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Subcutaneous Nitroglycerin to Prevent Radial Artery Occlusion in Pediatric Patients
A Randomized Clinical Trial

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IMPORTANCE Pediatric patients are at an increased risk of postprocedural radial artery occlusion (RAO) owing to their small vessels and high tendency for vasospasm after catheterization. Although subcutaneous nitroglycerin increases the success rate of radial artery catheterization by vasodilation and preventing vasospasm, its effect on RAO prevention after catheter removal remains unknown.

OBJECTIVE To evaluate the efficacy and safety of subcutaneous nitroglycerin for RAO prevention.

DESIGN, SETTING, AND PARTICIPANTS This double-blind randomized clinical trial was conducted at a single tertiary center and included pediatric patients younger than 3 years who required radial artery catheterization during general anesthesia. Study data were analyzed from April to July 2025.

INTERVENTIONS Patients were randomized to receive either subcutaneous nitroglycerin (5 µg/kg/0.5 mL) or normal saline (0.5 mL) above the chosen radial artery before radial arterial catheterization and catheter removal under ultrasound guidance.

MAIN OUTCOMES AND MEASURES The primary outcome was the RAO incidence after catheter removal, assessed using the reverse Barbeau test with pulse oximetry on the ipsilateral index finger.

RESULTS A total of 200 pediatric patients were initially enrolled, but 68 were excluded for protocol violations. In the per-protocol analysis with 132 participants (median [IQR] age, 5.5 [2.0-16.6] months; 73 female [55.3%]), RAO incidence was lower in the nitroglycerin group than in the control group (25.4% [17 of 67] vs 73.8% [48 of 65]; $P < .001$; odds ratio [OR], 0.12; 95% CI, 0.06-0.26; absolute risk reduction, 48.5%; 95% CI, 33.6%-63.4%). After catheter removal, the nitroglycerin group showed higher peak blood flow velocity (mean [SD], 13.0 [11.0] cm/s vs 7.4 [9.2] cm/s; 95% CI for mean difference, 2.1-9.1 cm/s; $P = .002$) and perfusion index (mean [SD], 1.37 [1.09] vs 0.65 [0.49]; 95% CI for mean difference, 0.43-1.01; $P < .001$) of the radial artery than did the control group. There was no significant intergroup difference in RAO duration. There was no hypotension or localized adverse effects.

CONCLUSIONS AND RELEVANCE Subcutaneous nitroglycerin injection before radial artery catheterization and catheter removal significantly reduced the incidence of RAO after catheter removal and may promote safe recovery in pediatric patients younger than 3 years.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT05443061

Visual Abstract

Multimedia

Supplemental content

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The radial artery is commonly used for arterial catheterization owing to its superficial location and relatively large diameter.[1,2] However, in small pediatric patients, radial artery catheterization is challenging due to the small vessel size and increased risk of complications such as vasospasm and hematoma, which may lead to catheter malfunction and radial artery occlusion (RAO).[1-4]

RAO is considered common in small pediatric patients due to their smaller vessels and greater tendency for vasospasm after radial artery catheterization.[1,5] A previous observational study[6] on neonates reported that RAO, confirmed by Doppler ultrasound, was observed in 63% of patients after radial artery catheter removal, and restoration of blood flow required 1 to 29 days. Severe complications such as peripheral ischemia and necrosis have also been reported,[7-9] particularly in pediatric patients with prolonged catheter duration, use of larger or longer catheters, or systemic infection.[10,11] These risk factors are frequently observed in pediatric patients who require surgery at a young age.

Nitroglycerin is a potent vasodilator that is used to prevent or treat arterial vasospasm.[12-18] It increases the radial artery diameter,[12,16] thereby facilitating arterial cannulation and reducing RAO incidence in adult cardiac catheterization.[14,15,17] In pediatric patients, both subcutaneous[1] and topical nitroglycerin[19] have been shown to improve first-attempt success and reduce procedure time. However, its role in preventing RAO after catheter removal in small children remains unclear.

We hypothesized that subcutaneous nitroglycerin injection before radial artery catheterization and catheter removal would dilate the radial artery and prevent RAO. The aim of this study was to compare the preventive effects against RAO of a subcutaneous injection of nitroglycerin (5 µg/kg) vs saline before radial artery catheter removal in pediatric patients younger than 3 years.

Key Points

Question Does subcutaneous nitroglycerin administered before radial artery catheterization and catheter removal reduce the incidence of radial arterial occlusion (RAO) in pediatric patients younger than 3 years compared with control group (saline)?

Findings In this randomized clinical trial involving 132 patients, subcutaneous nitroglycerin significantly reduced the incidence of RAO compared with that in the control group.

Meaning This study found that RAO after catheter removal was a notable risk in small pediatric patients, and subcutaneous nitroglycerin proved effective in preventing RAO, supporting its potential clinical utility in this vulnerable population.

Methods

Study Design and Participants

This prospective, parallel-arm, double-blinded, randomized clinical trial was approved by the Seoul National University Hospital Institutional Review Board and conducted at a tertiary pediatric hospital in Korea (Supplement 1). The authors evaluated the eligibility of patients and obtained written informed consent to enroll the participants before anesthesia. The study included patients younger than 3 years undergoing elective surgery under general anesthesia requiring invasive arterial monitoring. All participants in this study were East Asian and of Korean nationality. Exclusion criteria included nitroglycerin hypersensitivity or contraindications, prior radial artery puncture, infection at the catheterization site, peripheral vascular disease, unstable vital signs, and arrhythmias. This study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines.

Randomization

Participants were randomized 1:1 to receive subcutaneous nitroglycerin (5 µg/kg/0.5 mL) or saline via computer-generated randomization.[20] A study nurse prepared syringes based on body weight and group allocation, using opaque sealed envelopes. The operators who performed radial artery catheterization and catheter removal (Y.E.J. and J.B.P.), as well as the outcome assessor (S.H.J.) who evaluated the presence or absence of RAO and measured the depth and diameter of the radial artery using stored ultrasound images, were blinded to group assignment.

Nitroglycerin Solution

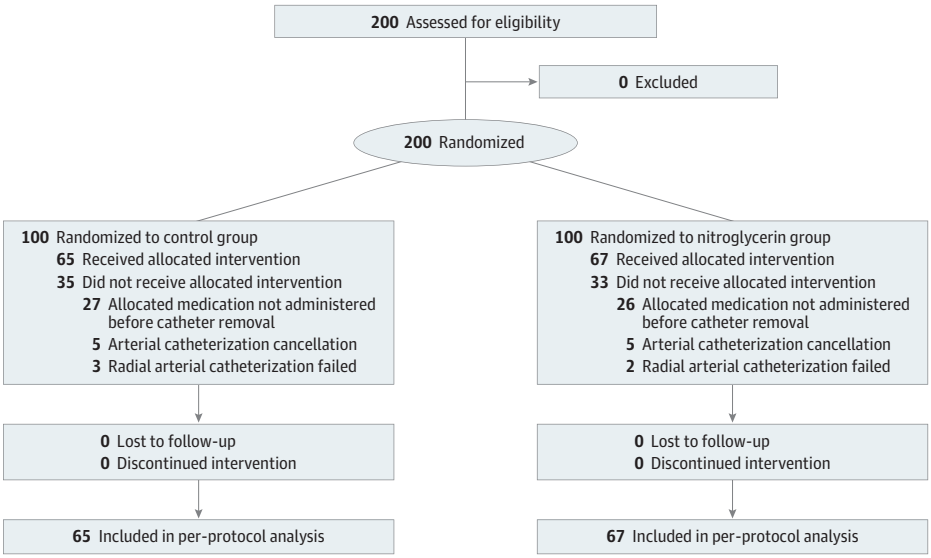
Nitroglycerin (5 µg/kg/0.5 mL) was previously used to induce vasodilation of the radial artery in pediatric patients younger than 2 years.[1] For subcutaneous injection, a trained study nurse prepared the syringe of nitroglycerin (5 µg/kg/0.5 mL) or placebo (0.5 mL saline) according to group allocation.

Radial Artery Catheterization and Catheter Removal

Radial artery assessment, selection of catheterization site, and catheterization were performed by 2 blinded anesthesiologists (Y.E.J. and J.B.P.), both with extensive experience in pediatric arterial catheterization. After anesthesia induction, the Allen test was performed to ensure ulnar arterial patency. The wrist was extended to maintain a constant angle, and all procedures were performed under sterile conditions. A pulse oximetry sensor (the RD rainbow SET-2 Neo [Masimo Corp] for patients <3 kg and the RD rainbow SET-2 Inf [Masimo Corp] for patients 3-30 kg) was placed on the ipsilateral index finger to monitor oxygen saturation and the perfusion index (PI).

Baseline measurements of the radial artery diameter and peak blood flow velocity were recorded using an 8- to 17-MHz linear ultrasound IO8-17T probe with an E-CUBE i7 unit (ALPINION Medical Systems), and the PI was recorded using the same pulse oximetry. In the nitroglycerin group, 5 µg/kg/0.5 mL of nitroglycerin was subcutaneously injected above the radial artery under ultrasound guidance (**Video**),[1] whereas the control group received 0.5 mL of saline. Three minutes later, these parameters were reassessed. A 24-gauge 0.7 × 19-mm over-the-needle catheter (Jelco) was used. If catheterization failed after 2 attempts or 10 minutes, the participant was excluded from the study. After catheterization measurements—including radial artery diameter, peak blood flow velocity, and PI of the ipsilateral index finger—were repeated, and complications such as hematoma and vasospasm were assessed using

Figure 1. The Consolidated Standards of Reporting Trials (CONSORT) Flow Diagram



ultrasonography. Catheter malfunction was monitored until the end of surgery. If malfunction occurred, a subcutaneous injection was administered according to group allocation, followed by catheter removal.

Before catheter removal, the same pulse oximeter sensor was placed on the ipsilateral index finger, and the radial artery diameter, peak blood flow velocity, and PI were recorded. Then, either 5 µg/kg/0.5 mL of nitroglycerin or 0.5 mL of normal saline was subcutaneously injected, and the same measurements were repeated 3 minutes later. After catheter removal, manual compression was applied for at least 5 minutes until complete hemostasis was achieved, and the compression duration was recorded. Once the hemostasis was confirmed, the radial artery diameter, peak blood flow velocity, and PI were reassessed. If the researcher was unable to visit the patient during catheter removal, the patient was excluded from the study, as the randomized medication could not be administered and the outcome variables could not be measured.

Evaluation of Radial Artery Patency and Occlusion

After catheter removal and complete hemostasis, the presence of RAO was assessed by a blinded outcome assessor (S.H.J.) using the reverse Barbeau test with digital plethysmography.[17,18,21] Both the radial and ulnar arteries were compressed, and the loss of the plethysmographic signal was confirmed. The radial artery was then released while maintaining ulnar compression. The return of the plethysmographic signal was considered evidence of radial artery patency, whereas the absence of a plethysmographic signal during ulnar compression was defined as RAO. Radial artery patency was assessed every 24 hours during hospitalization until RAO was resolved. The duration of RAO was defined as the number of days until the return of the digital plethysmographic signal at the ipsilateral index finger, as assessed using the reverse Barbeau test.

Statistical Analysis

The following data were collected for every patient: age, weight, sex, the American Society of Anesthesiologists (ASA) physical status classification, surgery type, vasopressor use during catheterization and its duration, and the patient's sedation, intubation status, and body temperature at catheter removal. The primary outcome was the incidence of RAO after catheter removal. Secondary outcomes included the diameter of the radial artery, peak blood flow velocity of the radial artery, PI measured before and after the subcutaneous injection and after catheterization and catheter removal, duration of catheterization, duration of hemostasis, and the duration of RAO. The incidence of catheter malfunction at the chosen radial artery was also measured until the end of surgery. We defined a systemic adverse effect of subcutaneous nitroglycerin as a decrease in the mean blood pressure of more than 20% compared with baseline, and intravenous phenylephrine (0.1- to 1.0-µg/kg bolus) was used. If hemostasis was not achieved within 10 minutes, it was defined as localized bleeding due to vasodilation.

The sample size was calculated based on previous studies.[6,14] The RAO incidence after radial artery catheter removal was 63% in neonates[6] and 13.9% in adults but decreased to 5.4% in the subcutaneous nitroglycerin group.[14] We assumed the incidence of RAO in the control and nitroglycerin groups to be 35% and 15%, respectively. With an α error of .05 and a power (1 − β error) of 0.85, the sample size for each group was calculated as 83. Considering a 20% dropout rate, a total of 200 patients were recruited.

All data are expressed as mean (SD) or median (IQR) unless otherwise specified. Distribution was tested using the Shapiro-Wilk normality test. The primary outcome was evaluated using the χ^2 test. Secondary outcomes were evaluated using the χ^2 test, t test, and Mann-Whitney U test. Exploratory subgroup analyses were conducted based on the cath-

Table 1. Patient Characteristics

Characteristic	Intention-to-treat (n = 200)		Per-protocol (n = 132)	
	Control (n = 100)	Nitroglycerin (n = 100)	Control (n = 65)	Nitroglycerin (n = 67)
Age, median (IQR) [range], mo	5.0 (2.0-13.0) [0-32]	5.0 (2.0-15.0) [0-35]	4.0 (2.0-13.0) [1-32]	7.0 (2.0-20.0) [0-35]
Sex, No. (%)				
Female	48 (48.0)	45 (45.0)	36 (55.4)	37 (55.2)
Male	52 (52.0)	55 (55.0)	29 (44.6)	30 (44.8)
Weight, median (IQR) [range], kg	6.7 (4.8-9.2) [2.2-16.9]	7.3 (5.1-9.5) [1.7-16.1]	6.6 (3.8-9.2) [2.2-14.0]	8.1 (5.3-10.4) [1.7-16.1]
Gestational age <60 wk, No. (%)	46 (46.0)	44 (44.0)	32 (54.2)	27 (40.3)
ASA physical status, No. (%)				
I	1 (1.0)	1 (1.0)	0	1 (1.5)
II	23 (23.0)	23 (23.0)	17 (26.2)	18 (26.9)
III	73 (73.0)	70 (70.0)	46 (70.8)	45 (67.1)
IV	3 (3.0)	5 (5.0)	2 (3.0)	3 (4.5)
Surgery, No. (%)				
Cardiothoracic surgery	65 (65.0)	72 (72.0)	43 (66.2)	45 (67.2)
General surgery	14 (14.0)	10 (10.0)	10 (15.4)	11 (16.4)
Neurosurgery	18 (18.0)	15 (15.0)	10 (15.4)	9 (13.4)
Other[a]	3 (3.0)	3 (3.0)	2 (3.0)	2 (3.0)
Continuous infusion at time of catheter removal, No. (%)				
Dopamine	16 (16.0)	19 (19.0)	10 (15.4)	10 (14.9)
Epinephrine	2 (2.0)	6 (6.0)	1 (1.5)	2 (3.0)
Norepinephrine	0	2 (2.0)	0	2 (3.0)
Dobutamine	1 (1.0)	3 (3.0)	10 (15.4)	10 (14.9)
Milrinone	21 (21.0)	22 (22.0)	11 (16.9)	9 (13.4)
Nitroglycerin	20 (20.0)	33 (33.0)	11 (16.9)	16 (23.9)
Nitroprusside	5 (5.0)	12 (12.0)	0	6 (9.0)
Vasopressor use for >50% of the arterial catheter dwell time, No. (%)	32 (32.0)	35 (35.0)	18/65 (27.7)	20 (29.9)
Sedated at catheter removal, No. (%)	31 (31.0)	29 (29.0)	19/65 (29.2)	21 (31.3)
Intubated at catheter removal, No. (%)	31 (31.0)	29 (29.0)	19/65 (29.2)	21 (31.3)
Body temperature at catheter removal, mean (SD), °C	36.8 [0.52]	36.8 [0.50]	36.8 [0.59]	36.8 [0.52]

Abbreviation: ASA, American Society of Anesthesiologists.

[a] Other surgery includes 4 pediatric urology procedures (3 ureteronephrocystectomies and 1 bilateral Wilms tumor excision) and 2 pediatric otolaryngology procedures (cochlear implantations).

eter dwell time and vasopressor use for greater than 50% of the catheterization period. A multivariable logistic regression analysis was performed to identify the independent risk factors associated with RAO.

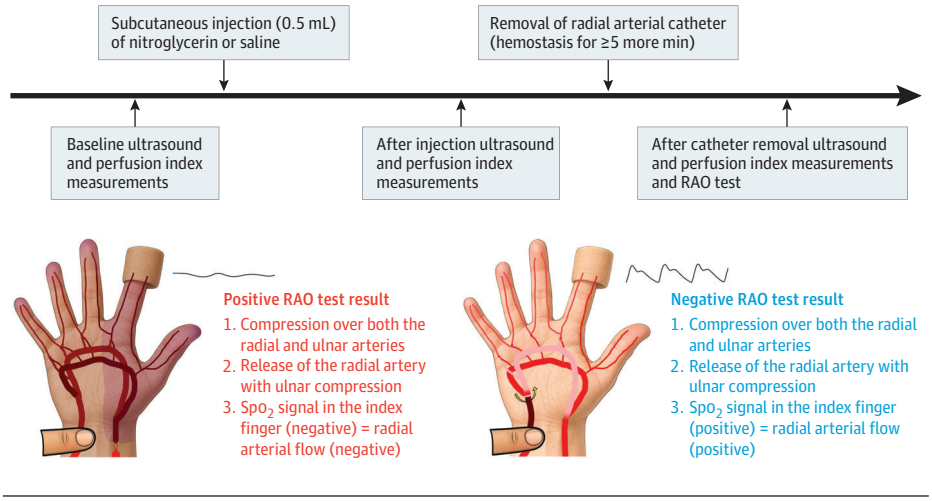
Statistical analyses were performed from April to July 2025 using SPSS Statistics, version 22 (IBM Corp). We performed a Bonferroni correction for 1 primary outcome and 13 secondary outcomes, and a 2-sided $P < .004$ indicated statistical significance.

Results

From September 8, 2022, to March 24, 2025, 200 pediatric patients (nitroglycerin, n = 100 and control, n = 100) were enrolled (**Figure 1**). Due to protocol violations, 68 patients were excluded and 132 patients (median [IQR] age, 5.5 [2.0-16.6] months; 73 female [55.3%]; 59 male [44.7%]) were included in the per-protocol analysis. All participants included in the analysis were East Asian/Korean. Baseline patient characteristics are summarized in **Table 1** and eTable 1 in Supplement 2. In both groups, cardiac surgery was the most performed surgery (88 of 132 patients [66.7%]) and over 70% of patients (96 of 132 [72.7%]) had ASA class III or higher.

The primary outcome, RAO incidence (the presence of which was assessed using the reverse Barbeau test with digital plethysmography outlined in **Figure 2**), was significantly lower in the nitroglycerin group than in the control group (25.4% [17 of 67] vs 73.8% [48 of 65]; $P < .001$; odds ratio [OR], 0.12; 95% CI, 0.06-0.26; absolute risk reduction, 48.5%; 95% CI, 33.6%-63.4%) (**Table 2**). There was no intergroup difference in the RAO duration. Among patients who developed

Figure 2. Subcutaneous Injection Before Catheter Removal and Radial Artery Occlusion (RAO) Test After Catheter Removal



The diameter, peak blood flow velocity, and perfusion index were measured at baseline, 3 minutes after the subcutaneous injection (after injection), and after catheter removal. The presence of RAO was assessed using the reverse Barbeau test with digital plethysmography. Both the radial and ulnar arteries were compressed, and the loss of the plethysmographic signal was confirmed. The radial artery was then released while maintaining ulnar compression. The return of the plethysmographic signal was considered evidence of radial artery patency, whereas the absence of a plethysmographic signal during ulnar compression was defined as RAO. SPO_2 indicates oxygen saturation.

RAO, flow recovery before discharge occurred in 82.4% (14 of 17) of those in the nitroglycerin group and 41.7% (20 of 48) in the control group (OR, 6.53; 95% CI, 1.66-25.78; *P* = .005).

Subcutaneous nitroglycerin injection increased the radial artery diameter after catheterization compared with that in the control group (mean [SD], 1.4 [0.3] mm vs 1.2 [0.3] mm; 95% CI for mean difference, 0.1-0.3 mm; *P* < .001) (eTable 2 in Supplement 2). The mean (SD) peak blood flow velocity was 16.9 (7.4) cm/s in the nitroglycerin group and 13.0 (9.4) cm/s in the control group after catheterization (95% CI, −6.9 to −1.0 cm/s; *P* = .01). The mean (SD) PI was 1.58 (0.98) in the nitroglycerin group and 1.19 (0.96) in the control group after catheterization (95% CI, −0.72 to −0.05; *P* = .02). Catheter-related complications occurred less frequently in the nitroglycerin group than in the control group (3.0% [2 of 67] vs 20.0% [13 of 65]; *P* = .002; OR, 0.12; 95% CI, 0.03-0.57). No intergroup differences were observed in the duration of catheterization and the time required for hemostasis. Results from the comparison of catheter dwell time and vasopressor use between the nitroglycerin and control groups are available in eTable 3 in Supplement 2.

Before catheter removal, the nitroglycerin group showed higher PI than the control group (mean [SD], 1.59 [1.30] vs 0.94 [0.80]; 95% CI, 0.28-1.03; *P* = .001) (Table 2). Subcutaneous nitroglycerin injection significantly increased the radial artery diameter (mean [SD], 1.4 [0.4] mm vs 1.1 [0.4] mm; 95%, 0.1-0.4 mm; *P* < .001) and PI (mean [SD], 1.58 [1.37] vs 0.96 [0.91]; 95% CI, 0.21-1.01; *P* = .003) compared with those in the control group (**Figure 3**). After catheter removal, the nitroglycerin group demonstrated significantly higher peak blood flow velocity (mean [SD], 13.0 [11.0] cm/s vs 7.4 [9.2] cm/s; 95% CI, 2.1-9.1 cm/s; *P* = .002) and PI (mean [SD], 1.37 [1.09] vs 0.65 [0.49]; 95% CI, 0.43-1.01; *P* < .001) than those of the control group. The mean (SD) radial artery diameter was 1.3 (0.5) mm in the nitroglycerin group and 1.0 (0.8) mm in the control group (*P* = .02) (eFigure 1 in Supplement 2). There were no systemic adverse effects (hypotension) or local bleeding at the injection site (eTable 4 in Supplement 2).

Discussion

This randomized clinical trial demonstrated that subcutaneous nitroglycerin injection before radial artery catheter removal was highly effective in preventing RAO in pediatric patients younger than 3 years. It increased the peak blood flow velocity of the radial artery, thereby improving the PI of the area supplied and leading to more favorable recovery from RAO.

The incidence of RAO in the control group was high (73.8%), with approximately 60% experiencing persistent RAO at discharge. This is similar to the incidence reported in neonates (63%)[6] but higher than that observed in previous studies investigating arterial thrombosis.[22] It may be attributable to the greater proportion of patients who underwent cardiac surgery. Furthermore, we performed prospective and systematic assessments of RAO using PI and ultrasound measurements, which may have enabled more sensitive detection of RAO.

The pathophysiology of RAO is multifactorial, involving direct mechanical trauma from catheter insertion, endothelial disruption, vasospasm, flow turbulence, and blood stasis during compression—all of which promote a vasoconstriction and prothrombotic environment.[23] Owing to anatomical and physiological vulnerabilities, infants and young children are at a significantly increased risk of developing RAO.[6] The radial artery is narrow and more fragile[1,11,24] and the catheter to vessel diameter ratio is frequently disproportionately large, which increases the likelihood of endothelial trauma, vasospasm, and thrombosis.[10] Moreover, multiple, prolonged catheterizations are frequently required in patients with congenital anomalies or those requiring early or multiple surgery, prolonged intensive care, or mechanical ventilation throughout their treatment. In high-risk groups—such as preterm infants or those with congenital heart disease, low cardiac output syndrome, cyanosis, dehydration, or systemic infection—these factors converge to exacerbate distal hypoperfusion.[25]

Table 2. Results of Radial Artery Catheterization and Catheter Removal

Variable[a]	No./total No. (%)		OR (95% CI of OR or mean difference)	ARR (95% CI of ARR)	*P* value[b]
	Control (n = 65)	Nitroglycerin (n = 67)			
Radial artery occlusion after catheter removal (primary outcome)[c]	48/65 (73.8)	17/67 (25.4)	0.12 (0.055 to 0.263)	48.5 (33.6 to 63.4)	<.001
Duration of catheterization, mean (SD) [95% CI], h[d]	48.9 (61.0) [33.8 to 64.0]	45.6 (51.8) [33.0 to 58.2]	NA (−16.2 to 22.8)	NA	.74
Time required for hemostasis, mean (SD) [95% CI]	5.1 (1.1) [4.8 to 5.4]	5.5 (1.6) [5.1 to 5.9]	NA (−0.85 to 0.88)	NA	NR
Duration of RAO, mean (SD) [95% CI], d	3.2 (2.1) [2.4 to 4.0]	3.2 (2.5) [1.7 to 4.7]	NA (−1.7 to 1.6)	NA	NR
Recovery of radial artery flow before discharge	20/48 (41.7)	14/17 (82.4)	6.53 (1.66 to 25.78)	−40.7 (−62.6 to −17.8)	NR
Radial artery diameter, mean (SD) [95% CI]					
Baseline diameter, mm	1.1 (0.4) [1.0 to 1.2]	1.2 (0.3) [1.1 to 1.3]	NA (−0.2 to 0.0)	NA	NR
Diameter, after subcutaneous injection, mm	1.1 (0.4) [1.0 to 1.2]	1.4 (0.4) [1.3 to 1.5]	NA (−0.4 to −0.1)	NA	NR
Diameter, after catheter removal, mm[d]	1.0 (0.8) [0.8 to 1.2]	1.3 (0.5) [1.2 to 1.4]	NA (−0.5 to 0.0)	NA	.02
Peak blood flow velocity of the radial artery, mean (SD) [95% CI]					
Baseline peak flow velocity, cm/s	9.8 (9.5) [7.4 to 12.1]	11.3 (9.9) [8.9 to 13.7]	NA (−4.9 to 1.9)	NA	NR
Peak flow velocity, after subcutaneous injection, cm/s	9.1 (9.3) [6.8 to 11.4]	12.7 (8.7) [10.6 to 11.8]	NA (−6.8 to −0.5)	NA	NR
Peak flow velocity, after catheter removal, cm/s[d]	7.4 (9.2) [5.1 to 9.7]	13.0 (11.0) [10.3 to 15.7]	NA (−9.1 to −2.1)	NA	.002
Perfusion index of ipsilateral index finger, mean (SD) [95% CI]					
Baseline perfusion index	0.94 (0.80) [0.74 to 1.14]	1.59 (1.30) [1.27 to 1.91]	NA (−1.03 to −0.28)	NA	NR
Perfusion index, after subcutaneous injection	0.96 (0.91) [0.74 to 1.19]	1.58 (1.37) [1.24 to 1.91]	NA (−1.01 to −0.21)	NA	NR
Perfusion index, after catheter removal[d]	0.65 (0.49) [0.52 to 0.77]	1.37 (1.09) [1.10 to 1.63]	NA (−1.01 to −0.43)	NA	<.001

Abbreviations: ARR, Absolute risk reduction; NA, not applicable; NR, not reported (exploratory outcome); OR, odds ratio.

[a] All variables are exploratory outcomes except for the primary outcome and secondary outcomes.

[b] A 2-sided *P* value <.004 indicates statistical significance.

[c] Primary outcome.

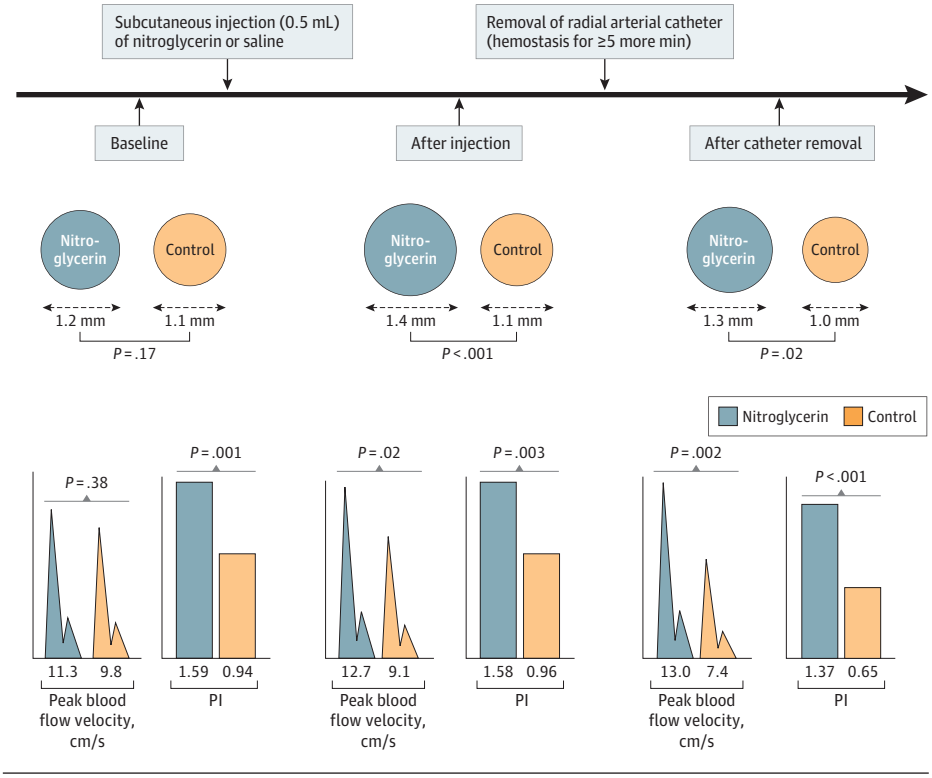
[d] Secondary outcome.

RAO may result in permanent vessel damage, compromising both immediate clinical management and future vascular access. Therefore, RAO prevention in pediatric patients holds considerable clinical importance.

In the present study, RAO incidence was reduced, and recovery from RAO was more favorable in the nitroglycerin group. These results suggest that nitroglycerin likely plays a role in preventing RAO onset and reducing its severity. Prior studies in adults have demonstrated that intra-arterial, topical, and subcutaneous nitroglycerin can significantly reduce RAO.[14,15,17] Nitroglycerin facilitates vasodilation, enhances antegrade flow during hemostasis, and may reduce endothelial injury and thrombosis.[21] Given the unique anatomical challenges in small children, such as smaller diameter, thinner walls, and a heightened susceptibility for vasospasm, the benefit of vasodilation may be even more pronounced.[1,26] We observed that the effects of subcutaneous nitroglycerin remained for an extended period, helping to prevent subsequent intraoperative catheter malfunction. Furthermore, the more favorable baseline PI observed in the nitroglycerin group following prolonged catheterization may suggest a prolonged benefit of nitroglycerin in preserving vascular integrity.[12,14,15] Notably, subcutaneous nitroglycerin did not prolong hemostasis time or increase bleeding, which supports its safety profile in surgical pediatric patients.

The present study showed that nitroglycerin-induced vasodilation increased radial artery blood flow, as reflected by peak blood flow velocity and PI after catheterization and catheter removal. The simultaneous increase in vessel diameter and flow velocity suggests the overall enhancement of arterial perfusion. Peripheral perfusion can be assessed using the PI, which is an indirect marker of pulsatile flow over nonpulsatile flow and reflects the tissue perfusion.[27] Reference PI values typically range between 0.8 to 1.2 in neonates and infants.[28] In our study, the mean (SD) PI after catheter removal was 1.37 (1.09) and 0.65 (0.49) in the nitroglycerin and control groups, re-

Figure 3. Diagram of the Radial Artery During Catheter Removal



The diameter, peak blood flow velocity, and perfusion index (PI) were measured at baseline, 3 minutes after the subcutaneous injection (after injection), and after catheter removal. After injection, the nitroglycerin group showed a significantly larger diameter (mean [SD], 1.4 [0.4] mm) compared with the baseline diameter (mean [SD], 1.2 [0.3] mm; 95% CI of mean difference, 0.24-0.11; $P < .001$) and the control group (mean [SD], 1.1 [0.4] mm; 95% CI of mean difference, 0.13-0.40 mm; $P < .001$). The nitroglycerin group also demonstrated significantly higher peak blood flow velocity than the control group after injection and after catheter removal. Additionally, the nitroglycerin group exhibited a significantly higher PI compared with the control group at baseline, after injection, and after catheter removal.

spectively, indicating a meaningful improvement in distal perfusion by nitroglycerin, which could enhance tissue oxygenation.[27] Additionally, as the peak flow velocity of the radial artery in infants and young children has not been well established, the data presented in this study may serve as an initial reference for this population and contribute to future clinical and research applications.

The discrepancy between trends in peak blood flow velocity and PI may be attributable to the PI measurement site—the second digit—which receives blood flow from both the radial and ulnar arteries via the palmar arch. Nonetheless, the higher PI in the nitroglycerin group suggests increased radial artery blood flow substantially contributed to overall perfusion. Given its simplicity and feasibility for bedside monitoring, PI may prove to be a useful adjunct for the longitudinal assessment of arterial patency during and after catheterization in pediatric patients.

Strengths and Limitations

This study has several strengths. The present study was the first, to the authors' knowledge, to implement an intervention to prevent RAO in pediatric patients. The results of the present study highlight that RAO occurs frequently in small pediatric patients who require surgery at a young age owing to underlying conditions and offer an effective intervention to prevent this complication. Moreover, this study was the first, to the authors' knowledge, to collect data on radial artery diameter and parameters reflecting radial perfusion, including peak blood flow velocity and PI.

The present study also has some limitations. First, we were unable to control for the timing of catheter removal and postoperative events, such as wrist movements, catheter-site dressing, and the infusion of vasoactive drugs while the catheter was inside the radial artery. Therefore, missing data occurred for patients who did not receive the subcutaneous injection of the intervention drug before catheter removal. The result of the intention-to-treat analysis, in which missing values for the primary outcome (incidence of RAO) were handled using multiple imputation, are provided in the eAppendix in Supplement 2. The characteristics of the patients who dropped out and the tipping point sensitivity analysis for the missing data are presented in eTable 1 and eFigure 2 in the Supplement 2, respectively. Second, RAO in a true no-injection control group was not compared with that in the subcutaneous injection of saline or nitroglycerin group. However, because there were no changes in the vessel diameter, peak blood flow velocity, or PI after the subcutaneous injection in the control group, it can be inferred that saline did not have a significant impact on the incidence of RAO. Third, there was no long-term follow-up data on the duration of RAO, as it was only assessed during the hospitalization period. Future studies with extended follow-up of radial arterial function are warranted to clarify whether early pharmacologic intervention translates into sustained vascular benefits in high-risk pediatric patients. Fourth, we did not measure the peak flow velocity of the ulnar artery, therefore, we do not know about the compensation of ulnar artery flow after RAO.

Conclusions

In conclusion, results of this randomized clinical trial show that subcutaneous nitroglycerin injection before radial artery catheterization and catheter removal decreased the incidence of RAO after the removal of the catheter in pediatric patients younger than 3 years. These findings support the potential role of nitroglycerin in enhancing vascular preservation and promoting safe recovery after arterial catheter removal in young children.

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