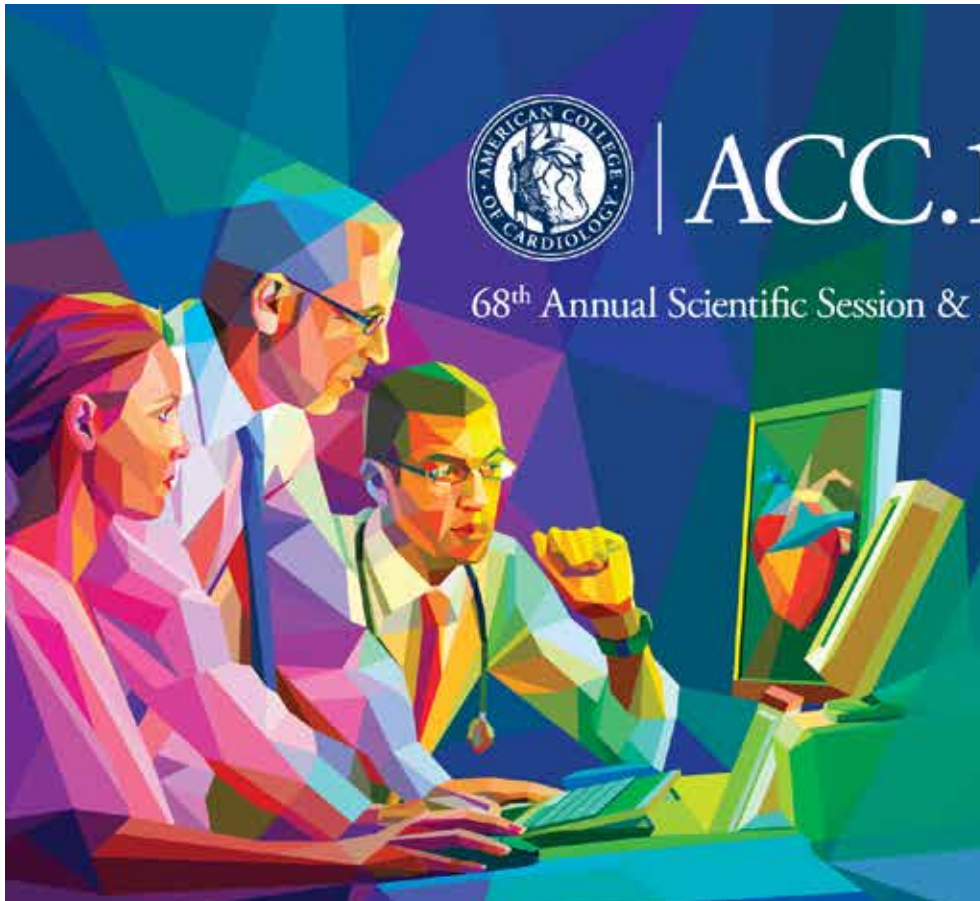

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68th Annual Scientific Session & Expo

NEW ORLEANS
MARCH 16 - 18
2019

The SAfety and Efficacy of Femoral Access vs Radlal Access in STEMI:

The SAFARI-STEMI Trial

ClinicalTrials.gov identifier: NCT01398254

Michel R Le May MD, FRCP, FACC
University of Ottawa Heart Institute,
Ottawa, Ontario,
Canada

The SAfety and Efficacy of Femoral Access vs. Radlal Access in ST-Elevation Myocardial Infarction (SAFARI-STEMI) trial

Investigators: Michel R. Le May, George A. Wells, Derek Y. So, Aun Yeong Chong, Michael Froeschl, Alexander Dick, Christopher Glover, Benjamin Hibbert, Jean-François Marquis, Melissa Blondeau, Christina Osborne, Andrea MacDougall, Malek Kass, Vernon Paddok, Ata Quraishi, Marino Labinaz.

Participating Centers:

University of Ottawa Heart Institute, Ottawa, Ontario

New Brunswick Heart Centre, Saint John Regional Hospital, New Brunswick

Thunder Bay Regional Heath Sciences Centre, Thunder Bay, Ontario

St. Boniface General Hospital, Winnipeg, Manitoba

Queen Elizabeth II Health Science Centre , Halifax, Nova Scotia

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SAFARI-STEMI

Background: Radial vs Femoral Access

- Radial access has been endorsed because
  - bleeding is reported to be less frequent than with femoral access, and
  - bleeding associated with PCI is linked to mortality
- Previous trials suggest that radial access is associated with lower mortality in STEMI pts
- Mortality advantage for radial access over femoral access in pts undergoing primary PCI is controversial.
- **Objective:**

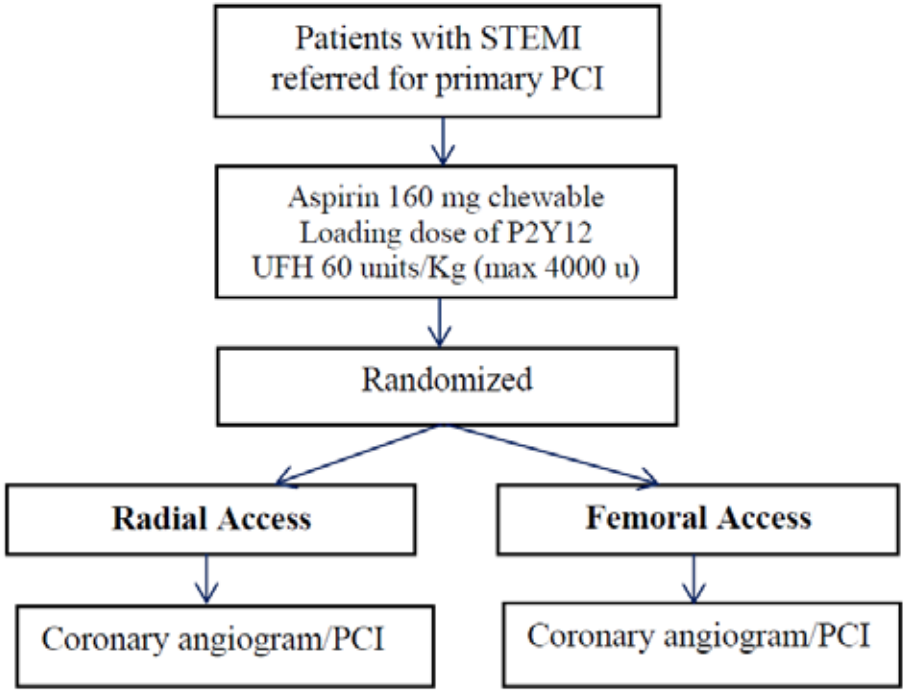
  Determine if radial access improves survival when compared to femoral access in pts referred for primary PCI

SAFARI-STEMI

STUDY DESIGN

- Investigator-driven, multi-center, prospective, randomized open-label trial with blinded evaluation of outcomes
- **Inclusion:**

  STEMI pts referred for primary PCI with symptom onset ≤12 hrs
- **Main exclusion criteria:**
  - Fibrinolytic therapy
  - Oral anticoagulants
  - Prior CABG



SAFARI-STEMI

Outcomes

Primary outcome:

- all-cause mortality measured at 30 days

Key secondary outcomes at 30 days:

- stroke
- reinfarction
- stent thrombosis
- bleeding (TIMI definition)

SAFARI-STEMI

Sample size

- Expected 30-day mortality of 4.0% in femoral access group
- Minimal clinically important difference of 1.5% between femoral and radial access
- Crossover rate: radial access 5% vs.1% femoral access
- Loss to follow-up of 0.5%
- Sample size of 2442 pts per group (total of 4884 pts) required with a level of significance of 0.05 and 80% power

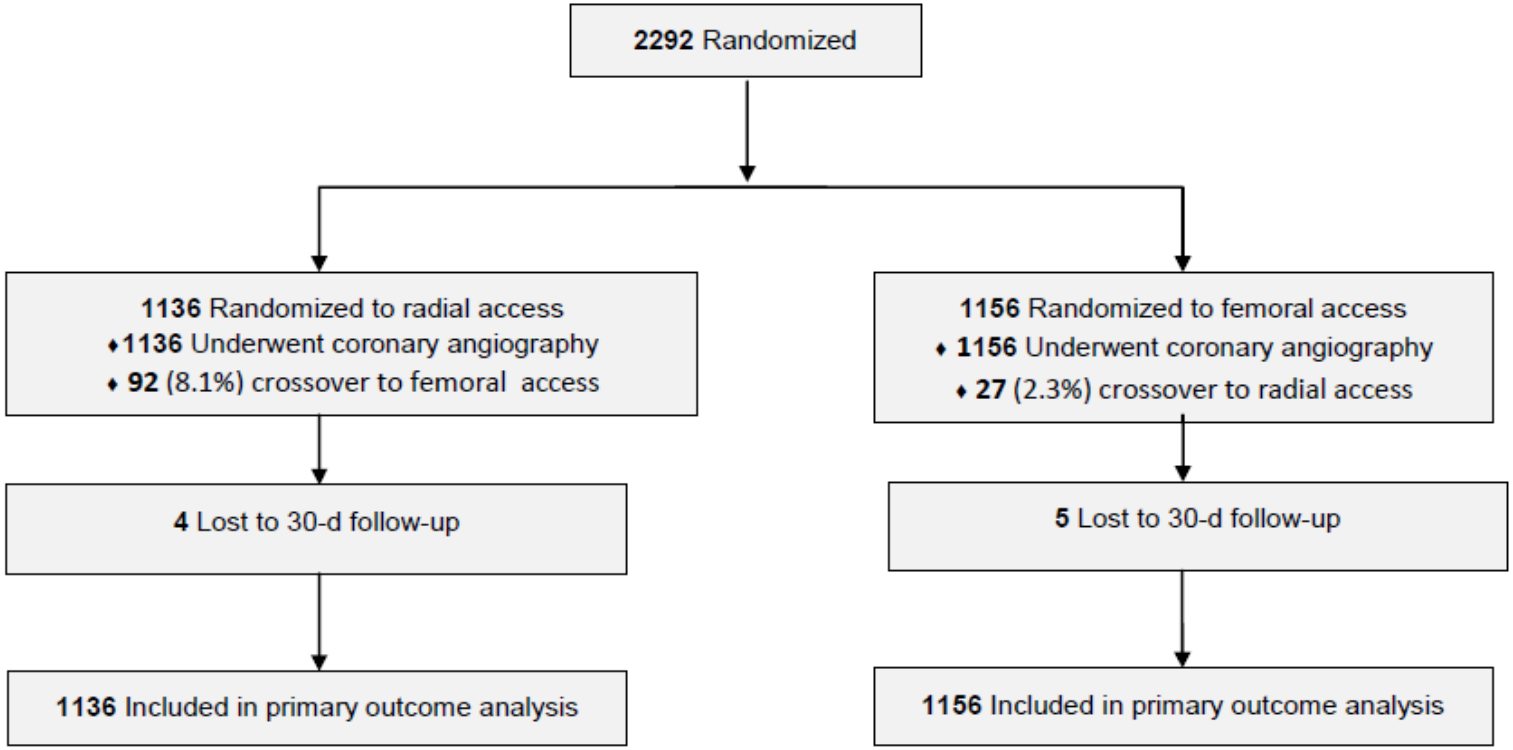
SAFARI-STEMI

Role of DSMB

- An independent DSMB oversaw the safety and scientific validity of the trial
- On December 7, 2018, recruitment was stopped early as recommended by the DSMB

SAFARI-STEMI

Patient Flow Diagram



SAFARI-STEMI

Baseline Characteristics

Characteristic	Radial Access (n=1136)	Femoral Access (n= 1156)
Age, mean ± SD, y	61.6 ± 12.3	62.0 ± 12.1
Male sex	77.7%	77.9%
Hypertension	49.1%	46.8%
Diabetes mellitus	16.7%	18.3%
Current smoker	39.6%	38.2%
Dyslipidemia	37.2%	37.3%
Previous MI	11.0%	10.0%
Previous PCI	9.2%	9.0%
Previous stroke or TIA	3.6%	3.5%
Anterior myocardial infarction	37.7%	34.3%
Heart rate, mean ± SD, beats per minute	76.7 ± 30.3	77.5 ± 25.5
Systolic blood pressure, mean ± SD, mm Hg	141.0 ± 28.5	142.4 ± 27.7
Killip class II, III, or IV	7.0%	6.7%
Body-mass index, mean ± SD kg/m^2	28.2 ± 4.9	28.2 ± 4.9

SAFARI-STEMI

Medications for the Procedure

Before Procedure

	Radial Access (n=1136)	Femoral Access (n= 1156)
Aspirin	99.9%	99.6%
P2Y12 inhibitor		
Clopidogrel*	18.6%	20.4%
Prasugrel	0.1%	0.1%
Ticagrelor	**91.5%**	**91.5%**
UFH, 60 units/kg (max 4000 u)	**98.2%**	**97.5%**

During Procedure

	Radial Access (n=1136)	Femoral Access (n= 1156)
Antithrombin		
Bivalirudin	**88.1%**	**92.4%**
UFH	11.9%	7.6%
Glycoprotein IIb/IIIa inhibitor	**6.1%**	**5.9%**

*Pts already given a LD of clopidogrel, additional LD of ticagrelor allowed

SAFARI-STEMI

Cardiac Catheterization/PCI Results

Variable	Radial Access (n=1136)	Femoral Access (n= 1156)
Coronary angiography	100%	100%
PCI performed	95.2%	95.9%
Stent insertion	91.3%	92.6%
Stents per patient, mean ± SD	1.5 ±1.2	1.5 ±1.0
Drug-eluting, % of pts stented	87.3%	88.4%
Manual aspiration thrombectomy, % of PCI	38.8%	42.9%
No of diagnostic & guiding catheters/pt, mean ± SD	3.2 ±1.4	3.1 ±1.0
Intraaortic balloon pump	1.8%	2.5%
Impella device or ECMO	0.26%	0.35%
Peak activated clotting time, mean ± SD, sec	395 ±130	389 ±116
Crossover	8.1%	2.3%
Use of vascular closing device	5.5%	68.2%

SAFARI-STEMI

Key Time Intervals: median (q1,q3) - min

Interval	Radial Access (n=1136)	Femoral Access (n= 1156)	P Value
Symptom onset to first balloon inflation/device	166 (111-247)	161 (109-239)	0.42
Arrival at PCI center to first balloon inflation/device	47 (35-63)	44 (33-60)	0.007
Arrival at catheterization laboratory to first balloon inflation/device	20 (16-25)	18 (14-22)	<0.0001
Lidocaine administration to first balloon inflation/device	13 (10-17)	11 (9-14)	<0.0001
Fluoroscopy time	9.4 (6.5-13.5)	8.2 (6.0-12.5)	<0.0001

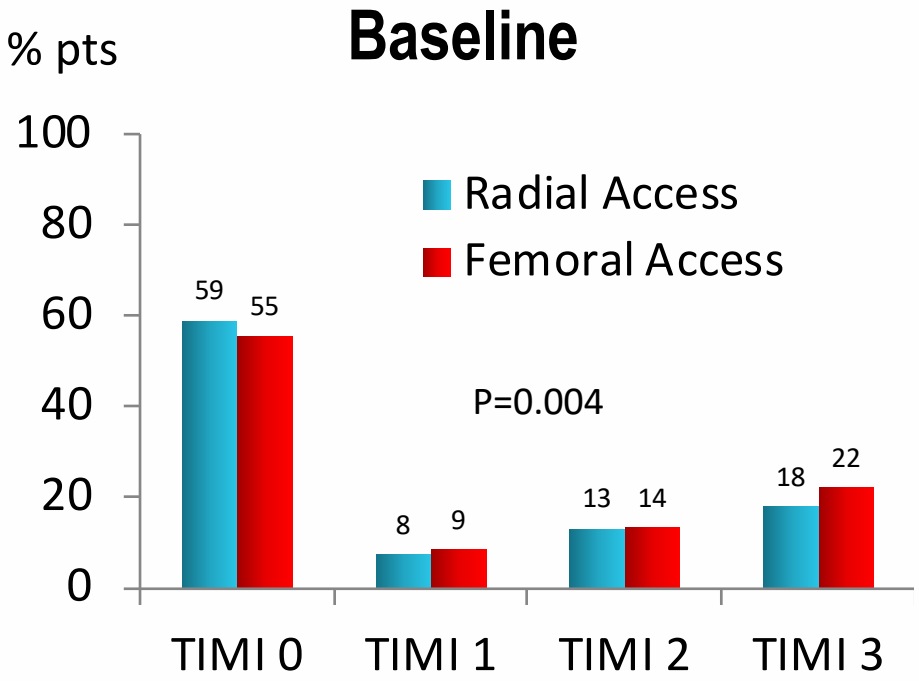
SAFARI-STEMI

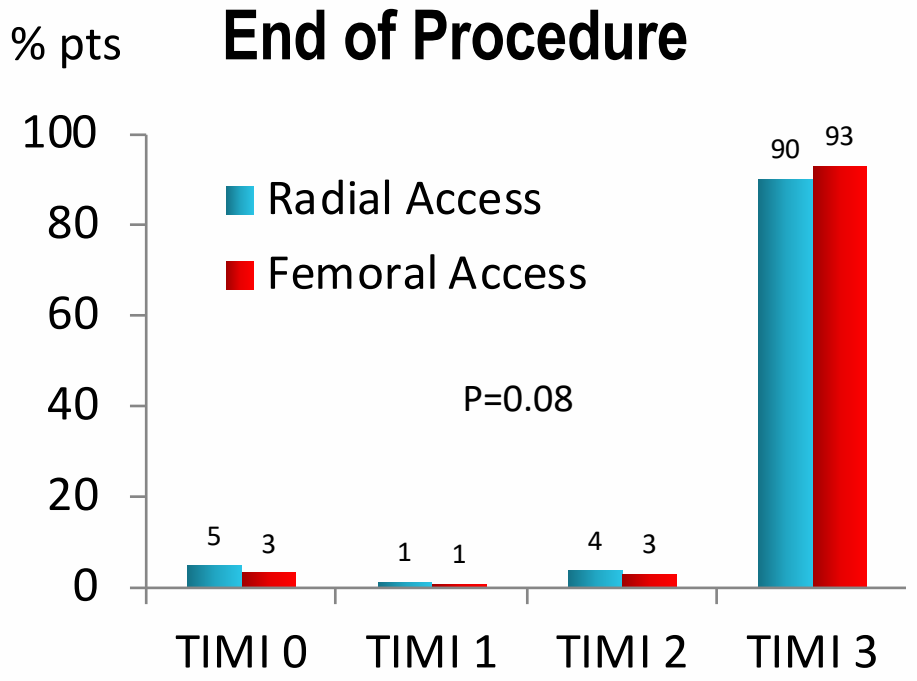
Angiographic results

	Radial Access (n=1136)	Femoral Access (n= 1156)
Multivessel disease	57.0%	58.3%
Infarct-related coronary artery		
Left main	0.53%	0.9%
Left anterior descending	40.1%	36.9%
Left circumflex	13.9%	15.2%
Right	44.0%	45.3%
Unknown	1. 5%	1.6%

SAFARI-STEMI

TIMI Flow Grade





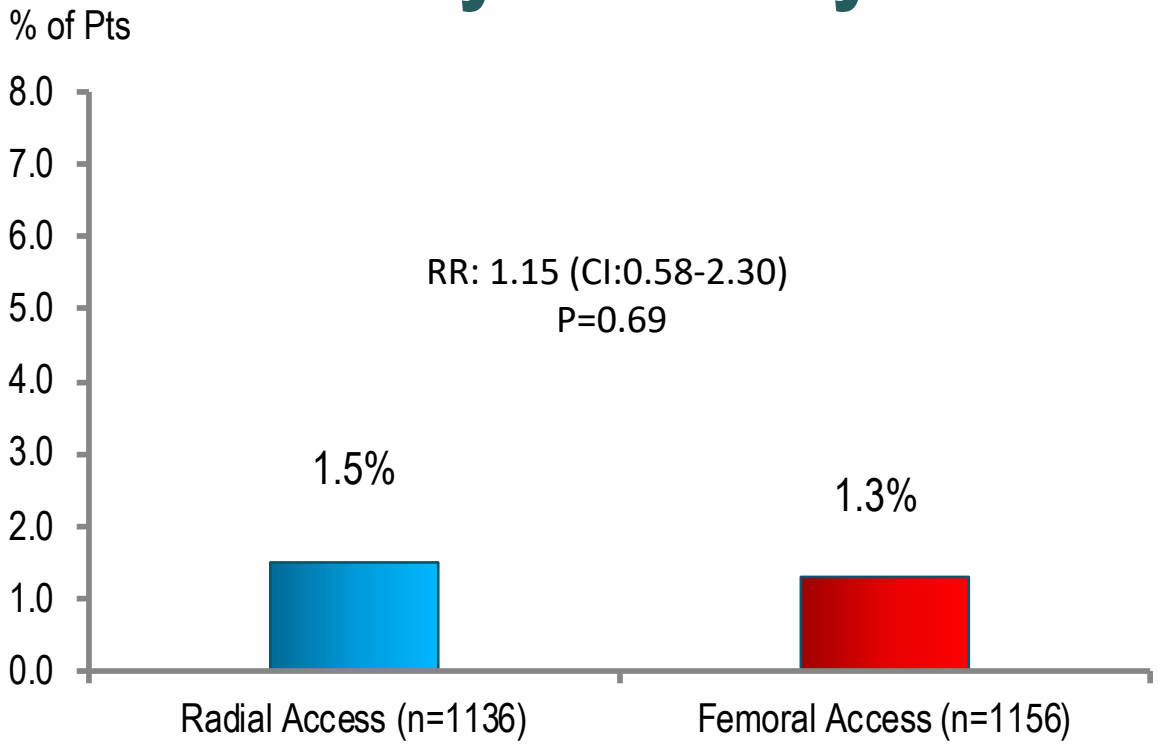
SAFARI-STEMI

DSMB's Recommendation

- As a result of a continual lower than expected rate of the primary outcome, the DSMB requested a **futility analysis**
- **A futility index of 0.83 for the primary outcome was calculated**
- Based on this analysis, the DSMB recommended terminating the trial because it was highly unlikely that the trial would show a clinically important difference in 30-day all-cause mortality between the access site strategies
- The steering committee met to discuss the recommendation and enrollment was terminated on Dec 7 2018
- 2292 pts enrolled and 30-day follow-up available on 2283 (99.6%)

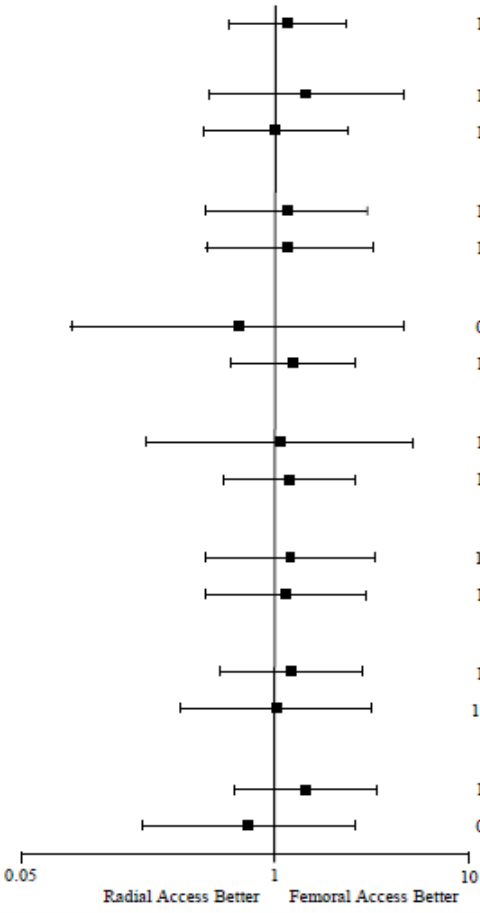
SAFARI-STEMI

Primary Outcome: 30-day Mortality



SAFARI-STEMI

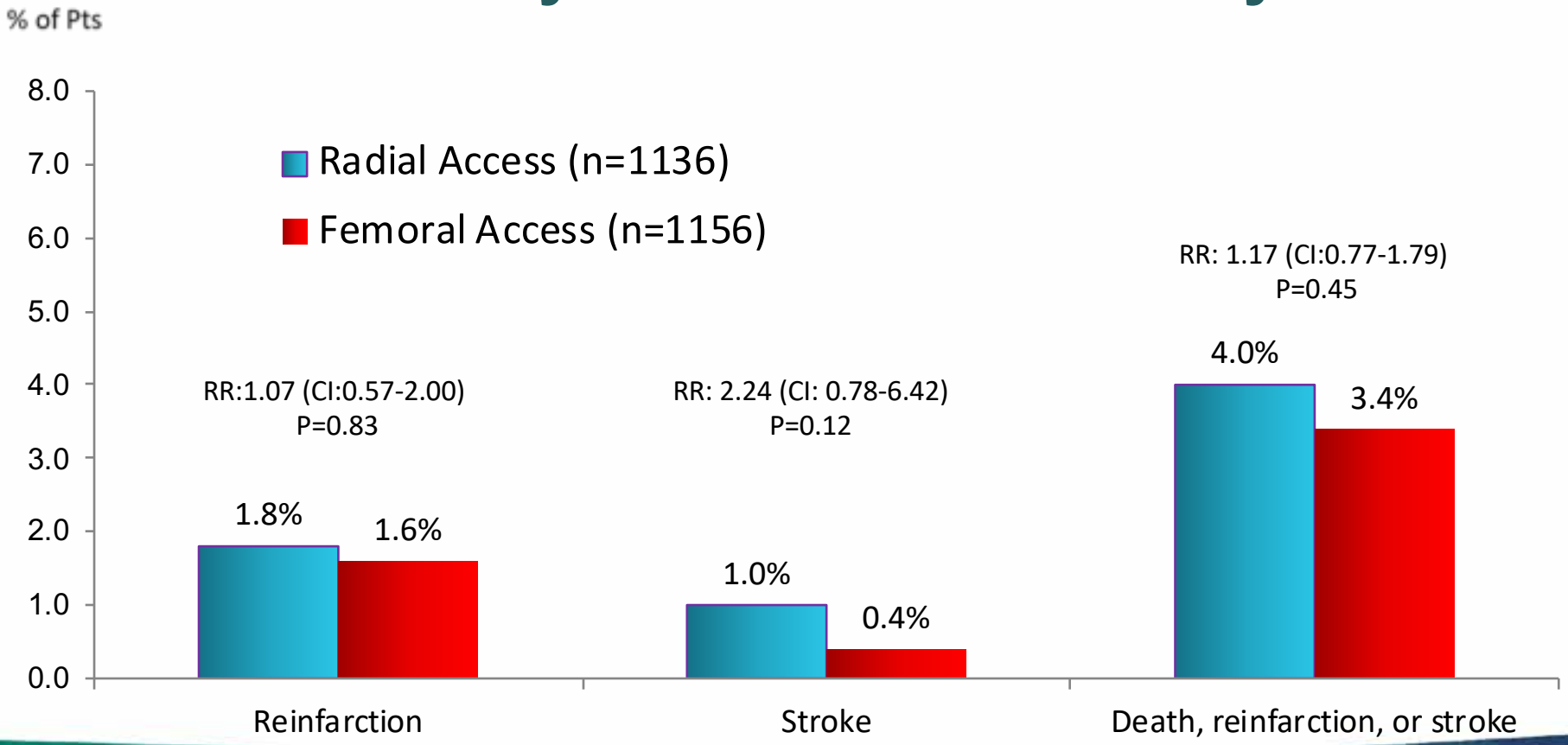
Subgroup	Radial Access	Femoral Access	RR (95% CI)	P value	P value for interaction
Overall	17/1136	15/1156	1.15 (0.58-2.30)	0.69	
Age					0.63
< 75 yr	7/950	5/970	1.43 (0.46-4.49)	0.54	
≥ 75 yr	10/186	10/186	1.00 (0.43-2.35)	1.00	
Gender					0.99
Male	9/883	8/901	1.15 (0.44-2.96)	0.78	
Female	8/253	7/255	1.15 (0.42-3.13)	0.78	
Bivalirudin Given					0.55
No	2/135	2/88	0.65 (0.09-4.54)	0.65	
Yes	15/1001	13/1068	1.23 (0.59-2.57)	0.58	
Loaded with Ticagrelor					0.87
No	3/96	3/98	1.02 (0.21-4.93)	1.00	
Yes	14/1040	12/1058	1.19 (0.55-2.55)	0.66	
Body Mass Index					0.93
<25 kg/m2	8/292	7/307	1.132 (0.44-2.92	0.72	
≥25 kg/m2	9/844	8/849	1.13 (0.44-2.95)	0.80	
Creatinine Clearance					0.80
<60 ml/min	11/149	9/148	1.21 (0.52-2.84)	0.65	
≥60 ml/min	6/987	6/1008	1.021 (0.33-3.16)	0.97	
Diabetes					0.39
No	13/945	9/944	1.44 (0.62-3.36)	0.39	
Yes	4/190	6/212	0.74 (0.21-2.60)	0.75	



Subgroup Analysis of the Primary Outcome

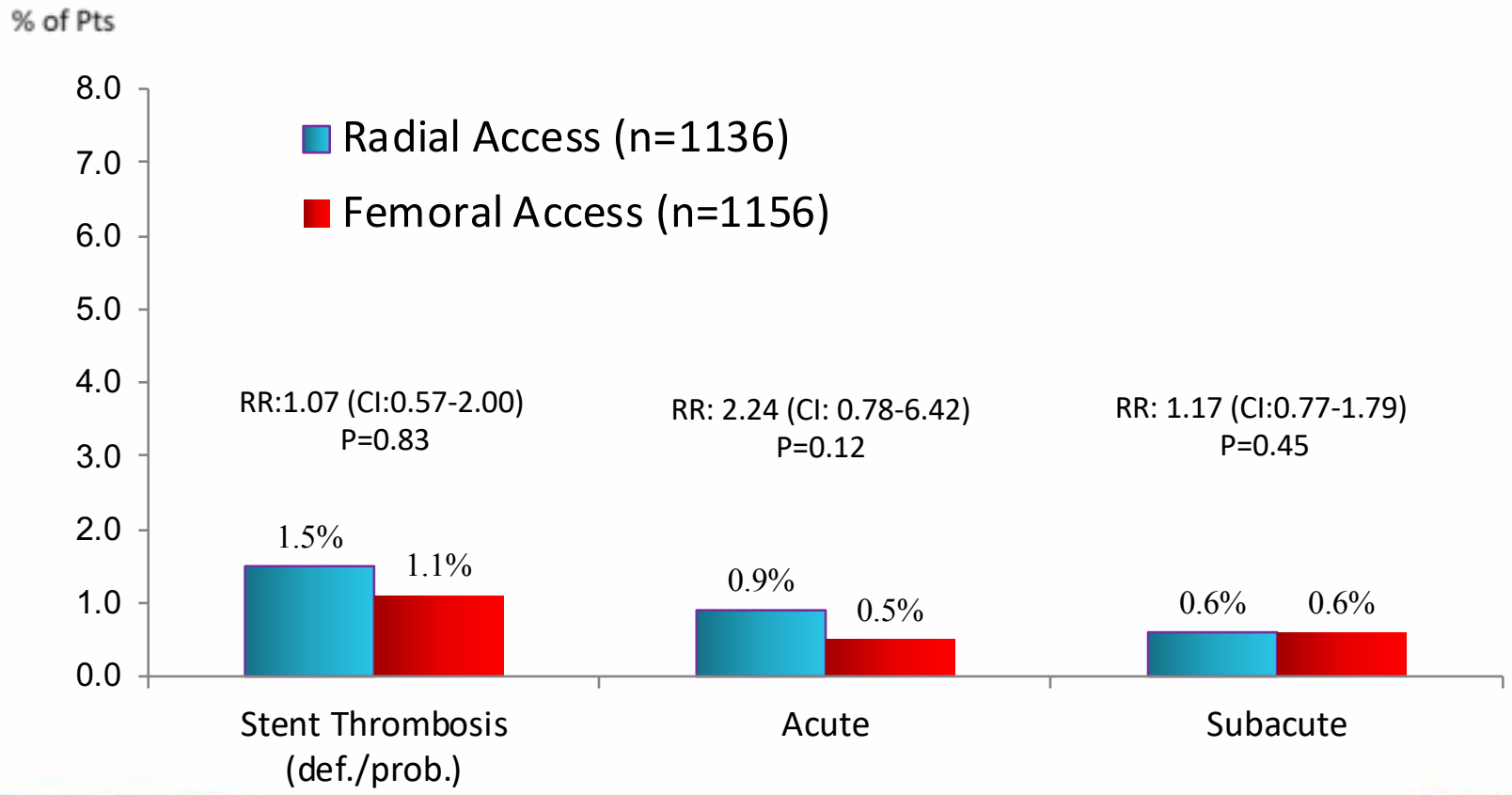
SAFARI-STEMI

Secondary Outcomes at 30 days



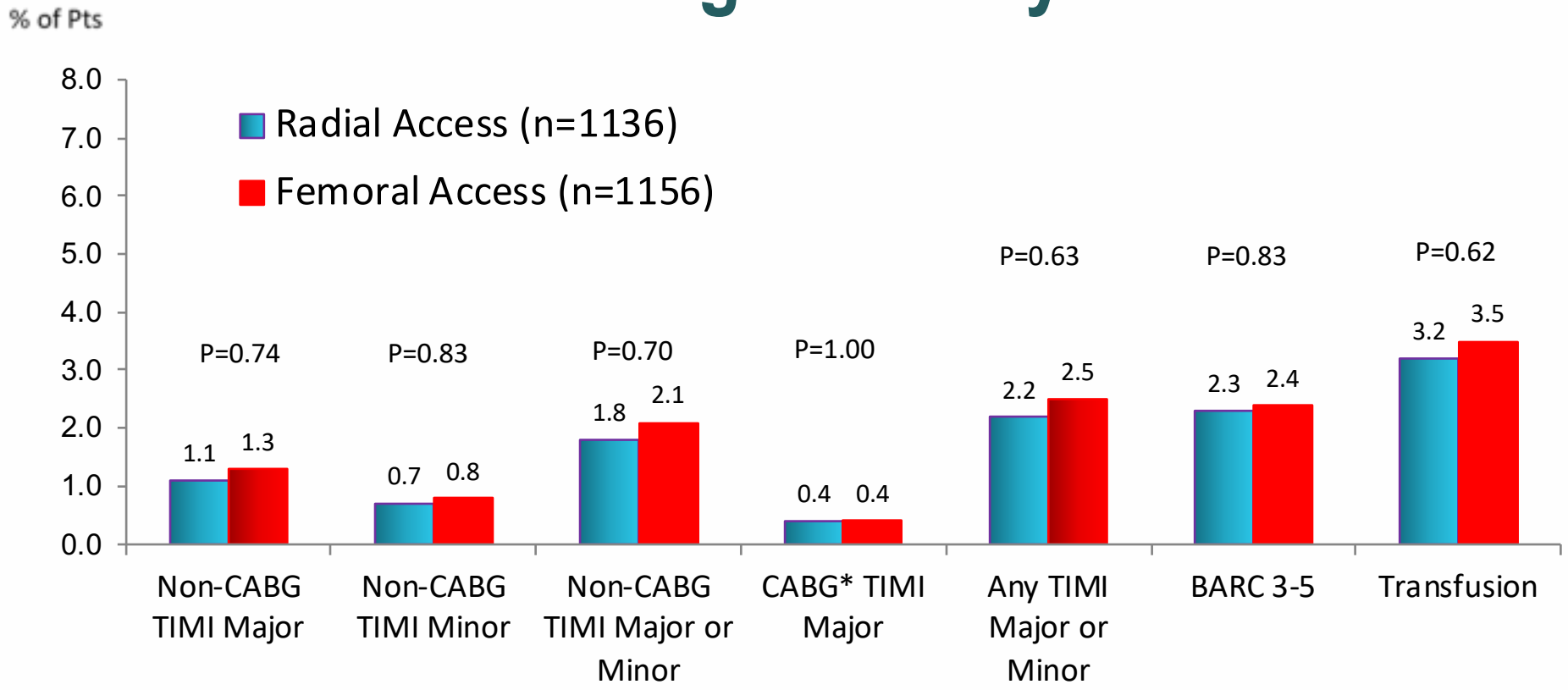
SAFARI-STEMI

Stent Thrombosis



SAFARI-STEMI

Bleeding at 30 days

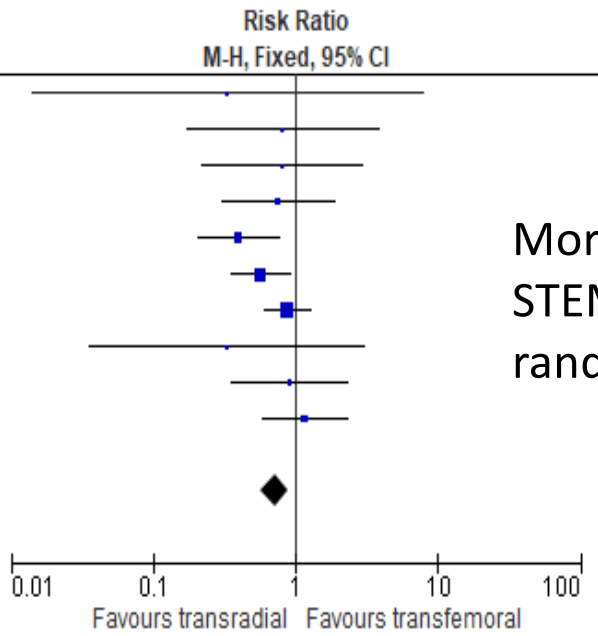


*CABG done in 3.8% radial and 3.5% femoral

SAFARI-STEMI

Study or Subgroup	Transradial Events	Transradial Total	Transfemoral Events	Transfemoral Total	Weight	Risk Ratio M-H, Fixed, 95% CI
RADIAL-AMI 2005	0	25	1	25	0.8%	0.33 [0.01, 7.81]
Yan 2008	3	57	3	46	1.8%	0.81 [0.17, 3.81]
Hou 2010	4	100	5	100	2.8%	0.80 [0.22, 2.89]
STEMI-Radial 2012	8	348	11	359	6.0%	0.75 [0.31, 1.84]
RIVAL 2012	12	955	32	1003	17.4%	0.39 [0.20, 0.76]
RIFLE-STEACS 2012	26	500	46	501	25.6%	0.57 [0.36, 0.90]
MATRIX 2015	48	2001	55	2009	30.6%	0.88 [0.60, 1.28]
OCEAN RACE 2014	1	52	3	51	1.7%	0.33 [0.04, 3.04]
Vasquez-Rodriguez 2009	8	217	9	222	5.0%	0.91 [0.36, 2.31]
SAFARI 2019	17	1136	15	1156	8.3%	1.15 [0.58, 2.30]
Total (95% CI)		**5391**		**5472**	**100.0%**	**0.71 [0.57, 0.89]**
Total events	127		180			

Heterogeneity: Chi² = 8.08, df = 9 (P = 0.53); I² = 0%
Test for overall effect: Z = 2.98 (P = 0.003)

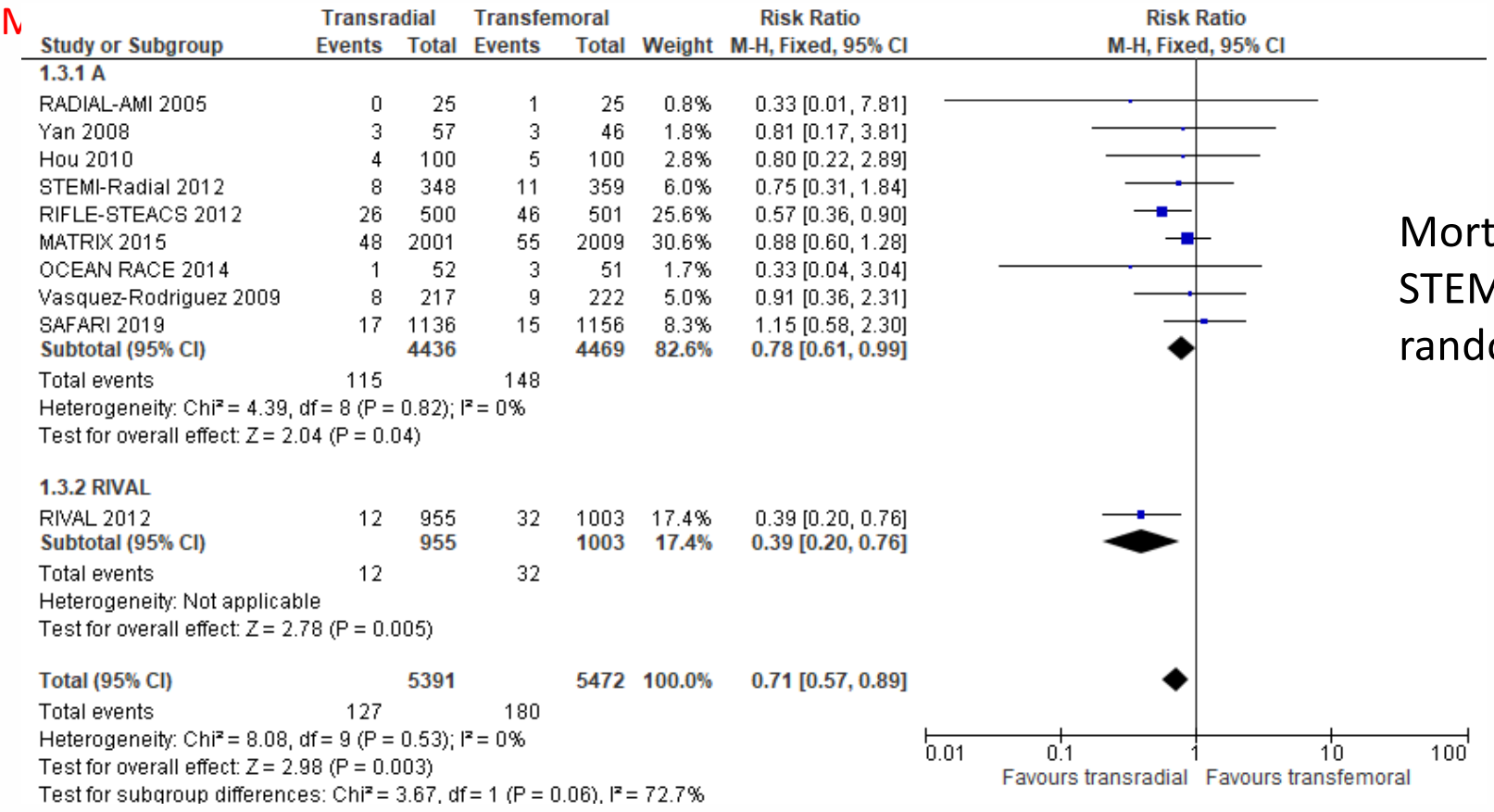


Mortality in STEMI pts in randomized trials

- SAFARI-STEMI is largest study after MATRIX and the largest dedicated PPCI study
- Precision similar to RIVAL and RIFLE-STEACS
- More consistent with other studies than RIVAL and RIFLE-STEACS
- Influence analysis – RIVAL corresponds to most significant interaction p-value (P=0.06)

SAFARI-

STEM



Study or Subgroup	Transradial Events	Total	Transfemoral Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.3.1 A						
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Hou 2010	4	100	5	100	2.8%	0.80 [0.22, 2.89]
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Vasquez-Rodriguez 2009	8	217	9	222	5.0%	0.91 [0.36, 2.31]
SAFARI 2019	17	1136	15	1156	8.3%	1.15 [0.58, 2.30]
Subtotal (95% CI)		**4436**		**4469**	**82.6%**	**0.78 [0.61, 0.99]**
Total events	115		148			
Heterogeneity: Chi² = 4.39, df = 8 (P = 0.82); I² = 0%						
Test for overall effect: Z = 2.04 (P = 0.04)						
1.3.2 RIVAL						
RIVAL 2012	12	955	32	1003	17.4%	0.39 [0.20, 0.76]
Subtotal (95% CI)		**955**		**1003**	**17.4%**	**0.39 [0.20, 0.76]**
Total events	12		32			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.78 (P = 0.005)						
Total (95% CI)		**5391**		**5472**	**100.0%**	**0.71 [0.57, 0.89]**
Total events	127		180			
Heterogeneity: Chi² = 8.08, df = 9 (P = 0.53); I² = 0%						
Test for overall effect: Z = 2.98 (P = 0.003)						
Test for subgroup differences: Chi² = 3.67, df = 1 (P = 0.06), I² = 72.7%						

Mortality in STEMI pts in randomized trials

SAFARI-STEMI

CONCLUSIONS

- In pts with STEMI referred for primary PCI, we did not find a difference in survival at 30 days between the use of radial access and femoral access
- Our findings suggest that adequately trained operators should be able to achieve similar results using either radial or femoral access for primary PCI

Acknowledgment

University of Ottawa Heart Institute,
Ottawa, Ontario

St. Boniface General Hospital,
Winnipeg, Manitoba

New Brunswick Heart Centre,
Saint John Regional Hospital, NB

1) Cath lab nurses/staff
2) CCU nurses /staff
3) Coordinators
4) Cardiology residents
5) Members of adjudication committee
6) Members of DSMB

,

Thunder Bay Regional Heath Sciences Centre,
Thunder Bay, Ontario

Queen Elizabeth II Health Science Centre ,
Halifax, Nova Scotia