

NAPOLI, 17-20 maggio 2017

XXI CONGRESSO
NAZIONALE **AMD**



PER UNA DIABETOLOGIA PREDITTIVA, PREVENTIVA, PERSONALIZZATA E PARTECIPATIVA

Il trattamento intra-ospedaliero del paziente diabetico con Sindrome Coronarica Acuta

Lelio Morviducci

Az. Osp. S. Camillo-Forlanini
Roma

DISCLOSURE

Novo Nordisk

Eli-Lilly

Sanofi

Lifescan

Boehringer

Medtronic

CASO CLINICO




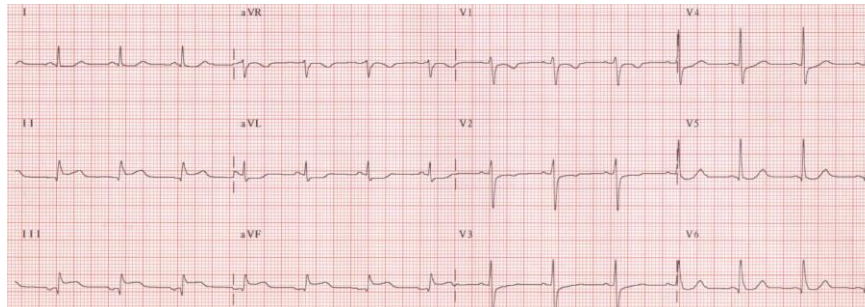
Giorgio
63 anni
impiegato

Diabetico da 4 anni (iDPP-4 + metformina)
Iperteso (sartano + HCT)
Sovrappeso

dolore epigastrico dal mattino

nel pomeriggio, dopo pranzo abbondante, peggioramento del quadro clinico con lieve difficoltà respiratoria

 PRONTO SOCCORSO



marcatori cardiaci elevati

Glicemia 196 mg<dl

- 1. Mantengo terapia domiciliare?**
- 2. Inizio insulina?**
- 3. Attendo?**

1. Mantengo terapia domiciliare?
- 2. Inizio insulina?**
3. Attendo?

- 1. Sliding scale?**
- 2. Basal-bolus?**
- 3. Insulina e.v.?**

1. Sliding scale?
2. Basal-bolus?
3. **Insulina e.v.?**

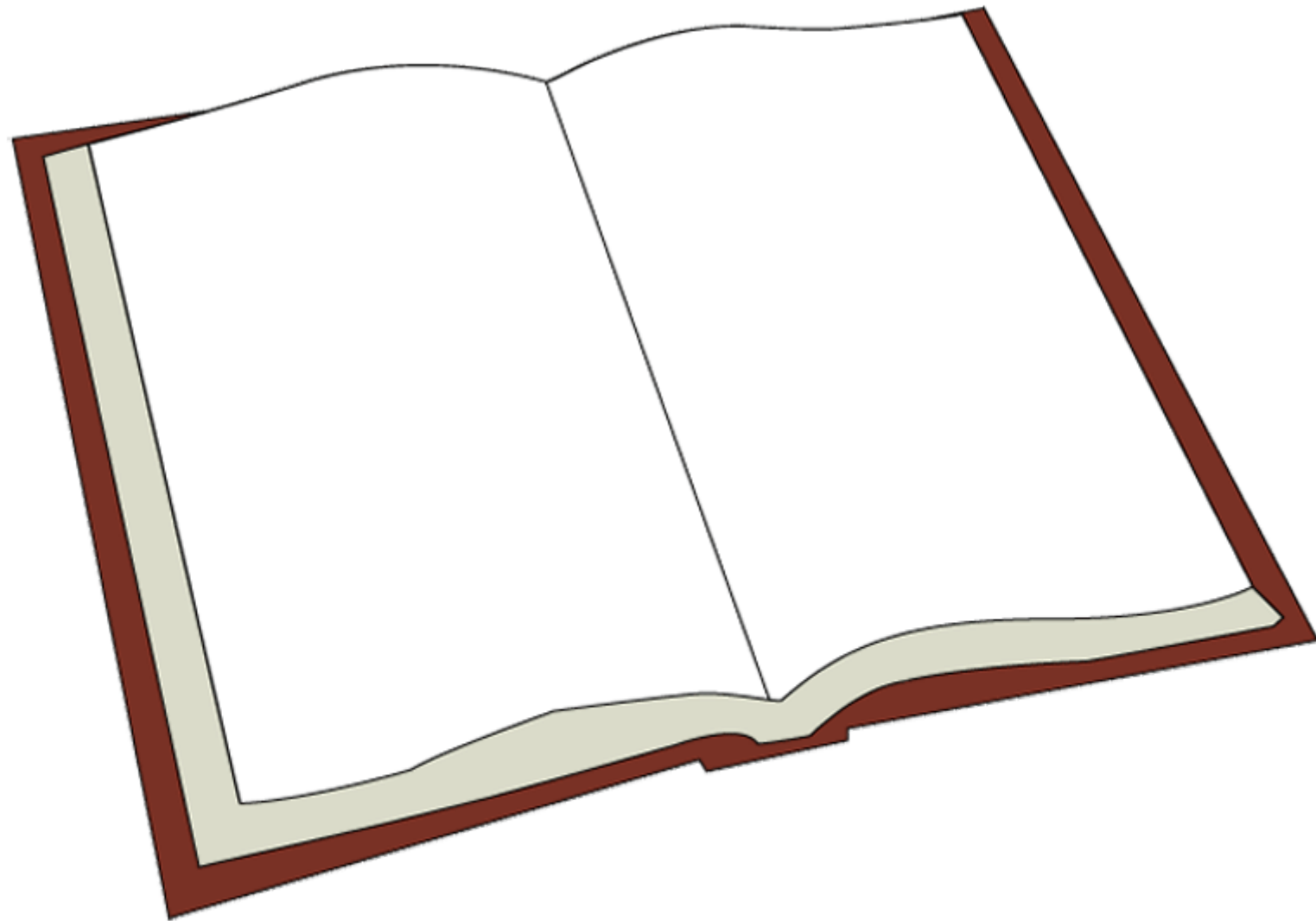
Quale target glicemico

- 1. 110 - 160 mg/dl?**
- 2. 140 - 180 mg/dl?**
- 3. 140 - 200 mg/dl?**

Quale target glicemico

1. 110 - 160 mg/dl?
- 2. 140 - 180 mg/dl?**
3. 140 - 200 mg/dl?





In-hospital mortality

Bellodi
Gasior
ICONS
JACCS
Lewandowicz
Nordin
O'Sullivan
Oswald
Ravid
Sewdarsen
Shen
Soler
Stranders
Worcester AHS
Overall

3.47 (2.07-5.82)
7.25 (3.02-17.43)
6.85 (1.94-24.20)
3.54 (2.25-5.57)
4.91 (2.08-11.58)
4.67 (0.99-22.01)
1.06 (0.24-4.74)
3.81 (1.35-10.71)
5.82 (2.87-11.79)
3.59 (1.55-8.33)
5.84 (2.29-14.93)
3.55 (1.13-11.16)
12.81 (0.72-221.07)
2.92 (1.32-6.46)
3.20 (2.55-4.03)
3.62 (3.09-4.24)

30-day mortality

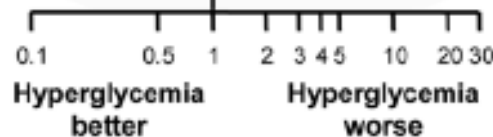
Ishihara
Peturscn
Suleiman
Overall

2.31 (2.24-2.39)
4.03 (1.73-9.39)
6.99 (4.45-10.98)
9.22 (4.48-18.95)
4.81 (2.18-10.61)

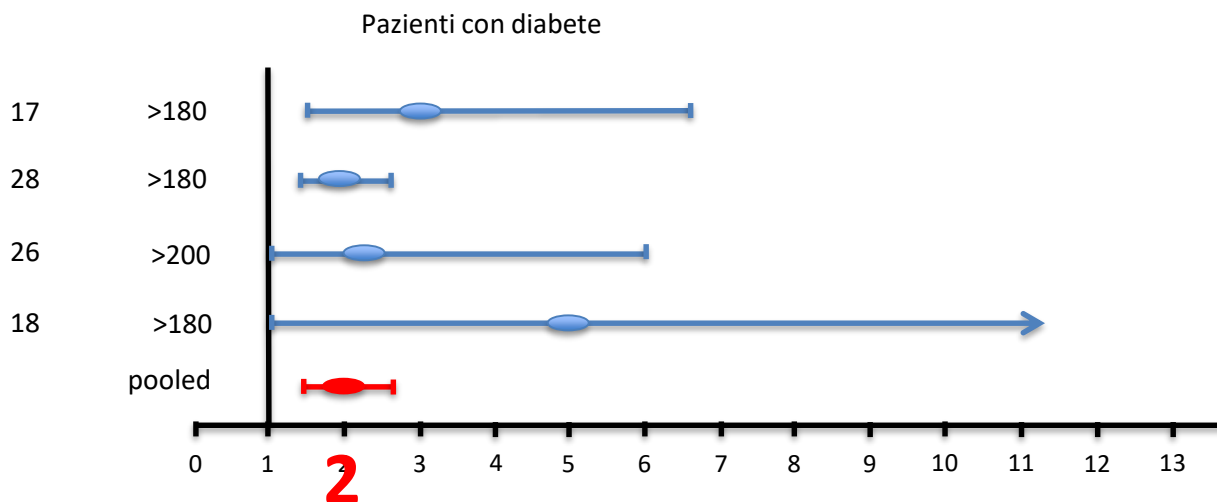
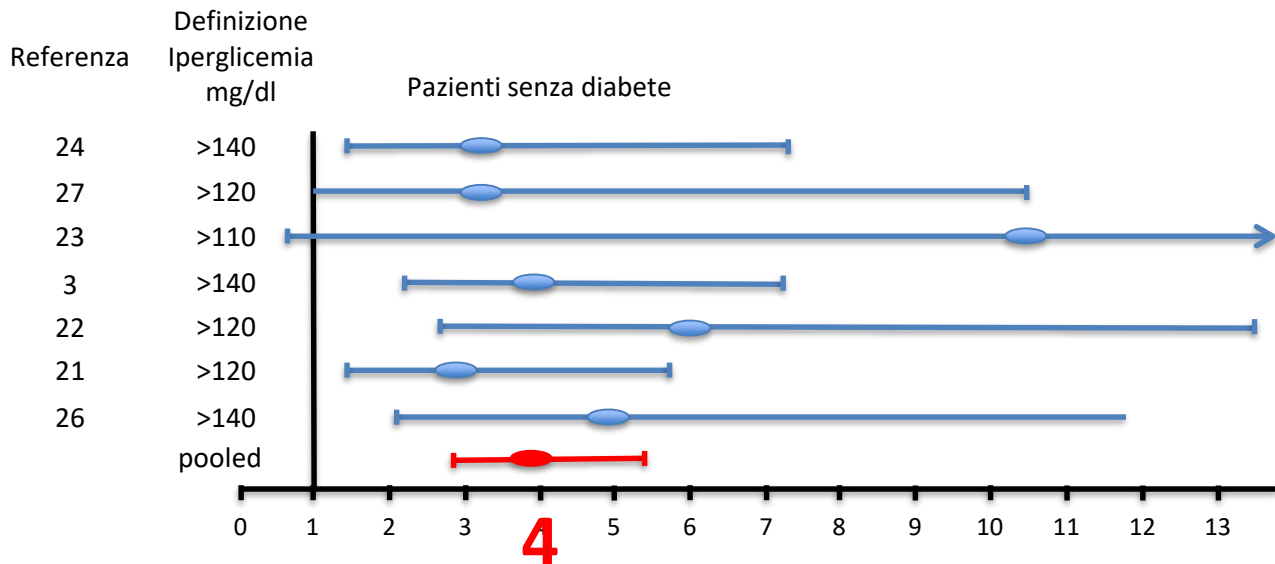
Long-term mortality

Amia
CCP
GRACE
Gasior
ICONS
Ishihara
Nordin
Peturscn
Scott
Stranders
Valiant
Zwolle
Overall

5.59 (3.58-8.73)
1.91 (1.85-1.96)
3.59 (2.01-6.39)
1.71 (0.88-3.29)
0.32 (0.10-1.02)
2.97 (1.61-5.48)
3.50 (0.96-12.83)
1.78 (1.16-2.73)
2.20 (1.74-2.78)
1.08 (0.76-1.53)
1.58 (1.26-1.99)
1.90 (0.96-3.77)
2.02 (1.62-2.51)

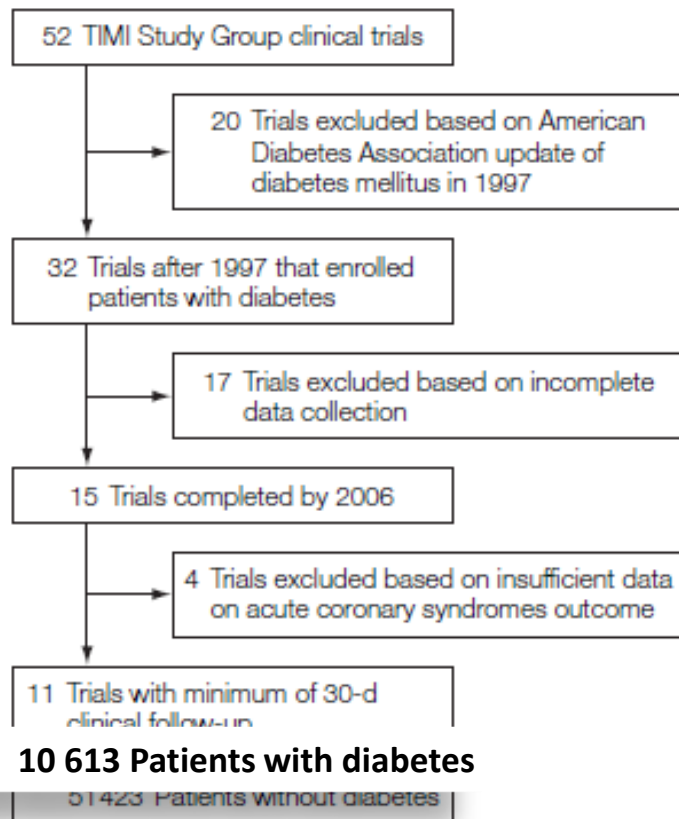


Mortality Rate



Diabetes and Mortality Following Acute Coronary Syndromes

JAMA 2007

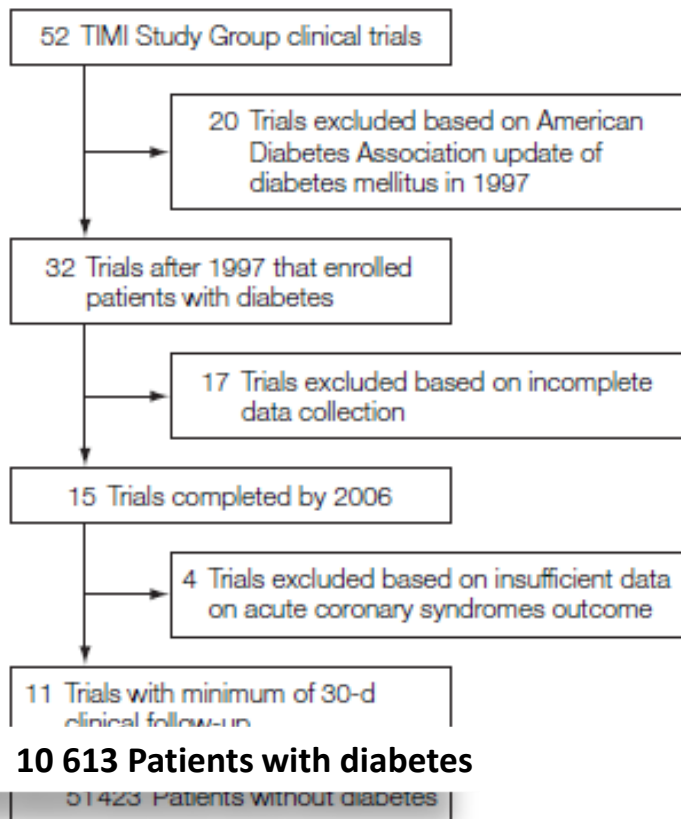


TIMI indicates Thrombolysis in Myocardial Infarction.

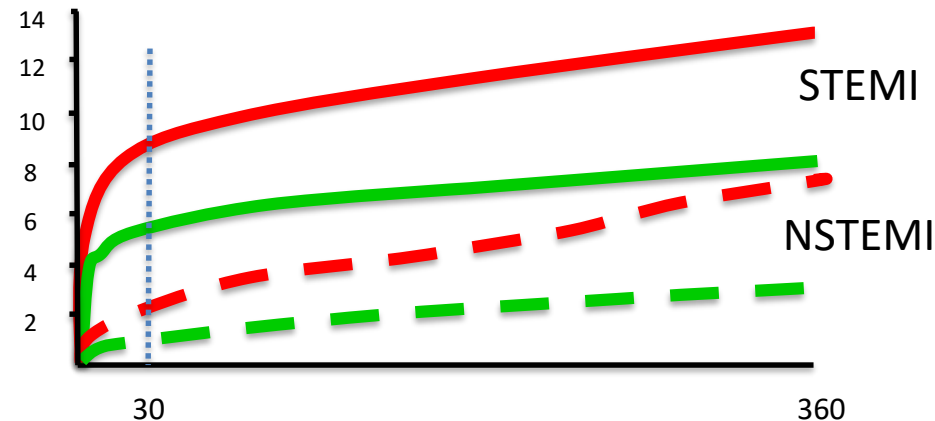
Variables	Incidence of Stent Thrombosis, No./Total (%)	Hazard Ratio (95% Confidence Interval)	P Value
Categorical Variables			
Premature antiplatelet therapy discontinuation	5/17 (29)	152 (52-442)	<.001
Prior brachytherapy	2/23 (8.7)	7.49 (1.78-31.49)	.006
Renal failure	8/127 (6.2)	11.67 (5.17-26.35)	<.001
Bifurcation with 2 stents	13/336 (3.9)	4.62 (2.22-9.62)	<.001
Bifurcation lesion	18/507 (3.6)	6.50 (3.02-13.98)	<.001
Unprotected left main artery	3/92 (3.3)	0.95 (0.67-1.36)	.81
Hyperglycaemia	15/591 (2.5)	3.45 (1.66-7.18)	.001
Thrombus	7/30 (2)	1.33 (0.27-7.00)	.80
Unstable angina	8/590 (1.4)	1.24 (0.56-2.73)	.58
Male sex	22/1907 (1.2)	0.80 (0.30-2.11)	.66
B2 or C type	21/1698 (1.2)	1.19 (0.48-2.94)	.69
Calcification	4/392 (1)	0.74 (0.26-2.14)	.58
Sirolimus-eluting stent	9/1062 (0.8)	0.50 (0.22-1.10)	0.09

Diabetes and Mortality Following Acute Coronary Syndromes

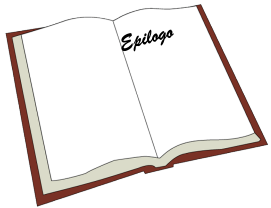
JAMA 2007



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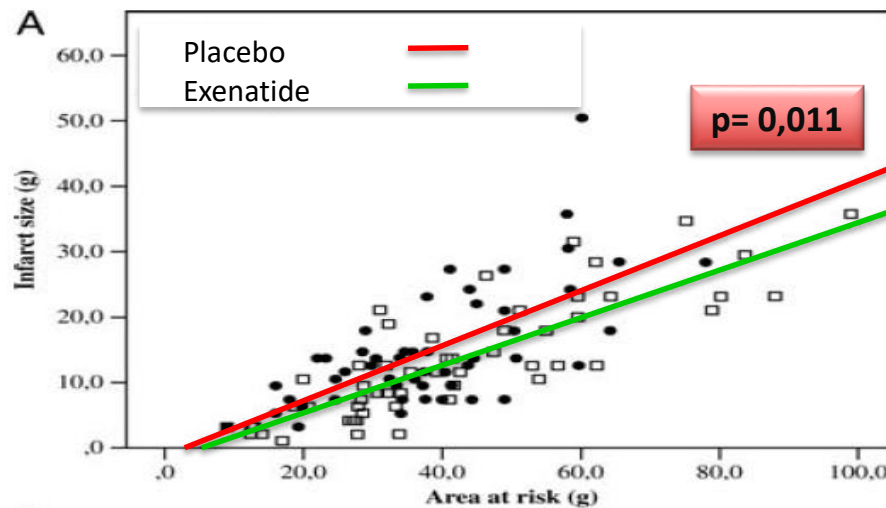


Il trattamento

L'utilizzo dei principali farmaci ipoglicemizzanti orali o iniettivi diversi dall'insulina (secretagoghi, biguanidi, tiazolidinedioni, incretine, gliflozine) presenta notevoli limitazioni in caso di patologie acute

.....La somministrazione di insulina e pertanto la terapia di scelta nel paziente diabetico ospedalizzato non stabilizzato.

(Livello della prova VI, Forza della raccomandazione B)



La terapia infusionale endovenosa trova una sua precisa indicazione nell'ambito dei reparti di terapia intensiva

	soluzione	Target	UI/h
Markowitz (Trence)	100 UI Insulina In Fis 100 (1UI/1ml)	80 - 180	4 schemi
Leuven	50 UI insulina In Fis 50 (1UI/1ml)	80- 110	1- 4
Yale	50 UI insulina In Fis 50 (1UI/1ml)	110-140	0.5-25
Portland	125 UI insulina In Fis 250 (1UI/2ml)	100-150	0.5-8
Digami	80 UI insulina 500 ml Gluc	125-180	0.5->>
Van den Bergh	50 UI insulina In Fis 50 (1UI/1ml)	80-110	2-4

	Sodio Cloruro	Destrosio	Stabilità
ASPART	✓	✓	24h
GLULISINE	✓		48h
LISPRO	✓	✓	48h

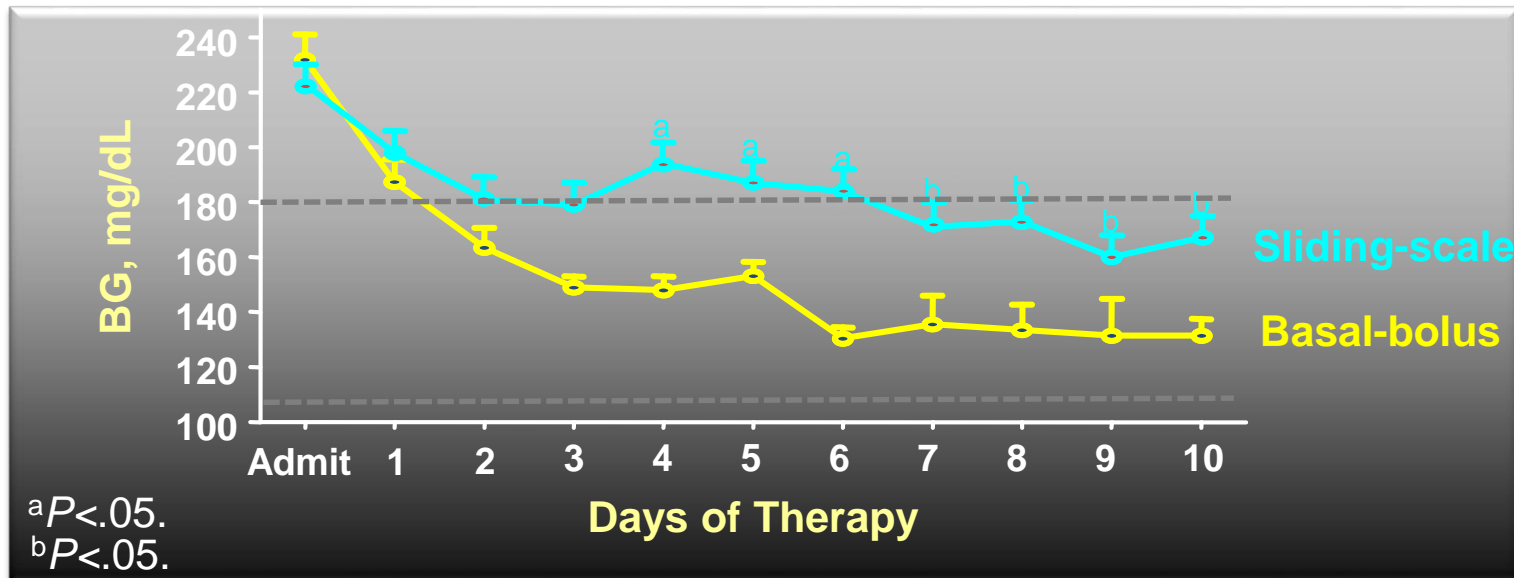
The Ideal IV Insulin Protocol

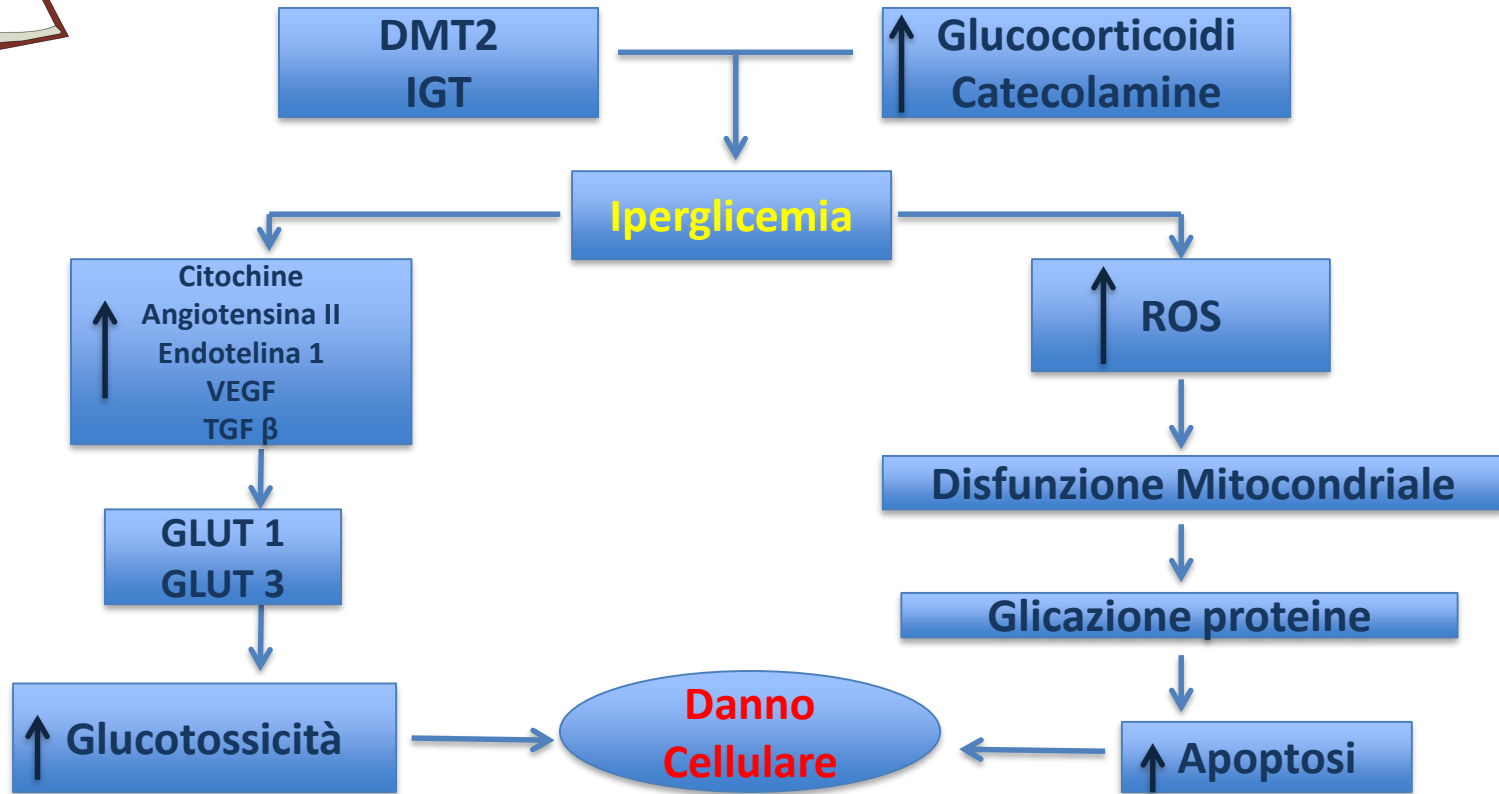
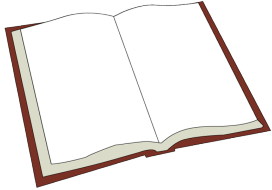
- ✓ Gli algoritmi vanno condivisi e validati nel proprio contesto assistenziale
- ✓ Devono essere **semplici e sicuri**
- ✓ A gestione Infermieristica
- ✓ Easily implemented
- ✓ Able to be used hospital wide

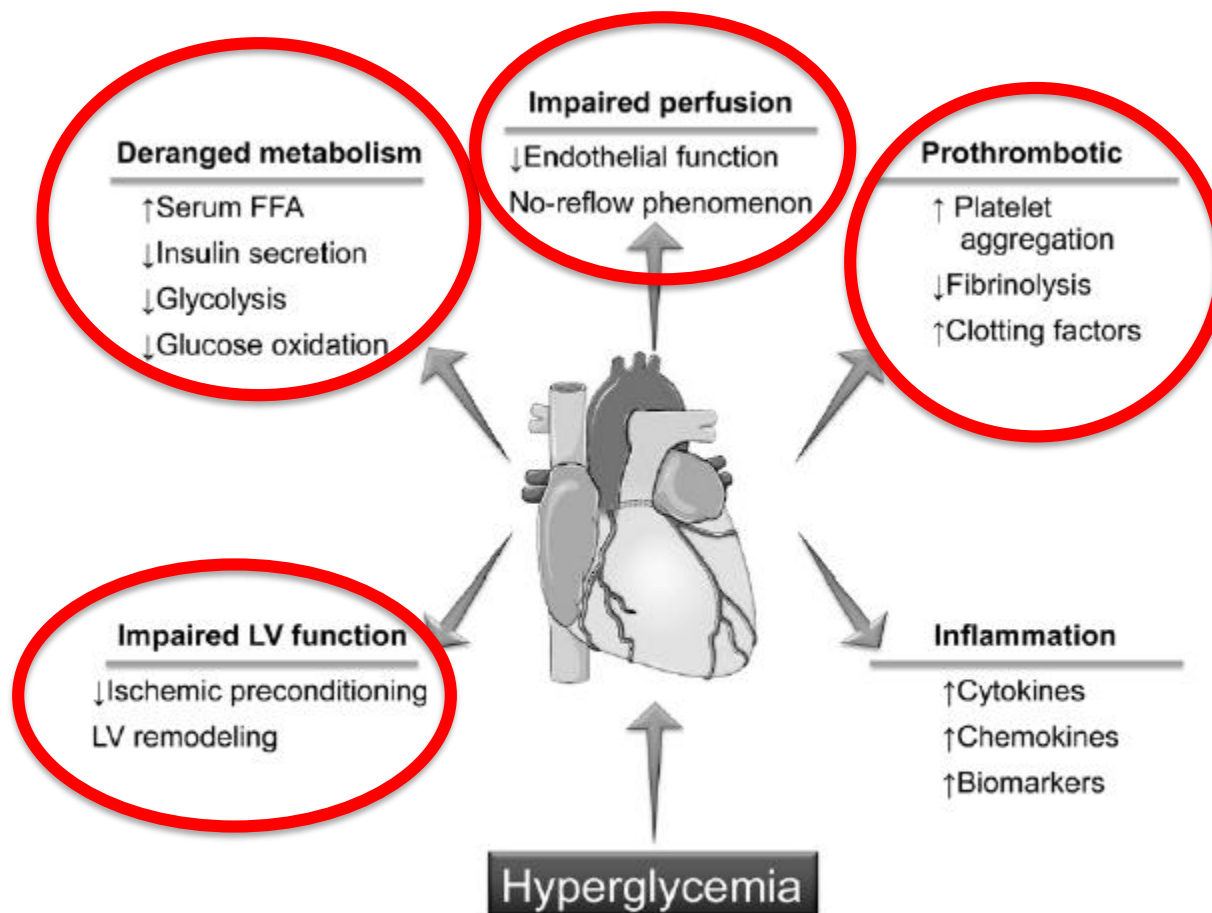
ALGORITMI: Digami - Clement – Portland -Markovitz –**Yale modificato** - Mayo Clinic - Van Den Berghe – Desio - **AMD-SID-OSDI**

La terapia insulinica per via sottocutanea deve seguire uno schema programmato che preveda l'uso di insulina basale. Questo schema deve essere integrato da un algoritmo di correzione basato sulla Il metodo di praticare insulina solamente "al bisogno" (*sliding scale*) deve essere abbandonato.

(Livello della prova IV, Forza della raccomandazione B)

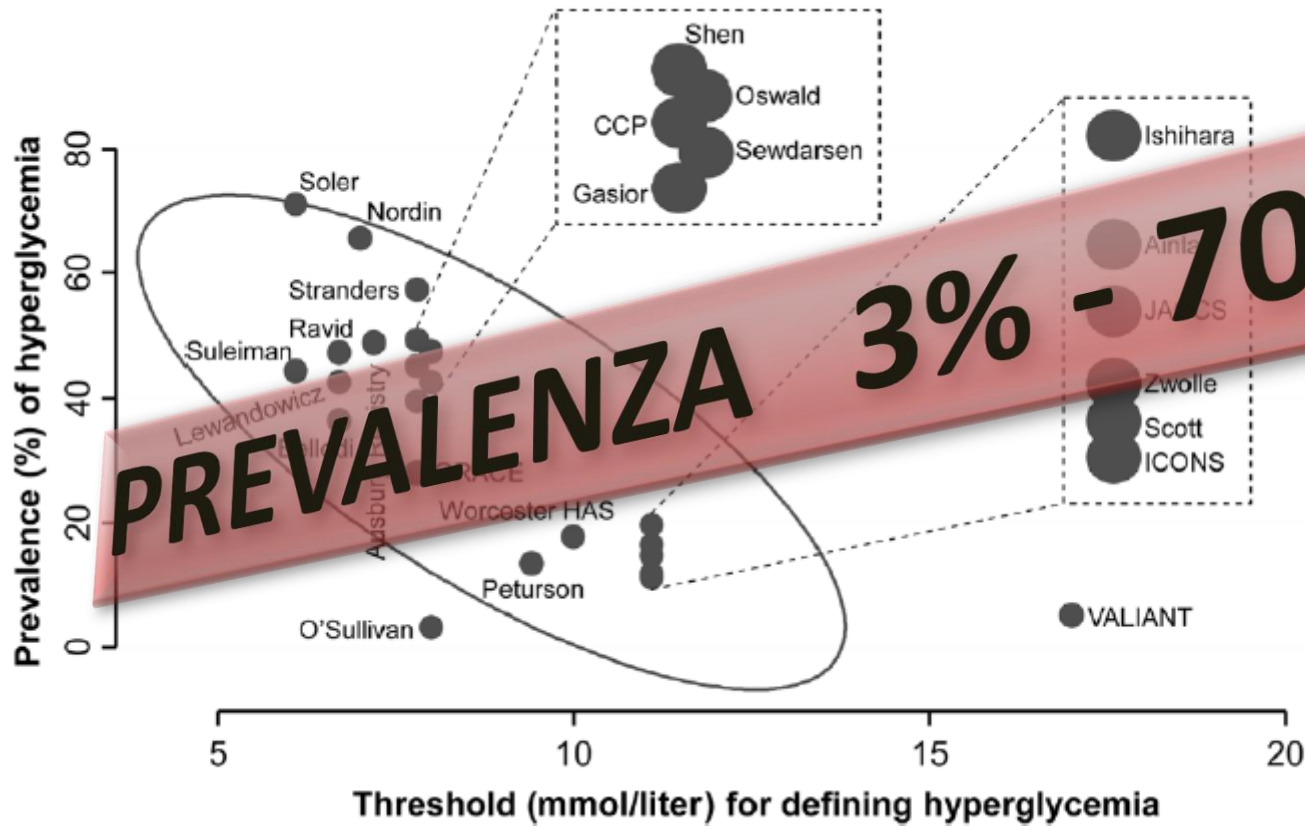


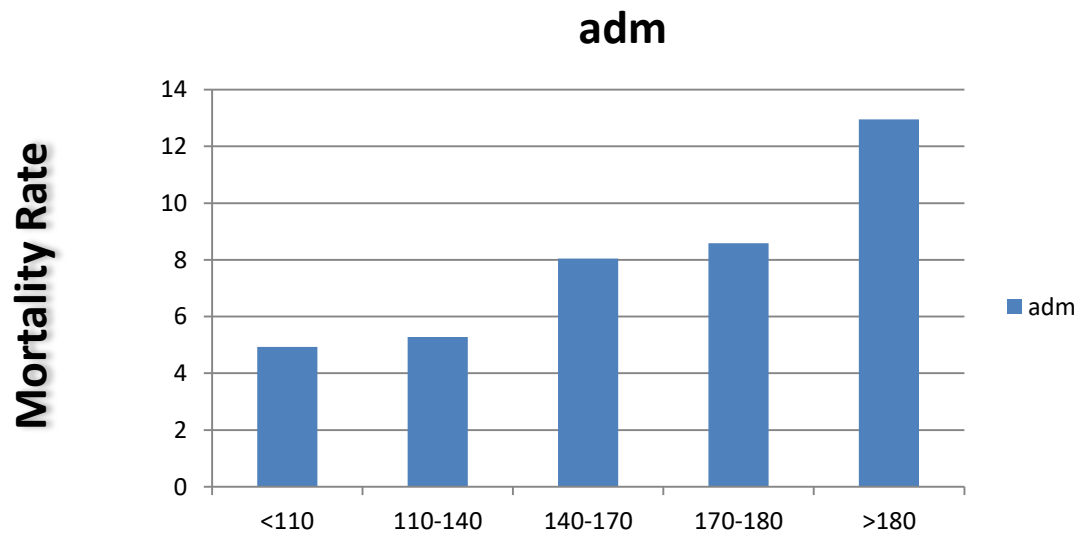
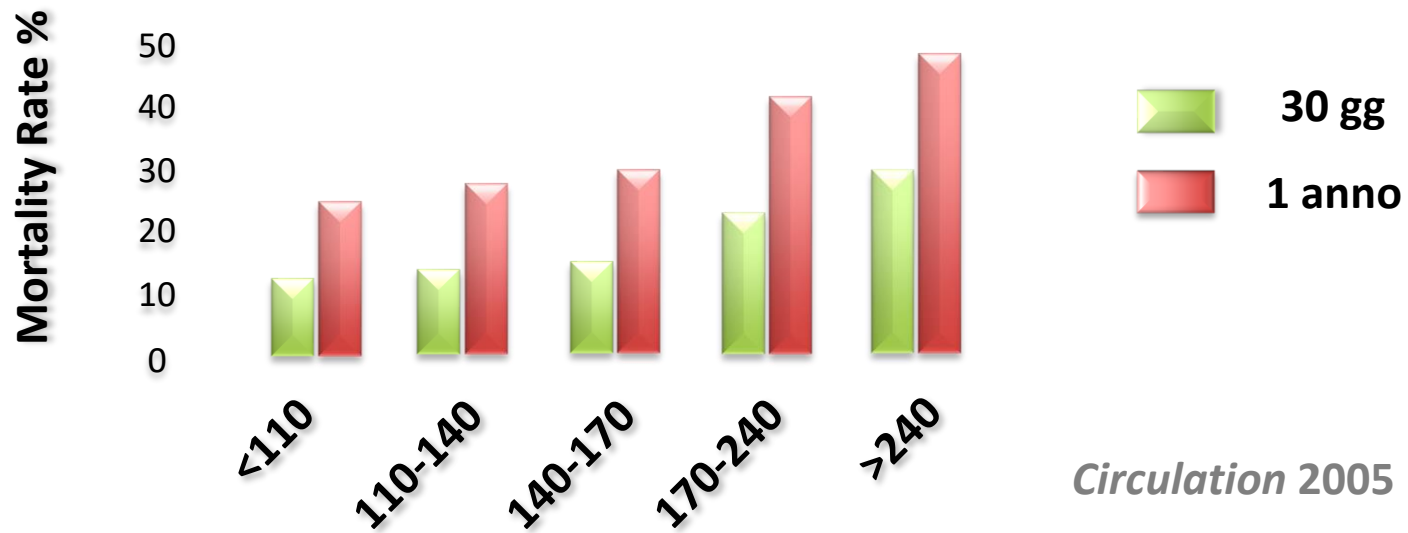


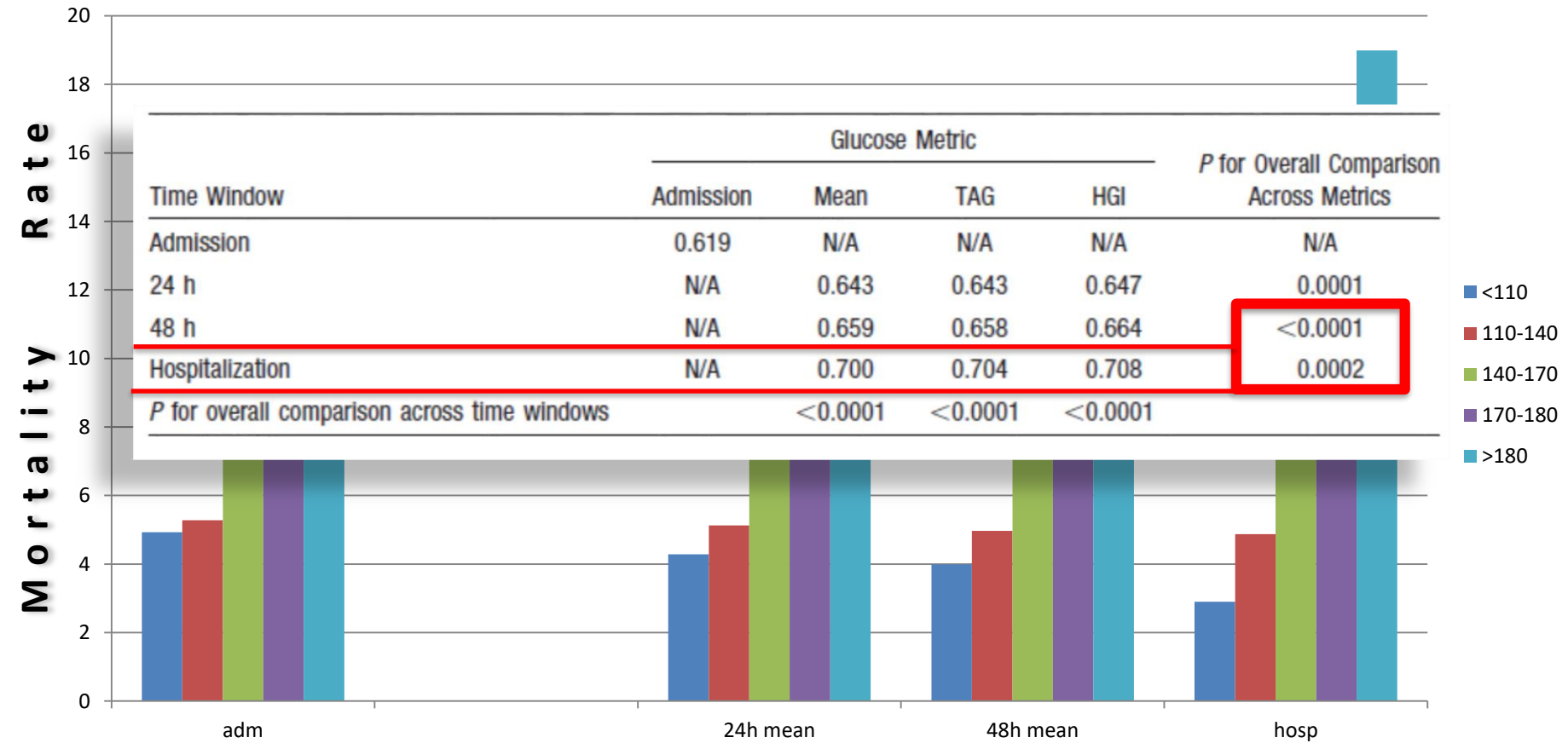


Qual è il valore soglia di glicemia da usare come marker diagnostico di iperglicemia?

Study	Setting	Threshold (mmol/liter)	r) Timing	Prevalence (%)
		≥ 11.1		
		> 7.2		
		≥ 6.7		
Ainla	ACS	≥ 7.8	adm	16.39
Ausburg Registry	ACS	≥ 7.8	adm	48.89
Bellodi	ACS	≥ 7.8	adm	36.39
CCP	ACS in elderly	≥ 11.1	adm	45.25
Gasior	ACS treated PCI	≥ 11.1	adm	39.5
GRACE	ACS	≥ 11.1	fasting > 12 h	28.05
ICONS	ACS	≥ 11.1	adm	11.13
Ishihara	ACS treated with PCI	≥ 6.7	adm	19.66
JACCS	ACS treated with PCI	> 7	adm	14.72
Lewandowicz	ACS	≥ 8	24h	42.50
Nordin	ACS treated with PCI	≥ 8	adm	65.57
O'Sullivan	ACS	> 9.4	after 8 h overnight	3.22
Oswald	ACS	≥ 6.7	adm (mean 9 h)	47.46
Peturson	ACS	≥ 11.1	adm	13.36
Ravid	ACS	≥ 11.1	within 72 h	47.34
Scott	ACS	≥ 8	adm	11.33
Sewdarsen	ACS	≥ 7.8	adm	42.60
Shen	ACS treated with PCI	≥ 6.1	adm	49.35
Soler	ACS	≥ 7.8	24 h	70.97
Stranders	ACS	≥ 6.1	adm	57.39
Suleiman	AMI		≥ 8 h fasting sample within 24 h	44.35
VALIANT	ACS (HR/LVSD)	> 17	adm/Rand (4, 9 days)	5.13
Worcester HAS	ACS	≥ 10	adm	17.7
Zwolle	ACS treated with PCI	≥ 11.1	adm	11.80





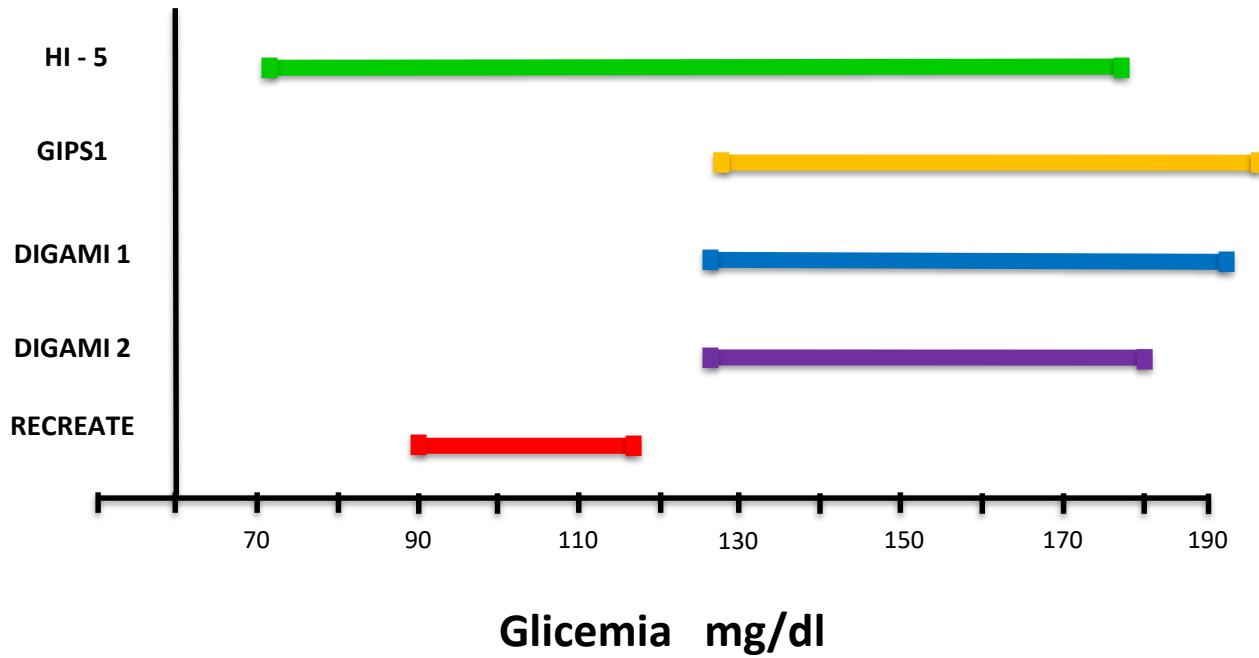


Kosiborod 2008

HI-5 study	24-h mean blood glucose level ≤ 8 mmol/l	24-h mean blood glucose level ≥ 8.1 mmol/l
Inpatient mortality	0%	7%
3-month mortality	2%	9%
6-month mortality	2%	11%

**Qual è il target glicemico
da mantenere?**

Target glicemico



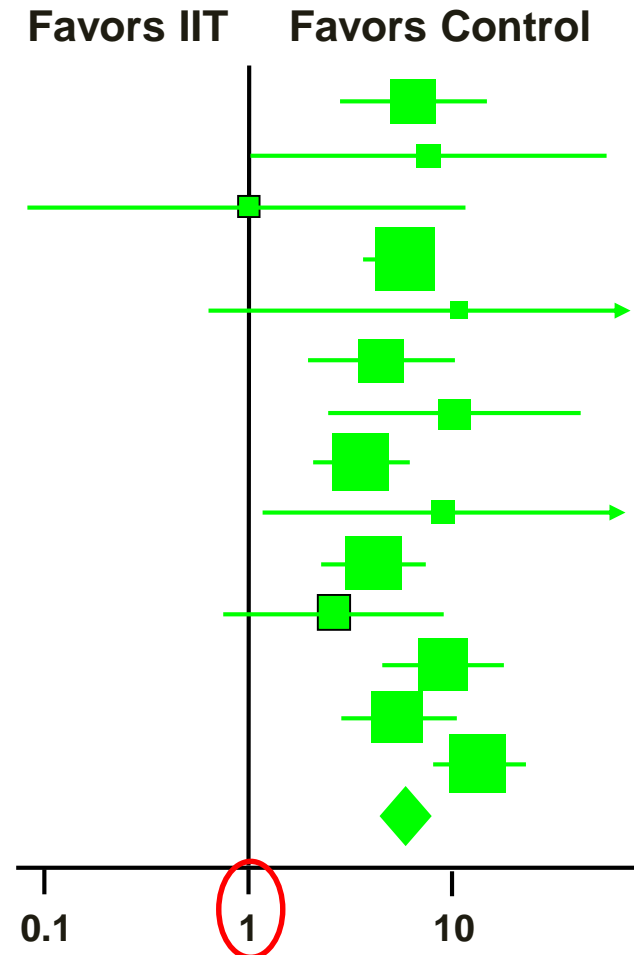
TRIALS	OUTCOMES	HYPO %
DIGAMI (1997)	SI	15
ECLA-GIK (1998)	NO	n.r.
GIPS-1 (2003)	NO	0
KRLIJANAC (2005)	SI	2
POL-GIK (1999)	NO (forse peggiorativo?)	7,6
REVIVAL (2004)	NO (ma positivo salvage index)	n.r.
DIGAMI-2 (2005)	NO	11
CREATE-ECLA (2005)	NO	0,4
GIPS-II (2006)	NO	n.r.
Hi-5 (2006)	NO (ma meglio per reinfarto a 3 mesi)	10
OASIS-6 (2007)	NO	n.r.
OASIS-6 +CREATE ECLA (2007)	NO	n.r.
IMMEDIATE (2012)	NO	n.r.
RECREATE (2012)	NO	23

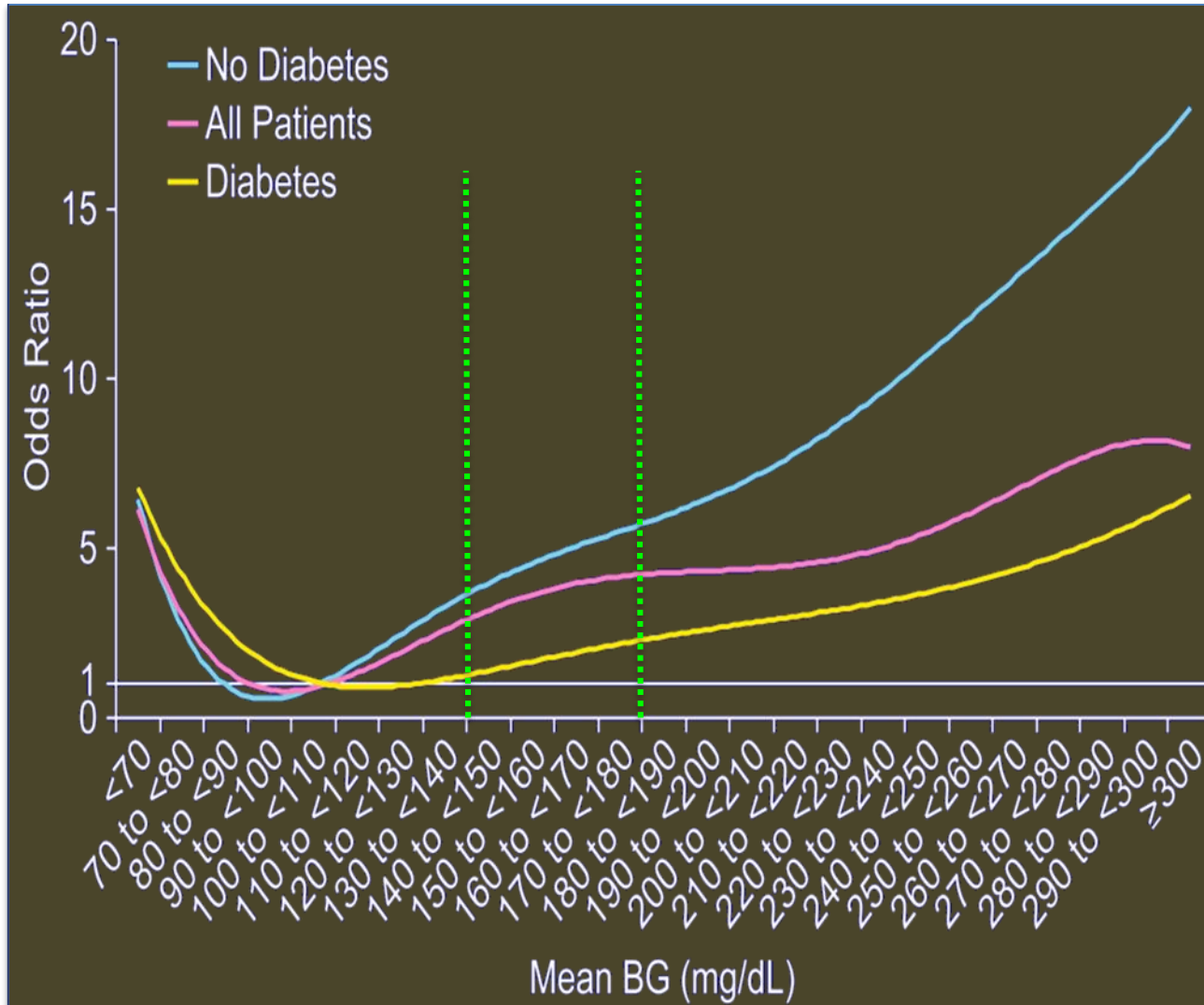
Intensive Insulin Therapy and Hypoglycemic Events in Critically Ill Patients

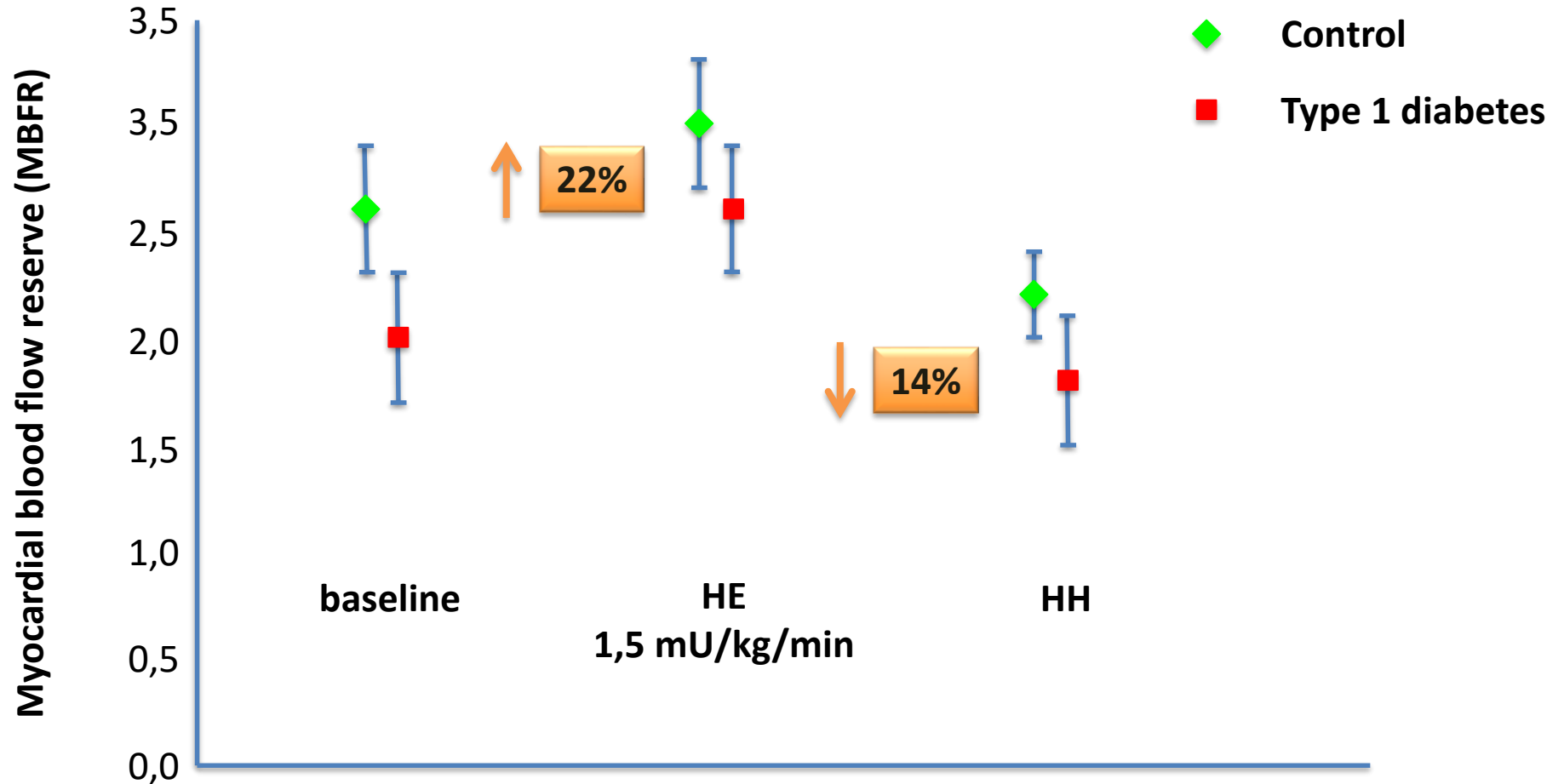
No. Events/Total No. Patients

Study	IIT	Control	Risk ratio (95% CI)
Van den Berghe et al	39/765	6/783	6.65 (2.83-15.62)
Henderson et al	7/32	1/35	7.66 (1.00-58.86)
Bland et al	1/5	1/5	1.00 (0.08-11.93)
Van den Berghe et al	111/595	19/605	5.94 (3.70-9.54)
Mitchell et al	5/35	0/35	11.00 (0.63-191.69)
Azevedo et al	27/168	6/169	4.53 (1.92-10.68)
De La Rosa et al	21/254	2/250	10.33 (2.45-43.61)
Devos et al	54/550	15/551	3.61(2.06-6.31)
Oksanen et al	7/39	1/51	9.15 (1.17-71.35)
Brunkhorst et al	42/247	12/290	4.11(2.2-7.63)
Iapichino et al	8/45	3/45	2.67 (0.76-9.41)
Arabi et al	76/266	8/257	9.18 (4.52-18.63)
Mackenzie et al	50/121	9/119	5.46 (2.82-10.60)
NICE-SUGAR	206/3016	15/3014	13.72 (8.15-23.12)
Overall	654/6138	98/6209	5.99 (4.47-8.03)

Hypoglycemic Events







TRIALS	Insulin Dose mU/kg/min
DIGAMI (1997)	1,2
ECLA-GIK (1998)	1,3
GIPS-1 (2003)	titrated on glucose
KRLIJANAC (2005)	0,8
POL-GIK (1999)	0,3
REVIVAL (2004)	1,2
DIGAMI-2 (2005)	1,2
CREATE-ECLA (2005)	1,3
GIPS-II (2006)	2,3
Hi-5 (2006)	0,5
OASIS-6 (2007)	1,3
OASIS-6 +CREATE ECLA (2007)	1,3
IMMEDIATE (2012)	1,3
RECREATE (2012)	titrated on glucose

Mortality
AMI



Infarct Size

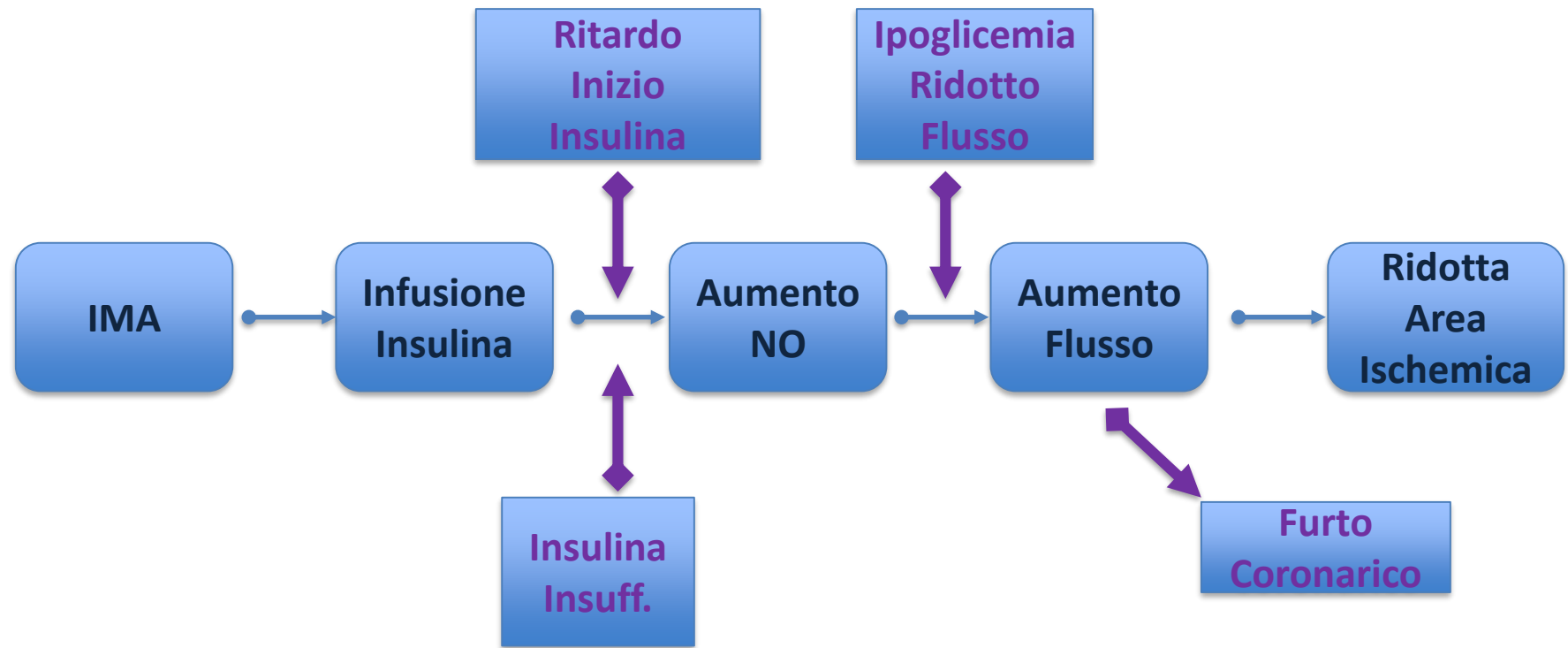


Ischemic Area
Duration of Ischemia

55 min



19 h

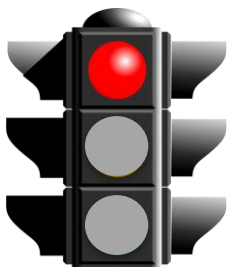


CONCLUSIONI

Standard italiani
per la cura del
diabete mellito
2016



- ✓ **Esiste una relazione stretta fra iperglicemia ed esito finale in pazienti ricoverati in unita coronarica.**
- ✓ **La somministrazione di insulina è la terapia di scelta nel paziente diabetico ospedalizzato non stabilizzato.**
- ✓ **In pazienti critici, la terapia insulinica deve essere effettuata in infusione venosa continua, applicando algoritmi basati su frequenti controlli dei valori glicemici e validati nel contesto di applicazione.**



**<110 mg/dl non sicuri
>180 mg/dl non accettabile**



140-180 mg/dl

Iniziare insulina e.v. ad una soglia non superiore a 180 mg/dl.

Grazie