

2014 ESC/EACTS guidelines on myocardial revascularisation

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Summary

The joint European Society of Cardiology and European Association of Cardio-Thoracic Surgery (ESC/EACTS) guidelines on myocardial revascularisation provide a contemporary overview of decision-making, management and treatment across the spectrum of coronary artery disease (CAD), including stable CAD as well as acute coronary syndromes. The 2014 document, issued 50 years after the first coronary artery bypass graft procedure (CABG), is based on a systematic review of randomised clinical trials comparing different strategies of myocardial revascularisation including CABG, balloon angioplasty and percutaneous coronary interventions with bare-metal stents, early- and new-generation drug-eluting stents with medical treatment. The present review focuses on some relevant aspects of these guidelines as well as on notable changes compared with previous recommendations.

Key words: guidelines; myocardial revascularisation; stent; coronary artery disease; surgery; medical therapy

Introduction

The joint European Society of Cardiology and European Association of Cardio-Thoracic Surgery (ESC/EACTS) 2014 guidelines on myocardial revascularisation provide a contemporary overview of decision-making, management and treatment across the spectrum of coronary artery disease (CAD), including stable CAD as well as acute coronary syndromes [1]. The 2014 document, issued 50 years after the first coronary artery bypass graft procedure (CABG) and 37 years after the first percutaneous coronary intervention (PCI), is based on a systematic review of randomised clinical trials comparing different strategies of myocardial revascularisation, including CABG, balloon angioplasty, PCI with bare-metal stents (BMS), and early- and new-generation drug-eluting stents (DES) with medical treatment. A total of 314 recommendations are included: 47% class I, 31% class IIa, 11% class IIb, and 11% class III recommendations. Regarding the level of evidence, 29% of recommendations are based on level A, 33% on level B, and 38% on level C evidence. The present

review focuses on some relevant aspects of these guidelines as well as on notable changes compared with previous recommendations [2].

The role of the heart team in decision-making: elective procedures for patients with multivessel coronary artery disease

The concept of the heart team, introduced in the 2010 ESC myocardial revascularisation guidelines [2], is reinforced in the 2014 document. The heart team, typically consisting of clinical or noninvasive cardiologists, cardiac surgeons and interventional cardiologists, has the objective to enhance a balanced, multidisciplinary decision-making process. The role of the heart team in the management of patients with multivessel CAD is dual: (i) development of shared, evidence-based institutional protocols for common case scenarios to avoid the need for systematic case-by-case review of all diagnostic angiograms; and (ii) interdisciplinary discussion and selection of the optimal revascularisation strategy on an individual patient basis whenever decision-making is complex and not covered by the institutional protocol. Multidisciplinary decision-making within a heart team can minimise specialty bias and prevent self-referral from interfering with optimal patient care. Of note, there is no uniform code for setting up a heart team in view of the diverse nature of institutions, healthcare systems, referral patterns and local expertise. Rather, hospitals and healthcare networks are called upon to develop institutional protocols to customise the heart team to best reflect the local environment.

The role of risk scores in decision-making

Current guidelines place emphasis on selected risk scores as valuable tools for individual patient risk stratification and guides to decision-making regarding the preferred revascularisation modality (PCI vs CABG) [1]. The Society of Thoracic Surgeons (STS) score is recognised as the recommended tool to stratify surgical risk among patients considered for CABG (I/B rec-

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ommendation). The use of the classic EuroScore is discouraged as it overestimates the surgical risk, whereas the more recently introduced EuroScore II (an update of the logistic EuroScore in a more contemporary cohort) overcomes this limitation and can also be considered for stratification of surgical risk (IIa/B recommendation).

The SYNTAX score, a comprehensive angiographic scoring system for quantifying CAD complexity, can effectively risk-stratify stable patients with three-vessel and left main coronary artery disease considered for PCI, and is recommended for guiding the choice between revascularisation with PCI or CABG (I/B). A detailed guide to calculating the SYNTAX score is provided in the guideline document to facilitate its use as an effective, comprehensive tool in routine clinical practice. The recently introduced SYNTAX II score combines anatomical and clinical factors and may further refine the treatment selection between PCI and CABG (currently IIa/B recommendation).

Revascularisation in stable coronary artery disease

Depending on its symptomatic, functional and anatomic complexity, stable CAD can be treated with medical therapy alone or combined with revascularisation using PCI or CABG. Two critical issues addressed in the guidelines are (i) the indications for revascularisation, and (ii) the relative merits of CABG and PCI in different patterns of stable CAD.

Indications for revascularisation

The guidelines summarise evidence regarding the benefits of medical therapy and revascularisation in patients with chronic stable CAD and highlight the rationale for myocardial revascularisation in this setting [1]. They emphasise that patients with stable CAD should receive guideline-recommended medical treat-

ment owing to its well-established benefits in terms of long-term prognosis and symptom relief. It is important to consider revascularisation and medical therapy as complementary, rather than competing, treatment strategies. Indications for revascularisation with either PCI or CABG include improvement of prognosis in certain anatomical patterns of CAD or in the presence of a significant ischaemic territory, and persistence of symptoms despite medical therapy (table 1).

The aforementioned indications are supported by robust evidence. In a network meta-analysis comparing revascularisation with medical therapy in stable CAD and including 93553 randomised patients, CABG was associated with a significantly reduced risk of mortality, myocardial infarction and need for repeat revascularisation compared with medical therapy alone. Similarly, PCI with new-generation DES, but not balloon angioplasty, BMS or early-generation DES, was more beneficial than medical therapy in terms of mortality and repeat revascularisation [3]. Similarly, the FAME-2 study demonstrated lower rates of the primary endpoint (all-cause mortality, myocardial infarction and urgent revascularisation) in stable CAD patients with haemodynamically relevant lesions [as exemplified by fractional flow reserve (FFR) values <0.80] treated with percutaneous placement of a DES compared with medical therapy alone [4]. Of note, FAME-2 was an open-label trial that was stopped prematurely by the data and safety monitoring board because of a highly significant difference in the incidence of the primary endpoint in favour of FFR-guided PCI.

Ischaemia is also of prognostic importance in patients with stable CAD [5]. Revascularisation relieves myocardial ischaemia caused by flow-limiting coronary stenoses more effectively than medical treatment [6]; the greater the ischaemic burden, the larger the benefits of revascularisation [7]. Hence, the absence of a difference in mortality between patients treated with PCI with BMS and patients receiving medical therapy alone

Table 1: Indications for revascularisation in patients with stable angina or silent ischaemia. Reproduced from: Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J.* 2014;35(37):2541–619, with permission.

	Extent of CAD (anatomical and/or functional)	Class	Level
For prognosis	Left main disease with stenosis >50% *	I	A
	Any proximal LAD stenosis >50% *	I	A
	Two-vessel or three-vessel disease with stenosis >50% * with impaired LV function (LVEF <40%)	I	A
	Large area of ischemia (>10% LV)	I	B
	Single remaining patent coronary artery with stenosis >50% *	I	C
For symptoms	Any coronary stenosis >50% * in the presence of limiting angina or angina equivalent, unresponsive to medical therapy	I	A

* with documented ischaemia or fractional flow reserve ≤ 0.80 for diameter stenosis <90%.

CAD = coronary artery disease; LAD = left anterior descending; LVEF = left ventricular ejection fraction.

in the COURAGE trial needs to be interpreted in view of the moderate severity of CAD and absent or only mild ischaemia in the majority of patients (70%) [8].

Regarding CAD symptoms, angina is associated with impaired quality of life, reduced physical endurance, depression, recurrent hospitalisations and outpatient visits. Revascularisation by PCI or CABG more effectively relieves angina, reduces the use of antianginal drugs, and improves exercise capacity and quality of life, compared with medical therapy alone [9]. It should be noted that, currently, optimal revascularisation results are achieved with PCI and use of new-generation DES, and with CABG employing maximal use of arterial grafts.

Optimal revascularisation modality in patients with stable coronary artery disease

In patients with stable CAD, the potential advantages of PCI (less invasive intervention, shorter hospitalisation, lower risk of cerebrovascular events) need to be carefully weighed against those of CABG (more complete revascularisation, fewer repeat revascularisations, protection against future events). The decision in the elective setting is determined largely by the localisation and complexity of disease, as well as the underlying surgical risk as detailed below. It is also important to note that adherence to guideline-recommended medical therapy improves clinical outcomes following PCI or CABG, and that all the components of evidence-based medical therapy (antiplatelet therapy, statins, β -blockers, angiotensin converting-enzyme inhibitors / angiotensin receptor blockers) are important for reducing adverse outcomes irrespective of revascularisation strategy [10]. The role of nonpharmacological measures, including lifestyle modifications and cardiac rehabilitation when indicated, is also emphasised for secondary prevention and improved quality of life.

Revascularisation of the left main coronary artery

Growing evidence indicates that both CABG and PCI provide effective treatment for selected patients with left main CAD, namely those with low to intermediate anatomical disease complexity. A prespecified analysis of the SYNTAX trial focused on patients with left main disease ($n = 705$) [11]. In patients with low and intermediate SYNTAX scores (SYNTAX score ≤ 22 and 23–32, respectively), 5-year rates of the primary endpoint, a composite of death, myocardial infarction, stroke and repeat revascularisation, were similar for PCI and CABG ($p = 0.74$ and $p = 0.88$, respectively, for low and intermediate SYNTAX scores). In contrast, mortality and repeat revascularisations were higher in the PCI group in patients with high SYNTAX scores (≥ 33) [11]. Based on these and other consistent data, current guidelines upgraded the indication for PCI to left main CAD with low anatomical complexity (SYNTAX score ≤ 22), whereby PCI and CABG can be considered on equal terms as mode of revascularisation in this setting (I/B recommendation for both modalities). PCI can also be considered in patients with intermediate SYNTAX scores of 23–32 (IIa/B), although CABG remains the preferred revascularisation modality (I/B). Conversely, PCI should not be applied among elective patients with left main CAD, high anatomic complexity (SYNTAX score > 32) and acceptable surgical risk (table 2). It is notable that currently available evidence is based exclusively on studies with early-generation DES. Ongoing randomised trials comparing PCI with new-generation DES vs CABG for treatment of unprotected left main CAD [the EXCEL trial (NCT01205776) and the NOBLE trial (NCT01496651)] are expected to provide important insights in this respect.

Table 2: Recommendation for the type of revascularisation (CABG or PCI) in patients with stable CAD and left main disease with suitable coronary anatomy for both procedures and low predicted surgical mortality. Reproduced from: Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J. 2014;35(37):2541–619, with permission.

	ESC 2014 Guidelines [1]				ESC 2010 Guidelines [2]			
	CABG		PCI		CABG		PCI	
	Class	Level	Class	Level	Class	Level	Class	Level
Left main disease with SYNTAX score ≤ 22	I	B	I	B	I	A	II a/b *	B
Left main disease with SYNTAX score 23–32	I	B	IIa	B	I	A	IIb **	B
Left main disease with SYNTAX score > 32	I	B	III	B	I	A	III	B

CABG = coronary artery bypass grafting; CAD = coronary artery disease; ESC = European Society of Cardiology; PCI = percutaneous coronary intervention.

* IIa indication for ostial or shaft left main lesions; IIb indication for distal bifurcation left main lesions.

** Indication for left main disease in the context of two- or three-vessel disease and SYNTAX score ≤ 32 .

Table 3: Recommendation for the type of revascularisation (CABG or PCI) in patients with stable, three-vessel CAD with suitable coronary anatomy for both procedures and low predicted surgical mortality. Reproduced from: Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J.* 2014;35(37):2541–619, with permission.

	ESC 2014 Guidelines [1]				ESC 2010 Guidelines [2]			
	CABG		PCI		CABG		PCI	
	Class	Level	Class	Level	Class	Level	Class	Level
Three-vessel disease with a SYNTAX score ≤ 22	I	A	I	B	I	A	IIa	B
Three-vessel disease with SYNTAX score 23–32	I	A	III	B	I	A	III	A
Three-vessel disease with SYNTAX score > 32	I	A	III	B	I	A	III	A

CABG = coronary artery bypass grafting; CAD = coronary artery disease; ESC = European Society of Cardiology; PCI = percutaneous coronary intervention.

Revascularisation for three-vessel, stable coronary artery disease

In the current guidelines, PCI is recommended for treatment of three-vessel disease and low anatomic complexity (SYNTAX score ≤ 22) with the same class I indication as CABG. In contrast, PCI is not recommended in more complex anatomies (SYNTAX score > 22) in view of increased rates of repeat revascularisation, as well as of ischaemic endpoints (table 3). These recommendations regarding PCI for low-complexity disease are in contrast to the 2010 guidelines [2], where the corresponding recommendation for PCI was class IIa. This change was based, among other reasons, on the 5-year follow-up results of the SYNTAX trial, where PCI demonstrated similar outcomes as CABG in patients with SYNTAX score ≤ 22 [12].

Revascularisation of the proximal left anterior descending artery

In patients with involvement of the proximal left anterior descending (LAD) artery, available evidence indicates comparably good results with PCI and CABG regarding long-term mortality and myocardial infarction. These results were consistent in patients treated for isolated proximal LAD disease or two-vessel disease including proximal LAD [13]. Two meta-analyses, one including 1210 patients with isolated proximal LAD lesions [14] and the other including 1952 patients with isolated proximal LAD lesions [15], reported no significant difference in mortality, myocardial infarction or stroke, but a higher risk of recurrent angina and repeat revascularisation with PCI compared with CABG. In the current guidelines, the indication for PCI of the proximal LAD was upgraded compared with the previous 2010 ESC Guidelines from IIa to I and now assumes the same level of recommendation as CABG for treatment of the proximal LAD disease (either alone, or in the context of two-vessel disease).

Revascularisation for acute coronary syndromes

The most notable and novel aspects regarding revascularisation for acute coronary syndromes (ACS) are summarised as follows.

In the setting of primary PCI for ST-elevation myocardial infarction (STEMI), new-generation DES are strongly recommended over BMS (I/A); radial access should be preferred over femoral access with a IIa/B indication if performed by experienced radial operators [16]. Thrombus aspiration is not recommended routinely in primary PCI; instead, it may be considered in selected patients to improve Thrombolysis in Myocardial Infarction (TIMI) 3 flow or prevent stent thrombosis (IIb/A). This indication is based largely on the TASTE randomised trial [17] and is corroborated further by the results of the TOTAL trial that was published after the present guidelines were released [18]. It is recommended that primary PCI should be limited to the culprit vessel, with the exception of cardiogenic shock and persistent ischaemia after PCI of the culprit lesion (IIa/B). Revascularisation of significant nonculprit lesions during the primary PCI procedure may, however, be considered in selected patients (IIb/B), based on the findings of the PRAMI and similar trials [19]. In the recently published CvLPRIT randomised trial, complete revascularisation during index admission lowered the rate of the composite primary endpoint at 12 months compared with treating only the infarct-related artery in 296 patients [20]; larger studies are needed to establish optimal timing of staged procedures in this setting. Finally, based on the findings of the IABP-SHOCK II trial [21], routine use of the intra-aortic balloon pump (IABP) is discouraged in patients with STEMI and cardiogenic shock, assuming III/A indication in the current document [1]. Selected IABP use can still be considered in the event of mechanical complications (IIa/C).

Revascularisation in patients with diabetes

In diabetic patients presenting with ACS, the benefits of revascularisation are particularly pronounced. In patients presenting with STEMI, primary PCI (if feasible within recommended time limits) is strongly recommended over fibrinolysis (I/A). In the setting of non-ST-elevation ACS (NSTEMI-ACS), an early invasive strategy is recommended over noninvasive management (I/A).

For diabetic patients with chronic, stable CAD and multivessel disease, revascularisation in the presence of documented ischaemia assumes a class I/B indication. In diabetics with multivessel disease, CABG is recommended over PCI for revascularisation (I/A), provided that the surgical risk is acceptable. This recommendation is largely based on the results of the FREEDOM trial [22], the diabetic substudy of the SYNTAX trial [23], and a meta-analysis of available trials [24]. The FREEDOM randomised trial compared CABG with PCI involving the use of early-generation DES (94%) in 1900 diabetic patients undergoing elective revascularisation for multivessel disease without LM coronary stenosis. The trial reported higher rates of the primary endpoint (a composite of death, myocardial infarction, and stroke), death, and myocardial infarction in patients treated with PCI, whereas stroke was more frequent in the CABG group [22]. Consistent results were reported in the diabetic substudy of the SYNTAX trial [22] as well as in meta-analytic evaluation of these two trials [24]. In patients with less complex disease, as quantified by SYNTAX scores ≤ 22 , PCI assumes a class IIa/B indication as an alternative to surgery, based on the reported nondiffering rates in mortality in diabetic patients with low (≤ 22) SYNTAX scores revascularised by means of PCI or CABG [23, 24]. If PCI is performed, new-generation DES are strongly recommended (I/A).

Recommendations regarding stent type

New-generation DES are characterised by thin-strut, metallic platforms that release limus-based antiproliferative drugs from durable polymers with improved biocompatibility and lower polymer mass, biodegradable polymers, or polymer-free surfaces. Compelling evidence has established that the transition from BMS to early- to new-generation DES has been associated with markedly improved efficacy as well as safety of PCI. In a network meta-analysis comparing revascularisation with medical therapy in stable CAD, including 100 randomised trials and 262 090 patient-years of follow-up, new-generation DES, but not balloon angioplasty, BMS or first-generation DES, resulted in significant mortality reduction compared with medical ther-

apy alone [3]. This analysis is consistent with recent studies demonstrating substantial reductions of cardiac mortality, myocardial infarction and stent thrombosis with new-generation DES compared with earlier device types across patient and lesion subsets [25, 26] including women [27], patients with diabetes [28], treatment of native lesions as well as saphenous vein bypass grafts [29], left main and multivessel disease, as well as in-stent restenosis [30]. New-generation DES have addressed previous concerns about very late stent thrombosis and are at least as safe as BMS during long-term follow-up.

On the basis of this evidence, the 2014 guidelines recommend the unrestricted use of new-generation DES across the spectrum of clinical CAD manifestations and lesion subsets [1]. Previous concerns from early-generation DES associated with discontinuation of early dual antiplatelet therapy (DAPT) were not confirmed in investigations with new-generation DES, and there is no clear evidence of a difference between DES and BMS in the risk of stent thrombosis following unplanned disruption of DAPT [31]; therefore, new-generation DES can also be used in patients who may require earlier discontinuation of antiplatelet therapy. For treatment of in-stent restenosis, in particular, both DES and drug-eluting balloons assume a class I/A recommendation.

Recently, bioresorbable polymer-based or resorbable metallic (magnesium) scaffolds have shown promising results in restoring the vasomotion of treated segments and enhancing positive vessel remodelling with late lumen enlargement [32], but these devices remain subject to ongoing clinical research. Randomised trials published after the 2014 guidelines demonstrated the noninferiority of drug-eluting, bioresorbable stents compared with new-generation metallic DES within 1 year [33], but larger studies with longer-term follow-up and inclusion of more complex lesion subsets are warranted to guide the indications for these devices.

Recommendations regarding antiplatelet treatment

In current guidelines, routine pretreatment with clopidogrel of elective patients scheduled for a diagnostic coronary angiogram is no longer recommended, based on the findings of a meta-analysis including >37 000 patients [34]. However, treatment with 600 mg clopidogrel is recommended in patients scheduled for elective PCI in whom anatomy is known, preferably 2 hours or more before the procedure (I/A). Prasugrel or ticagrelor are recommended as first-line treatment in patients with ACS, either NSTEMI-ACS or STEMI (I/B indi-

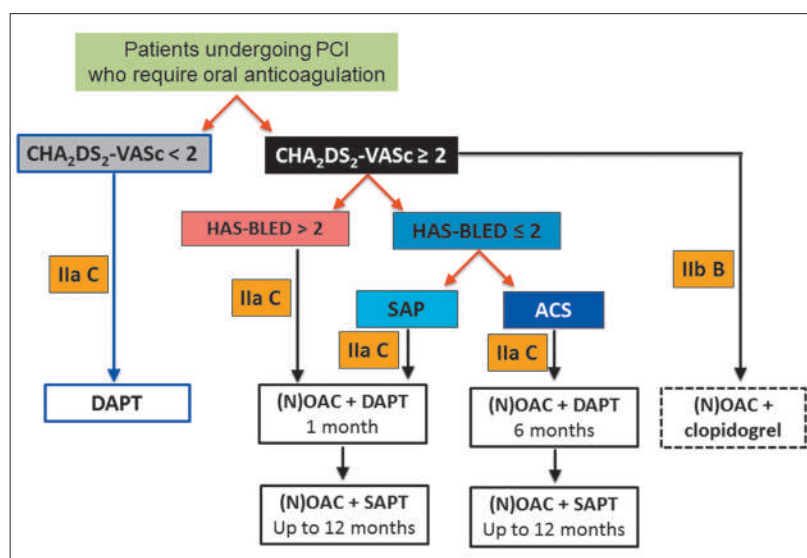


Figure 1: Recommendations for antithrombotic treatment in patients undergoing PCI who require oral anticoagulation. ACS = acute coronary syndrome; DAPT = dual antiplatelet therapy; (N)OAC = (novel) oral anticoagulation; SAP = stable angina pectoris.

cation for both agents), whereas clopidogrel should be used only when prasugrel and ticagrelor are not available or are contraindicated (I/B). New in the current guidelines is the contraindication for prasugrel before coronary angiography in patients with NSTEMI-ACS, based on the increased risk of major bleeding without ischaemic benefit in the ACCOAST trial [35]. The recommended duration of DAPT following PCI for ACS is 12 months irrespective of stent type used (BMS or DES), although new-generation DES are to be preferred (I/A).

Recommendations regarding anticoagulant therapy

Changes in recommendations concerning peri- and postprocedural anticoagulation in the current guidelines compared with previous guidelines are summarised as follows. First, bivalirudin now assumes a class IIa indication as anticoagulant in the setting of primary PCI for STEMI as compared with a class I indication for unfractionated heparin. Second, in patients with compelling indication for oral anticoagulation (OAC), the guidelines now provide recommendations regarding specific durations of triple antithrombotic therapy (OAC plus DAPT) on the basis of each patient's ischaemic and bleeding risk and their clinical indication for PCI (i.e., stable CAD or ACS) (fig. 1).

Conclusions and future perspectives

The 2014 ESC/EACTS Guidelines provide recommendations concerning diagnosis, decision-making, procedural and adjunctive medical management of patients

with CAD who are eligible for myocardial revascularisation. These guidelines are informed by review of randomised trials, which provide the highest level of evidence to support recommendations and inform practice. Key aspects include emphasis on individual risk stratification and on evidence-based recommendations regarding the preferred type of revascularisation (PCI vs CABG) for each patient. Briefly, in elective interventions for patients with stable CAD, PCI is an alternative to CABG for single- or two-vessel CAD with proximal LAD lesions; left main CAD with SYNTAX score ≤ 32 , and three-vessel CAD with SYNTAX score ≤ 22 . CABG is preferred over PCI in diabetic patients with multivessel disease. New-generation DES are now indicated in all patient and lesion subsets. Finally, volume–outcome relationships and minimal operator and institutional proficiency as well as training requirements are advocated.

Evidence published after the release of these guidelines needs to be considered, including new evidence regarding DAPT type and duration [36, 37] or regarding the beneficial impact of transradial access in patients undergoing PCI for ACS [38]. Aspects where additional evidence from future studies is required include (but are not limited to) randomised trials comparing new-generation DES with CABG in patients with multivessel disease; optimal timing of treatment of non-culprit lesions in STEMI patients; longer-term, broadly inclusive studies to establish indications for bioresorbable stents; studies addressing the value of routine intracoronary imaging-based evaluation and imaging-guided PCI for optimisation of acute results and improvement of longer-term clinical outcomes [39]; and consideration of geriatric aspects (e.g., frailty) that are currently missing in risk stratification tools. As new studies covering broad aspects of CAD management become available, official guideline documents will continue to provide contemporary, evidence-based recommendations to inform our practice, aiming at reducing the burden of CAD-related morbidity and mortality in the community and offering optimal treatment for each individual patient. In this context, the 2015 edition of the ESC Guidelines on non-ST-segment elevation acute coronary syndromes is also notable providing a further update in this patient population [40].

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References

The full list of references is included in the online article at www.cardiovascmed.ch

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