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Clevidipine versus nitroglycerin for blood pressure control during carotid endarterectomy: a cohort study

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Abstract

Background Clevidipine is an ultrafast-acting dihydropyridine calcium channel antagonist with selective arteriolar-dilating effects that may be suitable for afterload reduction during surgeries requiring tight blood pressure control. The objective of this single-center retrospective observational study was to evaluate the role of clevidipine to control blood pressure during carotid endarterectomy.

Methods Patients undergoing elective carotid endarterectomy from October 2024 to March 2025 who received clevidipine or nitroglycerin for intraoperative blood pressure management were included. The primary endpoint was the area under the curve of systolic blood pressure excursions outside the predefined target range of 140–160 mmHg. Secondary outcomes included corresponding measurements for mean arterial pressure and heart rate, as well as the incidence of significant clinical complications.

Results Of 40 included patients, 20 received clevidipine and 20 received nitroglycerin. Patients in the clevidipine group spent significantly less time outside the goal systolic blood pressure range than the nitroglycerin group (10 min vs. 37.5 min, $p < 0.001$). The median normalized area under the curve per five-minute intervals was 29.59 mmHg × min (interquartile range, 15.83 to 49.35) in the clevidipine group versus 60.30 mmHg × min (interquartile range 42.79 to 74.38) in the nitroglycerin group ($p = 0.005$). There were no significant differences in mean arterial pressure, heart rate, or clinical complications between the groups.

Conclusions Clevidipine was associated with significantly fewer blood pressure excursions outside the target goal range compared to nitroglycerin during carotid endarterectomy.

Keywords Antihypertensive agents, Carotid endarterectomy, Clevidipine, Nitroglycerin, Vascular surgery, Perioperative hypertension

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Background

Carotid surgery is inherently complex and requires meticulous maintenance of adequate cerebral perfusion. This necessitates rapid titration of blood pressure depending on the surgical phase, with higher targets typically required during clamping of the diseased carotid artery [1, 2]. Uncontrolled hypertension and perioperative hemodynamic fluctuations increase the risk of bleeding and neurological events, serving as important contributors to excess morbidity and mortality in patients undergoing carotid surgery [2, 3]. Therefore, tight blood pressure control throughout the procedure is essential to optimize patient outcomes and minimize perioperative risks.

In the setting of carotid endarterectomy, hemodynamic fluctuations are further exacerbated by a combination of surgery-specific factors such as hemorrhage and intermittent vascular clamping; the effects of anesthesia and regional techniques, including blunting of the carotid baroreceptor response from superficial cervical plexus blockade, and the presence of multiple comorbidities, including pre-existing hypertension [4, 5]. This interplay can result in fluctuating blood pressure, with alternating episodes of hypertension and hypotension that increase the risk of periprocedural stroke and embolization from the surgical site [6].

The ideal antihypertensive agent in this context should have a rapid onset and short duration of action, and act primarily on arteriolar resistance vessels, with minimal effects on the venous capacitance, thus allowing for precise and dynamic blood pressure control. Although nitroglycerin is commonly used for blood pressure management in vascular surgery, its role in carotid endarterectomy may be less suitable due to its non-negligible hemodynamic side effects. Its predominant action on capacitance vessels results in a marked reduction in diastolic and mean arterial pressure (MAP) – the principal determinants of cerebral perfusion pressure – thereby potentially compromising cerebral blood flow during critical phases of the procedure [7]. Moreover, by promoting vasodilation in non-ischemic brain regions, nitroglycerin may exacerbate cerebral steal phenomenon, diverting blood flow away from ischemic areas and potentially worsening neurological outcomes in patients with stroke [8].

In contrast, clevidipine – a third-generation dihydropyridine calcium channel blocker – exhibits pharmacological properties that make it a compelling option for blood pressure control during carotid endarterectomy. It is ultra-short acting, with rapid onset and offset due to metabolism by plasma esterases, making it well-suited for tight intraoperative blood pressure control [9]. Notably, clevidipine exerts its antihypertensive effect through direct arteriolar vasodilation, acting selectively

on resistance vessels without affecting venous capacitance. This results in a preferential reduction in systolic blood pressure (SBP) while preserving diastolic pressure and thereby supporting cerebral perfusion during critical intraoperative phases [10, 11]. While empirical evidence suggests clevidipine is safe in the perioperative setting, its role during carotid endarterectomy is not well characterized [12].

The objective of this study was to assess the effectiveness of clevidipine to control hemodynamic fluctuations in patients undergoing carotid endarterectomy compared to the standard of care nitroglycerin.

Materials and methods

Study design and patient selection

This was a single-center retrospective study of a prospectively collected database including all consecutive adult patients undergoing carotid endarterectomy at the Department of Vascular Surgery of a tertiary referral center university-hospital between October 2024 and March 2025. Patients aged ≥ 18 years were eligible for inclusion if their treating clinician deemed carotid endarterectomy necessary for their underlying carotid stenosis and if the attending cardiac anesthesiologist planned to use either clevidipine or nitroglycerin to maintain SBP within the range of 140 to 160 mmHg. Patients were excluded if they underwent other vascular surgical procedures involving the carotid artery, showed an ejection fraction lower than 50% or declined to participate.

As all patients had provided written informed consent for scientific data management and data were obtained as part of routine clinical activity and subsequently de-identified, the requirement for any additional ethical committee approval and informed consent was waived by the IRCCS Ospedale San Raffaele human research committee, in accordance with the current Italian legislation (Law No. 3/2018 and subsequent Legislative Decree 52/2019). The study conformed to the ethical standards of the 1975 Declaration of Helsinki and was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement guidelines (Supplementary Material, Supplemental Table 1).

Perioperative and surgical management

According to current guidelines, all antihypertensive medications were withheld on the day of surgery. Baseline laboratory tests included blood cell counts, electrolytes, liver function tests, serum creatinine, and coagulation tests. Carotid endarterectomy surgery was performed in the operating rooms of the Department of Anesthesia and Intensive Care of a tertiary referral center university-hospital. Standard monitoring was performed in all patients and encompassed invasive blood pressure

measurement via an intraarterial radial catheter, continuous five-lead electrocardiographic recording, pulse oximetry, and serial arterial blood gas analysis. Throughout the procedure, patients were allowed to breathe ambient air spontaneously. An oxygen source and a flow-inflating bag were kept readily available.

All patients received mild sedation and underwent ultrasound-guided superficial and intermediate cervical plexus block prior to surgery. For sedation, patients received a remifentanyl infusion at 0.01 to 0.05 $\mu\text{g/kg/min}$ during the entire procedure to maintain the Modified Observer's Alertness/Sedation scale of 5. Heparin (100 units/kg) was administered with additional dosing as needed to maintain an activated clotting time above 250 s throughout the duration of the procedure. Carotid endarterectomy was performed in a consistent manner throughout the study period, as previously described [13].

Cerebral perfusion was assessed by continuous monitoring of mental status and contralateral motor function. Patients exhibiting speech deficits, marked agitation or confusion, contralateral upper limb weakness, seizures, or unresponsiveness received selective shunting. Intraoperative completion angiography was performed in all patients via direct puncture of the common carotid artery, in accordance with hospital protocol. Postoperative computed tomography or magnetic resonance angiography was performed only in the event of an adverse cerebral outcome [13].

Drug administration

A single 20G peripheral venous catheter was used exclusively for administration of the study antihypertensive drugs, without concurrent infusions of other medications or fluids. All patients were managed using a standard infusion set and a 20-cm extension line primed with 1 mL of study drug. During the procedure, afterload reduction was initiated if the SBP exceeded 160 mmHg. Clevidipine or nitroglycerin was used at the discretion of the attending cardiac anesthesiologist and was administered via a dedicated peripheral venous catheter using an infusion pump. The infusion rate was titrated by the attending anesthesiologist to achieve an SBP within the predetermined range of 140 to 160 mmHg and continued until the end of the surgical procedure. Specifically, for patients in the clevidipine group, a continuous infusion was initiated at a rate of 2 mg/h, with subsequent dose adjustments made by sequential increments of 1 mg/h titrated according to patient hemodynamic response, up to a maximum of 10 mg/h. Similarly, nitroglycerin infusion was initiated at an infusion rate of 5 mcg/min and further titrated according to patient hemodynamic response up to 100 mcg/min.

Dose adjustments of the study drug were made if no response was observed within 1 min, in accordance with the pharmacokinetics and pharmacodynamics of the study drugs and local practice. Treatment failure was defined as the inability to achieve adequate afterload reduction despite administration of the maximum permitted dose of the assigned study drug, necessitating crossover to the other group. The use of antihypertensive medications other than clevidipine and nitroglycerin during the procedure was not allowed. No boluses of clevidipine or nitroglycerin were given, and vasoactive agents were avoided, per institutional practice. Blood pressure management was standardized with first-line interventions including a reduction of antihypertensive therapy and, if necessary, fluids administration instead of vasoactive medications [14].

Data collection

Baseline patient demographic characteristics, functional status, medical history, and ongoing pharmacological therapy were recorded prior to the initiation of the procedure. Physiological parameters – including intraoperative variables such as SBP, MAP, and heart rate (HR), were documented at initiation of sedation and subsequently recorded at 5-minute intervals until patient discharge from the operating room. Clamping time and duration of surgery were recorded. Adverse events including intraoperative need for carotid shunting, in-hospital stroke, and death were recorded through hospital discharge. All recorded data were prospectively collected, underwent full anonymization before being entered into an electronic database and subsequently analyzed retrospectively.

Study endpoints

The primary outcome was the effectiveness of clevidipine compared with nitroglycerin in reliably controlling SBP. Effectiveness was determined by an area under the curve (AUC) analysis of SBP excursions beyond the predefined lower and upper limits (140 and 160 mmHg, respectively), normalized per five-minute intervals, as well as the total time each patient spent outside the target range. The target blood pressure was set based on the latest guidelines recommendations [15]. To improve contralateral cerebral perfusion, transient higher targets were applied as needed during carotid shunting. A larger number indicates more excursions outside the goal range and therefore less optimal hemodynamic control. Secondary outcomes included the effectiveness of clevidipine in controlling MAP and HR, and the occurrence of adverse events. These were assessed using AUC analysis of MAP and HR excursions beyond the predefined thresholds (i.e., 80 to 100 mmHg for MAP and 60 to 80 beats per

minute for HR), normalized per five-minute intervals, and the total out-of-range time per patient.

Sample size calculation

The sample size was calculated using a nonparametric approach based on the Mann–Whitney U test (Noether's procedure), which is appropriate for comparing medians between two independent groups. The ECLIPSE trial, which compared clevidipine and nitroglycerin for perioperative blood pressure control in cardiac surgery, reported a median area under the curve for SBP deviation (AUC SBP-D) of 83.7 mmHg × min/h in the clevidipine group and 108.6 mmHg × min/h in the nitroglycerin group, corresponding to a relative reduction of approximately 29% [16]. Based on these findings, we assumed a probability of 77% that a randomly selected patient treated with clevidipine would have a lower AUC SBP-D than a randomly selected patient treated with nitroglycerin. This probability was used as the effect size in the sample size calculation, with a two-sided significance level (α) of 0.05 and a statistical power of 80%. Based on these assumptions, a total of 36 evaluable patients (18

per group) were required. To account for a potential 10% dropout rate, the sample size was increased to 40 patients (20 per group), ensuring adequate power. The sample size calculation was performed using PASS 2025, version 25.0.1 (NCSS, LLC; Kaysville, UT, USA).

Statistical analysis

Baseline characteristics were summarized using standard descriptive statistics. Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed variables were reported as mean ± standard deviation (SD), and non-normally distributed variables as median with interquartile range (IQR). Categorical variables were presented as counts and percentages. Between-group comparisons were performed using the t-test for normally distributed continuous variables, and the Wilcoxon rank-sum test otherwise. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate based on expected frequencies.

To evaluate the time spent outside predefined hemodynamic thresholds, we calculated the duration (in minutes) during which MAP, SBP, or HR exceeded or fell below the clinically relevant intraoperative ranges: 80 to 100 mmHg for MAP, 140 to 160 mmHg for SBP, and 60 to 80 bpm for HR. These predetermined ranges are consistent with worldwide clinical practice [17]. For each patient, data were recorded at 5-minute intervals and transformed into a long format to reconstruct individual time-series profiles. We computed the total out-of-range time per patient, as well as the AUC, in mmHg × min or bpm × min beyond the upper or lower bounds using the trapezoidal technique to approximate the time integral. To standardize across patients due to variable monitoring durations, the AUC was normalized by the number of timepoints, yielding a per-interval average AUC. Differences between treatment groups in both total time spent out-of-range and normalized out-of-range AUC values were compared using the independent samples t-test and Wilcoxon rank-sum test, as appropriate. Group differences were also graphically represented using bar plots.

All tests were two-sided, with a significance level set at $p < 0.05$. All data were stored by Excel® sheet and analyzed using SPSS Statistics® software version 25 (IBM Corp., Armonk, NY, USA).

Results

General characteristics of the study population

A total of 40 patients, with 20 allocated to each group, were enrolled. Baseline demographic and clinical characteristics were comparable between the clevidipine and nitroglycerin groups (Table 1). Median (IQR) age was 78 (74 to 81) years, and most (65%) were male. Active smoking was significantly more common in the nitroglycerin group compared with the clevidipine group (45% vs. 10%;

Table 1 Baseline characteristics

Variables	Overall (N=40)	Clevidipine group (N=20)	Nitroglycerin group (N=20)	P-value
Male sex	26 (65%)	12 (60%)	14 (70.0%)	0.51
Age, years	78 (74–81)	76 (74–82)	78 (72–80)	0.54
Comorbidities				
Active Smoker	11 (27.5%)	2 (10.0%)	9 (45.0%)	0.03
Diabetes	14 (35.0%)	7 (35.0%)	7 (35.0%)	1.00
Hypertension	36 (90.0%)	19 (95.0%)	17 (85.0%)	0.61
PM	2 (5.0%)	1 (5.0%)	1 (5.0%)	1.00
ICD	1 (2.5%)	1 (5.0%)	0 (0.0%)	1.00
PTCA	7 (17.5%)	5 (25.0%)	2 (10.0%)	0.41
Dyslipidemia	37 (92.5%)	18 (90.0%)	19 (95.0%)	1.00
COPD	4 (10.0%)	2 (10.0%)	2 (10.0%)	1.00
CAD	9 (22.5%)	6 (30.0%)	3 (15.0%)	0.45
Previous MI	6 (15.0%)	3 (15.0%)	3 (15.0%)	1.00
Previous Stroke/TIA	6 (15.0%)	3 (15.0%)	3 (15.0%)	1.00
CKD	6 (15.0%)	4 (20.0%)	2 (10.0%)	0.66
Abdominal aortic aneurysm	4 (10.0%)	3 (15.0%)	1 (5.0%)	0.61
Antiplatelet therapy				
None	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a
Aspirin	31 (77.5%)	15 (75.0%)	16 (80.0%)	0.71
Clopidogrel	10 (25.0%)	6 (30.0%)	4 (20.0%)	0.72
Lysine Acetyl Salicylate	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a
Ticlopidine	1 (2.5%)	1 (5.0%)	0 (0.0%)	1.00

Data are expressed as n (%) or as median (interquartile range (IQR))

COPD Chronic obstructive pulmonary disease, CAD Coronary artery disease, MI Myocardial infarction, PTCA Percutaneous transluminal coronary angioplasty, TIA Transit ischemic attack, CKD Chronic kidney disease, PM Pacemaker, ICD Implantable Cardioverter-Defibrillator

$p = 0.03$). The cumulative surgical time and clamping time were similar between groups. The most frequent comorbidities were hypertension, diabetes, dyslipidemia, and coronary artery disease, with no significant differences between the groups.

Hemodynamic variations

Variations in SBP

The median AUC normalized exposure to SBP values outside the 140 to 160 mmHg target range was 29.59 mmHg $\times$ min (IQR 15.83 to 49.35) in the clevidipine group and 60.30 mmHg $\times$ min (IQR 42.79 to 74.38) in the nitroglycerin group ($p = 0.005$) (Fig. 1a). The observed difference remained statistically significant following the sensitivity analysis conducted on mean SBP values

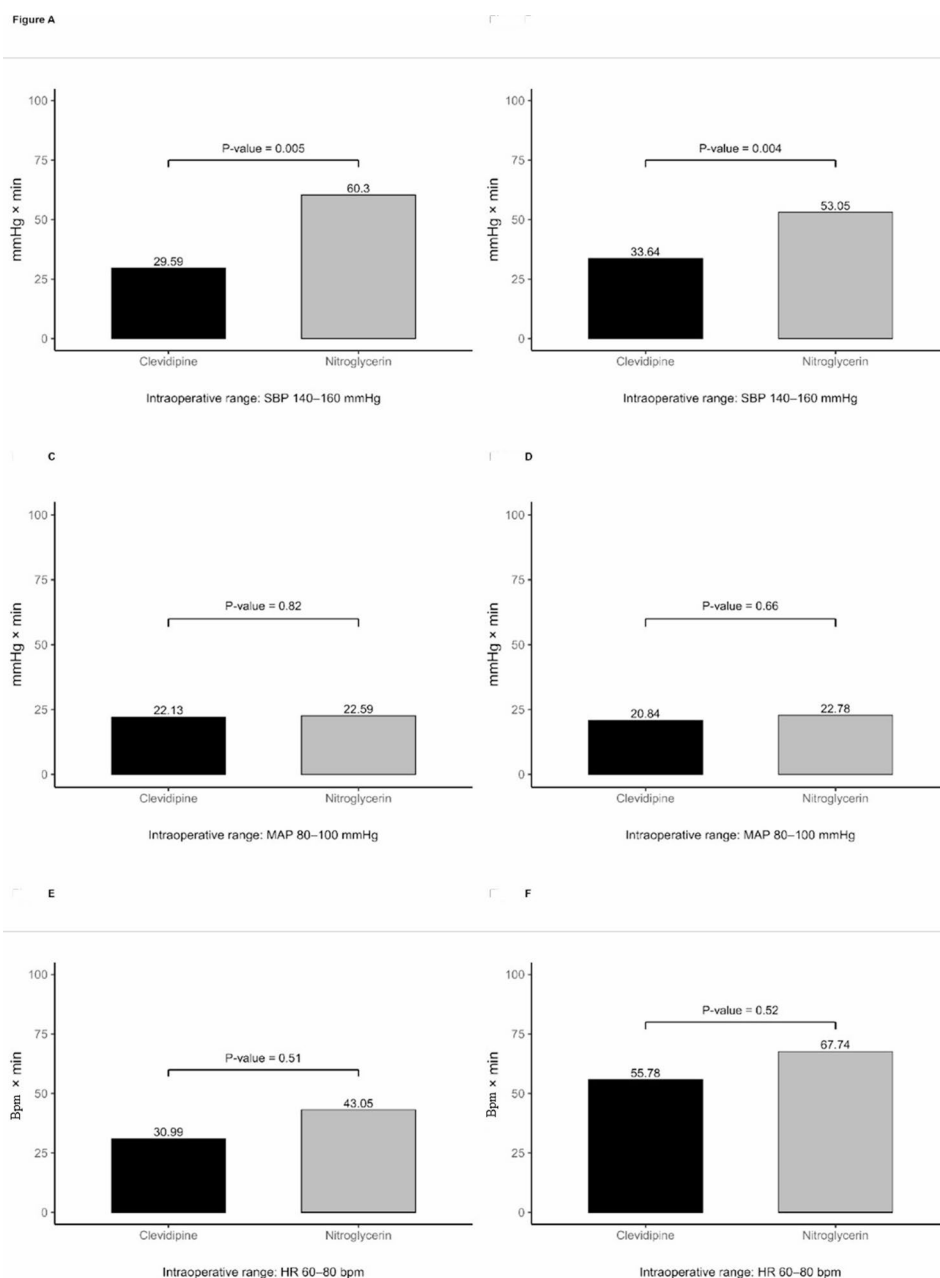


Fig. 1 Hemodynamic variations. **A** Median AUC normalized exposure to SBP outside the 140–160 mmHg target range; **B** Sensitivity analysis conducted on mean SBP values; **C** Median AUC normalized exposure to MAP outside the 80–100 mmHg target range; **D** Sensitivity analysis conducted on mean MAP values; **E** Median AUC normalized exposure to HR outside the 60–80 mmHg target range; **F** Sensitivity analysis conducted on mean HR values. AUC, area under the curve; SBP, systolic blood pressure; MAP, mean arterial pressure; HR, heart rate; mmHg: millimeters of mercury; Bpm: beats per minute

Table 2 Perioperative characteristics

Variables	Overall (N = 40)	Clevidipine group (N = 20)	Nitroglyc- erin group (N = 20)	P- val- ue
Crossover	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a
Need for shunting	7 (17.5%)	5 (25.0%)	2 (10.0%)	0.41
Clamping time, min	22 (16–26)	23 (17–26)	21 (14–26)	0.43
Cumulative surgical time, min,	73 (65–82)	76 (61–84)	72 (65–80)	0.38
Stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a
Neurological deficit	1 (2.5%)	0 (0.0%)	1 (5.0%)	1.00

Data are expressed as n (%) or as median (interquartile range (IQR))

(33.64 vs. 53.05 mmHg × min; $p=0.004$) (Fig. 1b). In terms of temporal exposure, clevidipine was associated with a markedly shorter median time spent outside the SBP target range (10.0 min [IQR 5.0 to 16.3]), compared to the nitroglycerin group (37.5 min [IQR 30.0 to 51.3]), $p<0.001$.

Variations in MAP

No significant differences in MAP AUC were observed between groups. The median normalized AUC was 22.13 mmHg × min (IQR 9.42 to 27.53) in the clevidipine group and 22.59 mmHg × min (IQR 10.28 to 30.23) in the nitroglycerin group ($p=0.82$) (Fig. 1c). Similarly, the mean AUC values were 20.84 mmHg × min in the clevidipine group and 22.78 mmHg × min in the nitroglycerin group ($p=0.66$), indicating comparable exposure intensity (Fig. 1d). Nevertheless, the time spent outside the MAP target range was significantly less in patients treated with clevidipine (10.0 min, IQR 10.0 to 16.3), compared to patients treated with nitroglycerin (25.0 min IQR 13.8 to 35.0), $p=0.016$.

Variations in HR

No significant difference was found in the occurrence of heart rate values outside the 60–80 bpm range between groups. The median AUC for heart rate was 30.99 bpm × min (IQR 16.25 to 101.69) in the clevidipine group and 43.05 bpm × min (IQR 19.00 to 100.85) in the nitroglycerin group ($p=0.51$) (Fig. 1e). Similarly, no significant difference was found in mean AUC values (55.78 bpm × min in the clevidipine group and 67.74 bpm × min in the nitroglycerin group, $p=0.52$) (Fig. 1f). The total time spent outside the target heart rate range was comparable between groups, with a median of 52.5 min (IQR 25.0 to 80.0) for clevidipine and 70.0 min (IQR 30.0 to 90.0) for nitroglycerin ($p=0.30$).

Adverse events

No crossover between treatment groups was observed. Intraoperative shunting of the internal carotid artery was required in 5 patients (20%) in the clevidipine group

and 2 patients (10%) in the nitroglycerin group ($p=0.41$). Major adverse events, such as stroke and in-hospital death, were not observed in either group (Table 2).

Discussion

Key findings

In this retrospective observational study of patients undergoing carotid endarterectomy, we found that patients receiving clevidipine spent less time exposed to SBP excursions outside the target range of 140 to 160 mmHg, resulting in a clinically meaningful 50% reduction in cumulative pressure burden. Furthermore, clevidipine led to a markedly lower median time spent outside the target blood pressure range. These findings indicate that clevidipine not only limits the magnitude of SBP excursions but also reduces their duration during carotid endarterectomy compared to nitroglycerin. Additionally, clevidipine achieved target MAP values more rapidly than nitroglycerin, suggesting a faster effect and more precise blood pressure control. Time outside the predefined MAP range favored clevidipine, whereas the MAP AUC did not, a pattern that aligns with the drug's well-characterized pharmacodynamic profile and is confirmed in this study of a high-risk population susceptible to hemodynamic instability. Notably, clevidipine preferentially reduces systolic blood pressure, having relatively little effect on diastolic pressure, which bears more directly on determining MAP. This pharmacologic distinction is particularly relevant in carotid endarterectomy, where maintenance of adequate cerebral perfusion pressure is critical. In this context, maintaining MAP while tightly controlling systolic pressure is advantageous, as it both preserves cerebral perfusion and reduces the risks associated with excessive systolic hypertension [15]. Taken together, these properties make clevidipine a highly suitable agent for intraoperative blood pressure management during CEA.

Relationship with the previous literature

Previous studies investigating the properties of clevidipine and its feasibility in the management of hemodynamic fluctuations in several surgical settings are available in the published literature [3, 12, 18, 19]. Specifically, in the context of cardiac surgery, the ECLIPSE trial found that clevidipine was superior to nitroglycerin, sodium nitroprusside, and nicardipine, with predictable effects on blood pressure control across patients [16]. Additionally, several case reports described the ease of use of clevidipine in the context of aneurysmectomy and in cases of intraoperative hypertension unresponsive to other anti-hypertensive drugs [20]. Similarly, clevidipine was found to be effective in the management of pheochromocytoma-related hypertension, even when the resulting hypertensive state was resistant to escalating

doses of other antihypertensive agents [21, 22]. Therefore, clevidipine's pharmacologic profile and the available literature suggest it may be particularly suitable for perioperative blood pressure management in the context of carotid endarterectomy [23].

Although clevidipine has shown favorable hemodynamic effects, tachycardia remains one of its most frequently reported adverse effects and may occasionally require additional pharmacologic interventions (e.g., beta-blockers) [24]. In addition, isolated reports have described episodes of severe hypoxemia, possibly related to pulmonary vasodilation and intrapulmonary shunting, during prolonged infusions [25]. In our cohort, HR did not differ substantially between clevidipine and nitroglycerin. Notably, beta-blockers were not required in the clevidipine group, and no episodes of severe hypoxemia were observed.

Significance of study findings and implications for clinical practice

To the best of our knowledge, this is the first study comparing the intraoperative administration of clevidipine versus nitroglycerin in patients undergoing carotid endarterectomy. Clevidipine was associated with greater effectiveness in achieving target SBP and minimizing blood pressure variability compared to nitroglycerin. These results are further supported by the fact that cumulative surgical and clamping times were similar between groups, indicating that differences in procedure duration did not influence the observed outcomes. We suspect that clevidipine's proportionally smaller impact on DBP – and, by extension, on MAP – may be advantageous in this context, as it may help preserve cerebral perfusion pressure while avoiding the detrimental effects of systolic hypertension [23]. Moreover, the absence of severe adverse events further supports its favorable safety profile. Overall, our results suggest that clevidipine represents a valuable option for intraoperative blood pressure management, with potential applicability to other surgical settings in which rapid and precise SBP titration is essential [1, 3, 26].

Strengths and limitations

Our study has both strengths and limitations worth noting. Despite the relatively small sample size, standardized monitoring protocols and predefined target ranges for SBP, MAP and HR were used enabling precise and reproducible assessment of hemodynamic control. Additionally, rigorous quantitative methods were applied to capture both the magnitude and duration of blood pressure excursions. The consecutive enrollment of participants also reduced the risk of selection bias. Although sample size is relatively limited, this study is a proof-of-concept investigation because no prior work

has evaluated intraoperative clevidipine in patients undergoing carotid surgery to maintain hemodynamics within a tightly predefined, guideline-recommended range. However, the methodology was rigorous in that we normalized the time spent outside the normal range for a number of important hemodynamic parameters and, based on our sample-size calculation, the study retained 80% power to detect a difference in the blood pressure AUC. Finally, the study was not designed or powered to assess downstream clinical outcomes, and larger confirmatory studies are needed to validate and extend these findings.

However, several limitations should be acknowledged. First, the retrospective observational design inherently introduces the possibility of selection bias and limits the ability to establish causal relationships between clevidipine use and hemodynamic outcomes. Although baseline characteristics were comparable between groups, unmeasured confounders may have residual influence on the results. In addition, while there is a theoretical possibility that the absence of randomization may have biased the choice of vasodilator used, the anesthesiology team did not change during the entire study and all staff had extensive prior experience with both clevidipine and nitroglycerin according to standardized clinical protocols. Thus, it is unlikely that the anesthesiologist's preferences biased or affected the study results. Second, the single-center nature of the study restricts the generalizability of the findings to other institutions with different surgical practices, patient populations, or perioperative protocols. Third, the relatively small sample size, while sufficient to detect statistically significant differences in SBP, limits the ability to assess less frequent adverse events or clinically relevant outcomes such as perioperative neurologic and cardiovascular complications. However, the improvement in blood pressure stability seen in this high-risk population does hint at a potential clinical benefit. Perioperative neurological events are multifactorial, influenced among the others by platelet function, atherosclerotic burden, diabetes, and collateral cerebral perfusion via the circle of Willis during carotid clamping. Blood pressure represents only one of these contributing factors, although systolic hypertension is recognized as a major risk factor for stroke [15]. The fact that clevidipine can effectively control systolic blood pressure may therefore mitigate one of the key triggers for neurological complications and thus supports its potential utility in patients undergoing CEA. Fourth, the absence of long-term follow-up beyond the intraoperative period precludes conclusions regarding the potential impact of improved hemodynamic control on postoperative recovery and morbidity. Fifth, in the United States, carotid endarterectomy is performed under regional anesthesia – typically a cervical block – in only 10–15% of cases,

according to large national registries [27]. Although this may limit the generalizability of the findings to settings where general anesthesia is more commonly employed, the present pragmatic study was specifically designed to assess the effects of clevidipine in a high-risk subpopulation with significant comorbidities and a pronounced hemodynamic fluctuation. Under general anesthesia, the cumulative hypotensive effects of anesthetic agents may reduce the need for additional antihypertensive therapy; however, the underlying patient profile and the inherent risk of neurological and ischemic/hemorrhagic complications remain comparable. From this point of view, results appear to be robust and consistent internally. Finally, although antihypertensive medications were not recorded systematically, withdrawal of these drugs on the day of surgery probably minimized any interaction between intraoperative antihypertensive agents and chronic therapy. Furthermore, since this was a uniform practice in both study groups, any effect would have been equally distributed, thus minimizing any risk of bias.

Conclusions and future perspectives

We found that clevidipine was associated with more reliable SBP control than nitroglycerin, resulting in a clinically meaningful 50% reduction in cumulative pressure burden during carotid endarterectomy. By significantly reducing both the extent and duration of blood pressure excursions beyond the target range, clevidipine appears to be a promising pharmacologic option for managing perioperative hypertension in high-risk vascular procedures. Future research should aim to confirm these findings in larger trials with sufficient statistical power to assess not only intraoperative hemodynamic parameters but also clinically meaningful outcomes, such as perioperative stroke, myocardial infarction, and long-term neurologic recovery related to excess intraoperative hypertension.

Abbreviations

AUC	area under the curve
AUC SBP-D	area under the curve for systolic blood pressure deviation
HR	heart rate
IQR	interquartile range
MAP	mean arterial pressure
SBP	systolic blood pressure
SD	standard deviation

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12871-025-03543-8>.

Supplementary Material 1.

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Authors' contributions

****RL:** ** Investigation, Data Curation and Writing – Original Draft. ****JDU:**** : Methodology, Writing – Original Draft and Writing – Review & Editing. ****SF:** ** Investigation, Data Curation and Writing – Original Draft. ****ABot:** ** Investigation, Methodology, Writing – Original Draft and Writing – Review & Editing. ****DP:** ** Methodology, Data Curation, Study Design, Data Analysis and Writing – Original Draft. ****OE:** ** Data Curation and Writing – Review & Editing. ****ML:** ** Data Curation and Writing – Review & Editing. ****ABon:** ** Data Curation and Writing – Review & Editing. ****PMW:** ** Methodology, Investigation and Writing – Review & Editing. ****FM**:** : Conceptualization, Supervision, Study design, Investigation, Methodology and Writing – Review & Editing.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

As all patients had provided written informed consent for scientific data management and data were obtained as part of routine clinical activity and subsequently de-identified, the requirement for any additional ethical committee approval and informed consent was waived by the IRCCS Ospedale San Raffaele human research committee, in accordance with the current Italian legislation (Law No. 3/2018 and subsequent Legislative Decree 52/2019). The study conformed to the ethical standards of the 1975 Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

PMW is a consultant for Wolters Kluwer/UpToDate. The other authors declare that they have no competing interests.

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