

# CORONARY ARTERY DISEASE

## Original Studies

### A Multidisciplinary Consensus Document on Follow-Up Strategies for Patients Treated With Percutaneous Coronary Intervention

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The number of percutaneous coronary interventions (PCI) is increasing worldwide. Follow-up strategies after PCI are extremely heterogeneous and can greatly affect the cost of medical care. Of note, clinical evaluations and non-invasive exams are often performed to low risk patients. In the present consensus document, practical advises are provided with respect to a tailored follow-up strategy on the basis of patients' risk profile. Three strategies follow-up have been defined and types and timing of clinical and instrumental evaluations are reported. Clinical and interventional cardiologists, cardiac rehabilitators, and general practitioners, who are in charge to manage post-PCI patients, equally contributed to the creation of the present document. © 2014 Wiley Periodicals, Inc.

**Key words:** health care policy; percutaneous coronary intervention; risk stratification

## INTRODUCTION

Percutaneous coronary intervention (PCI) in patients with coronary artery disease (CAD) is increasingly performed worldwide. Every year, over 130,000 PCIs are performed in Italy and over one million are performed in US [1,2]. Although several international guidelines have been published with respect to coronary revascularization, acute coronary syndromes (ACS), and stable CAD, follow-up strategies for PCI patients are often heterogeneous and arbitrary, with wide variations among centers [3–6]. Practice variation might significantly affect the cost of medical care. Redundant clinical and non-invasive examinations should not be considered as a marker for improved quality of post-PCI care but rather as a signal of increased health care utilization, as performance of useless testing sensibly increases the cost of medical care [7]. Testing is common after PCI across a broad range of patients, with rates up to 66% within 12 months after revascularization, a figure which greatly exceed the 15% 1-year rate of angina symptoms reported in previous registry reports [8]. Of note, freedom from angina can greatly vary from 66% in the PCI group of COURAGE [9] to 81% in the PCI group of FAME [10], a difference which may be explained by the near exclusive use of

drug-eluting stents (DES), reducing the rate of restenosis, in the latter. Asymptomatic, low-risk patients are often submitted to periodical, unuseful clinical evaluations and non-invasive exams, whereas paradoxically, patients with higher risk features at baseline are less likely to undergo post-PCI testing [8,11]. Increasing age, male sex, and most comorbidities are associated with a lower likelihood of any testing after PCI [8,11,12]. As a consequence, the revascularization rate is low on patients referred for routine stress test after PCI, with an average of 10% of patients undergoing revascularization within 90 days [8]. This may reflect a pattern of routine surveillance testing conflicting with clinical practice guidelines and Appropriate Use Criteria [3].

Taken together, these observations suggest that there may be opportunities to improve the selection of patients for testing. Of note, a standard follow-up strategy shared among cardiologists, cardiac rehabilitators, and general practitioners (GP) is lacking, further contributing to waste of follow-up resources.

## The “Post-PCI” Consensus Document

The Italian Society of Interventional Cardiology (SICI-GISE), the Italian National Association of Hospital Cardiologists (ANMCO), the Italian Association

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for Cardiovascular Prevention and Rehabilitation (GICR-IACPR) and Italian Society of General Practitioner (SIMG) promoted the creation of the present consensus document with regard to the optimal follow-up strategies for patients submitted to PCI due to stable CAD or ACS. The Writing Committee was composed by clinical and interventional cardiologists, cardiac rehabilitators, and GPs, who met in six meetings and equally contributed to drawing it up. In spite of the novelty of the present document and of the follow-up strategies proposed, the recommendations are based on International Guidelines [3–6]. Three specific patients subsets have been identified on the basis of clinical and procedural features and three standard follow-up strategies have been defined in parallel. Left ventricular ejection fraction (LVEF) at discharge, the presence of multivessel disease, diabetes mellitus (DM) incomplete or suboptimal PCI results, and clinical scenario (ACS vs. stable CAD), were recognised as main determinants of follow-up strategies. An individualized long-term follow-up has been defined for each patient at discharge. Follow-up focuses mainly on secondary prevention, patients' functional status, and symptoms, instead of CAD progression/restenosis only. Patients should be regularly followed-up by GP, who is supposed to visit the patient as soon as possible after discharge. By contrast, short or mid-term cardiologic clinical and/or instrumental re-evaluation should be scheduled at discharge only in high or intermediate risk patients. Of note, cardiologic consultation should be quickly provided in patients with new onset or worsening symptoms.

Figure 1 shows the flow-chart which leads to the identification of the 3 follow-up strategies

Strategy A follow-up (Fig. 2) is advised for patients at high risk, defined as patients undergoing PCI for ACS with reduced LVEF ( $LVEF \leq 45\%$ ), or PCI in patients with a recent finding of low LVEF, or PCI in patients with symptoms/signs of heart failure. Cardiac rehabilitation (CR) should be considered for all patients. In stable patients, strategy A advocates cardiologic consultation, ECG, and echocardiographic exam at least at 3 and 12 months, and according to clinical needs. The execution of a stress test should be considered on the basis of clinical/angiographic characteristics (see strategies B and C).

Strategy B follow-up (Fig. 3) is recommended for patients undergoing PCI and presenting 1 of the following clinical or procedural characteristics: ACS, diabetes mellitus, multivessel or left main or proximal left anterior descending artery disease, incomplete or suboptimal revascularization. If stable, these patients should undergo cardiologic consultation and ECG at 6

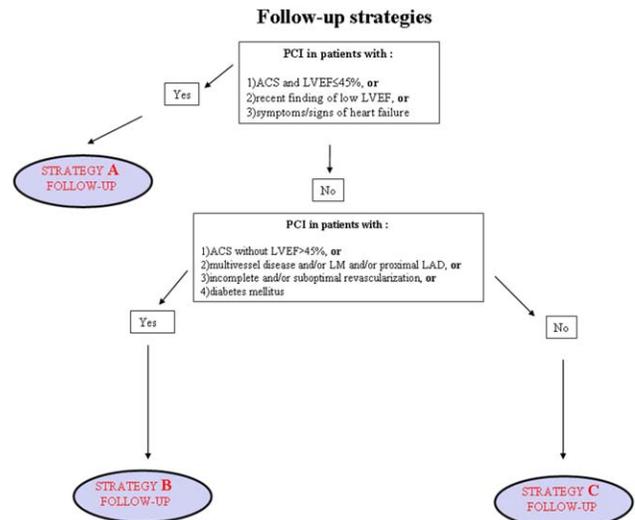


Fig. 1. Flow-chart leading to the identification of the 3 follow-up strategies.

and 12 months, and yearly afterward. Routine echocardiographic exam is not recommended in asymptomatic patients. Stress test at 3 months might be indicated in case of incomplete revascularization or suboptimal PCI result and should be repeated at 12 months and yearly afterward. Yearly stress test might be indicated in patients with silent ischemia at the time of index PCI and in diabetic patients, considered at high risk. In high risk diabetic patients with left ventricular dysfunction, yearly echocardiogram might be considered, even if clinically stable.

Strategy C follow-up (Fig. 4) is recommended to patients without relevant comorbidities and submitted to complete, successful PCI. Routine echocardiographic exam is not indicated in asymptomatic patients. If stable, these patients should undergo cardiologic consultation and ECG within 12 months (not routinely recommended afterward).

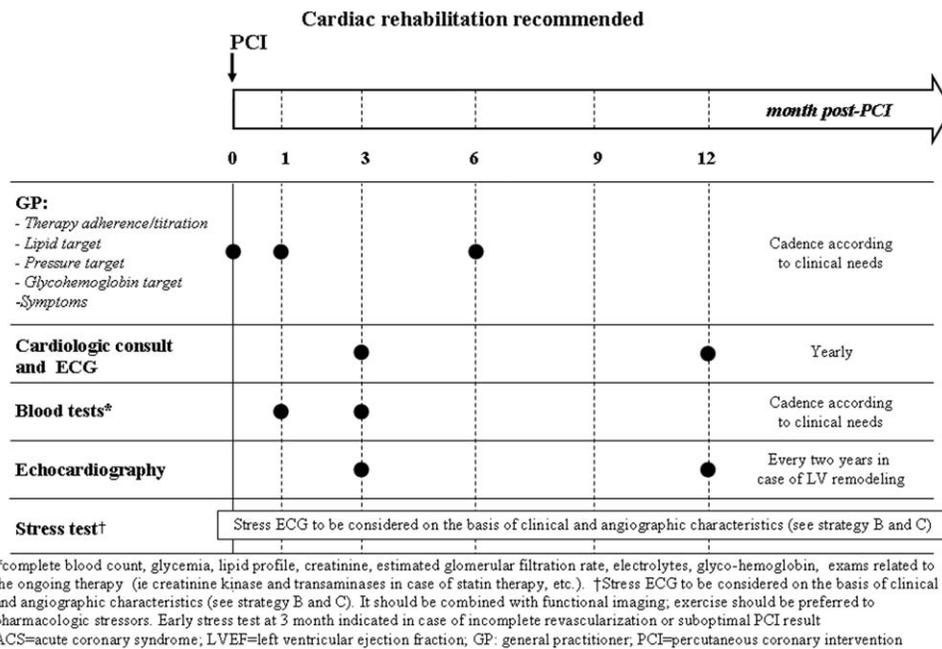
Follow-up strategy includes clinical and instrumental evaluation. GP ought to carefully monitor new onset or worsening of symptoms, adherence to prescribed therapy, and correction of risk factors. Cardiologists will perform clinical and instrumental follow-up in selected patients (i.e., high risk subsets or symptomatic patients) and will decide whether coronary angiography is required.

Of note, in patients (especially if diabetics or with multivessel disease) with newly diagnosed reduction of LVEF the presence of ischemia should be excluded and stress test and/or coronary angiography should be considered.

## Who Does What?

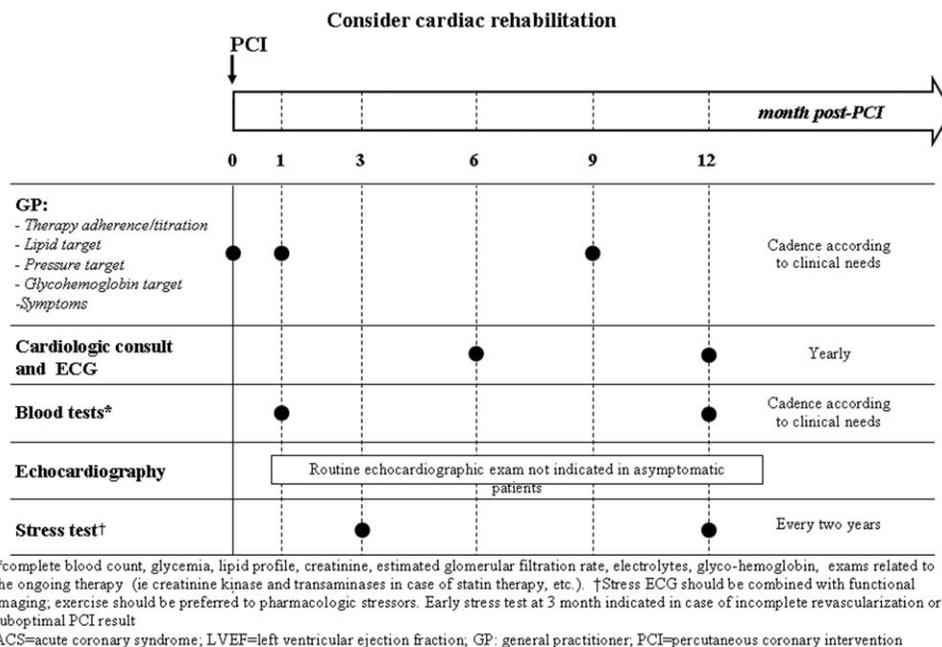
**The role of the cardiologist. Discharge document.** Essential information about the patient's

### Strategy A follow-up

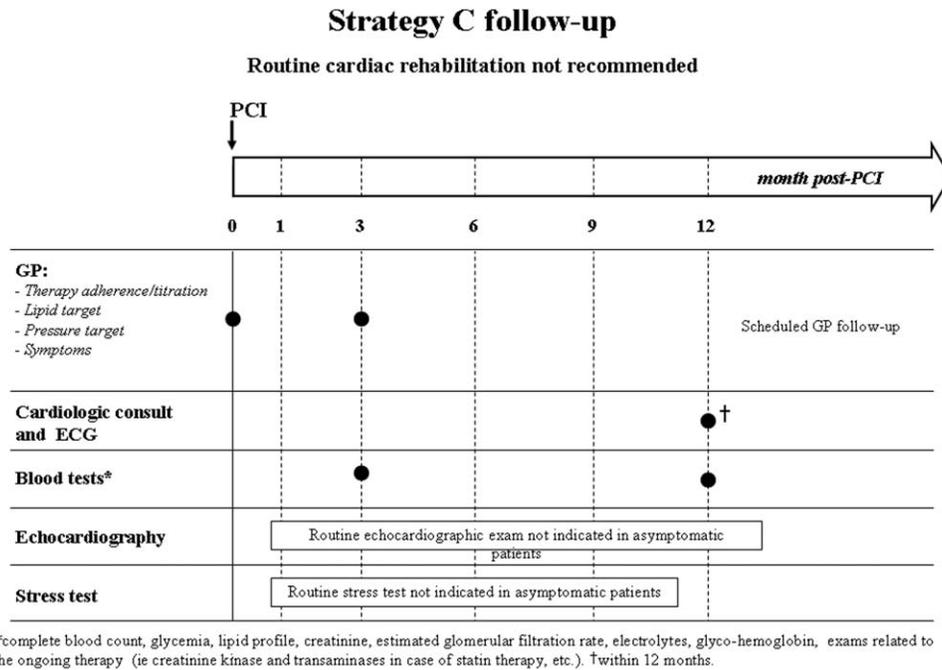


**Fig. 2. Strategy A follow-up.** It is recommended to patients with left ventricular dysfunction: percutaneous coronary intervention (PCI) in acute coronary syndrome (ACS) with reduction of left ventricular ejection fraction (LVEF) [LVEF ≤ 45%], or PCI in recent finding of low LVEF, or PCI in patients with symptoms/signs of heart failure).

### Strategy B follow-up



**Fig. 3. Strategy B follow-up.** It is recommended to patients with one of the following features: ACS, diabetes mellitus, multivessel or left main or proximal left anterior descending artery disease, incomplete or suboptimal revascularization (for acronyms, see Fig. 2 legend).



**Fig. 4. Strategy C follow-up. It is recommended to patients without relevant comorbidities and complete, successful PCI (for acronyms, see Fig. 2 legend).**

hospital stay and indications about follow-up strategy should be sent to the patient’s GP in the form of a discharge document. In particular, accurate reporting of all diagnoses, operations and procedures relevant to a patient’s admission is an essential part of the discharge document [13]. This information is central to the future care and management of the patient and essential for accurate coding and record keeping within hospital and GP records systems. Clear textual descriptions of these items must therefore be given. Also, the accurate recording of medicines is an essential component of the discharge document, as it has a direct impact on patient care and management and is an important factor in improving patient safety. Ultimately, a clear follow-up strategy should be provided in the discharge document for each patient.

**Cardiologic consultation and instrumental follow-up.**

Cardiologic consultation should be performed at different times according to the 3 different proposed follow-up strategies (Figs. 2–4) and is always indicated in case of worsening of the clinical status. The cardiologist ought to perform clinical evaluation once within the first 12 months in low-risk patients and periodically in intermediate and high risk patients. The cardiologist should also prescribe, when indicated, transthoracic echocardiography (TTE) and stress tests. Of note, routine echocardiography in asymptomatic patients is not recommended by international guidelines [14], whereas

it has a class I recommendation in patients with dyspnea and clinical signs of heart disease.

LVEF assessment should be performed in all patients hospitalized for an ACS [5]. LV dysfunction after acute myocardial infarction (AMI) may be caused by necrosis, myocardial stunning, hibernation, or to their combination. Assessment of LV function in patients with previous myocardial infarction when needed to guide possible implantation of implantable cardioverter-defibrillator is recommended with class IIa [14]. LVEF is the main predictor of death and congestive heart failure [15]. Short term LVEF assessment is crucial especially in patients with a severe reduction after the acute event, with respect to an accurate risk stratification also for arrhythmic events. Based on the LVEF, the proper indication to implantable cardioverter defibrillator and/or biventricular pace-maker implantation will be evaluated [5]. Assessment of late prognosis (greater than or equal to 2 years after AMI) is class IIb recommendation [14].

The indication for a stress test should be determined by a cardiologist [16]. The main rationale for stress testing in asymptomatic patients after PCI may reside in the search for silent ischemia caused by restenosis or disease progression. As a matter of fact, more than half of revascularized patients with recurrent ischemia at stress test are actually asymptomatic [17,18]. The long-term prognosis of patients with silent ischemia is remarkably worse than that of patients without

ischemia due to a significant increase in the overall incidence of major adverse cardiac events [17,18]. However, this increase in major adverse cardiac events is mainly driven by ischemic events and repeat revascularizations rather than death, while no survival benefit is observed in these patients from repeat revascularization [17,19]. Therefore, detection of silent ischemia might have significant clinical implications only in specific subsets of patients after revascularization (patients with incomplete or suboptimal PCI, especially in the setting of an AMI) whereas a routine stress testing strategy in the general population of asymptomatic patients after revascularization has no proven benefit and is not indicated [3]. Previously published guidelines and several authors warn against routine testing of asymptomatic patients [3,6]. Stress tests have been defined of indeterminate value late after PCI (>2 years), and inappropriate before this time frame. Increased use of testing after PCI is associated with a clear increase in repeat revascularization; however, the variation of testing and downstream revascularization does not result in decreased AMI or mortality [12]. The lack of association between stress testing use and clinical outcomes of death or AMI suggests that the more intensive testing use (implying a surveillance testing strategy) does not prevent or reduce post-PCI events in the short to medium term [7,20–22].

Early stress testing in order to verify that culprit lesions have been successfully treated may be recommended after incomplete or suboptimal revascularization as well as in other specific patient subsets (Fig. 3). The choice among imaging modalities is based on similar criteria to those used before intervention. In selected patients with new onset of typical angina or clear worsening of pre-existing angina, without clear contraindications to invasive procedures, it might be preferable to proceed to coronary angiography. Because of the high pre-test probability in these patients, the execution of stress test prior to coronary angiography would not be of value for diagnostic purposes, while delaying revascularization procedures.

The international guidelines on stable angina recommend to proceed to direct coronary angiography only male patients, aged >70 years, with typical angina [6]. Of note, this recommendation is based on existing databases, which addressed the probability of CAD in 2260 patients undergoing coronary angiography [23]. Only age, sex, and presence of typical angina were evaluated, whereas no information with respect to clinical risk factors such as diabetes, hypertension, dyslipidemia or known CAD were taken into account. Moreover, the definition of CAD was  $\geq 50\%$  diameter lumen reduction in 1 or more vessels, whereas the traditional understanding of CAD is that of a disease causing exercise- and stress-related chest symptoms due to narrowings of  $\geq 70\%$  in one or several of the major coronary arteries and  $\geq 50\%$  in the left main coronary artery.

**The role of the cardiac rehabilitator.** Cardiac rehabilitation (CR) and secondary prevention are an essential part of long-term management after PCI, as they can reduce future morbidity and mortality, in a cost-effective way [3–5]. Despite its well-documented benefits, CR is vastly underutilized [24]. Only about a third of CAD patients in Europe receive any form of CR [25].

CR and secondary prevention programs are implemented in or out of hospital, according to the clinical status and local facilities. National and international guidelines clearly define priority criteria for admission to CR centers as inpatients based on clinical risk [3–5,26].

After PCI, a structured in-hospital (residential or in a dedicated center) CR program ideal for high-risk patients [24,26], whereas medically supervised out-of-hospital programs might be prescribed after PCI to moderate-risk patients, as shown in Table I.

Despite a formal indication to CR, low-risk patients have a low-priority to enter in a medically supervised CR program; to these patients, lifestyle and risk factor modification should be guaranteed by GP after hospital discharge at the end of the acute phase.

The core components of CR intervention include patient assessment, secondary prevention measures,

**TABLE I. Indications to Structured In-hospital and Out-of-hospital Cardiac Rehabilitation (CR)**

In-hospital CR program: High risk patients	Out-of-hospital CR program: Moderate risk patients
Persistent clinical, hemodynamic or arrhythmic instability	Patients with high coronary anatomy complexity
Heart failure or LV dysfunction (LVEF $\leq 45\%$ )	Incomplete revascularization
Severe complications or comorbidities that are often associated with prolonged hospitalization during the acute phase	High cardiovascular risk because of the presence of DM and/or multiple risk factors
Old, frail patients or without very sedentary habits before the acute event	Low adherence to life style and risk factor modification programs, especially in younger patients
	Psycho social risk factors

CR = cardiac rehabilitation; LV = left ventricular, LVEF = left ventricular ejection fraction.

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physical activity counseling, and exercise training [24,26].

**Physical activity and exercise training.** Physical activity is defined as any bodily movement produced by contraction of skeletal muscles resulting in energy expenditure above the basal level and, as such, part of lifestyle intervention. Exercise training is defined as a sub-category of physical activity in which planned, structured, and repetitive bodily movements are performed to maintain or improve one or more attributes of physical fitness and thus it is a structured intervention over a defined period of time. It should be integrated within the physical activity intervention [24,26].

Specifically, after uncomplicated PCI, physical activity counseling can start the following day, and such patients can walk on the flat and up the stairs within a few days. After a large and/or complicated myocardial damage, physical activity should start after clinical stabilization, and be increased slowly, according to the symptoms [3–5,24,26].

In the presence of preserved exercise capacity without symptoms, patient can resume routine physical activity for 30–60 min, such as brisk walking, supplemented by an increase in daily activities (such as walking breaks at work, gardening, or household work); otherwise, the patient should resume physical activity at 50% of maximal exercise capacity and gradually increase. Physical activity should be a combination of activities like walking, climbing stairs, cycling.

For physical activity counseling and prescription, the execution of an exercise testing is not necessary. By contrast, an exercise testing is necessary for exercise training prescription.

Symptom-limited exercise testing can be safely performed 7–14 days after primary PCI for STEMI and as soon as 24 hr after elective PCI [3,5].

Algorithm for prescription of functional evaluation at the onset of an exercise training program after PCI is proposed in Fig. 1 according to the Guidelines of the European Society of Cardiology [3].

In patients post-ACS and post primary-PCI as well as those with stable CAD and elective PCI, an exercise training program should include at least 30 min, 5 days week<sup>-1</sup> aerobic exercise. Intensity of exercise should be at 70–85% of the peak heart rate, or at 70–85% of the heart rate at the onset of ischemia. In high risk patients because of LV dysfunction, CAD severity, comorbidities, exercise intensity at 50% of the peak heart rate is advisable [24,26].

**The role of the general practitioner.** In unselected patients submitted to PCI, cardiovascular death represents the most common mode of death only during the first month after revascularization whereas after

this time interval it only accounts about a third of the overall 3% annual mortality [27]. The GP should take a clinical history focusing particularly on current symptoms and functional status. Further questions should be asked concerning emotional aspects (depression, anxiety, worries, disappointment) and the patient's psychosocial situation, conception of illness, and behavior patterns, e.g., excessive caution. Because of the short hospital stay, even after an ACS, patients may not have reached an adequate perception of illness, which can negatively affect long-term adherence to medical therapy. The GP should support patients in understanding clinical implications of CAD and the importance of drugs and secondary prevention. At each visit, a physical examination should also be carried out, including heart and lungs auscultation, assessment of peripheral pulses, presence of edema, measurement of weight, body mass index, blood pressure, and heart rate.

Routine laboratory tests (electrolytes, complete blood count, liver and renal function tests) should be periodically performed according to the predefined pathways, as illustrated in Figs. 2–4. Particular attention should be paid to hemoglobine level, especially in patients at high hemorrhagic risk, contrast-induced nephropathy, and statin intolerance, if statin treatment has just been initiated (muscle symptoms, liver values).

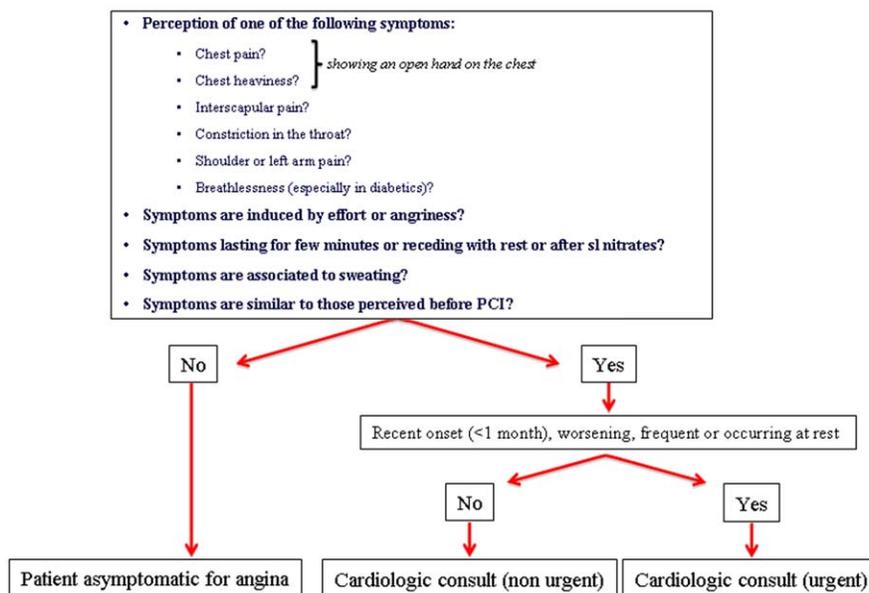
**Targets of secondary prevention.** In regular follow-up consultations, the GP (or the cardiac rehabilitator, when CR is performed) ought to:

1. monitor new onset or worsening of angina,
2. provide drug titration (especially of beta-blockers and ace inhibitors (ACE-I), angiotensin receptor blockers (ARB))
3. assess the patient's adherence to prescribed therapy,
4. promote the correction of risk factors

**Monitor new onset or worsening of angina.** The presence of angina is relevant and should be periodically, carefully assessed in each patient after PCI. In the CLARIFY study [28], the presence of angina ( $\pm$  documented ischemia) and non-silent ischemia were associated with poor prognosis. Noteworthy, angina should not be considered "tout court" as a synonymous of restenosis [29]. Especially if it occurs late after PCI, the potential for progression of coronary atherosclerosis in segments different from those treated with PCI should be taken into account, especially in high risk patients such as diabetics [30]. In the BARI trial, the use of DESs significantly lowered rates of restenosis in diabetics with multi-vessel CAD, but progression of coronary disease accounted for up to 57% of cases of repeat revascularization [31]. A sound diagnostic approach to chest pain recurring after successful PCI

## Angina Evaluation Questionnaire

(in patients who were asymptomatic after PCI)\*



\*: in chronically symptomatic patients the questionnaire is aimed at detecting changes in symptoms frequency or severity.

**Fig. 5. Angina evaluation questionnaire. The present questionnaire is aimed at allowing a better assessment of typical angina. Symptoms are characterized on the basis of clinical presentation, threshold, and correspondence to symptoms occurred prior to PCI.**

should start from an accurate evaluation of symptoms characteristics and temporal pattern of recurrence [29]. To allow a better assessment of the presence of typical angina, GP might use an *ad hoc*, standard questionnaire (Fig. 5). In the present questionnaire, symptoms are characterized on the basis of clinical presentation and correspondence to symptoms occurred prior to PCI. Cardiologic evaluation is strongly recommended in case of typical angina, (urgent consultation is advisable in case of unstable setting) and coronary angiography and/or stress test is advisable, according to the ESC guidelines [6]. Cardiologic evaluation and stress test might be recommended in cases of atypical symptoms in which a clear diagnosis is not provided.

**Drug titration.** Adequate titration of beta-blockers and ACE-I or ARB should be provided in all patients discharged on beta-blockers and ACE-I/ARB [32,33]. The initial dose should be small and increased slowly (double dose at not <2 weekly intervals) and progressively to the target dose used in the large clinical trials or, if not tolerated, the highest tolerated dose. Up-titration should be adapted to the individual response. Beta-blockers may reduce blood pressure and heart rate excessively, may temporarily induce myocardial depression and precipitate heart failure [32]. In addition, b-blockers may initiate or exacerbate asthma and induce peripheral vaso-

constriction. GP should monitor for evidence of heart failure symptoms, fluid retention, hypotension and bradycardia. Clinical status and blood pressure should be monitored at frequent intervals during the titration phase of ACE-I/ARB. Renal function and serum K ought to be regularly assessed, as well [33].

**Adherence.** Adherence has been defined as the “active, voluntary, and collaborative involvement of the patient in a mutually acceptable course of behavior to produce a therapeutic result” [34]. Medication adherence has been called the “next frontier in quality improvement” and is an important part of cardiovascular outcomes research. Adherence to medical therapy in chronic diseases such as heart failure, essential hypertension, hypercholesterolemia, diabetes mellitus has been demonstrated to be cost-effective both from clinical and economical point of view [35]. Over the last decade a growing attention to the issue of adherence to oral antiplatelet therapy has emerged, as demonstrated by the reduction in premature discontinuation of antiplatelet therapy in clinical trials. Of note, however, even in the most recent studies, one patient out of five still prematurely discontinues the antiplatelet therapy [36]. The most common causes of discontinuation are bleeding events, surgery, or dental procedures. Patients who discontinue antiplatelet therapy within the

first 12 months have a significantly greater incidence of overall major adverse cardiac effects, stent thrombosis, and death.

**Risk factors.** Supporting patients in achieving and maintaining lifestyle changes on an individualized basis, using defined therapeutic goals and strategies, continues to be a substantial challenge. Effective strategies for supporting patients in achieving positive lifestyle changes and improving self-management can be recommended [3]. The patient's tobacco use, physical activity, nutrition, and regular taking of medications should be assessed, and, if necessary, the patient should be encouraged to change his or her behavior in health-promoting ways. Cardiovascular drugs are not the unique long-term treatment useful for secondary prevention in chronic cardiovascular diseases: correct lifestyle has a cornerstone additive importance. Physical activity, correct (Mediterranean) diet and smoke withdrawal add a significant and independent prognostic benefit to conventional medical therapy, that emerges soon (30 days mortality) after AMI [37]. The benefit of a correct lifestyle can be an early "take-away" result and does not necessarily need a long time to be registered.

The GP should always refer the patient to the cardiologist whenever new symptoms and signs arise that might be due to CAD. Referral to the cardiologist may also be indicated if the GP cannot provide drug titration or achieve adequate correction of risk factors, including adherence to prescribed therapy, e.g. because of adverse effects, interactions, or non-compliance.

## CONCLUSIONS

Follow-up strategies of patients submitted to PCI are often heterogeneous, with wide variations among centers, which can significantly affect the cost of medical care. The present consensus document provides practical advises with respect to a "cost-effective" follow-up strategy, which is tailored on the basis of clinical and angiographic risk profile of each patient. These recommendations are shared among cardiologists, cardiologist rehabilitators, and GP, who should actively contribute to long-term management of patients after PCI. The implementation of the present recommendations in clinical practice should be monitored by national scientific societies.

## Limitations

The present consensus document derives mostly from experts' opinion rather than results of randomized trials, which represents the main limitation. Moreover, the strategy follow-up might change with time accord-

ing to clinical conditions. The effectiveness of the protocol depends on the efficiency of the network between cardiologists and GP. Of note, the national character of this document makes it not generalizable in other countries. Finally, studies which address the feasibility and cost-effectiveness of this protocol are warranted.

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