

Polish Forum for Prevention of Cardiovascular Diseases Guidelines on prophylactic pharmacotherapy

Wytyczne Polskiego Forum Profilaktyki Chorób Układu Krążenia
dotyczące farmakoterapii prewencyjnej

Piotr Podolec, Grzegorz Kopeć, Anetta Undas, Andrzej Pająk, Maciej Godycki-Ćwirko, Tomasz Zdrojewski,
Piotr Jankowski, Wojciech Drygas, Andrzej Rynkiewicz, Ryszard Piotrowicz, Danuta Czarnicka, Marek Naruszewicz,
Grzegorz Opala, Jerzy Stańczyk, Elżbieta Kozek, Adam Windak, Waldemar Banasiak, Tomasz Guzik

Polish Forum for Prevention of Cardiovascular Diseases Task Force on Guidelines

1. Prophylactic pharmacotherapy is, second only to a healthy lifestyle, the primary method of preventing cardiovascular disease (CVD). Its introduction explains about 20% reduction in mortality from coronary heart disease that have occurred in developed countries (changes in risk factors — about 50%, the introduction of invasive procedures — about 10%) [1].

2. Prophylactic pharmacotherapy includes the use of drugs which decrease the risk of developing CVD, and death from CVD, regardless of the impact on major CVD risk factors. It includes drugs:

- that improve survival (reduce the risk of death from any cause): antiplatelet drugs (aspirin and thienopyridine), statins (discussed in the PFP guidelines on dyslipidaemia) [2]; beta-blockers, angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), omega-3 fatty acids (discussed in the PFP guidelines on dyslipidaemia) [2];
- that reduce the risk of CVD events with no effect on overall survival: influenza vaccination (discussed in the Polish Forum for Prevention Guidelines on the so-called new cardiovascular risk factors and markers, which have a potentially significant role in the strategy for the prevention of CVD) [3], ivabradine [3].

3. Acetylsalicylic acid (ASA). In primary prevention, ASA reduces the risk of myocardial infarction (MI) in men by 32% and the risk of stroke in women by 17%, although it does not affect the risk of death. Its chronic use increases the risk of bleeding (including life-threatening gastrointestinal or intracranial bleeding).

It is recommended that patients be encouraged to use aspirin (75 mg once a day) only if the potential benefit from its use is greater than the risk of bleeding. This usually involves people who have a ten year risk of death from CVD > 10% as assessed by SCORE charts and adequate control of hypertension (< 140/90 mm Hg), and subjects with diabetes type 1, or type 2 > 50 years of age (men) and > 60 years of age (women), coexisting with at least one additional CVD risk factor, i.e.: positive family history, smoking, hypertension, hypercholesterolaemia or albuminuria.

It is recommended that aspirin not be used as primary prevention in men < 45 years or women < 55 years.

In the secondary prevention of CVD in patients with recent MI or ischaemic stroke, unstable or stable angina, peripheral artery disease, or transient ischaemic attack, and in patients with atrial fibrillation, the use of aspirin reduces the risk of death by 15%.

Aspirin is recommended as secondary prevention of CVD, unless there are contraindications:

- in a single loading dose of 150–325 mg in acute coronary syndromes and ischaemic stroke;
- indefinitely at a dose of 75–100 mg once a day in patients with diagnosed CVD; in cases of hypersensitivity to aspirin, clopidogrel is recommended at a dose of 75 mg once a day.

Contraindications: hypersensitivity or intolerance to the drug and active bleeding [4–7].

4. Clopidogrel. In acute MI, the addition of clopidogrel to aspirin throughout hospitalisation reduces the risk of death by 7%. Adding clopidogrel to aspirin for 3–12 months after

Address for correspondence:

prof. Piotr Podolec, MD, PhD, Department of Cardiac and Vascular Diseases, Institute of Cardiology, *Collegium Medicum*, Jagiellonian University, John Paul II Hospital, ul. Pędziczna 80, 31–202 Kraków, Poland, tel: +48 12 614 33 99, fax: +48 12 614 34 23, e-mail: ppodolec@interia.pl

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acute coronary syndrome (ACS) without ST segment elevation reduces the risk of CVD events in 12 months by 14%.

It is recommended that dual antiplatelet therapy be prescribed: clopidogrel in combination with aspirin in patients:

- with ACS in a loading dose;
- after an ACS for 12 months at a dose of 75 mg once a day;
- with stable coronary artery disease treated with percutaneous coronary intervention with implantation of a bare metal stent (for a month) or a drug-eluting stent (for 6–12 months) at a dose of 75 mg once a day.

Contraindications to the use of clopidogrel are: hypersensitivity to the drug, severe liver damage, active bleeding, pregnancy and lactation, recent stroke [8–12].

5. Beta-blockers, when used chronically after MI, reduce the risk of death by 23%. Bisoprolol, carvedilol and metoprolol (succinate) reduce the risk of death in patients with symptomatic heart failure (HF) and low left ventricular ejection fraction (LVEF < 35–45%) by 30%. Nebivolol reduces the risk of death or hospitalisation in patients with HF > 70 years of age by 14%. Beta-blockers used in combination with ACEI reduce the risk of death in asymptomatic patients with reduced LVEF by 25–30%.

It is recommended that beta-blockers be used indefinitely to prevent CVD events in patients:

- after MI; oral therapy is preferred and should be initiated after stabilisation of the haemodynamic status;
- with reduced LVEF < 40% in functional class I–IV [bisoprolol, carvedilol, metoprolol (succinate), nebivolol].

Beta-blockers are also used as antiarrhythmic, antihypertensive and antianginal drugs.

Contraindications: poorly controlled asthma and atrioventricular block of second or third degree, sick sinus syndrome, sinus bradycardia < 50/min. In the case of contraindications to beta-blockers in patients after MI without evidence of HF, verapamil should be considered as an alternative (it reduces the risk of death by 36%) [13–27].

6. ACE inhibitors reduce the risk of death in patients with coronary artery disease without HF by 13%, for patients with HF of different etiologies by 16–27%, and for patients with asymptomatic left ventricular dysfunction of different etiologies by 14–19%.

ACEIs are recommended to reduce the risk of CVD in patients:

- with reduced LVEF \leq 40%, irrespective of the presence of the clinical symptoms of HF;
- with ischaemic heart disease and diabetes or hypertension;
- with diabetes and albuminuria or hypertension;
- and in the treatment of hypertension.

Their use should be considered also in patients with diagnosed stable coronary artery disease and after MI.

ACEIs are not homogeneous drugs. When choosing a specific medication, one should consider the results of clinical studies and the lack of a class effect, especially in the prevention of vascular complications.

Contraindications: a history of angioedema, bilateral renal artery stenosis or stenosis of a single renal artery, pregnancy, cardiomyopathy with left ventricle outflow tract obstruction, severe aortic stenosis, serum potassium > 5 mmol/L (relative), serum creatinine > 220 mmol/L (2.5 mg/dL) (relative) [28–33].

7. Angiotensin receptor blockers. Adding ARBs to ACEIs in patients with HF and reduced LVEF reduces the risk of death from CVD by 16% and hospitalisations for HF by 17% to 34%, but does not affect the overall risk of death. In patients with HF and reduced ejection fraction who cannot tolerate an ACEI, the use of ARBs compared to a placebo reduces the risk of death from CVD by 20% and hospitalisation for HF by 39%. In patients after MI with HF or reduced ejection fraction, ARBs affect the risk of death similarly to ACEIs.

ARBs are recommended to improve prognosis in patients with hypertension, in patients after MI or HF who do not tolerate ACEI, and together with ACEI in patients with LVEF < 40% and with persistent symptoms of HF despite optimal medical treatment with ACEIs and beta-blockers, provided no aldosterone antagonist is used.

Contraindications are the same as for ACEI, except for angioedema. An ARB should not be added to patients receiving an ACEI and an aldosterone antagonist [34–38].

8. Aldosterone antagonists reduce the risk of death in patients with LVEF \leq 35% and functional class III or IV treated with an ACEI and a loop diuretic by 30% (spironolactone) and in patients after MI with LVEF \leq 40%, and symptoms of HF or diabetes treated with ACEI or ARB, diuretics and beta-blocker by 15% (eplerenone).

They are recommended to improve prognosis in patients with HF functional class III or IV, LVEF \leq 35%, who are optimally treated with beta-blockers and ACEIs or ARBs.

Contraindications: blood potassium > 5.0 mmol/L, serum creatinine > 220 mmol/L, the use of a combination of ACEI and ARB or the combination of potassium-sparing diuretic with potassium supplements [39, 40].

9. Pharmacotherapy plays an important role in modifying risk factors for CVD such as dyslipidaemia, hypertension and diabetes, and this modification significantly reduces the risk of CVD.

10. Some drugs used in patients with CVD do not affect the risk of CVD, but improve quality of life. This group includes for example nitrates used in stable coronary artery disease to abolish anginal symptoms, as well as digoxin or diuretics used in HF.

Conflict of interest: none declared

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