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ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ
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ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ
ΘΡΟΜΒΩΣΗ ΚΑΙ ΑΝΤΙΘΡΟΜΒΩΤΙΚΗ ΑΓΩΓΗ

Μεταπτυχιακή Διπλωματική Εργασία

"ΣΤΡΑΤΗΓΙΚΕΣ ΠΡΟΛΗΨΗΣ ΤΗΣ ΘΡΟΜΒΩΣΗΣ ΤΗΣ ΚΕΡΚΙΔΙΚΗΣ ΑΡΤΗΡΙΑΣ ΜΕΤΑ ΑΠΟ ΚΑΡΔΙΑΚΟ ΚΑΘΕΤΗΡΙΑΣΜΟ. ΣΥΣΤΗΜΑΤΙΚΗ ΑΝΑΣΚΟΠΗΣΗ"

υπό

ΔΗΜΗΤΡΙΟΥ Φ. ΚΑΡΕΛΑ

Ειδικευόμενου Καρδιολόγου

Υπεβλήθη για την εκπλήρωση μέρους των

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«Θρόμβωση και Αντιθρομβωτική Αγωγή»

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Τίτλος εργασίας στα αγγλικά:

Radial artery occlusion assessed by vascular ultrasound within 24 hours post coronary catheterization and preventive strategies. A systematic literature review.

Περίληψη

Υπόβαθρο: Η διακερκιδική προσέγγιση έχει εδραιωθεί ως η κύρια στρατηγική προσπέλασης για τον καθετηριασμό των στεφανιαίων αγγείων, λόγω των αποδεδειγμένων πλεονεκτημάτων όσο αφορά στις αγγειακές και αιμορραγικές επιπλοκές, τη διάρκεια παραμονής των ασθενών στο νοσοκομείο και το υγειονομικό κόστος περίθαλψης, συγκριτικά με τη διαμηριαία προσέγγιση. Παρά τα οφέλη, η διακερκιδική προσπέλαση μπορεί να συνοδεύεται από επιπλοκές με κυριότερη τη θρόμβωση της κερκιδικής αρτηρίας, η οποία αναφέρεται ότι εμφανίζεται μέχρι και στο 10% των ασθενών μετά από απλό στεφανιογραφικό έλεγχο ή αγγειοπλαστική. Από τη σύλληψη της ιδέας της χρήσης της διακερκιδικής προσπέλασης και έπειτα, καινοτόμες τεχνικές διαρκώς εξελίσσονται λόγω της ανάγκης μείωσης της έκθεσης των ασθενών σε περι-επεμβατικές επιπλοκές και κυρίως στη θρόμβωση της κερκιδικής αρτηρίας.

Στόχοι: Αυτή η συστηματική βιβλιογραφική ανασκόπηση συνοψίζει τις τρέχουσες γνώσεις που αφορούν στις στρατηγικές πρόληψης της θρόμβωσης της κερκιδικής αρτηρίας κατά τον καθετηριασμό των στεφανιαίων αγγείων.

Μέθοδοι: Η ηλεκτρονική βάση δεδομένων PubMed ελέγχθηκε με συστηματικό τρόπο για την εύρεση τυχαιοποιημένων μελετών οι οποίες ενέγραψαν ασθενείς που υπεβλήθησαν σε διαγνωστικό έλεγχο των στεφανιαίων αγγείων ή/και αγγειοπλαστική με διακερκιδική προσπέλαση (εγγύς, παραδοσιακή ή άπω) και εξετάστηκε η θρόμβωση της κερκιδικής αρτηρίας με τη χρήση υπερήχου ως πρωτεύον, μη-σύνθετο καταληκτικό σημείο μέσα σε χρονικό διάστημα 24 ωρών από το πέρας της στεφανιογραφίας. Επίσης, οι βιβλιογραφικές αναφορές των υπό εξέταση μελετών ερευνήθηκαν με την τεχνική της <<αντίστροφης χιονοστιβάδας>> (backwards snowballing method) με στόχο την αναζήτηση σχετικών άρθρων με το υπό εξέταση ερώτημα. Η αναζήτηση πραγματοποιήθηκε έως και την 1η Μαΐου 2022. Από αυτή τη στρατηγική αναζήτησης προέκυψαν 56 μελέτες και κάνοντας χρήση των προκαθορισμένων κριτηρίων αποκλεισμού, 13 μελέτες τέθηκαν υπό εκτενή ανασκόπηση και ανάλυση.

Συμπεράσματα: Οι βέλτιστες πρακτικές πρόληψης της θρόμβωσης της κερκιδικής αρτηρίας περιστρέφονται γύρω από τρεις άξονες: 1. τεχνική παρακέντησης και επιλογή καθετήρων και θηκαριών κατάλληλων ως προς τη διάμετρο του αγγείου, 2. περι-επεμβατικό σπασμολυτικό κοκτέιλ και επαρκής αντιθρομβωτική αγωγή, 3. βέλτιστη μετεπεμβατική φροντίδα του σημείου πρόσβασης, μη αποφρακτική αιμοστατική τεχνική συμπίεσης και ελάχιστος χρόνος αιμόστασης.

Λέξεις- Κλειδιά: κερκιδική αρτηρία, διακερκιδική προσπέλαση, θρόμβωση της κερκιδικής αρτηρίας, πρόληψη, στρατηγική, στεφανιογραφικός έλεγχος

Abstract

Background: Transradial access (TRA) has been established as the default strategy of coronary catheterization due to proven benefits in vascular and bleeding complications, length of hospital stay and healthcare costs compared with the transfemoral approach. Although advantageous, TRA is accompanied by radial artery occlusion (RAO) reported to occur in up to 10% of patients. Since TRA inception, novel techniques urged to evolve by the need to minimize patient exposure to procedural complications and prevent RAO risk.

Objectives: This systematic literature review was conducted to summarize current knowledge on strategies to prevent RAO following coronary catheterization.

Methods: PubMed electronic database was systematically searched for randomized control trials that enrolled patients undergoing transradial (conventional or distal) coronary angiography or percutaneous coronary intervention and evaluated radial artery occlusion for the first time with Doppler or vascular ultrasonography as a sole and non-composite primary outcome within 24-hours post-procedure. Additionally, reference lists of matched results and recent systematic reviews were screened in a backward snowballing method to identify relevant articles. The search was conducted until the 1st of May 2022. This search strategy yielded 56 results and by strict exclusion criteria 13 studies were left for in-depth review and analysis.

Conclusion: Best practices for RAO prevention rotate around 3 axies; pre-procedural puncture and cannulation techniques with appropriate catheter and sheath selection in respect to vessel's diameter; peri procedural spasmolytic cocktail and adequate anticoagulation regimen; post-procedural optimal care of the access site in respect to compression method and duration of non-occlusive patent hemostasis.

Keywords: radial access, radial artery occlusion, RAO, prevention, strategy, catheterization

Table of contents

ABBREVIATIONS

PCI: percutaneous coronary intervention

CAG: Coronary angiography

TRA: transradial approach

ICU: intensive care unit

ACS: acute coronary syndrome

ESC: European Society of Cardiology

AHA: American Heart Association

SCAI: Society of Cardiovascular Angiography and Interventions

NSTE-ACS: non-ST-Elevation acute coronary syndrome

RAO: radial artery occlusion

CTO: chronic total occlusion

CABG: coronary artery bypass graft surgery

INR: international normalized ratio

OD: once daily

PCD: pneumatic compression device

DRA: distal radial access

RHD: radial hemostatic device

UFH: unfractioned heparin

NTG: nitroglycerine

SC: subcutaneous

GSS6Fr: Glidesheath Slender 6-Fr

PH: patent hemostasis

ACT: activated clotting time

OR: odds ratio

CI: confidence interval

IVUS: intravascular ultrasound

BMI: body mass index

BSA: body surface area

CAD: coronary artery disease

GFR: glomerular filtration rate

OCT: optical coherence tomography

PO-FMD: prolonged occlusion flow-mediated dilatation

SH-GC: SheathLess hydrophilic-coated guide catheter

RAS: radial artery spasm

ULTRA: ULnar Artery Transient compression facilitating Radial Artery

RCT: randomized control study

GENERAL PART

Chapter 1 Introduction

1. INTRODUCTION

European Association of Percutaneous Coronary Interventions (EAPCI) Atlas survey of 2016 reported an annual median of 5000 diagnostic coronary angiographies (CAG) and 2500 PCIs per million people in Europe [1].

Transradial approach (TRA) gained overwhelmed popularity and has been established as the default strategy of coronary catheterization as evidence showed remarkable reduction in average intensive care unit (ICU) length of stay, profound cost-effectiveness, less vascular and bleeding complications, early mobilization of the patient and accelerated discharge pathways compared to the transfemoral access. In fact, benefits were maintained at 1-year follow-up in acute coronary syndrome (ACS) patients [2-9]. This norm of '*Radialism'* or '*radial-first strategy*' is also supported by the European Society of Cardiology (ESC), American Heart Association (AHA) and Society of Cardiovascular Angiography and Interventions (SCAI) guidelines for coronary interventions [10-12]. Interestingly, current data suggest that same-day discharge after uncomplicated PCI either for elective outpatients or for low-risk Non-ST-Elevation Acute Coronary Syndrome (NSTE-ACS) patients is safe as far as mortality, bleeding or readmission rates are concerned, prefered by the patients and cost-effective for healthcare systems [13-16].

Complications of TRA, though, may include hand dysfunction, hand ischemia, persistent post-procedural pain, neurological deficits, infection, aseptic granuloma, dissection, perforation, arteriovenous fistula, pseudoaneurysm, local hematomas, compartment syndrome, arterial spasm but most frequently radial artery occlusion (RAO) [17-22]. RAO incidence is reported to be 1-10%; 7.5% during the first 24 hours reduced to 5.5% at 30 days of follow-up due to spontaneous recanalization [23-26]. Although clinical silent and asymptomatic in acute setting given the presence of dual circulation and extensive anastomotic network to the hand [27], clinicians are concerned due to the fact that an occluded radial artery excludes future homolateral re-access point for repeat coronary procedures or complicated PCIs [i.e. Chronic Total Occlusions (CTO)] when dual access is needed. RAO also impedes the use of radial artery as a coronary artery bypass graft [28-30] or as a conduit for arteriovenous fistula formation for patients on hemodialysis [31-32]. A patent left radial offers ergonomical advantage of improved positioning both for the operator and the patient when cannulating the left internal mammary artery for patients with previous CABG (coronary artery bypass graft surgery) [33-34]. Finally, radial artery is utilized as a convenient access site for non–coronary procedures in interventional oncology and neuroradiology, in peripheral arterial

interventions and in anesthesiology and ICU for continuous arterial pressure monitoring and fluid replacement guidance [35-37].

Since TRA inception, novel techniques urged to evolve by the need to minimize patient exposure to procedural complications and prevent RAO risk. Best practices for RAO prevention rotate around 3 axies; pre-procedural puncture and cannulation techniques with appropriate catheter and sheath selection in respect to vessel's diameter; peri procedural spasmolytic cocktail and adequate anticoagulation regimen; and post-procedural access site non-occlusive patent hemostasis compression and care. Operator's and patient's ease and comfort are crucial aspects during the whole procedure. In all, this systematic literature review was conducted to summarize current knowledge on strategies to prevent RAO following coronary catheterization.

SPECIAL PART

Chapter 2 Methods

2.1 Objective

This systematic literature review summarizes current knowledge on strategies to prevent radial artery occlusion following coronary catheterization.

2.2 Inclusion Criteria (PICO)

Studies were considered for detailed screening and inclusion if their title and/or abstract potentially met one of the following criteria:

1. Randomized clinical studies enrolling over one-hundred participants evaluating radial occlusion.

2. Studies discussing RAO preventive strategies.

3. Studies assessing equipment (sheath and catheter size or type), pharmacology (antithrombotics and spasmolytics), access site care (hemostasis type and duration), radial artery diameter, and radial artery occlusion risk.

PICO	Inclusion criteria
Patient population	Randomized adults over 18 years of age undergoing transradial (conventional or distal) CAG or PCI and RAO evaluation
Intervention	Diagnostic CAG and/or PCI and ultrasound evaluation of radial artery patency to all subjects within 24 hours
Comparison	Equipment (sheath or catheter size or type), pharmacology (antithrombotics and spasmolytics), access site care (hemostasis type and duration), radial artery diameter, RAO risk
Outcome	RAO rate within 24-hours post-procedure

2.3 Search Strategy and description of study methodology

PubMed electronic database was systematically searched for randomized control trials that enrolled patients undergoing transradial (conventional or distal) coronary angiography or percutaneous coronary intervention and evaluated radial artery occlusion for the first time with Doppler or vascular ultrasonography as a sole and non-composite primary outcome within 24-hours post-procedure.

MeSH terms and database search techniques (truncation, quotations, parentheses, Boolean operators) were used. Full-length articles in English language only were taken into consideration.

The results derived were matched after having used combinations of the following key words: (radial artery occlusion OR RAO OR radial artery patency OR radial artery thrombosis) AND ("Coronary Angiography"[Mesh] OR "Percutaneous Coronary Intervention"[Mesh] OR "Cardiac Catheterization"[Mesh] OR "Coronary Vessels"[Mesh] OR "coronary procedure*") AND (transradial OR snuffbox OR dorsal) AND (ultrasound OR Doppler). Additionally, reference lists of matched results and recent systematic reviews were screened in a backward snowballing method to identify relevant articles. In case of multiple publications with the same population or substudies, the first original report was used. The search was conducted until the 1st of May 2022.
In the present systematic review, definition of RAO was restricted by Doppler or vascular ultrasonography confirmed lack of antegrade blood flow evaluated to all subjects within 24 hours post-procedure regarding the eligibility of included studies. Therefore, studies reporting RAO based on clinical grounds only i.e., palpation, clinical examination, Allen's test, reverse Allen's test or Barbeau's test alone or in combination and studies evaluating RAO for the first time in a period of more than 24-hours post-catheterization were excluded.

Electronic database search strategy yielded 54 results. Of these, 2 studies were duplicates or examined the same population, 15 studies were excluded by title and 15 by abstract. From the backward snowballing method 2 more studies were found. Finally, 23 studies overall were retrieved for detailed evaluation and eligibility. Strict exclusion criteria left 13 studies for in-depth review and analysis [Table 1].

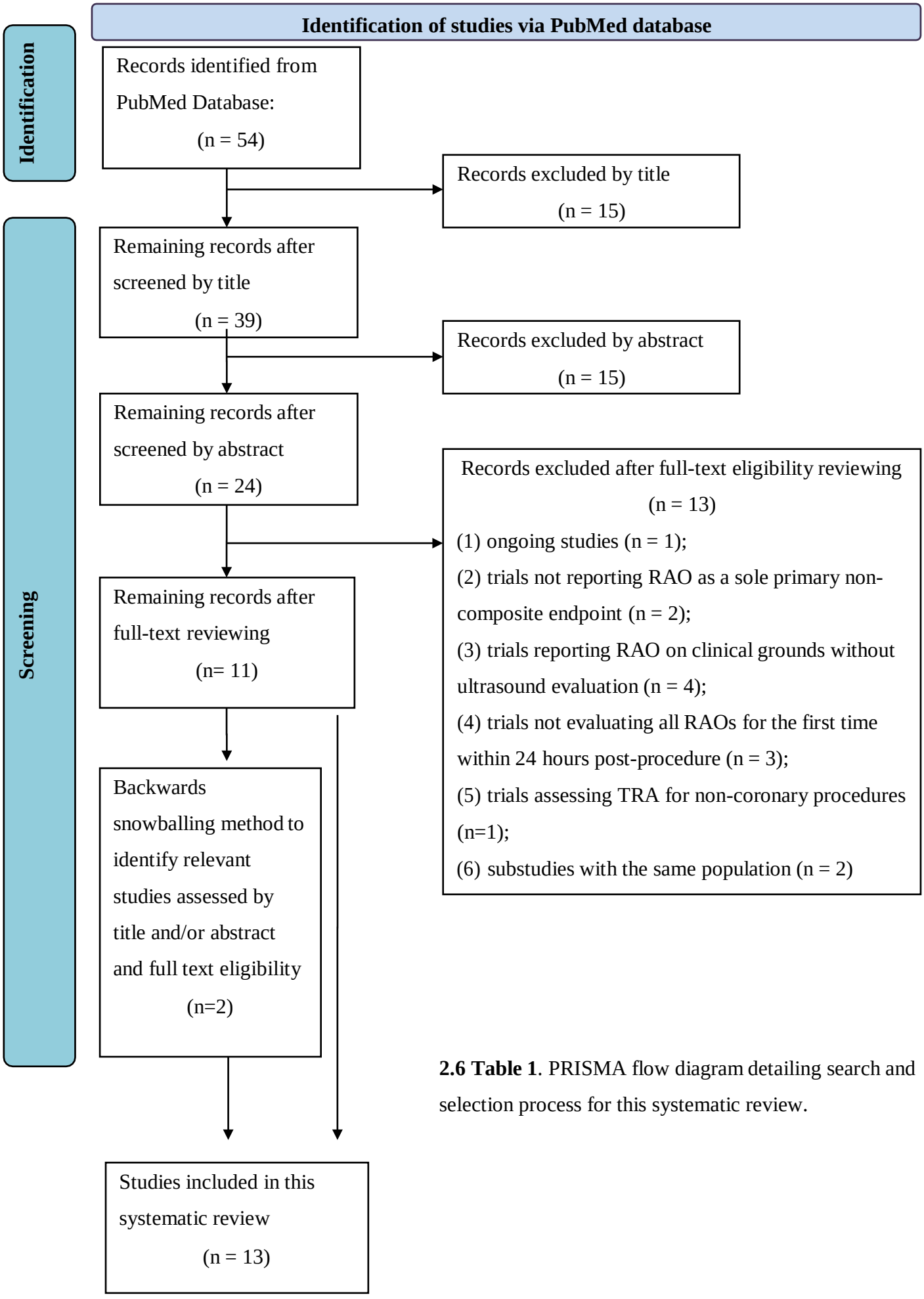
2.4 Exclusion criteria:

1. irretrievable data;
2. ongoing studies;
3. non-randomized clinical trials;
4. studies including less than 100 participants
5. studies not reporting RAO as a sole and non-composite primary endpoint;
6. studies reporting RAO on clinical grounds only without ultrasound evaluation for all subjects in the first instance;
7. studies evaluating RAO for the first time in a time period of more than 24 hours post-procedure;
8. studies including subjects with transradial access for non-coronary procedures
9. duplicate reports or substudies with the same population;
10. studies in language other than English

The present systematic review is presented in agreement with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines.

2.5 Data Extraction

The search of literature, selection of studies and extraction of data was initiated by 1 investigator (D.K) using a standardized systematic approach. In order to form the final tables presented herein, the following data were retrieved whenever possible from each study reviewed and recorded in a master Excel spreadsheet: type of study; country; number of patients, operators and centers; primary and secondary endpoints; outcomes of interest; defining study characteristics/arms; time of ultrasound evaluation; indication for CAG and/or PCI; procedural characteristics: dosage of unfractioned heparin, GP IIbIIIa inhibitors, nitroglycerine and verapamil, activated clotting time values, puncture attempts, size and type of sheaths and catheter, proximal and distal radial diameter, total procedural time and duration of hemostasis; all access-site complications including: RAO rates at discharge, 24 hours, 30 days or later and recanalization rates; RAO predictors from univariate or multivariate analysis; patient demographics, cardiovascular risk factors, medication, platelet count, hemoglobin, INR; and other variables or numerical data reported in the section “outcomes”.



2.6 Table 1. PRISMA flow diagram detailing search and selection process for this systematic review.

Chapter 3 Results

3.1 Tables of excluded and selected studies.

Table 2. List of excluded studies (First name, Journal, Year) based on methodology-set criteria.

	Studies								
Exclusion Criterion	**Title**		**Abstract**		**Ongoing**	**First RAO evalation on clinical grounds**	**First ultrasound evaluation after 24 hours post-procedure**	**Non-coronary procedures included**	**Composite and not sole primary endpoint**
	1. Filho Arq Bras Cardiol. 2003	9. Geng Chin Med J (Engl). 2014	1. Slagboom Catheter Cardiovasc Interv. 2005	9. Ünal Rev Port Cardiol. 2017	1. Aminian Am Heart J. 2022	1. Cubero Catheter Cardiovasc Interv. 2009	1. Kindel Clin Res Cardiol. 2008	1. Dharma Catheter Cardiovasc Interv. 2015	1. Horie EuroIntervention. 2018
	2. Ruiz-Salmeron Catheter Cardiovasc Interv. 2005	10. Wang Catheter Cardiovasc Interv. 2017	2. Choi J Invasive Cardiol. 2005	10. Dangoisse Am J Cardiol. 2017		2. Takeshita Am J Cardiol. 2014	2. Hahalis JACC Cardiovasc Interv. 2018		2. Tebaldi Cardiology. 2018
	3. Aptecar Catheter Cardiovasc Interv. 2006	11. Erden J Interv Cardiol. 2017	3. Beyer Int J Cardiol. 2013	11. Batchelor Am Heart J. 2018		3. Lavi J Am Heart Assoc. 2017			
	4. Li Chin Med J (Engl). 2010	12. Valgimigli Lancet. 2018	4. Hizoh J Am Heart Assoc. 2014	12. Haq Cardiovasc Revasc Med. 2019		4. Ognerubov J Interv Cardiol. 2020			
	5.Sciahbasi Cardiovasc Revasc Med. 2012	13. Dharma J Invasive Cardiol. 2018	5. Aykan Int J Cardiol. 2015	13. Didagelos Future Cardiol. 2022					
	6. Liu Circ J. 2012	14. Fan Cardiol J. 2021	6. Turan Cardiovasc Revasc Med. 2015	14. Tsigkas JACC Cardiovasc Interv. 2022					
	7. Jolly JACC Cardiovasc Interv. 2013	15. Gorgulu JACC Cardiovasc Interv. 2022	7. Déry Catheter Cardiovasc Interv. 2016	15. Safirstein JACC Cardiovasc Interv. 2022					

	8. Deftereos JACC Cardiovasc Interv. 2013		8. Pancholy JACC Cardiovasc Interv. 2016		

Table 3. Randomized studies assessing RAO incidence with ultrasound examination within 24 hours following coronary catheterization (diagnostic or PCI) as a primary, non-composite endpoint included in this review.

Year	First Author (Trial name) Ref#	Country	Patients	Primary endpoints	Outcomes of interest	Defining study characteristic, subjects in arms	Overall early RAO rate (%)	Early RAO rate in study arms (%)	P-value
2022	Liang D. (RESTORE) [116]	China	382	RAO at 24h with rivaroxaban 10mg OD for 7 days vs. placebo.	1. Post-procedure rivaroxaban (10mg OD) did not significantly reduce the 24-hour RAO compared with placebo. 2. Short-term use significantly reduced 1-month RAO compared with placebo.	Control group, n=191	10.2	11.5	0.398
						Rivaroxaban, n=191		8.9	
2021	Pathan AZ. [139]	Pakistan	597	RAO at 6- to 24-hours after CAG between two compression devices (InnoSEAL and PCD) and difference in hemostasis time and radial monitoring termination time.	1. InnoSEAL with compression bandage achieved earlier hemostasis with shorter time to termination of radial monitoring, compared to a PCD. 2. There was no significant difference in RAO rates or bleeding events.	InnoSEAL, n=299	8.7	8.5	> 0.05
						PCD, n=298		9.4	
2021	Eid-Lidt G. (DAPRAO) [65]	Mexico	282	Superiority of DRA vs. conventional TRA for proximal RAO at 24-hours.	Proximal RAO evaluated 24-hours post-procedure was significantly lower in the DRA group compared with TRA, meeting criteria for superiority.	Distal, n=140	4.6	0.7	0.002
						Conventional, n=142		8.4	

2021	Lavi S. (PRACTICAL-2)[130]	Canada	450	RAO risk with small sheaths, no heparin and quick hemostatic device weaning starting at 10, 20 or 30 minutes post-procedure.	TRA CAG with modern small-diameter radial introducer sheaths, no adjunctive heparin and a fast RHD weaning protocol [gradual release over 20 minutes with a quarter turn of the RHD knob every 5 minutes, followed by RHD removal] was associated with relatively low overall RAO incidence.	10min, n=150	7.7	7	0.26
						20min, n=150		11	
						30min, n=150		6	
2019	Shah S. [75]	USA	129	RAO rates and hematoma formation when evaluating the start of the radial compression weaning process [accelerated (20 min) vs. adjusted (30, 60 or 120 min)].	An accelerated weaning protocol is safe and effective at achieving hemostasis without increasing RAO or hematoma formation.	Group A – Accelerated protocol 1. wean at 20 min	7.7	5	0.337

	Shah S. [75]					Group B – Adjusted protocol 1. Diagnostic procedure: wean at 30min 2. PCI with UFH or Bivalirudin: wean at 60min 3. PCI with GPIIB/IIIa or INR > 2: wean at 120min		10.1	
2018	Campos MAC. [132]	Brazil	303	Occurrence of hemostasis and vascular complications (including immediate and late RAO) with 30 and 60 minutes of compression.	Compressive dressing for 30 minutes after elective TRA CAG is as effective and safe as when maintained for 60 minutes with respect to hemostasis and occurrence of immediate and late complications.	Compression for 30min, n=152	12.5	13.2	0.75
						Compression for 60min, n=151		11.9	
2018	Chiang CY. [141]	Taiwan	260	RAO rate 24-hours and 1-month after TRA CAG with QuikClot-Kaolin pad compression vs. sterile gauze.	1. Kaolin QuikClot pads with a short compression time did not significantly reduce RAO incidence. 2. Heparin dose and radial artery size were not correlated with RAO.	QuikClot-Kaolin, n=130	5	4.6	0.7760
						Sterile gauze, n=130		5.4	

2018	Chen Y. [100]	China	182	RAO rate after pre-procedure injection of nitroglycerin at the radial artery puncture site vs. placebo.	Early RAO incidence was substantially lower in the NTG treated group than in the placebo group.	SC NTG, n=92	9.8	5.4	0.04
						Placebo, n=90		14.4	
2018	Petroglou D. (MEMORY) [118]	Greece	595	Early (24-hours) RAO incidence after TRA GAC with manual vs. mechanical compression.	RAO incidence at 24-hours post-procedure was similar whether manual or mechanical compression was used.	Manual compression, n=304	10.18	12	0.176
						Mechanical compression, n=285		8	
2017	Aminian A. (RAP and BEAT) [94]	Japan, Europe, USA	1838	RAO at discharge when assessing non-inferiority of the GSS6Fr against the GS5Fr, and superiority of PH vs. institutional protocols.	1. Overall RAO incidence for the entire study cohort was low. 2. The hypothesis that the new GSS6Fr would provide similar RAO rates to a conventional 5 Fr sheath could not be confirmed. 3. PH did not reduce RAO rate compared to institutional protocols.	GSS6Fr and PH, n=448	2.61	3.6	1
						GSS6Fr without PH, n=473		3.4	
						GS5Fr and PH, n=470		1.7	1
						GS5Fr without PH, n=447		1.8	

2015	Dai N. [136]	China	600	Radial artery outcomes (including RAO) with a compression device vs. a Chitosan-based pad.	Chitosan-based pad showed better hemostatic efficacy and a lower RAO incidence compared to a compression device.	Compression device, n= 300	8.6	11.7	< 0.05
						Chitosan, n=300		5.4	
2011	Bernat I. [123]	Chech Republic, Canada	465	1. RAO incidence with 2 heparin dosage regimens after TRA CAG. 2. Efficacy and safety of transient homolateral ulnar artery compression for acute radial artery recanalization.	1. RAO incidence remained significantly lower with a higher anticoagulation level. 2. 5Fr sheaths and PH technique do not change the need of a higher heparin dose to prevent RAO. 3. Acute RAO after TRA can be recanalized by early 1-hour homolateral ulnar artery compression.	2000IU UFH, n=222	4.3	5.9	0.17
						5000IU UFH, n=243		2.9	
2010	Schiano P. (AWARE) [112]	France	162	Radial artery permeability within 24-hours after elective 5Fr TRA CAG with 5000IU vs. 50IU/kg, < 5000IU of UFH.	1. A weight-adjusted dose of UFH is safe and efficient, without any increased RAO risk in elective 5 Fr TRA CAG. 2. Compared to a single dose of 5,000 UI, it limits the ACT level achieved and significantly reduces the compression time required for hemostasis.	5000IU UFH, n=79	0	0	1
						50IU/kg, <5000IU, n=83		0	

RAO: radial artery occlusion, OD: once daily, CAG: coronary angiography, PCD: pneumatic compression device, DRA: distal radial access, TRA: traditional radial access, RHD: radial hemostatic device, PCI: percutaneous coronary intervention, UFH: unfractioned heparin, GPIIbIIIa: glycoprotein IIbIIIa, INR: international normalized ratio, NTG: nitroglycerine, SC: subcutaneous, GSS6Fr: Glidesheath Slender 6-Fr, PH: patent hemostasis, ACT: activated clotting time

Chapter 4 Discussion

RAO incidence following coronary catheterization is reported to be 1-10%; 7.5% during the first 24 hours reduced to 5.5% at 30 days of follow-up due to spontaneous recanalization [23-26]. Best practices for RAO prevention rotate around 3 axies: pre-procedural puncture and cannulation techniques with appropriate catheter and sheath selection in respect to vessel's diameter; peri procedural spasmolytic cocktail and adequate anticoagulation regimen; and post-procedural access site care, non-occlusive hemostatic compression and duration. Operator's and patient's ease and comfort are crucial aspects during the whole procedure. Risk factors for RAO in 24-hours post-coronary catheterization are summarized in Table 4.

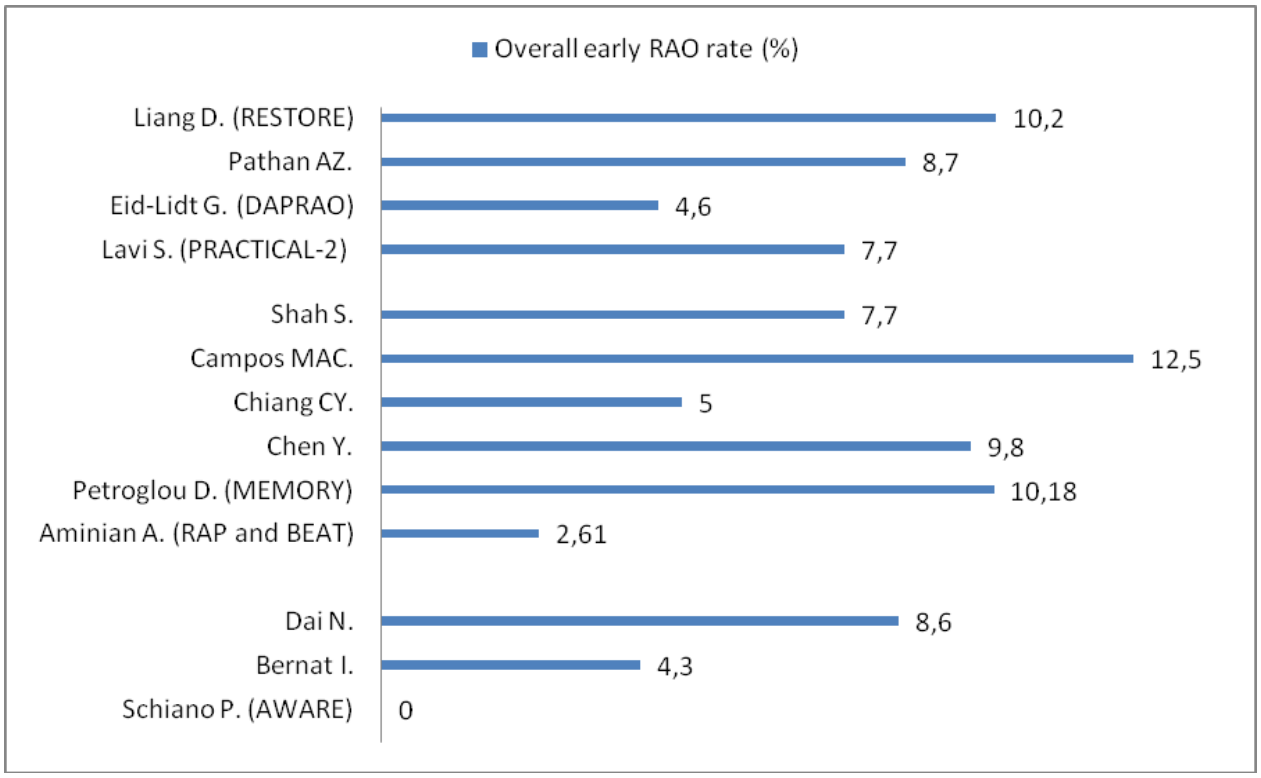


Figure 1. Overall early (24-hours) RAO rate (%) reported in each study reviewed for analysis.

Table 4. Synopsis of independent RAO risk factors reported in each study at 24-hours after regression analysis.

	Independent RAO risk factors at 24-hours after regression analysis
Liang 2022	Multivariate analysis significant: age (OR: 0.97, CI: 0.93–0.99; P=0.033), procedure duration (OR: 1.04, CI: 1.01–1.08; P=0.008), radial artery lumen diameter (OR: 0.40, CI: 0.20–0.83; P=0.014) non-significant: PCI or IVUS, UFH dose, hemostasis time, rivaroxaban group
Pathan 2021	NA
Lidt 2021	Multivariate analysis significant: proximal TRA (OR: 12.8; 95% CI: 1.6–100.0; P=0.015) non-significant: diagnostic or interventional study, antiplatelet or anticoagulant use, statins
Lavi 2021	Unadjusted analysis non-significant: age, sheath in the artery duration, male, GSS5Fr, previous TRA, aspirin, clopidogrel, ticagrelor
Shah 2019	Unadjusted analysis non-significant: technique puncture, number of puncture attempts, sheath diameter, duration of procedure
Campos 2018	NA
Chiang 2018	Univariate analysis: non-significant: age, sex, height, body weight, blood pressure, dyslipidemia, previous myocardial infarction, duration of the procedure, ACT, UFH dose
Chen 2018	NA

Petroglou 2018	Multivariate analysis: significant: number of puncture attempts (OR: 2.69; 95% CI: 1.42–5.14; P=0.003), ACT (OR: 0.98; 95% CI: 0.96–1.01; P=0.068), radiation time (OR: 0.79; 95% CI: 0.63–0.99; P=0.046), and patent hemostasis (OR: 0.08; 95% CI: 0.02–0.34; P<0.001) non-significant: age, male/female, BMI, BSA, indication for coronary angiography (CAD, valvular/other), history of CAD, hypertension, diabetes mellitus, dyslipidemia, smoking, family history of CAD, hemoglobin, creatinine, GFR, peri-procedural treatment characteristics, antiplatelet agents (aspirin, clopidogrel, ticagrelor, prasugrel, triflusal), vasodilators (nitrates, verapamil), heparin, arm (right/left), radial artery spasm, puncture attempts, sheath length, sheath time, radiation time, ACT, distal or proximal radial artery diameter, contrast volume
Aminian 2017	Univariate analysis significant: male (vs. female) (OR: 0.56, CI: 0.31–0.99; P=0.045), aspirin use (OR: 0.35, CI: 0.19–0.62; P < 0.001), PCI (OR: 0.42, CI: 0.13–1.35; P=0.132), GSS6Fr (OR: 2.03, CI: 1.10–3.72; P=0.02), spasm (OR: 4.11, CI: 1.87–9.07, P<0.001), pain during procedure (OR: 3.13, CI: 1.75–5.61; P<0.001), vascular access-site complications (OR: 8.60, CI: 1.81–40.94; P=0.001), non-successful hemostasis (OR: 2.34, CI: 1.17–4.65; P=0.013), procedural failure (OR: 4.82, CI: 1.08–21.58; P=0.023) non-significant: current smoker (OR:1.89, CI: 0.97–3.69; P=0.056), P2Y12 inhibitor use (OR: 0.53, CI: 0.28–1.03; P=0.059), Multivariate analysis significant: GSS6Fr (OR: 1.96, 95% CI: 1.06–3.83, P=0.032), pain during procedure (OR: 1.83, 95% CI: 1.24–2.72, P=0.003), age >65 years (OR: 0.97, 95% CI: 0.95–0.99, P=0.009), successful hemostasis (OR: 0.48, 95% CI: 0.24–0.99, P=0.046) and aspirin use (OR:0.38, 95% CI: 0.21–0.70, P=0.002)
Dai 2015	NA

Bernat 2011	NA
Schiano 2010	NA

Statistically significant if P-value < 0.05, NA: no answer, OR: odds ratio, CI: confidence interval, IVUS: intravascular ultrasound, UFH: unfractioned heparin, GSS5Fr: 5Fr-Glidesheath Slender sheath, ACT: activated clottingtime, BMI: body mass index, BSA: body surface area, CAD: coronary artery disease, GFR: glomerular filtration rate

4.1 Pre-procedural axis

Arterial puncture especially if repeated due to first hit access failure causes patient's discomfort and anxiety. Local anesthesia with subcutaneous or ointment lidocaine and mild sedation with midazolame reduces anxiety, irritability and pain perception during needle or sheath insertion and prevents vasoconstriction [38-41].

Access point (proximal, convenient, distal) has to be carefully selected. The anatomic snuffbox is a sunken triangular area (6cm in length x 1.5cm in width) on the dorsal side of the hand circumscribed laterally by the tendons of abductor pollicis longus and extensor pollicis brevis muscles and medially by the tendon of extensor pollicis longus muscle best seen when extending the thumb [42]. Radial artery transverses through the carpal tunnel giving off a rich anastomotic network of branches in the volar surface of the wrist; namely the superficial palmar arch; and its distal part crosses the snuffbox floor (distal radius, scaphoid, trapezium, and the base of the first metacarpal bone) to form the deep palmar arch [43] [Figure 2A-C]. Normally, TRA is performed at the distal third of the forearm 2–3 cm proximal to the styloid process of the wrist; a site quite near to the superficial palmar artery branch of the radial artery [Figure 1D]. On the contrary, the access point of DRA is located at the intersection of the thumb and the first digit over wrist's bones, distal to the origin of the superficial palmar arch branch [44]. The course of the distal artery, its anatomic arrangement with adjacent structures and the extended intercommunication between the superficial and deep palmar arches [27] lead to uncompromised distal blood flow in case of RAO as the origin of the superficial palmar artery is let clear [34,43,45-47]. Smaller diameter also shortens hemostasis time and risk for hematoma is reduced [48].

The Distal Radial Access Doppler Study [49] supported the background notion that DTRA perfomed in the snuffbox boundaries would forestall retrograde clot extension to the forearm and antegrade blood supply would be conserved by the branches of the superficial palmar arch artery [50]. Kaledin et al. [51] were the first to conceptualize this hypothesis, Babunashvilli et al. [52] first described DRA as an access site for recanalization of occluded ipsilateral radial artery and finally Kiemenej et al. [34] first practiced (left) DTRA for coronary interventions.

Since DRA inception, case reports and series, observational and randomized studies tested its feasibility and safety for coronary interventions and assessed complications rates compared with TRA demonstrating better outcomes on RAO incidence, hemostasis duration, radiation exposure and overall improved operator's and patient's comfort during the procedure because of a securing semiprone and otherwise neutral hand position [34,44,53-70].

A retrospective Optical Coherence Tomography (OCT)-based study by Kim et al. [55] in 46 Korean patients undergoing DRA CAG reported infrequent incidence of acute conventional radial artery injury including intimal tear, intraluminal thrombi or medial dissection. Tsigkas et. al. in ANGIE Trial [68] randomized one thousand forty-two consecutive patients to right DTRA or TRA and evaluated forearm RAO rate with Doppler ultrasound as a primary endpoint at 60 days of follow-up reporting significantly reduced incidence (3.7% vs. 7.9%, P = 0.014) and shorter hemostasis time but a higher crossover rate and a longer procedural time. In DAPRAO study [65], Lidt et al. randomized 268 patients to DRA and TRA and reported significantly reduced forearm RAO rates in the distal group both at 24-hours (0.7% vs. 8.4%; P < 0.002, odds ratio [OR]: 12.8, 95% confidence interval [CI]: 1.6–100.0) and at 30-days follow up (0.7% vs. 5.6%, P < 0.019, OR: 8.2; 95% CI: 1.0–67.2) with the sole independent risk factor for proximal RAO being the TRA. Pacchioni et al. [71], though, criticized its statistical power based on the fact that DAPRAO's investigators during inception overcalculated the expected RAO rate in the conventional group contrary to recent data (8% vs. 3.5%) [25] and consequently their sample size was considerably small (268 vs. 1098) for solid outcomes. A propensity score matching analysis of 1163 patients [54] compared the incidence of forearm RAO and hemostasis characteristics between distal and conventional transradial approach and reported lower RAO rates (0% vs. 4.8%, P < 0.0001), higher percentage of preserved flow (PF) (97.2% vs. 78.5%, P < 0.0001) and reduced time-to-hemostasis (147 ± 99 min vs. 285 ± 138 min, P < 0.0001) in favor of the distal arm. DORA Trial [56] evaluated a series of 970 patients of whom 485 patients underwent dorsal radial access (more distally to the snuffbox) CAG with 5-Fr sheaths and reported 96% success rate and 2% of forearm RAO 12 hours post-procedure with Doppler ultrasound confirmation. On the contrary, Bi et al. [72] assessed a more proximal approach aiming to compare RAO risk with Doppler ultrasound examination evaluated in two days and one year after the coronary intervention and demonstrated that RAO incidence in correlation with the puncture distance from the radius styloid process was significantly higher at sites 0 or 1 cm away (P = 0.002 and P = 0.001, respectively) but significantly less at 4 cm proximally (P = 0.001). Finally, a meta-analysis by Sattar et al. [53] comparing DRA vs. TRA for RAO incidence demonstrated lower RAO rates (OR 0.51, 95% CI 0.29–0.90, I^2 = 42.6%, P = 0.02) and similar occurence of procedure-related complications (access site pain, hematoma, bleeding, spasm or radial artery dissection). Overall, reported higher number of puncture attempts and/or higher rate of access site failure with consequent longer time to cannulation, cross-over punctures and the relatively smaller diameter of the distal radial artery compared to its proximal part constitute the non-bright side of the DTRA technique.

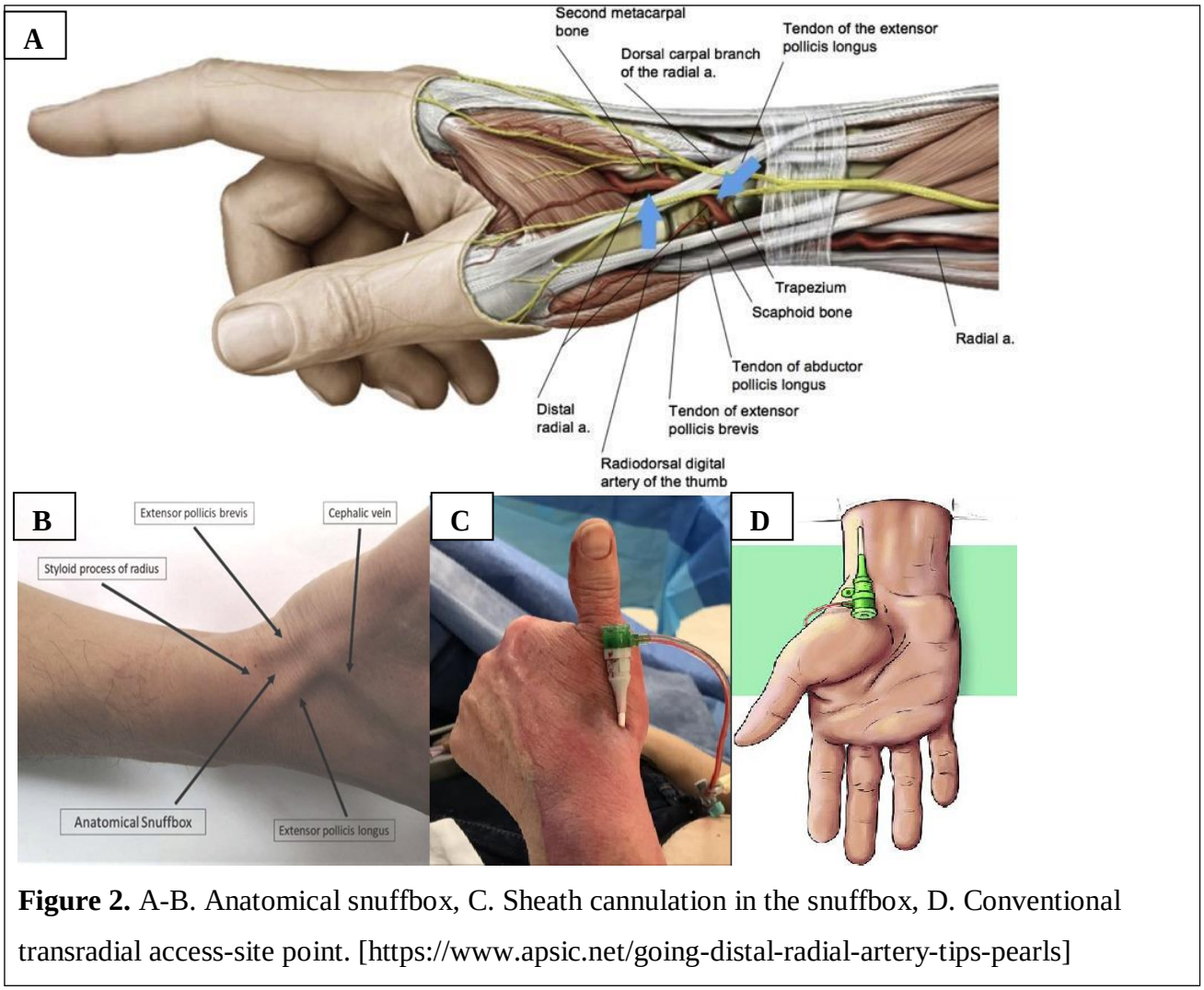


Figure 2. A-B. Anatomical snuffbox, C. Sheath cannulation in the snuffbox, D. Conventional transradial access-site point. [https://www.apsic.net/going-distal-radial-artery-tips-pearls]

Pre-procedural ultrasound offers another step towards the best access site option and Phi match between radial's artery ID and appropriate sheath and catheter size selection [73,74]. The randomized RAUST trial demonstrated reduced time and number of attempts to achieve arterial access with ultrasound guidance in patients with cardiogenic shock [75]. SCAI 2020 guidelines [12] recommended that operators should be familiar with pre-procedural ultrasound so as to ameliorate the chances of successful first hit and avoid insertion of unsuitable materials in respect to vessel's size provoking patient's discomfort or artery's spasm. Yet, the significance of such a practice is under question in real-world daily practice mostly because of procedural time extension and healthcare costs related issues [76,77].

To continue, after assessing 1706 consecutive patients undergoing TRA catheterization with Doppler ultrasound, Dharma et al. [78] reported that there is no matching between radial's artery diameter and body mass index (BMI) but females are anticipated to have smaller vessel diameter.

Radial's artery internal diameter (ID) is reported to be 2.7–3.1 mm [69,70,79] and constitutes this vessel quite fine and delicate. Despite its superficial and easily palpable course in the forearm or snuffbox, extreme caution and dexterity are important assets when puncturing, wiring, inserting a sheath maneuvering and navigating. In the RADIAL trial [80] investigators randomized 1156 patients and implemented a prolonged occlusion flow-mediated dilatation (PO-FMD) protocol to dilate the radial artery prior to puncturing and reported reduced failure rates and puncture attempts. RAO incidence though was not significantly different in the two arms (3.9% vs. 5.7%, P=0.2). The outer diameter (OD) of sheaths and catheters needs to match radial's artery ID otherwise friction or vascular stretch will occur, activation of the surface endothelium and coagulation cascade will ensue and chronic intimal thickening will finally arise compromising blood flow [81-85] [Figure 3]. Noteworthy, that adverse luminal remodeling with intimal hyperplasia, thickening, focal stenoses, and radial diameter reduction may be outcomes of prior RA catheterizations [86-88]. Interestingly, Yonetsu et al. [84] based on OCT findings found that more than half of the intimal tears were observed at the proximal end of the sheath and close to the artery's ostium.

Motivated by the need to overtake sheath-to-ratio mismatch restrictions, industry proceeded to the development of special finer, thin-walled, hydrophilic sheaths and operators experimented with sheathless approaches [89-92]. A hydrophilically coated introducer sheath significantly decreases friction both during insertion and removal [93], hence further reducing intimal damage [Figure 4]. Aminian et al. in the RAP and BEAT randomized multicenter trial [94] in 12 centers in Japan, Europe and the USA evaluated the sheath size for transradial access using a novel 6-Fr Glidesheath Slender (GSS6Fr) against the standard GS5Fr in terms of RAO rates at discharge as a primary endpoint and reported low overall RAO incidence (2.61%) but the GSS6Fr group did not show statistical significant non-inferiority vs. the control group (3.47% vs. 1.74%, risk difference 1.73%, 95% CI: 0.51–2.95%; $P_{non\text{-}inferiority}$=0.150). Of note, RAO is expected to be more frequent with increasing sheath sizes creating an environment of hypoperfusion and suffocation in the radial artery lumen [23]. One study [95], compared RAO incidence between sheathless and conventional technique with a hydrophilic introducer sheath and interestingly reported significantly higher RAO rates in the sheathless arm group attributed to intimal injury of the arterial entry site from the sheathless catheter insertion. On the other hand, an open-label, single-center, randomized study of 600 consecutive Asian patients undergoing TRA CAG compared 6.5-Fr Sheathless hydrophilic-coated guide catheter (SH-GC) with a GSS6Fr and reported a significant reduction in its primary composite endpoint of RAO and radial artery spasm (RAS) (0.7% vs. 3.7%, P=0.021). In this study none of the SH-GC group patients experienced 30-days RAO evaluated with ultrasonography as opposed to five patients of the GSS group (0.0% vs. 1.7%, P=0.062) [91].

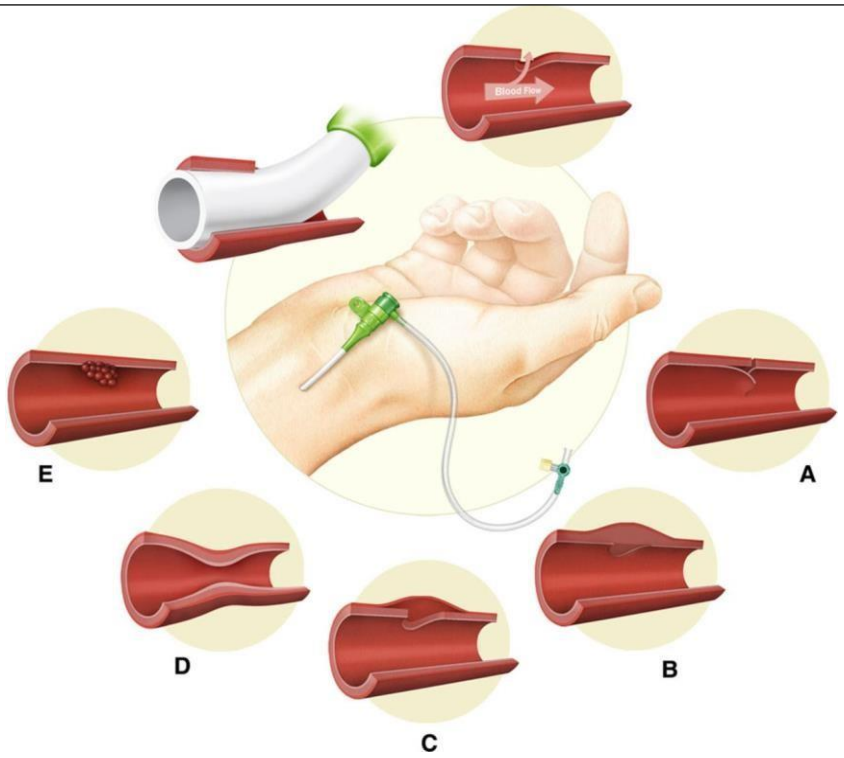


Figure 3. Radial cannulation and injuries. In the upper part, sheath removal and consequent trauma. In the lower part, acute wall injuries of the radial artery following cannulation observed with high-resolution ultrasound: dissection (**A**), intramural hematoma (**B**), pseudoaneurysm (**C**), spasm (**D**), and thrombus formation (**E**). [Costa F. et al. Circ Cardiovasc Interv. 2016]

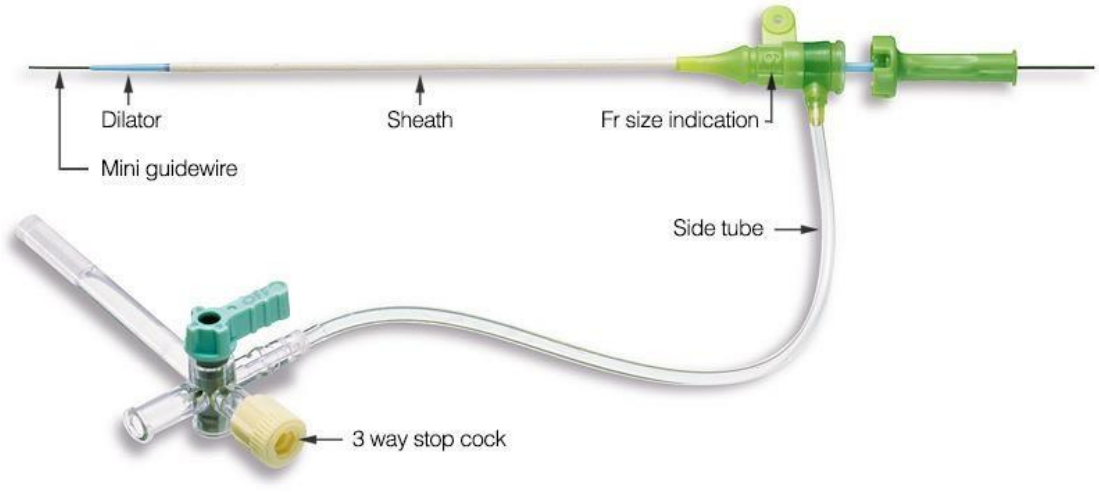


Figure 4. Radifocus Introducer II Standard Kit B, Introducer sheath [https://www.terumo-europe.com/en-emea/products/radifocus%E2%84%A2-introducer-ii-standard-kit-a-introducer-sheath]

4.2 Peri-procedural spasmolytics and anticoagulation

Wire advancement and friction between the arterial wall and the sheath or catheter further worsens endothelial function and precipitate to patient's discomfort, artery's spasm and ultimately to RAO. In fact, transradial catheterization may lead to anatomical and functional changes on vessel's wall in the long-term (6-months) due to puncture or material-associated trauma, inflammation and loss of endothelium's NO vasodilatory response [97]. A meta-analysis [98] showed that an intra-arterial cocktail of vasodilators (verapamil 5 mg and nitroglycerine 100 or 200 mcg) reduces radial artery spasm and should be administered following sheath insertion, catheter changes and just before sheath removal. In addition, two studies evaluated pre-puncture and post-procedure pre-hemostasis intraarterial delivery of nitroglycerine reporting significantly decreased RAO incidence [99,100]. Chen et al. [100] randomized 182 patients to subcutaneous nitroglycerine (NTG) or placebo and reported statistically significant decreased post-procedure 24-hour RAO rates (5.4% vs. 14.4%; P=0.04) and radial artery dilatation (by 0.03±0.10 mm, P=0.003) for the NTG arm group. PATENS Trial [101], however, found that the routine use of nitroglycerin was not associated with a reduction in RAO rate, regardless of the administration time point. The VERMUT study [102] showed that the combination of verapamil, hydrophilic equipment, patent hemostasis, and intravenous unfranctioned heparin (UFH) only in the case of PCI didn't statistically affect early (24-hours) or late (30-days) RAO occurrence but lessened RAS incidence due to verapamil's topical vasodilator effect.

Another pillar strategic measure to block RAO initiation following vessel's wall injury focuses on the peri-procedural antithrombotic method used. Strong evidence supports the systematic "high-dose" UFH administration strategy (at least 5000 IU or >75 IU/kg) over a "low-dose" protocol (<5,000 IU or up to 50 IU/kg body weight) either intravenously or through the sheath to reduce RAO risk [103-112]. In "The Spirit of ARTEMIS Study" [107] investigators reported significantly reduced RAO rates in the high-dose group (3.0% vs. 8.1%; OR: 0.35; 95% CI: 0.22–0.55; P<0.001), regardless of patients' characteristics, hemostasis protocol, and time of ultrasound evaluation. Unpredictable and varying action of UFH [113], however, motivated Pacchioni et al. [114] to assess whether activated clotting time (ACT) would benefit patients undergoing CAG to predict RAO risk. Eight-hundred and thirty-seven patients were divided into 3 distinctive groups by ACT measurements (<150sec, 150-249sec and >250sec) before sheath removal to match RAO occurrence with ACT values. Optimal range was between 175-274sec corresponding to less than 4% for RAO probability, while values <150sec showed increased RAO risk (OR: 3.53; 95% CI: 1.677–7.43; P=0.001). Paradoxically, excessive antithrombotic administration leading to extreme high values also predisposed to RAO by hemostasis duration prolongation.

Post-catheterization anticoagulation to prevent RAO has not been investigated as extensively as peri-procedural regiments have. One observational study addressed the issue and evaluated patients on warfarin regimen finally reporting lower RAO rates [115]. The RESTORE trial [116] randomized 382 anticoagulant-naïve patients to placebo or rivaroxaban 10 mg once daily for a period of 7 days and assessed medication's impact on RAO prevention at 24 hours (primary outcome) and 1-month (secondary outcome) by Doppler ultrasound. Short-term post-procedure rivaroxaban prescription did not affect 24-hour RAO incidence [8.9% vs. 11.5%; P=0.398, OR: 0.75 (95% CI: 0.39–1.46); P=0.399] but improved 1-month RAO [3.8% vs. 11.5%; P=0.011, OR: 0.22 (95% CI: 0.08–0.65); P=0.006], because of a higher radial artery recanalization occurence (69.2% vs. 30.0%; P=0.027). Data for patients on chronic oral anticoagulation regimen is scarce and dedicated studies are needed.

4.3 Post-procedural access site hemostasis, evaluation and care

Non-occlusive patent hemostatic compression is crucial when sealing the access point manually or mechanically to stop post-procedural bleeding. Patent hemostasis (PH) concept is built on the ground that persistent antegrade blood flow in the radial artery will counteract thrombus formation produced by a hypoperfused environment from stagnant or fully ceased blood flow with "occlusive hemostatic compression pressure" [117]. Different types of wristbands (balloon inflation, rotator tourniquet etc.) that resemble to manual compression (folded pieces of gauze with adhesive straps)are usually applied [Figure 5]. The MEMORY Study [118] compared manual and mechanical (pneumatic) strategies following TRA CAG and reported similar early (24-hours) RAO rates (12% vs. 8%, P= 0.176) assessed by ultrasonography, but significantly shorter hemostasis time for the manual group.

The PROPHET study [119] reported a significant decrease in early (24-hours) and late (30-days) RAO rates (from 12% to 5%, $P < 0.05$ and 7% to 1.8%, $P < 0.05$; respectively) using a pulse oximetry-guided HemoBand® patent hemostasis strategy compared with the conventional technique. In the other hand, TR band® significantly decreased RAO incidence compared to the HemoBand [120]. Aminian et al., however reported no difference between patent or institutional hemostasis strategies [94]. The RACOMAP [121] study reported a significant RAO rate reduction when investigators evaluated mean arterial pressure-guided radial artery compression with the TR band vs. the conventional 15 ml inflation strategy (1.1% vs. 12.0%, $P < 0.0001$). Additional benefit and further RAO incidence decrease was documented when investigators evaluated the ULnar Artery Transient compression facilitating Radial Artery (ULTRA) patent hemostasis technique. In other words, preferential flow to the radial artery by simultaneous ipsilateral ulnar artery compression is advantageous because of the radial's artery hemodynamic and hydrodynamic boosting response [12,122,123]. PROPHET II [124], compared standard patent hemostasis protocol alone with that of an additional prophylactic compression device on to the ipsilateral ulnar artery with respect to radial's artery patency and statistically significant reduction in 24-hour and 30-day RAO incidence was documented (from 4.3% to 1.0%, $P < 0.0001$ and 3.0% to 0.9%, $P = 0.0001$, respectively). Despite proven benefits, however, high rates of failure to stick to the protocol are reported to occur as high as in 20-50% of patients [12,106,107,119, 124]. This may be explained by a loose nursery staff engagement with the PH protocol that demands constant and repeated radial flow evaluation with palpation or oximetry plethysmography. Appropriate staff education on successfully adapting the hemostatic compression pressure is crucial to avoid tingling, prolonged numbness, clumsiness, hand or finger pain, paraesthesia or sensory deficit, skin tenderness, edema, discoloration or reduced temperature.

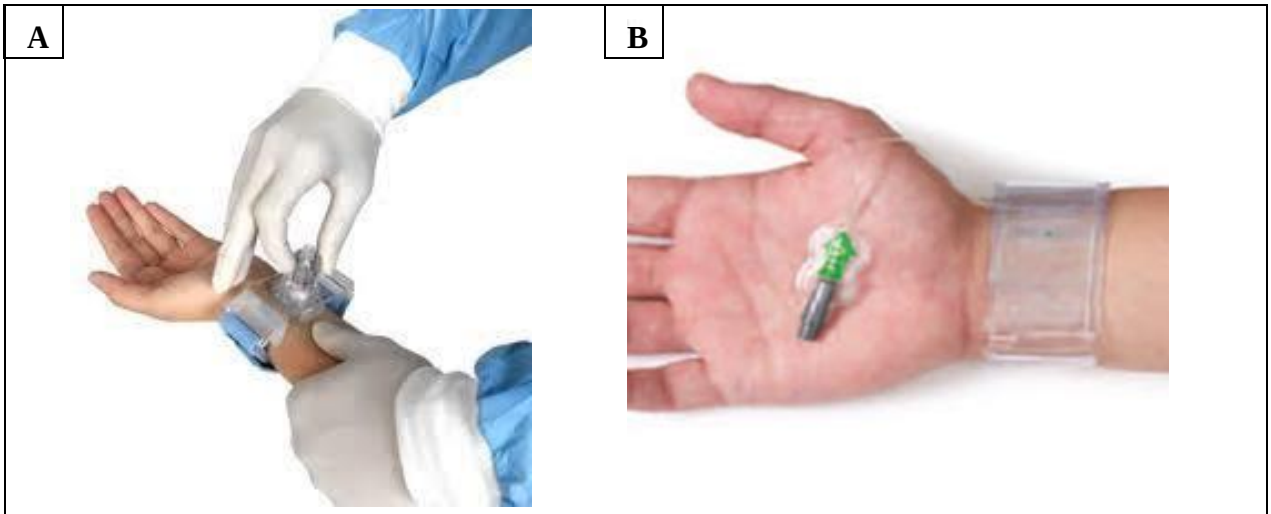


Figure 5. Radial artery compression devices. **A**. Rotator type/tourniquet wristband; **B**. Air-titrated balloon type - TR band [https://www.terumois.com/products/closure/tr-band.html]

Current evidence strongly suggests that shorter compression duration (up to 120 min) is associated with reduced RAO risk [25,125]. In fact, The CRASOC trials highlighted the effectiveness in preventing RAO with minimal pressure and short compression duration [126]. A facilitated patent hemostasis protocol with early deflation of a TR-band with minimal pressure applied 15 min after sheath removal and a mean final TR band volume of 8.1 ± 2 cc achieved PH by 95% and depicted low rates of early RAO, as compared with the standard deflation technique (2% vs. 14.5%; $P < 0.005$) [127]. However, in case of initial failure to perform 'accelerated' patent hemostasis or rebleeding occurs necessitating recompression of the access point, a longer hemostasis time will further increase the risk of RAO by prolonging the duration of blood stasis [76,126,128]. RESCUE-RAO TRIAL [129] randomized one thousand patients to short (3-hours) or prolonged (8-hours) hemostasis protocol and compared RAO incidence after elective TRA CAG or PCI at first assessed by oximetry plethysmography and then confirmed by ultrasound and reported outweighed outcomes with less RAO rates immediately after the procedure and at hospital discharge [(3.2% vs. 10.1%, $P < 0.001$) and (1.4% vs. 10.1%, $P < 0.001$), respectively] in favor of the 3-hours compression protocol. Interestingly, PRACTICAL-2 [130] randomized 450 individuals to very short radial hemostasis duration groups (10, 20, and 30 minutes with gradual release over 20 minutes) and reported low RAO incidence (7.7%) assessed by ultrasound 1-hour after device removal in patients undergoing diagnostic only CAG with small-caliber sheaths (5-Fr) and no adjunctive heparin. One randomized study [131], though, enrolled 129 patients and failed to report statistically significant

difference in early RAO rates (12- and 48-hours) either with an accelerated protocol in which weaning was initiated 20 min after sheath removal or with an adjusted strategy, in which weaning was dependent on the amount of antiplatelet or anticoagulation regimen used starting at 30, 60 or 120 minutes (5% vs. 10.1%, P= 0.337). One RCT [132] with 303 patients reported no significant impact on immediate or 30-days RAO rates assessed with Doppler vascular ultrasonography (13.2% vs. 11.9%, P=0.7) and (5.5% vs. 8.2%, P=0.4) in the two arms of a 30- and 60-min compression time protocol, respectively.

Finally, studies assessed the adjunctive use of pro-coagulant hemostatic patches based either on ferrum [133,134], chitosan [135-137] or kaolin [138] on top of the compression wristbands and reported less RAO, better patient comfort and significant shorter hemostasis time. Pathan et al. [139] used a catecholamine-chitosan pad (InnoSEAL) and compared it with a pneumatic compression device (PCD) in 606 randomized patients evaluating RAO rates in 6- to 24-hours by ultrasound. RAO incidence was similar (8.5% vs. 9.4%, $P > 0.05$) but hemostatic duration was significantly shorter (42 vs. 225 min, $P < 0.01$) for the InnoSEAL group. Another randomized study with 600 patients evaluated a chitosan-based pad vs. a PCD and reported shorter hemostasis time (127.6 ± 33.0min vs. 181.6 ± 32.2min, $P < 0.001$) and lower early (24-hours) or late (30-days) RAO rates [(5.4% vs. 11.7%, $P < 0.05$); (5% vs. 10%, $P < 0.05$), respectively] [140]. A cross-sectional randomized study of 260 patients compared compression strategy with a kaolin-filled pad (QuikClot) with the conventional hemostasis plan and failed to show significantly different RAO rates evaluated with color duplex ultrasound at 24-hours (4.6% vs. 5.4%, $P = 0.776$) or at 1-month follow-up (5.4% vs. 6.1%, $P = 0.789$), regardless of whether it was a first or a repeated TRA CAG [141].

Study limitations

This study has several limitations. First of all, it was initiated solely by one investigator for the purposes of a dissertation thesis. Secondly, only PubMed database was searched. Thirdly, studies assessing radial artery occlusion with vascular ultrasound to all subjects within 24-hours post-procedure were taken into consideration for review, excluding those that first evaluated RAO on clinical grounds and ultrasound confirmation followed.

Chapter 5 Conclusions

Best practices for RAO prevention rotate around 3 axies; pre-procedural puncture and cannulation techniques with appropriate catheter and sheath selection in respect to vessel's diameter; peri procedural spasmolytic cocktail and adequate anticoagulation regimen; and post-procedural optimal care of the access site in respect to non-occlusive compression method and duration of hemostasis.

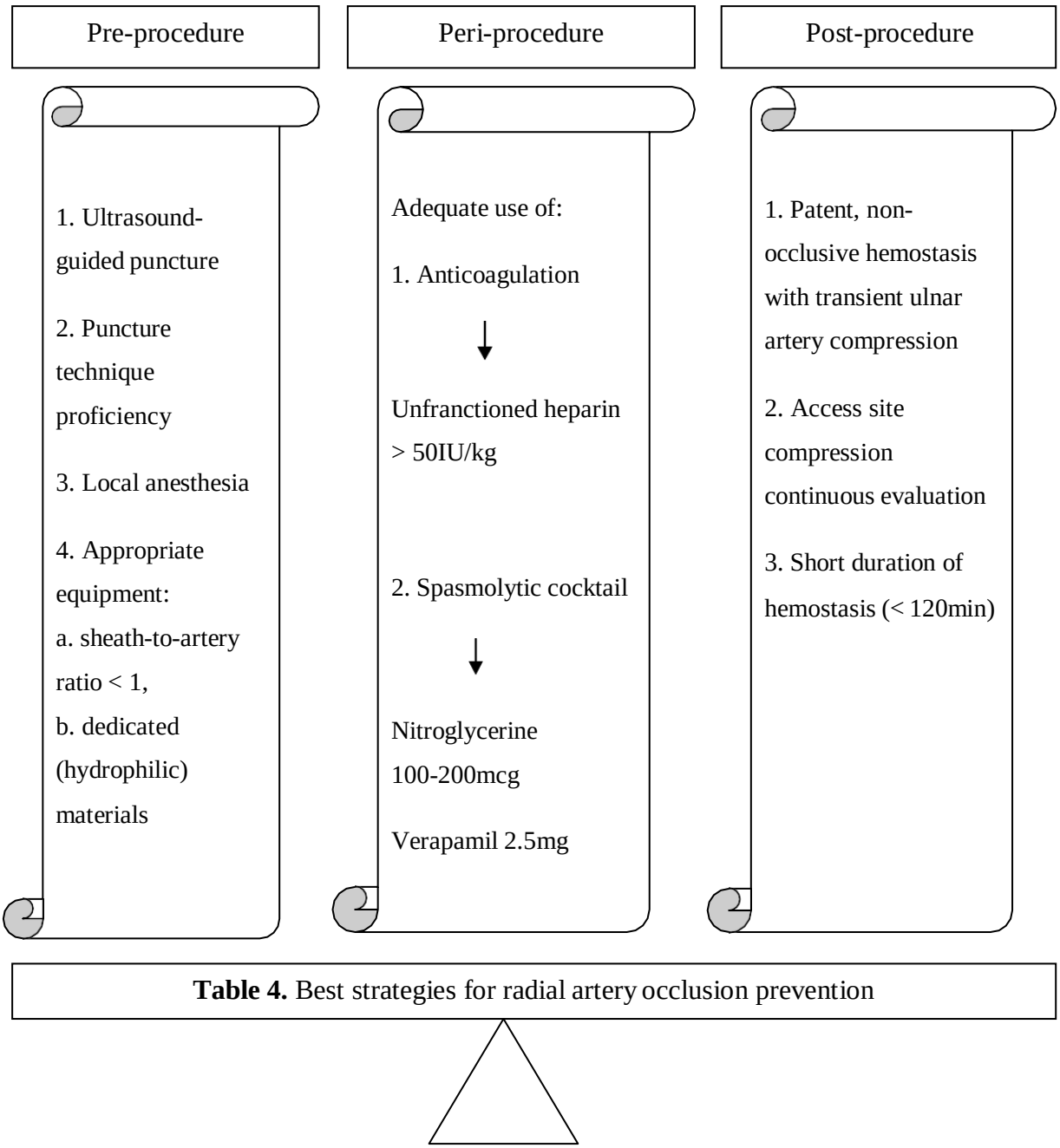


Table 4. Best strategies for radial artery occlusion prevention

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