



Kidney function in acromegaly: evidence from a long-term observational study

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Accepted: 24 March 2025
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Abstract

Purpose Growth hormone (GH) and insulin-like growth factor 1 (IGF-1) are critical regulators of renal development and function. Acromegaly, characterized by chronic GH hypersecretion, leads to renal hypertrophy and glomerular hyperfiltration. While immediate treatment of acromegaly mitigates hyperfiltration, the long-term risk of renal damage in treated patients remains unclear. Our study aimed to assess renal function over time in patients with acromegaly who were followed long-term at our institution.

Methods This study analyzed 80 patients with acromegaly from a single center. Creatinine values were recorded to assess kidney function before and after treatment. The estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI 2021 formula. eGFR variations were evaluated over the first 12 months after treatment (acute slope) and during long-term follow-up with a mean duration of 11.28 years (chronic slope). Descriptive statistics and multivariable regression analyses were performed.

Results Among the 80 patients (43.7 years, 46 male), 51 underwent surgery (11 of whom also received subsequent radiotherapy), while 29 received exclusively medical therapy. Comorbidities included diabetes (31.25%) and hypertension (65%). eGFR decreased acutely after treatment in all groups, with a more pronounced decline in surgically treated patients (mean -15.15 mL/min/1.73 m²; $p=0.042$). The mean chronic eGFR loss was -1.28 mL/year, with age (OR 1.09 per year) and diabetes (OR 5.66) significantly associated with a greater decline in eGFR ($p<0.01$).

Conclusions Renal hyperfiltration in acromegaly tends to normalize following treatment, with a more rapid response observed in patients who undergo surgery. Chronic kidney disease is highly prevalent in acromegaly and is closely linked to diabetes, which further contributes to the increased cardiovascular risk seen in these individuals.

Keywords Acromegaly · Kidney · CKD · IGF-1 · eGFR · GH

Introduction

Acromegaly is characterized by the hypersecretion of growth hormone (GH), usually caused by a pituitary adenoma, leading to abnormalities in multiple target organs,

including the kidney. Exposure to supraphysiological GH levels in patients with acromegaly has been associated with renal hypertrophy, increased glomerular filtration, extracellular volume expansion, and hypercalciuria [1].

Although treatment for acromegaly can improve kidney hyperfiltration [2, 3], no study to date evaluated whether different treatment modalities influence this outcome. Emerging evidence suggests an association between acromegaly and an increased risk of renal cysts [4] and end-stage renal disease (ESRD) [5], yet long-term renal function in this condition remains poorly characterized.

The aim of our study was to evaluate post-treatment renal function and its changes over time in a large cohort of patients followed long-term at our institution.

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Table 1 Demographic and clinical characteristics of our cohort of patients with acromegaly. Data are expressed as mean (standard deviation) for continuous variables and as frequency (percentage) for categorical variables. BMI, body mass index; eGFR, estimated glomerular filtration rate; DA, dopamine agonist; SRL, somatostatin receptor ligands; GHRA, growth hormone receptor antagonist

Demographic and Clinical Characteristics	Acromegaly cohort (n=80)
Age at diagnosis (years)	43.7 (14.0)
Duration of disease (years)	22.3 (12.7)
Sex (F)	34 (42.5%)
Baseline BMI (kg/m ²)	26.9 (4.9)
Baseline eGFR (mL/min/1.73 m ²)	99.0 (19.3)
Comorbidities at baseline	
Diabetes	25 (31.3%)
Hypertension	52 (65.0%)
Dislipidemia	29 (36.3%)
Acromegaly treatment	
Surgery	51 (63.8%)
Radiotherapy	11 (13.8%)
Medical Therapy (at last follow-up)	58 (75.0%)
DA	6 (10.3%)
DA+SRL	8 (13.8%)
SRL	34 (58.6%)
GHRA	10 (17.2%)
Remission	55 (68.8%)

Table 2A Acute loss of eGFR. Linear regression analysis examining the acute loss (up to one year after intervention) of estimated eGFR associated with different treatment groups and patients' characteristics

Acute Loss of eGFR	Coefficient	SE	p-value
Therapy (mean baseline eGFR±SD)			
(i) Medical Therapy (101.3 ml±12.3)	Reference		
(ii) Medical Therapy+Surgery* (103.6 ml±13.6)	1.16 ml	5.62	0.838
(iii) Only Surgery* (107.9 ml±12.3)	-13.32 ml	6.37	0.049
Age (per year)	-0.46 ml	0.22	0.054
Sex (female)	1.45 ml	4.11	0.726
Diabetes	2.13 ml	5.43	0.7
Hypertension	-7.05 ml	4.61	0.14

* Compared to Medical Therapy (reference variable)

Population and methods

Eighty patients with acromegaly from Papa Giovanni XXIII Hospital, Bergamo, were identified through electronic health records. Clinical data were collected from the initial evaluation to the most recent visit. All patients provided informed consent for the anonymized use of their data.

Creatinine values were recorded from the first therapeutic intervention. If pre-treatment values were unavailable, the earliest available creatinine measurement was used. The estimated glomerular filtration rate (eGFR) was calculated

using the CKD-EPI 2021 formula. Acute eGFR changes (acute slope) were determined by comparing pre-treatment values with those obtained within 12 months post-treatment. Chronic eGFR decline (chronic slope) was assessed through regression analysis of eGFR values in patients with at least three post-intervention creatinine measurements.

Chronic Kidney Disease (CKD) was defined as an eGFR of less than 60 mL/min/1.73 m², while ESRD as an eGFR of less than 15 mL/min/1.73 m².

Descriptive statistics were used to summarize patient characteristics, with continuous variables presented as mean values (standard deviation) and categorical variables as frequencies and percentages. Multivariable regression analysis was performed to examine acute and chronic slopes across treatment groups, adjusting for relevant covariates. A two-sided p-value ≤ 0.05 was considered statistically significant. All analyses were conducted using STATA 16.1.

Results

Demographic and clinical characteristics are detailed in Table 1. The mean age at diagnosis was 43.7 (SD 14) years, mean disease duration was 22.3 (SD 12.7) years. Forty-six patients (57.5%) were male. Eight patients (10%) died during follow-up.

Transsphenoidal (TNS) surgery was performed in 51 patients (63.8%), three of whom required a second TNS surgery. Eleven patients (13.7%) underwent radiotherapy, including 9 after the first surgery and 2 after the second. Thirty-one patients (60.8%) did not achieve remission (defined as normalized IGF-1 [6]) and were subsequently treated with medical therapy. Primary medical therapy was administered to 29 patients (36.2%). Overall, 55 out of 80 patients (68.7%) achieved remission. Comorbidities included diabetes in 25 patients (31.3%), and hypertension in 52 (65%).

Among the 80 patients, 29 (36.2%) had pre- and post-treatment creatinine measurements within 12 months of intervention. These patients were categorized into three groups: (i) medical therapy only (n=6), (ii) medical therapy followed by surgery (n=12), and (iii) surgery only (n=11). The mean acute eGFR loss was -6.64 mL/min/1.73 m² (SD 9.06) in group (i), -3.22 mL/min/1.73 m² (SD 8.56) in group (ii), and -15.15 mL/min/1.73 m² (SD 13.87) in group (iii), with significant differences between groups (p=0.042, Kruskal-Wallis test).

Multivariable linear regression (Table 2A) examined the relationship between acute eGFR changes and treatment groups, adjusting for demographic and clinical factors. The surgery-only group (iii) exhibited a significantly steeper

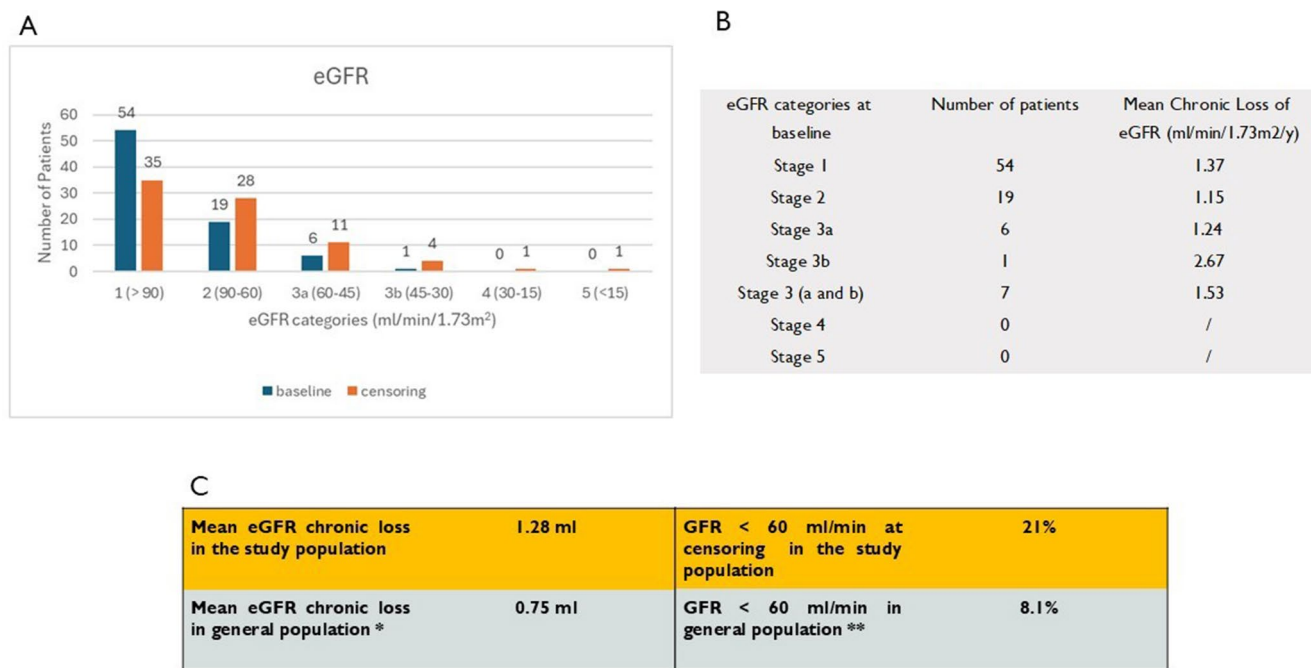


Fig. 1 Histogram illustrating the distribution of patients across CKD stages at baseline and at study censoring, depicting the associated chronic loss of eGFR (in mL/min/1.73 m²) for each CKD stage. * Mean chronic loss of our population was compared to a longitudinal

Table 2B Risk of CKD. Logistic regression analysis showing the probability of having CKD at last follow-up, based on treatment groups and patients' characteristics

CKD	OR	SE	p-value
Surgery	1.15	0.81	0.837
Age (per year)	1.09	0.35	0.008
Sex (female)	0.77	0.53	0.708
Diabetes	5.66	3.85	0.011
Hypertension	1.63	1.49	0.586

SE, Standard Error; OR, Odds Ratio; eGFR, estimated Glomerular Filtration Rate; CKD, Chronic Kidney Disease

decline in eGFR compared to the medical therapy group ($p=0.049$).

The mean follow-up duration for chronic slope evaluation was 11.68 (SD 5.5) years. The mean chronic eGFR decline during follow-up was -1.28 (SD 1.52) mL/min/1.73 m² per year. Of the 80 patients, 7 (9%) had CKD at baseline, while 17 (21%) developed CKD by the study's conclusion (Fig. 1A).

At the univariable analysis, age (OR 1.12 per year, $p<0.01$), presence of diabetes (OR 7.02, $p<0.01$) and of hypertension (OR 5.29, $p=0.04$) were significantly associated with CKD, whereas no significant differences were found between patients in remission and those with uncontrolled disease. Similarly, no significant association was observed for medical treatment (Supplementary Table 1).

study of renal function in healthy subjects [7]. ** Prevalence of CKD in our population was compared to a pooled meta-analysis assessing prevalence of CKD in general population [16]

At the multivariable logistic regression (Table 2B) age (OR 1.09 per year, $p=0.008$) and diabetes (OR 5.66, $p=0.011$) confirmed as significant predictors of CKD.

Discussion

Our study confirms that glomerular hyperfiltration caused by excessive GH secretion is acutely reversible with treatment [2] and reveals that this effect is more pronounced in patients undergoing surgery than in those receiving medical therapy. This likely reflects the rapid suppression of GH hypersecretion achieved through surgery, whereas medical therapy requires more time to normalize IGF-1 levels.

In the long-term, patients with acromegaly experience a greater decline in eGFR compared to the healthy population. Previous studies have reported a mean yearly eGFR decline of 0.75 mL/min in a relatively healthy cohort [7], which included patients with diabetes but excluded those with hypertension or renal disease, and of 0.63 mL/min in healthy kidney donors [8]. In contrast, the eGFR decline in our cohort of patients with acromegaly was nearly twice these rates.

By the end of follow-up, 21% of patients had CKD, underscoring acromegaly as a significant risk factor for kidney damage, contributing to greater renal function loss than aging alone. Consistent with our findings, Hong et

al. [5] reported an association between acromegaly and an increased risk of ESRD. In our cohort, the prevalence of ESRD was 1.25%, higher than the estimated 0.1% in the general population [9]. However, this finding should be interpreted with caution, as it is based on a single case out of 80 patients.

Acromegaly is associated with comorbidities, particularly diabetes and hypertension, both of which negatively impact renal function. In our cohort, diabetes was significantly associated with a greater chronic decline in eGFR, supporting findings from a large cohort study [5] that identified diabetes as a mediator of renal damage risk in acromegaly. Conversely, no predictive relationship between hypertension and eGFR decline was identified in our cohort. These findings suggest that the combined effects of prolonged GH excess and a higher prevalence of diabetes in patients with acromegaly outweigh the impact of hypertension, which, in contrast, is reported to be the leading cause of ESRD in general population [10]. Together, these factors contribute to an increased risk of adverse cardiovascular events in individuals with acromegaly.

No statistically significant associations were observed between disease status (active vs. remission) and the progression of chronic kidney disease (CKD). Our findings agree with other studies, which also found no differences in disease-related comorbidities prevalence between controlled and uncontrolled patients [11, 12]. We hypothesize that the renal function deterioration in acromegaly may primarily be driven by comorbidities, particularly diabetes, rather than directly correlating with disease control.

We also considered the potential impact of treatment with somatostatin receptor ligands (SRL) but found no association with chronic eGFR changes. In evaluating this finding, it has to be considered the impact of several confounding factors. Somatostatin receptor ligands (SRLs) have demonstrated potential in the treatment of chronic kidney disease by reducing renal hyperfiltration and glomerular hypertension [13]; However, they also elevate the risk of hyperglycemia, particularly with pasireotide [14], which could exacerbate kidney damage. This risk can be managed through careful monitoring of diabetes and timely interventions. Additionally, improvements in acromegaly achieved with these therapies may contribute to better glycemic control [15]. Finally, the cohort receiving SRL comprised patients either ineligible for surgery or with incomplete remission following surgery, which may introduce a selection bias.

Limitations of our study include the availability of pre-operative data for less than half of the patients, and the heterogeneity of the study cohort in terms of clinical characteristics and follow-up duration. Furthermore, the albumin/creatinine ratio (ACR) was not consistently measured during the follow-up, limiting our ability to classify the degree

of cardiorenal risk more precisely. On the other hand, to the best of our knowledge, our study is the first to analyze the long-term progression of renal function in patients with acromegaly, which represents its main strength.

In conclusion, our study demonstrated that:

- a). Acute treatment of acromegaly leads to normalization of renal hyperfiltration state associated with the disease, occurring more rapidly in surgically treated patients than in those receiving medical therapy.
- b). A significant proportion of patients with acromegaly develop CKD, particularly those with diabetes mellitus.

Given the frequent coexistence of hypertrophic cardiomyopathy and elevated cardiovascular risk in acromegaly, our findings emphasize the need for careful monitoring and management of cardiovascular risk factors in these patients. Specifically, our data highlight the importance of monitoring renal function (eGFR and ACR), and considering the early use of renin-angiotensin system (RAS) inhibitors, sodium-glucose cotransporter 2 inhibitors (SGLT2i), and glucagon-like peptide-1 receptor agonists (GLP-1 RAs), particularly in patients with diabetes mellitus, in light of recent data demonstrating their ability to mitigate cardio-renal -metabolic risk.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11102-025-01520-5>.

Author contributions All authors whose names appear on the submission-made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data; or the creation of new software used in the work; -drafted the work or revised it critically for important intellectual content; -approved the version to be published; -agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding Open access funding provided by Università degli Studi di Milano - Bicocca within the CRUI-CARE Agreement. This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

Ethical approval Data collection and analysis were approved by an appropriate Institutional Review Board of the local ethical committee. The study was performed in accordance with the Helsinki Declaration of 1964 (and its later amendments) and Good Clinical Practice Guidelines and agreed with national regulations.

Consent to participate/publish Informed consent was obtained from all individual participants for both participation in the study and publication of the results.

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