ANESTHESIOLOGY

Subcutaneous Nitroglycerin for Radial Arterial Catheterization in Pediatric Patients

A Randomized Controlled Trial

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ABSTRACT

Background: Pediatric radial artery cannulation is challenging because of the small vessel size. Nitroglycerin is a potent vasodilator and facilitates radial artery cannulation by increasing the internal diameter and preventing the vasospasm in adult patients. The authors hypothesize that subcutaneous nitroglycerin injection will improve the success rate of pediatric radial artery cannulation.

Methods: This double-blind, randomized, controlled, single-center study enrolled pediatric patients (n = 113, age less than 2 yr) requiring radial artery cannulation during general anesthesia. The participants were randomized into the nitroglycerin group (n = 57) or control group (n = 56). After inducing general anesthesia, nitroglycerin solution (5 µg/kg in 0.5 ml), or normal saline (0.5 ml) was subcutaneously injected above the chosen radial artery over 10 s with ultrasound guidance. Three minutes later, the ultrasound-guided radial artery cannulation was performed. Radial artery diameter was measured before and after the subcutaneous injection and after cannulation. The primary outcome was the first-attempt successful cannulation rate. The secondary outcomes included the diameter of the radial artery and the overall complication rate including hematoma and vasospasm.

Results: A total of 113 children were included in the analysis. The nitroglycerin group had a higher first-attempt success rate than the control group (91.2% [52 of 57] *vs.* 66.1% [37 of 56]; $P = 0.002$; odds ratio, 5.3; 95% CI, 1.83 to 15.6; absolute risk reduction, –25.2%; 95% CI, –39.6 to –10.7%). Subcutaneous nitroglycerin injection increased the diameter of the radial artery greater than normal saline (25.0 ± 19.5% *vs.* 1.9 ± 13.1%; 95% CI of mean difference, 16.9 to 29.3%; $P < 0.001$). Overall complication rate was lower in the nitroglycerin group than in the control group (3.5% [2 of 57] *vs.* 31.2% [18 of 56]; $P = 0.001$; odds ratio, 0.077; 95% CI, 0.017 to 0.350; absolute risk reduction, 28.6%; 95% CI, 15.5 to 41.8%).

Conclusions: Subcutaneous nitroglycerin injection before radial artery cannulation improved the first-attempt success rate and reduced the overall complication rates in pediatric patients.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Radial artery cannulation in infants can be technically challenging
- In adult patients, nitroglycerin has been found to facilitate radial artery cannulation

What This Article Tells Us That Is New

- In children less than 2 yr of age, infiltration around the radial artery with 5 mcg/kg of nitroglycerin in 0.5 ml of saline increased the first success rate of arterial cannulation

The radial artery is the most frequently used site for arterial cannulation because it is superficial and has a relatively large diameter compared to other peripheral arteries.[1] However, cannulation of the radial artery is difficult in small pediatric patients because of the small vessel size.[1–3] As a result, the first-attempt success rate of pediatric radial artery cannulation ranges from 18 to 56% with the pulse palpation technique.[4,5] Although ultrasound guidance provides a significant improvement in the success rate of radial artery cannulation,[5,6] its first-attempt success rate ranges from 48 to 83% in small pediatric patients.[1,5–7]

Failure of cannulation during the first attempt results in multiple cannulation attempts, longer procedure time, and complications such as vasospasm, hematoma, or distal ischemia.[8] Radial artery spasm reduces the internal diameter of the artery and in turn, the success rate of cannulation.[9] Therefore, increasing the internal diameter and preventing vasospasm are important for successful radial artery cannulation in small pediatric patients.

Nitroglycerin is a potent vasodilator and has been used to dilate the artery, and to prevent or treat arterial spasm.[10–18] In adults, nitroglycerin facilitates radial artery cannulation by increasing the internal diameter,[17,18] shortening the procedure time, improving the success rate,[13,15,16] and decreasing the incidence of radial arterial occlusion after cardiac catheterization.[11,14] However, there have been no previous

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studies on utilizing nitroglycerin for radial artery cannulation in pediatric patients. Considering the small internal diameter of radial artery and the associated technical difficulties, the application of nitroglycerin might improve the cannulation success rate in small pediatric patients.

We hypothesized that the subcutaneous injection of nitroglycerin would dilate the radial artery and increase the first-attempt success rate. Thus, this study compares the effects of subcutaneous injection of nitroglycerin (5 μg/kg) *versus* normal saline during radial artery cannulation in small pediatric patients.

Materials and Methods

Subjects and Study Design

This prospective, parallel-arm, double-blinded, randomized controlled trial was approved by the Seoul National University Hospital Institutional Review Board, Seoul, Korea (Chairperson Byung-Joo Park) on February 2, 2019 (no. 1810-077-979). The trial was registered before patient enrollment at ClinicalTrials.gov (NCT03849183; registered February 18, 2019, principal investigator Jin-Tae Kim). This study was conducted at a single site, tertiary teaching children's hospital Seoul National University Hospital, Seoul, Republic of Korea, to evaluate the superiority of nitroglycerin over the placebo control. The authors evaluated the eligibility of patients and individually approached the parents or guardians of the children and obtained written informed consent to enroll the participants before surgery. We included pediatric patients (less than 2 yr) scheduled for elective surgery (neurosurgery, cardiac, general, others) under general anesthesia, and requiring invasive arterial blood pressure monitoring or frequent blood sampling. Patients with hypersensitivity or contraindication to nitroglycerin (glaucoma, increased intracranial pressure, intracranial hemorrhage, and recent use of sildenafil or vardenafil); recent history of radial artery puncture; wound, infection, or hematomas at cannulation site; peripheral vascular disease; and unstable vital signs including shock or significant arrhythmia were excluded from the study.

Randomization

Subjects were allocated to either the nitroglycerin group or the normal saline (control) group at an allocation ratio of 1:1 by block randomization. Group allocations were generated by computer-generated randomization software (https://www.randomizer.org) and sealed in sequentially numbered, opaque envelopes that were opened by a trained study nurse before the induction of general anesthesia. Each envelope contained the group allocation with instructions for the subcutaneous medication (nitroglycerin or normal saline). Operators of the ultrasound and radial artery cannulation were blinded to the patients' group allocation. Another anesthesiologist who measured the depth and diameter of the radial artery from the stored images was also blinded to the group allocation.

Preparing the Nitroglycerin Solution

Since there was no study using subcutaneous nitroglycerin for arterial cannulation in pediatric patients, the dose of nitroglycerin was determined based on the effective subcutaneous dose in adult studies and the safe intravenous dose in pediatric patients. In adult cardiac patients, 400 to 500 μg nitroglycerin is subcutaneously injected to facilitate radial artery cannulation,[13,15,16] and to prevent radial arterial occlusion[14] without systemic hypotension. In children and adolescents, intravenous nitroglycerin at doses as high as 40 μg/kg/min did not decrease the mean arterial pressure less than 55 mmHg or more than one third of baseline mean arterial pressure.[19] Therefore, in the current study, the dose of nitroglycerin was determined to be 5 μg/kg based on the dose used in adult patients. The rate of administration was limited to 0.5 μg/kg/s (30 μg/kg/min) to avoid systemic vasodilation by accidental intravenous/intra-arterial injection.

The volume of nitroglycerin solution or saline was determined to optimize the depth of radial artery. Previous study showed that the first-attempt success rate and the overall success rate is higher for radial artery depth between 2 to 4 mm than those that are less than 2 mm or 4 mm or more in small pediatric patients.[20] Therefore, we used a small volume (0.5 ml) of nitroglycerin solution or saline to avoid shifting the radial artery deeper than 4 mm.

A trained study nurse prepared the syringe of placebo (0.5 ml of normal saline) or nitroglycerin (5 μg/kg in 0.5 ml) according to the group allocation. In the nitroglycerin group, the study nurse prepared the 1 ml syringe of nitroglycerin (10 μg/kg in 1.0 ml) according to the nearest body weight of each patient: 25 μg/ml for 2.5 kg, 50 μg/ml for 5 kg, 75 μg/ml for 7.5 kg, 100 μg/ml for 10 kg, 125 μg/ml for 12.5 kg, and 150 μg/ml for 15 kg. During subcutaneous injection, only 0.5 ml was used.

Anesthesia and Ultrasound-guided Radial Artery Cannulation

For the intention-to-treat evaluation, operators could choose the left or right radial artery according to their preferences. After general anesthesia, Allen's test was performed to ensure ulnar arterial patency. Noninvasive arterial blood pressure was measured every 2.5 min before the radial artery cannulation at the chosen arm. After the radial artery cannulation, invasive arterial blood pressure was monitored. The patient's wrist was extended over a roll to keep the angle of the wrist unchanged. In both groups, hand hygiene was done before gloving and a sterile barrier was placed. Skin preparation was done with alcohol-based chlorhexidine antiseptic.[21] Assessment of the radial artery and its cannulation using ultrasonography was performed by one of three pediatric anesthesiologists blinded to group allocation. All three pediatric anesthesiologists (Y.E.J., S.H.J., and J.T.K.) had performed more than 100 arterial cannulations in neonates and infants. We used an E-CUBE

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i7 unit (ALPINION Medical Systems Co., Korea) with a high-frequency (8 to 17 MHz) linear hockey stick–shaped IO8-17T probe (ALPINION Medical Systems Co., Korea) with a small footprint (31 × 6 mm). A short-axis (out-of-plane) view of the radial artery was obtained to measure the internal diameter and depth of the radial artery. In the nitroglycerin group, 5 µg/kg nitroglycerin in 0.5 ml saline solution was subcutaneously injected above the radial artery over 10 s with ultrasound guidance to avoid intra-arterial injection. In the control group, the same procedure was performed with 0.5 ml normal saline without nitroglycerin.

Three minutes later, a short-axis view of the radial artery was obtained at the same location to reassess the diameter and depth of the radial artery. Arterial cannulation was performed using the long-axis view (in-plane) technique with a 24-gauge, 0.7 mm × 1.9 cm over-the-needle catheter (Jelco, Smiths Medical, USA). During arterial cannulation, the operator could use the transfixion technique (intentionally puncturing both walls of the artery) at one's discretion. However, to eliminate the influence of other techniques on the success rate and the procedure time, the use of guidewire was not allowed in the study population. Cannulation was considered complete when the arterial waveform was confirmed on the monitor. If cannulation was unsuccessful within the second attempt or within 10 min, the case was considered a failure at the chosen radial artery. After the failure, an alternative site such as a contralateral radial artery, or dorsalis pedis artery, or posterior tibial artery was used for cannulation without subcutaneous injection of the study drugs. The overall procedure time of arterial cannulation was defined as the time interval from the first skin puncture by the over-the-needle catheter to confirmation of the arterial waveform on the monitor irrespective of the location of the arterial cannulation.

After the procedure, the diameter and depth of the radial artery and the occurrence of hematoma or vasospasm were evaluated with ultrasonography. Procedure-related complications and the function of the catheter were evaluated until the end of anesthesia.

Statistical Analyses and Outcome Variables

The following data were collected for every patient: age, weight, sex, American Society of Anesthesiologists physical status classification, and surgery type. The primary outcome was the first-attempt success rate of radial artery cannulation. The number of attempts was defined as the number of skin punctures for radial arterial cannulation. Successful artery cannulation was confirmed by arterial waveform on the monitor. The secondary outcomes included the diameter and depth of the radial artery before subcutaneous injection, after subcutaneous injection, and after the cannulation, and the time between the subcutaneous injection and ultrasound exam of diameter and depth. For the radial artery cannulation at the chosen radial artery, procedure time to success within the first and second attempt, the second-attempt success rate (within 10 min), and overall complications including hematoma, vasospasm (more than 25% decrease in the radial artery diameter after cannulation without intra-arterial hematoma), distal ischemia, and hypotension (more than 20% decrease in the mean blood pressure within 20 min after subcutaneous injection) were recorded. The incidence of catheter malfunction at the chosen radial artery (monitoring or sampling failure despite catheter flush or changing the catheter dressing) was also measured during anesthesia. The overall procedure time and the overall number of attempts of arterial cannulation were recorded. The outcome assessor (J.H.L) blinded to group allocation measured the depth and diameter of radial artery of all patients from the stored ultrasound images.

The sample size was calculated based on that of previous studies. The first-attempt success rate of ultrasound-guided radial artery cannulation ranged from 48 to 83% in children under 2 yr.[1,6] We assumed that the first-attempt success rate for radial artery cannulation would be 85% in the nitroglycerin group and 60% in the control group. Assuming a power of 0.8 for the 25% difference, with a two-sided alpha of 0.05, the sample size for each group was calculated as 52. Considering an attrition rate of 10%, 116 patients in total were recruited.

All data were expressed as mean ± SD or median (interquartile range) unless otherwise specified. Distribution was tested using the Shapiro–Wilk normality test. Baseline characteristics of the study population were evaluated using the *t* test and Mann–Whitney *U* test. The primary outcome was evaluated using the χ^2 test. Secondary outcomes were evaluated using the χ^2 test, the *t* test, and the Mann–Whitney *U* test.

Using proportional hazards assumption, Kaplan–Meier analysis of the overall procedure time to successful cannulation of the chosen radial artery was performed, and the data were compared between the groups using the log-rank test. Statistical analyses were performed using IBM SPSS Statistics 22 (SPSS Inc., IBM Corporation, USA) and R software version 3.4.4 (R Foundation for Statistical Computing, Austria), and the package "survival" was used for Kaplan–Meier survival curves. A two-sided *P*-value less than 0.05 indicated statistical significance.

Results

From March 20 to July 22, 2019, we enrolled 116 pediatric patients. After excluding three patients (recent radial artery puncture = 1, unstable vital signs = 1, and refusal to participate in study = 1), 113 patients were randomized into the nitroglycerin (n = 57) and control (n = 56) groups (fig. 1). No study protocol violation was reported during the entire study period, and 113 patients were included in the analysis.

The baseline patient characteristics are summarized in table 1. Cardiac surgery was the most commonly performed surgery in both groups, followed by neurosurgery, and

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general surgery. Three anesthesiologists (Y.E.J., S.H.J., and J.T.K.) performed radial artery cannulation in 56 (nitroglycerin = 29, control = 27), 34 (nitroglycerin = 17, control = 17), and 23 (nitroglycerin = 11, control = 12) cases, respectively.

The primary outcome, first-attempt success rate of radial artery cannulation, was significantly higher in the nitroglycerin group than in the control group (91.2% [52/57] *vs.* 66.1% [37/56]; $P = 0.002$; odds ratio, 5.3; 95% CI, 1.83 to 15.6; absolute risk reduction, –25.2%; 95% CI, –39.6 to -10.7%). The procedure time to the first-attempt success was shorter in the nitroglycerin group (median, 37 s; 25th to 75th percentile, 25 to 47 s; range, 16 to 199 s) than the control group (median, 48 s; 25th to 75th percentile, 36 to 59 s; range, 18 to 183 s; $P = 0.011$). The second-attempt success rate at the chosen radial artery was not higher in the nitroglycerin group than in the control group (96.5% [55/57] *vs.* 85.7% [48/56]; $P = 0.062$; odds ratio, 4.6; 95% CI, 0.93 to 22.6; absolute risk reduction, –10.8%; 95% CI, –21.1 to –0.4%). The procedure time to success within the second attempt was shorter in the nitroglycerin group (median, 37 s; 25th to 75th percentile, 25 to 53 s; range, 16 to 285 s) than the control group (median, 57 s; 25th to 75th percentile, 37 to 168 s; range, 18 to 548 s; $P < 0.001$). The use of the transfixion technique was not statistically different between the nitroglycerin and control groups (10.5% [6/57] *vs.* 19.6% [11/56]; $P = 0.181$; odds ratio, 0.48; 95% CI, 0.164 to 1.41; absolute risk reduction, 9.1%; 95% CI, –4.0 to 22.2%).

The overall procedure time of arterial cannulation was shorter in the nitroglycerin group (median, 38 s; 25th to 75th percentile, 27 to 57 s; range, 16 to 746 s) than the control group (median, 60 s; 25th to 75th percentile, 41 to 294 s; range, 18 to 893 s; $P < 0.001$). The overall number of attempts was smaller in the nitroglycerin group (median, 1; 25th to 75th percentile, 1 to 1; range, 1 to 4) than the

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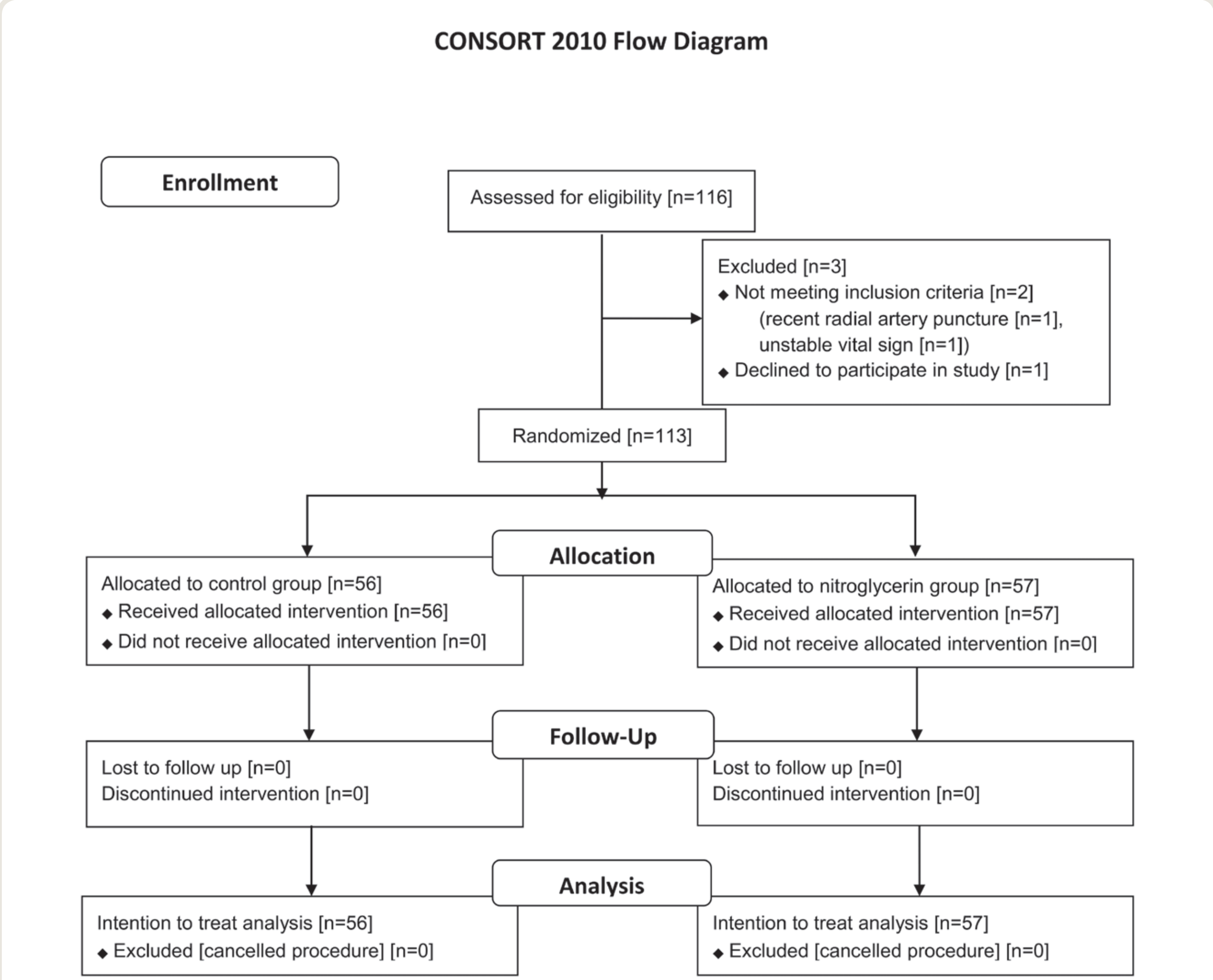

Fig. 1. The Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

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Table 1. Patient Characteristics of Control Group and Nitroglycerin Group for Radial Artery Cannulation

	Control (n = 56)	Nitroglycerin (n = 57)
Age (month)	6.5 (2.0–15.0) [1.0–23.0]	6.0 (3.0–13.5) [1.0–23.0]
Male	27 (48.2%)	26 (45.6%)
Female	29 (51.8%)	31 (54.4%)
Weight (kg)	7.4 ± 2.8	7.6 ± 2.7
Gestational age < 50 weeks	17 (30.4%)	16 (28.1%)
ASA Physical Status		
I	22 (39.3%)	30 (52.6%)
II	13 (23.2%)	9 (15.8%)
III	20 (35.7%)	18 (31.6%)
IV	1 (1.8%)	0 (0%)
Surgery		
Cardiac surgery	26 (46.4%)	25 (43.9%)
Neurosurgery	14 (25.0%)	19 (33.3%)
General surgery	13 (23.2%)	9 (15.8%)
Others	3 (5.4%)	4 (7.0%)

Values are mean ± SD, median (interquartile range) [range], or number (proportion).
ASA, American Society of Anesthesiologists.

control group (median, 1; 25th to 75th percentile, 1 to 2; range, 1 to 5; $P = 0.001$).

Overall complications were significantly lower in the nitroglycerin group than in the control group (3.5% [2/57] *vs.* 31.2% [18/56]; $P = 0.001$; odds ratio, 0.077; 95% CI, 0.017 to 0.350; absolute risk reduction, 28.6%; 95% CI, 15.5 to 41.8%), including vasospasm (1.8% [1/57] *vs.* 19.6% [11/56]; $P = 0.014$; odds ratio, 0.073; 95% CI, 0.009 to 0.59; absolute risk reduction, 17.9%; 95% CI, 6.9 to 28.8%), and hematoma (1.8% [1/57] *vs.* 23.2% [13/56]; $P = 0.008$; odds ratio, 0.059; 95% CI, 0.007 to 0.47; absolute risk reduction, 21.5%; 95% CI, 9.9 to 33.0%).

After subcutaneous injection, the internal diameter and the cross-sectional area of the radial artery increased in the nitroglycerin group compared to the control group (25.0 ± 19.5% *vs.* 1.9 ± 13.1%; 95% CI of mean difference, 16.9 to 29.3%; $P < 0.001$ and 60.0 ± 49.5% *vs.* 5.6 ± 26.7%; 95% CI of mean difference, 39.6 to 69.2%; $P < 0.001$, respectively; fig. 2). There was no difference in the depth of radial artery between the two groups throughout the procedure (table 2).

In the control group, vasospasm was observed in 10 (52.6%) of the 19 patients who experienced cannulation failure at the first attempt. In the second cannulation attempt of these patients, the cannulation was successful in only 3 of 10 patients (30%). In the nitroglycerin group, vasospasm was observed in one (20%) of the five patients who experienced cannulation failure at the first attempt. In the second cannulation attempt of this patient, the cannulation was failed. Putting the two groups together, the second cannulation attempt at the chosen radial artery was successful in 3 (27.3%) of 11 patients with vasospasm after the failure at the first attempt.

Catheter malfunction at the chosen radial artery occurred in four patients, and they showed both monitoring and sampling failure. In the control group, 3/48 (6.25%) patients developed catheter malfunction during anesthesia. One patient showed vasospasm after successful cannulation at the first attempt, and two patients were successfully cannulated at the second attempt but showed vasospasm and hematoma after the procedure. In the nitroglycerin group, 1/55 (1.8%) patient developed catheter malfunction during anesthesia. However, this patient showed no hematoma and vasospasm after the radial artery cannulation.

There was no difference in the mean blood pressure between the nitroglycerin and control groups before and after subcutaneous injection (53.4 ± 12.2 mmHg *vs.* 53.7 ± 15.1 mmHg; 95% CI of mean difference, –5.4 to 4.9 mmHg; $P = 0.921$ and 60.5 ± 13.1 mmHg *vs.* 58.1 ± 14.1 mmHg; 95% CI of mean difference, –2.7 to 7.4 mmHg; $P = 0.360$, respectively). No patient in either group developed hypotension within 20 min after subcutaneous injection. No patient in either group developed distal ischemia. Kaplan–Meier analysis showed that the overall procedure time to successful cannulation of the chosen radial artery was shorter in the nitroglycerin group than in the control group ($P < 0.0001$; fig. 3).

Discussion

The primary finding of this study is that the subcutaneous injection of nitroglycerin before radial artery cannulation increases the first-attempt success rate by increasing the internal diameter of the radial artery in small pediatric patients. We also found that subcutaneous injection of nitroglycerin decreases the number of cannulation attempts, procedure time, and procedure-related complications.

The major challenge to a successful radial artery cannulation in pediatric patients is the small arterial size. A recent study reported that the mean internal diameter of the radial artery is 1.3 ± 0.2 mm in children aged less than 2 yr,[1] consistent with our findings of 1.2 ± 0.3 mm in which the baseline radial artery diameter was 1 mm or less in 37.2% of patients. Therefore, radial artery cannulation with a standard 24-gauge catheter with an external diameter of 0.7 mm is not easy. Subcutaneous injection of nitroglycerin before cannulation increased the internal diameter and cross-sectional area of the radial artery in our study, thus explaining the higher first-attempt success rate.

Success at the first attempt is crucial during pediatric peripheral artery cannulation,[22] as the resulting vasospasm or hematoma from failed attempts further decreases the internal diameter of artery (fig. 4). Because the radial artery is α1-adrenoceptor–dominant, it is susceptible to vasospasm during cannulation attempts.[23] Temporary vasospasm occurs in up to 57% of cases immediately after radial

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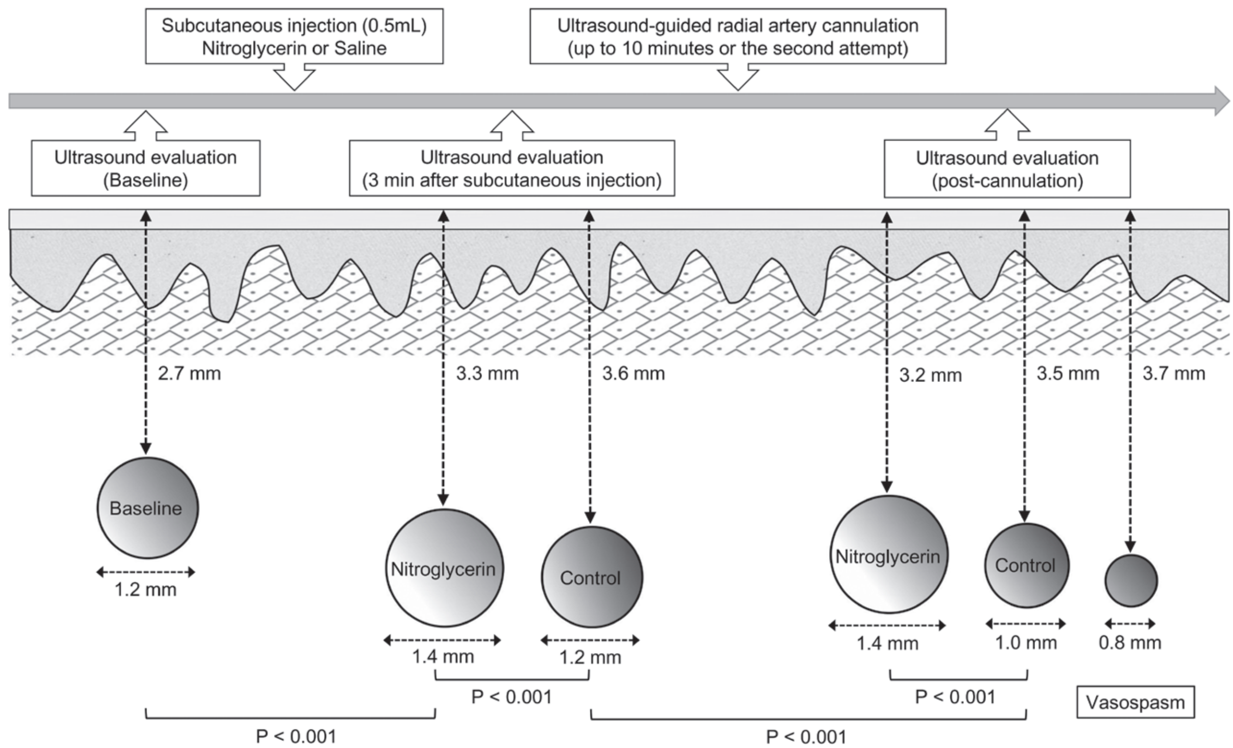

Fig. 2. Diagram of the diameter and depth of the radial artery throughout the procedure. After subcutaneous injection, nitroglycerin group showed significant vasodilation (1.4 ± 0.3 mm) compared to the baseline (1.2 ± 0.3 mm; 95% CI of mean difference, 0.22 to 0.33; $P < 0.001$) and the control group (1.2 ± 0.3 mm; 95% CI of mean difference, 0.14 to 0.37 mm; $P < 0.001$). The time between the subcutaneous injection and ultrasound exam of diameter and depth was 224 ± 27 s (95% CI, 216 to 232 s; range, 188 to 294 s) in the control group and 220 ± 17 s (95% CI, 214 to 223 s; range, 188 to 283 s; 95% CI of mean difference, –12 to 6 s; $P = 0.495$) in the nitroglycerin group. After radial artery cannulation, radial artery diameter decreased in the control group (1.0 ± 0.3 mm; 95% CI of mean difference, –0.24 to –0.14 mm; $P < 0.001$), while the nitroglycerin group showed no significant change (1.4 ± 0.3 mm; 95% CI of mean difference, 0 to 0.1 mm; $P = 0.460$). Patients with vasospasm (n = 12) showed a narrow radial artery with a median diameter of 0.8 mm (interquartile range, 0.4 to 1.0 mm).

arterial cannulation,[24] and sustained vasospasm occurs in 4 to 20% during transradial cardiac catheterization in adults.[9] Vasospasm makes cannulation and catheter advancement into the artery more difficult,[4] and decreases the success rate of radial artery cannulation.[9] A recent case report of radial artery spasm in an 8-month-old infant after failed cannulation showed the internal diameter to decrease from 2.1 mm to 0.4 mm.[25] In the current study, the second-attempt success rate at the chosen radial artery was very low (3/11, 27.3%) after the occurrence of vasospasm. All three patients in the control group who were successfully cannulated at the chosen radial artery despite the vasospasm showed catheter malfunction during anesthesia. The risk of delayed vasospasm or total occlusion was higher in the control group because the smaller radial artery is more susceptible to endothelial damage during cannulation. Vasospasm was observed in only one patient in the nitroglycerin group. A relatively larger internal diameter due to subcutaneous nitroglycerin administration might have increased the second-attempt success rate and decreased catheter malfunction.

Various routes such as intra-arterial,[10–12] topical,[17,18] and subcutaneous[13–16] routes are used to administer nitroglycerin for radial artery dilation in adult patients. Intra-arterial nitroglycerin can reduce vasospasm and occlusion of the radial artery in adult cardiac patients.[10–12] However, this route is not suitable before radial artery cannulation in children. Topical nitroglycerin cream has the advantage of being noninvasive and shows significant vasodilatory effects on the radial artery in healthy adult patients.[17,18] However, topical nitroglycerin should be applied on the skin for at least 30 min before radial artery cannulation. Additionally, transdermal absorption of topically applied nitroglycerin is difficult to predict in pediatric patients. Therefore, the authors chose to inject nitroglycerin subcutaneously above the radial artery. This route of administration is the most effective for localized vasodilation without the possible systemic side effects.[13,15]

In the current study, the dose of 5 μg/kg in 0.5 ml subcutaneous nitroglycerin produced a significant increase in the diameter of radial artery without systemic effects

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Table 2. Results of Radial Artery Cannulation in Control Group and Nitroglycerin Group

Variables	Control (n = 56)	Nitroglycerin (n = 57)	Odds Ratio	95% CI of Odds Ratio or Mean Difference	Absolute Risk Reduction (95% CI of Absolute Risk Reduction)	*P* Value
Radial artery cannulation at the first chosen radial artery						
First-attempt success rate	37/56 (66.1%)	52/57 (91.2%)	5.3	1.83 to 15.6	–25.2% (–39.6% to –10.7%)	0.002
Procedure time to success within the first attempt (s)	48 (36 to 59) [18 to 183]	37 (25 to 47) [16 to 199]	Not applicable	Not applicable	Not applicable	0.011
Second-attempt success rate within 10 min	48/56 (85.7%)	55/57 (96.5%)	4.6	0.93 to 22.6	–10.8% (–21.1% to –0.4%)	0.062
Procedure time to success within the second attempt (s)	57 (37 to 168) [18 to 548]	37 (25 to 53) [16 to 285]	Not applicable	Not applicable	Not applicable	< 0.001
Catheter malfunction	3/48 (6.25%)	1/55 (1.8%)	0.278	0.028 to 2.76	4.4% (–3.3 to 12.1%)	0.336
Use of another artery	8/56 (14.3%)	2/57 (3.5%)	0.218	0.44 to 1.08	10.8% (0.44 to 21.1%)	0.062
Contralateral radial artery	4/56 (7.1%)	0 (0%)				
Posterior tibial artery	2/56 (3.6%)	1/57 (1.8%)				
Dorsalis pedis artery	2/56 (3.6%)	1/57 (1.8%)				
Use of the transfixion technique	11/56 (19.6%)	6/57 (10.5%)	0.48	0.164 to 1.41	9.1% (–4.0 to 22.2%)	0.181
Overall procedure time of arterial cannulation (s)	60 (41 to 294) [18 to 893]	38 (27 to 57) [16 to 746]	Not applicable	Not applicable	Not applicable	< 0.001
Overall number of attempts	1 (1 to 2) [1 to 5]	1 (1 to 1) [1 to 4]	Not applicable	Not applicable	Not applicable	0.001
Overall complication at first chosen radial artery	18/56 (32.1%)	2/57 (3.5%)	0.077	0.017 to 0.350	28.6% (15.5 to 41.8%)	0.001
Vasospasm	11/56 (19.6%)	1/57 (1.8%)	0.073	0.009 to 0.59	17.9% (6.9 to 28.8%)	0.014
Hematoma	13/56 (23.2%)	1/57 (1.8%)	0.059	0.007 to 0.47	21.5% (9.9 to 33.0%)	0.008
Distal ischemia	0 (0%)	0 (0%)	Not applicable	Not applicable	Not applicable	Not applicable
Hypotension (>20% decrease in the mean blood pressure) within 20 min after subcutaneous injection	0 (0%)	0 (0%)	Not applicable	Not applicable	Not applicable	Not applicable
Radial artery size						
Baseline diameter (mm)	1.2 ± 0.3 (1.1 to 1.2)	1.2 ± 0.3 (1.1 to 1.2)	Not applicable	–0.1 to 0.1	Not applicable	0.985
Time between the subcutaneous injection and ultrasound exam of diameter and depth (s)	224 ± 27 (216 to 232)	220 ± 17 (214 to 223)	Not applicable	–12 to 6	Not applicable	0.495
Diameter, after subcutaneous injection (mm)	1.2 ± 0.3 (1.1 to 1.2)	1.4 ± 0.3 (1.3 to 1.5)	Not applicable	0.1 to 0.4	Not applicable	< 0.001
Diameter, postcannulation (mm)	1.0 ± 0.3 (0.9 to 1.1)	1.4 ± 0.3 (1.3 to 1.5)	Not applicable	0.3 to 0.5	Not applicable	< 0.001
Percentage change of diameter between baseline and after injection (%)	1.9 ± 13.1 (–1.6 to 5.4)	25.0 ± 19.5 (19.8 to 30.2)	Not applicable	16.9 to 29.3	Not applicable	< 0.001
Percentage change of area between baseline and after injection (%)	5.6 ± 26.7 (–1.5 to 12.7)	60.0 ± 49.5 (46.9 to 73.1)	Not applicable	39.6 to 69.2	Not applicable	< 0.001
Baseline depth (mm)	2.7 ± 1.4 (2.3 to 3.0)	2.6 ± 0.9 (2.4 to 2.9)	Not applicable	–0.4 to 0.4	Not applicable	0.966
Depth, after subcutaneous injection (mm)	3.6 ± 1.3 (3.2 to 3.9)	3.3 ± 1.0 (3.1 to 3.6)	Not applicable	–0.7 to 0.2	Not applicable	0.288
Depth, postcannulation (mm)	3.5 ± 1.3 (3.2 to 3.9)	3.2 ± 0.9 (3.0 to 3.5)	Not applicable	–0.7 to 0.2	Not applicable	0.205

Values are mean ± SD (95% CI), median (interquartile range) [range], or number (proportion).

in the study subjects. This makes subcutaneous nitroglycerin a treatment option for critically ill pediatric patients who frequently need invasive arterial blood pressure monitoring or frequent blood sampling. Additionally, the depth of radial artery is an important factor for ultrasound-guided cannulation in pediatric patients under 3 yr of age.[20] In the current study, the volume of 0.5 ml was used, and the mean depth of the radial artery was within the 2 to 4 mm range after subcutaneous injection in both groups without a significant difference. Therefore, the effect of the depth of radial artery on the success rate was controlled.

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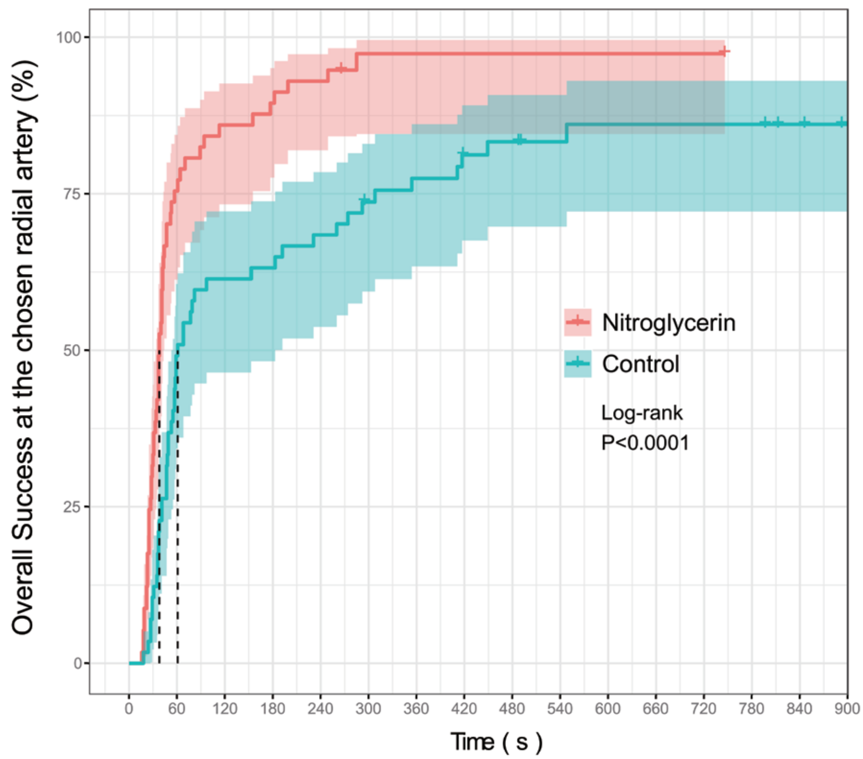

Number of patients need arterial cannulation

	0	60	120	180	240	300	360	420	480	540	600	660	720	780	840	900
Nitroglycerin	57	14	8	6	4	1	1	1	1	1	1	1	1	0	0	0
Control	56	28	21	20	17	13	11	8	7	5	4	4	4	4	2	0

Cumulative number of overall success at the chosen radial artery

	0	60	120	180	240	300	360	420	480	540	600	660	720	780	840	900
Nitroglycerin	0	43	49	51	53	55	55	55	55	55	55	55	55	55	55	55
Control	0	28	35	36	39	42	44	46	47	47	48	48	48	48	48	48

Cumulative number of right-censoring

	0	60	120	180	240	300	360	420	480	540	600	660	720	780	840	900
Nitroglycerin	0	0	0	0	0	1	1	1	1	1	1	1	1	2	2	2
Control	0	0	0	0	0	1	1	2	2	4	4	4	4	4	6	8

Fig. 3. Kaplan–Meier estimates for the overall procedure time to successful cannulation of the chosen radial artery within two attempts and 10 min (nitroglycerin *vs.* control group, $P < 0.0001$). The median cannulation time of the chosen radial artery was 37 s (interquartile range, 25 to 53 s) in the nitroglycerin group and 57 s (interquartile range, 37 to 168 s) in the control group.

There are some precautions for the subcutaneous injection of nitroglycerin in infants and small children. First, because the radial artery is small and shallow, subcutaneous injection with palpation is inaccurate and may result in intra-arterial injection. Therefore, ultrasound-guidance would be helpful to locate the radial artery and prevent intra-arterial injection. Second, dilatation of the radial artery occurs locally near the nitroglycerin injection site. Accordingly, the subcutaneous injection should be performed near the target site of the radial artery. Third, subcutaneously injected air bubbles can mask the underlying radial artery in the ultrasound image (fig. 4H), hence care should be taken to minimize air bubbles in the syringe.

The current study has some limitations. First, the success rates and complications of a true no-injection control group (without subcutaneous saline or nitroglycerin)

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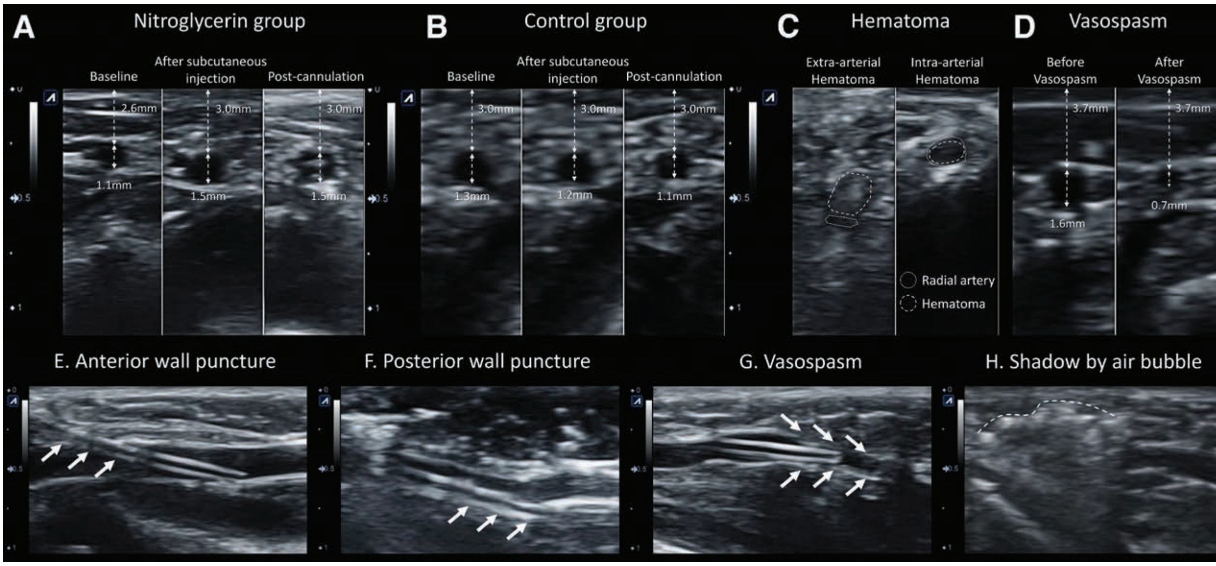

Fig. 4. Ultrasound images of the radial artery cannulation. Examples of changes in the diameter and depth of the radial artery after subcutaneous injection and postcannulation. (*A*) A 3-month-old infant in the nitroglycerin group showed significant vasodilation after subcutaneous injection and maintained the increased diameter after cannulation. (*B*) A 1-month-old infant in the control group showed no change in the radial arterial diameter after subcutaneous injection. (*C*) Hematomas and (*D*) vasospasm after failed attempt. Long-axis images of (*E*) anterior arterial wall puncture, (*F*) posterior arterial wall puncture, (*G*) vasospasm proximal to the catheter tip, and (*H*) shadow by air bubble due to subcutaneous injection.

were not compared to the subcutaneous injection of saline or nitroglycerin in the current study. Second, the anesthesiologists who performed the ultrasound assessment of the radial artery and its cannulation could notice a change in the radial artery diameter after subcutaneous injection. However, we think that if a different anesthesiologist performed artery cannulation, the arterial puncture and probe application site can be different from the injection site. Additionally, the change in the diameter of radial artery was not always matched with group allocation in both groups. Third, we evaluated the diameter of radial artery and distal perfusion only during the intraoperative period. Because the timing of the catheter removal varied depending on the surgery type and clinical situation, we were not able to evaluate the diameter of radial artery and distal perfusion after catheter removal. Fourth, general anesthesia could potentially affect the diameter of the radial artery. It has been shown that the diameter of the radial and ulnar artery increase considerably (about 5 to 12%) after induction with propofol and maintenance with sevoflurane in adult patients.[26] Because of the vasodilatory effect of general anesthetics, the diameter of radial artery in the current study might be larger than that of the nonanesthetized patients, and the vasodilatory effect of nitroglycerin could be attenuated. Therefore, the vasodilatory effect of subcutaneous nitroglycerin would be more significant in nonanesthetized patients. Fifth, the anesthesiologists were experienced in ultrasound-guided arterial cannulation of pediatric patients. Therefore, the effect of subcutaneous nitroglycerin on pediatric radial artery cannulation by physicians with less experience is not known. Sixth, the statistical significance of multiple secondary outcomes should be regarded with caution because they were not adjusted for multiplicity.

In conclusion, subcutaneous injection of nitroglycerin before radial artery cannulation improves the first-attempt success rate and lowers procedure-related complications in pediatric patients under 2 yr of age.

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Competing Interests

The authors declare no competing interests.

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Full protocol available at: jintae73@snu.ac.kr. Raw data available at: jintae73@snu.ac.kr.

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ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

Shadowing the Abbot: Wood Library-Museum Graphic Illustrators Bill and Janet Lyle

An earlier vignette reflected Wood Library-Museum (WLM) exhibit designer John Byrne "Shadowing the Abbess." We now segue with "Shadowing the Abbot": Father John Henry (*bottom, standing left*), the final Abbot of St. Herman's Monastery in Cleveland, Ohio. When the monastery's wheelchair lift at the men's shelter needed repairs, these were funded by the author and accomplished by electrician William "Bill" Lyle (*upper left*). Before mastering the Ohio electrical code to full licensure *without a mentor*, Mr. Lyle had taught himself every graphics version of Photoshop and Illustrator. I have never met a brighter fellow. Bill composed signage for the Wood Library-Museum's Park Ridge galleries, generated Wood Library-Museum exhibit graphics for American Society of Anesthesiologists Annual Meetings (2000 to 2011), and illustrated the initial 115 Reflections for Anesthesiology. After Bill suffered a devastating stroke in May of 2011, his wife Janet (*upper right*) grabbed the computer keyboard and generated 600-plus additional Anesthesiology Reflection images before retiring in April of 2020. The Wood Library-Museum thanks the Lyles for all of their artistic contributions to Anesthesiology and to the Wood Library-Museum over the past 28 years. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

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