PROVA SCRITTA N. 1

Embolia polmonare a rischio intermedio: trattamento e follow-up

PROVA SCRITTA N. 2

Trattamento della pericardite acuta clinicamente stabile

PROVA SCRITTA N. 3

SGLt2i: indicazioni e trattamento nello scompenso cardiaco

MASCHIO
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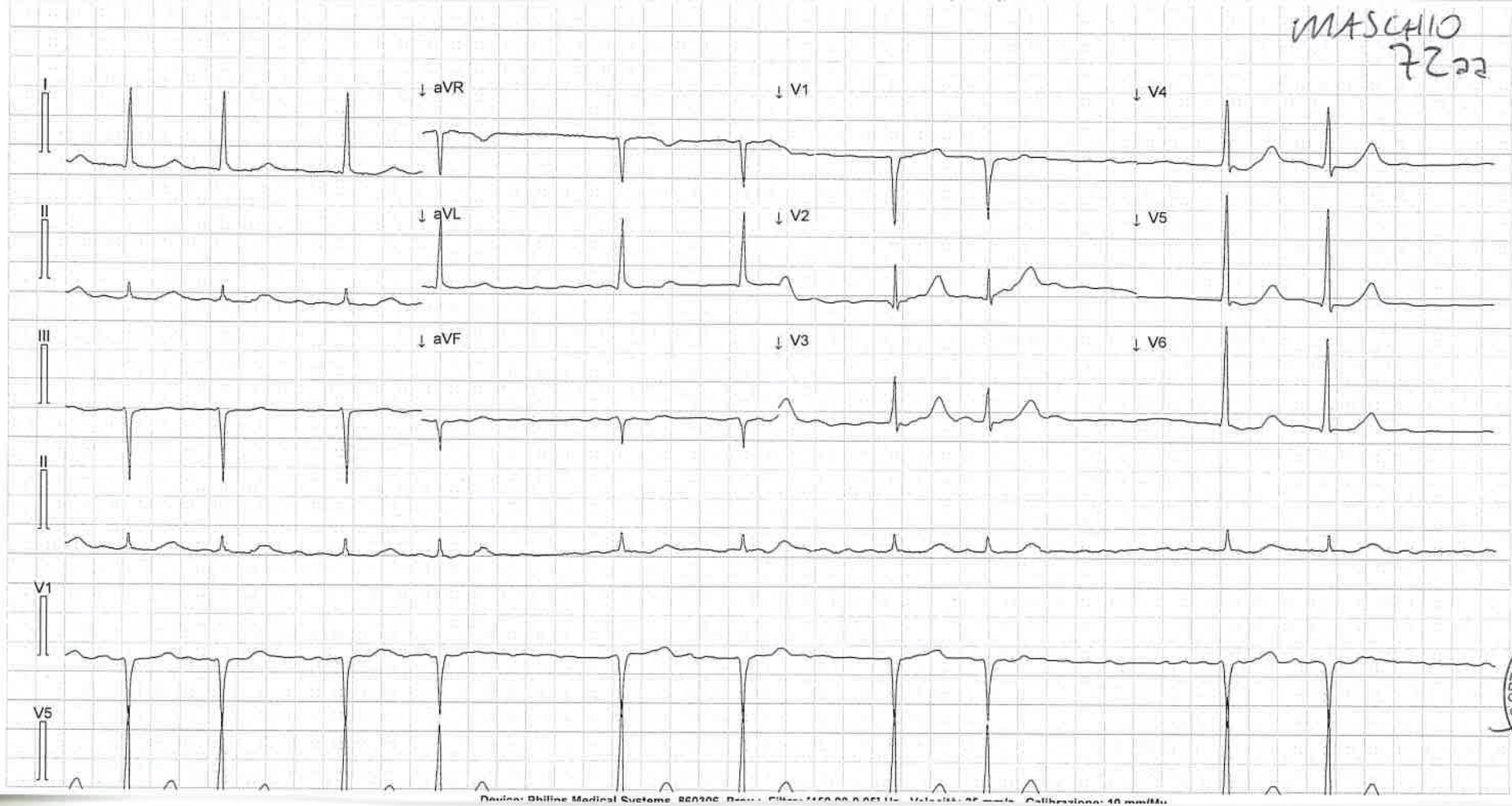
PROVA PRATICA N. 1



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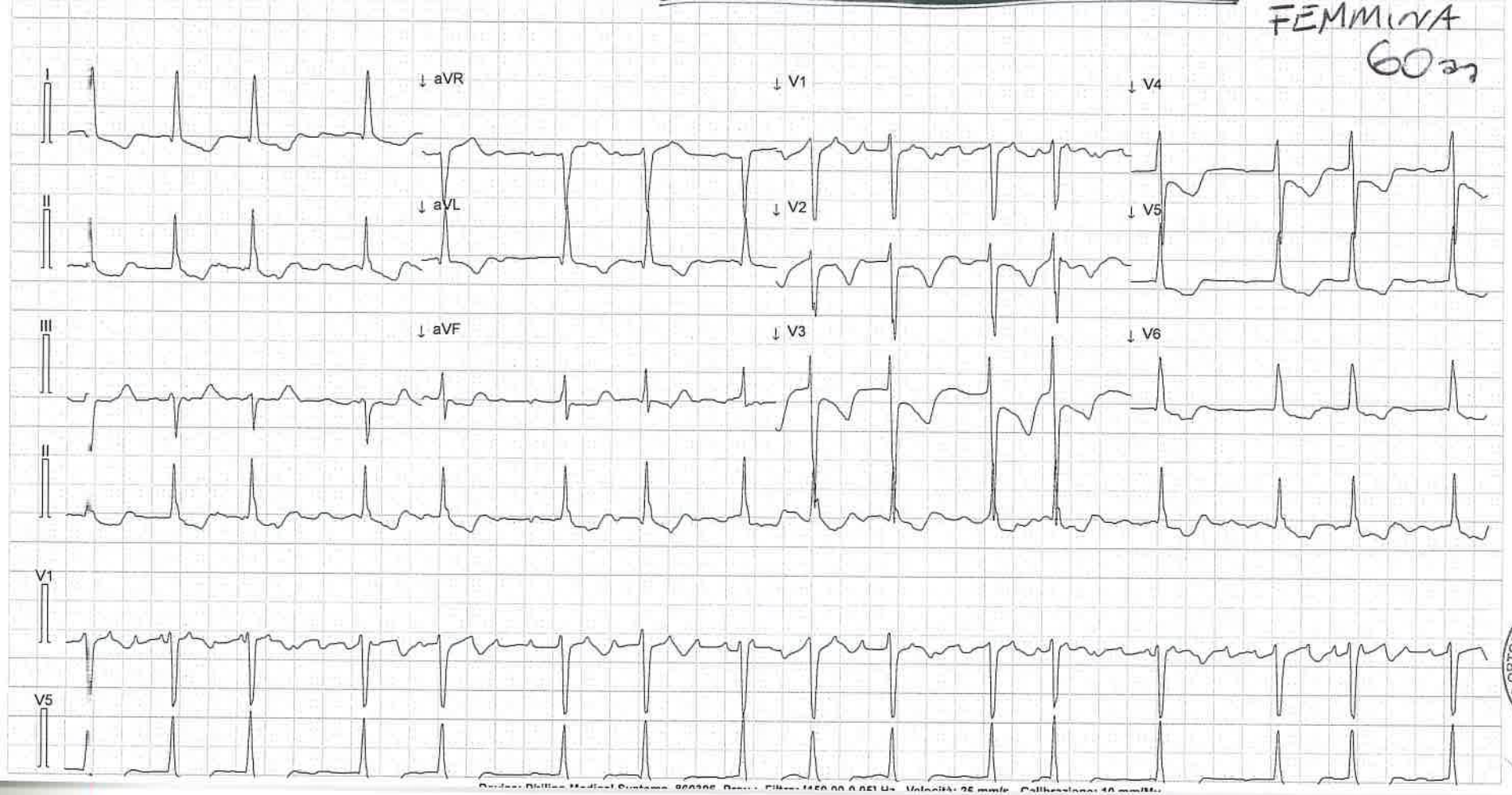

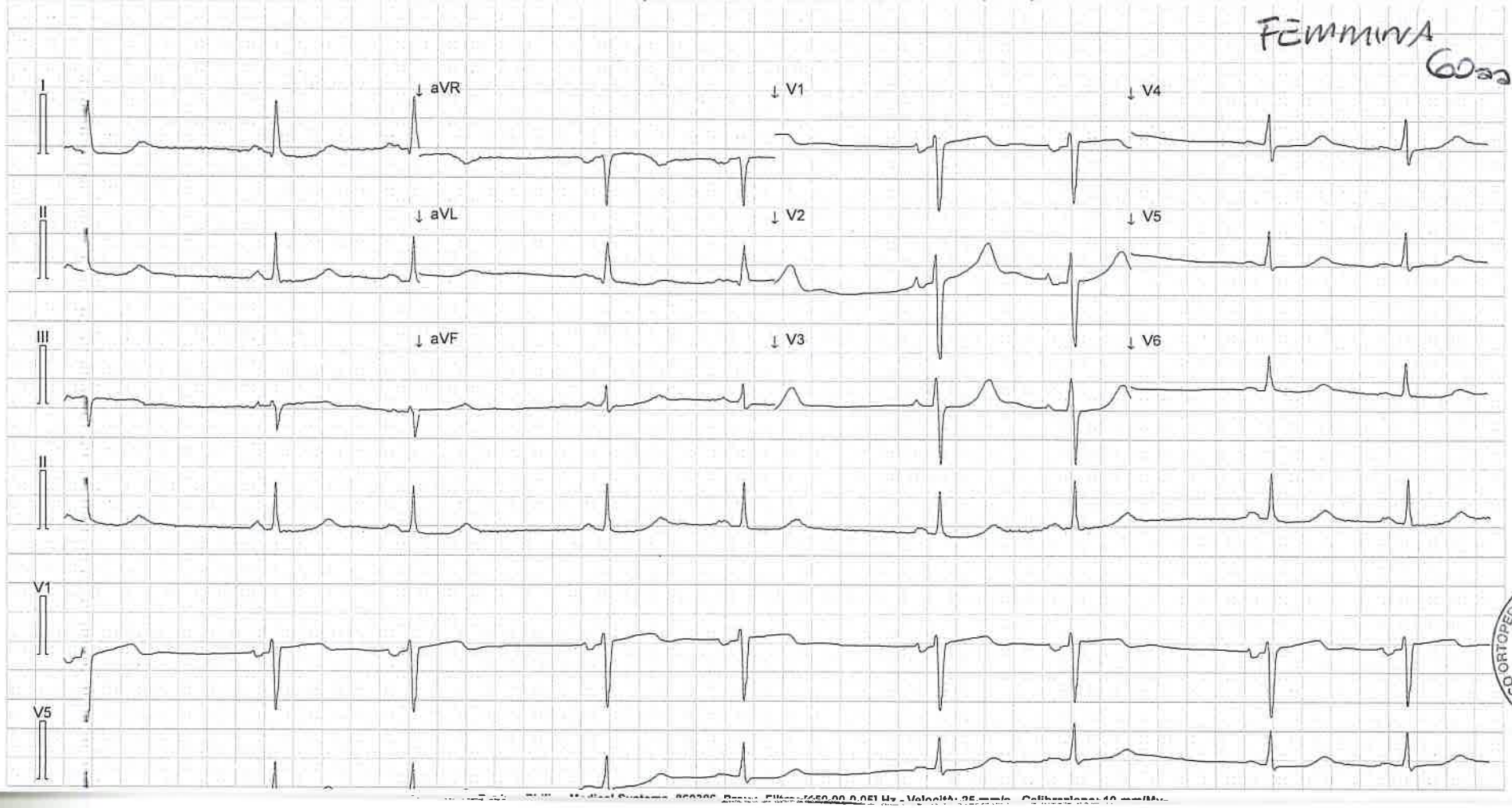

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PROVA PRATICA N. 3

CENTRO SPECIALISTICO ORTOPEDICO TRAUMATOLOGICO MILANO

PROVA ORALE N. 1

Stratificazione del rischio del paziente con NSTE: novità dalle Linee Guida ESC 2023

PROVA ORALE N. 2

I nuovi farmaci ipolipemizzanti iniettivi: quali pazienti beneficiano di un trattamento più aggressivo

PROVA ORALE N. 3

La riabilitazione cardiologica nel malato con scompenso cardiaco dopo una riacutizzazione

DOMANDA INFORMATICA

Cos'è il Phishing

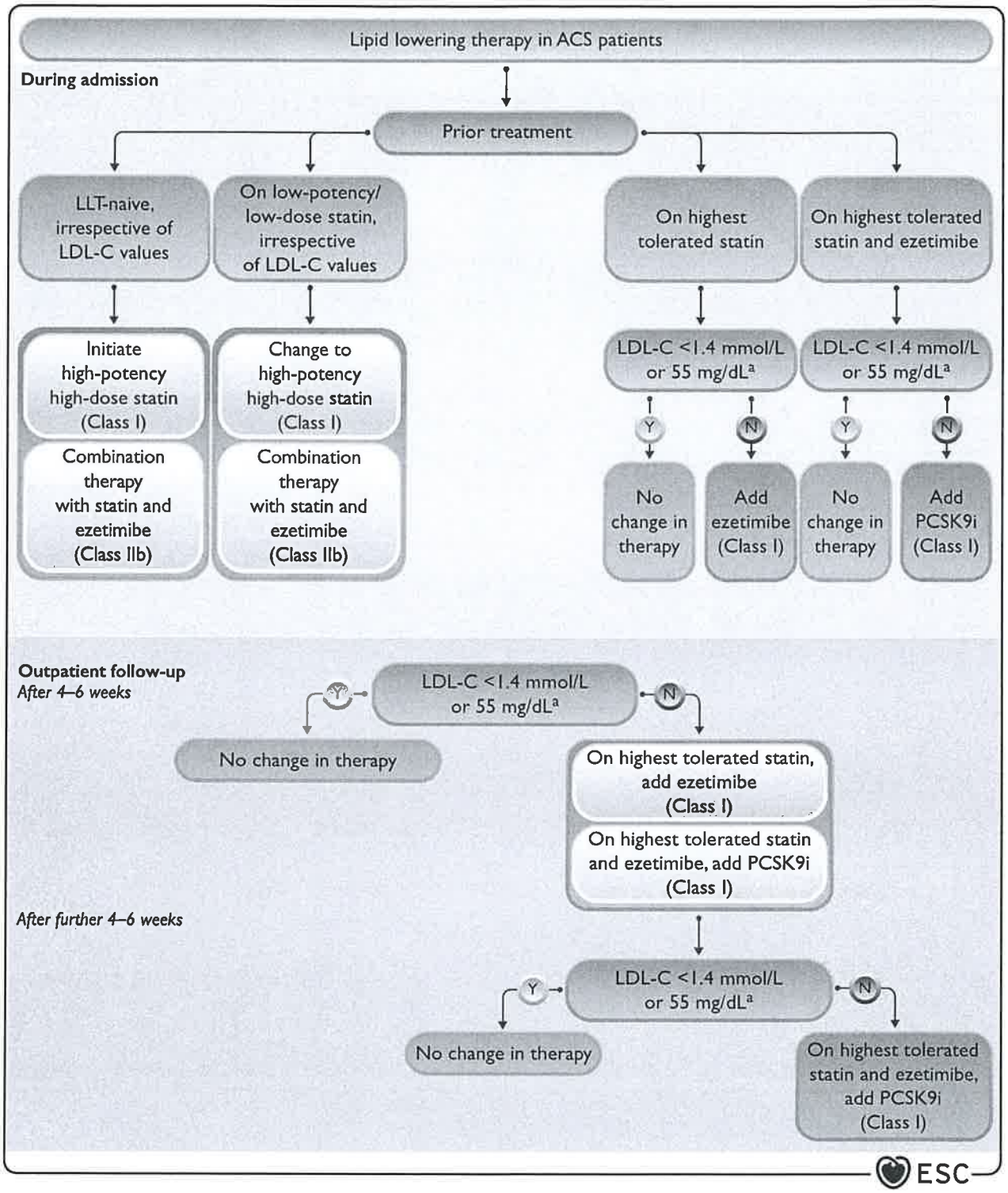

Figure 18 Lipid-lowering therapy in ACS patients. ACS, acute coronary syndrome; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor. [a]Consider LDL-C <1.0 mmol/L if recurrent event.

13.3.3. Beta-blockers

The clinical benefit of beta-blockers after ACS in patients with reduced LVEF is supported by evidence from contemporary trials.[557,798–800] However, the evidence for prescribing beta-blockers after uncomplicated ACS in patients with LVEF >40% is less well established. With the exception of the CAPRICORN (CArvedilol Post-infaRct survIval COntRolled evaluatioN) trial, which only recruited patients with LVEF ≤40%, all large RCTs testing the benefits of post-MI beta-blocker maintenance were performed in the pre-reperfusion era.[801] Pooled data demonstrated that post-MI beta-blocker therapy reduced the

risk of death by >20%. These trials mostly enrolled patients with STEMI, making the evidence for their benefit in NSTEMI less robust. In addition, since these trials were performed, the clinical scenario has changed dramatically, with improvements in invasive strategies and associated pharmacotherapy resulting in an improved prognosis for patients with ACS.[718] Modern observational studies and meta-analyses of these trials have yielded mixed results, with some studies suggesting a benefit of beta-blocker therapy irrespective of LVEF, and others reaching the opposite conclusion.[557,800,802–804]

There is only one small, open-label trial, CAPITAL-RCT (Carvedilol Post-Intervention Long-Term Administration in Large-scale Randomized Controlled Trial), that randomized 801 STEMI patients with successful PPCI and preserved LVEF to carvedilol or control.[805] During a 3-year follow-up, the incidence of a composite of all-cause death, MI, hospitalization for HF, and hospitalization for ACS was not significantly different between the two groups. However, the trial was underpowered and therefore this scientific question remains open. There are four ongoing pragmatic prospective large-scale RCTs in Europe randomizing ACS patients without reduced LVEF to beta-blocker or control: REBOOT-CNIC (TREatment With Beta-blockers After myOcardial Infarction withOut Reduced Ejection fracTion), 8468 ACS patients with LVEF >40%; REDUCE-SWEDEHEART (Evaluation of Decreased Usage of Betablockers After Myocardial Infarction in the SWEDEHEART Registry), 5000 ACS patients with LVEF ≥50% (NCT03278509); BETAMI (BEtablocker Treatment After Acute Myocardial Infarction in Patients Without Reduced Left Ventricular Systolic Function), 10 000 ACS patients with LVEF >40%; and DANBLOCK (Danish Trial of Beta Blocker Treatment After Myocardial Infarction Without Reduced Ejection Fraction), 3570 ACS patients with LVEF >40%.[806–808]

The duration of beta-blocker therapy after uncomplicated ACS is also another controversial topic. There are some observational studies suggesting that the clinical benefit of beta-blocker therapy is restricted to the first year after the index ACS event, but the non-randomized nature of the studies limits their conclusions.[809] There are two ongoing large-scale RCTs testing the impact of beta-blocker withdrawal after 6–12 months following uncomplicated ACS in patients with preserved LVEF: AβYSS (Beta Blocker Interruption After Uncomplicated Myocardial Infarction; NCT03498066) and SMART-DECISION (Long-term Beta-blocker Therapy After Acute Myocardial Infarction; NCT04769362).[810]

13.3.4. Nitrates and calcium channel blockers

Intravenous nitrates may be useful during the acute phase in STEMI patients with hypertension or HF, provided there is no hypotension or RV infarction. In the ISIS-4 (Fourth International Study of Infarct Survival) trial, oral nitrates had no survival benefit in MI patients.[811] Their use is therefore restricted to the control of residual angina, as recommended in the 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes.[195] Calcium channel blocker use was not associated with prognostic benefit in a systematic review including 28 trials.[812] Calcium channel blocker use can be considered in the context of residual angina and for blood pressure control as recommended in the 2021 ESC Guidelines on CVD prevention and the 2019 ESC Guidelines for the diagnosis and management of CCS.[195,646]

13.3.5. Renin–angiotensin–aldosterone system inhibitors

Angiotensin-converting enzyme (ACE) inhibitors have been demonstrated to improve outcomes in post-MI patients with additional conditions, such as clinical HF and/or LVEF ≤40%, diabetes, CKD, and/or hypertension.[813–817] A systematic overview of (old) trials of ACE inhibition early in STEMI showed that their use is associated with a small but significant reduction in 30-day mortality, especially in anterior MIs.[818]

In the VALsartan In Acute myocardial iNfarcTion (VALIANT) trial, valsartan was found to be non-inferior to captopril in patients with a recent MI plus HF and/or LVEF ≤40%.[819]

There is established evidence that patients with heart failure with reduced ejection fraction (HFrEF), regardless of aetiology, benefit from ACE inhibitors.[820–823] Angiotensin receptor/neprilysin inhibitors (ARNI) have been shown to be superior to ACE inhibitors in patients with established HF (of different aetiologies) and LVEF ≤40%.[824] However, in the more recent PARADISE-MI (Prospective ARNI vs ACE Inhibitor Trial to Determine Superiority in Reducing Heart Failure Events After MI), a dedicated study in patients with recent ACS (1–7 days) complicated by HF and/or LVEF ≤40%, an ARNI combination (sacubitril plus valsartan) was not associated with a significantly lower incidence of death from CV causes or incident HF in comparison to the active comparator ramipril.[825]

In general, ACE inhibitors (or sacubitril plus valsartan as a replacement for them) are recommended for patients with established HFrEF regardless of the aetiology.[557] These agents may be considered for patients with HF with mildly reduced ejection fraction.[557] Patients who tolerate neither ACE inhibitors nor ARNI are recommended to be treated with an angiotensin receptor blocker.

In the Eplerenone Post-AMI Heart failure Efficacy and SUrvival Study (EPHESUS), the mineralocorticoid receptor antagonist (MRA) eplerenone was associated with reduced mortality and CV hospitalizations in patients with a recent MI and LV dysfunction with symptoms of either HF or diabetes.[826] The Double-Blind, Randomized, Placebo-Controlled Trial Evaluating The Safety And Efficacy Of Early Treatment With Eplerenone In Patients With Acute Myocardial Infarction (REMINDER) trial randomized 1012 patients with acute STEMI without HF to eplerenone or placebo within 24 h of symptom onset.[827] The primary endpoint was the composite of CV mortality, rehospitalization, or extended initial hospital stay due to diagnosis of HF, sustained VT or VF, ejection fraction ≤40%, or elevated BNP/NT-pro BNP at 1 month or more after randomization. Eplerenone was associated with a significant reduction in the primary composite endpoint, although this difference was primarily driven by BNP levels.[827]

13.3.6. Medications for diabetes

13.3.6.1. Sodium–glucose co-transporter 2 inhibitors

Pharmacological blockade of SGLT2 induces glycosuria with lowering of plasma glucose levels, improving glycaemic control without hypoglycaemia, and leading to reductions in weight and blood pressure.[828] In patients with type 2 diabetes and established ASCVD, three trials (with empagliflozin, canagliflozin, and dapagliflozin) have demonstrated significant CV benefits.[656,829,830] In a meta-analysis of these three trials, MACE were reduced by 11%, with no clear effect on stroke or MI. This benefit was only seen in patients with established ASCVD.[698] The benefits of SGLT2 inhibitors may relate more to cardio-renal haemodynamic effects than to atherosclerosis.[646] Further recommendations for patients with diabetes can be found in the current ESC Guidelines on diabetes, pre-diabetes,and cardiovascular diseases.[831]

In patients with HF regardless of their LVEF, dapagliflozin and empagliflozin have been shown to significantly reduce the risk of worsening HF or CV death, both in the presence or absence of type 2

diabetes.[702,703,832,833] In the EMMY (EMpagliflozin in patients with acute MYocardial infarction) trial, empagliflozin led to a significant improvement in NT-pro BNP reduction over 26 weeks post-MI, accompanied by a significant improvement in echocardiographic functional and structural parameters.[834] Ongoing outcome trials in ACS populations will be useful to better define the role of these agents in the absence of HF.[835]

13.3.6.2. Glucagon-like peptide-1 receptor agonists

In a systematic review and meta-analysis of seven trials (56 004 patients with type 2 diabetes) testing different GLP1-RAs, their use was associated with reductions in the incidence of MACE, CV death, all-cause mortality, MI, and stroke.[699]

13.3.7. Proton pump inhibitors

Proton pump inhibitors (PPIs) reduce the risk of upper gastroduodenal bleeding in patients treated with antiplatelet agents.[287,836,837] Therapy with a PPI is indicated for patients receiving any antithrombotic regimen who are at high risk of gastrointestinal bleeding (for details see *Section 8.2.2.3*, Bleeding risk assessment, in the Supplementary data online).

PPIs that inhibit CYP2C19, particularly omeprazole and esomeprazole, may reduce the pharmacodynamic response to clopidogrel, though there is no strong evidence that this results in an increased risk of ischaemic events or stent thrombosis in clinical trials and propensity score-matched studies.[287,288,838–842] Importantly, no interaction between the concomitant use of PPIs and aspirin, prasugrel or ticagrelor has been observed.

13.3.8. Vaccination

An annual influenza vaccination in patients with stable ASCVD appears to be associated with reduced incidence of MI, an improved prognosis in patients with HF, and decreased CV risk in adults aged 65 years and older.[843,844] In addition, influenza vaccination given early after an MI or in high-risk CAD has been shown to result in a lower risk of all-cause death and CV death at 12 months.[845–847] Therefore, influenza vaccination is recommended for all ACS patients and should be given preferentially during index hospitalization during influenza season for those not protected by a seasonal influenza vaccination.

13.3.9. Anti-inflammatory drugs

Inflammation plays a central role in the pathogenesis of atherosclerosis and acute coronary events. Several recent trials have tested the role of the anti-inflammatory agent colchicine in acute and chronic coronary syndromes.[848,849] In the Colchicine Cardiovascular Outcomes Trial (COLCOT), which enrolled 4745 patients with a recent ACS event, low-dose colchicine (0.5 mg daily) was associated with a significant reduction of the primary composite endpoint (CV death, resuscitated cardiac arrest, MI, stroke, or urgent revascularization) in comparison to placebo.[850] Of note, pneumonia was more frequent in the colchicine group. The Low-dose Colchicine trial-2 (LoDoCo2) enrolled 5522 patients with CCS (84% of whom had prior ACS) who were randomized to colchicine (0.5 mg daily) or placebo.[851] The primary endpoint (composite of CV death, MI, stroke, or ischaemia-driven coronary revascularization) rate was significantly lower in the colchicine group; however, the incidence of non-CV death was higher in the colchicine group. The benefits of colchicine in reducing CV events have been shown to be consistent irrespective of history and timing of prior ACS.[852]

13.3.10. Hormone replacement therapy

For further information on hormone replacement therapy in patients with ACS, please see the Supplementary data online.

Recommendation Table 16 — Recommendations for long-term management

Recommendations	Class[a]	Level[b]
Cardiac rehabilitation		
It is recommended that all ACS patients participate in a medically supervised, structured, comprehensive, multidisciplinary exercise-based cardiac rehabilitation and prevention programme.[721–724,853,854]	I	A
Lifestyle management		
It is recommended that ACS patients adopt a healthy lifestyle, including: • stopping all smoking of tobacco • healthy diet (Mediterranean style) • alcohol restriction • regular aerobic physical activity and resistance exercise • reduced sedentary time[724,761,763,772,773,776,777,855–858]	I	B
In smokers, offering follow-up support, nicotine replacement therapy, varenicline or bupropion, individually or in combination, should be considered.[859–864]	IIa	A
Pharmacological treatment		
Lipid-lowering therapy		
It is recommended that high-dose statin therapy is initiated or continued as early as possible, regardless of initial LDL-C values.[787,865–867]	I	A
It is recommended to aim to achieve an LDL-C level of <1.4 mmol/L (<55 mg/dL) and to reduce LDL-C by ≥50% from baseline.[868,869]	I	A
If the LDL-C goal is not achieved despite maximally tolerated statin therapy after 4–6 weeks, the addition of ezetimibe is recommended.[788]	I	B
If the LDL-C goal is not achieved despite maximally tolerated statin therapy and ezetimibe after 4–6 weeks, the addition of a PCSK9 inhibitor is recommended.[785,786,795,796]	I	A
It is recommended to intensify lipid-lowering therapy[c] during the index ACS hospitalization for patients who were on lipid-lowering therapy before admission.	I	C
For patients with a recurrent atherothrombotic event (recurrence within 2 years of first ACS episode) while taking maximally tolerated statin-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.[785,786]	IIb	B
Combination therapy with high-dose statin plus ezetimibe may be considered during index hospitalization.[788]	IIb	B

Continued

Beta-blockers		
Beta-blockers are recommended in ACS patients with LVEF ≤40% regardless of HF symptoms.[801,870–872]	I	A
Routine beta-blockers for all ACS patients regardless of LVEF should be considered.[798,873–878]	IIa	B
RAAS system inhibitors		
Angiotensin-converting enzyme (ACE) inhibitors[d] are recommended in ACS patients with HF symptoms, LVEF ≤40%, diabetes, hypertension, and/or CKD.[195,813–817,879]	I	A
Mineralocorticoid receptor antagonists are recommended in ACS patients with an LVEF ≤40% and HF or diabetes.[826,880]	I	A
Routine ACE inhibitors for all ACS patients regardless of LVEF should be considered.[816,817]	IIa	A
Adherence to medication		
A polypill should be considered as an option to improve adherence and outcomes in secondary prevention after ACS.[753]	IIa	B
Imaging		
In patients with pre-discharge LVEF ≤40%, repeat evaluation of the LVEF 6–12 weeks after an ACS (and after complete revascularization and the institution of optimal medical therapy) is recommended to assess the potential need for sudden cardiac death primary prevention ICD implantation.	I	C
Cardiac magnetic resonance imaging should be considered as an adjunctive imaging modality in order to assess the potential need for primary prevention ICD implantation.	IIa	C
Vaccination		
Influenza vaccination is recommended for all ACS patients.[843,845–847]	I	A
Anti-inflammatory drugs		
Low-dose colchicine (0.5 mg once daily) may be considered, particularly if other risk factors are insufficiently controlled or if recurrent cardiovascular disease events occur under optimal therapy.[850,851]	IIb	A

Continued

ACS, acute coronary syndrome; CKD, chronic kidney disease; HF, heart failure; ICD, implantable cardioverter defibrillator; LDL-C, low-density lipoprotein-cholesterol; LVEF, left ventricular ejection fraction; PCSK9, proprotein convertase subtilisin/kexin type 9; RAAS, renin–angiotensin–aldosterone system.

[a]Class of recommendation.

[b]Level of evidence.

[c]Increase statin potency/dose if the patient was on low-potency/low-dose statin, add ezetimibe if the patient was only on statins at highest tolerated dose, or add PCSK9 inhibitor if the patient was on statins plus ezetimibe.

[d]Angiotensin receptor blockers in cases of intolerance.

14. Patient perspectives

14.1. Patient-centred care

The management of patients with ACS should not only consider the best available evidence with regard to clinical management strategies, but also should be mindful of the provision of care that is respectful of and responsive to individual patient preferences, needs, and values, ensuring that these values are included in clinical decision-making.[881]

Patient-centred care should be guided by ethical values when considering a patient's physical, emotional, and psychological needs. Adopting a person-centred care approach after an ACS event improves patient outcomes and enhances quality of life.[882] Patients who are regarded as equal partners in their ACS medical management are more likely to actively engage and participate in their own healthcare.[883]

Educating and involving patients in their care should be seen as a continuous process. Engaging and educating the patient is a key component of ACS care and should take place throughout their patient journey, from admission to hospital discharge and cardiac rehabilitation (*Figure 19*).

Figure 19 A person-centred approach to the ACS journey. ACS, acute coronary syndrome.

14.2. Shared decision-making

Shared decision-making is a process, during which the patient and a healthcare professional work together to make an informed decision about the patient's care.[884] During this process, information is provided, comprehension checked, and the patient is given an opportunity to ask questions in order to equip them with the tools needed to make an informed decision.

Using a shared decision-making approach during the consent process allows the patient's preferences to be established.[884] Discovery of the patient's concerns, goals, preferences, and values should be a central component of this process. The use of validated decision aids and audio-visual tools may also be helpful to facilitate informed consent and promote patient involvement.[884–887]

14.3. Informed consent

Informed consent should include the components listed in Supplementary data online, *Table S18*.[885,888] Informed consent is an opportunity to educate patients about the proposed procedure, the associated risks and benefits, and any available alternative interventions or treatments.[886,887] Assessment of the patient's understanding of the information given to them during the informed consent process using the 'teach back' technique should be considered (Supplementary data online, *Figure S6*).[885,889–891] The teach back method assesses understanding by asking patients to state in their own words what they need to know or do about their health.

Informed consent is an ethical and legal obligation for medical practitioners and is required before any invasive procedure. The information

13.1. Cardiac rehabilitation

13.1.1. Comprehensive cardiac rehabilitation

Secondary prevention is most effectively provided through cardiac rehabilitation (CR).[716,717] All ACS patients should participate in a comprehensive CR programme, which should start as early as possible after the ACS event.[716,717,719] CR may be performed in inpatient or outpatient settings, taking age, frailty, results of prognostic risk stratification, and comorbidities into account.[716] Comprehensive CR is a multidisciplinary intervention, supervised and performed by a team and usually co-ordinated by a cardiologist.[716] The core components of CR include patient assessment, management and control of CV risk factors, physical activity counselling, prescription of exercise training, dietary advice, tobacco counselling, patient education, psychosocial management, and vocational support.[716] Several studies have found that CR programmes after atherosclerotic cardiovascular disease (ASCVD) events or revascularization reduce CV hospitalizations, MI, CV mortality and, in some studies, all-cause mortality.[720–725] Despite proven benefits, the rates of referral to, participation in, and implementation of CR programmes are low.[726–730] Another identified issue is that many patients adopt healthier lifestyles during CR but relapse to pre-morbid habits when returning to everyday life.[731] Therefore, there is an unmet need for complementary pathways to the classical centre-based CR model. In addition to alternatives to CR, there is also a need for stronger endorsement of CR by physicians, cardiologists, and healthcare professionals.[732,733] It is also important to initiate and establish a strong partnership between patients and healthcare professionals as early as possible.[732–734]

13.1.2. Digital health

Telerehabilitation may be an effective strategy to maintain a healthy lifestyle over time and can support or even partially replace conventional, centre-based CR.[729] Telerehabilitation means rehabilitation from a distance, covering all CR core components, including telecoaching, social interaction, telemonitoring, and e-learning.[735,736] Studies in patients with CAD have shown that telerehabilitation can be equivalent to traditional CR in terms of achieving functional improvement, managing risk factors, and increasing patient well-being.[737–741] Few data are available about the effect of telerehabilitation on recurrent events.[742] Nevertheless, in a meta-analysis no significant difference was found between mortality following telehealth interventions and centre-based supervised CR.[743] Also, most trials have only focused on one of the CR core components—exercise training and/or physical activity.[742] Therefore, more research on the impact of telerehabilitation on outcomes is still needed, as are investigations into health and digital literacy in CR.

13.1.3. Adherence and persistence

Promotion of both adherence (the extent to which a patient adheres to a prescribed treatment or lifestyle advice) and persistence (the length of time between initiation and discontinuation of a prescribed treatment or lifestyle advice) are key in preventing recurrent CV events after ACS. Adherence to medication has been shown to be sub-optimal, ranging from 50% in primary prevention to 66% in secondary prevention. It is estimated that 9% of ASCVD events in Europe occur as a result of sub-optimal medication adherence.[646] Contributors to sub-optimal adherence and persistence are multidimensional and include: polypharmacy, drug regimen complexity, the doctor–patient relationship, a lack of patient-centred care and disease acceptance, concern regarding side effects, cognitive ability, mental and physical disorders, financial aspects, living alone, and depression.[646,744–749] Polypills, which include guideline-recommended treatments for secondary prevention, have been shown to increase adherence in post-ACS patients and may improve therapeutic targets.[750–752] The Secondary Prevention of Cardiovascular Disease in the Elderly (SECURE) study is the only RCT testing the impact of a strategy based on a polypill (containing aspirin, ramipril, and atorvastatin) vs. usual care on hard outcomes in ACS patients. The polypill strategy was associated with a significant reduction in major CV events, driven by a significant 33% reduction in CV mortality.[753] The use of technology to improve medication adherence is also generating interest: mobile phone applications and mobile health (mHealth) tools may improve medication adherence, but clinical trials of sufficient size and duration are needed.[754–756] Finally, it is important to recognize that adherence has complex underlying psychological drivers, and therefore a whole-systems approach is mandatory. This should include the education of health professionals, the use of patient-reported outcomes and experience measures, patient education, and patient-centred care.[734,757,758]

13.2. Lifestyle management

Lifestyle management is one of the cornerstones of comprehensive CR.[716] While most of the evidence regarding the benefits of a healthy lifestyle on prognosis comes from primary prevention, studies in secondary prevention settings indicate similar beneficial effects.[716,724,759–763]

13.2.1. Tobacco

Tobacco abstinence is associated with a reduced risk of re-infarction (30–40%) and death (35–45%) after ACS.[763–765] Measures to promote cessation of smoking are therefore a priority after ACS. Interventions for smoking cessation should begin during hospitalization using a combination of behavioural interventions, pharmacotherapy, and counselling.[18,766] Many patients continue or resume smoking after ACS, in particular patients with depression and environmental exposures.[646] During encounters with smokers, the 'very brief advice' evidence-based intervention should be used to facilitate dialogue between the patient and healthcare worker.[646] Drug interventions, including nicotine-replacement therapy (NRT), bupropion and varenicline, should be considered along with behavioural support. All forms of NRT are effective, and the anti-depressant bupropion aids in long-term smoking cessation with similar efficacy to NRT.[646,766] Varenicline is the most effective medical treatment to support smoking cessation and is safe to use in ACS patients.[767–770] An average weight gain of 5 kg can be expected when a person quits smoking, but it is important to recognize that the CV risk from continued smoking outweighs the CV risk from gaining weight.[646]

E-cigarettes have been used to help smokers quit, but evidence on their impact on successful smoking cessation is insufficient, particularly with regard to whether using e-cigarettes actually helps the person remain tobacco free. While e-cigarettes do contain nicotine, they do not contain as many tobacco chemicals as cigarettes. Caution should be given with respect to the use of e-cigarettes, as current evidence suggests they are harmful to CV health by increasing arterial stiffness, heart rate and blood pressure, and by causing endothelial dysfunction.[771]

13.2.2. Nutrition and alcohol

A healthy diet and eating habits influence CV risk. Adopting a Mediterranean-style diet can help reduce CV risk in all individuals, including persons at high CV risk and patients with ASCVD.[761,762,772]

Supplementary data online, *Table S17* summarizes the characteristics of a healthy diet that should be adhered to. For further details on nutrition, please refer to the 2021 ESC Guidelines on cardiovascular disease prevention.[646]

With regard to alcohol consumption, recent data suggest that alcohol abstainers have the lowest risk of CVD outcomes, that any amount of alcohol uniformly increases blood pressure and body mass index, and that a weekly consumption of >100 g of alcohol is associated with decreased life expectancy.[773–775] Accordingly, it is recommended to restrict alcohol consumption to a maximum of 100 g per week (same limit for men and women).[646]

13.2.3. Physical activity and exercise

Based on extensive data from the general population, sedentary behaviour, defined as time spent sitting or lying with low energy expenditure, while awake, is an independent risk factor for all-cause mortality.[776,777] According to recommendations from the World Health Organization, adults with chronic conditions should limit their amount of sedentary time, replacing it with physical activity of any intensity (including light intensity).[646,778] General physical activity recommendations include a combination of regular aerobic physical activity and resistance exercise throughout the week, which also forms the basis of recommendations for patients post-ACS.[646,778] However, it is important to recognize that daily physical activity does not replace participation in exercise-based CR. With support from multiple randomized trials, exercise training is a pivotal part of comprehensive CR and participation in exercise-based CR should be offered to all patients after ACS.[779] Cardiorespiratory fitness is a strong predictor of future prognosis both in the general population and in post-ACS patients.[780]

13.2.4. Psychological considerations

There is a two-fold risk of anxiety and mood disorders in patients with heart disease. Depression, anxiety, and psychological stress are associated with worse outcomes. Psychological and pharmacological interventions can have a beneficial effect and should be considered for ACS patients with depression, anxiety, and stress.[781] It is recommended that all patients have their mental well-being assessed using validated tools before discharge, with consideration of onward psychological referral when appropriate.[782] For further details, please refer to the 2021 ESC Guidelines on cardiovascular disease prevention.[646]

13.2.5. Resumption of activities

Information on the resumption of activities, sexual activity, and environmental factors is presented in the Supplementary data online, *Section 13.1.2.*

13.3. Pharmacological treatment

13.3.1. Antithrombotic therapy

Recommendations for antithrombotic therapy are included in *Section 6.*

13.3.2. Lipid-lowering therapy

Dyslipidaemia should be managed according to the current dyslipidaemia guidelines, with a combination of lifestyle and pharmacological interventions.[783] Trials have consistently demonstrated that lower low-density lipoprotein-cholesterol (LDL-C) levels after ACS are associated with lower CV event rates.[784] The current treatment goal for secondary prevention is to lower LDL-C to <1.4 mmol/L (<55 mg/dL) and to achieve a ≥50% LDL-C reduction from baseline. For patients who experience a second CV event within 2 years (not necessarily of the same type as the first event), an LDL-C goal of <1.0 mmol/L (<40 mg/dL) appears to confer additional benefit.[783,785,786]

After an ACS event, lipid-lowering treatment should be initiated as early as possible, both for prognostic benefit and to increase patient adherence after discharge. It is recommended that a high-intensity statin (e.g. atorvastatin or rosuvastatin) is initiated as early as possible after hospital admission, preferably before planned PCI, and prescribed up to the highest tolerated dose in order to reach the LDL-C goals.[783,787] The intensity of statin therapy should be increased in patients who were receiving low- or moderate-intensity statin treatment before the ACS event. In IMPROVE-IT (Improved Reduction of Outcomes: Vytorin Efficacy International Trial), ezetimibe treatment early after ACS (within 10 days) was added on top of prior statin therapy or initiated concomitantly in statin-naïve patients (two-thirds of patients) and compared with statin monotherapy.[788] Treatment with ezetimibe was shown to be safe and provided long-term benefits for CV outcomes. As such, if patients are on a maximally tolerated statin dose, or have no prior statin treatment, and have LDL-C levels which indicate it is unlikely that targets will be reached with statin therapy alone, initiating ezetimibe in addition to a statin (or statin plus ezetimibe combination treatment) may be considered during the ACS hospitalization.[783,788] In the ODYSSEY OUTCOMES (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab) trial, treatment with the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor alirocumab was initiated as early as 1 month after ACS.[786] Treatment with PCSK9 inhibitors has been shown to be safe and effective in lowering LDL-C in patients hospitalized with ACS.[789–791] Recent data have also shown improvements in plaque phenotype and plaque regression in ACS patients treated with PCSK9 inhibitors.[792,793] Combined with the data from trials on the long-term benefits of PCSK9 inhibitors and observational data on the importance of lowering LDL-C early after ACS, PCSK9 inhibitor treatment should be initiated during ACS hospitalization in patients who were not at their LDL-C goal despite being on statin and ezetimibe treatment before admission.[785,786,794–796]

In all cases, lipid levels should be re-evaluated 4–6 weeks after each treatment or dose adjustment to determine whether treatment goals have been achieved and to check for any safety issues; the therapeutic regimen can then be adapted accordingly. If the LDL-C goals are not achieved with the maximum tolerated dose of a statin alone after 4–6 weeks following ACS, adding ezetimibe is recommended.[783,788] Initiation of PCSK9 inhibitor treatment is recommended in patients who do not reach their LDL-C goal despite maximum tolerated statin and ezetimibe therapy.[783,785,786] Finally, icosapent ethyl, at a dose of 2 g b.i.d., can be used in combination with a statin in patients with ACS and triglyceride levels of 1.5–5.6 mmol/L (135–499 mg/dL) despite statin treatment.[783,797] An algorithm for lipid-lowering management in ACS patients is outlined in *Figure 18.*

For a detailed description of the different lipid-lowering drug classes and respective trial data, please refer to the Supplementary data online.