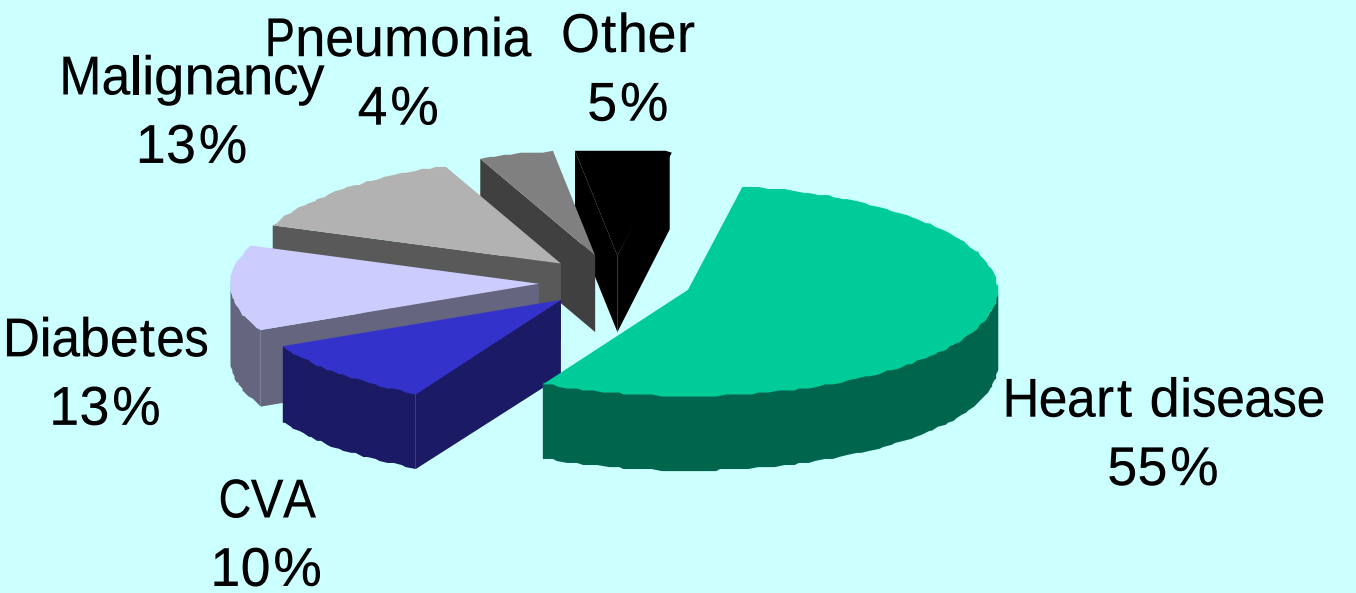
Metabolic Control of Diabetic Patients with Atherosclerosis

인제의대 상계백병원 내분비내과
고 경 수

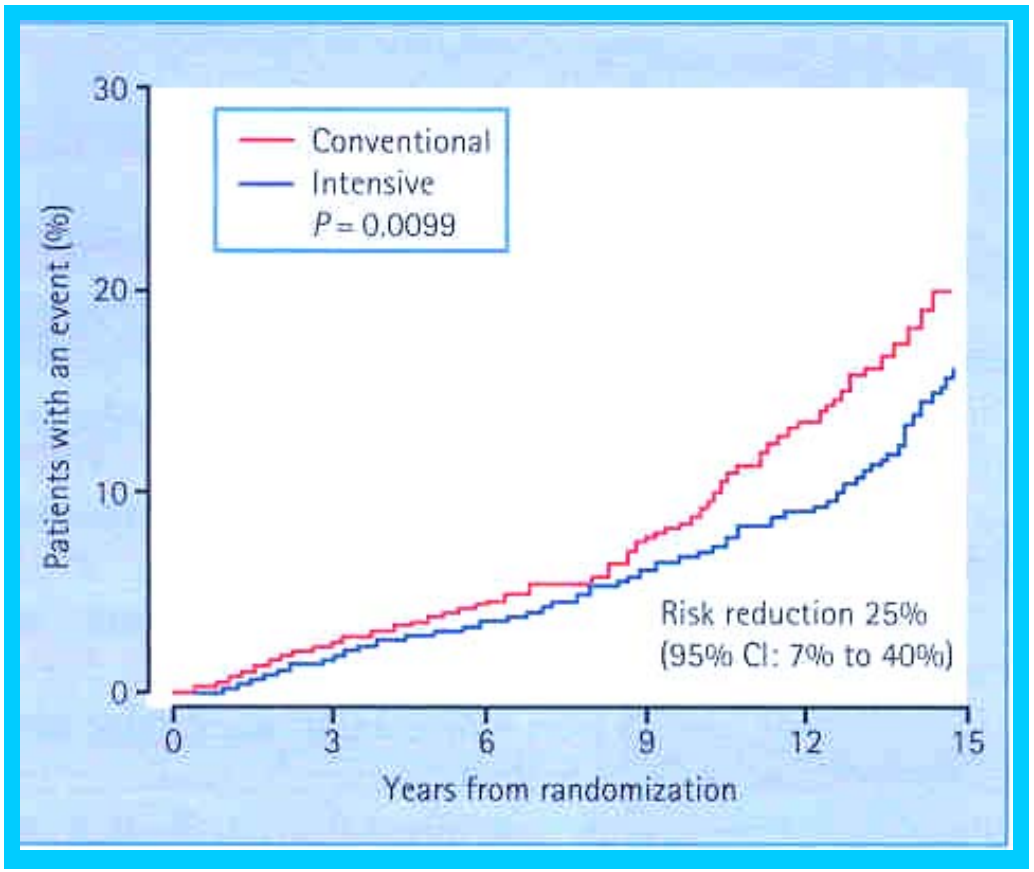
제2형 당뇨병

- **Chronic hyperglycemia**
- **Cardiovascular disease risk**
- **Worse prognosis**

Causes of mortality

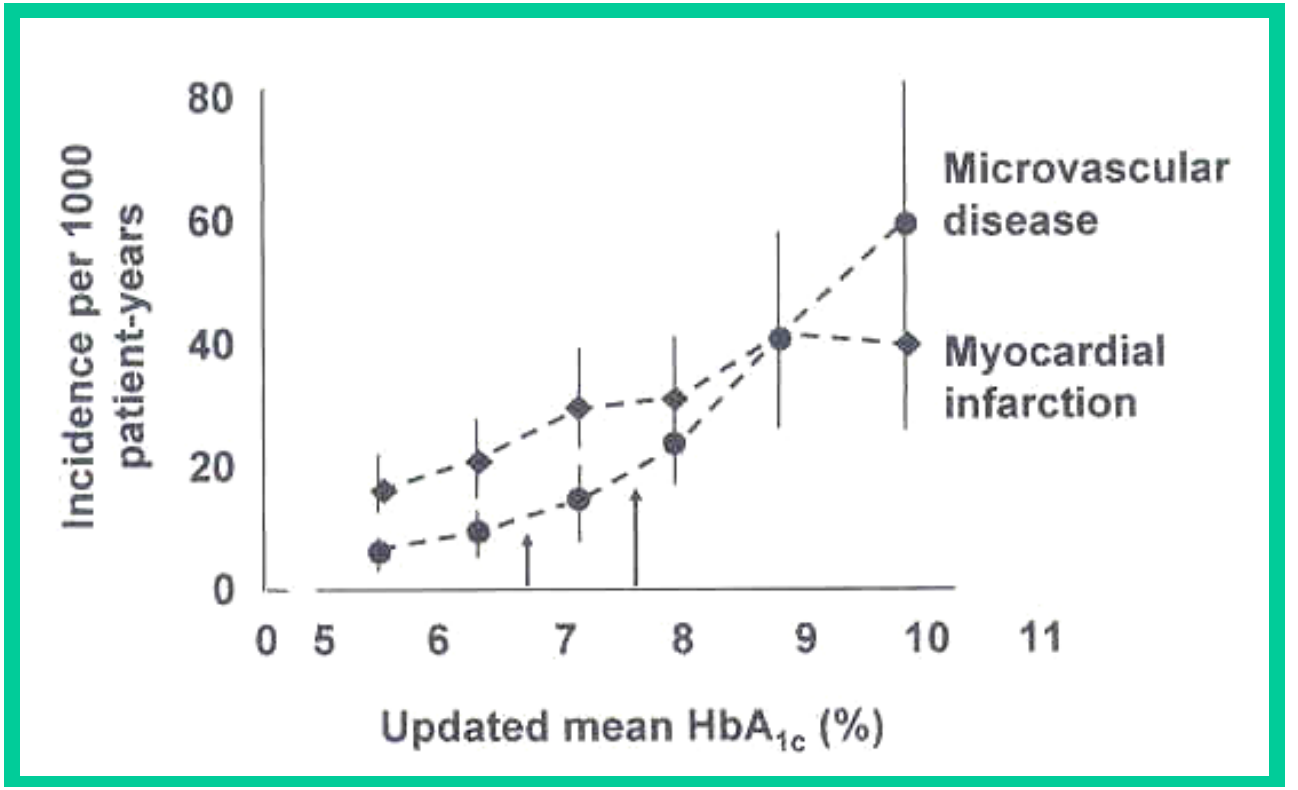


UKPDS



Development of microvascular complications

UKPDS



Development of micro-/macrovascular complications

UKPDS

Risk reduction for intensive therapy

Event	Main analysis	Metformin subgroup
Any diabetes-related end-point	12%	32%
Diabetes-related death	NS	42%
All-cause mortality	NS	36%
Myocardial infarction	16%	39%
Microvascular end-point	25%	NS
Fatal MI	NS	50%
Laser photocoagulation	29%	NS
Cataract extraction	24%	NS
Retinopathy at 12 yrs	21%	NS
Microalbuminuria at 12 yrs	33%	NS

Steno-2 study

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Multifactorial Intervention and Cardiovascular Disease in Patients with Type 2 Diabetes

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Steno-2 study

Goals of treatment

Systolic blood pressure

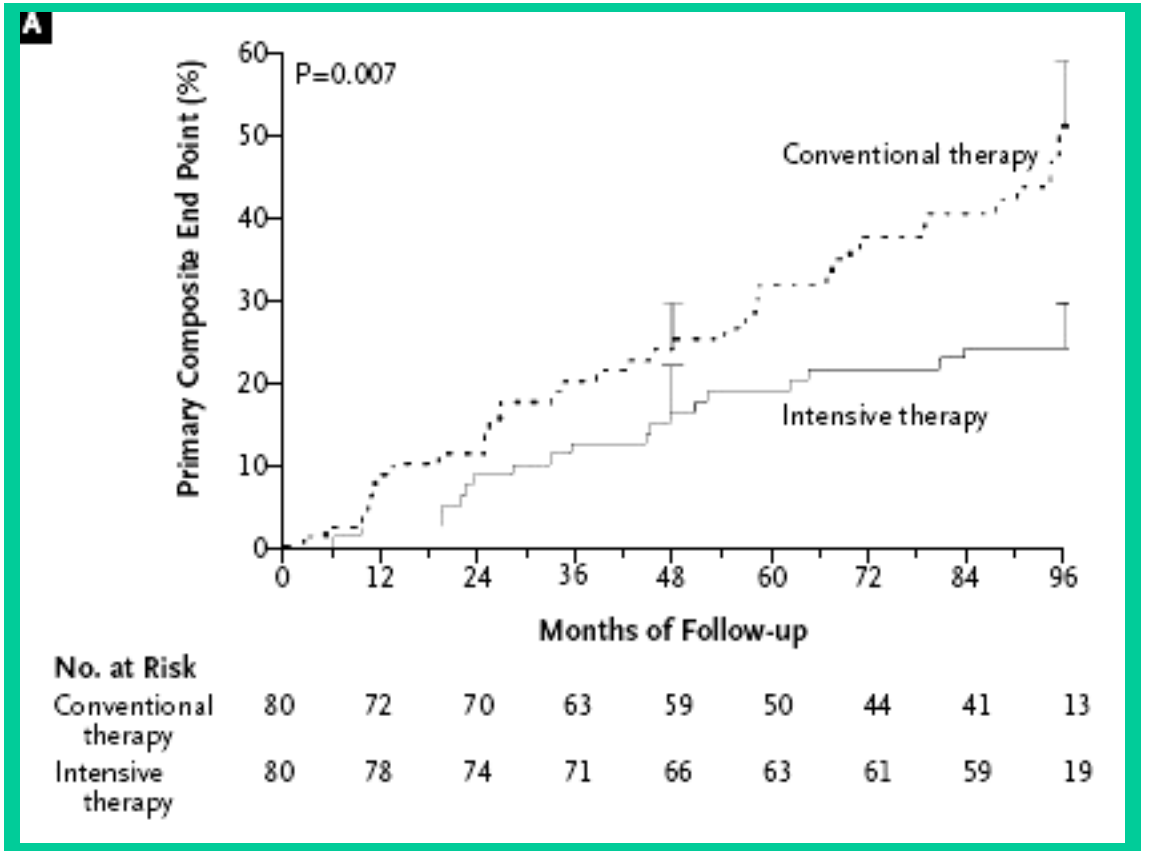
Diastolic blood pressure

Glycosylated hemoglobin

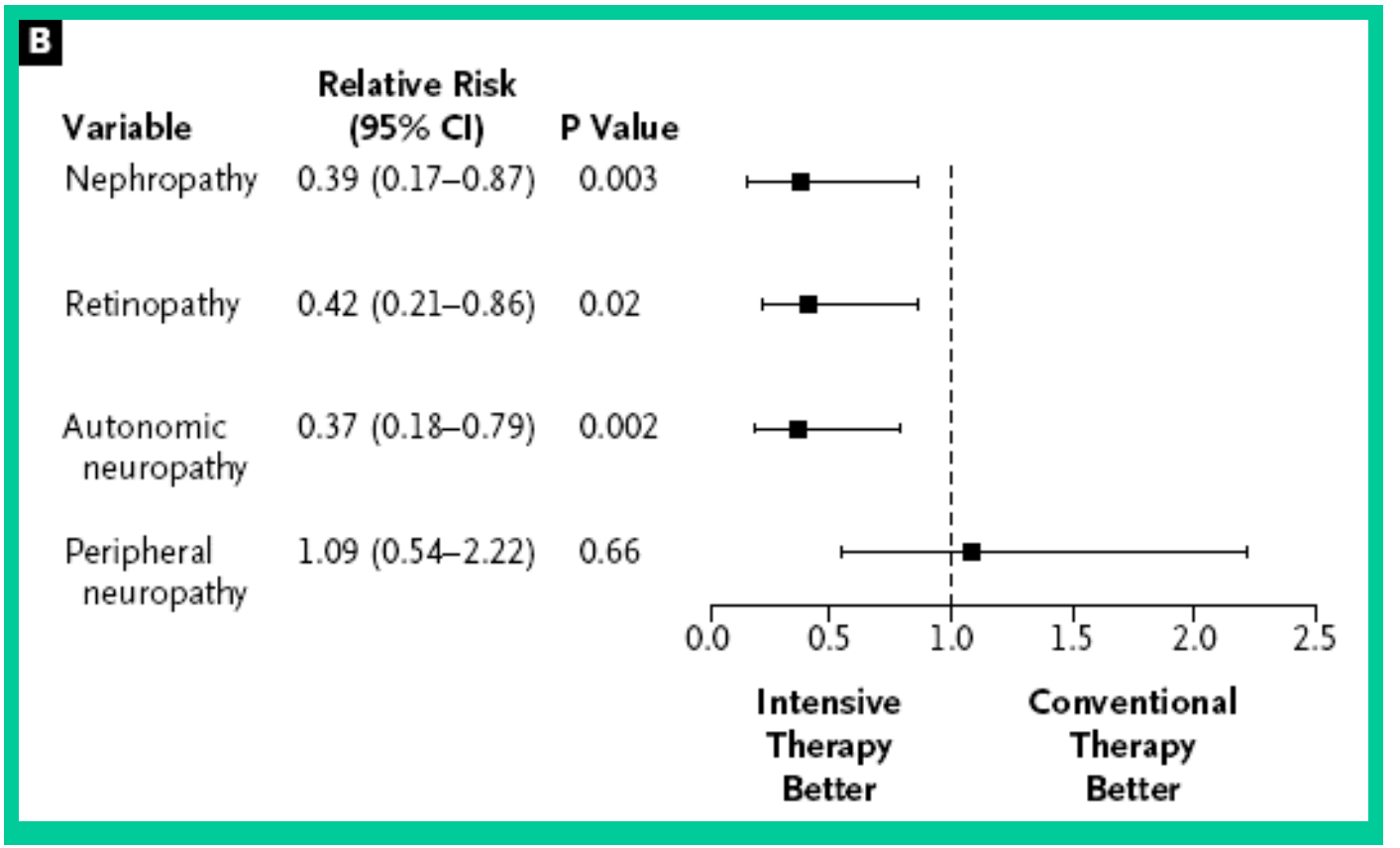
Total cholesterol

Triglyceride

Steno-2 study



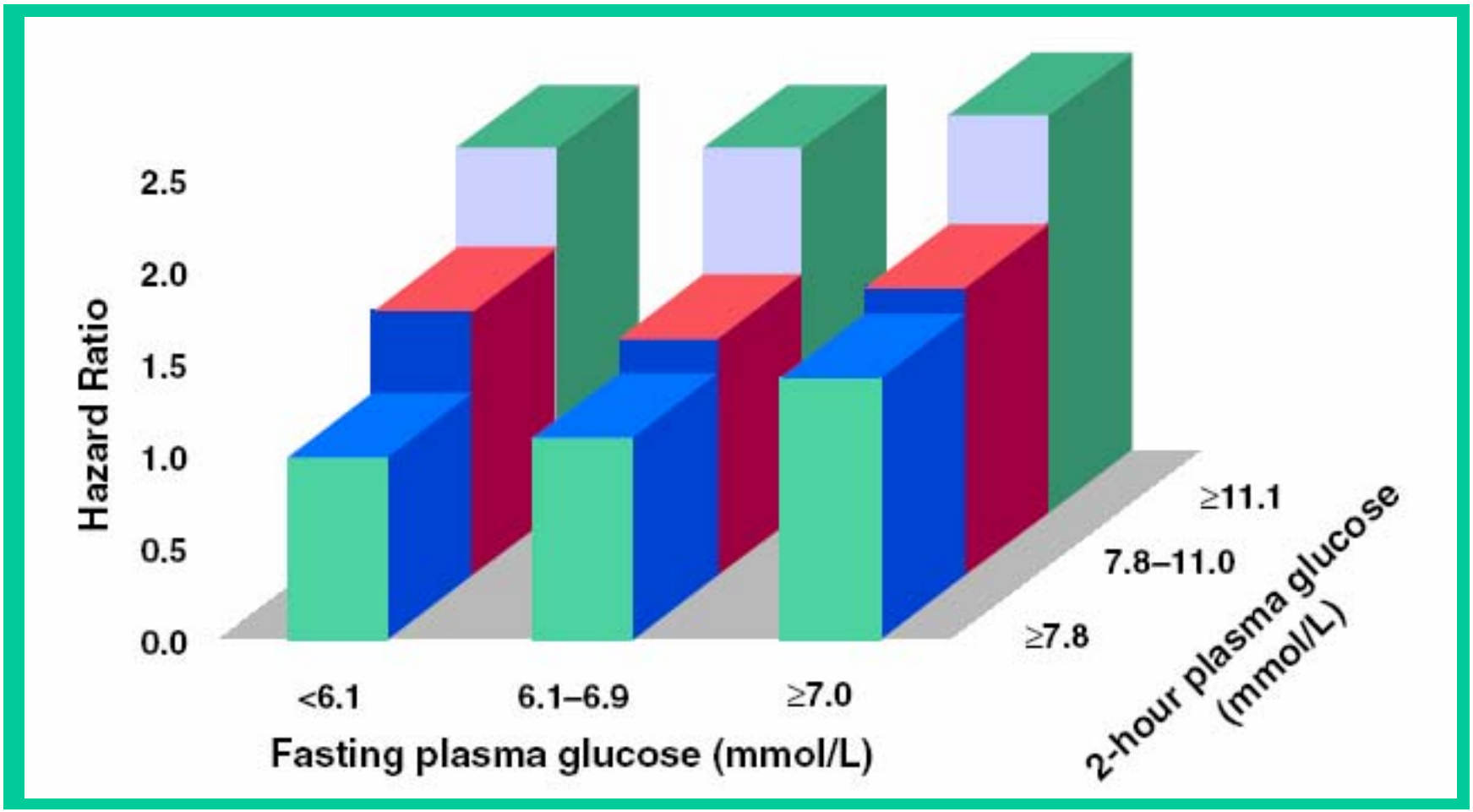
Steno-2 study



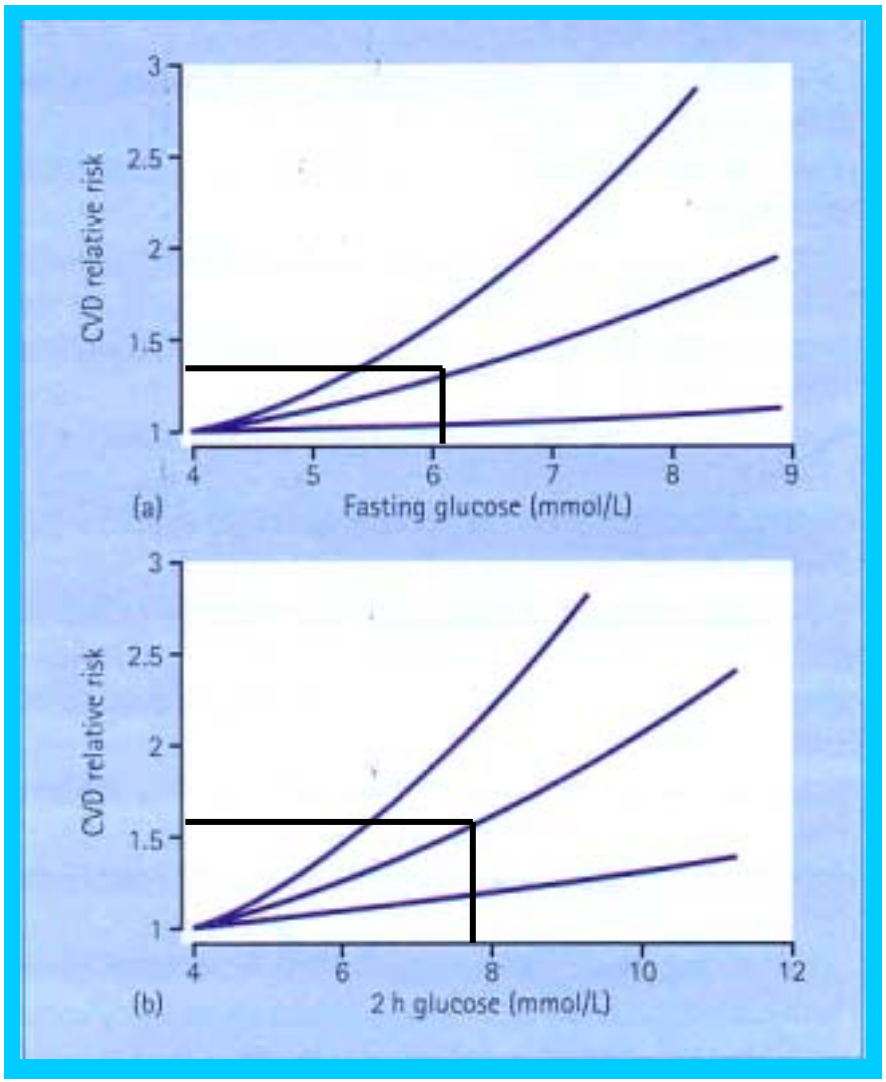
공복고혈당과 식후고혈당

공복혈당: 간의 포도당 생산

식후혈당: 간의 포도당 생산
간과 근육에서의 포도당 섭취
당불내인성의 초기 단계
대혈관합병증과 관련



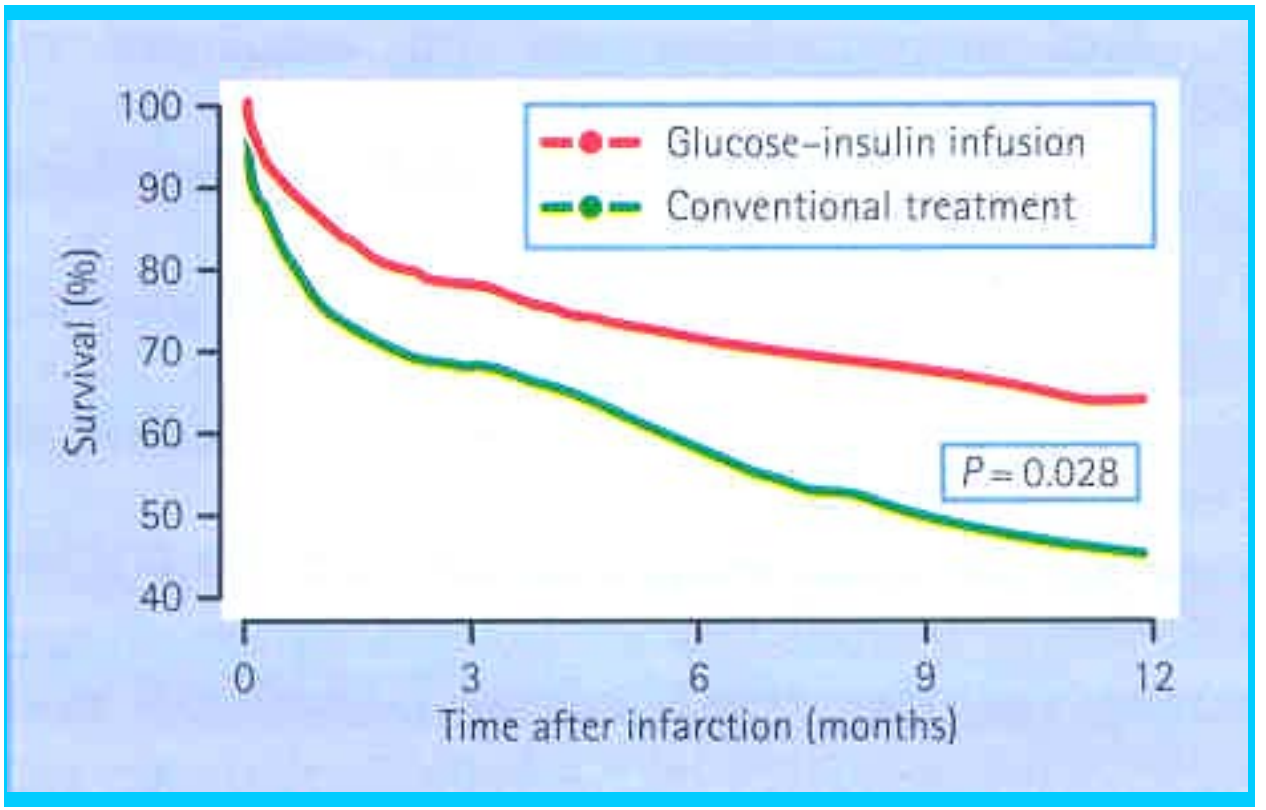
Mortality in terms of fasting and postprandial glucose level



Relationship between glucose and CVD (12 yr. F/U)

Prevention of CVD

Primary	Acute event	Secondary
Healthy eating	Thrombolysis	Aspirin
Exercise	IV insulin/glucose	β - blocker
Non-smoking	β-blocker	Risk factor reduction
Weight reduction	ACE inhibitor	revascularization
BP control		
Normal HbA_{1c}		
Aspirin		
Statin		
Fibrate		
ACE inhibitor		



DIGAMI protocol

Glycemic control

Beneficial?

Target?

Methods?

Benefit of glycemic control

UKPDS
Steno-2 study
DIGAMI trial

Target of glycemic control

Biochemical Control	Normal	Goal
HbA_{1C} (%)	<6.0	<7.0†
FPG (mg/dL)		
Average preprandial	<110	90-130‡
PPG (mg/dL)	<140	<180§

A1c target of current studies: 6.0~6.5%

Mode of glycemic control

- Insulin secretagogue
  - sulfonylurea
  - glinide
- Insulin sensitizer
  - metformin
  - thiazolidinedione
- α-glucosidase inhibitor
- Insulin

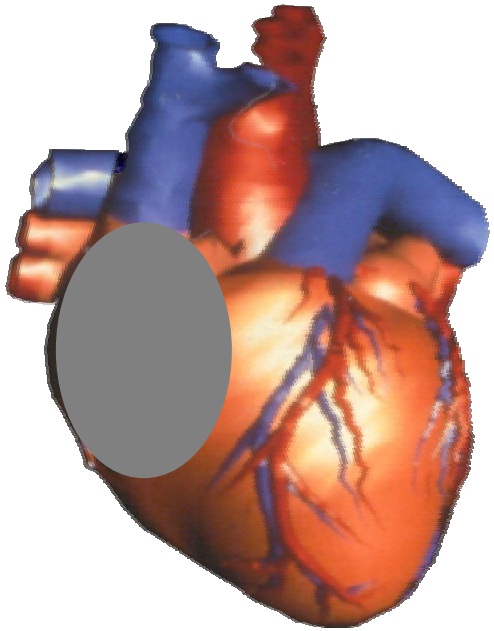
Sulfonylurea

University Group Diabetes Program (1971)
- Tolbutamide treatment may increase CV mortality

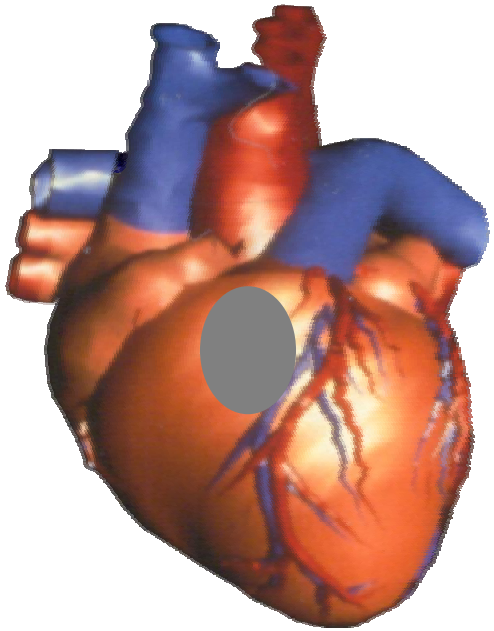
UKPDS
- slight reduction in myocardial infarction

Early mortality underwent balloon angioplasty
- after AMI (1999)

Ischemic Preconditioning (IP)

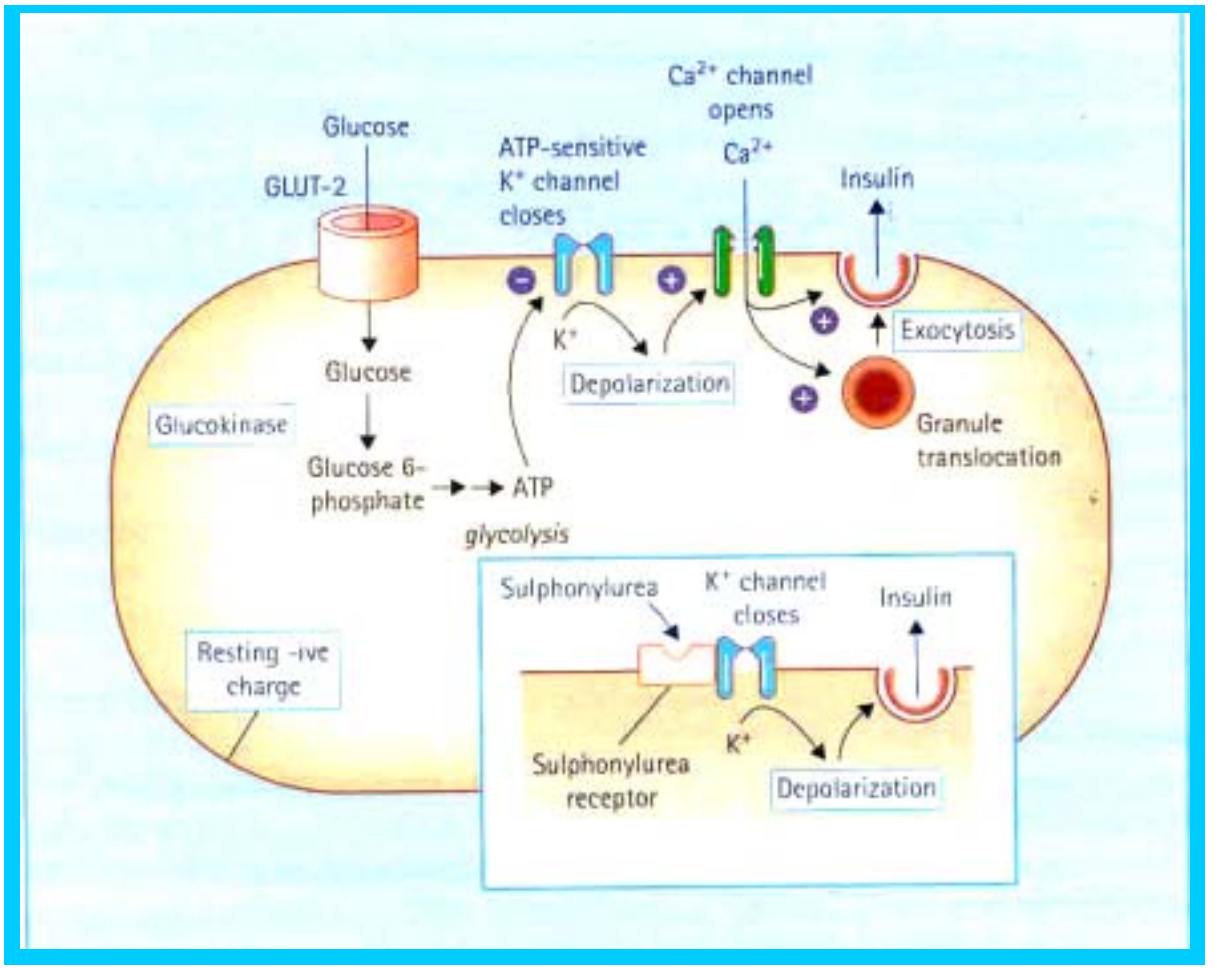


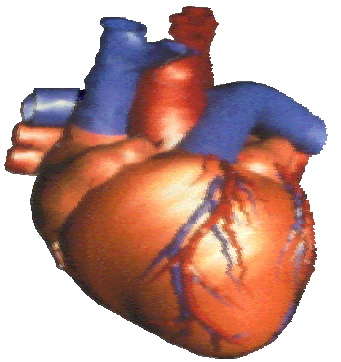
Prolonged occlusion of an epicardial artery leads to myocardial infarction

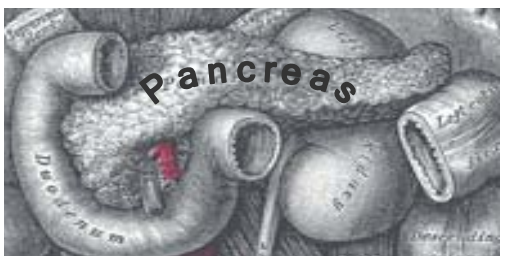


Repeated and brief occlusion of the same vessel conditions the myocardium such that subsequent prolonged occlusion leads to a smaller infarct (ischemic preconditioning)

인슐린분비촉진제의 작용기전







Kir6.2

SFU

SUR2A

Responsible for K^+ flux

68% homology

Kir6.2

SFU

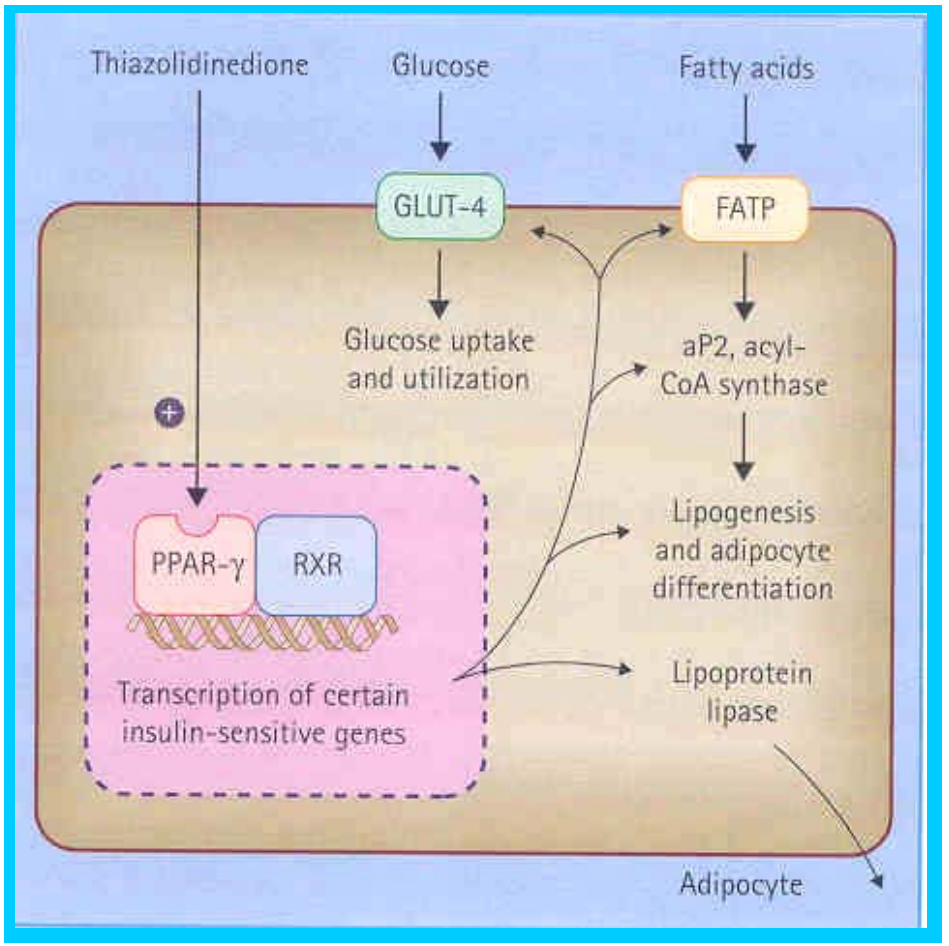
SUR1

Pancreatic K_{ATP} channels over channels in other tissue.

Metformin

- Greater reduction in CVD and mortality than SU and insulin
- Decrease TG, LDL-cholesterol
- Decrease PAI-1 activity

Thiazolidindiones



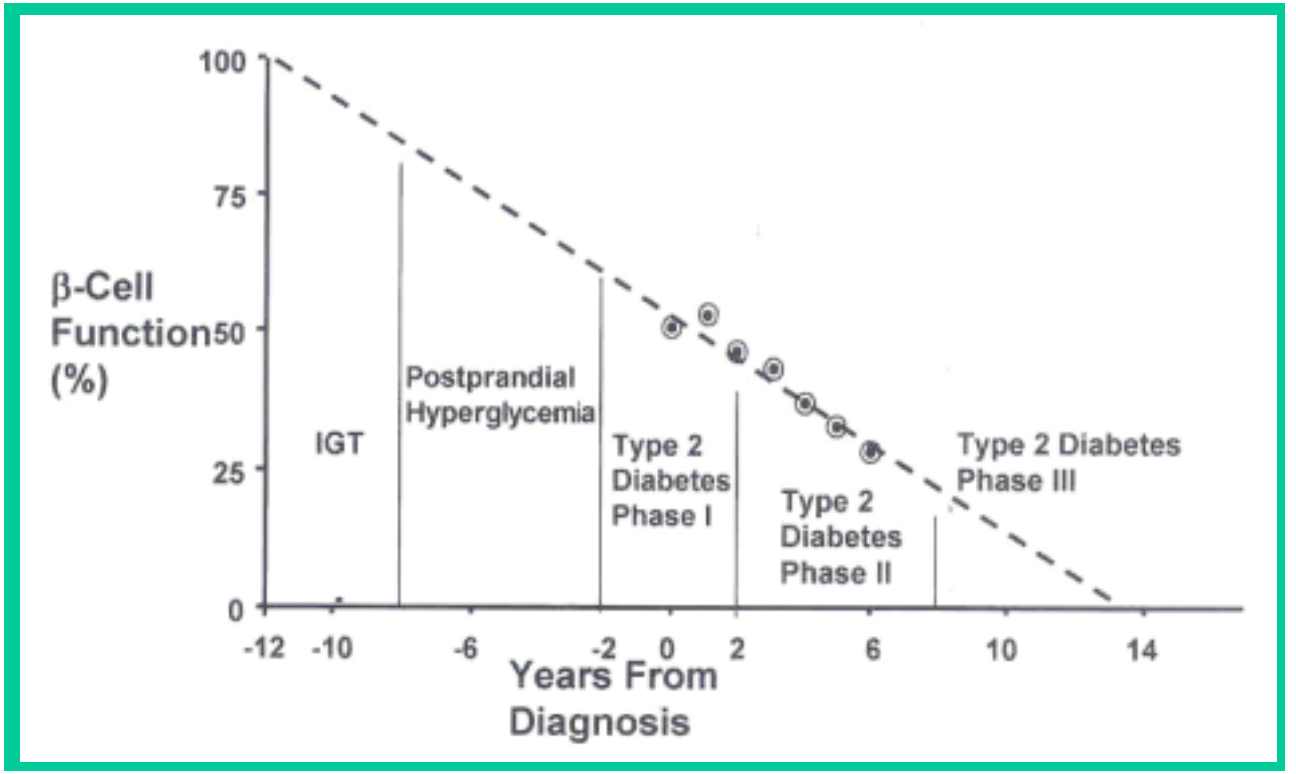
Mechanism of action

Thiazolidindiones

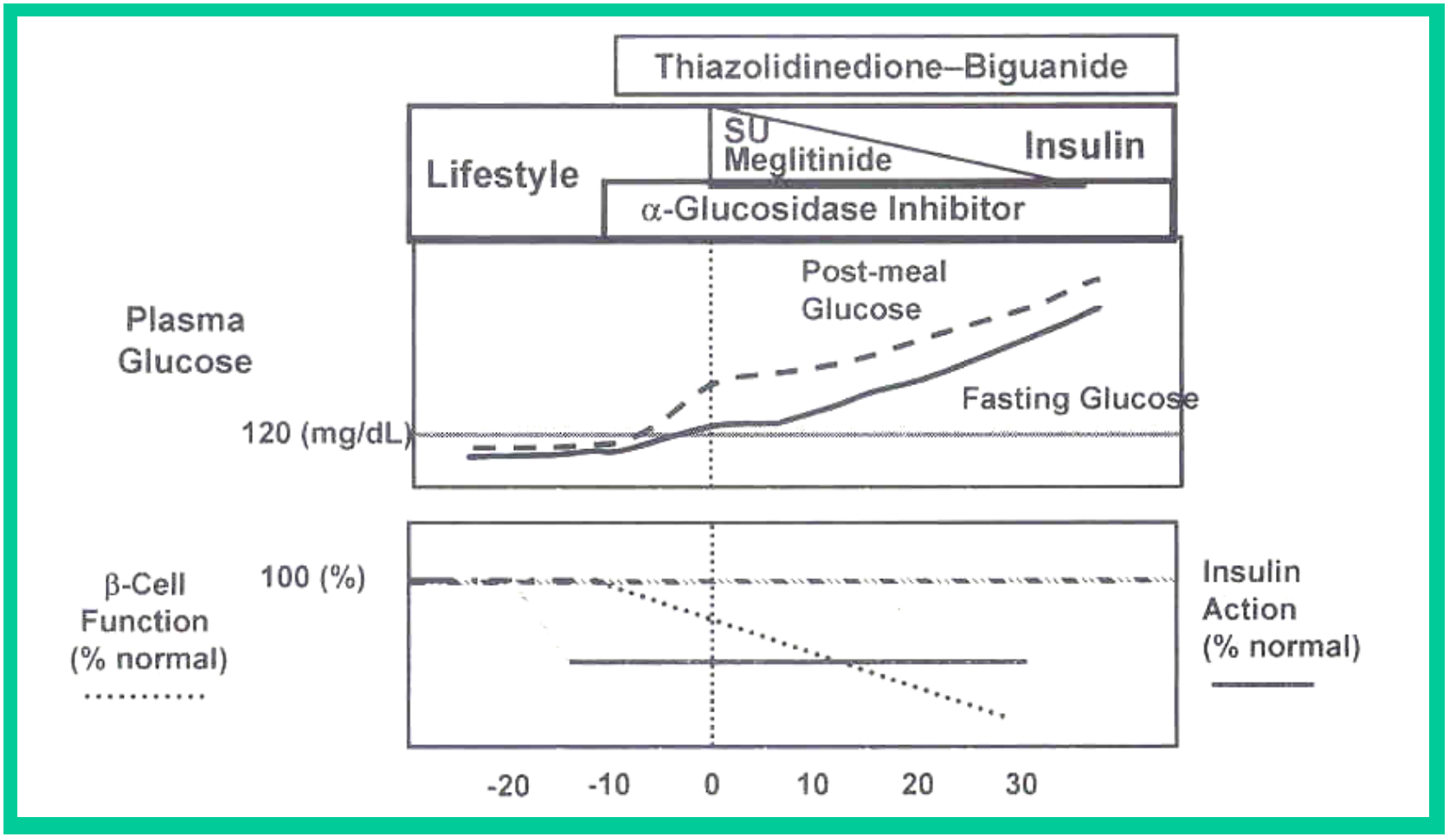
- Lipid metabolism and oxidation
- Blood pressure
- Endothelial function
- Vascular reactivity
- Fibrinolysis, coagulation, inflammation
- Albuminuria

Insulin

Insulin resistance and hyperinsulinemia



Stages of glucose intolerance



Matching pathophysiology with treatment

Summary

1. Diabetes and CV disease
2. Beneficial effect with strict glucose, lipid, blood pressure etc.
3. Insulin sensitizer