

Clonidine in patients having noncardiac surgery

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Background

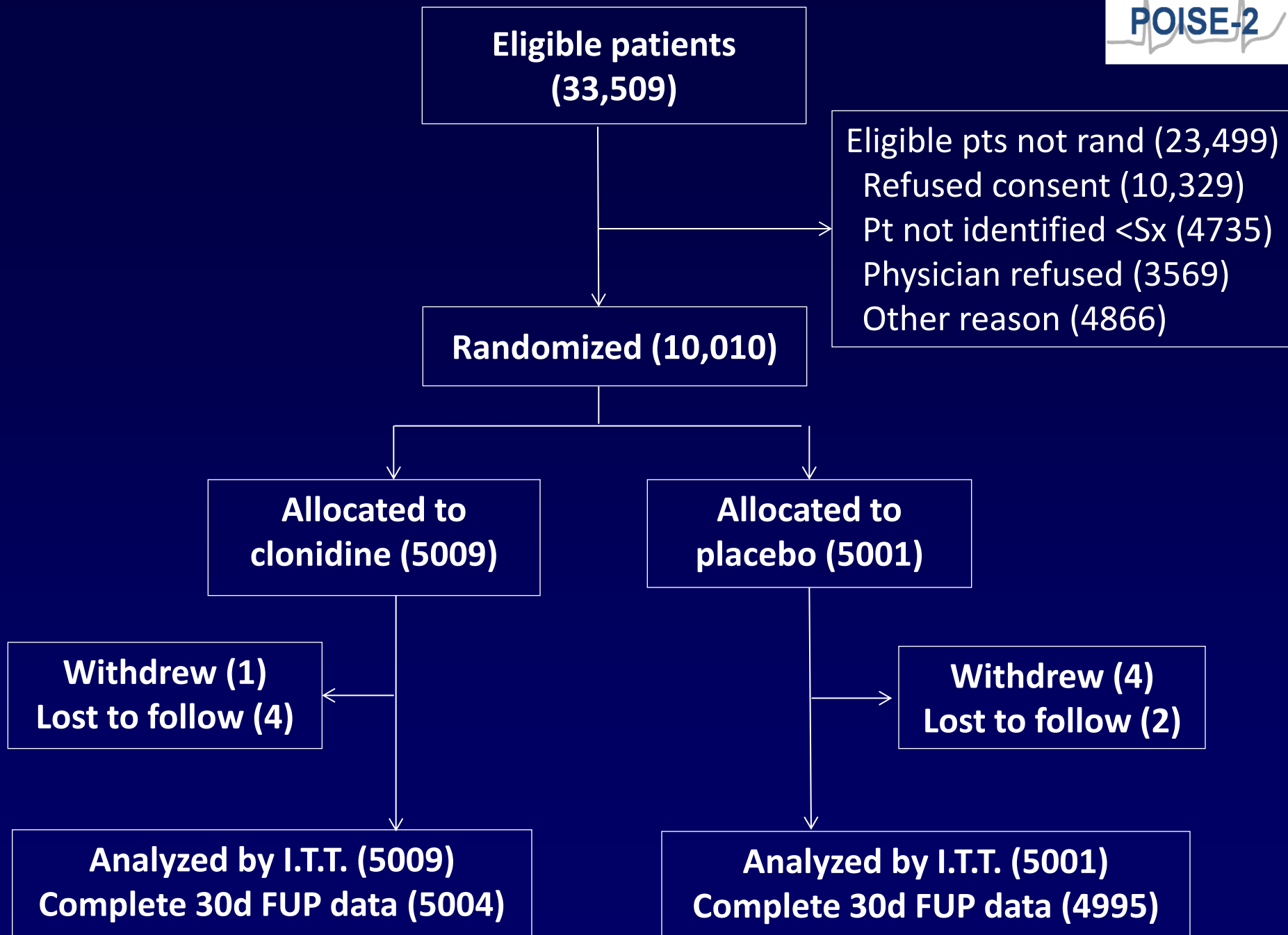
- **Myocardial injury is the leading cause of death after surgery**
 - 8% of surgical inpatients >45 years
 - 10% 30-day mortality
- **Safe prophylactic strategies unknown**
 - beta blockers decrease risk of MI
 - but increase risk of stroke and mortality
- **Clonidine**
 - decreases central sympathetic outflow
 - Analgesic and anti-inflammatory
- **Hypothesis:** clonidine reduces composite MI or death after noncardiac surgery

Subjects

- **10,010 patients** at 135 centers in 23 countries
- **Noncardiac inpatient surgery, age >45 years**
- **History of CAD, stroke, PVD, having vascular surgery**
 - or 3 of 9 risk factors
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Methods

- **Blinded 2 x 2 factorial randomized trial**
 - low-dose clonidine vs. placebo
 - 0.2 mg/day X 72 hours, started just before surgery
- **Primary outcome**
 - composite of death and MI at 30 days
- **Definitions**
 - MI: abnormal troponin *and* symptoms, ECG, or echo
 - Hypotension: systolic <90 mmHg *requiring treatment*
 - Bradycardia: HR <55 beats/min *requiring treatment*



Preoperative characteristics

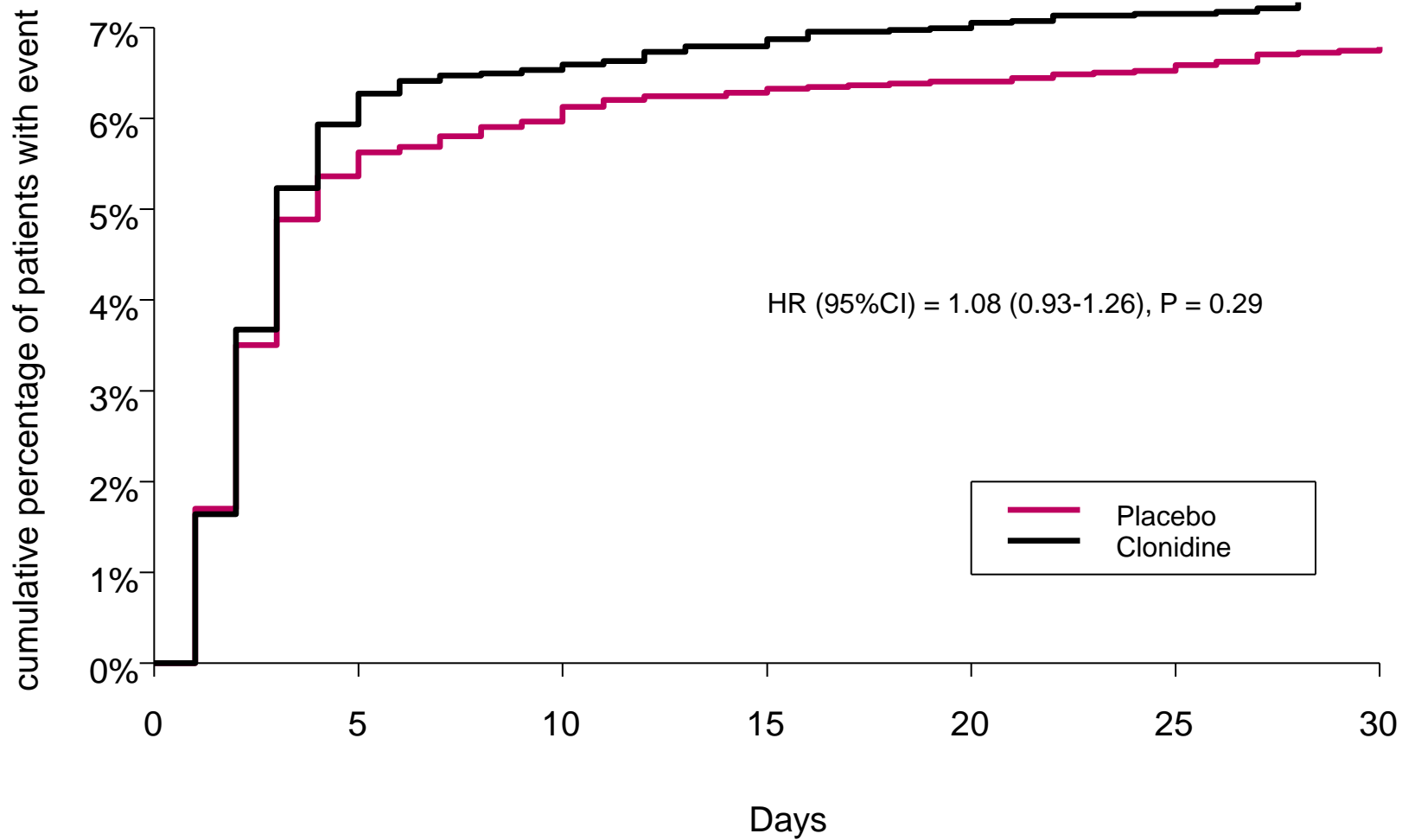
Characteristics	Clonidine (N=5009)	Placebo (N=5001)
Age – (mean years)	68	69
Male (%)	53	53
Known vascular disease (%)	32	33
Beta blocker taken ≤ 24 hours before Surgery (%)	29	28

30-day Results

Outcome	Clonidine (5009)	Placebo (5001)	HR (95% CI)	P
1 ^o outcome: death or MI	367 (7.3)	339 (6.8)	1.08 (0.93-1.26)	0.29
2 ^o outcome: death, MI, or stroke	380 (7.6)	352 (7.0)	1.08 (0.93-1.25)	0.30

No interactions with aspirin

Death or MI



Tertiary outcomes

Outcome	Clonidine (5009)	Placebo (5001)	HR (95% CI)	P
Total mortality	64 (1.3)	63 (1.3)	1.01 (0.72-1.44)	0.94
Vascular mortality	38 (0.8)	32 (0.6)	1.19 (0.74-1.90)	0.48
Myocardial infarction	329 (6.6)	295 (5.9)	1.11 (0.95-1.30)	0.18
Cardiac revascularisation	19 (0.4)	11 (0.2)	1.73 (0.82-3.63)	0.15
Pulmonary embolus	32 (0.6)	32 (0.6)	1.00 (0.61-1.63)	0.99
Nonfatal cardiac arrest	16 (0.3)	5 (0.1)	3.20 (1.17-8.73)	0.02

Safety outcomes

Outcome	Clonidine (5009)	Placebo (5001)	HR (95% CI)	P
Clinically important hypotension	2385 (48)	1854 (37)	1.32 (1.24-1.40)	<0.001
Clinically important bradycardia	600 (12)	403 (8)	1.49 (1.32-1.69)	<0.001
Stroke	18 (0.4)	17 (0.3)	1.06 (0.54-2.05)	0.87

Independent predictor of MI

Predictor	Adjusted HR (95% CI)	P
Clinically important hypotension	1.37 (1.16-1.62)	<0.001

Risk and duration of hypotension

Period	Clonidine (%)	Placebo (%)	P	Placebo duration minutes	Clonidine duration minutes	P
Surgery	39	32	<0.001	15	15	0.12
PACU	8	4	<0.001	30	30	0.30
Post-op Day 1	8	5	<0.001	150	180	0.13
Post-op Day 2	3	2	<0.001	110	160	0.03
Post-op Day 3	1.1	0.6	0.004	109	214	0.07

Conclusions

- Clonidine does not reduce postop MI or death
 - increases clinically important hypotension
- Low-dose clonidine should not be given to patients having noncardiac surgery in an effort to reduce perioperative mortality or MI
- A safe and effective way of preventing postoperative infarctions remains to be determined

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ORIGINAL ARTICLE

Clonidine in Patients Undergoing Noncardiac Surgery

P.J. Devereaux, D.I. Sessler, K. Leslie, A. Kurz, M. Mrkobra, P. Alonso-Coello, J.C. Villar, A. Sigamani, B.M. Bickard, C.S. Meyhoff, J.L. Parlow, G. Guyatt, A. Robinson, A.X. Garg, R.N. Rodseth, F. Botto, G. Lurati Buse, D. Xavier, M.T.V. Chan, M. Tiboni, D. Cook, P.A. Kumar, P. Forget, G. Malaga, E. Fleischmann, M. Amir, J. Eikelboom, R. Mizera, D. Torres, C.Y. Wang, T. VanHelder, P. Paniagua, O. Berwanger, S. Srinathan, M. Graham, L. Pasin, Y. Le Manach, P. Gao, J. Pogue, R. Whitlock, A. Lamy, C. Kearon, C. Chow, S. Pettit, S. Chrolavicius, and S. Yusuf, for the POISE-2 Investigators*