مقایسه اثربخشی تزریق میدازولام زیرجلدی و نیتروگلیسرین داخل شریانی در کاهش اسپاسم شریان رادیال در کاتتریسم ترانس رادیال عروق کرونری

شناسنامه طرح

کد رهگیری طرح	4020224
تاریخ تصویب پیش پروپوزال	
عنوان طرح	مقایسه اثربخشی تزریق میدازولام زیرجلدی و نیتروگلیسرین داخل شریانی در کاهش اسپاسم شریان رادیال در کاتتریسم ترانس رادیال عروق کرونری
عنوان لاتین طرح	Comparison of the effect of subcutaneous midazolam versus conventional Intra-arterial nitroglycerin in reducing radial artery spasm during trans-radial coronary catheterization
تلفن	09125055884
پست الکترونیکی	ehsankhalilipur@gmail.com
نوع مطالعه	کارآزمایی بالینی-Clinical trial
تاریخ شروع	1402/08/20
تاریخ خاتمه	1402/10/20
آیا طرح چند مرکزی است؟	خیر
مرکز/مراکز دیگر	
نام سازمان تصویب کننده اولیه پروپوزال	
محل اجرای طرح	
محل اجرای طرح	بیمارستان قلب شهید رجایی
سازمان مجری	بیمارستان قلب شهید رجایی
سازمان مجری	
دانشکده/محل خدمت	Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences
رشته تخصصی	قلب و عروق- اینترونشن
توضیحات	
نوع طرح ها	

مجری همکاران

نام و نام خانوادگی	سمت در طرح	نوع همکاری	توضیحات
احسان خلیلی پور	مجری اصلی / نویسنده مقاله	طراحی و تدوین طرح	
پرهام صادقی پور	همکار طرح	مشاور	
اسماعیل مهدی نژاد	مجری ونویسنده مقاله	نوشتن پروپوزال	
امیرحسین اکبرزاده پاشا	مجری ونویسنده مقاله	جمع آوری نمونه ها	
عطا فیروزی	همکار طرح	نظارت بر اجرای طرح	
علی زاهدمهر	همکار طرح	نظارت بر اجرای طرح	
محمد جواد عالم زاده انصاری	همکار طرح	نظارت بر اجرای طرح	
زهرا حسینی	همکار طرح	نظارت بر اجرای طرح	
محمدرضا بای	همکار طرح	نظارت بر اجرای طرح	
آرمین الهی فر	همکار طرح	نظارت بر اجرای طرح	
فرشاد شاکریان	همکار طرح	نظارت بر اجرای طرح	
محسن معدنی	همکار طرح	نظارت بر اجرای طرح	
رضا کیانی	همکار طرح	نظارت بر اجرای طرح	
عارفه قربانی	همکار طرح	سایر	

دانشده/مرکز مربوطه

رده	نوع ارتباط با مرکز
مرکز تحقیقات مداخلات قلبی و عروقی	وارد کننده

اطلاعات تفصیلی

آیتم ها	متن
بیان مسئله	The radial artery approach for coronary angiography is an effective and safe alternative to the femoral approach. The transradial technique has become increasingly popular due to fewer (vascular complications and immediate ambulation. (1 In particular, the radial approach is safe and effective for patients with obesity, aortoiliac disease, (therapeutic anticoagulation, and spinal problems. (2 Radial artery spasms are one of the most common complications operators encounter while performing transradial cardiac catheterization and PCI. It causes patient discomfort and reduces (the procedure success rate. (3 Radial artery spasm can be defined as a temporary, sudden narrowing of the radial artery. It is usually diagnosed clinically and angiographically during cardiac catheterization. Clinically, it is associated with pain in the forearm which is aggravated by movement of the catheter/sheath, and there is difficulty in manipulating the catheter. Also, loss of radial pulse and damping of radial

(arterial pressure is detected. (4

Unfortunately, even after using a vasodilator, RAS has been reported in 4 to 20% of the patients (undergoing transradial coronary angiography.(5

There is currently no definitive standard protocol for the optimal vasodilator cocktail to be (administered after successful insertion of the radial sheath. (3

ضرورت اجرا

Chen Y et al. showed that Subcutaneous injection of nitroglycerin at the radial artery puncture site dilates the radial artery and reduces the incidence of early radial artery occlusion (post-catheterization. (6

Midazolam is a water-soluble benzodiazepine which is characterized by rapid onset and short duration of action. Midazolam is largely used in clinical practice for induction of anesthesia and for sedation of patients in intensive care units. Midazolam is rapidly and extensively metabolized .almost exclusively by CYP3A isoforms

The subcutaneous injection of midazolam provides high bioavailability and reproducible plasma concentrations of it, which is comparable to intravenous administration. This suggests a possible alternative administration route in certain clinical settings in which intravenous injection is not .favorable

The absolute bioavailability of subcutaneous midazolam was found to be high (96%), with wide yet (acceptable inter-individual variations. (7

In a systematic review by Zaporowska-Stachowiak, et al in 2019, the bioavailability of midazolam was 96%, with onset of action in 5-10 minutes, and peak concentration being achieved in 31 (minutes. (8

The anxiolytic-sedative dose of midazolam in Scottish Palliative Care Guidelines is marked as (2-3mg. (9

Since there has been limited literature on the subcutaneous route of administration of midazolam, the present study is designed to investigate whether peri-radial subcutaneous administration of midazolam would reduce the occurrence of radial artery spasm in patients undergoing transradial .coronary catheterization in comparison to intravenous administration of the nitroglycerin

بررسی متون

Rathore S et al in 2010 showed hydrophilic sheath coating, but not sheath length, reduces the (incidence of radial artery spasm during transradial coronary procedures. (10

Coppola J et al in prospective, randomized trial on 379 patients found that the addition of a direct nitric oxide donor to nitroglycerin in an antispastic cocktail did not reduce the risk of spasm, and the use of nitroglycerin was found to be as effective as nitroprusside. Also, morphometric and mechanical factors played a significant role in predicting the occurrence of radial spasm. The sex of the patient, presence of diabetes, body surface area and smoking history appeared to play no (role in predicting the occurrence of radial spasm. (11

Jia DA et al found that the incidence of RAS during transradial coronary procedure was 7.8%.

Logistic regression analysis showed that female sex, small radial artery diameter, diabetes, and (unsuccessful access at first attempt were the independent predictors of RAS. (12

Deftereos S et al in 2012 showed that Routine administration of relatively low doses of an opioid/benzodiazepine combination during transradial interventional procedures is associated with a substantial reduction in the rate of spasm, the need for access site crossover, and the (procedure-related level of patient discomfort. (13

منابع

Kim SH, Kim EJ, Cheon WS, Kim M-K, Park WJ, Cho G-Y, et al. Comparative study of .1 nicorandil and a spasmolytic cocktail in preventing radial artery spasm during transradial coronary .angiography. Int J Cardiol. 2007;120(3):325-30

Hildick-Smith DJ, Walsh JT, Lowe MD, Shapiro LM, Petch MC. Transradial coronary .2 angiography in patients with contraindications to the femoral approach: an analysis of 500 cases. .Catheter Cardiovasc Interv. 2004;61(1):60-6

Ho HH, Jafary FH, Ong PJ. Radial artery spasm during transradial cardiac catheterization and .3 percutaneous coronary intervention: incidence, predisposing factors, prevention, and .management. Cardiovasc Revasc Med. 2012;13(3):193-5

Sandoval Y, Bell MR, Gulati R. Transradial artery access complications. Circ Cardiovasc Interv. .4 .2019;12(11):e007386

Varenne O, Jégou A, Cohen R, Empana JP, Salengro E, Ohanessian A, et al. Prevention of .5 arterial spasm during percutaneous coronary interventions through radial artery: the SPASM .study. Catheter Cardiovasc Interv. 2006;68(2):231-5

Chen Y, Ke Z, Xiao J, Lin M, Huang X, Yan C, et al. Subcutaneous injection of nitroglycerin at .6 the radial artery puncture site reduces the risk of early radial artery occlusion after transradial coronary catheterization: a randomized, placebo-controlled clinical trial. Circ Cardiovasc Interv. .2018;11(7):e006571

Pecking M, Montestruc F, Marquet P, Wodey E, Homery MC, Dostert P. Absolute bioavailability .7 of midazolam after subcutaneous administration to healthy volunteers. Br J Clin Pharmacol. 2002 .Oct;54(4):357-62

Zaporowska-Stachowiak I, Szyma□ski K, Oduah MT, Stachowiak-Szymczak K, Łuczak J, .8 Sopata M. Midazolam: Safety of use in palliative care: A systematic critical review. Biomedicine & Pharmacotherapy. 2019 Jun 1;114:108838

Scotland NH. Scottish palliative care Guidelines-Mouth care. NHS Scotland: Edinburgh, UK. .9 2019:1-1.10. Rathore S, Stables RH, Pauriah M, Hakeem A, Mills JD, Palmer ND, Perry RA, Morris JL. Impact of length and hydrophilic coating of the introducer sheath on radial artery spasm during transradial coronary intervention: a randomized study. JACC Cardiovasc Interv. 2010 .May;3(5):475-83

Coppola J, Patel T, Kwan T, Sanghvi K, Srivastava S, Shah S, Staniloae C. Nitroglycerin, .11 nitroprusside, or both, in preventing radial artery spasm during transradial artery catheterization. J .Invasive Cardiol. 2006 Apr;18(4):155-8

Jia DA, Zhou YJ, Shi DM, Liu YY, Wang JL, Liu XL, Wang ZJ, Yang SW, Ge HL, Hu B, Yan .12
ZX, Chen Y, Gao F. Incidence and predictors of radial artery spasm during transradial coronary
.angiography and intervention. Chin Med J (Engl). 2010 Apr 5;123(7):843-7

Deftereos S, Giannopoulos G, Raisakis K, Hahalis G, Kaoukis A, Kossyvakis C, Avramides D, .13
Pappas L, Panagopoulou V, Pyrgakis V, Alexopoulos D, Stefanadis C, Cleman MW. Moderate
procedural sedation and opioid analgesia during transradial coronary interventions to prevent
.spasm: a prospective randomized study. JACC Cardiovasc Interv. 2013 Mar;6(3):267-73

اهداف: هدف اصلی، اهداف اختصاصی، هدف کاربردی

هدف کلي طرح:

Comparison of the effect of subcutaneous midazolam versus conventional Intra-arterial
.nitroglycerin in reducing radial artery spasm during trans-radial coronary catheterization

اهداف اصلی طرح:

Determine the rate of RAS incidence in the post radial artery catheterization in the midazolam .1
.treated group

Determine the rate of RAS incidence in the post radial artery catheterization in the .2
.nitroglycerin-treated group

Comparison of the rate of RAS incidence in the post radial artery catheterization in the .3
.midazolam treated group and nitroglycerin treated group according to the age

Comparison of the rate of RAS incidence in the post radial artery catheterization in the .4
.midazolam treated group and nitroglycerin treated group according to the sex

Comparison of the rate of RAS incidence in the post radial artery catheterization in the .5
.midazolam treated group and nitroglycerin treated group according to the smoking history

Comparison of the rate of RAS incidence in the post radial artery catheterization in the .6
midazolam treated group and nitroglycerin treated group according to the underlying diseases
(... ,(Diabetes Mellitus, hypertension

Comparison of the rate of RAS incidence in the post radial artery catheterization in the .7
.midazolam treated group and nitroglycerin treated group according to the creatinine level

Comparison of the rate of RAS incidence in the post radial artery catheterization in the .8
midazolam treated group and nitroglycerin treated group according to the history of trans-radial
catheterization

Comparison of the rate of RAS incidence in the post radial artery catheterization in the .9
midazolam treated group and nitroglycerin treated group according to the INR

اهداف فرعي طرح:

Determine the rate of forearm hematoma incidence in the post radial artery catheterization in .1
.the midazolam treated group

Determine the rate of forearm hematoma incidence in the post radial artery catheterization in .2 .the nitroglycerin-treated group Determine the rate of radial artery pseudoaneurysm incidence in the post radial artery .3 .catheterization in the midazolam treated group Determine the rate of radial artery pseudoaneurysm incidence in the post radial artery .4 .catheterization in the nitroglycerin-treated group Comparison of the rate of systemic hypotension incidence in the post radial artery .5 catheterization in the midazolam treated group and nitroglycerin treated group Comparison of the rate of bleeding incidence in the post radial artery catheterization in the .6 midazolam treated group and nitroglycerin treated group Comparison of the rate of osteofascial compartment syndrome incidence in the post radial .7 artery catheterization in the midazolam treated group and nitroglycerin treated group Comparison of the rate of cardiac arrhythmia incidence in the post radial artery catheterization .8 in the midazolam treated group and nitroglycerin treated group Comparison of the rate of flushing incidence in the post radial artery catheterization in the .9 midazolam treated group and nitroglycerin treated group Comparison of the rate of skin rash incidence in the post radial artery catheterization in the .10 midazolam treated group and nitroglycerin treated group **هدف كاربردي طرح:** Finding an effective drug for preventing RAS as one of the most critical complications in .trans-radial cardiac catheterization might help improve interventional coronary procedures	
what is the rate of RAS incidence in the post radial artery catheterization in the midazolam .1 ?treated group what is the rate of RAS incidence in the post radial artery catheterization in the nitroglycerin .2 ?treated group There is a difference in the rate of RAS incidence in the post radial artery catheterization in the .3 .midazolam treated group and nitroglycerin treated group according to the age There is a difference in the rate of RAS incidence in the post radial artery catheterization in the .4 .midazolam treated group and nitroglycerin treated group according to the sex There is a difference in the rate of RAS incidence in the post radial artery catheterization in the .5 .midazolam treated group and nitroglycerin treated group according to the smoking history There is a difference in the rate of RAS incidence in the post radial artery catheterization in the .6 midazolam treated group and nitroglycerin treated group according to the underlying diseases .(... ,(Diabetes Mellitus, hypertension There is a difference in the rate of RAS incidence in the post radial artery catheterization in the .7	**فرضيات يا سوالات پژوهشی**

.midazolam treated group and nitroglycerin treated group according to the creatinine level

There is a difference in the rate of RAS incidence in the post radial artery catheterization in the .8 midazolam treated group and nitroglycerin treated group according to the procedure time

There is a difference in the rate of RAS incidence in the post radial artery catheterization in the .9 midazolam treated group and nitroglycerin treated group according to the number of radial artery puncture

what is the rate of forearm hematoma incidence in the post radial artery catheterization in the .10 ?midazolam treated group

what is the rate of forearm hematoma incidence in the post radial artery catheterization in the .11 ?nitroglycerin–treated group

what is the rate of radial artery pseudoaneurysm incidence in the post radial artery .12 ?catheterization in the midazolam treated group

what is the rate of radial artery pseudoaneurysm incidence in the post radial artery .13 ?catheterization in the nitroglycerin treated group

There is a difference in the rate of systemic hypotension incidence in the post radial artery .14 catheterization in the midazolam treated group and nitroglycerin treated group

There is a difference in the rate of bleeding incidence in the post radial artery catheterization .15 in the midazolam treated group and nitroglycerin treated group

There is a difference in the rate of osteofascial compartment syndrome incidence in the post .16 radial artery catheterization in the midazolam treated group and nitroglycerin treated group

There is a difference in the rate of cardiac arrhythmia incidence in the post radial artery .17 catheterization in the midazolam treated group and nitroglycerin treated group

There is a difference in the rate of flushing incidence in the post radial artery catheterization in .18 the midazolam treated group and nitroglycerin treated group

There is a difference in the rate of skin rash incidence in the post radial artery catheterization .19 in the midazolam treated group and nitroglycerin treated group

مشخصات ابزار جمع آوری اطلاعات و نحوه جمع آوری آن

.Patients' information will be collected through filling variables data sheets

متغیر	کیفی اسمی	کیفی ترتیبی	کمی گسسته	کمی پیوسته	نحوه اندازه‌گیری	تعریف علمی- عملی	مقیاس
Age			X		based on medical patient's records	patient's age	years
Sex	X				based on medical patient's records	patient's sex	male/female
Height				X	measuring tape	patient's height	centimeters

kilograms	patient's weight	calibrated digital weighing scale		X			Weight
yes/no	suffering from diabetes mellitus	based on American Diabetes Association criteria for diabetes mellitus				X	DM
yes/no	suffering from hypertension	based on written history ((and drug history				X	HTN
yes/no	eGFR < 90 mL/min for the past 3 months	based on written history ((and drug history				X	CKD
yes/no	use of cigarettes and/or hookah	based on written history				X	Cigarette smoking
yes/no	body mass index > 30kg/m2	based on written history				X	Obesity
yes/no	previous history of transradial catheterization	based on written history and patient's medical records				X	PMHx of transradial catheterization
gr/dL	hemoglobin level	based on results from Rajaei Heart Center laboratory	X				Hb
x10^3/μL	blood platelet count	based on results from Rajaei Heart Center laboratory		X			Plt
–	ratio of patient's PT to control PT	based on results from Rajaei Heart Center laboratory kits	X				INR
mg/dL	serum creatinine level	based on results from Rajaei Heart Center laboratory kits	X				Cr
yes/no	use of ASA	based on written drug history				X	ASA
yes/no	use of P2Y12is	based on written drug history				X	P2Y12is
yes/no	use of Statins	based on written drug history				X	Statins
yes/no	use of BBs	based on written drug history				X	BBs
yes/no	use of CCBs	based on written drug history				X	CCBs
yes/no	use of Nitrates	based on written drug history				X	Nitrates

yes/no	use of ACE/ARBs	based on written drug history				X	ACE/ARBs
yes/no	use of Ranolazine	based on written drug history				X	Ranolazine
Coronary Angiography ------- ------- Simple PCI and/or FFR ------- ------- Complex and High-risk Coronary Intervention ((CHIP	type of procedure ---------- CHIP: تعاریف CTO lesion: 100% occluded lesion with complete interruption of antegrade flow (TIMI flow grade 0) that had been present for at least 3 months. Bifurcation lesion: The division of a vessel into at least two branches, with the plaque extending from at least one of the limbs to the branching point Left main lesion: greater than 50 percent left main angiographic narrowing Multivessel disease: Significant stenosis (>70%) in two or more major coronary arteries of 2.5mm diameter or more Type C lesion: -Diffuse -Excessive tortuosity of proximal segment -Extremely angulated, >90° -Inability to protect major side branch -Degenerated vein graft with friable lesions	based on physician's written report				X	Procedure
Minutes	procedure time length	since vascular sheath insertion to vascular sheath removal		X			Duration of sheath insertion
Minutes	preparing and sheath insertion time length	since local anesthesia injection to vascular sheath insertion		X			Duration of procedure
IU (international (unit	total intravenous UFH injected during the procedure	nurse/physician's written report		X			UFH dosage
yes/no	patient's feeling pain/discomfort or difficulty relocating the catheter	based on physical examination and nurse/physician's written report				X	Radial artery spasm

yes/no	tenderness and bulging at the site of vascular access (during and after (procedure	based on physical examination, nurse/physician's written report, and an expert radiologist's sonography report				X	Forearm hematoma
yes/no	SBP <100/60mmHg during the procedure	based on blood pressure monitoring during the procedure and nurse/physician's written report				X	Hypotension
yes/no						X	Radial artery occlusion
yes/no	compartment syndrome signs and (symptoms (5P	based on physical examination and physician's written report				X	Compartment syndrome
yes/no	skin rashes	based on physical examination and nurse/physician's written report				X	Skin rash
yes/no	pseudoaneurysm formation at the site of vascular access	based on an expert radiologist's sonography report				X	Pseudoaneurysm
yes/no	formation of arteriovenous fistula at the site of vascular access	based on an expert radiologist's sonography report				X	AV fistula
yes/no	flushing of skin and face	based on physical examination and nurse/physician's written report				X	Flushing
yes/no	tachycardia (heart (rate >100bpm	based on cardiac monitoring during the procedure and nurse/physician's written report				X	Cardiac arrhythmia
yes/no	bleeding at the site of vascular access	based on physical examination and nurse/physician's written report				X	Bleeding

روش اجرا

This study, which will be conducted over a period of 3 months, is a prospective, non-randomized double-blinded clinical trial. All patients undergoing diagnostic or therapeutic trans-radial cardiac catheterization in our center will be evaluated according to inclusion and exclusion criteria. Since we lack the resources and personnel to perform randomization for each and every patient, and considering the fact that the results of randomized and non-randomized clinical trials are suggested to be closely correlated in the literature, we decided to assign patients to one of the study groups in a non-randomized fashion. Patients attending our center in November 2023 will be allocated to the control group, and patients attending our center in December 2023 will be assigned to the intervention group. Informed consent will be obtained from all patients. For every participant, we will collect demographic data on age, sex, smoking history, hypertension, diabetes mellitus, coronary catheterization history, serum creatinine, medications, unfractionated heparin dose, procedure time, and complications (incidence of RAO, forearm hematoma, radial artery

pseudoaneurysm, hypotension, osteofascial compartment syndrome, skin rash, flushing, and tachycardia, respectively. Demographic data will be matched between 2 groups. Five hundred seventy patients undergoing transradial cardiac catheterization will be assigned into either the midazolam treated group and the nitroglycerin group (285 patients in each group). Heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP) will be recorded. After sterile preparation, 2 mg of midazolam with 1 ml of 2% lidocaine will be injected (with 2 ml syringe, but with insulin syringe needle) subcutaneously 1–2 cm proximal to styloid process of the radius. In the other group, 200μg of nitroglycerin with 20 ml normal saline will be injected intra-arterially in the radial artery after radial sheet insertion. In the midazolam group, we will use 20 ml normal saline instead of conventional intra-arterial nitroglycerin. Both patients and observers will be blinded to the intervention. The preparation for subcutaneous and intra-arterial injections will be done by an independent researcher, and syringes will be labeled as subcutaneous and intra-arterial for blind injection. As all patients in each time point are allocated to the same group, the labeling of the syringes will not indicate the real study group. The interventional cardiologists performing the procedure, but neither the participants nor the observers, knew which participants received subcutaneous injection of midazolam or intra-arterial nitroglycerin. Coronary catheterization via the right radial artery will be performed by experienced interventional cardiologists. After puncture of radial artery with 21-gauge needle and sheath insertion (radial introducer set-6 french-7cm-0.018 wire of tabeeb darmaan pajouhesh ghalb company), the subjects will be receiving at least 5000 units of intra-arterial unfractionated heparin injection and then undergo coronary angiography (in cases of percutaneous coronary intervention or FFR, the heparin dosage will be increased). At the completion of the procedure, a TR-band inflated by 15 mL of air will be applied at the puncture site, and the radial sheath will be removed. Two hours later, the TR-band will be gradually deflated at the rate of 2 mL of air every 20 minutes, until hemostasis is achieved and then the TR-band will be removed. All participants will undergo ultrasound measurements of the radial artery, one day after the transradial coronary catheterization procedure. The ultrasound measurements will be conducted by an experienced operator who is blinded to the study groups, using an Acuson SC2000 ultrasound system .((Siemens, Germany

Radial artery spasm will be defined as difficulty in relocating or entrapment of the catheter or sheath, leading to pain during catheter manipulation or when removal is attempted, accompanied .by concomitant pressure damping or angiographical evidence during the procedure

:Inclusion criteria

All patient who are referred for transradial diagnostic or therapeutic coronary catheterization

:Exclusion criteria

Patients with more than 75 years old of age, pure stenotic valve lesions, atrioventricular block, glaucoma, altered liver function, unstable hemodynamics, known hypersensitivity to midazolam or other benzodiazepines, acute or severe pulmonary insufficiency, chronic respiratory insufficiency, severe respiratory depression, untreated sleep apnea syndrome, myasthenia gravis, severe left ventricular dysfunction (EF: <30%), chronic renal failure, and those who are going under catheterization in emergency settings, have undergone CABG, or do not consent to participate in the study

روش محاسبه حجم نمونه و تعدادآن	According to the incidence of RAO in nitroglycerin group equal to 5% (Subcutaneous Injection of Nitroglycerin at the Radial Artery Puncture Site Reduces the Risk of Early Radial Artery Occlusion After Transradial Coronary Catheterization: A Randomized, Placebo-Controlled Clinical Trial) and considering the incidence of this endpoint in intervention group about 1%, and assuming α = 0.05 and statistical power = 0.8, sample size can be calculated as 285 patients in each group, equally by using the z approximation tests for the proportions and GPower software (total sample size = 570).
ملاحظات اخلاقی	.Informed consent will be obtained from patients .The cost of midazolam will be borne by the project manager A qualified investigator, unblinded to study groups and treatments, will be responsible for protocol deviations and intervention cessation as needed. In the unfortunate event of patients experiencing complications during the study, our foremost priority is to ensure their well-being. Therefore, we will conduct a comprehensive medical assessment and provide necessary treatment promptly, without imposing any additional financial burden on the patients.
معیارهای ورود (فقط مربوط به طرحهای کارآزمایی بالینی)	All patient who are referred for transradial diagnostic or therapeutic coronary catheterization
معیارهای خروج (فقط مربوط به طرحهای کارآزمایی بالینی)	Patients with more than 75 years old of age, pure stenotic valve lesions, atrioventricular block, glaucoma, altered liver function, unstable hemodynamics, known hypersensitivity to midazolam or other benzodiazepines, acute or severe pulmonary insufficiency, chronic respiratory insufficiency, severe respiratory depression, untreated sleep apnea syndrome, myasthenia gravis, severe left ventricular dysfunction (EF: <30%), chronic renal failure, and those who are going under catheterization in emergency settings, have undergone CABG, or do not consent to participate in the study
چگونگی تصادفی سازی و Concealment (فقط مربوط به طرحهای کارآزمایی بالینی)	This study, which will be conducted over a period of 3 months, is a prospective, non-randomized double-blinded clinical trial. All patients undergoing diagnostic or therapeutic trans-radial cardiac catheterization in our center will be evaluated according to inclusion and exclusion criteria. Since we lack the resources and personnel to perform randomization for each and every patient, and considering the fact that the results of randomized and non-randomized clinical trials are suggested to be closely correlated in the literature, we decided to assign patients to one of the study groups in a non-randomized fashion. Patients attending our center in November 2023 will be allocated to the control group, and patients attending our center in December 2023 will be assigned to the intervention group.
تعریف گروه مداخله (فقط مربوط به طرحهای کارآزمایی	mg of midazolam with 1 ml of 2% lidocaine will be injected (with 2 ml syringe, but with insulin 2

بالینی)	.syringe needle) subcutaneously 1–2 cm proximal to styloid process of the radius
تعریف گروه شاهدیامقایسه (فقط مربوط به طرحهای کارآزمایی بالینی)	200μg of nitroglycerin with 20 ml normal saline will be injected intra-arterially in the radial artery .after radial sheet insertion
چگونگی کورسازی (**Blinding**) (فقط مربوط به طرحهای کارآزمایی بالینی)	Both patients and observers will be blinded to the intervention. The preparation for subcutaneous and intra-arterial injections will be done by an independent researcher, and syringes will be labeled as subcutaneous and intra-arterial for blind injection. As all patients in each time point are allocated to the same group, the labeling of the syringes will not indicate the real study group. The interventional cardiologists performing the procedure, but neither the participants nor the observers, knew which participants received subcutaneous injection of midazolam or intra-arterial .nitroglycerin
پیگیری (**follow up**) (فقط مربوط به طرحهای کارآزمایی بالینی)	At the completion of the procedure, a TR-band inflated by 15 mL of air will be applied at the puncture site, and the radial sheath will be removed. Two hours later, the TR-band will be gradually deflated at the rate of 2 mL of air every 20 minutes, until hemostasis is achieved and then the TR-band will be removed. All participants will undergo ultrasound measurements of the radial artery, one day after the transradial coronary catheterization procedure. The ultrasound measurements will be conducted by an experienced operator who is blinded to the study groups, .(using an Acuson SC2000 ultrasound system (Siemens, Germany

جدول متغیرها

نام متغیر	نقش متغیر	نوع متغیر کمی – پیوسته است؟	نوع متغیر کمی – گسسته است؟	نوع متغیر کیفی – رتبه ای است؟	نوع متغیر کیفی – اسمی است؟	واحد اندازه گیری	تعریف کاربردی	نحوه اندازه گیری
Age	مستقل	☐	☒	☐	☐	years	patient's age	based on medical patient's records
Sex	مستقل	☐	☐	☐	☒	male/female	patient's sex	based on medical patient's records
Height	مستقل	☒	☐	☐	☐	centimeters	patient's height	measuring tape
Weight	مستقل	☐	☒	☐	☐	kilograms	patient's weight	calibrated digital weighing scale
Diabetes Mellitus	مستقل	☐	☐	☐	☒	yes/no	suffering from diabetes mellitus	based on American Diabetes Association criteria for diabetes mellitus
Hypertension	مستقل	☐	☐	☐	☒	yes/no	suffering from hypertension	based on written history (and (drug history

جدول متغیرها

نام متغیر	نقش متغیر	نوع متغیر کمی – پیوسته است؟	نوع متغیر کمی – گسسته است؟	نوع متغیر کیفی – رتبه ای است؟	نوع متغیر کیفی – اسمی است؟	واحد اندازه گیری	تعریف کاربردی	نحوه اندازه گیری
CKD	مستقل	☐	☐	☐	☒	yes/no	eGFR < 90 mL/min for the past 3 months	based on written history (and drug history)
Cigarette smoking	مستقل	☐	☐	☐	☒	yes/no	use of cigarettes and/or hookah	based on written history
Obesity	مستقل	☐	☐	☐	☒	yes/no	body mass index > 30kg/m2	based on written history
PMHx of transradial catheterization	مستقل	☐	☐	☐	☒	yes/no	previous history of transradial catheterization	based on written history and patient's medical records
Hemoglobin	مستقل	☒	☐	☐	☐	gr/dL	hemoglobin level	based on results from Rajaei Heart Center laboratory
INR	مستقل	☒	☐	☐	☐	ratio	ratio of patient's PT to control PT	based on results from Rajaei Heart Center laboratory
Pletelets	مستقل	☐	☒	☐	☐	x10^3/μL	blood platelet count	based on results from Rajaei Heart Center laboratory
Creatinine	مستقل	☒	☐	☐	☐	mg/dL	serum creatinine level	based on results from Rajaei Heart Center laboratory kits
ASA	مستقل	☐	☐	☐	☒	yes/no	use of ASA	based on written drug history
P2Y12is	مستقل	☐	☐	☐	☒	yes/no	use of P2Y12is	based on written drug history
Statins	مستقل	☐	☐	☐	☒	yes/no	use of Statins	based on written drug history
Beta Blockers	مستقل	☐	☐	☐	☒	yes/no	use of BBs	based on written drug history
Calcium Channel Blockers	مستقل	☐	☐	☐	☒	yes/no	use of CCBs	based on written drug history
Nitrates	مستقل	☐	☐	☐	☒	yes/no	use of Nitrates	based on written drug history
ACE inhibitors and ARBs	مستقل	☐	☐	☐	☒	yes/no	use of ACEi/ARBs	based on written drug history
Ranolazine	مستقل	☐	☐	☐	☒	yes/no	use of Ranolazine	based on written drug history

جدول متغیرها

نام متغیر	نقش متغیر	نوع متغیر کمی – پیوسته است؟	نوع متغیر کمی – گسسته است؟	نوع متغیر کیفی – رتبه ای است؟	نوع متغیر کیفی – اسمی است؟	واحد اندازه گیری	تعریف کاربردی	نحوه اندازه گیری
Procedure	مستقل	☐	☐	☐	☒	Coronary Angiography / Simple PCI and/or FFR / Complex and High-risk Coronary Intervention ((CHIP	type of procedure	based on physician's written report
Duration of procedure	مستقل	☐	☒	☐	☐	Minutes	procedure time length	since vascular sheath insertion to vascular sheath removal
Duration of sheath insertion	مستقل	☐	☒	☐	☐	Minutes	preparing and sheath insertion time length	since local anesthesia injection to vascular sheath insertion
Unfractioned Heparin dosage	مستقل	☐	☒	☐	☐	IU (international unit)	total intravenous UFH injected during the procedure	nurse/physician's written report
Radial artery spasm	وابسته	☐	☐	☐	☒	yes/no	patient's feeling pain/discomfort or difficulty relocating the catheter	based on physical examination and nurse/physician's written report
Forearm hematoma	وابسته	☐	☐	☐	☒	yes/no	tenderness and bulging at the site of vascular access (during and after procedure)	based on physical examination, nurse/physician's written report, and an expert radiologist's sonography report
Hypotension	وابسته	☐	☐	☐	☒	yes/no	SBP <100/60mmHg during the procedure	based on blood pressure monitoring during the procedure and nurse/physician's written report
Radial artery occlusion	وابسته	☐	☐	☐	☒	yes/no	based on an expert radiologist's sonography report	Radial artery thrombosis and/or lack of flow
Compartment syndrome	وابسته	☐	☐	☐	☒	yes/no	compartment syndrome signs and (symptoms (5P	based on physical examination and physician's written report

جدول متغیرها

نام متغیر	نقش متغیر	نوع متغیر کمی ـ پیوسته است؟	نوع متغیر کمی ـ گسسته است؟	نوع متغیر کیفی ـ رتبه ای است؟	نوع متغیر کیفی ـ اسمی است؟	واحد اندازه گیری	تعریف کاربردی	نحوه اندازه گیری
Skin rash	وابسته	☐	☐	☐	☒	yes/no	skin rashes	based on physical examination and nurse/physician's written report
Pseudoaneurysm	وابسته	☐	☐	☐	☒	yes/no	pseudoaneurysm formation at the site of vascular access	based on an expert radiologist's sonography report
AV fistula	وابسته	☐	☐	☐	☒	yes/no	formation of arteriovenous fistula at the site of vascular access	based on an expert radiologist's sonography report
Flushing	وابسته	☐	☐	☐	☒	yes/no	flushing of skin and face	based on physical examination and nurse/physician's written report
Cardiac arrhythmia	وابسته	☐	☐	☐	☒	yes/no	tachycardia (heart rate >100bpm)	based on cardiac monitoring during the procedure and nurse/physician's written report
Bleeding	وابسته	☐	☐	☐	☒	yes/no	bleeding at the site of vascular access	based on physical examination and nurse/physician's written report

زمانبندی و اجرا

شرح مختصر مرحله	درصد مرحله	مدت زمان اجرا ـ ماه	از تاریخ	تا تاریخ
proposal preparation		1		
proposal presentation and acceptance		1		
sampling and trial		2		
statistical analysis		1		
final report and presentation		1		
writing article		1		

سایر هزینه ها

نوع هزینه	مبلغ ـ ریال
خدمات انجام شده	100,000,000

جمع کل هزینه های طرح

هزینه پرسنلی (هیات علمی و غیر هیات علمی)	هزینه مواد مصرفی	هزینه مواد غیر مصرفی	هزینه تجهیزات،موادوخدمات موجوددر مرکز	هزینه مسافرت	هزینه چاپ و تکثیر	سایر هزینه ها	جمع کل هزینه ـ ریال
0	0	0	0	0	0	100,000,000	100,000,000