

# Systematic Renal Function Evaluation Using Iohexol or Inuline Clearance Before Lung Transplantation in Adult CF patients

E. Novel-Catin<sup>1</sup>; S. Pelletier<sup>1</sup>; R. Nove Josserand<sup>2</sup>; Q. Reynaud<sup>2</sup>; S. Durupt<sup>2</sup>; L. Dubourg<sup>3</sup>; M. Laville<sup>1</sup>; D. Fouque<sup>1</sup>; I. Durieu<sup>2</sup>



1- Department of nephrology, Hôpital Lyon Sud, Pierre Bénite, France 2- Cystic Fibrosis Adult Center, Hôpital Lyon Sud, Pierre Bénite, France 3- Explorations Fonctionnelles Rénales, Hôpital Edouard Herriot, Lyon, France



## INTRODUCTION

Cystic fibrosis (CF) is not particularly known to have any significant renal consequences by itself, despite the presence of the CFTR receptor on all segments of the nephron (1).

Better management of the disease has allowed for a significant improvement in CF patient survival over the last decades, with a median life expectancy of 41 years in 2011 (2).

The betterment of this population's life expectancy raises the question of the long term renal consequences of both the disease itself and its treatment. Around 30% of cystic fibrosis patient suffer from insulin-requiring diabetes. Moreover, one of the pillars of the treatment of lung exacerbations is nephrotoxic antibiotics such as aminoglycoside or cotrimoxazole.

Due to low muscle mass, the usual equations estimating the glomerular filtration rate (GFR) such as Cockcroft or CKD-EPI are not adapted to the CF population (3).

The aim of our study was to measure precisely the GFR of adult CF patients before lung transplantation using a gold standard method.

## METHODS

Iohexol or Inuline clearance was realized in 25 adult CF patients from the Cystic Fibrosis Adult Center of the Lyon Sud University Hospital in Lyon, France. Renal clearance measurement was realized when they entered the lung transplant waiting list (n=17).

No patient was treated with aminoglycoside at the time of GFR measurement.

BMI, history of diabetes mellitus and high blood pressure were recorded. Exposure to IV aminoglycoside within 5 years before GFR measurement was calculated. Urine samples were collected to check for albuminuria.

## RESULTS

Precise exposure to aminoglycoside therapy over the last 5 years before GFR measurement was available for 23 of the 25 patients. The most used aminoglycoside was tobramycin at the mean posology of 7,6 mg/kg a day.

Mean measured GFR was 106mL/min/1.73m<sup>2</sup>, ranging from 46 to 138mL/min/1,73m<sup>2</sup> (table 2). 52% of patients had significant micro albuminuria.

Only one patients had an abnormal GFR of 46 mL/min/1,73m<sup>2</sup> and had a history of acute renal injury associated with glycopeptide overdose.

Table 1 : Patient characteristics (n=25)

Male	36%
Mean age (yrs)	32 (22-50)
Mean Body mass index (kg/m <sup>2</sup> )	19 (15-25)
History of high BP	1%
History of Diabetes	28%
Albuminuria 30 -300mg/L	52%
Homozygous $\Delta F508$ mutation	32%
Mean exposure to IV aminoglycoside (days)	165 (60-280)

Table 2 : Estimated and measured GFR results in 25 CF patients

Mean estimated GFR (CKD EPI)	125 mL/min/1,73m <sup>2</sup> (ranging 77-167)
Mean measured GFR (Iohexol/inulin)	106 mL/min/1,73m <sup>2</sup> (ranging 46-138)

## DISCUSSION

This is to our knowledge the first time that the renal function of CF patients is systematically measured using a gold standard method before lung transplantation. Our cohort seems representative of the adult CF population, with a wide range of age (See table 1) and the same prevalence of diabetes mellitus (4).

There seems to be no decline in the GFR of adult CF patients before lung transplantation despite a high prevalence of diabetes and extensive use of aminoglycoside therapy at the high doses of 7,6mg/kg/day when the FDA approved posology for the non CF population if only 3mg/kg/day.

The only patient with a significantly decreased GFR had a history of acute renal injury associated with glycopeptide overdose in an ICU setting.

Our work also seems to confirm that the CKD EPI equation systematically over estimates the actual GFR of CF patients, sometimes by up to 50% (See graphic 1).

## CONCLUSION

There is no significant decline in kidney function in adult patients with CF before lung transplantation.

Our next goal will be to longitudinally follow these patients and repeat GFR measurement using the same gold standard method 12 to 18 months after lung transplantation to study its impact on kidney function.

### References

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Graphic 1 : difference between Gold Standard and estimated GFR

