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Impact of Nitroglycerine Injection on Radial Artery Outcomes in Distal Transradial Access

ABSTRACT

Background: Preventive measures for radial artery complications in distal transradial approach are not fully studied. Our aim was to investigate the role of nitroglycerine injection in patients undergoing coronary angiography via distal transradial access.

Methods: In this study, 168 patients who underwent angiographic procedures performed via distal transradial route with or without nitroglycerine injection were evaluated. Demographic, angiographic, and laboratory characteristics were recorded. Radial artery outcomes, including radial artery spasm, radial artery occlusion, and hematoma were compared between these groups and *P* values < .05 indicated significant differences.

Results: Radial artery outcome occurred in 22% of the study population (n = 37), with radial artery spasm being the most encountered complication (n = 28, 16.7%). The groups were not different in terms of radial artery complications. Procedural features were also comparable except for the total contrast volume used.

Conclusion: Coronary angiographic procedures could be performed safely using distal trans-radial access without nitroglycerine injection.

Keywords: Distal transradial accessnitroglycerineradial artery spasm

ORIGINAL INVESTIGATION

INTRODUCTION

Transradial access has emerged as a preferred approach for coronary angiography and percutaneous coronary intervention (PCI) due to its lower rates of access site complications, reduced bleeding risk, and faster patient ambulation compared to traditional femoral access.[1] Distal transradial access (dTRA) via the anatomical snuffbox is a novel approach introduced by Kiemeneij in 2017.[2] This method has been shown to be a safe and effective alternative for performing coronary angiography and interventions, with the added benefit of reducing hemostasis time.[2] The anatomical snuffbox, as a distal access site, offers potential advantages over traditional radial access in terms of patient comfort and hand mobility during the post-procedure period.[3] However, compared to other approaches, conventional transradial access (cTRA) may present some challenges due to factors like the low release of nitric oxide, potential endothelial damage, and reduced blood flow resulting from the insertion of the sheath and catheter. As a consequence, cTRA is associated with a higher risk of complications such as radial artery spasm and radial artery occlusion (RAO).[4,5] These complications can lead to longer procedure times, consideration of alternative arterial access sites, and increased discomfort for the patient.

Intra-arterial nitroglycerine injection after sheath insertion has been proposed as a default strategy to reduce radial artery spasm and improve the success rate of dTRA.[5,6] Nitroglycerine, a vasodilator, relaxes the radial artery smooth muscles, facilitates smooth catheter manipulation, and reduce the incidence of spasm-related complications.[7,8] Despite its potential benefits, the impact of intra-arterial nitroglycerine injection on procedural outcomes and complications in the context of dTRA remains less explored.

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The aim of this retrospective study was to compare the clinical characteristics, angiographic findings, procedural outcomes, and complications between 2 groups of patients undergoing coronary angiography and PCI through the distal transradial route, with and without intra-arterial nitroglycerine injection.

METHODS

Study Design and Patient Population

Patients who underwent elective or emergency coronary angiography and/or percutaneous coronary interventions via distal transradial artery access between the years 2021 and 2022 were enrolled in this study retrospectively. Patients with no palpable pulses, diagnosed with vasculitis, and who had arterio-venous fistula or planned for hemodialysis program were excluded. The study population was divided into 2 groups based on nitroglycerine injection after sheath insertion. Demographic, clinical, and angiographic features of these 168 patients were recorded and compared between those groups. Radial artery complications, including radial artery spasm, RAQ, perforation, hematoma, and radial nerve injury, were the primary outcomes of nitroglycerine (−) and nitroglycerine (+) groups. Radial artery hematoma and spasm were classified into 5 and 4 categories respectively according to their severity. Patients who experienced arm claudication or absence of pulse after the procedure underwent Doppler evaluation to determine RAO. The study protocol was approved by the Institutional Review Board. Neither artificial intelligence nor assisted technologies were used when preparing this article.

Procedure and Management

All procedures were performed by experienced interventionalists. The d-TRA approach involved accessing the radial artery at the anatomical snuffbox, a triangular depression located on the radial aspect of the wrist when the thumb is fully extended. Intra-arterial 5000 IU heparin was administered via the sheath to all patients. A loading dose of clopidogrel (600 mg) and acetylsalicylic acid (300 mg) for patients who underwent a PCI procedure was administered. Nitroglycerine 100 µg/mL was introduced via the radial artery sheath at the discretion of the operator. Radial artery occlusion was detected by the absence of anterograde flow as detected by vascular Doppler ultrasound following catheterization for up to 24 hours. Radial artery spasm was managed by calcium channel blocking agents, warm compression, or sedatives. Hemostasis was achieved by manual compression after sheath removal.

Statistical Analysis

All data were presented as mean ± SD for variables with normal distribution and as median [inter-quantile range] for variables with non-normal distribution. Categorical variables were reported as numbers and percentages. Continuous variables were checked for the normal distribution assumption using Kolmogorov–Smirnov statistics. Categorical variables were tested by Pearson's χ^2 test and Fisher's exact test. Differences between groups were evaluated using the Mann–Whitney *U* test or the Student *t*-test, when appropriate. A *P*-value < .05 was considered statistically significant. All statistical studies were carried out using Statistical Package for Social Sciences software (SPSS 22.0 for Windows, SPSS Inc., Chicago, Illinois, USA).

HIGHLIGHTS

- Radial artery cannulation is the default access site for widespread procedures including coronary angiography and percutaneous interventions.
- Distal transradial access is a safe and reliable option alongside radial artery access, providing lower complication rates, mainly radial artery occlusion.
- Despite increasing evidence on the feasibility of distal transradial access, more research is needed to define it as a standard technique.

RESULTS

A total of 168 patients (mean age: 63 ± 10, male n = 118, 70.2%) who underwent diagnostic coronary angiography and/or percutaneous coronary intervention by dTRA route were retrospectively evaluated. Patients were divided into 2 categories based on intraarterial nitroglycerine injection after sheath insertion. Demographic features, clinical characteristics, and angiographic findings were comparable between these groups. However, several laboratory findings differed significantly, including lipid profile, full blood count parameters, and acute phase reactants without a causal relationship. These data are depicted in Table 1. The prevalence of hyperlipidemia was slightly higher in the nitroglycerine-injected group (48.8% vs. 34.9%, *P* = .06), but it did not reach statistical significance.

Except for the total contrast volume, which was higher in the nitroglycerine (−) group, procedural characteristics such as sheath size, number of puncture attempts, sheath insertion time, use of sedatives, and total procedure time were similar between these groups. These data are demonstrated in Table 2. The overall procedural success rate was 98.8%, with only 2 patients crossed to conventional transradial route, and no transition to femoral access was observed.

The incidence of complications is shown in Table 2 as study outcome parameters. Symptomatic RAO occurred in 5 patients and did not differ between the groups. Radial artery spasm was observed in 28 patients (16.7%) and was mainly managed by additional calcium channel blockers or warm compression. The percentage of patients experiencing radial artery spasm was also similar between the nitroglycerine (+) and nitroglycerine (−) groups. Access site hematoma was observed in 4 patients and was managed by prolonged compression or ice-pack implementation and did not require further interventions. No complications such as radial perforation, radial nerve injury, or compartment syndrome were reported.

DISCUSSION

The main finding of this study was that the use of nitroglycerine during dTRA for coronary angiography and

Table 1. Clinical, Angiographic Characteristics, and Laboratory Parameters

Variables	Total (n = 168)	Nitrate (+) (n = 82)	Nitrate (–) (n = 86)	*P*
Clinical characteristics				
Age, years	63.2 ± 10	63.3 ± 9	63 ± 10	.881
Males, n (%)	118 (70.2)	58 (70.7)	60 (69.8)	.893
Hypertension, n (%)	108 (64.3)	56 (68.3)	52 (60.5)	.292
Diabetes mellitus, n (%)	70 (41.7)	38 (46.3)	30 (37.2)	.237
Previous CAD, n (%)	78 (46.4)	40 (48.8)	38 (44.2)	.556
PAD, n (%)	2 (1.2)	2 (2.4)	0 (0)	.145
CVA, n (%)	2 (1.2)	0 (0)	2 (2.3)	.164
Current smoking, n (%)	88 (52.4)	44 (53.7)	44 (51.2)	.740
Hyperlipidemia, n (%)	70 (41.7)	40 (48.8)	30 (34.9)	.061
Atrial fibrillation, n (%)	4 (2.4)	2 (2.4)	2 (2.3)	.960
BMI (kg/m^2), mean ± SD	27.9 ± 3.5	27.8 ± 3.9	28.1 ± 3.2	.682
Congestive heart failure, n (%)	2 (1.2)	0 (0)	2 (2.3)	.161
Angiographic findings				
ACS presentation, n (%)	50 (29)	24 (29)	26 (30)	.928
LAD lesion, n (%)	28 (16.7)	12 (14.6)	16 (18.6)	.529
LCx lesion, n (%)	21 (12.5)	11 (13.4)	10 (11.6)	.490
RCA lesion, n (%)	25 (14.8)	10 (12.2)	15 (17.4)	.261
Post-procedural flow < TIMI 3	2 (1.2)	0 (0)	2 (2.3)	.161
Use of stents, n (%)	74 (44)	34 (41.5)	40 (46.5)	.512
Laboratory analysis				
Hemoglobin (g/dL)	13.8 ± 1.6	12.5 ± 1.6	13.9 ± 1.6	**<.01**
Platelet (10^3 µ/L)	249 ± 76	251 ± 94	249 ± 73	.765
Lymphocyte	1.8 ± 0.8	1.2 ± 0.5	1.9 ± 0.8	**<.01**
Serum creatinine (mg/dL)	0.9 ± 0.4	1.0 ± 0.4	0.9 ± 0.4	**<.01**
Glucose (mg/dL)	158 ± 77	168 ± 88	156 ± 75	.091
Albumin (mg/dL)	3.8 ± 0.4	3.1 ± 0.6	3.9 ± 0.3	**<.01**
Total cholesterol (mg/dL)	181 ± 43	130 ± 28	188 ± 40	**<.01**
LDL cholesterol (mg/dL)	115 ± 35	80 ± 23	120 ± 34	**<.01**
HDL cholesterol (mg/dL)	38 ± 11	34 ± 12	38 ± 12	**<.01**
Triglyceride (mg/dL)	148 ± 88	105 ± 41	154 ± 91	**<.01**
C-reactive protein (mg/dL)	2.3 [4.4]	5.1 [9.6]	1.9 [4.2]	**<.01**
Uric aside (mg/dL)	5.2 ± 1.6	5.0 ± 1.6	5.3 ± 1.7	.064
c-Troponin I (ng/mL)	6.8 [44]	8.7 [99]	6.7 [42]	.112

ACS, acute coronary syndrome; BMI, body mass index; CAD, coronary artery disease; CVA, cerebrovascular accident; HDL, high density cholesterol; LAD, left anterior descending; LCx, left circumflex; LDL, low density cholesterol; PAD, peripheral arterial disease; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction. Values which have statistical significance written in bold.

Table 2. Procedural Features and Outcome Parameters of the Study Population

Variables	Total (n = 168)	Nitrate (+) (n = 82)	Nitrate (–) (n = 86)	*P*
Procedural features				
Sheat size, n (%)				
5F (French)	22 (13.1)	12 (14.6)	10 (11.6)	.560
6F (French)	146 (86.9)	70 (85.4)	76 (88.4)	.529
Catheter size, n (%)				
5F (French)	106 (63.1)	56 (68.3)	50 (58.1)	.178
6F (French)	62 (36.9)	26 (31.7)	36 (41.9)	.103
Puncture number	1.2 ± 0.6	1.29 ± 0.6	1.2 ± 0.5	.383
Sheat insertion time	1.3 ± 0.7	1.4 ± 0.8	1.2 ± 0.7	.334
Total contrast volume (mL)	138.2 ± 76	126 ± 59	149 ± 89	**.040**
Heparin dosage (IU/L)	5208 ± 797	5243 ± 930	5174 ± 644	.571
Total procedure time (min)	16.5 [24]	16 [20]	18 [29]	.422
Total fluoroscopy time (min)	7.2 [12]	7.1 [8]	7.6 [15]	.466
Total radiation dosage (mgray)	1183 [2097]	1209 [1584]	1157 [2557]	.459
Use of sedatives, n (%)	74 (44)	34 (41.5)	40 (46.5)	.510
Procedure success, n (%)	166 (98.8)	82 (100)	84 (97.7)	.160
Outcome parameters				
Radial artery spasm, n (%)	28 (16.7)	12 (14.6)	16 (18.6)	.521
Radial artery occlusion, n (%)	5 (2.9)	2 (2.4)	3 (3.4)	.266
Radial hematoma, n (%)	4 (2.4)	2 (2.4)	2 (2.3)	.966

percutaneous coronary intervention did not decrease radial artery complications.

The advantages of the transradial approach over the transfemoral approach for coronary angiography or PCI have been demonstrated in numerous studies. [9,10] The superiority of the transradial approach has been accepted worldwide and is also emphasized by guidelines.[11,12] Although uncommon, there are still some vascular complications associated with this approach, including radial artery injury, radial artery spasm, RAO, pseudoaneurysm, arteriovenous fistula, nerve damage, and complex regional pain syndrome.[13] While the trans-ulnar artery approach serves as an alternative method with comparable safety and effectiveness to the transradial approach in cardiac catheterization, it is not the preferred choice due to certain drawbacks such as increased requirement for wrist rotation during the procedure, which can lead to heightened patient discomfort.[14]

Recently, a new technique, namely distal radial artery access, has gained popularity due to complications arising from conventional radial artery access.[15] The anatomical snuffbox is a triangular depression located on the radial aspect of the wrist when the thumb is fully extended. The radial artery in this area is superficial and can be easily felt when palpated.[16] The vascular diameter of the distal radial artery within the anatomical snuffbox is typically smaller than that of the radial artery at the wrist, with a ratio of approximately 0.8-0.9.[17] Additionally, it has been observed that the diameter of the distal radial artery is larger in men compared to women,[18] which means successful catheterization or puncture of the distal radial artery appears to be more challenging. Approximately a 92% success rate in snuffbox puncture has been reported in the literature.[15] In our study, we achieved a success rate of 98% in puncturing the distal radial artery. In previously published studies, the snuffbox puncture time, defined as the time interval from local anesthesia induction to successful sheath cannulation, was recorded as 2.7 ± 1.6 minutes, and snuffbox puncture was successfully completed within 5 minutes in 95.3% of the patients.[19] In our study, we achieved an average of 1.3 minutes sheath insertion time compared to the literature.

As anticipated, the dTRA exhibits superior safety and patient satisfaction in cardiac interventions.[20] Being a novel approach for cardiac catheterization, operators should also consider access-related complications, including RAO, radial artery spasm, bleeding, hematoma, and injury to the superficial branch of the radial nerve.[21-24] The most common complication associated with dTRA is RAO, occurring in approximately 1%-10% of cases.[25-27] Endothelial injury of the radial artery and reduced blood flow following sheath and catheter insertion are believed to contribute to thrombus formation, making them predisposing factors for RAO.[28] Additionally, repeated cannulation of the radial artery can lead to intimal hyperplasia and increased intima-media thickness,[29,30] resulting in negative remodeling of the arterial wall and further increasing the risk of RAO.[31] Various vasodilator agents have been utilized during TRA to prevent radial artery spasm and RAO, including nitrates, calcium channel blockers, lidocaine, and alpha blockers. Several studies have demonstrated an increase in peri-procedural radial artery diameter with these agents.[32-34] Dharma et al[35] reported that the use of post-procedural/pre-hemostasis intra-arterial nitroglycerin significantly reduced the incidence of RAO compared to placebo (8.3% vs. 11.7%, $P = .006$). Despite it may be beneficial for radial artery cannulation, routine use of nitroglycerin does not seem to have a favorable effect on adverse outcomes such as RAO, spasm, or thrombosis.[35,36] The effects of nitroglycerin administration on outcomes in patients undergoing coronary interventions via the distal radial approach are still a matter of debate. Although research on this topic is scarce, several studies involving a limited number of patients have examined the effects of nitrate use on vascular complications associated with dTRA. Lee et al[37] demonstrated that the use of nitroglycerin in patients undergoing dTRA results in a greater radial artery diameter after the procedure compared to its diameter before the procedure. However, Murai et al[38] state that while nitroglycerin administration does not have a positive effect on hematoma and vasospasm, it does have beneficial effects on vascular access. These findings appear to be consistent with the results of our study.

While there are many procedural and tissue-related factors contributing to RAO and other radial artery complications, we believed that administering drugs through external injection would not prevent these occurrences. Therefore, the main focus of our study was to investigate the relationship between nitrate use and radial artery complications. In our study, out of a total of 168 patients, radial artery spasm in 28 patients (16.7%), RAO in 5 patients (2.9%), and radial hematoma in 4 patients (2.4%) were detected. When comparing 2 groups—nitrate (+) and nitrate (−) no statistically significant difference was observed (*P*-values were .52, .26, and .96, respectively). Based on these values, it can be concluded that there is no significant association between nitrate use and radial artery complications in d-TRA.

Study Limitations

This study has several limitations. First, the inclusion of patients with compromised vascular structures due to comorbidities was avoided, and thus, the results cannot be generalized to the overall population. Secondly, it involved a small number of patients, and the patient selection was based on the palpability of the distal radial artery, which may have introduced selection bias and should be acknowledged. Finally, our study has limitations attributed to its retrospective nature.

CONCLUSION

In conclusion, our study supports the safety and feasibility of distal radial artery access for coronary angiography and percutaneous coronary intervention. The use of nitroglycerin during dTRA did not show a significant reduction in radial artery complications. However, larger-scale prospective and randomized studies are needed to further explore the potential benefits and limitations of this approach in clinical practice.

Ethics Committee Approval: The study was approved by the Memorial Ataşehir Hospital Ethics Committee (Ethical approval date and ID: August 23, 2024, 2024/11).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.K.; Design – M.K.; Supervision – B.D.; Resources – M.K, B.D.; Materials – M.K.; Data Collection and/or Processing – M.K.; Analysis and/or Interpretation – M.K., B.D.; Literature Search – M.K.; Writing – M.K.; Critical Review – M.K., B.D.

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