



Hypotension-avoidance strategy versus hypertension-avoidance strategy in patients undergoing noncardiac surgery

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Background

- >300 millions/year adult noncardiac surgeries
- Major vascular complications frequent
- Hemodynamics abnormalities frequent
 - >25% intraoperative and/or postoperative hypotension
 - linked to major vascular complications
- >50% take chronic antihypertensive medications
 - commonly continued perioperatively (although practice varies)

Rationale

- Small studies with methodological limitations suggest
 - withholding ACEIs/ARBs may reduce perioperative hypotension and vascular complications
 - withholding beta-blockers may increase perioperative vascular complications
- Intraoperative mean arterial pressure (MAP) targets ≥ 60 mm Hg are commonly used
 - however, based on observational data, it has been questioned whether MAP targets ≥ 80 mm Hg would improve outcomes

Uncertainty remains regarding optimal perioperative blood pressure management

Research question

- In patients undergoing noncardiac surgery who are at risk of vascular events
 - what are effects of perioperative hypotension-avoidance strategy versus hypertension-avoidance strategy on
 - 30-day incidence of major vascular complications?

Design

- 10,000 patients in tranexamic acid or placebo trial
- Partial 2x2 factorial design
- Expected 6,500 patients in blood pressure trial
- Patients, healthcare providers, and study personnel aware of blood pressure treatment assignment
- Outcome adjudicators masked to treatment assignment

Eligibility criteria

- Included patients
 - ≥45 years old, undergoing inpatient noncardiac surgery
 - at risk of perioperative cardiovascular events
 - chronically taking ≥1 antihypertensive medication
- Excluded patients
 - NYHA class III-IV, or LVEF ≤30%

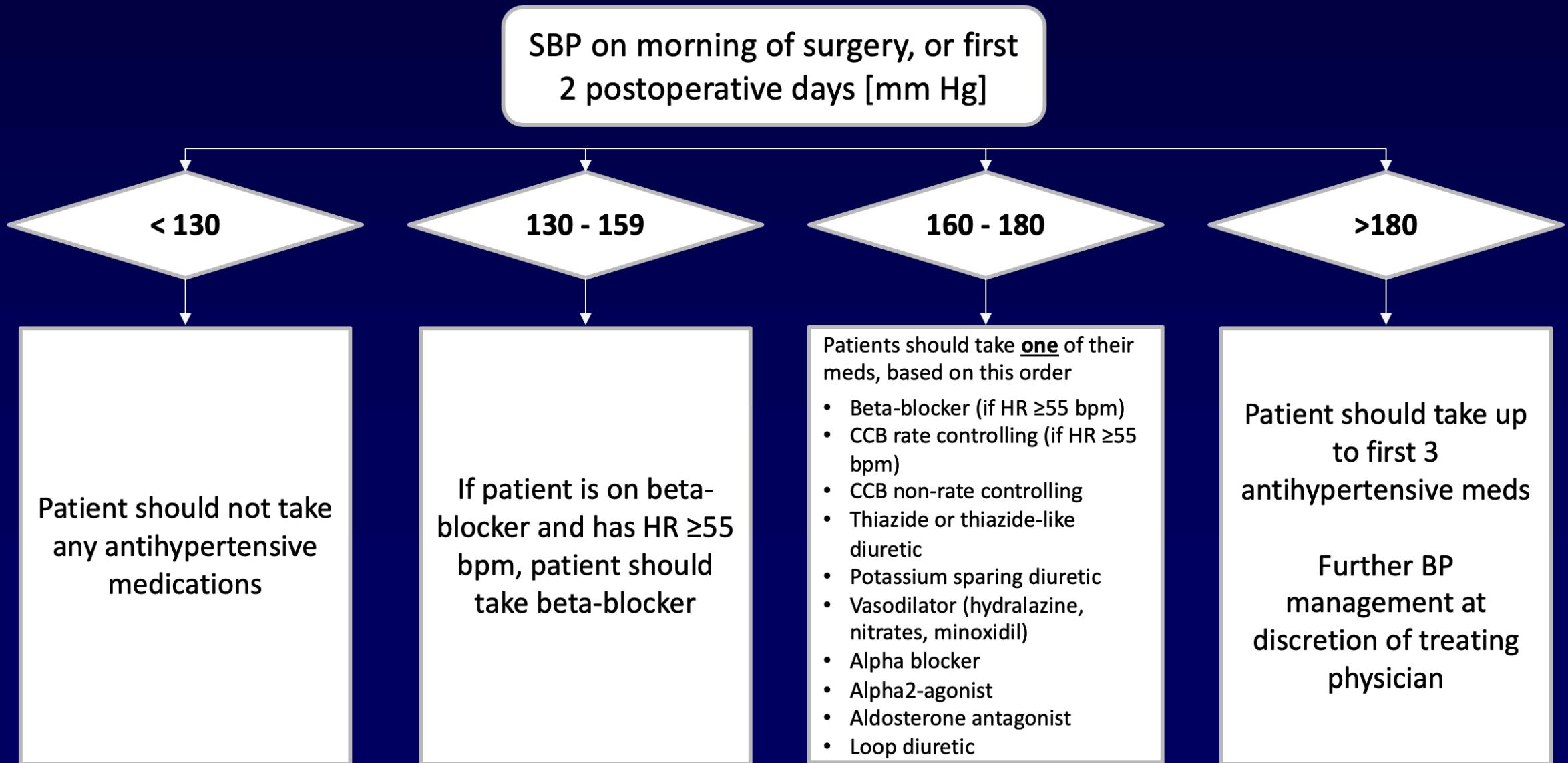
Intervention

- Patients told not to take antihypertensive medications night before and morning of surgery
 - bring medications to preoperative holding area
- hypotension-avoidance vs hypertension-avoidance
 - based on blood pressure abnormality preferentially intended to avoid

Hypotension-avoidance strategy

- Preoperative management
 - hold chronic ACEI/ARBs
 - other chronic antihypertensive meds based on algorithm
- Intraoperative management
 - target MAP ≥ 80 mm Hg
- Postoperative management for first 2 days after surgery
 - hold chronic ACEI/ARBs
 - other chronic antihypertensive meds based on algorithm

Hypotension-avoidance algorithm



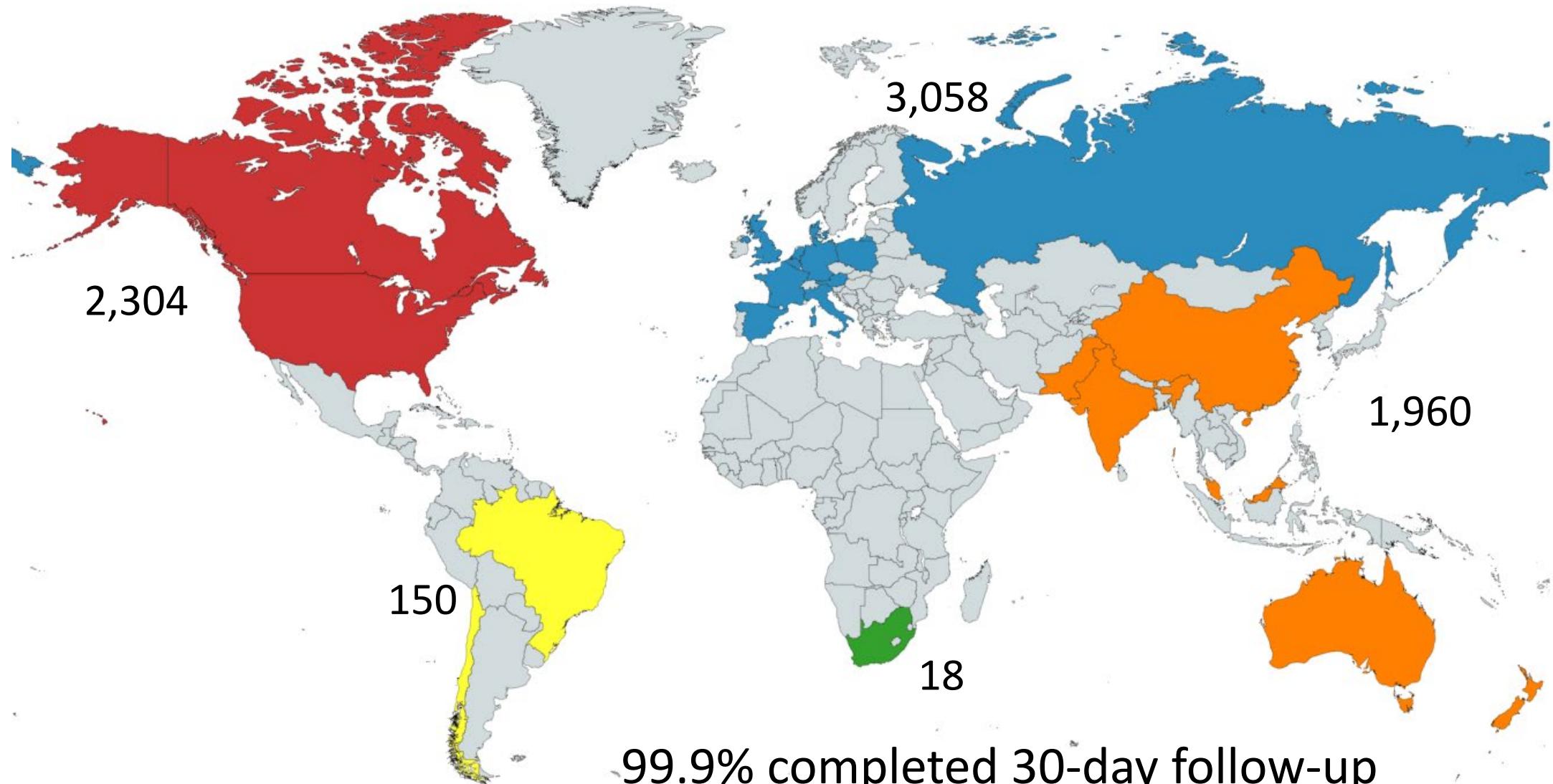
Hypertension-avoidance strategy

- Preoperative management
 - given chronic antihypertensive medications
- Intraoperative management
 - target MAP \geq 60 mm Hg
- Postoperative management
 - restart chronic antihypertensive medications after surgery

Primary outcome

- Major vascular complication
 - composite of vascular death and nonfatal myocardial injury after noncardiac surgery (MINS), stroke, and cardiac arrest at 30 days after randomization

**7490 patients randomized
110 centres, 22 countries**



Baseline characteristics

	Hypotension-avoidance (N = 3742)	Hypertension-avoidance (N = 3748)
age, years	70	70
male	2075 (56%)	2096 (56%)
number of chronic antihypertensive meds		
mean (sd)	2 (1)	2 (1)
≥3 meds	1038 (28%)	1011 (27%)
chronic ACEI or ARB	2684 (72%)	2684 (72%)
chronic beta-blocker	1668 (45%)	1601 (43%)

Intraoperative compliance

	Hypotension-avoidance (N = 3742)	Hypertension-avoidance (N = 3748)	Median difference (95% CI)
Intraoperative MAPs	Minutes, median (IRQ)*		
MAP <60	0 (0 - 0)	0 (0 - 2)	NA
MAP 60-79	25 (5 - 63)	56 (20 - 108)	-31 (-34 to -28)
MAP ≥80	101 (55 - 165)	70 (26 - 125)	31 (27 to 36)

*mean duration of surgery 170 minutes

Pre- and postoperative compliance

	Hypotension-avoidance (N = 3742)	Hypertension-avoidance (N = 3748)
Day	% compliance (95% CI)	
Day of Surgery*	68 (67 - 70)	57 (55 - 58)
Postoperative day 1	75 (73 - 76)	67 (65 - 68)
Postoperative day 2	72 (71 - 74)	70 (69 - 72)

*before and after surgery

Medications received perioperatively

	Day of surgery		Day 1 after surgery		Day 2 after surgery	
	Hypo	Hyper	Hypo	Hyper	Hypo	Hyper
received ACEI/ARB	5%	38%	6%	47%	7%	50%
received beta-blocker	23%	32%	25%	36%	28%	37%
received ≥ 1 antihypertensive	36%	70%	39%	79%	42%	83%

Hypo = hypotension-avoidance
Hyper = hypertension-avoidance

Primary outcome

	Hypotension-avoidance N = 3742 n (%)	Hypertension-avoidance N = 3748 n (%)	Hazard ratio (95% CI)	P value
Major vascular complication	520 (13.9)	524 (14.0)	0.99 (0.88-1.12)	0.92

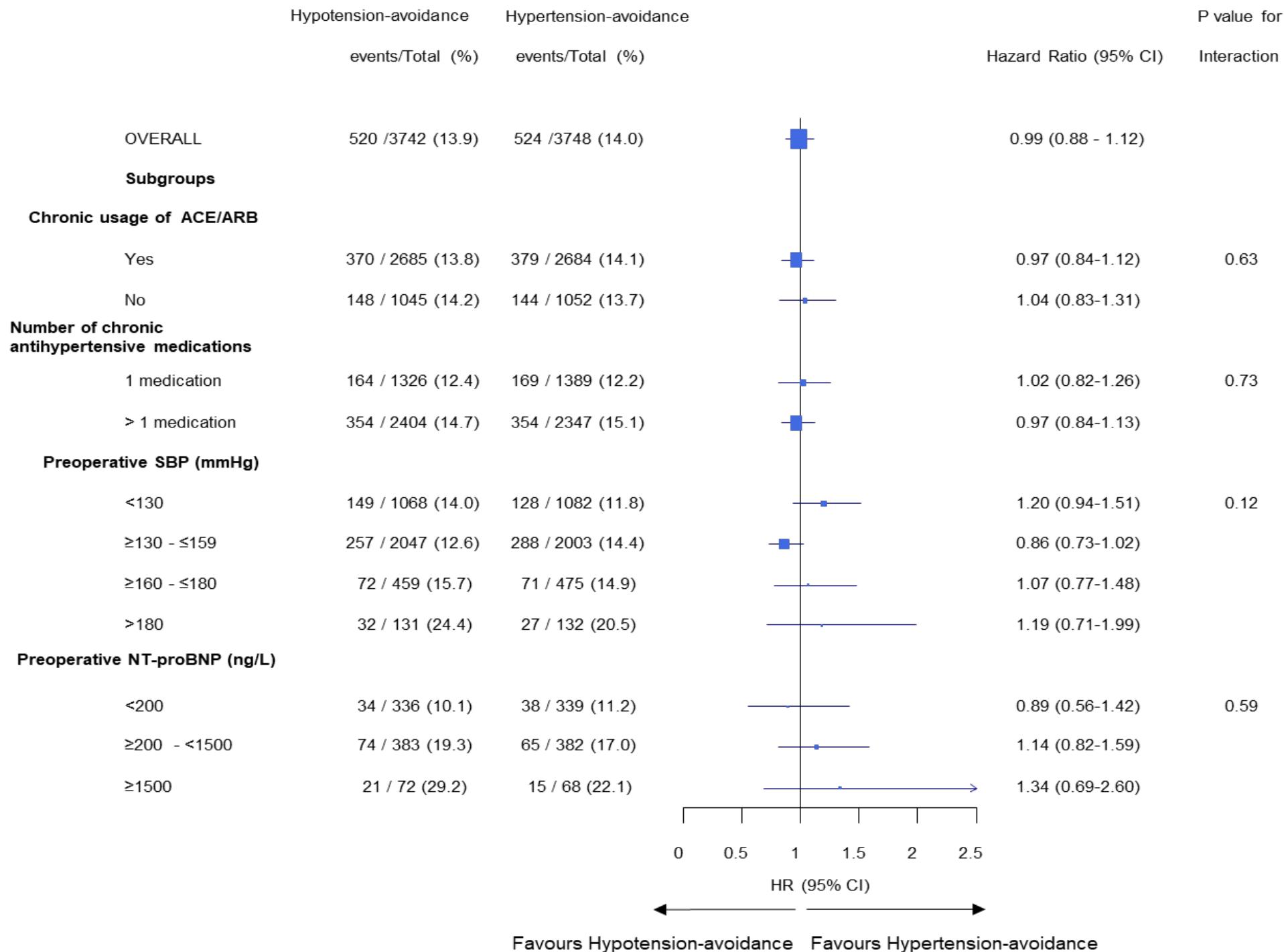
- Results not modified by status of randomization to tranexamic acid or placebo group (interaction P=0.54)

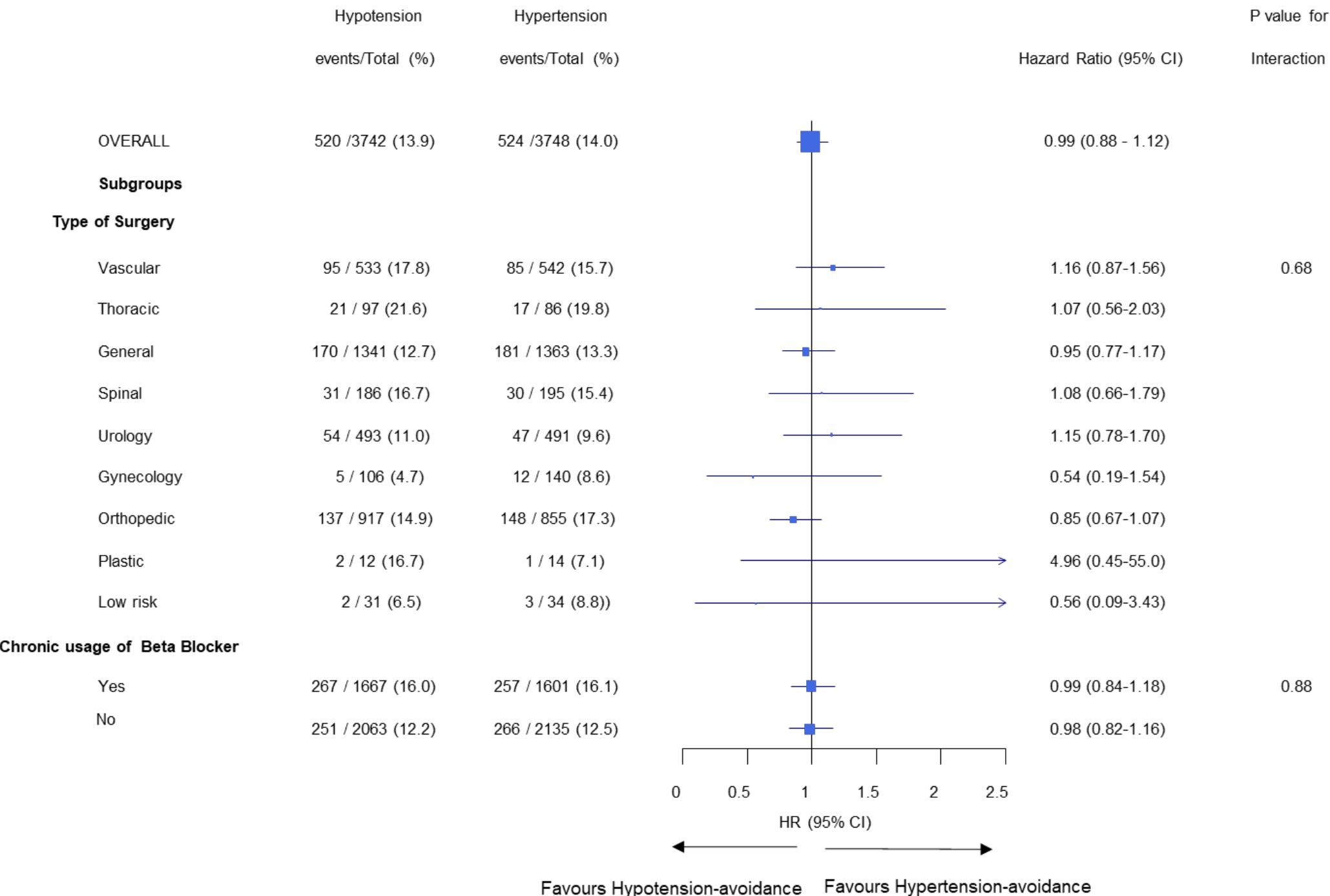
Secondary outcomes

	Hypotension-avoidance N = 3742 n (%)	Hypertension-avoidance N = 3748 n (%)	Hazard ratio (95% CI)	P value
Myocardial injury after noncardiac surgery (MINS)	474 (12.7)	481 (12.8)	0.99 (0.87-1.12)	0.84
MINS not fulfilling universal definition of MI	424 (11.3)	439 (11.7)	0.97 (0.85-1.10)	0.61
Myocardial infarction	54 (1.4)	46 (1.2)	1.18 (0.80-1.75)	0.41
Stroke	17 (0.5)	17 (0.5)	1.00 (0.51-1.96)	>0.99
Vascular mortality	25 (0.7)	24 (0.6)	1.04 (0.60-1.83)	0.88
All-cause mortality	50 (1.3)	43 (1.1)	1.17 (0.78-1.75)	0.46

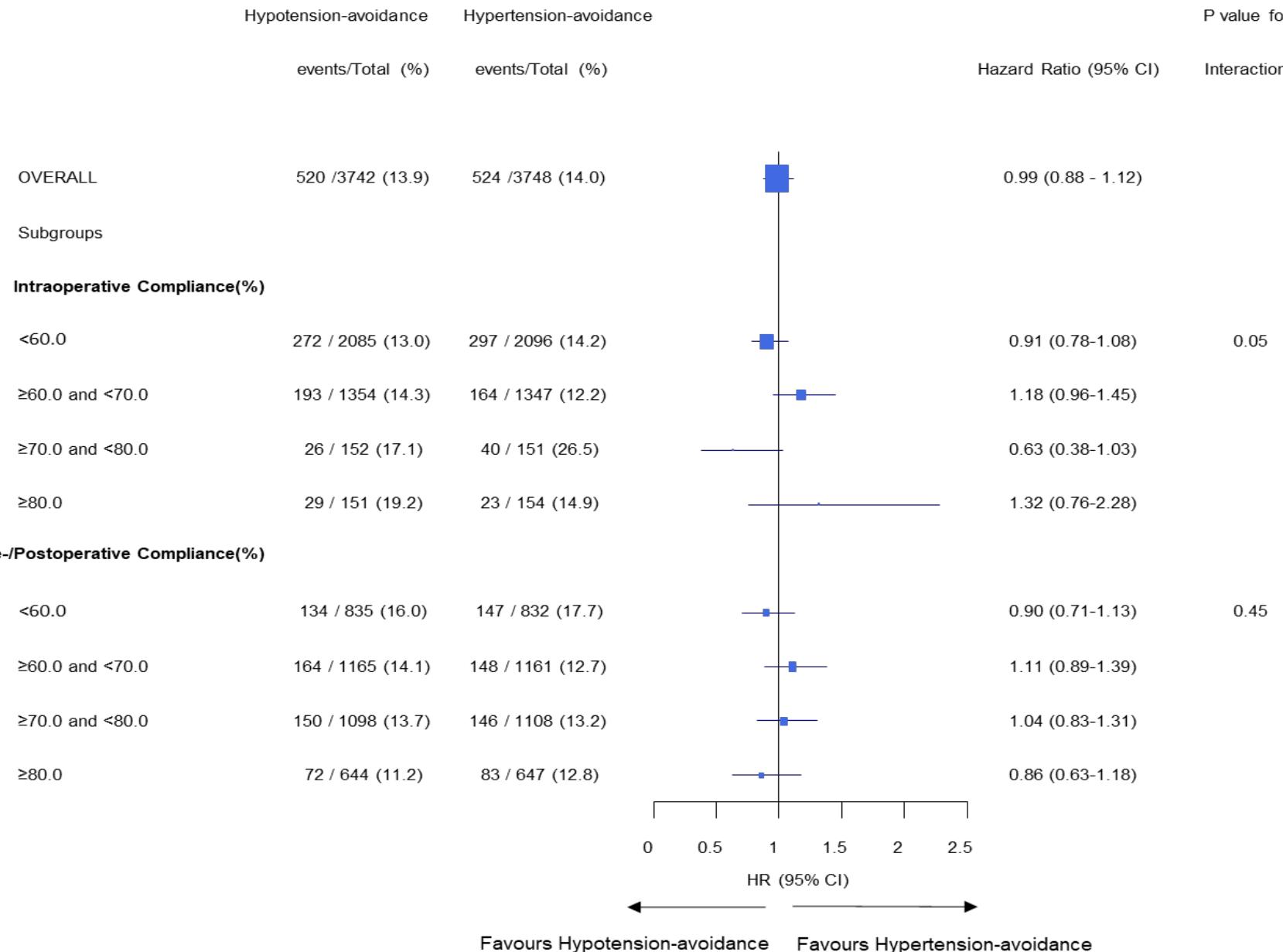
Tertiary outcomes

	Hypotension-avoidance N = 3742 n (%)	Hypertension-avoidance N = 3748 n (%)	Hazard ratio (95% CI)	P value
Non-fatal cardiac arrest	7 (0.2)	3 (<0.1)	2.34 (0.60-9.04)	0.22
Hemorrhagic stroke	0 (0.0)	1 (<0.1)	-	-
Non-hemorrhagic stroke	17 (0.5)	16 (0.4)	1.07 (0.54-2.11)	0.86
Acute congestive heart failure	21 (0.6)	18 (0.5)	1.17 (0.62-2.19)	0.63
New clinically important AF	62 (1.7)	44 (1.2)	1.42 (0.96-2.08)	0.08
Sepsis	47 (1.3)	57 (1.5)	0.88 (0.60-1.29)	0.51





Effects on primary outcome by centre compliance



Effects on hemodynamics

Post-randomization time	Hypotension-avoidance mean	Hypertension-avoidance mean	Mean difference (95% CI)
Systolic blood pressure, mm Hg			
before anesthetic induction	147.5	146.5	1.0 (0.0, 2.0)
in PACU (2 hrs from surgery)	132.5	131.3	1.2 (0.1, 2.3)
upon arrival to surgical ward	132.1	130.4	1.7 (0.7, 2.7)
day 1 after surgery	129.0	127.4	1.6 (0.8, 2.4)
day 2 after surgery	131.8	130.7	1.1 (0.2, 2.0)
Heart rate, bpm			
before anesthetic induction	75.4	74.8	0.6 (0.0, 1.2)
in PACU (2 hrs from surgery)	76.0	74.7	1.3 (0.5, 2.1)
upon arrival to surgical ward	76.6	75.2	1.4 (0.7, 2.1)
day 1 after surgery	77.0	75.8	1.2 (0.6, 1.8)
day 2 after surgery	78.7	77.3	1.4 (0.7, 2.1)

Effects on hemodynamics by centre compliance

- Effects of blood pressure strategies on hemodynamics consistent across centres with different compliance
 - Interaction P=0.72 for systolic blood pressure
 - Interaction P=0.15 for heart rate

Conclusions

- Perioperative hypotension-avoidance strategy did not differ from hypertension-avoidance strategy regarding effects on 30-day major vascular complications

Implications

- POISE-3 informs questions that commonly confront physicians taking care of patients undergoing surgery
 - during surgery: target MAPs ≥ 60 or ≥ 80 produced similar vascular outcomes
 - perioperatively: holding ACEI/ARBs and continuing other chronic antihypertensive meds based on blood pressure, versus continuing all antihypertensive meds, resulted in no substantial impact on hemodynamics and vascular outcomes
- Further research is needed to evaluate perioperative interventions that can modify hemodynamics to extent and in direction that will lead to favorable impact on clinical outcomes