

Special article

Update in Cardiology: Vascular Risk and Cardiac Rehabilitation



Enrique Galve,^{a,*} Alberto Cordero,^b Vicente Bertomeu-Martínez,^b Lorenzo Fácila,^c Pilar Mazón,^d Eduardo Alegría,^e Jaime Fernández de Bobadilla,^f Esteban García-Porrero,^g Manuel Martínez-Sellés,^h and José Ramón González-Juanatey^d

^a Servicio de Cardiología, Hospital Universitari Vall d'Hebron, Barcelona, Spain

^b Departamento de Cardiología, Hospital Universitario de San Juan, San Juan de Alicante, Alicante, Spain

^c Servicio de Cardiología, Consorcio Hospital General de Valencia, Valencia, Spain

^d Servicio de Cardiología, Hospital Universitario Santiago de Compostela, Santiago de Compostela, A Coruña, Spain

^e Servicio de Cardiología, Policlínica Gipuzkoa, San Sebastián, Guipúzcoa, Spain

^f Servicio de Cardiología, Hospital La Paz, Madrid, Spain

^g Servicio de Cardiología, Complejo Hospitalario Universitario de León, León, Spain

^h Servicio de Cardiología, Hospital General Universitario Gregorio Marañón, Madrid, Spain

Article history:

Available online 9 January 2015

Keywords:

Update
Risk factors
Physical exercise
Smoking
Hypertension
Diabetes

ABSTRACT

As in other fields, understanding of vascular risk and rehabilitation is constantly improving. The present review of recent epidemiological update shows how far we are from achieving good risk factor control: in diet and nutrition, where unhealthy and excessive societal consumption is clearly increasing the prevalence of obesity; in exercise, where it is difficult to find a balance between benefit and risk, despite systemization efforts; in smoking, where developments center on programs and policies, with the electronic cigarette seeming more like a problem than a solution; in lipids, where the transatlantic debate between guidelines is becoming a paradigm of the divergence of views in this extensively studied area; in hypertension, where a nonpharmacological alternative (renal denervation) has been undermined by the SYMPLICITY HTN-3 setback, forcing a deep reassessment; in diabetes mellitus, where the new dipeptidyl peptidase-4 and sodium-glucose cotransporter type 2 inhibitors and glucagon like peptide 1 analogues have contributed much new information and a glimpse of the future of diabetes treatment, and in cardiac rehabilitation, which continues to benefit from new information and communication technologies and where clinical benefit is not hindered by advanced diseases, such as heart failure. Our summary concludes with the update in elderly patients, whose treatment criteria are extrapolated from those of younger patients, with the present review clearly indicating that should not be the case.

© 2014 Sociedad Española de Cardiología. Published by Elsevier España, S.L.U. All rights reserved.

Novedades en cardiología: riesgo vascular y rehabilitación cardiaca

RESUMEN

El conocimiento en las áreas de riesgo vascular y rehabilitación, como en otras, se enriquece constantemente. Esta revisión aborda las novedades en los campos de la epidemiología, terreno que muestra lo lejos que se está de alcanzar un buen control de los factores de riesgo: en alimentación y nutrición, donde se hace patente la creciente obesidad de una sociedad que consume mal y en exceso; en ejercicio, donde tan difícil es lograr el equilibrio entre beneficio y riesgo, aunque se están haciendo esfuerzos de sistematización; en tabaquismo, donde lo nuevo se centra en programas y políticas, área en que el cigarrillo electrónico aparece más como problema que como solución; en lípidos, donde el debate transatlántico entre guías se erige como paradigma de divergencia de criterio en un aspecto profundamente estudiado; en hipertensión, donde la alternativa no farmacológica (la denervación renal) ha visto surgir el contratiempo del SYMPLICITY HTN-3, lo que obliga a un replanteamiento en profundidad; en diabetes mellitus, donde los nuevos fármacos inhibidores de la dipeptidil peptidasa-4 y del cotransportador sodio-glucosa tipo 2 y análogos del péptido similar al glucagón tipo 1 aportan mucha información nueva y anticipan la que está por llegar, y en rehabilitación cardiaca, que las nuevas tecnologías de información y comunicación siguen enriqueciendo y con la cual la enfermedad más avanzada, como insuficiencia cardiaca, no es óbice para obtener beneficio. Se finaliza con las novedades

Palabras clave:

Novedades
Factores de riesgo
Ejercicio físico
Tabaco
Hipertensión arterial
Diabetes

* Corresponding author: Servicio de Cardiología, Hospital Vall d'Hebron, Pg. Vall d'Hebron 119, 08035 Barcelona, Spain.
E-mail address: egalve@vhebron.net (E. Galve).

en el paciente anciano, al que se aplican los mismos criterios que se extrapolan de los más jóvenes, cuando la presente revisión establece que no debe ser así.

© 2014 Sociedad Española de Cardiología. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

Abbreviations

BP: blood pressure
CR: cardiac rehabilitation
CV: cardiovascular
HT: hypertension

INTRODUCTION

Cardiovascular (CV) prevention befits advanced societies that not only act before disease appearance, but adopt more demanding criteria when the disease is already present. In keeping with the times, the concepts of effectiveness, efficiency, pharmacoconomics, opportunity cost, and general health economics are interwoven in our daily work.¹ Interventions in primary CV prevention have a lower individual cost than those of the disease stages, but are applied to such broad swathes of the public that they end up costing much more and require a more thorough analysis, which is far from being well established. The present article covers the most important update of the past year in vascular risk and rehabilitation, with an effort made to summarize the developments most relevant to clinical practice.

EPIDEMIOLOGICAL ASPECTS

Just a century ago, CV disease caused less than 10% of all deaths. Propelled by industrialization, urbanization, and lifestyle changes, the 20th century saw an unprecedented increase in life expectancy, with a radical change in the causes and rates of mortality. Now the number one cause of death, CV disease is responsible for more than 30% of deaths worldwide, with a preferential distribution in economically developed countries.² Given the modifiable character of certain known risk factors, the efficient application of preventive strategies and therapies might alter the natural course of the epidemiological transition worldwide and thereby reduce the global impact of CV diseases. However, we are far from reaching excellence in this regard.

The data of the EUROASPIRE IV registry³ showed that only 51% of patients had stopped smoking between 6 months and 3 years after a coronary event, 43% had blood pressure (BP) readings above target values, 81% failed to achieve the lipid control targets, and 59% had not participated in any CV risk prevention program.⁴ These data agree with results of the PURE study,⁵ conducted in patients with atherosclerotic CV or cerebrovascular disease. In this study, there was a low prevalence of healthy lifestyles, with only half quitting smoking, 39% following a suitable diet, and 35% performing physical activity. The Spanish data from the EUROASPIRE IV registry were slightly better than the European average (Figure 1), with 73% of patients quitting smoking, 40% with suboptimal control of BP, and 59% failing to achieve the target levels of low-density lipoprotein cholesterol, results that concur with those published in the ENRICA and BARBANZA group studies.^{6,7} Notably, a high percentage of patients in most studies were receiving the treatments recommended by the guidelines, but most patients failed to achieve the control targets for their risk factors, indicating the need to encourage both the attending

physician and the patient to individualize the dose and type of drug, as well as to prompt lifestyle changes.

The European guidelines on CV prevention are aware of this need, as well as the importance of tailoring the preventive strategy to the baseline patient risk.⁸ Accordingly, the guidelines establish specific recommendations for controlling each risk factor, stratifying the baseline risk in accordance with the SCORE (Systematic Coronary Risk Evaluation) system. Cardiac rehabilitation (CR) is currently a class I recommendation in all clinical practice guidelines, meaning that its use is based on a demonstrated benefit in multiple studies; nonetheless, CR continues to be underused. Thus, all of the data appear to support the need to strengthen comprehensive and multidisciplinary prevention programs in which both patients and their families participate, as well as ensuring an organizational model that integrates primary and specialized care.⁹

DIET AND WEIGHT

The review of Arós and Estruch¹⁰ on the Mediterranean diet is recommended nutrition-related reading because it summarizes the global impact of the Spanish PREDIMED study.¹¹ This trial has indisputably emerged as a benchmark in CV prevention and the researchers involved continue to publish data on the preventive aspects of the diet (30 articles already on PubMed from 2014 and more than 110 overall).¹² Similarly, the SUN study,¹³ showed a reduced incidence of metabolic syndrome with a “pro-vegetarian” diet.

Another interesting publication is the epidemiological study Di@bet.es, which showed a high percentage of obesity (body mass

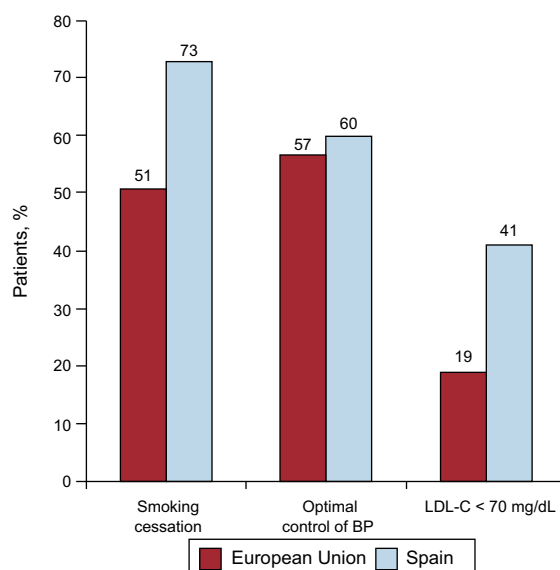


Figure 1. Distribution of patients with adequate control of cardiovascular risk factors after a coronary event, according to European Action on Secondary and Primary Prevention through Intervention to Reduce Events IV. BP, blood pressure; LDL-C, low-density lipoprotein cholesterol. Adapted with permission from Galve et al.⁹

index > 30) in people older than 18 years in Andalusia (37%), a significantly higher rate than the rest of Spain (27%).¹⁴ Another Spanish weight-related study, REDINSCOR,¹⁵ showed improved survival in heart failure patients with higher BMIs (until a certain limit). Recently, Spanish groups have also studied the prevalence of infant obesity (which, although high, seems to have stabilized in the last decade) and its hemodynamic consequences.^{16,17}

Among the relevant international studies, one with strong results analyzed 20 studies in obese patients (body mass index > 40), showing a life expectancy 10 years shorter due to death from any cause, not just CV related.¹⁸ The Swedish Obese Subjects study caused great commotion; after a long follow-up, the study showed the tremendous benefits of bariatric surgery on diabetes mellitus and macrovascular complications.¹⁹ The CARDIA study²⁰ analyzed the influence of 5 lifestyle measures (obesity, low alcohol intake, a healthy diet, physical activity, smoking) in Americans aged between 18 and 30 years at baseline, finding a clear relationship with subclinical atherosclerosis parameters 20 years later.

Regarding nutritional supplements, it seems that studies of multivitamins have been put on hold following the negative results of the Physicians' Health Study II.²¹ Studies of Ω -3 fatty acids limp onward, fanning continued controversy; due to recent failures to link them to prevention of atrial fibrillation, attention has lately turned to their preventive effects on CV mortality.²²

One important study was the Cochrane review of nutritional supplements in familial hypercholesterolemia; as expected with such a high bar (short-term mortality and ischemia heart disease), there were no important findings.²³

EXERCISE AND VASCULAR RISK

Sedentary lifestyles and excess weight are first-order health care problems that explain the high levels of hypertension (HT), diabetes mellitus, and hypercholesterolemia in both developed and developing countries. Physical exercise (PE) is implicated in the onset and development of vascular risk factors and is thus a cornerstone of their control. Accordingly, PE is recommended in all clinical practice guidelines. However, despite the unanimity concerning its importance, the adoption of heart-healthy lifestyles that include habitual PE remains a pending issue.

An important part of the work of health care professionals should be to help people to achieve long-term lifestyle changes. On one hand, this approach would require specific training for professionals to establish a monitoring strategy in the population habitually practicing PE, above all in the important subgroup of individuals that practice amateur sport but at high intensity, which carries risks of arrhythmic and ischemic complications and even sudden death. In this context, it is important to identify the at-risk individuals, to guide training to optimize cardiac adaptation, and to differentiate between normal and pathological cardiac adaptation.²⁴

On the other hand, the "prescription" of PE should be made in a structured manner. Generic and empirical recommendations are habitually made, although they generally are abandoned. First of all, the terminology should be defined. Physical activity, PE, and sport are wrongly considered synonymous:

- *Physical activity*: combination of body movements produced by the contraction of skeletal muscles that expend energy.
- *Physical exercise*: planned, structured, and repetitive physical activity that has as intermediate and final objectives an improvement or maintenance of physical fitness and an increase in the functional capacity of the body.
- *Sport*: the practice of PE according to certain playing rules and a competition-oriented system.

Although PE prescription manuals and studies use the terms physical activity and PE interchangeably, it is more correct to speak of PE because not all physical activity positively stimulates health. The objective of a PE prescription is to obtain greater health benefits with fewer risks, while considering any specific and individual needs.

These aspects have been addressed in the past year by 2 publications. The PE prescription guidelines²⁵ aim to promote the correct and individualized prescription of PE for healthy persons and patients with CV risk factors, based on the latest scientific evidence, and to provide health care support professionals with the format for its correct prescription. In addition, the ninth edition of the "Guidelines for exercise testing and prescription" of the American College of Sports Medicine was published,²⁶ which reviewed the indications for the testing of individuals performing sporting activities and the guidelines for their correct prescription.

SMOKING

One notable psychosocial work on the impact of warning labels (which some consider of neutral or transitory effectiveness) showed that such labels can support smoking cessation by prompting smokers to consider the risks of smoking; the more striking and eye-catching the labels, the more effective they are.²⁷

Many people believe that it is almost impossible to get adolescents to stop smoking. One study²⁸ identified predictors of smoking cessation in nascent adolescent smokers. During follow-up, 40% quit smoking. Male sex, age, and the practice of sport were associated with greater abstinence, whereas substance abuse, excess weight, and family stress were related to greater difficulty in smoking cessation.

The relationship between sexual orientation and smoking was studied in 28 198 participants in Sweden.²⁹ The authors hypothesized that there would be a higher prevalence of smoking in sexual minorities, partly because they have less social capital (understood as structures, networks, and social relationships) due to discriminatory societal attitudes: although it was confirmed that homosexual and bisexual people smoke more, the trend persisted after adjusting for social capital, indicating the involvement of other factors.

In a Cochrane review³⁰ of antidepressants and smoking (quitting can trigger depressive episodes), bupropion (44 trials) and nortriptyline (6 trials) significantly improved long-term abstinence; the mechanism appears to be independent of their antidepressant effect. There was no efficacy with reuptake serotonin inhibitors or monoamine oxidase inhibitors.

The growing social phenomenon of electronic cigarettes should now be considered a threat to public health in Spain because of the lack of evidence for their usefulness in smoking cessation or reducing tobacco risk and because they are tending to normalize smoking behavior, threatening the as-yet unconsolidated achievements of legislation.³¹

LIPIDS

Published at the end of 2013, the new guidelines of the American Heart Association/American College of Cardiology on dyslipidemia clearly recapitulate the new update in this field.³² The guidelines recommend intensive treatment with statins for patients with atherothrombotic CV disease or at high risk of it, which marks a clear difference from the European guidelines³³ that identify some specific cholesterol targets for each risk category. The American guidelines base their risk estimation on 4 key points: presence of CV disease, low-density lipoprotein cholesterol \geq 190 mg/dL, diabetes mellitus, and estimated 10-year

risk based on a custom scale (Figure 2). Because this scale had not been validated, it has been widely criticized.³⁴ Moreover, a combined analysis of 3 prospective studies of primary prevention showed that the risk equation proposed by the American guidelines overestimates the risk by between 75% and 150% and increases the number of patients that should begin statin therapy by between 40% and 50%.³⁴ However, the approach of the American guidelines appears correct for secondary prevention. Finally, the debate over the ideal treatment for dyslipidemia continues, as shown by an initiative to improve the treatment and evaluation of dyslipidemia.³⁵

As already mentioned, a subanalysis of the PREDIMED study has shown benefits of a diet supplemented with nuts and olive oil on total cholesterol and low-density lipoprotein cholesterol, as well as on BP and blood sugar.³⁶

HYPERTENSION

After almost 11 years, the latest report of the JNC 8³⁷ on the management of HT in adults appeared in 2014, offering 9 recommendations based on scientific evidence (Table).

The SYMPLICITY HTN-3³⁸ study heralded a radical change in HT interventionism. Previously, the clinical approach relied on unblinded studies showing that renal artery denervation reduced BP in resistant HT. However, the publication of a more rigorous study (blinded and with a sham control arm) revealed unexpected results: there were no significant differences in systolic BP and outpatient BP monitoring at 6 months in 535 patients. The earlier success could be explained by a placebo effect or other circumstances (eg, the Hawthorne effect), or treatment adherence, or perhaps because the treated HT was not actually refractory. This result sullies the once-promising future of the technique. The problem may be patient selection (to define whether a certain subgroup benefits), the technique used, or the suitability of the denervation device.

In this respect, a Spanish cross-sectional study (with its inherent limitations) has been published on primary care for resistant HT (63 167 patients), showing that 1 out of 4 patients is older than 80 years (associated with female sex, obesity, diabetes mellitus, heart disease, and kidney disease), whereas in those younger than 50 years this form of HT was associated with male sex, obesity, stroke, and kidney disease.³⁹ In addition, 2 prognostic studies have been published. The first publication showed that a morning increase in systolic BP > 23 mmHg in elderly patients with treated hypertension was an independent factor for stroke in individuals with a circadian dipper rhythm, but not in those with a non-dipper rhythm.⁴⁰ The second study analyzed 1.25 million people without CV disease (20% on antihypertensive therapy), with a 5.2-year follow-up; the group with lower risk had a systolic BP between 90 and 90-114 mmHg and a diastolic BP between 60 and 74 mmHg without a J-shaped curve.⁴¹

Finally, an intriguing and useful study in 102 patients showed that outpatient monitoring of BP for only 1 h during daytime hours is valid for HT diagnosis and subpopulation classifications (white coat, refractory).⁴²

DIABETES MELLITUS

The debate continues over the CV safety of the new antidiabetics, beyond their effectiveness in controlling hyperglycemia. Various related meta-analyses have been published in the last year. Increased heart failure has been shown in patients treated with dipeptidyl peptidase-4 inhibitors (odds ratio = 1.19; $P < .015$)⁴³; this finding is based only on studies designed with CV

endpoints and it had not been seen in a meta-analysis prior to the publication of the SAVOR and EXAMINE studies.⁴⁴

Glucagon-like peptide 1 agonists have been evaluated in 37 trials. In low-risk patients, a reduction was seen in CV events with these drugs vs placebo and vs pioglitazone, as well as a favorable trend (although nonsignificant) vs dipeptidyl peptidase-4 inhibitors,⁴⁵ but we have to wait for ongoing trials with CV endpoints to confirm the results (the first results will be available in 2015).⁹

Sodium-glucose cotransporter-2 inhibitors have shown a good safety profile and lipid-lowering efficacy (reduction of glycated hemoglobin, 0.5%-0.6%) and additional benefits such as weight loss, reduced BP, and increased high-density lipoprotein cholesterol; however, development of mild genitourinary infections was reported.⁴⁶ Nonetheless, we have to wait for the results of two trials with CV endpoints, CANVAS (CANagliflozin cardioVascular Assessment Study) with canagliflozin in 2017 and DECLARE-TIMI 58 (Dapagliflozin Evaluation of Cardiovascular Events-Thrombolysis In Myocardial Infarction 58) with dapagliflozin in 2019.

Another important issue is the treatment of hyperglycemia in acute coronary syndrome. Platelet function is altered in diabetic

Table

Summary of the Recommendations of the Eighth Joint National Committee

1	In the general population older than 60 years, pharmacological treatment is initiated with SBP > 150 mmHg or DBP > 90 mmHg; target BP, SBP < 150 mmHg and DBP < 90 mmHg (A)
2	In the general population younger than 60 years, pharmacological treatment is initiated with DBP > 90 mmHg; target BP, DBP < 90 mmHg (A).
3	In the general population younger than 60 years, pharmacological treatment is initiated with SBP > 140 mmHg; target BP, SBP < 140 mmHg (E).
4	In the population older than 18 years with chronic kidney disease, pharmacological treatment is initiated if SBP is > 140 mmHg or DBP is > 90 mmHg; target BP, SBP < 140 mmHg and DBP < 90 mmHg (E).
5	In the general population older than 18 years with diabetes mellitus, pharmacological treatment is initiated with SBP > 140 mmHg or DBP > 90 mmHg; target BP, SBP < 140 mmHg and DBP < 90 mmHg (E).
6	In the general nonblack population, including those with diabetes, the initial treatment should include thiazides, calcium antagonists, ACE inhibitors, or ARB (B).
7	In the general black population, including those with diabetes, the initial treatment should include thiazides or calcium antagonists (B).
8	In the population older than 18 years with chronic kidney disease and HT, the initial treatment (or second drug) should include ACE inhibitors or ARB to improve renal function (this is applicable to all patients with HT, regardless of race or diabetes status) (B).
9	Management strategy: if the BP targets are not met following 1 month of treatment, the drug dose should be increased or a second drug should be added (thiazides, ACE inhibitors, ARB or calcium antagonists). If the BP targets are not reached with the second drug, a third should be added, without using ACE inhibitors + ARB. If the BP targets are not reached with the 4 recommended drugs (whether due to a contraindication or because more than 3 drugs are needed), other antihypertensives can be used. Patients should be referred to a specialist if the BP targets cannot be achieved despite following all these indications and after all therapeutic steps (E).

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers; BP, blood pressure; DBP, diastolic blood pressure; HT, hypertension; SBP, systolic blood pressure.

The capital letter at the end of each recommendation denotes the strength of the recommendation, from A (maximum evidence) to E (only expert opinion).

Adapted with permission from James et al.³⁷

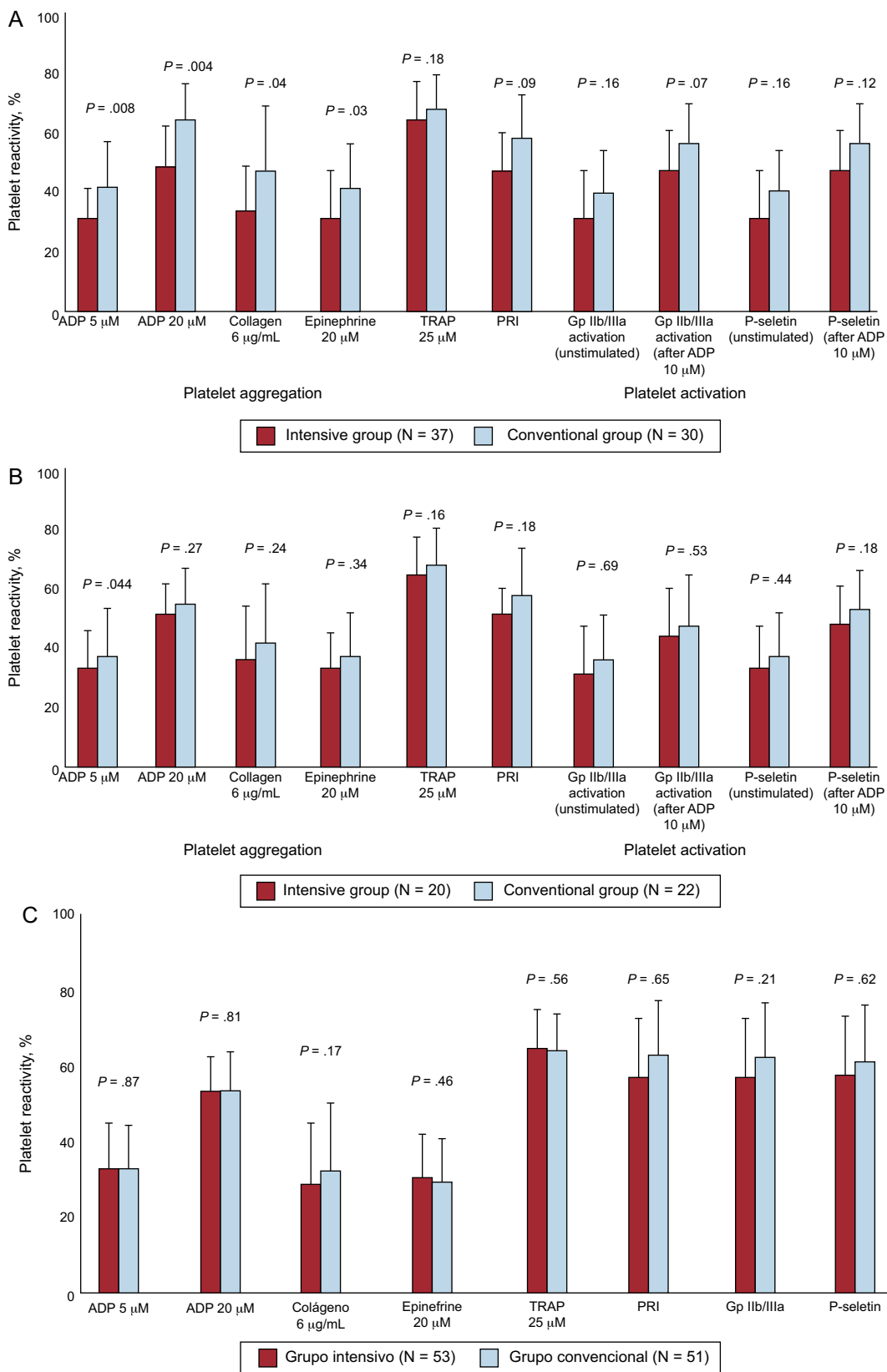


Figure 2. Results of the *Control de Hiper glucemia y Actividad Plaquetaria en Pacientes con Síndrome Coronario Agudo* study. Platelet reactivity in patients intensively treated with insulin vs conventional therapy. At the moment of hospital discharge. A: patients with worse glycemic control (glycated hemoglobin > 6.5%). B: patients with better glycemic control (glycated hemoglobin > 6.5%). C: One-year follow-up. ADP, adenosine diphosphate; GPIIb/IIIa, glycoprotein IIb/IIIa; PRI, platelet reactivity index; TRAP, thrombin receptor activating peptide. Reproduced with permission from Vivas et al.^{47,48}.

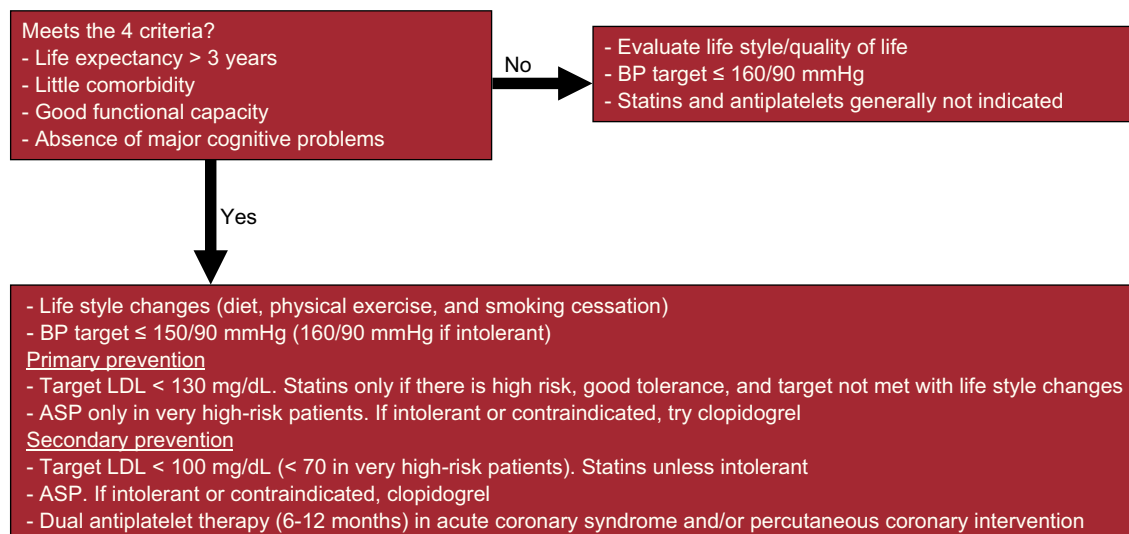


Figure 3. Summary of the recently published recommendations on the treatment of cardiovascular risk factors of octogenarians. ASA, acetylsalicylic acid; BP, blood pressure; LDL-C, low-density lipoprotein cholesterol. *Low-dose (75-100 mg). Reproduced with permission from Gómez-Huelgas et al.⁵⁶.

patients and hyperglycemia-associated platelet hyperactivation is produced by multiple independent pathways of thromboxane A₂. A beneficial relationship between intensive treatment with insulin and platelet reactivity was only found in patients with elevated glycated hemoglobin in the CHIPS study of Vivas et al⁴⁷ (Figures 2A and B). In the 1-year follow-up, and despite continued significant differences in blood glucose control (104 mg/dL in the intensive treatment group vs 119 mg/dL), there was no significant difference in platelet aggregation between the groups (Figure 2C).⁴⁸ An interesting finding of this study was that implementation of an aggressive protocol for long-term outpatient management of hyperglycemia in patients with acute coronary syndrome was feasible and potentially safe, with a low percentage of severe hypoglycemia, and may reduce renal deterioration progression compared with a conventional protocol.⁴⁹

CARDIAC REHABILITATION

As a general comment, we must highlight the abundance of publications on CR authored by nursing staff. Many studies have stressed the different characteristics of CR in different countries. The most-studied aspects are CR in heart failure and the use of smartphones.

A review of CR in cardiac surgery patients detailed all aspects of the multidisciplinary strategy used.⁵⁰ The American registry of CR after myocardial infarction showed a progressive increase in the number of patients referred to these programs between 2007 and 2012.⁵¹

The Cochrane review of CR in heart failure⁵² supports the conclusions of an earlier review showing reduced hospital admissions and noteworthy improvements in quality of life. Another Cochrane review⁵³ to promote patient approval and CR adherence found weak evidence for the effectiveness of interventions aimed at recruiting patients to CR.

The article of Ades et al⁵⁴ reviewed the current evidence on the benefits and risks of exercise and self-care advice in patients with heart failure in CR, offered recommendations for patient selection, and discussed the role of CR in the promotion of self-care and behavioral changes. In the study of Völer et al,⁵⁵ patients who underwent transcatheter aortic valve implantation benefited from CR despite their advanced age and comorbidity.

ELDERLY PATIENTS

For the first time in Spain, a consensus document has been published on the treatment of the vascular risk factors of octogenarians.⁵⁶ The document stresses lifestyle modifications, a less stringent BP target ($\leq 150/90$ mmHg or $\leq 160/90$ mmHg if there is intolerance or relevant comorbidity), and avoiding systolic BP < 120 mmHg and diastolic BP < 80 mmHg. The remaining recommendations are summarized in Figure 3. Physicians should determine if the octogenarian meets 4 criteria (life expectancy > 3 years, little comorbidity, good functional capacity, and absence of major cognitive problems). If so, the treatment can be more aggressive. A more conservative approach has to be adopted if any criterion is not met. In this document, as in other recent ones,^{57,58} primary prevention with statins is not recommended for octogenarians. The recommendation of a previous document⁵⁹ was also ratified: for fragile and diabetic elderly patients, the blood glucose control targets should be lax (glycated hemoglobin $< 8.5\%$) due to the known risks of overtreating diabetes mellitus in elderly patients, except in those with symptomatic hypoglycemia or hyperglycemia.⁶⁰

Regarding antihypertensive combinations, the APOLLO study⁶¹ in hypertensive elderly patients (mean age, 72 years) showed that combined treatment is safe and achieves greater BP reductions, with a trend toward a reduction in CV events. Having said that, a greater reduction in BP was accompanied by a risk of symptomatic hypertension and injurious falls.⁶²

CONCLUSIONS

Because they concern the vast majority of the population, each year sees the appearance of broadly applicable findings in the broad network of areas comprising vascular risk and CR. The present article has summarized these results, emphasizing the most relevant. The developments have involved researchers, health care professionals, scientific societies, and health care authorities. A noteworthy effort has been made in the systemization and structuring of recent knowledge. The considerable accumulation of findings gives rise to reviews that continuously engender clinical practice guidelines and consensus documents, which help physicians in clinical practice. However, in an era marked by evidence-based medicine, clinical practice is seen as more fragile than previously thought, due to the divergences and

controversies emanating from the standards and recommendations.⁶³ However, knowledge is not monolithic, and even dissemination is valuable.

CONFLICTS OF INTEREST

None declared.

REFERENCES

- Annemans L, Witttrup-Jensen K, Bueno H. A review of international pharmacoeconomic models assessing the use of aspirin in primary prevention. *J Med Econ.* 2010;13:418–27.
- World Health Organization. *World Health Statistics 2013.* Geneva: WHO; 2013.
- Kotseva K, Wood D, De Backer G, De Bacquer D, Pyörälä K, Keil U; EUROASPIRE Study Group. Cardiovascular prevention guidelines in daily practice: a comparison of EUROASPIRE I, II and III surveys in eight European countries. *Lancet.* 2009;14:929–40.
- Gielen S, Landmesser U. The Year in Cardiology 2013: cardiovascular disease prevention. *Eur Heart J.* 2014;35:307–12.
- Teo K, Lear S, Islam S, Mony P, Dehghan M, Li W, et al. Prevalence of a healthy lifestyle among individuals with cardiovascular disease in high-, middle- and low-income countries. The Prospective Urban Rural Epidemiology (PURE) Study. *JAMA.* 2013;309:1613–21.
- Guallar-Castillón P, Gil-Montero M, León-Muñoz LM, Graciani A, Bayán-Bravo A, Taboada JM, et al. Magnitud y manejo de la hipercolesterolemia en la población adulta de España, 2008–2010: el estudio ENRICA. *Rev Esp Cardiol.* 2012;65:551–8.
- Vidal-Perez R, Otero-Raviña F, Franco M, Rodríguez García JM, Liñares Stolle R, Esteban Alvarez R, et al.; BARBANZA investigators. Determinants of cardiovascular mortality in a cohort of primary care patients with chronic ischemic heart disease. BARBANZA Ischemic Heart Disease (BARIHD) study. *Int J Cardiol.* 2013;167:442–50.
- Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, et al. Guía europea sobre prevención de la enfermedad cardiovascular en la práctica clínica (versión 2012). *Rev Esp Cardiol.* 2012;65:e1–66.
- Galve E, Alegría E, Cordero A, Fácila L, Fernández de Bobadilla J, Lluís-Ganella C, et al. Temas de actualidad en cardiología: riesgo vascular y rehabilitación cardíaca. *Rev Esp Cardiol.* 2014;67:203–10.
- Arós F, Estruch R. Dieta mediterránea y prevención de la enfermedad cardiovascular. *Rev Esp Cardiol.* 2013;66:771–4.
- Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, et al.; PREDIMED Study Investigators. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med.* 2013;368:1279–90.
- Konstantinidou V, Ruiz LA, Ordovás JM. Personalized nutrition and cardiovascular disease prevention: From Framingham to PREDIMED. *Adv Nutr.* 2014;5:368S–71S.
- Pimenta AM, Toledo E, Rodriguez-Diez MC, Gea A, Lopez-Iracheta R, Shivappa N, et al. Dietary indexes, food patterns and incidence of metabolic syndrome in a Mediterranean cohort: The SUN project. *Clin Nutr.* 2014. Available at: doi: 10.1016/j.clnu.2014.06.002.
- Valdés S, García-Torres F, Maldonado-Araque C, Goday A, Calle-Pascual A, Sorriquer F, et al.; grupo de estudio Di@bet.es. Prevalencia de obesidad, diabetes mellitus y otros factores de riesgo cardiovascular en Andalucía. Comparación con datos de prevalencia nacionales. Estudio Di@bet.es. *Rev Esp Cardiol.* 2014;67:442–8.
- Puig T, Ferrero-Gregori A, Roig E, Vazquez R, Gonzalez-Juanatey JR, Pascual-Figal D, et al.; investigadores de REDINSCOR. Valor pronóstico del índice de masa corporal y el perímetro de cintura en los pacientes con insuficiencia cardíaca crónica (Registro Español REDINSCOR). *Rev Esp Cardiol.* 2014;67:101–6.
- Sánchez-Cruz JJ, Jiménez-Moleón JJ, Fernández-Quesada F, Sánchez MJ. Prevalencia de obesidad infantil y juvenil en España en 2012. *Rev Esp Cardiol.* 2013;66:371–6.
- Marrodán Serrano MD, Cabañas Armesilla MD, Carmenate Moren MM, González-Montero de Espinosa M, López-Ejeda N, Martínez Álvarez JR, et al. Asociación entre adiposidad corporal y presión arterial entre los 6 y los 16 años. Análisis en una población escolar madrileña. *Rev Esp Cardiol.* 2013;66:110–5.
- Kitahara CM, Flint AJ, Berrington de Gonzalez A, Bernstein L, Brotzman M, MacInnis RJ, et al. Association between class III obesity (BMI of 40–59 kg/m²) and mortality: a pooled analysis of 20 prospective studies. *PLoS Med.* 2014;11:e1001673.
- Sjöström L, Peltonen M, Jacobson P, Ahlin S, Andersson-Assarsson J, Anveden A, et al. Association of bariatric surgery with long-term remission of type 2 diabetes and with microvascular and macrovascular complications. *JAMA.* 2014;311:2297–304.
- Spring B, Moller AC, Colangelo LA, Siddique J, Roehrig M, Daviglus ML, et al. Healthy lifestyle change and subclinical atherosclerosis in young adults: Coronary Artery Risk Development in Young Adults (CARDIA) study. *Circulation.* 2014;130:10–7.
- Sesso HD, Christen WG, Bubes V, Smith JP, MacFadyen J, Schwartz M, et al. Multivitamins in the prevention of cardiovascular disease in men: the Physicians' Health Study II randomized controlled trial. *JAMA.* 2012;308:1751–60.
- Kromhout D, De Goede J. Update on cardiometabolic health effects of Ω -3 fatty acids. *Curr Opin Lipidol.* 2014;25:85–90.
- Malhotra A, Shafiq N, Arora A, Singh M, Kumar R, Malhotra S. Dietary interventions (plant sterols, stanols, omega-3 fatty acids, soy protein and dietary fibers) for familial hypercholesterolaemia. *Cochrane Database Syst Rev.* 2014;6:CD001918.
- Coleman KJ, Ngor E, Reynolds K, Quinn VP, Koebnick C, Young DR, et al. Initial validation of an exercise "vital sign" in electronic medical records. *Med Sci Sports Exerc.* 2012;44:2071–6.
- Abellán Alemán J, Sainz de Baranda Andújar P, Ortín Ortín EJ. Guía para la prescripción de ejercicio físico en pacientes con riesgo cardiovascular. Madrid: Sociedad Española de Hipertensión-Liga Española para la Lucha contra la Hipertensión Arterial; 2014.
- American College of Sports Medicine. Guidelines for exercise testing and prescription. American College of Sports Medicine; 2014. Available at: www.acsm.org
- Yong HH, Borland R, Thrasher JF, Thompson ME, Nagelhout GE, Fong GT, et al. Medialation pathways of the impact of cigarette warning labels on quit attempts. *Health Psychol.* 2014;33:1410–20.
- O'Loughlin JL, Sylvestre MP, Dugas EN, Karp I. Predictors of the occurrence of smoking discontinuation in novice adolescent smokers. *Cancer Epidemiol Biomarkers Prev.* 2014;23:1090–101.
- Lindström M, Axelsson J, Modén B, Rosvall M. Sexual orientation, social capital and daily tobacco smoking: a population-based study. *BMC Public Health.* 2014;14:565.
- Hughes JR, Stead LF, Hartmann-Boyce J, Cahill K, Lancaster T. Antidepressants for smoking cessation. *Cochrane Database Syst Rev.* 2014;1:CD000031.
- Fernández de Bobadilla J, Dalmau R, Galve E; grupo «Legislación del Tabaco y Síndrome Coronario Agudo en España». Impacto de la legislación que prohíbe fumar en lugares públicos en la reducción de la incidencia de síndrome coronario agudo en España. *Rev Esp Cardiol.* 2014;67:349–52.
- Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2014;63:2889–934.
- Anguita M, Alegría E, Barrios V, Casasnovas JA, Escobar C, León M, et al. Comentarios a las guías de práctica clínica sobre manejo de las dislipemias de la Sociedad Europea de Cardiología y la Sociedad Europea de Aterosclerosis 2011. Un informe del Grupo de Trabajo del Comité de Guías de Práctica Clínica de la Sociedad Española de Cardiología. *Rev Esp Cardiol.* 2011;64:1090–5.
- Ridker PM, Cook NR. Statins: new American guidelines for prevention of cardiovascular disease. *Lancet.* 2013;382:1762–5.
- Millán Núñez-Cortés J, Pedro-Botet J, Brea-Hernando A, Díaz-Rodríguez A, González-Santos P, Hernández-Mijares A, et al. Consenso de expertos sobre propuestas para la mejora del manejo de la dislipemia aterogénica. *Rev Esp Cardiol.* 2014;67:36–44.
- Doménech M, Roman P, Lapetra J, García de la Corte FJ, Sala-Vila A, De la Torre R, et al. Mediterranean diet reduces 24-hour ambulatory blood pressure, blood glucose, and lipids: one-year randomized, clinical trial. *Hypertension.* 2014;64:69–76.
- James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults. report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA.* 2014;311:507–20.
- Bhatt DL, Kandari DE, O'Neill WW, D'Agostino R, Flack JM, Katzen BT, et al.; SYMPLICITY HTN-3 Investigators. A controlled trial of renal denervation for resistant hypertension. *N Engl J Med.* 2014;370:1393–401.
- Gijón-Conde T, Graciani A, Banegas JR. Demografía y características clínicas de la hipertensión resistente en 6.292 pacientes en atención primaria. *Rev Esp Cardiol.* 2014;67:270–6.
- Pierdomenico SD, Pierdomenico AM, Cucurullo F. Morning blood pressure surge, dipping, and risk of ischemic stroke in elderly patients treated for hypertension. *Am J Hypertens.* 2014;27:564–70.
- Rapsomaniki E, Timmis A, George J, Pujades-Rodriguez M, Shah AD, Denaxas S, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet.* 2014;383:1899–911.
- Mas-Heredia M, Molés-Moliner E, González-de Paz L, Kostov B, Ortiz-Molina J, Mauri-Vázquez V, et al. Validez y aplicabilidad de un nuevo método de registro para la hipertensión arterial. *Rev Esp Cardiol.* 2014;67:717–23.
- Monami M, Dicembrini I, Mannucci E. Dipeptidyl peptidase-4 inhibitors and heart failure: a meta-analysis of randomized clinical trials. *Nutr Metab Cardiovasc Dis.* 2014;24:689–97.
- Monami M, Ahren B, Dicembrini I, Mannucci E. Dipeptidyl peptidase-4 inhibitors and cardiovascular risk: a meta-analysis of randomized clinical trials. *Diabetes Obes Metab.* 2013;15:112–20.
- Monami M, Dicembrini I, Nardini C, Fiorelli I, Mannucci E. Effects of glucagon-like peptide-1 receptor agonists on cardiovascular risk: a meta-analysis of randomized clinical trials. *Diabetes Obes Metab.* 2014;16:38–47.
- Monami M, Nardini C, Mannucci E. Efficacy and safety of sodium glucose cotransport-2 inhibitors in type 2 diabetes: a meta-analysis of randomized clinical trials. *Diabetes Obes Metab.* 2014;16:457–66.
- Vivas D, García-Rubira JC, Bernardo E, Angiolillo DJ, Martín P, Calle-Pascual A, et al. Influence of HbA_{1c} levels on platelet function profiles associated with tight glycaemic control in patients presenting with hyperglycemia and an acute

- coronary syndrome. A subanalysis of the CHIPS Study (“Control de Hiperglucemia y Actividad Plaquetaria en Pacientes con Síndrome Coronario Agudo”). *J Thromb Thrombolysis*. 2013;35:165–74.
48. Vivas D, García-Rubira JC, Bernardo E, Angiolillo DJ, Martín P, Calle A, et al. Efecto del tratamiento optimizado con insulina en la reactividad plaquetaria tras el alta de pacientes hiperglucémicos con síndrome coronario agudo. *Rev Esp Cardiol*. 2014;67:22–7.
 49. Puig Domingo M. Función plaquetaria e hiperglucemia en el síndrome coronario. *Rev Esp Cardiol*. 2014;67:3–5.
 50. Hernández García S, Prendes Lago E, Mustelie Oquendo JA, Rivas Estany E. Fase hospitalaria de la rehabilitación cardíaca. Protocolo para la cirugía cardíaca. *CorSalud*. 2014;6:246–56.
 51. Beatty AL, Li S, Thomas L, Amsterdam EA, Alexander KP, Whooley MA. Trends in referral to cardiac rehabilitation after myocardial infarction: data from the National Cardiovascular Data Registry 2007 to 2012. *J Am Coll Cardiol*. 2014;63:2582–3.
 52. Taylor RS, Sagar VA, Davies EJ, Briscoe S, Coats AJ, Dalal H, et al. Exercise-based rehabilitation for heart failure. *Cochrane Database Syst Rev*. 2014; 4:CD003331.
 53. Karmali KN, Davies P, Taylor F, Beswick A, Martin N, Ebrahim S. Promoting patient uptake and adherence in cardiac rehabilitation. *Cochrane Database Syst Rev*. 2014;6:CD007131.
 54. Ades PA, Keteyian SJ, Balady GJ, Houston-Miller N, Kitzman DW, Mancini DM, et al. Cardiac rehabilitation exercise and self-care for chronic heart failure. *JACC Heart Fail*. 2013;1:540–7.
 55. Völler H, Salzwedel A, Nitardy A, Buhler H, Treszl A, Wegscheider K. Effect of cardiac rehabilitation on functional and emotional status in patients after transcatheter aortic-valve implantation. *Eur J Prev Cardiol*. 2014. Available at: doi: 10.1177/2047487314526072.
 56. Gómez-Huelgas R, Martínez-Sellés M, Formiga F, Alemán Sánchez JJ, Camafort M, Galve E, et al. Tratamiento de los factores de riesgo vascular en el paciente mayor de 80 años. *Med Clin (Barc)*. 2014;143. 134.e1-11.
 57. Reiner Z. Primary prevention of cardiovascular disease with statins in the elderly. *Curr Atheroscler Rep*. 2014;16:420.
 58. Stone NJ, Intwala S, Katz D. Statins in very elderly adults (debate). *J Am Geriatr Soc*. 2014;62:943–5.
 59. Gómez Huelgas R, Díez-Espino J, Formiga F, Lafita Tejedor J, Rodríguez Mañas L, González-Sarmiento E, et al.; Grupo de Trabajo para el Documento de Consenso sobre el tratamiento de la diabetes tipo 2 en el anciano. Tratamiento de la diabetes tipo 2 en el paciente anciano. Documento de consenso. *Med Clin (Barc)*. 2013;140. 134.e1-12.
 60. Andrews MA, O'Malley PG. Diabetes overtreatment in elderly individuals: risky business in need of better management. *JAMA*. 2014;311:2326–7.
 61. Teo KK, Pfeffer M, Mancina G, O'Donnell M, Dagenais G, Diaz R, et al.; Aliskiren Prevention of Later Life Outcomes trial Investigators. Aliskiren alone or with other antihypertensives in the elderly with borderline and stage 1 hypertension: the APOLLO trial. *Eur Heart J*. 2014;35:1743–51.
 62. Berry SD, Kiel DP. Treating hypertension in the elderly: should the risk of falls be part of the equation? *JAMA Intern Med*. 2014;174:596–7.
 63. Lobos Bejarano JM, Galve E, Royo-Bordonada MA, Alegría Ezquerro E, Armario P, Brotons Cuixart C, et al. Posicionamiento del Comité Español Interdisciplinario de Prevención Cardiovascular y la Sociedad Española de Cardiología en el tratamiento de las dislipemias. Divergencia entre las guías europea y estadounidense. *Rev Esp Cardiol*. 2014;67:913–9.