International Journal of Cardiology xxx (xxxx) xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Short communication

*P*ostprocedural *R*adial *A*rtery *C*ompression *T*ime *I*n *C*hronic *A*nticoagu*L*ated patients using StatSeal: The PRACTICAL-SEAL study

Rodrigo Bagur [a,*], Luiz F. Ybarra [a], Zeev Israeli [b], Amir Solomonica [c], Hussein Taleb [a], Panagiotis Savvoulidis [a], Shubrandu S. Sanjoy [d], Shahar Lavi [a]

[a] *London Health Sciences Centre, London, Ontario, Canada*
[b] *Division of Cardiology, Ziv Medical Center, Safed, Israel*
[c] *Interventional Cardiology Unit, Rambam Healthcare Campus, Haifa, Israel*
[d] *Research Department, Saskatchewan Health Authority, Regina, Saskatchewan, Canada*

ARTICLE INFO

Keywords:
Radial access
Angiography
Anticoagulation
Percutaneous coronary intervention

ABSTRACT

Background: Patients on uninterrupted chronic oral anticoagulation (OAC) therapy are at high-risk of bleeding during cardiac catheterization. We aimed to investigate the safety and efficacy of the StatSeal® disc for adjunct hemostasis in patients undergoing transradial coronary angiography under uninterrupted OAC therapy.

Methods: Patients who underwent transradial cardiac catheterization without interrupted OAC therapy were included in this study.

Results: Among 180 patients, 85 (47.2%) patients were on warfarin and 95 (52.8%) patients on novel oral anticoagulants (NOACs). Patients on NOACs were older (72.9 ± 9.6 versus 69.7 ± 10.8 years, $P < 0.001$) and had more atrial fibrillation/flutter (94.7% versus 62.4%, $P < 0.001$), whereas patients on Warfarin were more often women (43.5% versus 26.3%, $P = 0.02$) and had mechanical heart valves (27.1% versus 0%, $P < 0.001$). Intravenous unfractioned heparin (UFH) was administered in 96.5% of patients on warfarin (3799 ± 1342 units) and 93.7% patients on NOACs (4028 ± 1362 units), $P = 0.27$. There were no differences in terms of type and sheath size and the need for ad hoc coronary intervention. Time-to-first release of the hemostatic wristband was 56.2 ± 12.6 min and complete hemostasis was achieved in 71.1 ± 13.0 min, with shorter times among patients on NOACs (54.1 ± 11.7 and 58.5 ± 13.2 min, 68.9 ± 11.7 versus 73.6 ± 14.0 min, $P = 0.02$, for both). There were no significant differences in terms of bleeding. There was no radial artery occlusion among 112 participants who underwent color Doppler ultrasound.

Conclusion: The present study shows that in patients undergoing transradial coronary angiogram under contemporary uninterrupted OAC therapy and periprocedural administration of UFH, the use of StatSeal® disc for adjunctive hemostasis was associated with short times to complete hemostasis.

1. Introduction

Transradial approach for coronary angiography and percutaneous coronary intervention (PCI) is considered safer than a transfemoral approach [1–3]. A specific subset of patients that is at high-risk of bleeding and needs further attention is that of patients on chronic oral anticoagulation (OAC) therapy (i.e., patients with atrial fibrillation, mechanical heart valves, status post thromboembolism, etc.). This cohort of patients is growing and will inevitably continue to do so during the next years. Moreover, during the past several years, robust evidence supporting the use of novel oral anticoagulants (NOACs) is available and the number of patients using these medications has grown accordingly [4]. Yet, data regarding their management when in need for coronary procedures are lacking.

Current recommendations support uninterrupted vitamin-K antagonists (VKA) for both elective and urgent cases [5]. This strategy has been associated with similar outcomes in terms of safety, and appears to be safer than interrupted VKAs and bridging with heparin in patients

; NOACs, Novel oral anticoagulants; RAO, Radial artery occlusion; UFH, Unfractioned heparin; OAC, Oral anticoagulants; VKA, Vitamin-K antagonists; PCI, Percutaneous coronary intervention.

* Corresponding author at: University Hospital, London Health Sciences Centre, 339 Windermere Road, N6A 5A5 London, Ontario, Canada.
E-mail address: rodrigobagur@yahoo.com (R. Bagur).

https://doi.org/10.1016/j.ijcard.2021.11.011
Received 8 September 2021; Received in revised form 20 October 2021; Accepted 7 November 2021
Available online 10 November 2021

undergoing coronary angiography with or without PCI [6,7]. Nonetheless, information regarding NOACs is very limited and somewhat contradicting, hence, recommendations suggest withholding NOACs before coronary angiogram or PCI [5,8].

Importantly, the recommendations also favour the use of radial approach in this subset of patients. However, studies have shown that prolonged radial compression times for hemostasis (i.e., >2 h) were associated to increased risk of radial artery occlusion (RAO) [9,10].

The StatSeal (Biolife, Sarasota, FL, USA) disc is a hemostasis adjunct that works in conjunction with any radial hemostatic device or manual pressure and aims to reduce bleeding, thereby shortening compression times. Therefore, we sought to investigate the safety and efficacy of the StatSeal® disc for adjunct hemostasis in patients undergoing transradial coronary angiography under uninterrupted OAC.

2. Material and methods

Patients who underwent transradial diagnostic cardiac catheterization without interrupted OAC were included in this feasibility study between October 2016 and April 2020. Intravenous unfractionated heparin (UFH) administration (50 U/Kg for diagnostic angiogram and 70–100 U/Kg for coronary intervention, imaging, or physiology assessment) was left at operator's discretion. After completion of the transradial procedure, the sheath was removed, and a StatSeal® disc was placed at the access-site along with a hemostatic wristband applied for 40–60 min as per local institutional protocol and practices (Fig. 1). Patent haemostasis, whenever possible, was recommended. To provide further insight on the study population, participants were separated into warfarin and NOACs groups (Table 1). The primary efficacy endpoint was the time-to-complete hemostasis, and the primary safety outcome was access-site related bleeding complications. Institutional review board and ethics committee approval was obtained from The Western University Health Science Research Ethics Board.

Continuous variables are expressed as a mean ± standard deviation and categorical variables as n (%). Comparison of continuous variables was performed using the two-sided Student's *t*-test, and categorical variables were compared using the Chi-square test. Statistical tests were two-tailed, and differences were considered statistically significant when a *P*-value was <0.05. Statistical analyses were performed using R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

Among 180 patients, 85 (47.2%) patients were on warfarin and 95 (52.8%) patients on NOACs. Patients on NOACs were older (72.9 ± 9.6 versus 69.7 ± 10.8 years, $P < 0.001$) and had more atrial fibrillation/flutter (94.7% versus 62.4%, $P < 0.001$), whereas patients on Warfarin were more often women (43.5% versus 26.3%, $P = 0.02$) and had mechanical heart valves (27.1% versus 0%, $P < 0.001$). Patients on NOACs had more frequently CHA_2DS_2-VASc score ≥ 2 ($P = 0.01$), and there were differences between groups with regards to the indication for coronary angiogram ($P = 0.03$) (Table 1).Intravenous UFH was administered in 96.5% of patients on warfarin (3799 ± 1342 units) and 93.7% patients on NOACs (4028 ± 1362 units), $P = 0.27$. There were no differences in terms of type and sheath size and the need for ad hoc coronary intervention. Time-to-first release of the hemostatic wristband was 56.2 ± 12.6 min and complete hemostasis was achieved in 71.1 ± 13.0 min, with shorter times among patients on NOACs (54.1 ± 11.7 and 58.5 ± 13.2 min, 68.9 ± 11.7 versus 73.6 ± 14.0 min, $P = 0.02$, for both). There were no significant differences in terms of bleeding (Table 1). There was no RAO among 112 patients assessed by color Doppler ultrasound. All outpatients were discharged home the same day.

Three patients in the warfarin group developed a small pseudoaneurysm, which resolved after 60 min of ultrasound-guided focalized compression with a RadAR (Advanced Vascular Dynamics, WI, USA) wristband. The patients were brought back the day after for follow-up, the pseudoaneurysms sealed and the radial artery was patent in the 3 cases.

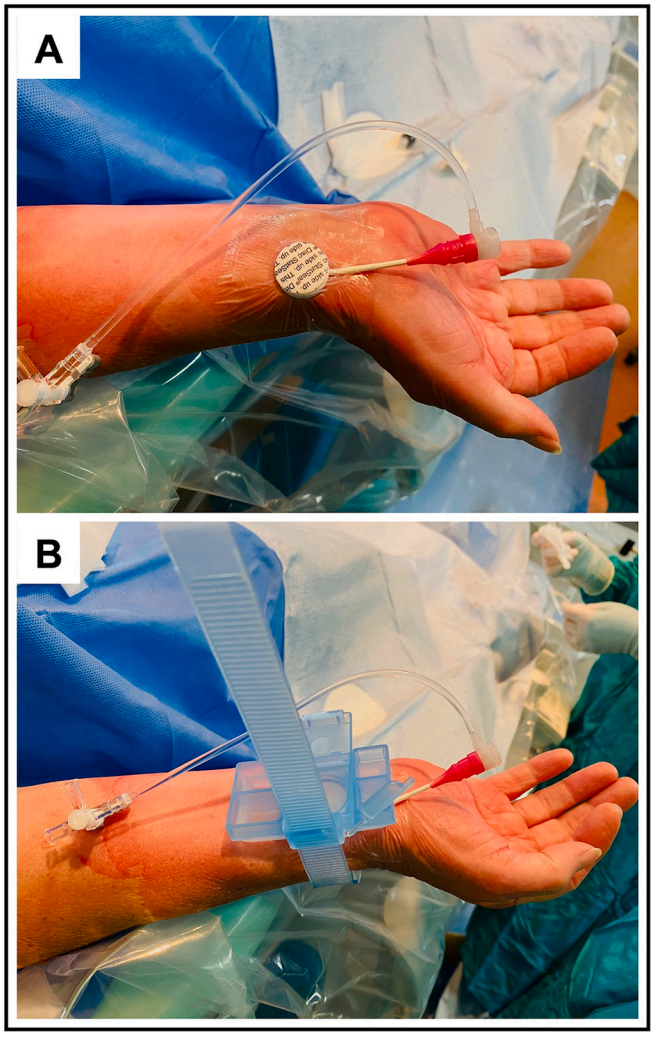

Fig. 1. StatSeal disc application. (A) The introducer sheath is pulled out halfway, then, a StatSeal disc is applied right at the access site. A small transparent film dressing is applied on top of it to secure it in position. **(B)** The hemostatic wristband is applied, and the sheath is completely removed.

4. Discussion

The radial StatSeal® disc has been assessed in trials post coronary angiography [11,12]. Seto et al. [11] showed that the use of StatSeal® disc was associated with a significantly lower mean time-to-full TR Band (Terumo Corp., Tokyo, Japan) deflation as compared to the control group (43 ± 14 versus 160 ± 43 min, $P < 0.001$). Ayyaz Ul Haq et al. [12] followed the same line showing a significantly lower compression-time using the Helix compression device (Vascular Perspectives Ltd. Holmfirth, England) plus StatSeal® disc compared to standard compression (79.7 ± 41.2 versus 165.8 ± 63.1 min, $P < 0.001$). Another adjunct for accelerating radial hemostasis is the QuikClot Radial pad (QuikClot Radial; Z-Medica), that was used in a 30-patient study where the authors allocated 10 patients to 3 groups and showed significant reduction in compression times (30.7 ± 2.2 versus 60.9 ± 2.9 and 149.4 ± 36.5 min, $P < 0.001$) for the 30-min, 60-min and TR Band alone, respectively [13].

Individuals that are nowadays on VKAs may be limited to those with mechanical heart valves or other specific conditions. Whenever VKAs

Table 1
Baseline characteristics of the study population.

Variables	All $n = 180$	Warfarin $n = 85$	NOACs $n = 95$	P-value
Age (years)	71.4 ± 10.3	69.7 ± 10.8	72.9 ± 9.6	**<0.001**
Female	62 (34.4)	37 (43.5)	25 (26.3)	**0.02**
Weight (kg)	86.6 ± 20.8	85.4 ± 22.7	87.7 ± 19.0	0.45
Height (cm)	171.2 ± 10.5	170.4 ± 10.7	171.8 ± 10.3	0.38
Body mass index (kg/m^2)	29.5 ± 6.2	29.3 ± 6.8	29.7 ± 5.7	0.69
Hypertension	145 (80.6)	66 (77.6)	79 (83.2)	0.46
Diabetes	42 (23.3)	18 (21.2)	24 (25.3)	0.64
Dyslipidemia	130 (72.2)	57 (67.1)	73 (76.8)	0.19
Smoking status (current or former)	94 (52.2)	48 (56.5)	46 (48.4)	0.35
Previous myocardial infarction	23 (12.8)	11 (12.9)	12 (12.6)	1.00
Previous PCI	16 (8.9)	8 (9.4)	8 (8.4)	1.00
Previous CABG	12 (6.7)	9 (10.6)	3 (3.2)	0.09
Previous mechanical heart valve	23 (12.8)	23 (27.1)	0 (0)	**<0.001**
Atrial fibrillation/flutter	143 (79.4)	53 (62.4)	90 (94.7)	**<0.001**
Cerebrovascular disease (stroke/TIA)	32 (17.8)	13 (15.3)	19 (20.0)	0.53
Chronic kidney disease*	57 (31.7)	31 (36.5)	26 (27.4)	0.25
Left ventricular ejection fraction (%)	48.3 ± 15.4	48.8 ± 13.9	47.8 ± 16.7	0.67
Hemoglobin (g/dL)	13.2 ± 2.1	13.0 ± 2.2	13.3 ± 2.0	0.44
Platelets (x1000/uL)	217.1 ± 74.3	209.5 ± 74.9	223.8 ± 73.6	0.20
Creatinine (mg/dL)	1.2 ± 0.6	1.3 ± 0.8	1.2 ± 0.5	0.24
Concomitant aspirin	71 (39.4)	38 (44.7)	33 (34.7)	0.23
$CHADS_2$ score	2.2 ± 1.3	2.0 ± 1.3	2.3 ± 1.3	0.09
$CHADS_2$ score (category)				
0 (Low)	10 (5.6)	8 (9.4)	2 (2.1)	
1 (Intermediate)	53 (29.4)	27 (31.8)	26 (27.4)	0.07
≥2 (High)	117 (65.0)	50 (58.8)	67 (70.5)	
CHA_2DS_2-VASc score	3.5 ± 1.7	3.4 ± 1.9	3.7 ± 1.6	0.17
CHA_2DS_2-VASc score (category)				
0 (Low)	5 (2.8)	5 (5.9)	0 (0)	
1 (Intermediate)	16 (8.9)	10 (11.8)	6 (6.3)	**0.01**
≥2 (High)	159 (88.3)	70 (82.8)	89 (93.7)	
Peri-procedural data				
Elective or outpatient setting	170 (94.4)	80 (94.1)	90 (94.7)	0.86
International normalized ratio	2.4 ± 0.9	2.8 ± 0.7	1.5 ± 0.6	**<0.001**
International normalized ratio < 3	92 (74.2)	55 (64.7)	37 (94.9)	
International normalized ratio 3–4	26 (21.0)	25 (29.4)	1 (2.6)	**0.001**
International normalized ratio > 4	6 (4.8)	5 (5.9)	1 (2.6)	
Indication for coronary angiogram				
Stable angina	16 (8.9)	8 (9.4)	8 (8.4)	
Acute coronary syndrome	10 (5.6)	6 (7.1)	4 (4.2)	
Cardiomyopathy	33 (18.3)	10 (11.8)	23 (24.2)	
Preoperative liver transplant	4 (2.2)	4 (4.7)	0 (0)	**0.03**
Preoperative SAVR	38 (21.1)	19 (22.4)	19 (20.0)	
Preoperative MVR/repair	33 (18.3)	16 (18.8)	17 (17.9)	
Preoperative TAVI	21 (11.7)	6 (7.1)	15 (15.8)	
	3 (1.7)	2 (2.4)	1 (1.1)	
Preoperative tricuspid valve surgery				
Preoperative aortic root replacement	9 (5.0)	6 (7.1)	3 (3.2)	
Congestive heart failure	8 (4.4)	3 (3.5)	5 (5.3)	
Ventricular tachycardia/cardiac arrest	5 (2.8)	5 (5.9)	0 (0)	
Type and size of sheath[#]				
5-French Slender Glidesheath	48 (26.7)	20 (23.5)	28 (29.5)	
5-French	103 (57.2)	48 (56.5)	55 (57.9)	0.48
6-French Slender Glidesheath	15 (8.3)	8 (9.4)	7 (7.4)	
6-French	14 (7.8)	9 (10.6)	5 (5.3)	
Intravenous heparin	171 (95.0)	82 (96.5)	89 (93.7)	0.50
Units/Kg (range)	40–50	40–50	40–50	–
Units/Kg (minimum-maximum)	20–130	20–130	25–100	–
Total Units, mean	3918 ± 1353	3799 ± 1342	4028 ± 1362	0.27
Total Units, median (IQR)	4000 (3000–4500)	4000 (3000–4500)	4000 (3000–4500)	0.43
Procedural time (minutes), median (IQR)	15.0 (9.0–25.0)	16.0 (10.0–30.0)	14.0 (8.0–20.5)	0.08
Ad hoc coronary intervention (PCI/FFR)	18 (10.0)	10 (11.8)	8 (8.4)	0.62
Time to first release hemostatic wrist band (min)	56.2 ± 12.6	58.5 ± 13.2	54.1 ± 11.7	**0.02**
Total compression time (complete hemostasis, min)	71.1 ± 13.0	73.6 ± 14.0	68.9 ± 11.7	**0.02**
Need for hemostatic wristband retightening	6 (3.3)	4 (4.7)	2 (2.1)	0.42
Type of wrist band				
Bengal[†]	164 (91.1)	77 (90.6)	87 (91.6)	
RadAR[‡]	14 (7.8)	7 (8.2)	7 (7.4)	1.00
TRAcelet[¥]	2 (1.1)	1 (1.2)	1 (1.1)	
Hematoma (EASY scale)				
Grade 1	5 (2.8)	3 (3.5)	2 (2.1)	0.35
Grade 2	2 (1.1)	2 (2.4)	0 (0)	
Pseudo aneurysm	3 (1.7)	3 (3.5)	0 (0)	0.53

Values are expressed as n (%), mean ± SD, median (interquartile range, IQR) unless otherwise noted. Some percentages may not add up to 100 because of rounding. *Estimated glomerular filtration rate < 60 mL/min/1.72m^2. [#]Terumo Corp., Tokyo, Japan. NOACs: novel oral anticoagulants. PCI: percutaneous coronary intervention. CABG: coronary artery bypass graft. TIA: transient ischemic attack. CHADS: Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes, prior Stroke or TIA. CHA_2DS-VASc: Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes, prior Stroke or TIA, Vascular disease, Age 65–74 years, Sex category. SAVR: surgical aortic valve replacement. TAVI: transcatheter aortic valve implantation. MVR: mitral valve replacement. FFR: fractional flow reserve. †Benrikal Services Inc., QC, Canada. [‡]Advanced Vascular Dynamics, WI, USA. [¥]Medtronic, Inc. EASY: Early Discharge After Transradial Stenting of Coronary Arteries.

are interrupted, bridging with low molecular wight heparin (i.e., outpatient setting) or UFH (i.e., inpatient setting) is required to prevent thromboembolic events or mechanical heart valve thrombosis. However, the strategy of bridging with heparin has been associated with increased risk of bleeding complications [6,7] and, also, its inherent prolonged length of hospital stays. Nonetheless, in patients with atrial fibrillation and low CHA_2DS_2-VASc score that are under NOACs, these can be stopped for 24 h prior to the angiogram, then be resumed either at

night-time or the day after.

Notably, in studies that showed the safety of coronary procedures on patients under uninterrupted VKAs or NOACs, the reported compression times for hemostasis ranged from 2 to 4 h [14–16]. Our study extends previous knowledge on the usefulness of StatSeal® disc for adjunctive hemostasis, now among individuals on chronic uninterrupted OAC and periprocedural administration of UFH, also achieving short times to complete hemostasis.

5. Limitations

The present study presents with limitations. First, there is no comparator group (no-heparin or lower dose i.e., 25–30 U/Kg, and no-StatSeal), however, due to an expected slow-rate of enrolment (3 1/2 years) considering the very selected population, we pre-specified a feasibility-study design to assess the performance of the StatSeal® disc in this subset of patients. Second, we are in a high-volume university hospital where each operator performs >500 radial procedures yearly, thus, these results may help to expand the use of radial approach on patients under uninterrupted OAC without the necessity to discontinue VKAs and bridging with heparin, further preventing a hospital admission to do so, or simply delaying coronary angiography among those admitted on NOACs.

6. Conclusion

In patients undergoing transradial coronary angiogram and intervention under contemporary uninterrupted OAC therapy and periprocedural administration of UFH, the use of StatSeal® disc for adjunctive hemostasis was associated with short times to complete hemostasis.

Author contributions

Each author has contributed to the present work as follows:

Rodrigo Bagur: 1) Conception and design of the study. 2) Acquisition, analysis and interpretation of data; 3) drafting of the manuscript; and 4) final approval of the manuscript submitted.

Luiz F. Ybarra, Zeev Israeli, Amir Solomonica, Hussein Taleb, Panagiotis Savvoulidis, Shubrandu S. Sanjoy, and Shahar Lavi: 1) Acquisition, analysis and interpretation of data; 2) revising critically the manuscript for important intellectual content; and 3) final approval of the manuscript submitted.

Declaration of Competing Interest

The authors have no conflicts of interest inherent to the content of this manuscript.

Acknowledgement

No source of funding.

References

[1] O.F. Bertrand, R. Bagur, O. Costerousse, J. Rodes-Cabau, Transradial vs femoral percutaneous coronary intervention for left main disease in octogenarians, Indian Heart J. 62 (2010) 234–237.

[2] R. Bagur, O.F. Bertrand, J. Rodes-Cabau, et al., Comparison of outcomes in patients > or =70 years versus <70 years after transradial coronary stenting with maximal antiplatelet therapy for acute coronary syndrome, Am. J. Cardiol. 104 (2009) 624–629.

[3] A. Sirker, C.S. Kwok, R. Kotronias, et al., Influence of access site choice for cardiac catheterization on risk of adverse neurological events: a systematic review and meta-analysis, Am. Heart J. 181 (2016) 107–119.

[4] M.V. Huisman, K.J. Rothman, M. Paquette, et al., The changing landscape for stroke prevention in AF: findings from the GLORIA-AF registry phase 2, J. Am. Coll. Cardiol. 69 (2017) 777–785.

[5] Lip GYH, J.P. Collet, M. Haude, et al., Joint European consensus document on the management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous cardiovascular interventions: a joint consensus document of the European Heart Rhythm Association (EHRA), European Society of Cardiology Working Group on Thrombosis, European Association of Percutaneous Cardiovascular Interventions (EAPCI), and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), Latin America Heart Rhythm Society (LAHRS), and Cardiac Arrhythmia Society of Southern Africa (CASSA), Europace 21 (2018) 192–193, 2019.

[6] M. Kowalewski, P. Suwalski, G.M. Raffa, et al., Meta-analysis of uninterrupted as compared to interrupted oral anticoagulation with or without bridging in patients undergoing coronary angiography with or without percutaneous coronary intervention, Int. J. Cardiol. 223 (2016) 186–194.

[7] D. Siegal, J. Yudin, S. Kaatz, J.D. Douketis, W. Lim, A.C. Spyropoulos, Periprocedural heparin bridging in patients receiving vitamin K antagonists: systematic review and meta-analysis of bleeding and thromboembolic rates, Circulation. 126 (2012) 1630–1639.

[8] A.N. Raval, J.E. Cigarroa, M.K. Chung, et al., Management of patients on non-vitamin K antagonist oral anticoagulants in the acute care and periprocedural setting: a scientific statement from the American Heart Association, Circulation. 135 (2017) e604-e33.

[9] S. Lavi, A. Cheema, A. Yadegari, et al., Randomized trial of compression duration after transradial cardiac catheterization and intervention, J. Am. Heart Assoc. 6 (2017), https://doi.org/10.1161/JAHA.116.005029.

[10] S. Lavi, S.R. Mehta, R. Bajwa, et al., Short Durations of radial hemostatic device after diagnostic transradial cardiac catheterization: the PRACTICAL-2 randomized trial, Can. J. Cardiol. 37 (2021) 276–283.

[11] A.H. Seto, W. Rollefson, M.P. Patel, et al., Radial haemostasis is facilitated with a potassium ferrate haemostatic patch: the Statseal with TR Band assessment trial (STAT), EuroIntervention. 14 (2018) e1236-e42.

[12] M. Ayyaz Ul Haq, S.A. Nazir, M. Rashid, et al., Accelerated patent hemostasis using a procoagulant disk; a protocol designed to minimize the risk of radial artery occlusion following cardiac catheterization, Cardiovasc Revasc Med 20 (2019) 137–142.

[13] J.S. Roberts, J. Niu, J.A. Pastor-Cervantes, Comparison of hemostasis times with a kaolin-based hemostatic pad (QuikClot Radial) vs mechanical compression (TR band) following transradial access: a pilot prospective study, J. Invasive Cardiol. 29 (2017) 328–334.

[14] C.M. Lippe, E.A. Reineck, A.R. Kunselman, I.C. Gilchrist, Warfarin: impact on hemostasis after radial catheterization, Catheter. Cardiovasc. Interv. 85 (2015) 82–88.

[15] J.G. Cordoba-Soriano, J.F. Oteo, A. Gutierrez-Diez, et al., Percutaneous coronary intervention without interruption of oral anticoagulation, Circ. Cardiovasc Interv. 14 (2021), e009949.

[16] N. Chongprasertpon, A. Zebrauskaite, J.J. Coughlan, et al., Performing diagnostic radial access coronary angiography on uninterrupted direct oral anticoagulant therapy: a prospective analysis, Open Heart. 6 (2019), e001026.