ENFERMEDAD CORONARIA Y DIABETES MELLITUS EN EL ANCIANO.

ACADEMIA LATINOAMERICANA DE MEDICINA DEL ADULTO MAYOR

ALMA

UNIVERSIDAD DE SALAMANCA
DEPARTAMENTO DE MEDICINA

XI Curso ALMA
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Salamanca, España
"El Anciano con Diabetes"

Organización Panamericana de la Salud

Oficina Regional de la Organización Mundial de la Salud

Introducción

- La enfermedad coronaria es la principal causa de morbilidad y mortalidad en DM2.

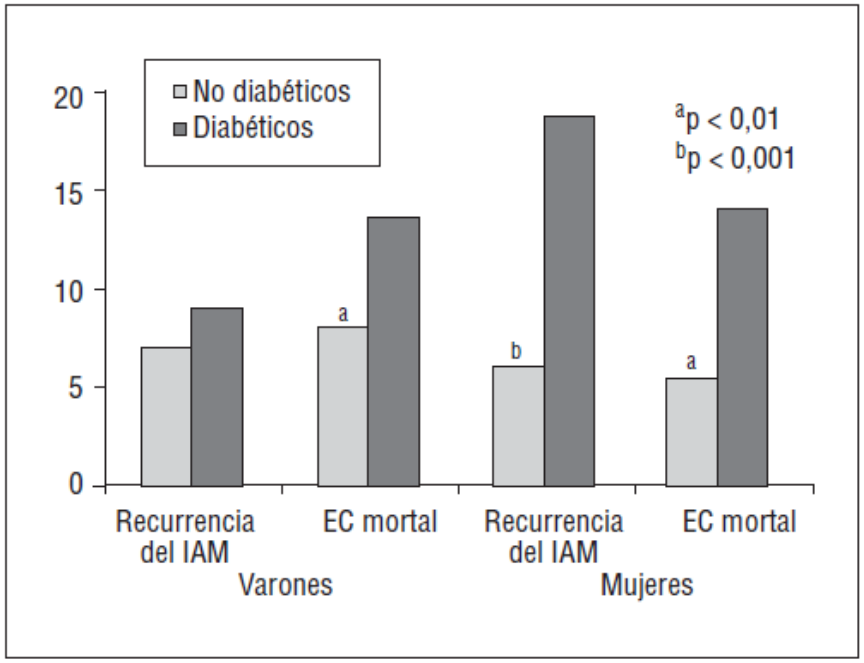

Fig. 2. Pronóstico del infarto agudo de miocardio en los pacientes diabéticos (adaptada de Miettinen et al[38] y Sala et al[39]). IAM: infarto agudo de miocardio; EC: enfermedad coronaria.

Buse JB, et al. American Heart Association; American Diabetes Association: Primary prevention of cardiovascular diseases in people with diabetes mellitus: a scientific statement from the American Heart Association and the American Diabetes Association. Circulation 2007, 115(1): 114-126.

Alteraciones de la glicemia en DM

Hiperglicemia crónica sostenida

- Cambios estructurales en pared arterial
- Estado procoagulante
- Disfx diastólica
- Cardiopatía DM
- Aumento masa ventricular

Fluctuaciones de la glicemia

- Activa el estrés oxidativo
- Formación excesiva de productos finales de la glucosa
- ↓apoptosis en células endoteliales
- Disfunción simpática
- Rol en patogénesis de ateroesclerosis
- FR de complicaciones cardiovasculares

Ceriello A, Esposito K, et al: Oscillating glucose is more deleterious to endothelial function and oxidative stress than mean glucose in normal and type 2 diabetic patients. Diabetes 2008, 57(5):1349-1354.
Monnier L, Mas E, et al: Activation of oxidative stress by acute glucose fuctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes.JAMA 2006, 295(14):1681-1687.
Hu Y, Liu W, et al: Postchallenge plasma glucose excursions, carotid intima-media thickness, and risk factors for atherosclerosis in Chinese population with type 2 diabetes. Atherosclerosis 2010, 210(1):302.

Association of glycemic variability and the presence and severity of coronary artery disease in patients with type 2 diabetes

Gong Su[1], Shuhua Mi[1], Hong Tao[1], Zhao Li[2], Hongxia Yang[1], Hong Zheng[1], Yun Zhou[1], Changsheng Ma[1*]

Cardiovascular Diabetology 2011, **10**:19

Medidas:

•Amplitud media de las desviaciones de glucosa: **(MAGE):** media aritmética de diferencias entre picos y valles

• La media de las diferencias diarias **(MODD):** media de las diferencias absolutas en 2 días consecutivos

•Las desviaciones de la glucosa post prandial **(PPGE):** incrementos en la glucosa post desayuno

Resultados

MAGE y PPGE significativamente mayores en pacientes con enfermedad coronaria.

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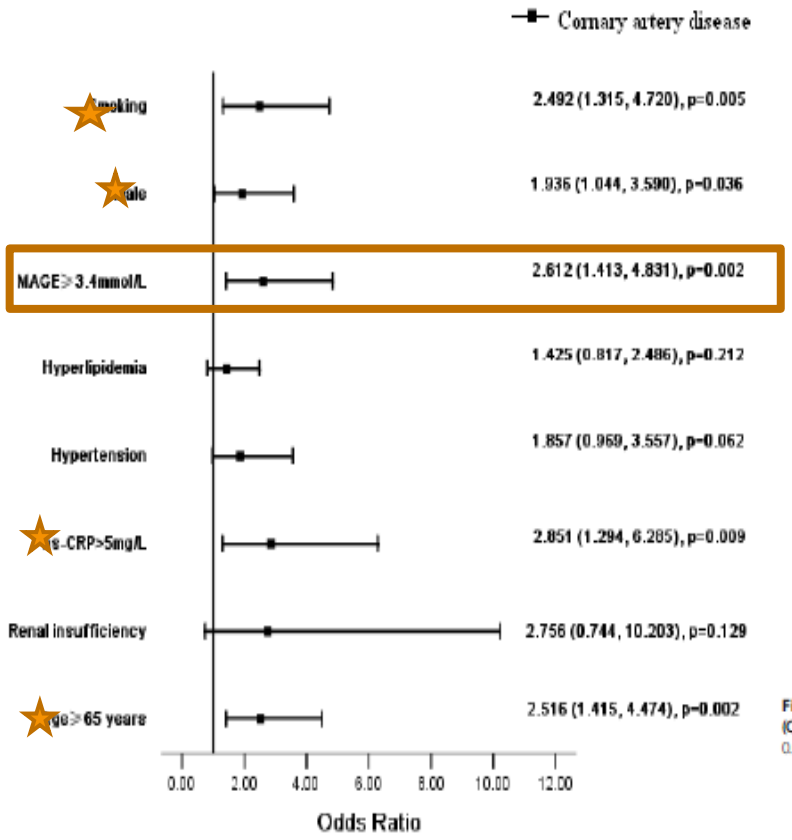

Figure 3 Multivariate analysis for independent determinants of coronary artery disease (CAD). Smoking, male, older age, MAGE and hs-CRP were independent risk factors for CAD.

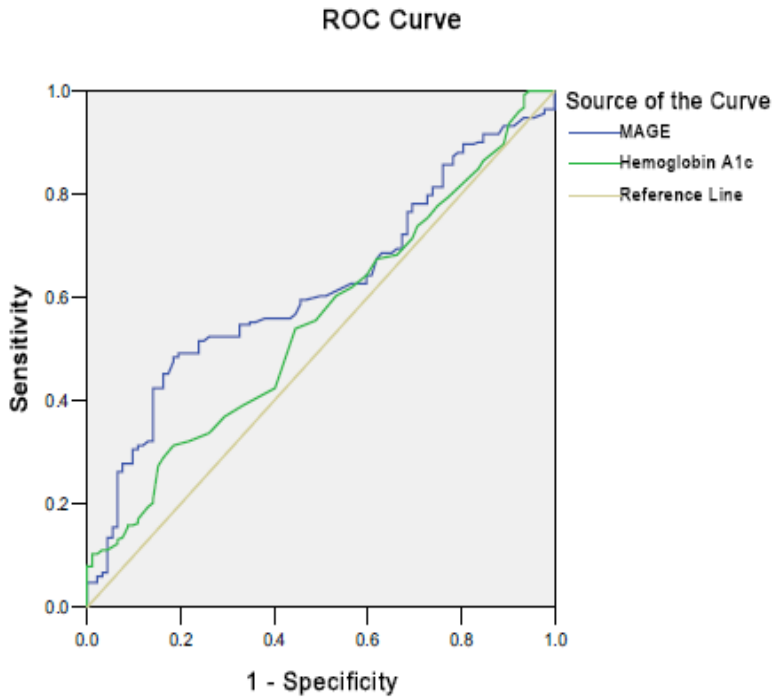

Figure 4 Receiver-operating characteristic (ROC) curve for MAGE and hemoglobin A_{1c} (HbA_{1c}) in predicting coronary artery disease (CAD) in patients with type 2 diabetes (T2DM). Area under the receiver-operating characteristic curve: MAGE 0.618 (95% CI 0.555, 0.680), p = 0.001; HbA_{1c} 0.554 (95% CI 0.487, 0.620), p = 0.129. MAGE, but not HbA_{1c} displayed significant value in predicting CAD in patients with T2DM.

Su *et al. Cardiovascular Diabetology* 2011, **10**:19

Fluctuaciones de la glucosa y enf coronaria

- Las fluctuaciones de la glucosa se asocian con la presencia y la severidad de la enf coronaria y al desarrollo de ateroesclerosis en pacientes con DM2.
- Se deben controlar:
  - Hemoglobina glicosilada
  - Glucosa post prandial
  - Fluctuaciones de la glucosa

Control de glucosa y enf coronaria

Estudios	Población	Tratamiento	Objetivo	Resultados
UKPDS	3867 53.3a Dx reciente Hb A1c: 7.1 Seguim: 10a	SU Insulina Metformina Vs dieta	FPG<108mg/dl	**RR IM no fatal: 0.79 (0.58-1.09)** **RR IM fatal: 0.94 (0.68-1.30)** Metformina ↓42% muerte por DM ↓36% mortalidad total
UKPDS Follow up	Seguim: 10a			Pérdida de diferencias de Hb A1c. **Grupo SU, insulina: ↓ 15% IMA y 13% mortalidad total**
ACCORD	10251 62.2 a 10 evolución Hb A1c: 8.3 35% enf macrovascular Seguim: 3.4 a	ADO Insulina	Intensivo Hb A1c<6% vs Standard: Hb A1c 7-7.9%	**HR IM no fatal+ACV+mortCV:** 0.90 (0.82-0.93) **HR IM no fatal: 0.76 (0.62-0.92)** **HR Mortalidad Total: 1.22 (1.01-1.46)**
ACCORD Follow up	17 meses seguim		Intensivo Hb A1 7.2% vs Standard: Hb A1c 7.6%	**IM no fatal: 0.82 (0.70-0.96)** Mortalidad total a 5 años: 19% mayor en tx intensivo

Does Aggressive Glycemic Control Benefit Macrovascular and Microvascular Disease in Type 2 Diabetes?: Insights from ACCORD, ADVANCE, and VADT

Curr Cardiol Rep (2012) 14:79–88

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Estudios	Población	Tratamiento	Objetivo	Resultados
ADVANCE	11140 65.8a 8 a evolución Hb A1c: 7.5 23% enf macrovascular Seguim: 5 a	Glicazida vs otros tx	Intensivo Hb A1c<6.5% vs Standard: Basado en guías	**HR IM no fatal: 0.98 (0.78-1.23)** No diferencias en mortalidad total o muerte CV
VADT	1791 60.4 a 11 a evolución Hb A1c: 9.4% 40% enf macrovascular Seguimiento 5.6 a	Metformina+ rosiglitazona Glimepiride+ rosiglitazona Insulina vs Mitad dosis intensivo	Intensivo↓ Hb A1c 1.5	**Eventos CV+mort total: 0.88 (0.74-1.05)** **HR Mortalidad total: 1.07 (0.81-1.42)** **HR mort CV: 1.32 (0.81-2.14)**

• Reaven P, Moritz T, Schwenke D, et al. Intensive glucose-lowering therapy reduces cardiovascular disease events in veterans affairs diabetes trial participants with lower calcified coronary atherosclerosis. Diabetes 2009, 58:2642–2648.

- 301 participantes del VADT con ateroesclerosis coronaria basal (medido con TAC)
- **Resultados en pacientes con menos ateroesclerosis**
  - **HR control intensivo : 0.08 (0.008-0.77)**
- Resultados en pacientes con ateroesclerosis mas avanzada: ningún beneficio significativo en eventos cardiovasculares

Pharmacologic Prevention of Microvascular and Macrovascular Complications in Diabetes Mellitus

Implications of the Results of Recent Clinical Trials in Type 2 Diabetes

Nikhil Tandon,[1] *Mohammed K. Ali*[2] and *K.M. Venkat Narayan*[2]

- Pacientes ancianos con DM avanzada y enf cardiaca previa no se benefician del control intensivo de la glucosa.
- Pacientes recientemente diagnosticados sin complicaciones cardiovasculares se benefician del control intensivo.

Hipertensión arterial y enf coronaria

Estudios	Objetivo	Resultados
UKPDS-BP Captopril, atenolol+ Furosemida , nifedipino	Intensivo PA< 150/85 estándar PA <180/105	↓ 10mmhg: ↓ 12% complicaciones DM ↓15% muerte CV **↓ 11% IM** Beneficio no persiste durante seguimiento.
ADVANCE Perindopril+ indapamina+ terapia usual		↓18% mortalidad CV ↓14% Mortalidad total **↓14% eventos coronarios**
ACCORD 3.4 antihipertensivos Vs 2.1	Intensivo Psist< 120 estándar Psist <140	**Ninguna diferencia en eventos** **Exceso de eventos adversos serios (3.3% vs 1.3%)**

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Am J Cardiovasc Drugs 2012; 12 (1): 7-22

Dislipidemia y enfermedad coronaria

Colhoun HM, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. Lancet. 2004;364(9435):685–696.

- 2838, DM2 sin enf CV, LDL≤ 160 mg/dl
- Atorvastatina 10mg
- ↓ **eventos CV (IMA), revascularización coronaria y stroke : 37%**

Keech A, et al. Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial. Lancet. 2005;366(9500):1849–1861

- 9795 DM
- **↓24% IMA no fatal**
- **↓ 21%revascularización coronaria**
- **↑mortalidad enf coronaria. HR: 1·19 (0·90–1·57).**

Vascular Health and Risk Management
23 August 2011

Dislipidemia

Ginsberg HN, Elam MB, Lovato LC, et al. Effects of combination lipid therapy in type 2 diabetes mellitus. The ACCORD study. N Engl J Med. 2010;362(17): 1563–1574.

- Adición de fenofibrato a simvastatina no muestra beneficio cardiovascular extra a simvastatina sola.
- ↓ 31% incidencia de eventos CV en pacientes con dislipidemia mixta

Efficacy of cholesterol-lowering therapy in 18 686 people with diabetes in 14 randomised trials of statins: a meta-analysis

Lancet 2008; 371: 117–25

*Cholesterol Treatment Trialists' (CTT) Collaborators**

- Meta análisis incluye 18 686 diabéticos
- 14 ensayos, estatinas
- Resultados: cada mmol/L disminución LDL
  - ↓ 9% mortalidad total
  - ↓ 13% mortalidad cardiovascular
  - ↓ 21% eventos CV mayores
  - ↓ 22 IM o muerte coronaria
  - ↓ 25% reduccción en revascularización coronaria
  - ↓ 21% stroke

- Beneficios independientes de antecedente de enf vascular previa.
- Conclusión: todos los Diabéticos que tienen riesgo vascular suficiente para ser tratados con estatinas deben ser tratados independientemente de su nivel de colesterol.

Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials

Lancet 2010; 375:735–42

Naveed Sattar, David Preiss, Heather M Murray, Paul Welsh, Brendan M Buckley, Anton J M de Craen, Sreenivasa Rao Kondapally Seshasai,

Findings We identified 13 statin trials with 91 140 participants, of whom 4278 (2226 assigned statins and 2052 assigned control treatment) developed diabetes during a mean of 4 years. Statin therapy was associated with a 9% increased risk for incident diabetes (odds ratio [OR] 1·09; 95% CI 1·02–1·17), with little heterogeneity (I^2=11%) between trials. Meta-regression showed that risk of development of diabetes with statins was highest in trials with older participants, but neither baseline body-mass index nor change in LDL-cholesterol concentrations accounted for residual variation in risk. Treatment of 255 (95% CI 150–852) patients with statins for 4 years resulted in one extra case of diabetes.

Interpretation Statin therapy is associated with a slightly increased risk of development of diabetes, but the risk is low both in absolute terms and when compared with the reduction in coronary events. Clinical practice in patients with moderate or high cardiovascular risk or existing cardiovascular disease should not change.