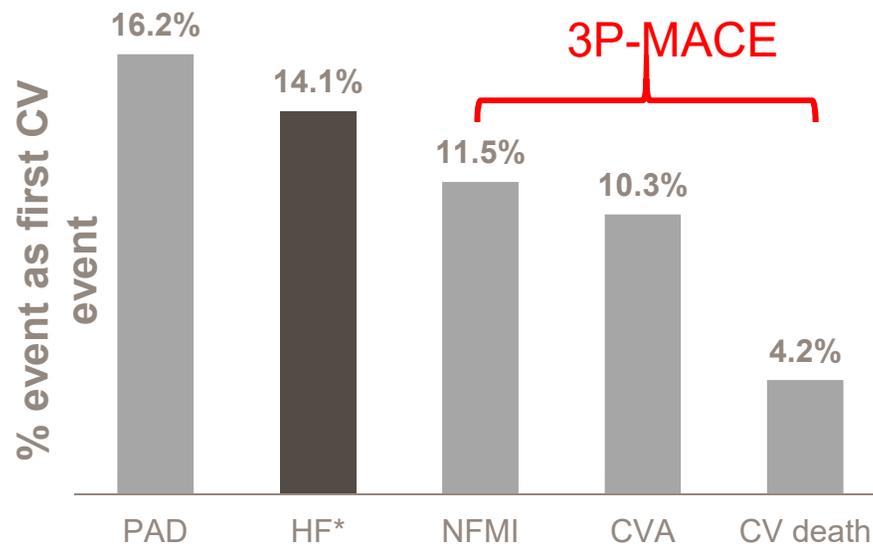


# **DIABETES MELLITUS IN DER PRAXIS – UPDATE DES EXPERTEN**

**PROF. DR. MED. MARC DONATH,  
FACHARZT FÜR ENDOKRINOLOGIE/DIABETOLOGIE  
& FÜR ALLGEMEINE INNERE MEDIZIN**

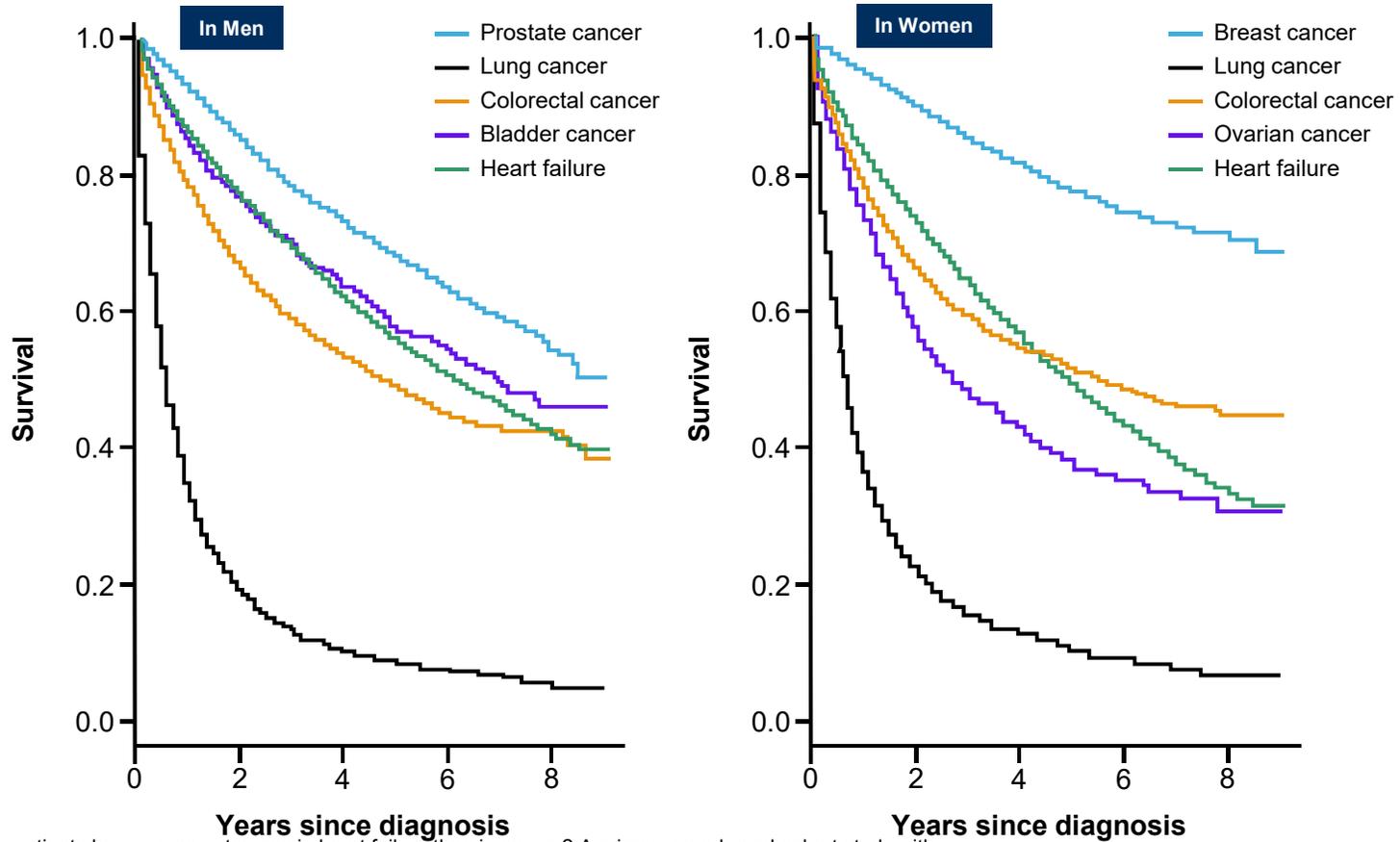
## HF occurs earlier than MI or stroke as a T2DM complication

Cohort study of patients (n= 1.9 million) with T2DM and incidence of CV disease



\*Heart failure post MI was not included in this definition of HF

## Despite advances in management, HF as 'malignant' as cancer

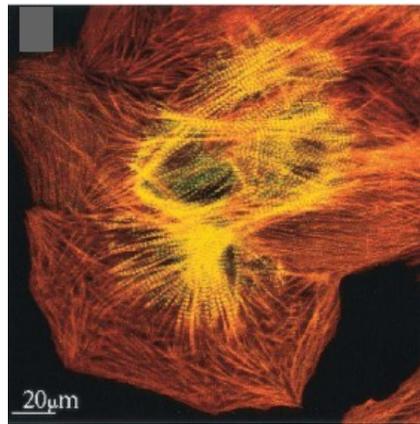


HF, heart failure

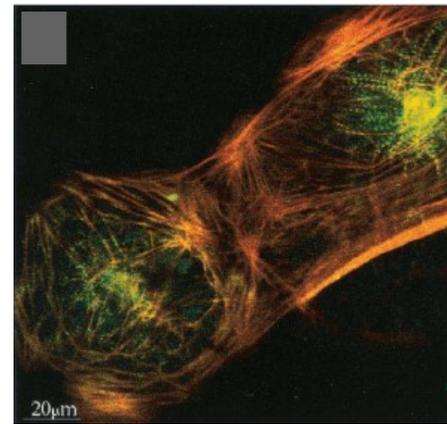
Mamas MA. et al. Do patients have worse outcomes in heart failure than in cancer? A primary care-based cohort study with 10-year follow-up in Scotland *Eur J of Heart Failure* 2017;19:1095-1104

# Cardiomyocytes

Control



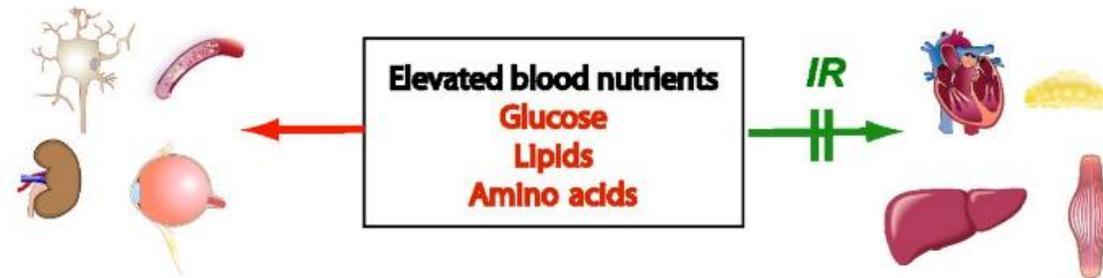
Glucose



## Therapeutic approaches to obesity-related type 2 diabetes with refractory glycemic control

**Vascular complications eventually occur unless glycemia is controlled**

**Insulin resistance provides defense against nutrient-induced injury of insulin-sensitive tissues**



**Nutrient off-loading  
+/- low-dose insulin**

Lifestyle  
Bariatric surgery  
GLP-1R agonists  
 $\alpha$ -glucosidase inhibitors

Metformin  
SGLT2 inhibitors  
Thiazolidinediones?  
DPP-4 inhibitors ?

**Reduced metabolic stress in ALL tissues  
Reduced short- and long-term complications**

**Overriding insulin resistance in refractory patients**

High-dose insulin  
Sulfonylureas?

**Insulin-induced metabolic stress  
Short-term injury of insulin-sensitive tissues**

C.J. Nolan N.B. Ruderman<sup>2</sup>, S. E. Kahn, O. Pedersen, M. Prentki. *Diabetes* 2015;64:673-686

Type 2 diabetes

=

Protection against Overnutrition

Islet:

Protection

=

Insulin production ↓

Kidney:

Protection

=

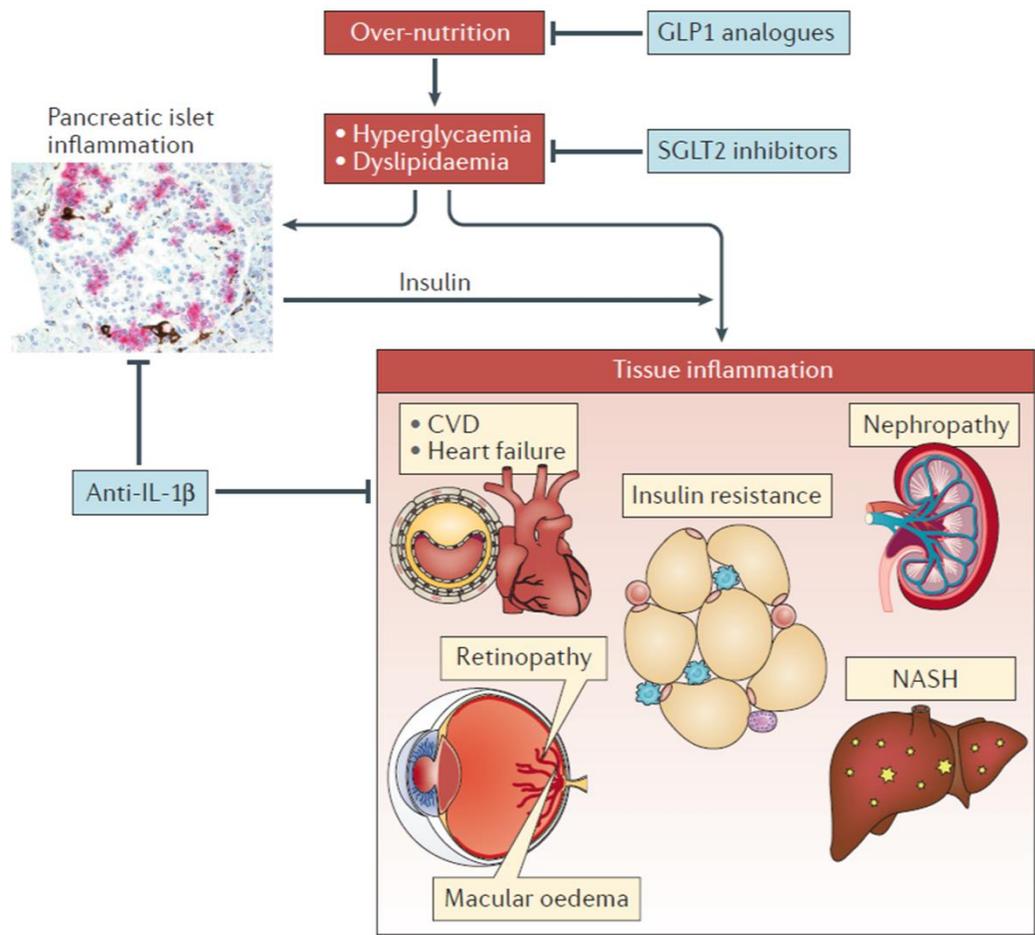
Glucosuria

Fat, liver, muscle:

Protection

=

Insulin sensitivity ↓



Donath et al, *Nature Reviews Immunology*, in Press

## Treatment of Typ 2 Diabetes

1. Prevention – Life-style intervention
  - Sport is the best drug
2. Anti-obesity treatment
  - GLP-1, GLP1-Glucagon etc.
3. Glucose lowering without tissue accumulation
  - SGLTi, bariatric surgery
4. Damage limitation
  - DPP-Ivi, Anti-inflammation

## Glycemic targets

- HbA1c < 7.0%

Individualization is key:

- Tighter targets (6.0 - 6.5%)
  - younger, healthier
- Looser targets (7.5 - 8.0%)
  - older, comorbidities, hypoglycemia prone, etc.
- Avoidance of **hypoglycemia**

Patient, 47 year old:

- Polyuria & polydipsia for 3 weeks
- BMI 28
- HbA1c 14.8%
- Urin keton bodies +++++

➤ 2 l saline & lifestyle intervention

## Exercise improves

- **Well being**
- **Glucose uptake in muscles**
- **Insulin production (cross-talk muscle-islet)**
- **Body weight (?)**



# THE BEND-ER STUDY

Bicycle Exercise in Newly Diagnosed  
Diabetics in the Emergency Room



# Food legalisation



# Incretins

- DPP-IV inhibitors
- GLP-1 analoga

## **DPP-IV inhibitors**

- No Hypoglycaemia
- No changes in Body weight
- Safe

But no demonstrated cardiovascular protection

## DPP-IV inhibitors

- Sitagliptin (Januvia und Xelevia bzw. Janumet & Velmetia)
- Vildagliptin (Galvus und Galvumet)
- Saxagliptin (Onglyza und Kombiglyze XR)
- Linagliptin (Trajenta und Jentadueto)

## GLP-1 analoga

### **Twice-daily**

- Exenatide (Byetta)

### **Daily**

- Liraglutide (Victoza) & Liraglutide & Degludec (Xultophy)
- Lixisenatid (Lyxumia) & Lixisenatid & Glargin (Suliqua)

### **Once-weekly**

- Exenatide Once Weekly Sustained-release (Bydureon)
- Dulaglutide (Trulicity)
- Semaglutide (Ozempic)

## SGLT2 Inhibitors

1. Canagliflozin (Invokana)
2. Dapagliflozin (Forxiga)
3. Empagliflozin (Jardiance)
4. Ertugliflozin (Steglatro)

## SGLT2 Inhibitors

- HbA1c↓
- Body weight ↓( 80-100 gr. glucose = ~ 300-400 cal/day)
- Blood pressure ↓
- No hypoglycemia
- All combination possible (incretin limits)

BUT:

- Genital infections
- Ketoacidosis
- New drug (Glucagon secretion ↑)

# Insulin

- Insulatard
- Lantus
- Levemir
- Tresiba
- Toujeo

## Konkretes vorgehen:

- Basisinsulin (um 10 IE)
- Dosis erhöhen bis FPG < 5,5 mmol/l
- +/- DPP-IVi oder GLP-1 Analoga
- Bolus insulin: nur falls nötig !

# Therapeutic scheme

1. Lifestyle
2. Metformin
3. Individualization :
  - A. Early case: DPP4i, GLP-1a (BMI>28) or SGLT2i
  - B. Established cardiovascular disease:
    - SGLT2i (heart failure)
    - GLP-1a (obese)
  - C. Uncontrolled diabetes or GFR < 30 : Basal insulin (& GLP-1a or DPP4i)
  - D. BMI>35: consider bariatric surgery