

## Background

Renal insufficiency in HIV infected patients may mean that the dose and regimen of combination antiretroviral therapy need to be adapted to reduce the risk of toxic effects in the short term and severe co-morbidity and increased risk of mortality in the long term.

There are a range of methods of quantifying renal function using serum creatinine. The use of each of these methods can lead to substantially different proportions of patients requiring dose adjustment [1]. There is also little published data on the prevalence of and outcomes following renal insufficiency in HIV positive populations [2].

We used two formulas and patients' measurements of serum creatinine to estimate patients' glomerular filtration rates to describe the prevalence of renal insufficiency in the population of HIV positive patients in the Netherlands. We also compared the results of the two formulas at a population level and presented the characteristics of patients with and without renal insufficiency.

## Methods

We used data from the national ATHENA cohort study [3] to estimate the prevalence of renal insufficiency. We defined renal insufficiency as:

- a confirmed moderately decreased estimated glomerular filtration rate (30 to 60 mL/min/1.73m<sup>2</sup>).
- a confirmed severely decreased estimated glomerular filtration rate (15 to 30 mL/min/1.73m<sup>2</sup>).
- confirmed kidney failure (estimated glomerular filtration rate under 15 mL/min/1.73m<sup>2</sup>).
- or kidney dialysis for a period of at least 91 days or a previous kidney transplant.

We estimated glomerular filtration rate using each patient's first routine or clinically indicated measurement of serum creatinine in 2008 and the Cockcroft-Gault [4] and Mayo Quadratic [5] formulas. We do not record data on race and hence did not use the Modification of Diet in Renal Disease or Chronic Kidney Disease Epidemiology Collaboration formulas.

If a patient's estimated glomerular filtration rate from this measurement was below 60 mL/min/1.73m<sup>2</sup>, we also estimated glomerular filtration rate from a measurement made at least 91 days earlier. Confirmed estimated glomerular filtration rate was defined as the highest level obtained at the two time points.

**Table 1. The number of 10,840 patients with moderately and severely decreased estimated glomerular filtration rate and kidney failure.**

	Estimated glomerular filtration rate mL/min/1.73m <sup>2</sup>			Kidney dialysis or transplant
	59 to 30	29 to 15	Under 15	
<i>Estimated using the Cockcroft-Gault formula</i>				
<b>Single measurement*</b>	272 (2.5%)	24 (0.2%)	13 (0.1%)	21 (0.2%)
<b>Confirmed</b>	184 (1.7%)	18 (0.2%)	6 (0.1%)	21 (0.2%)
<i>Estimated using the Mayo Quadratic formula</i>				
<b>Single measurement*</b>	118 (1.1%)	25 (0.2%)	18 (0.2%)	21 (0.2%)
<b>Confirmed</b>	71 (0.7%)	20 (0.2%)	9 (0.1%)	21 (0.2%)

\* First measurement of serum creatinine in 2008

## Results

A total of 10819 patients had at least one measurement of serum creatinine in 2008, but were not on kidney dialysis and had never had a kidney transplant, 19 were on long term dialysis and two had had a kidney transplant. Hence, the results presented are based on data from 10,840 patients.

The prevalence of renal insufficiency is 229/10,840 (2.1%) if the Cockcroft-Gault formula is used and 121/10,840 (1.1%) if the Mayo Quadratic formula is used (Table 1).

Patients with renal insufficiency, as defined using the Cockcroft-Gault formula, were more likely to be male, aged over 44 years, have become HIV positive via homosexual contact, to be on combination antiretroviral therapy and to die within a year of the first measurement of serum creatinine in 2008 (Table 2). However, further multivariate analyses are needed to confirm these relationships.

**Table 2. The characteristics of patients without and with renal insufficiency (RI).**

	Patients without RI n = 10611	Patients with RI n = 229	P-value**
<b>Male</b>	8398 (79%)	155 (68%)	< 0.0001
<b>Aged over 44 years</b>	5226 (49%)	196 (86%)	< 0.0001
<b>Born in the Netherlands</b>	6248 (59%)	132 (58%)	0.7059
<b>Homosexual transmission</b>	6163 (58%)	83 (36%)	< 0.0001
<b>On combination antiretroviral therapy*</b>	8864 (84%)	224 (98%)	< 0.0001
<b>On tenofovir*</b>	4889 (46%)	88 (38%)	0.0216
<b>Died within a year*</b>	123 (1%)	17 (7%)	< 0.0001

\* at/of the first measurement of creatinine in 2008.  
\*\* based on chi-squared tests.

## Conclusions

The prevalence of renal insufficiency in our population is low. However, estimating glomerular filtration rate using the Cockcroft-Gault rather than the Mayo Quadratic formula leads to nearly twice as many patients being classified as having renal insufficiency. This confirms earlier results [1], which showed that the prevalence of renal insufficiency can vary substantially depending on how glomerular filtration rate is estimated.

Our results underline the need for the standardization of definitions of renal function in HIV positive populations [2], particularly if they are to influence the type or dosage of antiretroviral medication that clinicians prescribe for individual patients.

## References

- [1] van Griensven J, Sopheak T, Koole O, Verpooten GA, Lynen L. Determination of kidney function before tenofovir initiation: four-fold difference in need of tenofovir dose reduction depending on method used. *JAIDS*. 2011 Jun 1; 57(2): e21-e23.
- [2] Mocroft A. The difficulties of classifying renal disease in HIV-infected patients. *HIV Med*. 2011 Jan;12(1):1-3.
- [3] van Sighem A, Smit C, Gras LA, van Sighem A, Smit C, et al. Monitoring Report 2011. Human Immunodeficiency Virus (HIV) Infection in the Netherlands. Stichting HIV Monitoring, Amsterdam, The Netherlands. Available to download from <http://www.hiv-monitoring.nl>.
- [4] Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron*. 1976; 16(1):31-41.
- [5] Rule AD, Larson TS, Bergstralh EJ, Slezak JM, Jacobsen SJ, Cosio FG. Using serum creatinine to estimate glomerular filtration rate: accuracy in good health and in chronic kidney disease. *Ann Intern Med* 2004 Dec 21;141(12):929-37.

## Contact

Rebecca Holman  
Stichting HIV Monitoring  
E: r.holman@amc.uva.nl  
[www.hiv-monitoring.nl](http://www.hiv-monitoring.nl)