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VIII CONGRESSO NAZIONALE
ECOCARDIOCHIRURGIA 2016
MILANO, 21 - 22 - 23 MARZO 2016

MINI CORSO
MEDICINA D'URGENZA
Quale strategia in PS per la SCA NSTEMI

21/03/2016

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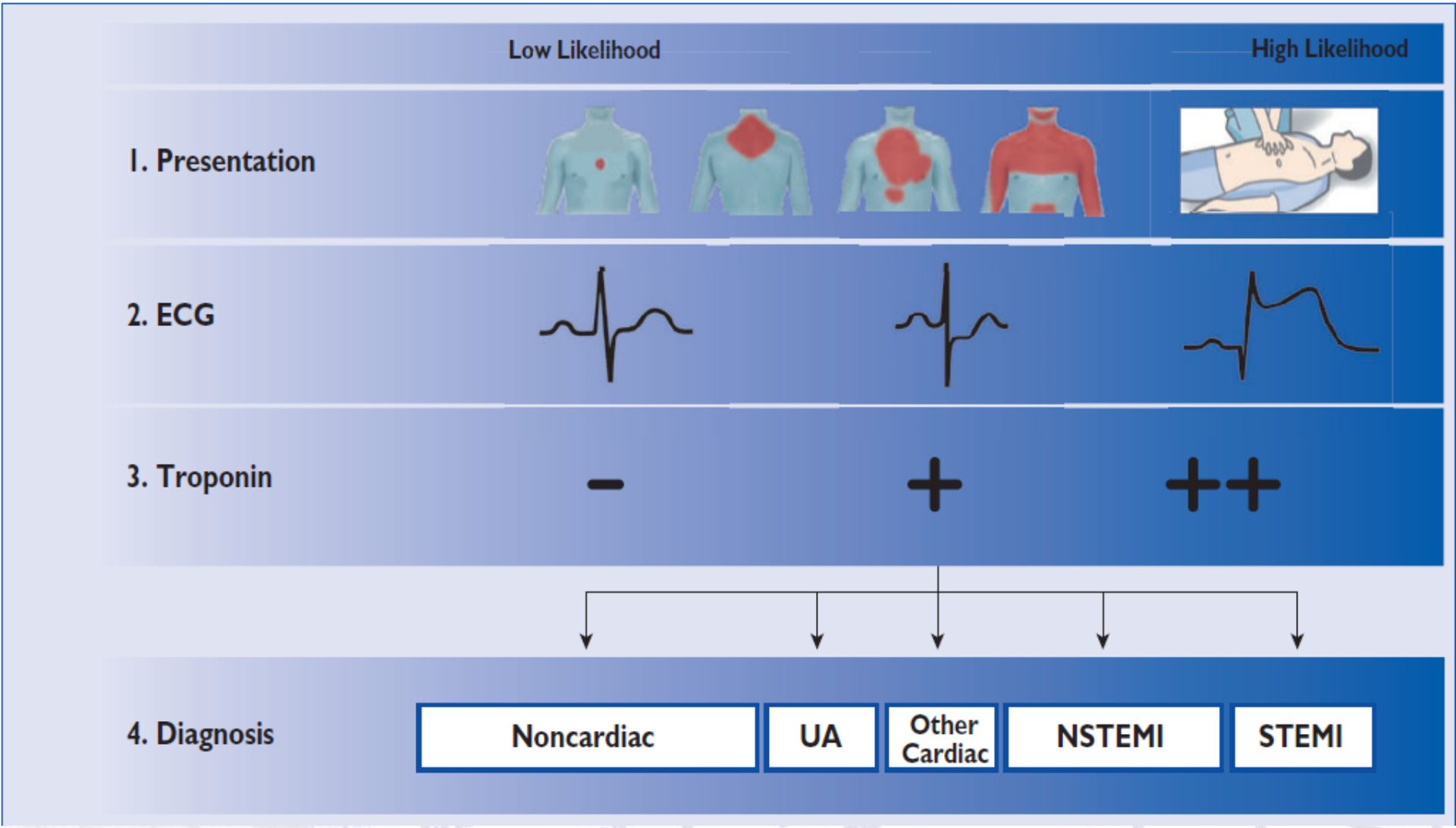

Eur Heart J 2016;37:267-315

ED triage of low-risk patients presenting with chest pain and possible ACS

1. To improve cost-effectiveness *(early discharge strategy)* various strategies have been proposed
2. The primary goal (for ED department) is *exclusion of ACS* rather than detection of CAD (safety priority, i.e. ↑ sensitivity and NPV)

Circulation 2010;122:1756-1776

Array of new diagnostic strategies

1. New cardiac biomarkers (hs-cTn)
2. New risk scores
3. Accelerated diagnostic protocols (ADP)
4. Noninvasive imaging

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European Heart Journal Advance Access published August 29, 2015

European Heart Journal
doi:10.1093/eurheartj/ehv320

ESC GUIDELINES

2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC)

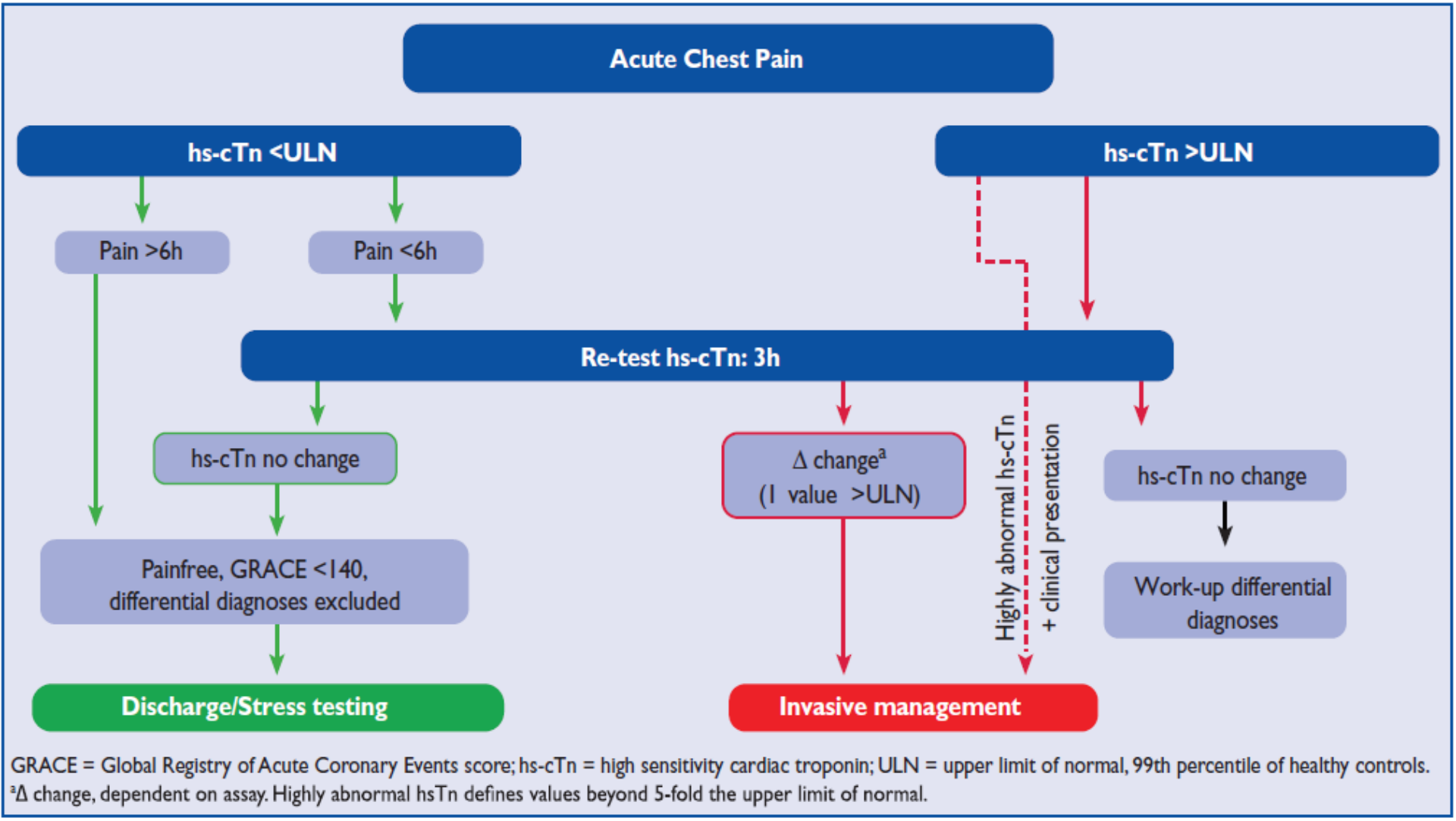
Eur Heart J 2016;37:267-315

Clinical implications of hs-cTn assays

Compared with standard cardiac troponin assays, high-sensitivity assays:
• Have higher negative predictive value for acute MI.
• Reduce the "troponin-blind" interval leading to earlier detection of acute MI.
• Result in a ~4% absolute and ~20% relative increase in the detection of type 1 MI and a corresponding decrease in the diagnosis of unstable angina.
• Are associated with a 2-fold increase in the detection of type 2 MI.
Levels of high-sensitivity cardiac troponin should be interpreted as quantitative markers of cardiomyocyte damage (i.e. the higher the level, the greater the likelihood of MI):
• Elevations beyond 5-fold the upper reference limit have high (>90%) positive predictive value for acute type 1 MI.
• Elevations up to 3-fold the upper reference limit have only limited (50–60%) positive predictive value for acute MI and may be associated with a broad spectrum of conditions.
• It is common to detect circulating levels of cardiac troponin in healthy individuals.
Rising and/or falling cardiac troponin levels differentiate acute from chronic cardiomyocyte damage (the more pronounced the change, the higher the likelihood of acute MI).

Eur Heart J 2016;37:267-315

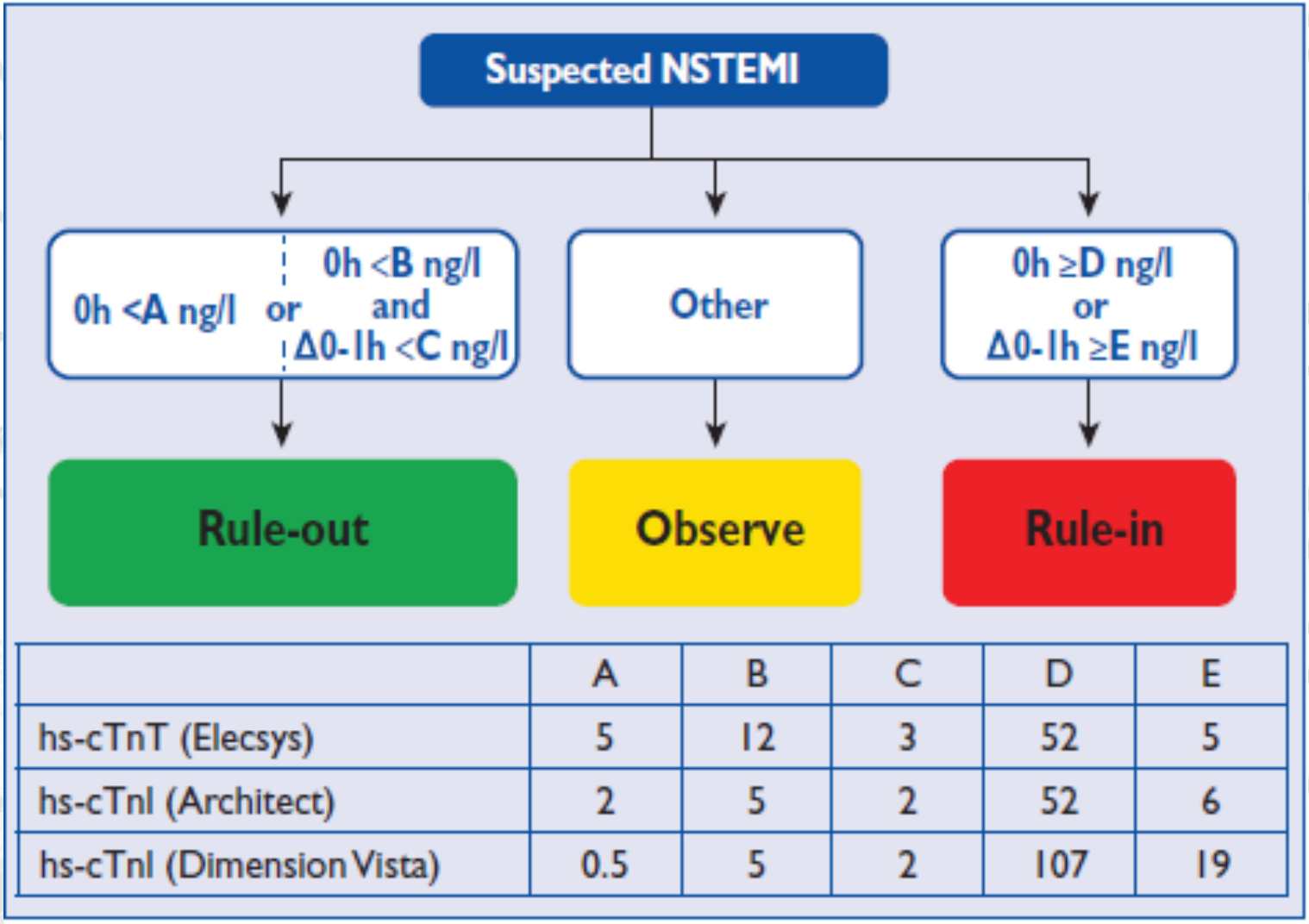
0 h/3 h rule-out algorithm of NSTEMI-ACS using hs-cTn



GRACE = Global Registry of Acute Coronary Events score; hs-cTn = high sensitivity cardiac troponin; ULN = upper limit of normal, 99th percentile of healthy controls.
[a]Δ change, dependent on assay. Highly abnormal hsTn defines values beyond 5-fold the upper limit of normal.

Eur Heart J 2016;37:267-315

0 h/1 h rule-out and rule-in algorithms of NSTEMI-ACS using hs-cTn



	A	B	C	D	E
hs-cTnT (Elecsys)	5	12	3	52	5
hs-cTnI (Architect)	2	5	2	52	6
hs-cTnI (Dimension Vista)	0.5	5	2	107	19

NPV: >98%, PPV 75-80%

Eur Heart J 2016;37:267-315

Array of new diagnostic strategies

1. New cardiac biomarkers (hs-cTn)
2. **New risk scores**
3. Accelerated diagnostic protocols (ADP)
4. Noninvasive imaging

What is the HEART Score?

H = History

E = ECG

A = Age

R = Risk Factors

T = Troponin

HEART

HEART score for chest pain patients			
History	Highly suspicious	2	
	Moderately suspicious	1	
	Slightly suspicious	0	
ECG	Significant ST-deviation	2	
	Non specific repolarisation disturbance / LBTB / PM	1	
	Normal	0	
Age	≥ 65 years	2	
	> 45 and < 65 years	1	
	≤ 45 years	0	
Risk factors	≥ 3 risk factors or history of atherosclerotic disease*	2	
	1 or 2 risk factors	1	
	No risk factors known	0	
Troponin	≥ 3x normal limit	2	
	> 1 and < 3x normal limit	1	
	≤ 1x normal limit	0	
		Total	

***Risk factors for atherosclerotic disease:**

Hypercholesterolemia	Cigarette smoking
Hypertension	Positive family history
Diabetes Mellitus	Obesity

Int J Cardiol 2013;168:2153-2158

International Journal of Cardiology 168 (2013) 2153–2158

Contents lists available at ScienceDirect

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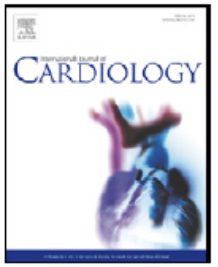

A prospective validation of the HEART score for chest pain patients at the emergency department ☆

B.E. Backus [a,b,*], A.J. Six [c], J.C. Kelder [d], M.A.R. Bosschaert [d], E.G. Mast [e], A. Mosterd [f], R.F. Veldkamp [g], A.J. Wardeh [h], R. Tio [i], R. Braam [j], S.H.J. Monnink [k], R. van Tooren [e], T.P. Mast [l], F. van den Akker [l], M.J.M. Cramer [a], J.M. Poldervaart [m], A.W. Hoes [m], P.A. Doevendans [a]

Array of new diagnostic strategies

1. New cardiac biomarkers (hs-cTn)
2. New risk scores
3. **Accelerated diagnostic protocols (ADP)**
4. Noninvasive imaging

2 h rule-out protocol (TIMI risk score+ ECG at presentation and 99th hs-cTn at 0 and 2 h)

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Validation of High-Sensitivity Troponin I in a 2-Hour Diagnostic Strategy to Assess 30-Day Outcomes in Emergency Department Patients With Possible Acute Coronary Syndrome

J Am Coll Cardiol 2013;62:1242–9

Accuracy (95% CI) of ECG, hs-TnI, TIMI, and ADP for exclusion of MACE

		ECG*	hs-TnI†	TIMI = 0	TIMI ≤1	TIMI = 0 and ECG* and hs-TnI†	TIMI ≤1 and ECG* and hs-TnI†
Sensitivity	ADAPT cohort	18.6 (14.3–23.9)	91.9 (87.8–94.6)	98.4 (95.9–99.4)	85.0 (80.0–88.9)	100 (98.5–100)	99.2 (97.1–99.8)
	APACE cohort	51.9 (43.8–60.0)	82.7 (75.8–88.3)	99.4 (96.5–100)	92.3 (87.0–96.0)	100 (97.7–100)	99.4 (96.5–100)
Negative predictive value	ADAPT cohort	86.9 (85.1–88.5)	98.5 (97.7–99.0)	98.8 (96.9–99.5)	94.9 (93.1–96.3)	100 (98.8–100)	99.7 (98.9–99.9)
	APACE cohort	87.7 (86.0–91.0)	96.3 (94.6–97.5)	99.6 (97.8–100)	97.2 (95.1–98.5)	100 (98.4–100)	99.7 (98.4–100)
Specificity	ADAPT cohort	95.8 (94.6–96.8)	93.1 (91.6–94.3)	23.3 (21.1–25.6)	50.1 (47.4–52.7)	23.1 (20.9–25.3)	48.7 (46.1–51.3)
	APACE cohort	78.1 (75.0–81.0)	91.8 (89.6–93.6)	33.1 (29.7–36.6)	54.3 (50.7–57.9)	30.5 (27.3–34.0)	46.5 (42.9–50.1)
Positive predictive value	ADAPT cohort	44.2 (35.1–53.8)	70.3 (65.1–75.0)	18.6 (16.6–20.8)	23.3 (20.6–26.1)	18.8 (16.8–21.0)	25.6 (22.9–28.5)
	APACE cohort	32.9 (27.1–39.2)	67.5 (60.4–74.1)	23.5 (20.3–27.0)	29.5 (25.5–33.8)	23.0 (19.9–26.3)	27.8 (24.1–31.7)

*ECG alone; any new ischemia at 0 or 2 h is positive. †hs-TnI at 0 and 2 h ≤26.2 ng/l.
ADP = accelerated diagnostic protocol; CI = confidence interval; other abbreviations as in Table 1.

J Am Coll Cardiol 2013;62:1242–9

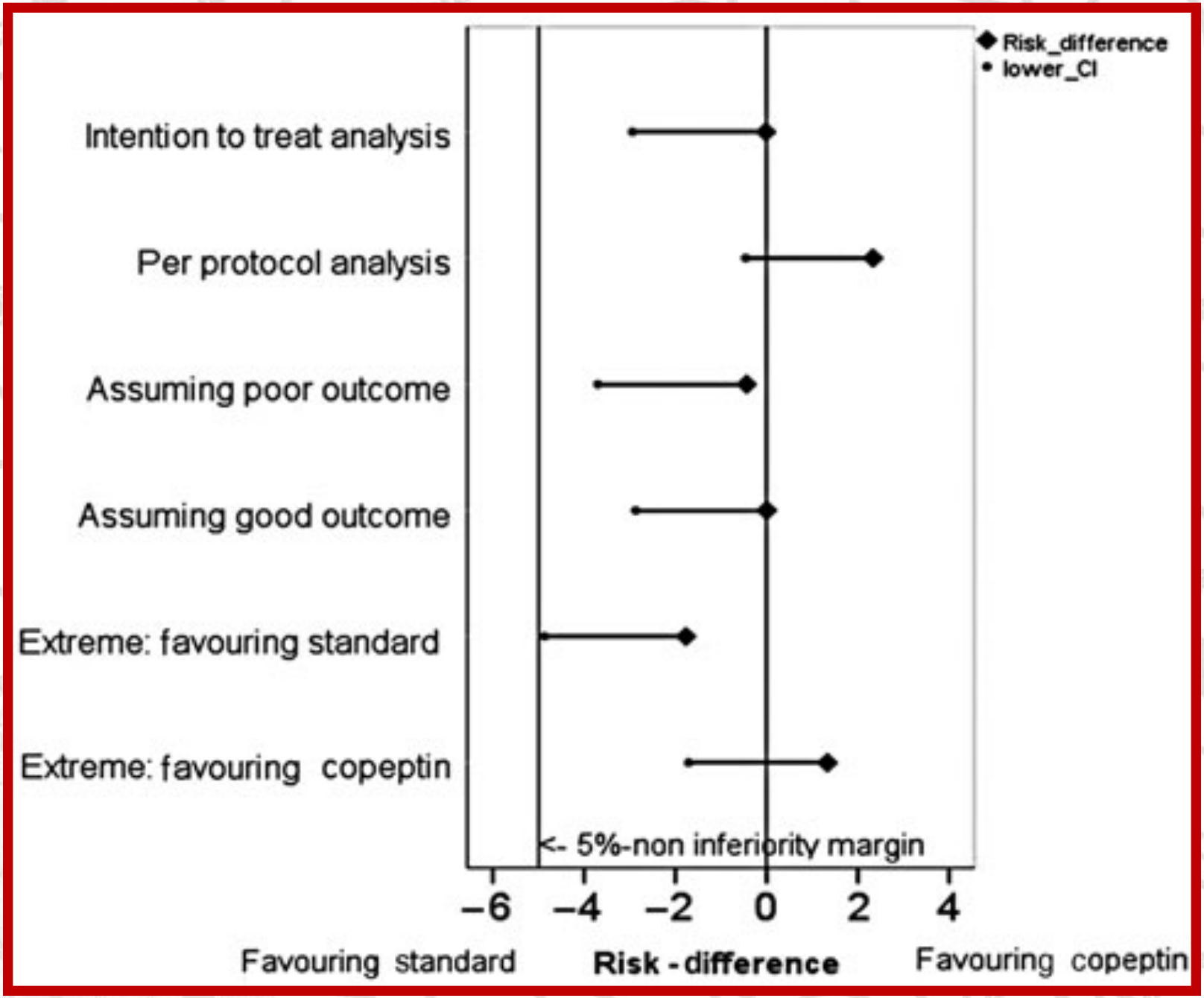
Single dual marker early rule-out strategy (cTn + copeptin)

European Heart Journal (2015) **36**, 369–376
doi:10.1093/eurheartj/ehu178

CLINICAL RESEARCH
Acute coronary syndromes

Early discharge using single cardiac troponin and copeptin testing in patients with suspected acute coronary syndrome (ACS): a randomized, controlled clinical process study

Martin Möckel[1]*, Julia Searle[1], Christian Hamm[2,3], Anna Slagman[1], Stefan Blankenberg[4], Kurt Huber[5], Hugo Katus[6], Christoph Liebetrau[2,3], Christian Müller[7], Reinhold Muller[8], Philipp Peitsmeyer[4], Johannes von Recum[1], Milos Tajsic[5], Jörn O. Vollert[9], and Evangelos Giannitsis[6]



Eur Heart J 2015;36:369–376

Array of new diagnostic strategies

1. New cardiac biomarkers (hs-cTn)
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4. **Noninvasive imaging**

APPROPRIATE UTILIZATION OF CARDIOVASCULAR IMAGING

2015 ACR/ACC/AHA/AATS/ACEP/ASNC/NASCI/SAEM/SCCT/SCMR/SCPC/SNMMI/STR/STS Appropriate Utilization of Cardiovascular Imaging in Emergency Department Patients With Chest Pain

A Joint Document of the American College of Radiology Appropriateness Criteria Committee and the American College of Cardiology Appropriate Use Criteria Task Force

J Am Coll Cardiol 2016;67:853-79

Suspected NSTEMI ACS: early assessment pathway

- With this strategy, imaging may be used early in the evaluation process, with the goal of ruling-in or ruling-out ACS through the identification of rest wall motion abnormalities, perfusion defects, or obstructive CAD *without the need to wait for serial biomarker analysis (triage decision)*

J Am Coll Cardiol 2016;67:853-79

Predictive accuracy of TTE in patients presenting with acute chest pain

	N	Event+	Event−	PPV (%)	NPV (%)
Kontos et al [3]	130	RWA+ 15	29	34	
		RWA− 6	80		93
Sabia et al [4]	169	RWA+ 27	60	31	
		RWA− 2	80		98
Kontos et al [5]	260	RWA+ 41	53	44	
		RWA− 4	162		98
Korosoglou et al [6]	98	RWA+ 19	2	90	
		RWA− 18	59		77
Saeian et al [7]	60	RWA+ 22	3	88	
		RWA+ 2	33		94
Sasaki et al [8]	46	RWA+ 17	1	94	
		RWA− 6	22		79
Horowitz et al [9]	65	RWA+ 34	2	94	
		RWA− 2	27		93
Peels et al [10]	35	RWA+ 22	4	85	
		RWA− 3	14		82
Mohler et al [11]	92	RWA+ 27	0	100	
		RWA− 28	37		57

Cardiol Clin 2005; 23:531–539

Rest MPI in Pts with acute chest pain and a nonischemic ECG

Reference	n	Radiopharmaceutical	Sensitivity, %	Specificity, %	NPV, %	Outcome
Varetto et al[111]	64	Tc-mibi	100	92	100	CAD
Hilton et al[112]	102	Tc-mibi	94	83	99	CAD/AMI
Tatum et al[113]	438	Tc-mibi	100	78	100	AMI
Kontos et al[116]	532	Tc-mibi	93	71	99	AMI
Heller et al[115]	357	Tc-tet	90	60	99	AMI
Kontos et al[114]	620	Tc-mibi	92	67	99	AMI
Udelson et al*[71]	1215	Tc-mibi	96	NR	99	AMI
Schaeffer et al[117]	479	Tc-mibi	77	92	99	ACS

Circulation 2010;122:1756-1776

Outcomes After Coronary Computed Tomography Angiography in the Emergency Department

A Systematic Review and Meta-Analysis of Randomized, Controlled Trials

Edward Hulten, MD, MPH,* Christopher Pickett, MD,† Marcio Sommer Bittencourt, MD,* Todd C. Villines, MD,† Sara Petrillo, MD,‡ Marcelo F. Di Carli, MD,* Ron Blankstein, MD*

Boston, Massachusetts; and Bethesda and Rockville, Maryland

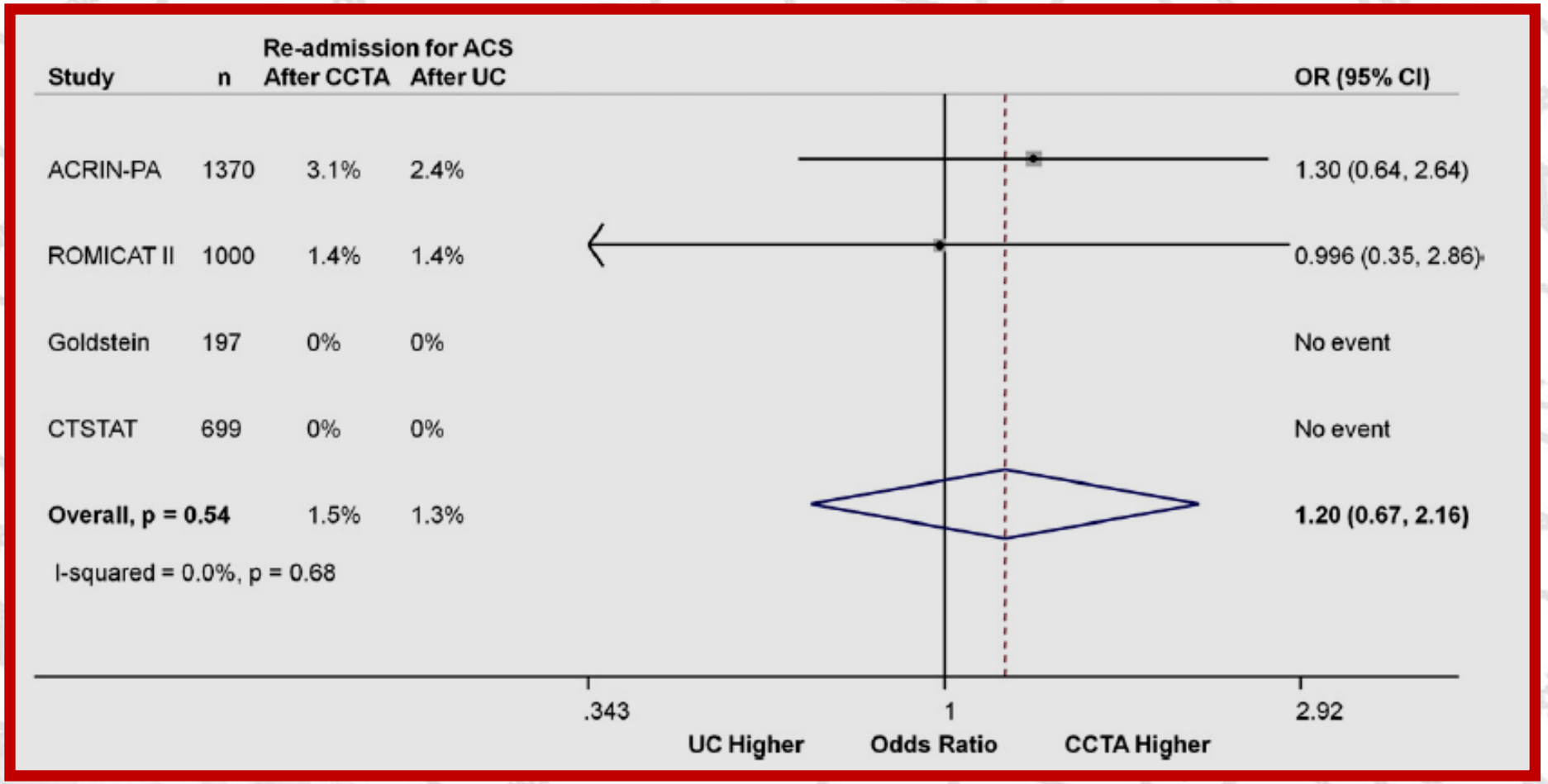
Objectives The aim of the study was to systematically review and perform a meta-analysis of randomized, controlled trials of coronary computed tomography angiography (CCTA) versus usual care (UC) triage of acute chest pain in the emergency department (ED).

Background CCTA allows rapid evaluation of patients presenting to the ED with acute chest pain syndromes; however, the impact of such testing on patient management and downstream testing has emerged as a concern.

Methods We systematically searched for randomized, controlled trials of CCTA in the ED and performed a meta-analysis of clinical outcomes.

Results Four randomized, controlled trials were included, with 1,869 patients undergoing CCTA and 1,397 undergoing UC. There were no deaths and no difference in the incidence of myocardial infarction, post-discharge ED visits, or rehospitalizations. Four studies reported decreased length of stay with CCTA and 3 reported cost savings; 8.4% of patients undergoing CCTA versus 6.3% of those receiving UC underwent invasive coronary angiography (ICA), whereas 4.6% of patients undergoing CCTA versus 2.6% of those receiving UC underwent coronary revascularization. The odds ratio of ICA for CCTA patients versus UC patients was 1.36 (95% confidence interval [CI]: 1.03 to 1.80, $p = 0.030$), and for revascularization, it was 1.81 (95% CI: 1.20 to 2.72, $p = 0.004$). The absolute increase in ICA after CCTA was 21 per 1,000 CCTA patients (95% CI: 1.8 to 44.9), and the number needed to scan was 48. The absolute increase in revascularization after CCTA was 20 per 1,000 patients (95% CI: 5.0 to 41.4); the number needed to scan was 50. Both percutaneous coronary intervention and coronary artery bypass graft surgery independently contributed to the significant increase in revascularization.

Conclusions Compared with UC, the use of CCTA in the ED is associated with decreased ED cost and length of stay but increased ICA and revascularization. (J Am Coll Cardiol 2013;61:880–92)

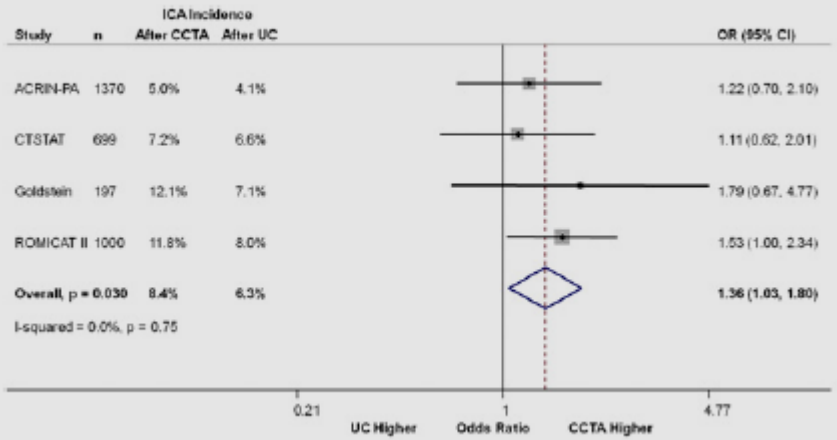


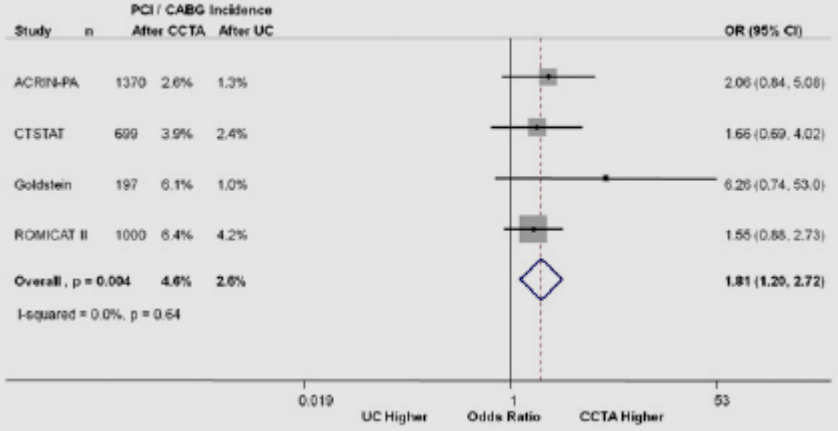
J Am Coll Cardiol 2013;61:880–92

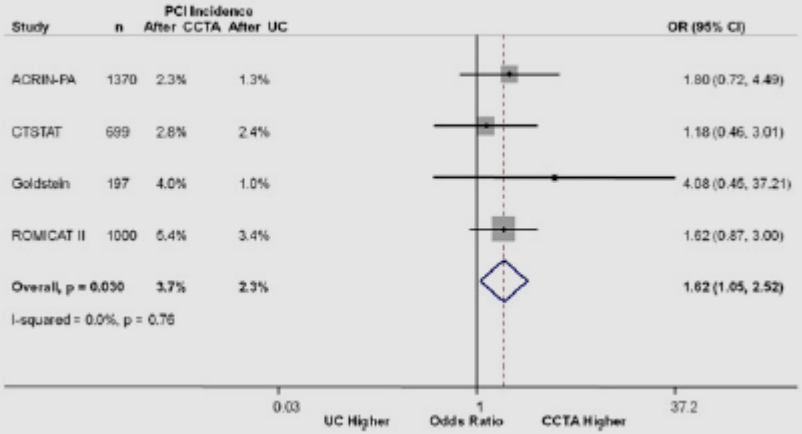
LOS and cost outcomes

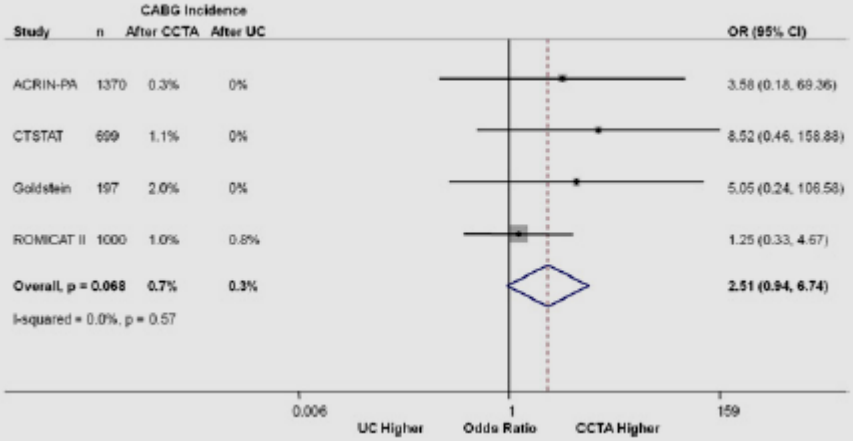
	Goldstein et al. (18)	CT-STAT (19)	ACRIN-PA (21)	ROMICAT II (20)	
Primary outcome	Safety, diagnostic efficiency	Time to diagnosis	Safety	Hospital LOS	
LOS definition	Time to diagnosis	Time to diagnosis	Hospital duration	Time to diagnosis	Hospital duration
UC LOS, h	15.0 (7.3–20.2)	6.2 (4.2–19.0)	24.8	18.7 (11.8)	30.8 (28.0)
CCTA LOS, h	3.4 (2.3–14.8)	2.9 (2.1–4.0)	18	10.4 (12.6)	23.2 (37.0)
UC-CCTA LOS, h	11.6*	3.4*	6.8*	8.3*	7.6*
Reduction, %	77.3*	54.8*	27.4*	44.3*	24.7*
Cost Definition	**ED Cost**	**ED Cost**	**N/A**	**ED Cost**	**Total Hospital**
UC cost, US$	1,872 (1,727–2,069)	3,458 (2,900–4,297)	N/A	2,566 (1,323)	3,874 (5,298)
CCTA cost, US$	1,586 (1,413–2,059)	2,137 (1,660–3,077)	N/A	2,101 (1,070)	4,026 (6,792)
UC-CCTA cost, US$	286*	1,321*	N/A	465*	−152
Reduction, %	15.3*	38.2*	N/A	18.1*	−3.9

J Am Coll Cardiol 2013;61:880–92









J Am Coll Cardiol 2013;61:880–92

Low/intermediate likelihood initial diagnosis of NSTEMI (early assessment pathway)

Normal o nonischemic on initial ECG, normal initial troponin	Appropiate use
Echocardiography	R
CMR	R
SPECT	M*
CCTA (coronary CT angiography)	A
Ccath (catheter-based coronary angiography)	R

A: appropiate
M*:may be appropiate as determined by lack of consensus by rating panel
R: rarely appropriate
M: may be appropiate with rating panel consensus

J Am Coll Cardiol 2016;67:853-79

Equivocal initial diagnosis of NSTEMI (early assessment pathway)

Equivocal initial troponin or single troponin elevation without additional evidence of ACS	Appropiate use
Echocardiography	M*
CMR	M*
SPECT	A
CCTA (coronary CT angiography)	A
Ccath (catheter-based coronary angiography)	R

A: appropiate
M*:may be appropiate as determined by lack of consensus by rating panel
R: rarely appropriate
M: may be appropiate with rating panel consensus

J Am Coll Cardiol 2016;67:853-79

Suspected NSTEMI ACS: observational pathway

- Pts in this pathway have undergone initial ECG and biomarker testing that has not led to a clear diagnosis of ACS, but ACS is still a consideration. Thus, *serial ECG and troponin biomarker analysis are used* to rule out NSTEMI or ACS (or rule it in)
- By definition, at least *9-24 h out from ED presentation*

J Am Coll Cardiol 2016;67:853-79

Studies of exercise ECG in accelerated diagnostic protocols

Reference	No. of Patients	Positive Tests, %†	Negative Predictive Value, %‡	Positive Predictive Value, %‡	Adverse Exercise Test Events
Tsakonis et al[78]	28	18	100		0
Kerns et al[79]	32	0	100		0
Gibler et al[80]	782	1	99	44	0
Gomez et al§[69]	100	7	100	0	0
Zalenski et al[81]	224	8	98	16	0
Polanczyk et al[82]	276	24	98	15	0
Kirk et al[83]	212	13	100	57	0
Diercks et al[84]	747	3	99	37	0
Sarullo et al[86]	190	30	99	77	0
Amsterdam et al[77]	1000	13	89	33	0
Ramakrishna et al[85]	125	27	100	8	0

Circulation 2010;122:1756-1776

Stress echocardiography in Pts presenting to the ED with chest pain

Reference	Test	No. of Patients	Follow-Up, mo	Positive Test, n	ACE With Positive Test, n	PPV, %	Negative Test, n	ACE With Negative Test, n	NPV, %
Geleijnse[127]	DSE	80	6	36	0 Death 0 MI 9 UA 10 Revasc	53	44	0 Death 1 MI 1 UA 2 Revasc	89
Bholasingh[124]	DSE	377	6	26	1 Death 2 MI 2 UA 3 Revasc	30	351	1 Death 0 MI 6 UA 7 Revasc	96
Nucifora[125]	DSE	107	2	20	0 Death 0 MI 1 Revasc	5	87	0 Death 4 MI 4 Revasc	100
Trippi[94]	DSE	137	3	7	1 MI 1 UA	29	130	0 Death 0 MI 0 Revasc	98

Circulation 2010;122:1756-1776

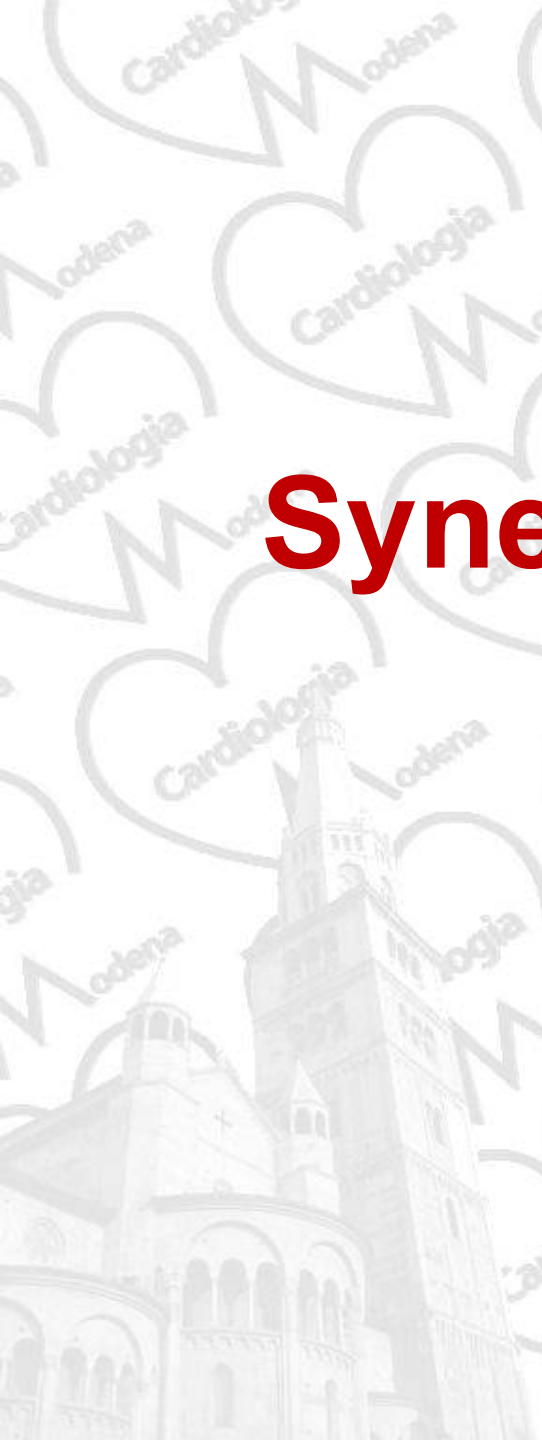
Suspected NSTEMI (observational pathway)

Serial ECG and troponin negative for NSTEMI/ACS		Appropiate use
Exercise ECG		A
Echocardiography	Rest	R
	Stress/Rest	A
CMR	Rest	R
	Stress/Rest	A
SPECT/PET	Rest	R
	Stress/Rest	A
CCTA (coronary CT angiography)		A
Ccath (catheter-based coronary angiography)		R

A: appropiate
M*:may be appropiate as determined by lack of consensus by rating panel
R: rarely appropriate
M: may be appropiate with rating panel consensus

J Am Coll Cardiol 2016;67:853-79

Synergistic workflows



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hs-Troponin I Followed by CT Angiography Improves Acute Coronary Syndrome Risk Stratification Accuracy and Work-Up in Acute Chest Pain Patients

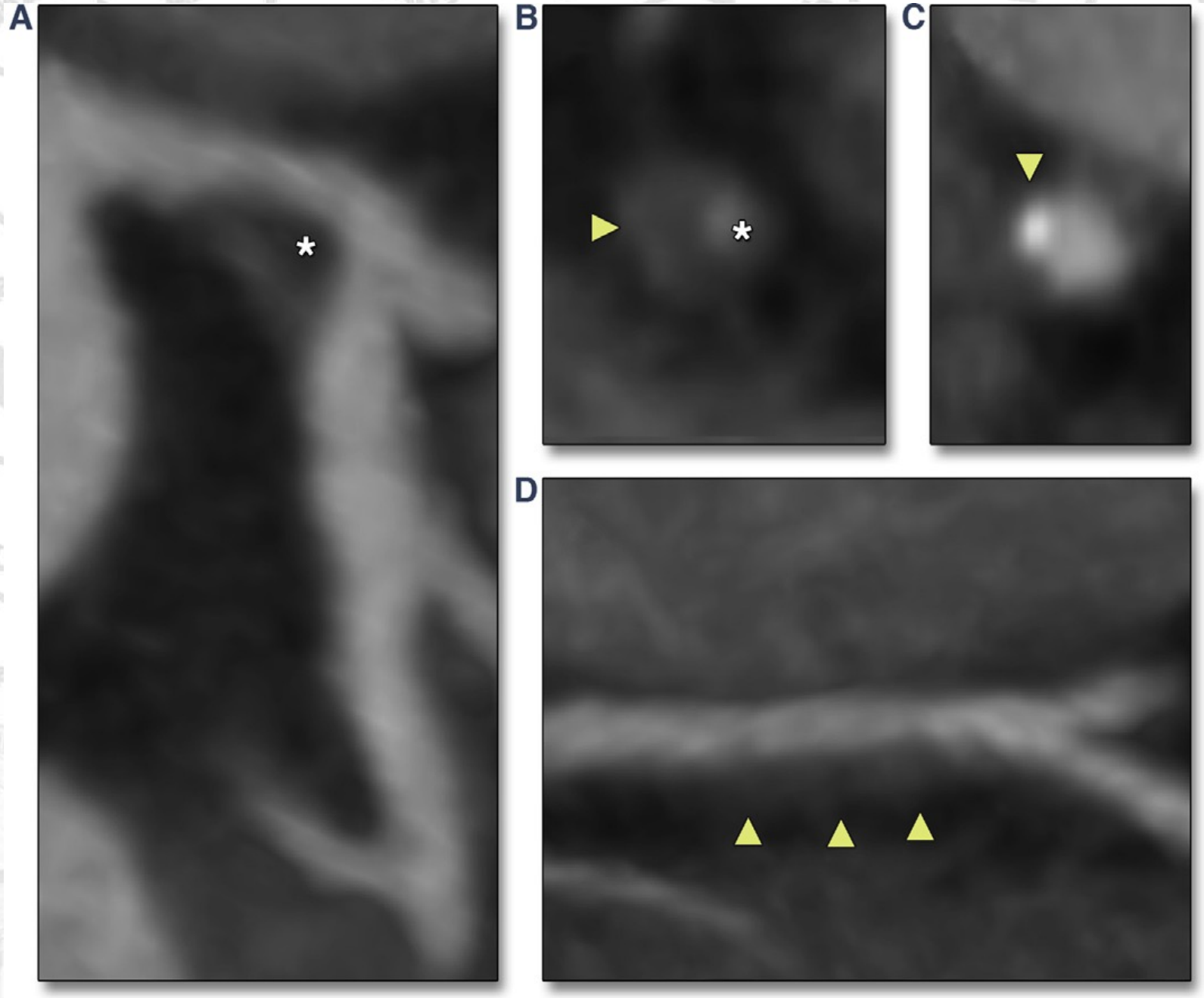
Results From ROMICAT II Trial

Maros Ferencik, MD, PhD,*†‡ Ting Liu, MD,†‡§ Thomas Mayrhofer, PhD,†‡ Stefan B. Puchner, MD,†‡‖ Michael T. Lu, MD,†‡ Pal Maurovich-Horvat, MD, MPH,¶ J. Hector Pope, MD,# Quynh A. Truong, MD, MPH,†‡** James E. Udelson, MD,†† W. Frank Peacock, MD,‡‡ Charles S. White, MD,§§ Pamela K. Woodard, MD,‖‖ Jerome L. Fleg, MD,¶¶ John T. Nagurney, MD, MPH,## James L. Januzzi, MD,*** Udo Hoffmann, MD, MPH†‡***

hsTnI + early advanced coronary CTA

- *Traditional features* of CAD (no CAD, nonobstructive CAD, ≥50% stenosis)
- *Advanced features* of CAD (≥ 50% stenosis, high-risk plaque features: positive remodeling, low <30-Hounsfield units plaque, napkin-ring sign, spotty calcium)

J Am Coll Cardiol Img 2015;8:1272–81



J Am Coll Cardiol Img 2015;8:1272–81

Diagnostic accuracy for ACS of conventional cTn + traditional CTA VS hsTnI + advanced CTA

	Sensitivity	Specificity	PPV	NPV	AUC
Conventional troponin and traditional CTA	100.0 (82.4-100.0)	48.2 (39.7-56.8)	20.7 (12.9-30.4)	100.0 (94.7-100.0)	0.74 (0.70-0.78)
hsTnI and advanced CTA	100.0 (82.4-100.0)	68.1 (59.7-75.7)	29.7 (18.9-42.4)	100.0 (96.2-100.0)	0.84 (0.80-0.88)

p < 0.001

J Am Coll Cardiol Img 2015;8:1272–81

Caveats

Intermediate-risk patients

- *Prior history of CAD (PCI)*
- ECG with ST-segment depression 0.05-0.10 mV and/or flat or inverted T waves <0.20 mV deep
- Diabetes mellitus
- Chronic kidney disease
- Advanced age

Patterns confounding the ECG diagnosis of ACS

Chest pain as a marker of restenosis after PCI

Author	Year	Patients (N.)	Time to follow-up angiography (months)	Sensitivity (%)	Specificit (%)	PPV (%)	NPV (%)	Accuracy (%)
Nobuyoshi [9]	1988	229	6-12	41	95	91	59	66
Hect [11]	1991	116	6	64	34	59	39	52
Hernandez [12]	1992	839	6-9	52	NA	NA	NA	NA
Legrand [13]	1997	325	6	56	86	51	89	80
Ruygrok [8]	2001	2690	6	45	NA	NA	NA	NA

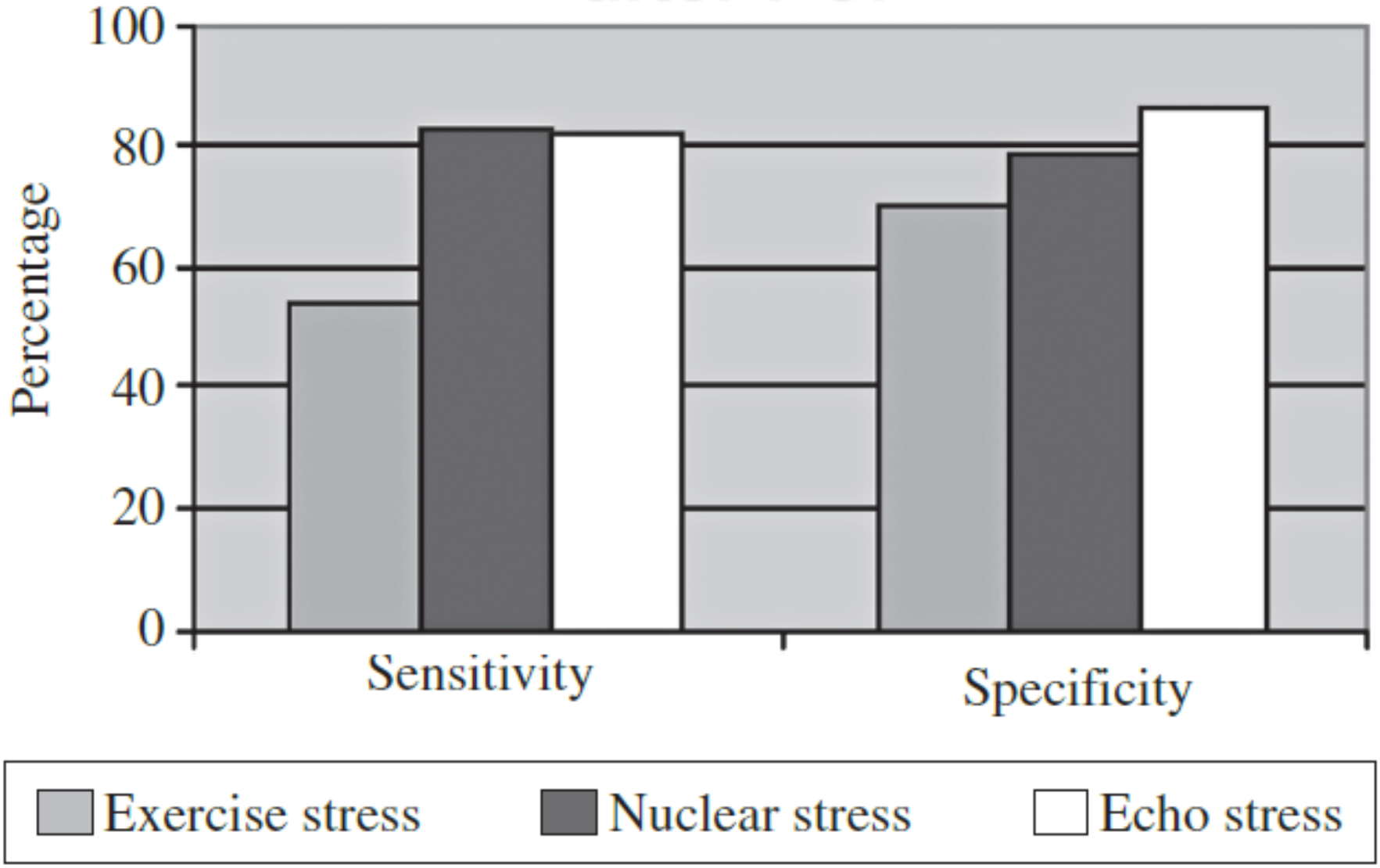
Minerva Cardioangiol 2011;59:321-30

- The ability to detect ischemia on stress imaging seems to be related to time from initial PCI (appeared *non-informative within the first 30-days* due to high-rates of FP results)

- Hence, when confronted with a Pt presenting with *early recurrence* of symptoms, a clinician may consider proceeding directly to coronary angiography

J Am Coll Cardiol 1994;24:260-6
Am Heart J 1997;133:240-8

Detecting restenosis of symptomatic Pts after PCI



Minerva Cardioangiol 2011;59:321-30

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2013 ESC guidelines on the management of stable coronary artery disease

The Task Force on the management of stable coronary artery disease of the European Society of Cardiology

An imaging stress test should be considered in symptomatic patients with prior revascularization (PCI or CABG).	IIa	B

Coronary CTA is not recommended in patients with prior coronary revascularization. | III | C

5-THM

1. Basic clinical tools provide powerful estimates of ACS risk diagnosis
2. High-risk Pts require any further testing
3. Low risk individuals should be triaged via available testing options
4. Array of new diagnostic (early discharge) strategies
5. Lacking of synergistic workflow and comparative studies