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Routine ultrasound guidance for femoral vascular access for cardiac procedures: A randomized trial (UNIVERSAL)

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On Behalf of UNIVERSAL investigators

Disclosure Statement of Financial Interest

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Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
Grant/Research Support	Boston Scientific
Consulting Fees/Honoraria	Medtronic, Penumbra
Major Stock Shareholder/Equity	None
Royalty Income	None
Ownership/Founder	None
Intellectual Property Rights	None
Other Financial Benefit	None

Faculty disclosure information can be found on the app

We need to avoid Femoral Access Bleeding

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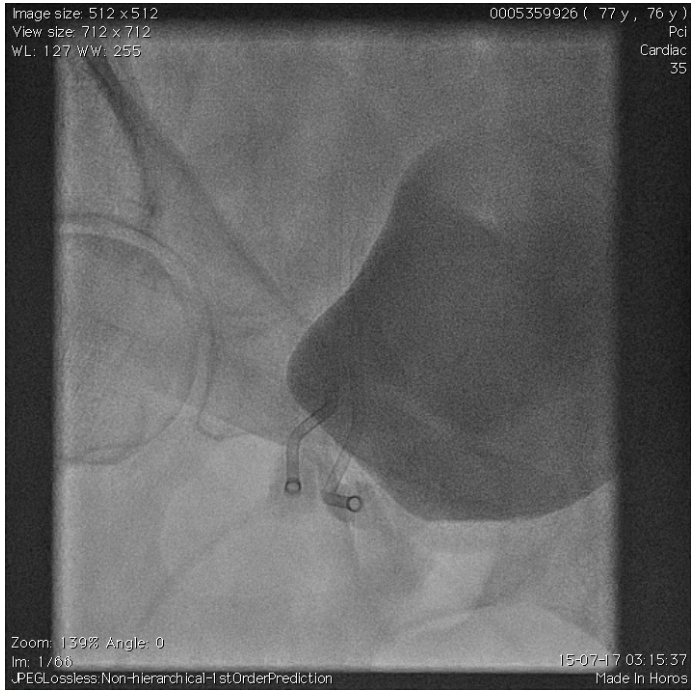

Background and Rationale

- Transradial first reduces access site bleeding by more than 60%
- Still need femoral access for large bore, occluded radial

- Randomized trials of US guidance have shown mixed results
- US used in about a third of cases for femoral access in surveys

Gargiulo et al. Circ. 2022: online.
Seto et al. JACC Int, 2010;3(7):751-8.
Nguyen et al. Eurointervention. 2019:15(6):e22-30

Design of UNIVERSAL Trial

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14% Control event rate, 80% power for a 50% RRR

Patients with planned femoral access for coronary procedures, N=621

Randomized 1:1

US guided Access

No US guided Access

Fluoroscopy landmarking for both groups

Primary Outcome: BARC 2, 3 or 5 Bleeding and Major Vascular Complications within 30 days (blinded outcome assessment)

Eligibility Criteria

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Inclusion

- Patients were eligible if referred for coronary angiography or percutaneous coronary intervention (PCI) with planned femoral access

Exclusion

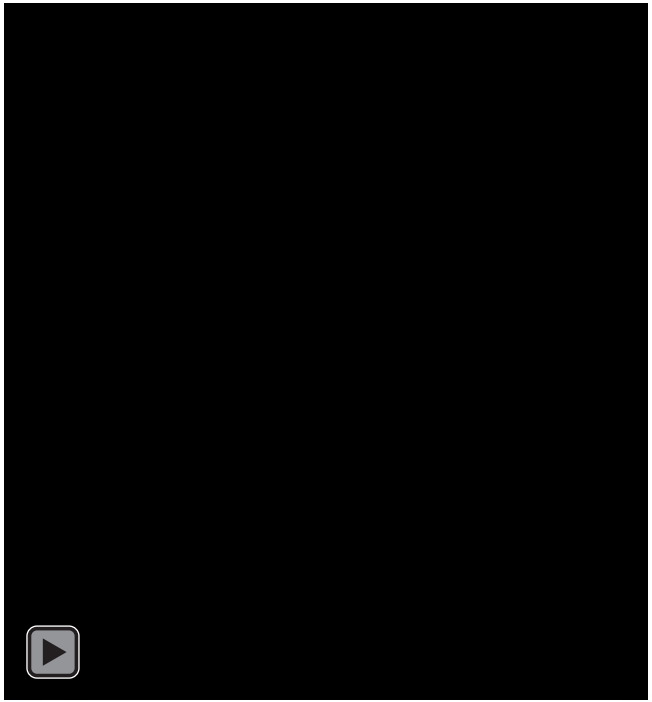
- < 18 years
- Acute ST-elevation myocardial infarction
- Absence of a palpable femoral pulse

Requirement for Operators

- Needed to demonstrate following prior to enrolling:
  - Identifying femoral bifurcation and femoral head
  - Real time tracking of needle including indentation of anterior wall
  - Confirming wire position in orthogonal views prior to sheath insertion

- Each operator was approved after performing 10 cases demonstrating these skills

Ultrasound for femoral Access can potential reduce complications



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Baseline Characteristics

	US n = 311	No US n = 310
Age	70.5	70.7
Female Sex (%)	25.7	25.2
Diabetes (%)	42.8	41.3
Previous PCI (%)	45.0	44.5
Previous CABG (%)	57.2	56.5
Peripheral Artery Disease (%)	18.3	17.1

Procedural Characteristics

	US n = 311	No US n = 310
PCI performed (%)	43.1	41.3
CTO PCI (%)	13.5	14.8
≥7 French used (%)	20.0	18.0
Closure Device (%)	53.8	50.5
Angioseal (%)	44.1	45.1
Perclose (%)	9.1	5.4

Procedural Outcomes

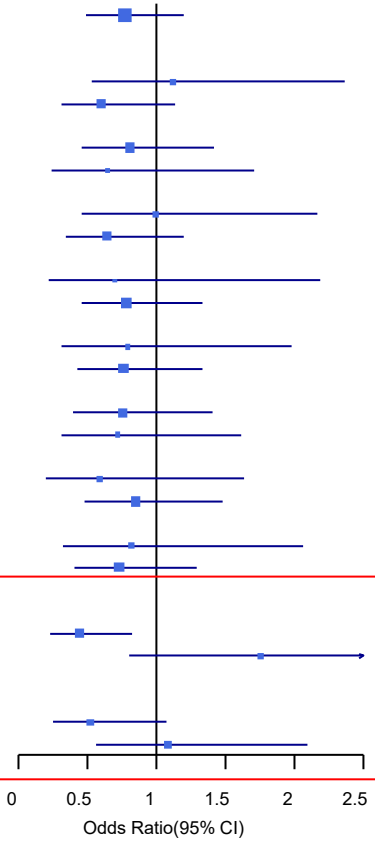
	US* n = 320	No US* n = 317	*P* Value
First Attempt Access	86.6%	70.0%	<0.001
Number of Attempts	1.16	1.43	<0.001
Accidental Venipuncture	3.1%	11.7%	<0.001
Time local to sheath insertion (mean)	114s	129s	0.34

*By Access

Clinical Outcomes

	US N=311	No US n = 310	*P* Value
BARC 2, 3 or 5 bleeding or major vascular complications*	12.9%	16.1%	0.25
BARC 2, 3 or 5 bleeding	10.0%	10.7%	0.78
Major Vascular Complications	6.4%	9.4%	0.18
BARC 2 Bleeding	9.7%	10.3%	0.78

	US and Fluoroscopy events/Total (%)	Fluoroscopy events/Total (%)	Odds Ratio (95% CI)	P value for Interaction
OVERALL	40 /311 (12.9)	50 /310 (16.1)	0.77 (0.49 - 1.20)	
Subgroups				
Age				
>=75	19 / 108 (17.6)	20 / 125 (16.0)	1.12 (0.53-2.37)	0.18
<75	21 / 203 (10.3)	30 / 185 (16.2)	0.60 (0.31-1.13)	
Sex				
Male	30 / 231 (13.0)	36 / 232 (15.5)	0.81 (0.46-1.42)	0.67
Female	10 / 80 (12.5)	14 / 78 (18.0)	0.65 (0.24-1.71)	
BMI				
>=30	19 / 133 (14.3)	17 / 119 (14.3)	1.00 (0.46-2.17)	0.34
<30	21 / 178 (11.8)	33 / 191 (17.3)	0.64 (0.34-1.20)	
Peripheral Vascular Disease				
Yes	8 / 57 (14.0)	10 / 53 (18.9)	0.70 (0.22-2.19)	0.85
No	32 / 254 (12.6)	40 / 257 (15.6)	0.78 (0.46-1.33)	
Clinical Presentation				
NSTE-ACS	12 / 91 (13.2)	14 / 87 (16.1)	0.79 (0.31-1.98)	0.93
Elective	28 / 220 (12.7)	36 / 223 (16.1)	0.76 (0.43-1.33)	
Use of femoral access				
PCI	27 / 134 (20.2)	32 / 128 (25.0)	0.76 (0.40-1.41)	0.92
Angiography alone	13 / 177 (7.3)	18 / 182 (9.9)	0.72 (0.31-1.62)	
Type of Procedure				
CTO	10 / 42 (23.8)	16 / 46 (34.8)	0.59 (0.20-1.64)	0.5
Non-CTO	30 / 269 (11.2)	34 / 264 (12.9)	0.85 (0.48-1.48)	
Sheath Size				
>=7	14 / 61 (23.0)	15 / 56 (26.8)	0.82 (0.32-2.06)	0.82
<7	26 / 250 (10.4)	35 / 254 (13.8)	0.73 (0.41-1.29)	
Post randomization variable - Actual Closure device use				
Yes	20 / 170 (11.8)	37 / 158 (23.4)	0.44 (0.23-0.82)	0.004
No	20 / 141 (14.2)	13 / 152 (8.6)	1.76 (0.80-4.03)	
Post hoc subgroup - Staff position and fellow				
Staff	16 / 157 (10.2)	26 / 146 (17.8)	0.52 (0.25-1.07)	0.12
Fellow	24 / 154 (15.6)	24 / 164 (14.6)	1.08 (0.56-2.09)	



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Subgroup finding with Closure devices

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Biologically plausible

- US allows for a single puncture
- US helps choose a site without disease and Ca

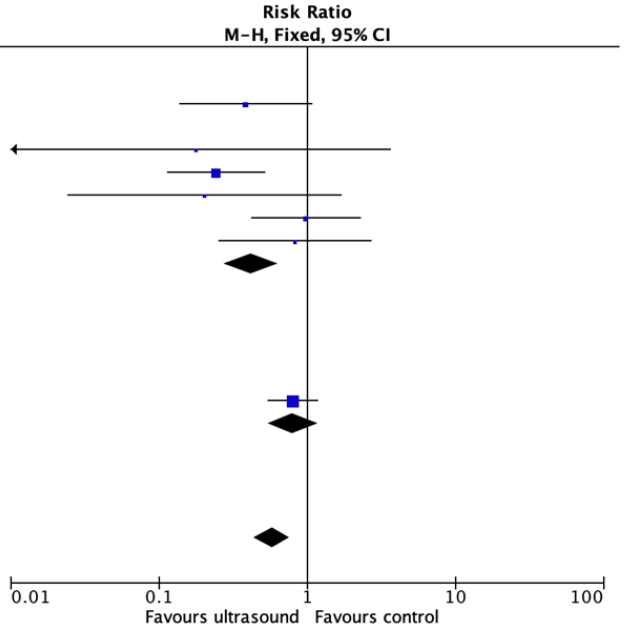
- Caution: Post randomization subgroup

Limitations

- Not powered for modest 20-25% risk reductions
- Likely trainees still on learning curve
- Outcome driven by BARC 2 bleed (less important)

Meta-Analysis for Composite of Major Bleed or Major vascular complications

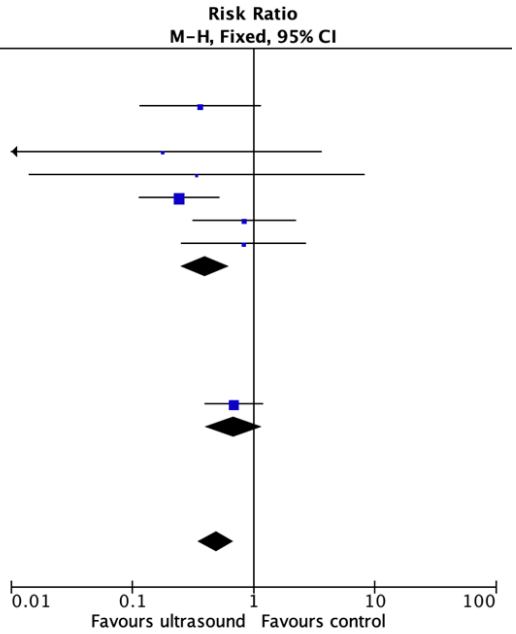
Study or Subgroup	Ultrasound Events	Ultrasound Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
1.1.1 RCTs before UNIVERSAL							
Dudeck 2004	0	56	0	56		Not estimable	2004
Seto 2010	5	503	13	501	10.7%	0.38 [0.14, 1.07]	2010
Gedikoglu 2013	0	108	0	100		Not estimable	2013
Slattery 2015	0	53	2	47	2.2%	0.18 [0.01, 3.61]	2015
Katircibasi 2018	8	449	36	490	28.3%	0.24 [0.11, 0.52]	2018
Marquis-Gravel 2018	1	64	5	65	4.1%	0.20 [0.02, 1.69]	2018
Nguyen 2019	10	319	11	343	8.7%	0.98 [0.42, 2.27]	2019
Stone 2020	5	319	6	316	5.0%	0.83 [0.25, 2.68]	2020
Subtotal (95% CI)		**1871**		**1918**	**58.9%**	**0.42 [0.28, 0.64]**	
Total events	29		73				
Heterogeneity: $Chi^2 = 7.95$, df = 5 (P = 0.16); $I^2 = 37\%$							
Test for overall effect: Z = 4.02 (P < 0.0001)							
1.1.2 UNIVERSAL							
Jolly 2022	40	311	50	310	41.1%	0.80 [0.54, 1.17]	2022
Subtotal (95% CI)		**311**		**310**	**41.1%**	**0.80 [0.54, 1.17]**	
Total events	40		50				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.15 (P = 0.25)							
Total (95% CI)		**2182**		**2228**	**100.0%**	**0.58 [0.43, 0.76]**	
Total events	69		123				
Heterogeneity: $Chi^2 = 11.78$, df = 6 (P = 0.07); $I^2 = 49\%$							
Test for overall effect: Z = 3.83 (P = 0.0001)							
Test for subgroup differences: $Chi^2 = 4.81$, df = 1 (P = 0.03), $I^2 = 79.2\%$							



RR 0.58 ; 95% CI 0.43-0.76

Meta-Analysis for Major vascular complications

Study or Subgroup	Ultrasound Events	Ultrasound Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
2.1.1 RCTs before UNIVERSAL							
Dudeck 2004	0	56	0	56		Not estimable	2004
Seto 2010	4	503	11	501	11.8%	0.36 [0.12, 1.13]	2010
Gedikoglu 2013	0	108	0	100		Not estimable	2013
Slattery 2015	0	53	2	47	2.8%	0.18 [0.01, 3.61]	2015
Marquis-Gravel 2018	0	64	1	65	1.6%	0.34 [0.01, 8.16]	2018
Katircibasi 2018	8	449	36	490	36.9%	0.24 [0.11, 0.52]	2018
Nguyen 2019	7	319	9	343	9.3%	0.84 [0.32, 2.22]	2019
Stone 2020	5	319	6	316	6.5%	0.83 [0.25, 2.68]	2020
Subtotal (95% CI)		**1871**		**1918**	**68.9%**	**0.40 [0.25, 0.63]**	
Total events	24		65				
Heterogeneity: $Chi^2 = 5.67$, df = 5 (P = 0.34); $I^2 = 12\%$							
Test for overall effect: Z = 3.97 (P < 0.0001)							
2.1.2 UNIVERSAL							
Jolly 2022	20	311	29	310	31.1%	0.69 [0.40, 1.19]	2022
Subtotal (95% CI)		**311**		**310**	**31.1%**	**0.69 [0.40, 1.19]**	
Total events	20		29				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.34 (P = 0.18)							
Total (95% CI)		**2182**		**2228**	**100.0%**	**0.49 [0.34, 0.69]**	
Total events	44		94				
Heterogeneity: $Chi^2 = 7.48$, df = 6 (P = 0.28); $I^2 = 20\%$							
Test for overall effect: Z = 4.04 (P < 0.0001)							
Test for subgroup differences: $Chi^2 = 2.27$, df = 1 (P = 0.13), $I^2 = 56.0\%$							



RR 0.49 ; 95% CI 0.34-0.69

Conclusions

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- US improved first attempt success but did not reduce bleeding or vascular complications in UNIVERSAL
- US beneficial when closure device used

- Updated meta-analyses support the benefit of US guided femoral access

Perspective

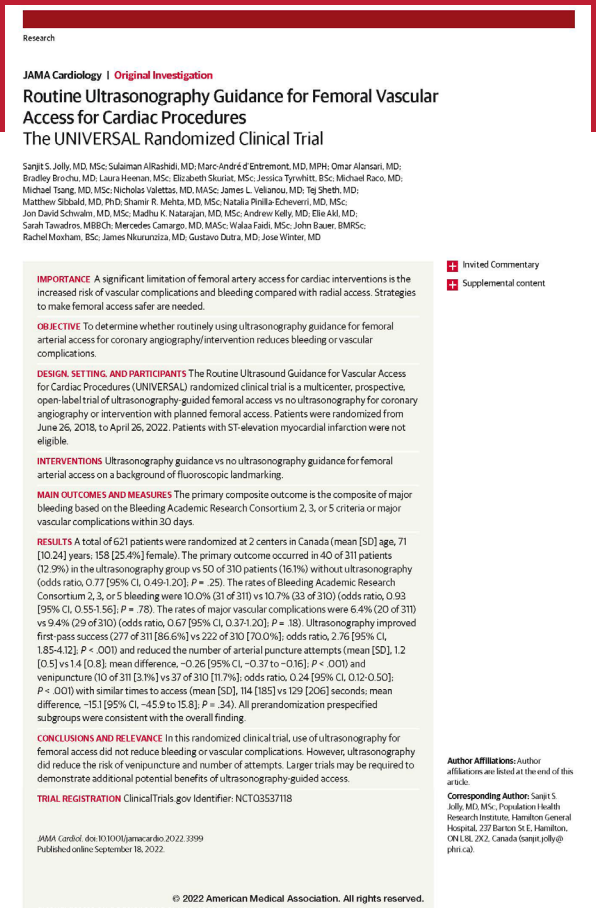
- US has no risks
- Widely available
- We need to focus on training and expertise

- Transradial access is still safest approach

Acknowledgements

Study Team	Statistical Support	ICT Support
J Tyrwhitt MA d'Entremont E Skuriat C Agrippa	K Balasubramanian L Heenan A Wang	H Wilton J Orellana A Pineau

Site Staff	
Investigators	E Akl, O Alansari, S Alradshidi, B Brochu, G Dutra, A Kelly, S Mehta, M Natarajan, N Pinilla-Echeverri, M Raco, JD Schwalm, T Sheth, M Sibbald, M Tsang, N Valettas, J Velianou, J Winter
Coordinators	S Tawadros, M Camargo, W Faidi, J Ferguson, B Sirotnik
Angiographic Core laboratory	J Bauer, R Moxham



Research

JAMA Cardiology | Original Investigation

Routine Ultrasonography Guidance for Femoral Vascular Access for Cardiac Procedures
The UNIVERSAL Randomized Clinical Trial

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Invited Commentary
Supplemental content

IMPORTANCE A significant limitation of femoral artery access for cardiac interventions is the increased risk of vascular complications and bleeding compared with radial access. Strategies to make femoral access safer are needed.

OBJECTIVE To determine whether routinely using ultrasonography guidance for femoral arterial access for coronary angiography/intervention reduces bleeding or vascular complications.

DESIGN, SETTING, AND PARTICIPANTS The Routine Ultrasound Guidance for Vascular Access for Cardiac Procedures (UNIVERSAL) randomized clinical trial is a multicenter, prospective, open-label trial of ultrasonography-guided femoral access vs no ultrasonography for coronary angiography or intervention with planned femoral access. Patients were randomized from June 26, 2018, to April 26, 2022. Patients with ST-elevation myocardial infarction were not eligible.

INTERVENTIONS Ultrasonography guidance vs no ultrasonography guidance for femoral arterial access on a background of fluoroscopic landmarking.

MAIN OUTCOMES AND MEASURES The primary composite outcome is the composite of major bleeding based on the Bleeding Academic Research Consortium 2, 3, or 5 criteria or major vascular complications within 30 days.

RESULTS A total of 621 patients were randomized at 2 centers in Canada (mean [SD] age, 71 [10.24] years; 158 [25.4%] female). The primary outcome occurred in 40 of 311 patients (12.9%) in the ultrasonography group vs 50 of 310 patients (16.1%) without ultrasonography (odds ratio, 0.77 [95% CI, 0.49-1.20]; $P = .25$). The rates of Bleeding Academic Research Consortium 2, 3, or 5 bleeding were 10.0% (31 of 311) vs 10.7% (33 of 310) (odds ratio, 0.93 [95% CI, 0.55-1.56]; $P = .78$). The rates of major vascular complications were 6.4% (20 of 311) vs 9.4% (29 of 310) (odds ratio, 0.67 [95% CI, 0.37-1.20]; $P = .18$). Ultrasonography improved first-pass success (277 of 311 [86.6%] vs 222 of 310 [70.0%]; odds ratio, 2.76 [95% CI, 1.85-4.12]; $P < .001$) and reduced the number of arterial puncture attempts (mean [SD], 1.2 [0.5] vs 1.4 [0.8]; mean difference, −0.26 [95% CI, −0.37 to −0.16]; $P < .001$) and venipuncture (10 of 311 [3.1%] vs 37 of 310 [11.7%]; odds ratio, 0.24 [95% CI, 0.12-0.50]; $P < .001$) with similar times to access (mean [SD], 114 [185] vs 129 [206] seconds; mean difference, −15.1 [95% CI, −45.9 to 15.8]; $P = .34$). All prerandomization prespecified subgroups were consistent with the overall finding.

CONCLUSIONS AND RELEVANCE In this randomized clinical trial, use of ultrasonography for femoral access did not reduce bleeding or vascular complications. However, ultrasonography did reduce the risk of venipuncture and number of attempts. Larger trials may be required to demonstrate additional potential benefits of ultrasonography-guided access.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03537118

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