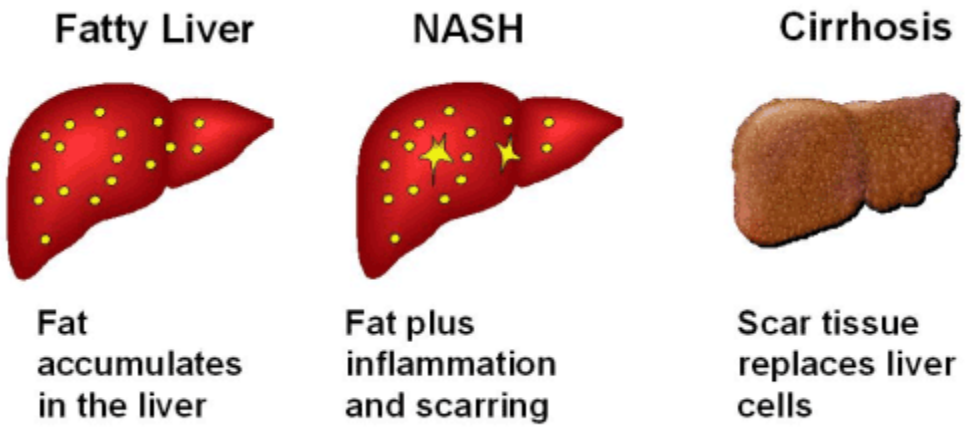
# LA STEATOEPATITE NON ALCOLICA

**Gianluigi Vendemiale**

UNIVERSITÀ DEGLI STUDI DI FOGGIA

# DEFINIZIONE

**Vasto spettro di lesioni istologiche nel fegato di soggetti che non assumono alcol**



## NAFLD

Presenza di infiltrazione grassa nel fegato (> 5-10% di steatosi macrovescicolare in campioni bioptici)

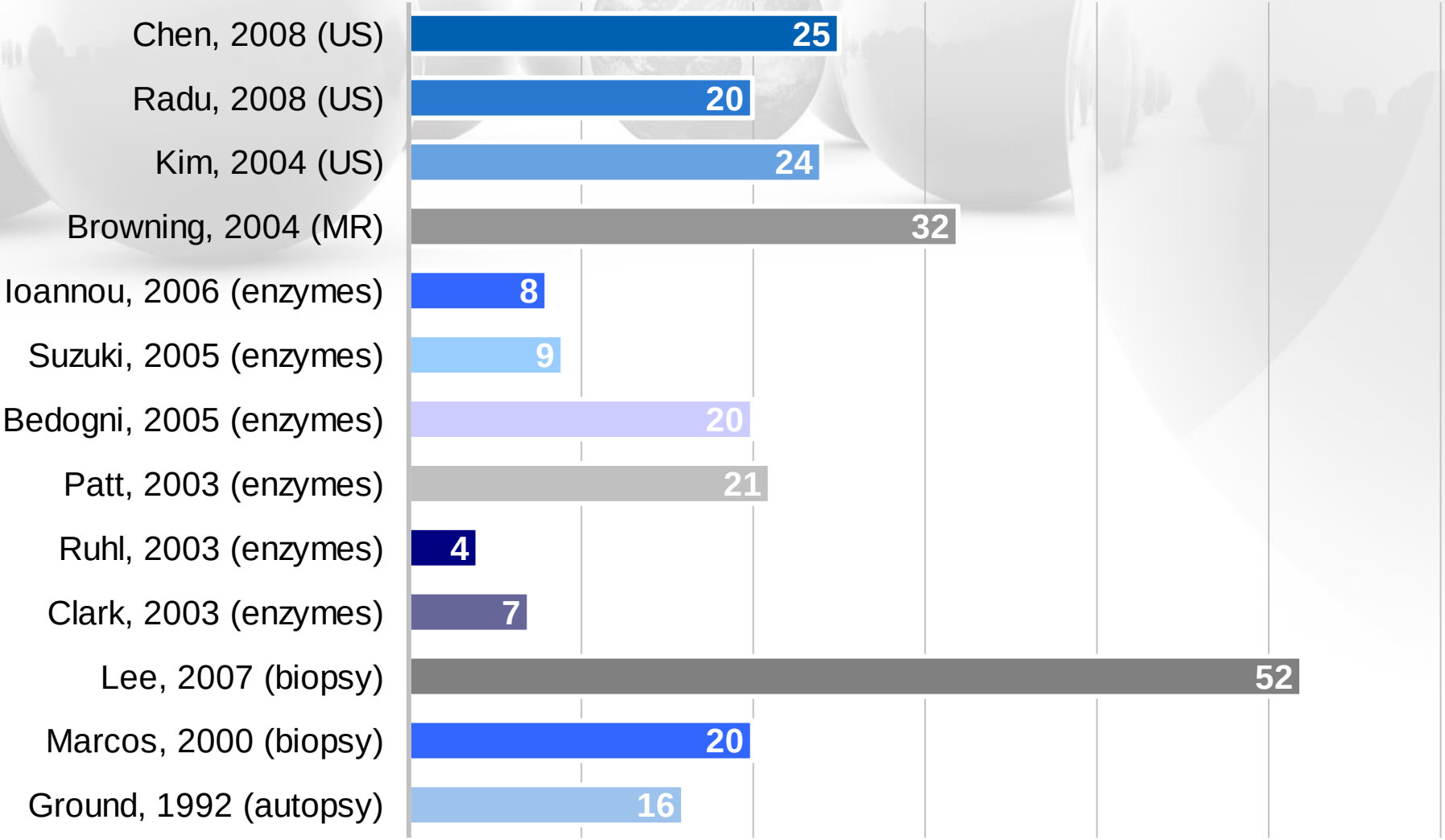
| | |
|---|---|
| **Steatosi semplice** | NAFLD senza infiammazione né fibrosi |
| **NASH** | NAFLD con infiammazione, epatociti balloniformi, +/- fibrosi, ad inizio solitamente attorno alla vena centrolobulare, che può progredire in cirrosi |

| | |
|---|---|
| **NAFLD/NASH primaria** | Associata ad obesità centrale e/o DM2 ma senza un'etiologia specifica |
| **NAFLD/NASH secondaria** | Associata a cause specifiche come ad esempio farmaci (assenza di IR) |

| | |
|---|---|
| **NAFLD/NASH presunta** | Aumento delle aminotransferasi sieriche, sierologia virale negativa, anomalie US suggestive di steatosi epatica |

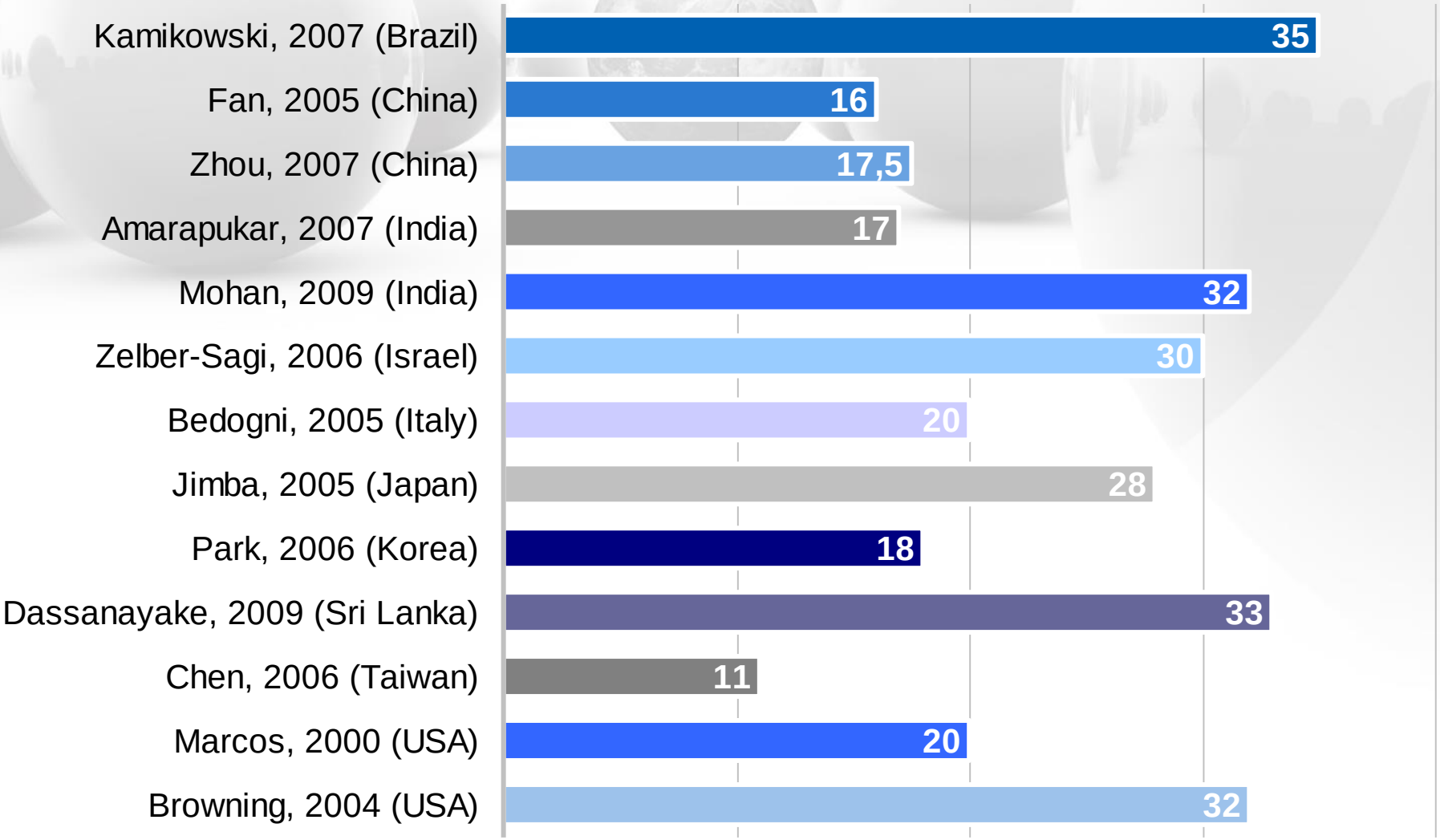
# EPIDEMIOLOGIA

Prevalenza della NAFLD nella popolazione generale (%)



# EPIDEMIOLOGIA

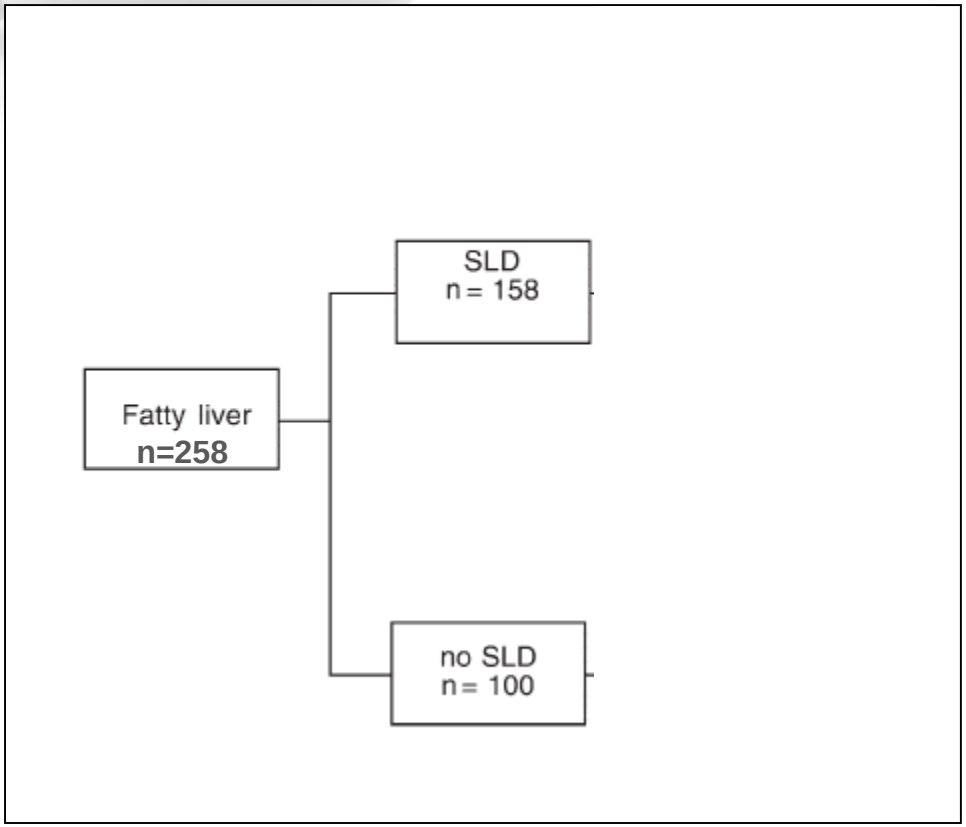
Prevalenza della NAFLD nella popolazione generale (%)



# Prevalence of and Risk Factors for Nonalcoholic Fatty Liver Disease: The Dionysos Nutrition and Liver Study

Giorgio Bedogni,[1,2] Lucia Miglioli,[2] Flora Masutti,[2] Claudio Tiribelli,[1,2] Giulio Marchesini,[3] and Stefano Bellentani[1,2,4]

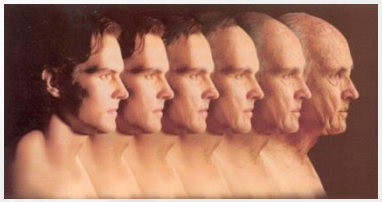
HEPATOLOGY, Vol. 42, No. 1, 2005

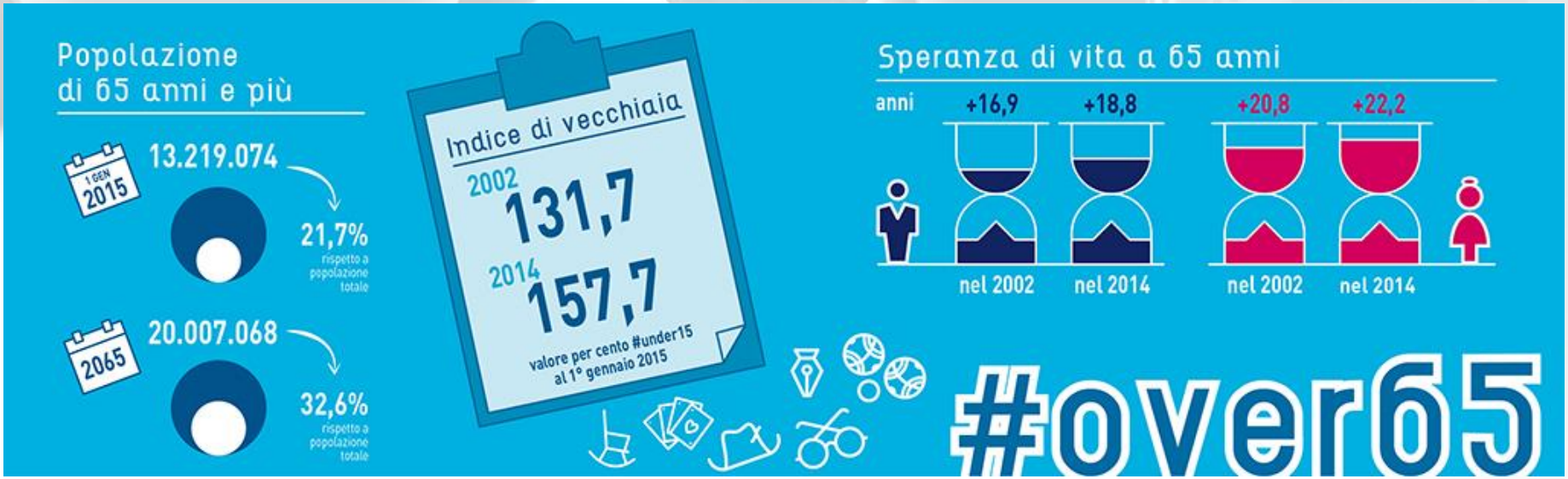


# Gruppi ad alto rischio

## ANZIANI

46%



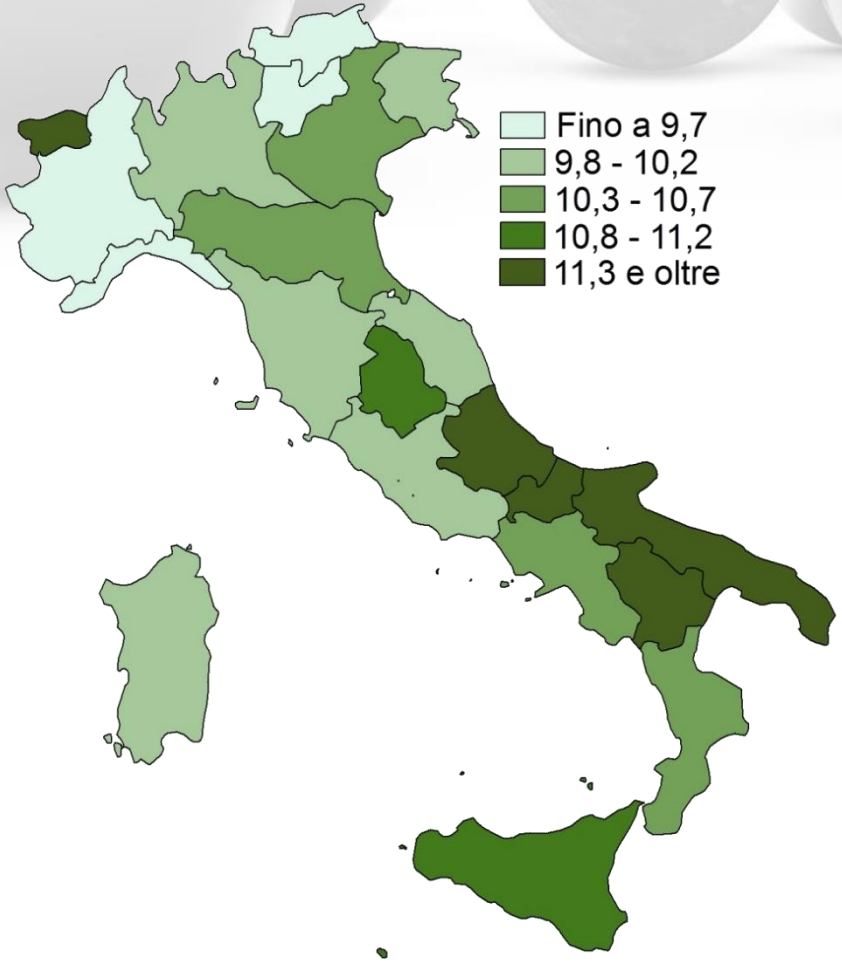


**Dati ISTAT 2015**

# Gruppi ad alto rischio

## OBESI

85%



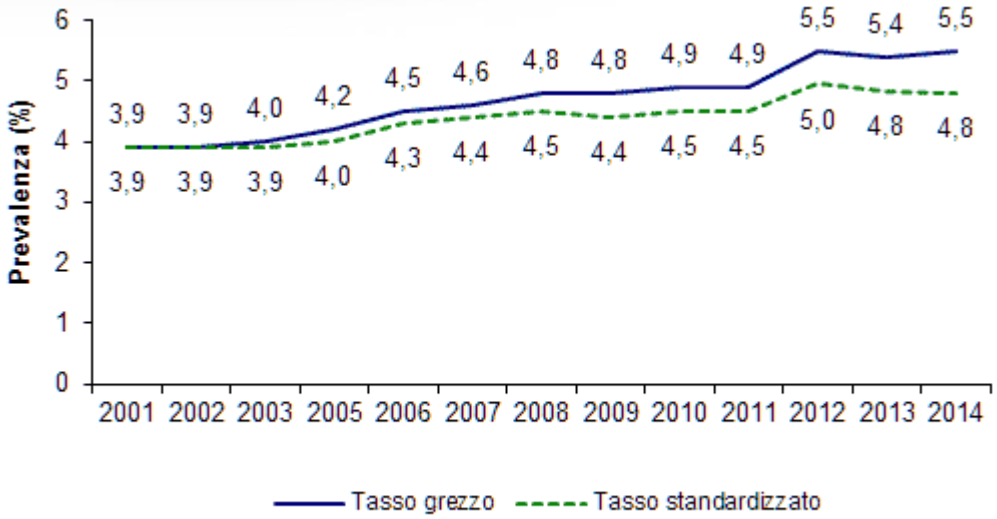

**Dati ISTAT 2013**

**Italia = 10.3%**

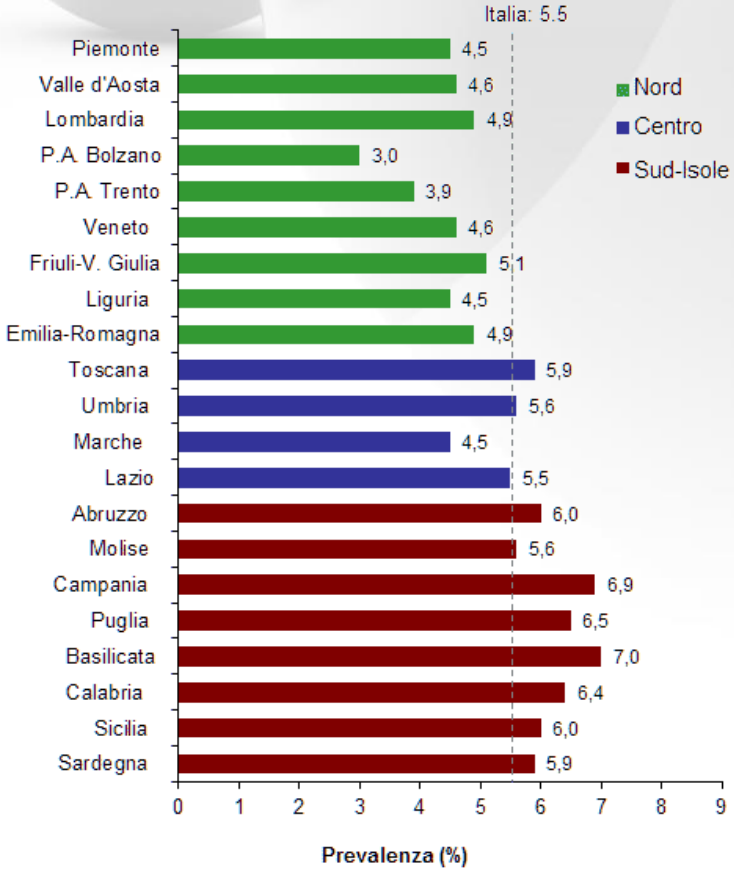
# Gruppi ad alto rischio

## DIABETICI

**75%**




Fonte ISTAT 2014, elaborazione ISS




Fonte ISTAT 2014, elaborazione ISS

# Gruppi ad alto rischio

## SINDROME METABOLICA

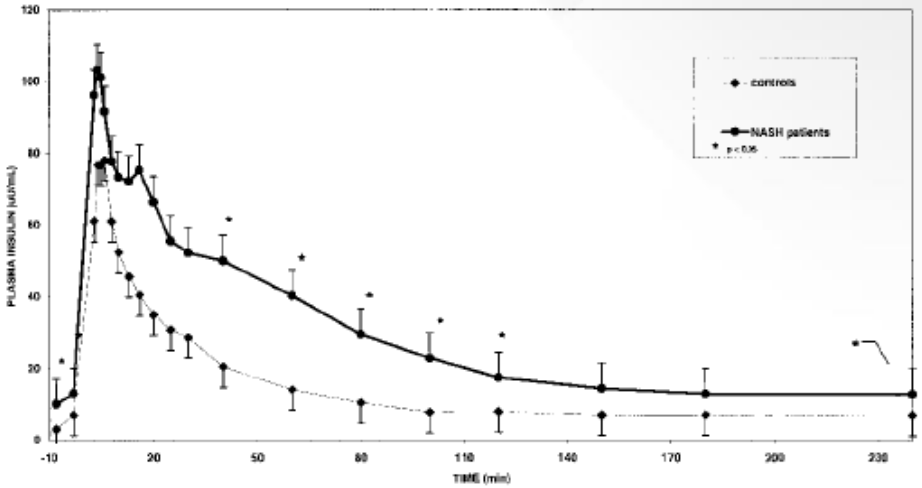
| Caratteristiche | OMS | NCEP ATP III |
|---|---|---|
| VALORI PRESSORI | Terapia antipertensiva e/o PA ≥ 140/90 mmHg | Terapia antipertensiva e/o PA ≥ 130/85 mmHg |
| DISLIPIDEMIA | Trigliceridi > 1,7 mmol/L (150 mg/dl) e/o HDL < 0,9 mmol/L (35 mg/dl) negli uomini e < 1,0mmol/L (< 40 mg/dl) nelle donne | Trigliceridi > 150 mg/dL, colesterolo HDL < 40 mg/dL negli uomini e < 50 mg/dl nelle donne |
| OBESITÀ | BMI > 30 e/o rapporto vita/fianchi > 0,90 negli uomini, > 0,85 nelle donne | Circonferenza alla vita > 102 cm negli uomini e > 88 cm nelle donne |
| GLICEMIA | Diabete mellito di tipo 2 o IGT* | Glicemia a digiuno ≥ 110 mg/dL |
| ALTRO | Microalbuminuria = secrezione urinaria di albumina (diuresi notturna) >20 mcg/min (30mg/g Cr) | |
| PER LA DIAGNOSI | Diabete mellito di tipo 2 o IGT ed 1 altro criterio. Se non è presente la ridotta tolleranza di glucosio devono essere presenti almeno 3 criteri | 3 criteri |

* Ridotta tolleranza al glucosio

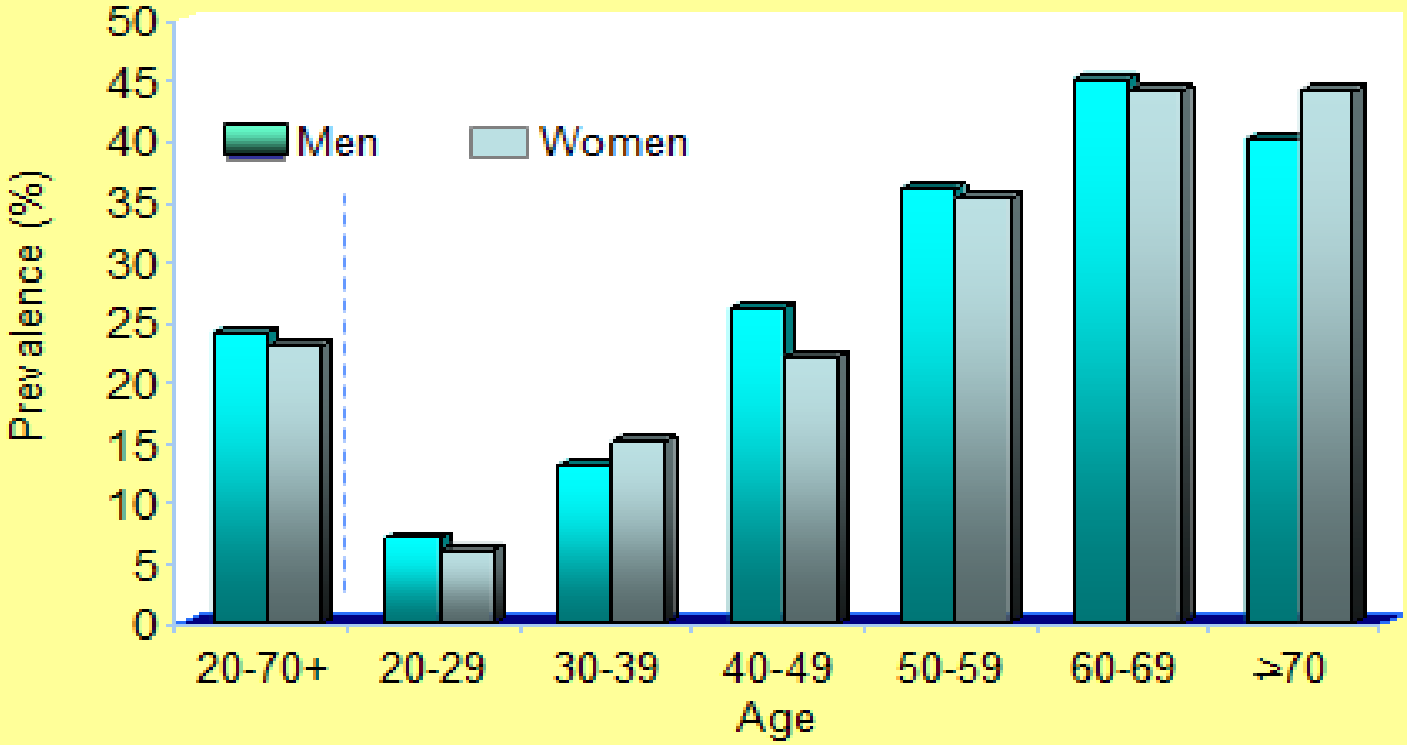
**Nonalcoholic Steatohepatitis, Insulin Resistance, and Metabolic Syndrome: Further Evidence for an Etiologic Association**

Gianfranco Pagano,[1] Giovanni Pacini,[2] Giovanni Musso,[1] Roberto Gambino,[1] Fabio Mecca,[1] Nadia Depetris,[1] Maurizio Cassader,[1] Ezio David,[3] Paolo Cavallo-Perin,[1] and Mario Rizzetto[4]

HEPATOLOGY 2002;35:367-372.

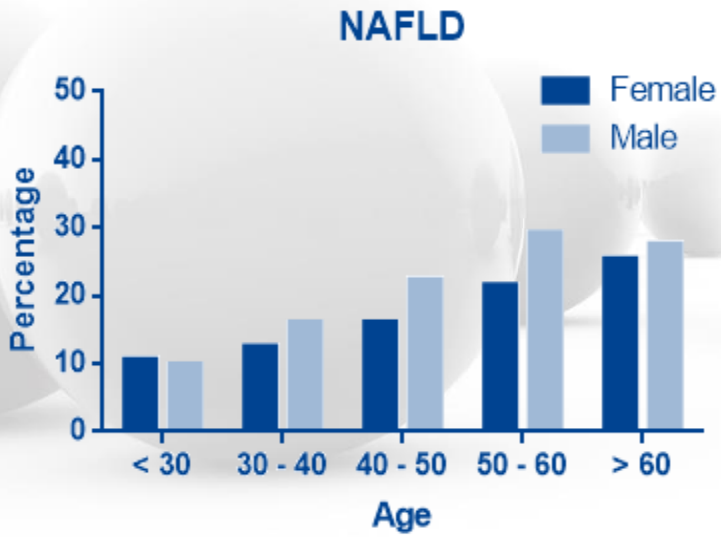


# Increasing Prevalence of NCEP Metabolic Syndrome with Age (NHANES III)

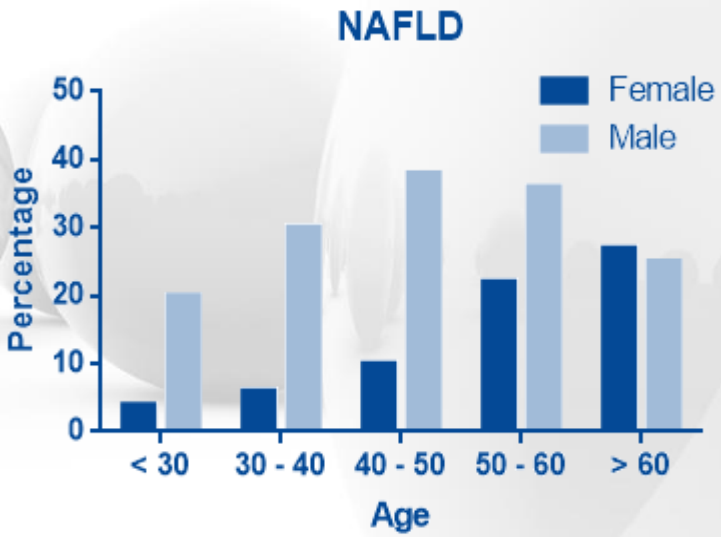


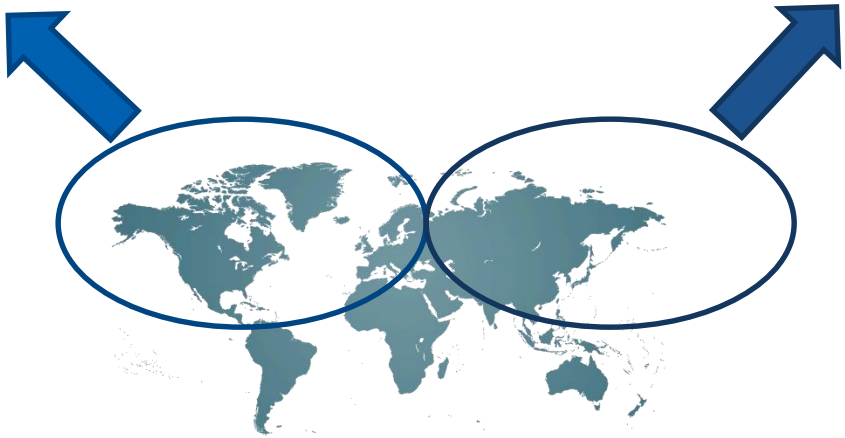

Ford E et al. *JAMA*. 2002;287:356-359.

Age-specific prevalence of NAFLD in 12454 participants.




Age-specific prevalence of fatty liver disease in 7371 participants.



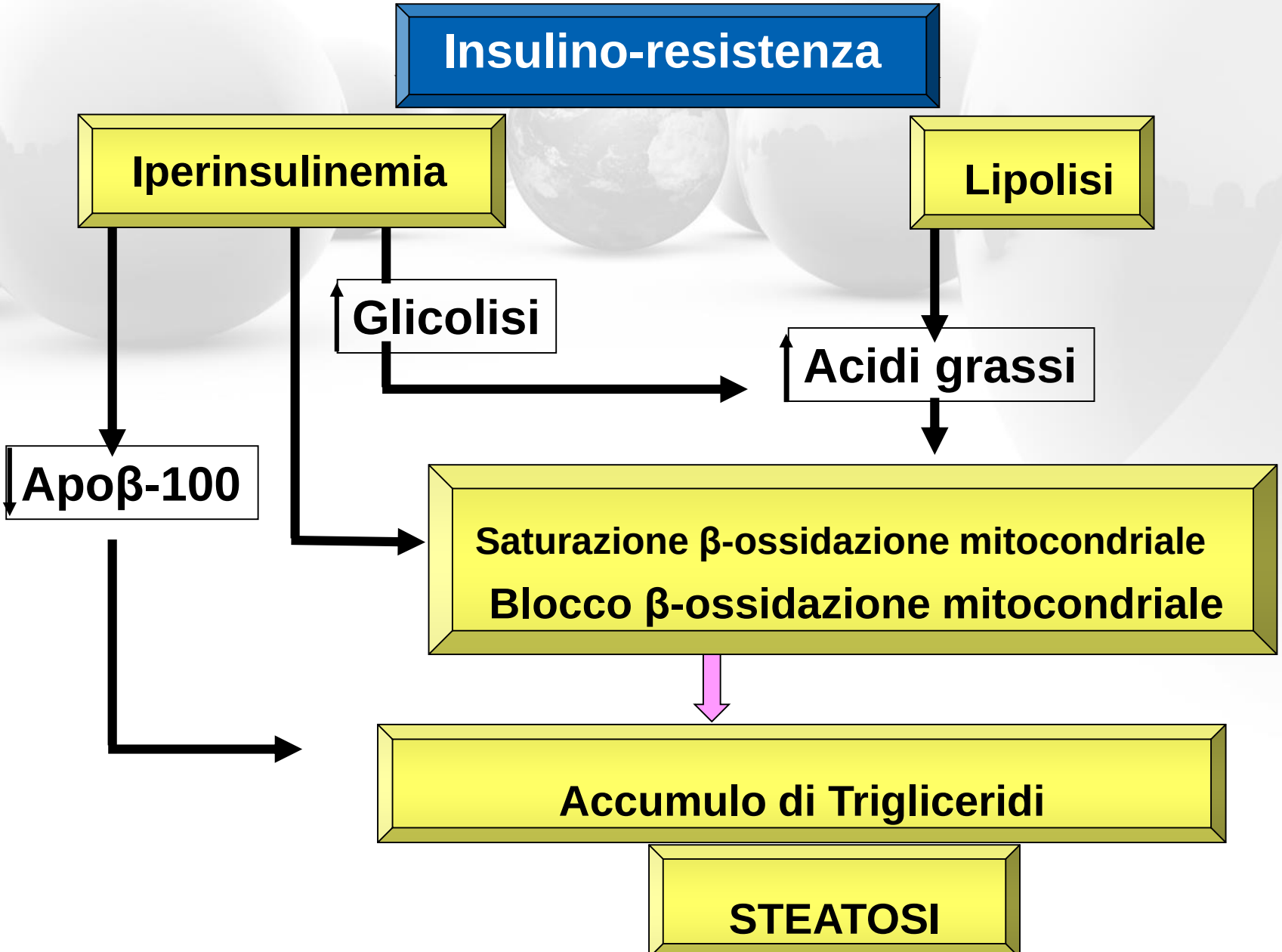
**Western Countries**

**Eastern Countries**

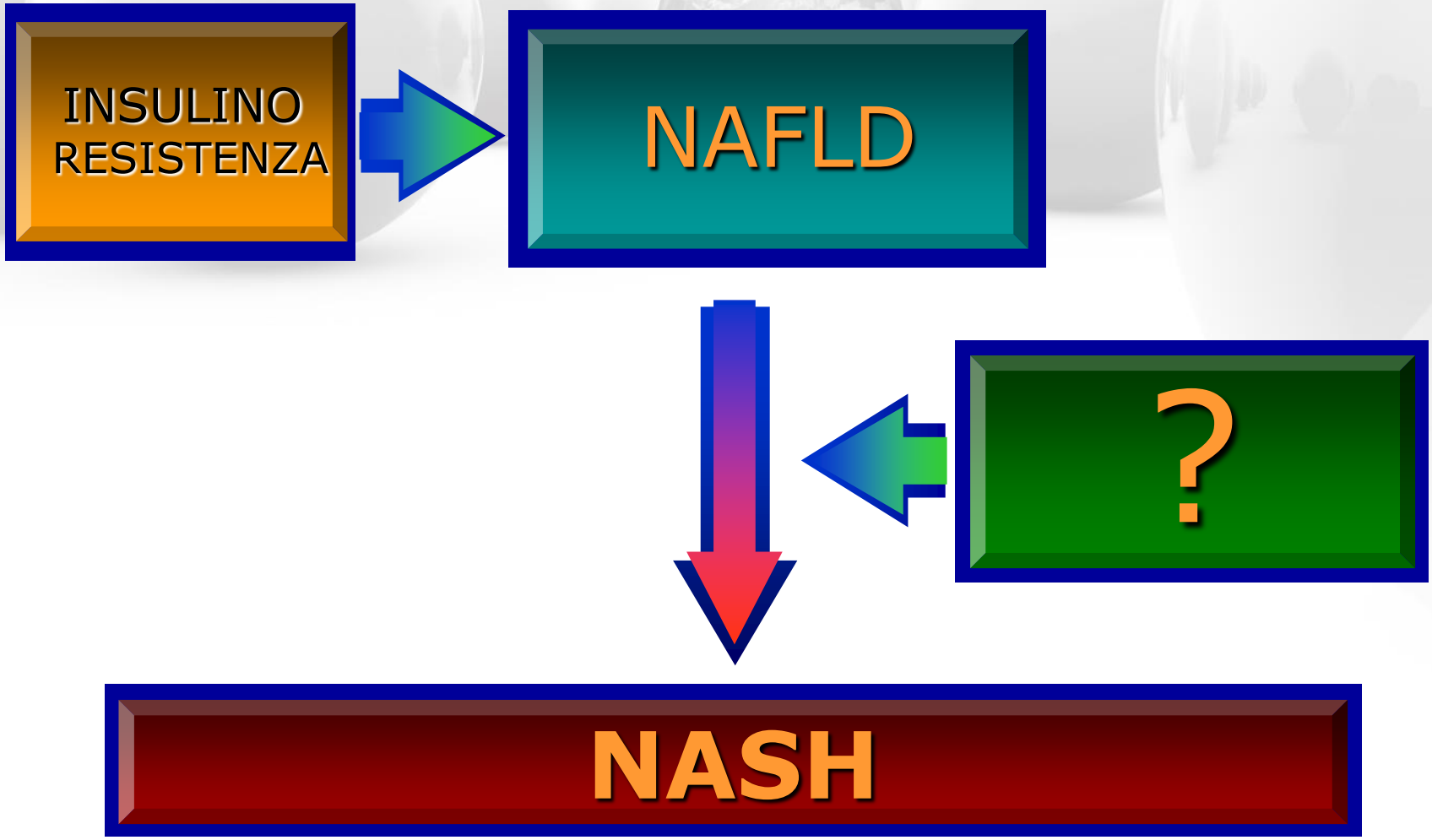
*Lazo M et al., Am J Epidemiol 2012*

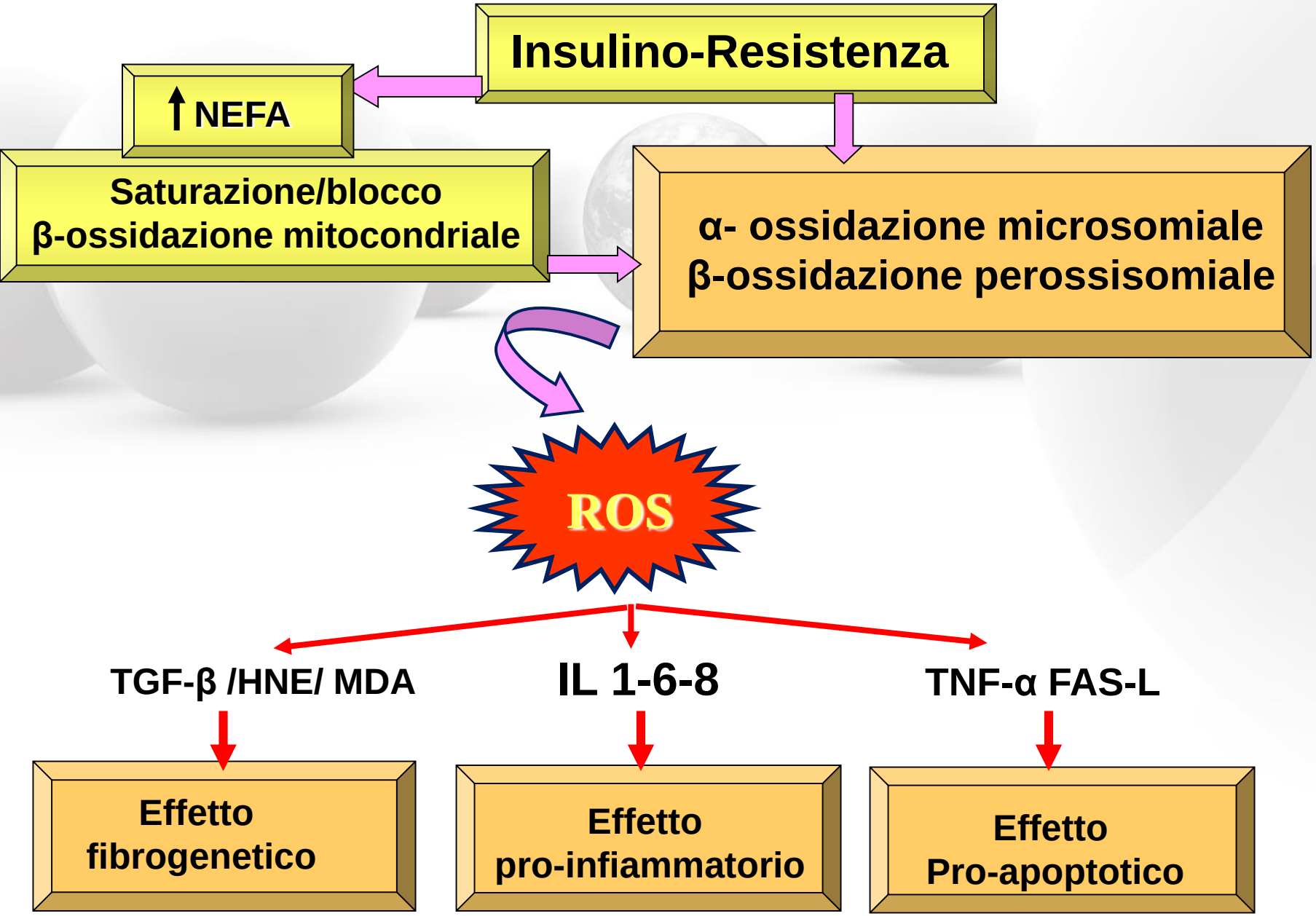
*Wang Z et al., Exp Gerontol 2013*

# PATOGENESI DELLA STEATOSI SEMPLICE

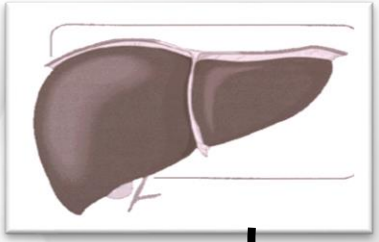


# PATOGENESI



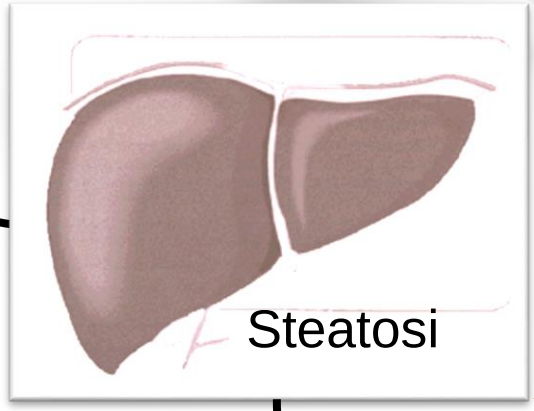

Insulino-Resistenza
↑ NEFA
Saturazione/blocco
β-ossidazione mitocondriale
α- ossidazione microsomiale
β-ossidazione perossisomiale
ROS
TGF-β /HNE/ MDA
IL 1-6-8
TNF-α FAS-L
Effetto
fibrogenetico
Effetto
pro-infiammatorio
Effetto
Pro-apoptotico

# THE TWO-HITS THEORY



First hit

Obesità
Diabete
Dislipidemia
Insulino-resistenza



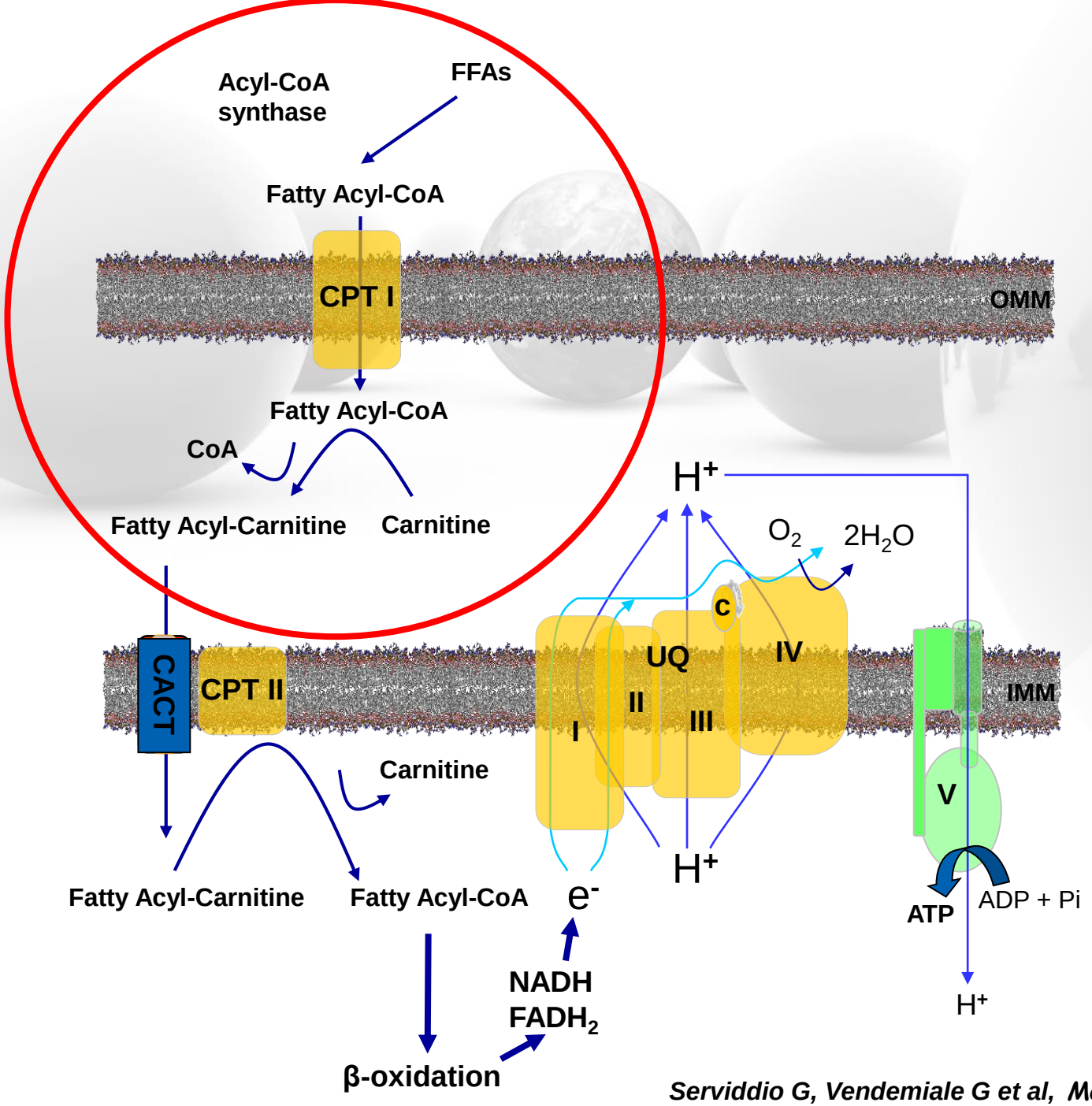

Second hit

Stress Ossidativo
Perossidazione lipidica
Induzione Citochine
Endotossinemia

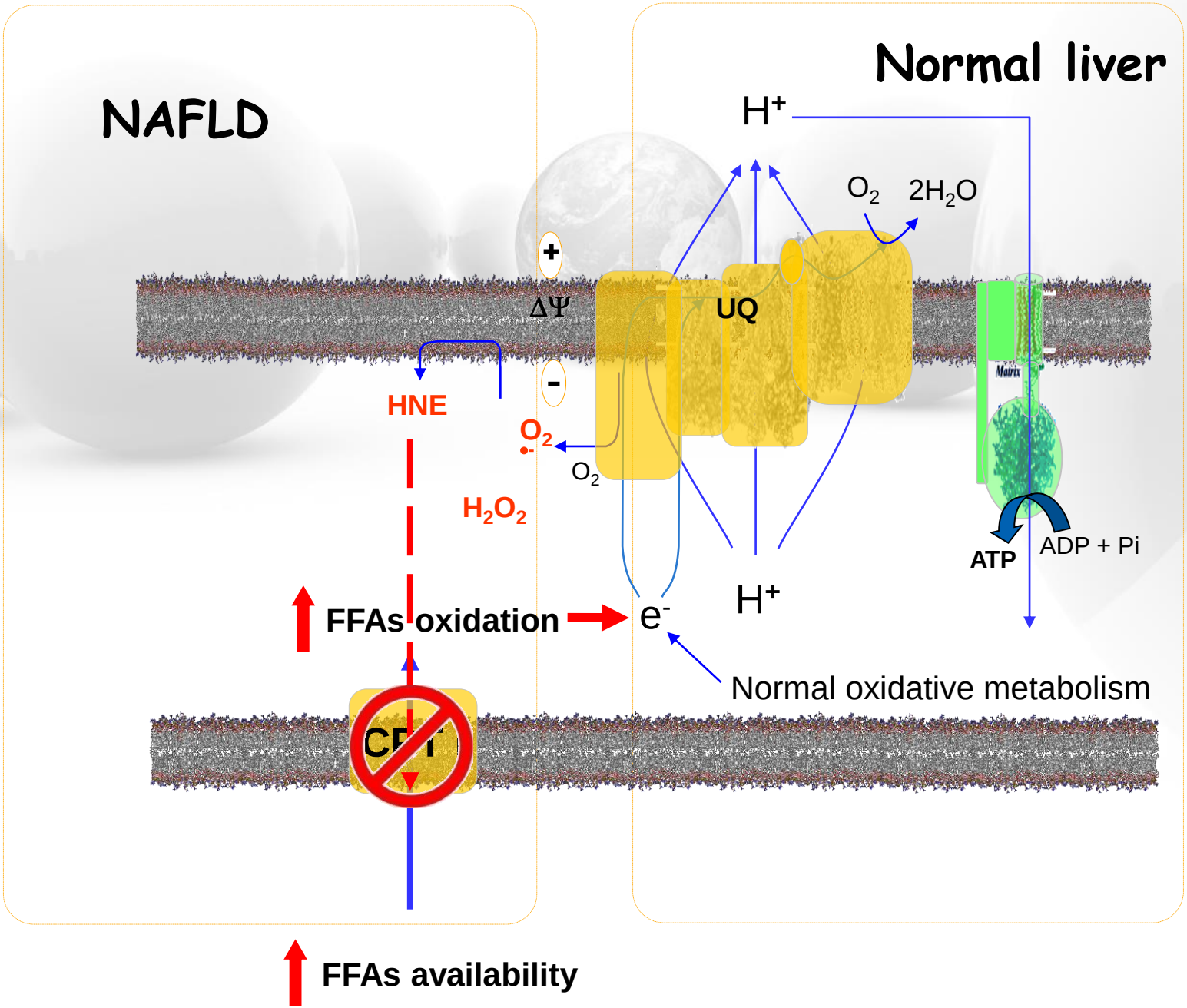
Apoptosi/Necrosi
Flogosi
Fibrosi
Cirrosi

# Tuttavia:

| | |
|---|---|
| 1 | **Molti soggetti con steatosi epatica non alcolica non svilupperanno mai una steatoepatite** |
| 2 | **Non tutti i soggetti affetti da NASH presentano insulino-resistenza** |

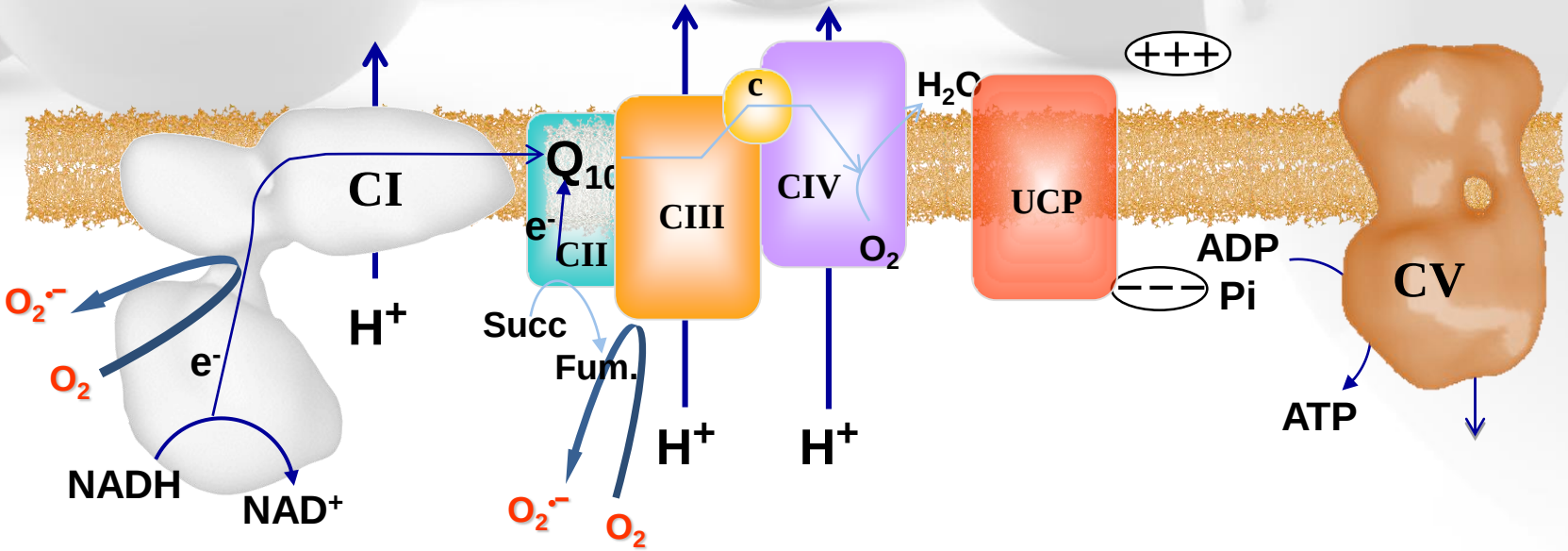



*Serviddio G, Vendemiale G et al, Mol Aspects Med 2008*




*Serviddio G, Vendemiale G. PLoS One 2011*

# Uncoupling protein-2 induces mitochondrial proton leak and increases susceptibility of NASH liver to ischaemia-reperfusion injury.




*Serviddio G, Vendemiale G et al, Gut 2008*

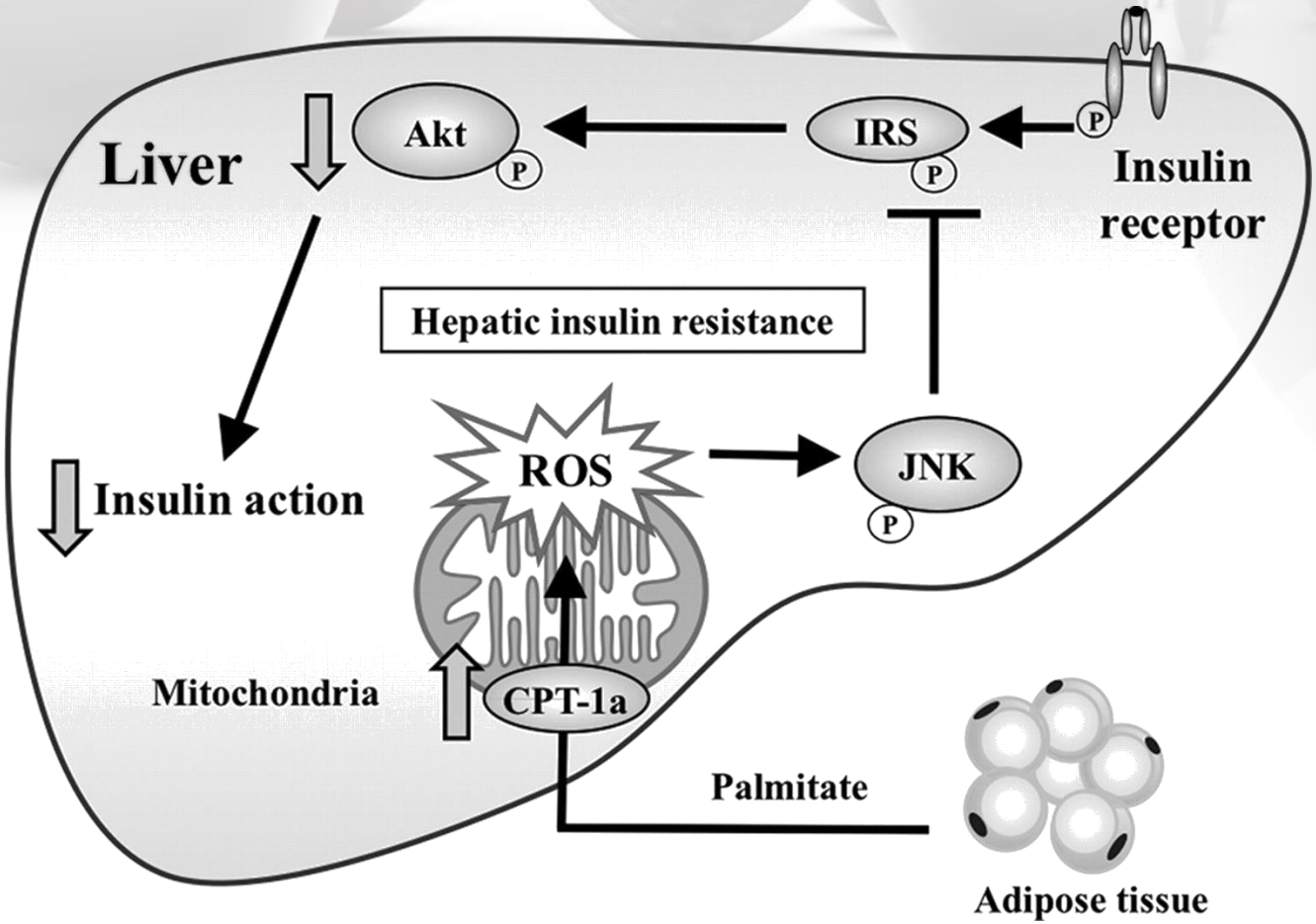
✖ Author's Choice

THE JOURNAL OF BIOLOGICAL CHEMISTRY VOL. 284, NO. 22, pp. 14809–14818, May 29, 2009
© 2009 by The American Society for Biochemistry and Molecular Biology, Inc. Printed in the U.S.A.

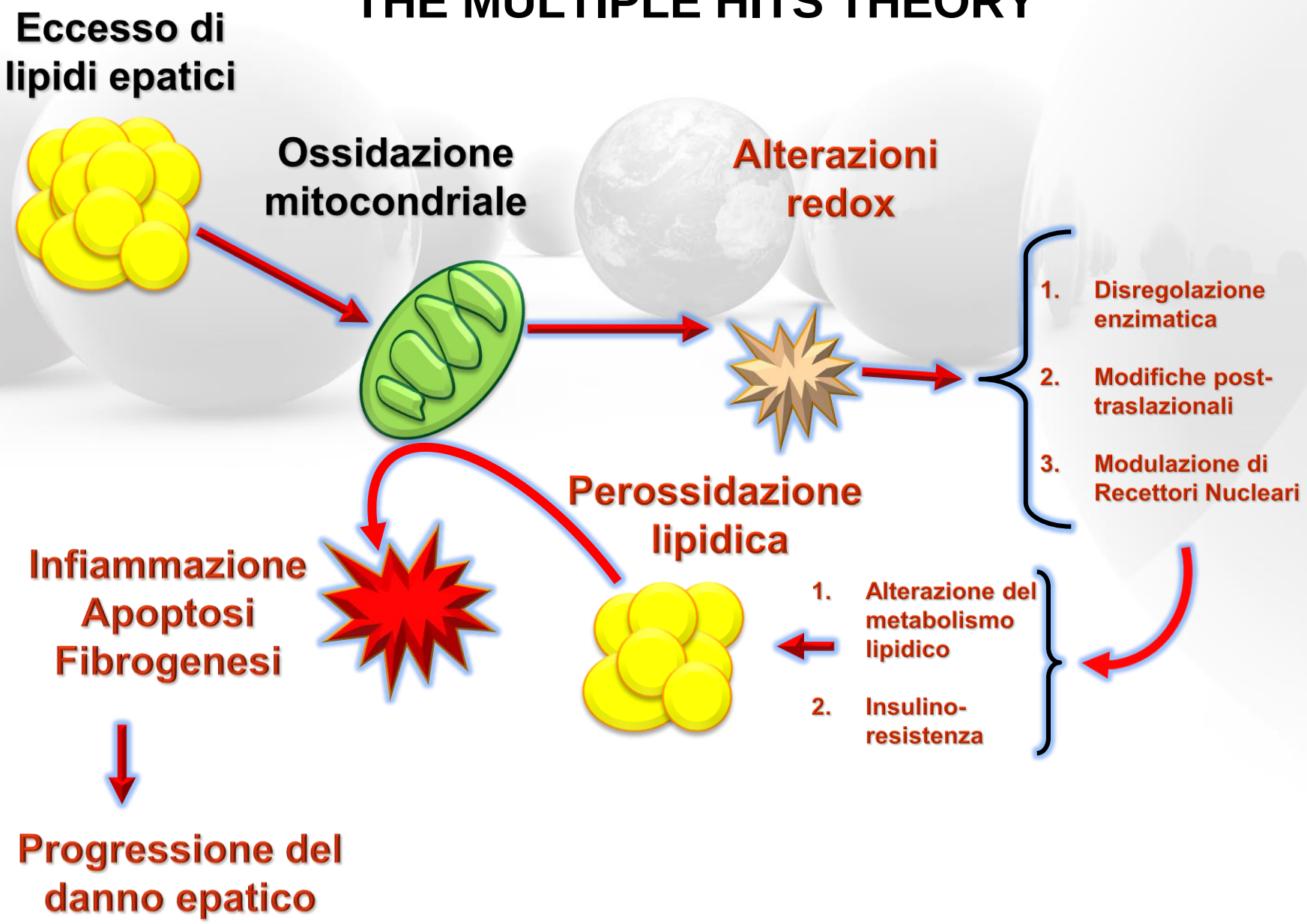
# Palmitate Induces Insulin Resistance in H4IIEC3 Hepatocytes through Reactive Oxygen Species Produced by Mitochondria*[S]

Received for publication, March 5, 2009 Published, JBC Papers in Press, March 30, 2009, DOI 10.1074/jbc.M901488200

Seiji Nakamura[‡], Toshinari Takamura[‡1], Naoto Matsuzawa-Nagata[§], Hiroaki Takayama[‡], Hirofumi Misu[‡], Hiroyo Noda[‡], Satoko Nabemoto[‡], Seiichiro Kurita[‡], Tsuguhito Ota[‡], Hitoshi Ando[‡], Ken-ichi Miyamoto[§], and Shuichi Kaneko[‡]



# THE MULTIPLE HITS THEORY




*adattato da G Serviddio, F Bellanti, G Vendemiale.*
*Free radical biology for medicine: learning from nonalcoholic fatty liver disease.*
*Free Rad Biol Med 65(2013) 963-68.*

Free Radical Biology and Medicine 65 (2013) 952–968

Contents lists available at ScienceDirect

Free Radical Biology and Medicine

journal homepage: www.elsevier.com/locate/freeradbiomed

Review Article

# Free radical biology for medicine: learning from nonalcoholic fatty liver disease

Gaetano Serviddio *, Francesco Bellanti, Gianluigi Vendemiale

*C.U.R.E. Centre for Liver Disease Research and Treatment, Institute of Internal Medicine, Department of Medical and Surgical Sciences, University of Foggia, 71122 Foggia, Italy*

# Alterations of hepatic ATP homeostasis and respiratory chain during development of non-alcoholic steatohepatitis in a rodent model

G. Serviddio*, F. Bellanti*, R. Tamborra*, T. Rollo*, A. D. Romano*, A. M. Giudetti†, N. Capitanio*, A. Petrella‡, G. Vendemiale*§ and E. Altomare*

*University of Foggia, Foggia, Italy, †University of Lecce, Lecce, Italy, ‡Istituto Zooprofilattico di Puglia e Basilicata, Foggia, Italy, §IRCCS-Casa Sollievo della Sofferenza, San Giovanni Rotondo, Foggia, Italy

EXPERT REVIEWS

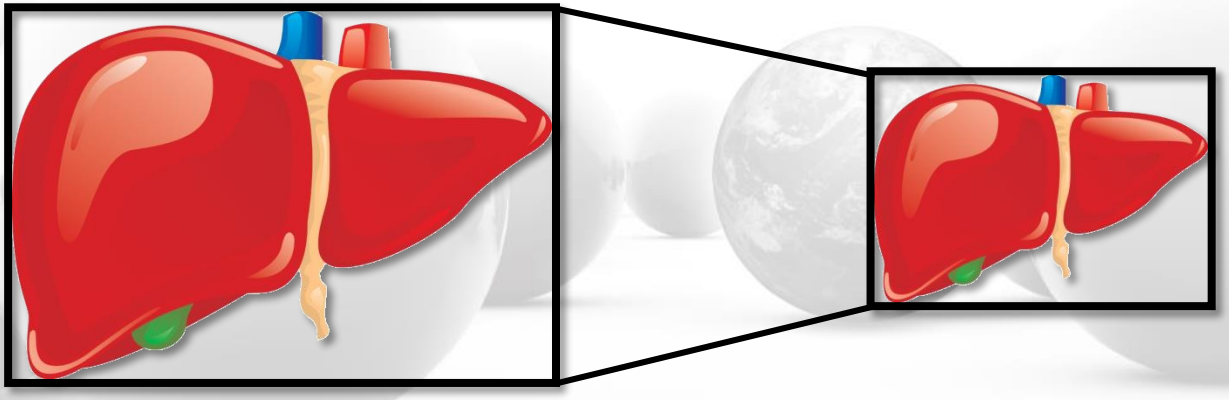
# Mitochondrial dysfunction in nonalcoholic steatohepatitis

*Expert Rev. Gastroenterol. Hepatol.* 5(2), 233–244 (2011)

Gaetano Serviddio[†1], Francesco Bellanti[1], Gianluigi Vendemiale[1,2] and Emanuele Altomare[1]

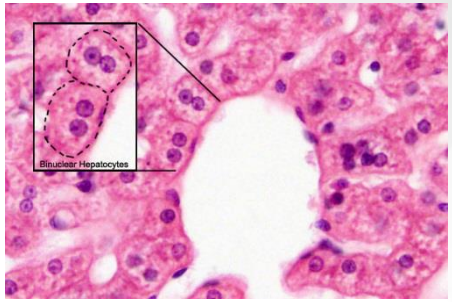
[1]*CURE (Centre for Liver Disease Research and Treatment), Department of Medical and Occupational Sciences, University of Foggia, 70124 Foggia, Italy*

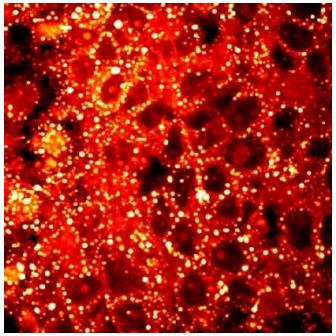
# THE AGING LIVER



**Reduction of size and blood flow**

**Macrohepatocytes with polyploidy**



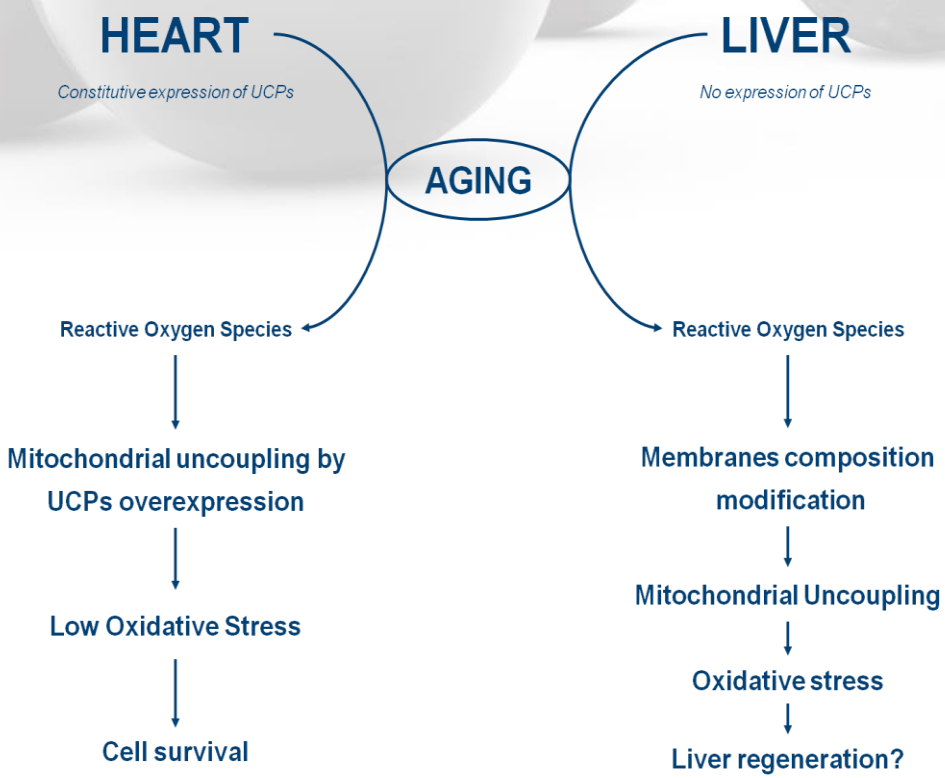



**Increase in lipid droplets**

*Jones K et al, Ageing Res Rev 2012*

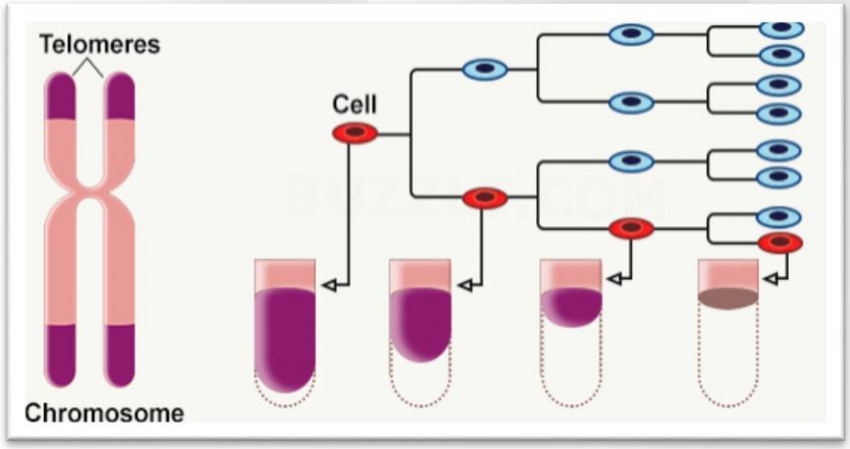
# THE AGING LIVER: REPLICATIVE SENESCENCE

## Failure in redox adaptations




Bellanti F, Vendemiale G *et al*
*J Gerontol A Biol Sci Med Sci 2013*

## Telomeres shortening

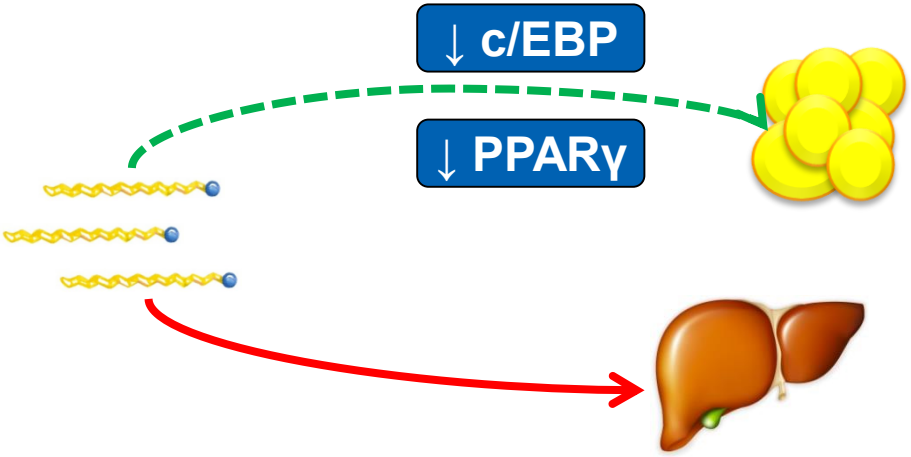



Aravinthan A *et al*, *J Hepatology 2013*

# THE AGING LIVER: LIPID DYSMETABOLISM

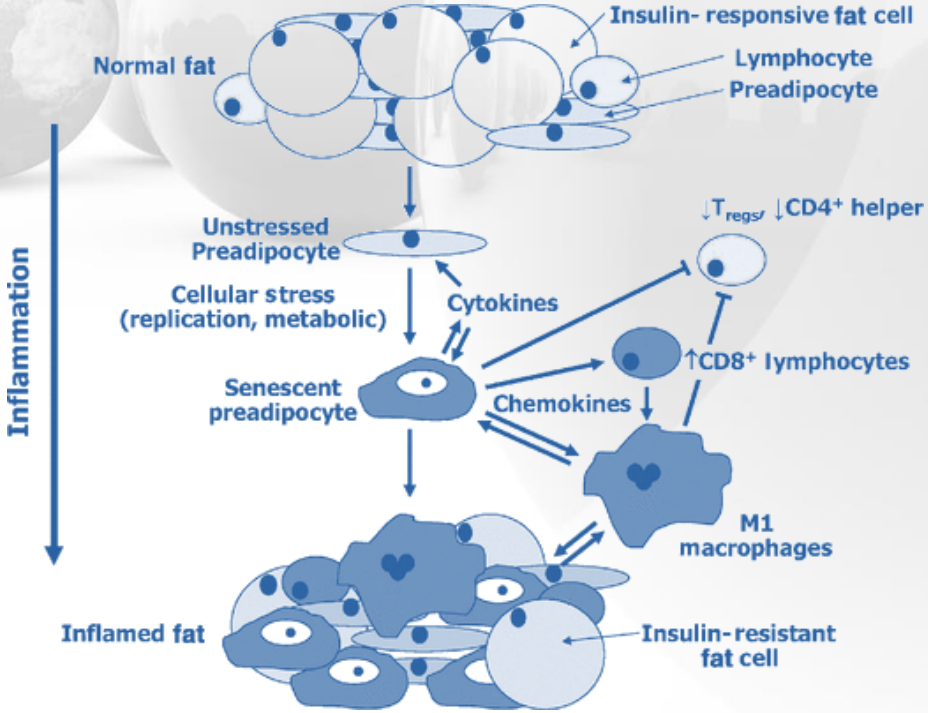
**Increase in visceral fat**

*Stramaglia G, Vendemiale G et al, J Nutr Health Aging 2010*




**Impaired adipogenesis by FAs**

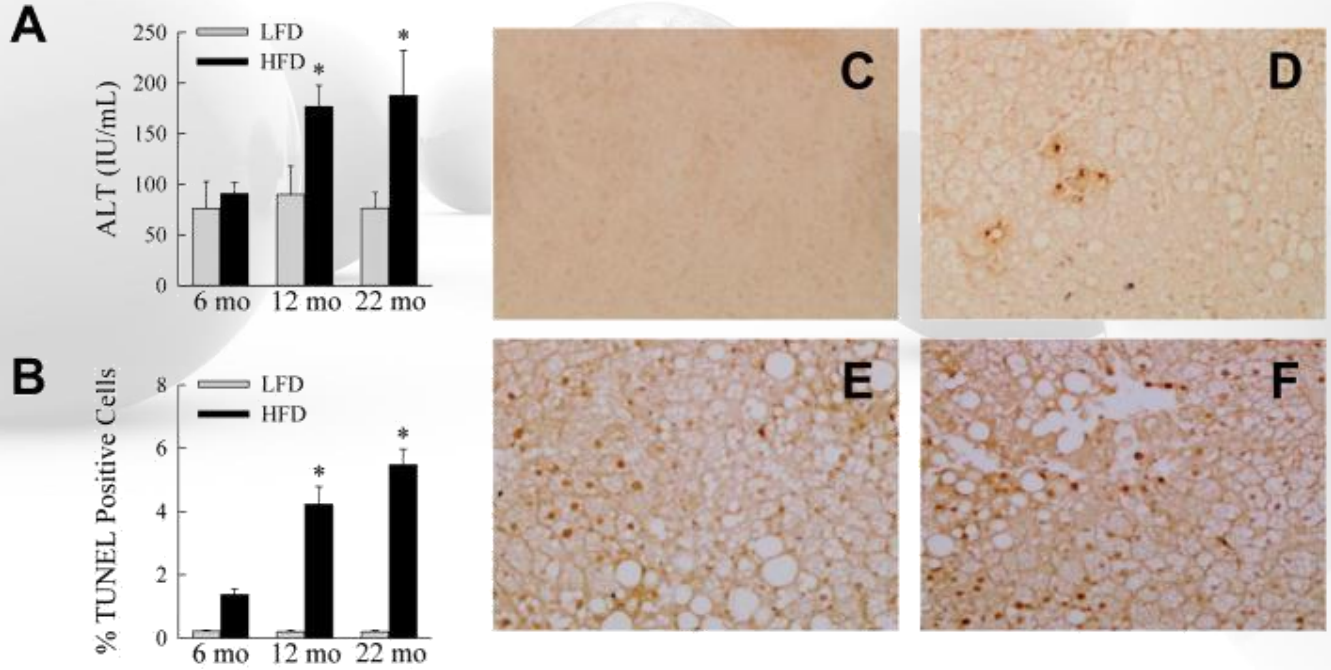
*Go W et al, Am J Physiol Endocrinol Metab 2007*




**Senescent and pro-inflammatory pre-adipocytes**

*Tchkonia T et al, Aging Cell 2010*

# THE AGING LIVER: “INFLAMM-AGING”




**Sensitization to the Fas death pathway**

**Increased M1 macrophage polarization**

Fontana L et al, Hepatology *2013*

# THE AGING LIVER: EXTRAHEPATIC COMPLICATIONS

| | |
|---|---|
| 1 | Coronaric risk factor independent of gender and obesity (non obese NAFLD patients are at higher risk) |

*Akahoshi M et al, Hypertens Res 2001*

| | |
|---|---|
| 2 | Risk factor for osteoporotic fractures |

*Li M et al, J Clin Endocrinol Metab 2012*

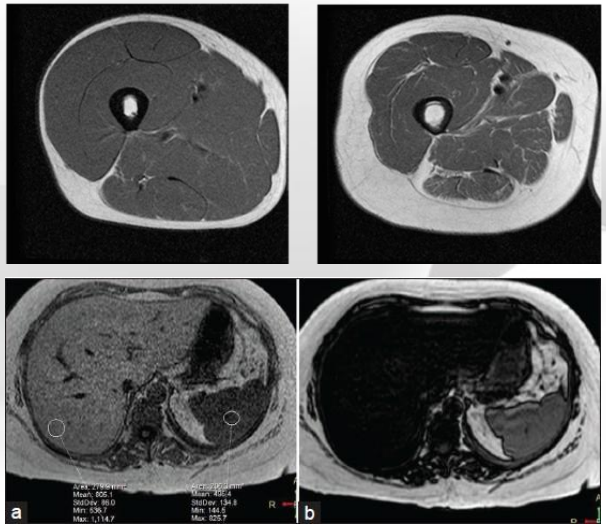
| | |
|---|---|
| 3 | NASH (but not steatosis) is an indipendent risk factor for colonic neoplasia |

*Wong VW et al, Gut 2011*

| | |
|---|---|
| 4 | Association with atrial fibrillation in DM2 |

*Targher G et al, PLoS One 2013*

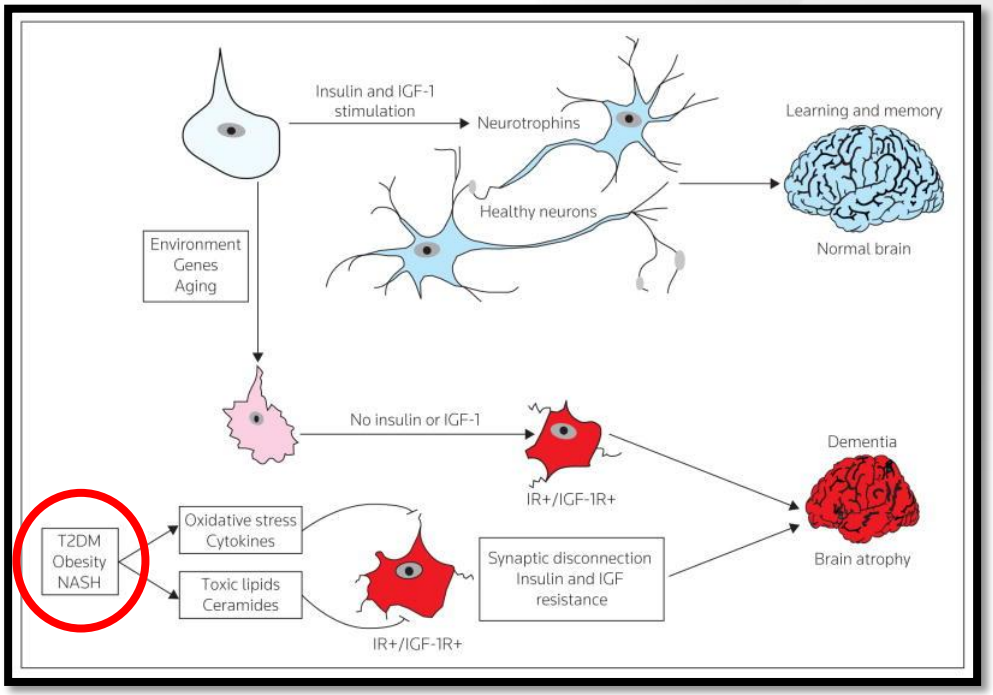
# LA NAFLD E LE SINDROMI GERIATRICHE




**Sarcopenia**

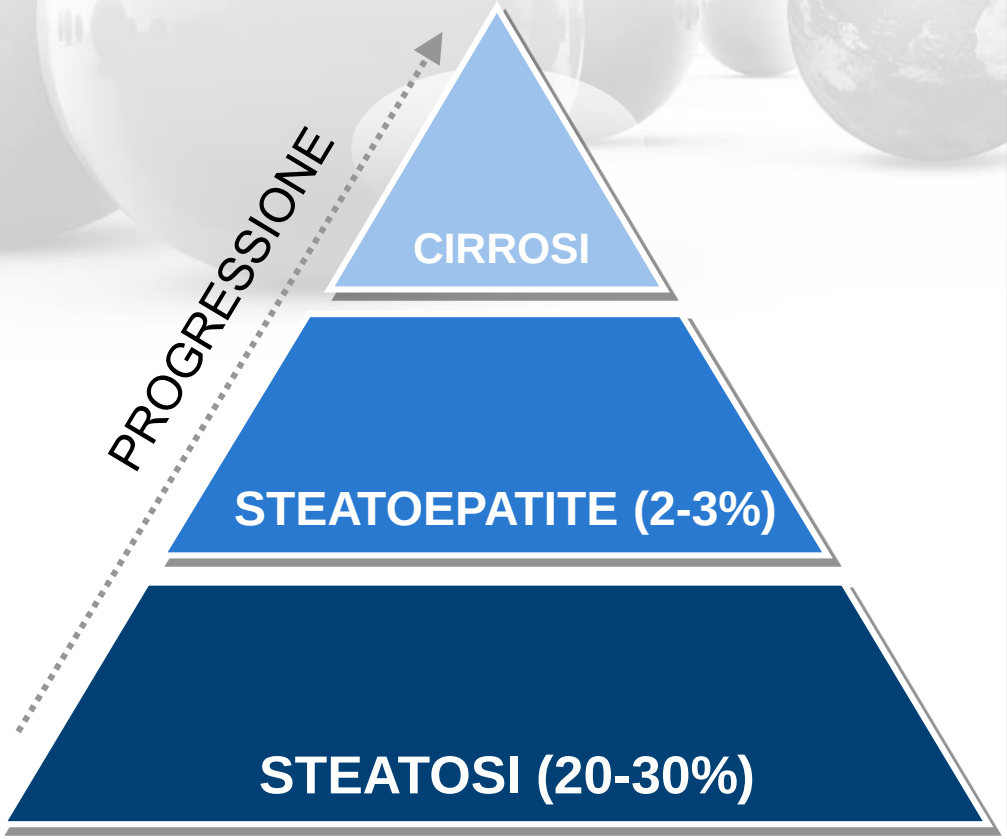
*Hong HC et al, Hepatology 2014*

**Neurodegenerazione**




*de la Monte SM et al, Current Opin Investig Drugs 2009*

# EVOLUZIONE DELLA NAFLD




## STORIA NATURALE

La NAFLD ha elevata mortalità derivante da cause epatiche e CV (OR: **1.57**, 95% CI: 1.18-2.10),ed un rischio raddoppiato di DM.

La NASH ha una mortalità da cause epatiche ancora maggiore (OR NASH: **5.71**, 2.31-14.13; OR NASH con fibrosi avanzata: **10.06**, 4.35-23.25), ma non da cause CV (OR: 0.91, 0.42-1.98).

*Musso G et al.* ***Meta-analysis: Natural history of non-alcoholic fatty liver disease (NAFLD) and diagnostic accuracy of non-invasive tests for liver disease severity.*** *Ann Med 2010*

# Management del paziente con NAFLD

**Sospettare la NAFLD presunta**

**Stimare la presenza di fibrosi**

**Follow-up periodico**

Step 1 → Step 2 → Step 3 → Step 4 → Step 5

**Confermare la NAFLD presunta**

**Gestione terapeutica**

# Step n° 1: sospettare la NAFLD presunta

**'OSPEDALI RIUNITI - FOGGIA'**
Azienda Ospedaliero - Universitaria
I° Laboratorio Analisi Chimico-Cliniche
*Direttore: Dr. F. Simone*

Pagina 1

Data Prelievo: 27/08/2011 09:38
Data Referto: 27/08/2011 12:15
Identificativo: 2820654
Data Nascita: [redacted]

[redacted]
MEDICINA UNIVER.

| Esame | Risultato | | u.m. | Valori di Riferimento |
|---|---|---|---|---|
| BILIRUBINA TOTALE | 0,65 | | mg/dl | 0,20 - 1,20 |
| BILIRUBINA DIRETTA | 0,16 | | mg/dl | 0,02 - 0,30 |
| BILIRUBINA INDIRETTA | 0,49 | | mg/dl | 0,10 - 0,90 |
| TRANSAMINASI GOT | 20 | | U/L | 2 - 40 |
| TRANSAMINASI GPT | 45 | H | U/L | 2 - 40 |
| GAMMA GT | 26 | | U/L | 7 - 38<br>1 - 6 mesi: 5 - 125 |
| FOSFATASI ALCALINA | 60 | | IU/L | 30 - 120<br>Adulti: 30 - 120<br>Bambini: 50 - 350 |
| CREATININEMIA | 0,62 | | mg/dl | 0,20 - 1,10 |
| AZOTEMIA | 33 | | mg/dl | 10 - 50 |
| GLUCOSIO | 164 | H | mg/dl | 50 - 110 |
| COLESTEROLO TOTALE | 137 | L | mg/dl | 140 - 200 |
| COLESTEROLO HDL<br>COL.HDL<br>Fattore di rischio (Col. Tot / Col HDL) | <br>35<br>3,9 | | mg/dl | 35 - 60<br>Basso rischio fino a 3,43<br>Medio rischio 3,44 a 4,97<br>Alto rischio 4,98 a 9,55 |
| COLESTEROLO LDL | 84 | | mg/dl | 70 - 150 |
| TRIGLICERIDI | 88 | | mg/dl | 40 - 170 |
| ACIDO URICO | 6,20 | H | mg/dl | 2,30 - 6,10 |
| SIDEREMIA | 46 | L | ug/dl | 49 - 151 |
| PROTEINE TOTALI | 6,40 | | g/dl | 6,10 - 8,30<br>Neonati: da 4,1 a 6,5 |
| CALCEMIA | 8,80 | | mg/dl | 8,40 - 10,50 |
| FOSFOREMIA | 3,50 | | mg/dl | 2,70 - 4,50<br>0 - 10 anni: 3,6 - 6,1 |

... segue ...

**Solo se steatosi > 30%**

**ALT > AST**
↓ ↓
**NASH ASH**

# Quando si parla di ipertransaminasemia?

## Clinical and Histologic Spectrum of Nonalcoholic Fatty Liver Disease Associated With Normal ALT Values

Pouneh Mofrad,[1] Melissa J. Contos,[2] Mahmadul Haque,[1] Carol Sargeant,[1] Robert A. Fisher,[3] Velimir A. Luketic,[1] Richard K. Sterling,[1] Mitchell L. Shiffman,[1] Richard T. Stravitz,[1] and Arun J. Sanyal[1]

HEPATOLOGY 2003;37:1286-1292.

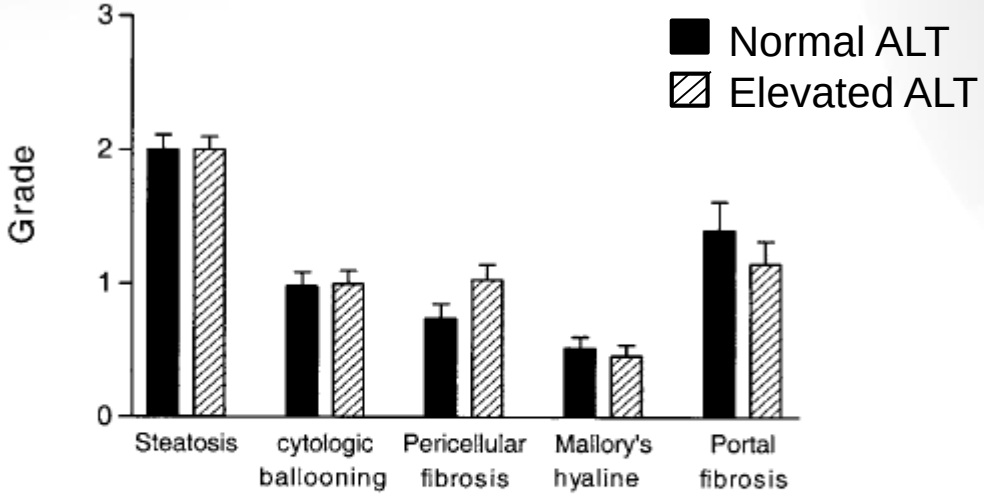


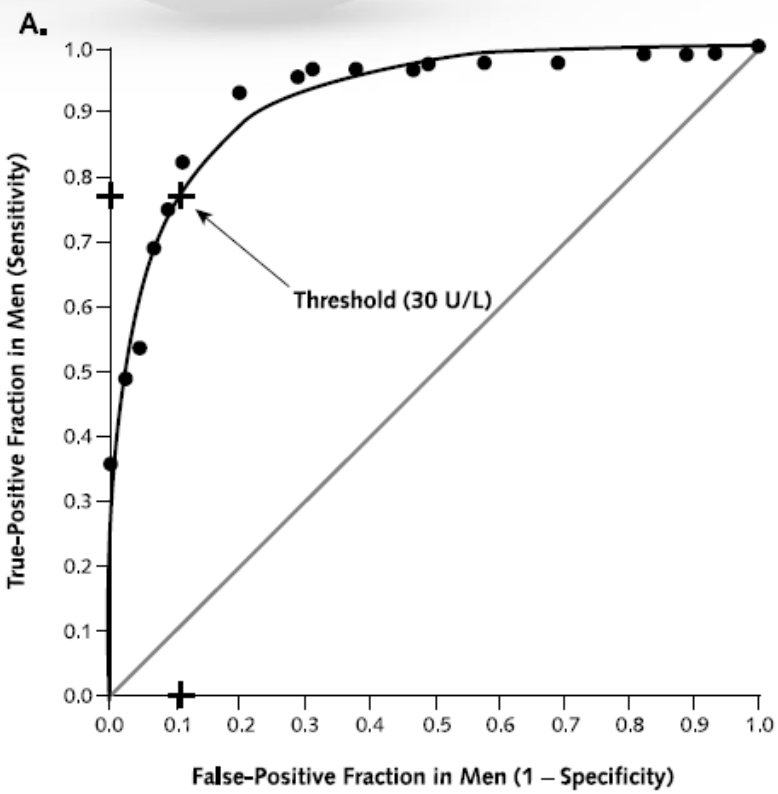

Fig. 1. The mean (±SD) grade of the individual histologic findings of NAFLD in 51 subjects with NAFLD and normal ALT (■) and 50 subjects with NAFLD and elevated ALT levels (▨). There was no significant difference with respect to the grade of steatosis, cytologic ballooning, Mallory bodies, pericellular fibrosis, or portal fibrosis. These data indicate that the histologic spectrum of NAFLD in those with normal ALT are comparable with those with elevated ALT.

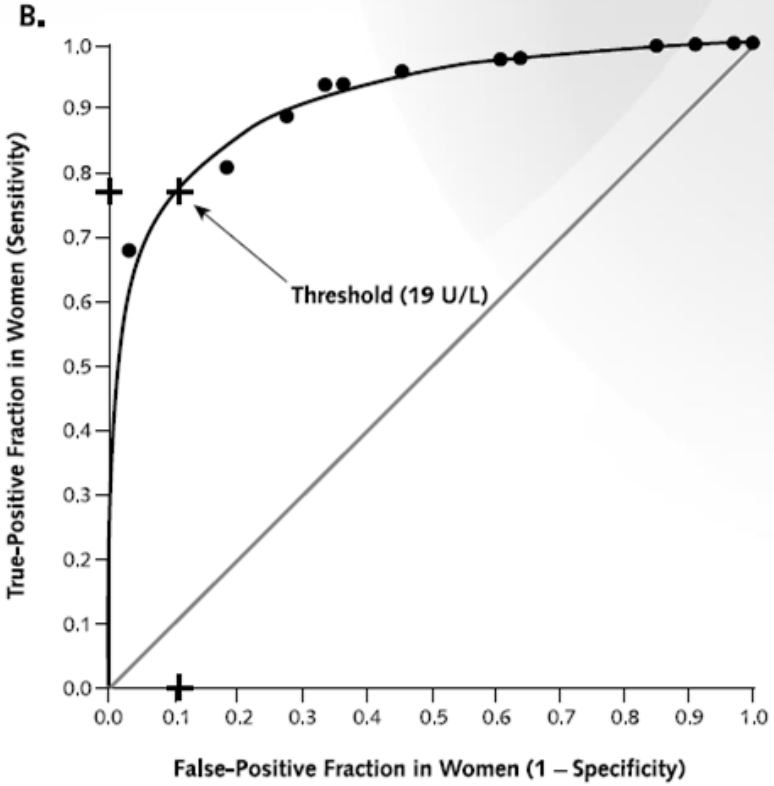
# Quando si parla di ipertransaminasemia?

## Updated Definitions of Healthy Ranges for Serum Alanine Aminotransferase Levels

Daniele Prati, MD; Emanuela Taioli, MD, PhD; Alberto Zanella, MD; Emanuela Della Torre, DSc; Sonia Butelli, DSc; Emanuela Del Vecchio, DSc; Luciana Vianello, MD; Francesco Zanuso, MD; Fulvio Mozzi, DSc; Silvano Milani, PhD; Dario Conte, MD; Massimo Colombo, MD; and Girolamo Sirchia, MD, FRCPath (Edin)

*Ann Intern Med.* 2002;137:1-9.



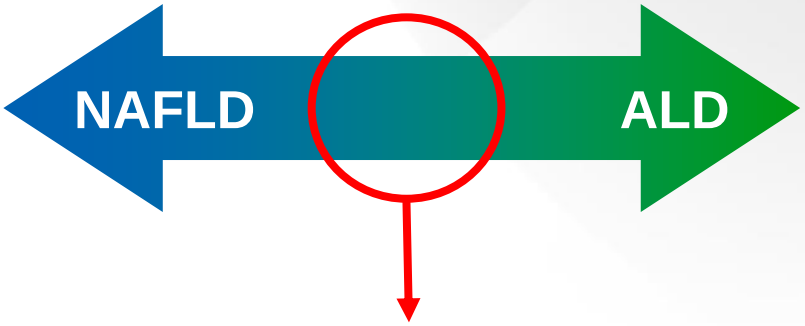
# Step n° 2: confermare la NAFLD presunta

## Anamnesi

- Alimentazione
- Alcol
- Attività fisica
- Modificazioni del peso corporeo
- Assunzione di farmaci o tossici
- Malattie autoimmunitarie
- PCOS

## Quanto alcol?

<20 g/die | <10 g/die




***«Alcuni pazienti con NAFLD possono invece essere affetti da epatopatia alcolica. È necessario ottenere una storia accurata riguardo all'assunzione di alcol in passato».***

# Step n° 2: confermare la NAFLD presunta

## Esame Obiettivo

- Indice di Massa Corporea
- Circonferenza Addominale
- Pressione arteriosa
- Rapporto Vita/Fianchi

## Test di laboratorio

- Esame emocromocitometrico
- PT, PTT
- AST, ALT, GGT, FA
- Proteine totali, elettroforesi proteica
- Glicemia ed insulinemia a digiuno
- Col. totale ed HDL, trigliceridemia
- HBsAg, Ab-anti HCV
- ASMA, ANA, LKM I-II, p-ANCA,
- c-ANCA, EMA
- Sideremia, transferrina e ferritina
- Alfa 1-antitripsina
- Cupremia, ceruloplasmina
- TSH

# Diagnosi Differenziale



**Table 5**
Causes of fatty liver disease [106].

| Nutritional | Drugs[a] | Metabolic or genetic | Other |
|---|---|---|---|
| Protein–calorie malnutrition[b] | Glucocorticoids[b] | Lipodystrophy[b] | Inflammatory bowel disease[b] |
| Starvation[b] | Synthetic estrogens[b] | Dysbetalipoproteinemia[b] | Small-bowel diverticulosis with bacterial overgrowth[b] |
| Total parenteral nutrition[b] | Aspirin[c] | Weber–Christian disease[b] | Human immunodeficiency |
| Rapid weight loss[b] | Calcium-channel blockers[b] | Wolman's disease[d] | Virus infection[b] |
| Gastrointestinal surgery for obesity[b] | Amiodarone[d] | Cholesterol ester storage[d] | Environmental hepatotoxins |
| | Tamoxifen[b] | Acute fatty liver of pregnancy[c] | Phosphorus[c] |
| | Tetracycline[c] | | Petrochemicals[b,c] |
| | Methotrexate[b] | | Toxic mushrooms[b] |
| | Perhexiline maleate[d] | | Organic solvents |
| | Valproic acid[c] | | *Bacillus cereus* |
| | Cocaine[c] | | Toxins[c] |
| | Antiviral agents | | |
| | Zidovudine[b] | | |
| | Didanosine[c] | | |
| | Fialuridine[c] | | |

[a] This is a partial list of agents that produce fatty liver. Some drugs produce inflammation as well. The association of fatty liver with calcium-channel blockers and valproic acid is weak, whereas the association with amiodarone is strong. Drug-induced fatty liver may have no sequelae (e.g., cases caused by glucocorticoids) or can result in cirrhosis (e.g., cases caused by methotrexate and amiodarone).
[b] This factor predominantly causes macrovesicular steatosis (mostly owing to imbalance in the hepatic synthesis and export of lipids).
[c] This factor predominantly causes microvesicular steatosis (mostly owing to defects in mitochondrial function).
[d] This factor causes hepatic phospholipidosis (mostly owing to the accumulation of phospholipids in lysosomes).

# Step n° 3: stimare la presenza di fibrosi

## NAFLD fibrosis score
### Online calculator

Angulo P, Hui JM, Marchesini G et al. **The NAFLD fibrosis score**
*A noninvasive system that identifies liver fibrosis in patients with NAFLD*
Hepatology 2007;45(4):846-854 doi:10.1002/hep.21496

| | |
|---|---|
| Age (years) | 60 |
| BMI (kg/m²) | 35 |
| IGF/diabetes | ☑ |
| AST | 40 |
| ALT | 38 |
| Platelets (x10⁹/l) | 250 |
| Albumin (g/l) | 3 |
| **Score** | 2.00 |
| Original score | 2.559 |

< -1.455: predictor of **absence** of significant fibrosis (F0-F2 fibrosis)
≤ -1.455 to ≤ 0.675: indeterminate score
> 0.675: predictor of **presence** of significant fibrosis (F3-F4 fibrosis)

BMI: body mass index
IGF: impaired fasting glucose

© 2009 nafldscore.com

concept: Dr Matthew Armstrong
site construction and design: Dr Jeremy Jones

# Step n° 3: stimare la presenza di fibrosi

Available online at www.sciencedirect.com

ScienceDirect

Digestive and Liver Disease

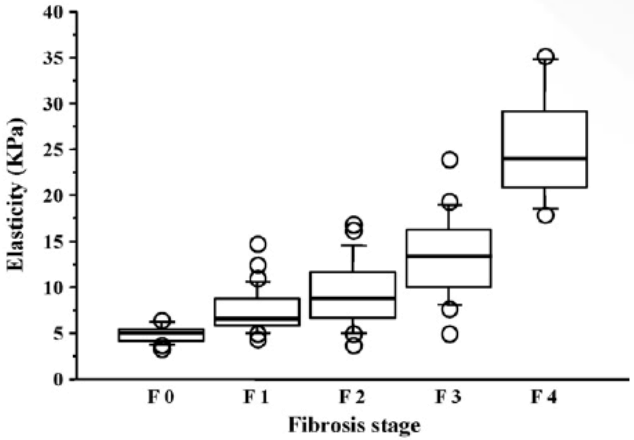
Digestive and Liver Disease 40 (2008) 371–378

www.elsevier.com/locate/dld

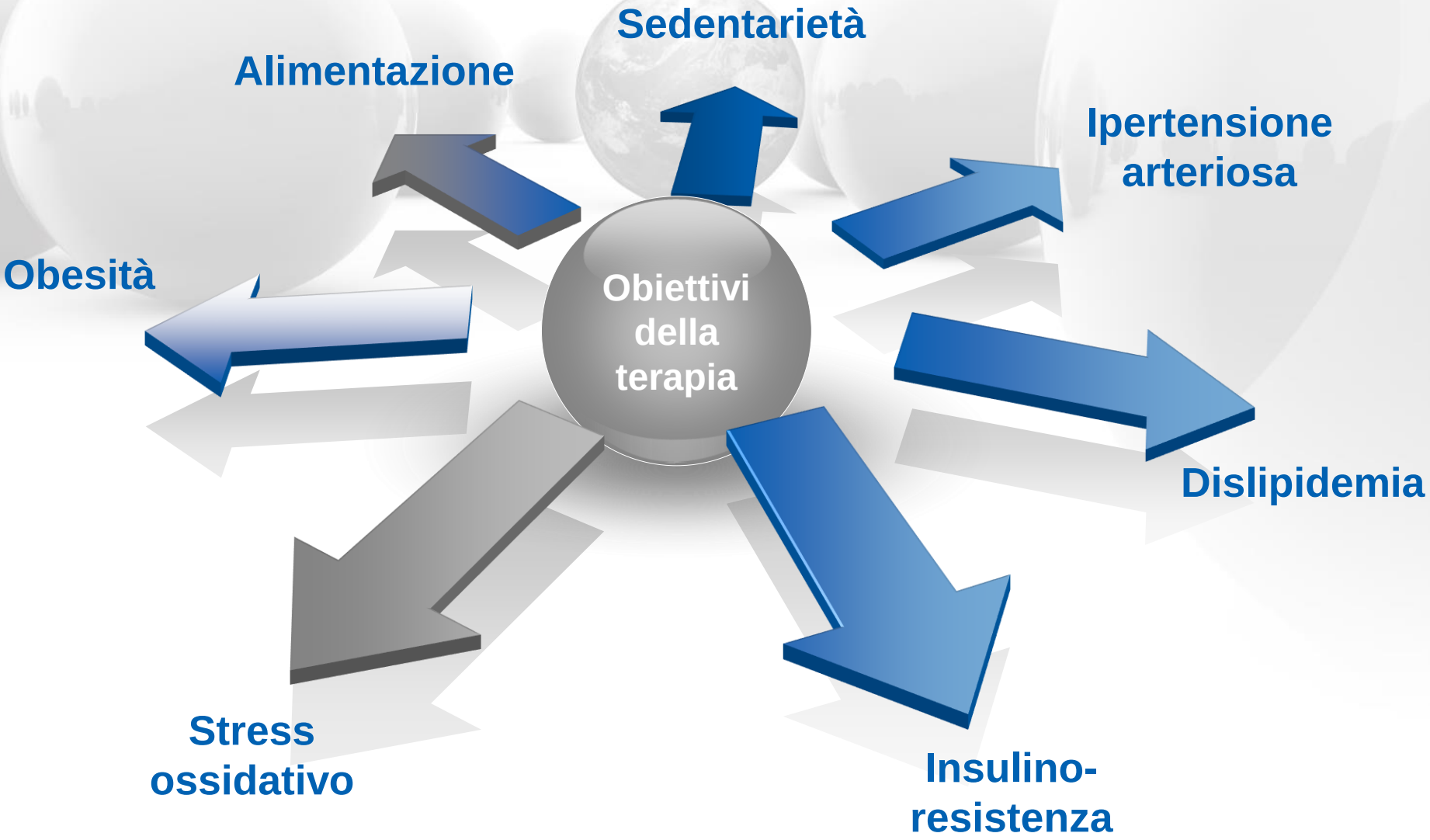
Liver, Pancreas and Biliary Tract

## Noninvasive assessment of liver fibrosis by measurement of stiffness in patients with nonalcoholic fatty liver disease (NAFLD)

M. Yoneda[a,1], M. Yoneda[c,1], H. Mawatari[a], K. Fujita[a], H. Endo[a], H. Iida[a], Y. Nozaki[a], K. Yonemitsu[a], T. Higurashi[a], H. Takahashi[a], N. Kobayashi[a], H. Kirikoshi[a], Y. Abe[a], M. Inamori[a], K. Kubota[a], S. Saito[a], M. Tamano[c], H. Hiraishi[c], S. Maeyama[d], N. Yamaguchi[b], S. Togo[b], A. Nakajima[a,*]



# Step n° 4: gestione terapeutica



Review

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

# Lifestyle interventions for the treatment of non-alcoholic fatty liver disease in adults: A systematic review

Christian Thoma[1,2,3], Christopher P. Day[1,2], Michael I. Trenell[1,2,3,*]

[1]Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK; [2]NIHR Biomedical Research Centre for Ageing & Age-related Disease, Newcastle University, Newcastle upon Tyne, UK; [3]MRC Centre for Brain Ageing & Vitality, Newcastle University, Newcastle upon Tyne, UK

## Key Points

- Gli interventi sullo stile di vita che determinano perdita di peso riducono l'accumulo epatico di lipidi
- L'entità del calo ponderale si riflette sul grado di steatosi epatica
- L'esercizio fisico determina un modesto – ma significativo – effetto sulla steatosi epatica, anche senza perdita di peso
- I dati che documentano l'impatto delle modificazioni dello stile di vita sull'istologia epatica sono molto limitati

# Gli anziani rispondono meno degli adulti ai cambiamenti nello stile di vita?

*J Appl Physiol* 100: 1584–1589, 2006.
First published December 22, 2005; doi:10.1152/japplphysiol.01336.2005.

## Exercise-induced reversal of insulin resistance in obese elderly is associated with reduced visceral fat

**Valerie B. O'Leary,[1,2] Christine M. Marchetti,[1,2] Raj K. Krishnan,[1,2] Bradley P. Stetzer,[5] Frank Gonzalez,[5] and John P. Kirwan[1,2,3,4]**

## Diet and Exercise Interventions Reduce Intrahepatic Fat Content and Improve Insulin Sensitivity in Obese Older Adults

**Krupa Shah[1], Abby Stufflebam[1], Tiffany N. Hilton[2], David R. Sinacore[1,2], Samuel Klein[1] and Dennis T. Villareal[1]**

*Obesity* (2009) **17,** 2162–2168. doi:10.1038/oby.2009.126

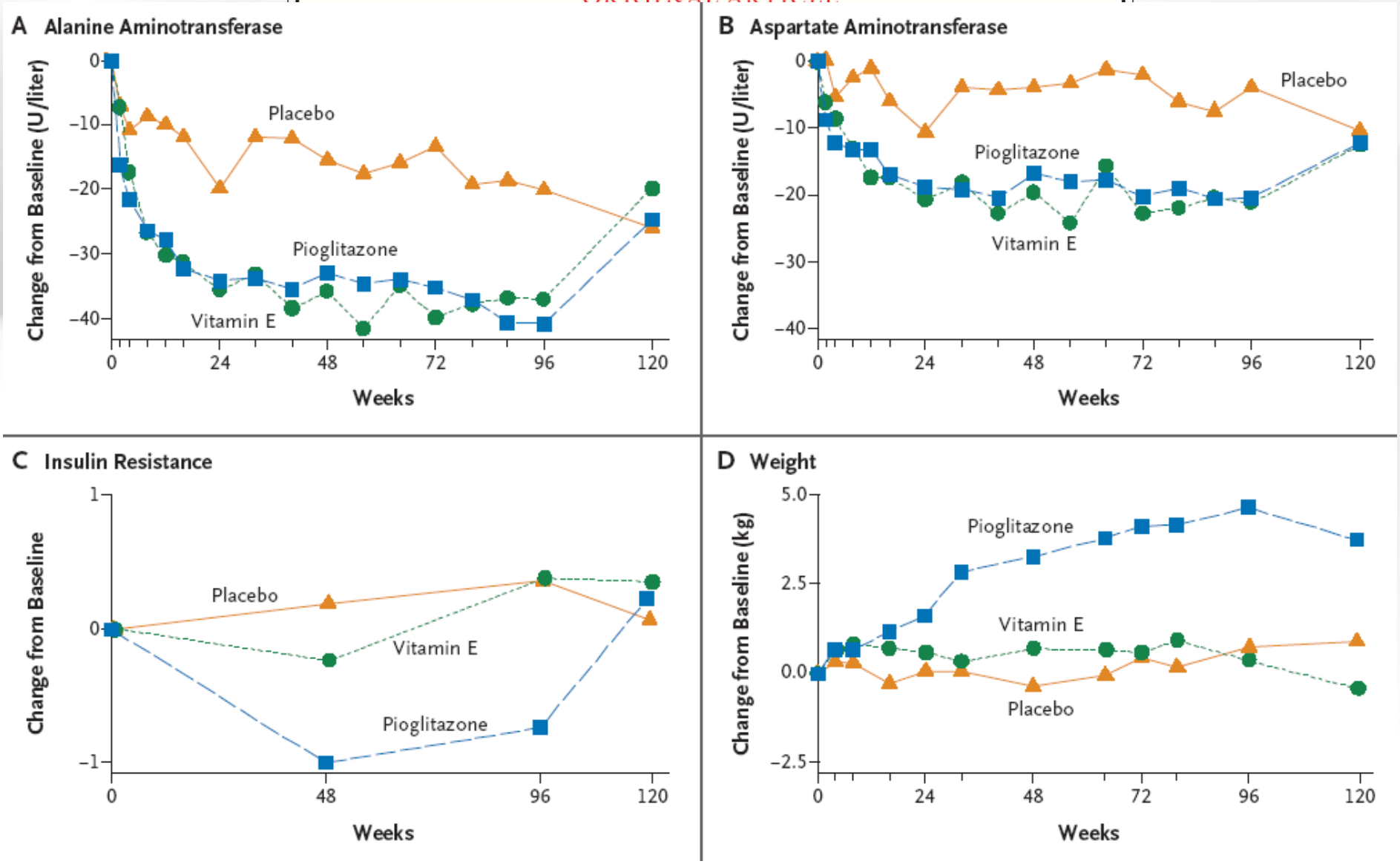
# A Meta-Analysis of Randomized Trials for the Treatment of Nonalcoholic Fatty Liver Disease

Giovanni Musso,[1] Roberto Gambino,[2] Maurizio Cassader,[2] and Gianfranco Pagano[2]

HEPATOLOGY 2010;52:79-104

1. Il calo ponderale migliora l'attività istologica, ma più del 50% dei pazienti non raggiunge il peso desiderato
2. I tiazolidinedioni migliorano la steatosi e l'infiammazione ma determinano aumento del peso corporeo
3. I PUFA hanno migliorato markers biochimici e radiologici di NAFLD
4. Pentossifillina, telmisartan ed L-carnitina hanno migliorato l'istologia epatica in pazienti con NASH
5. RCTs che hanno utilizzato antiossidanti sono molto eterogenei e mostrano risultati controversi

ORIGINAL ARTICLE



# IL TRATTAMENTO FARMACOLOGICO DELLA NAFLD NELL'ANZIANO

**1** **Non esistono raccomandazioni specifiche per pazienti di età > 65 anni**

*Nascimbeni F et al, J Hepatol 2013*

**2** **Le scelte terapeutiche tra adulti ed anziani sono simili**

*Premoli A et al, Minerva Gastroenterol Dietol 2009*

**3** **Gli anziani in polifarmacoterapia hanno maggior rischio di epatotossicità da farmaci**

*Shah BM et al, Clin Geriatr Med 2012*

# Take Home Messages

- La NAFLD è una malattia diffusa e potenzialmente evolutiva soprattutto nell’anziano, associandosi con maggiore frequenza a complicanze epatiche ed extraepatiche
- L’approfondimento diagnostico specialistico deve considerarne l’inquadramento nel contesto delle sindromi geriatriche (fragilità, sarcopenia, demenza).
- La gestione dell’anziano affetto da NAFLD, pur richiedendo un cambiamento nello stile di vita, deve tener conto delle limitazioni fisiche e dell’adeguato apporto calorico. Il trattamento farmacologico deve considerare le comorbidità ed il rischio aumentato di tossicità epatica.

# LA STEATOEPATITE NON ALCOLICA

**Gianluigi Vendemiale**

UNIVERSITÀ DEGLI STUDI DI FOGGIA