Journal Club del Venerdì
Gruppo di Ricerca Geriatrica
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# BPCO e insufficienza renale misconosciuta: un problema prettamente geriatrico

Piera Ranieri

U.O. Medicina, Istituto clinico S.Anna, Brescia

Gruppo di Ricerca Geriatrica

# Perché parlare di BPCO e di insufficienza renale?

- La BroncoPneumopatia Cronica Ostruttiva ( BPCO ) è una malattia respiratoria cronica caratterizzata da ostruzione al flusso persistente ed evolutiva legata a rimodellamento delle vie aeree periferiche ed enfisema.

- La BPCO è prevenibile ed efficacemente curabile ed è variabilmente associata a significativi effetti extrapolmonari e comorbilità, che possono contribuire alla sua gravità.

- L'ostruzione, il rimodellamento delle vie aeree periferiche e l'enfisema sono dovuti ad una abnorme risposta infiammatoria delle vie aeree e del parenchima polmonare all'inalazione di fumo di sigaretta o di altri inquinanti.

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- Insufficienza cardiaca cronica
- Coronaropatia e Infarto miocardico
- Vasculopatia periferica
- Neoplasia polmonare
- Sindrome metabolica/Diabete mellito
- Osteoporosi
- Depressione
- Insufficienza renale cronica
- Embolia polmonare
- Aritmie

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La BPCO si associa frequentemente ad altre malattie croniche, definite comorbidità.

Le comorbidità possono essere classificate come:

1. con-causali, quando condividono con la BPCO fattori di rischio, ad es. fumo ed età per la cardiopatia ischemica.
2. complicanti, quando rappresentano effetti extrapolmonari della BPCO, ad es. osteoporosi o depressione.
3. concomitanti, ovvero malattie croniche coesistenti senza relazione causale nota con la BPCO.

Tuttavia, in rapporto al livello di conoscenze attuali, è spesso difficile classificare una comorbidità in modo univoco.

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**Infiammazione sistemica** (aumento di PCR, IL-6, IL-8, TNF-α; cellule infiammatorie circolanti; stress ossidativo sistemico)

**Alterazioni nutrizionali e cachessia** (aumento del dispendio energetico e del catabolismo, alterata composizione del corpo, carenze di micronutrienti come la vit D o i folati)

**Stato procoagulatorio**

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**Sarcopenia**

**Patologie cardiovascolari** (malattia aterosclerotica pluridistrettuale)

**Ridotta densità minerale ossea** (osteopenia, osteoporosi)

**Alterazioni ematologiche** (anemia, prevalentemente normocitica e normocromica)

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# Patterns of Comorbidities in Newly Diagnosed COPD and Asthma in Primary Care*

*Joan B. Soriano, MD, PhD; George T. Visick, PhD; Hana Muellerova, PhD; Nassrin Payvandi, PhD; and Anna L. Hansell, MD, PhD*

**Table 2—*Rate per 10,000 and RR by Major Organ Systems in COPD and Asthma***

| Disorders | COPD | RR (95% CI) | Asthma | RR (95% CI) |
|---|---|---|---|---|
| Blood and lymphatic system | 277.8 | 1.74 (1.4–2.1) | 216.9 | 1.61 (1.3–2.0) |
| Cardiac | 2,256.3 | 4.01 (3.6–4.4) | 648.1 | 3.52 (3.0–4.1) |
| Congenital, familial, and genetic | 48.1 | 1.18 (0.8–1.8) | 75.6 | 1.28 (0.9–1.8) |
| Ear and labyrinth | 881.8 | 1.44 (1.3–1.6) | 1,218.0 | 1.27 (1.2–1.4) |
| Endocrine | 385.3 | 1.22 (1.1–1.4) | 192.9 | 1.49 (1.2–1.9) |
| Eye | 870.69 | 1.32 (1.2–1.5) | 769.1 | 1.46 (1.3–1.6) |
| GI | 2,756.5 | 1.69 (1.6–1.8) | 1,995.9 | 1.49 (1.4–1.6) |
| General and administration site | 2,252.6 | 1.75 (1.6–1.9) | 1,457.6 | 1.78 (1.6–1.9) |
| Hepatobiliary | 96.33 | 2.89 (1.9–4.3) | 30.26 | 1.50 (0.8–2.6) |
| Immune system | 481.6 | 1.78 (1.5–2.1) | 822.1 | 2.54 (2.2–2.9) |
| Infections and infestations | 3,923.6 | 2.13 (2.0–2.2) | 3,995.7 | 1.52 (1.4–1.6) |
| Injury, poisoning | 607.6 | 1.23 (1.1–1.4) | 747.7 | 1.50 (1.3–1.7) |
| Metabolism/nutrition | 485.3 | 1.66 (1.4–1.9) | 177.8 | 1.72 (1.3–2.2) |
| Musculoskeletal and connective tissue | 2,867.7 | 1.45 (1.4–1.5) | 1,654.3 | 1.60 (1.5–1.7) |
| Neoplasms benign, malignant, and unspecified | 385.3 | 1.09 (0.9–1.3) | 363.1 | 1.40 (1.2–1.6) |
| Nervous system | 1,207.8 | 1.48 (1.3–1.6) | 800.7 | 1.54 (1.4–1.7) |
| Pregnancy, puerperium, and perinatal | 11.1 | 0.43 (0.2–0.9) | 148.8 | 1.27 (1.0–1.6) |
| Psychiatric | 1,063.3 | 1.98 (1.8–2.2) | 747.7 | 1.68 (1.5–1.9) |
| Renal and urinary | 566.8 | 1.53 (1.3–1.7) | 303.9 | 1.37 (1.1–1.6) |
| Reproductive system and breast | 377.9 | 1.17 (1.1–1.4) | 480.4 | 1.40 (1.2–1.6) |
| Respiratory, thoracic, and mediastinal | 2,897.3 | 3.14 (2.9–3.4) | 2,635.2 | 2.57 (2.4–2.8) |
| Skin and subcutaneous tissue | 1,726.5 | 1.57 (1.4–1.7) | 1,668.1 | 1.54 (1.4–1.7) |
| Social circumstances | 292.7 | 1.80 (1.5–2.2) | 184.1 | 2.12 (1.6–2.7) |
| Surgical and medical | 2,315.6 | 1.51 (1.4–1.6) | 1,480.3 | 1.35 (1.2–1.5) |
| Vascular | 926.2 | 1.41 (1.3–1.6) | 315.2 | 1.20 (1.0–1.4) |

- Elevated serum cadmium and lead levels in smokers resulting in glomerular dysfunction
- Nephropathies are accelerated by nicotine with an increased incidence of microalbuminuria progressing to proteinuria
- Cigarette smoke-induced renal damage is due, at least in part, to activation of the sympathetic nervous system resulting in an elevation in blood pressure
- Ethanol, nicotine, or concurrent intake significantly increases lipid peroxidation in liver, and decreased superoxide dismutase activity and increased catalase activity in the kidney
- Both active and passive smoking is toxic to renal function

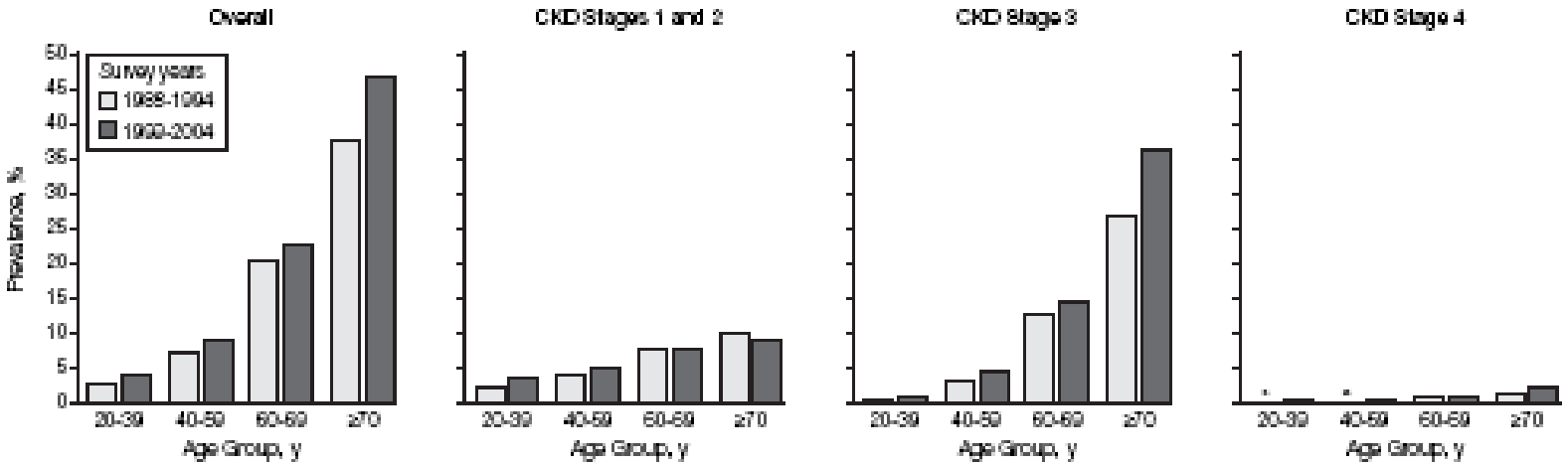
# Chronic Renal Failure (CRF)

- CRF rises in prevalence with age and is frequently associated with chronic diseases such as congestive heart failure and diabetes mellitus
- When present as a comorbidity, CRF carries negative prognostic implications and impacts the therapeutic strategy

# Prevalence of Chronic Kidney Disease in the United States

Josef Coresh, MD, PhD
Elizabeth Selvin, PhD, MPH
Lesley A. Stevens, MD, MS
Jane Manzi, PhD
John W. Kusek, PhD
Paul Eggers, PhD
Frederick Van Lente, PhD
Andrew S. Levey, MD

**Figure 2.** Prevalence of Chronic Kidney Disease (CKD) Stages by Age Group in NHANES 1988-1994 and 1999-2004




NHANES Indicates National Health and Nutrition Examination Surveys.
[a]There were no cases in 1988–1994.

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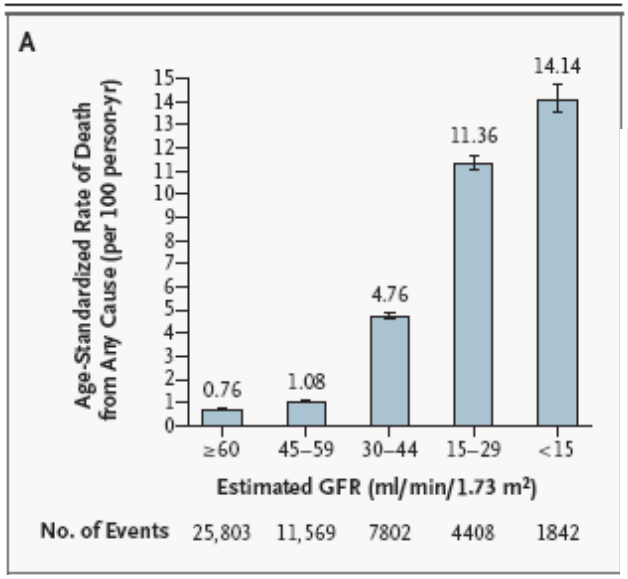
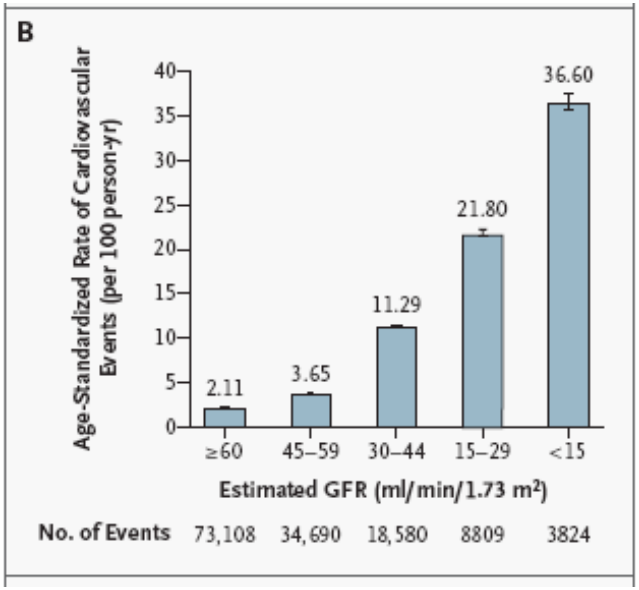
The NEW ENGLAND JOURNAL of MEDICINE

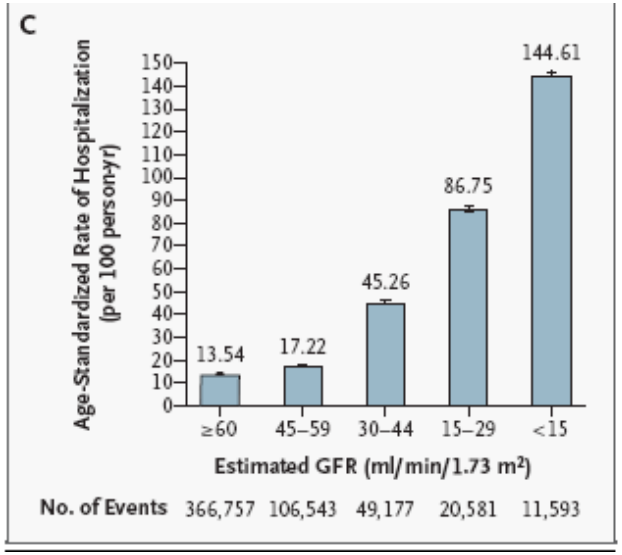
ORIGINAL ARTICLE

# Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization

Alan S. Go, M.D., Glenn M. Chertow, M.D., M.P.H., Dongjie Fan, M.S.P.H., Charles E. McCulloch, Ph.D., and Chi-yuan Hsu, M.D.



# BPCO e INSUFFICIENZA RENALE CRONICA

Molti studi che considerano la comorbilità della BPCO spesso si riferiscono a popolazioni selezionate (con esclusione dei pazienti affetti da insufficienza renale), non specificano in che modo è stata posta la diagnosi di insufficienza renale, o non includono l'insufficienza renale tra le diagnosi self-reported

# Co-morbidity contributes to predict mortality of patients with chronic obstructive pulmonary disease

R. Antonelli Incalzi*, L. Fuso**, M. De Rosa**, F. Forastiere+, E. Rapiti+,
B. Nardecchia**, R. Pistelli**

*Co-morbidity contributes to predict mortality of patients with chronic obstructive pulmonary disease. R. Antonelli Incalzi, L. Fuso, M. De Rosa, F. Forastiere, E. Rapiti, B. Nardecchia, R. P*

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**tion or ischaemia (HR 1.42; 95% CI 1.02–1.96), $FEV_1$ <590 mL (HR 1.49; 95% CI 0.97–2.27). A score based upon these variables predicted mortality at 5 yrs with a sensitivity of 63% and a specificity of 77%.**

**Selected co-morbid diseases and electrocardiogram signs of right ventricular hypertrophy play a major prognostic role in advanced chronic obstructive pulmonary disease. The clinical assessment of patients with chronic obstructive pulmonary disease should include these important and easily measurable variables.**

*Eur Respir J 1997; 10: 2794–2800.*

*Dept of Geriatrics and **Dept of Respiratory Physiology Catholic University,
t,

Unico lavoro che correla l'insufficienza renale cronica e la mortalità. La prevalenza di insufficienza renale cronica è del 6% e predice la mortalità a lungo termine in modo indipendente. Insufficienza renale valutata con creatininemia (sottostimata)

Table 3. – Survival of patients with chronic obstructive pulmonary disease, according to various characteristics

| Variables significantly correlated with mortality | Survival yrs | | Gehan's Wilcoxon | p-value |
|---|---|---|---|---|
| | Presence of risk | Absence of risk | | |
| $P_{A\text{-}a,O_2}$+ | 1.76 (0.29–4.25) | 3.29 (1.46–5.04) | 3.071 | 0.001 |
| Chronic renal failure | 0.84 (0.25–2.35) | 3.17 (1.29–4.99) | 2.917 | 0.002 |
| ECG signs of RVH or overload | 2.62 (0.89–4.35) | 3.50 (1.06–5.53) | 2.371 | 0.009 |
| FEV1† | 2.88 (0.73–4.79) | 3.89 (2.35–5.80) | 2.235 | 0.012 |
| Length of hospital stay+ | 2.23 (0.65–4.57) | 3.36 (1.39–5.04) | 2.195 | 0.014 |
| ECG signs of ischaemic heart disease | 2.19 (0.69–3.97) | 3.26 (1.27–5.21) | 1.913 | 0.027 |
| Chronic liver disease | 1.45 (0.33–3.76) | 3.11 (1.04–5.04) | 1.839 | 0.033 |
| ECG evidence of ventricular arrhythmias | 2.39 (0.48–3.45) | 3.12 (0.98–5.04) | 1.822 | 0.034 |
| History of myocardial infarction | 0.84 (0.50–3.20) | 3.12 (1.14–5.02) | 1.738 | 0.041 |

Survival values are presented as median values with interquartile ranges in parentheses. $P_{A\text{-}a,O_2}$: alveolar-arterial oxygen difference; ECG: electrocardiogram; RVH: right ventricular hypertrophy; FEV1: forced expiratory volume in one second. †: lowest quartile *versus* other quartiles; +: highest quartile *versus* other quartiles.

Table 4. – Results of the multivariate Cox regression analysis

| Variables | β coefficient | Hazard rate (95% CI) | t-value | p-value |
|---|---|---|---|---|
| Age (per year) | 0.038 | 1.04 (1.02–1.05) | 4.88 | 0.00001 |
| ECG signs of RVH or overload | 0.565 | 1.76 (1.30–2.38) | 3.67 | 0.0003 |
| Chronic renal failure | 0.580 | 1.79 (1.05–3.02) | 2.16 | 0.032 |
| ECG signs of ischaemic heart disease | 0.349 | 1.42 (1.02–1.96) | 2.10 | 0.037 |
| FEV1† | 0.398 | 1.49 (0.97–2.27) | 1.97 | 0.049 |
| Chronic liver disease | 0.508 | 1.66 (0.95–2.88) | 1.80 | 0.073 |
| ECG evidence of ventricular arrhythmias | 0.470 | 1.60 (0.93–2.75) | 1.70 | 0.089 |
| $P_{A\text{-}a,O_2}$+ | 0.231 | 1.26 (0.92–1.72) | 1.44 | 0.149 |
| Length of hospital stay+ | 0.124 | 1.13 (0.83–1.55) | 0.77 | 0.441 |
| Year of recruitment | -0.016 | 0.98 (0.94–1.03) | -0.72 | 0.471 |
| Female gender | -0.031 | 0.97 (0.67–1.41) | -0.16 | 0.869 |
| History of myocardial infarction | 0.053 | 1.05 (0.54–2.05) | 0.15 | 0.876 |

95% CI: 95% confidence intervals; ECG: electrocardiogram; RVH: right ventricular hypertrophy; FEV1: forced expiratory volume in one second; $P_{A\text{-}a,O_2}$: alveolar-arterial oxygen difference. †: lowest quartile *versus* other quartiles; +: highest quartile *versus* other quartiles.

Nell’anziano fragile affetto da comorbilità, l’insufficienza renale cronica è spesso associata a normali valori di creatininemia, una condizione conosciuta come INSUFFICIENZA RENALE MISCONOSCIUTA o OCCULTA

Nephrol Dial Transplant (2006) 21: 88–92
doi:10.1093/ndt/gfi163
Advance Access publication 11 October 2005

Nephrology Dialysis

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**Results.** Creatinine and albuminuria were measured in the preceding 2 years in 82.3 and 55.2% of subjects, respectively. In patients with CKD, normoalbuminuria was present in 48.8%, and serum creatinine was normal (≤120 μmol/l) in 54.7%. An abnormal serum creatinine (≥120 μmol/l) had a sensitivity and specificity of 45.3 and 100%, respectively, to identify CKD. The combination of abnormal creatinine and albuminuria had an improved performance but still failed to detect a large number with CKD (sensitivity 82.4%, specificity 75.4%). Serum creatinine failed to identify CKD more often in females (OR 8.22, CI 6.56–10.29).

earlier in the natural history of the disease and enable early effective treatment to delay progression of CKD.

# Come identificare l'insufficienza renale con creatininemia normale

- La creatinina sierica non è affidabile nell'anziano a causa delle alterazioni età-correlate della composizione corporea, che porta alla progressiva perdita di massa magra, e forse anche del ridotto apporto proteico
- E' quindi sempre consigliabile ricorrere alla misurazione della clearance della creatinina oppure della velocità di filtrazione glomerulare
- I metodi per la valutazione diretta della funzione renale non sono tuttavia facilmente applicabili e presentano dei grossi limiti (soprattutto nel paziente anziano)

# Come identificare l'insufficienza renale con creatininemia normale

- Nella pratica clinica la funzione renale è comunemente valutata utilizzando delle equazioni che partendo dalla creatinina sierica forniscono una stima della clearance della creatinina (formula di Cockroft Gault) o della velocità di filtrazione glomerulare (MDRD)
- L'affidabilità di queste formule è molto discussa ed i risultati ottenuti sono influenzati da numerosi fattori
- Nonostante nessuna formula sia ottimale nel predire la funzione renale soprattutto nei pazienti anziani, l'utilizzo di queste equazioni sono un metodo di facile utilizzo che permette di individuare con buona affidabilità i pazienti con ridotta funzione renale in presenza di creatinina sierica normale

# Does concealed chronic kidney disease predict survival of older patients discharged from acute care hospitals?

Corsonello A, Pedone C, Lattanzio F, Garasto S, Corica F, Bustacchini S, Guffanti, EE, Abbatecola AM, Mari V, Fimognari FL, Incalzi RA.

Rejuvenation Res. 2010 Oct;13(5):539-45.

We aimed at verifying whether unrecognized chronic kidney disease (CKD) (i.e., reduced estimated glomerular filtration rate in spite of normal serum creatinine) has prognostic significance in an unselected population of older patients discharged from 11 acute care hospitals located throughout Italy. Our series consisted of 396 participants aged 70 and older. Estimated glomerular filtration rate (eGFR) was calculated by the Modification of Diet in Renal Disease (MDRD) study equation. We compared three groups: Normal renal function (normal serum creatinine levels and normal eGFR), concealed (normal serum creatinine levels and reduced eGFR), or overt (increased creatinine levels and reduced eGFR) renal failure. The relationship between renal function and 1-year mortality was evaluated using Kaplan-Meier curves and Cox regression analysis including potential confounders. Overall, 56 patients died over a cumulative follow-up time of 335 months, with an estimated incidence rate of 16.7/100 person-year (PY). The corresponding figures in patients with normal renal function, concealed CKD, and overt CKD were 9.8/100 PY (95% CI, 5.7-15.7), 28.3/100 PY (95% CI, 13.6-52.1), and 23.0 (95% CI, 15.4-33.0), respectively (log rank test p = 0.006). According to the fully adjusted model, both concealed (hazard ratio [HR], 2.35; 95% CI, 1.09-6.01) and overt CKD (HR, 2.09; 95% CI, 1.05-5.34) were significantly associated with the outcome. Concealed CKD contributes to profile the elderly patient at greater risk of death after being discharged from acute care medical wards. If confirmed in broader populations, this finding might have both clinical and epidemiological implications.

# Concealed Renal Insufficiency and Adverse Drug Reactions in Elderly Hospitalized Patients

*Andrea Corsonello, MD; Claudio Pedone, MD; Francesco Corica, MD; Chiara Mussi, MD; Pierugo Carbonin, MD; Raffaele Antonelli Incalzi, MD; for the Gruppo Italiano di Farmacovigilanza nell'Anziano (GIFA) Investigators*

**Table 1. Sociodemographic and Clinical Characteristics of Patients Divided According to Their Renal Function***

| Characteristic | Normal Renal Function, % (n = 7195) | Concealed Renal Insufficiency, % (n = 1631) | Overt Renal Insufficiency, % (n = 2861) | *P* Value |
|---|---|---|---|---|
| Age ≥80 y | 22.6 | 44.5† | 42.1§ | .001 |
| Male sex | 47.1 | 52.7† | 64.5§‖ | .001 |
| Alcohol consumption >0.5 L | 11.0 | 6.7† | 9.9‖ | .001 |
| Dependent in at least 1 ADL | 12.5 | 15.7‡ | 15.5§ | .001 |
| Cognitive impairment | 22.3 | 32.6† | 29.7§ | .001 |
| Medicine ward | 38.2 | 33.3† | 33.4§ | .001 |
| >4 Prescribed drugs | 58.1 | 69.3† | 72.9§ | .001 |
| >4 Diagnoses | 28.5 | 33.6† | 41.1§‖ | .001 |
| Length of stay >14 d | 33.3 | 33.8 | 37.2§ | .01 |
| Serum albumin <3.5 g/dL | 23.2 | 42.5† | 35.0§‖ | .001 |
| BMI <20 | 9.3 | 10.0 | 7.6‖¶ | .01 |
| Diabetes | 16.2 | 21.0† | 22.6§ | .001 |
| CHF | 7.9 | 13.5† | 18.9§‖ | .001 |
| Hypertension | 29.2 | 32.4 | 37.0§# | .001 |

Abbreviations: ADL, activities of daily living; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); CHF, congestive heart failure.

*Normal renal function: estimated glomerular filtration rate (GFR) higher than or equal to 60 mL/min × 1.73 $m^2$ body surface area (BSA) and serum creatinine level lower than or equal to 1.2 mg/dL (≤106 µmol/L); concealed renal insufficiency: estimated GFR lower than 60 mL/min × 1.73 $m^2$ BSA and serum creatinine level lower than or equal to 1.2 mg/dL (≤106 µmol/L); overt renal insufficiency: estimated GFR lower than 60 mL/min × 1.73 $m^2$ BSA and serum creatinine level higher than 1.2 mg/dL (>106 µmol/L). *P* values in the last column refer to the 3 (groups) by 2 (level) $\chi^2$ test

†*P*<.001 (concealed renal insufficiency vs normal renal function).

‡*P*<.01 (concealed renal insufficiency vs normal renal function).

§*P*<.001 (overt renal insufficiency vs normal renal function).

‖*P*<.001 (overt renal insufficiency vs concealed renal insufficiency).

¶*P*<.01 (overt renal insufficiency vs normal renal function).

#*P*<.01 (overt renal insufficiency vs concealed renal insufficiency).

ORIGINAL INVESTIGATION

# Concealed Renal Insufficiency and Adverse Drug Reactions in Elderly Hospitalized Patients

*Andrea Corsonello, MD; Claudio Pedone, MD; Francesco Corica, MD; Chiara Mussi, MD; Pierugo Carbonin, MD; Raffaele Antonelli Incalzi, MD; for the Gruppo Italiano di Farmacovigilanza nell'Anziano (GIFA) Investigators*

**Table 4. Summary Regression Models of Selected Risk Factors to the Occurrence of ADR During Hospital Stay***

| Demographic/Clinical Characteristic | Any ADR (n = 941) | ADR to Hydrosoluble Drugs (n = 301) | ADR to Any Other Drugs (n = 640) |
|---|---|---|---|
| Age, y | | | |
| <65 | 1.00 (Referent) | 1.00 (Referent) | 1.00 (Referent) |
| 65-79 | 0.96 (0.80-1.16) | 1.18 (0.84-1.65) | 0.90 (0.73-1.11) |
| ≥80 | 0.93 (0.76-1.14) | 1.27 (0.89-1.82) | 0.83 (0.66-1.05) |
| Male sex | 0.83 (0.72-0.95) | 0.80 (0.63-1.01) | 0.85 (0.72-1.0) |
| Serum albumin <3.5 g/dL | 1.12 (0.97-1.30) | 1.12 (0.88-1.43) | 1.12 (0.94-1.33) |
| Medicine ward | 0.82 (0.71-1.01) | 0.94 (0.73-1.21) | 0.79 (0.70-1.01) |
| Length of stay >14 d | 1.85 (1.61-2.12) | 2.08 (1.64-2.63) | 1.70 (1.45-2.0) |
| >4 Diagnoses | 1.50 (1.31-1.73) | 1.62 (1.28-2.06) | 1.44 (1.22-1.71) |
| >4 Prescribed drugs | 2.65 (2.20-3.19) | 2.46 (1.77-3.42) | 2.61 (2.10-3.24) |
| Renal function | | | |
| Normal renal function | 1.00 (Referent) | 1.00 (Referent) | 1.o0 (Referent) |
| Concealed renal insufficiency | 0.97 (0.78-1.19) | 1.61 (1.15-2.25) | 0.83 (0.65-1.08) |
| Overt renal insufficiency | 1.26 (1.08-1.48) | 2.02 (1.54-2.65) | 1.01 (0.83-1.23) |

Abbreviations: ADR, adverse drug reaction; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters).
*Data are given as odds ratio (95% confidence interval) (calculated by entering all variables simultaneously in logistic regression model).

European Heart Journal (2008) **29**, 1029–1036
doi:10.1093/eurheartj/ehn102

**CLINICAL RESEARCH**
*Heart failure/cardiomyopathy*

# Prevalence and significance of unrecognized renal insufficiency in patients with heart failure

**Aims** Renal insufficiency (RI) is a strong predictor of adverse outcome in patients with heart failure (HF). We aimed to determine the prevalence of RI being unrecognized and its significance in patients hospitalized with HF.

**Methods and results** We analysed data from a prospective survey of 4102 hospitalized patients with HF. RI [defined as estimated glomerular filtration rate (eGFR) $< 60$ mL/min/1.73 $m^2$] was present in 2145 (57%) patients but, based on medical records, was unrecognized in 872 [41%, 95% confidence interval (CI) 39–43%] of them. Patients with unrecognized RI were more likely to be women, elderly, and with better functional class, compared with patients with recognized RI. In-hospital and 1 year mortality was significantly higher among patients with recognized and unrecognized RI compared with patients without RI: 6.5 and 7.1 vs. 2.1%, and 38.8 and 30.9 vs. 18.8% ($P < 0.001$), respectively. After adjustment, recognized and unrecognized RI comparably predicted increased in-hospital mortality: odds ratio (OR) and 95% CI of 2.34 (1.43–3.87), $P < 0.001$, and 2.30 (1.45–3.72), $P < 0.001$. After 1 year, recognized RI remained an independent predictor for mortality: OR 1.79 (1.45–2.20), $P < 0.001$, whereas there was a trend for increased mortality predicted by unrecognized RI: OR 1.22 (0.97–1.53), $P = 0.08$.

**Conclusion** A high proportion of RI remains unrecognized among hospitalized patients with HF. As co-morbid RI has important prognostic and therapeutic implications, patients with HF may benefit from routine assessment of GFR.

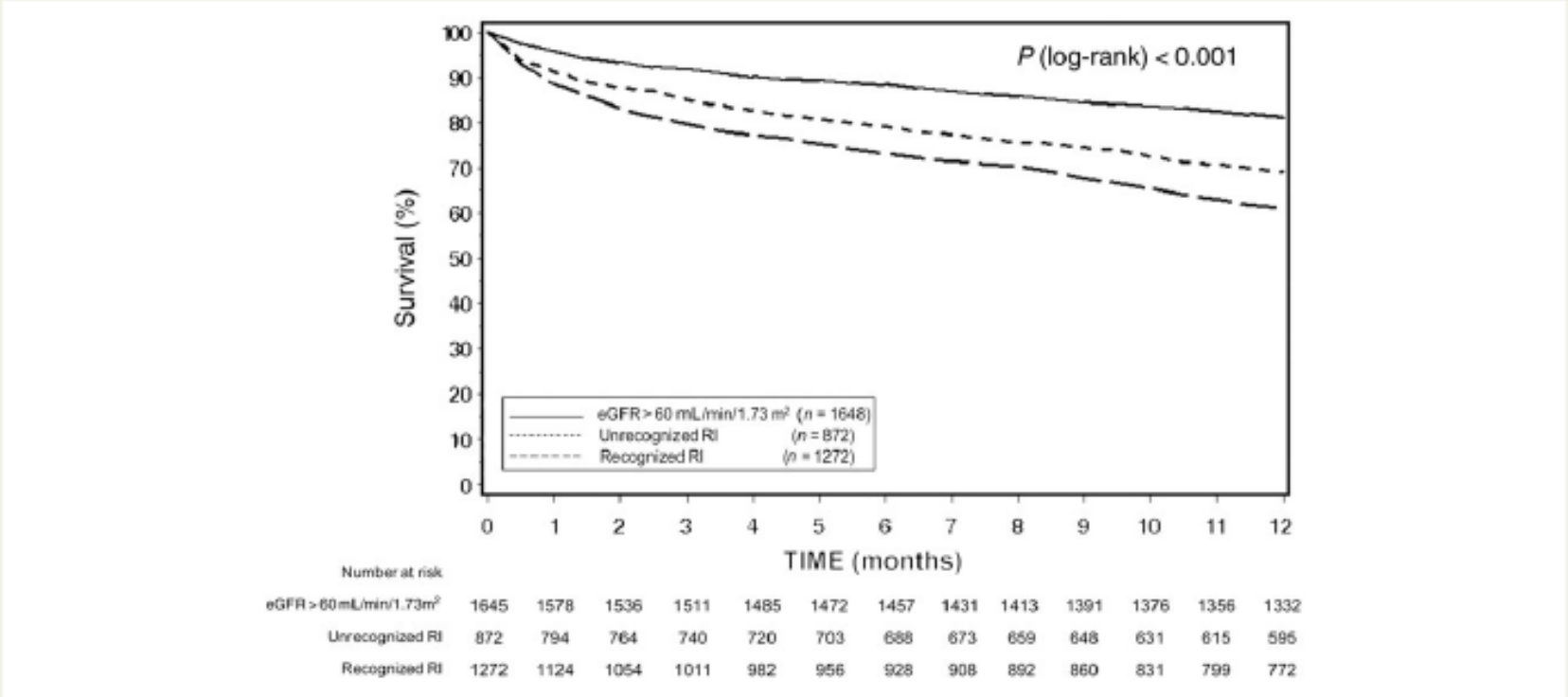



**Figure 2** Kaplan–Meier survival curves of patients with recognized renal insufficiency, unrecognized renal insufficiency, and patients with estimated glomerular filtration rate ≥60 mL/min/1.73 $m^2$.

# Summary and implications

Among hospitalized patients with HF, unrecognized RI is a common, independent predictor of increased mortality. However, a high proportion (41%) of RI remains clinically unrecognized. With the expanding population of HF patients, it is important to identify the subset of patients with HF who are at the highest risk for poor outcomes, so that clinicians can treat modifiable risk factors. The ability to identify chronic RI may promote early implementation of treatment that might arrest or delay the progression of renal damage, enable effective treatment of its complications, and reduce the risk of drug-induced nephrotoxicity. Thus, we suggest the routine use of calculated eGFR, preferably routinely reported by the local laboratory along with serum creatinine, to enhance early recognition of RI in HF patients.

CHEST

Original Research

COPD

# Chronic Renal Failure

## A Neglected Comorbidity of COPD

*Raffaele Antonelli Incalzi, MD; Andrea Corsonello, MD; Claudio Pedone, MD; Salvatore Battaglia, MD; Giuseppe Paglino, MD; and Vincenzo Bellia, MD, FCCP; on behalf of the Extrapulmonary Consequences of COPD in the Elderly Study Investigators**

***Background:*** **To the best of our knowledge, the association between COPD and chronic renal failure (CRF) has never been assessed. Lean mass is frequently reduced in COPD, and the glomerular filtration rate (GFR) might be depressed in spite of normal serum creatinine (concealed CRF). We investigated the prevalence and correlates of both concealed and overt CRF in elderly patients with COPD.**

***Methods:*** **We evaluated 356 consecutive elderly outpatients with COPD enrolled in the Extrapulmonary Consequences of COPD in the Elderly Study and 290 age-matched outpatients free from COPD. The GFR was estimated using the Modification of Diet in Renal Disease Study Group equation. Patients were categorized as having normal renal function (GFR ≥ 60 mL/min/1.73 m²), concealed CRF (normal serum creatinine and reduced GFR), or overt CRF (increased serum creatinine and reduced GFR). Independent correlates of CRF were investigated by logistic regression analysis.**

***Results:*** **The prevalence of concealed and overt CRF in patients with COPD was 20.8% and 22.2%, respectively. Corresponding figures in controls were 10.0% and 13.4%, respectively. COPD and age were significantly associated with both concealed CRF (COPD: odds ratio [OR] = 2.19, 95% CI = 1.17-4.12; age: OR = 1.06, 95% CI = 1.04-1.09) and overt CRF (COPD: OR = 1.94, 95% CI = 1.01-4.66; age: OR = 1.06, 95% CI = 1.04-1.10). Diabetes (OR = 1.96, 95% CI = 1.02-3.76), hypoalbuminemia (OR = 2.83, 95% CI = 1.70-4.73), and muscle-skeletal diseases (OR = 1.78, 95% CI = 1.01-3.16) were significant correlates of concealed CRF. BMI (OR = 1.05, 95% CI = 1.01-1.10) and diabetes (OR = 2.25, 95% CI = 1.26-4.03) were significantly associated with overt CRF.**

***Conclusions:*** **CRF is highly prevalent in patients with COPD, even with normal serum creatinine, and might contribute to explaining selected conditions such as anemia that are frequent complications of COPD.** *CHEST 2010; 137(4):831–837*

**Abbreviations:** CRF = chronic renal failure; GFR = glomerular filtration rate; OR = odds ratio

**Table 2—*Demographic and Clinical Characteristics of Patients Divided According to Renal Function***

| Characteristics | Normal Renal Function, n = 203 | Concealed Renal Dysfunction, n = 74 | Overt Renal Dysfunction, n = 79 | *P* Value |
|---|---|---|---|---|
| Age, y | 74.3 ± 6.2 | 76.3 ± 5.8 | 75.8 ± 6.0 | .026 |
| Gender, males | 170 (83.7) | 54 (73.0)[a] | 62 (78.5) | .122 |
| $FEV_1$, % | 54.9 ± 18.1 | 57.3 ± 17.2 | 56.5 ± 17.2 | .565 |
| Pack-years | 47.0 ± 40.0 | 40.7 ± 44.4 | 50.7 ± 36.5 | .330 |
| Barthel score, self-care | 47.4 ± 6.4 | 48.0 ± 4.8 | 46.2 ± 7.8 | .219 |
| Barthel score, mobility | 42.2 ± 8.2 | 42.9 ± 7.1 | 41.8 ± 7.7 | .668 |
| Barthel score, total | 89.4 ± 13.6 | 90.9 ± 10.5 | 87.9 ± 14.1 | .381 |
| 6WD, m | 330 ± 143 | 303 ± 118 | 291 ± 123 | .090 |
| 6WD, % | 76.2 ± 31.6 | 73.9 ± 24.1 | 70.5 ± 26.3 | .453 |
| pH | 7.42 ± 0.04 | 7.42 ± 0.03 | 7.41 ± 0.04 | .051 |
| $nPaco_2$, mm Hg | 43.0 ± 9.4 | 39.1 ± 5.2[a] | 41.2 ± 6.2 | .011 |
| $Pao_2$, mm Hg | 72.4 ± 12.7 | 76.8 ± 14.8 | 76.3 ± 11.7 | .037 |
| $Sao_2$, % | 94.1 ± 2.9 | 94.8 ± 2.4 | 94.1 ± 2.8 | .215 |
| Respiratory drugs, n | 1.7 ± 1.2 | 1.4 ± 0.9 | 1.7 ± 1.6 | .150 |
| Comorbidities, n | 3.5 ± 2.4 | 4.2 ± 2.7 | 5.2 ± 3.2[b] | .001 |
| Hypertension | 111 (54.7) | 47 (63.5) | 53 (67.1) | .115 |
| Cardiovascular diseases | 51 (25.1) | 19 (25.7) | 19 (24.1) | .972 |
| Muscle-skeletal diseases | 52 (25.6) | 29 (39.2)[a] | 20 (25.3) | .068 |
| Gastrointestinal diseases | 59 (29.1) | 20 (27.0) | 24 (30.4) | .899 |
| Diabetes | 34 (16.7) | 19 (25.7) | 28 (35.4)[c] | .003 |
| Cerebrovascular diseases | 14 (6.9) | 6 (8.1) | 10 (12.7) | .292 |

Data are number of cases (percentage) or mean ± SD. Cardiovascular diseases: heart failure, coronary heart disease, history of pulmonary embolism, venous thrombosis, arrhythmias, valvular diseases, peripheral vascular disease. Muscle-skeletal diseases: osteoporosis, arthritis, kyphosis, scoliosis, fractures, myastenia. Gastrointestinal diseases: gastroesophageal reflux disease, peptic ulcer, liver diseases, inflammatory and/or vascular bowel diseases, chronic pancreatitis. Cerebrovascular diseases: transient ischemic attack, stroke, chronic cerebrovascular disease. 6WD = 6-min walk distance; $Sao_2$ = arterial oxygen saturation.

[a] $P < .05$ vs normal renal function.

[b] $P < .01$.

[c] $P < .001$.

**Table 4—*Backward Stepwise Logistic Regression Models of Selected Variables to Concealed or Overt Renal Dysfunction vs Normal Renal Function***

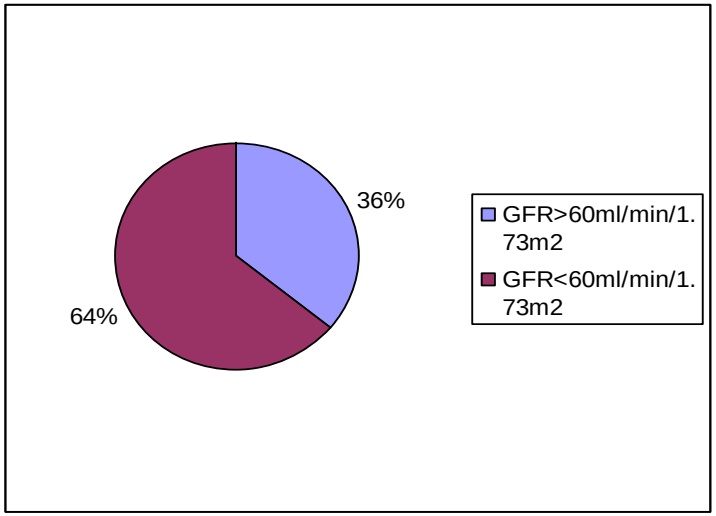
| Variables | OR | 95% CI |
|---|---|---|
| Concealed renal dysfunction[a] | | |
| Age, y (for each 1-y increase) | 1.06 | 1.04-1.09 |
| COPD | 2.19 | 1.17-4.12 |
| Serum albumin < 3.5 g/dL | 2.83 | 1.70-4.73 |
| Muscle-skeletal disease | 1.78 | 1.01-3.16 |
| Diabetes | 1.96 | 1.02-3.76 |
| Overt renal dysfunction[b] | | |
| Age, y (for each 1-y increase) | 1.06 | 1.04-1.10 |
| BMI | 1.05 | 1.01-1.10 |
| COPD | 1.94 | 1.01-4.66 |
| Diabetes | 2.25 | 1.26-4.03 |

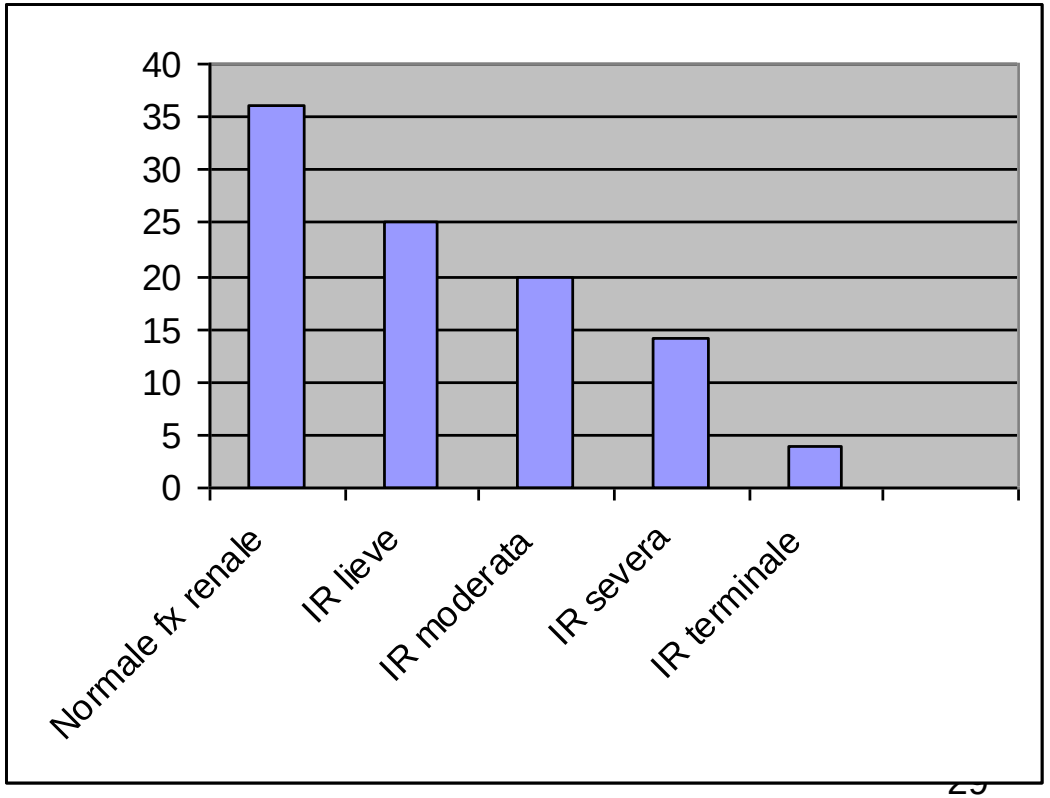
OR = odds ratio.

[a]Cardiovascular disease and gender were removed on step 2, hypertension and BMI were removed on step 3, and cerebrovascular disease was removed on step 4.

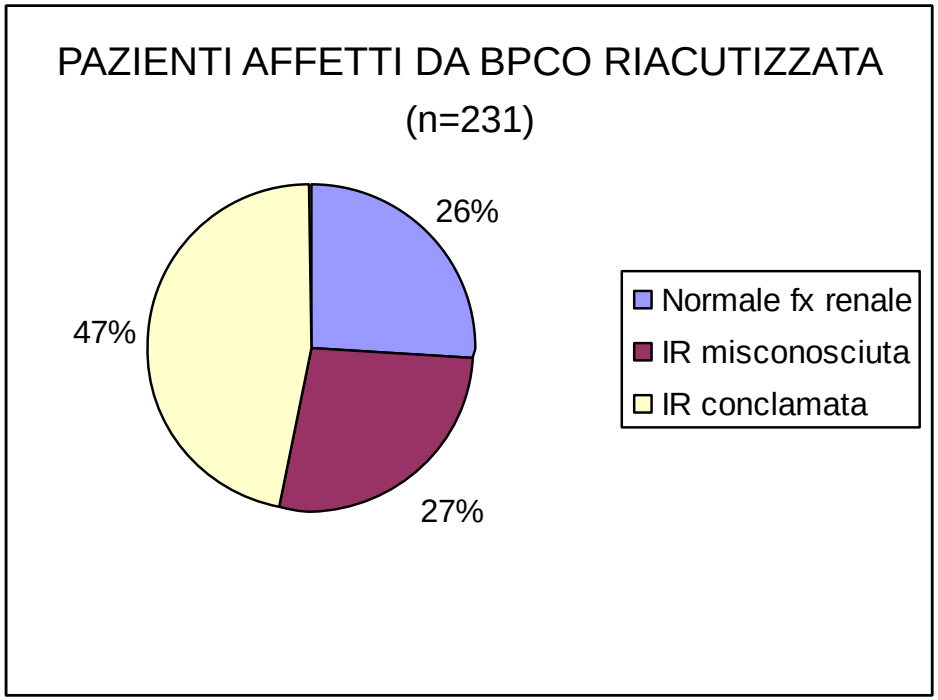
[b]Hypoalbuminemia and muscle-skeletal disease were removed on step 2, cardiovascular disease was removed on step 3, and gender was removed on step 4; hypertension and cerebrovascular disease were removed on step 5.

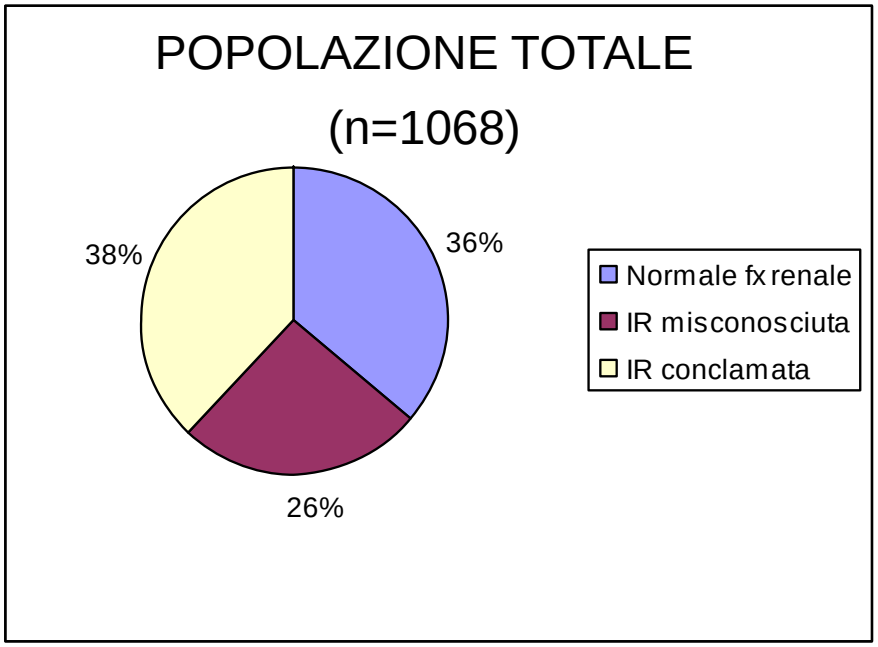
# Prevalenza e gravità di insufficienza renale nella popolazione totale di pazienti ricoverati in U.O Medicina S'Anna (1068 pz)



# Prevalenza di insufficienza renale misconosciuta e conclamata



# Characteristics of study population stratified for the presence of chronic renal failure (CRF) in AECOPD patients (229 pts).

| Variables | No CRF (n=60) | Occult CRF (n=61) | p* | | Occult CRF (n=61) | Overt CRF (n=108) | p* |
|---|---|---|---|---|---|---|---|
| Age (years) | 78,0±7.2 | 83,6±6.7 | ,000 | | 83,6±6.7 | 82.4±6.6 | n.s. |
| Gender (Female) | 40 | 62 | ,011 | | 62 | 61 | n.s. |
| Body Mass Index (Kg/m$^2$) | 23.7±4.8 | 24.8±5.5 | n.s. | | 24.8±5.5 | 26.0±5.5 | n.s. |
| Mini Mental State Examination (MMSE) | 23.1±3.9 | 19.9±6.2 | ,002 | | 19.9±6.2 | 20.0±7.3 | n.s. |
| Geriatric Depression Scale (GDS) | 5.2±3.0 | 5.0±3.0 | n.s. | | 5.0±3.0 | 4.3±3.0 | n.s. |
| IADL (functions lost) | 2.5±2.5 | 4.5±3.1 | ,000 | | 4.5±3.1 | 4.6±2.9 | n.s. |
| Barthel index (BI) pre-admission | 82.8±24.2 | 76.2±26.1 | n.s. | | 76.2±26.1 | 72.8±26.4 | n.s. |
| Barthel index at admission | 60.9±32.5 | 51.6±34.9 | n.s. | | 51.6±34.9 | 51.5±32.8 | n.s. |
| Barthel index at discharge | 78.0±26.0 | 68.4±28.2 | ,05 | | 68.4±28.2 | 65.8±30.6 | n.s. |
| Numbers of medications at admission | 4.8±2.7 | 4.9±3.0 | n.s. | | 4.9±3.0 | 6.3±2.8 | ,003 |
| Numbers of medications at discharge | 5.8±2.4 | 5.9±2.5 | n.s. | | 5.9±2.5 | 6.9±2.2 | ,004 |
| Apache II score | 9.0±4.0 | 8.3±2.8 | n.s. | | 8.3±2.8 | 10.7±4.1 | ,000 |
| Adverse events | 20 | 39 | ,02 | | 39 | 35 | n.s. |

# Characteristics of study population stratified for the presence of chronic renal failure (CRF) in AECOPD patients (229 pts).

| Variables | No CRF (n=60) | Occult CRF (n=61) | p* | | Occult CRF (n=61) | Overt CRF (n=108) | p* |
|---|---|---|---|---|---|---|---|
| Charlson Index | 3.4±1.9 | 3.7±1.2 | n.s. | | 3.7±1.2 | 4.4±1.8 | ,002 |
| Ischemic Heart disease | 17 | 18 | n.s. | | 18 | 14 | n.s. |
| Congestive Heart Failure | 28 | 56 | ,002 | | 56 | 52 | n.s. |
| Cerebrovascular disease | 30 | 21 | n.s. | | 21 | 43 | ,004 |
| Dementia | 21 | 15 | ,04 | | 21 | 14 | n.s. |
| Diabetes mellitus | 17 | 29 | ,07 | | 29 | 28 | n.s. |
| Diabetes complicated | 3 | 3 | n.s. | | 3 | 13 | ,03 |
| Serum cholesterol (mg/dl) | 183.6±35.6 | 171.4±44.0 | ,09 | | 171.4±44.0 | 172.2±44.4 | n.s. |
| Serum albumin (mg/dl) | 3.6±0.5 | 3.4±0.4 | ,02 | | 3.4±0.4 | 3.4±0.4 | n.s. |
| Hemoglobin (gr/dl) | 13.3±1.6 | 12.6±1.4 | ,02 | | 12.6±1.4 | 12.0±2.0 | ,03 |
| Urea (mg/dl) | 35.1±10.7 | 47.3±15.5 | ,000 | | 47.3±15.5 | 78.7±39.6 | ,000 |
| Creatinine (mg/dl) | 0.8±0.1 | 1.0±0.1 | ,000 | | 1.0±0.1 | 1.7±0.9 | ,000 |
| *e*-GFR (MDRD) | 72.8±15.1 | 52.1±5.3 | ,000 | | 52.1±5.3 | 31.6±9.7 | ,000 |
| ESR (mm/h) | 32.3±23.0 | 40.7±26.3 | ,06 | | 40.7±26.3 | 43.3±28.4 | n.s. |
| CRP (mg/dl) | 52.2±47.0 | 55.6±51.1 | n.s. | | 55.6±51.1 | 52.9±47.8 | n.s. |
| FEV1 (% of pred.) | 67.7±25.6 | 68.3±25.1 | n.s. | | 68.3±25.1 | 68.6±28.0 | n.s. |
| Length of stay (days) | 8.4±5.3 | 7.8 ±3.1 | ,08 | | 7.8 ±3.1 | 8.8±3.9 | ,09 |

In una regressione logistica multivariata l'insufficienza renale misconosciuta (rispetto alla funzione renale normale) risultava essere associata in modo indipendente a:

| | O.R. | 95%CI | p |
|---|---|---|---|
| Età | 1.09 | 1.01-1.18 | .020 |
| Scompenso Cardiaco | 3.58 | 1.35-9.47 | .010 |
| Complicanze Diabete | 2.92 | 0.96-8.82 | .058 |
| Eventi Avversi | 3.68 | 1.17-11.59 | .026 |

# CONCLUSIONI

- Questi dati confermano l'alta prevalenza di IR misconosciuta nella popolazione anziana ospedalizzata, in particolare nei pazienti ricoverati per BPCO riacutizzata
- La presenza di IR misconosciuta identifica una categoria di pazienti "più fragili" (dal punto di vista cognitivo, funzionale e somatico) che non possono essere identificati dalla semplice valutazione della creatininemia
- La presenza di IR misconosciuta risulta associata in modo indipendente alla comorbilità cardiaca e diabetica ed a un aumentato rischio di sviluppare reazioni avverse intraospedaliere
- L'IR dovrebbe comunque essere considerata come una comorbidità frequente della BPCO e bisognerebbe implementare nella pratica clinica routinariamente il suo riconoscimento attraverso la valutazione del filtrato glomerulare, essendo la cretaininemia un parametro non attendibile

# Spunti di discussione

- L’alta prevalenza di insufficienza renale nei pazienti affetti da BPCO potrebbe avere importanti implicazioni cliniche
- Tale associazione potrebbe aiutare a capire e spiegare meglio il legame tra BPCO ed anemia
- L’associazione con le reazioni avverse da farmaci andrebbe sempre presa in considerazione nei pazienti affetti da BPCO riacutizzata che necessitano frequentemente di polifarmacologia (soprattutto corticosteroidea ed antibiotica)