GIMBE®

*Gruppo Italiano per la Medicina Basata sulle Evidenze*

Evidence-Based Medicine Italian Group

**Decisioni Cliniche e Prove di Efficacia**

La pratica clinica è dissociata dalle evidenze?

*Rimini, 25-26 marzo 2006*


## Workshop Clinici Interattivi (2)

# La gestione ambulatoriale del paziente con insufficienza renale

## Il Medico di Famiglia è un optional?

Leonardo Cagnoli
Modesto Fantini

# Scenario Clinico

- Il signor Matteo è un pensionato di 63 anni, ex commerciante in sovrappeso (172 cm x 80 kg, BMI 27)
- E' un buon mangiatore che non disdegna un bicchiere di vino ai pasti.
- Ha fumato 20 sigarette/die da 15 a 55 anni, quando ha smesso in seguito al decesso di un cugino fumatore per carcinoma polmomare.
- Anamnesi familiare negativa per patologie cardiovascolari

# Scenario Clinico

- A 55 anni tiroidectomia totale - per carcinoma papillifero della tiroide - e conseguente terapia sostitutiva (tiroxina 150 mcg/die)
- Da molti anni, riscontro di dislipidemia mista mai trattata farmacologicamente, con valori elevati sia di di colesterolo LDL (> 150 mg%), sia di trigliceridi (200-400 mg%).
- Da circa tre anni, riscontro di ipertensione lieve (155/90 mmHg), per la quale non assume alcun farmaco
- Riferisce nicturia da qualche anno

# Scenario Clinico

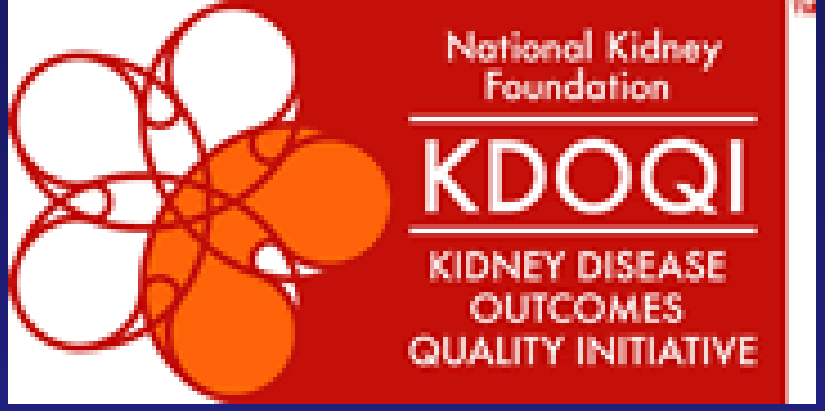
- Nel giugno 2005, in occasione del controllo annuale, riscontro occasionale di creatininemia di 1.5 mg% (azotemia 58 mg%), mai riscontrata in precedenza.
- Esami di routine nella norma, tranne profilo lipidico (LDL-C 148 mg%, trigliceridi 280 mg%).
- Il signor Matteo rimane assolutamente asintomatico
- Obiettivamente:
  - PAO 145/90 mmHg
  - FC 74 bpm
  - nessun altro reperto da segnalare

# CLINICAL QUESTIONS

# 1. Lo screening dell'IRC è appropriato in tutti i pazienti con ipertensione?

1. No
2. Sì, con la creatininemia
3. Sì, con la velocità di filtrazione glomerulare*
4. Sì, con la proteinuria
5. 3+4

*Glomerular Filtration Rate (GFR)




# K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification

*Am J Kidney Dis, 2002*

| *Clinical recommendation* | *Evidence rating* |
|---|---|
| All adults with risk factors for chronic kidney disease should be screened with a serum creatinine determination for GFR estimation and analysis of a random urine sample for proteinuria. | C |

- Although screening methods for chronic kidney disease have not been evaluated in randomized controlled trials, the high prevalence of the disease in at-risk populations, the ease of screening, and the availability of effective treatments during early asymptomatic stages of the disease provide sufficient rationale for screening.

*K/DOQI. Am J Kidney Dis, 2002*

# Main high-risk groups that should be screened for chronic kidney disease

- Family history of renal disease
- Diabetes
- Hypertension
- Recurrent urinary tract infections
- Urinary obstruction
- Systemic illness that affects the kidneys

*K/DOQI. Am J Kidney Dis, 2002*

*Boulware LE, Jaar BG, Tarver-Carr ME, et al.*

# Screening for proteinuria in US adults: a cost-effectiveness analysis

*JAMA 2003;290:3101-14*

# Main high-risk groups that should be screened for chronic kidney disease

- Screening all patients older than 60 years is cost-effective even when other risk factors for chronic kidney disease are absent;

- Screening low-risk patients younger than 60 years does not appear to be cost-effective.

*Boulware LE, et al. JAMA, 2003*

# How to screen

- Significant kidney disease can present with decreased GFR or proteinuria, or both.

- K/DOQI guidelines recommend screening for kidney disease with:
  - serum creatinine for use in GFR estimation
  - analysis of a random urine sample for albuminuria

*K/DOQI. Am J Kidney Dis, 2002*

## Stages of Chronic Kidney Disease Based on Estimated GFR

| *Stage* | *GFR (mL per minute per 1.73 $m^2$)* |
|---|---|
| 1 | ≥90 |
| 2 | 60 to 89 |
| 3 | 30 to 59 |
| 4 | 15 to 29 |
| 5 | <15 or dialysis |

*GFR = glomerular filtration rate.*

*K/DOQI. Am J Kidney Dis, 2002*

*Table 4.* **National Kidney Foundation Kidney Disease Outcomes Quality Initiative Classification, Prevalence, and Action Plan for Stages of Chronic Kidney Disease***

| Stage† | Description | GFR, *mL/min per 1.73 m²* | Prevalence, *n (%)*‡ | Action§ |
|---|---|---|---|---|
| — | At increased risk | ≥60 (with chronic kidney disease risk factors) | — | Screening; chronic kidney disease risk reduction |
| 1 | Kidney damage with normal or increased GFR | ≥90 | 5 900 000 (3.3) | Diagnosis and treatment; treatment of comorbid conditions; slowing progression; CVD risk reduction |
| 2 | Kidney damage with mild decreased GFR | 60–89 | 5 300 000 (3.0) | Estimating progression |
| 3 | Moderately decreased GFR | 30–59 | 7 600 000 (4.3) | Evaluating and treating complications |
| 4 | Severely decreased GFR | 15–29 | 400 000 (0.2) | Preparation for kidney replacement therapy |
| 5 | Kidney failure | <15 (or dialysis) | 300 000 (0.1) | Kidney replacement (if uremia present) |

*K/DOQI. Ann Intern Med, 2003*

## Formulas for Estimating GFR in Adults*

### Abbreviated MDRD study equation[12]†

$$\text{GFR (mL per minute per 1.73 m}^2) = 186 \times (S_{Cr})^{-1.154} \times (\text{age})^{-0.203} \times (0.742, \text{ if female}) \times (1.210, \text{ if black})$$

### Cockcroft-Gault equation[13]

$$C_{Cr}\ (\text{mL per minute}) = \frac{(140 - \text{age}) \times \text{weight}}{72 \times S_{Cr}} \times (0.85, \text{ if female})$$

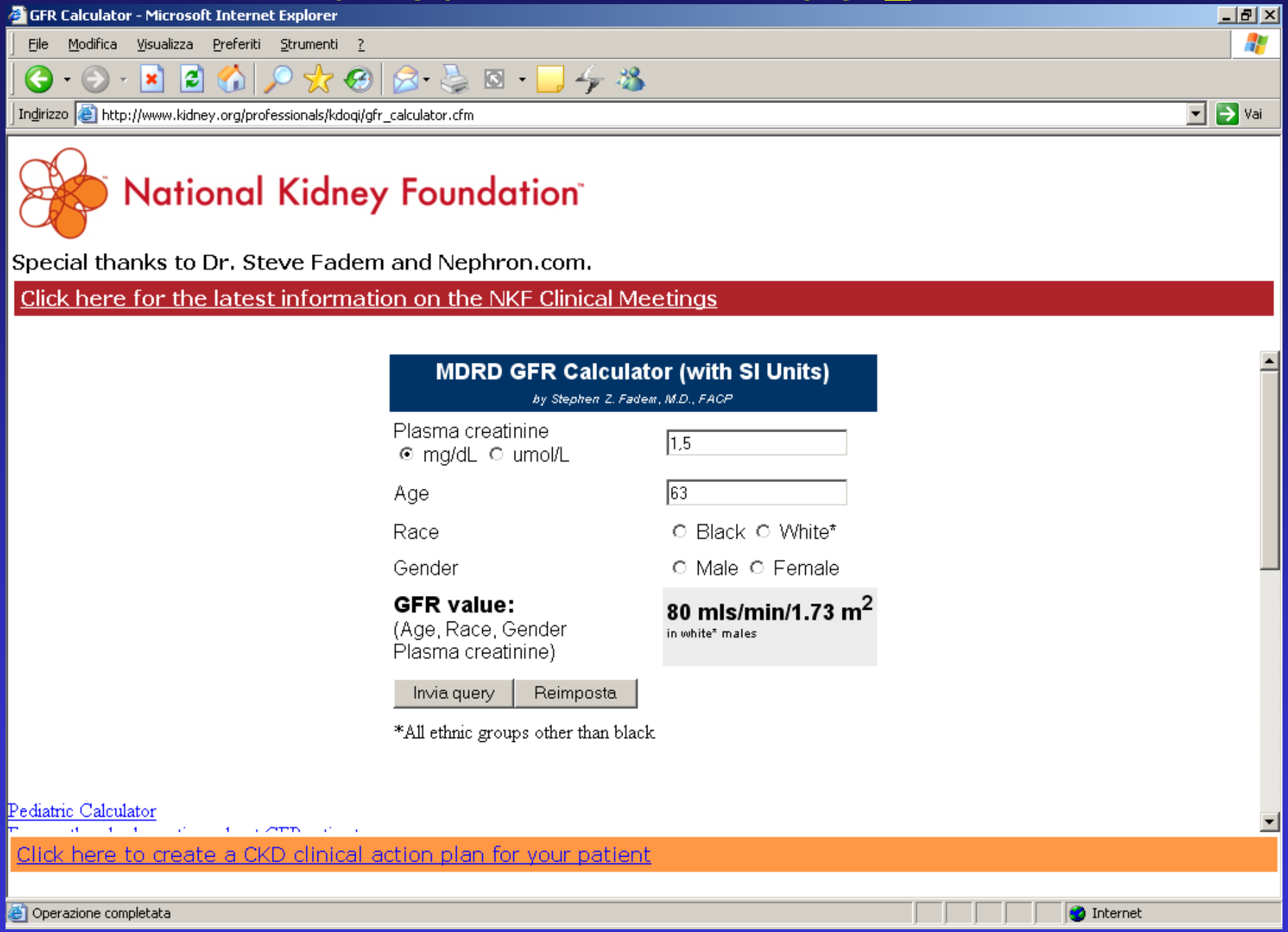
*GFR = glomerular filtration rate; MDRD = Modification of Diet in Renal Disease; $S_{Cr}$ = serum creatinine concentration; $C_{Cr}$ = creatinine clearance.*

**—For each equation, $S_{Cr}$ is in milligrams per deciliter, age is in years, and weight is in kilograms.*

*†—In validation studies,[14-17] the MDRD study equation performed as well as versions with more variables; however, a recent study[18] found that the equation underestimated the GFR in patients who did not have chronic kidney disease.*

*K/DOQI. Am J Kidney Dis, 2002*

# www.kidney.org/professionals/kdoqi/gfr_calculator.cfm



## Preferred Methods for Assessing Kidney Function

| *Method* | *Situations for use* |
|---|---|
| MDRD study equation for estimating GFR* | Patients with diabetic kidney disease† |
| | Patients with chronic kidney disease in middle-age (average age: 51 years)† |
| | Black patients with hypertensive chronic kidney disease† |
| | Patients with a kidney transplant† |
| Cockcroft-Gault equation for estimating creatinine clearance* | Older patients (performs better than the MDRD study equation) |
| 24-hour urine collection for creatinine clearance | Pregnant women |
| | Patients with extremes of age and weight |
| | Patients with malnutrition |
| | Patients with skeletal muscle diseases |
| | Patients with paraplegia or quadriplegia |
| | Patients with a vegetarian diet and rapidly changing kidney function |

*MDRD = Modification of Diet in Renal Disease; GFR = glomerular filtration rate.*

**—Requires stable kidney function.*

†*—Validated for use in these patients.*



K/DOQI. Am J Kidney Dis, 2002

# Albuminuria

- The K/DOQI guidelines recommend screening for microalbuminuria in all patients at risk for kidney disease.

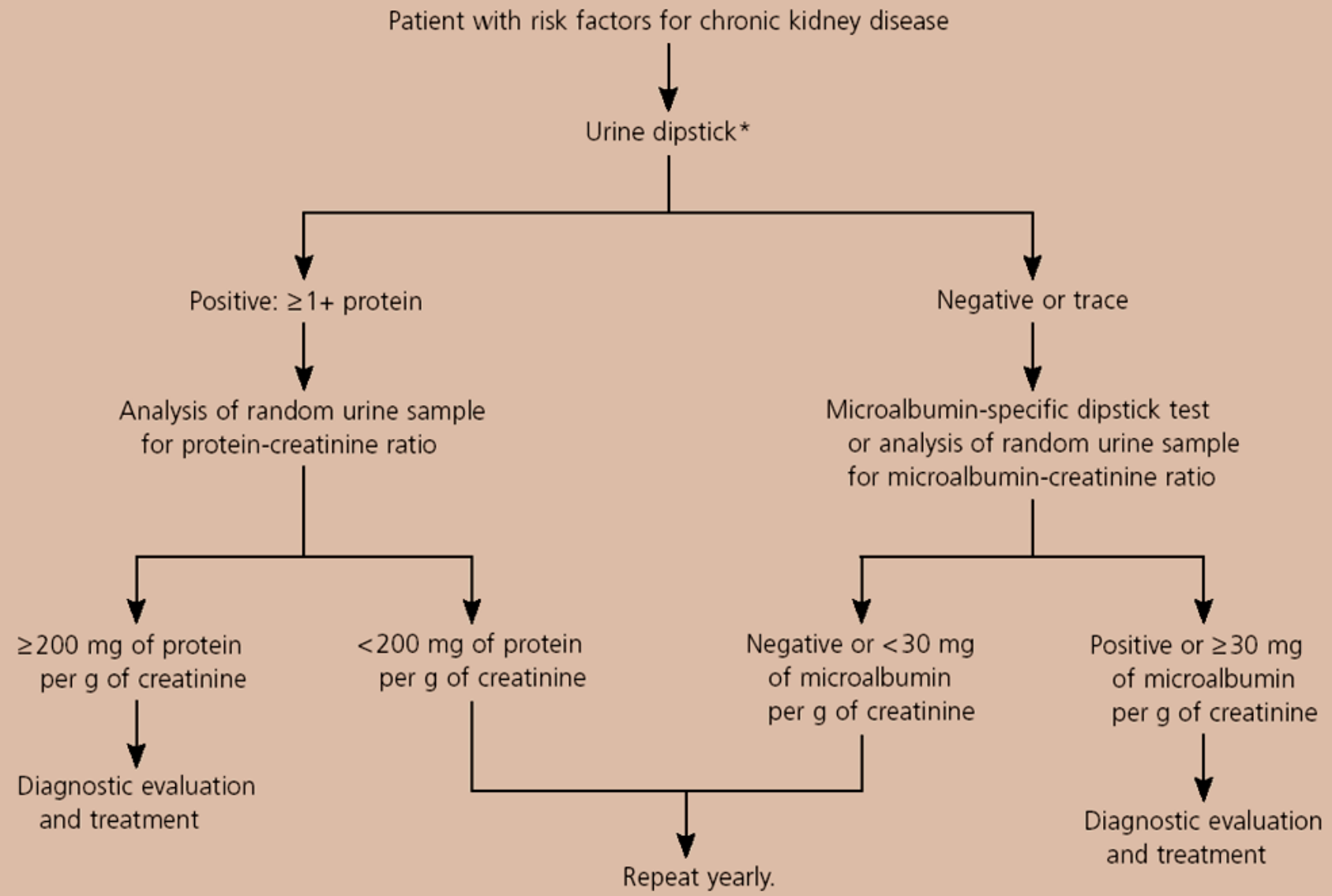
- Screening can be performed using a microalbumin-sensitive dipstick or analysis of a random morning urine sample to determine the microalbumin-creatinine ratio.

- Microalbumin dipsticks have a sensitivity of 51 to 100 percent and a specificity of 27 to 97 percent

- The protein-creatinine ratio in an early-morning random urine sample correlates well with 24-hour urine protein excretion and is much easier to obtain.

*K/DOQI. Am J Kidney Dis, 2002*

# Evaluation for Proteinuria and Microalbuminuria




*—If available, an albumin-specific dipstick may be used in place of a standard urine dipstick as the initial step in screening.*



*K/DOQI. Am J Kidney Dis, 2002*

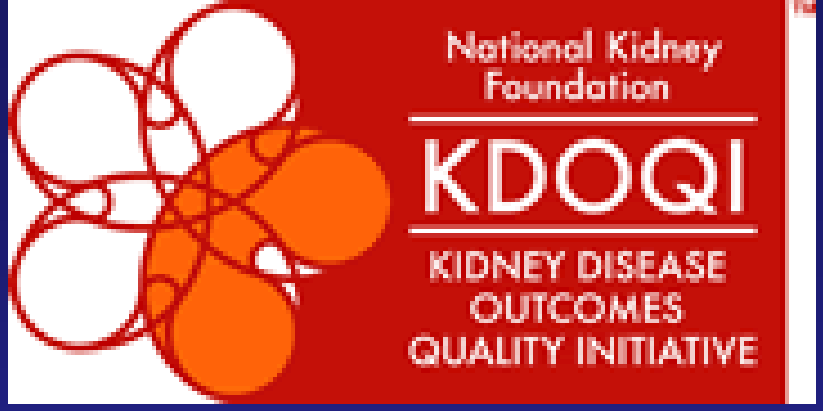
# Scenario Clinico

- Sollecitato dal signor Matteo, visibilmente preoccupato, decido di ricontrollare azotemia e creatinina a breve distanza
- Dopo circa un mese i valori sono sovrapponibili ai precedenti
- Microalbuminuria 200 mg/die
- Clearance della creatinina (formula di Cockroft): 60 ml/min
- PAO 150/90 mmHg

# CLINICAL QUESTIONS

## 2. Ritieni necessario trattare l'ipertensione del sig. Matteo?

1. No
2. Sì, con ACE inibitore
3. Sì, con sartanico
4. Sì, con calcio antagonista
5. Sì, con altro antipertensivo




# Clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease

*Am J Kidney Dis, May 2004*

A blood pressure goal of 130/80 mm Hg is recommended in patients with normal urinary albumin concentrations, and a blood pressure goal of 125/75 mm Hg is recommended in patients with proteinuria equal to or greater than 1 g per 24 hours. B

- A long-term follow-up study of patients with nondiabetic kidney disease and an average GFR of 32 mL found that the patients randomized to a low blood pressure target were one third less likely to develop kidney failure than were the patients randomized to a usual blood pressure goal.

*K/DOQI. Am J Kidney Dis, 2004*

*Sarnak MJ, Green T, Wang X, et al.*

# The effect of a lower target blood pressure on the progression of kidney disease: long-term follow-up of the Modification of Diet in Renal Disease Study

*Ann Intern Med 2005;142:342-51*

# Strengh of evidence

1. Most patients with nondiabetic kidney disease are hypertensive (**Strong**).

**Table 113. Prevalence of Hypertension in Nondiabetic Kidney Disease**

| Type of Kidney Disease | Prevalence (%) |
|---|---|
| Glomerular Diseases | 85% |
| Vascular Diseases | 100% |
| Tubulointerstitial Diseases | 62% |
| PKD | 87% |

Data from MDRD Study [21]

2. Higher levels of blood pressure are associated with more rapid progression of nondiabetic kidney disease (**Strong**).

*K/DOQI. Am J Kidney Dis, 2004*

# Strengh of evidence

3. Multiple antihypertensive agents are usually required to reach target blood pressure (**Strong**).

**Table 114. Summary of Number of Antihypertensive Agents to Reach Target Blood Pressure**

| Study, Year, Reference | Target BP | Achieved BP | Mean Number of Agents |
|---|---|---|---|
| Wright[141] | <125/75 | 125/76 | 3.5 |
| | <140/90 | 140/84 | 2.7 |
| Klahr[446] | <125/75 | 125/78 | 1.9 |
| | <140/90 | 138/78 | 1.5 |
| Maschio [447] | Diastolic ≤90 | 135/84(ACE inhibitor) | 1.7 |
| | | 144/89(placebo) | 2.1 |

*K/DOQI. Am J Kidney Dis, 2004*

# Strengh of evidence

4. ACE inhibitors are more effective than other agents in slowing the progression of most nondiabetic kidney diseases (**Strong**).

5. The beneficial effect is greater in patients with higher levels of proteinuria (**Strong**).

**Table 116. Type of Kidney Disease, Level of Proteinuria, and Strength of Recommendation for ACE Inhibitors in Nondiabetic Kidney Disease**

| Common Types of Nondiabetic Kidney Disease | Usual Level of Proteinuria (Spot Urine Protein-to-Creatinine Ratio, mg/g)* | | Strength of Evidence for ACE Inhibitors to Slow Progression of CKD |
|---|---|---|---|
| | Total Protein | Albumin | |
| Glomerular diseases | >500-1,000 | >300 | Strong |
| Hypertensive nephrosclerosis | <500-1,000 | <300 | Strong |
| Tubulointerstitial diseases | <200 | <30 | Weak |
| Polycystic kidney disease | <200 | <30 | Weak |

*Levels are not exact. They are meant to provide only a general guide to diagnosis.

*K/DOQI. Am J Kidney Dis, 2004*

# Strengh of evidence

6. ARBs may be more effective than other antihypertensive agents in slowing the progression of nondiabetic kidney disease (**Weak**)

7. ACE inhibitors and ARBs in combination may be more effective than either alone in slowing the progression of nondiabetic kidney disease (**Weak**).

8. Diuretics may potentiate the beneficial effects of ACE inhibitors and ARBs in nondiabetic kidney disease (**Moderately Strong**)

*K/DOQI. Am J Kidney Dis, 2004*

# Strengh of evidence

9. ACE inhibitors, ARBs, and nondihydropyridine calcium-channel blockers have a greater antiproteinuric effect than other antihypertensive classes in nondiabetic kidney disease (**Strong**).

10. Dihydropyridine calcium-channel blockers are less effective than other agents in slowing the progression of nondiabetic kidney disease with proteinuria (**Moderately Strong**).



*K/DOQI. Am J Kidney Dis, 2004*

# Strengh of evidence

11. A SBP goal of <130 mm Hg is more effective in slowing the progression of nondiabetic kidney disease in patients with proteinuria (**Strong**).

12. An even lower blood pressure goal may be more effective in patients with proteinuria >500 to 1,000 mg/g (**Weak**).

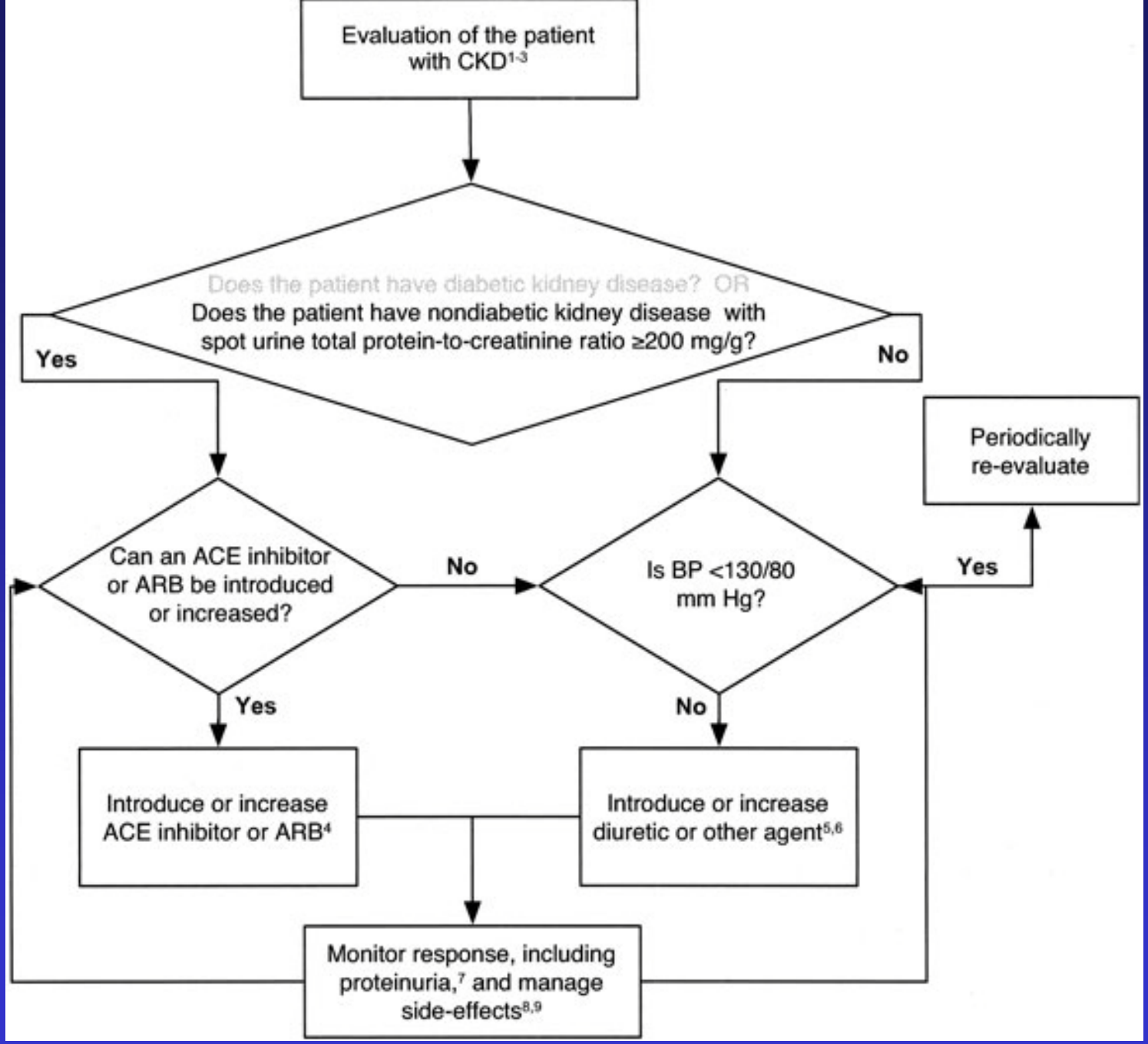
*K/DOQI. Am J Kidney Dis, 2004*

# Pharmacological therapy: nondiabetic kidney disease

- Target blood pressure in nondiabetic kidney disease should be <130/80 mm Hg.

- Patients with nondiabetic kidney disease and spot urine total protein to creatinine ratio ≥200 mg/g, with or without hypertension, should be treated with an ACE inhibitor or ARB

*K/DOQI. Am J Kidney Dis, 2004*






*K/DOQI. Am J Kidney Dis, 2004*

**Table 118. Summary of Recommendations in Nondiabetic Kidney Disease**

| | | |
|---|---|---|
| 1. | Evaluation | • CKD<br>• CVD and CVD risk factors |
| 2. | Diet and other therapeutic lifestyle changes for all patients | • Dietary sodium intake <2.4 g/d<br>• BMI ≤25 kg/m²<br>• Exercise and physical activity<br>• Moderation of alcohol intake<br>• Smoking cessation |
| 3. | Therapy for other CVD risk factors | • Diabetes therapy (ADA ) as necessary<br>• Dyslipidemia (NCEP guidelines, K/DOQI guidelines) |
| 4. | ACE inhibitor or ARB if spot urine total protein-to-creatinine ratio ≥200 mg/g | • ACE inhibitor preferred<br>• ARB can be used as alternative agent, if ACE inhibitor cannot be used.<br>• Use moderate to high doses (Guideline 11)<br>• Consider ACE inhibitor and ARB in combination |
| 5. | Diuretic if spot urine total protein-to-creatinine ratio <200 mg/g | • CKD Stages 1-3: Thiazide, loop, or potassium-sparing (use with caution with ACE inhibitor or ARB<br>• CKD Stages 4-5: Loop diuretic<br>• See Guideline 12 for dosages |
| 6. | Systolic blood pressure goal <130 mm Hg | • For patients treated initially with an ACE inhibitor or ARB<br>– Add diuretic first.<br>– Then add calcium-channel blocker or beta-blocker.<br>– Avoid dihydropyridine calcium-channel blocker without an ACE inhibitor or ARB.<br>• For patients treated initially with diuretics.<br>– Add ACE inhibitor, ARB, calcium-channel blocker or beta-blocker. |
| 7. | For patients with spot urine total protein-to-creatinine ratio >500-1000 mg/g | • Consider a lower systolic blood pressure goal<br>• Consider measures to reduce proteinuria<br>– Increase dose of ACE inhibitor or ARB<br>– Use ACE inhibitor or ARB in combination<br>– Add or increase dosage of other agents that lower proteinuria |
| 8. | Monitor serum potassium (Guidelines 11-12) | • ACE inhibitors and ARBs may cause hyperkalemia.<br>– Avoid other medications that cause hyperkalemia, if possible (potassium supplements, NSAIDs, Cox 2 inhibitors, potassium-sparing diuretics).<br>– Evaluate causes of hyperkalemia<br>– Treat hyperkalemia with diuretics<br>– Continue ACE inhibitor or ARB if serum potassium ≤5.5 mEq/L.<br>• Diuretics may cause hypokalemia.<br>– Evaluate causes of hypokalemia.<br>– Treat hypokalemia with caution in CKD. |
| 9. | Monitor GFR (Guideline 11-12) | • If GFR declines >30% from baseline within 4 weeks, evaluate causes<br>• Continue ACE inhibitor, ARB or diuretic if GFR decline is <30% from baseline value over four months. |



*idney Dis, 2004*

# Scenario Clinico

- Prescrivo:
  - Ecografia delle vie urinarie
  - Visita cardiologica ed ECG
  - Ramipril, 5 mg/die

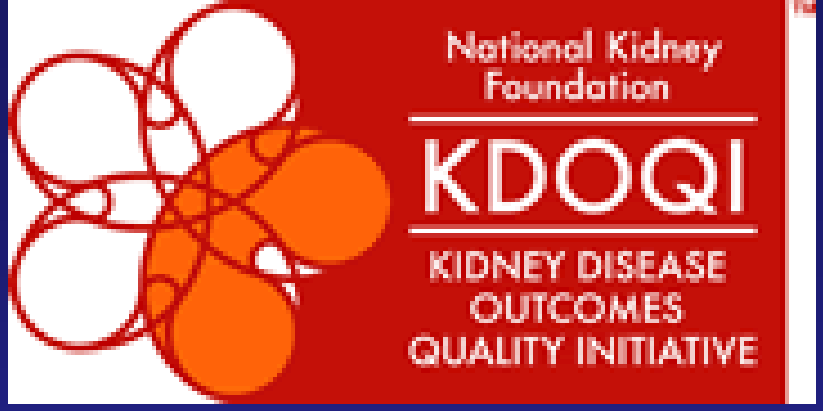
# Scenario Clinico

- Dopo circa 15 gg, il signor Matteo ritorna nel mio studio.
  - Visita cardiologia ed ECG negativi
  - Ecografia: “Lieve differenza tra i diametri longitudinali dei 2 reni (sn 10.5 cm, dx 11.5). Incremento della ecogenicità della corticale, che appare lievemente ridotta di spessore. Ipertrofia prostatica.
  - PAO 130/80 mmHg, con buona compliance del trattamento con ramipril, ben tollerato dal paziente.

# CLINICAL QUESTIONS

# 3. Condividi la decisione del cardiologo di non prescrivere una statina?

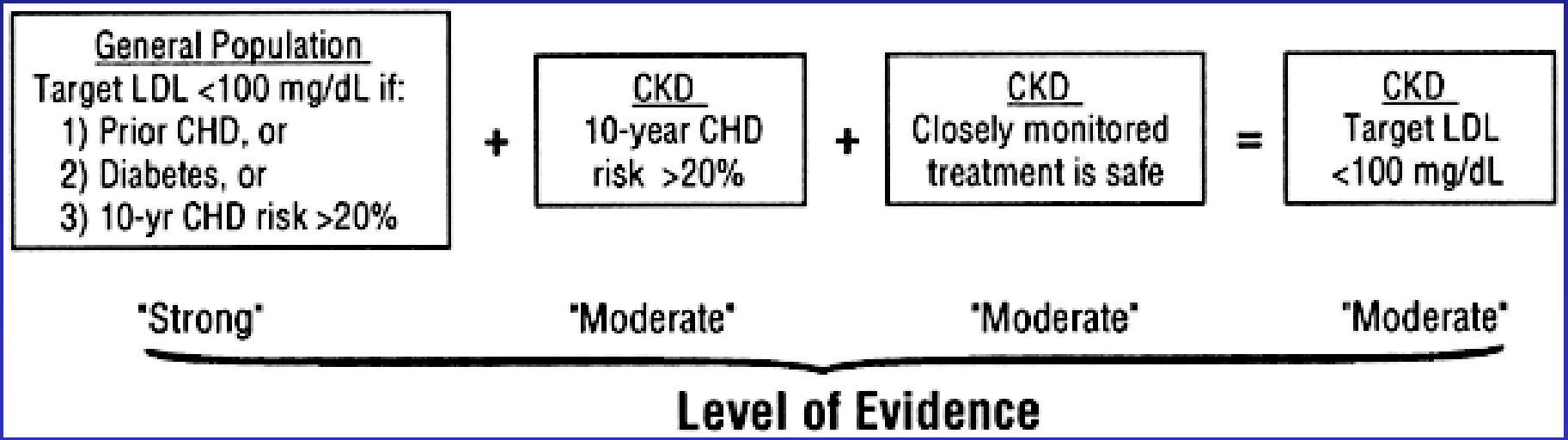
1. Sì
2. No



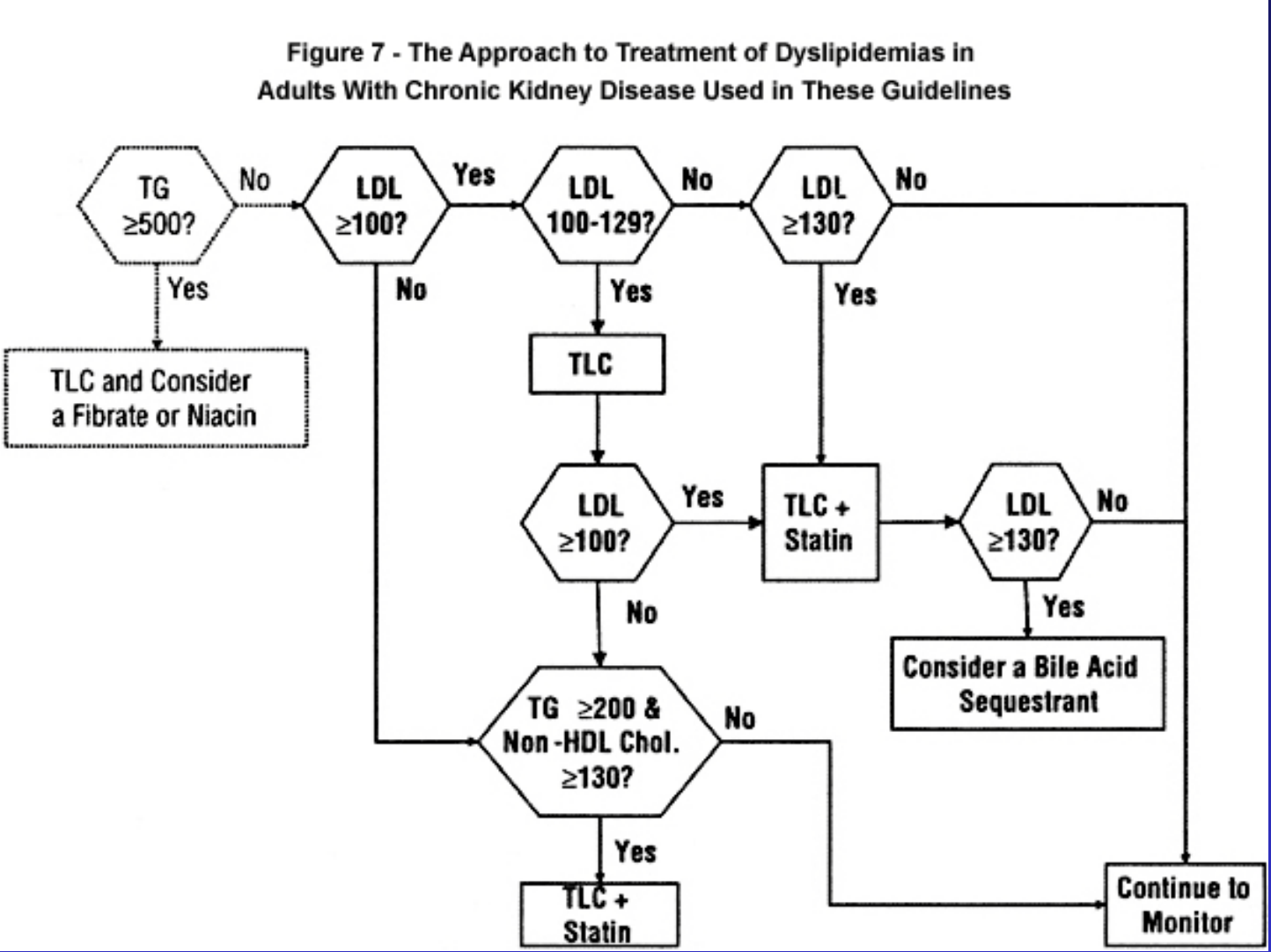

# Managing Dyslipidemias in Chronic Kidney Disease

*Am J Kidney Dis, April 2003*

A low-density lipoprotein goal of less than 100 mg per dL (2.60 mmol per L) is recommended for patients with chronic kidney disease, because these patients are statistically at highest risk for cardiovascular disease. C




*K/DOQI. Am J Kidney Dis, 2003*




TG, triglycerides; TLC, therapeutic lifestyle changes; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

*K/DOQI. Am J Kidney Dis, 2003*

# Scenario Clinico

- Tranquillizzo il signor Matteo, consigliando di controllare periodicamente la PA e di ripetere gli esami di funzionalità renale dopo circa 3 mesi.

# Scenario Clinico

- Dopo circa 4 mesi, il signor Matteo ritorna in ambulatorio con il suo controllo ematochimico
  - Creatinina 1.9 mg%
  - Azotemia 65 mg%
  - Sodiemia 140 UI/L
  - Potassiemia 5.1 UI/L

- Sospendo il ramipril e prescrivo manidipina 10 mg/die

- Richiedo una consulenza nefrologica

# CLINICAL QUESTIONS

# 4. Condividi la decisione del collega di sostituire l'ACE inibitore un calcio antagonista?

1. No
2. Sì, per l'incremento della creatinina
3. Sì, per l'incremento del potassio
4. 2 +3

## Table 144. Summary of Use of ACE Inhibitors and ARBs in CKD

| | | |
|---|---|---|
| 1. | Indications | • Diabetic kidney disease<br>• Nondiabetic kidney disease with spot urine total protein-to-creatinine ratio >200 mg/g<br>• Consider in kidney transplant recipients with spot urine total protein-to-creatinine ratio >500-1,000 mg/g |
| 2. | Doses Used in Controlled trials (mg/d) | • ACE inhibitors (benazepril 30, captopril 100, lisinopril 20, perindopril 4, ramipril 10, trandolopril 3)<br>• ARBs (candesartan 16, irbesartan 300, losartan 100, valsartan 160) |
| 3. | Side-Effects | • Hypotension, early decrease in GFR, hyperkalemia, cough, angioneurotic edema, rash, contraindicated in 2nd and 3rd trimesters of pregnancy (recommend contraception to women of child-bearing age) |
| 4. | Causes of Early Decrease in GFR | • ECF volume depletion, hypotension, renal artery disease (bilateral or unilateral with a solitary kidney) |
| 5. | Causes of Hyperkalemia | • Increased potassium intake (high potassium foods, supplements, herbal supplements, transfusions, salt substitutes)<br>• Metabolic acidosis<br>• Acute GFR decline<br>• Drugs (beta-blockers, heparin, NSAID, Cox 2 inhibitors, heparin, digoxin overdose, potassium supplements, herbal supplements, potassium-sparing diuretics, cyclosporine, tacrolimus, pentamidine, trimethoprim, lithium.<br>• Laboratory error |
| 6. | Frequency of Monitoring for Side Effects (Blood Pressure, GFR, Serum Potassium) | • If SBP <120 mm Hg, GFR <60 mL/min/1.73 m², change in GFR ≥15%, or serum potassium >4.5 mEq/L,<br>– ≤4 weeks after initiation or increase in dose, or<br>– 1-6 months after blood pressure is at goal and dose is stable. |
| 7. | Conditions in which ACE Inhibitors or ARBs Should Not be Used or Used with Caution | • Pregnancy<br>• History of cough, angioedema or other allergic reaction<br>• Bilateral renal artery stenosis<br>• Serum potassium >5.5 mEq/L despite treatment<br>• GFR decline >30% within 4 months without explanation |

# Scenario Clinico

- Il collega nefrologo, nell'ipotesi di una IRC su base vascolare, richiede:
  - ecodoppler delle arterie renali
  - studio del bilancio calcio-fosforo
  - controlli laboratoristici ogni 3-4 mesi

- Conferma la terapia con manidipina 20 mg/die (con 10 mg/die la PAO 140/80 mmHg) discretamente tollerata dal paziente (lieve succulenza alle caviglie)

- Non prescrive dieta ipoproteica

# CLINICAL QUESTIONS

# 5. Condividi la decisione dello specialista di non prescrivere al sig. Matteo una dieta ipoproteica?

1. No
2. Sì

*Fouque D, Wang PH, Laville M, Boissel JP.*

# Low protein diets for chronic renal failure in non diabetic adults

*Cochrane Database of Systematic Reviews 2006, Issue 1*

## SELECTION CRITERIA

• RCTs comparing two different levels of protein intake in adult patients suffering from moderate to severe renal failure, followed for at least one year.
• Diabetic nephropathy patients were excluded.

## DATA COLLECTION AND ANALYSIS

• Seven RCTs were selected and 1494 patients were analysed (753 with reduced protein intake and 741 with higher protein intake).
• Collection of the number of "renal deaths" defined as the need for starting dialysis, the death of a patient or a kidney transplant during the trial.



*Fouque D, et al. Cochrane Library, 2006*

# MAIN RESULTS

- 242 renal deaths were recorded, 101 in the low protein diet and 141 in the higher protein diet group, giving an odds ratio of 0.62 with a 95% confidence interval of 0.46 to 0.83 (p=0.006).
- To avoid one renal death, four to 56 patients need to be treated with a low protein diet during one year.



*Fouque D, et al. Cochrane Library, 2006*

# AUTHORS' CONCLUSIONS

- Reducing protein intake in patients with chronic renal failure reduces the occurrence of renal death by about 40% as compared with higher or unrestricted protein intake.
- The optimal level of protein intake cannot be confirmed from these studies

*Fouque D, et al. Cochrane Library, 2006*

# Scenario Clinico

- Eco-color-doppler aa renali: non alterazioni di rilievo.
- Bilancio calcio fosforo nella norma:
  - calcio 8.7 mg%
  - fosforo 3.3 mg%
  - paratormone 55 UI/L

# Scenario Clinico

- Ai controlli successivi:
  - la creatinina si stabilizza intorno a 1.90 mg%
  - il potassio rientra nella norma: 4.4 UI/L
  - persiste un lieve incremento dell'azotemia: 62 mg%
  - l'emoglobina si mantiene nella norma (14 gr%)

- La diagnosi è di IRC su base vascolare (nefroangiosclerosi).

# CLINICAL QUESTIONS

# 6. Ritieni appropriato l'iter diagnostico eseguito nel sig. Matteo?

1. Sì
2. No, sono state eseguite troppe indagini
3. No, avrei eseguito altre indagini

# Evaluation of Patients with CKD

- All patients with CKD should undergo urinalysis and renal imaging as part of the diagnostic evaluation.
- Patients with long-standing diabetes, hypertension, and a clinical course consistent with CKD secondary to these conditions may not require further evaluation.
- The evaluation of all patients is guided by the symptoms, family history of kidney disorders and known medical problems.

*K/DOQI. Am J Kidney Dis, 2002*

## Diagnostic Evaluation in Chronic Kidney Disease

| *Disorder* | *Clinical clues* | *Urine sediment* | *Protein-creatinine ratio* | *Additional tests* |
|---|---|---|---|---|
| Diabetes mellitus | Diabetes for >15 years, retinopathy | RBCs in <25 percent of affected patients | >30 to >3,500 mg of protein per g of creatinine | Fasting blood sugar, A1C |
| Essential hypertension | Left ventricular hypertrophy, retinopathy | Benign | >30 to 3,000 mg of protein per gram of creatinine | No additional tests |
| Glomerulonephritis | History and physical examination: infections; rash, arthritis; patient older than 40 years | Dysmorphic RBCs or RBC casts | >30 to >3,500 mg of protein per g of creatinine | C3 and C4 for all patients<br>Tests for infections: anti-ASO, ASK, HIV, HBsAg, HCV, RPR, blood cultures<br>Tests if there is rash or arthritis: ANA, ANCA, cryoglobulin, anti-GBM<br>Tests if patient is older than 40 years: SPEP, UPEP |
| Interstitial nephritis | Medications, fever, rash, eosinophilia | WBCs, WBC casts, eosinophils | 30 to 3,000 mg of protein per g of creatinine | ACE level; SS-A, SS-B |
| Low flow states | Volume depletion, hypotension, congestive heart failure, cirrhosis, atherosclerosis | Hyaline casts, eosinophils | <200 mg of protein per g of creatinine | FENa: <1 percent; eosinophilia |



K/DOQI. Am J Kidney Dis, 2002

## Imaging Options in Chronic Kidney Disease

| *Imaging study* | *What the study helps identify* |
|---|---|
| Plain-film radiography of kidneys, ureters, and bladder | Ureter or bladder stones |
| Renal ultrasonography | Kidney size, obstructive kidney disease, polycystic kidney disease |
| Renal Doppler ultrasonography | Renovascular disease, renal vein thrombosis |
| Radioisotope renal scanning | Individual kidney function, renovascular disease, obstructive uropathy |
| Computed tomography | Kidney mass or complex cyst |
| Magnetic resonance angiography | Renovascular disease |
| Renal angiography | Renovascular disease, renal artery thrombosis/thromboembolism, polyarteritis nodosa |
| Retrograde ureterography | Upper urinary tract obstruction |

NOTE: *Intravenous pyelography generally is not performed in patients with chronic kidney disease because it may precipitate acute renal failure.*

# Evaluation of Patients with CKD

- Renal ultrasonography helps establish the diagnosis and prognosis by documenting the size of the kidneys.
  - Normal size indicates kidney disease that may be amenable to medical treatment.
  - Small kidneys suggestirreversible disease.
  - Asymmetry in kidney size suggests renovascular disease.

*K/DOQI. Am J Kidney Dis, 2002*

| | | | | |
|---|---|---|---|---|
| Urinary tract obstruction | Urinary symptoms | Benign, or RBCs | None | KUB radiography, intravenous pyelography, spiral CT scanning, renal ultrasonography |
| Chronic urinary tract infection | Urinary symptoms | WBCs, RBCs | < 2,000 mg of protein per g of creatinine | Pelvic examination, urine culture, voiding cystourethrography, renal ultrasonography, CT scanning |
| Neoplasm, paraproteinemia | Patient older than 40 years, constitutional symptoms, anemia | RBCs, RBC casts, granular casts | False-negative result or > 30 to > 3,500 mg of protein per g of creatinine | SPEP, UPEP, calcium level, ESR |
| Cystic kidney disease | Palpable kidneys with or without family history of cystic kidney disease, flank pain | RBCs | 30 to 3,000 mg of protein per g of creatinine | Renal ultrasonography or CT scanning if there is a complex kidney cyst or mass |
| Renovascular disease | Late-onset or refractory hypertension, sudden onset of hypertension in young woman, smoking history, abdominal bruit | Benign | < 200 mg of protein per g of creatinine | Renal Doppler ultrasonography, radioisotope renal scanning, MRA, renal angiography |
| Vasculitis | Constitutional symptoms, peripheral neuropathy, rash, respiratory symptoms | RBCs; granular casts | > 30 to > 3,500 mg of protein per g of creatinine | C3, C4, ANA, ANCA; HBsAg, HCV, cryoglobulins, ESR, RF, SS-A, SS-B, HIV |



*K/DOQI. Am J Kidney Dis, 2002*

# CLINICAL QUESTIONS

## 7. Ritieni appropriata una visita specialistica per tutti i pazienti con aumento persistente della creatinina?

1. Sì
2. No

# Referral of patients with CKD

- Nephrology referral generally is recommended for patients with a serum creatinine level of 1.5 to 2.0 mg%

- The KDOQI endorses a model of collaboration between primary care physicians and subspecialists

*K/DOQI. Am J Kidney Dis, 2002*

*Kinchen KS, Sadler J, Fink N, et al.*

# The timing of specialist evaluation in chronic kidney disease and mortality

*Ann Intern Med 2002;137:479-86*

*Levinsky NG*

# Specialist evaluation in chronic kidney disease. Too little, too late.

*Ann Intern Med 2002;137:542-3*

## Indications for Nephrology Referral in Chronic Kidney Disease

Underlying cause unclear after basic work-up

Renal biopsy indicated

Management of underlying cause beyond the scope of primary care

Stage 3 chronic kidney disease (GFR <60 mL per minute per 1.73 $m^2$): consider comanagement

Stage 4 chronic kidney disease (GFR <30 mL per minute per 1.73 $m^2$): nephrologist involvement essential

Rapid progression of chronic kidney disease

Superimposed acute kidney failure

*GFR = glomerular filtration rate.*

*K/DOQI. Am J Kidney Dis, 2002*