C’è qualcosa di nuovo per la dissezione aortica

Medicina di Emergenza-Urgenza: il volto

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NAPOLI 18 - 11 -2016

x congresso nazionale
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NAPOLI 18-20 NOVEMBRE 2016

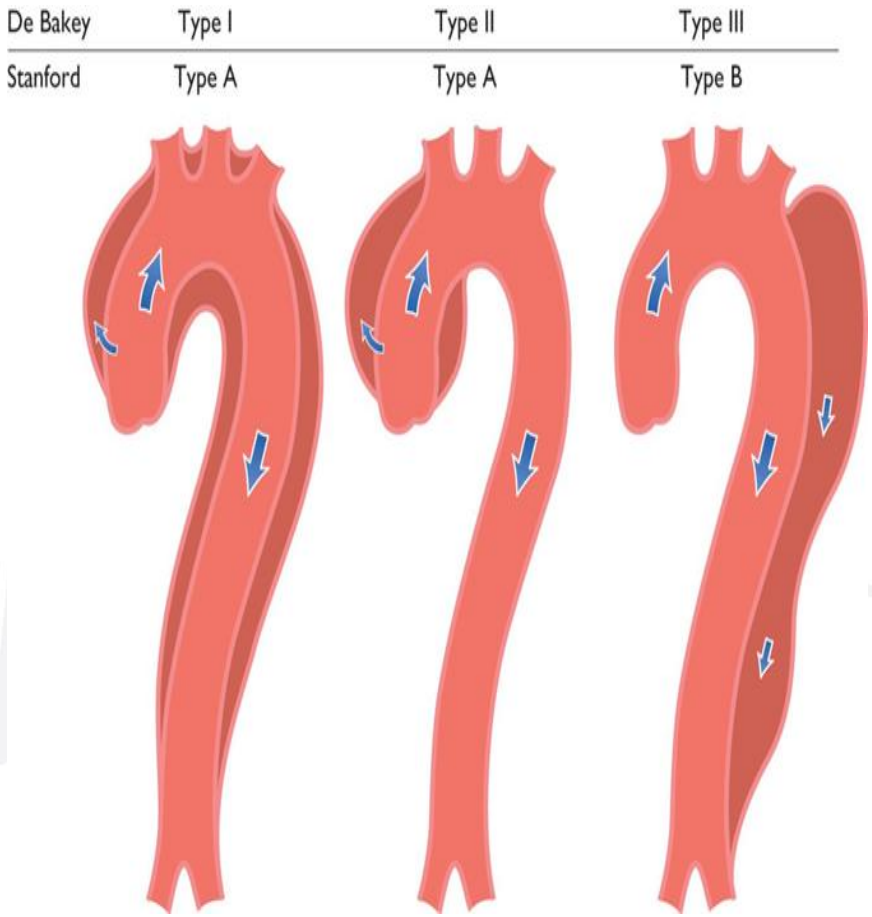
Sindrome Aortica Acuta (SAA)

- **Dissezione aortica** 80-90%
  Stanford A 60-70%
  Stanford B 20-30%

- **Ematoma intramurale aortico** 5-20%
  Stanford A 20-30%
  Stanford B 70-80%

- **Ulcera penetrante aortica** 2-7%

- **Rottura/fissurazione aortica**

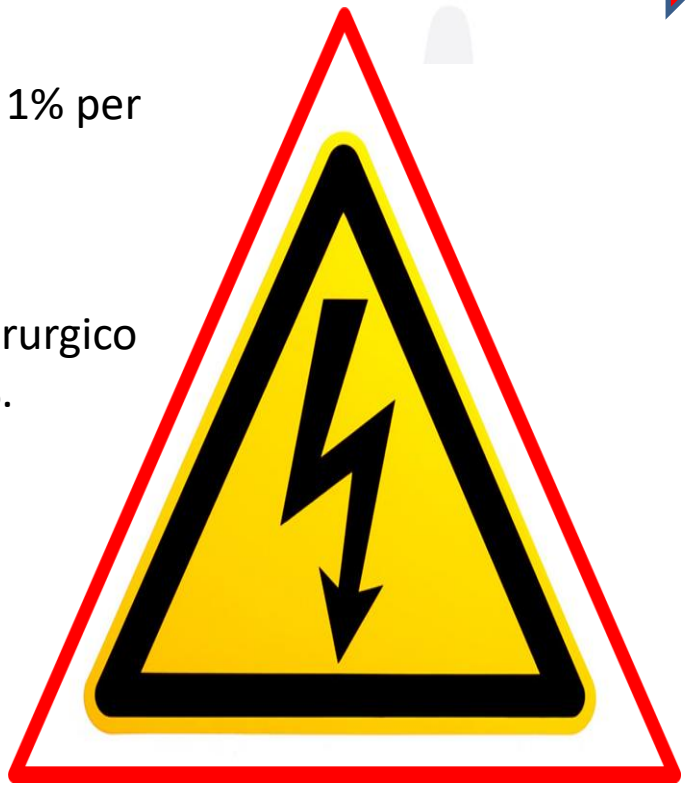


SAA: Epidemiologia e Clinica

Bassa incidenza

2,6-3,5 casi/100.000 persone/anno.
0.2-2% dei dolori toracici in Dip Emergenza.

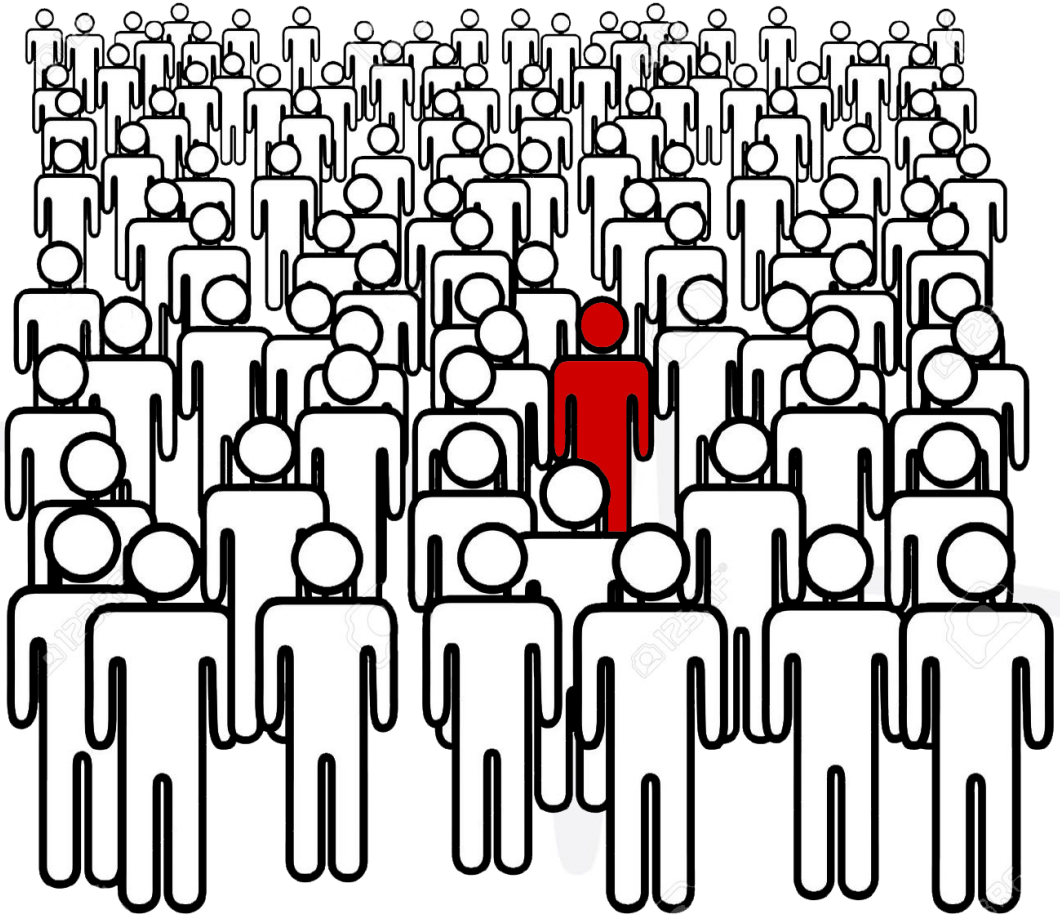
La mortalità aumenta del 1% per ogni ora trascorsa senza trattamento.
Mortalità a 1 mese 80%.
Il trattamento medico-chirurgico riduce la mortalità al 30%.



Numerose diagnosi differenziali.

Conseguenze mortali

Eterogeneità clinica



Clinical Policy: Critical Issues in the Evaluation and Management of Adult Patients with Suspected Acute Nontraumatic Thoracic Aortic Dissection

ACEP Board of Directors, Ann Emerg Med 2015

1) In adult patients with suspected acute nontraumatic thoracic aortic dissection, are there **clinical decision rules** that identify a group of patients at very low risk for the diagnosis of thoracic aortic dissection?

2) Is a negative serum **dimer** sufficient to identify a group of patients at very low risk for the diagnosis of thoracic aortic dissection?

3) Does a normal **chest X ray** rule out thoracic aortic dissection in patients at low risk?

4) Does an abnormal **bedside TTE** establish the diagnosis of thoracic aortic dissection?

Future Research - **Large prospective studies** are needed to better assess historical information, physical examination findings, and diagnostic testing combinations for the diagnosis of acute nontraumatic aortic dissection.

Future Research - A prospective study evaluating D-dimer levels on undifferentiated ED patients who present with signs and symptoms concerning for thoracic aortic dissection is warranted. **Studies clarifying the best way to integrate D-dimer testing into clinical algorithms that include risk stratification are needed**

Future research should address the **diagnostic characteristics of CXR and of bedside TTE by emergency physicians in ED** patients with acute presentations concerning for thoracic aortic dissection.

VIII Congresso Nazionale Rimini 19-21 Ottobre 2012

VIII Congresso Nazionale SIMEU
Rimini

COMUNICAZIONI

Sabato 20 Ottobre 2012*

Performance of D-dimer testing for the diagnosis of aortic dissection in the Emergency Department

F. Giachino, C. Moiraghi, F. Morello
DEA, AOU San Giovanni Battista, Torino, Italia

Usefulness of D-dimer associated with a standardized clinical score to rule out aortic dissection

P. Nazerian, L. Bitossi, S. Vanni, C. Gigli, G. Giannazzo, G. Pepe, S.Grifoni
Emergency Department, AOU Careggi, Florence, Italy

Original scientific paper

Diagnostic performance of the aortic dissection detection risk score in patients with suspected acute aortic dissection

Peiman Nazerian[1], Francesca Giachino[2], Simone Vanni[1], Maria G Veglio[2], Matteo Castelli[1], Davide Lison[2], Luca Bitossi[1], Corrado Moiraghi[2], Stefano Grifoni[1] and Fulvio Morello[2]

European Heart Journal Acute Cardiovascular Care
EUROPEAN SOCIETY OF CARDIOLOGY®

Medicine®
DIAGNOSTIC ACCURACY STUDY

OPEN

Plasma Lactate Dehydrogenase Levels Predict Mortality in Acute Aortic Syndromes

A Diagnostic Accuracy and Observational Outcome Study

Fulvio Morello, MD, PhD, Anna Ravetti, MD, Peiman Nazerian, MD, Giovanni Liedl, MD, Maria Grazia Veglio, MD, Stefania Battista, MD, Simone Vanni, MD, Emanuele Pivetta, MD, Giuseppe Montrucchio, MD, Giulio Mengozzi, MD, Mauro Rinaldi, MD, Corrado Moiraghi, MD, and Enrico Lupia, MD, PhD

Contents lists available at ScienceDirect

International Journal of Cardiology

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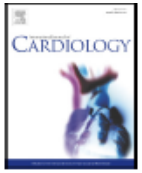


Combined use of aortic dissection detection risk score and D-dimer in the diagnostic workup of suspected acute aortic dissection

Peiman Nazerian [a,1,2], Fulvio Morello [b,*,1,2], Simone Vanni [a,1], Alessia Bono [b,1], Matteo Castelli [a,1], Daniela Forno [b,1], Chiara Gigli [a,1], Flavia Soardo [b,1], Federica Carbone [b,1], Enrico Lupia [b,1], Stefano Grifoni [a,1]

[a] *Department of Emergency Medicine, Careggi University Hospital, Firenze, Italy*
[b] *Department of Emergency, A.O. Città della Salute e della Scienza, Molinette Hospital, Torino, Italy*

Intern Emerg Med (2014) 9:665–670
DOI 10.1007/s11739-014-1080-9

EM - ORIGINAL

Diagnostic performance of emergency transthoracic focus cardiac ultrasound in suspected acute type A aortic dissection

Peiman Nazerian · Simone Vanni · Matteo Castelli · Fulvio Morello · Camilla Tozzetti · Giovanni Zagli · Giuseppe Giannazzo · Ruben Vergara · Stefano Grifoni

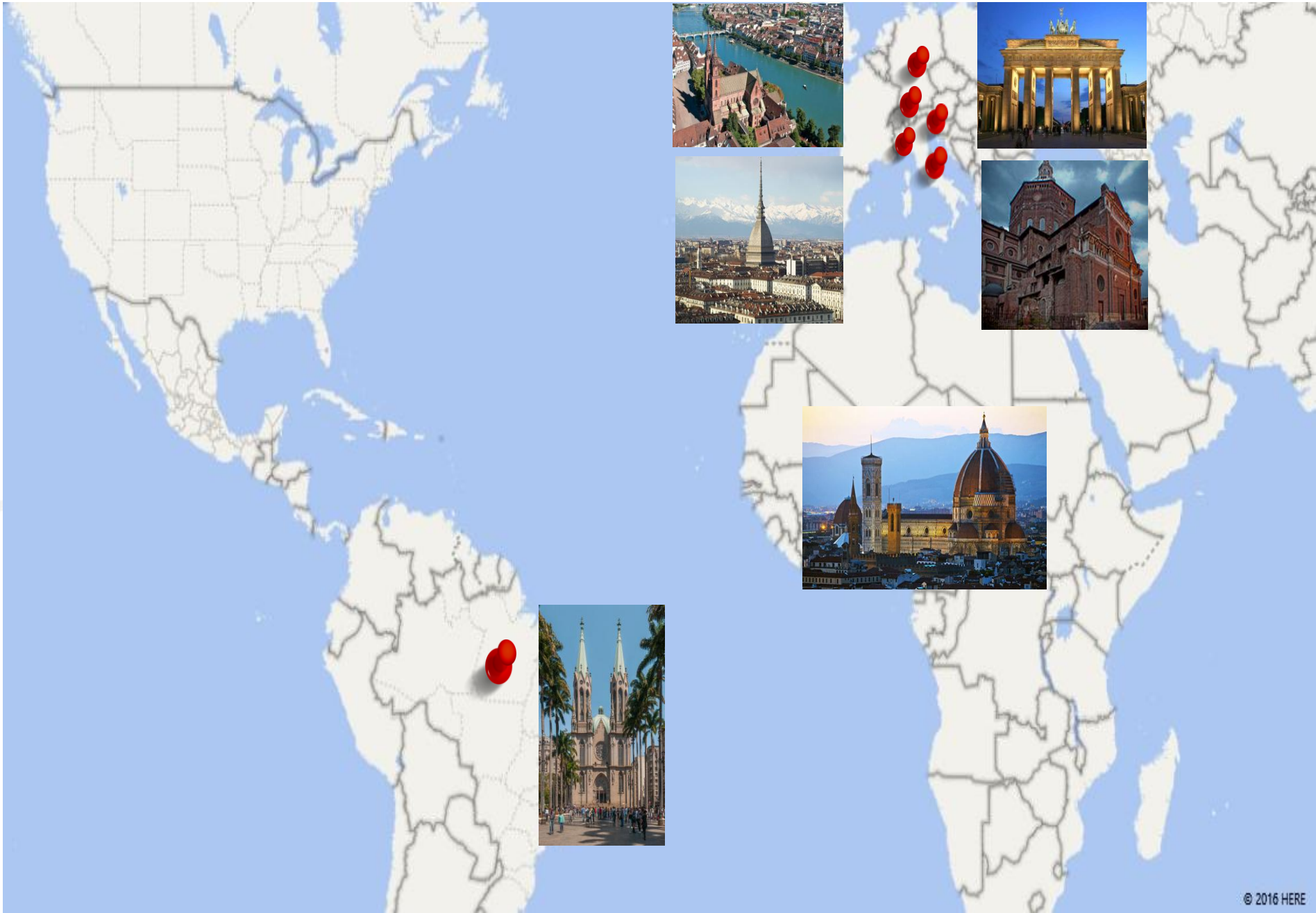
Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

ORIGINAL RESEARCH CONTRIBUTION

Diagnostic Performance of Focused Cardiac Ultrasound Performed by Emergency Physicians for the Assessment of Ascending Aorta Dilation and Aneurysm

Peiman Nazerian, MD, Simone Vanni, MD, PhD, Fulvio Morello, MD, PhD, Matteo Castelli, MD, Maddalena Ottaviani, MD, Claudia Casula, MD, Alessandra Petrioli, MD, Maurizio Bartolucci, MD, and Stefano Grifoni, MD

Studio ADvISED: Aortic DissectIon ScorE plus D-dimer



Metodi dello studio

Criteri d'arruolamento:
1. Sospetta SAA

Criteri d'esclusione:
1. Pazienti con trauma primario
2. Diagnosi alternativa ovvia
3. Non consenso

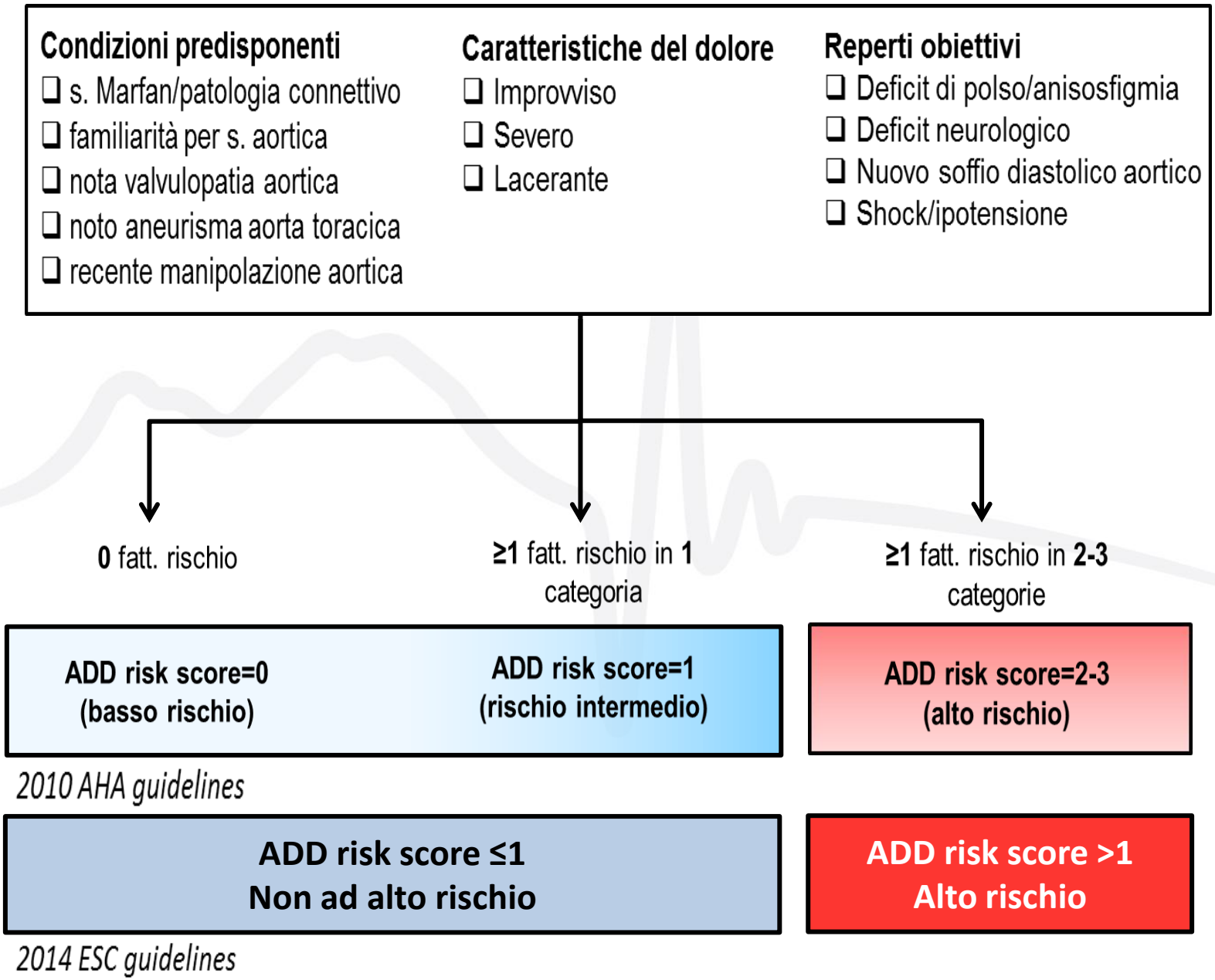
Valutazione clinica e calcolo ADD risk score

Cut-off 500ng/ml

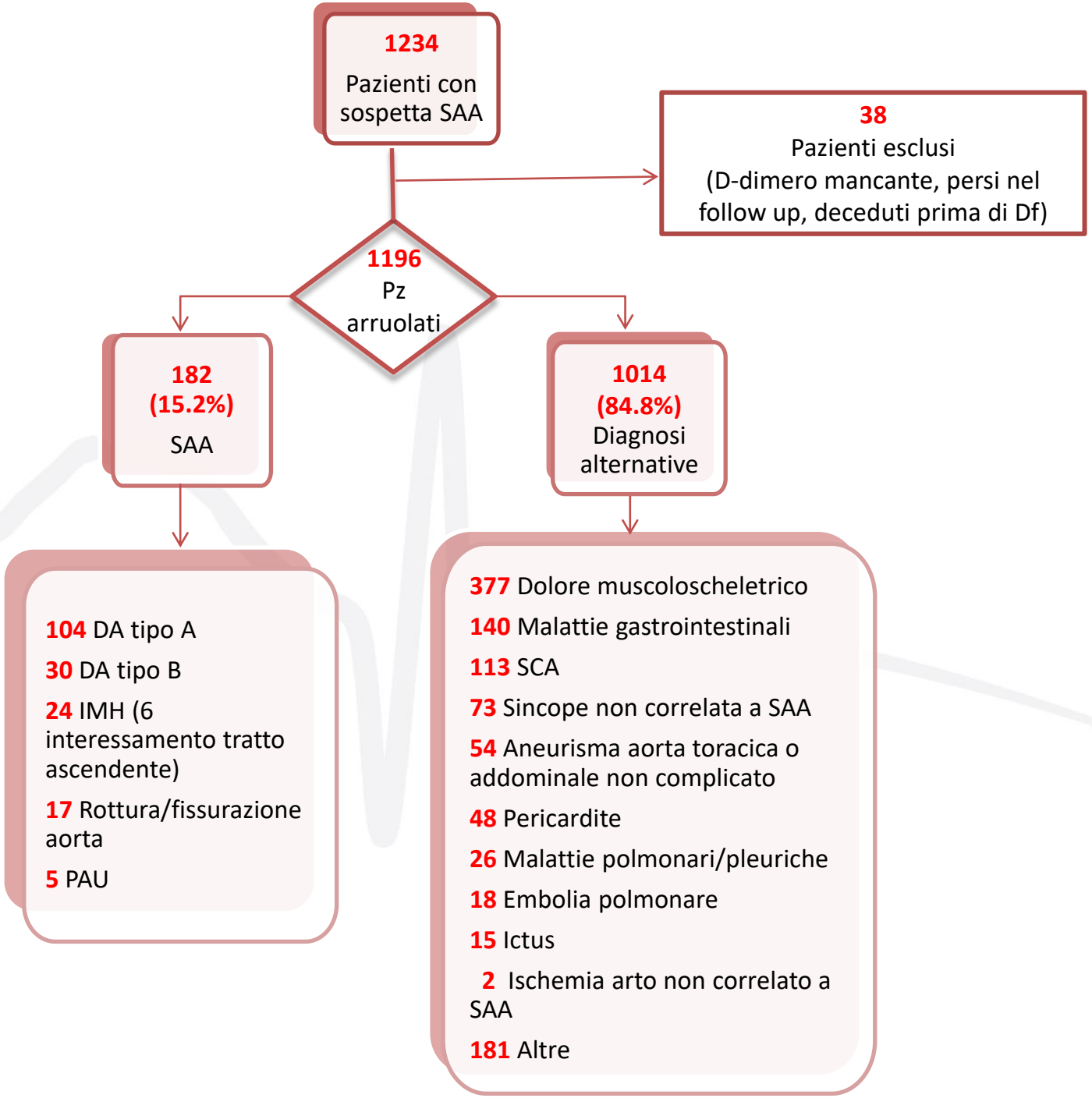
Angio TC
ETE
RM
Report operatorio
Autopsia
Follow up a 14 gg

24h/24 h, 7/7gg
1/06/2014 - 31/08/2016

Aortic Dissection Detection risk score

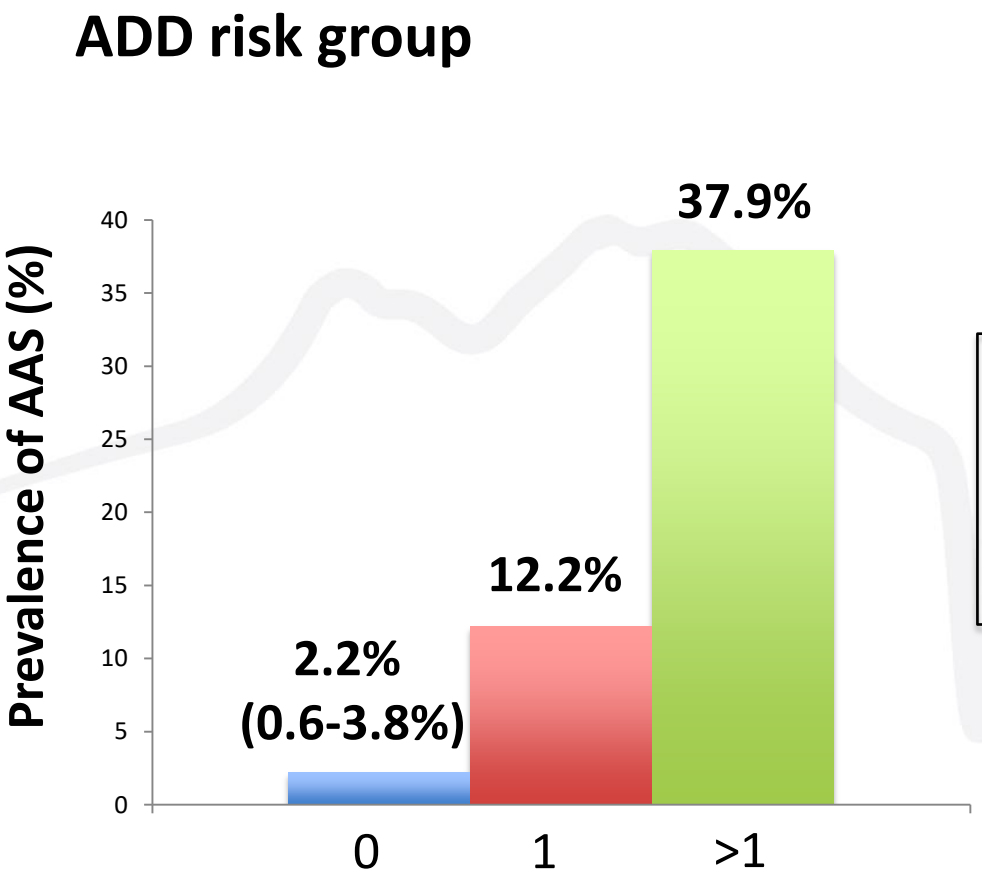


RISULTATI DEI CENTRI ITALIANI



RISULTATI DEI CENTRI ITALIANI	Pz con SAA N=182	Pz con Alt D N= 1014	P-value
Sesso femminile	51 (28%)	382 (37.7%)	**0.015**
Età (anni)	67.5 ±14.7	61.5 ± 16.7	0.05
CONDIZIONI ANAMNESTICHE A RISCHIO			
Sindrome di Marfan	1 (0.6%)	3 (0.3%)	0.479
Storia familiare di aortopatia	17 (9.5%)	38 (3.7%)	**0.003**
Nota valvulopatia aortica	14 (7.8%)	63 (6.2%)	0.41
Recente manipolazione aortica	3 (1.7%)	16 (1.6%)	1.000
Noto aneurisma aorta toracica	35 (21.8%)	95 (9.4%)	**<0.001**
CARATTERISTICHE DEL DOLORE			
Severo (VAS ≥7)	122 (67%)	393 (38.8%)	**<0.001**
Improvviso	112 (61.5%)	310 (30.6%)	**<0.001**
Lacerante/ pugnalante	25 (13.7%)	61 (6.0%)	**0.001**
REPERTI OBIETTIVI			
Asimmetria di polsi/differenza pressoria >20mmHg	34(18.7%)	52(5.1%)	**<0.001**
Nuovo soffio da insufficienza aortica	8 (4.4%)	11 (1.1%)	**0.004**
Deficit neurologico focale	21 (11.5%)	57 (5.6%)	**0.005**
Ipotensione-shock	48 (26.4%)	38 (3.8%)	**<0.001**

1) Are there clinical decision rules that identify a group of patients at very low risk for the diagnosis of thoracic aortic dissection?



N	**316**	**616**	**264**
SAA	7	75	100

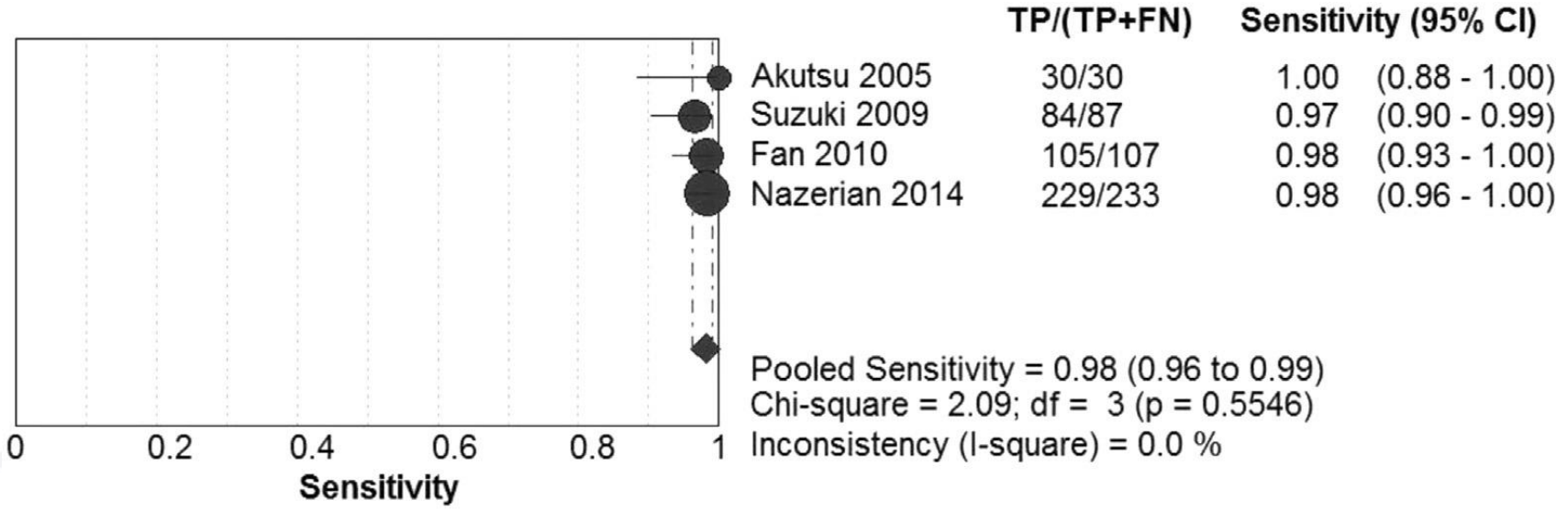
ADD risk score > 0

Sensibilità	95.1% (90.1-97.7%)
Specificità	30.5 (27.6-33.4)
Neg likely ratio	0.16 (0.08-0.31)

2) Is a negative serum dimer sufficient to identify a group of patients at very low risk for the diagnosis of thoracic aortic dissection?

A Systematic Review and Meta-analysis of D-dimer as a Rule-out Test for Suspected Acute Aortic Dissection

Asha S. Ann Emerg Med 2015



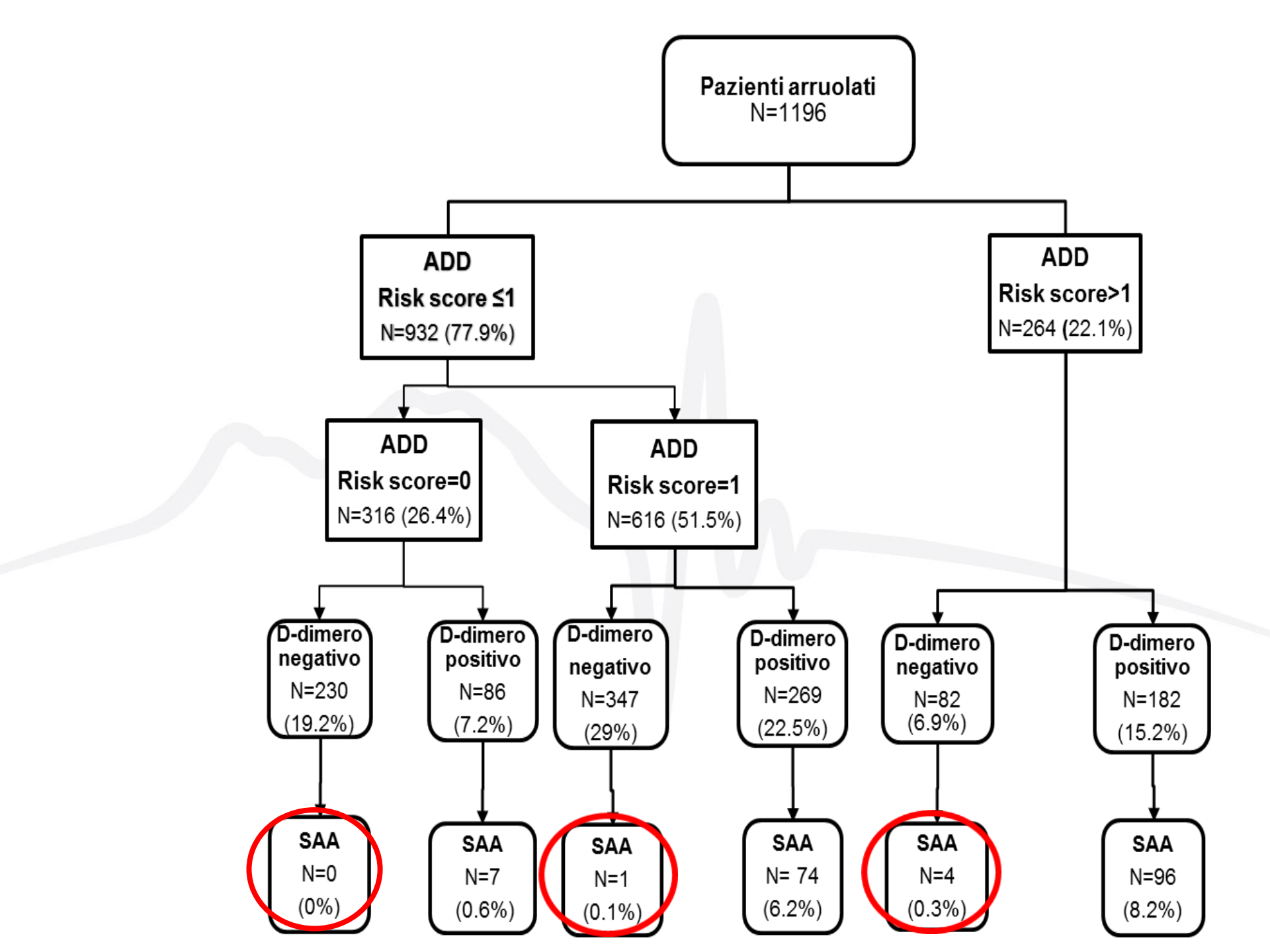
Risultati ADvISED

D-dimer <500	659 (55.1%)
SAA	5

D-dimer ≥ 500 ng/ml

Sensibilità	97.2% (93.7-99.1%)
Specificità	64.5% (61.5-67.4%)
Neg likely ratio	0.04 (0.02-0.1)

D-dimero inferiore al valore minimo fissato dal laboratorio	164 (13.7%)
SAA	0


Pazienti arruolati
N=1196
ADD
Risk score ≤1
N=932 (77.9%)
ADD
Risk score>1
N=264 (22.1%)
ADD
Risk score=0
N=316 (26.4%)
ADD
Risk score=1
N=616 (51.5%)
D-dimero negativo
N=230
(19.2%)
D-dimero positivo
N=86
(7.2%)
D-dimero negativo
N=347
(29%)
D-dimero positivo
N=269
(22.5%)
D-dimero negativo
N=82
(6.9%)
D-dimero positivo
N=182
(15.2%)
SAA
N=0
(0%)
SAA
N=7
(0.6%)
SAA
N=1
(0.1%)
SAA
N= 74
(6.2%)
SAA
N=4
(0.3%)
SAA
N=96
(8.2%)

ADD score + D-dimero

ADD RISK SCORE:	0, basso rischio (N=316)	≤1, non ad alto rischio (N=932)	>1, alto rischio (N=234)
Sensibilità	100% (64.6-100)	98.8% (93.4-99.9)	96% (90.1-98.9)
Specificità:	74.4%(69.2-79.2)	67.8% (64.5-71)	47.6%(39.7-55.5)
Neg likely ratio	0	0.02 (0-0.13)	0.08 (0.03-0.22)
Failure rate[a]	0%	0.2% (0-1)	4.9% (1.9-11.9)
Efficienza[b]	19.2% (17-21.4)	48.2% (45.4-51)	6.9% (5.5-8.3)

[a] Numero dei pz con diagnosi finale di SAA e D-dimero negativo diviso tutti i pazienti con D-dimero negativo della stessa categoria di rischio.

[b] Numero totale dei pz con D-dimero negativo dentro una categoria di rischio diviso tutti i pazienti arruolati nello studio.

- L’associazione di ADD=0 (basso rischio) e D-dimero negativo permette di escludere la diagnosi di SAA in circa 20% del totale dei sospetti.

- L’associazione di ADD$\leq$1 (non alto rischio) e D-dimero negativo esclude con elevata sicurezza la diagnosi di SAA in circa il 50% del totale dei sospetti.

- I pazienti ad alto rischio clinico (ADD>1) devono essere sottoposti immediatamente ad *imaging* di secondo livello, indipendentemente dai valori del D-dimero.

Descrizione clinica dei pazienti affetti da SAA (N=5) e D-dimero neg

Pz	Descrizione clinica	ADD risk score	D-dimero cut-off 500ng/ml	Diagnosi Finale
1	Uomo di 54 aa con storia di pregressa SAA, presenta dolore toracico anteriore iniziato improvvisamente da 23h	3	290 ng/ml Hemosil D-dimerHS	Rottura dell'aorta con interessamento del tratto ascendente
2	Uomo di 35 aa si presenta per episodio sincopale preceduto da dolore intenso e improvviso a livello del torace anteriore e posteriore da 2 h	1	258 ng/ml Innovance D-dimer	DA Stanford di tipo A
3	Uomo di 41 aa con storia familiare di SAA si presenta per dolore toracico anteriore improvviso iniziato da 1 h	2	270 ng/ml STA LIATEST D-DI	DA Stanford di tipo A
4	Uomo di 75 aa si presenta con dolore improvviso, severo e strappante a livello del torace anteriore e posteriore iniziato da 24h associato ad asimmetria dei polsi	2	470 ng/ml STA LIATEST D-DI	Ematoma intramurale con interessamento del tratto ascendente
5	Uomo 59 aa con storia di AAT si presenta per dolore severo, localizzato al torace posteriore e all'addome, iniziato improvvisamente da 2 h	2	270 ng/ml STA LIATEST D-DI	Ematoma intramurale con interessamento del tratto ascendente

3) Does a normal chest X ray rule out thoracic aortic dissection in patients at low risk?

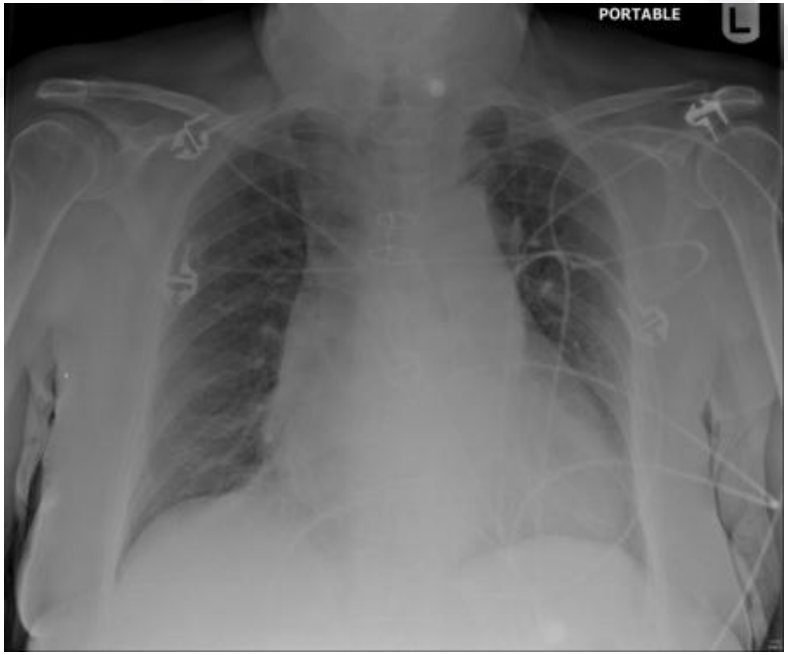
Widened mediastinum

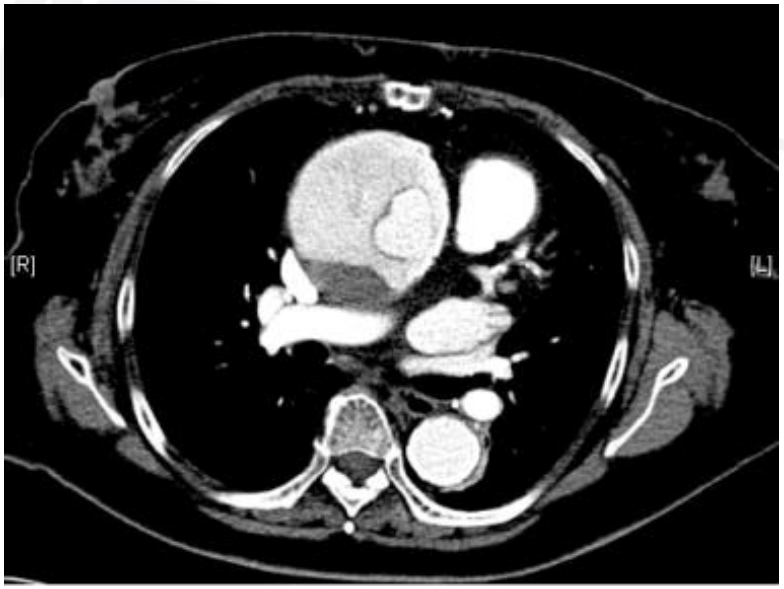
Maximum width >80 mm at the level of the aortic knob, a ratio of mediastinum to chest width >0.25

von Kodolitsch Y, et al. *Am J Med* 2004

Pooled data from 10 studies: Sens of a widened mediastinum 64%

Klompas M. JAMA 2002



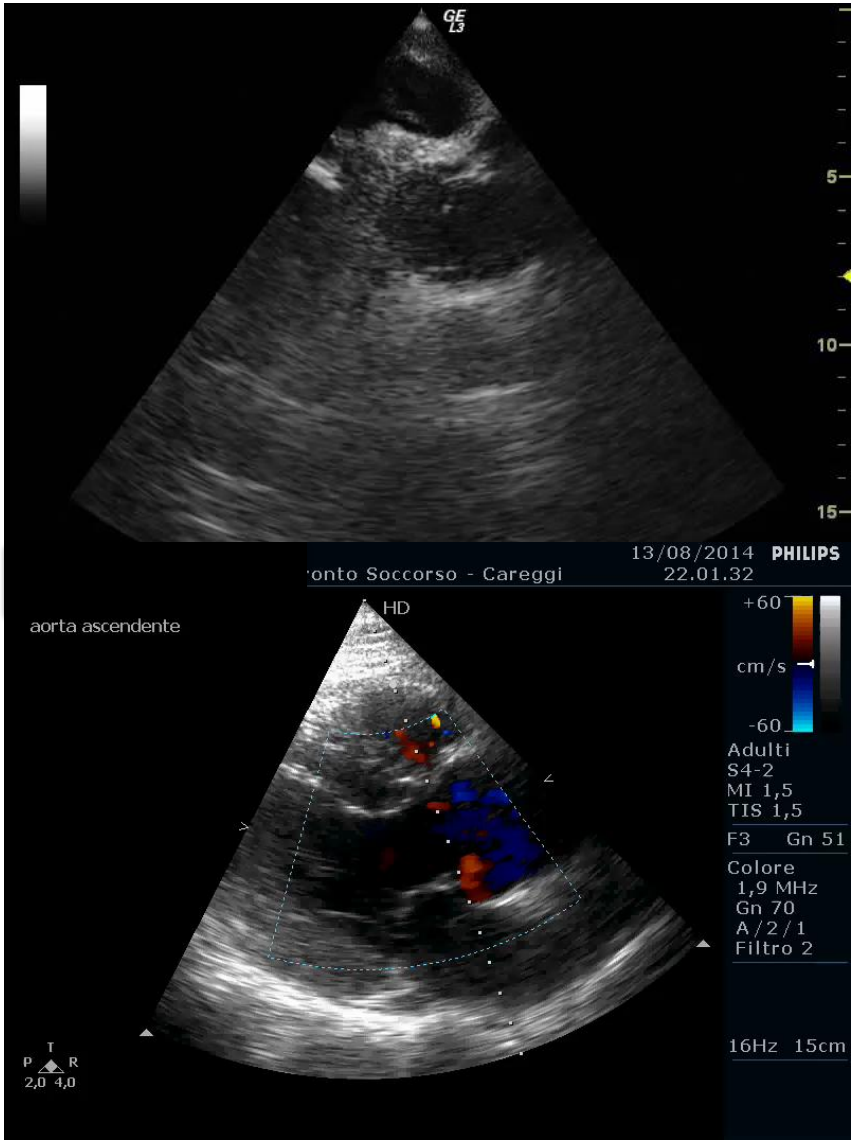


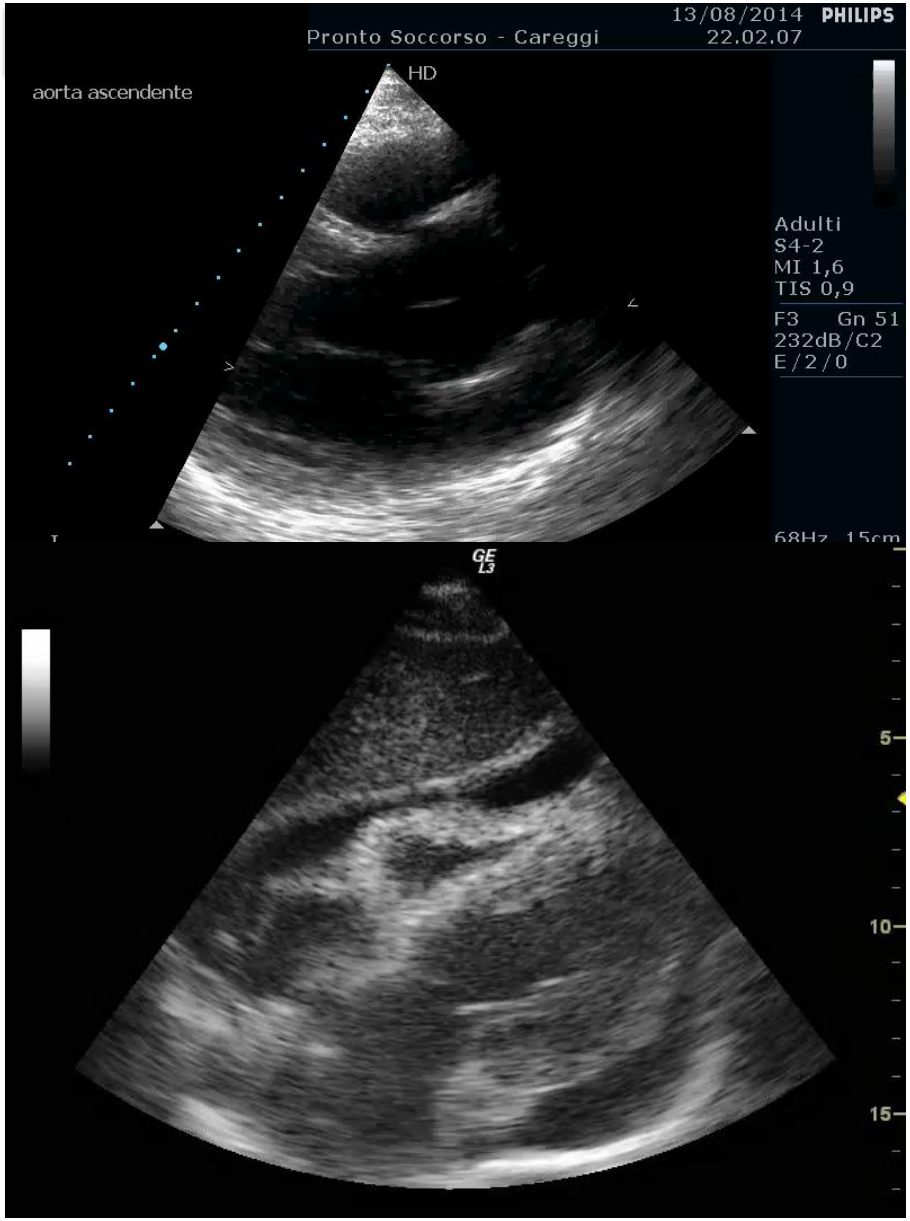
ADD score + Rx torace (slargamento del mediastino)

CXR normale nel gruppo ADD≤1	575
SAA	19

ADD RISK SCORE	≤1, non ad alto rischio (N=633 con cxr)
Sensibilità	32.1 % (15.9-52.3)
Specificità	91.9 % (89.4-93.9)
Neg likely ratio	0.74 (0.57-0.95)
Failure rate	3.4 % (2-5)

4) Does an abnormal bedside TTE establish the diagnosis of thoracic aortic dissection?





ADD score + FoCUS (any sonographic sign)

FoCUS normale nel gruppo ADD≤1	357
SAA	9

ADD RISK SCORE:	≤1, non ad alto rischio (N=452 con FoCUS)
Sensibilità	60.9 % (38.5-80.3)
Specificità	81.1 % (77.1-847)
Neg likely ratio	0.48 (0.29-0.8)
Failure rate	2.5 % (0.8-4.1)

FoCUS nei pazienti in shock o arresto cardiaco sospetti di SAA (N=54)

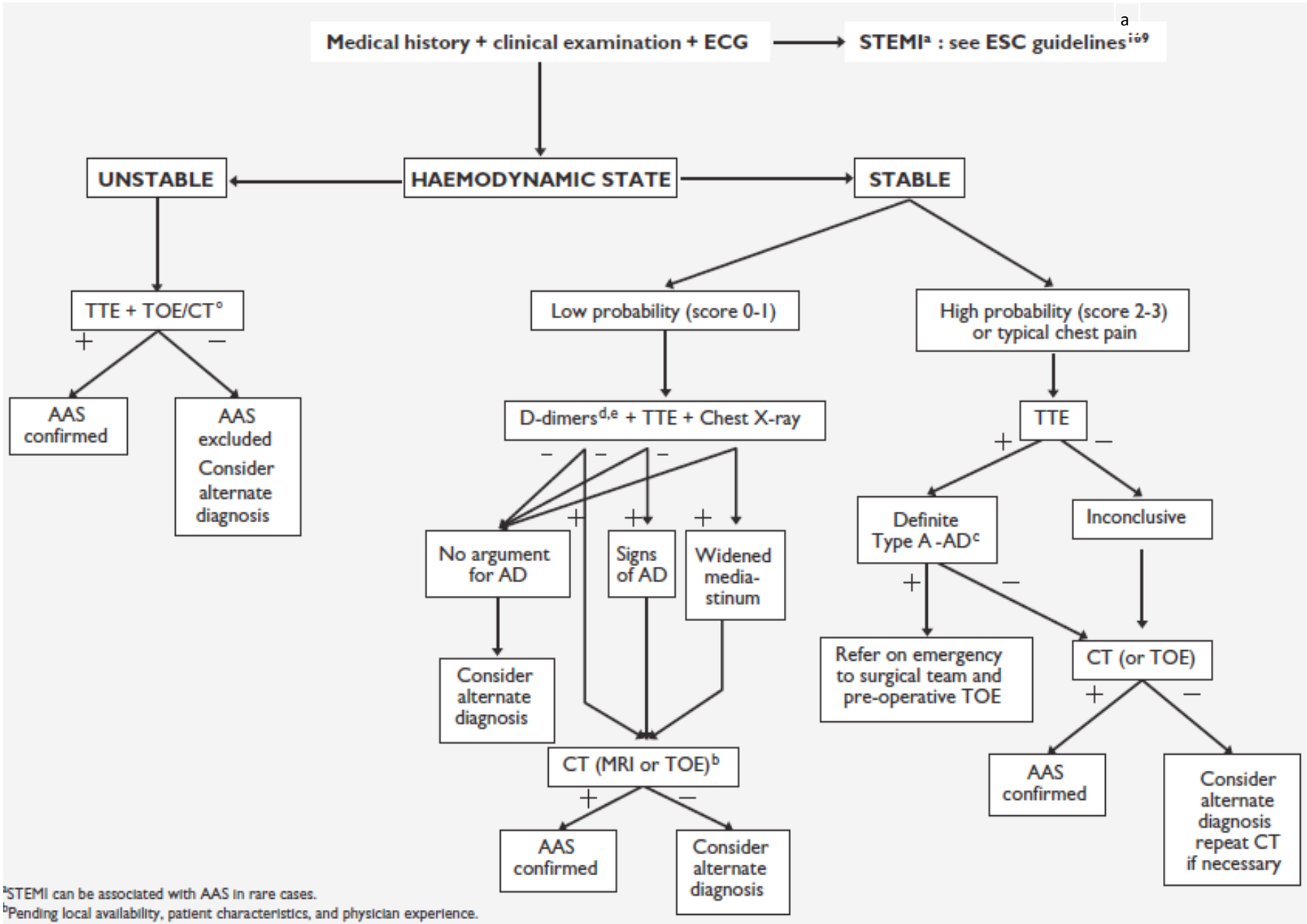
	Rilievo di flap intimale to rule in AAS
Sensibilità	27.8% (9.7-53.5)
Specificità	100 % (90.3-100)
Pos likely ratio	Inf.

La FoCUS

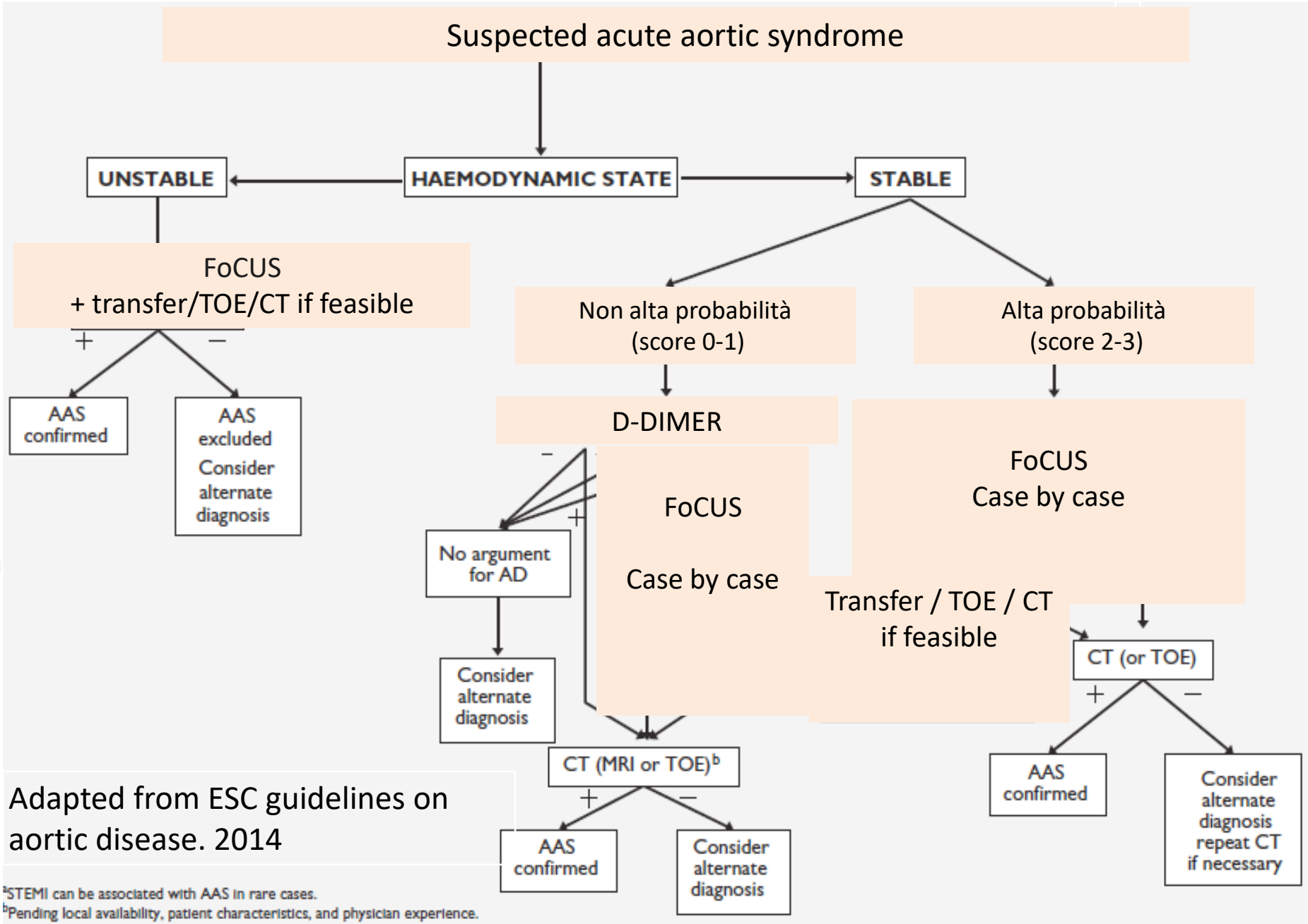
- da sola e in associazione con l'ADD score non può essere usata per il rule in e out della dissezione aortica

- può però dare informazioni rapide e cruciali nei pz sospetta dissezione aortica in shock/ipotensione o arresto cardiaco

- può essere utilizzata come strumento rapido bedside nei pz con sospetta dissezione aortica per procedere rapidamente a test di immaging di secondo livello o al trasferimento del paziente verso centri hub



[a]STEMI can be associated with AAS in rare cases.
[b]Pending local availability, patient characteristics, and physician experience.
[c]Proof of type-A AD by the presence of flap, aortic regurgitation, and/or pericardial effusion.
[d]Preferably point-of-care, otherwise classical.
[e]Also troponin to detect non–ST-segment elevation myocardial infarction.



Adapted from ESC guidelines on aortic disease. 2014

[a]STEMI can be associated with AAS in rare cases.
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[e]Also troponin to detect non–ST-segment elevation myocardial infarction.

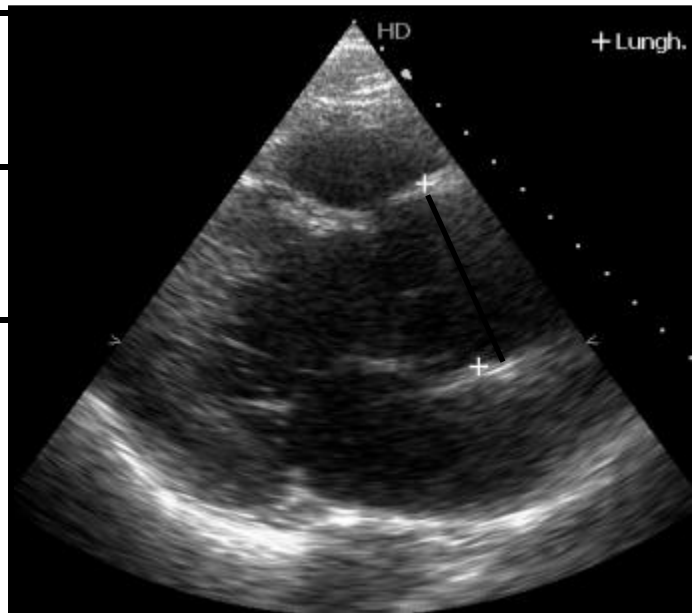
Grazie.

Peiman Nazerian
nazerianp@aou-careggi.toscana.it

Does an abnormal TTE establish the diagnosis of aortic dissection?

Diagnostic Performance of Focused Cardiac Ultrasound performed by Emergency Physicians for the Assessment of Ascending Aorta Dilation and Aneurysm (140 pts)

	Aortic dilation at FoCUS (diameter ≥ 4 cm)
Sens, % (95% CI)	78.6 (65.6-88.4)
Spec, % (95% CI)	93.9 (85.1-97.3)
PPV, % (95% CI)	88 (75.7-95.4)
NPV, % (95% CI)	86.7 (77.9-92.9)



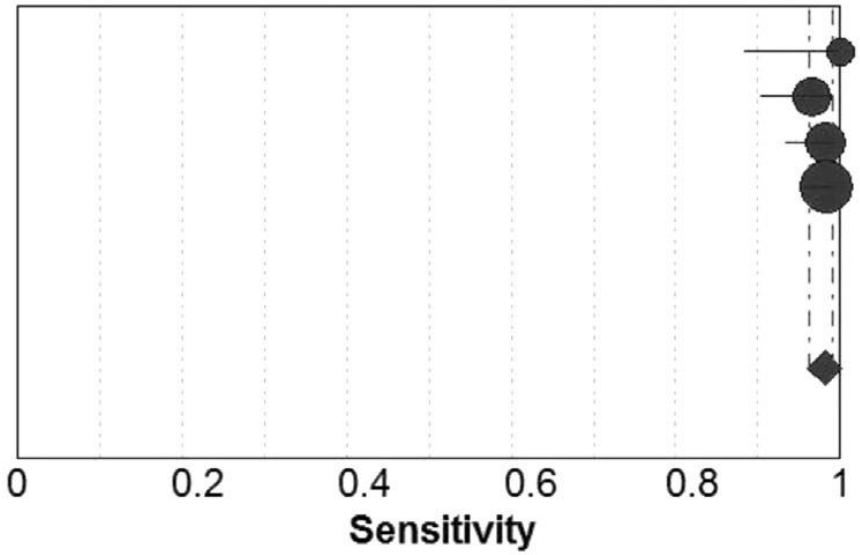
BACKGROUND - D-DIMER

A Systematic Review and Meta-analysis of D-dimer as a Rule-out Test for Suspected Acute Aortic Dissection

Stephen E. Asha, MBBS, MMed (Clin Epi)*; James W. Miers, BSc, MBBS

*Corresponding Author. E-mail: stephen.asha@sesiahs.health.nsw.gov.au.

http://dx.doi.org/10.1016/j.annemergmed.2015.02.013



	TP/(TP+FN)	Sensitivity (95% CI)
Akutsu 2005	30/30	1.00 (0.88 - 1.00)
Suzuki 2009	84/87	0.97 (0.90 - 0.99)
Fan 2010	105/107	0.98 (0.93 - 1.00)
Nazerian 2014	229/233	0.98 (0.96 - 1.00)

Pooled Sensitivity = 0.98 (0.96 to 0.99)
Chi-square = 2.09; df = 3 (p = 0.5546)
Inconsistency (I-square) = 0.0 %

STUDY AIMS

PRIMARY AIMS

✓ To prospectively evaluate the diagnostic accuracy of the ADD risk score

✓ To prospectively evaluate the sensitivity and negative predictive value of a diagnostic strategy combining ADD risk score stratification plus D-dimer for AAS rule-out.

SECONDARY AIMS

✓ To develop a simplified tool for patient risk stratification

✓ To pospectively evaluate US assessment

✓ To prospectively evaluate alternative biomarkers in addition to D-dimer

METHODS - STUDY SETTING AND DESIGN

Study type: observational diagnostic accuracy study

Design: prospective

Centers: international multicenter

Setting: Emergency Department of tertiary hospital

Period: recruitment started in Jun 2014

Population: consecutive outpatients

METHODS - ENROLMENT CRITERIA

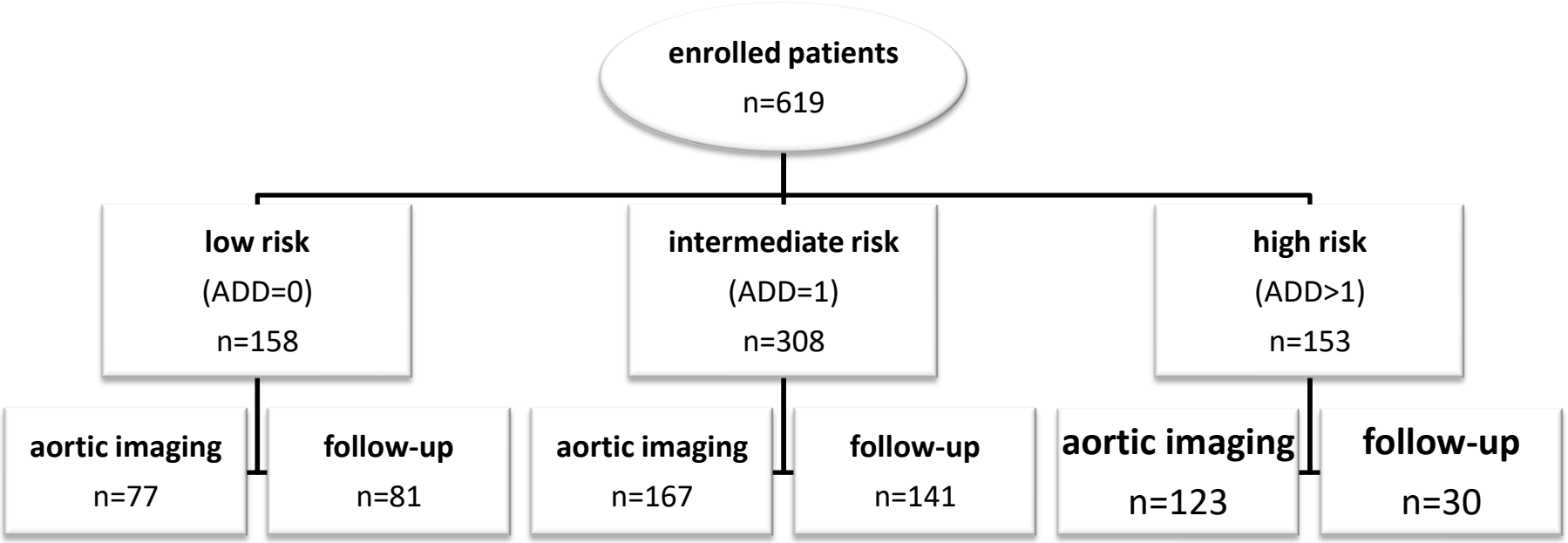
Inclusion criteria:

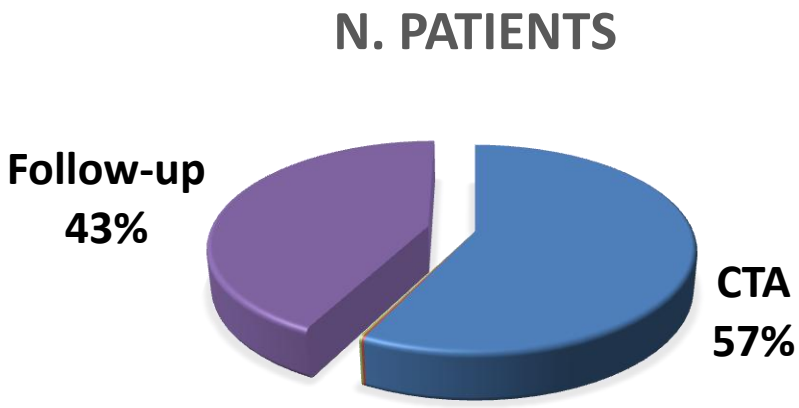
- acute onset (<14 days) of ≥1 signs/symptoms:
  - chest pain
  - back pain
  - abdominal pain
  - syncope
  - malperfusion signs/symptoms (limb, CNS etc.)
- acute aortic syndrome considered as a differential diagnosis

Exclusion criteria:

- trauma
- obvious alternative diagnoses to AAS
- patient's denial to participate

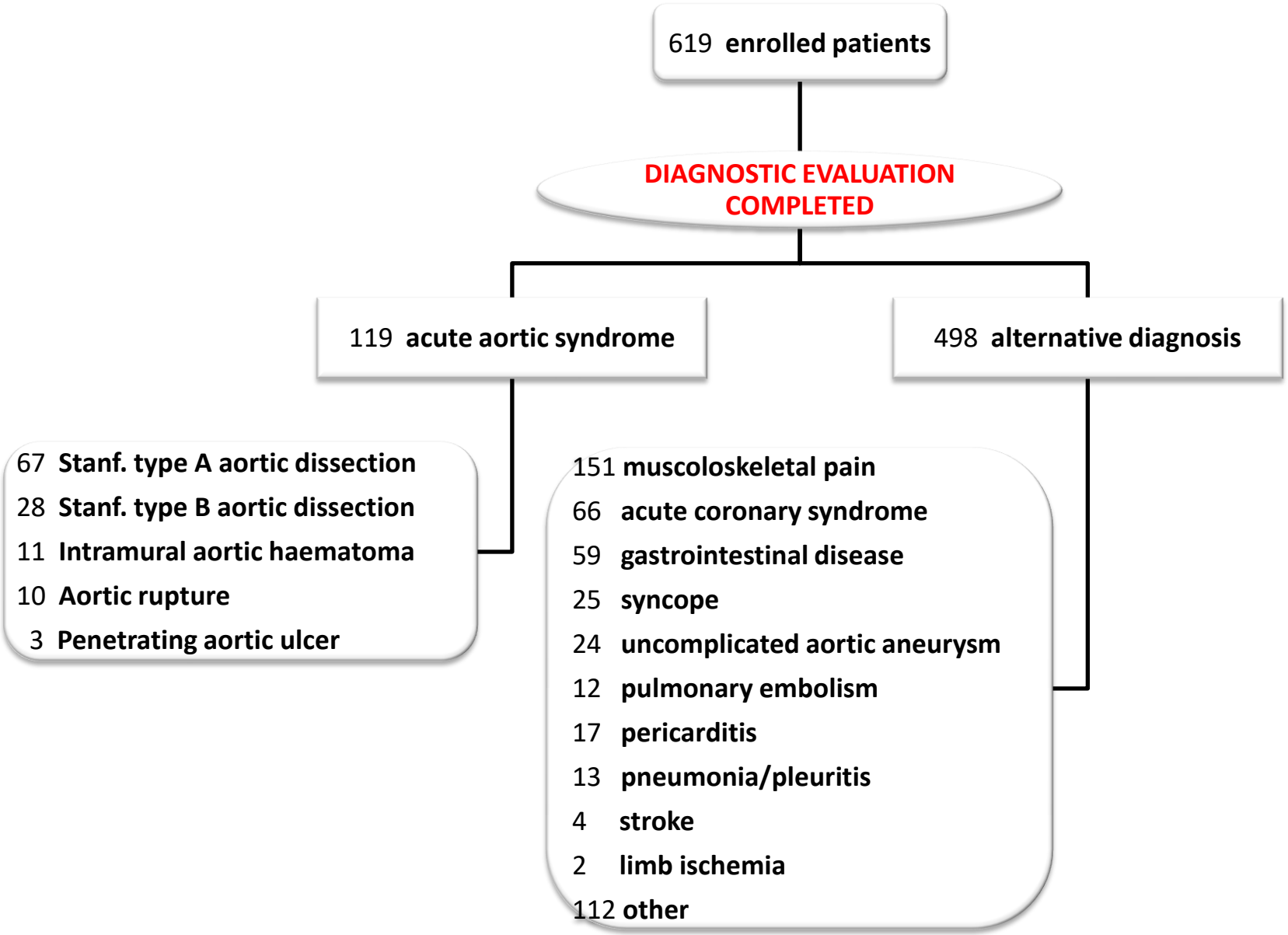
PRELIMINARY DATA – PATIENT CLASSIFICATION





Preliminary data - F. Morello, P. Nazerian - Oct. 2015

PRELIMINARY DATA – FINAL DIAGNOSIS

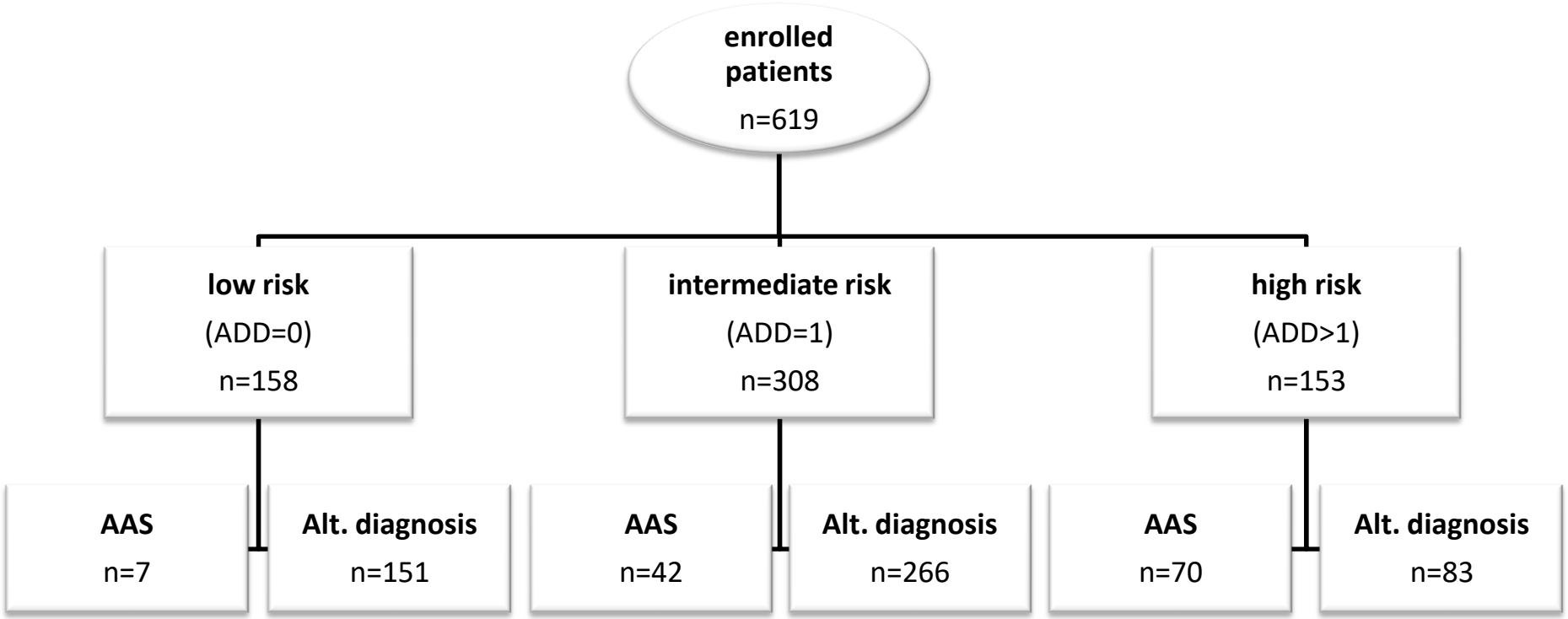


Preliminary data - F. Morello, P. Nazerian - Oct. 2015

PRELIMINARY DATA – STUDY POPULATION

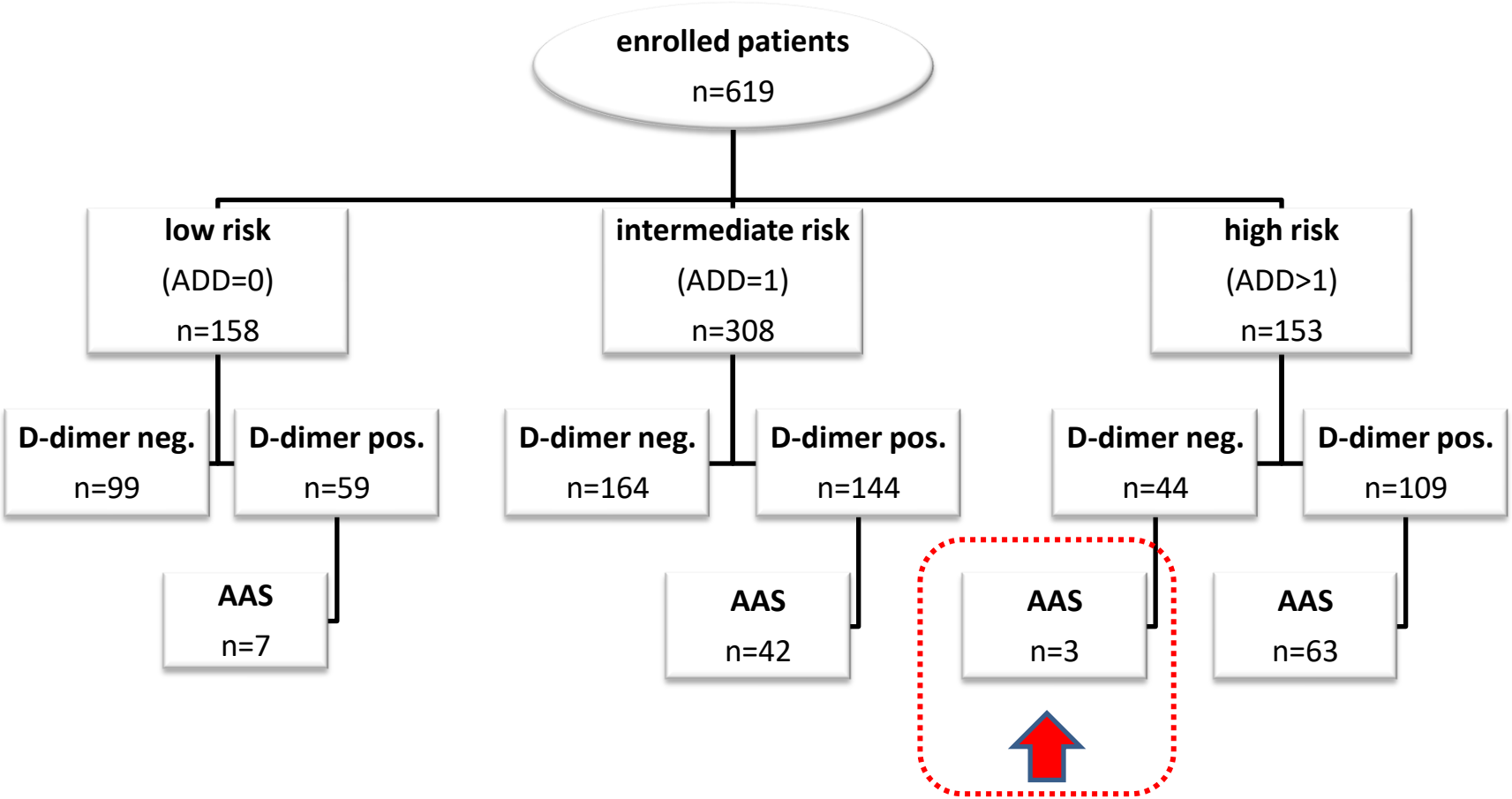
	AAS (119)	AltD (498)	*P*-value
Female gender	27.7%	38.2%	0.03
Age (years)	**65.5 ± 15.8**	**61.3 ± 16.3**	**0.013**
Hypertension	64.6%	56.7%	0.126
Smoke	27.4%	29.6%	0.642
Diabetes	8.0%	14.3%	0.072
CLINICAL PRESENTATION			
Ant. chest pain	68.3%	67.2%	0.826
Post. chest pain	34.5%	30.5%	0.406
Back pain	13.4%	10.4%	0.347
Abdominal pain	**22.7%**	**15.1%**	**0.044**
Syncope	**19.3%**	**11.0%**	**0.015**
Perfusion deficit	**21.8%**	**9.4%**	**<0.001**
Systolic blood pressure (mmHg)	**130 ± 40**	**142 ± 27**	**<0.001**

PRELIMINARY DATA – AORTIC IMAGING



Preliminary data - F. Morello, P. Nazerian - Oct. 2015

PRELIMINARY DATA – ADD risk score + D-dimer



Aortic rupture (54 years, ADD 3, previous AAS, Δt 10 h)
Stanf. A aortic dissection (46 years, ADD 2, Δt 28 h)
Stanf. A aortic dissection (41 years, ADD 2, Δt 1 h)

Preliminary data - F. Morello, P. Nazerian - Oct. 2015

ADD risk score + D-dimer

D-dimer (cutoff 500 ng/ml)	low prob. (n=466)	high prob. (n=153)
Sensitivity % (95% CI)	100% (90.9-100%)	95.7% (87.9-99.1%)
Specificity % (95% CI)	63.1% (58.2-67.7%)	45.6% (35.1-56.4%)
Failure rate % (95% CI)	0% (0-1.8%)	6.8% (1.8-19.7%)
Rule-out rate % (95% CI)	42.5% (38.6-46.5%)	7.1% (5.3-9.5%)

Preliminary data - F. Morello, P. Nazerian - Oct. 2015

conclusions

Preliminary multicenter prospective data indicate that:

- ✓ D-dimer is highly sensitive for the diagnosis of acute aortic syndrome in patients at low probability
- ✓ Combination of low probability + D-dimer <500 ng/ml is associated with very high negative predictive value
- ✓ Combination of low probability + D-dimer <500 ng/ml is highly efficient for the rule-out of acute aortic synromes, with potentially a major impact on the number of requested aortic imaging exams

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