management

100% GA (38% +EDA), 96% propofol/remifentanil TCI



No relevant differences in anesthetic Management

Results - Outcomes

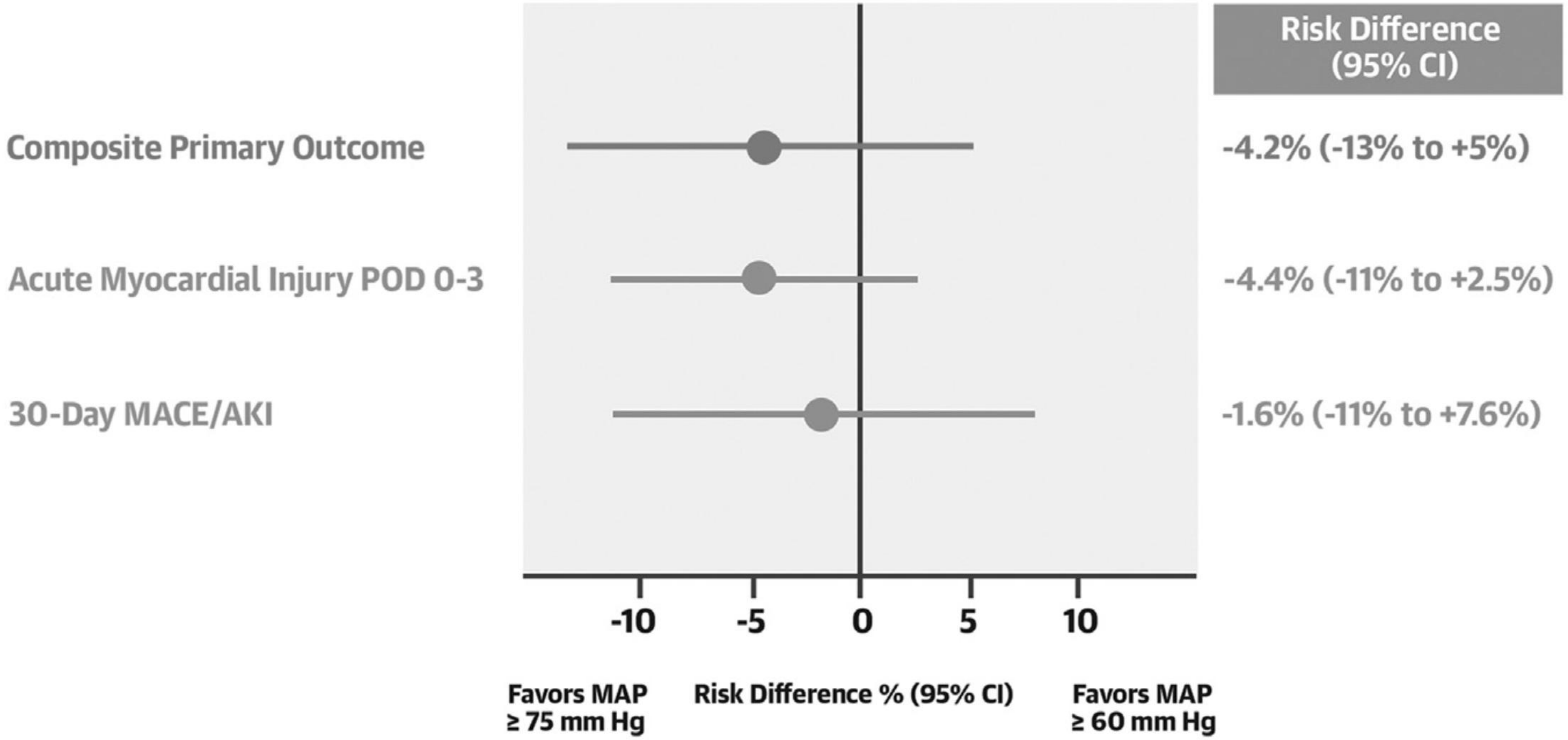
What Did We Do?	What Did We Find?

Intraoperative Randomization

Target Mean Arterial Blood Pressure (MAP) ≥75 mm Hg (Intervention)

VS

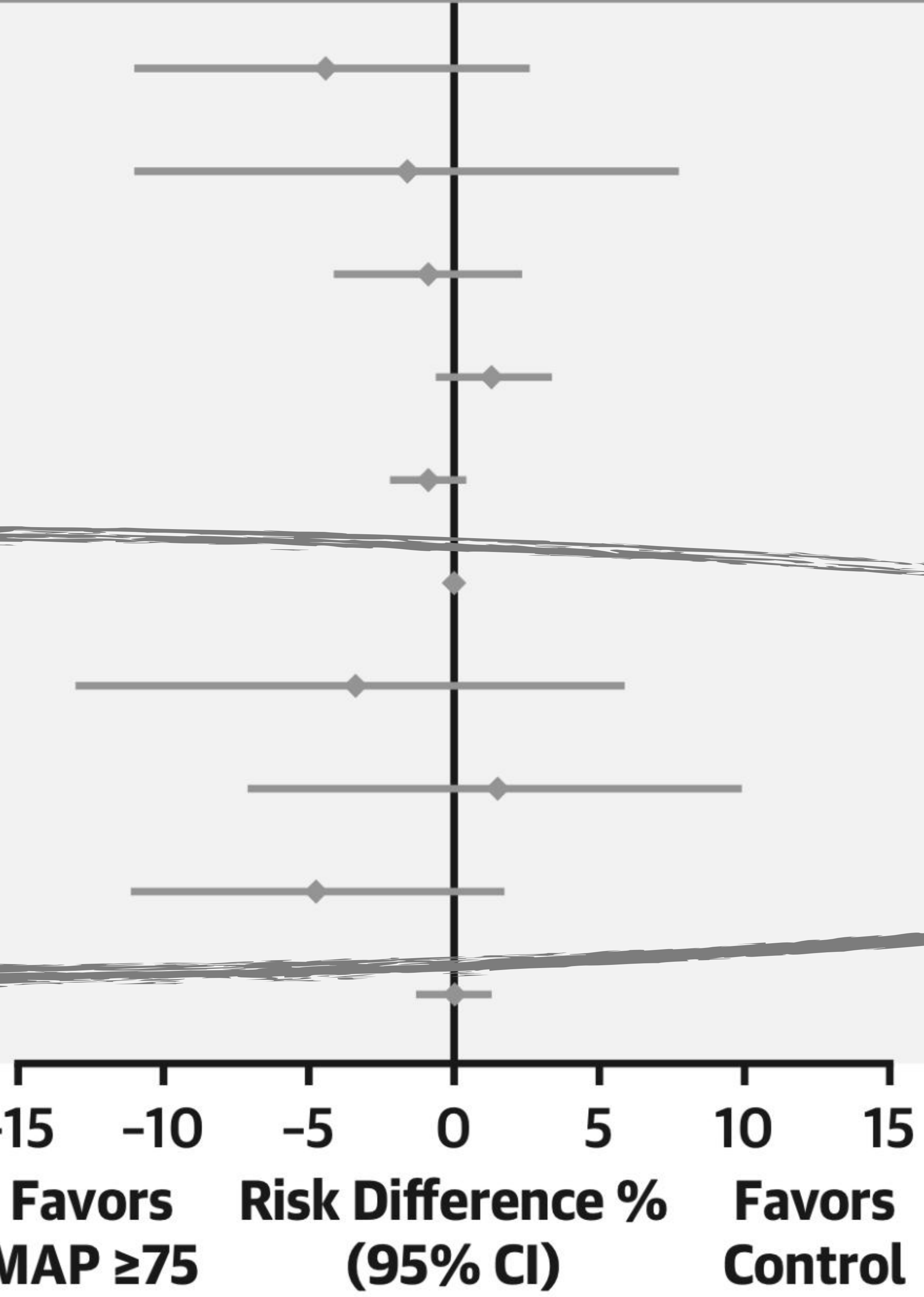
Target MAP ≥60 mm Hg (Control)



Results - Outcomes

FIGURE 3 **Effect of Targeting Higher Intraoperative Blood Pressures on MACE**

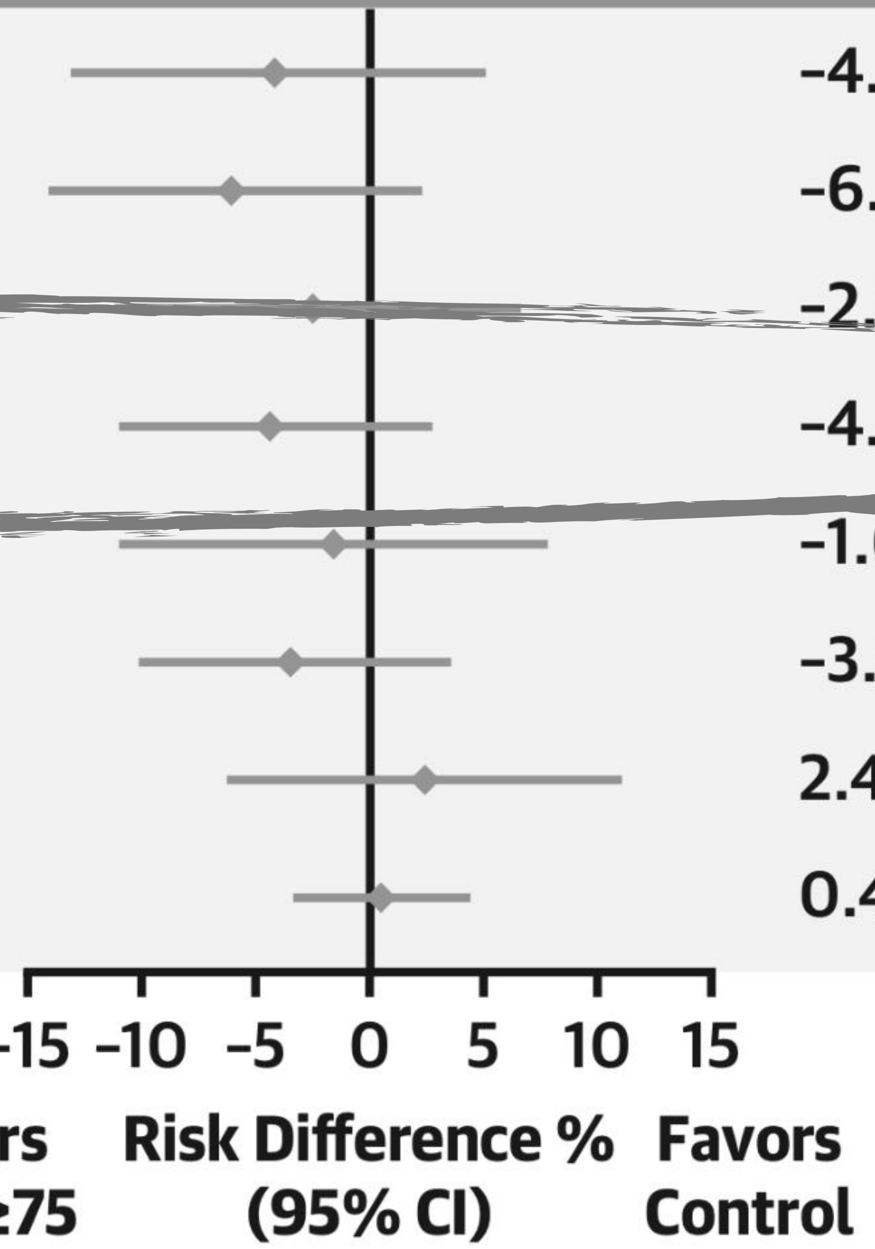
A	Control (n = 226)	MAP Target ≥75 (n = 225)	Risk Difference (95% CI)
Acute myocardial injury POD 0-3	43 (19%)	33 (15%)	-4.4% (-11% to 2.5%)
30-day MACE/AKI (composite outcome)	105 (46%)	101 (45%)	-1.6% (-11% to 7.6%)
ACS at 30 days	8 (3.5%)	6 (2.7%)	-0.87% (-4.1% to 2.3%)
CHF at 30 days	1 (0.44%)	4 (1.8%)	1.3% (-0.6% to 3.3%)
Coronary revascularization at 30 days	2 (0.88%)	0 (0%)	-0.88% (-2.1% to 0.34%)
Stroke at 30 days	0 (0%)	0 (0%)	0% (N/D)
AKI at 30 days	104 (46%)	96 (43%)	-3.4% (-13% to 5.8%)
Stage 1	66 (29%)	69 (31%)	1.5% (-7% to 9.9%)
Stages 2 & 3	38 (17%)	27 (12%)	-4.8% (-11% to 1.7%)
Death at 30 days	1 (0.44%)	1 (0.44%)	0.002% (-1.2% to 1.2%)



RESULTS - OUTCOMES

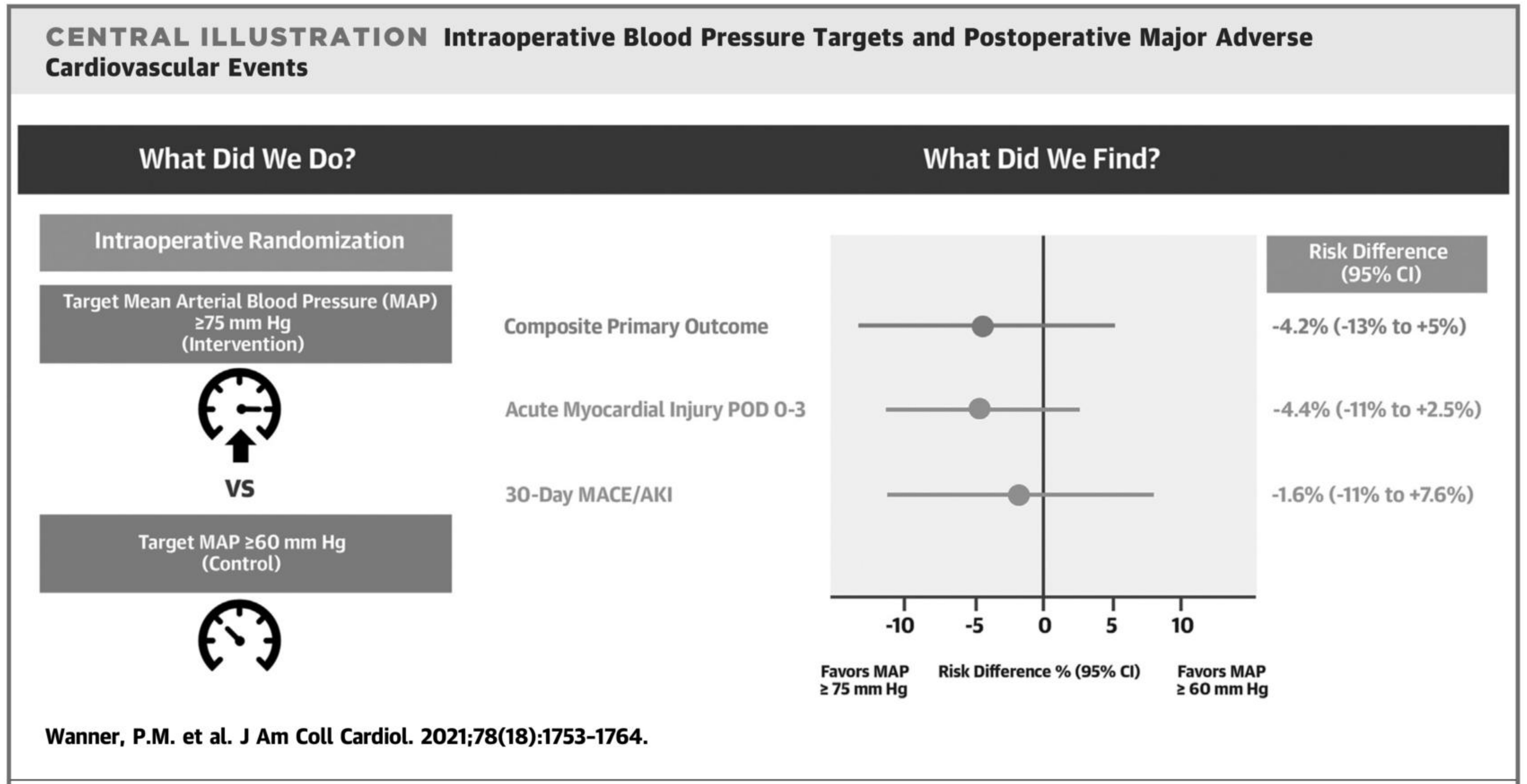
FIGURE 4 **Sensitivity Analysis of Primary Outcome and 30-Day MACE**

	Control (n = 226)	MAP Target ≥75 (n = 225)	Risk Difference (95% CI)
Primary endpoint per protocol	118 (52%)	108 (48%)	-4.2% (-13% to 5%)
Primary endpoint with AKI stages 2 & 3	68 (30%)	54 (24%)	-6.1% (-14% to 2.1%)
Primary endpoint with AKI defined only by lab constellation	90 (40%)	84 (37%)	-2.5% (-11% to 6.5%)
Primary endpoint without AKI	45 (20%)	35 (16%)	-4.4% (-11% to 2.7%)
30-day MACE/ AKI per protocol	105 (46%)	101 (45%)	-1.6% (-11% to 7.6%)
30-day MACE with AKI stages 2 & 3	43 (19%)	35 (16%)	-3.5% (-10% to 3.5%)
30-day MACE with AKI defined only by lab constellation	68 (30%)	73 (32%)	2.4% (-6.2% to 11%)
30-day MACE without AKI	9 (4%)	10 (4.4%)	0.46% (-3.2% to 4.2%)



Sensitivity analyses were performed to ascertain the effect of AKI definitions (per protocol, only stages 2 and 3, only lab constellation, without AKI) on the primary composite outcome (acute myocardial injury and/or 30-day MACE) and 30-day MACE alone, showing no significant differences in the study results. Abbreviations as in **Figure 3**.

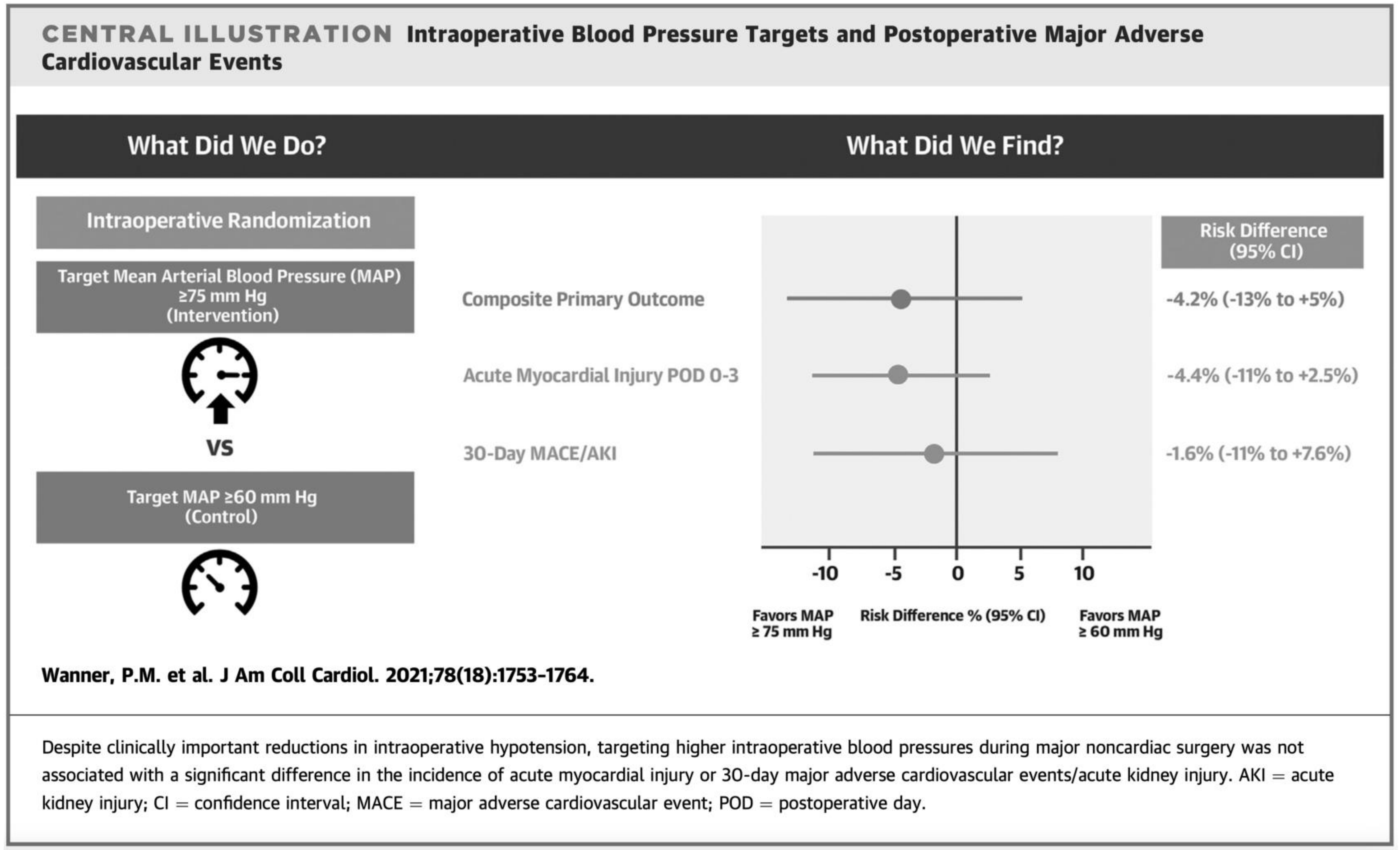
CONCLUSION



Despite clinically important reductions in intraoperative hypotension, targeting higher intraoperative blood pressures during major noncardiac surgery was not associated with a significant difference in the incidence of acute myocardial injury or 30-day major adverse cardiovascular events/acute kidney injury. AKI = acute kidney injury; CI = confidence interval; MACE = major adverse cardiovascular event; POD = postoperative day.

Results do not support universally targeting higher BPs to prevent myocardial injury or 30-day MACE/AKI.

CONCLUSION



<u>Results</u> do not support universally targeting higher BPs to prevent myocardial injury or 30-day MACE/AKI.

<u>Future research:</u> larger studies, focus on personalized BP management

WHAT ABOUT OTHER TRIALS ?

INPRESS

Findings of other trials - INPRESS

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery

A Randomized Clinical Trial

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French Multicenter RCT

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French Multicenter RCT

Patients > 50y, major surgery > 2h, at risk of AKI

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Patients > 50y, major surgery > 2h, at risk of AKI

Individualized vs. Standard BP therapy

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Study design

The Intraoperative Norepinephrine to control arterial PRESSure (INPRESS) trial is a multicenter, prospective, randomized, stratified, parallel-group clinical trial with concealed allocation of patients at high-risk of postoperative complications after abdominal surgery in a 1:1 ratio to a standard or an individualized treatment strategy:

- Control group = standard (curative) treatment strategy
  In the standard treatment group, patients will receive intravenous boluses of ephedrine to treat any drop in SBP below 80 mmHg or lower than 40% from the patient resting blood pressure (used as the reference value)

- Intervention group = individualized (preventive) treatment strategy
  In the individualized treatment group, patients will receive continuous infusion of norepinephrine to maintain SBP within ±10% of the patient resting blood pressure (used as the reference value)

In the two treatment groups, the patient resting blood pressure will be used as the reference value. If not available, the blood pressure value obtained in the surgical ward the day before surgery (after a 5-min rest while lying supine) will be used as reference value.

Findings of other trials - INPRESS

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Control:
SBP > 80, within 40% resting BP
<u>Ephedrine</u>

Findings of other trials - INPRESS

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In the two treatment groups, the patient resting blood pressure will be used as the reference value. If not available, the blood pressure value obtained in the surgical ward the day before surgery (after a 5-min rest while lying supine) will be used as reference value.

Intervention:
SBP within 10% resting BP
Noradrenaline

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The Intraoperative Norepinephrine to control arterial PRESSure (INPRESS) trial is a multicenter, prospective, randomized, stratified, parallel-group clinical trial with concealed allocation of patients at high-risk of postoperative complications after abdominal surgery in a 1:1 ratio to a standard or an individualized treatment strategy:

- Control group = standard (curative) treatment strategy
  In the standard treatment group, patients will receive intravenous boluses of ephedrine to treat any drop in SBP below 80 mmHg or lower than 40% from the patient resting blood pressure (used as the reference value)

- Intervention group = individualized (preventive) treatment strategy
  In the individualized treatment group, patients will receive continuous infusion of norepinephrine to maintain SBP within ±10% of the patient resting blood pressure (used as the reference value)

In the two treatment groups, the patient resting blood pressure will be used as the reference value. If not available, the blood pressure value obtained in the surgical ward the day before surgery (after a 5-min rest while lying supine) will be used as reference value.

Resting BP ~ values surgical ward day before surgery

Findings of other trials - INPRESS

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery

A Randomized Clinical Trial

Emmanuel Futier, MD, PhD; Jean-Yves Lefrant, MD, PhD; Pierre-Gregoire Guinot, MD, PhD; Thomas Godet, MD, PhD; Emmanuel Lorne, MD; Philippe Cuvillon, MD, PhD; Sebastien Bertran, MD; Marc Leone, MD, PhD; Bruno Pastene, MD; Vincent Piriou, MD, PhD; Serge Molliex, MD, PhD; Jacques Albanese, MD, PhD; Jean-Michel Julia, MD; Benoit Tavernier, MD, PhD; Etienne Imhoff, MD; Jean-Etienne Bazin, MD, PhD; Jean-Michel Constantin, MD, PhD; Bruno Pereira, PhD; Samir Jaber, MD, PhD; for the INPRESS Study Group

French Multicenter RCT

Patients > 50y, major surgery > 2h, at risk of AKI

Individualized vs. Standard BP therapy

Primary outcome: Posoperative organ dysfunction (SIRS + any organ failure: renal, CV, resp, neuro, coagulation)

Findings of other trials - INPRESS

Table 1. Baseline Characteristics of Patients

Characteristic	Individualized Treatment (n = 147)	Standard Treatment (n = 145)
Age		
Overall, mean (SD), y	69.7 (7.1)	70.0 (7.5)
Among those aged ≥70 y, mean (SD), y	75.6 (4.3)	76.1 (4.8)
≥70 y, No. (%)	71 (48.3)	73 (50.3)
Male, No. (%)	125 (85.0)	123 (84.8)
Height, mean (SD), cm	170.7 (7.4)	171.3 (7.6)
Predicted body weight, mean (SD), kg[a]	65.9 (7.8)	66.4 (8.1)
ASA physical status class, No. (%)[b]		
II	62 (42.2)	54 (37.2)
III	84 (57.1)	89 (61.4)
≥IV	1 (0.7)	2 (1.4)
Acute kidney injury risk index class, No. (%)[c]		
III	76 (51.7)	71 (49.0)
IV	51 (34.7)	52 (35.9)
V	20 (13.6)	22 (15.1)
Reference blood pressure, mean (SD), mm Hg[d]		
Systolic	135.4 (20.2)	135.3 (17.1)
Diastolic	75.1 (11.6)	77.4 (12.1)
Preexisting conditions, No. (%)		
Chronic arterial hypertension	120 (81.6)	120 (82.8)
Chronic heart failure	26 (17.7)	38 (26.2)
Ischemic heart disease	20 (13.6)	32 (22.1)
Renal impairment	28 (19.1)	17 (11.7)
Diabetes mellitus	77 (52.4)	73 (50.3)
Type of surgery, No. (%)		
Abdominal	138 (93.9)	140 (96.6)
Nonabdominal	9 (6.1)	5 (3.4)
Urgency of surgical procedure, No. (%)		
Elective	124 (84.4)	123 (84.8)
Emergency	23 (15.6)	22 (15.2)
Medication use, No. (%)		
Antihypertensive		
Overall	100 (68.0)	97 (66.9)
Angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker	71 (48.2)	72 (49.6)
Medications not taken within 24 h prior to surgery	61 (61.0)	58 (59.8)
Diuretic	24 (16.3)	20 (13.8)
Antidiabetic	72 (49.0)	68 (46.9)
Serum creatinine at inclusion, mean (SD), mg/dL	0.93 (0.30)	0.93 (0.34)
Estimated GFR[e]		
Overall, median (IQR), mL/min/1.73 m^2	88.0 (71.6-105.1)	87.8 (71.0-103.3)
Among those with estimated GFR <60 mL/min/1.73 m^2, median (IQR), mL/min/1.73 m^2	46.1 (43.6-54.6)	50.8 (43.8-55.6)
Estimated GFR <60 mL/min/1.73 m^2, No. (%)	20 (13.7)	17 (11.9)
Digit Symbol Substitution Test score at inclusion, mean (SD)[f]	30.4 (13.1)	29.3 (12.4)

95% abdominal surgery

Findings of other trials - INPRESS

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

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Table 3. Primary and Secondary Outcomes and Adverse Events

Variable	Individualized Treatment (n = 147)	Standard Treatment (n = 145)	Between-Group Absolute Difference, % (95% CI)	Unadjusted Relative Risk (95% CI)	*P* Value	Adjusted Relative Risk (95% CI)[a]	*P* Value
Primary Outcome							
Primary composite outcome, No. (%)[b]	56 (38.1)	75 (51.7)	−14 (−25 to −2)	0.74 (0.57 to 0.95)	.02	0.73 (0.56 to 0.94)	.02

[b] The primary outcome was a composite of SIRS and at least 1 organ system dysfunction for the renal, respiratory, cardiovascular, coagulation, and neurologic systems by day 7 after surgery.

Primary composite outcome

RR 0.74 (0.57 to 0.95)

Findings of other trials - INPRESS

Table 3. Primary and Secondary Outcomes and Adverse Events

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Secondary Outcomes							
Complications within 7 d							
SIRS							
No. (%)	108 (73.5)	105 (72.4)	1 (−9 to 11)	0.84 (0.65 to 1.10)	.20	1.01 (0.92 to 1.12)	.78
SIRS score, No. (%)[c]							
2	49 (33.3)	36 (24.8)	9 (−2 to 19)	1.18 (0.90 to 1.59)	.29	1.19 (0.89 to 1.59)	.25
≥3	59 (40.1)	69 (47.6)	−8 (−19 to 4)	0.84 (0.65 to 1.10)	.20	0.81 (0.64 to 1.02)	.07
Daily SIRS score, mean (95% CI)[c]	1.5 (1.3 to 1.7)	1.6 (1.4 to 1.7)			.62		.61
Acute kidney injury according to RIFLE criteria, No. (%)[d]							
Risk	23 (15.7)	36 (24.8)	−9 (−18 to 0)	0.63 (0.39 to 1.00)	.05	0.73 (0.47 to 1.14)	.17
Injury	16 (10.9)	26 (17.9)	−7 (−15 to 1)	0.61 (0.34 to 1.08)	.09	0.61 (0.34 to 1.08)	.09
Failure	9 (6.1)	9 (6.2)	0 (−6 to 5)	0.99 (0.40 to 2.41)	.98	0.97 (0.40 to 2.34)	.95
Use of renal replacement therapy, No. (%)	4 (2.7)	5 (3.5)	0 (−5 to 3)	0.79 (0.22 to 2.88)	.72	0.81 (0.22 to 2.97)	.76
Acute heart failure, No. (%)	1 (0.7)	0	1 (−1 to 2)				
Myocardial ischemia or infarction, No. (%)	0	1 (0.7)	−1 (−2 to 1)				
Altered consciousness, No. (%)[e]	8 (5.4)	23 (15.9)	−10 (−17 to −3)	0.34 (0.16 to 0.74)	.007	0.34 (0.16 to 0.75)	.007
Stroke, No. (%)	0	0					
Coagulation SOFA score ≥2, No. (%)	16 (11.0)	11 (7.6)	3 (−3 to 10)	1.44 (0.69 to 3.01)	.33	1.47 (0.07 to 2.23)	.07
Hypoxemia, No. (%)	21 (14.3)	33 (22.8)	−8 (−17 to 0)	0.63 (0.38 to 1.03)	.07	0.64 (0.40 to 1.03)	.07
Pneumonia, No. (%)	4 (2.7)	11 (7.6)	−5 (−10 to 0)	0.36 (0.12 to 1.10)	.07	0.36 (0.12 to 1.10)	.07
ARDS, No. (%)	7 (4.8)	7 (4.8)	0 (−5 to 5)	0.99 (0.35 to 2.74)	.98	0.98 (0.35 to 2.67)	.95
Reintubation, No. (%)	10 (6.8)	15 (10.3)	−4 (−10 to 3)	0.66 (0.31 to 1.42)	.28	0.66 (0.31 to 1.42)	.28
Need for noninvasive or invasive ventilation, No. (%)	25 (17.0)	36 (24.8)	−8 (−17 to 1)	0.68 (0.43 to 1.08)	.10	0.71 (0.45 to 1.11)	.13
SOFA score, median (IQR)[f]							
Day 1	1 (0-3)	1 (0-3)			.31		.36
Day 2	1 (0-2)	2 (0-3)			.19		.21
Day 7	0 (0-1)	0 (0-1)			.66		.68
Sepsis, No. (%)	13 (8.8)	23 (15.9)	−7 (−15 to 0)	0.56 (0.29 to 1.06)	.07	0.55 (0.29 to 1.04)	.07
Severe sepsis or septic shock, No. (%)	13 (8.8)	13 (9.0)	0 (−6 to 7)	0.99 (0.47 to 2.05)	.97	1.01 (0.49 to 2.11)	.97

Primary composite outcome
RR 0.74
(0.57 to 0.95)

Findings of other trials - INPRESS

Table 3. Primary and Secondary Outcomes and Adverse Events

Variable	Individualized Treatment (n = 147)	Standard Treatment (n = 145)	Between-Group Absolute Difference, % (95% CI)	Unadjusted Relative Risk (95% CI)	*P* Value	Adjusted Relative Risk (95% CI)[a]	*P* Value
Primary Outcome							
Primary composite outcome, No. (%)[b]	56 (38.1)	75 (51.7)	−14 (−25 to −2)	0.74 (0.57 to 0.95)	.02	0.73 (0.56 to 0.94)	.02
Secondary Outcomes							
Complications within 7 d							
SIRS							
No. (%)	108 (73.5)	105 (72.4)	1 (−9 to 11)	0.84 (0.65 to 1.10)	.20	1.01 (0.92 to 1.12)	.78
SIRS score, No. (%)[c]							
2	49 (33.3)	36 (24.8)	9 (−2 to 19)	1.18 (0.90 to 1.59)	.29	1.19 (0.89 to 1.59)	.25
≥3	59 (40.1)	69 (47.6)	−8 (−19 to 4)	0.84 (0.65 to 1.10)	.20	0.81 (0.64 to 1.02)	.07
Daily SIRS score, mean (95% CI)[c]	1.5 (1.3 to 1.7)	1.6 (1.4 to 1.7)			.62		.61
Acute kidney injury according to RIFLE criteria, No. (%)[d]							
Risk	23 (15.7)	36 (24.8)	−9 (−18 to 0)	0.63 (0.39 to 1.00)	.05	0.73 (0.47 to 1.14)	.17
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Use of renal replacement therapy, No. (%)	4 (2.7)	5 (3.5)	0 (−5 to 3)	0.79 (0.22 to 2.88)	.72	0.81 (0.22 to 2.97)	.76
Acute heart failure, No. (%)	1 (0.7)	0	1 (−1 to 2)				
Myocardial ischemia or infarction, No. (%)	0	1 (0.7)	−1 (−2 to 1)				
Altered consciousness, No. (%)[e]	8 (5.4)	23 (15.9)	−10 (−17 to −3)	0.34 (0.16 to 0.74)	.007	0.34 (0.16 to 0.75)	.007
Stroke, No. (%)	0	0					
Coagulation SOFA score ≥2, No. (%)	16 (11.0)	11 (7.6)	3 (−3 to 10)	1.44 (0.69 to 3.01)	.33	1.47 (0.07 to 2.23)	.07
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Severe sepsis or septic shock, No. (%)	13 (8.8)	13 (9.0)	0 (−6 to 7)	0.99 (0.47 to 2.05)	.97	1.01 (0.49 to 2.11)	.97

Altered Consc.
RR 0.34
(0.16 to 0.74)

Findings of other trials - INPRESS

Table 3. Primary and Secondary Outcomes and Adverse Events

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AKI RR 0.67 (0.50 to 0.89)

POISE-3

Findings of other trials - POISE-3 (ACC 2022)

Findings of other trials - POISE-3 (ACC 2022)

Multinational Partial 2x2 factorial RCT

Findings of other trials - POISE-3 (ACC 2022)

Multinational Partial 2x2 factorial RCT

Patients > 45y at risk of Cardiovasc. Events, chron. Antihypertensive tx

Findings of other trials - POISE-3 (ACC 2022)

Multinational Partial 2x2 factorial RCT

Patients > 45y at risk of Cardiovasc. Events, chron. Antihypertensive tx

Hypotension vs. Hypertension-avoidance strategy

HYPOtension-avoidance

HYPOTENSION-AVOIDANCE

ACE-I/ARB HELD PREOP AND FOR 2D POSTOP, ALGORITHM FOR OTHER ANTIHYPERTENSIVES

HYPOtension-avoidance

ACE-I/ARB held preop and for 2d postop, algorithm for other antihypertensives

Intraop. MAP target >= 80 mmHg

HYPERtension-avoidance

HYPERtension-avoidance

Periop. Continuation of all chronic antihypertensive meds

HYPERtension-avoidance

Periop. Continuation of all chronic antihypertensive meds

Intraop. MAP target >= 60 mmHg

Findings of other trials - POISE-3 (ACC 2022)

Multinational Partial 2x2 factorial RCT

Patients > 45y at risk of Cardiovasc. Events, chron. Antihypertensive tx

Hypotension vs. Hypertension-avoidance strategy

Findings of other trials - POISE-3 (ACC 2022)

Multinational Partial 2x2 factorial RCT

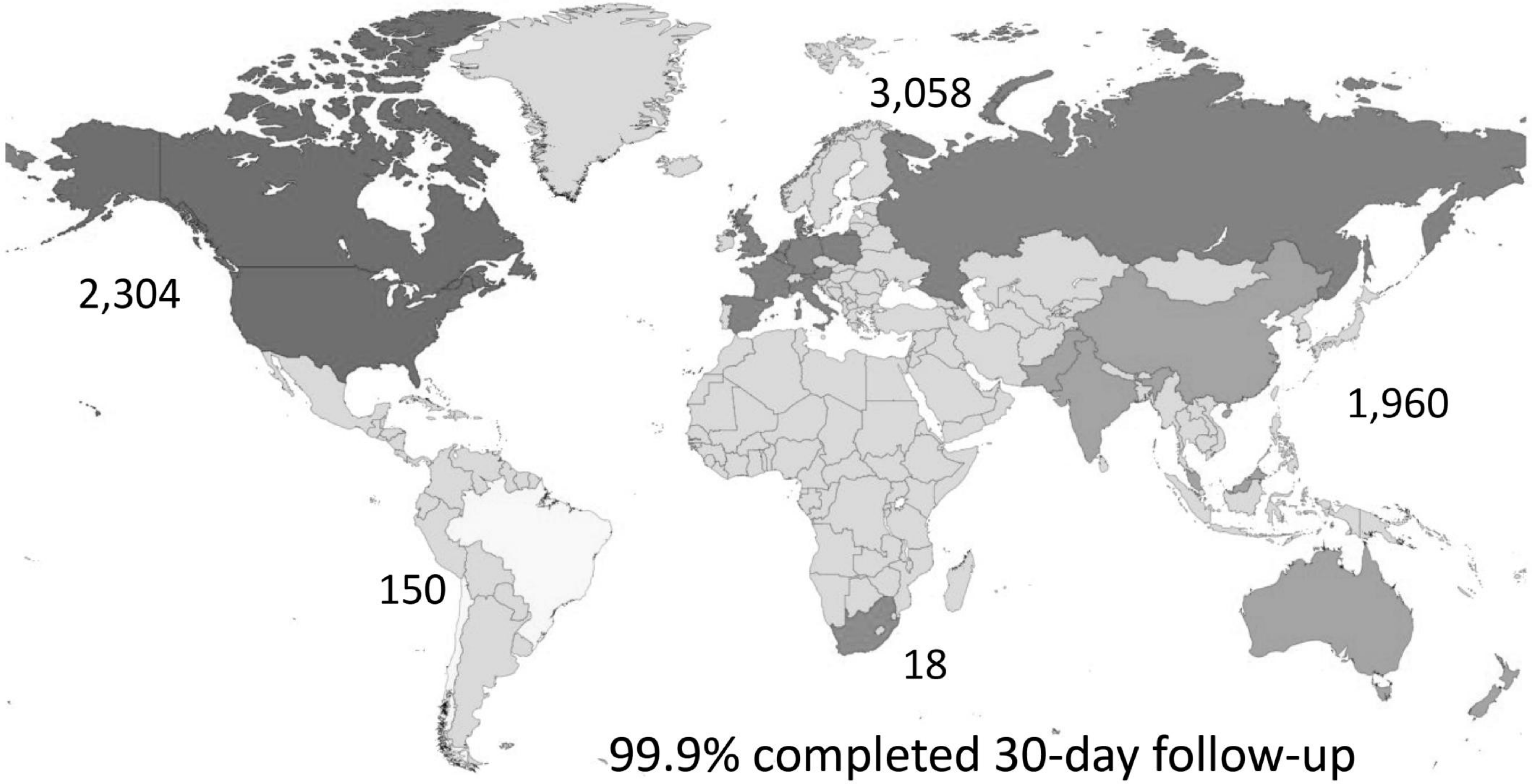
Patients > 45y at risk of Cardiovasc. Events, chron. Antihypertensive tx

Hypotension vs. Hypertension-avoidance strategy

Primary outcome: major vascular complication (vasc. Death, non-fatal MINS, stroke, cardiac arrest at 30 days)

Findings of other trials - POISE-3 (ACC 2022)

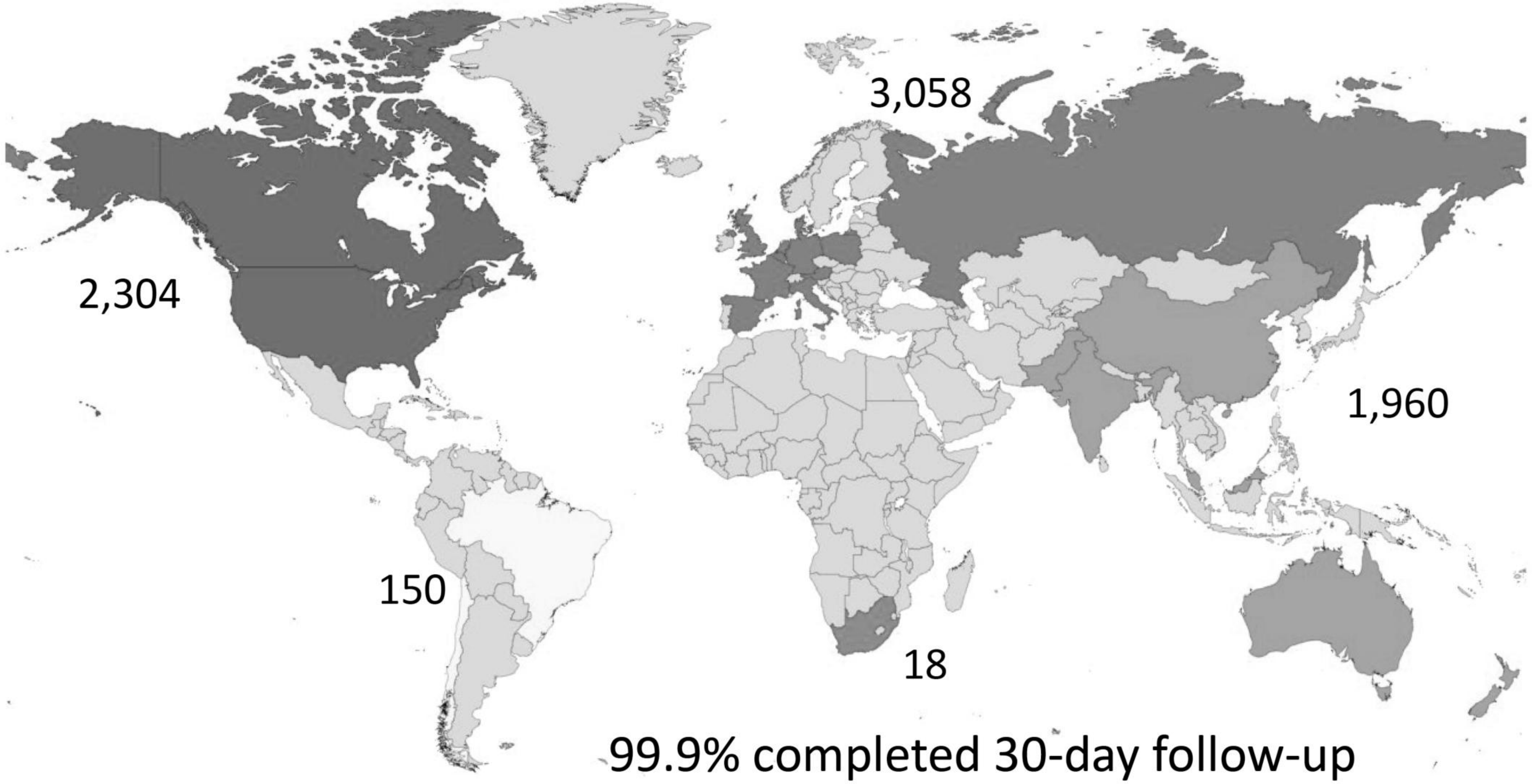
7490 patients randomized
110 centres, 22 countries



99.9% completed 30-day follow-up

Findings of other trials - POISE-3 (ACC 2022)

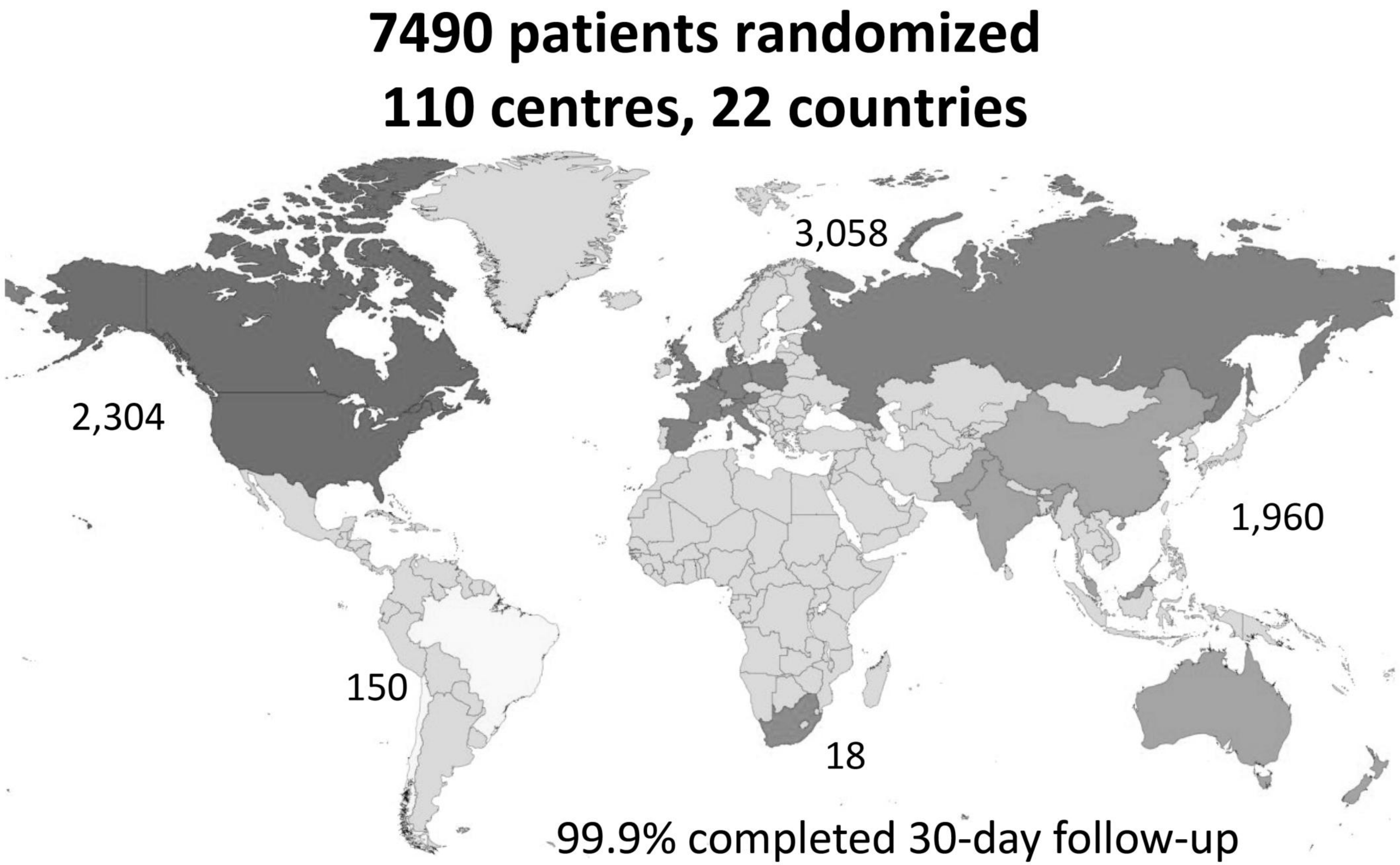
7490 patients randomized
110 centres, 22 countries



99.9% completed 30-day follow-up

36% general surgery
24% orthopedic surgery
14% vascular surgery

Findings of other trials - POISE-3 (ACC 2022)



HR 0.99 (0.88 to 1.12) for major vascular complications with Hypotension vs. Hypertension-avoidance

Results - Baseline characteristics

TABLE 1 Characteristics of Patients at Baseline

	Control (n = 226)	MAP Target ≥75 mm Hg (n = 225)
Age, y	69 ± 10	70 ± 8
Sex		
Male	182 (81)	186 (83)
Female	44 (19)	39 (17)
ASA physical status		
2	81 (36)	76 (34)
3	142 (63)	144 (64)
4	3 (1)	5 (2)
Charlson comorbidity index		
0	44 (19)	37 (16)
1	52 (23)	33 (15)
2	40 (18)	62 (28)
3	40 (18)	44 (20)
4	32 (14)	31 (14)
5	12 (5)	6 (3)
6	1 (0)	6 (3)
7	2 (1)	2 (1)
8	0 (0)	2 (1)
9	2 (1)	2 (1)
10	1 (0)	0 (0)
Revised cardiac risk index		
0	2 (1)	2 (1)
1	109 (48)	95 (42)
2	81 (36)	94 (42)
3	29 (13)	29 (13)
4	4 (2)	5 (2)
5	1 (0)	0 (0)
Fulfilment of ≥3 Lee criteria	38 (17)	34 (15)
History of coronary artery disease	84 (37)	111 (49)
History of peripheral artery disease	94 (42)	110 (49)
History of congestive heart failure	1 (0)	2 (1)
History of stroke	23 (10)	11 (5)
History of transient ischemic attack	7 (3)	9 (4)
Preoperative serum creatinine >175 µmol/L	33 (15)	34 (15)
Insulin-dependent diabetes mellitus	24 (11)	19 (8)
Preoperative brain-type natriuretic peptide	52 (29-102)	54 (28-108)
Preoperative high-sensitivity cardiac troponin I	10 (10-11)	10 (10-10)
ACE inhibitor		
None	160 (71)	147 (65)
Continued perioperatively	66 (29)	78 (35)
Stopped perioperatively	0 (0)	0 (0)
Angiotensin receptor blocker		
None	154 (68)	165 (73)
Continued perioperatively	71 (31)	59 (26)
Stopped perioperatively	1 (0)	1 (0)
Beta-blocker		
None	114 (50)	116 (52)
Continued perioperatively	112 (50)	108 (48)
Stopped perioperatively	0 (0)	1 (0)
Calcium-channel blocker		
None	169 (75)	163 (72)
Continued perioperatively	57 (25)	60 (27)
Stopped perioperatively	0 (0)	2 (1)
Operations		
Gynecological surgery	4 (2)	1 (0)
Orthopedic surgery	6 (3)	7 (3)
Thoracic surgery	11 (5)	18 (8)
Urological surgery	15 (7)	31 (14)
Vascular surgery	161 (71)	142 (63)
Visceral surgery	29 (13)	26 (12)

Continued on the next page

TABLE 1 Continued

Values are mean ± SD, n (%), or median (interquartile range).
ACE = angiotensin-converting enzyme; ASA = American Society of Anesthesiologists.

67% Vascular Surgery

12% Abdominal Surgery

10% Urological Surgery