

## Tumori e sindromi coronariche acute.

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Giancarlo Mareni



# “*Punti di contatto*” tra sindromi coronariche acute e tumori

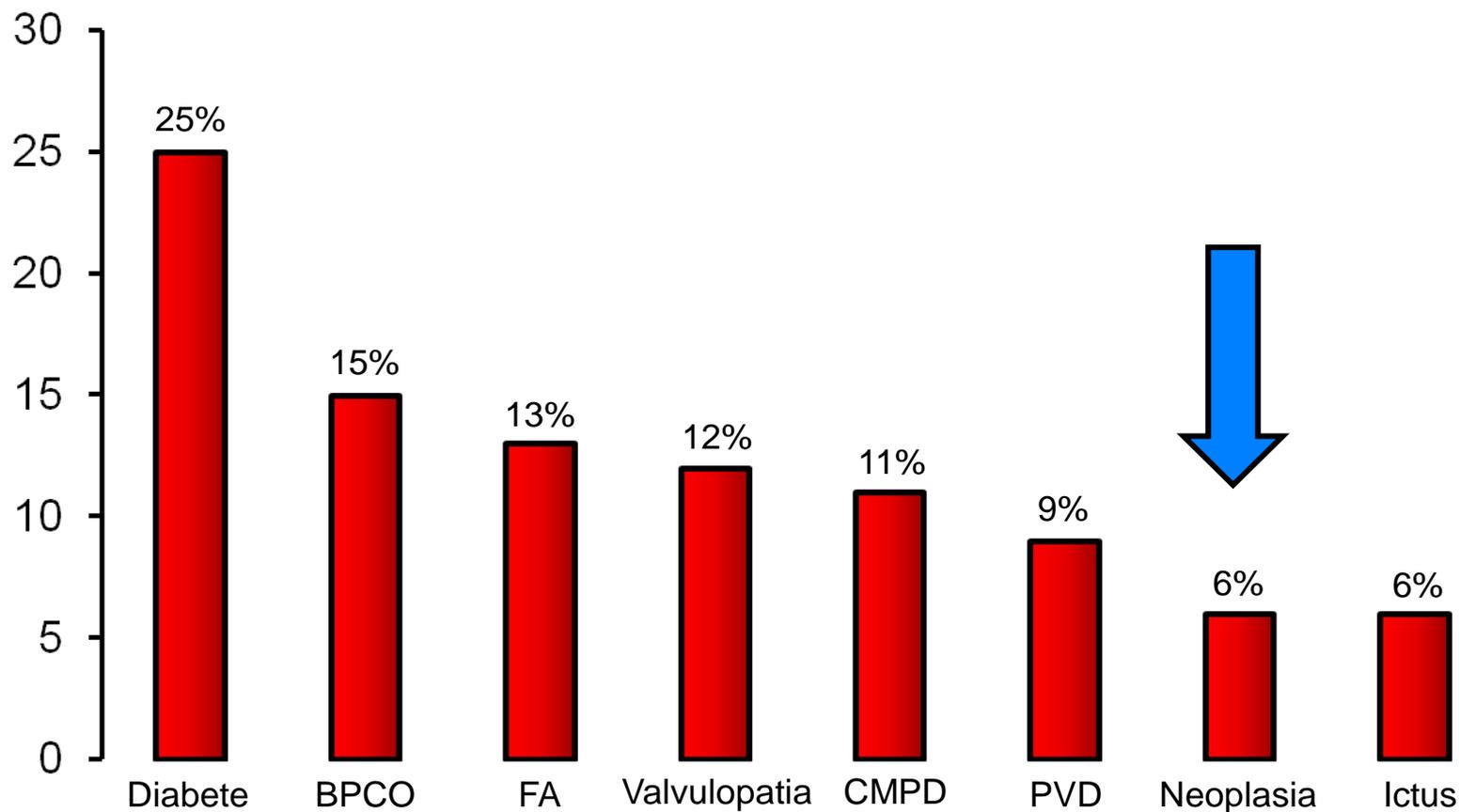
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- Cancro e malattie cardiovascolari sono le due più frequenti patologie

# Principali co-morbidità nelle SCA

## Registro Blitz-3

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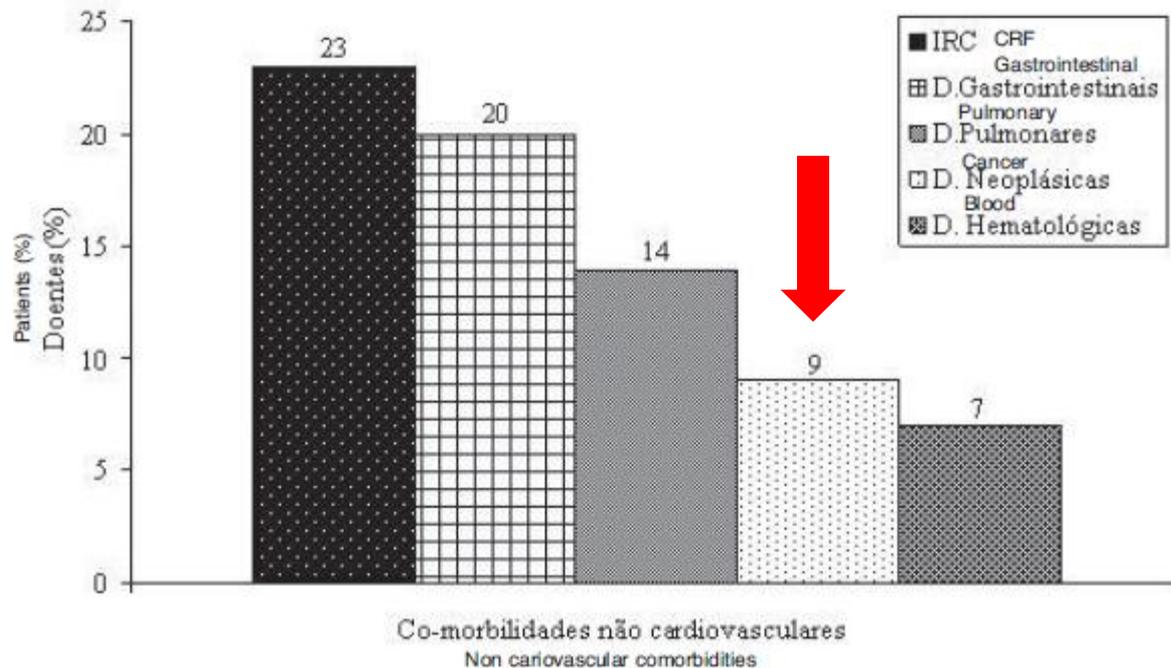


# Influence of Comorbid Conditions on One-Year Outcomes in Non-ST-Segment Elevation Acute Coronary Syndrome

TABLE 1. Comorbid Conditions Among Patients in the Derivation Cohort (N=1017)<sup>a</sup>

Current smoker	243 (24)
Hypertension	656 (65)
Hypercholesterolemia	494 (49)
Diabetes	404 (40)
Family history of ischemic heart disease	60 (6)
Previous myocardial infarction	249 (24)
Previous coronary stenosis	197 (19)
Previous coronary angioplasty	85 (8)
Previous coronary surgery	74 (7)
Previous admission for heart failure	75 (7)
Peripheral artery disease	93 (9)
Cerebrovascular disease	81 (8)
Chronic pulmonary disease	85 (8)
Diabetes with end-organ damage	59 (6)
Mild renal failure <sup>b</sup>	218 (21)
Severe renal failure <sup>b</sup>	27 (3)
 Cancer	59 (6)
Rheumatic disease	65 (6)
Peptic ulcer disease	42 (4)
AIDS	6 (0.6)
Mild liver disease	7 (0.7)
Severe liver disease	8 (0.8)
Hemiplegia	15 (1.5)
Dementia	14 (1.4)
Metastatic solid tumor	2 (0.2)
Anemia <sup>c</sup>	195 (19)

# Co-morbilidades médicas crónicas em doentes com síndrome coronária aguda [1]



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- Fattori di rischio comuni (fumo, ecc.)

# Mortality Attributable to Smoking in China

**Table 4. Relative Risk, Population Attributable Risk, and Absolute Number of Deaths Attributable to Smoking in China, According to Sex and Cause of Death.\***

Cause of Death	Men			Women		
	Multivariable-Adjusted Relative Risk (95% CI)†	Population Attributable Risk %	Absolute No. of Deaths Attributable to Smoking (95% CI) <i>thousands</i>	Multivariable-Adjusted Relative Risk (95% CI)†	Population Attributable Risk %	Absolute No. of Deaths Attributable to Smoking (95% CI) <i>thousands</i>
<b>Cancer</b>						
Any	1.55 (1.41–1.70)	28.0	240.4 (198.8–282.0)	1.62 (1.42–1.85)	5.7	27.8 (15.8–39.9)
Lung	2.44 (2.01–2.96)	50.6	113.0 (93.6–132.5)	2.76 (2.18–3.49)	14.8	16.0 (9.6–22.5)
Liver	1.36 (1.11–1.66)	20.3	37.2 (17.2–57.3)	1.44 (0.99–2.11)	NA	NA
Stomach	1.52 (1.23–1.89)	27.0	40.6 (23.3–58.0)	1.05 (0.71–1.56)	NA	NA
Esophageal	1.34 (1.03–1.75)	19.4	19.2 (5.2–33.3)	1.24 (0.75–2.05)	NA	NA
Colon and rectal	1.02 (0.71–1.48)	NA	NA	1.21 (0.73–1.99)	NA	NA
Other	1.26 (1.03–1.55)	15.6	24.5 (5.3–43.7)	1.42 (1.12–1.80)	4.0	6.3 (0–13.0)
<b>Respiratory disease</b>						
Any	1.14 (1.02–1.26)	8.8	48.6 (13.7–83.5)	1.43 (1.25–1.65)	4.1	18.2 (6.6–29.9)
Chronic obstructive pulmonary disease	1.19 (1.05–1.35)	12.1	47.3 (18.0–76.5)	1.61 (1.37–1.89)	5.6	17.1 (7.1–27.1)
<b>Cardiovascular disease</b>						
Any	1.17 (1.09–1.26)	10.7	126.6 (75.6–177.7)	1.21 (1.10–1.34)	2.1	19.6 (3.6–35.5)
Stroke	1.17 (1.07–1.28)	10.8	82.5 (41.7–123.4)	1.18 (1.03–1.34)	1.7	9.8 (0–22.1)
Coronary heart disease	1.21 (1.03–1.42)	12.9	30.4 (6.7–54.1)	1.41 (1.15–1.71)	3.8	7.3 (0–15.2)

\* Causes of death were coded according to the *International Classification of Diseases, Ninth Revision*. NA denotes not applicable.

† Data were adjusted for the age at baseline, educational level, geographic region (north vs. south), urbanization (rural vs. urban), and the presence or absence of hypertension, overweight status or obesity, alcohol consumption, and physical inactivity; the presence or absence of diabetes was considered as a time-dependent covariate.

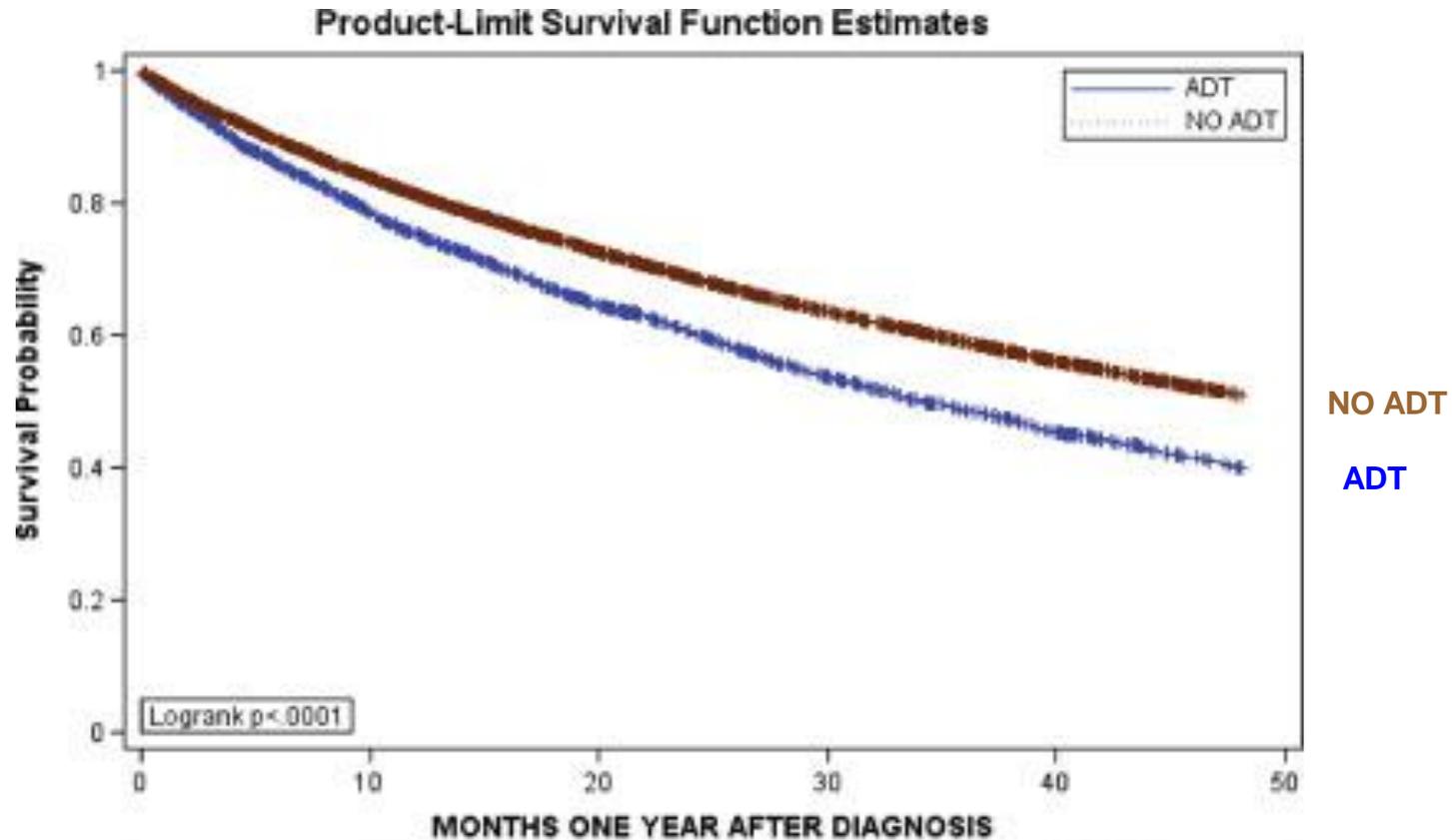
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- Terapia antineoplastica come fattore di rischio cardiovascolare

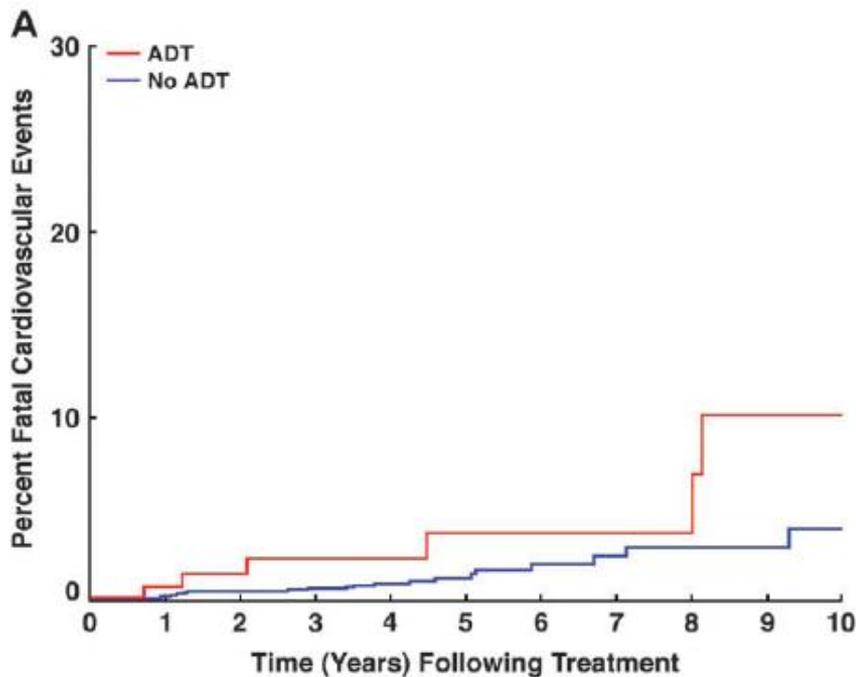
# Androgen Deprivation Therapy Increases Cardiovascular Morbidity in Men With Prostate Cancer

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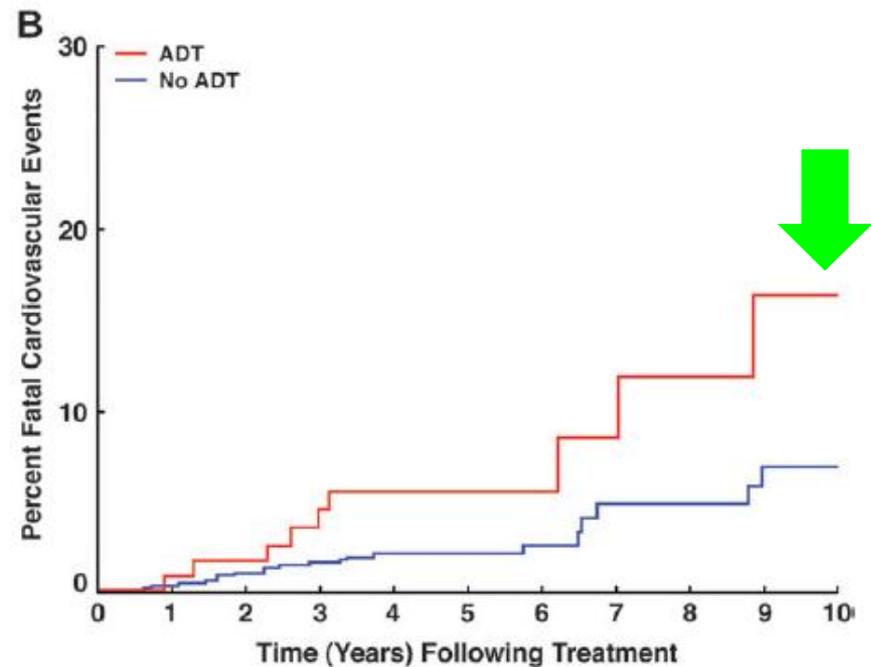


# Androgen Deprivation Therapy for Localized Prostate Cancer and the Risk of Cardiovascular Mortality

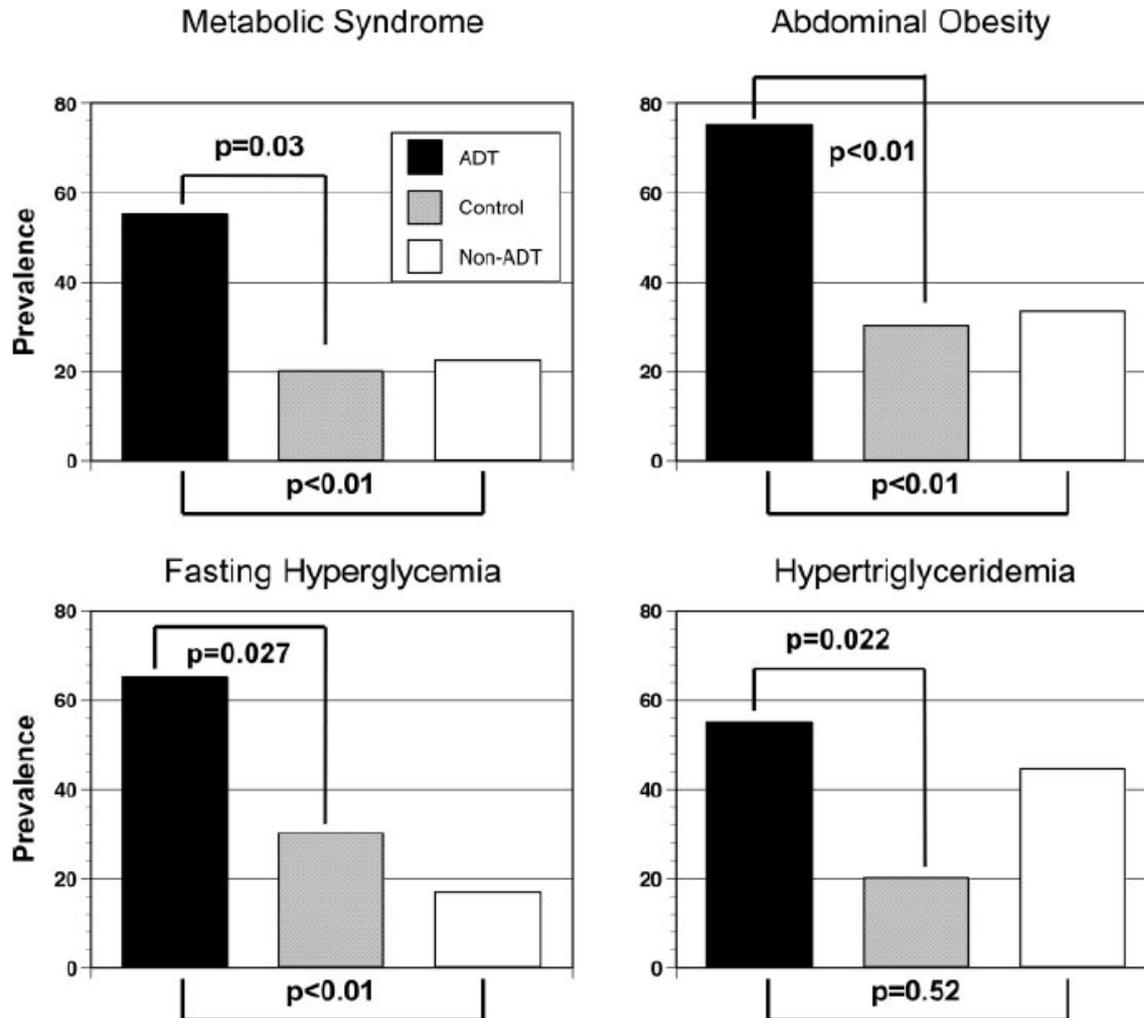
Patients who underwent radical prostatectomy and were <65 years of age at the time of surgery



Patients who underwent radical prostatectomy and were >65 years of age at the time of surgery



# Androgen Deprivation Therapy in Prostate Cancer and Metabolic Risk for Atherosclerosis



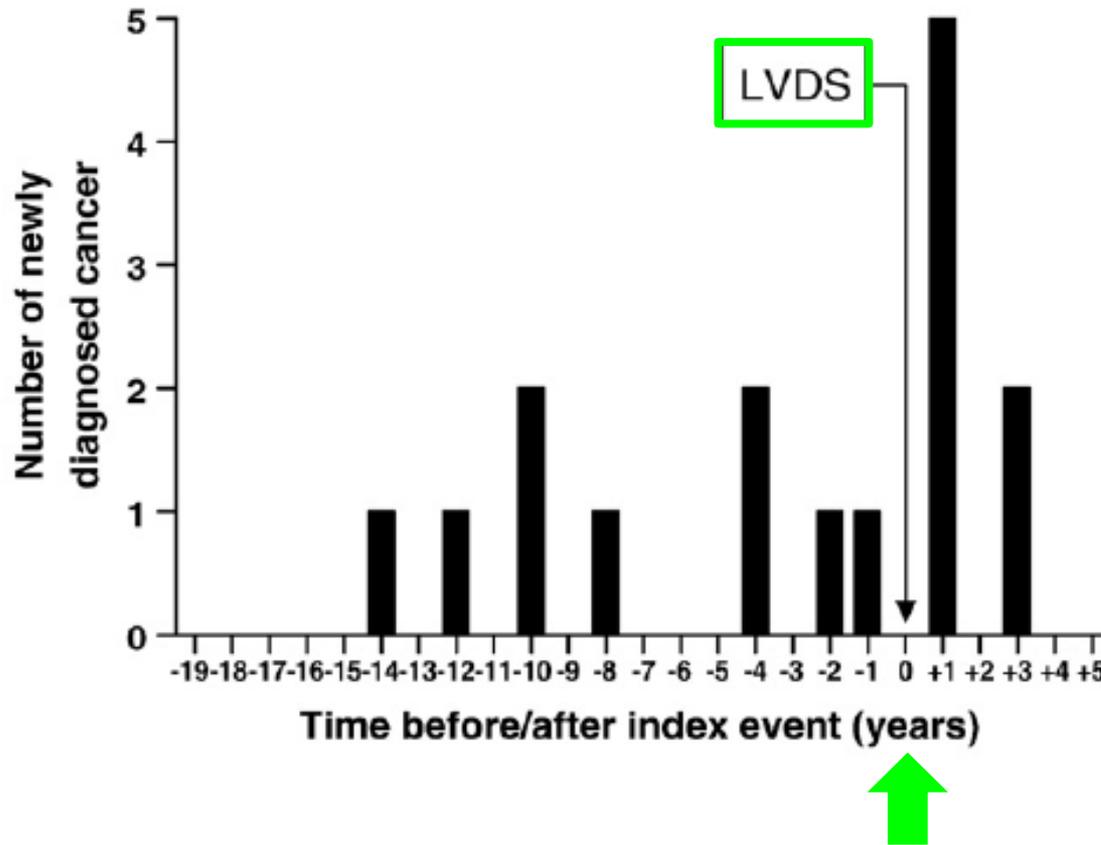
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- Fattori di rischio comuni (fumo, ecc.)
- Tumori e terapia antineoplastica come fattori di rischio cardiovascolare
- Tumori e terapia antineoplastica e SCA

# Long-term prognosis of the transient left ventricular dysfunction syndrome (Tako-Tsubo cardiomyopathy): Focus on malignancies

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**TABLE 2.** Incidences of side effects of selected chemotherapeutic agents

Left ventricular dysfunction	
Anthracyclines	+++
Cyclophosphamide (Cytoxan, high dose)	++
Ifosfamide (Mitoxana, high dose)	++++
Cisplatin (Platinol)	++
Mitomycin (Mutamycin)	++
Imatinib mesylate (Gleevec)	++++
Alemtuzumab (Campath)	+
Trastuzumab (Herceptin)	++
Interferon-alpha	+
Myocardial ischemia	
5-fluorouracil (Adrucil)	++
Capecitabine (Xeloda)	+
Interferon $\alpha$	+
Hypotension	
Etoposide (Vepesid)	++
All-trans-retinoic acid (Tretinoin)	++
Cytokines (eg, interleukin-2 and interferon $\alpha$ )	+++ to ++++
Monoclonal antibodies	+ to +++
Hypertension	
Bevacizumab (Avastin)	++
Interferon- $\alpha$	++
Thrombocytopenia	

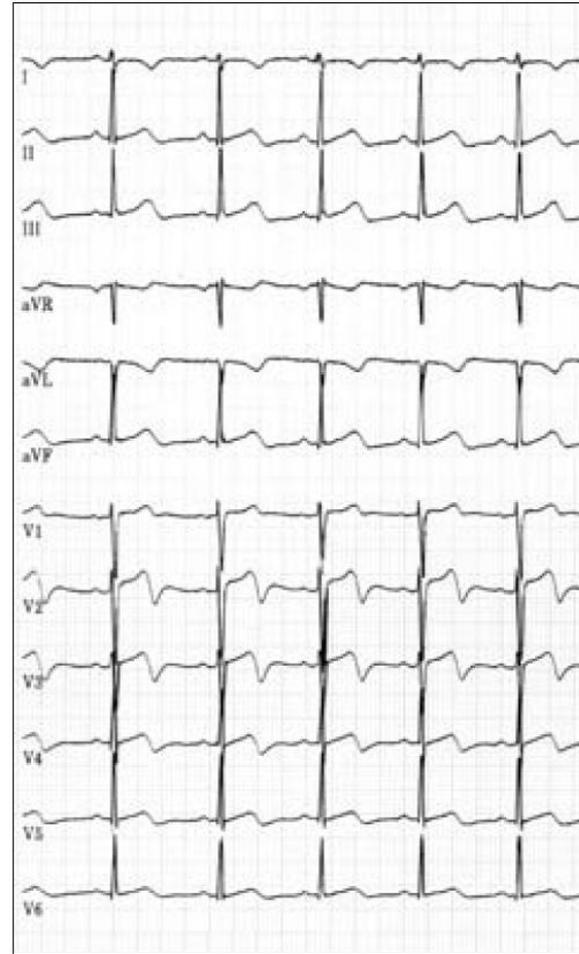
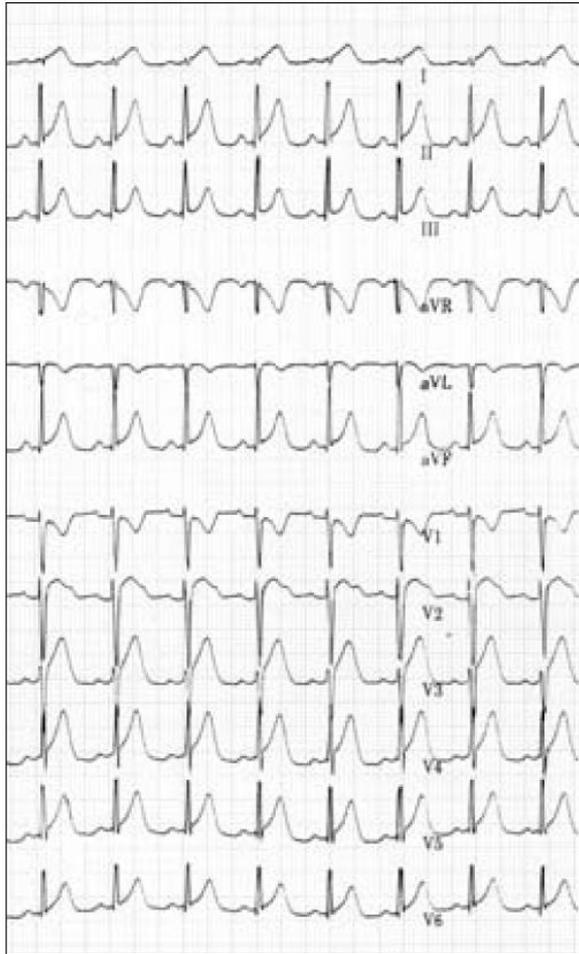
Among these agents are 5-FU and its prodrug capecitabine, paclitaxel, and interferon. All of these medications have been associated with ACS and nonobstructive CAD on coronary angiogram, suggesting coronary spasm as the cause for this type of ACS.

Cisplatin	++++
5-fluorouracil (Adrucil)	++++
QT-prolongation or Torsades de pointes	
Arsenic trioxide (Trisenox)	++++

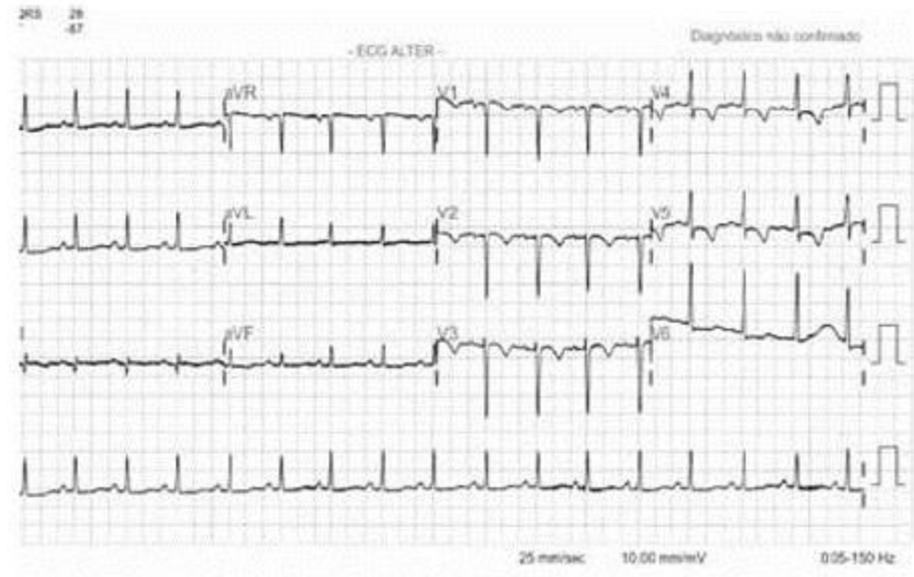
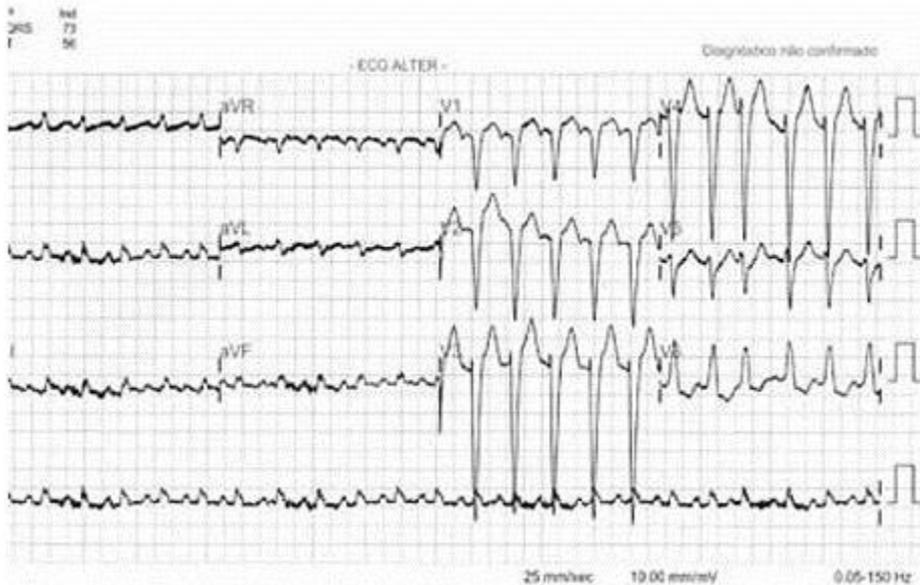
+, rare (<1%); ++, uncommon (1-5%); +++, common (6-10%); +++++, frequent (<10%).

# Acute coronary syndrome induced by oral capecitabine

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# Trastuzumab-Induced Myocardiotoxicity Mimicking Acute Coronary Syndrome



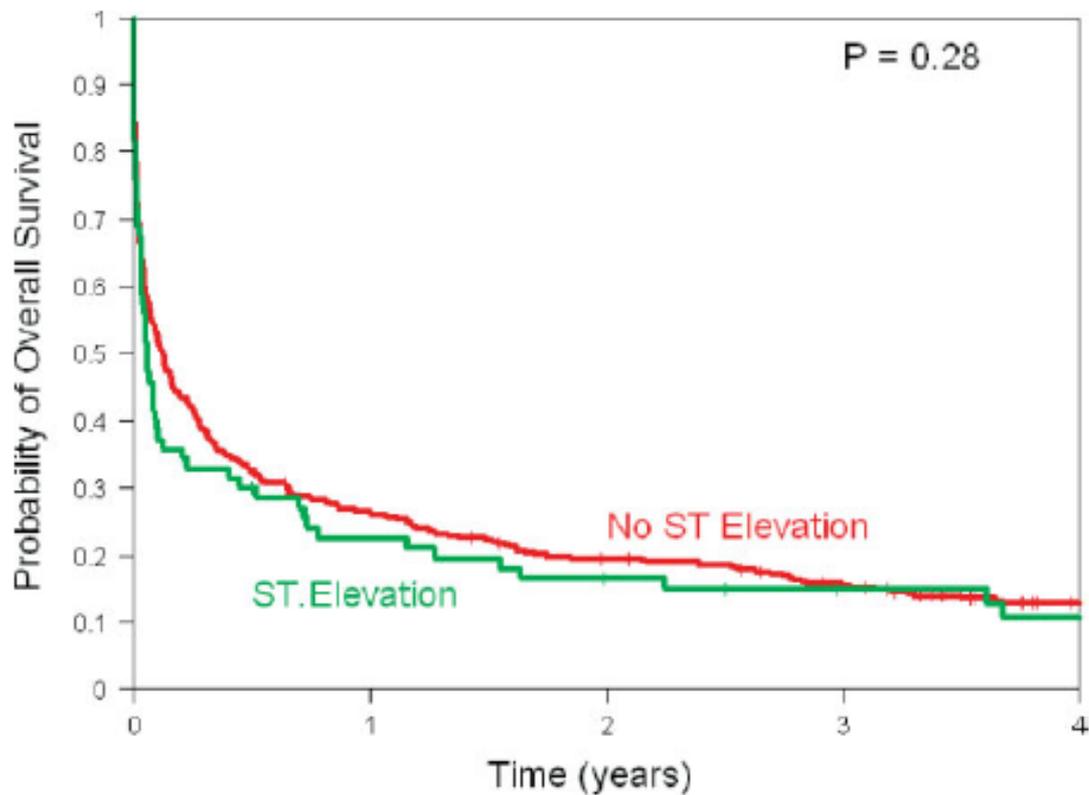
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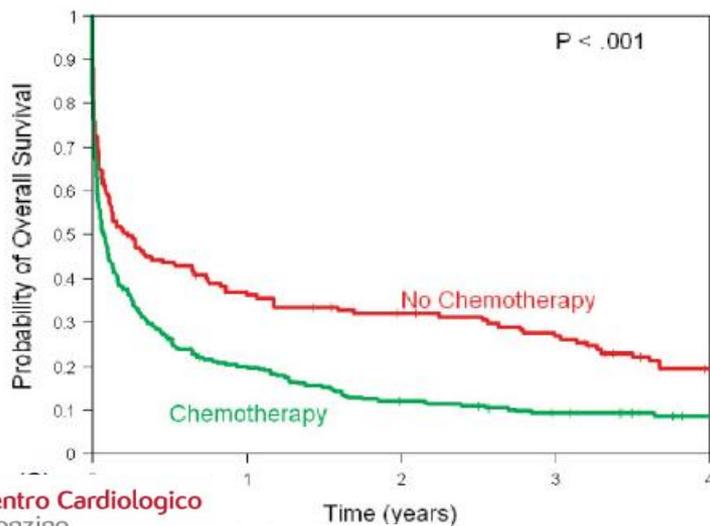
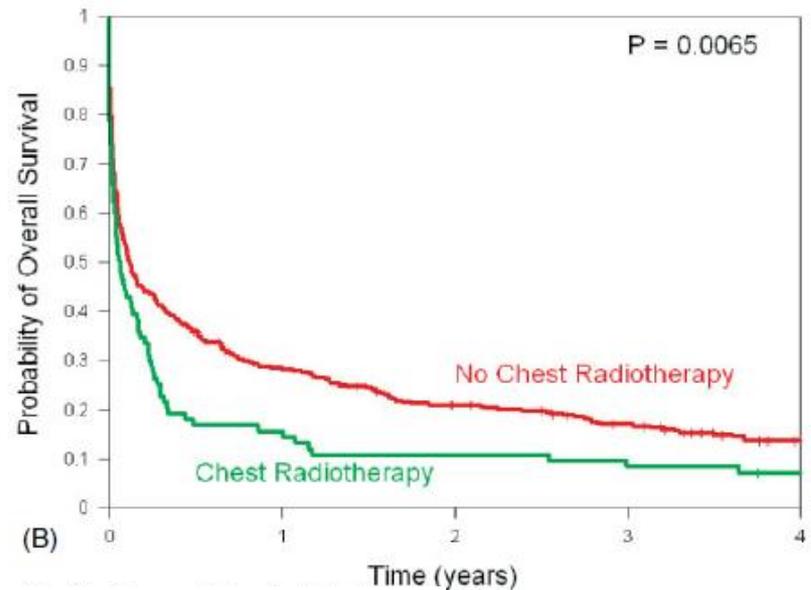
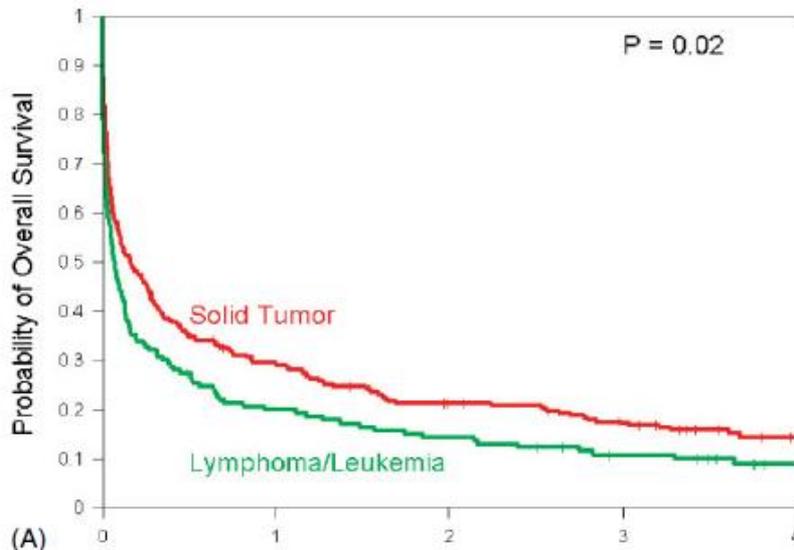
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- Fattori di rischio comuni (fumo, ecc.)
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- SCA e rischio aumentato nei pazienti con tumore

# Treatment and Outcomes of Acute Coronary Syndrome in the Cancer Population

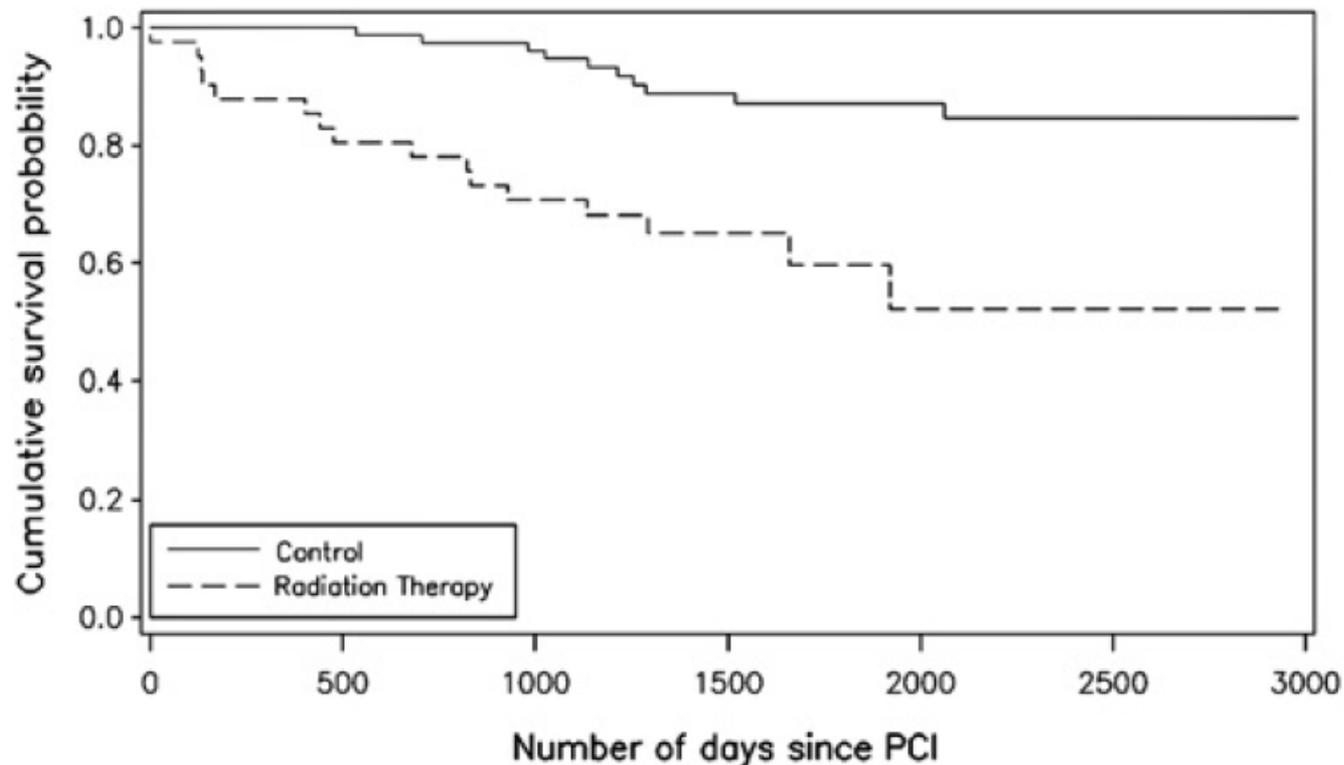
456 cancer patients with ACS (386 NSTEMI and 70 STEMI)



# Treatment and Outcomes of Acute Coronary Syndrome in the Cancer Population



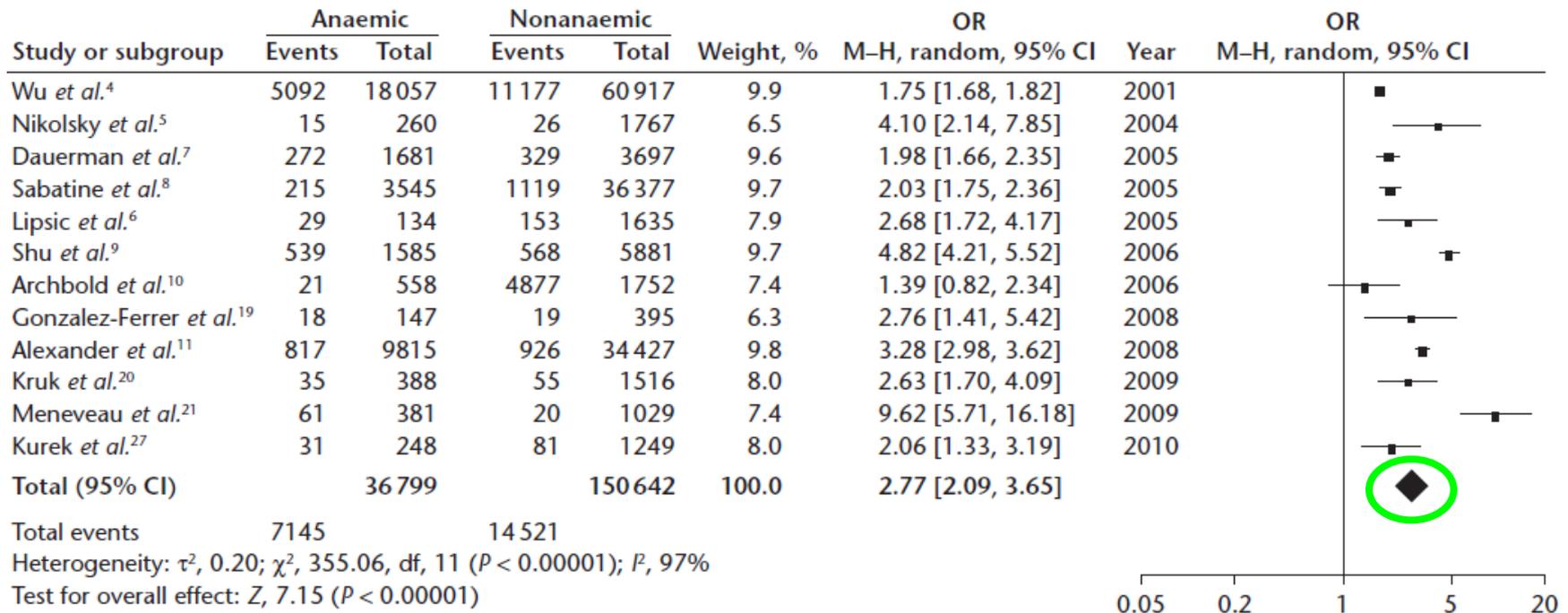
# Clinical outcome of coronary stenting after thoracic radiotherapy: a case-control study



In conclusion, our findings suggest an increased risk of all-cause and cardiac mortality in patients who underwent coronary stent implantation after previous thoracic RT. Verification in larger patient populations is warranted.

# Anaemia and Prognosis in Acute Coronary Syndromes: a Systematic Review and Meta-analysis

## Risk of short-term mortality for anaemic vs. nonanaemic ACS patients



# Anaemia and Prognosis in Acute Coronary Syndromes: a Systematic Review and Meta-analysis

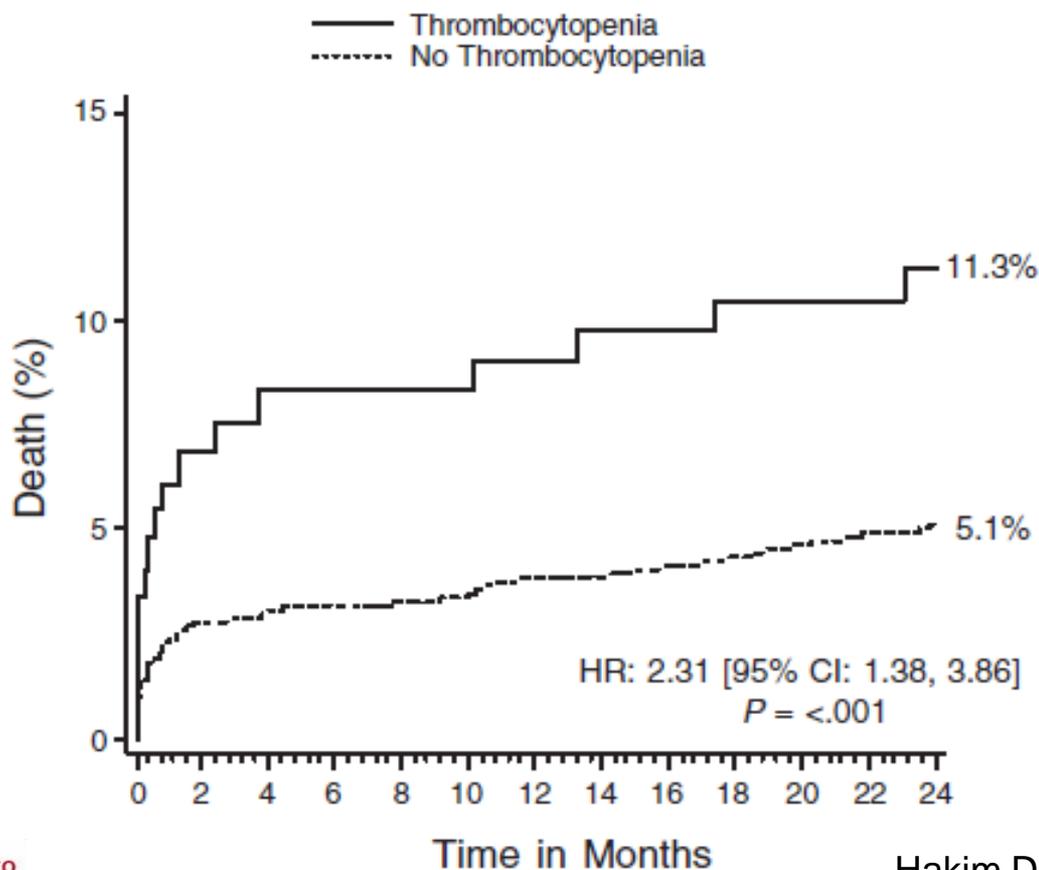
## Risk of long-term mortality for anaemic vs. nonanaemic ACS patients

Study or subgroup	Anaemic		Nonanaemic		Weight, %	OR M-H, random, 95% CI	Year	OR M-H, random, 95% CI
	Events	Total	Events	Total				
Al Falluji <i>et al.</i> <sup>15</sup> (1986)	335	996	3545	14 588	10.8	1.58 [1.38, 1.81]	2002	
Al Falluji <i>et al.</i> <sup>15</sup> (1996)	476	1510	3007	13 247	10.9	1.57 [1.40, 1.76]	2002	
Langston <i>et al.</i> <sup>23</sup>	48	145	77	378	8.9	1.93 [1.26, 2.96]	2003	
Nikolsky <i>et al.</i> <sup>5</sup>	53	260	306	1767	9.7	1.22 [0.88, 1.69]	2004	
Vaglio <i>et al.</i> <sup>12</sup>	46	248	53	790	8.9	3.17 [2.07, 4.84]	2005	
Valeur <i>et al.</i> <sup>25</sup>	331	437	937	1294	10.2	1.19 [0.93, 1.53]	2006	
Shu <i>et al.</i> <sup>9</sup>	423	1036	718	5313	10.8	4.42 [3.81, 5.11]	2006	
Aronson <i>et al.</i> <sup>24</sup>	76	361	81	1029	9.6	3.12 [2.22, 4.38]	2007	
Anker <i>et al.</i> <sup>26</sup>	313	1235	554	3775	10.7	1.97 [1.69, 2.31]	2009	
Kurek <i>et al.</i> <sup>27</sup>	51	248	141	1249	9.5	2.03 [1.43, 2.90]	2010	
Total (95% CI)		6476		43 430	100.0	2.03 [1.52, 2.71]		
Total events	2152		9419					

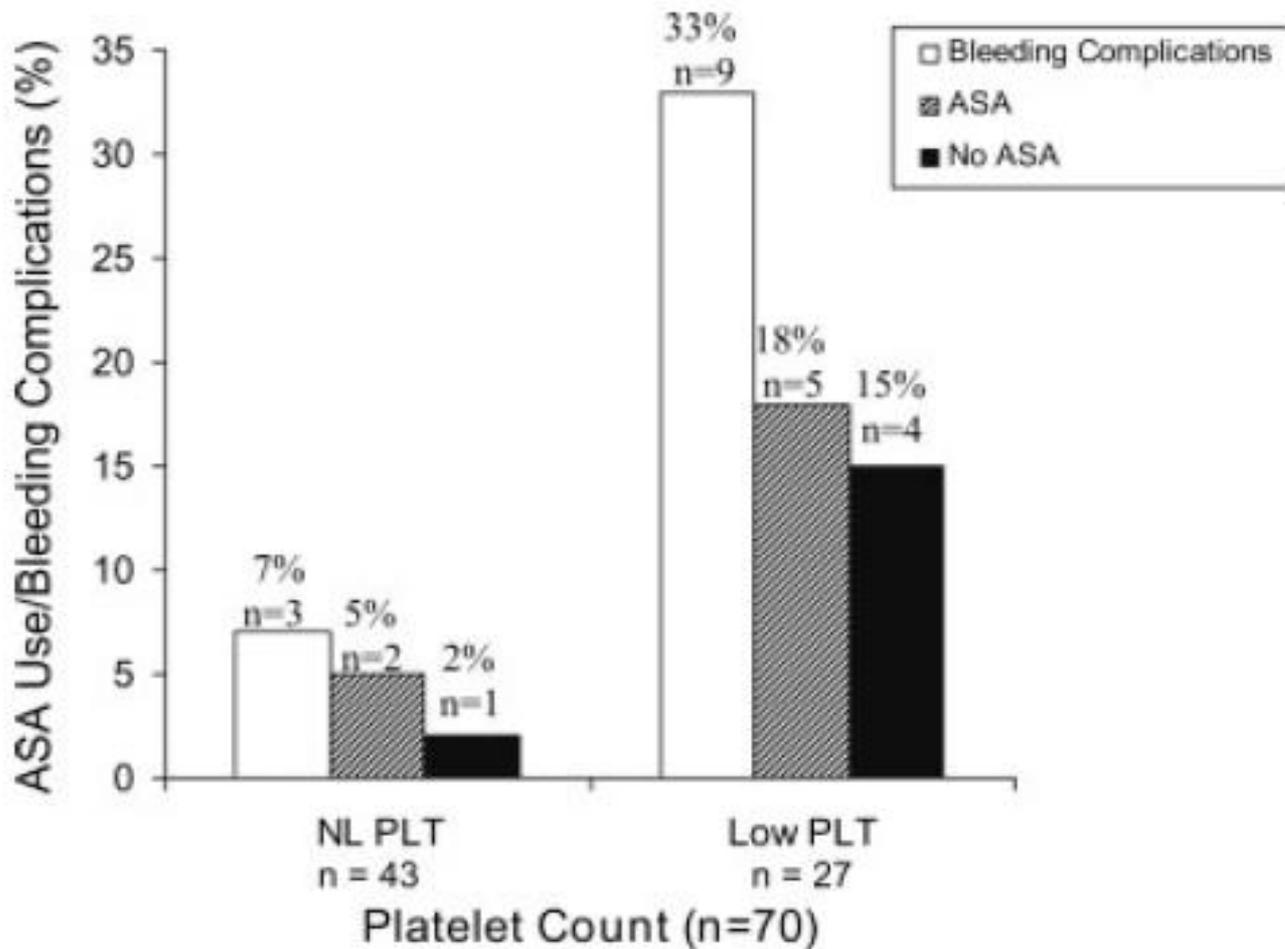
Heterogeneity:  $\tau^2$ , 0.20;  $\chi^2$ , 177.14, df, 9 ( $P < 0.00001$ );  $I^2$ , 95%  
 Test for overall effect:  $Z$ , 4.77 ( $P < 0.00001$ )

# Impact of baseline thrombocytopenia on the early and late outcomes after ST-elevation myocardial infarction treated with primary angioplasty: Analysis from the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial

Thrombocytopenia: <math><150,000</math> platelets/mm<sup>3</sup> (4.2%) (<math><100,000</math> excluded from the study)

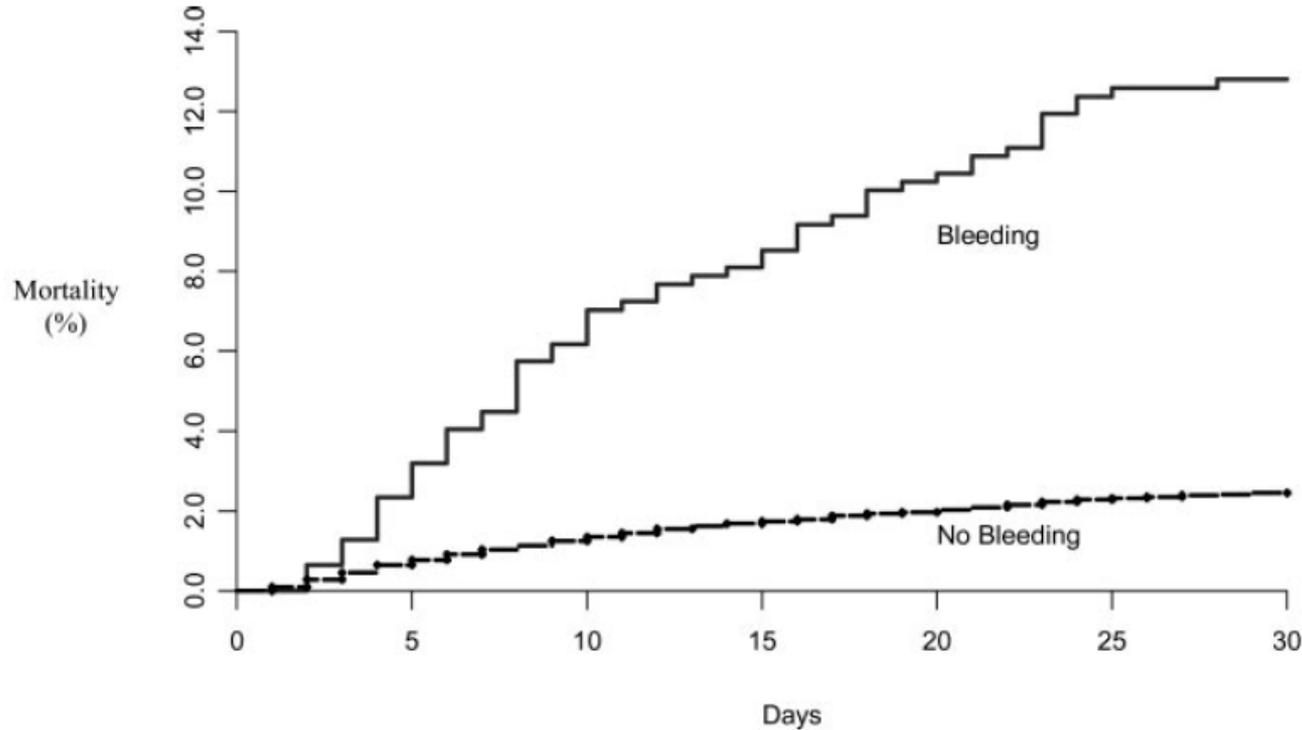


# Impact of Aspirin Therapy in Cancer Patients With Thrombocytopenia and Acute Coronary Syndromes

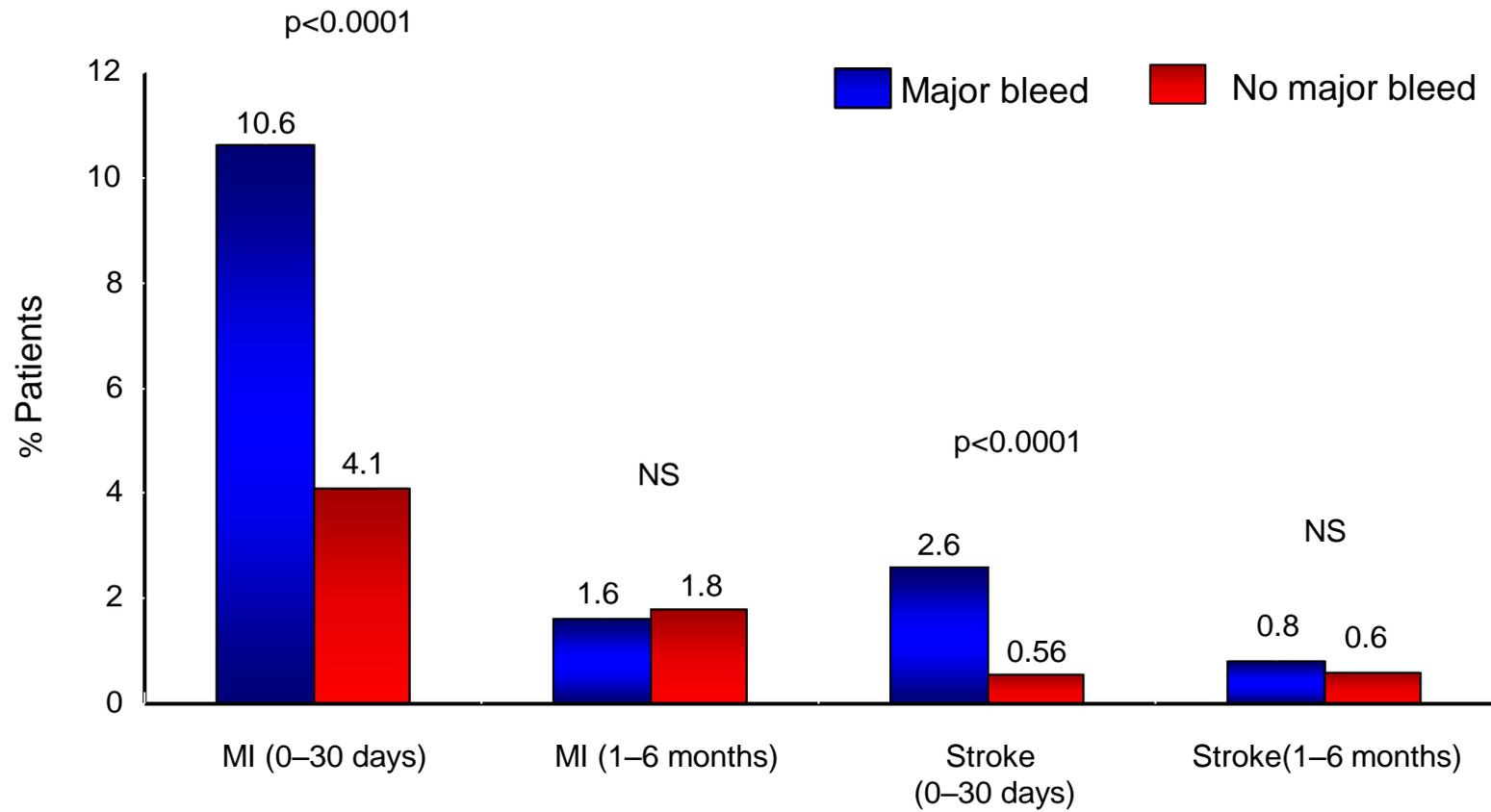


# Adverse Impact of Bleeding on Prognosis in Patients With Acute Coronary Syndromes

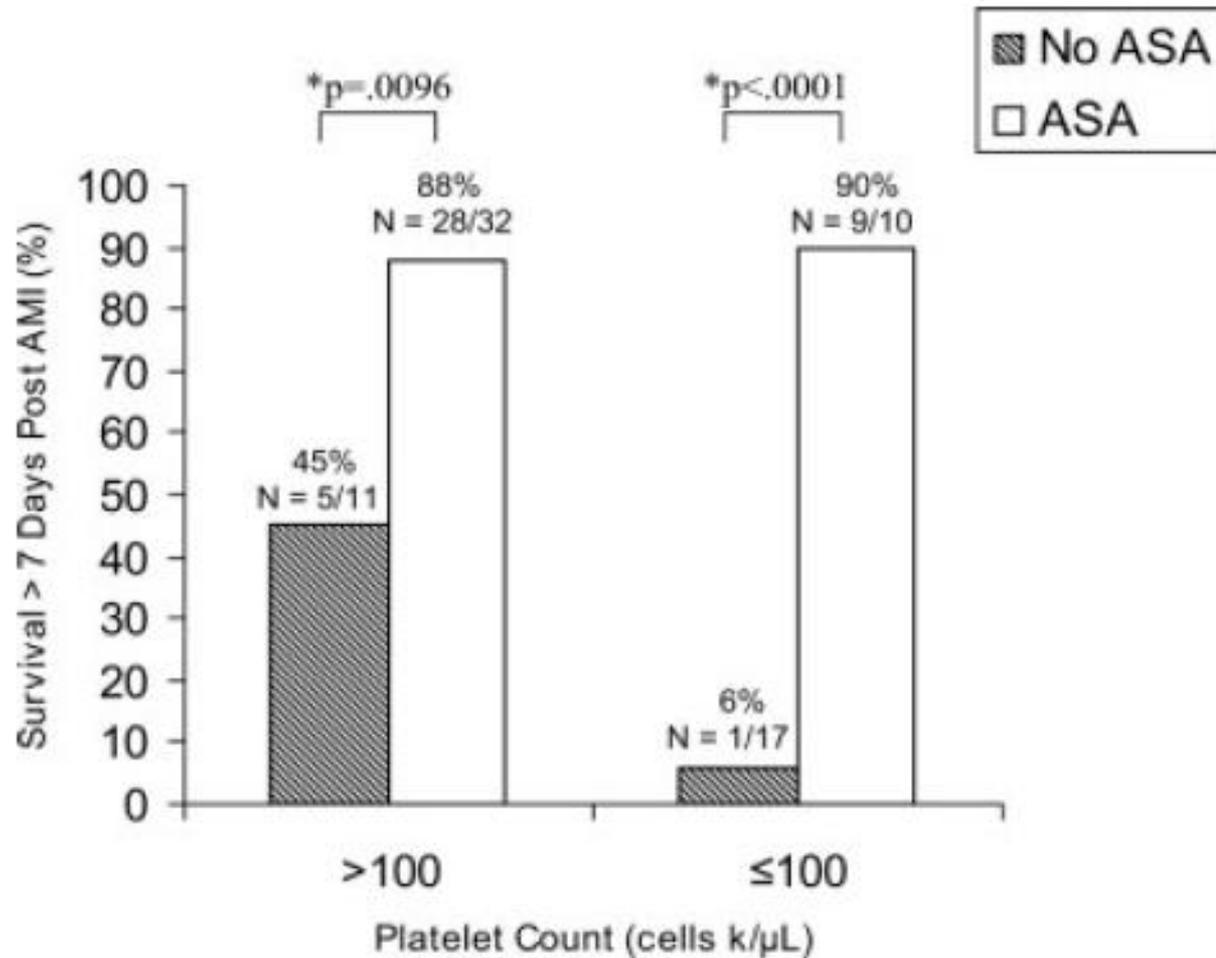
34,146 ACS patients from OASIS Registry, OASIS-2 and CURE trials



# Association between bleeding and CV events



# Impact of Aspirin Therapy in Cancer Patients With Thrombocytopenia and Acute Coronary Syndromes



# “*Punti di contatto*” tra sindromi coronariche acute e tumori

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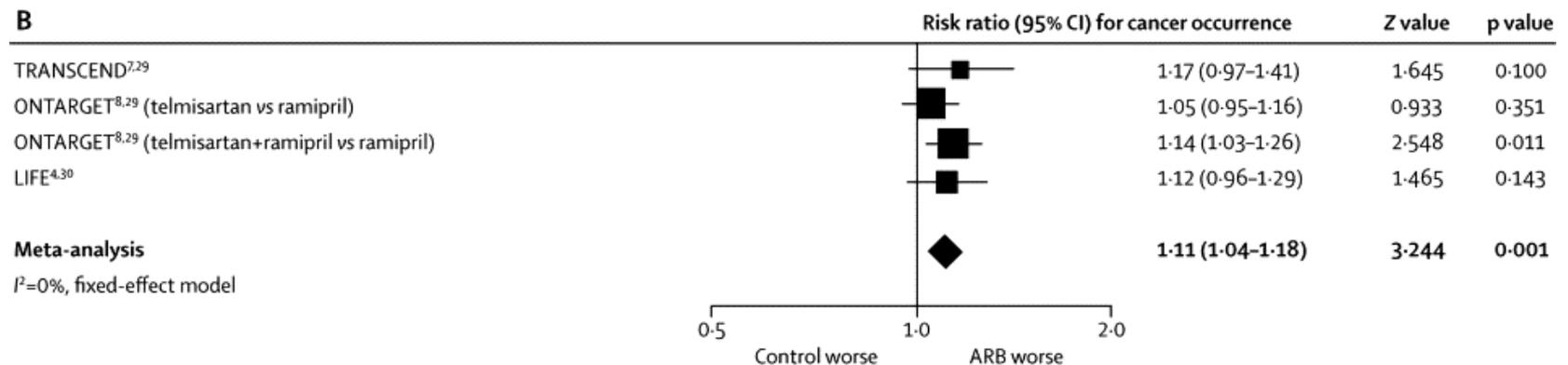
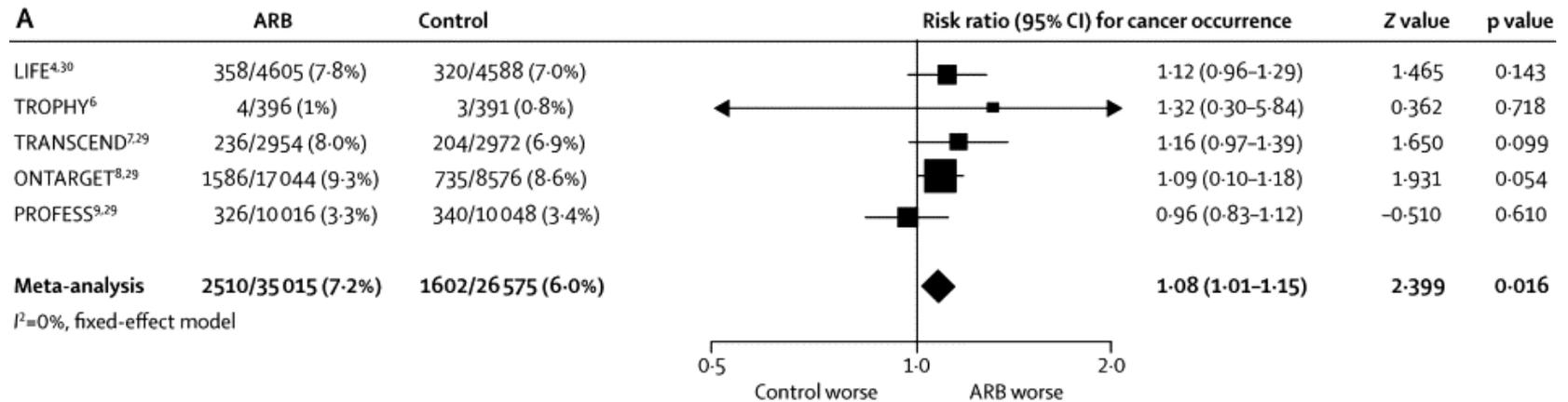
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- **Terapia delle SCA e rischio neoplastico**

# Cardiovascular Medications and Risk of Cancer

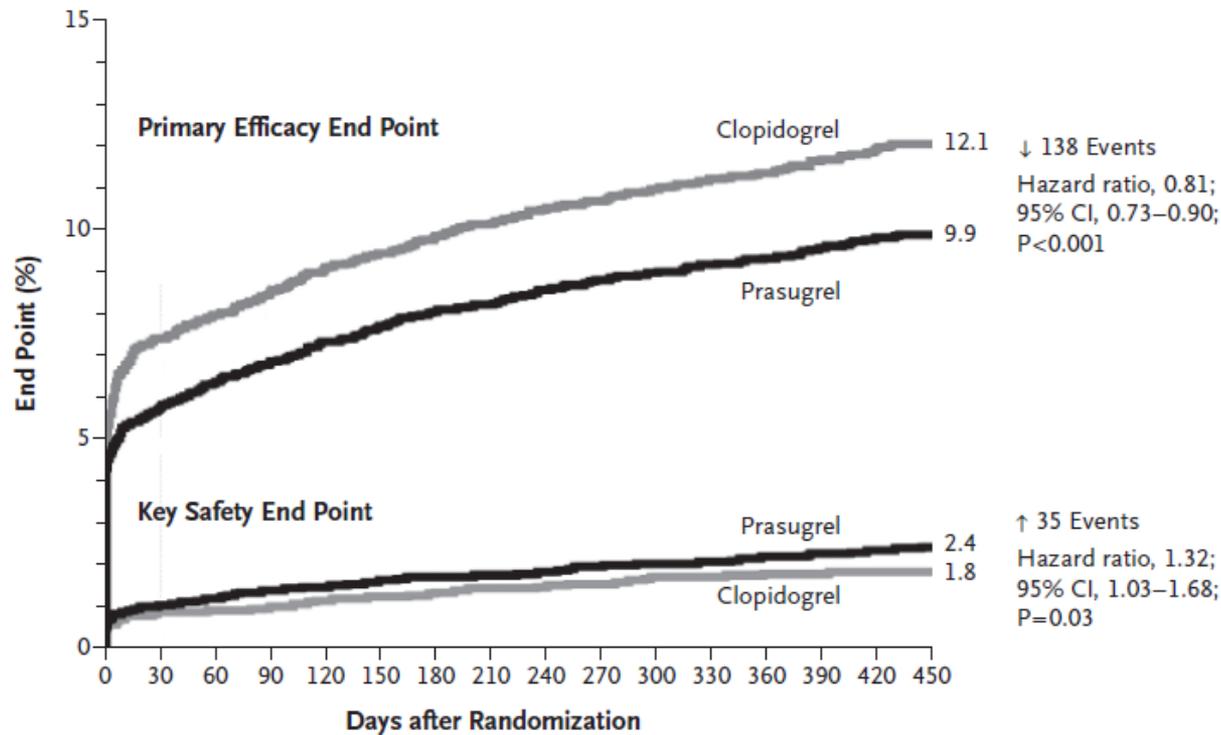
## Statins and risk for cancer

Study	Year	n	Type of Study	Average Age (yrs)	Agent	Type of Cancer	Outcome	Comments
Coogan et al <sup>24</sup>	2002	4,859	Case-control study	50–79	All statins	Breast and prostate	Breast cancer: OR 2.1, 95% CI 1.1–4.0; prostate cancer: OR 1, 95% CI 0.6–1.6	Yes
Pfeffer et al <sup>25</sup>	2002	19,592	Cohort	59	Pravastatin	Breast	Incidence 0.2% vs 0.1% (p = 0.08)	Yes
Friis et al <sup>29</sup>	2005	334,754	Cohort	30–80	All statins	All	RR 0.86, 95% CI 0.78–0.95	No*
Cauley et al <sup>27</sup>	2006	156,351	Cohort	50–79	All statins	Breast	HR 0.91, 95% CI 0.8–1.05 (p = 0.2); using E + P: HR 0.93, 95% CI 0.74–1.18	No*
Browning et al <sup>26</sup>	2006	103,573	Meta-analysis	—	All statins	All	RR 0.95, 95% CI 0.87–1.03 (p = 0.14)	No*
Dale et al <sup>55</sup>	2006	86,936	Meta-analysis	—	All statins	All	OR 1.02, 95% CI 0.97–1.07; deaths: OR 1.01, 95% CI 0.93–1.09	Yes
Murtola et al <sup>57</sup>	2007	49,446	Case-control	20–96	All statins	Prostate	OR 0.75, 95% CI 0.62–0.91	No*
Farwell et al <sup>30</sup>	2008	62,842	Cohort	66	All statins	All	9.4% vs 13.2%; HR 3.8%, 95% CI 3.3%–4.3% (p < 0.001); HR <sup>†</sup> 0.76, 95% CI 0.73–0.8	No*
Chiu et al <sup>66</sup>	2010	2,332	Case-control	≥50	All statins	Liver	OR 0.62, 95% CI 0.45–0.83	No*
Bradley et al <sup>64</sup>	2010	9,095	Case-control	≥85	All statins	Pancreas	OR 0.71, 95% CI 0.42–1.2	No*
Samadder et al <sup>65</sup>	2010	3,842	Case-control	≥60	Pravastatin and simvastatin	Colorectal	No IBD: OR 0.56, 95% CI 0.44–0.72; IBD: OR 0.10, 95% CI 0.01–1.31	No*

# Angiotensin-receptor blockade and risk of cancer: meta-analysis of randomised controlled trials



# Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes

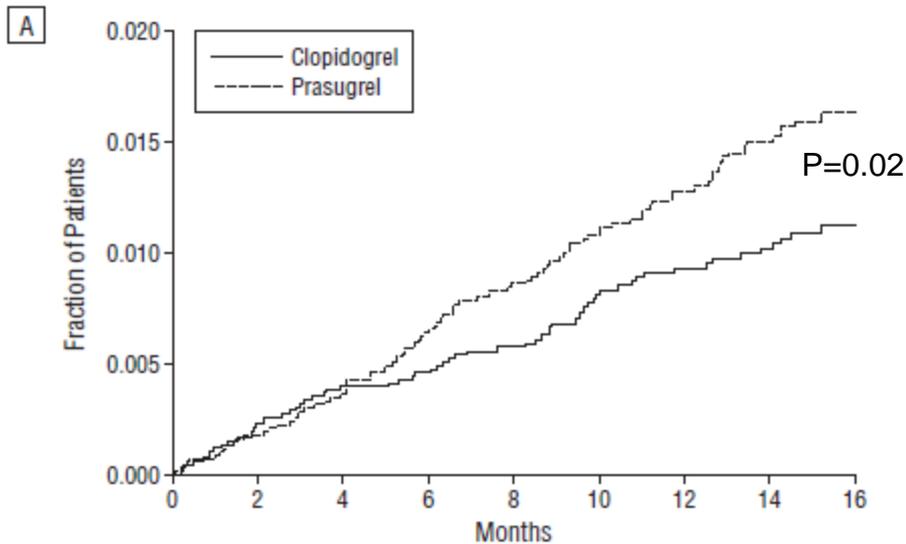


CV death, MI or stroke

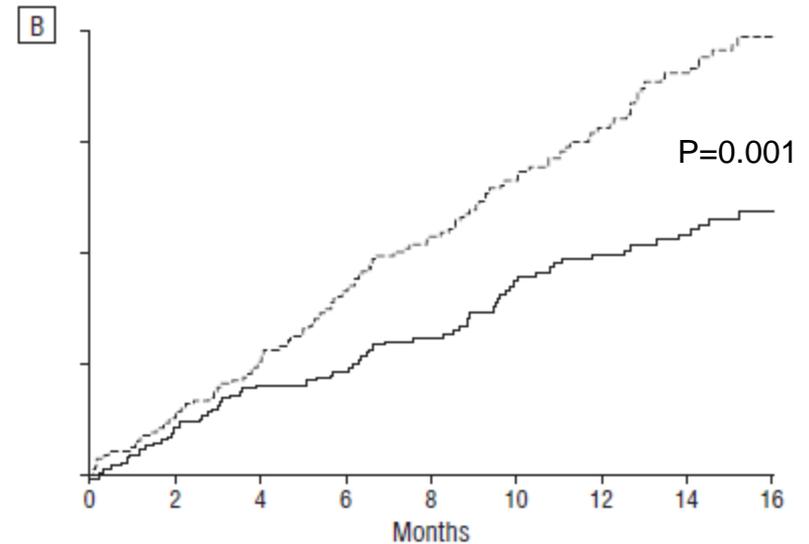
Major bleeding

# Prasugrel as a Potential Cancer Promoter: Review of the Unpublished Data

New solid tumors

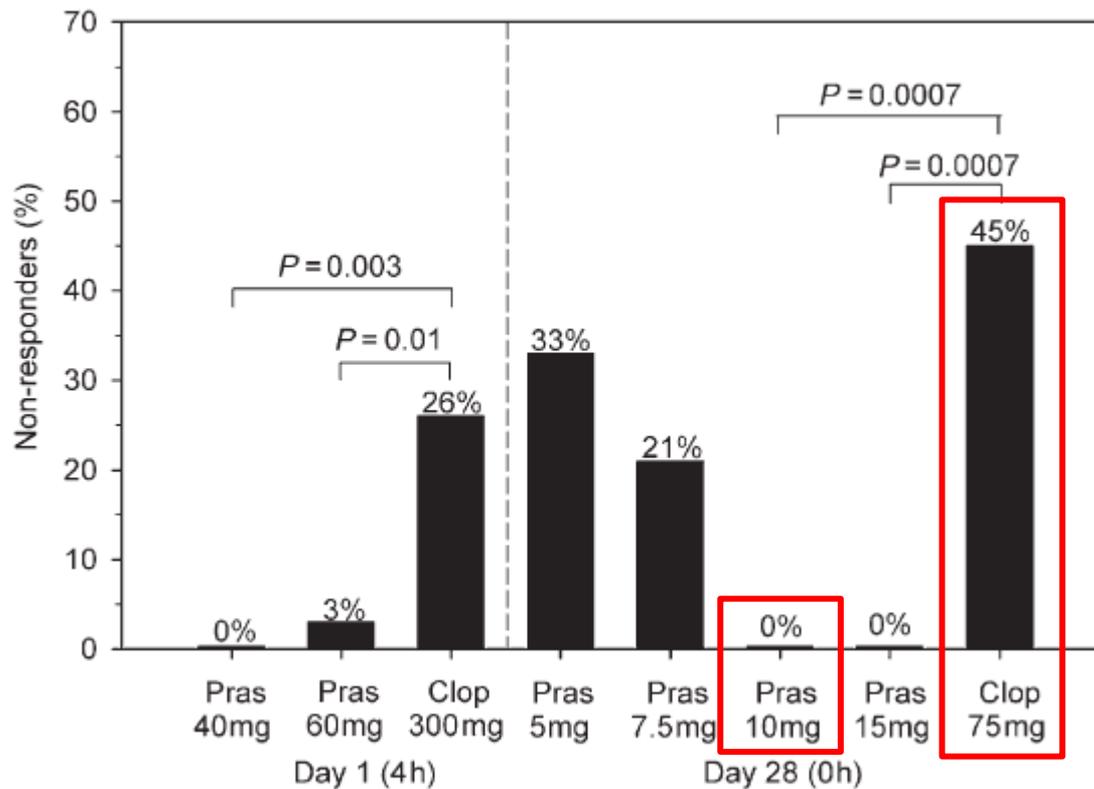


New and worse solid tumors



# Prasugrel achieves greater inhibition of platelet aggregation and a lower rate of non-responders compared with clopidogrel in aspirin-treated patients with stable coronary artery disease

Percentage of non-responders (inhibition of platelet aggregation induced by ADP <25%)



# Sindromi coronariche acute e tumori

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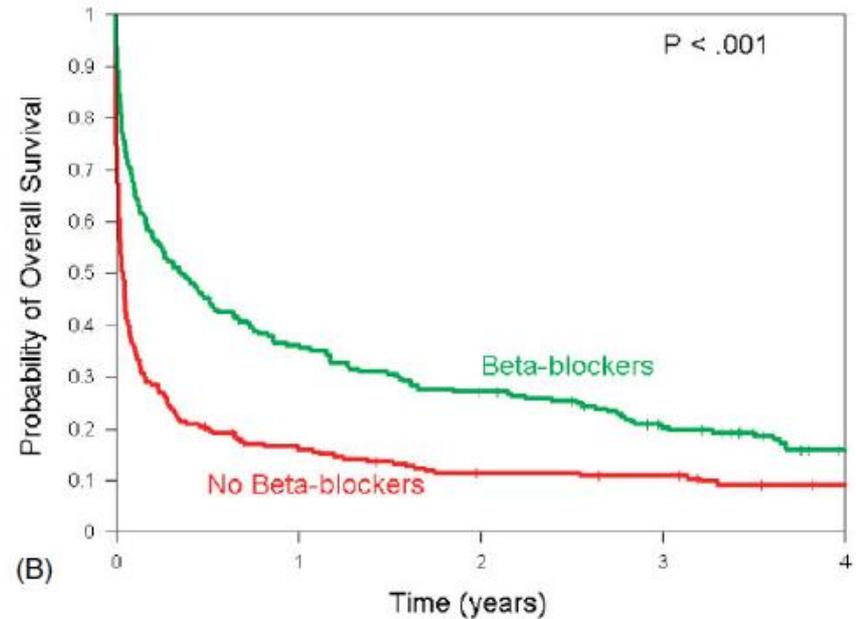
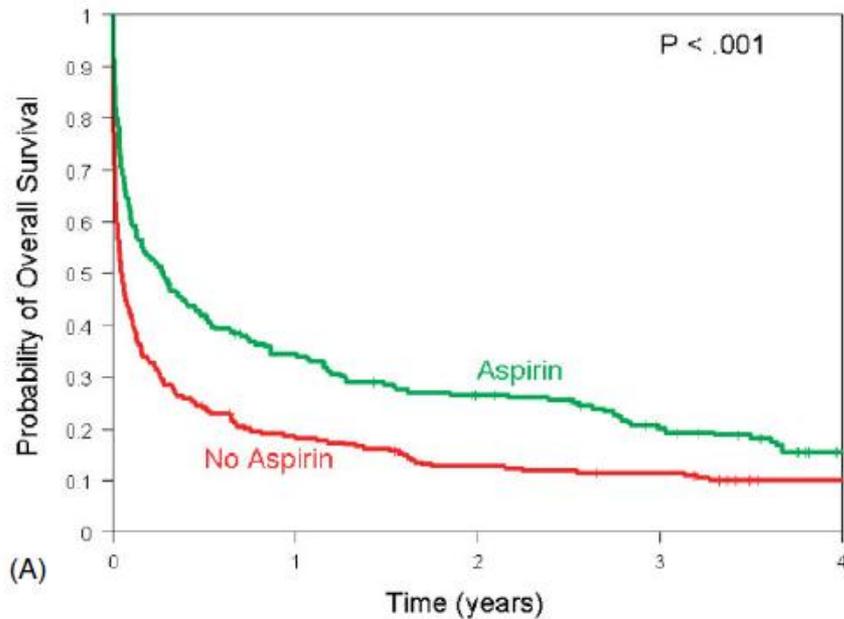
- ❑ Come dobbiamo trattare i pazienti neoplastici con SCA ?

# Sindromi coronariche acute e tumori

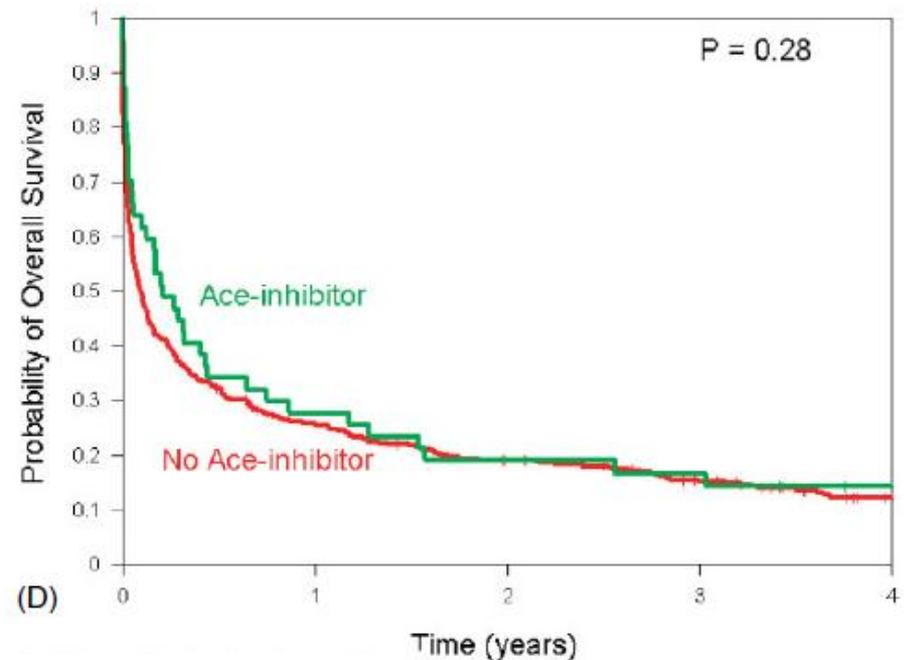
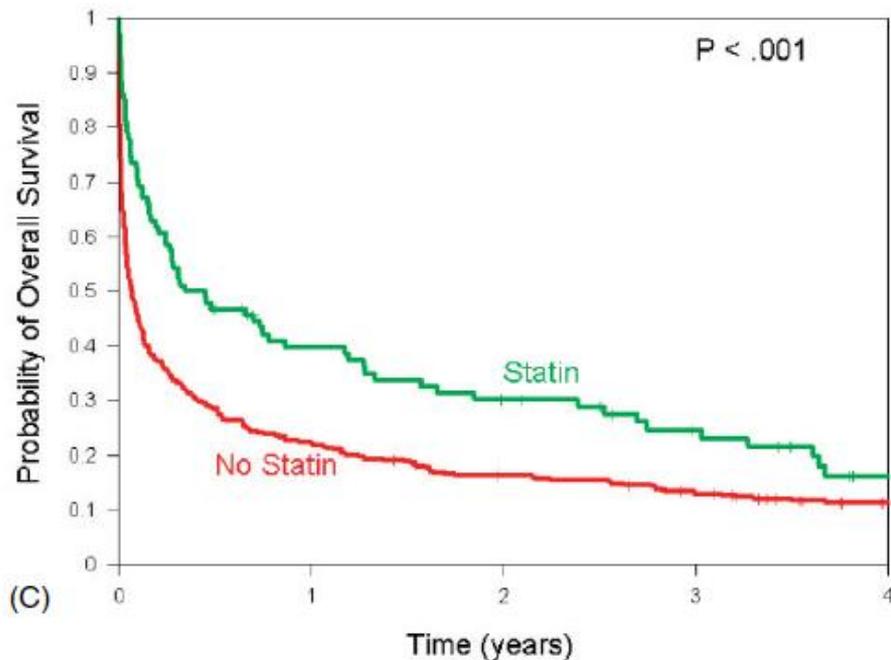
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- Quale tipo di tumore e quali patologie/rischi associati (anemia, piastrinopenia, IR)?
- Qual è la prognosi di base del paziente?
- Quale tipo di terapia antineoplastica è stata utilizzata e qual è il suo timing?
- Quali sono i futuri programmi terapeutici del paziente?
- Possiamo applicare le linee-guida?
- Che tipo di stent coronarico dobbiamo (possiamo) scegliere?
- Quale durata della duplice terapia antiaggregante possiamo permetterci?

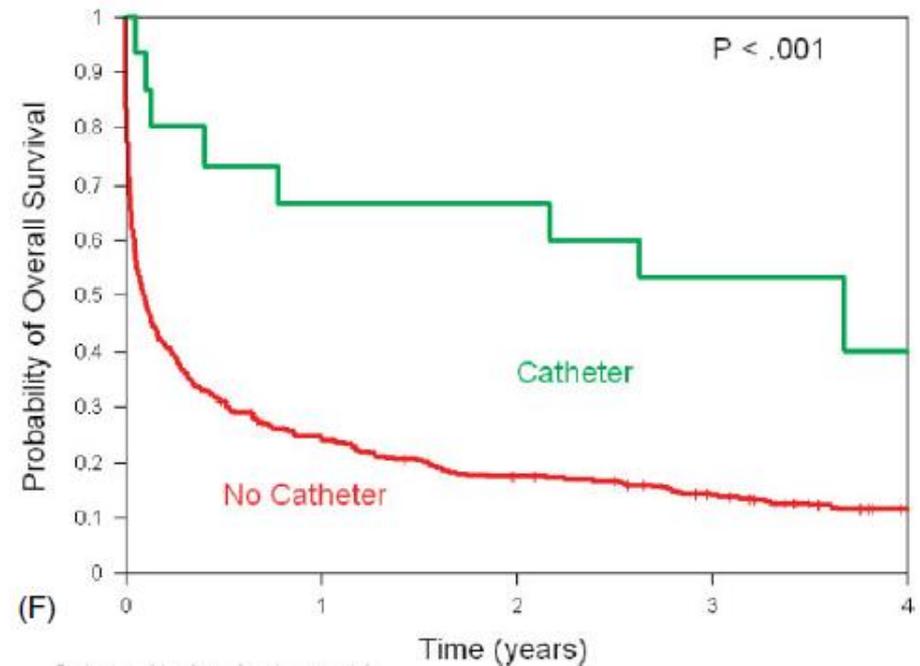
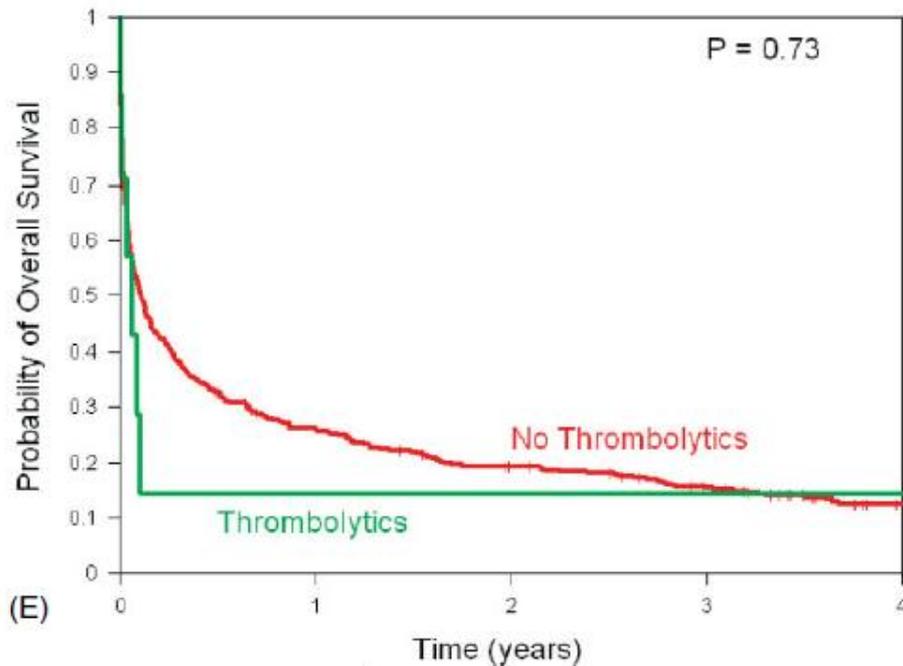
# Treatment and Outcomes of Acute Coronary Syndrome in the Cancer Population



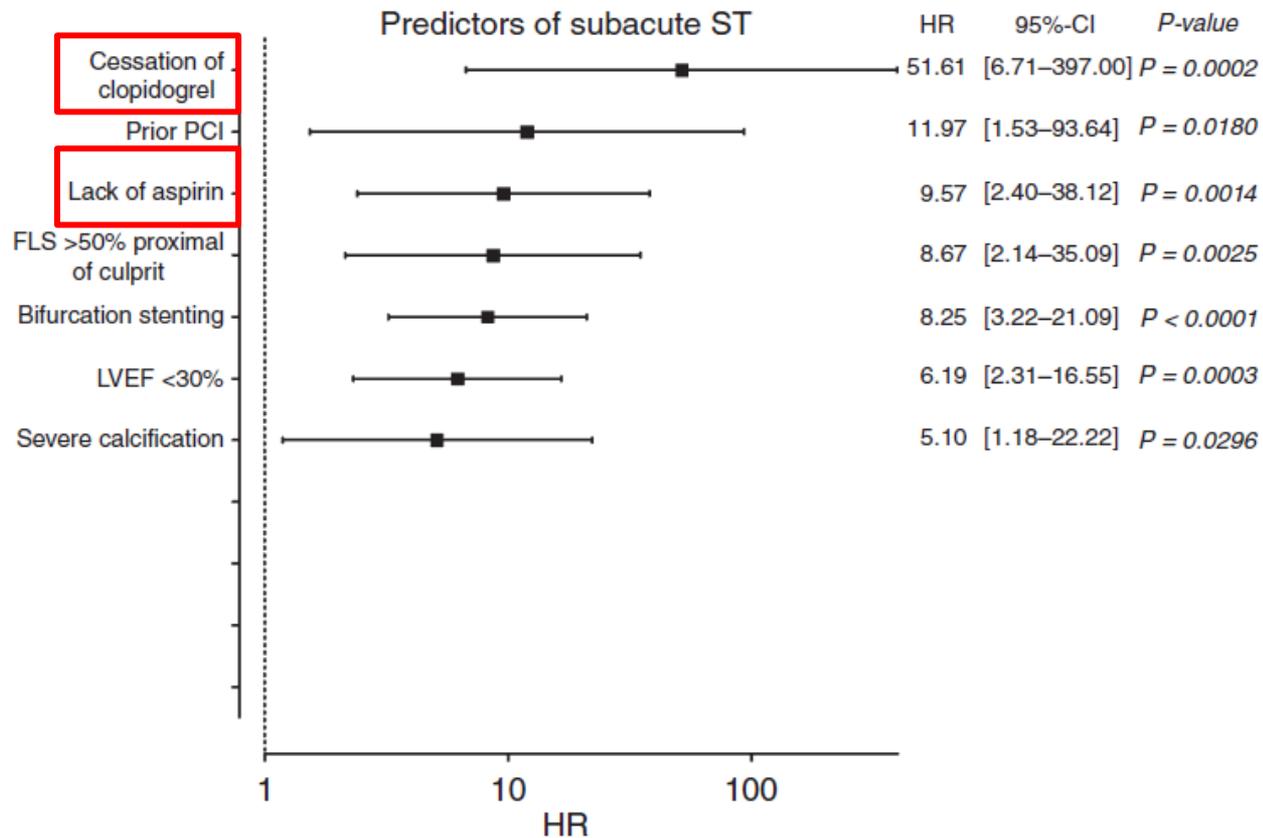
# Treatment and Outcomes of Acute Coronary Syndrome in the Cancer Population



# Treatment and Outcomes of Acute Coronary Syndrome in the Cancer Population



# Acute and subacute stent thrombosis after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: incidence, predictors and clinical outcome



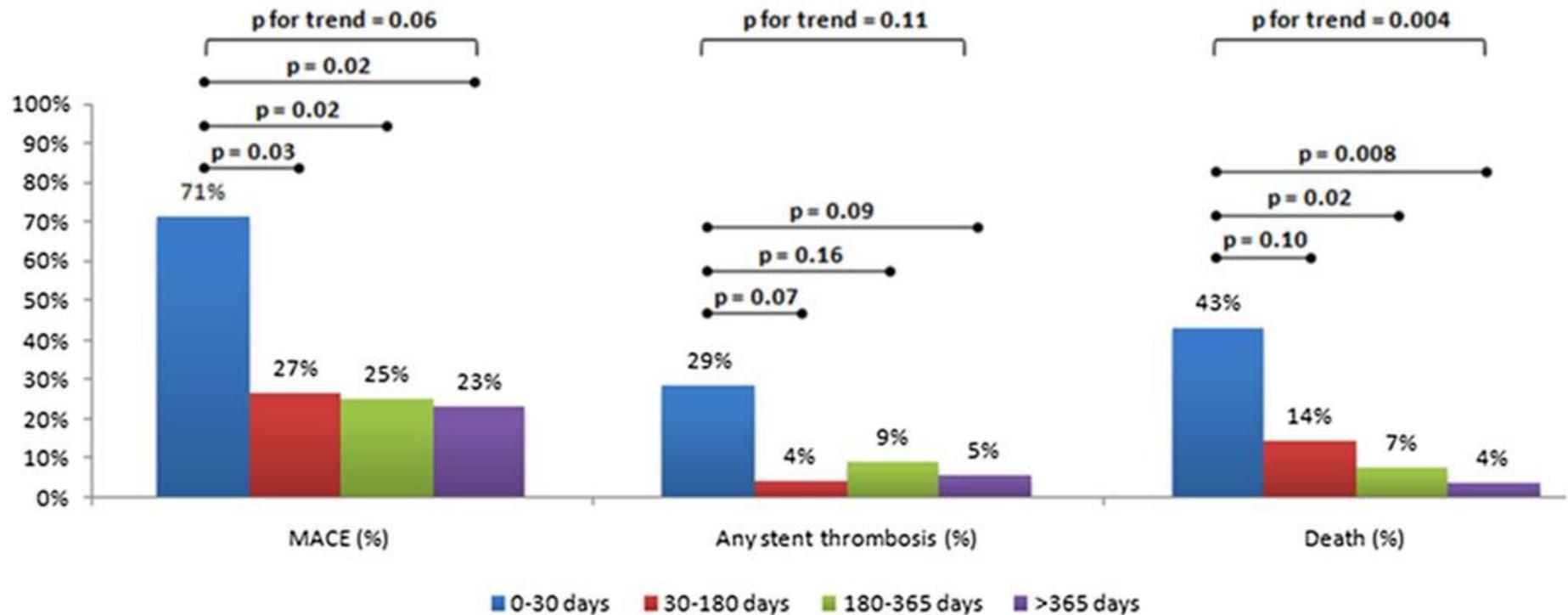
# Prevalence, Predictors, and Long-Term Prognosis of Premature Discontinuation of Oral Antiplatelet Therapy After Drug Eluting Stent Implantation

## Causes of antiplatelet therapy discontinuation

Event	Patients (n)
Early discontinuation of dual antiplatelet therapy (n = 119)	
Bleeding	41 (34.5%)
Surgery	25 (21.0%)
Medical decision	21 (17.6%)
Dental procedure	9 (7.6%)
Economic issues	7 (5.9%)
Oral anticoagulation started	6 (5.0%)
Allergy/intolerance	3 (2.5%)
Unknown	2 (1.7%)
Patient decision	2 (1.7%)
Patient mistake	2 (1.7%)
Trauma	1 (0.8%)

# Prevalence, Predictors, and Long-Term Prognosis of Premature Discontinuation of Oral Antiplatelet Therapy After Drug Eluting Stent Implantation

Outcome in relation to point of antiplatelet therapy discontinuation



# Comparison of Two Antiplatelet Regimens (*Aspirin* Alone Versus *Aspirin + Ticlopidine* or *Clopidogrel*) After Intracoronary Implantation of a *Carbofilm*-Coated Stent

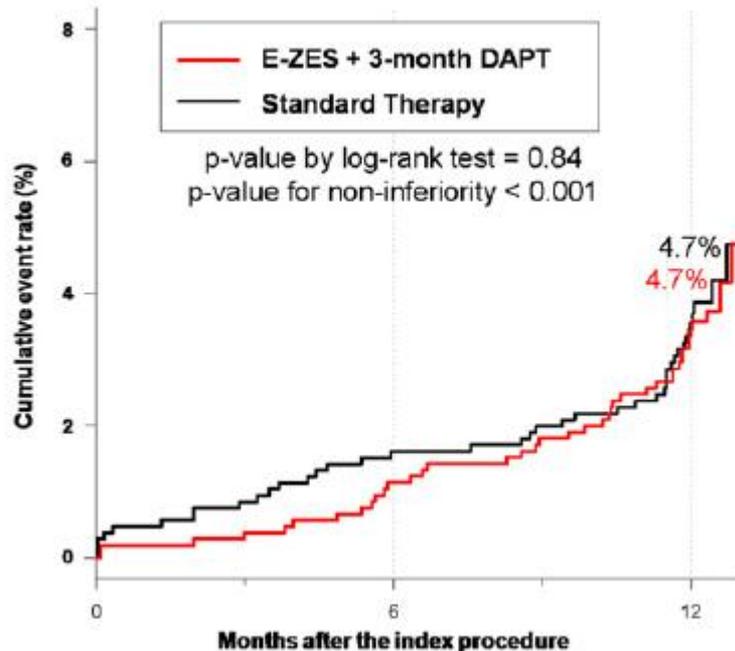
## Primary and secondary end points

	Aspirin Alone	Aspirin + Ticlopidine/Clopidogrel	p Value	RR (95% CI)
<b>ST</b>				
No. of patients	235	244		
Excluding protocol deviations				
Acute	0	0	—	—
Subacute	0	0	—	—
Including protocol deviations				
Acute	2 <sup>†</sup> (0.7%)	1* (0.32%)	0.61	0.47 (0.04–5.17)
Subacute	2 <sup>‡</sup> (0.7%)	0	0.23	—
Total	4 (1.4%)	1 (0.3%)	0.20	0.23 (0.03–2.08)
<b>MACEs</b>				
No. of patients	191	195		
Cardiac death	0	0	—	—
Myocardial infarction	0	1 (0.5%)	1.00	1.00 (0.99–1.02)
Target lesion revascularization	7 (4%)	15 (8%)	0.09	2.19 (0.87–5.50)
Coronary bypass	0	1 (0.5%)	1.00	1.00 (0.99–1.02)
Repeat angioplasty	4 (2%)	13 (7)	0.04	3.32 (1.07–10.43)
Repeat angioplasty + stent	3 (2%)	1 (0.5%)	0.37	0.32 (0.03–3.13)
Total	7 (4%)	16 (8%)	0.06	2.35 (0.94–5.85)

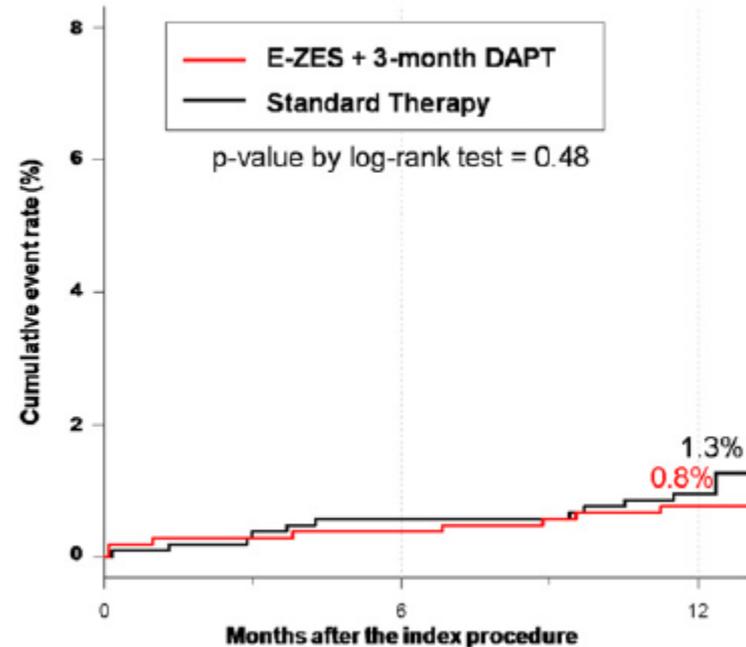
# A New Strategy for Discontinuation of Dual Antiplatelet Therapy

The RESET Trial (REal Safety and Efficacy of 3-month dual antiplatelet Therapy following Endeavor zotarolimus-eluting stent implantation)

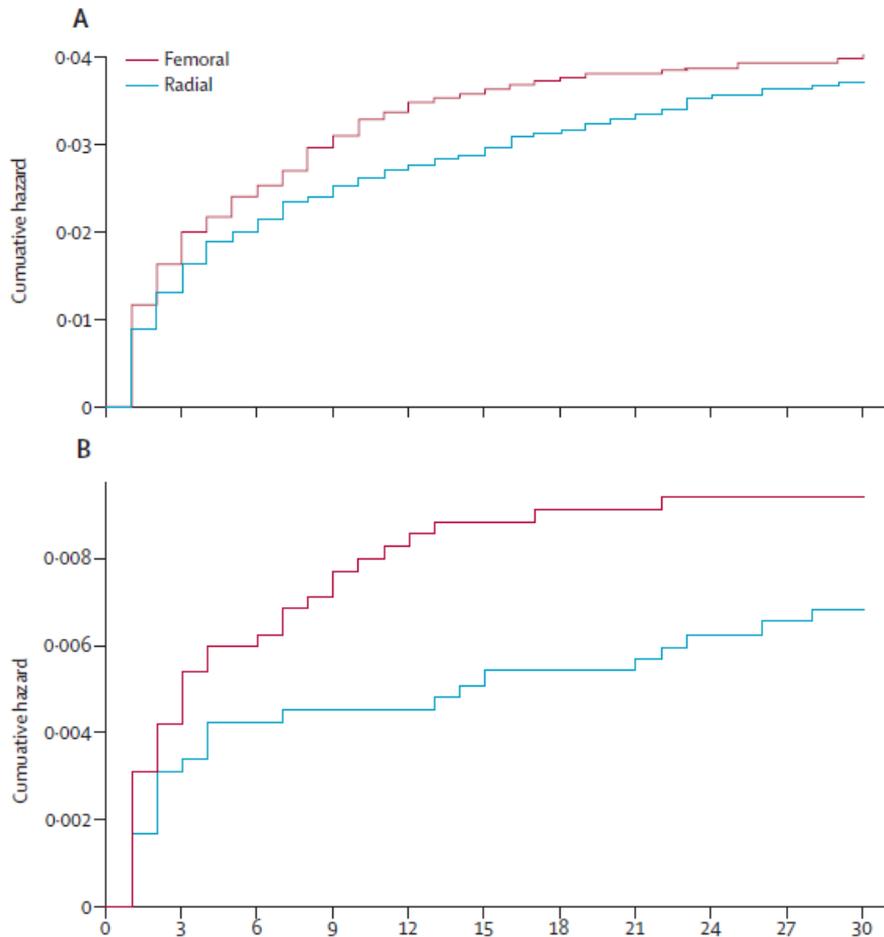
Composite of CV death, MI, stent thrombosis, target revascularization or bleeding



Composite of death from any cause, MI, stent thrombosis,



# Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial



Primary outcome:  
death, MI, stroke and major bleeding

Secondary outcome:  
major bleeding

# Conclusioni

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- ❑ I pazienti con tumore e SCA presentano una mortalità elevata e problematiche cliniche peculiari legate alla patologia di base, a cui la letteratura e le linee-guida non sono in grado ancora di dare una risposta (pazienti sempre esclusi dai trial).
- ❑ Analisi retrospettive suggeriscono che gran parte delle terapie classiche utilizzate nelle SCA (PCI, ASA, beta-bloccanti, statine) possano essere efficaci anche nei pazienti neoplastici
- ❑ La strategia terapeutica deve però essere sempre personalizzata, caso per caso, in rapporto alle numerose variabili che caratterizzano questi pazienti.