CONCIENTE ENTRE ÁCIDO ÚRICO Y CREATININA SÉRICA COMO PREDICTOR DE EVENTOS CARDIOVASCULARES.

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Original Article

OPEN

Serum uric acid / serum creatinine ratio as a predictor of cardiovascular events. Detection of prognostic cardiovascular cut-off values

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Objective: In the frame of the Uric Acid Right for Heart Health (URRAH) study, a nationwide multicenter study involving adult participants recruited on a regional community basis from all the territory of Italy under the patronage of the Working Group on Uric Acid and Cardiovascular Risk of the Italian Society of Hypertension, we searched for the cut-off values of the ratio between serum uric acid (SUA) and serum creatinine (sCr) able to predict cardiovascular (CV) events.

Methods: Among 20 724 participants followed-up for 126 ± 64 months, after detecting cut-off by the receiver operating characteristic curves, we calculated by Cox models adjusted for confounders having CV events as dependent variable the hazard ratio (HR) of SUA/sCr > cut-off. We also verified if the role of cut-off varied with increasing SUA/sCr.

Results: A plausible prognostic cut-off of SUA/sCr was found and was the same in the whole database, in men and in women (>5.35). The HR of SUA/sCr > cut-off was 1.159 (95% confidence interval [CI] 1.092–1.131, $P<0.03$) in all, 1.161 (95% CI 1.021–1.335, $P<0.02$) in men, and 1.444 (95% CI 1.012–1.113, $P<0.03$) in women. In increasing quintiles of SUA/sCr the cut-offs were >3.08, >4.87, >5.35, >6.22 and >7.58, respectively. The HRs significantly increased from the 3rd to the 5th quintile (1.21, 95% CI 1.032–1.467, $P=0.018$; 1.294, 95% CI 1.101–1.521, $P=0.002$; and 1.642, 95% CI 1.405–1.919, $P<0.0001$; respectively), that is, over 5.35, whereas the 2nd quintile was not significantly different from the 1st (reference).

Conclusion: Having SUA/sCr >5.35 is an independent CV risk indicator both in men and women. The cut-off is dynamic and significantly increases with increasing SUA/sCr.

Keywords: cardiovascular, creatinine, cut-off, epidemiology, uric acid

Abbreviations: CI, confidence interval(s); CV, cardiovascular; HR, hazard ratio(s); ICD-10, International Classification of Diseases – 10th Revision; OR, odds ratio (s); ROC, receiver operating characteristic; sCr, serum creatinine; SUA, serum uric acid; URRAH, Uric Acid Right for Heart Health

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El estudio italiano URRAH (Uric Acid Right for Heart Health) ha aportado evidencia en los últimos años sobre los posibles valores de corte para el ácido úrico sérico (AUs) que permiten predecir la posible incidencia de eventos cardiovasculares (también en diabéticos).

Debido a la influencia de la función renal sobre el ácido úrico sérico se presenta este estudio que analiza el cociente entre el ácido úrico sérico y la creatinina sérica (AUs/Crs) como predictor de eventos cardiovasculares

DISEÑO DEL ESTUDIO

ESTUDIO MULTICÉNTRICO, OBSERVACIONAL Y RETROSPECTIVO

n = 20724

OBJETIVO DEL ESTUDIO

Identificar los valores de corte entre el cociente entre el ácido úrico sérico y creatinina sérica capaces de predecir eventos cardiovasculares.

CARACTERÍSTICAS DE LA MUESTRA

Variables	Total (n= 20724)	Hombres (n=10229)	Mujeres (n=10495)	Valores P entre sexos
Edad (años)	57.2 ± 14.7	56.5 ± 14.2	58.0 ± 15.4	<0.0001
Hombres (%)	49.4	-	-	-
AUs (mg/dl)	5.04 ± 1.39	5.26 ± 1.38	4.83 ± 1.38	<0.0001
Crs (mg/dl)	0.93 ± 0.25	0.96 ± 0.22	0.90 ± 0.28	<0.0001
AUs/Crs	5.56 ± 1.74	5.60 ± 1.76	5.51 ± 1.71	<0.0001
Hábito tabáquico (sí %)	24.1	27.8	20.6	<0.0001
Ingesta alcohólica (%)	62.6	64.8	60.4	<0.0001
Diabetes (%)	10.6	10.6	10.5	0.80 (NS)
Hipertensión (%)	66.7	66.2	67.3	0.10 (NS)
FC (lpm)	71.8 ± 12.3	70.7 ± 12.5	72.9 ± 11.9	<0.0001
PA sistólica (mmHg)	143.3 ± 2.8	143.0 ± 22.6	144.3 ± 24.9	<0.0001
PA diastólica (mmHg)	85.4 ± 12.8	85.5 ± 12.5	85.3 ± 13.1	0.20 (NS)
IMC (kg/m²)	25.9 ± 4.2	26.6 ± 3.9	26.7 ± 4.6	0.03
LDL-C (mg/dl)	135.6 ± 35.8	134.8 ± 35.9	135.1 ± 35.4	0.53 (NS)

AUs: ácido úrico sérico; Crs: creatinina sérica; FC: frecuencia cardíaca; IMC: índice de masa corporal; LDL-C: low-density-lipoprotein serum cholesterol; NS: diferencia no estadísticamente significativa; PA: presión arterial.

Tabla 1. Características de la muestra. *Adaptado de artículo original.*

SEGUIMIENTO

240 meses

Durante el periodo de seguimiento, 2110 pacientes (10,2%) tuvieron un evento cardiovascular, siendo 1030 hombres y 1080 mujeres (*p*=0,6)

RESULTADOS

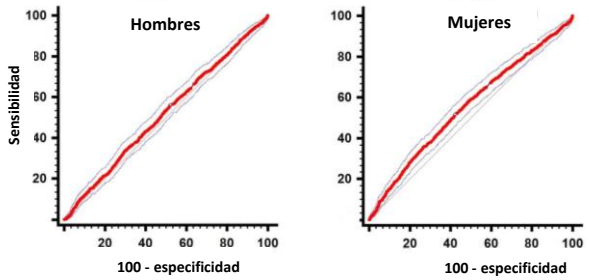

Imagen 1. Curvas ROC detectando el valor de corte pronóstico de AUs/Crs en hombres y mujeres, el cual es igual al análisis de la muestra total. *Adaptado de artículo original.*

	Área bajo la curva (95% IC)	Valor Z	Sensibilidad (%)	Especificidad (%)	Índice Youden	Valor de corte (95% IC)
Hombres	0.52 (0.51-0.53)	1.938	56.2	48.0	0.042	>5.35 (3.73-6.17)
Mujeres	0.55 (0.54-0.56)	5.733	51.7	57.9	0.091	>5.35 (5.27-6.62)

Tabla 2. Parámetros ROC del ratio AUs/Crs en hombres y mujeres, los cuales son iguales al análisis de la muestra total. *Adaptado de artículo original.*

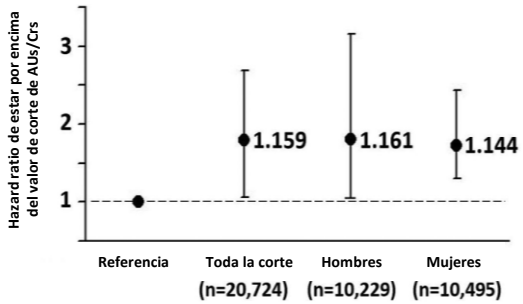

Imagen 2. *Hazard ratio* referente a tener el AUs/Crs superior al valor de corte en toda la corte, en hombres y en mujeres. Las barras verticales representan el 95% de IC. *Adaptado de artículo original.*

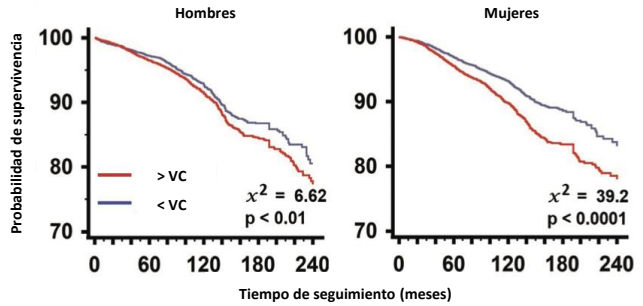

Imagen 3. Curvas de supervivencia *Kaplan-Maier* atendiendo a estar o no por encima del valor de corte (VC) de AUs/Crs en hombres y mujeres.
Adaptado de artículo original.

CONCLUSIONES

- Existe un valor de corte (>5,35) capaz de estratificar pacientes destinados a experimentar un evento cardiovascular en un periodo extenso de tiempo.
- El cociente AUs/Crs es un marcador fiable de bajo costo del riesgo de CV y puede ser usado como predictor de eventos cardiovasculares a largo plazo en hombres y mujeres.

COMENTARIO

Analizando los diferentes trabajos presentados por el grupo URRAH, podemos observar cómo AUs es un factor de riesgo independiente para eventos cardiovasculares a largo plazo. Ahora bien, en este estudio nos muestran cómo si indexamos los valores de AUs a la función renal, mejoramos la predicción a largo plazo de eventos cardiovasculares.

En esta línea, tras no observar cambios significativos a la hora de ajustar AUs a la función renal usando el valor sérico de creatinina o el ratio de filtrado glomerular, proponen el valor sérico de creatinina como variable predictiva por su accesibilidad y fácil uso en la práctica clínica. De modo que se debe valorar la función renal cuando se tiene el nivel de AUs como factor de riesgo cardiovascular independientemente del sexo.

Por otra parte, demuestran la existencia de un preciso valor de corte de AUs/Crs (5,35) que puede ser usado en hombres y mujeres como predictor de eventos cardiovasculares a largo plazo. Además, los resultados extraídos de la división de la corte por quintiles, proponen que estar por encima del límite representa un riesgo de CV creciente si la relación AUs/Crs es superior a 5,35.

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