11° CONGRESSO NAZIONALE AGE

Roma – 18/21 marzo 2015

ASP
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catanzaro

Iperuricemia e rischio globale nel paziente anziano

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Geriatra ASP Catanzaro

Roma - Hotel Aran Mantegna, 21 Marzo 2015

Key points

- Fisiopatologia del danno vascolare da iperuricemia
- Ruolo di fattore di rischio CV dell'iperuricemia: dati clinici a supporto
- Casi in cui l'acido urico **NON** causa un aumento del rischio CV

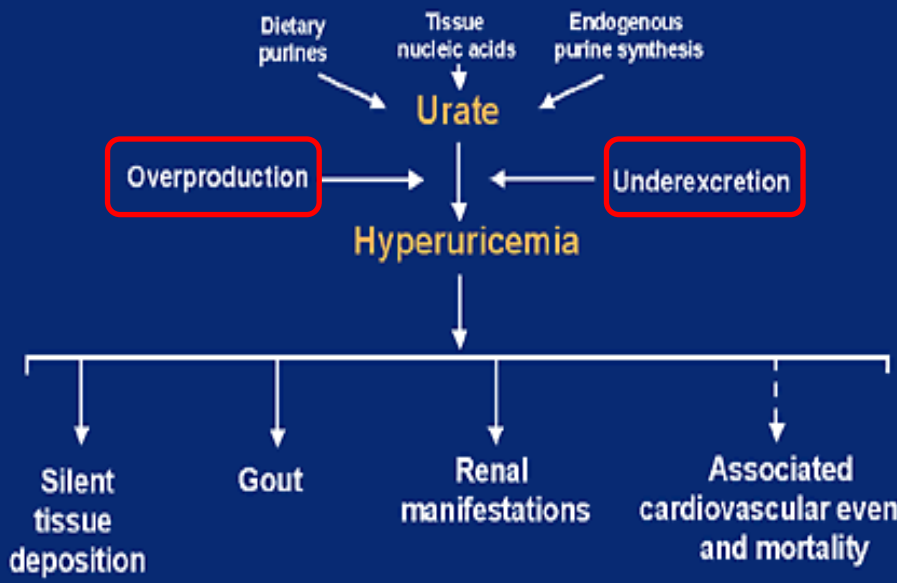
Iperuricemia

- L'acido urico è il prodotto finale del metabolismo purinico

- Definiamo iperuricemia quella condizione in cui i livelli sierici di acido urico superano i 6.8 mg/dL, per cui viene superata la soglia di solubilità e si verifica la precipitazione dei cristalli di urato

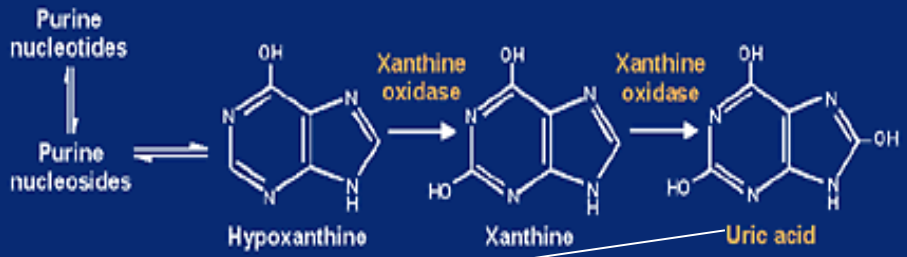
- L'iperuricemia può derivare da un eccesso di produzione o da una ridotta escrezione di acido urico

The Hyperuricemia Cascade



Purine Degradation to Uric Acid

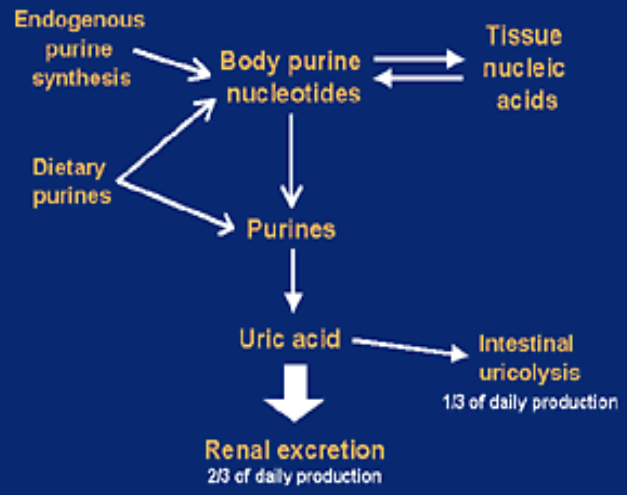
- **Xanthine oxidase** catalyzes the final conversions to uric acid



Prodotto finale del metabolismo purinico nell'uomo

Prodotto finale del metabolismo purinico Nella maggior parte dei mammiferi

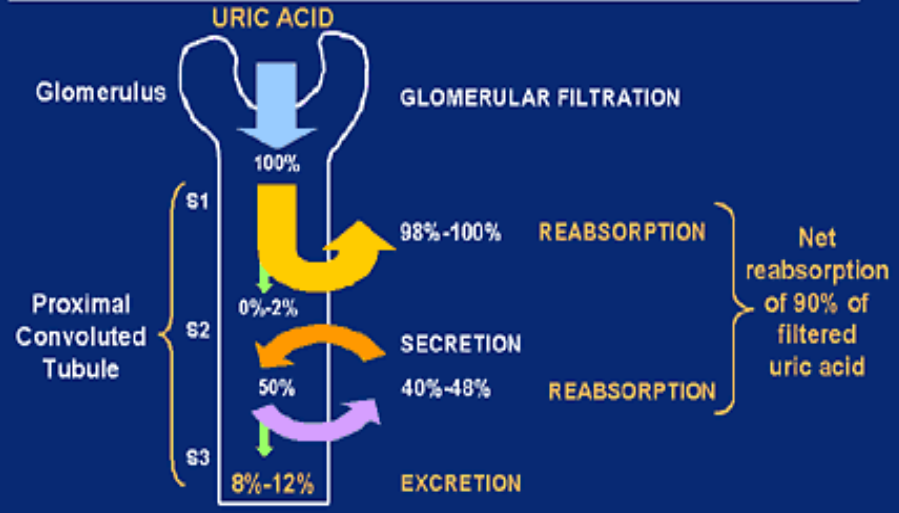
Schematic Overview of the Production and Elimination of Uric Acid



Koopman, ed. In: *Arthritis and Allied Conditions.* 14th ed. Lippincott, Williams and Wilkins; 2001:2283.

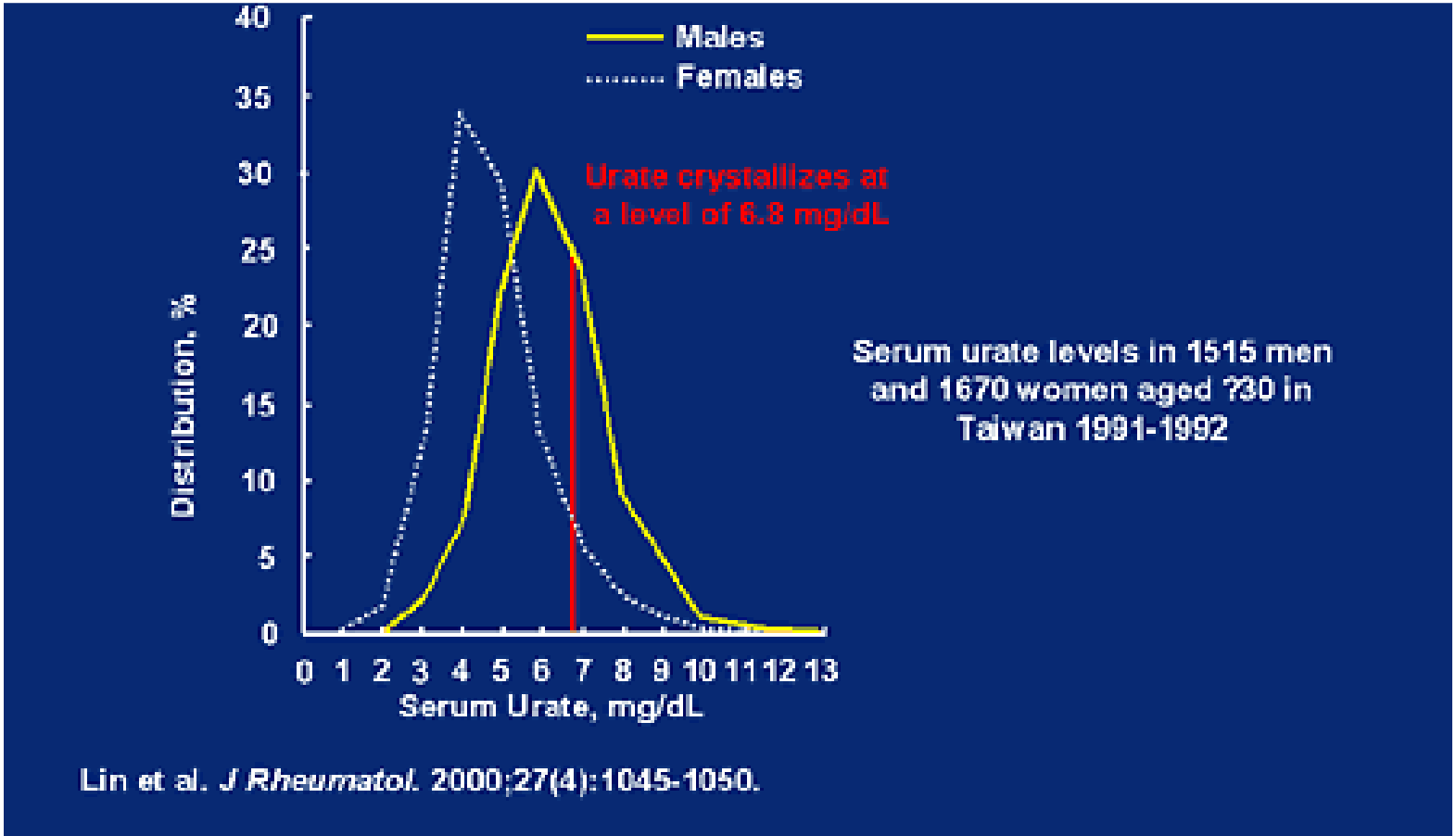
Renal Elimination of Uric Acid

Operationally Defined 4 Component Model of Renal Uric Acid Handling

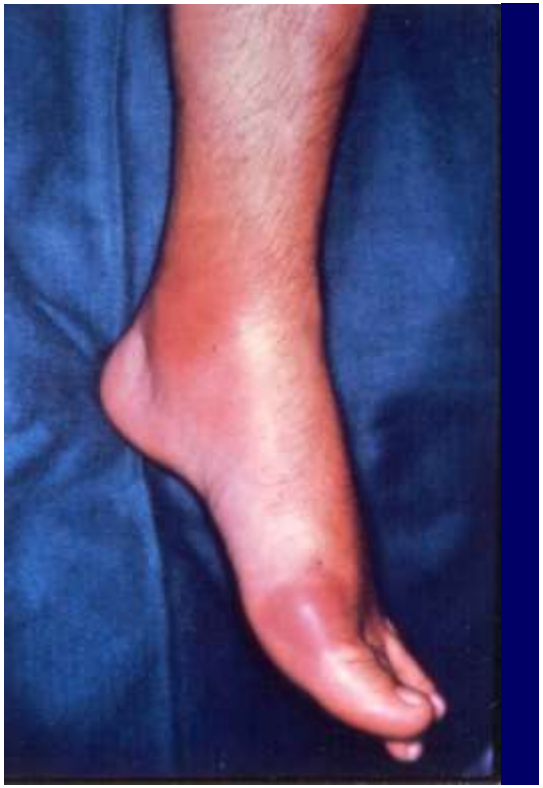


The multiple reabsorptive and secretory mechanisms may be regulated by a recently identified gene product of URAT-1 (Enomoto et al., Nature, 2002)

Distribuzione dei valori sierici di urati



Hyperuricemia as an Independent Risk Factor for Atherogenesis



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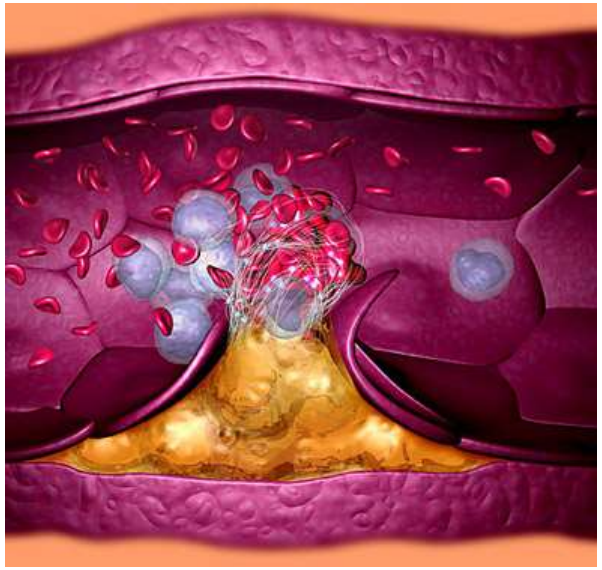
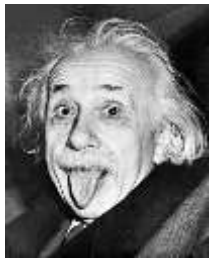


Uric Acid

The Good

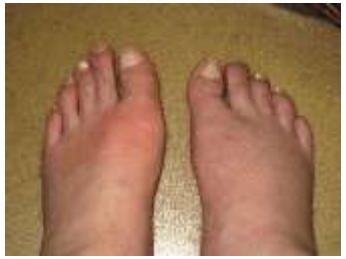


Intelligence

Alzheimer's

The Bad

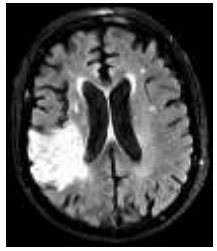
Tophi



Gout

Stone

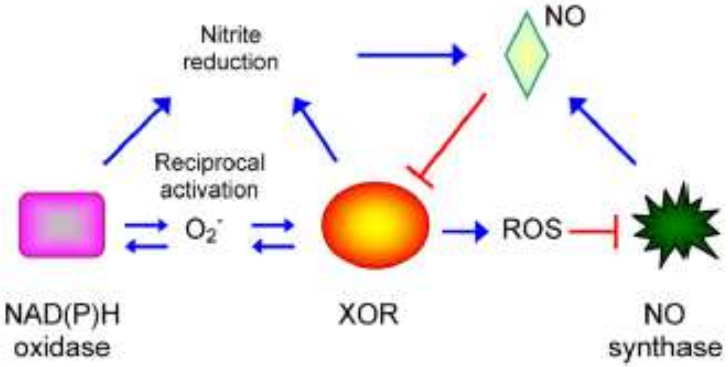
Parkinson's Disease

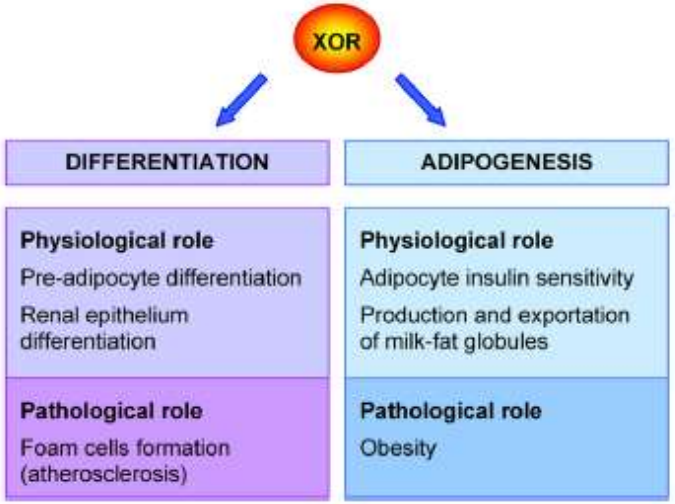


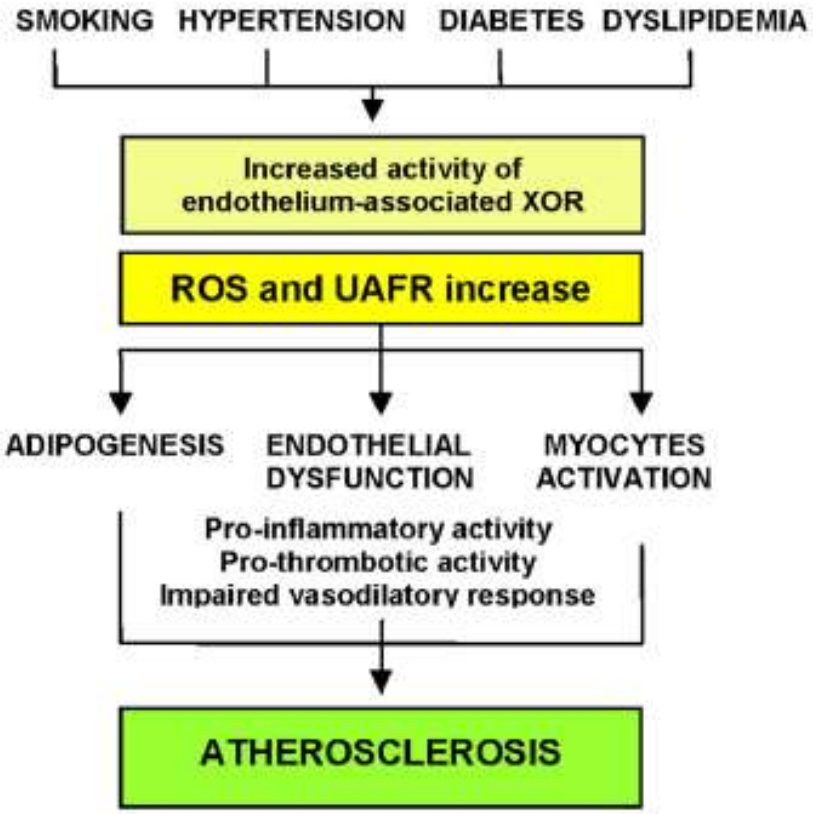
CVA

MI

Role of xantine oxidoreductase (XOR) in the pathogenesis of atherosclerosis







Battelli MG et al., Atherosclerosis 2014

Elevated SUA and CV-TOD

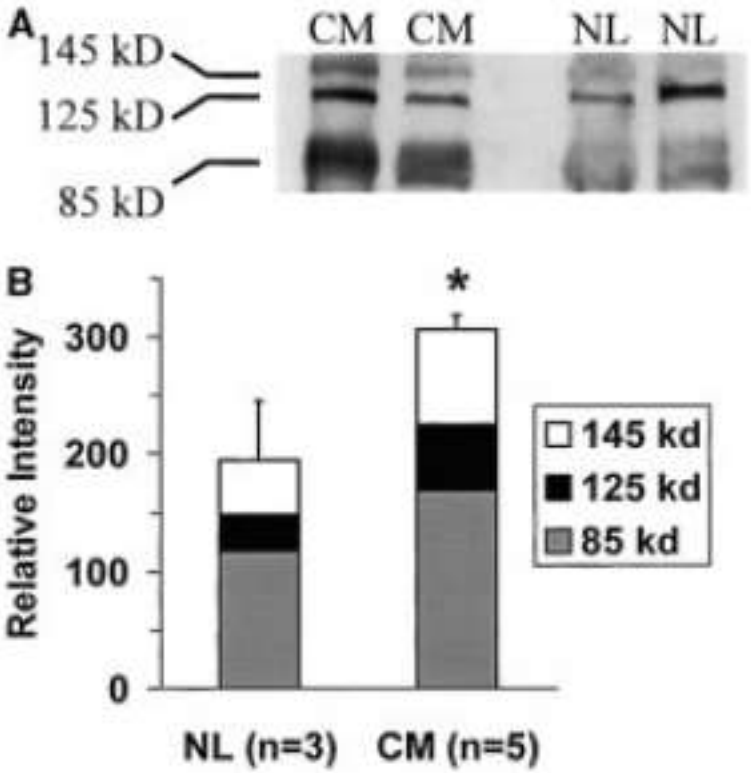
Elevated levels of SUA have been correlated with:

- **LV mass and structure** (Tze-Fan Chao et al., Int J Cardiol, 2013)
- **IMT** (Borghi et al J Hypertens 2013; Gomes-Marco et al. Am J Hypertens 2013)
- **PWV** (Vlachopoulos et al., Am J Hypertens 2011; Borghi et al. J Hypertens 2013, Mehta, Am J Hypertens 2014)
- **Microalbuminuria** (Viazzi et al., Am J Hypertens 2007)
- **Renal Vascular Resistance** (Viazzi et al., Am J Hypertens 2007)

Therapeutic Effects of Xanthine Oxidase Inhibitors: Renaissance Half a Century after the Discovery of Allopurinol

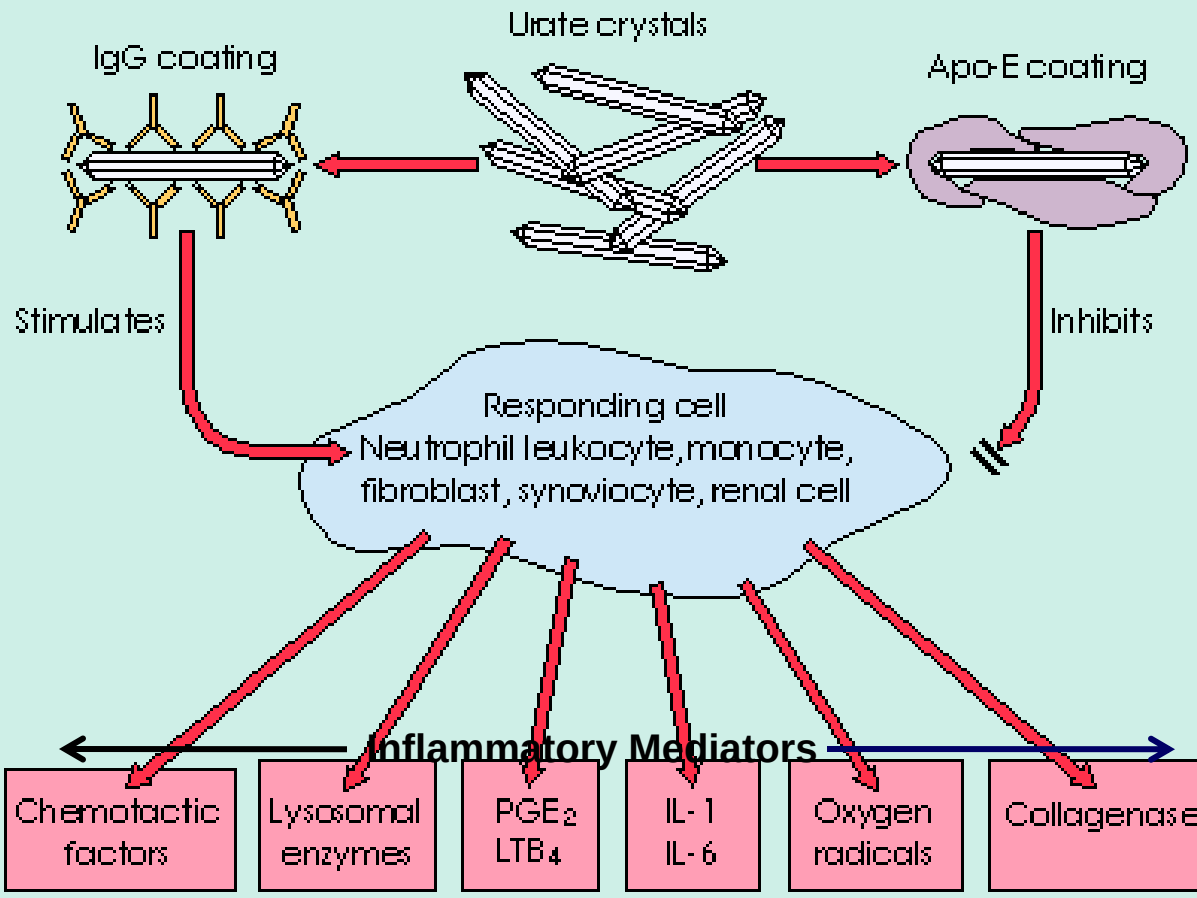
Pacher et al., 2006

XOR is up-regulated in patients with heart failure

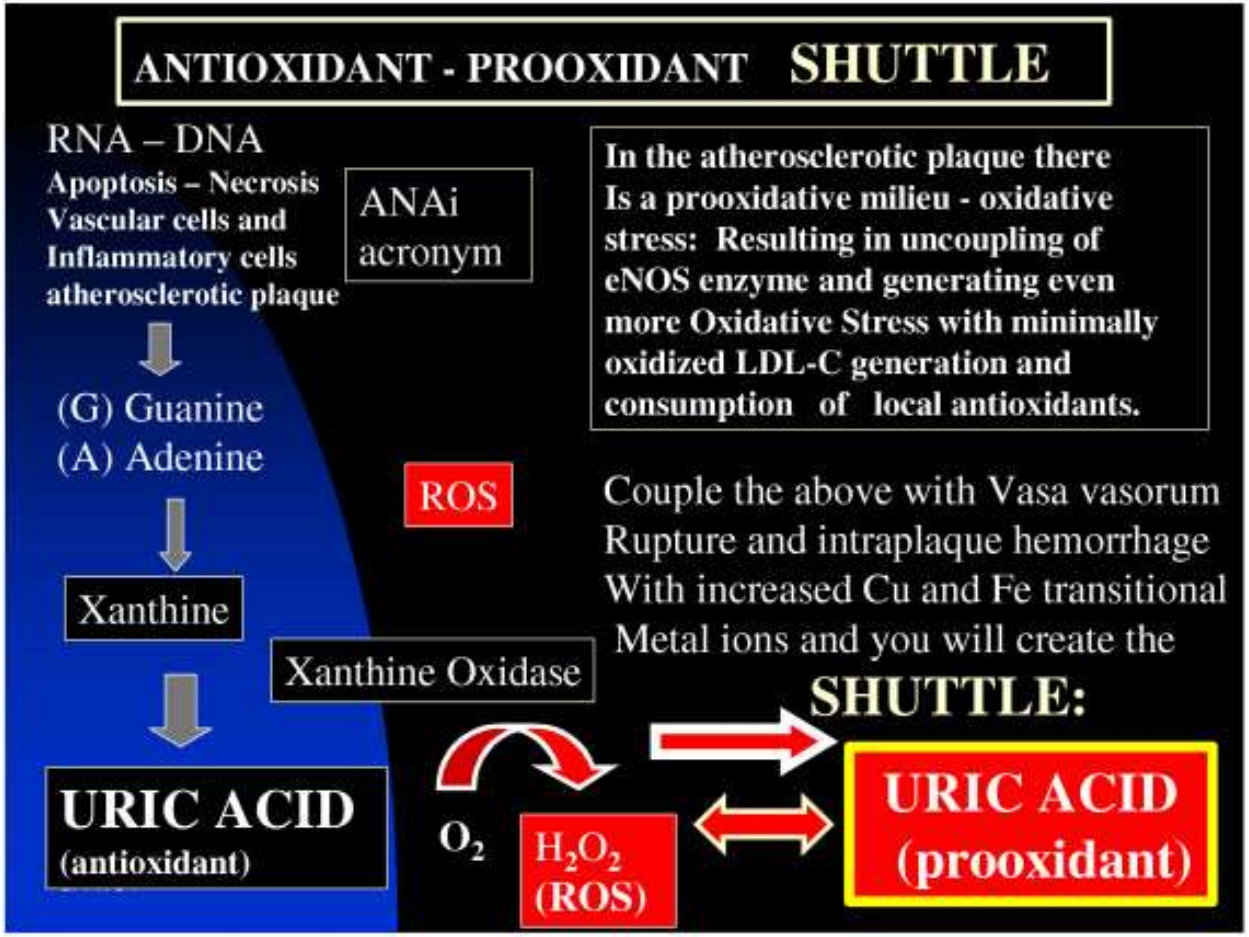


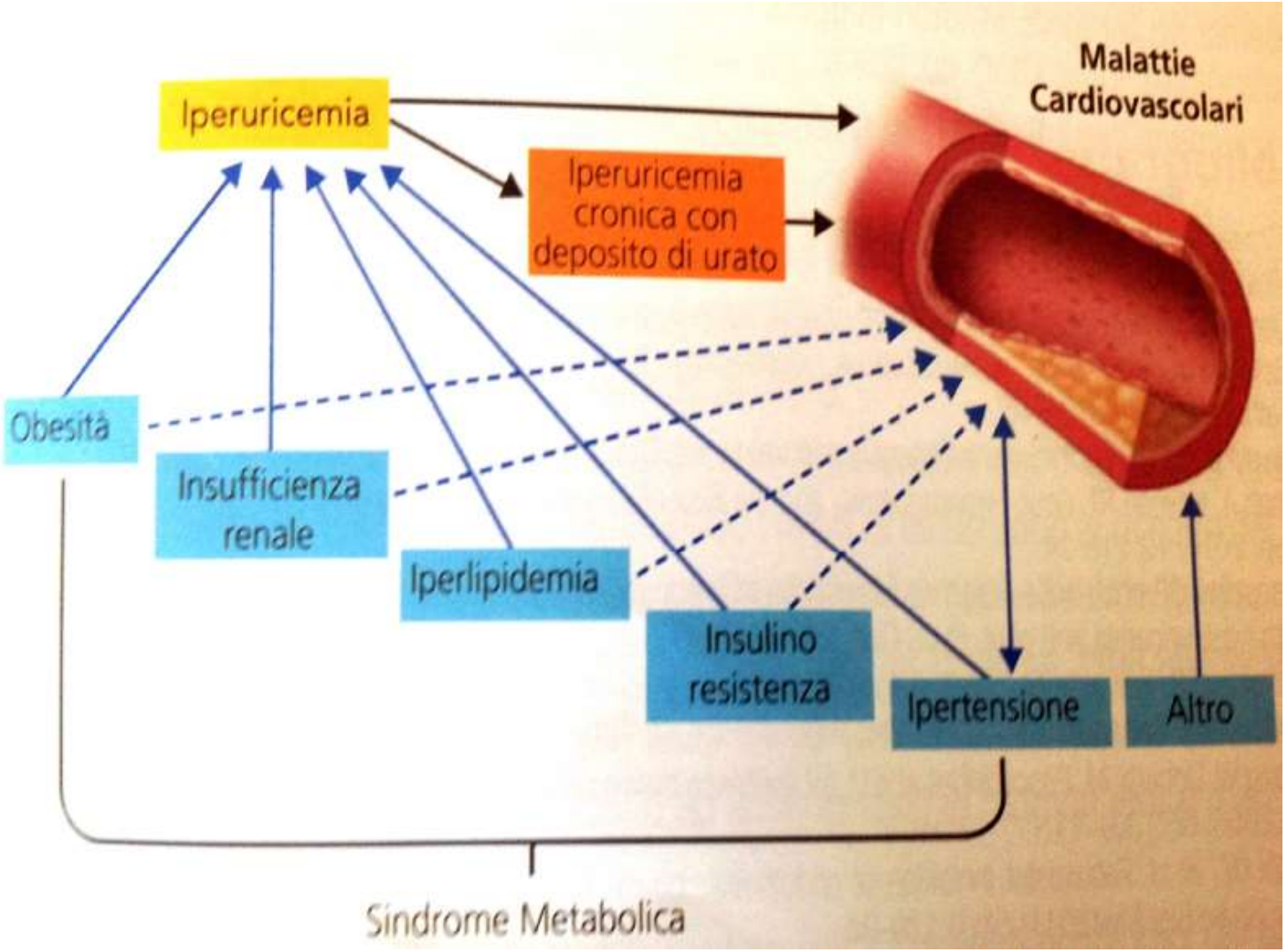
The total XDH/XO signal is increased by 60% in idiopathic dilated cardiomyopathy.

INFLAMMATORY MEDIATORS PRODUCED IN RESPONSE TO URATE CRYSTALS



I due volti dell'acido urico



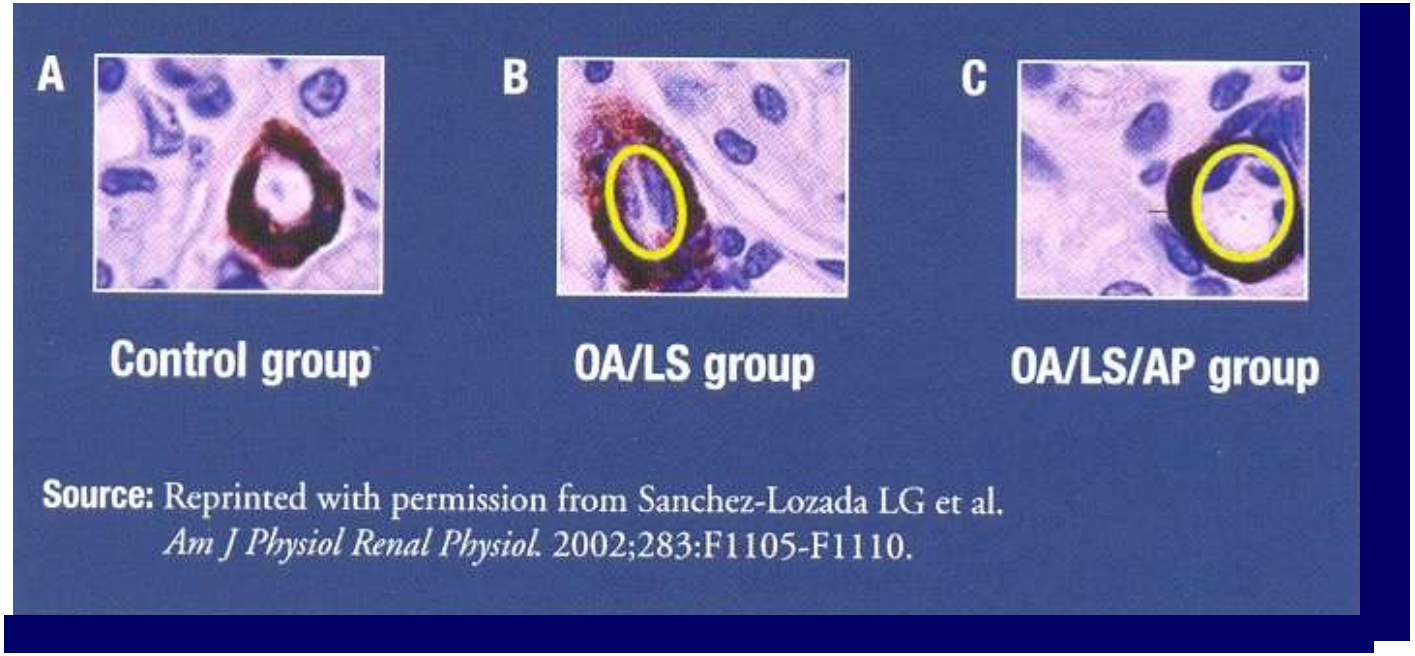

Malattie Cardiovascolari
Iperuricemia
Iperuricemia cronica con deposito di urato
Obesità
Insufficienza renale
Iperlipidemia
Insulino resistenza
Ipertensione
Altro
Sindrome Metabolica

Acido Urico: un'occhiata ad un vecchio fattore di rischio per CVD, syndrome metabolica e DM tipo 2

- **Role of UA, oxidative – redox stress, reactive O_2 species, decreased endothelial nitric oxide & endothelial dysfunction cannot be over emphasized**
- **In the pro – oxidative environment, the antioxidant properties of UA paradoxically become pro – oxidant**
- **This contributes to the oxidation of lipoproteins within atherosclerotic plaques**
- **Elevation of uric acid > 4 mg/ml should be a "red flag" to the increased risk of CVD & especially in those at risk for CVD**

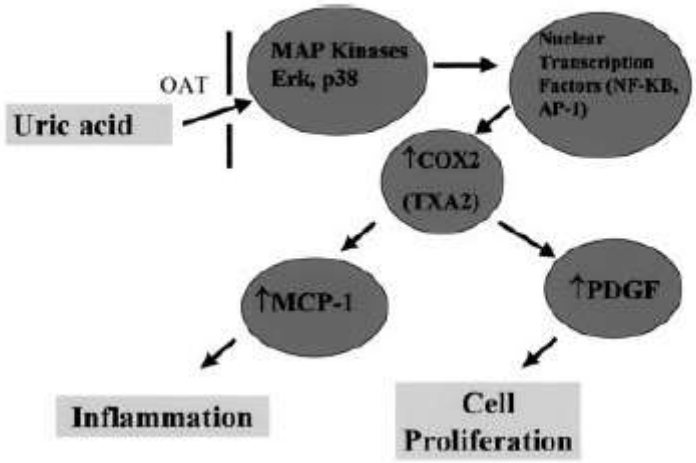
Hayden, MR & Tyagi SC. Nutrition & Metab. 2004; 1:10, 1 - 15

Uncontrolled hyperuricemia results in afferent arteriole with thick wall & small lumen (B). When urate normalized, arteriole thinner & the lumen larger (C).



Uric Acid, Vascular Smooth Muscle Cell Proliferation & Inflammation

- **Uric acid induces COX-2, TXA2 & PDGF A, which induces vascular smooth muscle cell proliferation[1]**
- **Soluble UA is pro – inflammatory[2]**
  - **Induces Monocyte Chemoattractant Protein-1**
  - **MCP-1 is a chemokine important in vascular disease & atherosclerosis[3]**
- **Soluble UA induces IL-1B, IL-6 & TNF-α[4]**



1. Rao GN et al. J Biol Chem. 1991; 266: 8604 – 8608.
2. Kanellis J et al. Hypertension. 2003; 41: 1287 – 1293.
3. Gu L et al. Mol Cell. 1998; 2: 275 -281.
4. Kang DH et al. Amer. Soc. Of Nephrol. 35th Annual Mtg Scientific Exposition, 2002; Abstract.

Hypertension
Journal of the American Heart Association

American Heart Association®

Is There a Pathogenetic Role for Uric Acid in Hypertension and Cardiovascular and Renal Disease?

Richard J. Johnson, Duk-Hee Kang, Daniel Feig, Salah Kivlighn, John Kanellis, Susumu Watanabe, Katherine R. Tuttle, Bernardo Rodriguez-Iturbe, Jaime Herrera-Acosta and Marilda Mazzali

- **U.A. stimulates vascular smooth muscle cell proliferation & induces endothelial dysfunction**
- **U.A. stimulates the production of cytokines from leukocytes & chemokines from vascular smooth muscle cells (TNF, IL-1, IL -6)**
- **Hyperuricemia activates circulating platelets**
- **Mild hyperuricemia inhibits the nitric oxide system in the kidney → vasoconstriction**

Hypertension 2003;41:1183

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Uric Acid Is Closely Linked to Vascular Nitric Oxide Activity

Evidence for Mechanism of Association With Cardiovascular Disease

Andrew J. Maxwell, MD, FACC, Kristen A. Bruinsma, MS

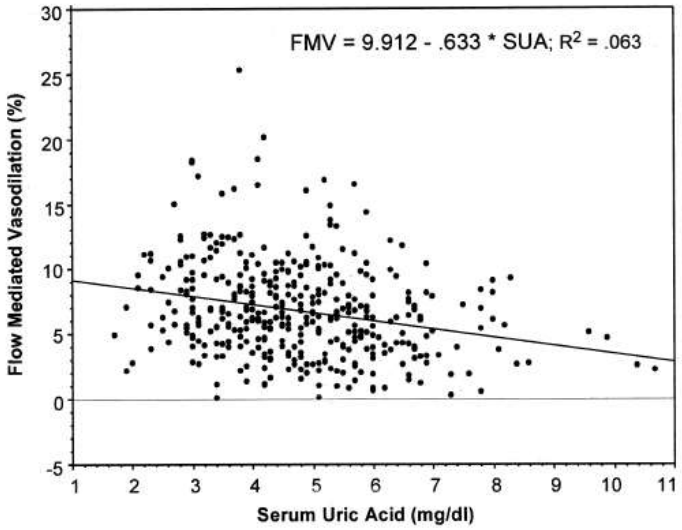
OBJECTIVES The study was undertaken to determine whether the mechanism of association of elevated serum uric acid level (SUA) with cardiovascular disease (CVD) is secondary to a common link with vascular nitric oxide (NO) activity.

BACKGROUND Epidemiologic studies demonstrate an association of elevated SUA with CVD. The mechanism of this association is unknown, but both may be linked via an impairment in vascular NO activity. To examine this, we determined the relationship of SUA to vascular NO activity and to CVD risk. We then determined the effect of enhancing vascular NO activity on SUA.

METHODS In part 1, individuals with various degrees of CVD (n = 458) were surveyed and underwent measurement of flow-mediated brachial artery vasodilation (FMV), a measure of vascular NO activity. In part 2, we performed an analysis of data pooled from six separate clinical trials of a medical food designed to enhance vascular NO activity in individuals with CVD (n = 217 subjects representing 253 treatment periods) to determine the effect on SUA.

RESULTS In part 1, of all risk factors tested, SUA was second only to age in correlation with FMV, accounting for 7% ($p < 0.0001$) of the variability in FMV. Both SUA and FMV were related to the degree of disease risk ($p < 0.0001$ and $p = 0.00025$ by analysis of variance, respectively). By multivariate analysis, SUA did not continue to contribute significantly to the determination of FMV. In part 2, enhancement of FMV (5.8 ± 4 to 8.6 ± 5, $p < 0.0001$) was associated with a decrease in SUA (5.5 ± 1.5 to 5.0 ± 1.5, $p < 0.0001$). There was no placebo effect on FMV or SUA.

CONCLUSIONS These results suggest that the association of elevated SUA with CVD may be a consequence of an impairment of vascular NO activity. This may be owing to an ability of NO to modulate uric acid production through its influence on xanthine oxidase activity. (J Am Coll Cardiol 2001;38:1850–8) © 2001 by the American College of Cardiology



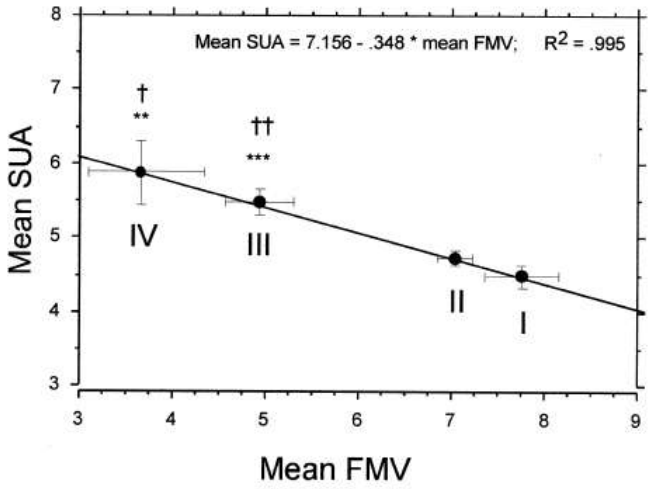


TABLE 1. Uric Acid Is Increased in Groups at Cardiovascular Risk

Group	Mechanism
Postmenopausal women and men	Estrogen is uricosuric[6]
African Americans[7]	Unknown
Renal disease	Decrease in GFR increases uric acid levels
Diuretics	Volume contraction promotes urate reabsorption
Obesity/insulin resistance	Insulin increases sodium reabsorption and is tightly linked to urate reabsorption[8]
Hypertension[9]	Urate reabsorption increased in setting of increased renal vascular resistance;[10] microvascular disease predisposes to tissue ischemia that leads to increased urate generation (from adenosine breakdown) and reduced excretion (due to lactate competing with urate transporter in the proximal tubule);[11] some hyperuricemic hypertension may be due to alcohol ingestion[12] or lead intoxication[13]
Alcohol use	Increases urate generation,[14] decreases urate excretion[15]

GFR indicates glomerular filtration rate.

Hypertension 2003;41:1183

TABLE 3. Hyperuricemia Predicts Cardiovascular Events: Studies of the Hypertensive Population

Study	Length of Follow-Up, y	Univariate Correlation with Events	Independent Predictor in Multivariate Analyses
Hypertension Detection Follow-Up Program Cooperative Research Group			
1985[36]	5	Yes	Yes
1987[37]			
Work site			
1999[38]			
PIUMA (Progetto Ipertensione Umbria Monitoraggio Ambulatoriale)			
2000[39]			
European Working Party on High BP in the Elderly			
1991[40]			
SHEP (Systolic Hypertension in the Elderly Program)*			
2001[41]	5	Yes	Yes
Syst-China*			
2001[42]	3	Yes	Yes
Syst-Eur*			
2002[43]	2	No	No

*Patients with isolated systolic hypertension; †subanalysis of patients on thiazides.

TABLE 4. Hyperuricemia Predicts Cardiovascular Events in Patients With Pre-Existing Cardiovascular Disease

Study	Univariate Correlation With Events	Independent Predictor in Multivariate Analyses
Coronary Drug Project Research Group, 1976[44]	Yes	No
French Canadian Study, 1973[45]	No	Not done
Atherogene Study, 2002[46]	Yes	Yes
The Heart Institute of Spokane, 2002[47]	Yes	Yes

Hypertension 2003;41:1183

Comorbidities associated with Hyperuricemia

- Renal manifestations[1]
- Obesity[2]
- Metabolic syndrome[3]
- Diabetes mellitus[4]
- Heart failure[5]
- Hyperlipidemia[2]
- Hypertension[6]
- Cardiovascular disease[7]

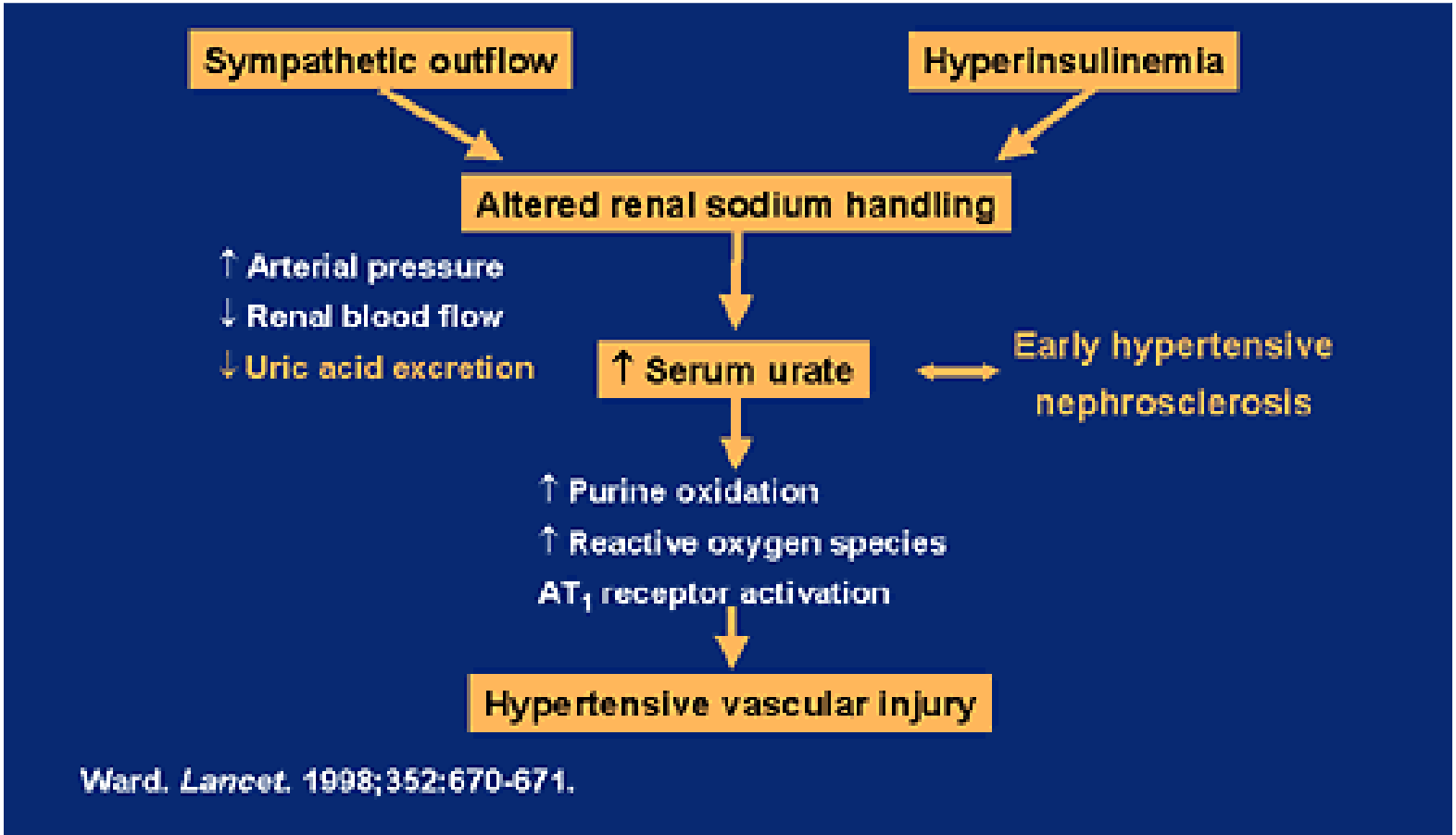
1. Vazquez-Mellado et al. Best Pract Res Clin Rheumatol. 2004;18:111-124
2. Nakakanishi et al. Int J Epidemiol. 1999;28:888-893
3. Ford et al. JAMA. 2002;287:356-359.
4. Boyko et al. Diabetes Care. 2000;23:1242-1248.
5. Anker et al. Circulation. 2003;107:1991-1997.
6. Gavin et al. Am J Cardiovasc Drugs. 2003;3:309-314.
7. Niskanen et al. Arch Intern Med. 2004;164:1546-1551.

Possibili spiegazioni che correlano l'iperuricemia alla sindrome metabolica

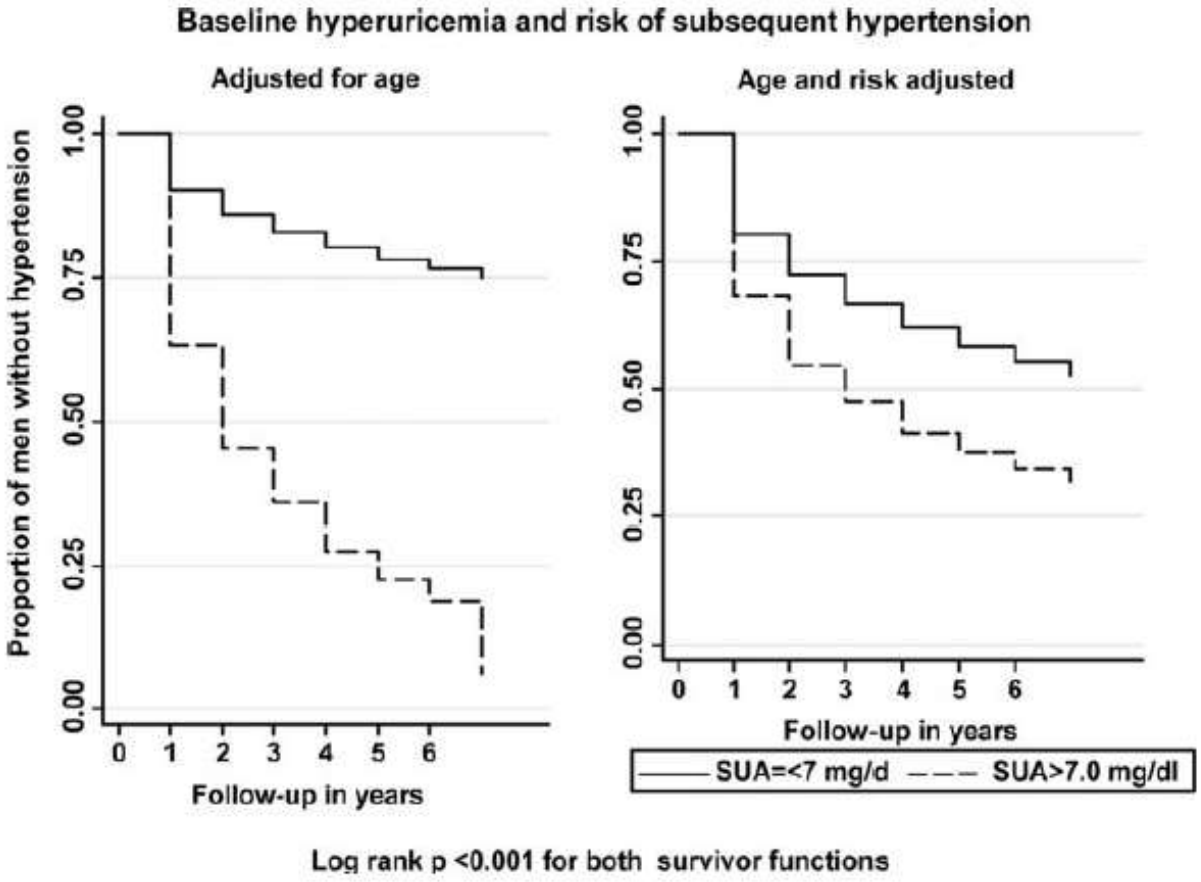
- **Role of insulin resistance**[1]
  ↑insulin → ↑urate reabsorption → hyperuricemia
- **Role of ammonium excretion**
  ↑NH_4 excretion → ↓urine pH → urolithiasis
- **Role of obesity**[2]
  obesity → ↑serum leptin → ↑uric acid

1. Vazquez-Mellado et al. *Best Practice and Res Clin Rheum.* 2004;18(2):111-124.
2. Fruehwald-Schultes et al. *Metabolism.* 1999;48(6):677-680.

Alterazioni dei livelli di acido urico e fisiopatologia dell'ipertensione – Possibile spiegazione per il link

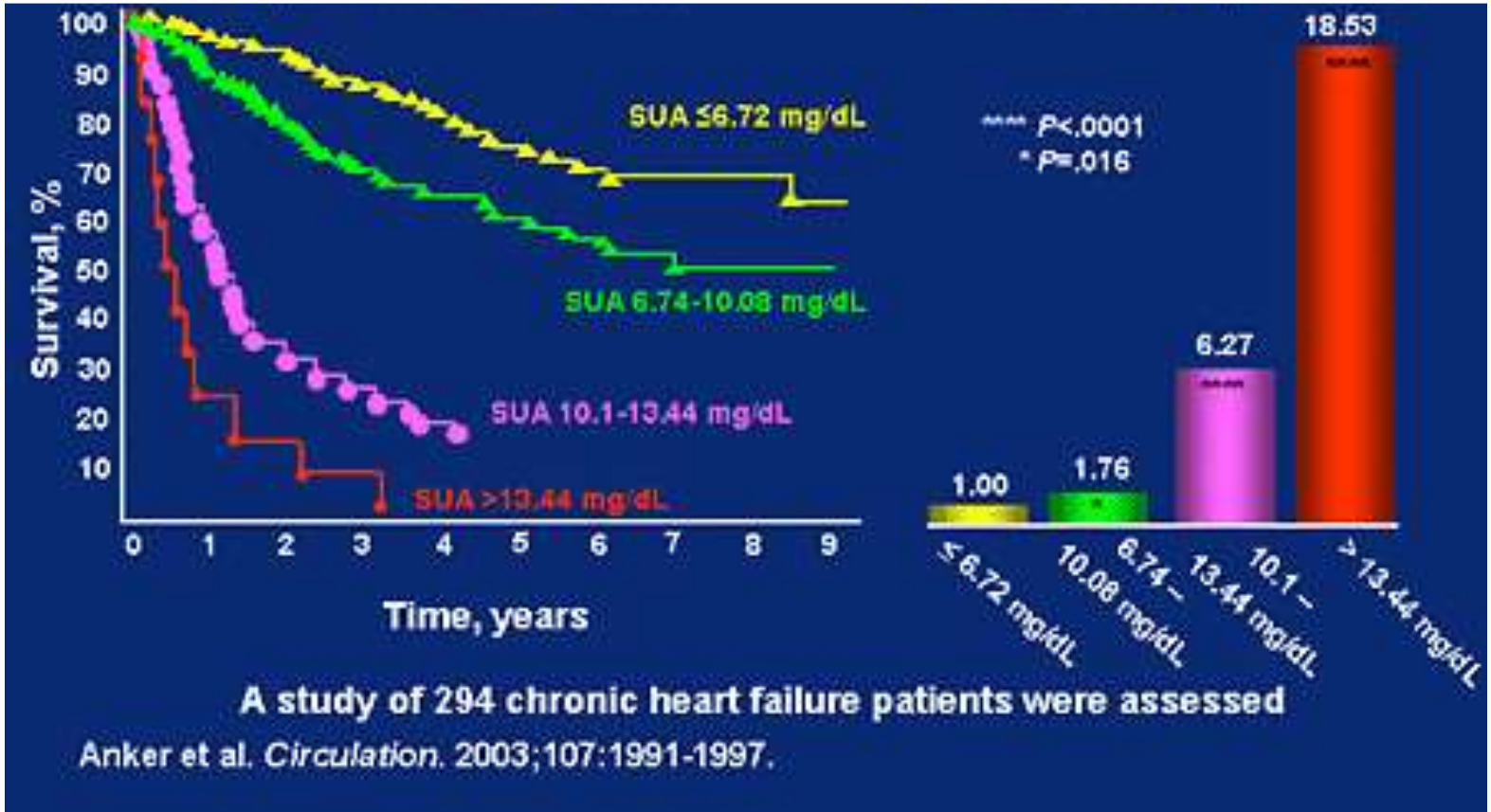


Time to develop hypertension among 803 men with baseline hyperuricemia (SUA 7.0 mg/dl) compared with 2270 men without hyperuricemia in the MRFIT study

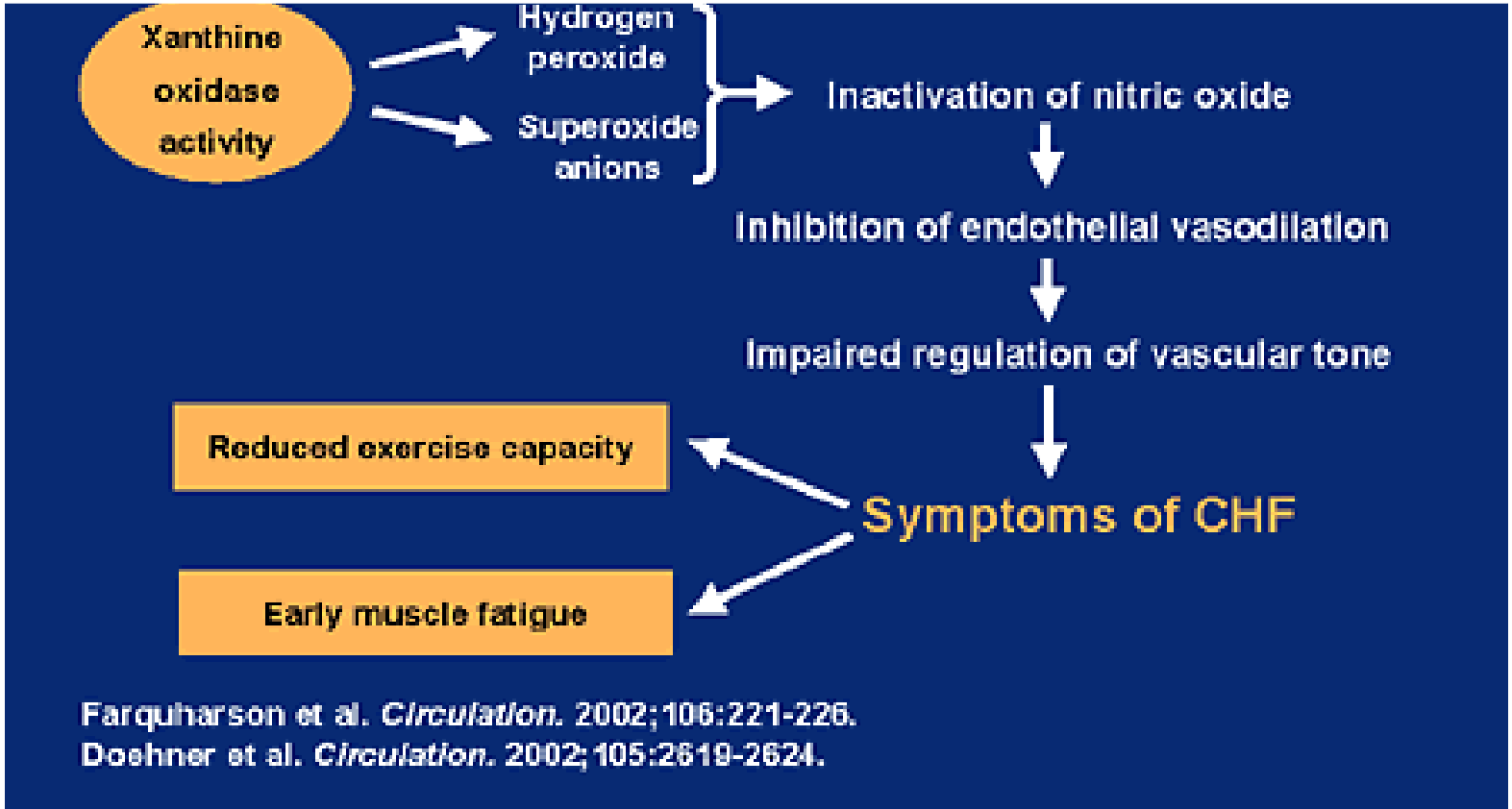


Krishnan et al., Hypertension 2007

Scompenso cardiaco
Correlazione tra SUA e sopravvivenza



Il legame allo scompenso cardiaco può considerarsi correlato all'attività della XO?



Farquharson et al. *Circulation*. 2002;106:221-226.
Doehner et al. *Circulation*. 2002;105:2619-2624.

Associazione tra iperuricemia, eventi cardiovascolari prematuri e mortalità

Finding	Supportive Studies
Hyperuricemia ↑ development of CVD, IHD, and/or CHD	✓ Breckenridge et al (*Lancet, 1966*) ✓ Framingham Heart Study *(Ann Intern Med, 1999)*
Hyperuricemia ↑ risk of CV events	✓ SHEP *(J Hypertens, 2000)* ✓ Worksite Treatment Program *(J Hypertens, 1998)* ✓ PIUMA *(Hypertension, 2000)* ✓ LIFE 2003 (*Kidney Int, 2000*) ✓ Darmawan et al *(J Rheumatol, 2003)* ✓ Lehto et al *(Stroke, 1998)*
Hyperuricemia ↑ mortality from CHD, IHD, and overall mortality	✓ NHANES (*JAMA, 2000*) ✓ Framingham Heart Study *(Ann Intern Med, 1999)* ✓ Bickel et al *(Am J Cardiol, 2002)* ✓ Darmawan et al *(J Rheumatol, 2003)* ✓ Niskanen et al (*Arch Int Med*, 2004)

Risultati NHANES III

- 15773 soggetti non istituzionalizzati seguiti per 6 anni negli USA
- Quartili di SUA (<4.3, 4.3-5.2, 5.2-6 e > 6mg/dl)
- Valutazione dei livelli di SUA e della presenza di iperuricemia cronica con deposito di urato con la mortalità cardiovascolare e totale
- Risultati: esiste una relazione indipendente tra iperuricemia con e senza deposito di urato e mortalità totale e cardiovascolare
- Correlazione lineare tra acido urico e mortalità con aumento del rischio di morte per ciascun incremento di 1 mg/dl di SUA

Stack et al., QJM 2013;106(7):647-58

Risultati dello studio LIFE

- Losartan vs atenolol over 4.8 years in population at high risk for CV events
- Mean serum urate at baseline NOT considered hyperuricemic (5.54 mg/dL for all patients)
  - Baseline serum urate still significantly associated with increased CV events
  - End-of-study increase in serum urate significantly greater in atenolol group vs losartan group (*P*<.001)
  - 29% of losartan effect may be explained by serum urate–lowering properties

Hoieggen et al. *Kidney Int.* 2004;65:1041-1049.

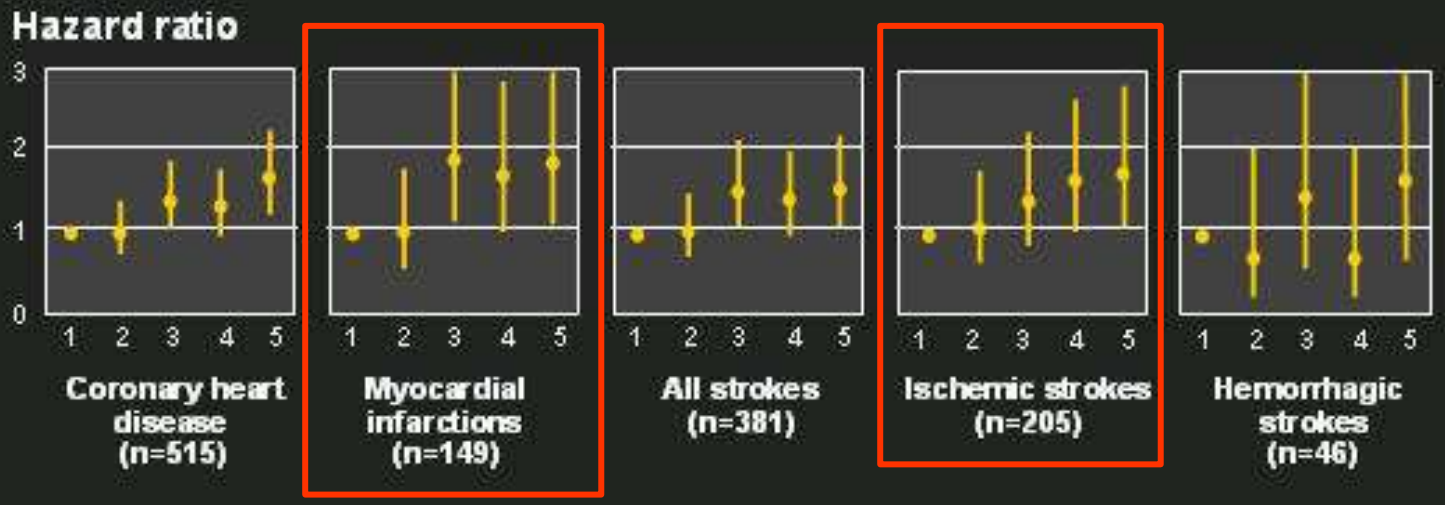
Ruolo potenziale degli urati nella cardiopatia ischemica

- L'iperuricemia promuove i seguenti fattori correlati all'aterosclerosi ed alla trombosi attraverso:
  - proliferazione delle cellule muscolari lisce
  - perossidazione lipidica
  - ossidazione delle LDL
  - produzione di radicali liberi dell'ossigeno
  - aumento dell'adesività e dell'aggregazione piastrinica
  - disfunzione endoteliale

Vazquez-Mellado et al., *Best Practice and Res Clin Rheum.* 2004; 18(2): 111-124

Acido urico come fattore di rischio per IMA e stroke (Studio Rotterdam)

- 4,385 participants aged ≥55 years; average follow-up 8.4 years
  Total of 36,794 person-years

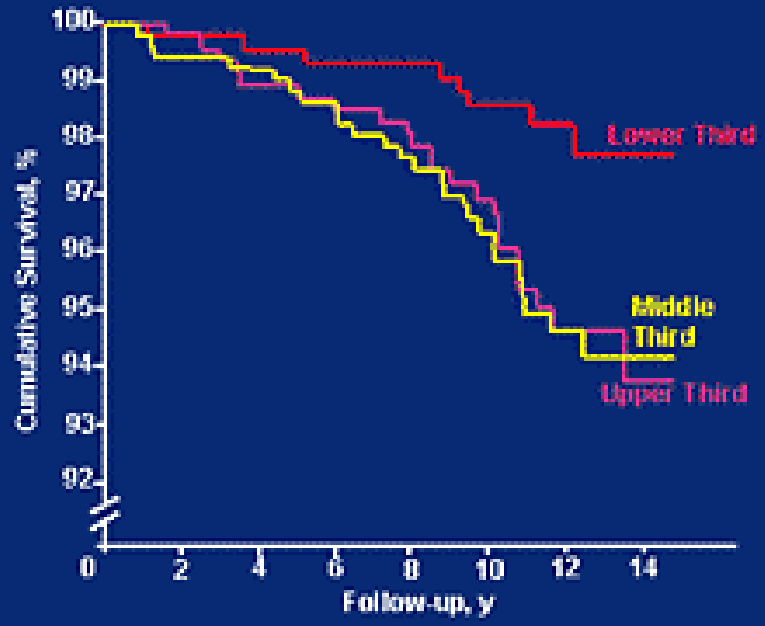


- High serum urate levels were associated with risk of MI and stroke
- Serum urate is a strong risk factor for myocardial infarction and stroke

Bos et al, Stroke 2006; 37: 1503–7

Mortalità cardiovascolare più elevata associata ad elevati valori sierici di urati

Prospective study done in 1423 healthy, middle-aged men



- Men divided into 3 groups according to serum urate levels
  - Lower third: 3.03-5.04 mg/dL
  - Middle third: 5.05-5.88 mg/dL
  - Upper third: 5.89-9.58 mg/dL

Niskanen et al. *Arch Intern Med.* 2004;164:1546-1551.

J Atheroscler Thromb. 2015 Feb 17. [Epub ahead of print]

Impact of the Serum Uric Acid Level on Subclinical Atherosclerosis in Middle-aged and Elderly Chinese.

Chen Y, Xu B, Sun W, Sun J, Wang T, Xu Y, Xu M, Lu J, Li X, Bi Y, Wang W, Ning Q.

Aim: The carotid intima-media thickness (CIMT) is now validated as a sensitive marker of atherosclerosis and is directly associated with an increased risk of cardiovascular disease. Considering that the independent association between the serum uric acid level and CIMT remains controversial due to the complex interrelationship with other known cardiovascular risk factors, further studies are needed. The aim of the present study is to explore the association between the serum uric acid level and CIMT in a general Chinese population and determine whether the association differs according to varied metabolic status. Methods: The present study was cross-sectional in design. A total of 10,281 community-based participants 40 years of age or older from Shanghai, China were included in the current analysis. All participants underwent a detailed questionnaire interview, anthropometric measurements and ultrasonography to assess the CIMT. Blood and urine samples were collected for the biochemical measurements. Results: **The serum uric acid levels were positively associated with obesity- and diabetes-related parameters and the CIMT**. In a logistic regression model controlling for potential confounders, compared with the participants in the first quartile of the uric acid level, those in the fourth quartile had a higher odds of an elevated CIMT in both men (odds ratio [OR]=1.37; 95% confidence interval [CI]=1.07-1.75) and women (OR=1.48; 95% CI=1.12-1.94). The subgroup analyses revealed that an association between an elevated CIMT and the serum uric acid level persisted regardless of diuretic use and the hypertension, diabetes mellitus and chronic kidney disease status. However, the association disappeared in the patients who consumed alcohol and in premenopausal women. Conclusions: **The serum uric acid level is positively associated with an elevated CIMT in middle-aged and elderly Chinese subjects, independent of known risk determinants of cardiovascular disease.**

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PLOS ONE

Uric Acid as a Risk Factor for Cardiovascular Disease and Mortality in Overweight/Obese Individuals

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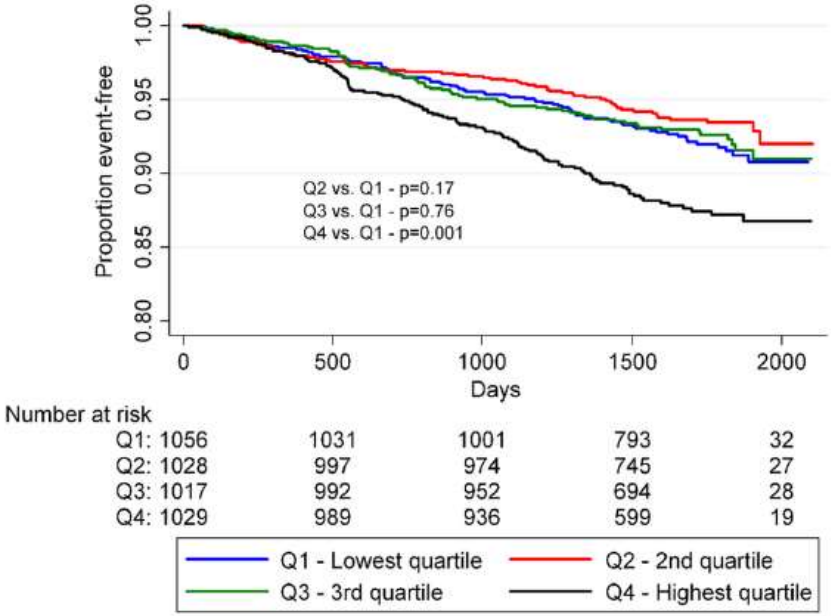
Abstract

Background: The predictive value of serum uric acid (SUA) for adverse cardiovascular events among obese and overweight patients is not known, but potentially important because of the relation between hyperuricaemia and obesity.

Methods: The relationship between SUA and risk of cardiovascular adverse outcomes (nonfatal myocardial infarction, nonfatal stroke, resuscitated cardiac arrest or cardiovascular death) and all-cause mortality, respectively, was evaluated in a post-hoc analysis of the Sibutramine Cardiovascular OUTcomes (SCOUT) trial. Participants enrolled in SCOUT were obese or overweight with pre-existing diabetes and/or cardiovascular disease (CVD). Cox models were used to assess the role of SUA as an independent risk factor.

Results: 9742 subjects were included in the study; 83.6% had diabetes, and 75.1% had CVD. During an average follow-up time of 4.2 years, 1043 subjects had a primary outcome (myocardial infarction, resuscitated cardiac arrest, stroke, or cardiovascular death), and 816 died. In a univariate Cox model, the highest SUA quartile was associated with an increased risk of cardiovascular adverse outcomes compared with the lowest SUA quartile in women (hazard ratio [HR]: 1.59; 95% confidence interval [CI]: 1.20–2.10). In multivariate analyses, adjusting for known cardiovascular risk factors the increased risk for the highest SUA quartile was no longer statistically significant among women (HR: 0.99; 95% CI: 0.72–1.36) nor was it among men. Analyses of all-cause mortality found an interaction between sex and SUA. In a multivariate Cox model including women only, the highest SUA quartile was associated with an increased risk in all-cause mortality compared to the lowest SUA quartile (HR: 1.51; 95% CI: 1.08–2.12). No relationship was observed in men (HR: 1.06; 95% CI: 0.82–1.36).

Conclusion: SUA was not an independent predictor of cardiovascular disease and death in these high-risk overweight/obese people. However, our results suggested that SUA was an independent predictor of all-cause mortality in women.



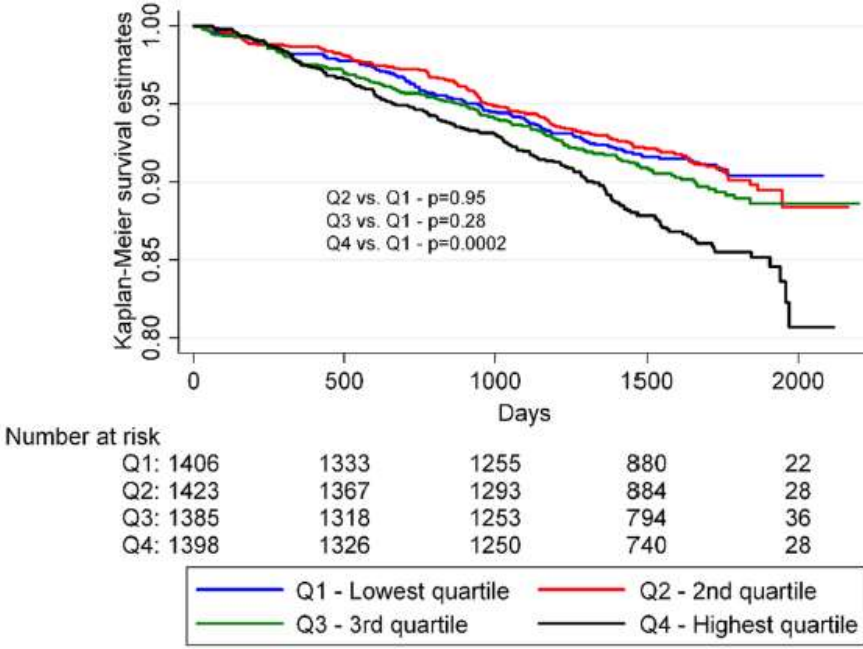


Figure 2. Proportion of event-free women by SUA quartiles. P-values were calculated using logrank statistics.
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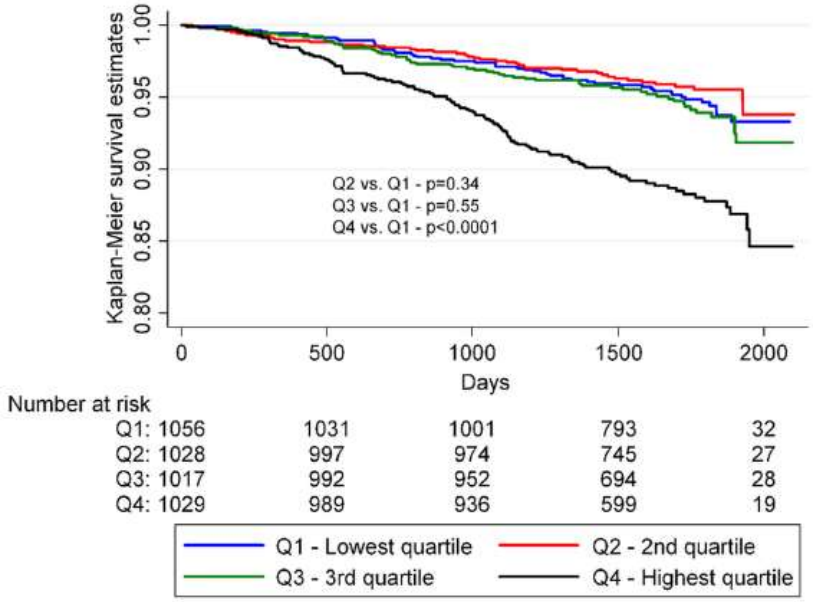

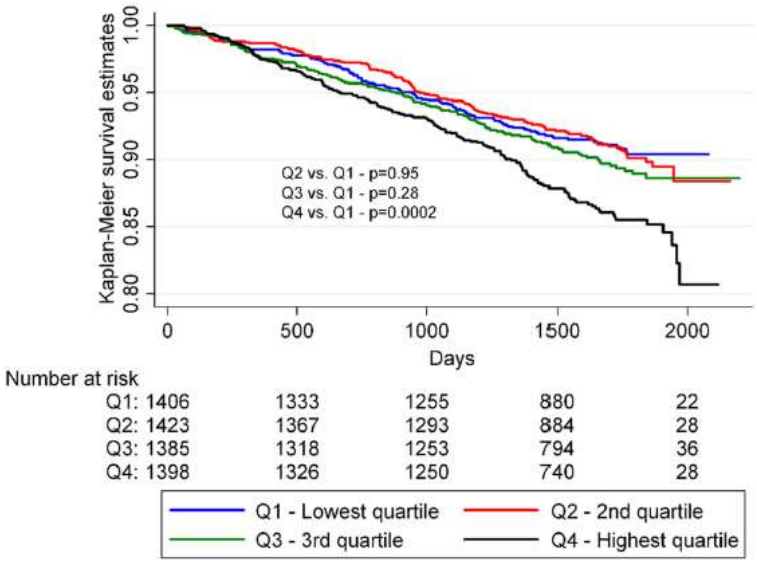

Figure 3. Kaplan-Meier survival analysis of men by SUA quartiles. P-values were calculated using logrank statistics.

Figure 4. Kaplan-Meier survival analysis of women by SUA quartiles. P-values were calculated using logrank statistics.

Uric Acid Levels and All-Cause and Cardiovascular Mortality in the Hemodialysis Population

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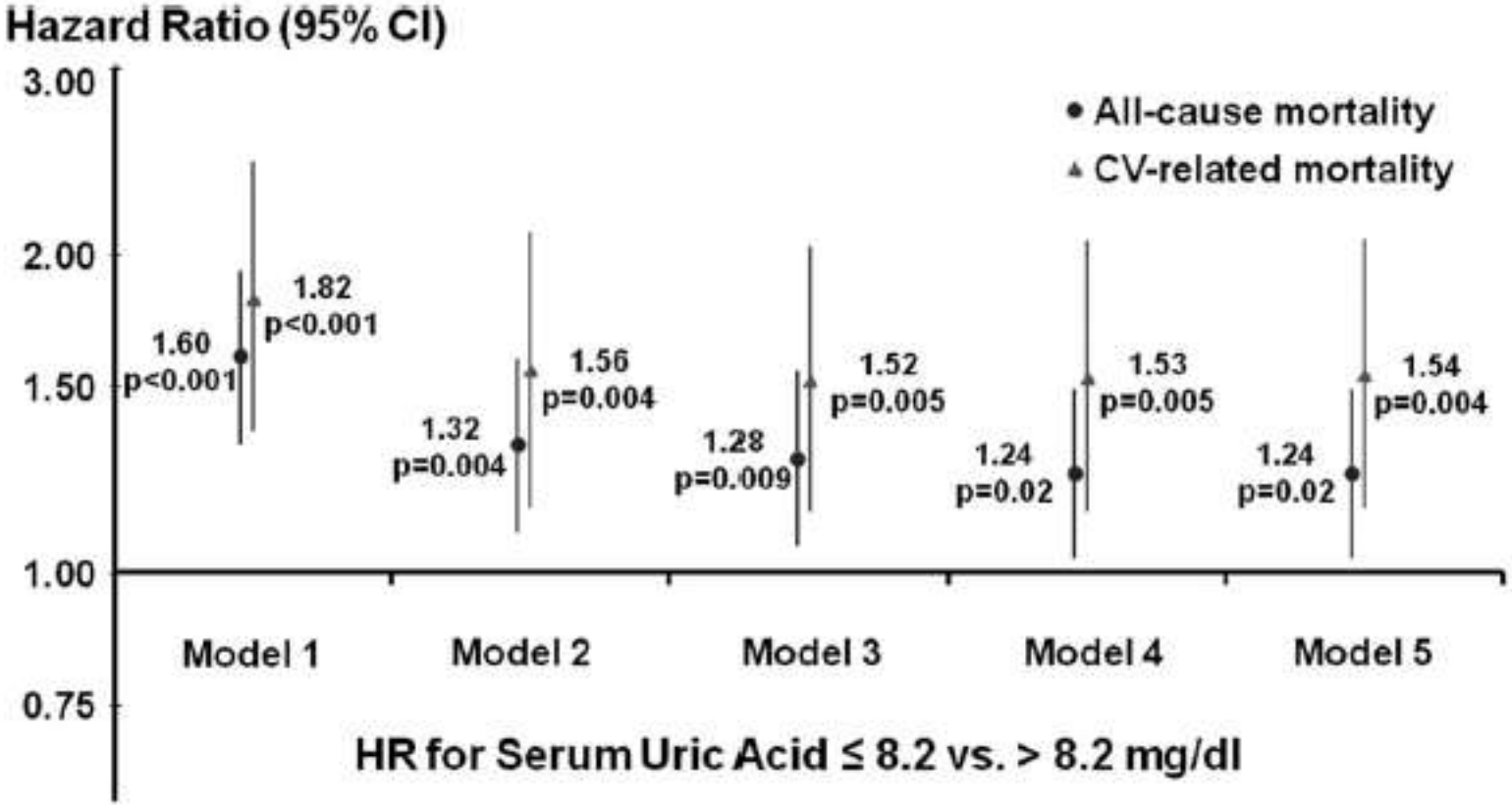
Mark R. Marshall,‡ Werner Kleophas,§ Nathan W. Levin,‖ Ananda Sen,¶ Bruce M. Robinson,†¶ and Rajiv Saran¶

Design, setting, participants, & measurements Data from 5827 patients on chronic hemodialysis from six countries affiliated with the Dialysis Outcomes and Practice Patterns Study (DOPPS) were analyzed. All laboratory data were based upon the initial cross-section of patients in DOPPS I and II. Cox regression was used to calculate the hazard ratio (HR) of all-cause and cardiovascular (CV) mortality with adjustments for case-mix including 14 classes of comorbidity.

Results There were no clinically significant differences in baseline characteristics between those who had measured uric acid (n = 4637) and those who did not (n = 1190). Uric acid level was associated with lower all-cause mortality (HR: 0.95, 95% confidence interval [CI]: 0.90 to 1.00 per 1 mg/dl higher uric acid level) and CV mortality (HR: 0.92, 95% CI: 0.86 to 0.99). When analyzed as a dichotomous variable, the adjusted HR at uric acid ≤8.2 mg/dl compared with >8.2 mg/dl was 1.24 (95% CI: 1.03 to 1.49) for all-cause mortality and 1.54 (95% CI: 1.15 to 2.07) for CV mortality.

Conclusions Higher uric acid levels were associated with lower risk of all-cause and CV mortality in the hemodialysis population. These results are in contrast to the association of hyperuricemia with higher cardiovascular risk in the general population and should be the subject of further research.

Clin J Am Soc Nephrol 6: 2470–2477, 2011



Model 1: Stratified by DOPPS phase and country and adjusted for facility clustering effects
Model 2: Model 1 + age, black race, gender, BMI, time since ESRD
Model 3: Model 2 + 14 summary comorbidities
Model 4: Model 3 + albumin-corrected calcium, albumin, ferritin, creatinine, phosphorus
Model 5: Model 4 + use of allopurinol;

Clin J Am Soc Nephrol 6: 2470–2477, 2011

- Higher uric acid among hemodialysis patients is a surrogate for better nutritional status, as evidenced by the positive association with higher nPCR, creatinine, phosphorous, and BMI.
- Similar to uric acid, homocysteine is also a marker of better nutritional status and higher protein intake
- Uric acid has been shown to have antioxidant properties *in vitro* and this property may account for some of the benefit observed in the hemodialysis population, where oxidative stress is thought to be mechanistically linked with the excess cardiovascular mortality

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GOUT AND THE RISK OF ALZHEIMER'S DISEASE: A POPULATION-BASED, BMI-MATCHED COHORT STUDY.

Lu N, Dubreuil M, Zhang Y, Neogi T, Rai SK, Ascherio A, Hernán MA, Choi HK.

OBJECTIVE:

While gout is associated with cardiovascular (CV)-metabolic comorbidities and their sequelae, the antioxidant effects of uric acid may have neuroprotective benefits. We evaluated the potential impact of incident gout on the risk of developing Alzheimer's disease (AD) in a general population context.

METHODS:

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RESULTS:

We identified 309 new cases of AD among 59 224 patients with gout (29% female, mean age 65 years) and 1942 cases among 238 805 in the comparison cohort over a 5-year median follow up (1.0 vs 1.5 per 1000 person-years, respectively). Univariate (age-matched, sex-matched, entry-time-matched and BMI-matched) and multivariate HRs for AD among patients with gout were 0.71 (95% CI 0.62 to 0.80) and 0.76 (95% CI 0.66 to 0.87), respectively. The inverse association persisted among subgroups stratified by sex, age group (<75 and ≥75 years), social deprivation index and history of CV disease. The association between incident OA and the risk of incident AD was null.

CONCLUSIONS:

These findings provide the first general population-based evidence that gout is inversely associated with the risk of developing AD, supporting the purported potential neuroprotective role of uric acid.

In ogni caso:

- L'assenza di manifestazioni cliniche dell'iperuricemia cronica con deposito di urato non implica necessariamente che il soggetto esaminato sia realmente sano
- Importanza di riconsiderare il concetto di asintomaticità nei pazienti iperuricemici

- Allopurinolo: isomero strutturale ipoxantina, inibitore competitivo XO;
- Febuxostat: inibitore non purinico della XO; azione antagonista nei confronti di entrambe le isoforme della XO; riduzione sia dei livelli di SUA che della produzione di anione superossido, antagonizzando così lo stress ossidativo

Take home messages (1)

- L'associazione tra iperuricemia ed altre comorbilità sembra essere biologicamente molto rilevante

Sono comunque necessarie maggiori informazioni

- L'iperuricemia è un fattore di rischio indipendente per malattia cardiovascolare o è solo un marker?

- Il trattamento dell'iperuricemia funziona davvero nella gestione delle comorbilità?

Take home messages (2)

- I livelli plasmatici di acido urico sono correlati alla malattia cardiovascolare in modo significativo
- Questa relazione può essere mediata dall'insorgenza di ipertensione arteriosa
- L'impatto cardiovascolare dei livelli sierici di acido urico può essere investigato precocemente nella vita a prescindere dalla presenza di gotta
- Il meccanismo responsabile di malattia cardiovascolare potrebbe riguardare l'interazione tra gli elevati livelli di acido urico e lo stress ossidativo associato all'attivazione della XOR
- L'effetto preventivo CV di strategie finalizzate alla riduzione dei livelli sierici di acido urico (inibizione XOR) è una sfida per il prossimo futuro

"I told him it wouldn't kill him to try to be nice once in a while, but I was wrong."


Grazie per l’attenzione