

La Cardiomiopatia Diabetica

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SID

Società Italiana
di Diabetologia



Conflitti di Interesse di Angelo Avogaro

Dichiaro che negli ultimi 5 anni ho ricevuto compensi per advisory board e relazioni dalle seguenti aziende:

AstraZeneca, Boehringer Ingelheim, Bayer, Eli Lilly, Mundipharma, Neopharmed, Amgen, Servier, Merck Sharp & Dohme, Novartis, Novo Nordisk, Sanofi, Takeda.

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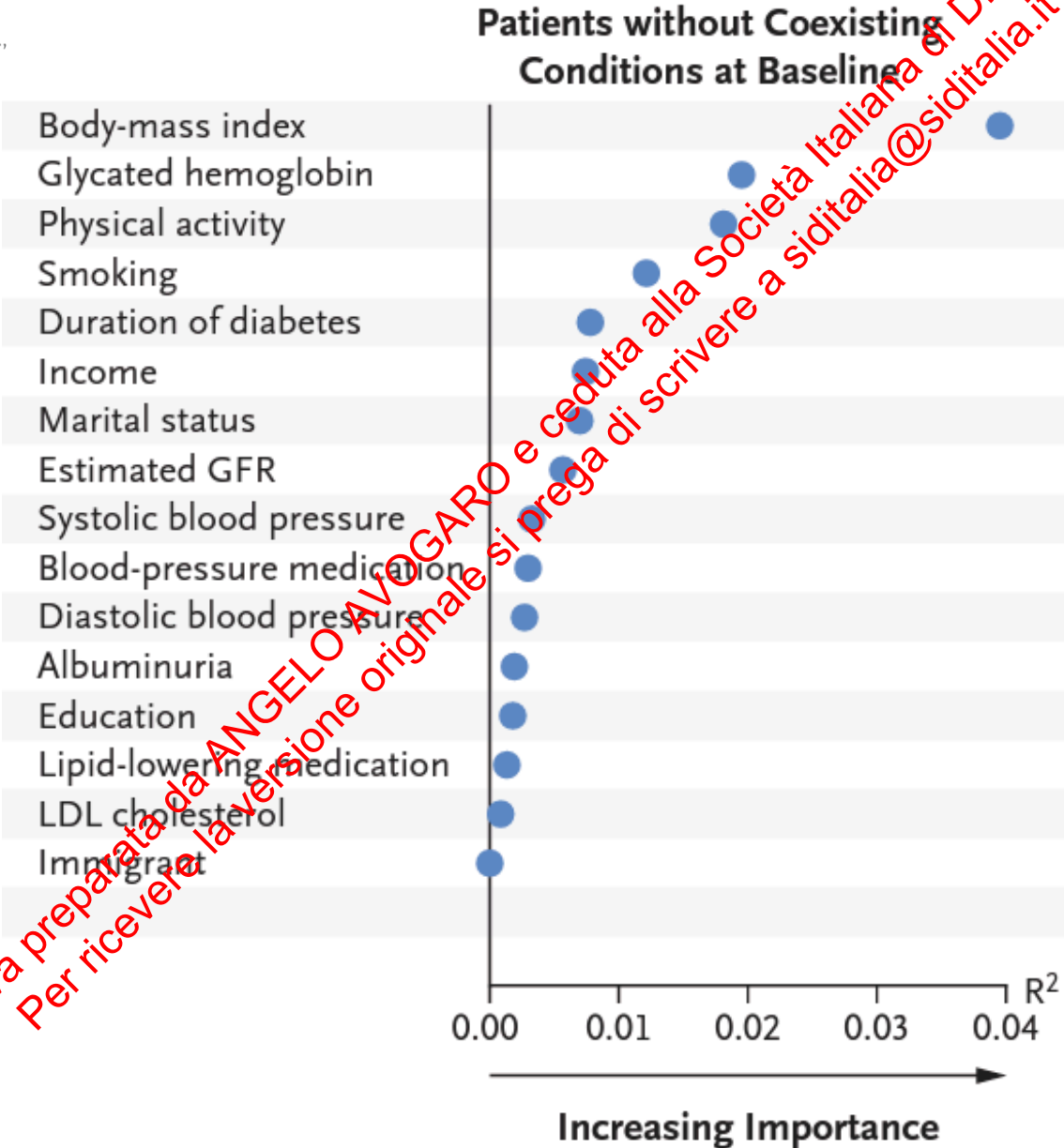
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1. La quantità di ATP prodotto e consumato in 1 giorno è pari a 15 volte il peso del cuore stesso
2. I mitocondri occupano quasi il 30% del volume cardiomiocitario
3. Il cuore pompa giornalmente 7000 litri di sangue
4. Il cuore rinnova completamente la sua componente proteica in 30 giorni

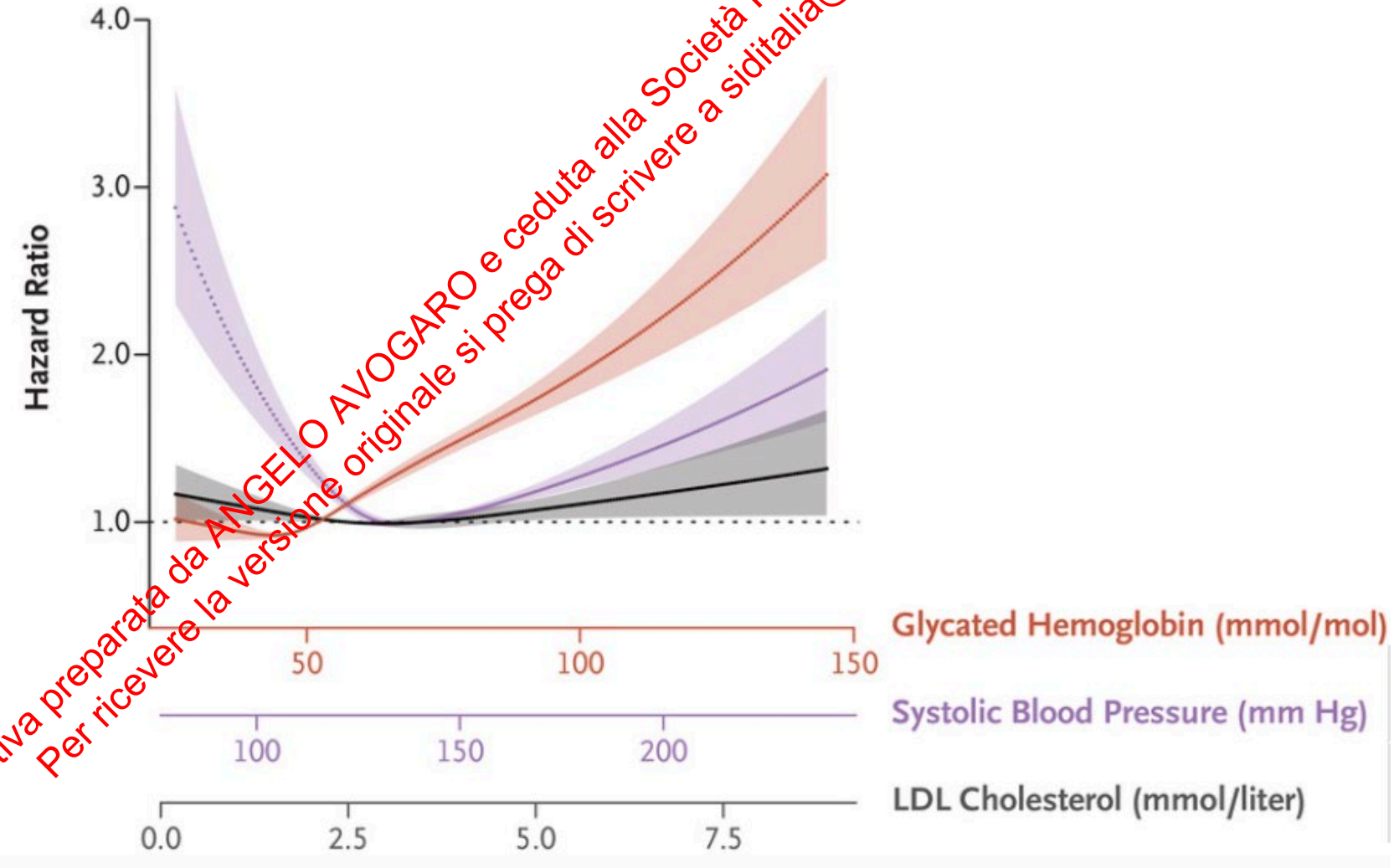
Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes

Aidin Rawshani, M.D., Araz Rawshani, M.D., Ph.D., Stefan Franzén, Ph.D.,
Naveed Sattar, M.D., Ph.D., Björn Eliasson, M.D., Ph.D., Ann-Marie Svensson, Ph.D.,
Björn Zethelius, M.D., Ph.D., Mervete Miftaraj, M.Sc.,
Darren K. McGuire, M.D., M.H.Sc., Annika Rosengren, M.D., Ph.D.,
and Soffia Gudbjörnsdottir, M.D., Ph.D.



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New Type of Cardiomyopathy Associated with Diabetic Glomerulosclerosis

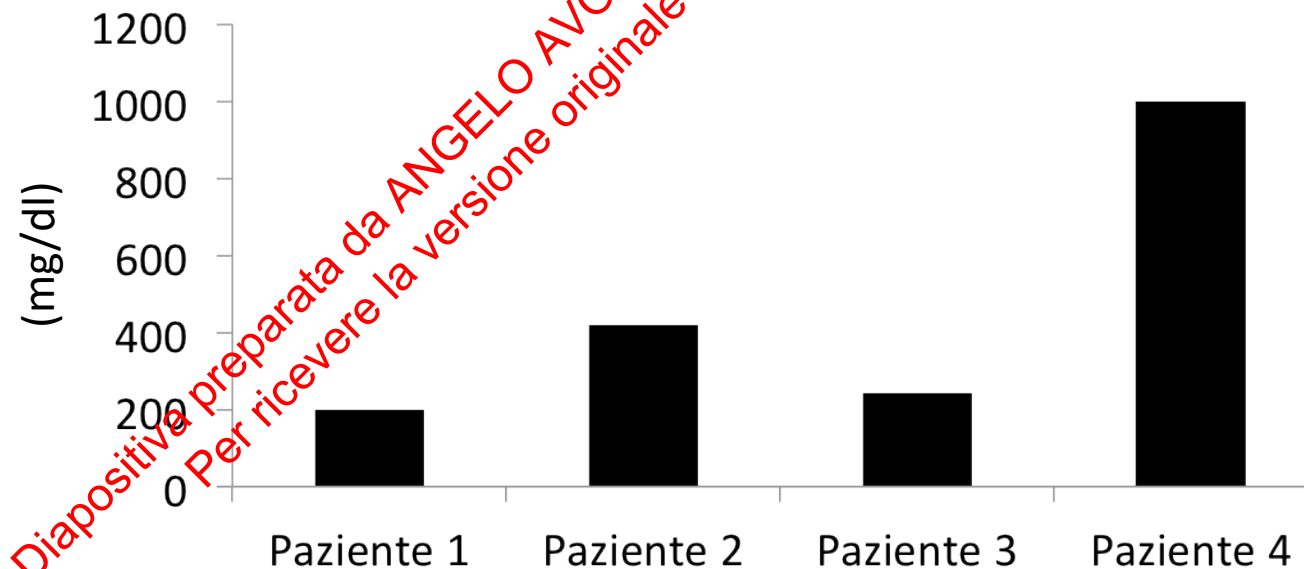
SHIRLEY RUBLER, MD, FACC
JOEL DLUGASH, MD
YUSUF ZIYA YUCEOGLU, MD, FACC
TARIK KUMRAL, MD
ARTHUR WHITLEY BRANWOOD, MD
ARTHUR GRISHMAN, MD, FACC

New York, New York

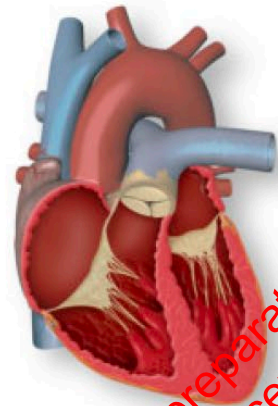
The postmortem findings and clinical records of 27 patients with proved diabetic glomerulosclerosis were examined and reviewed for evidence of primary myocardial disease. Twenty-three cases were excluded because of complicating conditions such as hypertension, significant obstruction of the major coronary arteries or valvular disease. Four patients demonstrated cardiomegaly and congestive heart failure of no known cause.

The autopsy findings consisted of left ventricular hypertrophy and,

Glicemia



- Mitochondrial dysfunction
- Insulin resistance
- Impaired insulin signaling
- Hyperglycemia
- ROS generation
- Inflammation
- Fibrosis
- Hypertrophy



HFrEF

Progression of diabetes

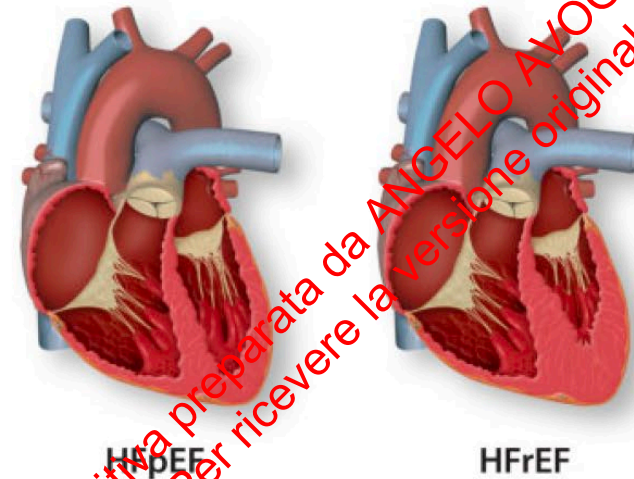
Early stage

Mid stage

Late stage

Final stage

- Mitochondrial dysfunction
- Insulin resistance
- Impaired insulin signaling
- Hyperglycemia
- ROS generation
- Inflammation
- Fibrosis
- Hypertrophy
- Dyslipidemia
- Perturbed Ca^{2+} handling
- Contractile protein dysfunction
- Autophagy
- Lipotoxicity
- Glucotoxicity
- Cell Death
- O-GlcNAcylation



Early stage

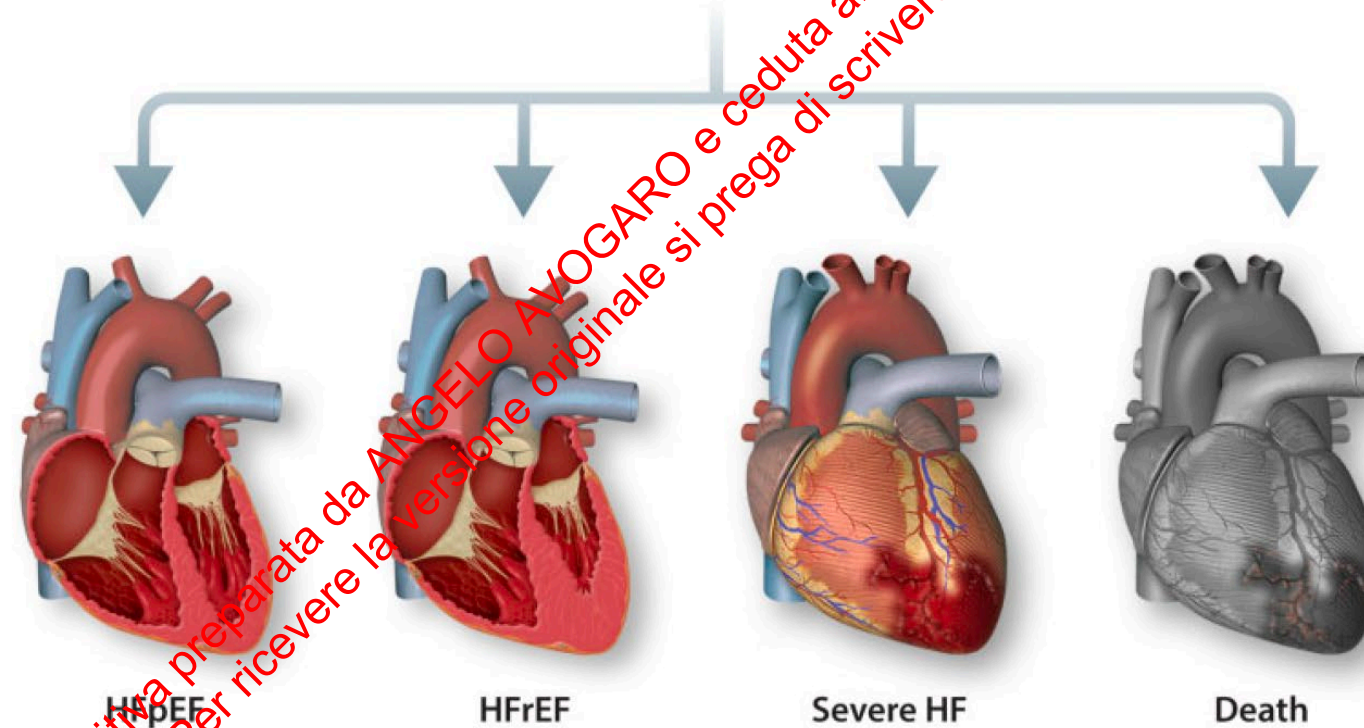
Mid stage

Late stage

Final stage

Progression of diabetes

- Mitochondrial dysfunction
- Insulin resistance
- Impaired insulin signaling
- Hyperglycemia
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- Inflammation
- Fibrosis
- Hypertrophy
- Dyslipidemia
- Perturbed Ca^{2+} handling
- Contractile protein dysfunction
- Autophagy
- Lipotoxicity
- Glucotoxicity
- Cell Death
- O-GlcNAcylation
- AGEs
- Neurohormonal mechanisms
- Ischemia
- Hypertension
- Renal failure
- Microangiopathy
- Coronary artery disease
- Macroangiopathy



Early stage

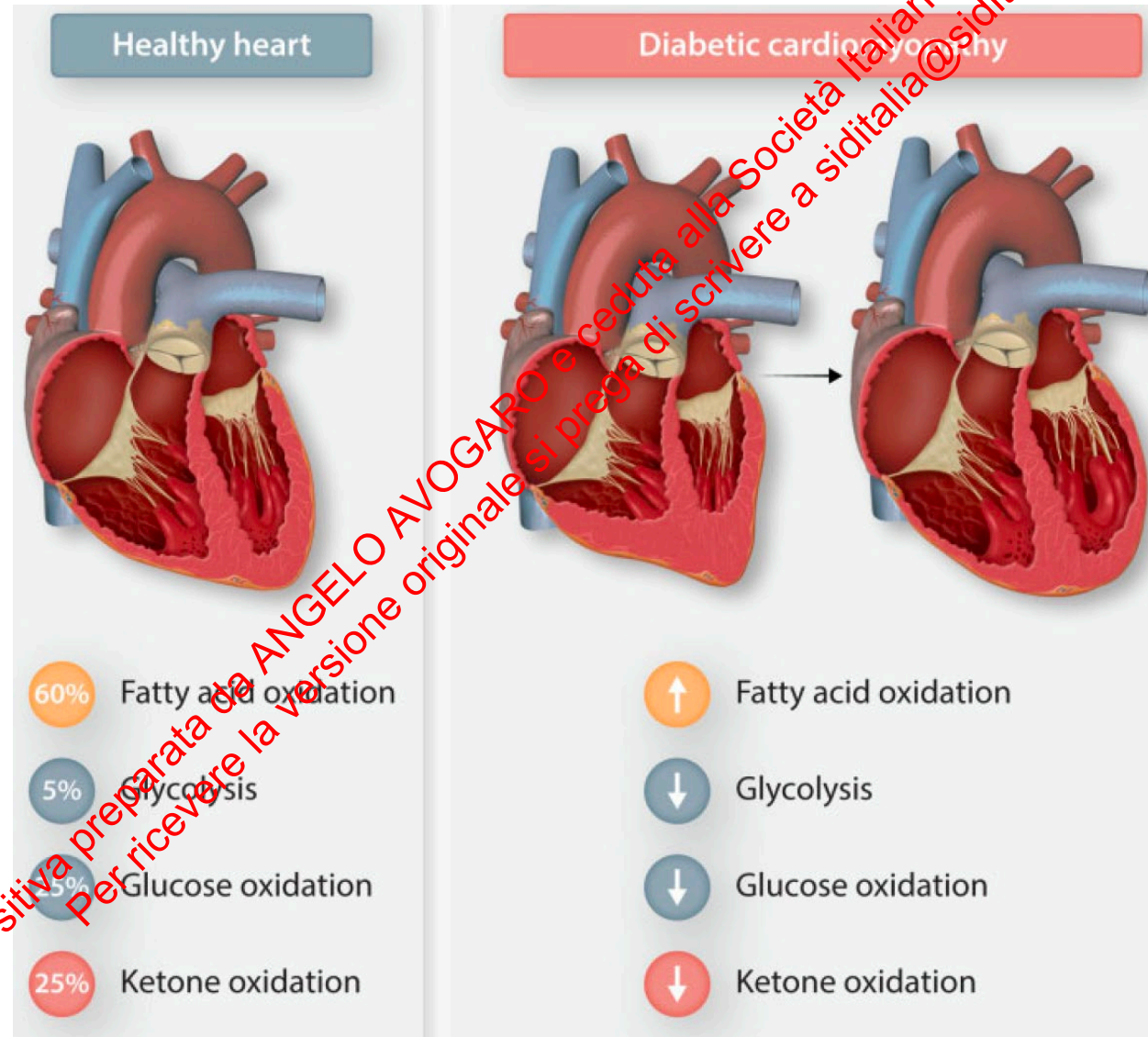
Mid stage

Late stage

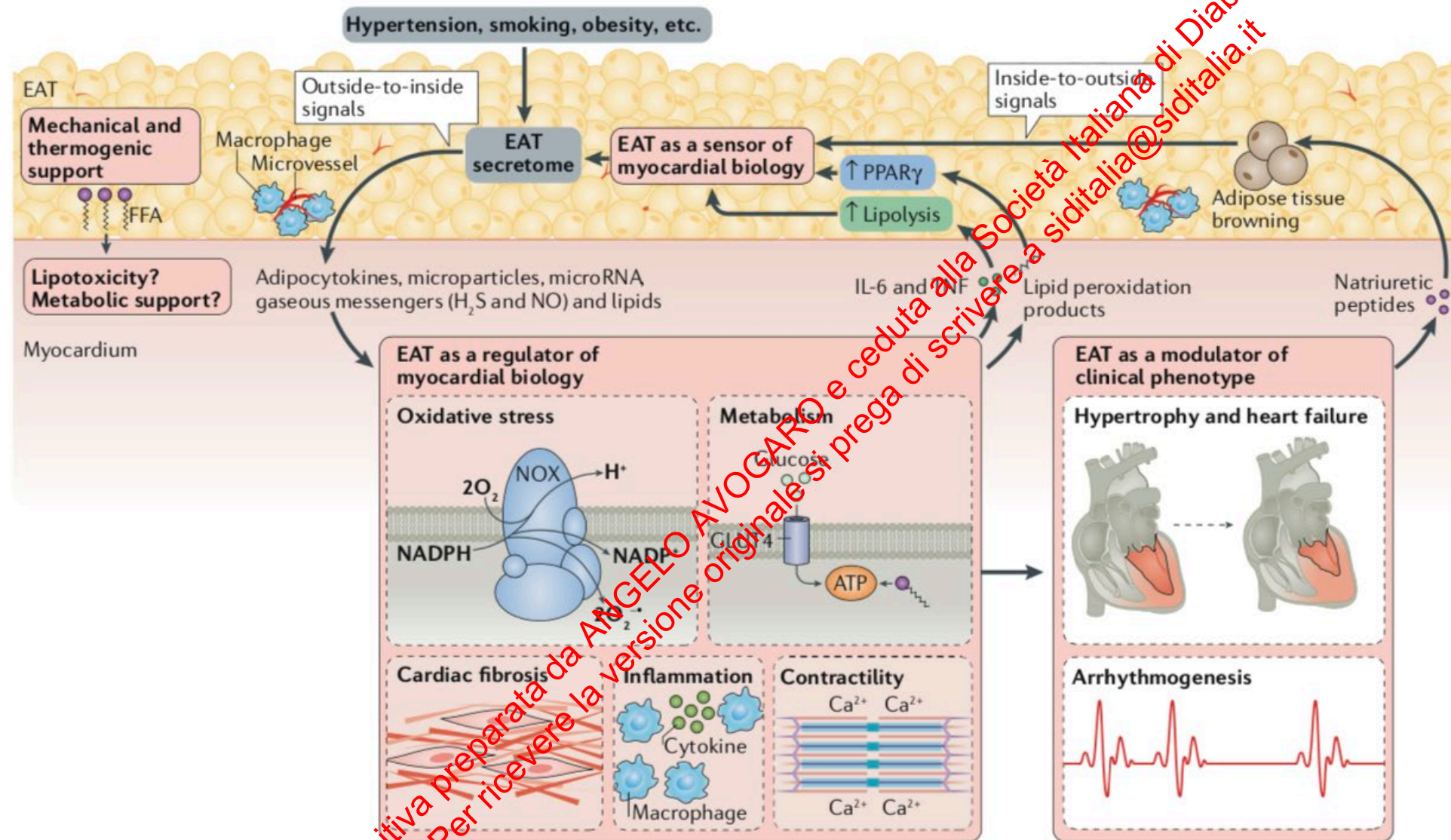
Final stage

Progression of diabetes

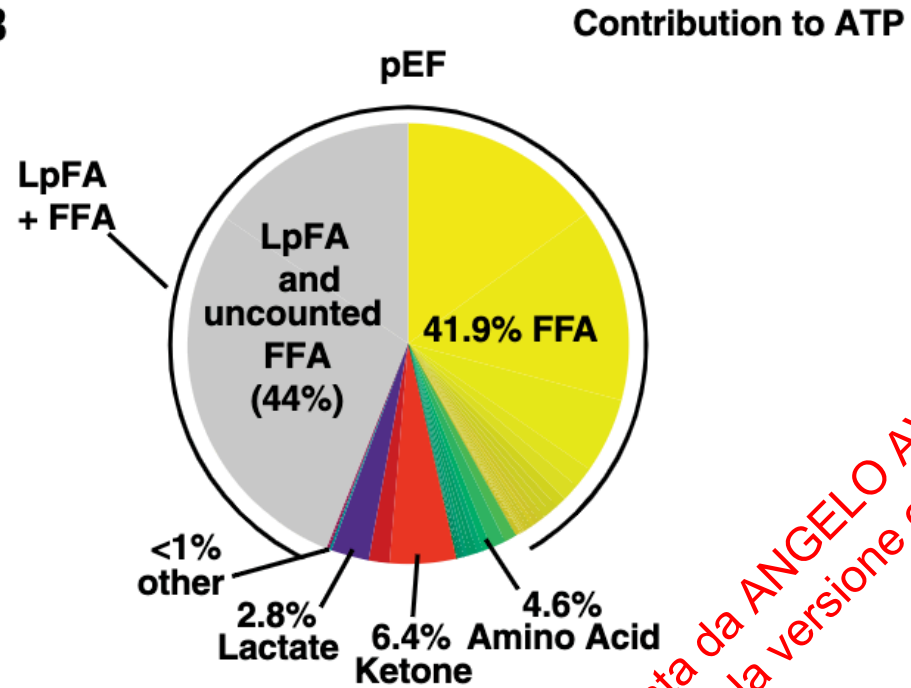
Energy metabolic changes in a healthy setting vs. diabetic cardiomyopathy.



Obesity is associated with fat «spillover»



B

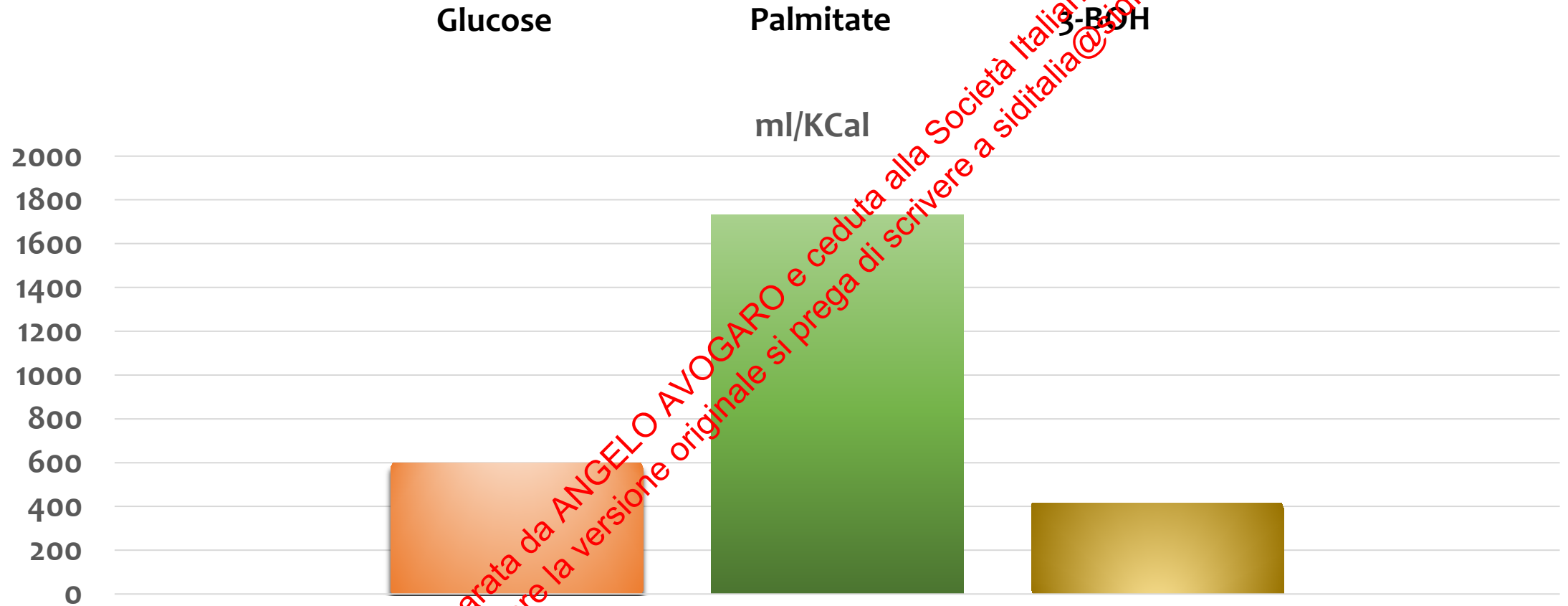


Substrate-specific contribution to cardiac ATP generation in patients with preserved ejection fraction (pEF) versus reduced ejection fraction (rEF)

Murashige et al. Science 2020

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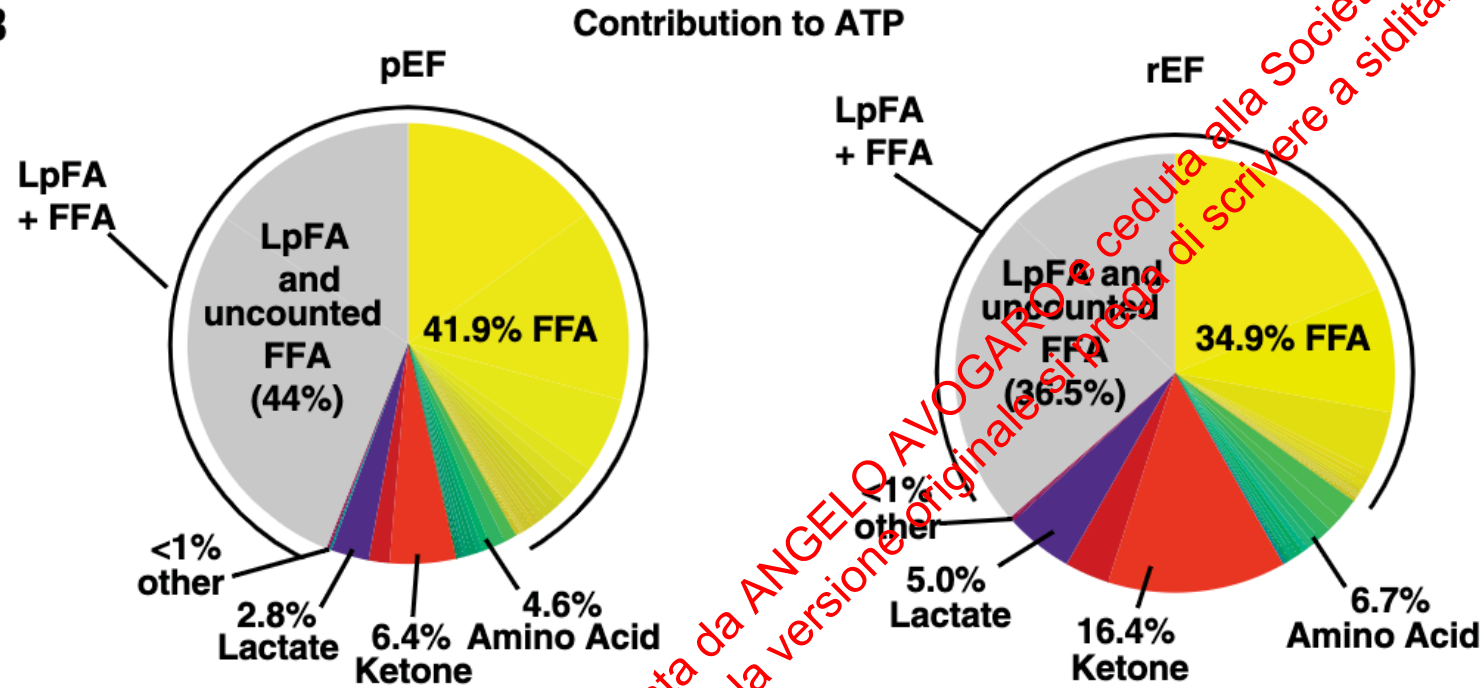
Heart Energetics



O₂ cost of calories for C₂

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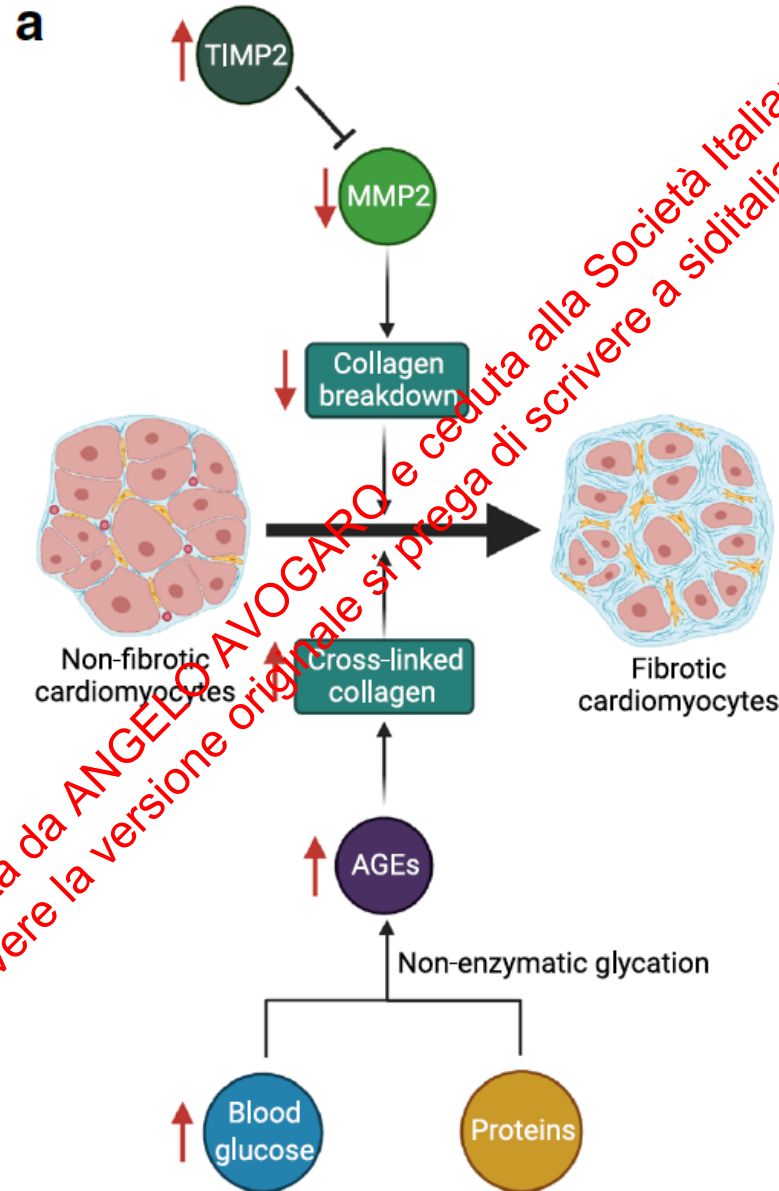
B



Substrate-specific contribution to cardiac ATP generation in patients with preserved ejection fraction (pEF) versus reduced ejection fraction (rEF)

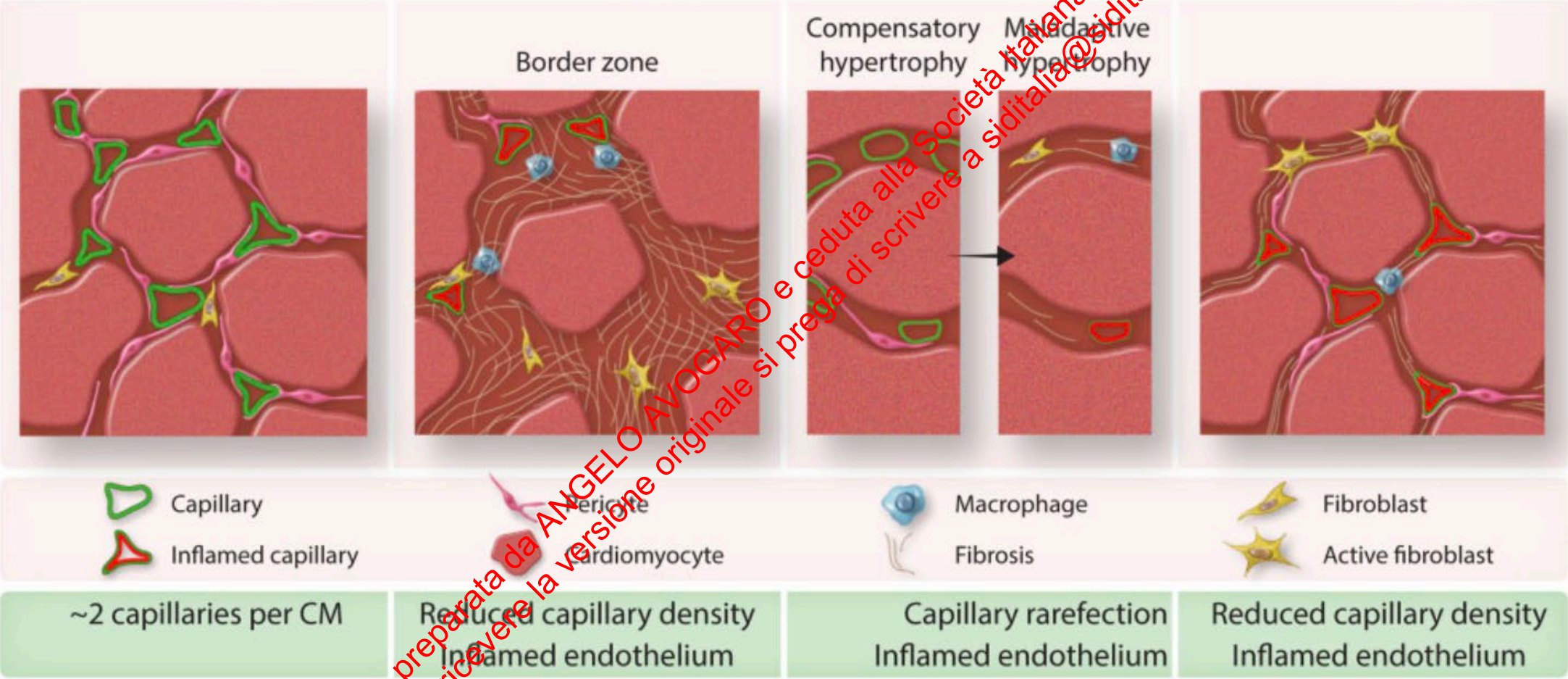
Murashige et al. Science 2020

Nella Cardiomiopatia diabetica esiste uno stato profibrotico

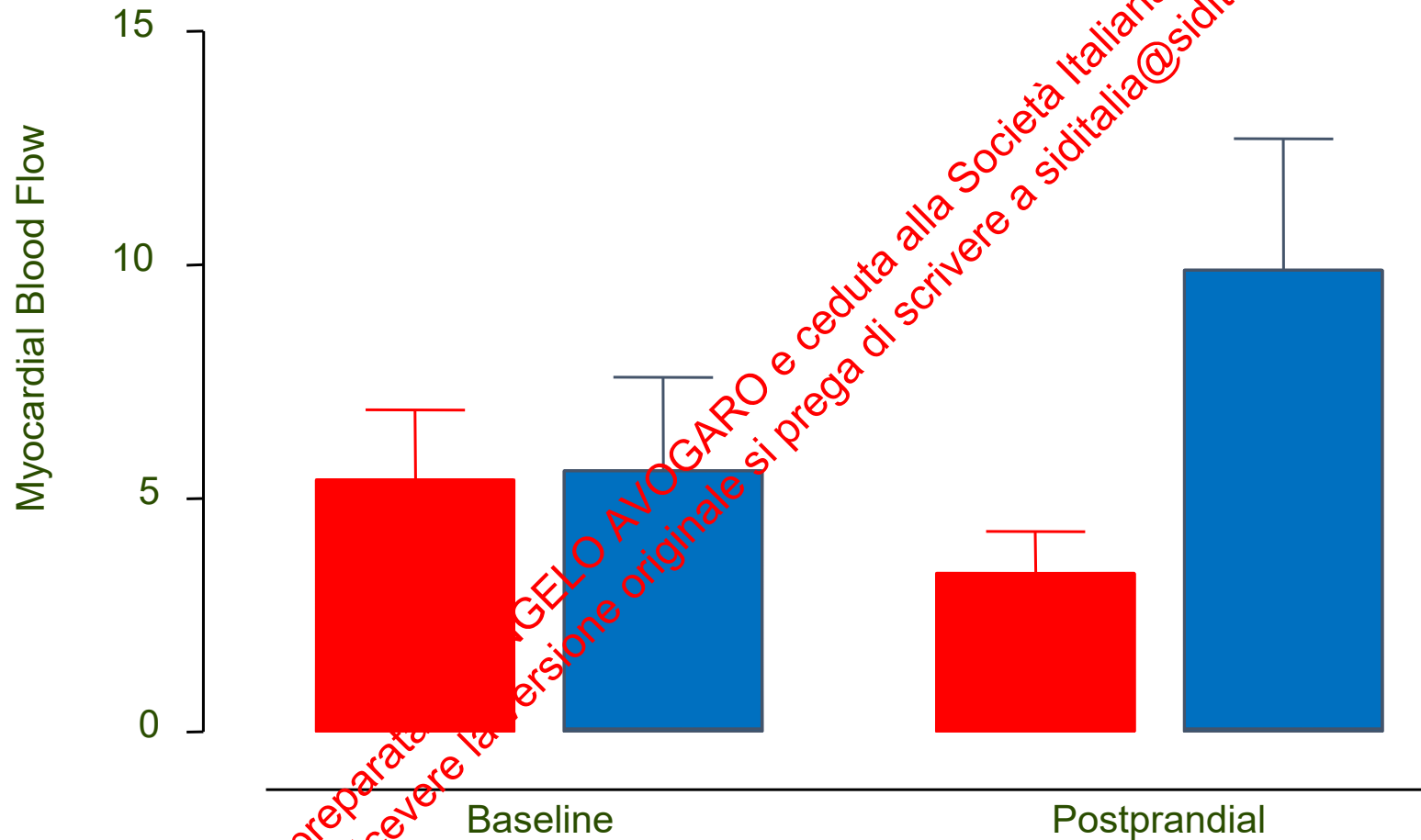


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Compared characteristics of the microvasculature in different pathological diseases



Patients with type 2 diabetes without ATS show compromised meal-related increase in myocardial blood-flow



Scognamiglio et al. Circulation, 2005

Microvascular
ischaemia

LVH

MI

No MI

"Transition to failure"

MI

No MI

Microvascular
ischaemia

cLVH

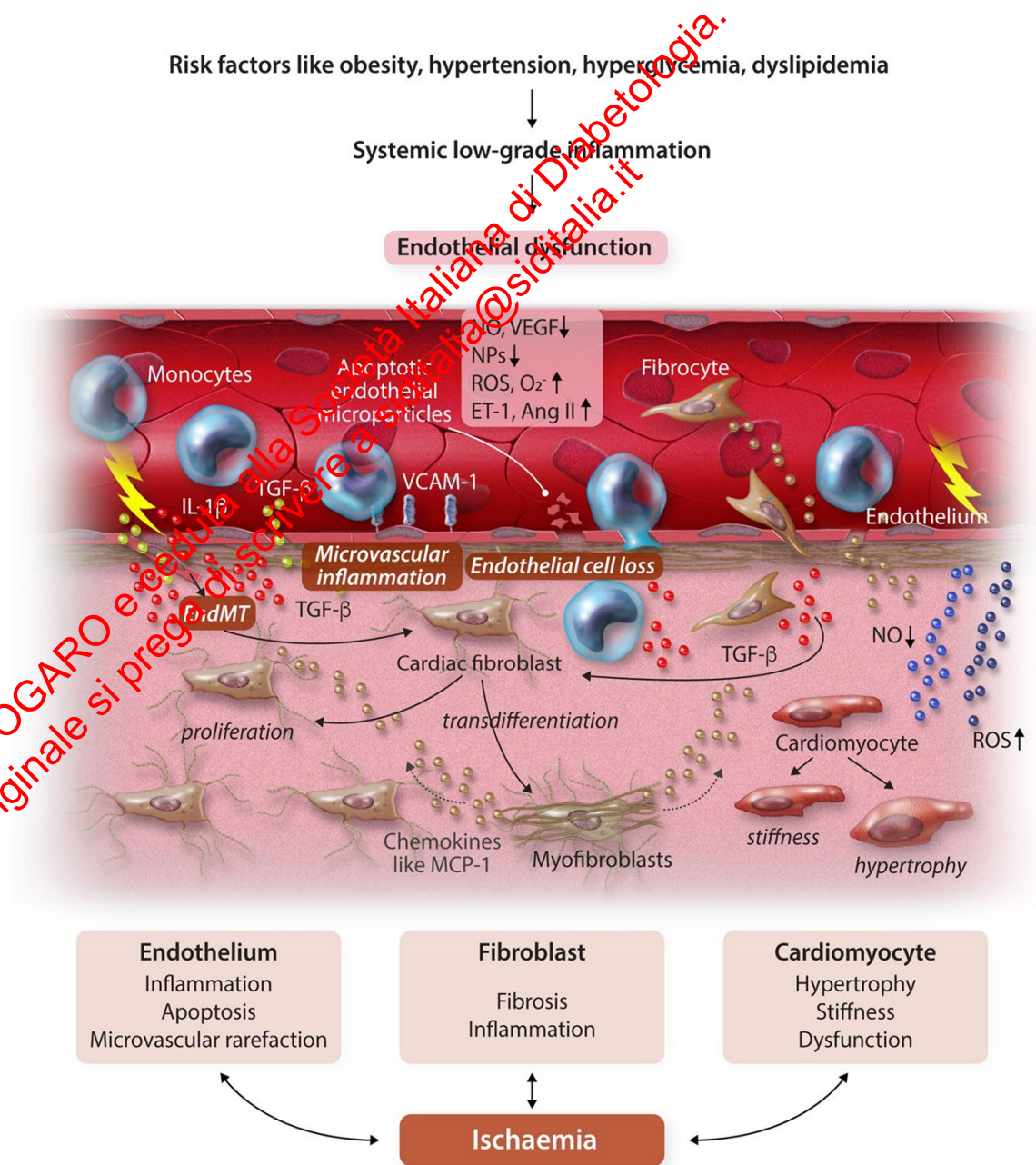
Low EF

Symptomatic heart
failure with **normal** EF

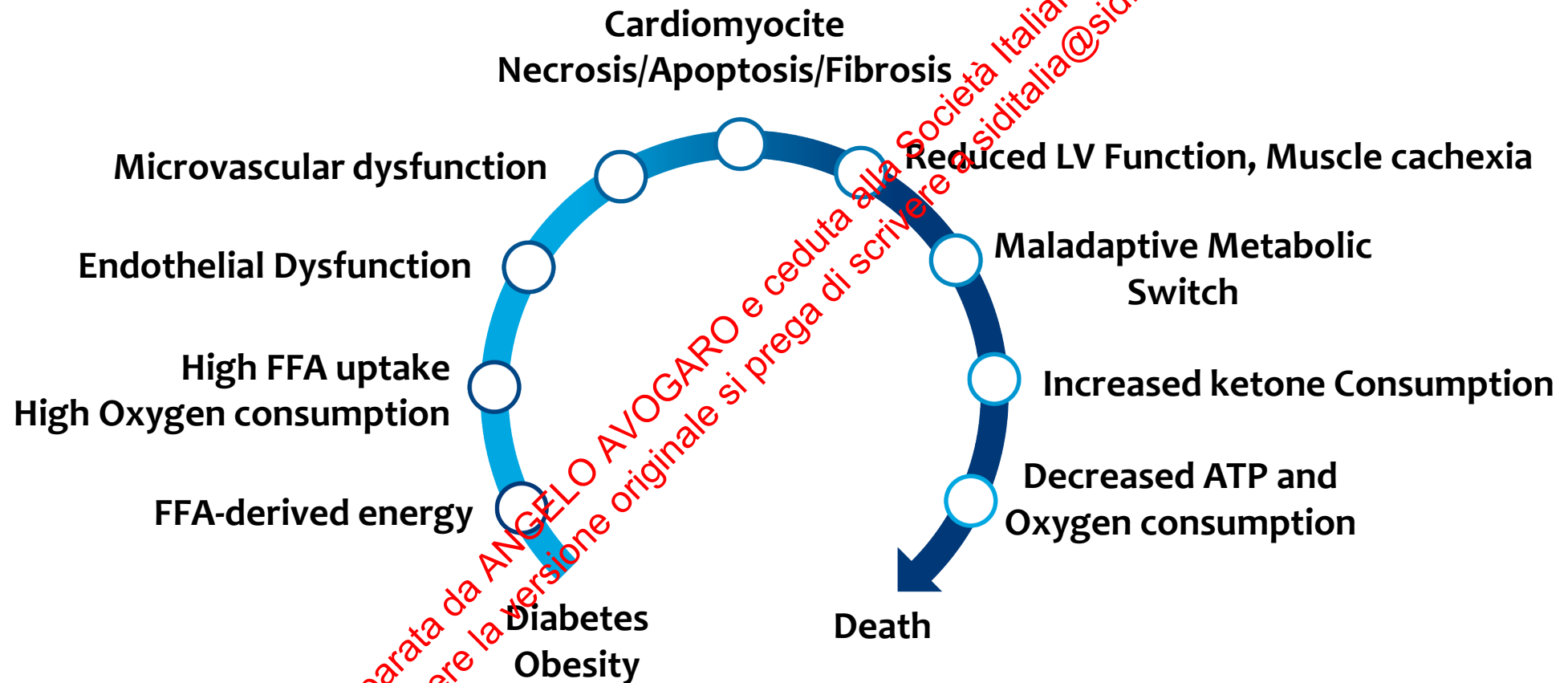
Symptomatic heart
failure with **low** EF

Contribution of
myocardial
ischaemia in the
progression from
LVH to heart
failure.

Endothelial dysfunction
provokes cardiomyocyte
stiffness/hypertrophy



HEART FAILURE: The functional metabolic continuum



Nello scompenso cardiaco gli acidi grassi liberi si associano a un ridotto consumo di ossigeno?

Si

No

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La cardiomiopatia diabetica è un marcatore di mediocre compenso glicemico?

Si

No

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