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Original article

Prognostic value of the increase in systolic blood pressure with exercise in patients with hypertension and known or suspected coronary artery disease☆

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ABSTRACT

Background and objective: The association of an exaggerated systolic blood pressure increase with exercise (EBPIE) with cardiovascular events remains controversial. Our aim was to determine the possible association of an EBPIE with survival and risk of serious cardiac events in patients with hypertension and known or suspected coronary artery disease (CAD).
Patients and methods: This is a retrospective observational study based on a sample of 5226 patients with a history of arterial hypertension and known or suspected CAD referred for exercise echocardiography. The EBPIE was defined as an increase in systolic blood pressure with exercise greater than or equal to the 95th percentile of this population (80 mmHg). The end points were all-cause mortality, cardiac death and myocardial infarction (MI).
Results: During a mean follow-up of 4.7 years, there were 978 deaths (including 371 cardiac) and 798 MI. Annual rates of all-cause mortality, cardiac mortality and MI were 2.73, 0.83 and 2.63% in patients with EBPIE and 4.4, 1.58 and 3.98% in those without EBPIE ($p < .001$, $p = .012$, and $p = .014$, respectively). After multivariate analysis, an EBPIE remained independently associated with a lower risk of all-cause mortality (HR: 0.70, 95% CI: 0.52–0.95; $p = .023$) and MI (HR: 0.69, 95% CI: 0.50–0.95; $p = .022$) but was not significantly associated with cardiac mortality (HR: 0.72, 95% CI: 0.43–1.20; $p = .2$).
Conclusions: EBPIE was associated with an increased likelihood of survival and lower rate of MI in hypertensive patients with known or suspected CAD.

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Valor pronóstico del incremento de la presión arterial sistólica con el ejercicio en pacientes hipertensos con enfermedad coronaria conocida o sospechada

RESUMEN

Fundamento y objetivos: La asociación entre un incremento exagerado de la presión arterial sistólica con el ejercicio (IEPASE) y la probabilidad de eventos cardiovasculares es controvertida. Nuestro propósito fue determinar la posible asociación de un IEPASE con la supervivencia y con el riesgo de eventos cardíacos graves en pacientes hipertensos con enfermedad coronaria conocida o sospechada.
Pacientes y métodos: Se trata de un estudio retrospectivo y observacional sobre una muestra de 5.226 pacientes con historia de hipertensión arterial y enfermedad coronaria conocida o sospechada referidos a ecocardiografía de ejercicio. El IEPASE se definió como un incremento de la presión arterial sistólica con el ejercicio igual o superior al percentil 95 de esta población (80 mmHg). Los objetivos fueron mortalidad total, mortalidad de origen cardíaco e infarto de miocardio (IM).

Resultados: En un seguimiento medio de 4,7 años, se registraron 978 muertes (371 de origen cardíaco) y 798 IM. Las tasas anuales de mortalidad, mortalidad de origen cardíaco e IM fueron del 2,73; 0,83 y 2,63% en pacientes con IEPASE y de 4,4; 1,58 y 3,98%, respectivamente en aquellos sin IEPASE (p < 0,001; p = 0,012 y p = 0,014, respectivamente). Tras un ajuste multivariado, el IEPASE resultó predictor de mortalidad por cualquier causa (HR: 0,70; IC 95%: 0,52–0,95; p = 0,023) e IM (HR: 0,69; IC 95%: 0,50–0,95; p = 0,022), pero la asociación con mortalidad cardiaca no alcanzó significación estadística (HR: 0,72; IC 95%: 0,43–1,20; p = 0,2).

Conclusiones: El IEPASE se asoció con mayor probabilidad de supervivencia y menor riesgo de IM en pacientes hipertensos con enfermedad coronaria conocida o sospechada.

Introduction

Hypertension at rest is a well-established risk factor for cardiovascular events.[1–3] However, the prognostic value of blood pressure (BP) response to exercise, particularly when too high, is discussed. The importance of adequately assessing the implications of an exaggerated blood pressure response to exercise is given by the possibility of predicting future cardiovascular complications beyond BP figures at rest. In recent years, studies have been published that have established an association between hypertensive response to exercise and a higher incidence of cardiovascular events[4–8] in healthy individuals. However, studies in patients with confirmed or suspected cardiovascular disease have generally reported conflicting results.[9–13] Our purposes in this study were to analyze the possible associations between increased systolic BP with exercise (especially exaggerated increases) with mortality and with severe heart events in hypertensive patients with known or suspected coronary heart disease referred to stress echocardiography.

Material and methods

Patients and study design

The study group was selected from 13,328 patients aged ≥18 years who were referred to treadmill stress echocardiogram in the Imaging and Heart Function Unit of the University Hospital Complex of A Coruña for known or suspected coronary artery disease from 1 March 1995 to 28 June, 2013. The referral of the patients to stress echocardiogram was in no case motivated by the evaluation of the BP response to exercise. Inclusion criteria were: history of hypertension, living in the reference area of our hospital, not having received beta-blocker treatment in the 48 h prior to the test (because of its effect on increasing BP with exercise) and not having reported hypotensive response to exercise (for its well-known negative prognostic value). The sample of our study finally consisted of a total 5226 patients. The study was approved by the Ethics Committee of Clinical Research of Galicia.

Clinical data

Demographic and clinical data were entered into a prospective database at the time of the tests. The definition of hypertension, hypercholesterolemia and diabetes mellitus was based on the previous history and previous treatment with antihypertensive, hypolipidemic or antidiabetic drugs, respectively. Patients referred for chest pain assessment were classified as patients with typical angina, probable/atypical angina, or nonspecific chest pain according to the Diamond scale.[14] Previous history of ischemic heart disease was defined as the history of myocardial infarction (MI), coronary artery revascularization, or previous angiographic report of any significant coronary artery stenosis, defined as the occurrence of any stenosis ≥50% of the left coronary artery trunk diameter or ≥70% of the diameter of any other epicardial coronary artery. The baseline ECG was considered non-interpretable in the presence of left bundle branch block, pacemaker rhythm, left ventricular hypertrophy with strain pattern, treatment with digoxin, preexcitation syndrome or other alterations of repolarization.

Stress test

All patients were studied through treadmill stress echocardiogram. Data on heart rate, BP (through auscultation) and 12-lead electrocardiogram procedure were obtained at baseline and at every stage of the exercise protocol, as usual in conventional ergometry. To perform the test, patients were encouraged to perform a treadmill exercise protocol to achieve one of the following objectives: physical exhaustion, limiting symptoms, significant arrhythmia, severe hypertension (systolic BP > 240 mmHg or diastolic BP > 110 mmHg), or a hypotensive response to exercise (systolic BP drop >20 mmHg from baseline). The increase of systolic BP with exercise ($\triangle$SBPE) was defined as the difference between the maximum systolic BP during the test and its value at rest. The exaggerated increase in systolic BP during exercise (EISBPE) was defined as $\triangle$SBPE ≥80 mmHg (value corresponding to the 95th percentile of the study population).

Ischemic ECG changes during the test were defined as the elevation or depression of the horizontal or downsloping ST segment ≥1 mm 80 ms away from the J point in ≥1 leads in patients with interpretable electrocardiogram. A submaximal test was defined as the inability to achieve 85% of the maximum theoretical heart rate.

A two-dimensional echocardiogram was performed on the standard apical and parasternal projections at baseline, peak exercise, and immediately after exercise.[15] Echocardiographic ischemia was defined as the development of new changes in segmental contractility or the worsening of previously existing ones, except the worsening of akinesia to dyskinesia[16] and isolated inferobasal segment hypokinesis.[17,18]

Follow-up

Follow-up data were obtained from the review of electronic medical records, hospital databases and death certificates. The endpoints of the study were total mortality, cardiac cause death, and MI. Most of these data were provided by the Information Technology Department of the A Coruña University Hospital Complex, in accordance with the information available in the hospital databases and in the health card database, which allows to know the vital state of the patients under study. This information was compared with that provided by the Galician Registry of Mortality, and the discrepancies were reviewed. The average follow-up was 4.4 years (median 3.3 years, interquartile range 0.2–7.4 years).