



68° CONGRESSO NAZIONALE **SIGG**

Ritorno al futuro

FIRENZE, 13-16 DICEMBRE 2023
PALAZZO DEI CONGRESSI



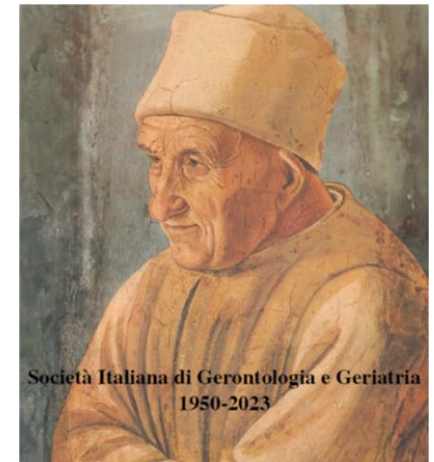
AGING KIDNEY: FISIOPATOLOGIA E CLINICA



Società Italiana di Gerontologia e Geriatria
1950-2023

Andrea Ungar

Università di Firenze



Società Italiana di Gerontologia e Geriatria
1950-2023



68° CONGRESSO NAZIONALE **SIGG**

Ritorno al futuro

FIRENZE, 13-16 DICEMBRE 2023
PALAZZO DEI CONGRESSI



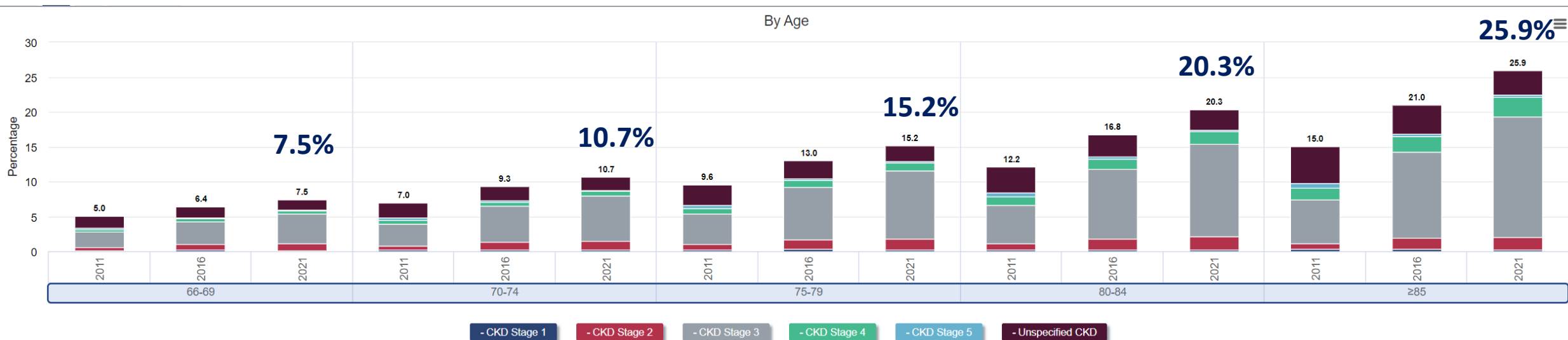
AGING KIDNEY: FISIOPATOLOGIA E CLINICA

La prevalenza



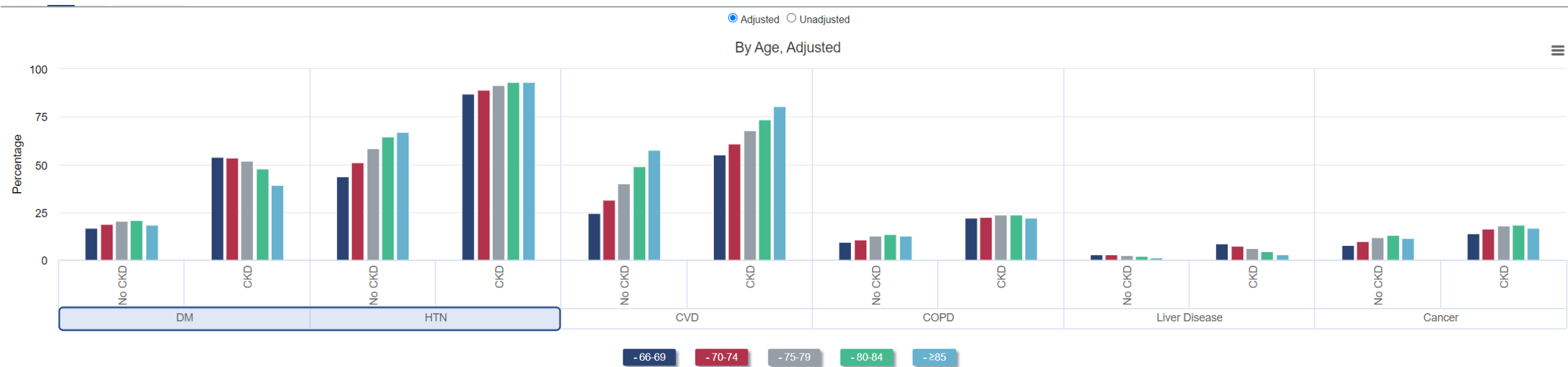


Prevalence of CKD overall and by stage in older adult Medicare FFS beneficiaries, 2011-2021



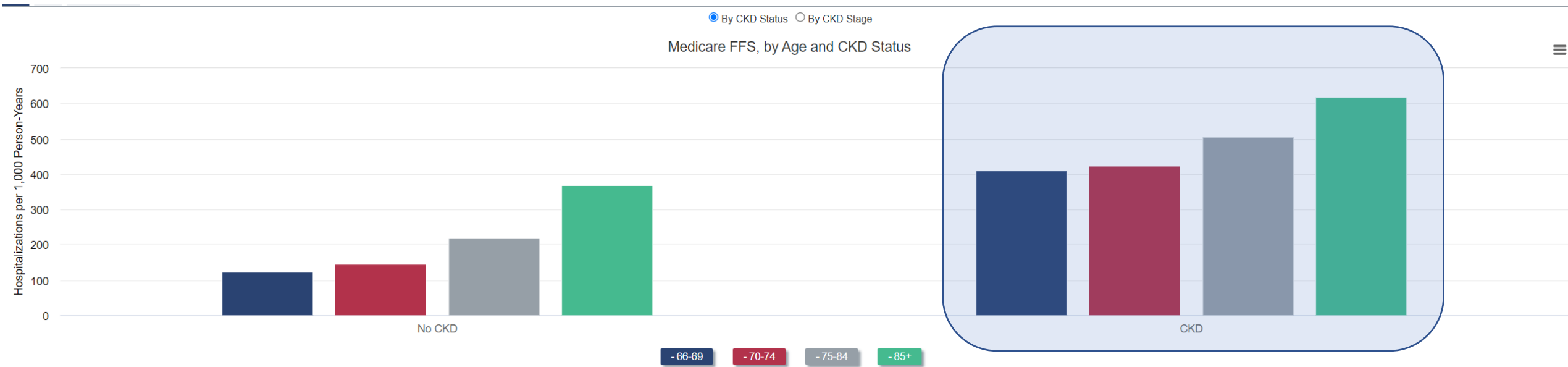


Prevalence of **comorbid conditions** in older adult Medicare FFS beneficiaries by age, 2021





Adjusted all-cause **hospitalization** rates in older adults, by Age and CKD, 2021





68° CONGRESSO NAZIONALE **SIGG**

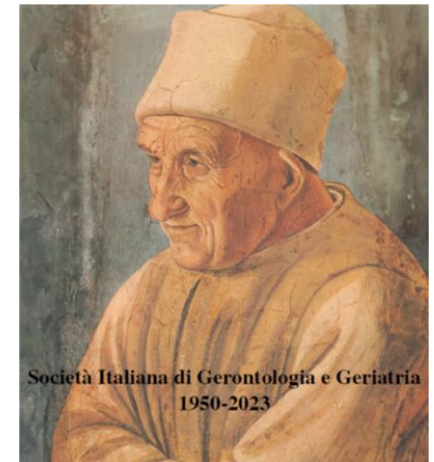
Ritorno al futuro

FIRENZE, 13-16 DICEMBRE 2023
PALAZZO DEI CONGRESSI



AGING KIDNEY: FISIOPATOLOGIA E CLINICA

Come misurare il
GFR





Original article



Low Creatinine Potentially Overestimates Glomerular Filtration Rate in Older Fracture Patients: A Plea for an Extensive Use of Cystatin C?

Iacopo Iacomelli ^{a,1}, Antonella Giordano ^{b,1}, Giulia Rivasi ^b, Martina Rafanelli ^b, Virginia Tortù ^b, Alessandro Cartei ^c, Carlo Rostagno ^c, Mauro Di Bari ^b, Niccolò Marchionni ^d, Enrico Mossello ^b, Andrea Ungar ^{b,*}

Valutazione funzione renale con Creatinina, Cistatina e Creatinina/Cistatina

Table 1

Characteristics of the study population at admission.

	All patients (n = 425)
Mean age (years)	84 ± 7.6
Female	325 (76.5)
Creatinine (mg/dL)	0.97 ± 0.58
Cystatin C (mg/L)	1.53 ± 0.65
MDRD (mL/min/1.73 m²)	71 ± 26.0
CKD-EPlcr(mL/min/1.73 m²)	65 ± 21.0
CKD-EPlcys(mL/min/1.73 m²)	46 ± 19.4
CKD-EPlcr/cys(mL/min/1.73 m²)	55 ± 20.0

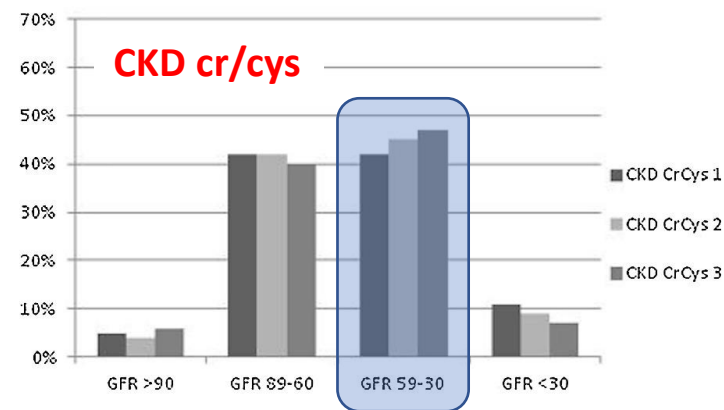
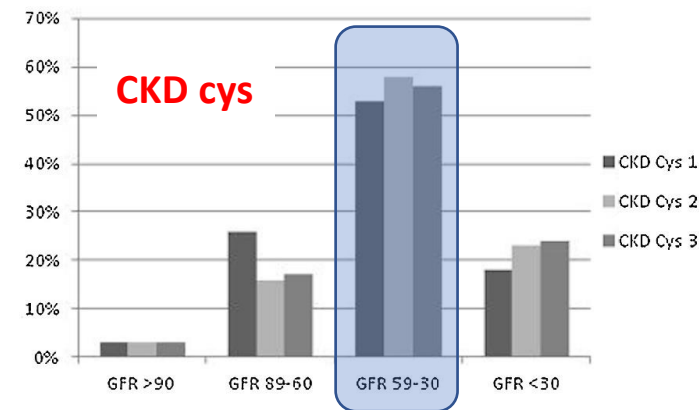
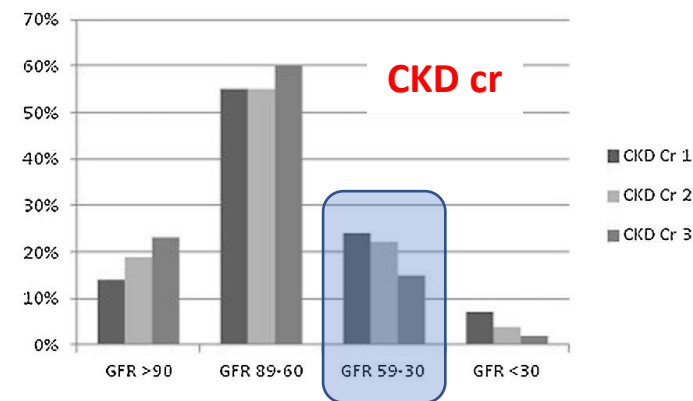
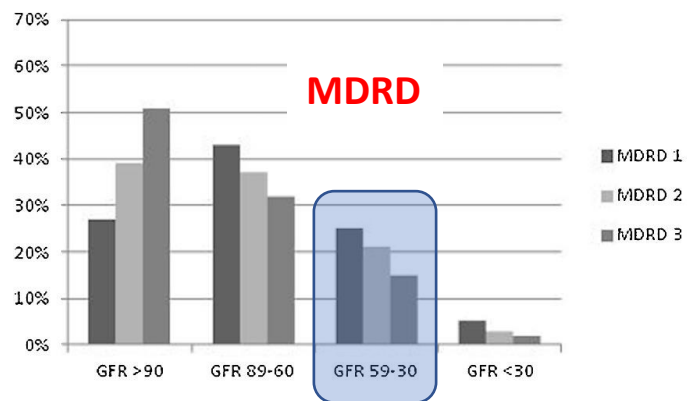


Original article



Low Creatinine Potentially Overestimates Glomerular Filtration Rate in Older Fracture Patients: A Plea for an Extensive Use of Cystatin C?

Iacopo Iacomelli^{a,1}, Antonella Giordano^{b,1}, Giulia Rivasi^b, Martina Rafanelli^b, Virginia Tortù^b,
Alessandro Cartei^c, Carlo Rostagno^c, Mauro Di Bari^b, Niccolò Marchionni^d, Enrico Mossello^b,
Andrea Ungar^{b,2}





Original article

Low Creatinine Potentially Overestimates Glomerular Filtration Rate in Older Fracture Patients: A Plea for an Extensive Use of Cystatin C?



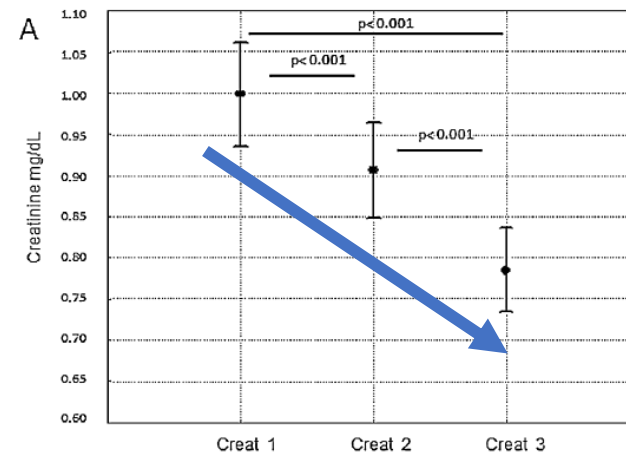
Iacopo Iacomelli^{a,1}, Antonella Giordano^{b,1}, Giulia Rivasi^b, Martina Rafanelli^b, Virginia Tortù^b, Alessandro Cartei^c, Carlo Rostagno^c, Mauro Di Bari^b, Niccolò Marchionni^d, Enrico Mossello^b, Andrea Ungar^{b,2}

Variazione Creatinina e Cistatina durante il ricovero

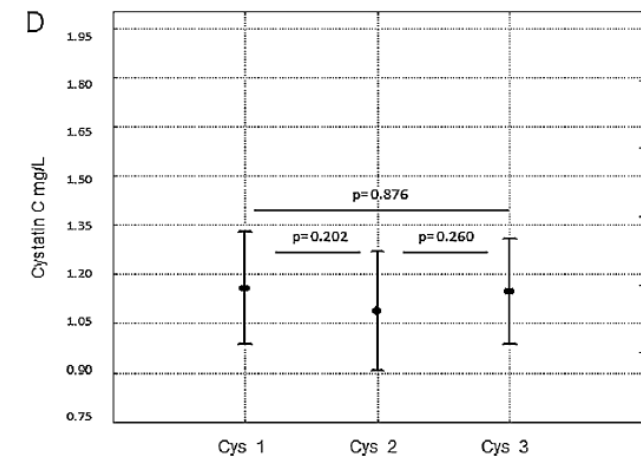
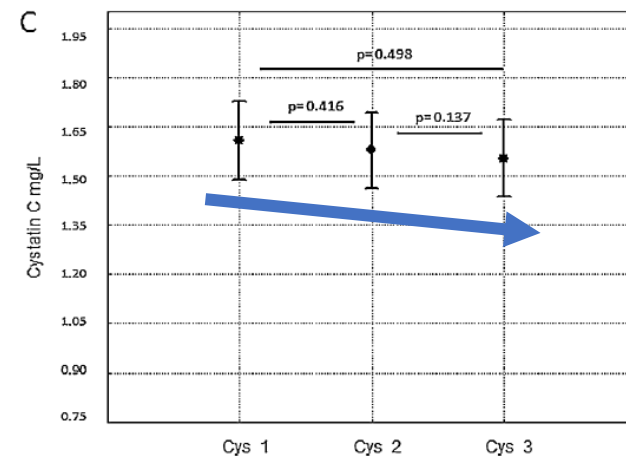
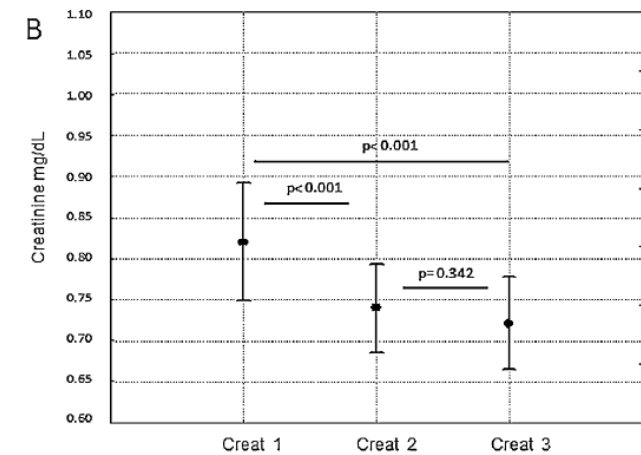
Creatinina

Cistatina

Frattura femore



Frattura omero





Contents lists available at ScienceDirect

European Journal of Internal Medicine

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



Renal function and delirium in older fracture patients: different information from different formulas?

Enrico Mossello^a, Giulia Rivasi^a, Virginia Tortù^a, Antonella Giordano^a, Iacopo Iacomelli^a, Maria Chiara Cavallini^a, Martina Rafanelli^a, Alice Ceccofiglio^a, Alessandro Cartei^b, Carlo Rostagno^b, Mauro Di Bari^a, Andrea Ungar^{a,*}

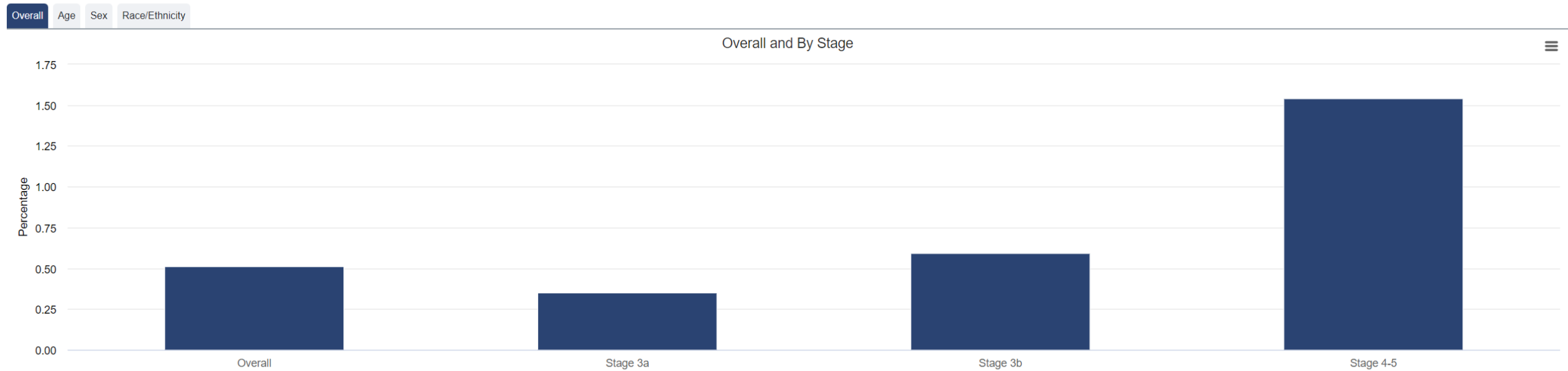
In older patients hospitalized for traumatic fractures, moderate renal dysfunction was independently associated with delirium in subjects aged 75–84, but not among the oldest ones.

In comparison with the most used CKD-EPIcr and MDRD formulas, the observed association was stronger when glomerular filtration rate was estimated with cystatin-based (CKD-EPIcys, CKD-EPIcr-cys, BIS-2)



Percentage of adults with stage 3-5 CKD receiving testing for cystatin C, 2019-2021

Figure 8.13 Percentage of adults with stage 3-5 CKD receiving testing for cystatin C, 2019-2021



Data source: M Health Fairview stages 3-5. December 31 point prevalent patients aged ≥18 years. 2019-2021 combined cohorts.



Percentage of adults with stage 3-5 CKD receiving testing for cystatin C, 2019-2021

Figure 8.13 Percentage of adults with stage 3-5 CKD receiving testing for cystatin C, 2019-2021

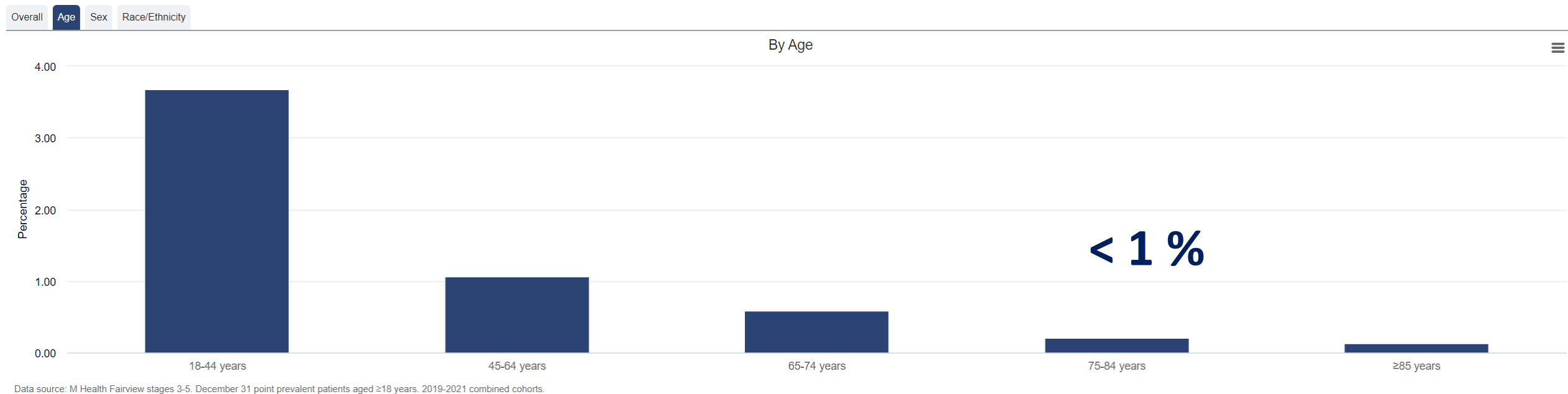


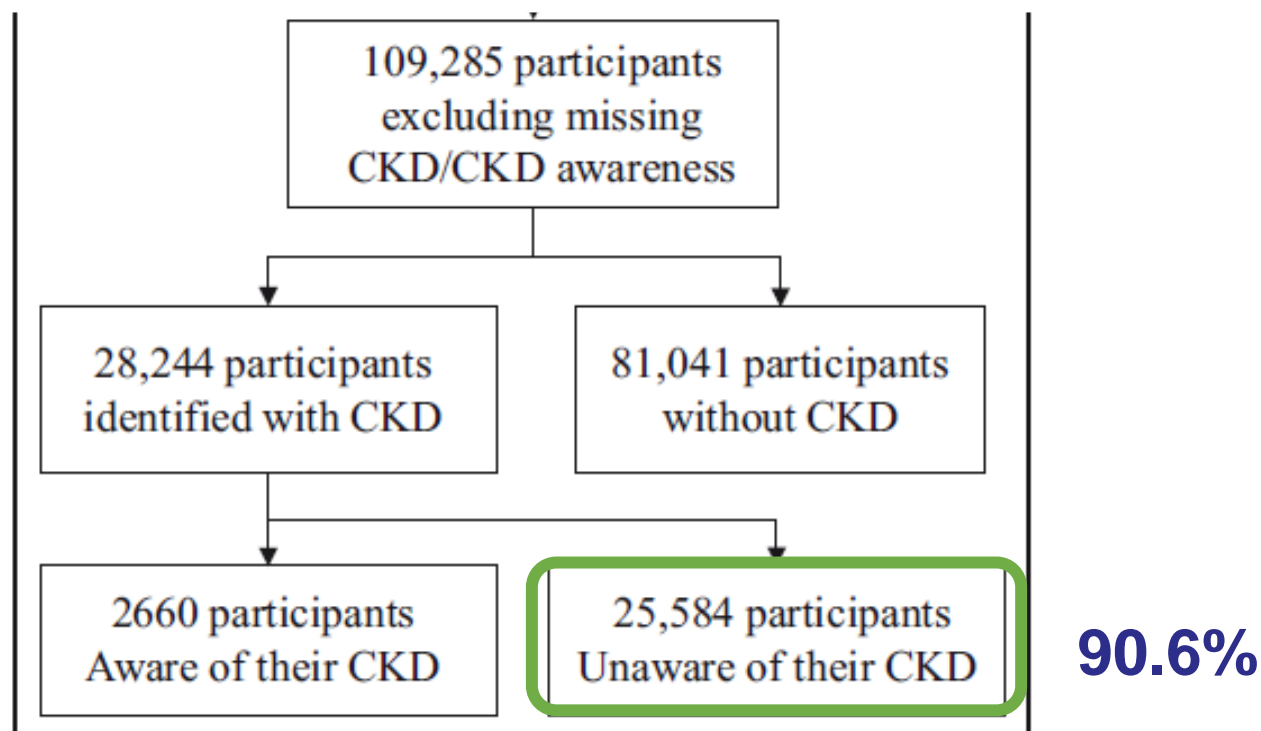
Figure 8.13 shows the percentage of patients from the M Health Fairview system who had stages 3-5 CKD based on serum creatinine values and clinical diagnoses who received a cystatin C test order in 2019-2021. Overall, 0.5% of patients had a cystatin C test order. The rate of test ordering was much higher among patients with more advanced CKD (e.g., 1.5% among those with stage 4 or 5 CKD), younger patients (3.7% among those aged 18-44 years), and Black patients (0.9% versus 0.47% among White patients).



Awareness of Kidney Disease and Relationship to End-stage Renal Disease and Mortality

THE AMERICAN
JOURNAL of
MEDICINE®

Adam Whaley-Connell, DO, MSPH,^a Michael G. Shlipak, MD, MPH,^b Lesley A. Inker, MD, MS,^c Manjula Kurella Tamura, MD, MPH,^d Andrew S. Bomback, MD, MPH,^e Georges Saab, MD,^f Susanna M. Szpunar, PhD,^g Samy I. McFarlane, MD, MPH,^h Suying Li, PhD,ⁱ Shu-Cheng Chen, MS,ⁱ Keith Norris, MD,^j George L. Bakris, MD,^k Peter A. McCullough, MD, MPH,^g on behalf of the Kidney Early Evaluation Program Investigators



2012

CardioLink

SCIENTIFIC NEWS

CALCOLO DEL
FILTRATO GLOMERULARE

SCARICA
LA NUOVA

APP



CALCOLO DEL FILTRATO GLOMERULARE

Edito da: **Andrea Ungar**

Centro di Riferimento Regionale per l'Ipertensione Arteriosa nell'Anziano - Cardiologia e Medicina Geriatrica. Azienda Ospedaliero-Universitaria Careggi, Università di Firenze

In collaborazione con: **Web Lab** di www.cardiolink.it

Leggi l'articolo **MISURA** sull'impiego delle diverse formule di calcolo del GFR

Creatinina Sierica

numero

mg/dL

μ mol/L

Cistatina C

numero

mg/L

Età

numero

anni

Peso

numero

kg

Razza

Nera

Altra Razza

Sesso

Maschio

Femmina

Riferibile a IDMS

No

Si

Calcola



Frailty and Chronic Kidney Disease: The Third National Health and Nutrition Evaluation Survey

Emilee R. Wilhelm-Leen, BA,^a Yoshio N. Hall, MD,^c Manjula K. Tamura, MD, MPH,^b Glenn M. Chertow, MD, MPH^b

Table 2 Prevalence of Frailty and Domains

	Overall % (SE)	No CKD % (SE)	Stage 1/2 % (SE)	Stage 3a % (SE)	Stage 3b, 4, 5 % (SE)
Shrinkage	2.64 (0.20)	2.32 (0.23)	3.66 (0.62)	2.07 (1.13)	3.01 (2.13)
Weakness	13.13 (0.83)	10.45 (0.65)	21.57 (1.87)	36.20 (4.71)	36.78 (4.82)
Exhaustion	4.01 (0.38)	2.55 (0.32)	6.81 (1.18)	11.31 (2.36)	27.12 (4.24)
Low activity	21.85 (0.70)	20.82 (0.72)	28.26 (1.96)	25.77 (4.31)	29.19 (4.81)
Slow walking ^a	13.35 (0.71)	7.33 (0.51)	15.17 (1.29)	28.73 (4.11)	31.54 (6.31)
Frail^b	2.77 (0.34)	1.47 (0.21)	5.94 (0.99)	10.74 (2.36)	20.90 (3.44)

CKD = chronic kidney disease; SE = standard error.

^aThe slowest-walking quintile adjusted for gender was defined before adjustment for complex survey design.

^bFrail persons exhibit ≥ 3 of 3 to 5 available frailty domains.



Frailty and Chronic Kidney Disease: The Third National Health and Nutrition Evaluation Survey

Emilee R. Wilhelm-Leen, BA,^a Yoshio N. Hall, MD,^c Manjula K. Tamura, MD, MPH,^b Glenn M. Chertow, MD, MPH^b

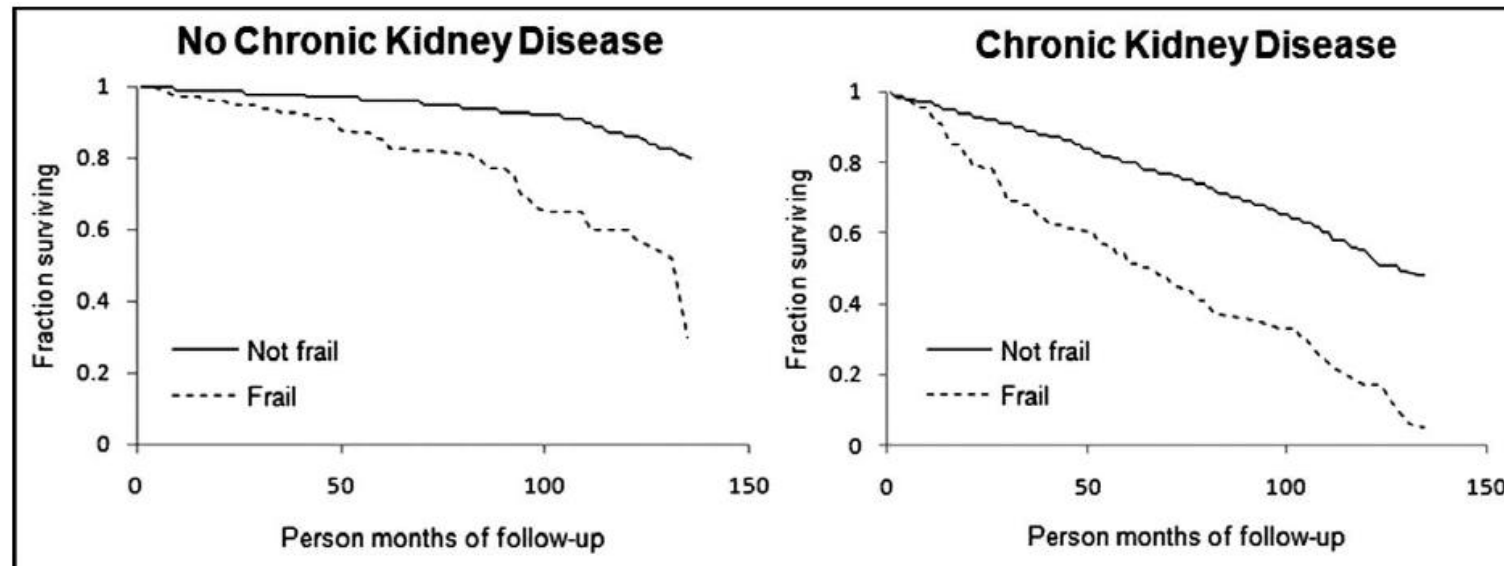


Figure 3 Frailty, chronic kidney disease, and survival.



68° CONGRESSO NAZIONALE **SIGG**

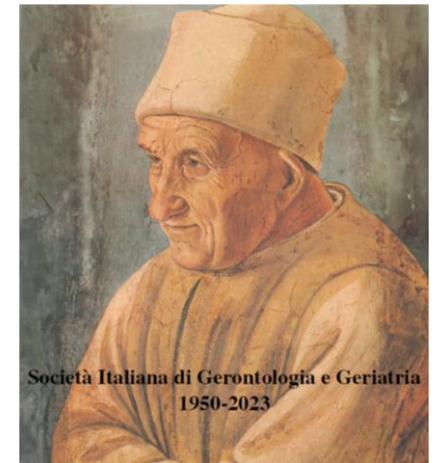
Ritorno al futuro

FIRENZE, 13-16 DICEMBRE 2023
PALAZZO DEI CONGRESSI



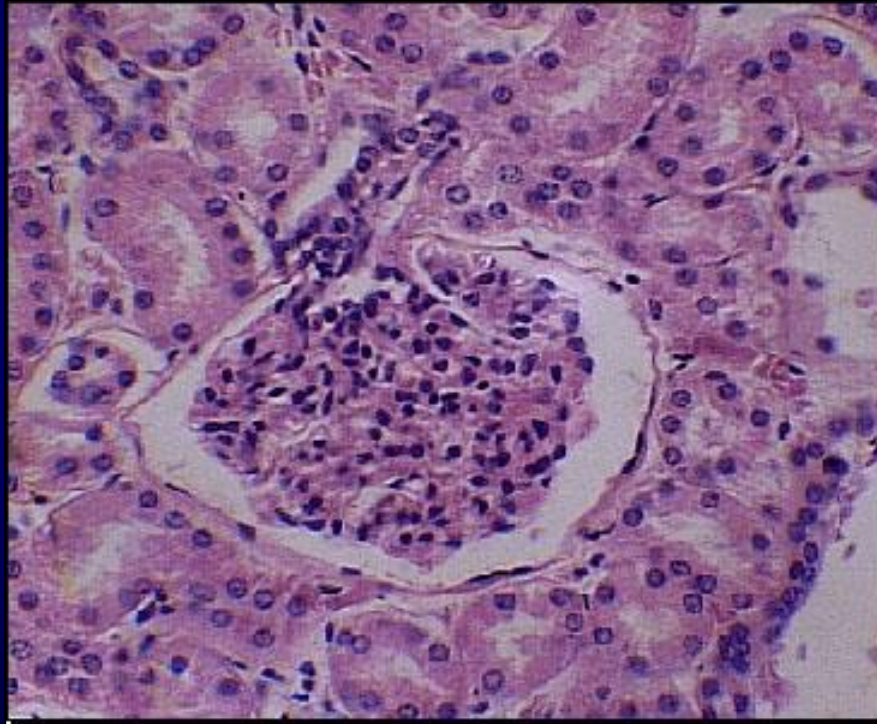
AGING KIDNEY: FISIOPATOLOGIA E CLINICA

La fisiopatologia



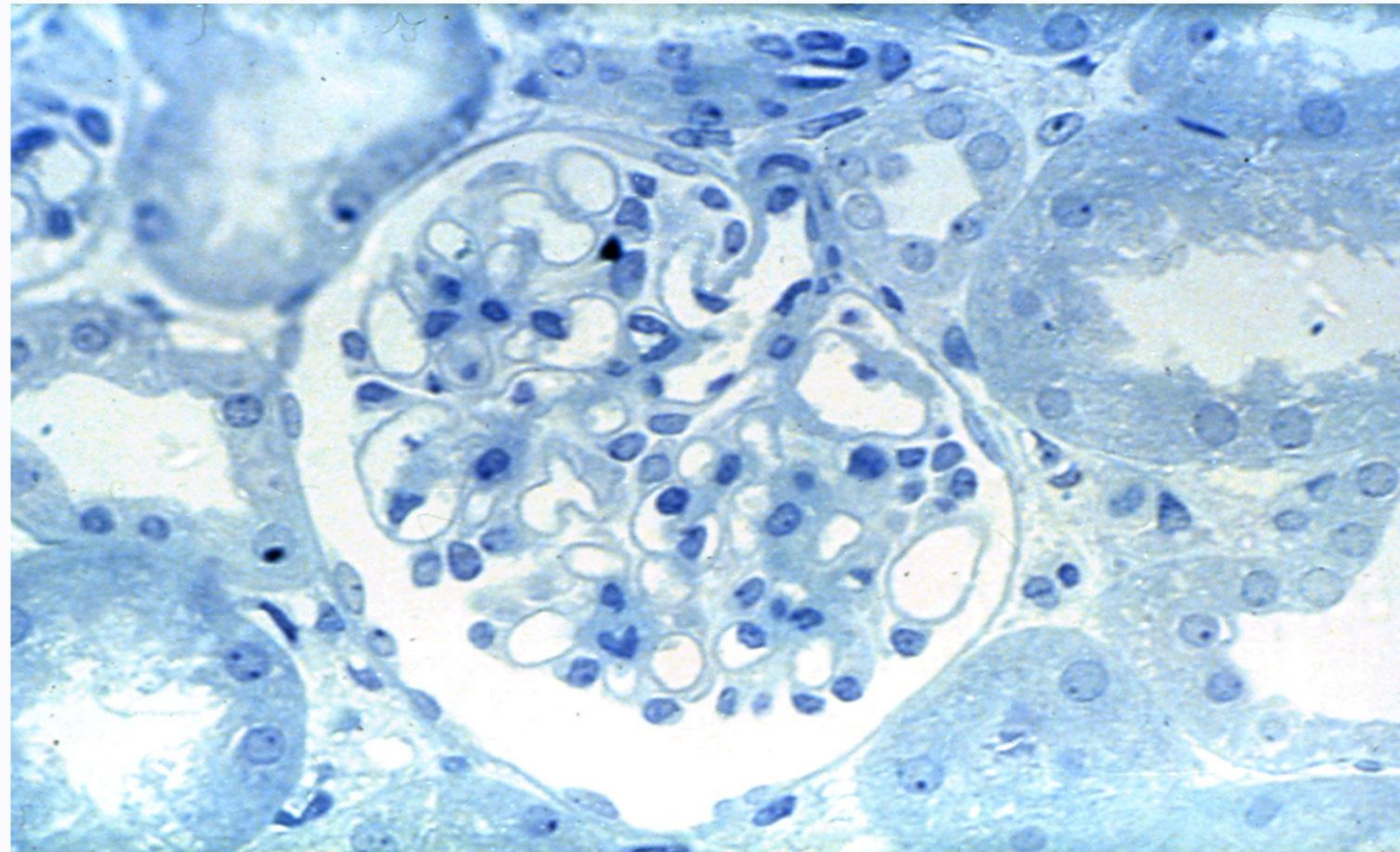


Il Glomerulo. La chiave del rene senile



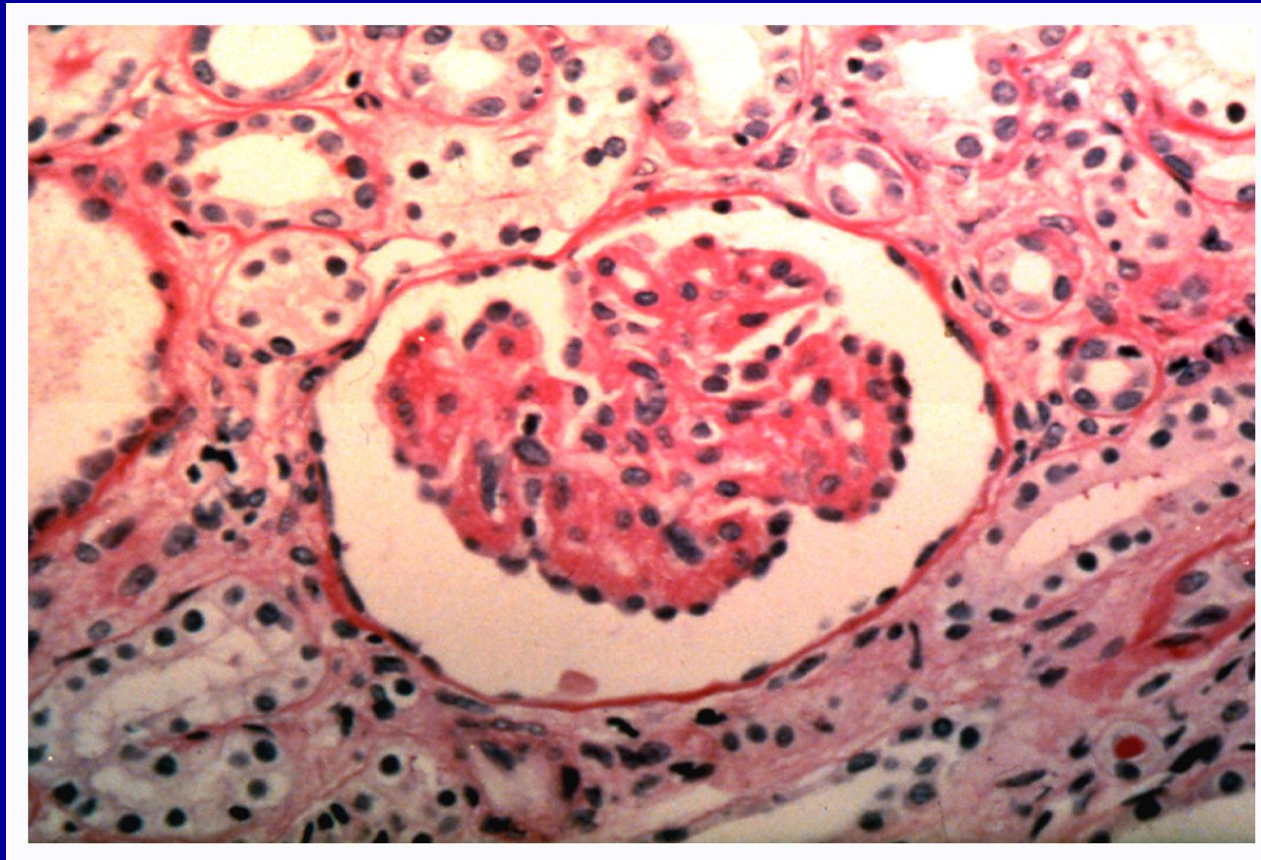


Normal Glomerulus



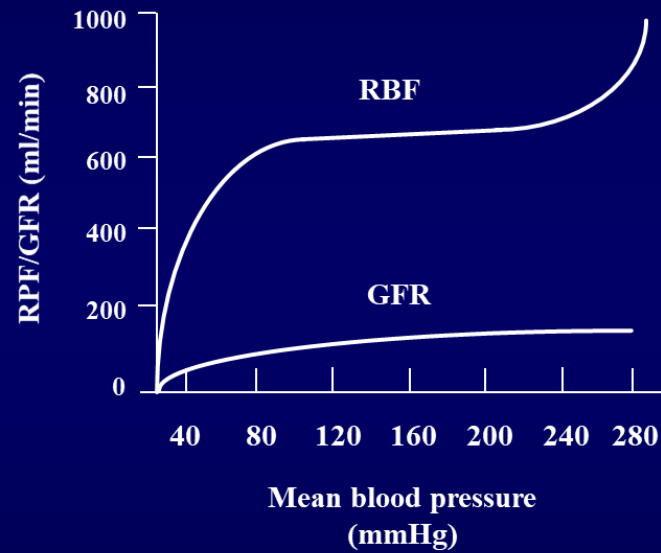


Sclerotic Glomerulus

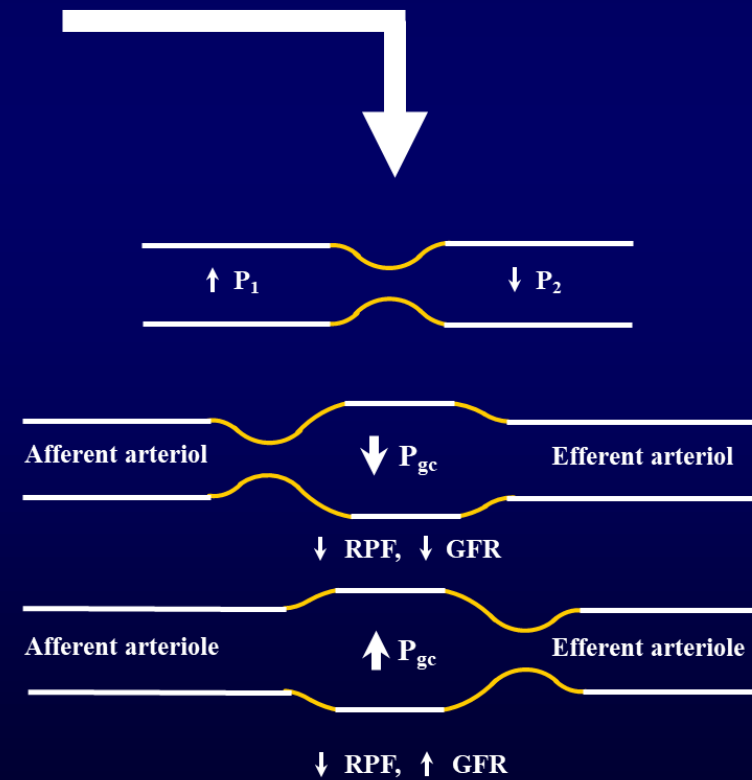




Autoregulation of renal plasma flow (RPF) and glomerular filtration rate (GFR)



Shiple RE et al, 1951





Paracrine factors and glomerular arteriolar resistance

	Arteriole	
	afferent	efferent
Angiotensin II	+	++
Endothelin 1	+	++
Norepinephrine	+	++
↑↑ Vasoconstrictors vs. Vasodilators ↓↓		
Nitric Oxide	++	+
PGE ₂	++	-
PGI ₂	++	++



Excessive vasoconstriction after stress by the aging kidney: Inadequate prostaglandin modulation of increased endothelin activity

SERGIO CASTELLANI, ANDREA UNGAR, CLAUDIA CANTINI, GIUSEPPE LA CAVA, CLAUDIA DI SERIO, ANNA ALTABELLI, BARBARA VALLOTTI, MARCO PELLEGGRI, ALESSANDRO BROCCHI, ALBERTO CAMAITI, MIRELLA COPPO, UGO MELDOLESI, GIANNI MESSERI, and GIULIO MASOTTI

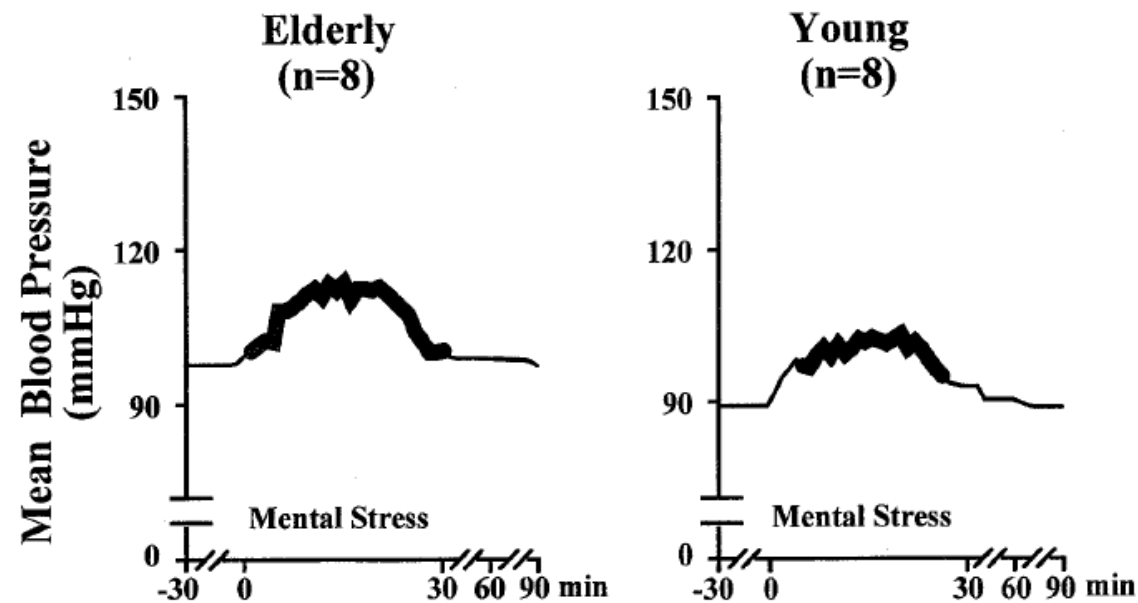


Fig 1. Effects of mental stress on MBP. ■, Values significantly different from baseline ($P < .001$, least significant difference test, ANOVA).



Excessive vasoconstriction after stress by the aging kidney: Inadequate prostaglandin modulation of increased endothelin activity

SERGIO CASTELLANI, ANDREA UNGAR, CLAUDIA CANTINI, GIUSEPPE LA CAVA, CLAUDIA DI SERIO, ANNA ALTABELLI, BARBARA VALLOTTI, MARCO PELLEGRINI, ALESSANDRO BROCCHI, ALBERTO CAMAITI, MIRELLA COPPO, UGO MELDOLESI, GIANNI MESSERI, and GIULIO MASOTTI

FIRENZE, ITALY

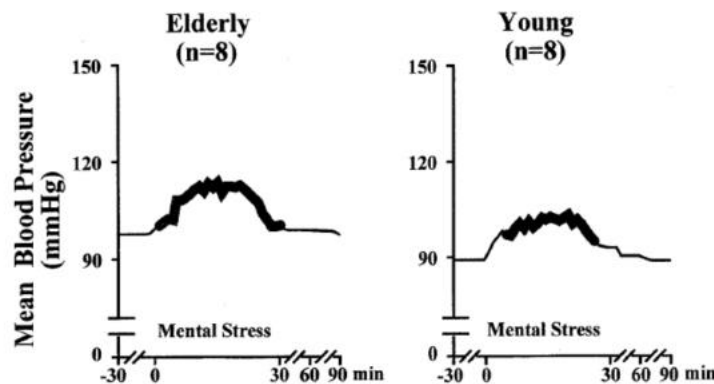
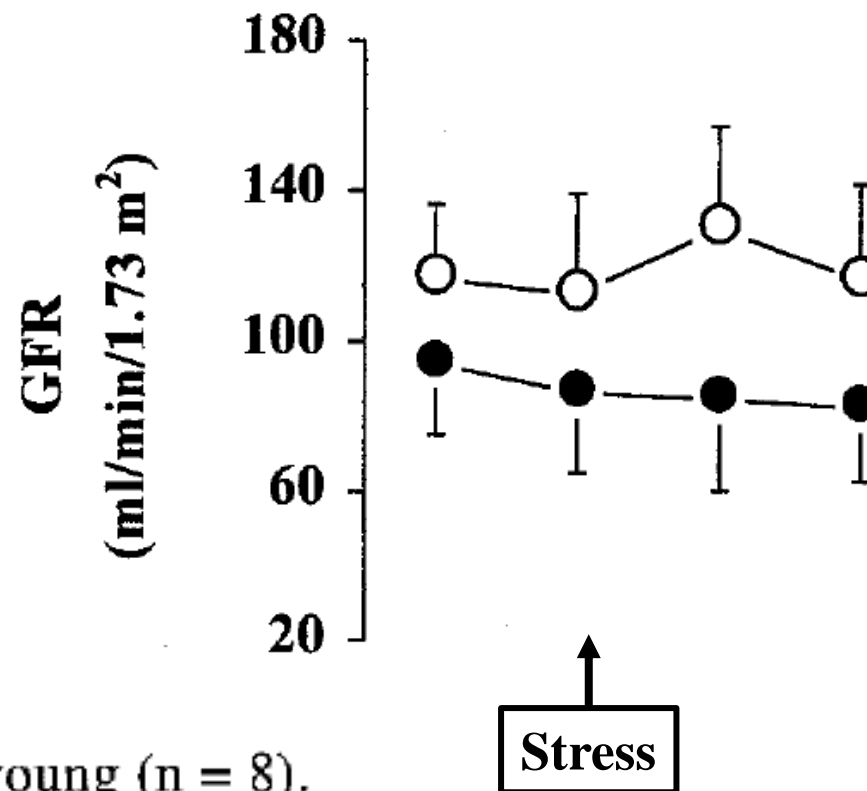


Fig 1. Effects of mental stress on MBP. ■, Values significantly different from baseline ($P < .001$, least significant difference test, ANOVA).

●, Elderly (n = 8); ○, young (n = 8).





Excessive vasoconstriction after stress by the aging kidney: Inadequate prostaglandin modulation of increased endothelin activity

SERGIO CASTELLANI, ANDREA UNGAR, CLAUDIA CANTINI, GIUSEPPE LA CAVA, CLAUDIA DI SERIO, ANNA ALTABELLI, BARBARA VALLOTTI, MARCO PELLEGRINI, ALESSANDRO BROCCHI, ALBERTO CAMAITI, MIRELLA COPPO, UGO MELDOLESI, GIANNI MESSERI, and GIULIO MASOTTI

FIRENZE, ITALY

●, Elderly (n = 8); ○, young (n = 8). * $P < .05$; ** $P < .01$; *** $P < .001$ vs baseline (least significant difference test, ANOVA). FF, Filtration fraction; RVR, renal vascular resistance.

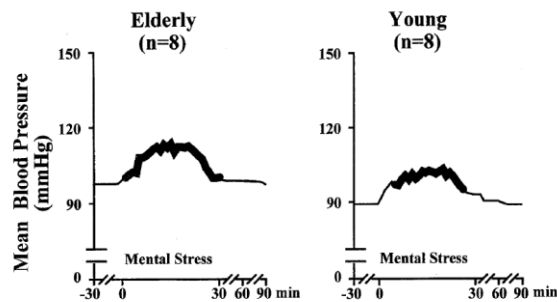
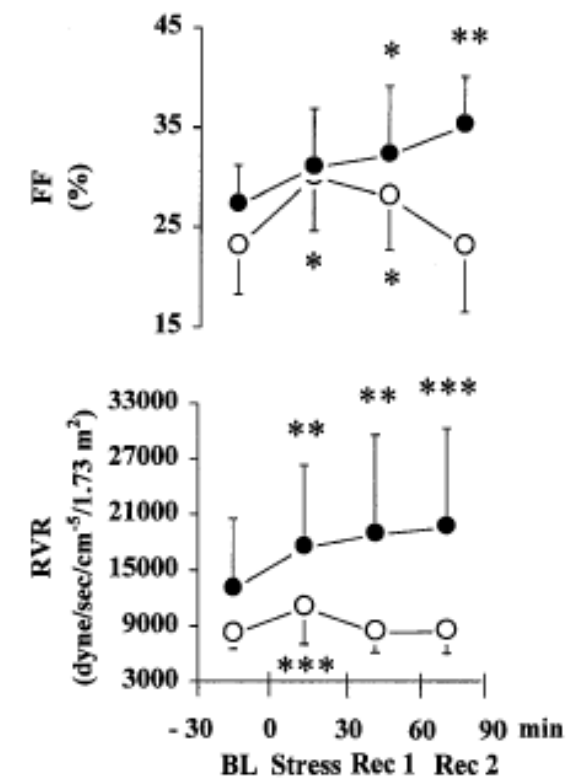
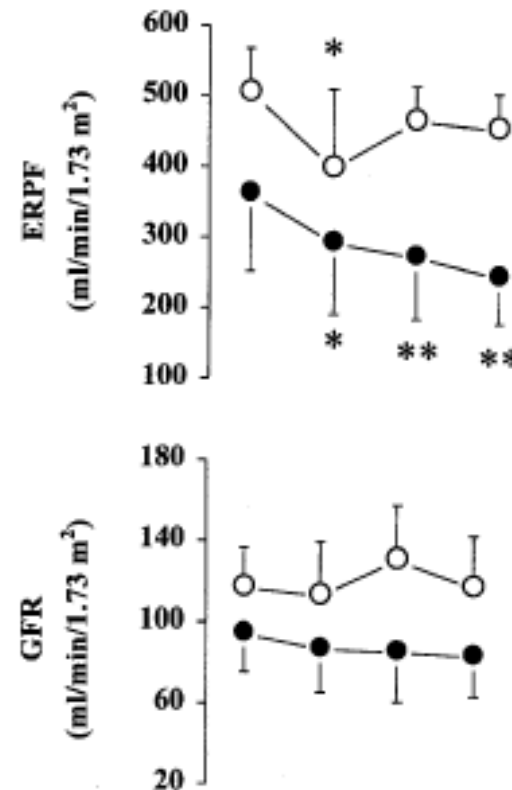


Fig 1. Effects of mental stress on MBP. ■, Values significantly different from baseline ($P < .001$, least significant difference test, ANOVA).





Excessive vasoconstriction after stress by the aging kidney: Inadequate prostaglandin modulation of increased endothelin activity

SERGIO CASTELLANI, ANDREA UNGAR, CLAUDIA CANTINI, GIUSEPPE LA CAVA, CLAUDIA DI SERIO, ANNA ALTABELLI, BARBARA VALLOTTI, MARCO PELLEGGRI, ALESSANDRO BROCCHI, ALBERTO CAMAITI, MIRELLA COPPO, UGO MELDOLESI, GIANNI MESSERI, and GIULIO MASOTTI

FIRENZE, ITALY

□ Young
■ Elderly

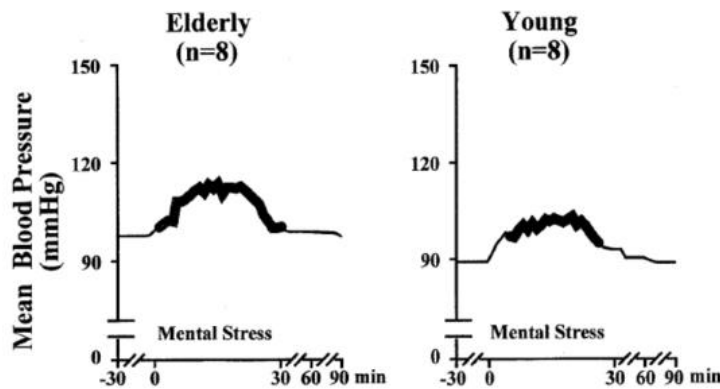
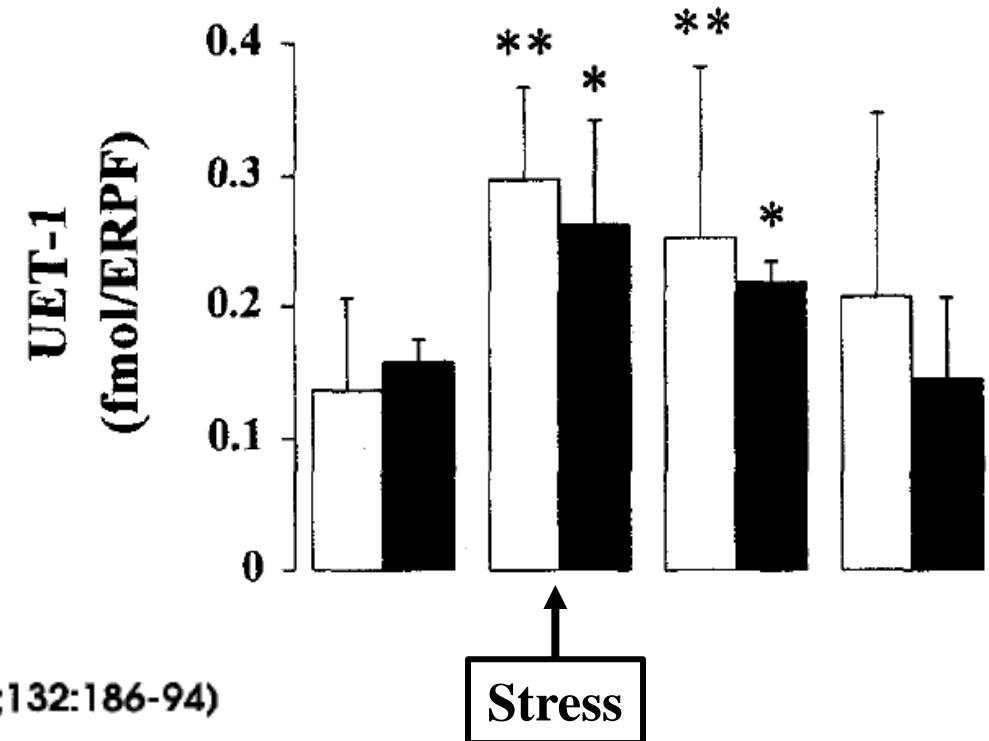


Fig 1. Effects of mental stress on MBP. ■ Values significantly different from baseline ($P < .001$, least significant difference test, ANOVA).

UET-1: urinary endothelin 1



(J Lab Clin Med 1998;132:186-94)

Excessive vasoconstriction after stress by the aging kidney: Inadequate prostaglandin modulation of increased endothelin activity

SERGIO CASTELLANI, ANDREA UNGAR, CLAUDIA CANTINI, GIUSEPPE LA CAVA, CLAUDIA DI SERIO, ANNA ALTABELLI, BARBARA VALLOTTI, MARCO PELLEGGRI, ALESSANDRO BROCCHI, ALBERTO CAMAITI, MIRELLA COPPO, UGO MELDOLESI, GIANNI MESSERI, and GIULIO MASOTTI

FIRENZE, ITALY

UPGE₂: Urinary Prostaglandin E₂

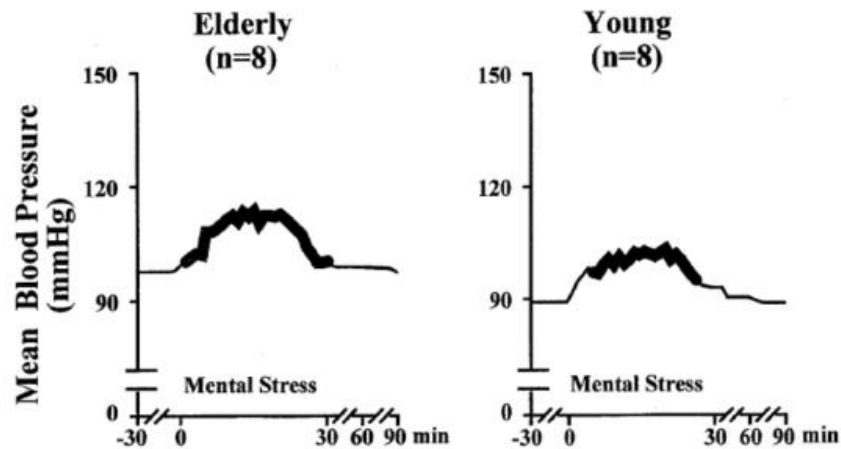
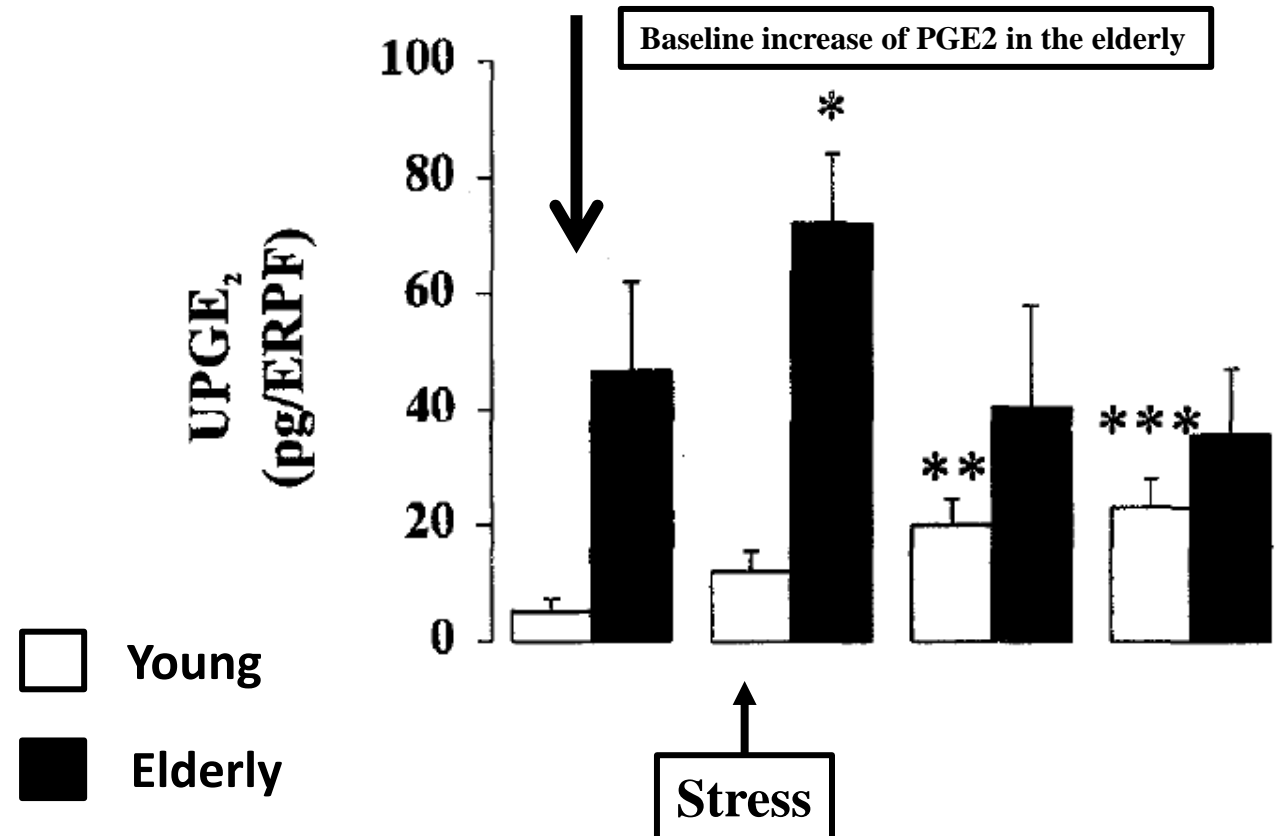


Fig 1. Effects of mental stress on MBP. ■, Values significantly different from baseline ($P < .001$, least significant difference test, ANOVA).



(J Lab Clin Med 1998;132:186-94)



Excessive vasoconstriction after stress by the aging kidney: Inadequate prostaglandin modulation of increased endothelin activity

SERGIO CASTELLANI, ANDREA UNGAR, CLAUDIA CANTINI, GIUSEPPE LA CAVA, CLAUDIA DI SERIO, ANNA ALTABELLI, BARBARA VALLOTTI, MARCO PELLEGGRI, ALESSANDRO BROCCHI, ALBERTO CAMAITI, MIRELLA COPPO, UGO MELDOLESI, GIANNI MESSERI, and GIULIO MASOTTI

FIRENZE, ITALY

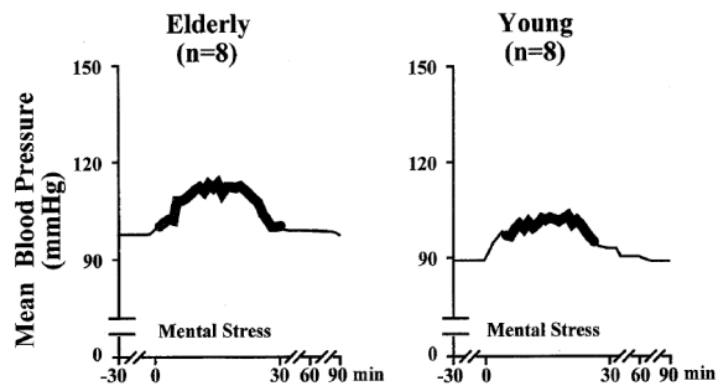
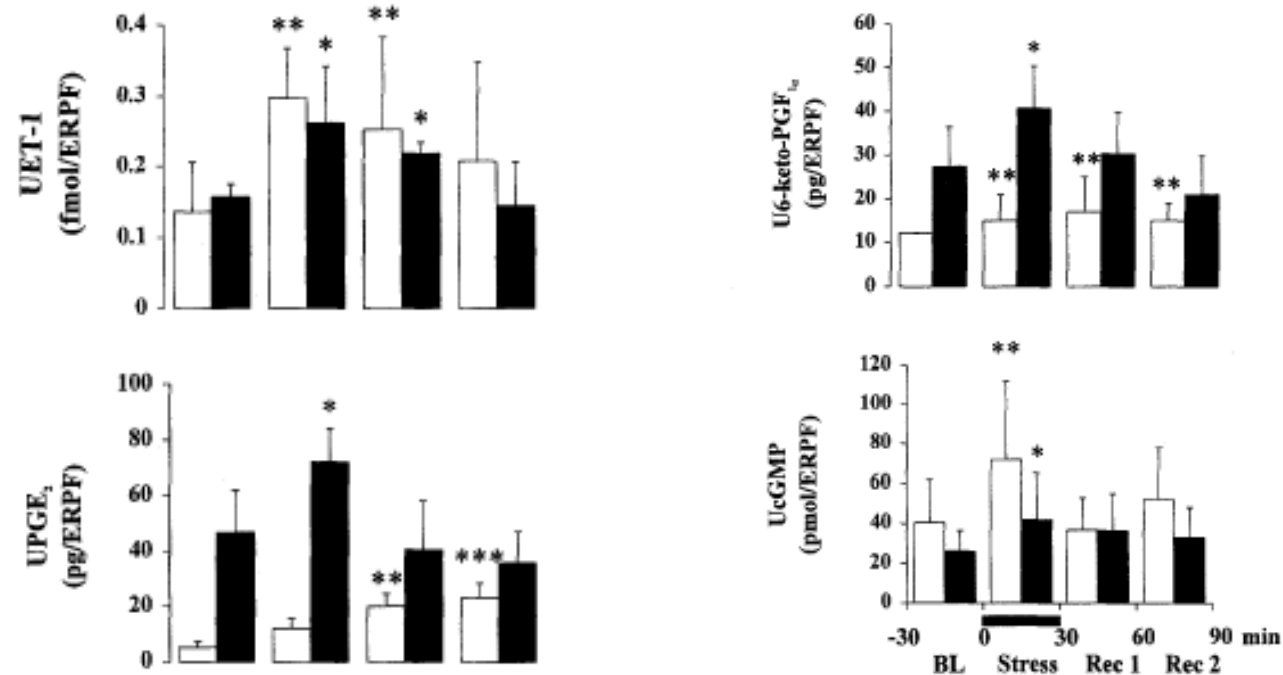


Fig 1. Effects of mental stress on MBP. ■, Values significantly different from baseline ($P < .001$, least significant difference test, ANOVA).

Fig 3. Effects of mental stress on UET-1, UPGE₂, 6-keto-PGF_{1α}, and UcGMP (mean ± SD). ■, Elderly (n = 8); □, young (n = 8). * $P < .05$, ** $P < .01$, and *** $P < .001$ vs baseline (least significant difference test, ANOVA).





Trandolapril, but not Verapamil nor their association, restores the physiological renal hemodynamic response to adrenergic activation in essential hypertension

LORELLA LAMBERTUCCI, CLAUDIA DI SERIO, SERGIO CASTELLANI, MONICA TORRINI, ELENA LOTTI, CLAUDIA CRISTOFARI, GIULIO MASOTTI, NICCOLO MARCHIONNI, and ANDREA UNGAR

Bolus infusion of PAH and Inulin

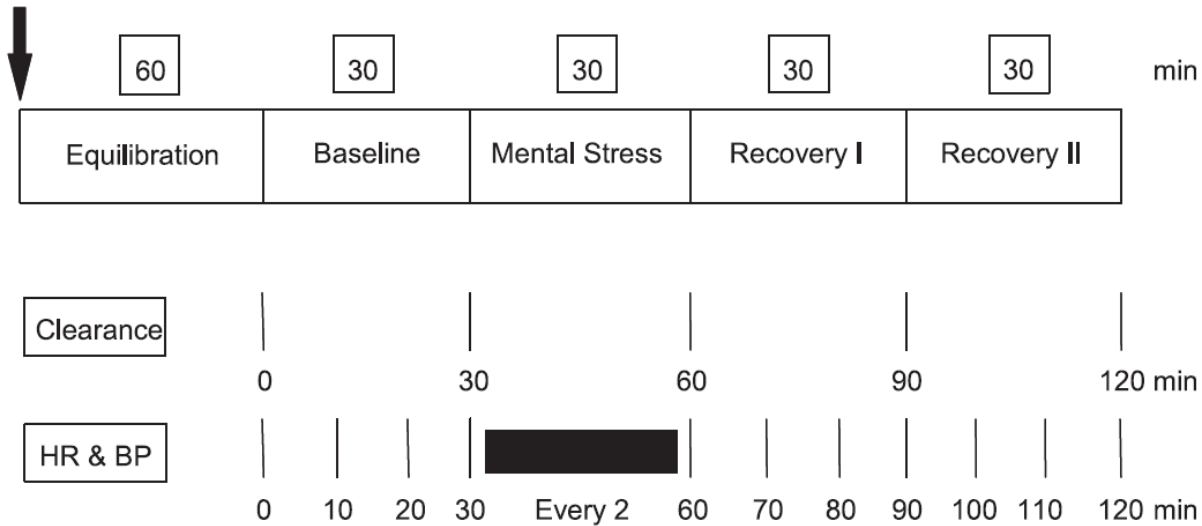


Fig 1. Study protocol.

Before and after 15 days of:

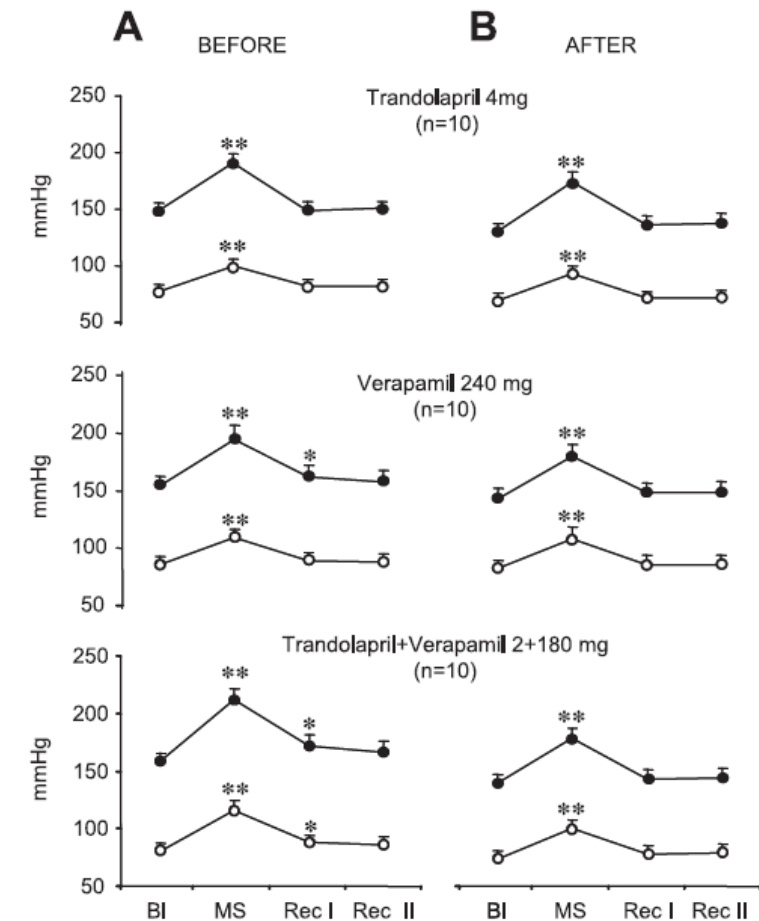
- Trandolapril 4 mg
- Verapamil 240 mg
- Trandolapril 2mg + Verapamil 180 mg



Trandolapril, but not Verapamil nor their association, restores the physiological renal hemodynamic response to adrenergic activation in essential hypertension

LORELLA LAMBERTUCCI, CLAUDIA DI SERIO, SERGIO CASTELLANI, MONICA TORRINI, ELENA LOTTI, CLAUDIA CRISTOFARI, GIULIO MASOTTI, NICCOLÒ MARCHIONNI, and ANDREA UNGAR

Blood Pressure

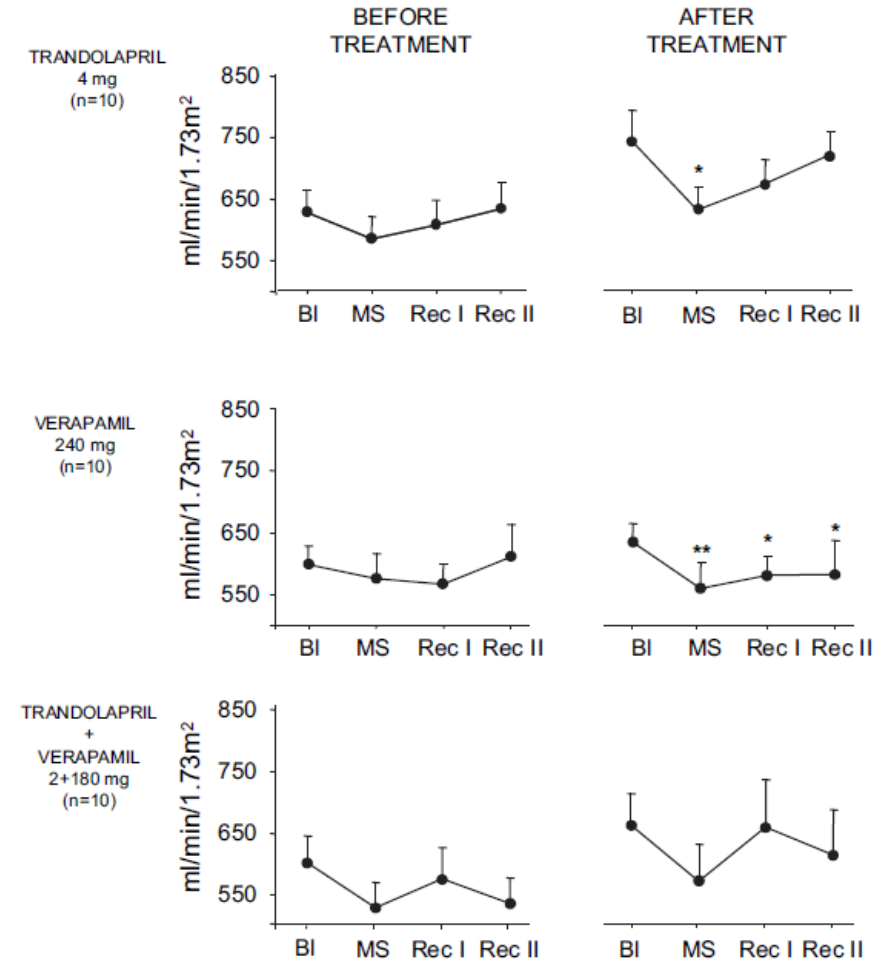




Trandolapril, but not Verapamil nor their association, restores the physiological renal hemodynamic response to adrenergic activation in essential hypertension

LORELLA LAMBERTUCCI, CLAUDIA DI SERIO, SERGIO CASTELLANI, MONICA TORRINI, ELENA LOTTI, CLAUDIA CRISTOFARI, GIULIO MASOTTI, NICCOLÒ MARCHIONNI, and ANDREA UNGAR

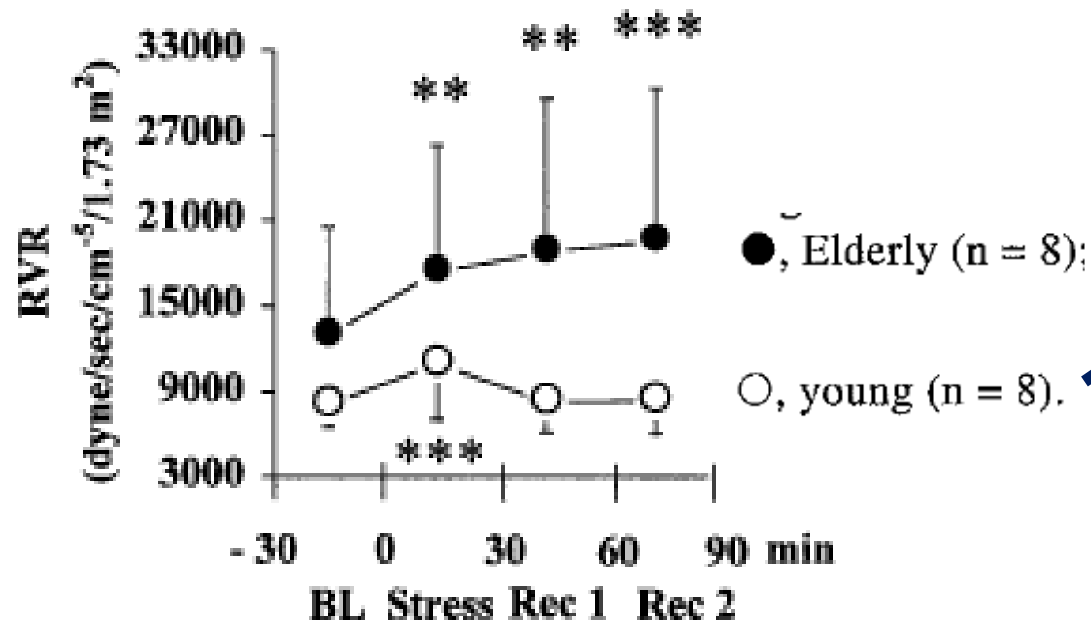
ERPF



Trandolapril, but not Verapamil nor their association, restores the physiological renal hemodynamic response to adrenergic activation in essential hypertension

LORELLA LAMBERTUCCI, CLAUDIA DI SERIO, SERGIO CASTELLANI, MONICA TORRINI, ELENA LOTTI, CLAUDIA CRISTOFARI, GIULIO MASOTTI, NICCOLO MARCHIONNI, and ANDREA UNGAR

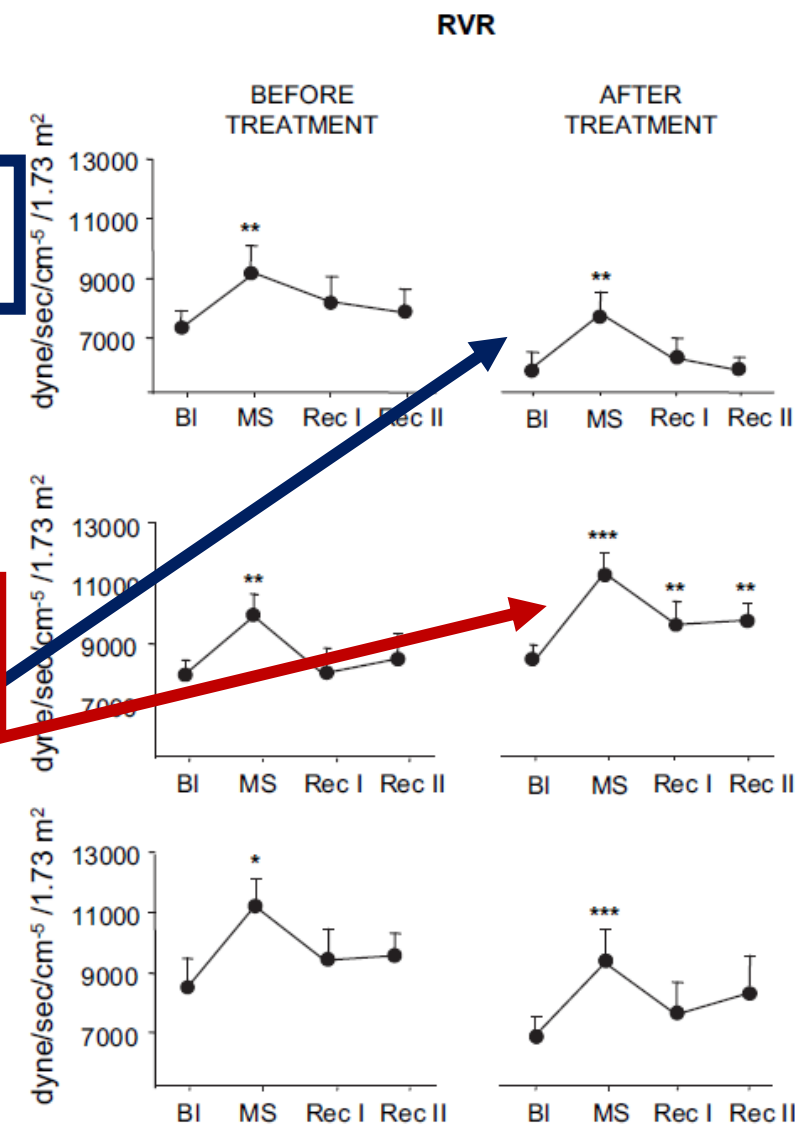
Translational Research 2011;157:348–356



TRANDOLAPRIL
4 mg
(n=10)

VERAPAMIL
240 mg
(n=10)

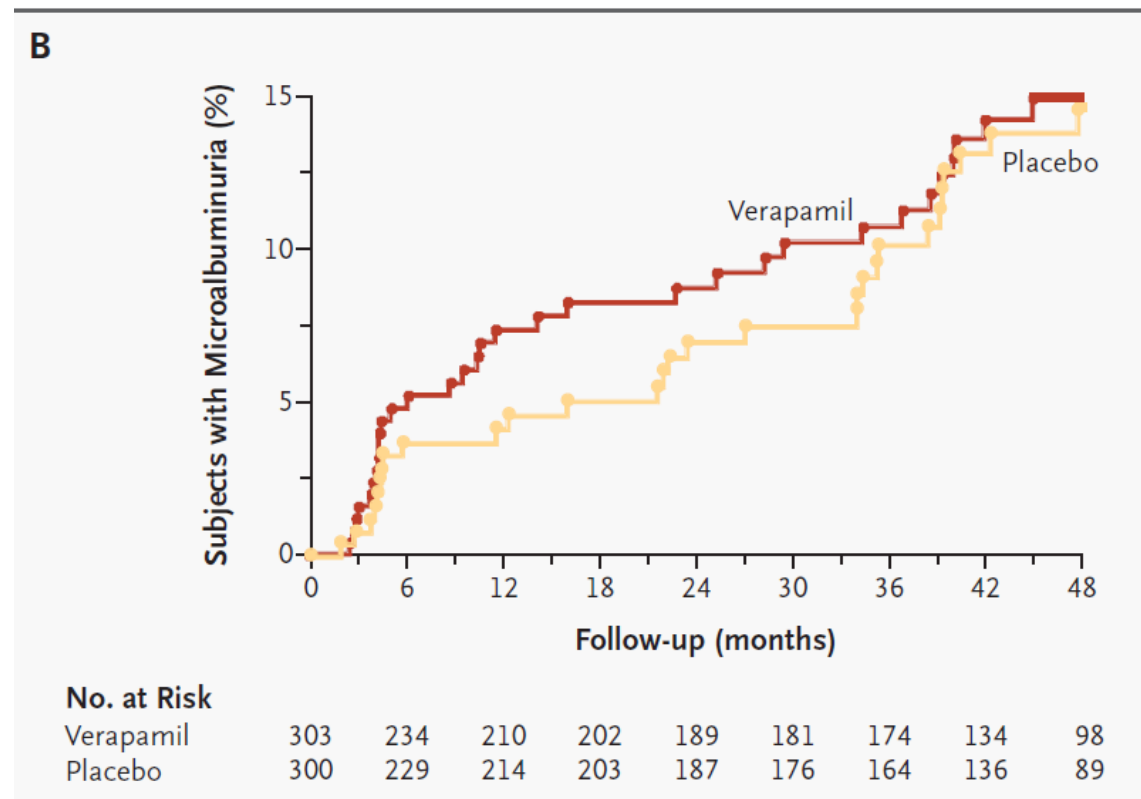
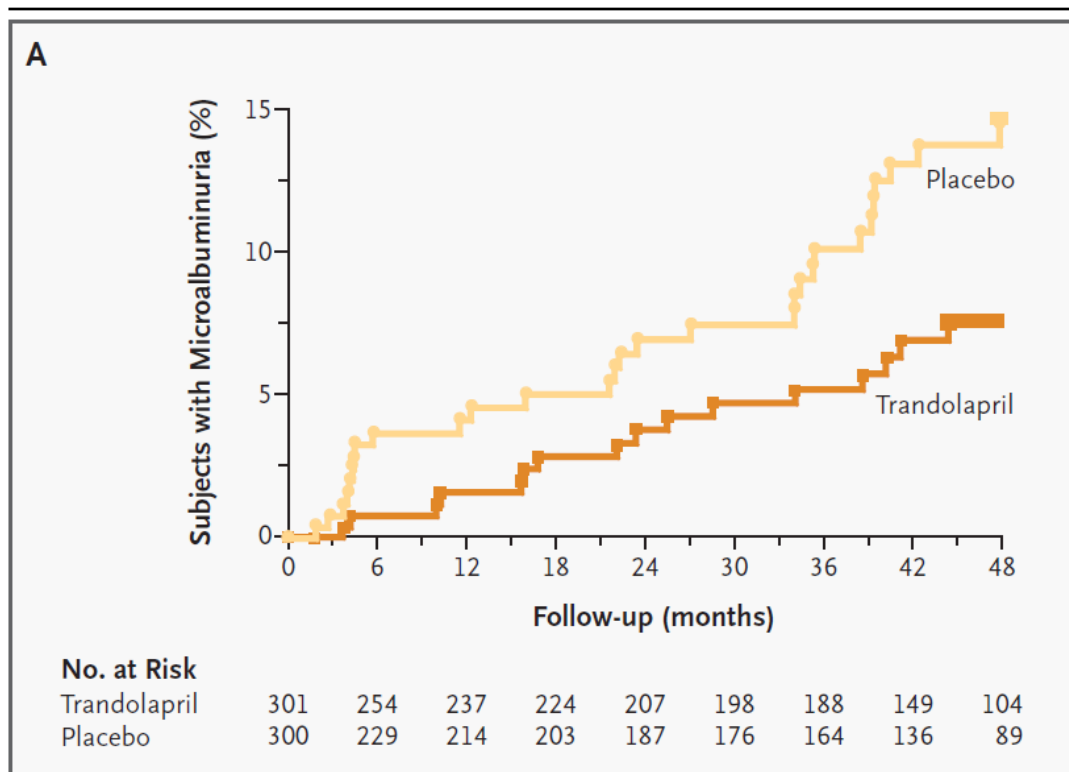
TRANDOLAPRIL +
VERAPAMIL
2+180 mg
(n=10)





Preventing Microalbuminuria in Type 2 Diabetes

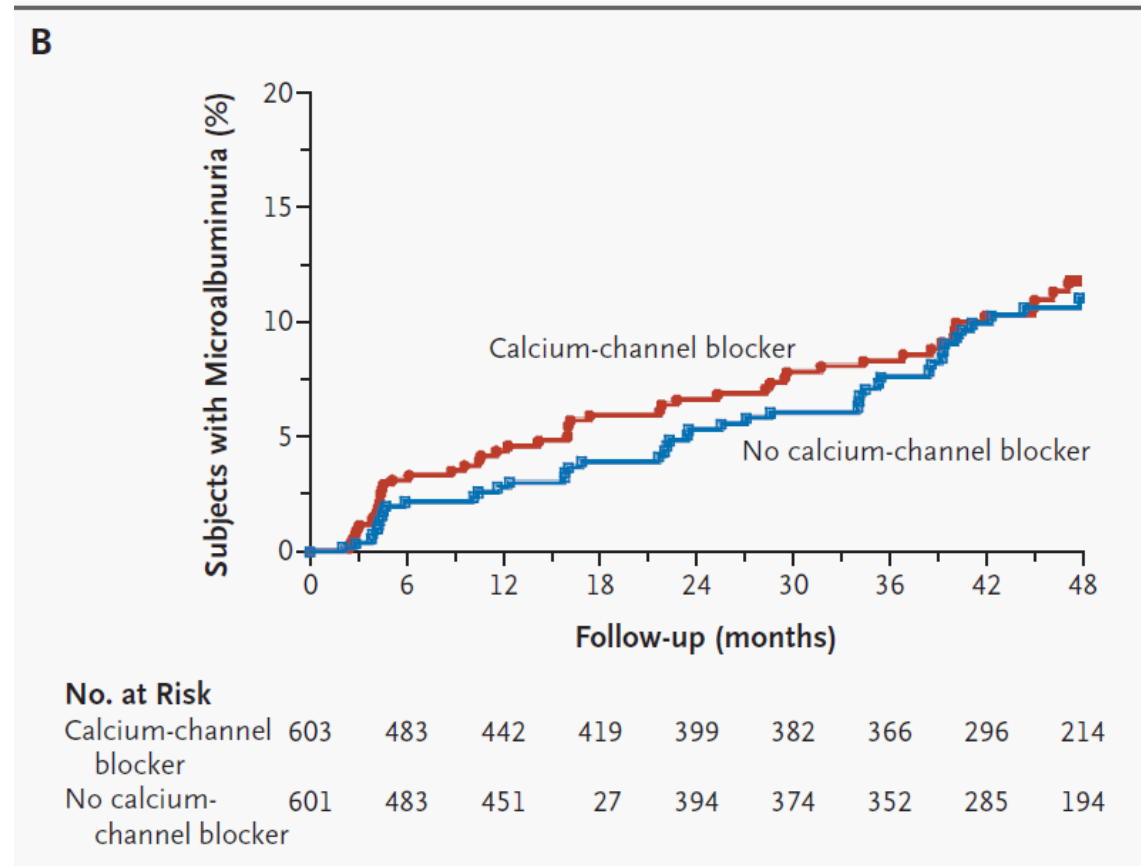
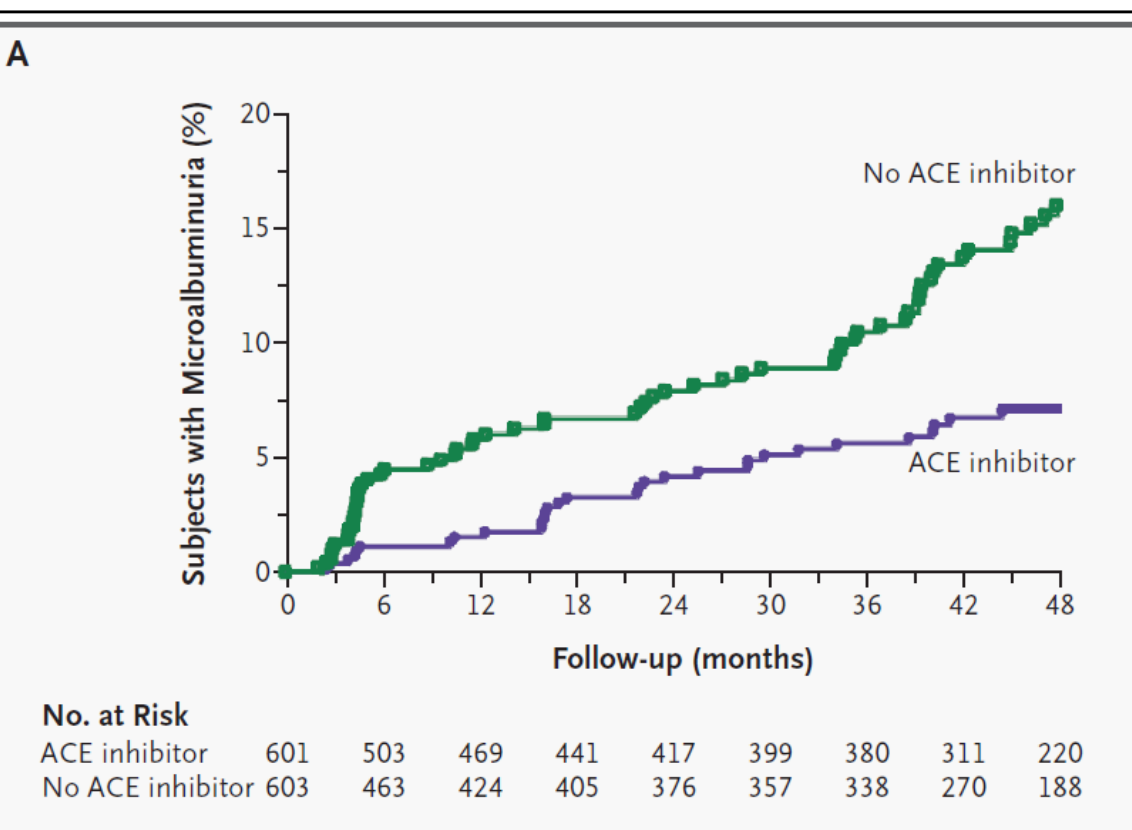
Piero Ruggenenti, M.D., Anna Fassi, M.D., Anelja Parvanova Ilieva, M.D., Simona Bruno, M.D.,





Preventing Microalbuminuria in Type 2 Diabetes

Piero Ruggenenti, M.D., Anna Fassi, M.D., Anelja Parvanova Ilieva, M.D., Simona Bruno, M.D.,





68° CONGRESSO NAZIONALE **SIGG**

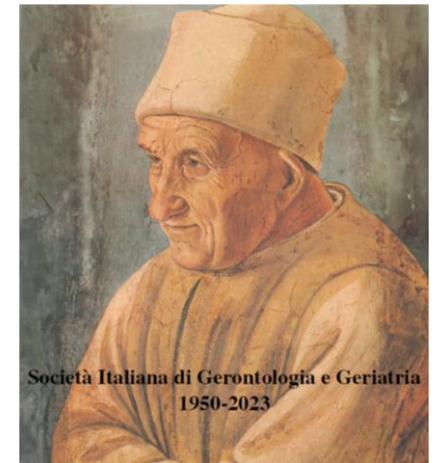
Ritorno al futuro

FIRENZE, 13-16 DICEMBRE 2023
PALAZZO DEI CONGRESSI



AGING KIDNEY: FISIOPATOLOGIA E CLINICA

**L'insufficienza
renale acuta**





Acute Kidney Injury in the Elderly: Problems and Prospects

Jonathan Himmelfarb, MD

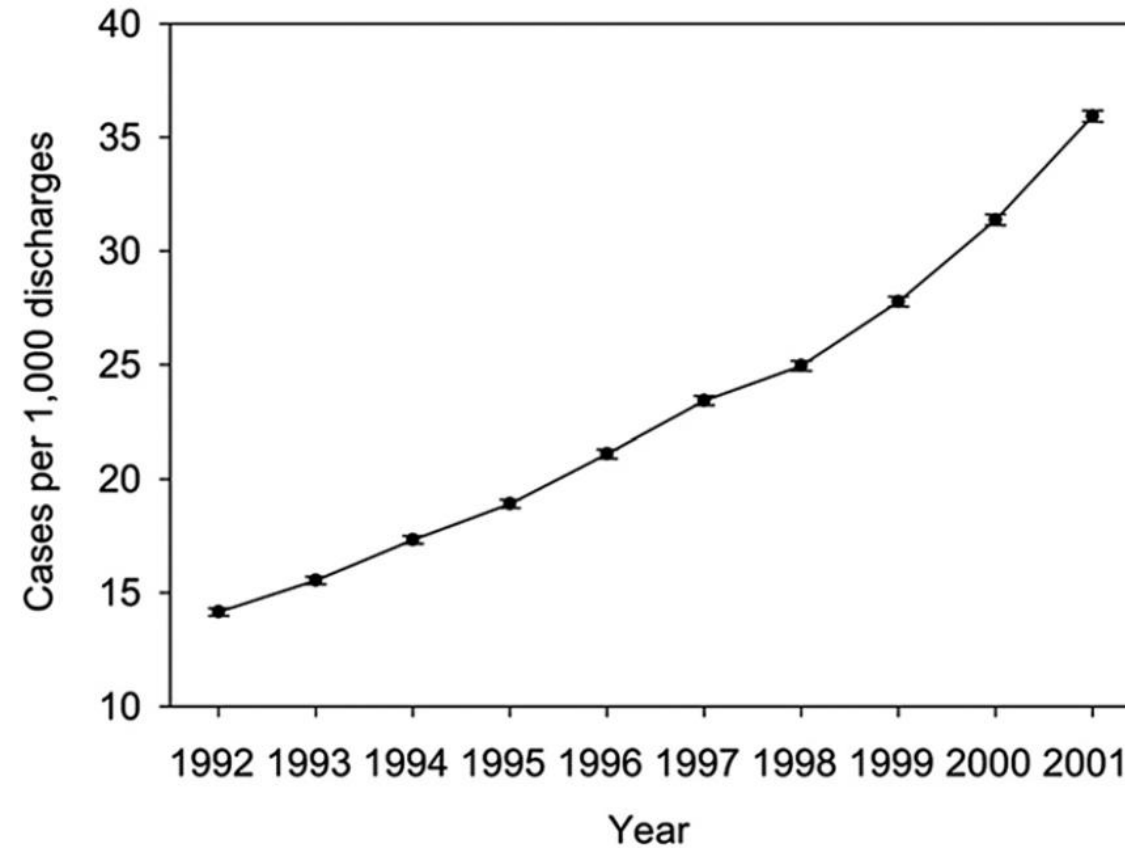


Figure 2. Increasing prevalence of AKI. Adapted from Xue et al.¹³

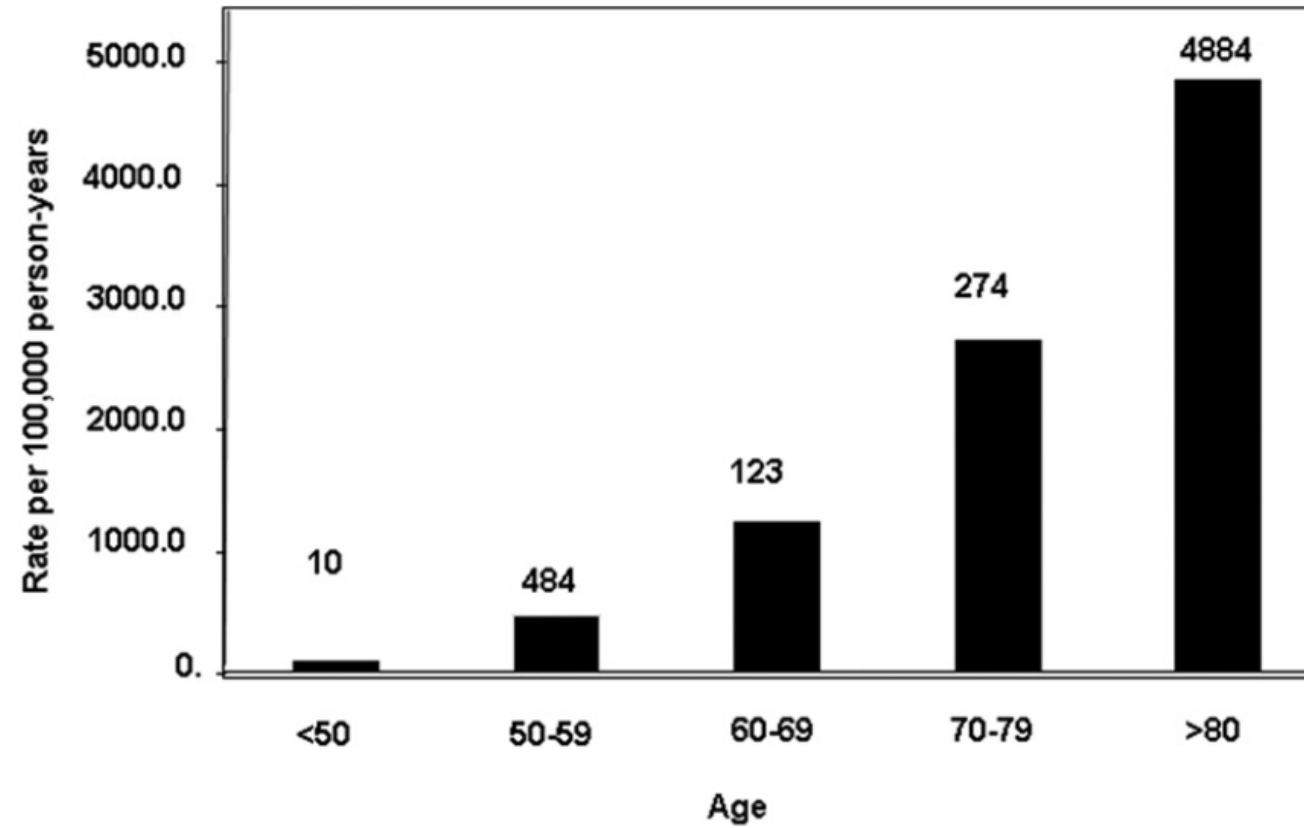


Figure 3. Age and incidence of community-acquired AKI. Adapted from Hsu et al.¹²



Renal function and functional reserve in healthy elderly individuals

Ciro Esposito, AnnaRita Plati, Tiziana Mazzullo, Gianluca Fasoli, Andreana De Mauri, Fabrizio Grosjean, Filippo Mangione, Francesca Castoldi, Nicoletta Serpieri, Flavia Cornacchia, Antonio Dal Canton

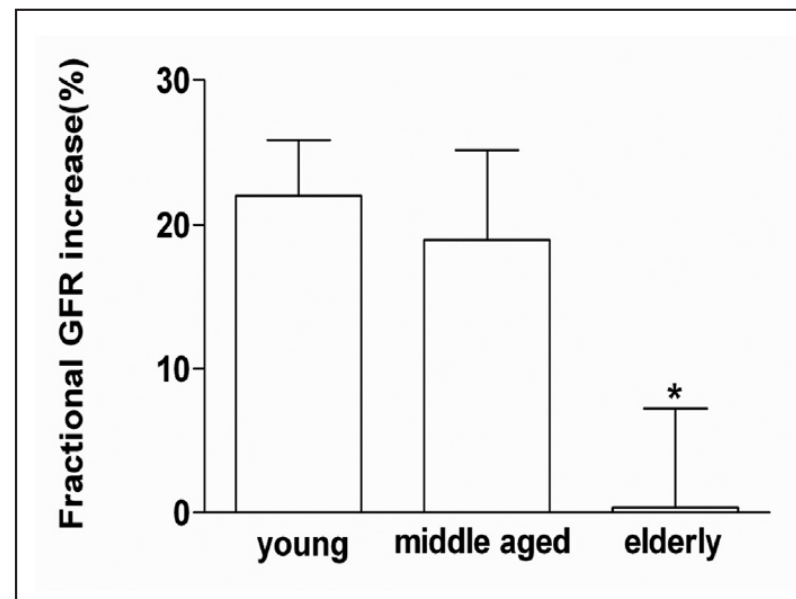
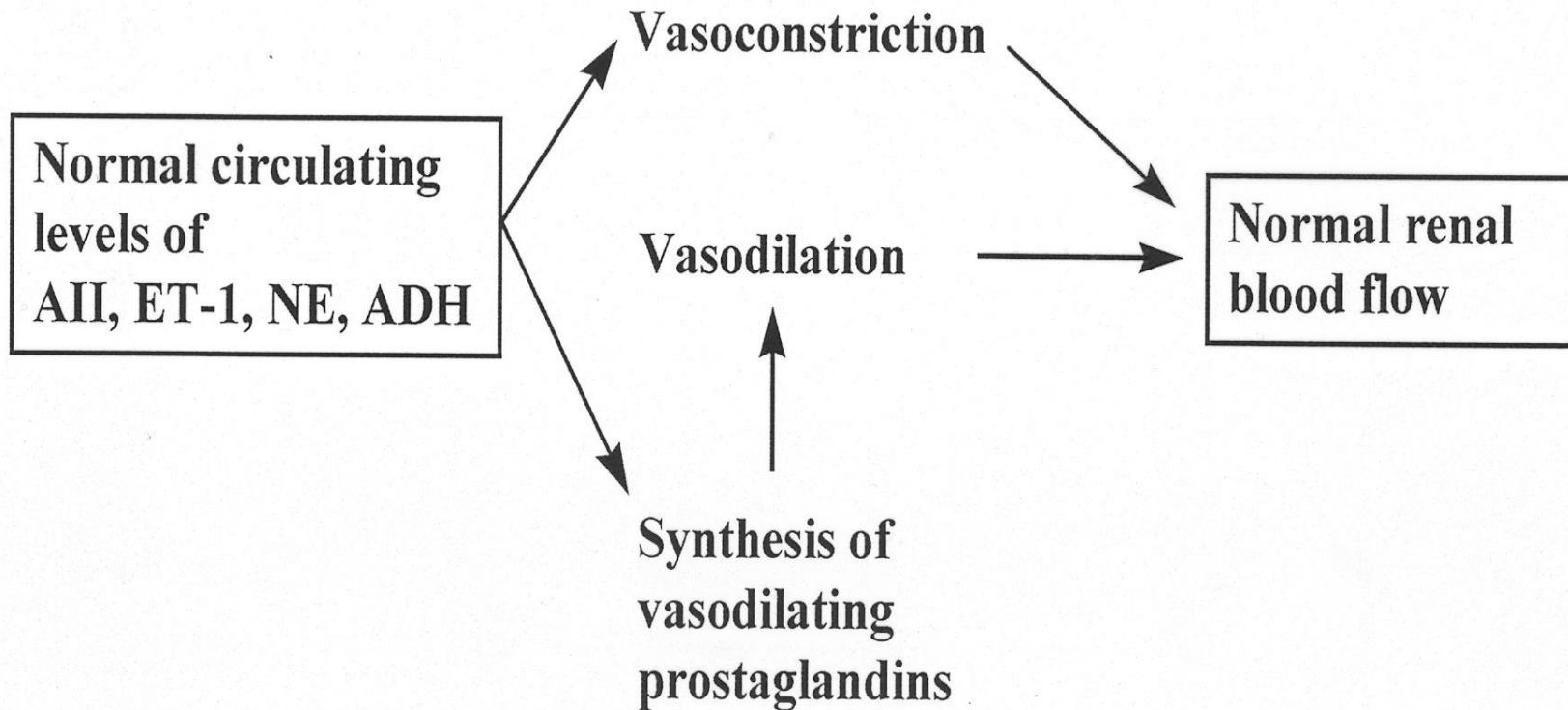


Fig. 2 - Fractional glomerular filtration rate (GFR) increase after vasodilating stimuli in young, middle-aged and elderly subjects. Values are means \pm SD; * $p < 0.01$, elderly vs. young and middle-aged subjects.

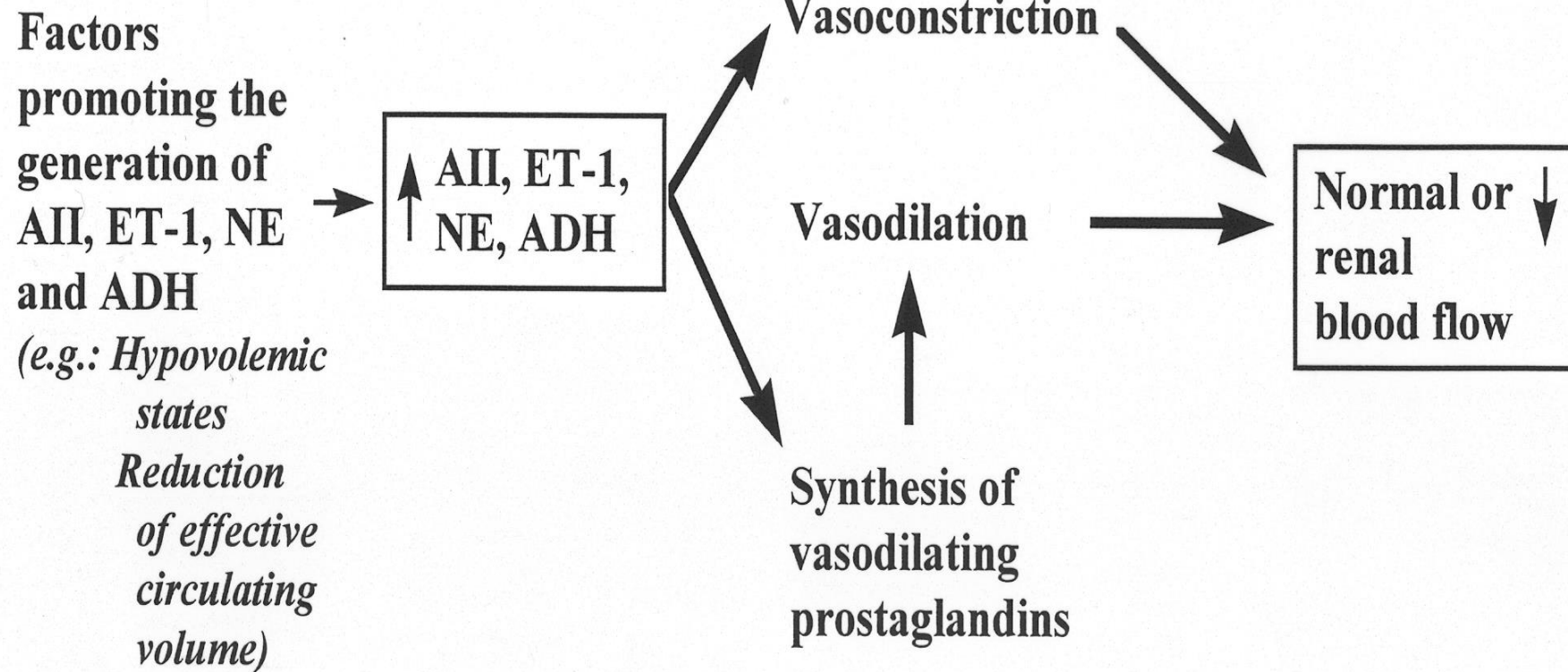


A - Normal conditions



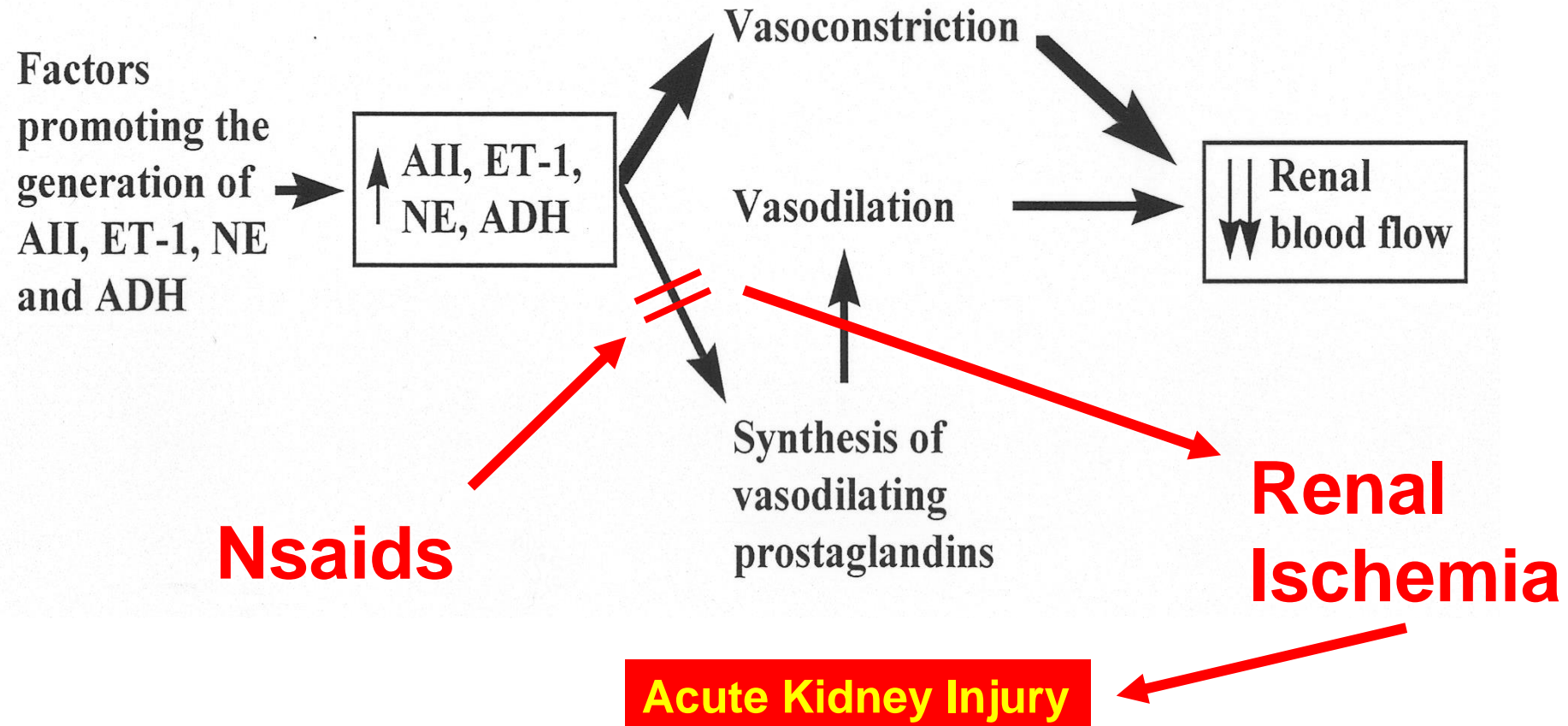


B - Increased vasoconstriction





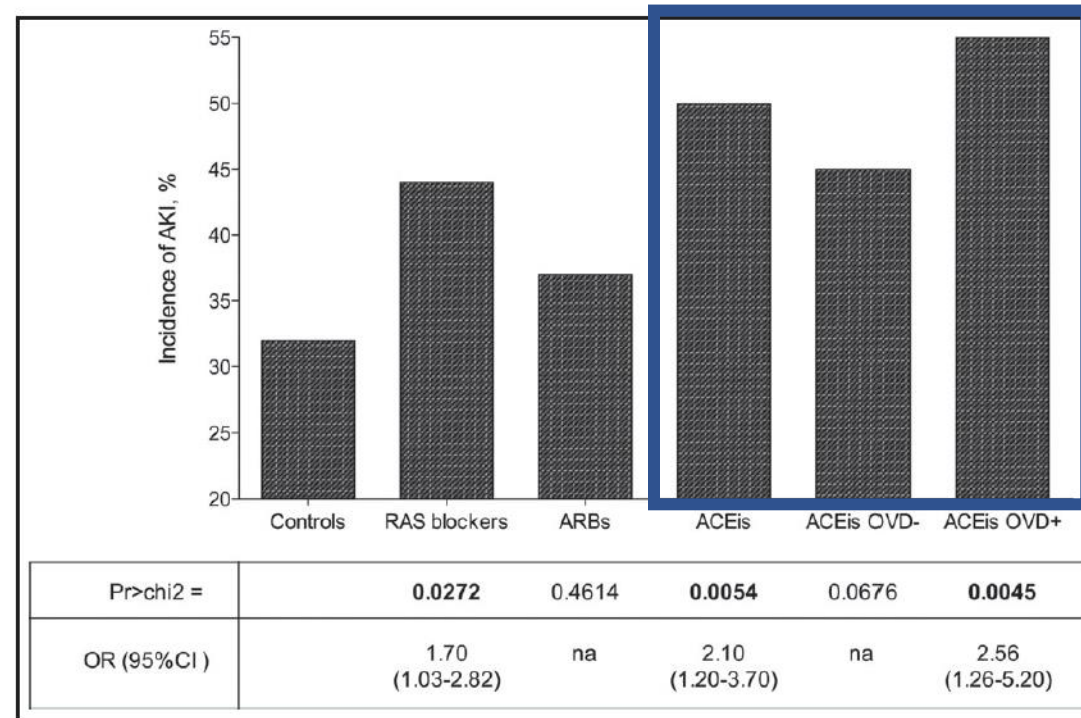
**C - Increased vasoconstriction
in the elderly**





Acute Kidney Injury in Elderly Patients With Chronic Kidney Disease: Do Angiotensin-Converting Enzyme Inhibitors Carry a Risk?

Martin Chaumont, MD;¹ Aline Pourcelet, MD;¹ Marc van Nuffelen, MD;² Judith Racapé, PhD;³ Marc Leeman, MD, PhD;⁴ Jean-Michel Hougardy, MD, PhD¹



OVD:
overdosed

FIGURE. Incidence of acute kidney injury (AKI) compared with controls depending on the class and dose of renin-angiotensin-aldosterone system (RAS) blockers. OR indicates odds ratio; ARB, angiotensin receptor blockers; ACEis, angiotensin-converting enzyme inhibitors; OVD, overdosed; CI, confidence interval; na, not available.

The Combined Effect of High Ambient Temperature and Antihypertensive Treatment on Renal Function in Hospitalized Elderly Patients

Iftach Sagy^{1,2,3}*, Alina Vodonos^{1,3}, Victor Novack^{1,2,3}, Boris Rogachev^{2,3,4}, Yosef S. Haviv^{2,3,4}, Leonid Barski^{2,3}

PLOS ONE | DOI:10.1371/journal.pone.0168504 December 19, 2016

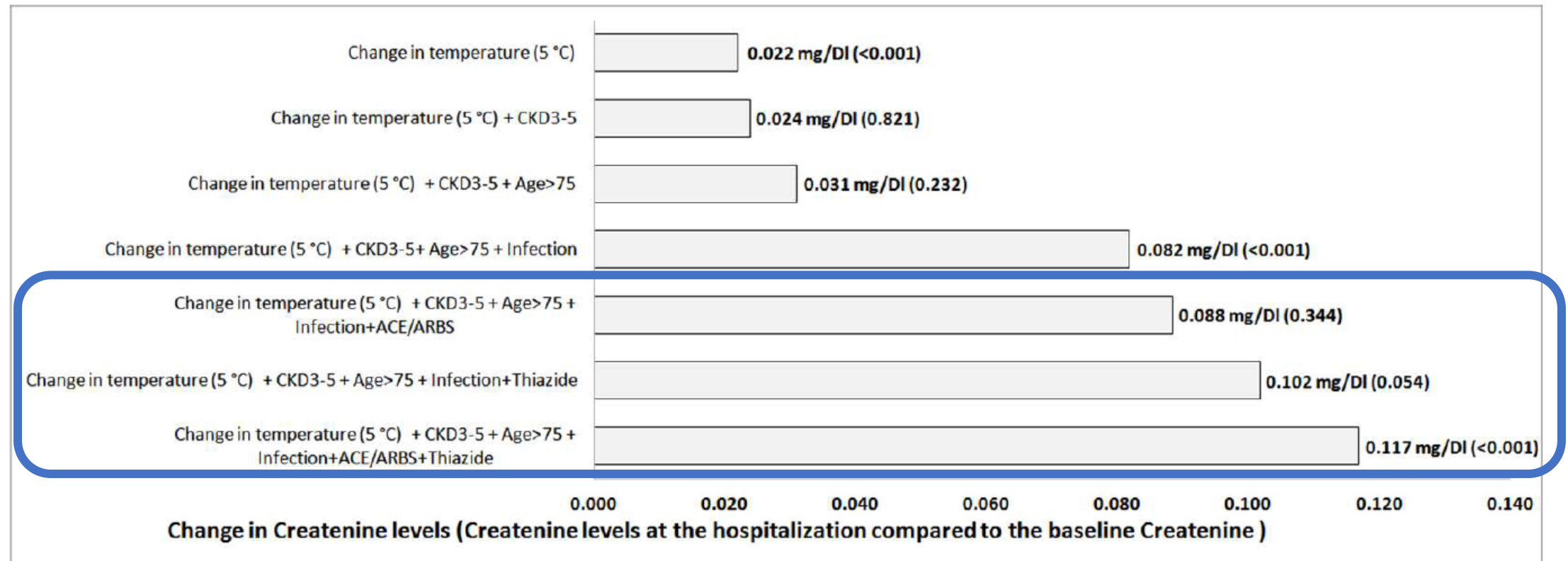
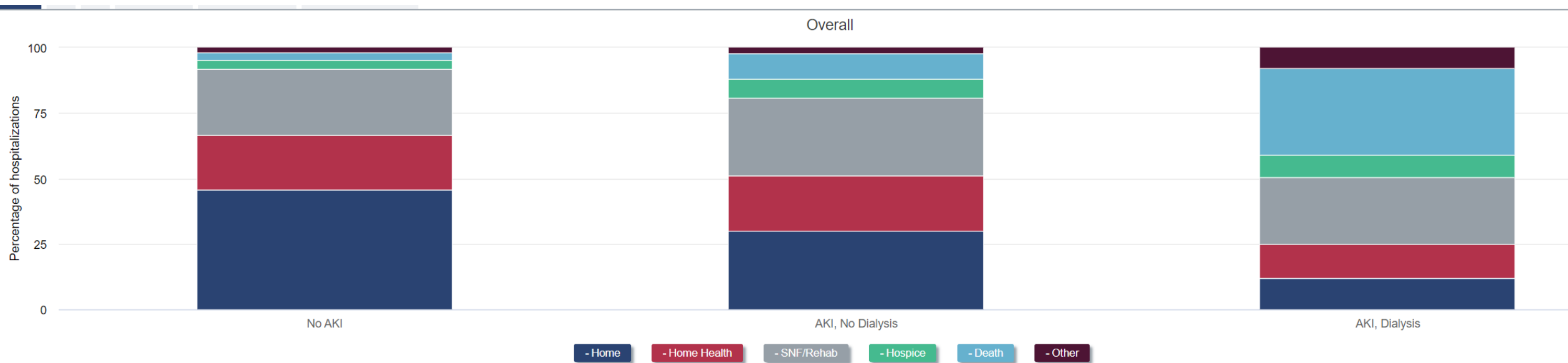


Fig 2. The cumulative increase in serum creatinine (mg/dL) for the addition of each clinical characteristic. The additional p value for each parameter is presented in brackets. ACE/ARBs—angiotensin-converting-enzyme inhibitor or angiotensin receptor blockers, CKD—chronic kidney disease



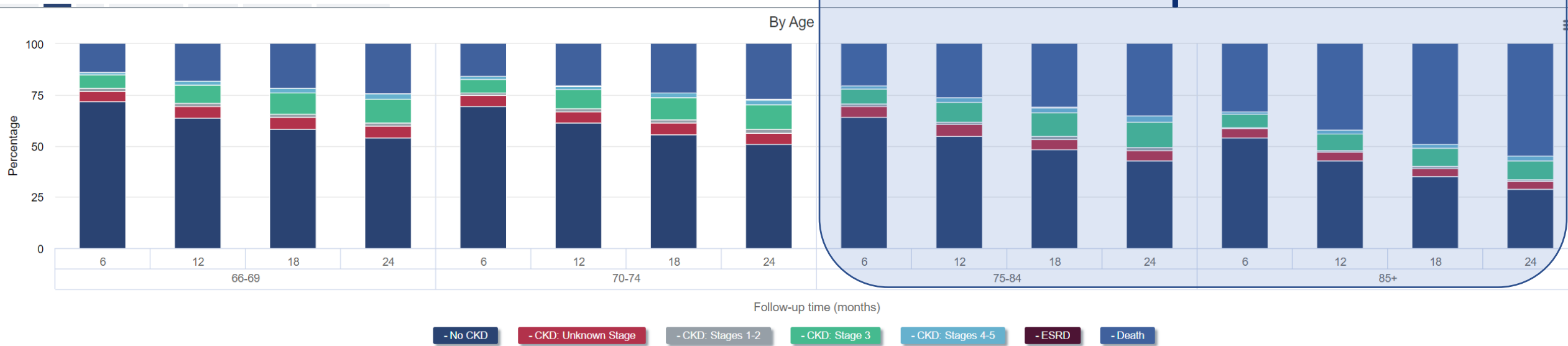
Discharge status of older adults hospitalized without acute kidney injury, with acute kidney injury, or with acute kidney injury requiring dialysis, 2021





Chronic kidney disease status during 24 months following live discharge from first hospitalization with acute kidney injury in older adults **without pre-existing CKD**, 2017-2019

> 50 % anziani > 75 anni esce dall'ospedale con CKD





Acute Kidney Injury in the Elderly: Problems and Prospects

Jonathan Himmelfarb, MD

Table 1. Hospital-Acquired AKI: Mortality and Cost Associated With Selected Changes in Serum Creatinine Level

Increase in Serum Creatinine Level	Multivariable OR (95% CI)	Area Under ROC Curve	Increase in Total Cost
0.3 mg/dL	4.1 (3.1-5.5)	0.84	\$4,886
0.5 mg/dL	6.5 (5.0-8.5)	0.86	\$7,499
1.0 mg/dL	9.7 (7.1-13.2)	0.84	\$13,200
2.0 mg/dL	16.4 (10.3-26)	0.83	\$22,023

OR, odds ratio; CI, confidence interval; ROC, receiving operating characteristic.
Adapted from Chertow et al.⁷



Conclusioni

Nell'anziano:

- **La prevalenza di CKD è elevata ed in continuo aumento**
- **La valutazione del GFR non è semplice, le formule vanno usate bene e spesso la creatinina non basta**
- **La riserva funzionale renale è ridotta**
- **I fattori paracrini, in particolare l'angiotensina II e le prostaglandine sono cruciali per l'autoregolazione renale**
- **ACE-inibitori, FANS e disidratazione sono le principali cause di IRA**
- **L'insufficienza renale acuta ha una elevata incidenza ed una prognosi molto sfavorevole**