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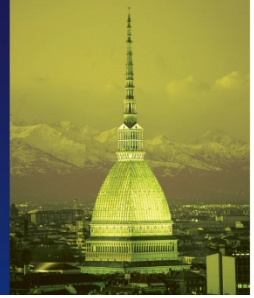

UNIVERSITÁ DEGLI STUDI DI TORINO

AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

Management of coronary artery disease in patients undergoing transcatheter aortic valve implantation: *look at ischemic burden*

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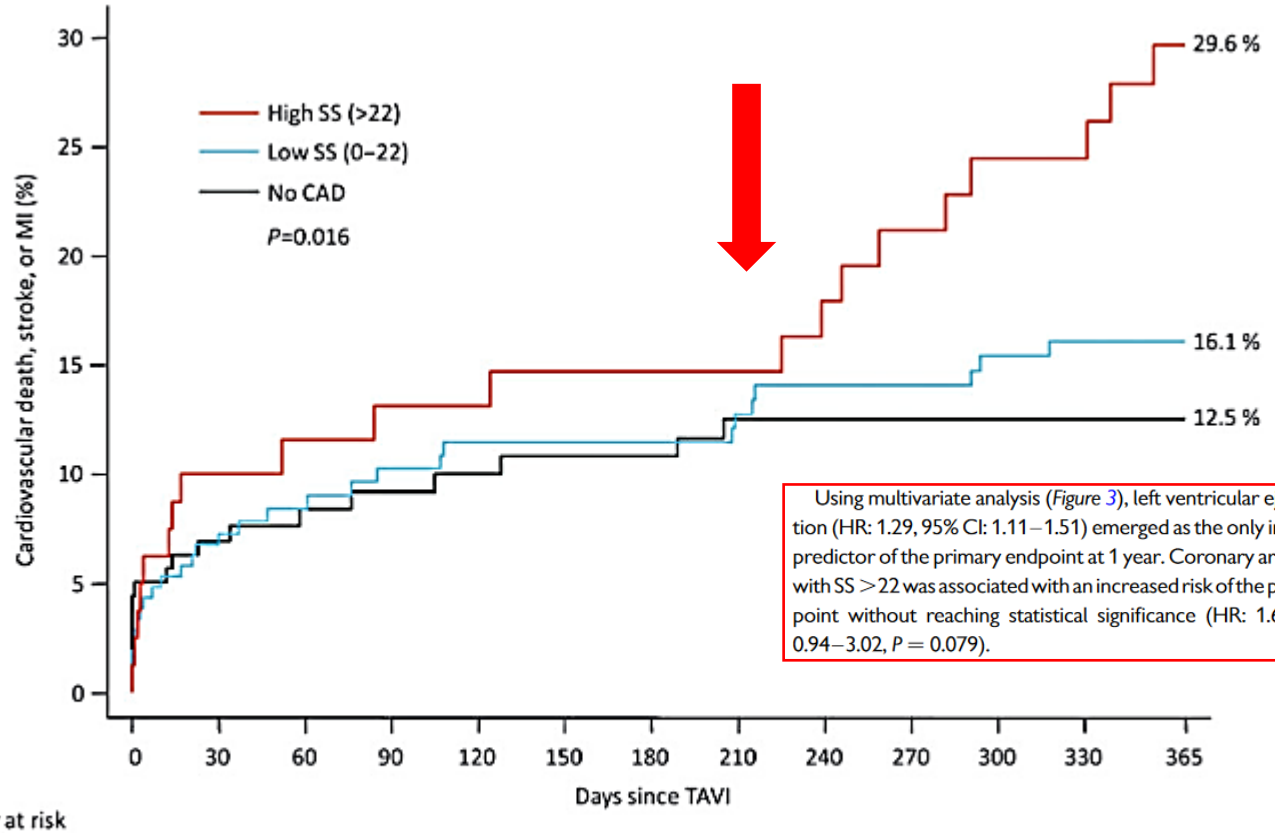
Disclosure

- I have consulted for Abbott Vascular and Bayer

CAD severity and post-TAVI outlook



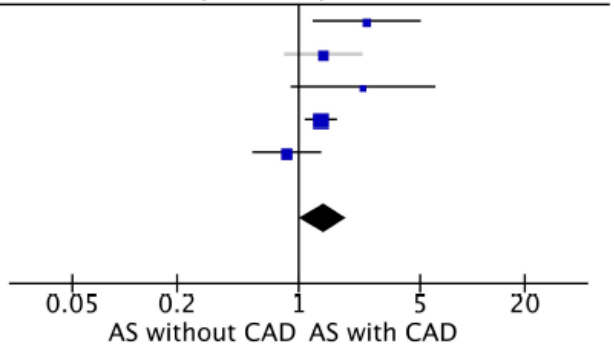
Using multivariate analysis (*Figure 3*), left ventricular ejection fraction (HR: 1.29, 95% CI: 1.11–1.51) emerged as the only independent predictor of the primary endpoint at 1 year. Coronary artery disease with SS >22 was associated with an increased risk of the primary endpoint without reaching statistical significance (HR: 1.68, 95% CI: 0.94–3.02, $P = 0.079$).

Stefanini et al, Eur Heart J 2014

CAD severity and post-TAVI outlook

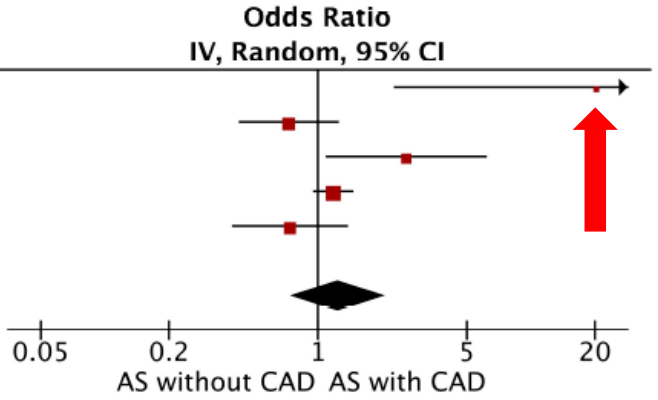
Study or Subgroup	AS with CAD Events	AS with CAD Total	AS without CAD Events	AS without CAD Total	Weight	Odds Ratio IV, Random, 95% CI
Dewey et al, 2010	30	84	16	87	13.1%	2.47 [1.22, 4.98]
Franzone et al, 2017	41	248	31	248	19.8%	1.39 [0.84, 2.29]
Mancio et al, 2015	17	46	9	45	8.4%	2.34 [0.91, 6.03]
Snow et al, 2015	246	1167	230	1387	36.2%	1.34 [1.10, 1.64]
Ussia et al, 2013	35	251	65	408	22.5%	0.86 [0.55, 1.33]
Total (95% CI)		**1796**		**2175**	**100.0%**	**1.39 [1.02, 1.88]**
Total events	369		351			

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 8.17$, df = 4 (P = 0.09); $I^2 = 51\%$
Test for overall effect: Z = 2.09 (P = 0.04)



Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Dewey et al, 2010	3.0106	1.1111	4.9%	20.30 [2.30, 179.17]
Franzone et al, 2017	-0.3147	0.27	24.4%	0.73 [0.43, 1.24]
Mancio et al, 2015	0.9555	0.4389	17.3%	2.60 [1.10, 6.15]
Snow et al, 2015	0.1655	0.1053	30.9%	1.18 [0.96, 1.45]
Ussia et al, 2013	-0.3011	0.3139	22.4%	0.74 [0.40, 1.37]
Total (95% CI)			**100.0%**	**1.25 [0.74, 2.11]**

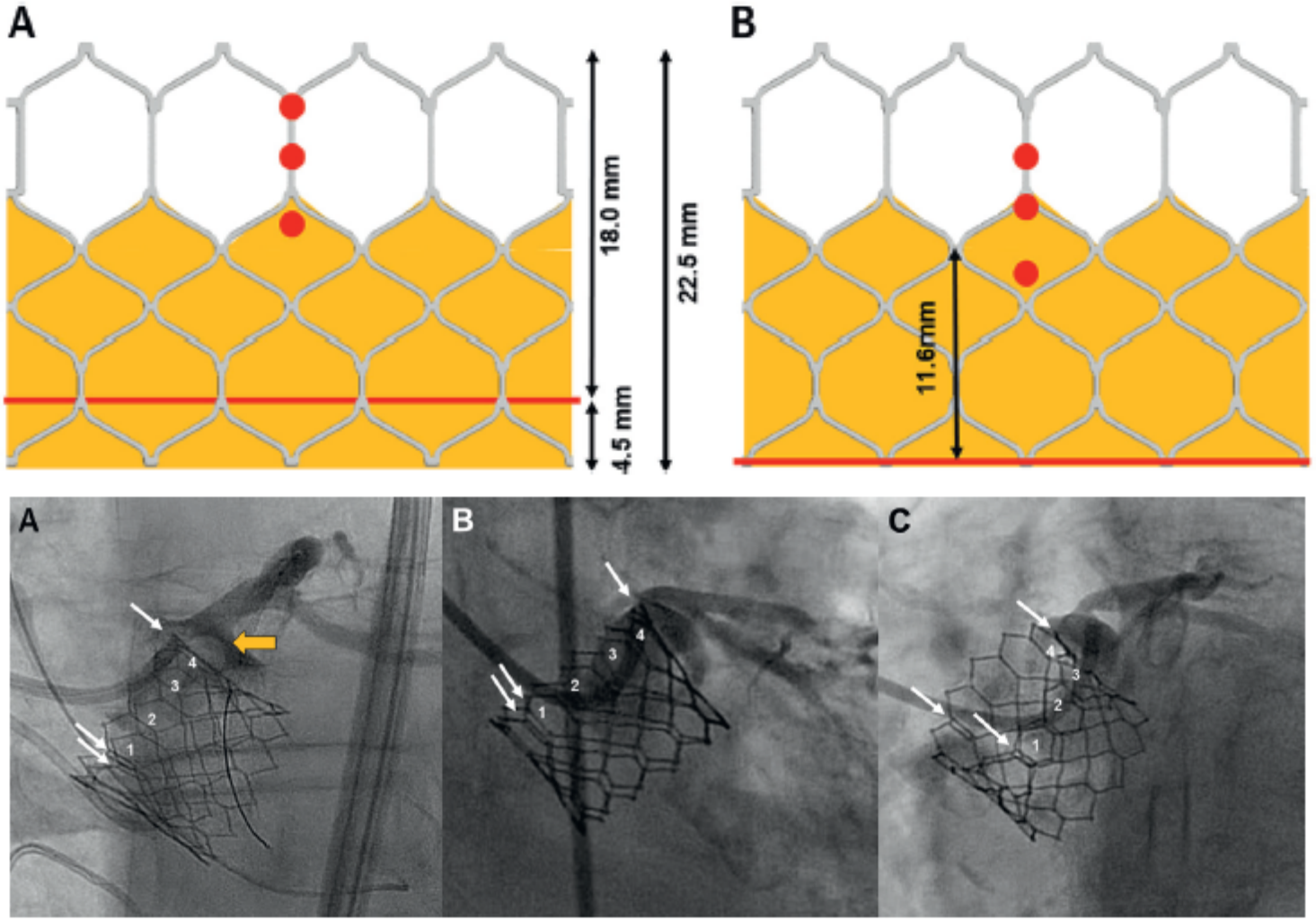
Heterogeneity: $Tau^2 = 0.22$; $Chi^2 = 14.97$, df = 4 (P = 0.005); $I^2 = 73\%$
Test for overall effect: Z = 0.82 (P = 0.41)



8 studies missing: selective reporting?

D'Ascenzo et al, EuroIntervention 2018

PCI after TAVI



Yudi et al, J Am Coll Cardiol 2018

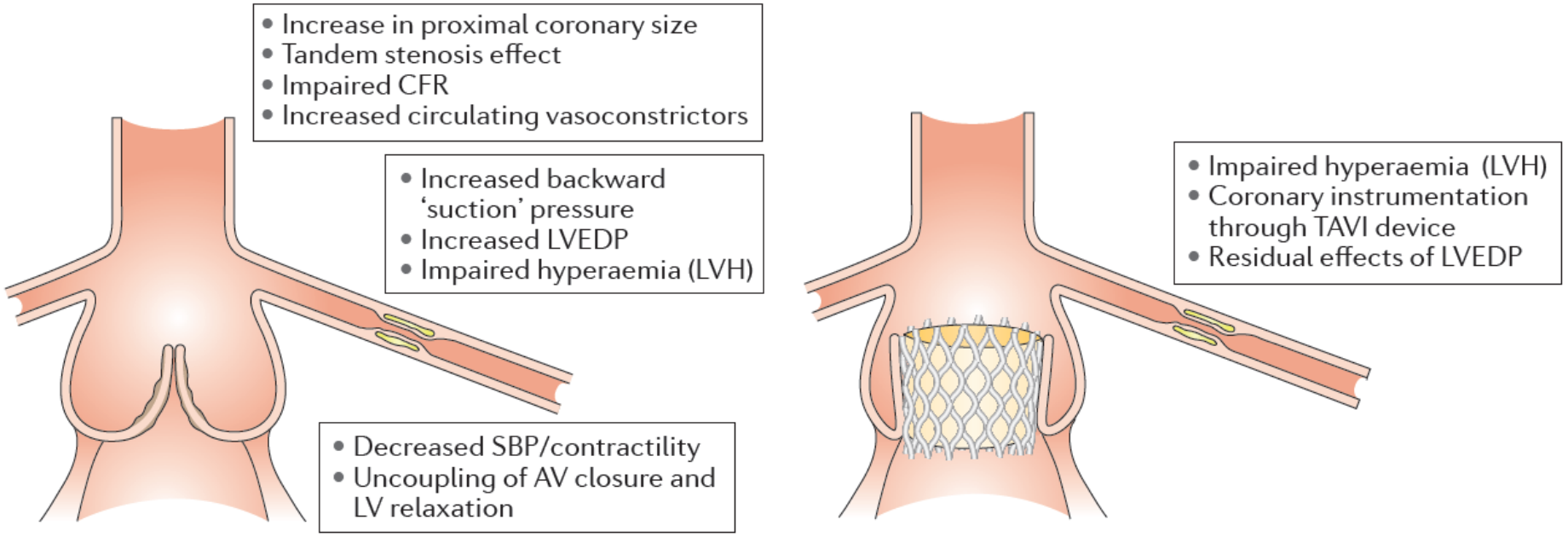
One- vs two-stage PCI and TAVI

Study	Conrad et al[13]	Wenaweser et al[14]	Aktug et al[15]	Griese et al[3]
30-d mortality				
Concomitant PCI+TAVR	2/7	4/36	0/8	3/17
Staged PCI+TAVR	0/21	2/23	7/49	7/48
Renal failure				
Concomitant PCI+TAVR	2/7	1/36	NR	1/17
Staged PCI+TAVR	0/21	0/23	NR	2/48
Life-threatening bleeding				
Concomitant PCI+TAVR	0/7	2/36	NR	1/17
Staged PCI+TAVR	0/21	3/23	NR	5/48
Periprocedural myocardial infarction				
Concomitant PCI+TAVR	0/7	0/36	NR	1/17
Staged PCI+TAVR	0/21	0/23	NR	2/48
Major stroke				
Concomitant PCI+TAVR	0/7	2/36	NR	0/17
Staged PCI+TAVR	0/21	0/23	NR	0/48

PCI = percutaneous coronary intervention, TAVR = transcatheter aortic valve replacement.

Yang et al, Medicine 2017

Confounding functional assessment



Danson et al, Nat Rev Cardiol 2016

Competing scenarios

- **Timing:**
  - Before vs after TAVI
- **CAD type:**
  - Atherothrombotic vs stable
  - Symptomatic vs asymptomatic
  - Functionally vs anatomically significant
- **Lesion subset:**
  - Simple vs complex
  - Low risk vs high risk
  - Proximal vs distal
  - Stenotic vs occluded

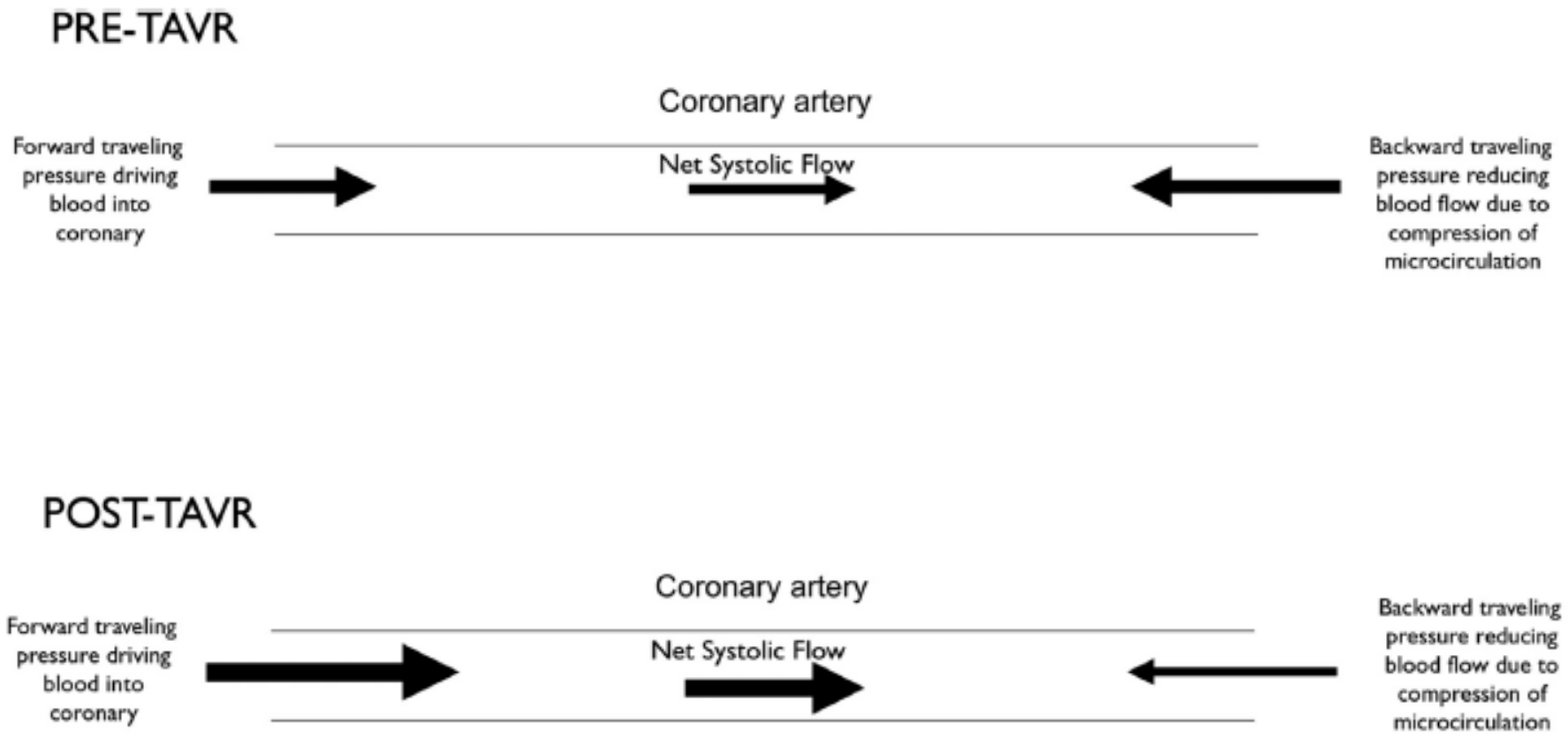
Nudi et al, J Nucl Cardiol 2018

Anatomic vs functional complexity

- **Scores:**
  - SYNTAX vs MIS vs others
- **Timing**:
  - Baseline vs residual
- **Anatomic definition**:
  - Diameter stenosis vs lumen area
- **Functional definition**:
  - Wall motion vs perfusion vs CFR vs FFR vs iFR

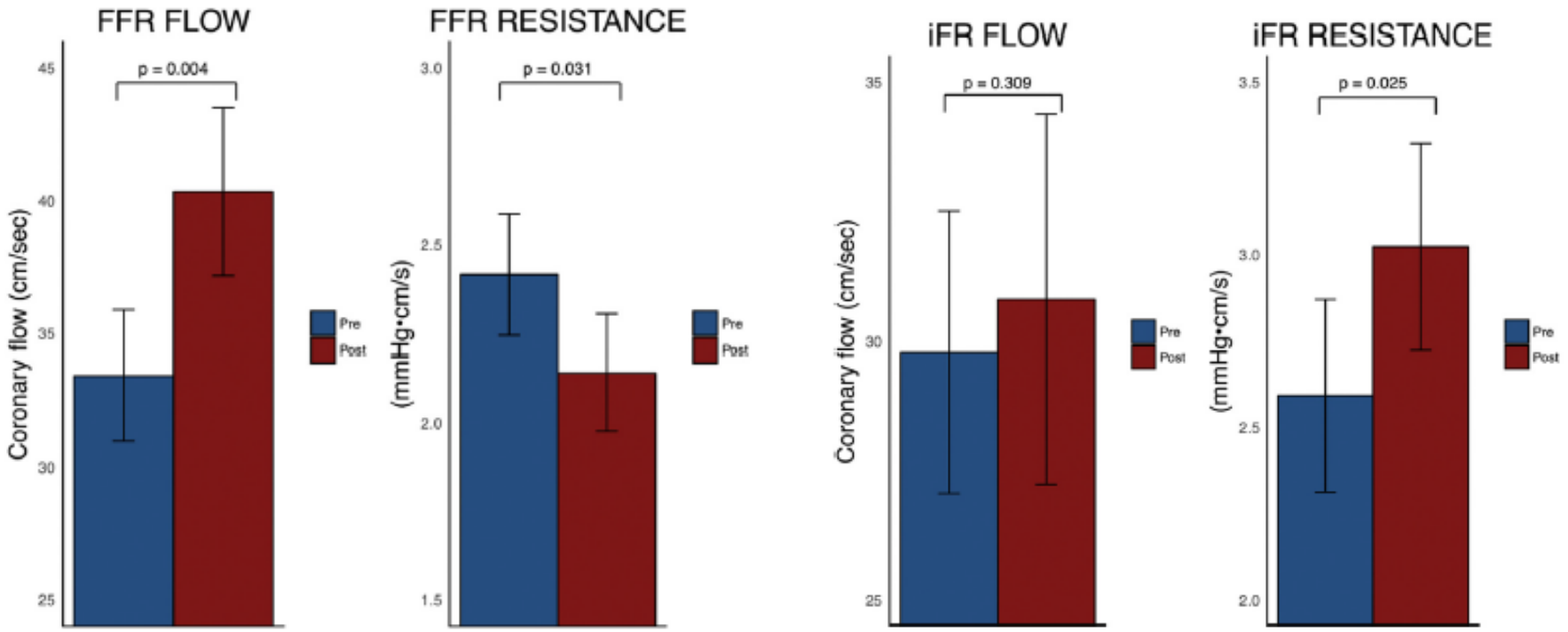
Nudi et al, J Nucl Cardiol 2014

FFR vs iFR



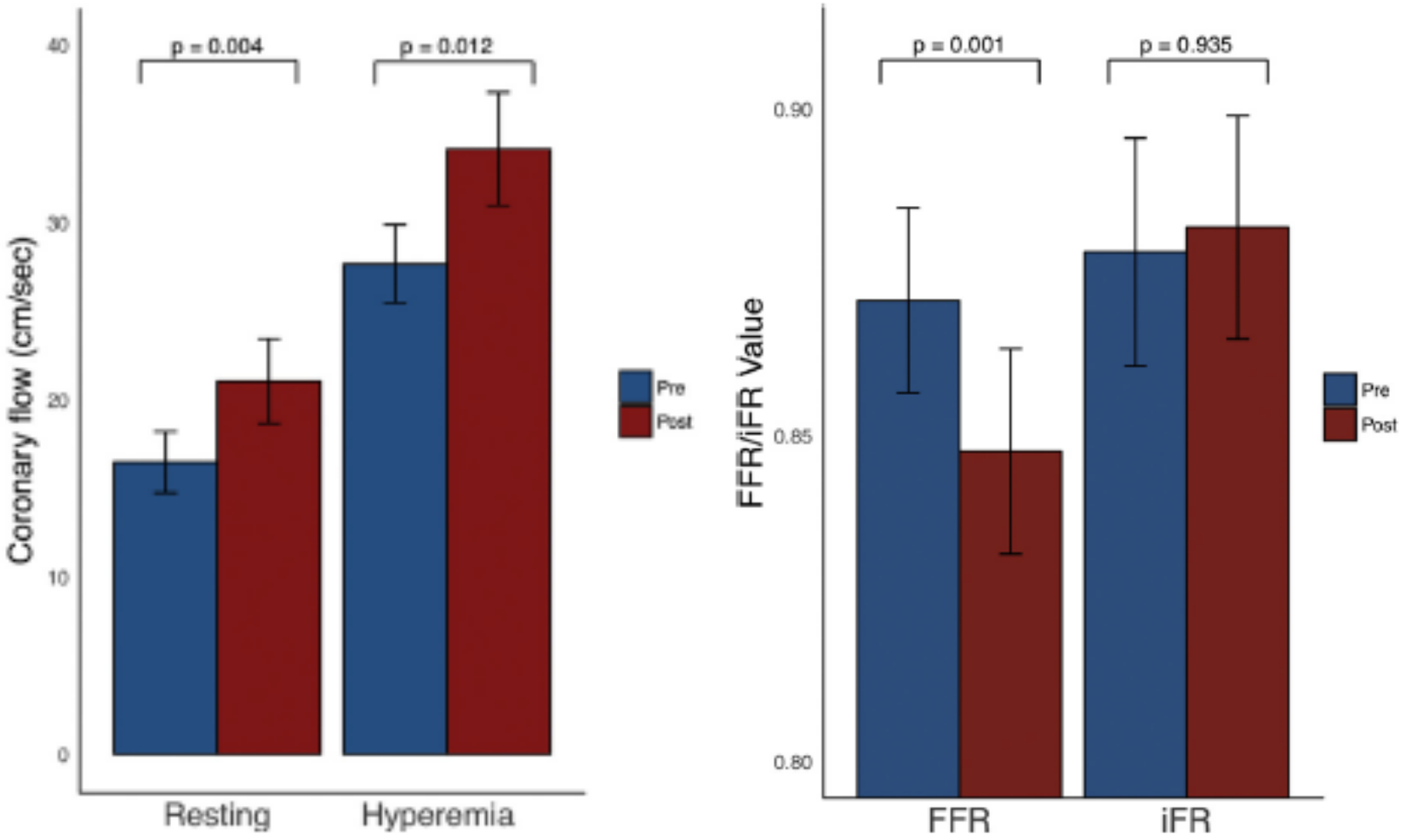
Ahmad et al, JACC Cardiovasc Interv 2018

FFR vs iFR



Ahmad et al, JACC Cardiovasc Interv 2018

FFR vs iFR



Ahmad et al, JACC Cardiovasc Interv 2018

Non-invasive functional testing

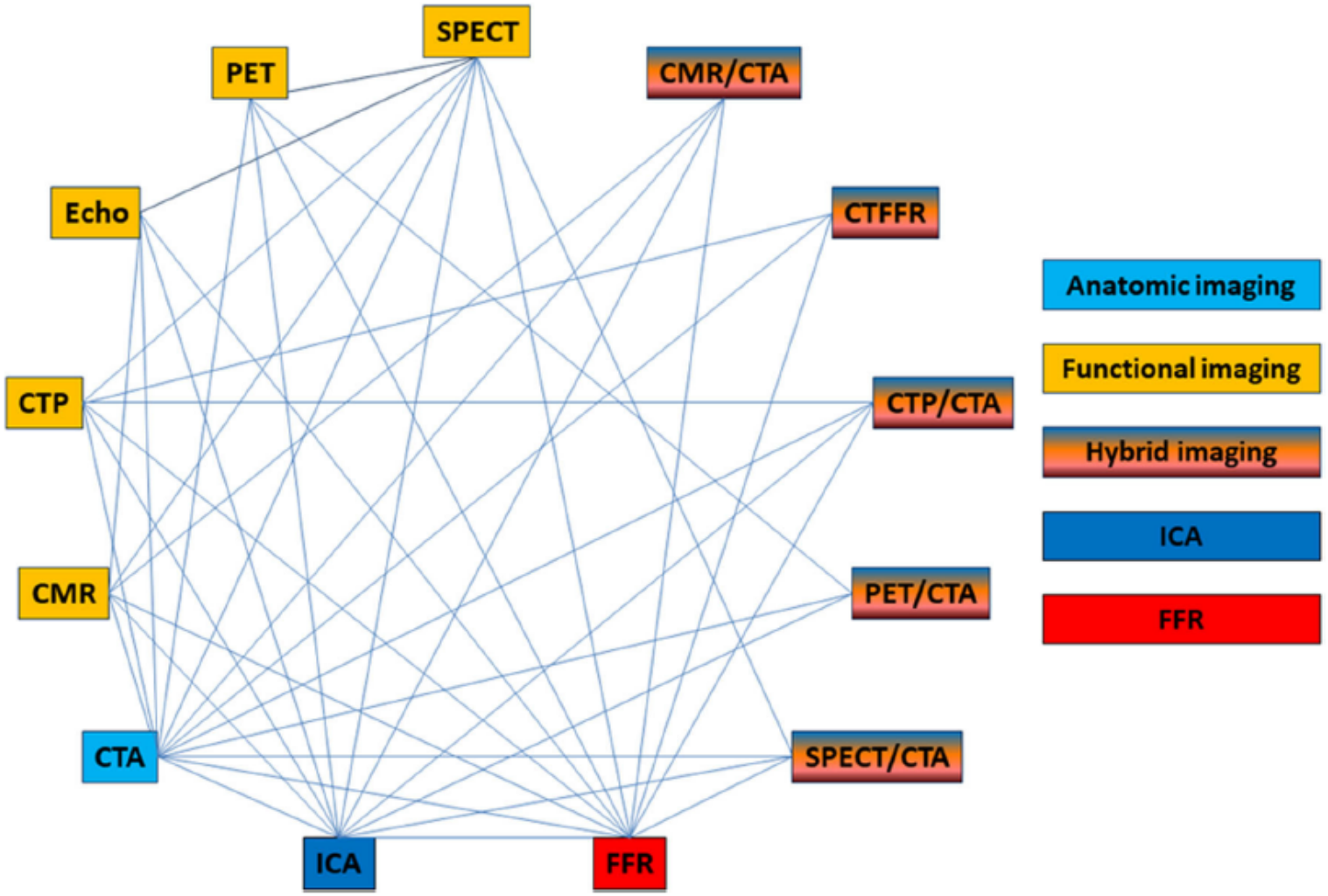
Table 5 | **Sensitivity and specificity of noninvasive stress testing for CAD**

Study	Patients (n)	Stressor	Imaging modality	Comparator modality	Sensitivity for CAD (%)	Specificity for CAD (%)
Cremer *et al.* (2014)[69]	50	Regadenoson	PET	Revascularization	91	—
Burgstahler *et al.* (2008)[70]	23	Adenosine	MRI	Angiography (stenosis >70%)	100	80
Patsilnakos *et al.* (2004)[71]	241	Adenosine	SPECT	Angiography (stenosis >70%)	88.6	72.5
Demirkol *et al.* (2002)[72]	390	Dipyridamole	SPECT	Angiography (stenosis >50%)	100	71
Patsilinakos *et al.* (1999)[73]	50	Adenosine	SPECT and TTE	Angiography (stenosis >70%)	• SPECT: 85 • TTE: 85	• SPECT: 76.7 • TTE: 96.7

CAD, coronary artery disease; MRI, magnetic resonance imaging; PET, positron emission tomography; SPECT, single-photon emission computed tomography; TAVI, transcatheter aortic valve implantation; TTE, transthoracic echocardiography.

Danson et al, Nat Rev Cardiol 2016

Hybrid imaging for CAD



Biondi-Zoccai et al, J Nucl Cardiol 2018

Hybrid imaging for CAD

Table 3. Studies and patients included distinguishing index and reference tests

Index test	Years	Sample size	Reference test: Invasive coronary angiography — Studies (*N* = 654)	Reference test: Invasive coronary angiography — Patients (71,712)	Reference test: Invasive fractional flow reserve — Studies (*N* = 96)	Reference test: Invasive fractional flow reserve — Patients (8764)
Anatomic imaging						
Computed tomography angiography	2010 (1998-2016)	77 (20-1372)	132 (20.3%)	14,592	20 (20.8%)	2157
Functional imaging						
Cardiac magnetic resonance	2009 (1999-2018)	66 (16-823)	93 (14.3%)	10,128	17 (17.7%	1531
Computed tomography perfusion	2013 (2009-2015)	70 (14-101)	5 (0.8%)	250	9 (9.4%)	562
Positron emission tomography	2006 (1988-2013)	53 (19-202)	18 (2.8%)	1144	1 (1.0%)	120
Single photon emission computed tomography	2000 (1982-2018)	76 (5-1853)	233 (35.9%)	28,841	21 (21.9%)	1811
Stress echocardiography	1997 (1988-2015)	70 (7-430)	151 (23.3%)	15,184	6 (6.3%)	373
Hybrid imaging						
Cardiac magnetic resonance/computed tomography angiography	2010 (2010-2013)	72 (47-88)	2 (0.3%)	119	1 (1.0%)	88
Computed tomography perfusion/computed tomography angiography	2013 (2009-2015)	65 (20-101)	8 (1.2%)	396	7 (7.3%)	480
Computed tomography-fractional flow reserve	2014 (2011-2016)	85 (7-254)	0	0	11 (1.5%)	1193
Positron emission tomography/computed tomography angiography	2012 (2009-2013)	74 (33-120)	2 (0.3%)	77	2 (2.1%)	224
Single photon emission computed tomography/ Computed tomography angiography	2013 (2009-2015)	134 (54-225)	5 (0.8%)	592	1 (1.0%)	225

Reported as median (minimum-maximum), sum, or count (%)

Biondi-Zoccai et al, J Nucl Cardiol 2018

Hybrid imaging for CAD

Table 4. Results of pairwise meta-analysis

Reference test	Index test	Sensitivity	Specificity	+ LR	− LR	DOR	AUC of SROC
Invasive coronary angiography	Anatomic imaging	0.95 (0.94-0.96)	0.83 (0.81-0.85)	5.7 (5.0-6.5)	0.06 (0.05-0.07)	94.7 (73.1-122.8)	0.99 (0.99-0.99)
	Functional imaging	0.83 (0.82-0.84)	0.76 (0.23-0.26)	3.5 (3.3-3.6)	0.22 (0.21-0.23)	15.8 (14.5-17.2)	0.90 (0.90-0.90)
	Hybrid imaging	0.90 (0.85-0.93)	0.89 (0.83-0.92)	7.8 (5.3-11.9)	0.11 (0.08-0.17)	68.8 (37.9-124.8)	0.98 (0.97-0.99)
Invasive fractional flow reserve	Anatomic imaging	0.94 (0.90-0.96)	0.46 (0.38-0.55)	1.7 (1.5-2.1)	0.14 (0.09-0.22)	12.2 (7.0-21.4)	0.93 (0.88-0.98)
	Functional imaging	0.78 (0.74-0.82)	0.80 (0.76-0.84)	4.0 (3.3-4.8)	0.27 (0.22-0.32)	14.9 (11.0-20.2)	0.88 (0.86-0.91)
	Hybrid imaging	0.87 (0.83-0.90)	0.82 (0.76-0.87)	4.9 (3.6-6.9)	0.16 (0.12-0.20)	31.0 (19.6-49.3)	0.94 (0.92-0.96)

+ *LR*, positive likelihood ratio; − *LR*, negative likelihood ratio; *AUC*, area under the curve; *DOR*, diagnostic odds ratio; *SROC*, summary receiver-operating curve

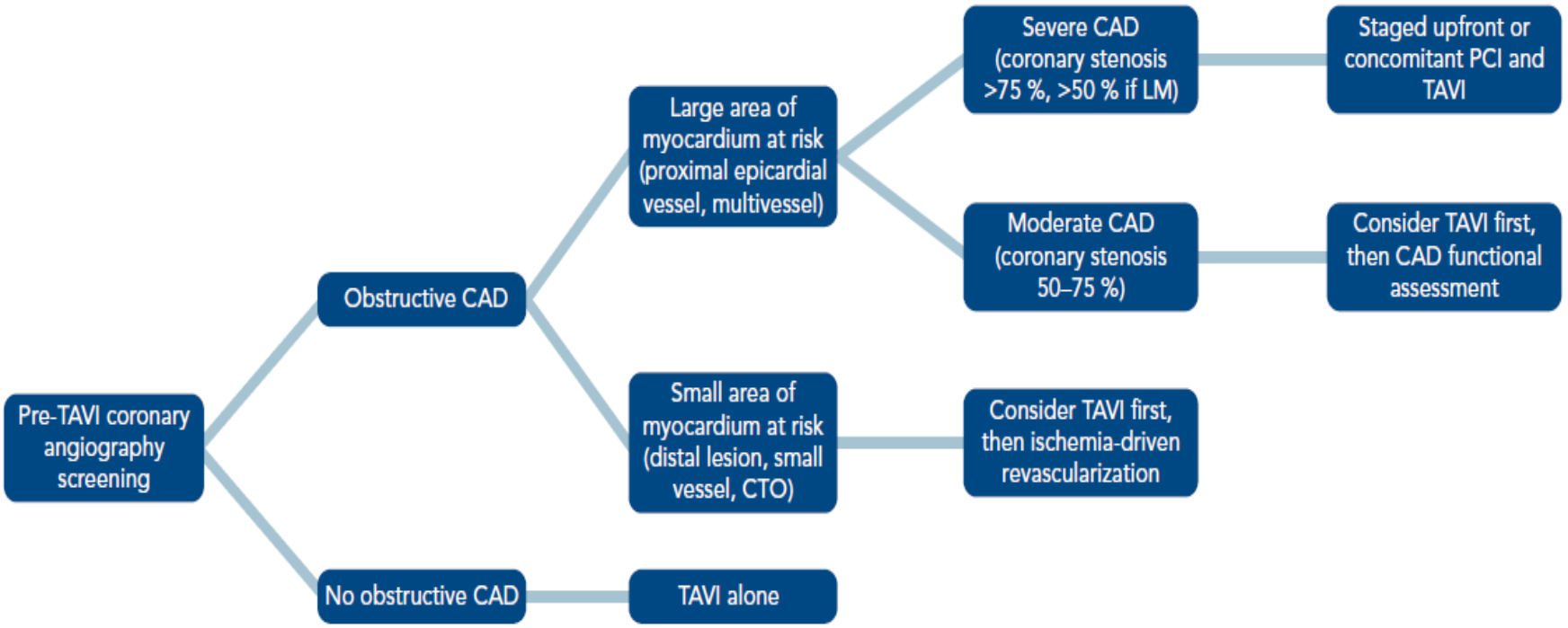
Table 5. Results of multivariate meta-analysis

Reference test	Index test	Sensitivity	Specificity	+ LR	− LR
Invasive coronary angiography	Anatomic imaging	0.96 (0.95-0.97)	0.83 (0.81-0.85)	12.3 (8.7-15.9)	0.16 (0.05-0.27)
	Functional imaging	0.84 (0.83-0.85)	0.77 (0.76-0.78)	6.1 (5.4-6.7)	0.32 (0.29-0.35)
	Hybrid imaging	0.91 (0.89-0.93)	0.87 (0.84-0.90)	13.6 (8.3-19.0)	0.17 (0-0.39)
Invasive fractional flow reserve	Anatomic imaging	0.95 (0.93-0.97)	0.46 (0.38-0.55)	2.0 (1.6-2.5)	0.38 (0.16-0.61)
	Functional imaging	0.79 (0.75-0.83)	0.81 (0.77-0.85)	6.3 (4.5-8.2)	0.42 (0.33-0.50)
	Hybrid imaging	0.88 (0.86-0.91)	0.82 (0.77-0.87)	7.2 (0-15.4)	0.27 (0.12-0.42)

+ *LR*, positive likelihood ratio; − *LR*, negative likelihood ratio

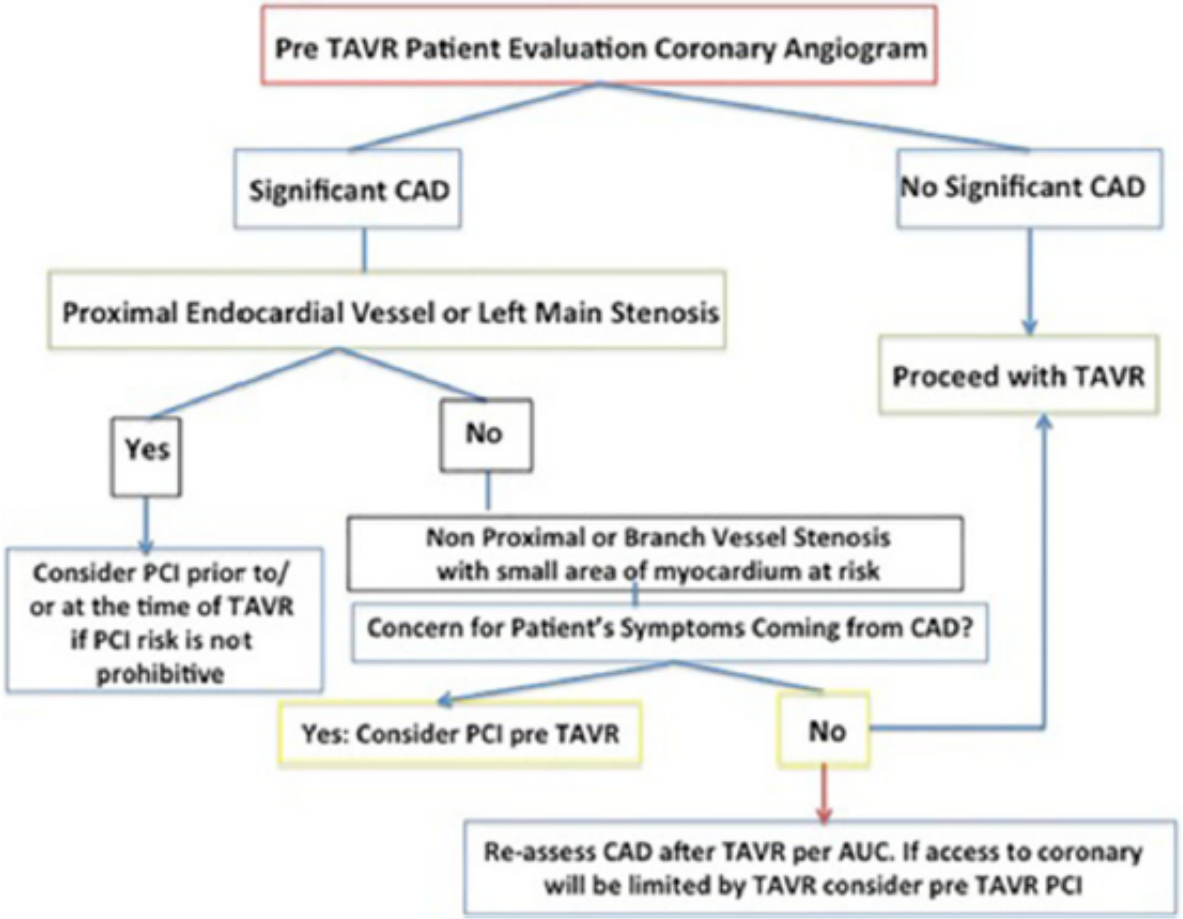
Biondi-Zoccai et al, J Nucl Cardiol 2018

Algorithm for CAD in AS



Cao et al, Interv Cardiol Rev 2018

Another algorithm for CAD in AS



Voudris et al, Curr Treat Options Cardio Med 2018

Upcoming RCT

- Title: PercutAneous Coronary inTerventIon prior to transcatheter aortic VAlve implantaTION: a randomised controlled trial (ACTIVATION)
- Principal investigator: Martyn Thomas
- Primary endpoint: Death or rehospitalization at 1 year
- Sample: 310 patients
- Methods: 1:1 randomisation of pre-TAVI PCI to no pre-TAVI PCI; coronary angiography will be used to identify significant CAD defined as ≥1 lesion of ≥70% in ≥1 epicardial coronary artery; patients without significant CAD will be enrolled into Registry 1; patients whose CAD is not suitable for percutaneous coronary intervention (PCI) will be enrolled into Registry 2
- Years: 2011-2015
- **Results: ??????????????????????????**

http://www.isrctn.com/ISRCTN75836930

Alternatives to EBM

- Eminence based medicine
- Vehemence based medicine
- Eloquence based medicine
- Providence based medicine
- Diffidence based medicine
- Nervousness based medicine
- Confidence based medicine

Isaacs et al, BMJ 1999

Alternatives to EBM

Basis of clinical practice

Basis for clinical decisions	Marker	Measuring device	Unit of measurement
Evidence	Randomised controlled trial	Meta-analysis	Odds ratio
Eminence	Radiance of white hair	Luminometer	Optical density
Vehemence	Level of stridency	Audiometer	Decibels
Eloquence (or elegance)	Smoothness of tongue or nap of suit	Teflometer	Adhesin score
Providence	Level of religious fervour	Sextant to measure angle of genuflection	International units of piety
Diffidence	Level of gloom	Nihilometer	Sighs
Nervousness	Litigation phobia level	Every conceivable test	Bank balance
Confidence*	Bravado	Sweat test	No sweat

* Applies only to surgeons.

Isaacs et al, BMJ 1999

Conclusions

- The management of patients scheduled for TAVI with non-invasive anatomic evidence of CAD remains uncertain
- Awaiting for randomized trials, a cooperative multidisciplinary approach is recommended
- On top of integrating different (sub)specialty expertises, it is paramount to combine functional and anatomic assessment of CAD
- Eventually, feasibility and prognosis remain the key factors in decision making

Many thanks for your attention!

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