

High risk patient, with CKD, in primary prevention

Arrigo F.G. Cicero

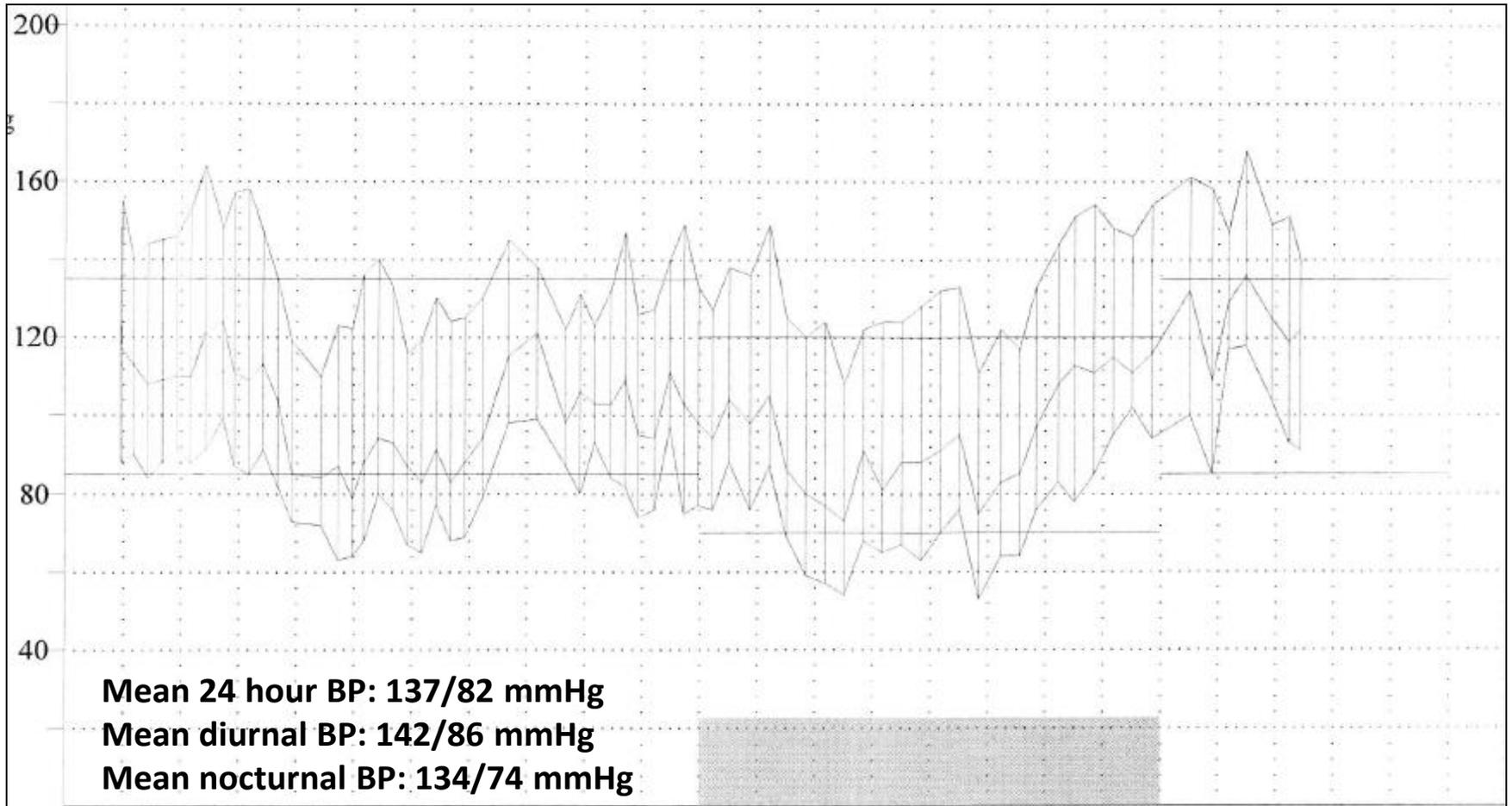
Mrs. Rossi, 64 years old

- Family history: mother died because of AMI at 65, father treated with TEA at 87 (no previous stroke)
- Personal history: fibromyalgia, overweight, hypertensive and hypercholesterolemic from the age of menopause (52 y.o.)
- Active smoker: 5-7 cigarettes/day since the age of 20
- Sedenterary, Mediterranean diet pattern

Some numbers

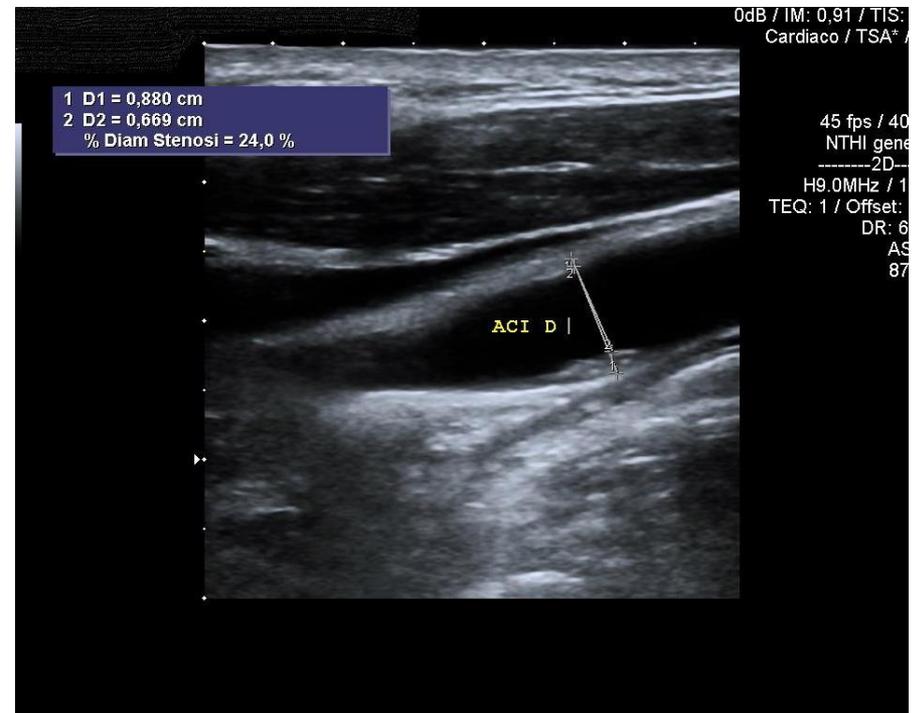
- Office BP= 144/86 mmHg (mean of 3 measurements)
- Home BP= 140/84 mmHg (mean of reported morning values)
- WC= 98 cm, BMI= 29,7 kg/m²
- FPG= 118 mg/dL
- Uric acid= 6,1 mg/dL
- eGFR= 58 ml/min
- No microalbuminuria
- TC= 239 mg/dL
- LDL-C= 131 mg/dL
- TG= 298 mg/dL
- HDL-C= 48 mg/dL
- Lp(a)= 54 mg/dL
- Liver transaminases, gGT in the normal range
- TSH in the normal range
- CPK= 294 U/L

Her latest ABPM



No pathological signs at standard ECG and echocardiography but ...

- **Diffuse Intima-Media Thickness (1.3-1.4 mm)**
- **Plaque at right internal carotid level (stenosis: 25-30%)**



Current treatment of the patient

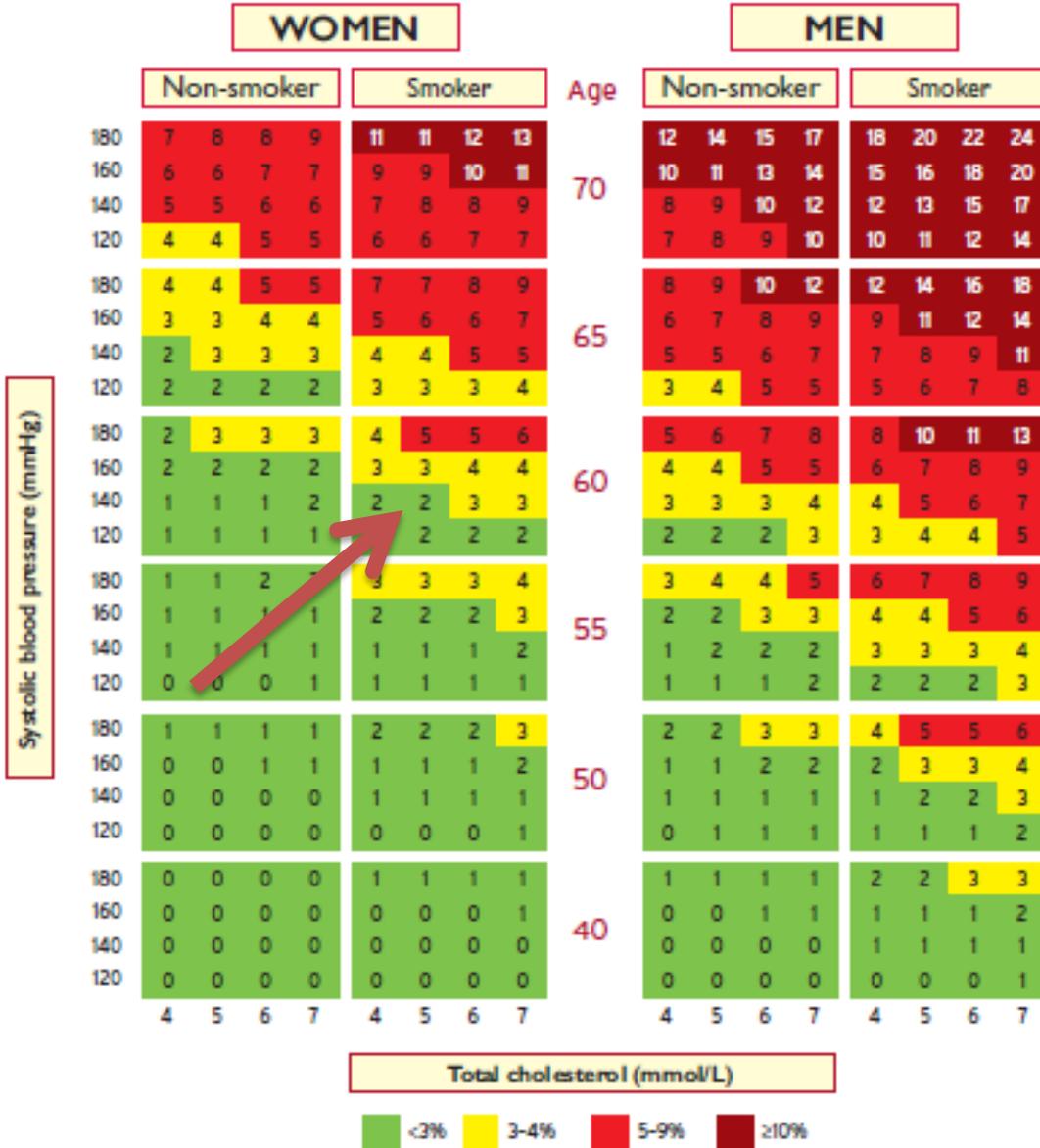
- **Ramipril 2.5 mg morning and evening**
- **Cardioaspirin**
- **Phytosterols 1600 mg/day**

What the risk for this patient?

- **Moderate**
- **High**
- **Very High**
- **Extreme**

SCORE Cardiovascular Risk Chart
10-year risk of fatal CVD

Low-risk regions of Europe



A «standard» risk classification

CKD and RISK

Box 5 Risk estimation: key messages

In apparently healthy persons, CVD risk is most frequently the result of multiple, interacting risk factors. This is the basis for total CV risk estimation and management.

Risk factor screening including the lipid profile should be considered in men >40 years old, and in women >50 years of age or post-menopausal.

A risk estimation system such as SCORE can assist in making logical management decisions, and may help to avoid both under- and overtreatment.

Certain individuals declare themselves to be at high or very high CVD risk without needing risk scoring, and all risk factors require immediate attention. This is true for patients with documented CVD, older individuals with long-standing DM, familial hypercholesterolaemia, chronic kidney disease, carotid or femoral plaques, coronary artery calcium score >100, or extreme Lp(a) elevation.

Table 4 Cardiovascular risk categories

Very-high-risk

People with any of the following:
Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound.
DM with target organ damage,² or at least three major risk factors, or early onset of T1DM of long duration (>20 years).
Severe CKD (eGFR <30 mL/min/1.73 m²).
A calculated SCORE \geq 10% for 10-year risk of fatal CVD.
FH with ASCVD or with another major risk factor.

High-risk

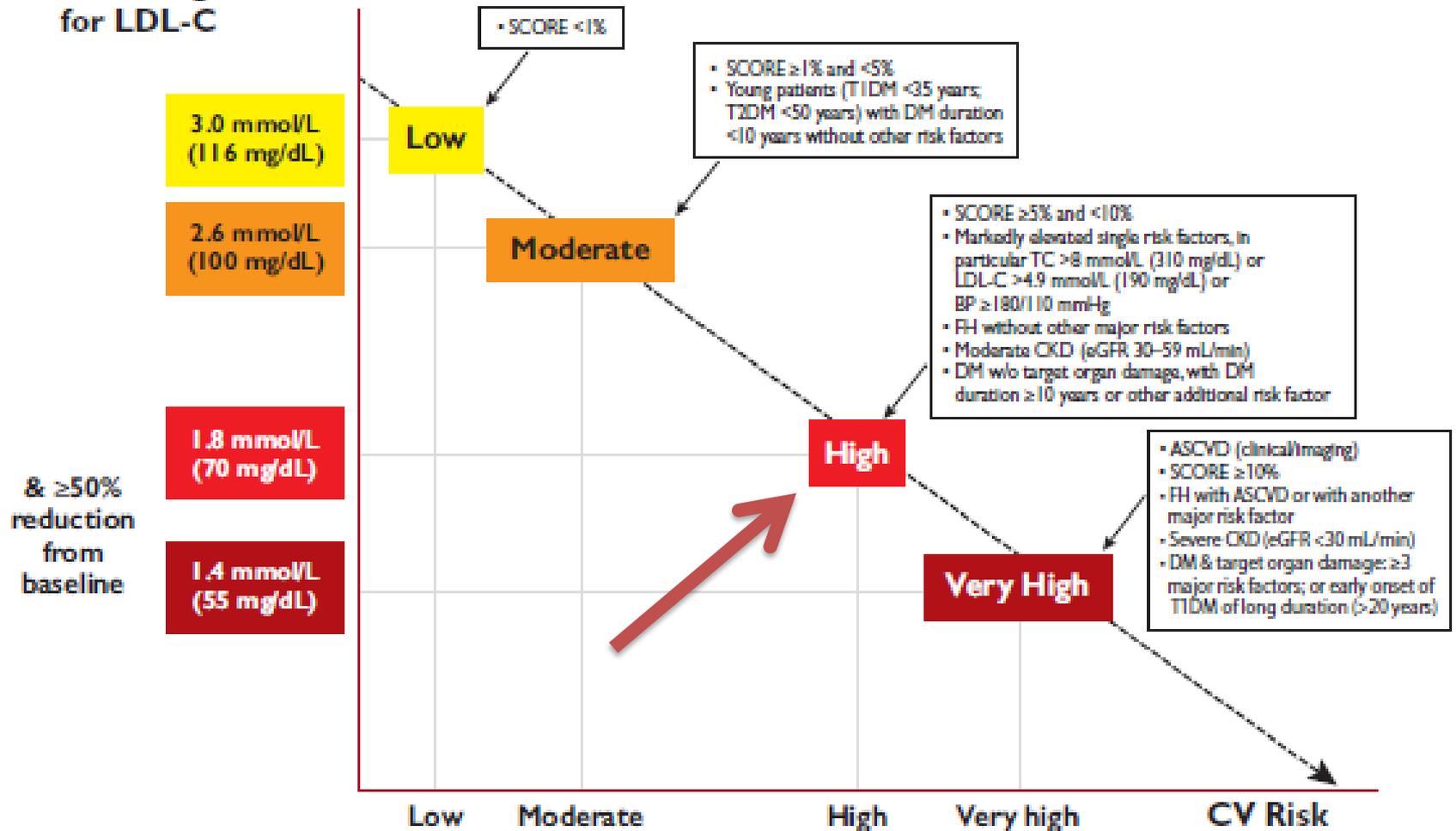
People with:
Markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), or BP \geq 180/110 mmHg.
Patients with FH without other major risk factors.
Patients with DM without target organ damage,² with DM duration \geq 10 years or another additional risk factor.
Moderate CKD (eGFR 30–59 mL/min/1.73 m²).
A calculated SCORE \geq 5% and <10% for 10-year risk of fatal CVD.

What LDL-C target for this patient?

- <115 mg/dL
- <100 mg/dL
- <70 mg/dL
- <55 mg/dL

The LDL-C goals

Treatment goal for LDL-C



Some numbers

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- Liver transaminases, gGT in the normal range
- TSH in the normal range
- CPK= 294 U/L

Current treatment of the patient

- **Ramipril 2.5 mg morning and evening**
- **Cardioaspirin**
- **Phytosterols 1600 mg/day**

What about statin safety in CKD patients?

- **As in non CKD patients**
- **Slightly higher than in non CKD patients**
- **Higher than in non-CKD patients**
- **Markedly higher than in non-CKD patients**

Statins risk in CKD patients

8.1.4.5 *Adverse effects on kidney function.* There is no clear evidence that statins have a clinically significant beneficial or adverse effect on renal function.²⁵³ An increased frequency of proteinuria has been reported for all statins, but has been analysed in more detail for rosuvastatin. With a dose of 80 mg, a frequency of 12% was reported. With the approved doses of <40 mg, the frequency is much lower and in line with the frequency for other statins. The proteinuria induced by statins is of tubular origin, usually transitory, and is believed to be due to reduced tubular reabsorption and not to glomerular dysfunction.^{254,255} In clinical trials, the frequency of proteinuria is generally low and, in most cases, is not higher than for placebo.²⁵⁶

What to change in therapy?

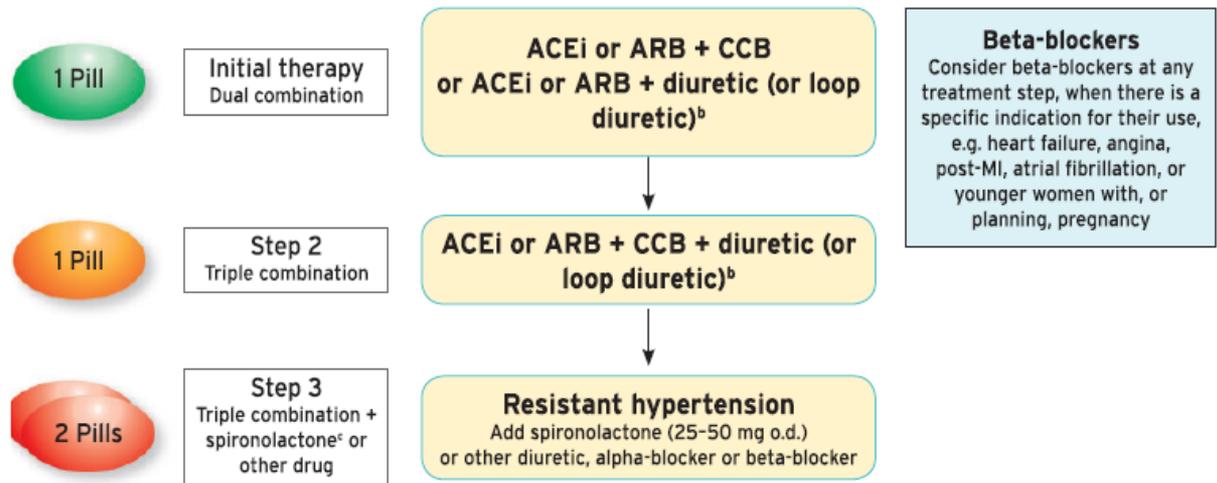
- **TLS intensification and recheck**
- **Antihypertensive treatment intensification**
- **Lipid-lowering treatment**
- **All of them**
- **No one of them**

The distance from target

- LDL-C= 131 mg/dL -> <70 mg/dL = ↓ min. 47%
- nonHDL-C= 191 mg/dL -> <100 mg/dL = ↓48%
- TG= 298 mg/dL -> <150 mg/dL = ↓ 50%

And what about her BP control ?

Recommendations	Class ^a	Level ^b
In patients with diabetic or non-diabetic CKD, it is recommended that an office BP of $\geq 140/90$ mmHg be treated with lifestyle advice and BP-lowering medication. ^{9,203,485}	I	A
In patients with diabetic or non-diabetic CKD: <ul style="list-style-type: none"> It is recommended to lower SBP to a range of 130–139 mmHg.^{9,487,489} Individualized treatment should be considered according to its tolerability and impact on renal function and electrolytes. 	I IIa	A C
RAS blockers are more effective at reducing albuminuria than other antihypertensive agents, and are recommended as part of the treatment strategy in hypertensive patients in the presence of microalbuminuria or proteinuria. ^{487,489}	I	A
A combination of a RAS blocker with a CCB or a diuretic ^c is recommended as initial therapy. ¹⁷⁵	I	A
A combination of two RAS blockers is not recommended. ²⁹⁸	III	A



Our first approach

- **TLS improvement**
- **Perindopril/Amlodipine 10/5 mg 1 tab/morning**
- **Cardioaspirin**
- **Simvastatin/Ezetimibe 40/10 mg/evening**

Recommendations for lipid management in patients with moderate-to-severe (Kidney Disease Outcomes Quality Initiative stages 3–5) chronic kidney disease

Recommendations	Class ^a	Level ^b
It is recommended that patients with Kidney Disease Outcomes Quality Initiative stage 3–5 ^c CKD are considered to be at high or very-high risk of ASCVD. ^{489–493}	I	A
The use of statins or statin/ezetimibe combination is recommended in patients with non-dialysis-dependent stage 3–5 CKD. ^{214,222,495,496}	I	A
In patients already on statins, ezetimibe, or a statin/ezetimibe combination at the time of dialysis initiation, continuation of these drugs should be considered, particularly in patients with ASCVD.	IIa	C
In patients with dialysis-dependent CKD who are free of ASCVD, commencement of statin therapy is not recommended. ^{220,221}	III	A

After 2 months ...

- Office BP= 133/82 mmHg (mean of 3 measurements)
- Home BP= 128/79 mmHg (mean of reported morning values)
- WC= 95 cm, BMI= 28,6 kg/m²
- FPG= 109 mg/dL
- Uric acid= 5,6 mg/dL
- eGFR= 59 ml/min
- No microalbuminuria
- TC= 165 mg/dL
- LDL-C= 71
- TG= 211 mg/dL
- HDL-C= 52 mg/dL
- Lp(a)= 52 mg/dL
- Liver transaminases, gGT in the normal range
- TSH in the normal range
- CPK= 294 U/ml

Next step?

- **To maintain the current therapy suggesting a further intensification of the TLS?**
- **To increase the simvastatin dose to 80 mg?**
- **To change simvastatin/ezetimibe 40/10 mg with atorvastatin 20 mg + ezetimibe 10 mg?**
- **To begin treatment with PCSK9 inhibitors?**

Thanks for your attention