Continuous *versus* bolus norepinephrine administration and arterial blood pressure stability during induction of general anaesthesia in high-risk noncardiac surgery patients: a randomised trial

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Desar 1
GHRMSA - 27/10/2025

Noradrénaline Bolus Vs PSE

BJA

Impact Factor 9,2

Hypotension artérielle post induction = risque d'insuffisance rénale aiguë

Patients à risques

Essai en simple aveugle (patient)

Randomisé

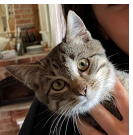
Un centre unique

71 participants

<u>Hypothèses :</u>

PSE Vs Bolus pour une meilleure stabilité hémodynamique

Durée d'administration plus importante / Sévérité de l'hypotension artérielle



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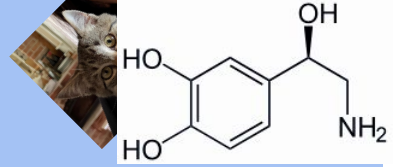
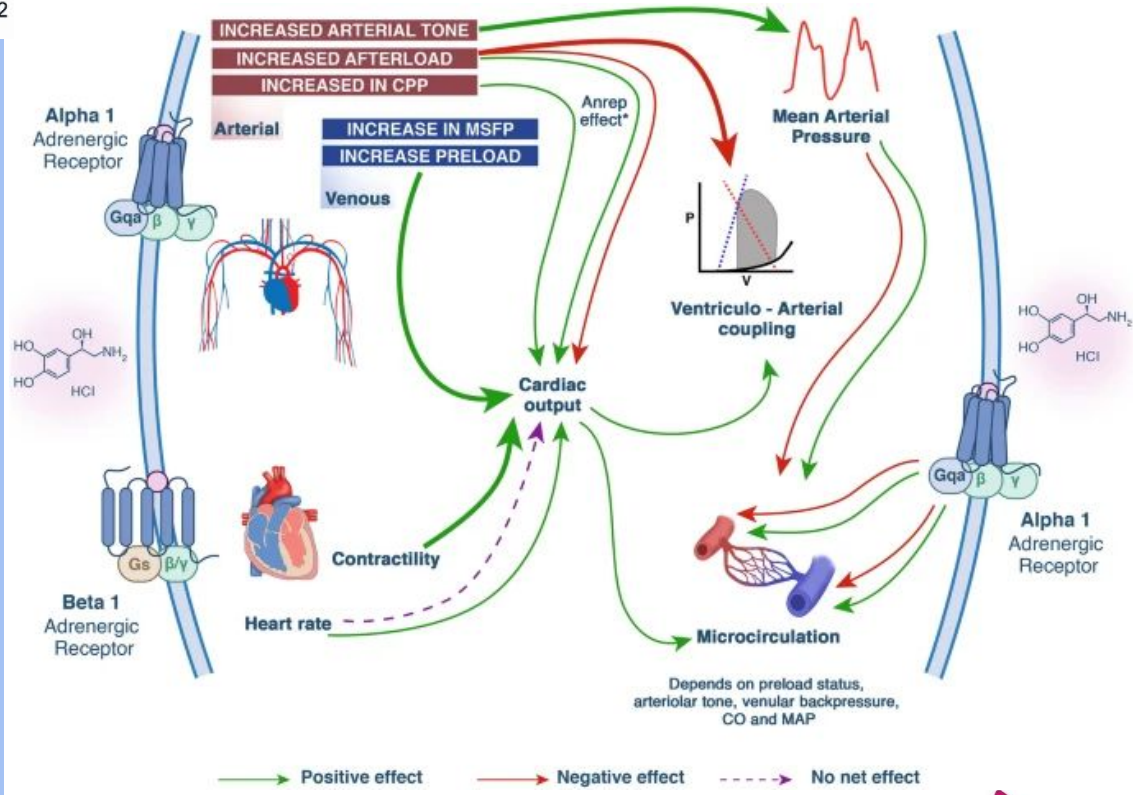


Rappel Physiopath Noradrénaline

Catécholamine endogène

Alpha agoniste ++ et beta

Durée d'action courte 2-3 minutes



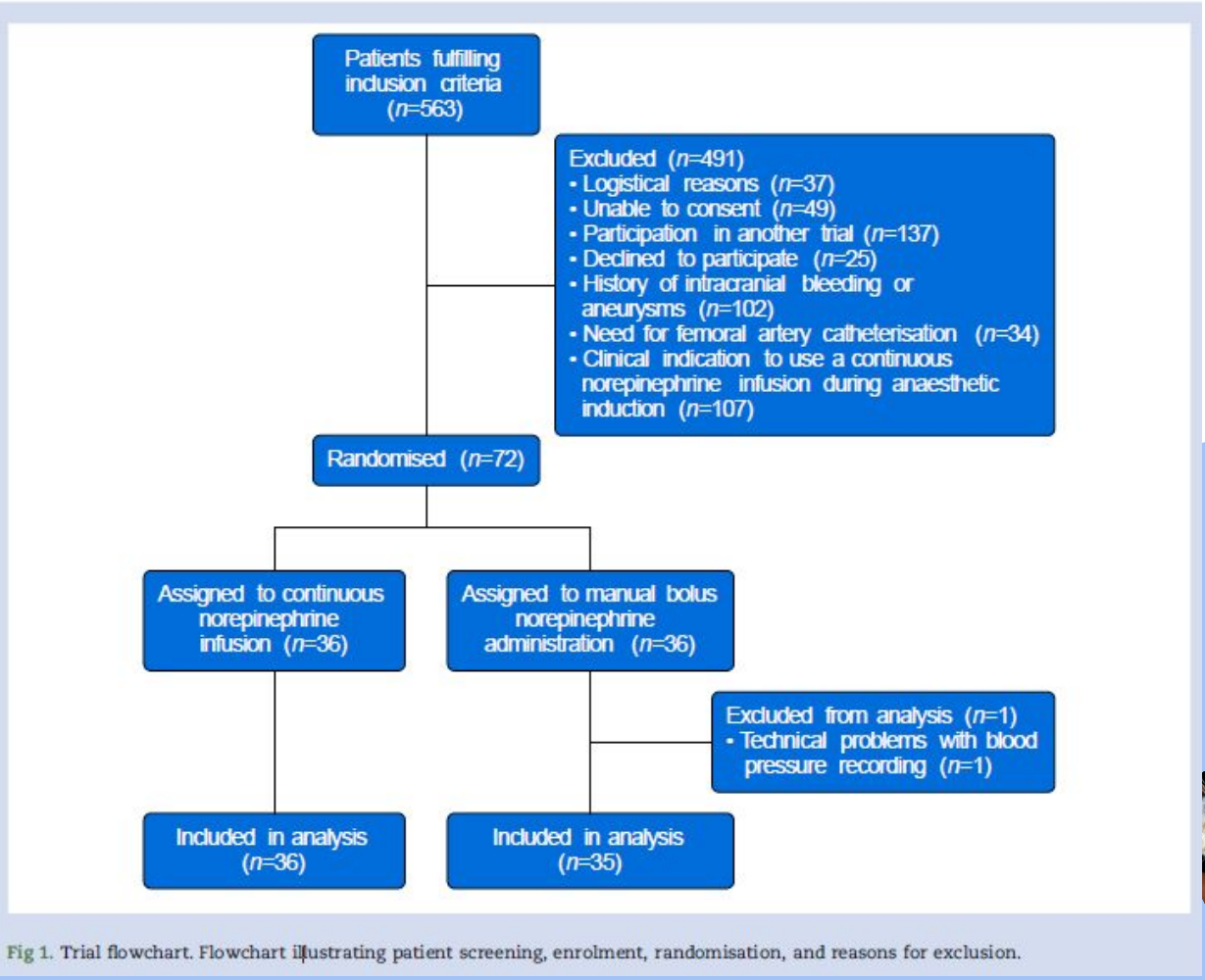


Fig 1. Trial flowchart. Flowchart illustrating patient screening, enrolment, randomisation, and reasons for exclusion.

Table 1 Participant characteristics and management during induction of general anaesthesia. Data are presented as mean (range or standard deviation), median (25th percentile, 75th percentile), or absolute number (percentage). Percentages may not sum up to 100% because of rounding.

Characteristic		Continuous norepinephrine infusion (n=36)	Manual bolus norepinephrine administration (n=35)
Age (yr)		67 (55-86)	64 (47-81)
Height (cm)		174 (10)	172 (10)
Weight (kg)		80 (21)	79 (21)
Sex	Female	15 (42)	19 (54)
	Male	21 (58)	16 (46)
ASA physical status (2; 3)	2	20 (56)	21 (60)
	3	16 (44)	14 (40)
Chronic arterial hypertension		19 (53)	17 (49)
Chronic obstructive pulmonary disease		3 (8)	1 (3)
Diabetes mellitus		3 (8)	9 (26)
Chronic heart failure		0 (0)	0 (0)
Liver disease		0 (0)	0 (0)
Chronic kidney disease		2 (6)	2 (6)
Coronary artery disease		1 (3)	2 (6)
Cerebrovascular disease		2 (6)	1 (3)
Type of surgery			
General surgery		14 (39)	17 (49)
Gynaecological surgery		3 (8)	4 (11)
Neurosurgery		8 (22)	8 (23)
Urological surgery		9 (25)	6 (17)
Trauma surgery		2 (6)	0 (0)
Management during induction of general anaesthesia			
Epidural block		18 (50)	12 (34)
Propofol dose during induction (mg kg^{-1})		2.6 (2.0, 3.7)	2.7 (2.0, 3.8)
Sufentanil use		27 (75)	27 (77)
Sufentanil dose during induction (μg kg^{-1})		0.5 (0.4, 0.6)	0.5 (0.5, 0.6)
Remifentanil use		9 (25)	9 (26)
Remifentanil dose during induction (μg kg^{-1} min^{-1})		0.5 (0.4, 0.5)	0.5 (0.5, 0.5)
Cumulative volume of crystalloids (ml)		275 (200, 350)	250 (200, 435)

Résultats significatifs

Variation de PAM

19 mmHg en PSE

25 mmHg en Bolus

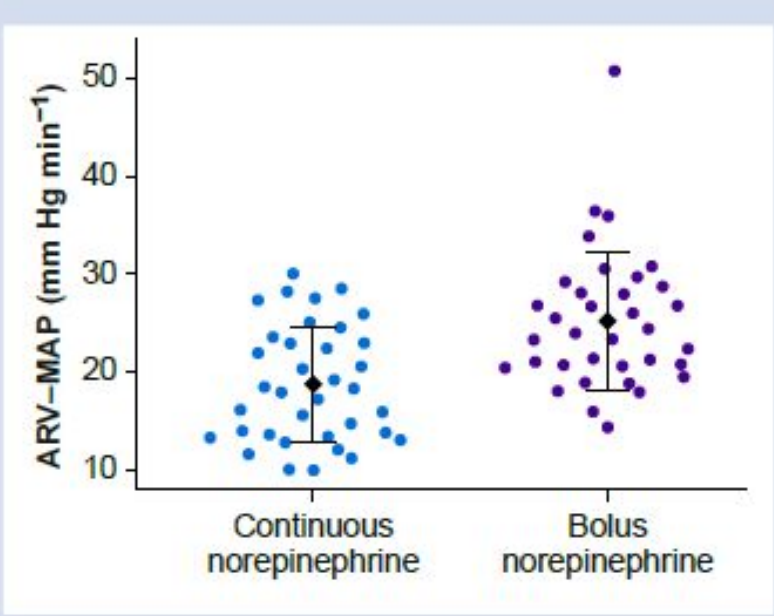


Fig 2. Generalised average real variability of mean arterial pressure (ARV-MAP). Means (black ◆) (standard deviation; error bars) are shown, with overlaying scatterplots in patients assigned to continuous norepinephrine infusion and manual bolus norepinephrine administration during induction of general anaesthesia.

Table 2 Secondary endpoints quantifying hypotension. Data are presented as median (25th percentile, 75th percentile). MAP, mean arterial pressure. *P-values correspond to Wilcoxon rank-sum tests with continuity correction.

Outcome	Continuous norepinephrine infusion (n=36)	Manual bolus norepinephrine administration (n=35)	P-value*	Cliff's delta
Area under a MAP of 65 mm Hg (mm Hg min)	3 (0, 18)	9 (1, 16)	0.178	0.19
Area under a MAP of 60 mm Hg (mm Hg min)	1 (0, 7)	2 (0, 6)	0.659	0.06
Area under a MAP of 50 mm Hg (mm Hg min)	0 (0, 0)	0 (0, 0)	0.465	−0.08
Area under a MAP of 40 mm Hg (mm Hg min)	0 (0, 0)	0 (0, 0)	0.182	−0.08
Cumulative duration of MAP values <65 mm Hg, min	0.8 (0.0, 2.4)	1.8 (0.5, 2.8)	0.027	0.30
Cumulative duration of MAP values <60 mm Hg, min	0.3 (0.0, 1.4)	0.7 (0.0, 1.5)	0.311	0.14
Cumulative duration of MAP values <50 mm Hg, min	0.0 (0.0, 0.2)	0.0 (0.0, 0.0)	0.534	−0.07
Cumulative duration of MAP values <40 mm Hg, min	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.169	−0.08

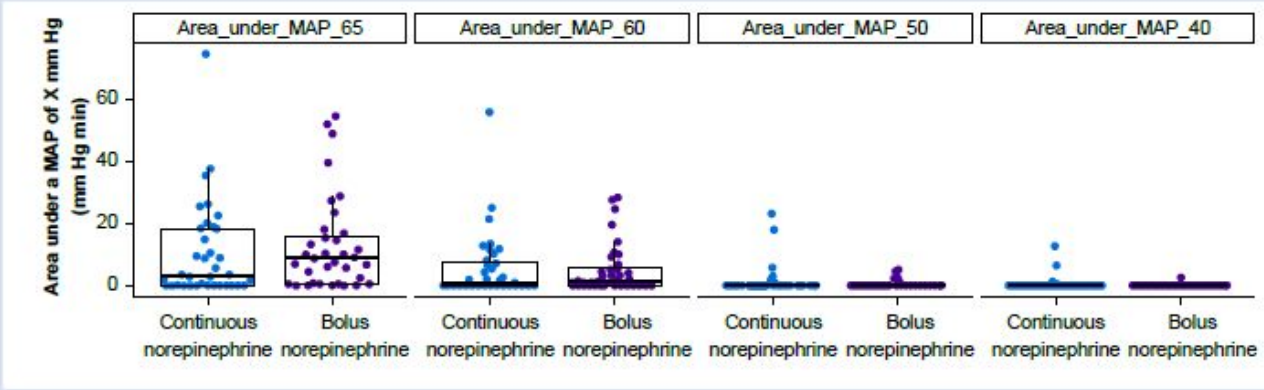


Fig 3. Areas under mean arterial pressure (MAP) values of 65, 60, 50, and 40 mm Hg in patients assigned to continuous norepinephrine infusion or manual bolus norepinephrine administration during induction of general anaesthesia. Boxplots with overlaying scatterplots are shown.

Table 3 Secondary endpoints quantifying hypertension. Data are presented as median (25th percentile, 75th percentile). MAP, mean arterial pressure. *P-values correspond to Wilcoxon rank-sum tests with continuity correction.

Outcome	Continuous norepinephrine infusion (n=36)	Manual bolus norepinephrine administration (n=35)	P-value*	Cliff's delta
Area above a MAP of 100 mm Hg (mm Hg min)	20 (2, 72)	16 (6, 53)	0.986	−0.003
Area above a MAP of 110 mm Hg (mm Hg min)	1 (0, 24)	2 (0, 19)	0.834	0.03
Area above a MAP of 120 mm Hg (mm Hg min)	0 (0, 1)	0 (0, 4)	0.454	0.09
Area above a MAP of 140 mm Hg (mm Hg min)	0 (0, 0)	0 (0, 0)	0.274	0.09
Cumulative duration of MAP values >100 mm Hg (min)	2.8 (0.6, 5.0)	2.3 (1.3, 4.3)	0.530	−0.09
Cumulative duration of MAP values >110 mm Hg (min)	0.6 (0.0, 3.2)	0.7 (0.0, 2.2)	0.701	−0.05
Cumulative duration of MAP values >120 mm Hg (min)	0.0 (0.0, 0.6)	0.0 (0.0, 0.6)	0.691	0.05
Cumulative duration of MAP values >140 mm Hg (min)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.244	0.09

The median cumulative dose of norepinephrine was 1.3 (1.0, 1.7) $\mu g\ kg^{-1}$ in participants assigned to continuous norepinephrine infusion and 0.5 (0.4, 0.7) $\mu g\ kg^{-1}$ in participants assigned to manual bolus norepinephrine administration (Cliff's delta: −0.87, P<0.001). *Post hoc* analyses for SAP are

Discussion / Limites

- PSE + bolus autorisé
- Dose x 2
- Hypotension post induction
- Essai unicentrique
- Validité externe - Noradrénaline
- Objectif de PAM
- Pose d’un cathéter artériel pré-opératoire

MERCI

RFE 2024

R1.1 – Il est probablement recommandé d'éviter un niveau de pression artérielle moyenne (PAM) peropératoire inférieure à 60-70 mmHg, chez le patient non hypertendu chronique, afin de diminuer la morbimortalité postopératoire.

GRADE 2 (Accord fort)

R1.2 – Les experts suggèrent de cibler un niveau de pression artérielle moyenne supérieur à 90 % de sa valeur habituelle ou une pression artérielle moyenne supérieure à 70 mmHg chez les patients hypertendus chroniques, pour diminuer la morbi-mortalité postopératoire.

Avis d'expert (Accord fort)

Tableau 1. Equivalence des différentes formulations de noradrénaline (14)

Formulation en sels	**Formulation en sels : dosage en mg**	**Formulation en Base : équivalence (mg)**
Hydrochloride de noradrénaline	1,22	1
Bitartrate de noradrénaline	1,89	1
Tartrate de noradrénaline	2	1