Антиагрегантна терапия при пациенти с ОКС и захарен диабет или бъбречна дисфункция

Д-р Борислав Борисов
Клиника по кардиология
МБАЛ Проф. Ст. Киркович – Университетска
Стара Загора

Euro Heart Survey

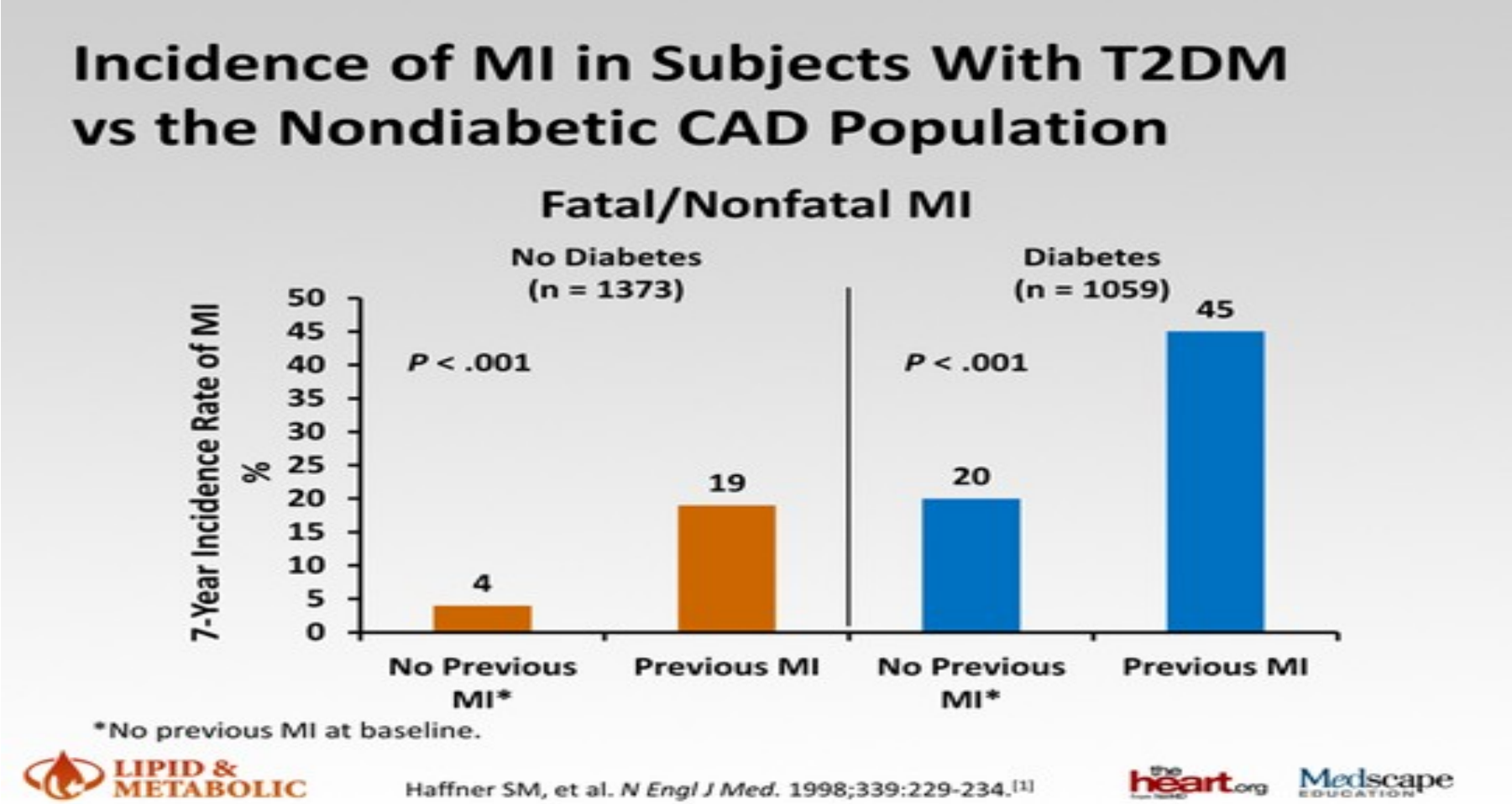
Около 37% от пациентите с ОКС са с известен или новодиагностициран ЗД.

По-често са:

1. Възрастни
2. Жени
3. С АХ и БН
4. Склонни към СН и кървене

Dotevall A, et. al., .Data from the Euro Heart Survey ACS. Diabet Med 2005;22: 1542–1550.

Миокарден инфаркт и захарен диабет

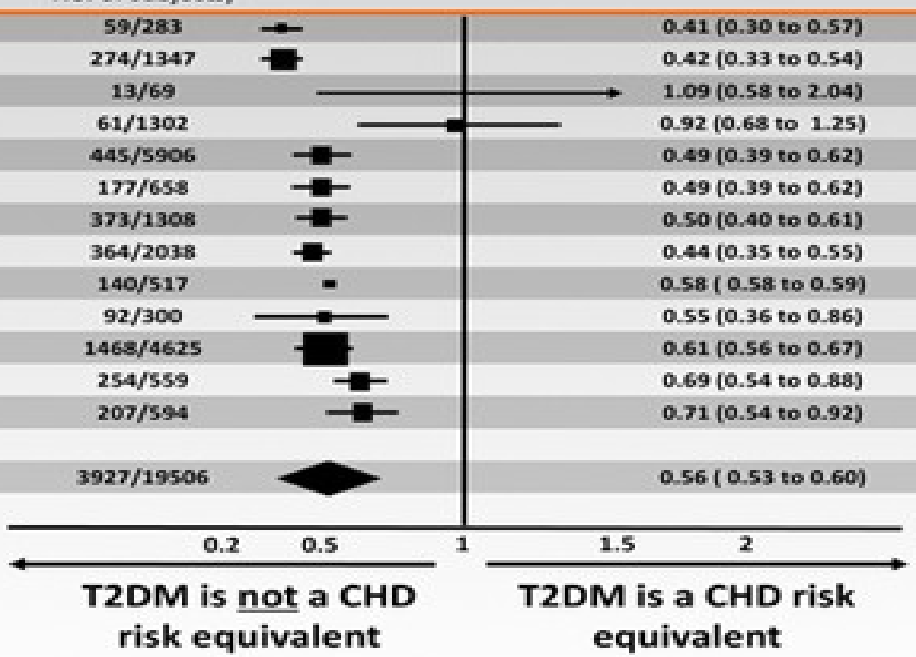


ЗД и коронарна болест - мета анализ

Is Type 2 Diabetes a Coronary Risk Equivalent?

13 studies involving 45,108 subjects

Study	Diabetes alone (No. of MI/ No. of subjects)	Prior MI alone (No. of MI/ No. of subjects)	Odds ratio (95% CI)	Odds ratio (95% CI)	Year
Lee *et al.*	141/1460	59/283		0.41 (0.30 to 0.57)	2004
Evan *et al.*	113/1155	274/1347		0.42 (0.33 to 0.54)	2002
Haffner *et al.*	180/890	13/69		1.09 (0.58 to 2.04)	1998
Hu FB *et al.*	161/3705	61/1302		0.92 (0.68 to 1.25)	2001
Lotufo *et al.*	89/2317	445/5906		0.49 (0.39 to 0.62)	2001
Eberly *et al.*	171/1122	177/658		0.49 (0.39 to 0.62)	2003
Hu G *et al.*	159/962	373/1308		0.50 (0.40 to 0.61)	2005
Cho *et al.*	113/1285	364/2038		0.44 (0.35 to 0.55)	2002
Wannamathee *et al.*	36/202	140/517		0.58 (0.58 to 0.59)	2004
Natarajan *et al.*	35/178	92/300		0.55 (0.36 to 0.86)	2003
Vaccaro *et al.*	1087/4809	1468/4625		0.61 (0.56 to 0.67)	2004
Pajunen *et al.*	191/525	254/559		0.69 (0.54 to 0.88)	2005
Natarajan *et al.*	127/462	207/594		0.71 (0.54 to 0.92)	2005
Total	2603/19072	3927/19506		0.56 (0.53 to 0.60)	



LIPID & METABOLIC

Bulugahapitiya U, et al. *Diabet Med*. 2009;26:142-148.[2]
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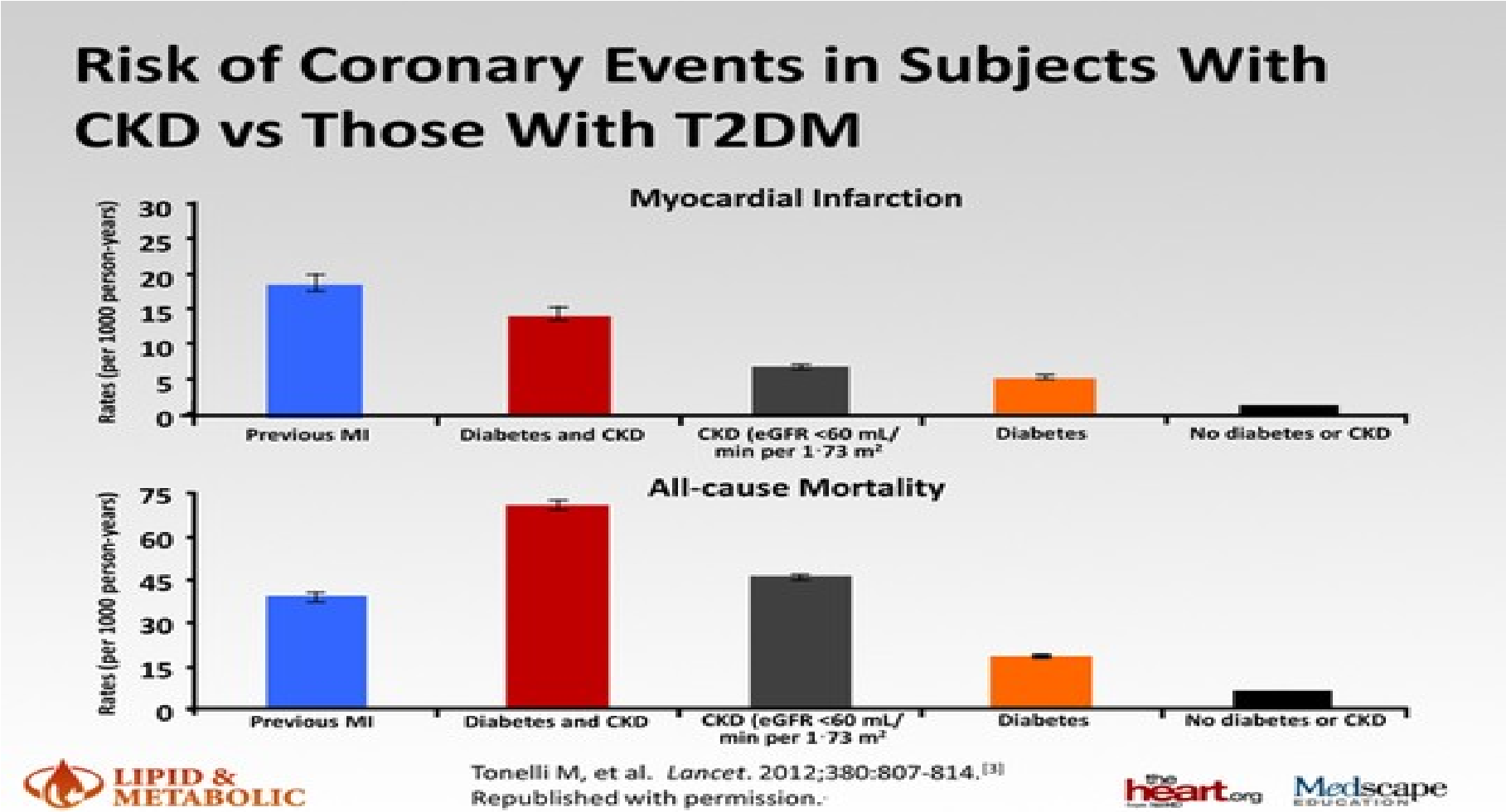
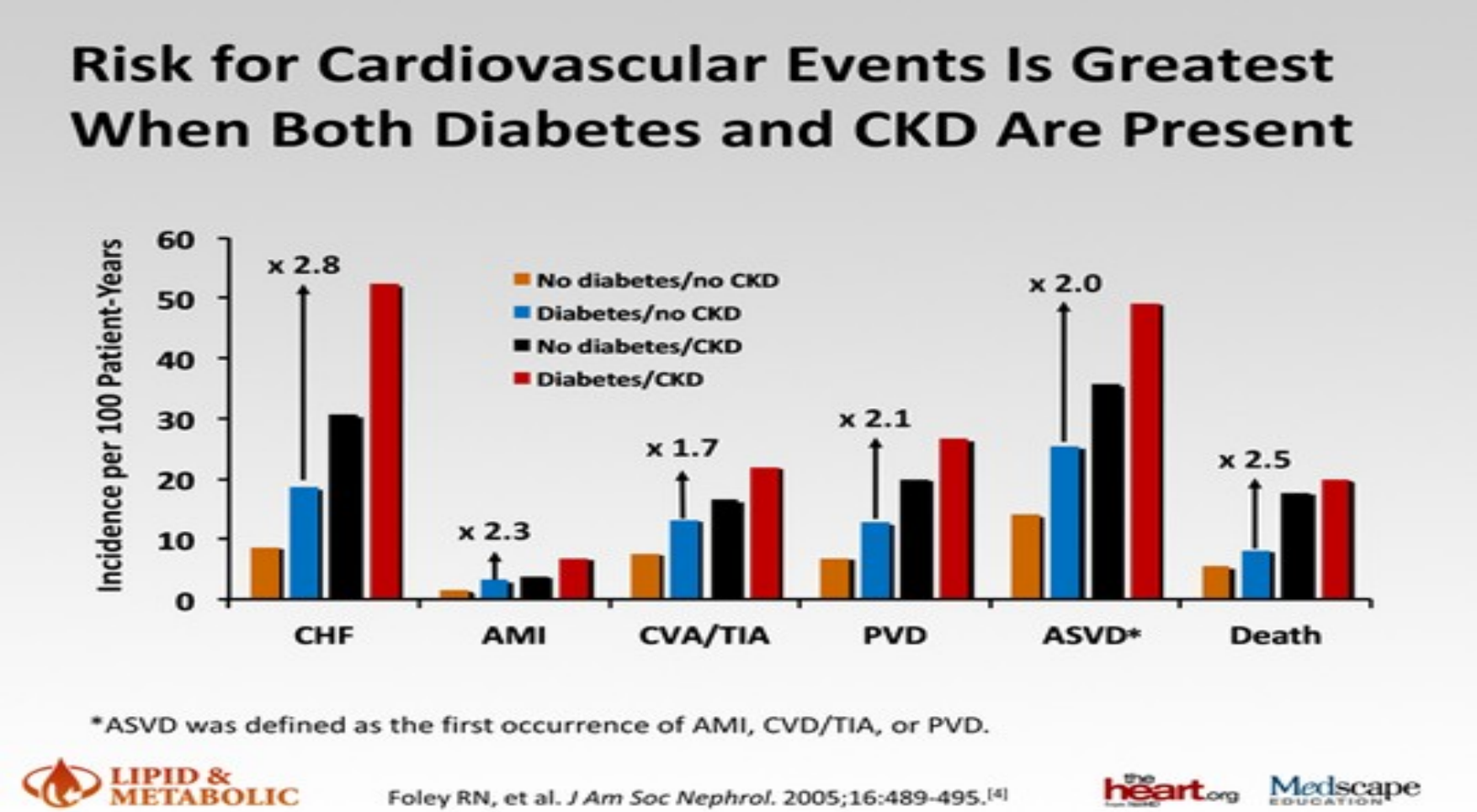
the heart.org

Medscape EDUCATION

ЗД, бъбречна дисфункция и коронарна болест



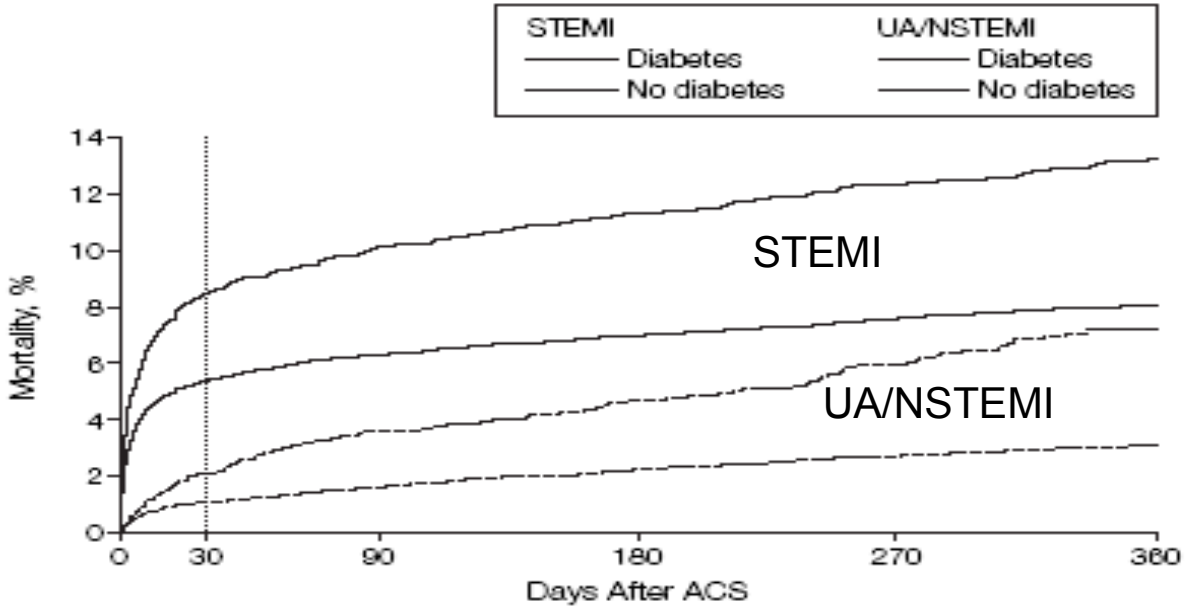
ЗД, бъбречна дисфункция и риск от съдово заболяване



Смъртност при ЗД и ОКС – метаанализ

1997-2006, 62036 пациента

30 дневна - 1.1-2.1% и 5.4-8.5%
1 г. – 3.1-7.2% и 8.1-13.2%



No. at Risk						
STEMI						
Diabetes	7156	6508	2947	2653	2118	1610
No diabetes	39421	37136	16685	15274	12276	9351
UA/NSTEMI						
Diabetes	3457	3313	2923	2339	1317	924
No diabetes	12002	11658	10505	8191	5141	4008

Donahoe S., JAMA, 2007, 298, 765-775

ЗД и по-висок риск при ОКС (1)

1. По-висока честота на нежелани събития – PURSUIT, ACUITY
2. По-често съчетание с АХ и бъбречно увреждане
3. По-висока честота на СН (особено “диастолна”)
4. Индукция на проинфламаторно и протромботично състояние с ендотелна дисфункция и активация на тромбоцитите
5. При инсулинова резистентност съществува повишена активност на $P2Y_{12}$ рецептора

1. Donahoe SM, et al. Diabetes and mortality following acute coronary syndromes. *JAMA*. 2007;298:765–775.

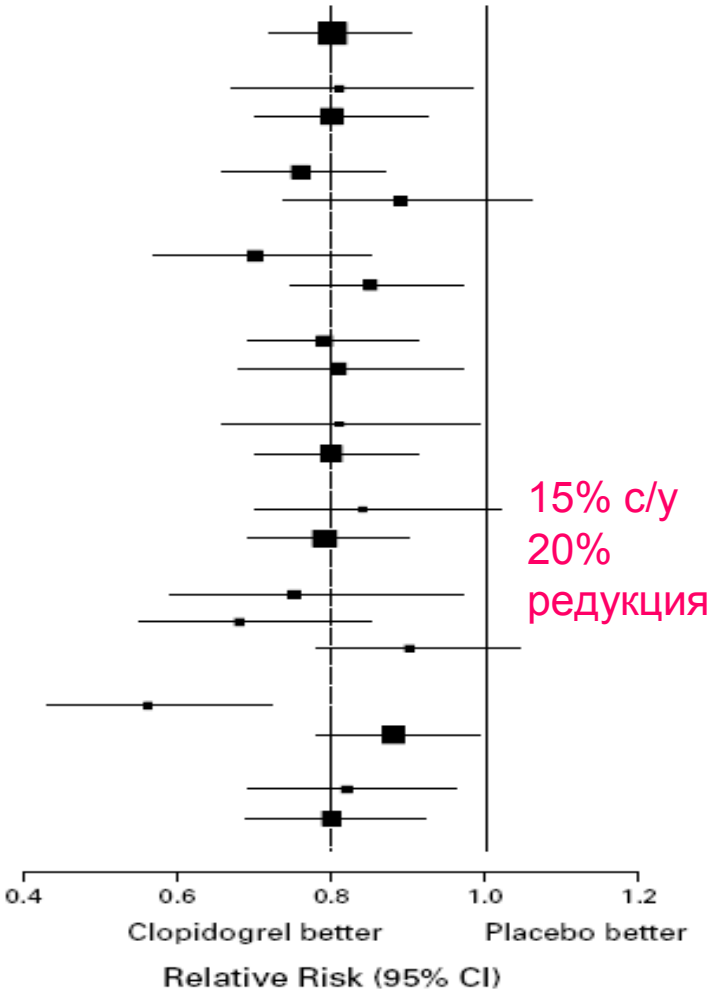
ЗД и по-висок риск след реваскуларизация

	No DM (n=10 462), %	DM (n=3146), %	HR (95% CI)	*P*
CVD/MI/CVA*	9.9	14.6	1.45 (1.29–1.62)	<0.0001
CVD/MI	9.2	13.1	1.39 (1.23–1.56)	<0.0001
MI†	8.0	10.7	1.30 (1.14–1.49)	0.0001
CVD	1.8	3.8	2.13 (1.68–2.70)	<0.0001
Stent thrombosis	1.4	2.8	1.95 (1.47–2.59)	<0.0001
Major bleed‡	2.0	2.6	1.28 (0.97–1.68)	0.08
Major or minor bleed‡	4.2	4.8	1.15 (0.95–1.41)	0.15
D/MI/CVA*/major bleed‡	11.9	16.9	1.40 (1.26–1.56)	<0.0001

Wiviott S., *Circulation*. 2008;118:1626-1636

CURE поданализ

Characteristic	No. of Patients	Percentage of Patients with Event	
		Placebo	Clopidogrel
Overall	12562	11.4	9.3
Associated MI	3283	13.7	11.3
No associated MI	9279	10.6	8.6
Male sex	7726	11.9	9.1
Female sex	4836	10.7	9.5
≤65 yr old	6354	7.6	5.4
>65 yr old	6208	15.3	13.3
ST-segment deviation	6275	14.3	11.5
No ST-segment deviation	6287	8.6	7.0
Enzymes elevated at entry	3176	13.0	10.7
Enzymes not elevated at entry	9386	10.9	8.8
Diabetes	2840	16.7	14.2
No diabetes	9722	9.9	7.9
Low risk	4187	6.7	5.1
Intermediate risk	4185	9.4	6.5
High risk	4184	18.0	16.3
History of revascularization	2246	14.4	8.4
No history of revascularization	10316	10.7	9.5
Revascularization after randomization	4577	13.9	11.5
No revascularization after randomization	7985	10.0	8.1

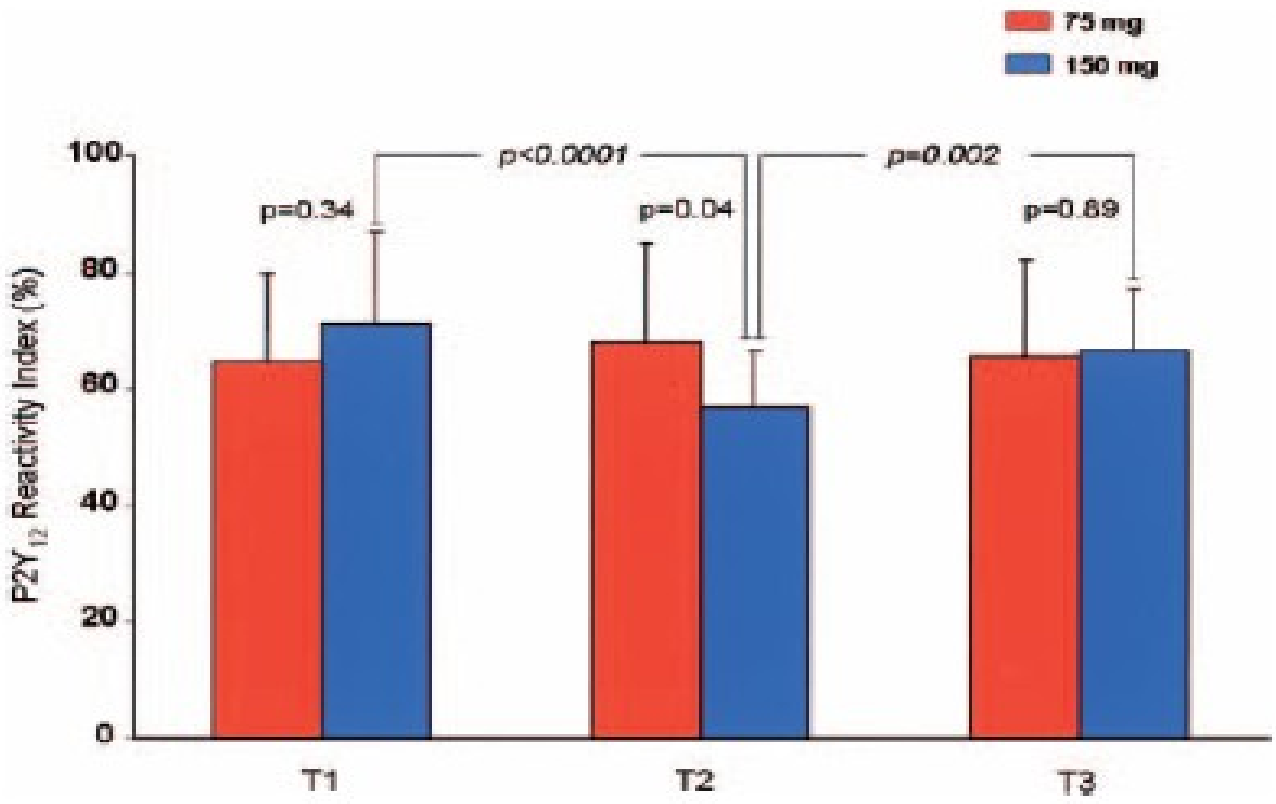


15% с/у
20%
редукция

Yusuf S et al., N Engl J Med, 2001, Vol. 345, No. 7

Доза зависим ефект на Клопидогрел при ЗД – Optimus trial

***Dominick A., Circulation*. 2007;115:708-716, включени след PCI 40 пациента от 64 или 62.5%**



Празугрел и ЗД
поданализ на TRYTON-TIMI 38

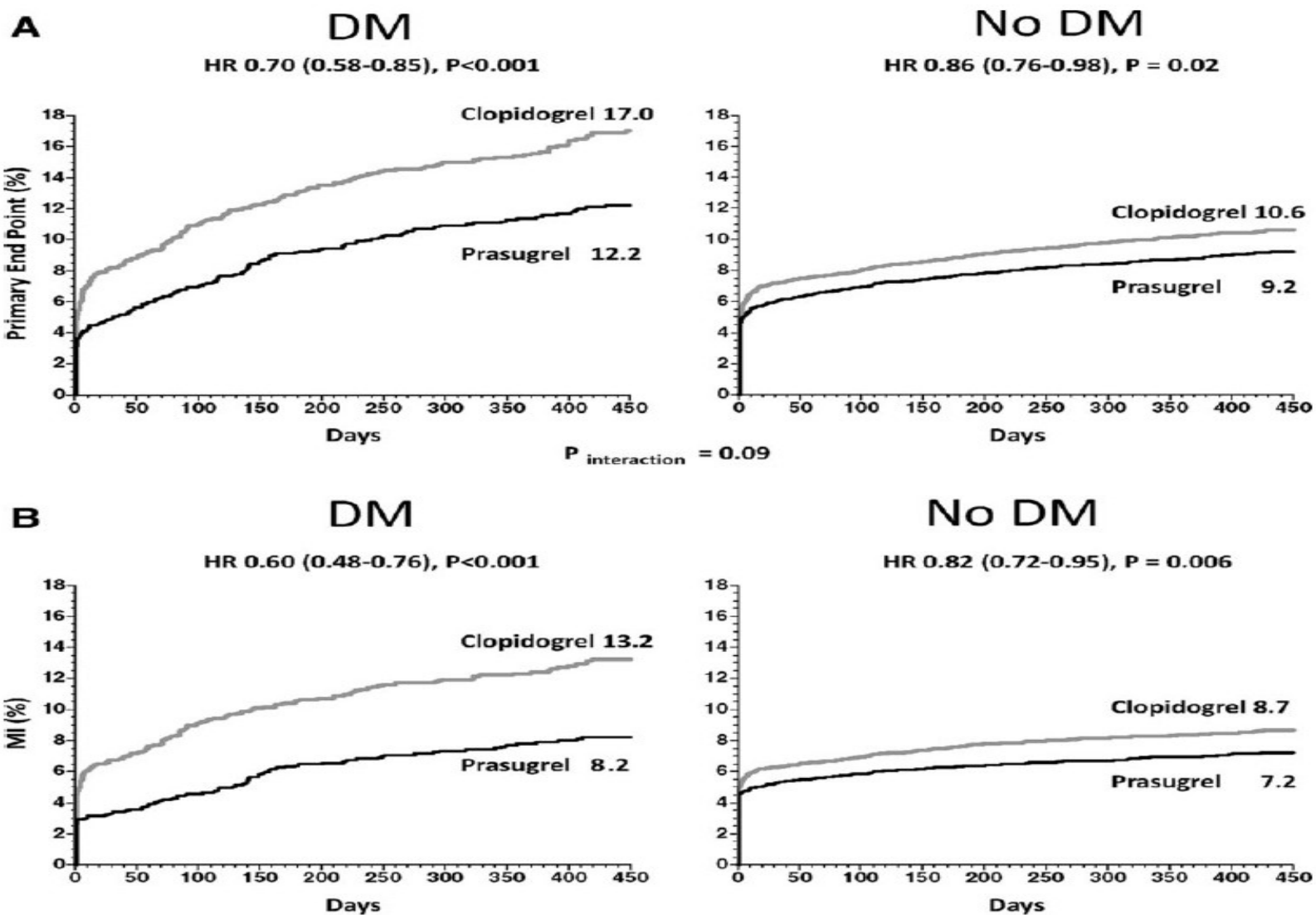
- От 13608 - 3146 са със ЗД (23.1%) Обхванати са пациенти с НАП след STEMI или за първична PTCA за STEMI
- От тях 776 на инсулин
- Крайни точки:

  - първични – сърдечно-съдова смъртност, МИ, инсулт

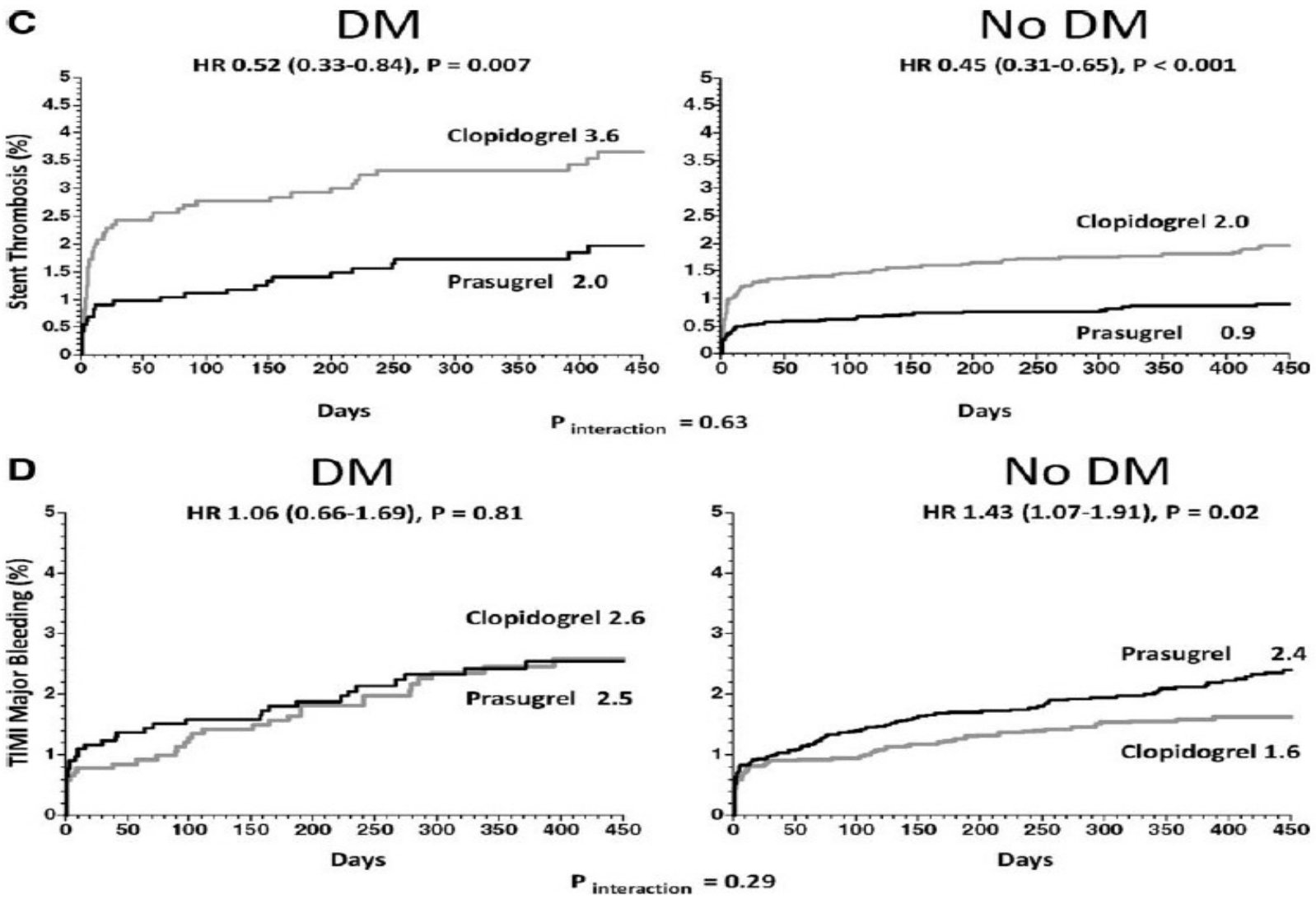
  - вторични – обща смъртност, МИ, инсулт, TIMI голямо кървене

Wiviott S., *Circulation*. 2008;118:1626-1636

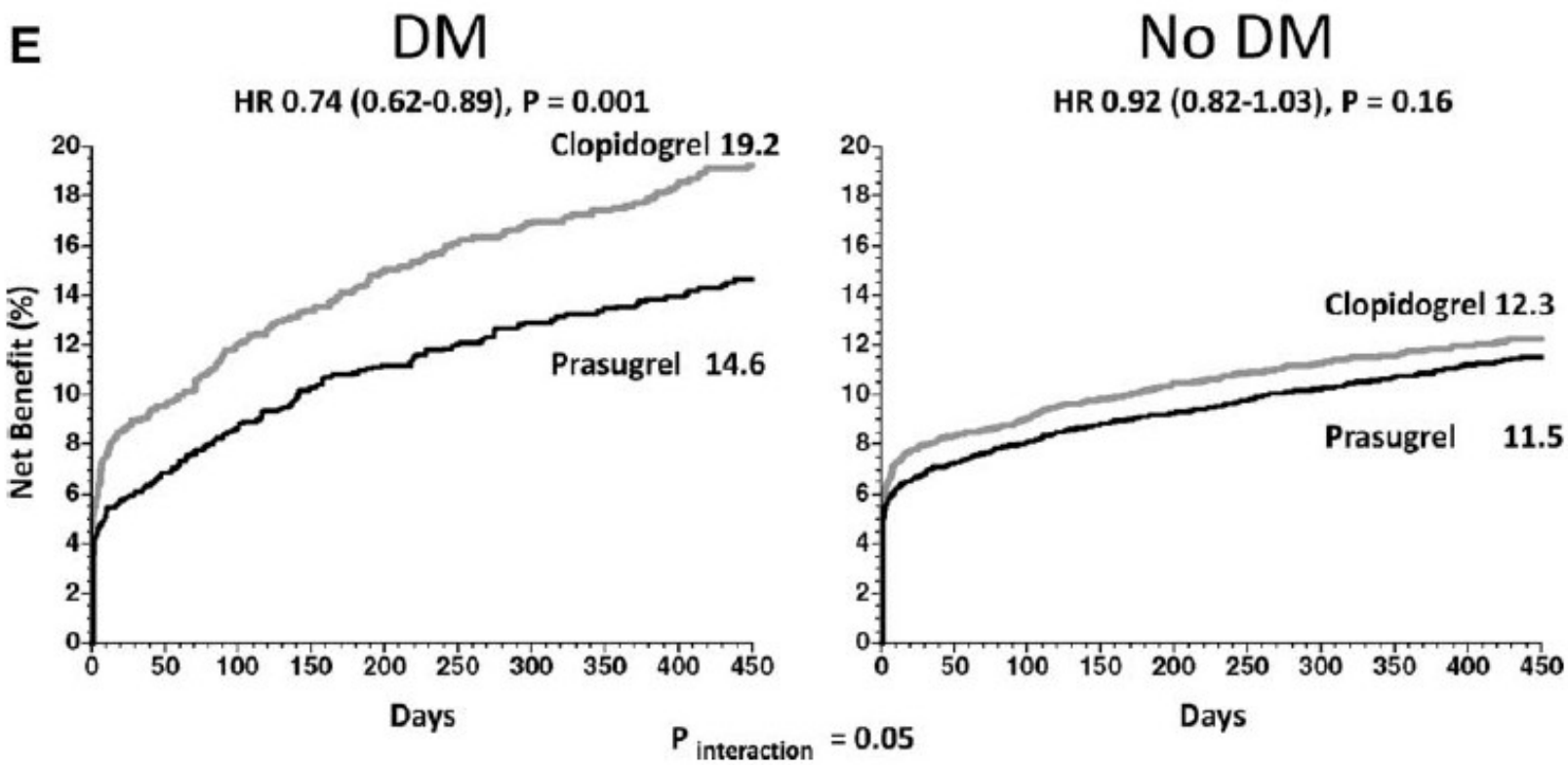
Резултати


A
DM
HR 0.70 (0.58-0.85), P<0.001
Clopidogrel 17.0
Prasugrel 12.2
Primary End Point (%)
Days
No DM
HR 0.86 (0.76-0.98), P = 0.02
Clopidogrel 10.6
Prasugrel 9.2
Days
P interaction = 0.09
B
DM
HR 0.60 (0.48-0.76), P<0.001
Clopidogrel 13.2
Prasugrel 8.2
MI (%)
Days
No DM
HR 0.82 (0.72-0.95), P = 0.006
Clopidogrel 8.7
Prasugrel 7.2
Days

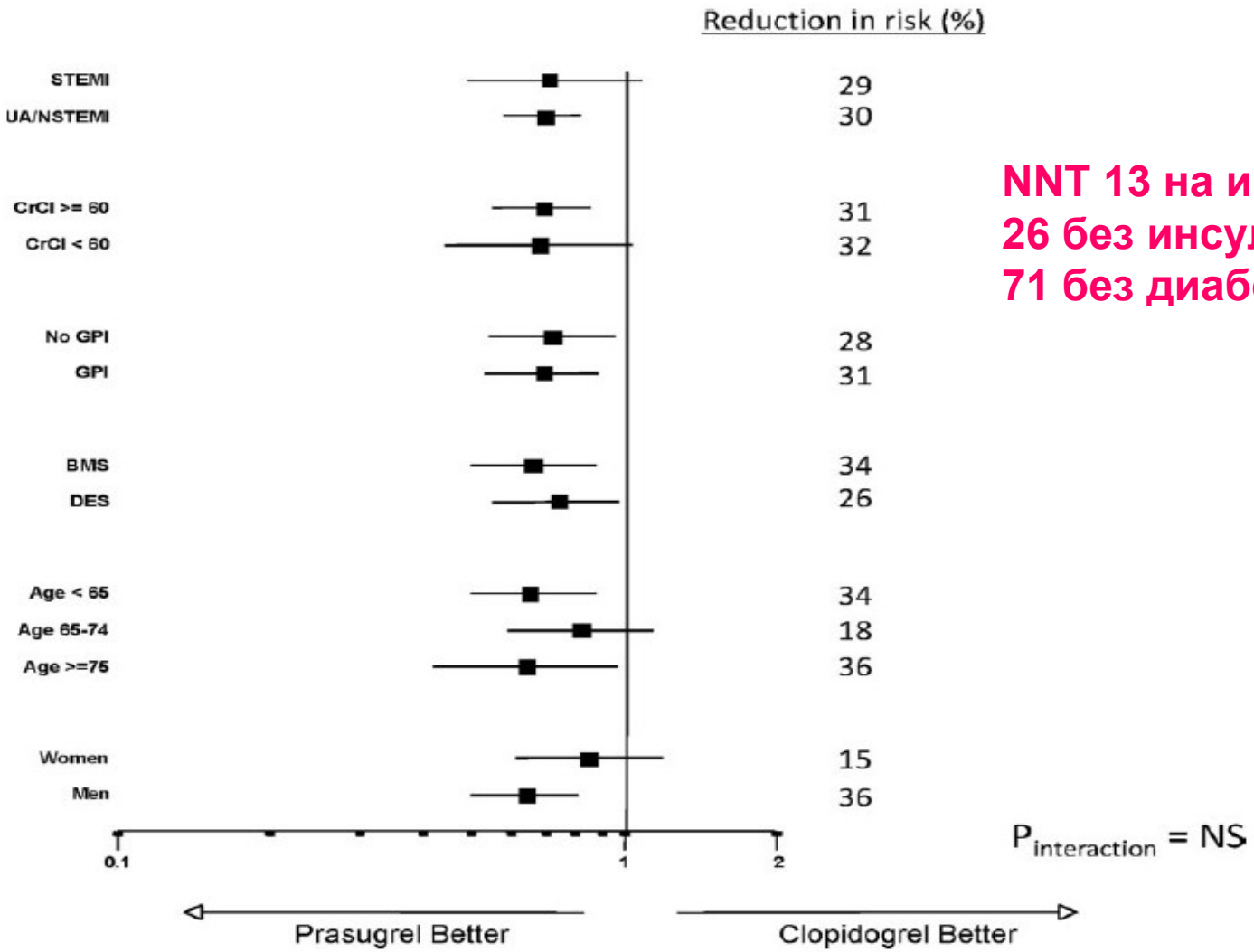
Резултати


C
DM
HR 0.52 (0.33-0.84), P = 0.007
Stent Thrombosis (%)
Clopidogrel 3.6
Prasugrel 2.0
Days
No DM
HR 0.45 (0.31-0.65), P < 0.001
Clopidogrel 2.0
Prasugrel 0.9
Days
P interaction = 0.63
D
DM
HR 1.06 (0.66-1.69), P = 0.81
TIMI Major Bleeding (%)
Clopidogrel 2.6
Prasugrel 2.5
Days
No DM
HR 1.43 (1.07-1.91), P = 0.02
Prasugrel 2.4
Clopidogrel 1.6
Days
P interaction = 0.29

Резултати


E
DM
HR 0.74 (0.62-0.89), P = 0.001
Clopidogrel 19.2
Prasugrel 14.6
Net Benefit (%)
Days
No DM
HR 0.92 (0.82-1.03), P = 0.16
Clopidogrel 12.3
Prasugrel 11.5
Days
P interaction = 0.05

Резултати



NNT 13 на инсулин,
26 без инсулин,
71 без диабет

Тикагрелор и ЗД
поданализ на PLATO

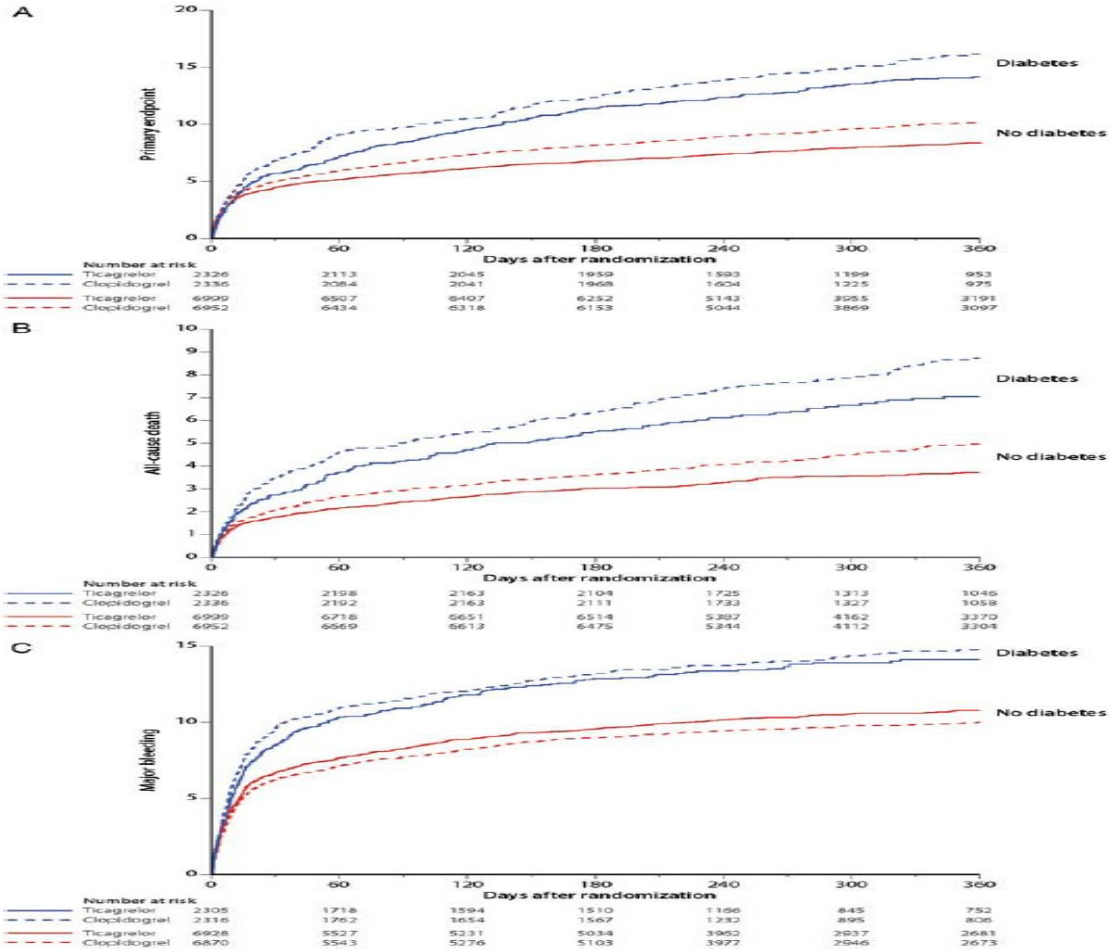
- От 18624 пациента с ОКС 4662 са със ЗД (25%), тип 2 - 96%
- От тях 1036 на инсулин
- По-често са с ОКС без ST-елевация
- Крайни точки

  - първични – сърдечносъдова смъртност, МИ, инсулт

  - вторични – смъртност, голямо кървене

James S, et al., EHJ (2010) 31, 3006–3016

ЗД и риск при ОКС



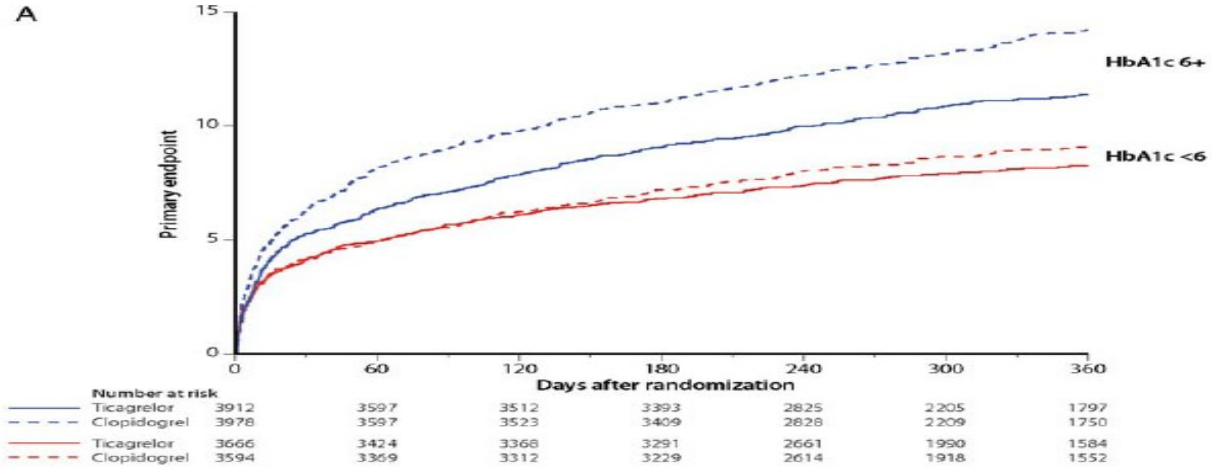
С.-с. смъртност, МИ, инсулт

Обща смъртност

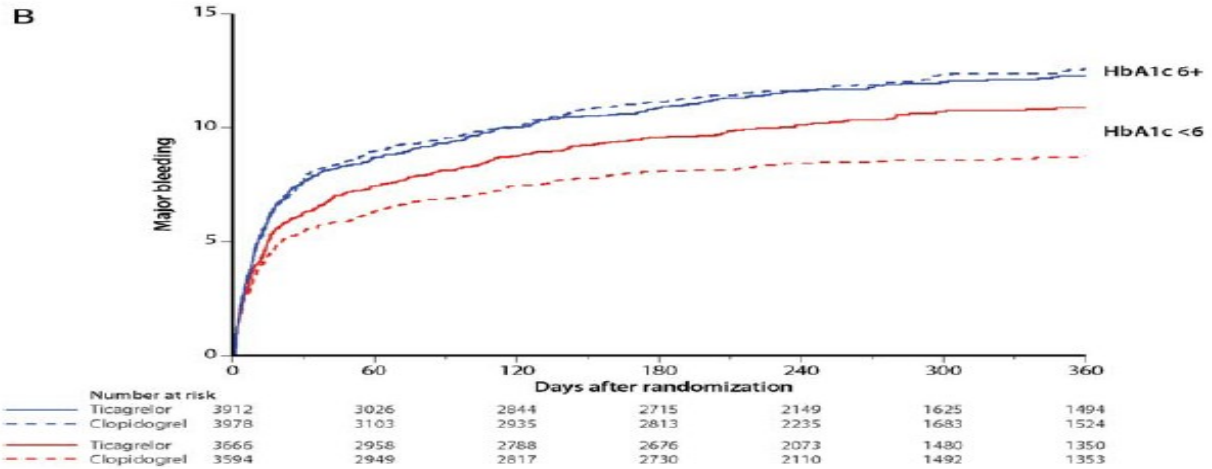
Голямо кървене

Първичен проследяван показател за ефикасност (%/годишно)	**(n=2,326)**	**(n=2,336)**	
СС смърт/МИ†/инсулт	**14.1**	**16.2**	**0.88 (0.76–1.03)**
Вторичен проследяван показател за ефикасност (%/годишно)	**(n=2,326)**	**(n=2,336)**	
Смърт по всякаква причина	**7.0**	**8.7**	**0.82 (0.66–1.01)**
МИ†	**8.4**	**9.1**	**0.92 (0.75–1.13)**
Дефинитивна стент тромбоза	**1.6**	**2.4**	**0.65 (0.36–1.17)**
Първичен проследяван показател за безопасност (%/годишно)	**(n=2,305)**	**(n=2,316)**	

Риск според HbA1c



С.-с. смъртност, МИ, инсулт



Голямо кървене

Table 4 Outcome in relation to diabetes status and glucose metabolic control

	n	Overall	Ticagrelor	Clopidogrel	HR (95% CI)	*P*-value (interaction)
CV death, myocardial infarction, or stroke						
No diabetes	13 951	9.3 (1219)	8.4 (555)	10.2 (664)	0.83 (0.74–0.93)	0.49
Diabetes	4662	15.2 (659)	14.1 (309)	16.2 (350)	0.88 (0.76–1.03)	
Glucose < 6.8 mmol/L	7604	8.9 (630)	8.0 (284)	9.7 (346)	0.83 (0.71–0.98)	0.52
Glucose ≥ 6.8 mmol/L	7646	12.8 (925)	11.7 (428)	14.0 (497)	0.85 (0.74–0.96)	
HbA1c < 6.0%	7260	8.6 (593)	8.2 (288)	9.0 (305)	0.93 (0.79–1.09)	0.24
HbA1c ≥ 6.0%	7890	12.8 (947)	11.4 (419)	14.2 (528)	0.80 (0.70–0.91)	
All-cause death						
No diabetes	13 951	4.3 (564)	3.7 (246)	5.0 (318)	0.77 (0.65–0.91)	0.66
Diabetes	4662	7.9 (341)	7.0 (153)	8.7 (188)	0.82 (0.66–1.01)	
Glucose < 6.8 mmol/L	7604	3.6 (252)	3.1 (110)	4.1 (142)	0.79 (0.62–1.01)	0.38
Glucose ≥ 6.8 mmol/L	7646	6.9 (492)	6.0 (218)	7.8 (274)	0.79 (0.66–0.94)	
HbA1c < 6.0%	7260	3.8 (256)	3.4 (114)	4.2 (142)	0.79 (0.62–1.01)	0.71
HbA1c ≥ 6.0%	7890	6.5 (475)	5.6 (206)	7.4 (269)	0.78 (0.65–0.93)	
Myocardial infarction						
No diabetes	13 951	5.6 (731)	5.0 (329)	6.2 (402)	0.81 (0.70–0.94)	0.32
Diabetes	4662	8.7 (366)	8.4 (175)	9.1 (191)	0.92 (0.75–1.13)	
Glucose < 6.8 mmol/L	7604	5.9 (415)	5.5 (192)	6.2 (223)	0.87 (0.72–1.06)	0.84
Glucose ≥ 6.8 mmol/L	7646	7.2 (500)	6.4 (227)	7.9 (273)	0.82 (0.68–0.97)	
HbA1c < 6.0%	7260	5.4 (369)	5.1 (179)	5.8 (190)	0.92 (0.75–1.13)	0.47
HbA1c ≥ 6.0%	7890	7.5 (540)	6.8 (241)	8.2 (299)	0.81 (0.68–0.96)	
Definite stent thrombosis						
No diabetes	8766	1.5 (130)	1.3 (53)	1.8 (77)	0.68 (0.48–0.97)	0.89
Diabetes	2518	2.0 (47)	1.6 (18)	2.4 (29)	0.65 (0.36–1.17)	
Glucose < 6.8 mmol/L	4383	1.1 (48)	1.2 (25)	1.0 (23)	1.07 (0.61–1.89)	0.45
Glucose ≥ 6.8 mmol/L	4882	1.9 (89)	1.5 (33)	2.4 (56)	0.60 (0.39–0.93)	
HbA1c < 6.0%	4592	1.4 (62)	1.4 (30)	1.4 (32)	0.91 (0.55–1.50)	0.51
HbA1c ≥ 6.0%	4636	1.7 (74)	1.3 (28)	2.0 (46)	0.62 (0.39–1.00)	
Major bleeding, PLATO defined						
No diabetes	13 798	10.4 (1298)	10.8 (674)	10.0 (624)	1.08 (0.97–1.20)	0.21
Diabetes	4621	14.4 (592)	14.1 (287)	14.8 (305)	0.95 (0.81–1.12)	
Glucose < 6.8 mmol/L	7604	10.7 (734)	11.0 (370)	10.4 (364)	1.04 (0.90–1.20)	0.35
Glucose ≥ 6.8 mmol/L	7646	11.5 (790)	12.0 (412)	11.1 (378)	1.09 (0.94–1.25)	
HbA1c < 6.0%	7260	9.8 (647)	10.9 (357)	8.8 (290)	1.22 (1.05–1.43)	0.08
HbA1c ≥ 6.0%	7890	12.4 (874)	12.3 (428)	12.6 (446)	0.98 (0.86–1.12)	
Non-CABG-related major bleeding, PLATO defined						
No diabetes	13 798	3.8 (461)	4.1 (253)	3.4 (208)	1.22 (1.01–1.46)	0.69
Diabetes	4621	5.2 (207)	5.5 (109)	4.9 (98)	1.13 (0.86–1.49)	
Glucose < 6.8 mmol/L	7604	3.7 (243)	3.9 (126)	3.4 (117)	1.10 (0.86–1.42)	0.97
Glucose ≥ 6.8 mmol/L	7646	4.4 (297)	4.9 (168)	3.9 (129)	1.30 (1.03–1.64)	
HbA1c < 6.0%	7260	3.5 (228)	4.2 (132)	2.9 (96)	1.36 (1.05–1.77)	0.47
HbA1c ≥ 6.0%	7890	4.5 (307)	4.8 (163)	4.2 (144)	1.16 (0.93–1.46)	
CABG-related major bleeding, PLATO defined						
No diabetes	13 798	7.0 (871)	6.8 (430)	7.1 (441)	0.97 (0.85–1.11)	0.51
Diabetes	4621	9.9 (402)	9.3 (189)	10.4 (213)	0.90 (0.74–1.09)	
Glucose < 6.8 mmol/L	7604	7.4 (510)	7.4 (252)	7.4 (258)	1.00 (0.84–1.19)	0.32
Glucose ≥ 6.8 mmol/L	7646	7.6 (515)	7.5 (254)	7.7 (261)	0.97 (0.81–1.15)	
HbA1c < 6.0%	7260	6.6 (436)	6.9 (230)	6.3 (206)	1.10 (0.91–1.33)	0.31

Continued

Тикагрелор и ЗД
поданализ на PLATO

Ползите са при всички подгрупи:

1. Независимо ОКС с ST-елевация или без ST-елевация
2. Независимо от стратегията – инвазивна или неинавазивна
3. Независимо от степента на бъбречно увреждане
4. Независимо от лечението с инсулин
5. Независимо от типа на диабета

Тикагрелор и ЗД
поданализ на PLATO

Статистическа значимост при нива на HbAc>6% за:

1. Първичната крайна точка с 2.8% (2.1%) и RRR с 30% (23%).
2. Обща смъртност с 1.8% и RRR с 24%.
3. МИ с 1.8% и RRR с 22%.

European Heart Journal (2011) 32, 2999–3054
doi:10.1093/eurheartj/ehr236

ESC GUIDELINES

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

The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

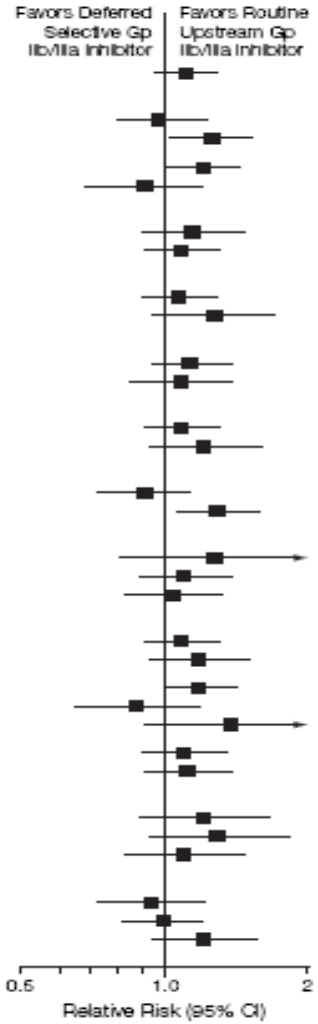
Ползите от приложението на мощните $P2Y_{12}$ инхибитори (празугрел или тика-грелор спрямо клопидогрел) са съ-ществени и увеличени при пациенти със захарен диабет.

IIb-IIIa инхибитори – ACUITY trial

(abciximab или eptifibatide, ОКС без STEMI, смъртност, МИ или непланова реваскуларизация на 30-ти ден)

Stone G., JAMA, February 14, 2007—Vol 297, No. 6

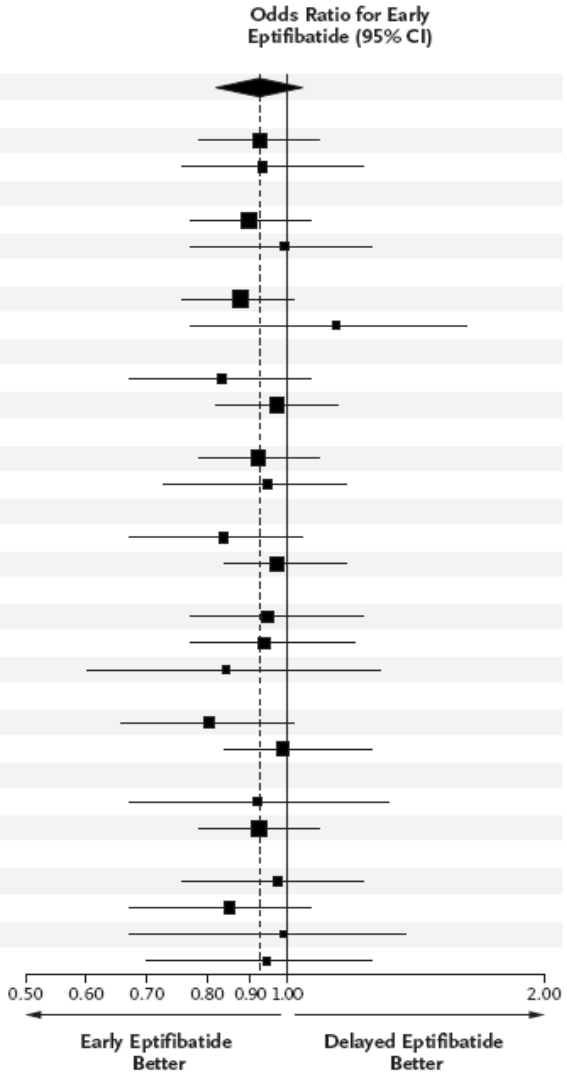
Group	No.	Composite Ischemia, %		Relative Risk (95% CI)	*P* Value for Interaction
		Deferred Gp IIb/IIIa Inhibitor	Upstream Gp IIb/IIIa Inhibitor		
All	9207	7.9	7.1	1.12 (0.97-1.29)	
Age, y					
<65	5054	6.4	6.6	0.98 (0.80-1.21)	.08
≥65	4153	9.8	7.7	1.27 (1.04-1.54)	
Men	6467	8.5	7.0	1.21 (1.02-1.43)	.08
Women	2740	6.5	7.2	0.91 (0.69-1.20)	
Diabetes					
Yes	2565	9.7	8.4	1.15 (0.90-1.48)	.68
No	6567	7.2	6.6	1.08 (0.91-1.30)	
Creatinine Clearance, mL/min					
≥60	6961	7.1	6.6	1.08 (0.90-1.28)	.29
<60	1650	11.8	9.2	1.28 (0.96-1.70)	
US Study Site					
Yes	5236	8.5	7.5	1.14 (0.95-1.37)	.74
No	3971	7.1	6.6	1.09 (0.86-1.37)	
Creatine Kinase MB/Troponin I or T					
Elevated	4962	9.1	8.3	1.09 (0.91-1.31)	.52
Normal	3469	6.6	5.4	1.22 (0.94-1.59)	
ST-Segment Deviation					
Yes	3246	8.6	9.5	0.91 (0.73-1.13)	.02
No	5961	7.5	5.8	1.31 (1.08-1.58)	
TIMI Risk Score					
0-2	1284	6.1	4.8	1.28 (0.81-2.02)	.78
3-4	4453	7.2	6.5	1.10 (0.89-1.37)	
5-7	2423	10.5	10.0	1.05 (0.83-1.33)	
Thienopyridine Preangiography					
Yes	5766	7.6	7.0	1.09 (0.91-1.31)	.56
No	3280	8.4	7.0	1.19 (0.94-1.51)	
PCI	5170	9.5	8.0	1.19 (1.00-1.42)	.15
Coronary Artery Bypass Graft Surgery	1048	13.5	15.3	0.88 (0.65-1.18)	
Medical Therapy	2989	3.3	2.4	1.39 (0.91-2.12)	
Randomized to Heparin*	4603	7.6	6.9	1.11 (0.90-1.36)	.89
Randomized to Bivalirudin	4604	8.2	7.3	1.13 (0.92-1.38)	
Randomization to PCI (Tertiles)					
Early (<2.67 h)	1708	9.5	7.8	1.22 (0.89-1.66)	.76
Intermediate (2.67-16.35 h)	1708	8.9	6.8	1.31 (0.94-1.82)	
Late (>16.35 h)	1708	10.1	9.2	1.10 (0.83-1.46)	
Prior Antithrombin					
No Prior Antithrombin	3106	6.6	7.0	0.94 (0.73-1.22)	†
Consistent Therapy	5425	7.2	7.2	1.00 (0.82-1.20)	
Crossover	3201	8.6	7.1	1.22 (0.96-1.55)	



IIb-IIIa инхибитори – EARLY ACS

eptifibatide при ОКС без ST елевация, смъртност, МИ, непланувана реваскуларизация Robert P. et al., N Engl J Med 2009;360:2176-90

Subgroup	Total No. of Patients	Early Eptifibatide %	Delayed Eptifibatide %
Overall	9406	9.3	10.0
Sex			
Male	6431	9.1	9.8
Female	2975	9.7	10.4
Age			
<75 yr	7026	8.6	9.5
≥75 yr	2377	11.4	11.4
Troponin			
Positive	7650	9.5	10.6
Negative	1468	7.7	6.8
Diabetes			
Yes	2860	8.9	10.6
No	6546	9.5	9.8
Early clopidogrel intended			
Yes	7057	8.8	9.5
No	2349	10.8	11.5
Time to randomization			
≤4 hr	3134	8.9	10.5
>4 hr	6271	9.5	9.8
TIMI risk score			
High (5–7)	3258	10.4	10.9
Intermediate (3–4)	4415	9.4	10.1
Low (0–2)	1521	6.8	8.0
Heparin use			
Unfractionated only	3237	9.1	11.0
Low-molecular-weight only	4973	9.9	9.9
Type of hospital care			
Primary	1770	9.0	9.7
Tertiary	7636	9.4	10.1
Region of the world			
North America	2888	10.3	10.6
Western Europe	3790	7.3	8.6
Eastern Europe	1018	11.2	11.2
Middle East, Africa, or Asia–Pacific	1710	10.9	11.5



European Heart Journal (2011) 32, 2999–3054
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Recommendations	Class	Level
Aspirin should be given to all patients without contraindications at an initial loading dose of 150-300 mg, and at a maintenance dose of 75-100 mg daily long-term regardless of treatment strategy.	I	A
A $P2Y_{12}$ inhibitor should be added to aspirin as soon as possible and maintained over 12 months, unless there are contraindications such as excessive risk of bleeding.	I	A
A proton pump inhibitor (preferably not omeprazole) in combination with DAPT is recommended in patients with a history of gastrointestinal haemorrhage or peptic ulcer, and appropriate for patients with multiple other risk factors (*H. elicobacter pylori* infection, age ≥ 65 years, concurrent use of anticoagulants or steroids).	I	A
Prolonged or permanent withdrawal of $P2Y_{12}$ inhibitors within 12 months after the index event is discouraged unless clinically indicated.	I	C
Ticagrelor (180 mg loading dose, 90 mg twice daily) is recommended for all patients at moderate-to-high risk of ischaemic events (e.g. elevated troponins), regardless of initial treatment strategy and including those pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced).	I	B
Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended for $P2Y_{12}$-inhibitor-naïve patients (especially diabetics) in whom coronary anatomy is known and who are proceeding to PCI unless there is a high risk of life-threatening bleeding or other contraindications.	I	B

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ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC)

Recommendations	Class	Level
Antiplatelet therapy		
Aspirin oral or i.v. (if unable to swallow) is recommended	I	B
An ADP-receptor blocker is recommended in addition to aspirin. Options are:	I	A
• Prasugrel in clopidogrel-naive patients, if no history of prior stroke/TIA, age < 75 years.	I	B
• Ticagrelor.	I	B
• Clopidogrel, preferably when prasugrel or ticagrelor are either not available or contraindicated.	I	C

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Recommendations for GP IIb/IIIa receptor inhibitors

Recommendations	Class[a]	Level[b]	Ref[c]
The choice of combination of oral antiplatelet agents, a GP IIb/IIIa receptor inhibitor, and anticoagulants should be made in relation to the risk of ischaemic and bleeding events.	I	C	–
Among patients who are already treated with DAPT, the addition of a GP IIb/IIIa receptor inhibitor for high-risk PCI (elevated troponin, visible thrombus) is recommended if the risk of bleeding is low.	I	B	152, 161
Eptifibatide or tirofiban added to aspirin should be considered prior to angiography in high-risk patients not preloaded with $P2Y_{12}$ inhibitors.	IIa	C	–
In high-risk patients eptifibatide or tirofiban may be considered prior to early angiography in addition to DAPT, if there is ongoing ischaemia and the risk of bleeding is low.	IIb	C	–
GP IIb/IIIa receptor inhibitors are not recommended routinely before angiography in an invasive treatment strategy.	III	A	151, 170
GP IIb/IIIa receptor inhibitors are not recommended for patients on DAPT who are treated conservatively.	III	A	150, 151

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Recommendations	Class	Level
GP IIb/IIIa inhibitors should be considered for bailout therapy if there is angiographic evidence of massive thrombus, slow or no-reflow or a thrombotic complication.	IIa	C
Routine use of a GP IIb/IIIa inhibitor as an adjunct to primary PCI performed with unfractionated heparin may be considered in patients without contraindications.	IIb	B
Upstream use of a GP IIb/IIIa inhibitor (vs. in-lab use) may be considered in high-risk patients undergoing transfer for primary PCI.	IIb	B
Options for GP IIb/IIIa inhibitors are (with LoE for each agent):		
• Abciximab		A
• Eptifibatide (with double bolus)		B
• Tirofiban (with a high bolus dose)		B

ОКС без ST елевация и бъбречна дисфункция

Relation Between Renal Function and Outcomes in Patients With Non–ST-Segment Elevation Acute Coronary Syndrome

Real-World Data From the European Public Health Outcome Research and Indicators Collection Project

Ilan Goldenberg, MD; Isaac Subirana, MA; Valentina Boyko, MA; Joan Vila, MA; Roberto Elosua, MD, PhD; Gaieta Permanyer-Miralda, MD; Ignacio Ferreira-González, MD; Michal Benderly, PhD; Victor Guetta, MD; Shlomo Behar, MD; Jaume Marrugat, MD, PhD, FESC

EUPHORIC Project database

Arch Intern Med. 2010;170(10):888-895

ОКС без ST елевация и бъбречна дисфункция

- Включени 13141 пациента от 3 ре-гистъра (от 2000 г. до 2006 г.) с данни за ГФ<60 ml/min/1.73 m2 по MDRD
- Анализирани са болничната смъртност и 30-дневната смъртност

Table 1. Patients With Available Renal Function (eGFR) Data Included in the Study

Study	Country	Year	Consecutive Patients	Hospitals, No.	University Hospitals, %	Country Representative	Patients, Total No.	NSTE-ACS, No.	eGFR Available, No.
MASCARA study	Spain	2005	Yes	32	75	Yes	7251	4091	3110
EHS-ACS I	Europe	2000	No	84	63	No	10 180	5936	5545
EHS-ACS II	Europe	2005	No	190	54	No	5160	2647	2275
ACSIS 2004	Israel	2004	Yes	25	70	Yes	2094	1121	1089
ACSIS 2006	Israel	2006	Yes	25	70	Yes	2077	1136	1122
Total							**26 762**	**14 931**	**13 141**

Резултати за смъртност

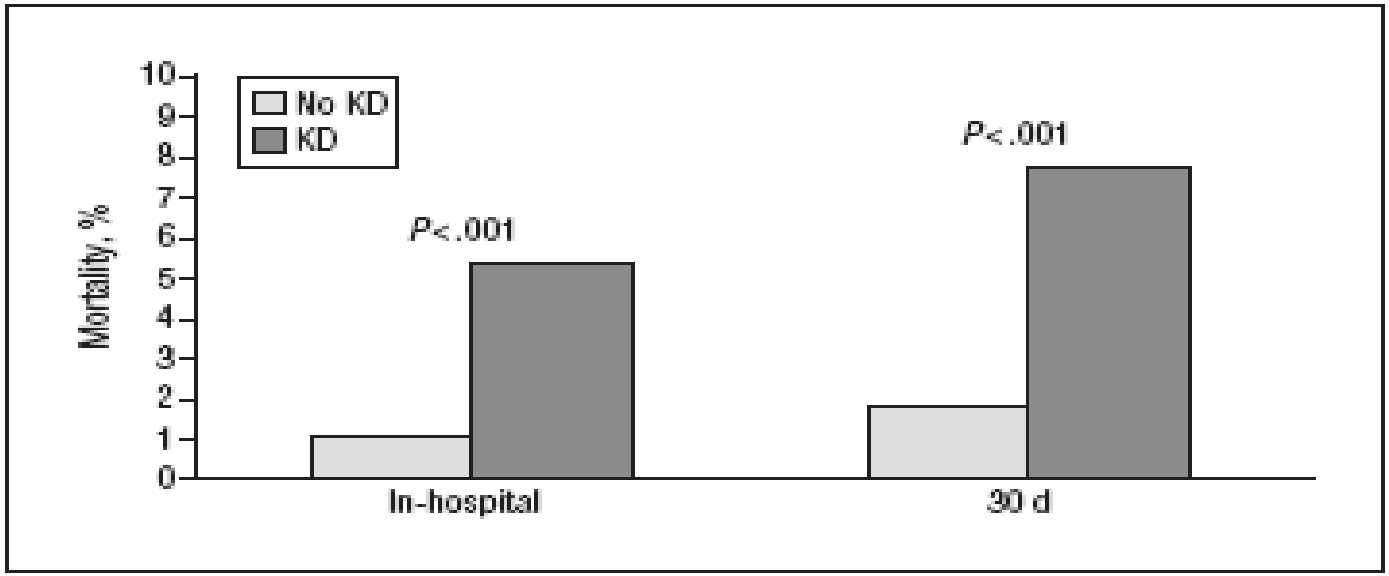

Figure 1. In-hospital and 30-day mortality rates in patients with and without kidney disease (KD).

x4

Резултати за смъртност

Table 4. Multivariate Analysis: Adjusted ORs for In-hospital and 30-Day Case Fatality[a]

	In-hospital Case Fatality (n = 9214)		30-d Case Fatality (n = 8528)	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
KD (eGFR, <60 mL/min/1.73 m^2) vs no KD (eGFR, ≥60 mL/min/1.73 m^2)	2.11 (1.48-3.00)	<.001	1.95 (1.46-2.61)	<.001
Moderate KD (eGFR, 30-59 mL/min/1.73 m^2) vs no KD[b]	1.71 (1.17-2.49)	.005	1.46 (1.07-2.00)	.01
Severe KD (eGFR, <30 mL/min/1.73 m^2) vs no KD[b]	4.11 (2.53-6.68)	<.001	4.84 (3.27-7.16)	<.001
Age	1.05 (1.04-1.07)	<.001	1.06 (1.05-1.08)	<.001
Female sex	0.70 (0.47-1.04)	.08	0.83 (0.60-1.14)	.25
Hypertension	0.78 (0.55-1.13)	.19	0.80 (0.59-1.07)	.13
Diabetes mellitus	1.20 (0.86-1.69)	.28	1.25 (0.95-1.66)	.11
History of CAD	0.90 (0.59-1.37)	.61	0.98 (0.69-1.38)	.90
Current smoking	1.01 (0.69-1.49)	.95	1.10 (0.80-1.50)	.57
Killip class >II[c]	42.2 (30.15-59.09)	<.001	17.99 (13.51-23.96)	<.001

Резултати смъртност и коронарография

(49.9% с БД, 67.8% без БД от пациентите са със СКАГ)

Table 5. Multivariate Analysis: Adjusted ORs of In-hospital and 30-Day Case Fatality for Coronary Angiography by the Presence and Severity of Kidney Disease[a]

Model	In-hospital Mortality		30-d Mortality	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Model 1: effect in the total population				
Angiography (yes/no)	0.53 (0.37-0.75)	<.001	0.53 (0.40-0.72)	<.001
Model 2: effect by the presence of kidney disease				
Angiography in those with eGFR ≥60 mL/min/1.73 m^2	0.45 (0.26-0.78)	.005	0.52 (0.34-0.79)	.001
Angiography in those with eGFR <60 mL/min/1.73 m^2	0.64 (0.41-1.00)	.05	0.60 (0.41-0.87)	<.001
Interaction eGFR <60 mL/min/1.73 m^2: angiography (yes/no)		.31		.83
Model 3: effect in kidney disease subgroups				
Angiography in those with eGFR ≥60 mL/min/1.73 m^2	0.46 (0.26-0.79)	.005	0.53 (0.34-0.81)	.001
Angiography in those with eGFR of 30-59 mL/min/1.73 m^2	0.52 (0.30-0.88)	.01	0.54 (0.34-0.85)	<.001
Angiography in those with eGFR <30 mL/min/1.73 m^2	1.31 (0.58-2.94)	.51	0.80 (0.41-1.54)	.17
Interaction eGFR in 3 categories: angiography (yes/no)		.09		.62

Резултати смъртност и коронарография

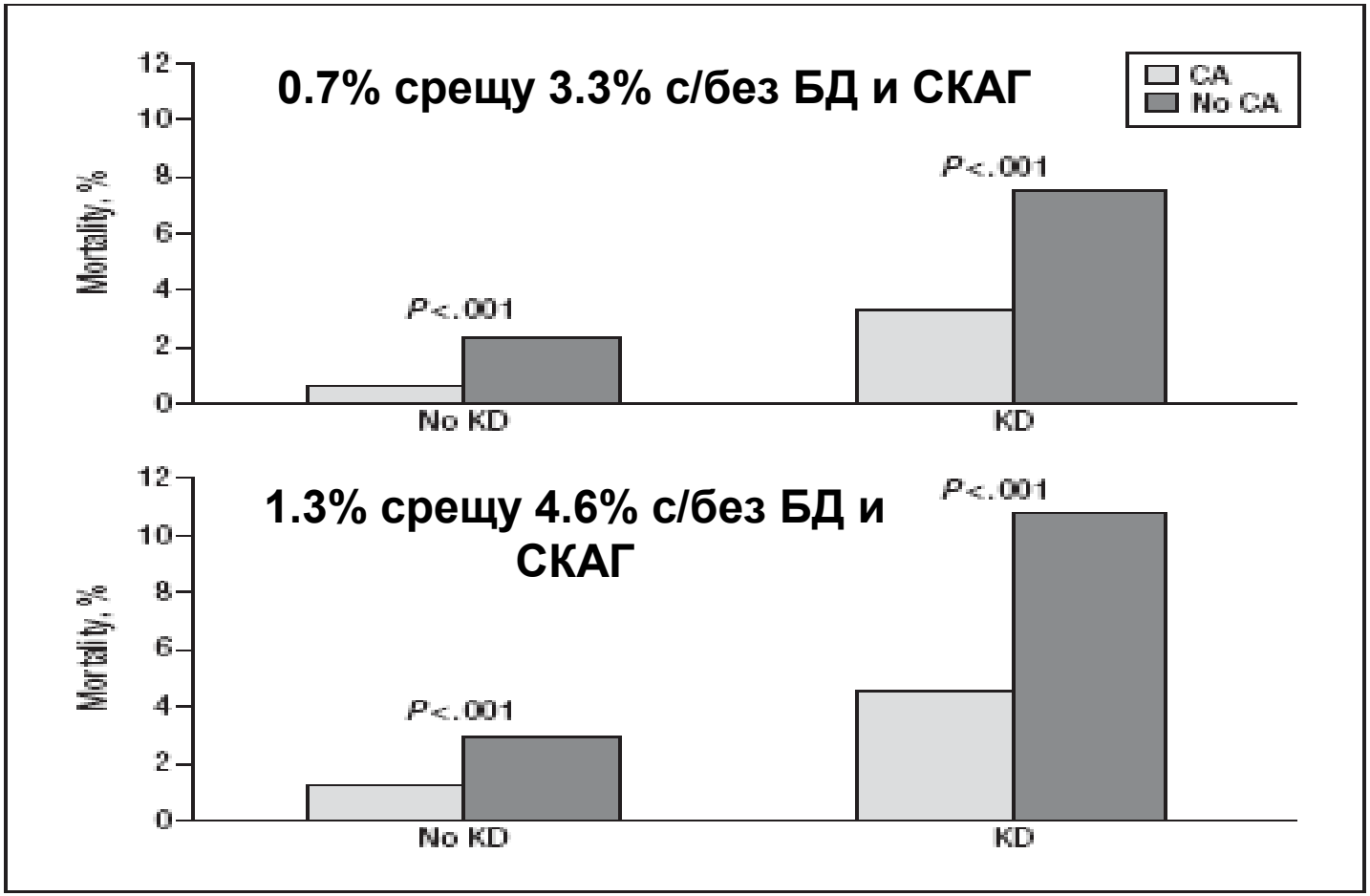

Figure 2. In-hospital (A) and 30-day (B) mortality rates in patients who did and did not undergo coronary angiography (CA) by the presence of kidney disease (KD).

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doi: 10.1111/j.1365-2796.2009.02204.x

Relation between renal function, presentation, use of therapies and in-hospital complications in acute coronary syndrome: data from the SWEDEHEART register

K. Szummer[1], P. Lundman[2], S. H. Jacobson[3], S. Schön[4], J. Lindbäck[5], U. Stenestrand[6], L. Wallentin[5] & T. Jernberg[1], for SWEDEHEART

57477 пациента с ОМИ 2003-2006 г.

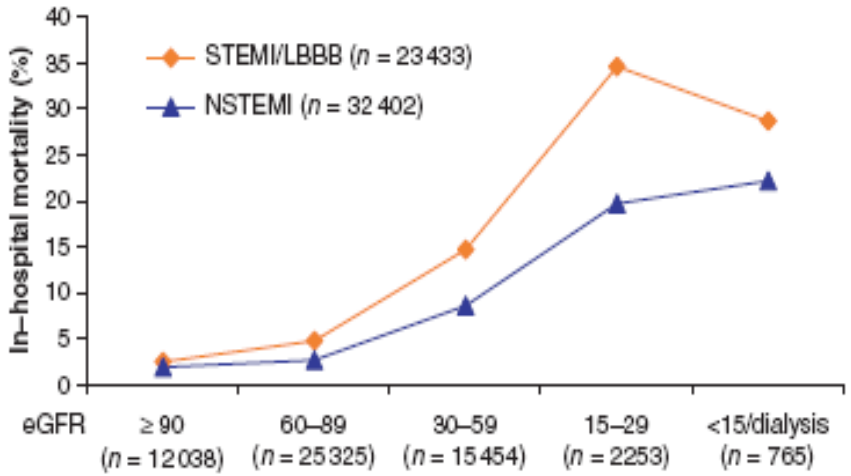

Fig. 3 *Unadjusted in-hospital mortality according to eGFR and ECG on admission.*

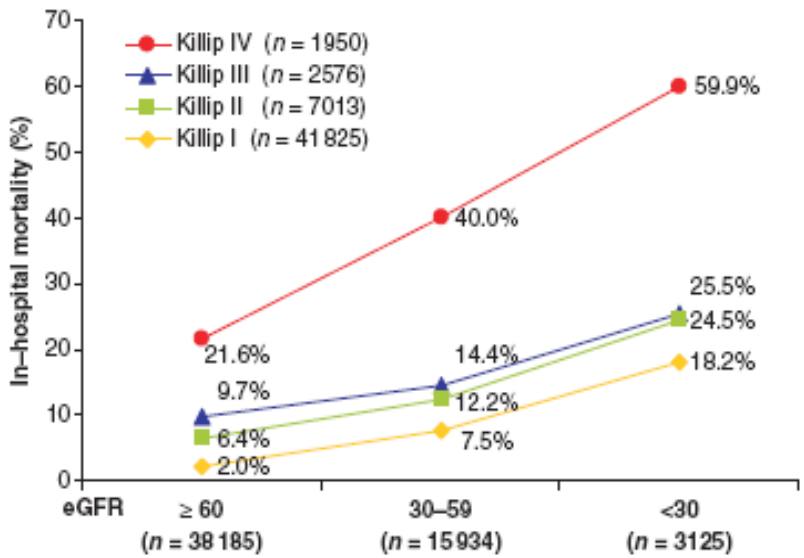

Fig. 4 *Unadjusted mortality according to eGFR and Killip class on admission.*

Резултати обобщение

1. В ежедневната практика около 1/3 от пациентите с ОКС без ST елевация са с БД
2. БД е независим показател за четирикратно по-висок риск за болнична и 30-дневна смъртност
3. Инвазивната стратегия на лечение на болните с БД е със значимо по-нисък риск, но отново по-висок от тези без БД
4. ГФ трябва да се използва за оценка на риска при пациенти с ОКС без ST елевация

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Table 10 Recommendations for the use of antithrombotic drugs in CKD

Drug	Recommendations
Clopidogrel	No information in patients with renal dysfunction.
Prasugrel	No dose adjustment necessary, including in patients with end-stage disease.
Ticagrelor	No dose reduction required; no information in dialysis patients.
Enoxaparin	Dose reduction to 1 mg/kg once daily in the case of severe renal failure (CrCl <30 mL/min). Consider monitoring of anti-Xa activity.
Fondaparinux	Contraindicated in severe renal failure (CrCl <20 mL/min). Drug of choice in patients with moderately reduced renal function (CrCl 30–60 mL/min).
Bivalirudin	Patients with moderate renal impairment (30–59 mL/min) should receive an infusion of 1.75 mg/kg/h. If the creatinine clearance is <30 mL/min, reduction of the infusion rate to 1 mg/kg/h should be considered. No reduction in the bolus dose is needed. If a patient is on haemodialysis, the infusion rate should be reduced to 0.25 mg/kg/h.
Abciximab	No specific recommendations for the use of abciximab, or for dose adjustment in the case of renal failure. Careful evaluation of haemorrhagic risk is needed before using the drug in the case of renal failure.
Eptifibatide	The infusion dose should be reduced to 1 μg/kg/min in patients with CrCl <50 mL/min. The dose of the bolus remains unchanged at 180 μg/kg. Eptifibatide is contraindicated in patients with CrCl <30 mL/min.
Tirofiban	Dose adaptation is required in patients with renal failure; 50% of the bolus dose and infusion if CrCl is <30 mL/min.

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ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

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Table 18 Initial dosing of antithrombotic agents in patients with chronic kidney disease (estimated creatinine clearance <60 mL/min)

	Recommendation
Aspirin	No dose adjustment.
Clopidogrel	No dose adjustment.
Prasugrel	No dose adjustment. No experience with end-stage renal disease/dialysis.
Ticagrelor	No dose adjustment. No experience with end-stage renal disease/dialysis.
Enoxaparin	No adjustment of bolus dose. Following thrombolysis, in patients with creatinine clearance <30 mL/min, the s.c. doses are given once every 24 h.
Unfractionated heparin	No adjustment of bolus dose.
Fondaparinux	No dose adjustment. No experience in patients with end-stage renal disease or dialysis patients.
Bivalirudin	• In patients with moderate renal insufficiency (GFR 30–59 mL/min) a lower initial infusion rate of 1.4 mg/kg/h should be given. The bolus dose should not be changed. • In patients with severe renal insufficiency (GFR <30 mL/min) and in dialysis-dependent patients bivalirudin is contraindicated.
Abciximab	No specific recommendation. Careful consideration of bleeding risk.
Eptifibatide	• In patients with moderate renal insufficiency (GFR ≥30 to <50 mL/min), an i.v. bolus of 180 μg should be administered followed by a continuous infusion dose of 1.0 μg/kg/min for the duration of therapy. • In patients with severe renal insufficiency (GFR <30 mL/min) eptifibatide is contraindicated.
Tirofiban	In patients with severe renal insufficiency (GFR <30 mL/min) the infusion dose should be reduced to 50%.

БЛАГОДАРЯ ЗА ВНИМАНИЕТО!