REFERENCES

1. Morris Jr JJ, Estes Jr EH, Whalen RE, Thompson Jr HK, McIntosh HD. P-wave analysis in valvular heart disease. Circulation. 1964;29:242–52.
2. Robitaille GA, Phillips JH. An analysis of the P wave in patients with transient benign atrial fibrillation. Dis Chest. 1967;52:806–12.
3. Ogawa M, Kumagai K, Vakulenko M, Yasuda T, Siegerman C, Garfinkel A, et al. Reduction of P-wave duration and successful pulmonary vein isolation in patients with atrial fibrillation. J Cardiovasc Electrophysiol. 2007;18:931–8.
4. Janin S, Wojcik M, Kuniss M, Berkowitsch A, Erkapic D, Zaltsberg S, et al. Pulmonary vein antrum isolation and terminal part of the P wave. Pacing Clin Electrophysiol. 2010;33:784–9.
5. Martín García A, Jiménez-Candil J, Hernández J, Martín García A, Martín Herrero F, Martín Luengo C. Morfología de la onda P y recurrencia tras cardioversión de fibrilación auricular aislada. Rev Esp Cardiol. 2012;65:289–90.

SEE RELATED ARTICLE:
DOI: 10.1016/j.rec.2012.01.017

doi:10.1016/j.rec.2012.02.004

Assessment of Renal Involvement by Cystatin C: A Forgotten Biomarker

Valoración de la afección renal mediante la cistatina C: un biomarcador olvidado

To the Editor,

We read with great interest the excellent article by Górriz Teruel et al.[1] on renal assessment in patients with cardiovascular disease. This extensive and excellent update did not mention cystatin C (CC), a biological marker that estimates kidney function and has lately gained importance due to its role in cardiovascular risk stratification.

Chronic kidney disease is usually associated with cardiovascular disease and greatly increases the patient's risk. Recent studies have shown that even mild renal impairment is associated with high risk, hence kidney function markers are now being considered true sentinel indicators of cardiovascular risk.[2]

CC is a cysteine protease inhibitor protein produced by all nucleated cells and exhibits a highly stable synthesis rate. Its low molecular weight and high isoelectric point mean that the protein is almost entirely excreted by glomerular filtration. Concentrations of the protein are unaffected by age, sex, or protein intake, and there is greater sensitivity to small changes in glomerular filtration rate. Because of these characteristics, plasma CC concentrations are one of the best markers of glomerular filtration rate.[3] Several recent publications report a correlation between elevated CC concentrations and the development of cardiovascular complications in patients with coronary disease.

Koenig et al.[4] studied the usefulness of CC to predict future cardiovascular events in a cohort of 1033 patients who had been diagnosed with coronary disease within 3 months before inclusion. Patients with renal failure as assessed by plasma creatinine or creatinine clearance (CrCl) presented CC values in the top quintile, compared to those who had mild renal impairment or normal kidney function. No significant differences in the incidence of cardiovascular adverse events were found among patients with differing degrees of renal dysfunction as assessed by plasma creatinine (5.4% incidence of events with creatinine >106 μmol/L vs 7% incidence with creatinine<106 μmol/L; *P*=.63) or by CrCl (7% incidence of events in patients with CrCl<60 mL/min, 9% in patients with CrCl 60-90 mL/min, and 6.3% in patients with CrCl>90 mL/min; *P*=.1). There were significant CC-related differences in the probability of developing a cardiovascular event according to CC quintile (14% for the top quintile and 7.7%, 4.3%, 3.9%, and 5% for the remaining quintiles in descending order; *P*<.0001).

A Spanish study among patients with acute coronary syndrome showed that those with higher CC concentrations presented worse cardiovascular prognosis, even in the group of patients with normal estimated glomerular filtration rate, which could have implications for risk stratification in this patient group.[5] Additionally, Cepeda et al.[6] conducted the first study in Spain to determine the prevalence of high CC and its correlation with cardiovascular risk factors among the general population.

Based on the scientific evidence published in the literature in recent years, we believe that CC should be considered a better marker of kidney function than other common measurements (serum creatinine and glomerular filtration rate) and a practical application is likely to be found for the various clinical settings for cardiovascular diseases.

Alberto Domínguez-Rodriguez[a,*] and Pedro Abreu-Gonzalez[b]

[a]*Servicio de Cardiología, Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain*
[b]*Departamento de Fisiología, Universidad de La Laguna, Santa Cruz de Tenerife, Spain*

* Corresponding author:
E-mail address: adrvdg@hotmail.com (A. Domínguez-Rodriguez).

Available online 20 April 2012

REFERENCES

1. Górriz Teruel JL, Beltrán Catalán S. Valoración de afección renal, disfunción renal aguda e hiperpotasemia por fármacos usados en cardiología y nefrotoxicidad por contrastes. Rev Esp Cardiol. 2011;64:1182–92.
2. Dharnidharka VR, Kwon C, Stevens G. Serum cystatin C is superior to serum creatinine as a marker of kidney function: a meta-analysis. Am J Kidney Dis. 2002;40:221–6.

3. Shlipak MG, Katz R, Sarnak MJ, Fried LF, Newman AB, Stehman-Breen C, et al. Cystatin C and prognosis for cardiovascular and kidney outcomes in elderly persons without chronic kidney disease. Ann Intern Med. 2006;145:237–46.
4. Koenig W, Twardella D, Brenner H, Rothenbacher D. Plasma concentrations of cystatin C in patients with coronary heart disease and risk for secondary cardiovascular events: more than simply a marker of glomerular filtration rate. Clin Chem. 2005;51:321–7.
5. García Acuña JM, González-Babarro E, Grigorian Shamagian L, Peña-Gil C, Vidal Pérez R, López-Lago AM, et al. La cistatina C aporta más información que otros parámetros de función renal en la estratificación del riesgo de los pacientes con síndrome coronario agudo. Rev Esp Cardiol. 2009;62:510–9.
6. Cepeda J, Tranche-Iparraguirre S, Marín-Iranzo R, Fernández-Rodríguez E, Riesgo-García A, García-Casas J, et al. Cistatina C y riesgo cardiovascular en población general. Rev Esp Cardiol. 2010;63:415–22.

SEE RELATED ARTICLES:
DOI: 10.1016/j.rec.2011.08.012
DOI: 10.1016/j.rec.2012.02.008

doi:10.1016/j.rec.2012.02.005

Assessment of Renal Involvement by Cystatin C: A Forgotten Biomarker. Response

Valoración de la afección renal mediante la cistatina C: un biomarcador olvidado. Respuesta

To the Editor,

We appreciate the interest shown in our study published in your journal[1] and would like to make a few comments on the subject. As described by Domínguez-Rodriguez and Abreu-Gonzalez, serum cystatin C (CC) is a biological marker both for determining renal function and for cardiovascular prognosis, with enormously promising medical implications. In recent studies, CC has provided an estimated glomerular filtration rate (GFR) almost as accurate as traditional formulae based on creatinine levels adjusted for age, sex, and race, independently of the patient's muscle mass. An equation that includes CC in combination with serum creatinine levels, age, sex, and race provides even more exact estimates.[2]

Given the widespread circulation of *Revista Española de Cardiología*, the primary goal of the article was to inform the reader as to the importance of evaluating renal involvement as an early detection method for individuals with a high risk of cardiovascular events and promote swift action, all from a clinical standpoint.[1] Since CC is not commonly determined in clinical practice, it was not addressed in the review. We would thus like to thank these comments, which add to the information provided in the article.

However, despite the fact that CC could be a promising marker for renal function, for the stratification of the risk, specially in those patients with intermediate risk, there are certain limitations to the standardized use of CC as such a marker. To be specific:

- There is no standard reference value for measuring CC, and there is a great deal of intra-individual variability.[3]
- CC concentrations increase with age, especially in patients older than 80 years.[4] Thus, it is not clear whether increases in CC in these patients are related to different levels of renal function or other factors that are unrelated to GFR.
- Several different factors influence CC levels, such as hypothyroidism, some inflammation markers such as C-reactive protein, treatment with steroids, body fat, and diabetes.[5]
- Few laboratories have the capability to measure CC, and the cost is still quite higher than for determining GFR using serum creatinine levels.

Therefore, until the technique has become standardized and more cost-effective methods of measurement have been developed, we should focus on ensuring that 100% of patients with cardiovascular diseases have their GFR and urinary albumin excretion determined using formulas derived from creatinine levels and the urine albumin/creatinine ratio, respectively.

This does not mean that CC is not a viable marker, but its role in the detection of cardiovascular risk and GFR determination has not been well established. It is probably simply a matter of time.

Jose Luis Górriz Teruel* and Sandra Beltrán Catalán

Servicio de Nefrología, Hospital Universitario Dr. Peset, Valencia, Spain

* Corresponding author:
E-mail address: jlgorriz@senefro.org (J.L. Górriz Teruel).

Available online 3 May 2012

REFERENCES

1. Górriz Teruel JL, Beltrán Catalán S. Valoración de afección renal, disfunción renal aguda e hiperpotasemia por fármacos usados en cardiología y nefrotoxicidad por contrastes. Rev Esp Cardiol. 2011;64:1182–92.
2. Stevens LA, Astor BC. Estimating GFR using serum cystatin C alone and in combination with serum creatinine: a pooled analysis of 3,418 individuals with CKD. Am J Kidney Dis. 2008;51:395–406.
3. Caravaca F. Cistatina C sí pero... Nefrologia. 2006;26:421–5.
4. Shlipak MG, Sarnak MJ, Katz R, Fried LF, Seliger SL, Newman AB, et al. Cystatin C and the risk of death and cardiovascular events among elderly persons. N Engl J Med. 2005;352:2049.
5. Knight EL, Verhave JC, Spiegelman D, Hillege HL, De Zeeuw D, Curhan GC, et al. Factors influencing serum cystatin C levels other than renal function and the impact on renal function measurement. Kidney Int. 2004;65:1416.

SEE RELATED ARTICLE:
DOI: 10.1016/j.rec.2012.02.005

doi:10.1016/j.rec.2012.02.008