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Continental variations in IgA nephropathy among Asians

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Abstract

Background/Aims—Local variations in patient demographics and medical practice can contribute to differences in renal outcomes in patients with IgA nephropathy. We report the experiences of two groups of Asians with IgA nephropathy across continents.

Materials and methods—We retrospectively examined two cohorts of Asian patients with IgA nephropathy from The King Chulalongkorn Memorial Hospital registry, Thailand (1994 – 2005), and The Metropolitan Toronto Glomerulonephritis registry, Canada (1975 – 2006), and compared their baseline characteristics. Slope of estimated glomerular filtration rate (eGFR) in each group was approximated using separate repeated measures regression models for each country.

Results—There were 152 Canadian and 76 Thai patients. At the time of first presentation, Thai patients were more likely to be female (63.2 vs. 44.1%, $p = 0.01$), have less baseline proteinuria (1.2 vs. 1.7 g/d, $p = 0.08$) and more likely to receive angiotensin-converting enzyme inhibitors (ACE-I) or angiotensin receptor blockers (ARB) (64.0 vs. 15.2%, $p < 0.01$), or prednisone (41.3 vs. 4.6%, $p < 0.01$). The annual change in estimated glomerular filtration rate (eGFR) for the Thai and Canadian groups were $-0.82 \text{ ml/min/1.73 m}^2/\text{year}$ and $-3.35 \text{ ml/min/1.73 m}^2/\text{year}$, respectively, after adjustment for age, sex, mean arterial pressure (MAP), proteinuria, body mass index, Haas histological grade, chronicity scores and baseline medications.

Conclusions—Although disease severity was similar among IgA nephropathy patients in Canada and Thailand, more Thai patients were on ACE-I/ARB or prednisone therapy at baseline. Further prospective research is needed to explore international differences in demographic and environmental factors, health resources, and disease management to determine how they may impact long-term outcomes in Asians with IgA nephropathy.

Keywords

IgA nephropathy; Asians; renal function; geographical variation; clinical presentation

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Conflict of interest statement

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Introduction

IgA nephropathy, first described by Berger in 1969, is still the most common primary glomerulonephritis worldwide [Berger 1969, Levy and Berger 1988]. The prevalence of IgA nephropathy varies between people of different ethnicities and is specifically higher in Asian patients. IgA nephropathy is the cause of 32.4 – 42% of primary glomerulonephritis in East/Southeast Asia [Szeto et al. 2001, Woo et al. 1999, Yu et al. 2005]. In comparison its prevalence in Australia, Finland and North America is 2 – 10% [Donadio and Grande 2002]. In addition, patients living in the USA who are of Asian and the Pacific Island background have higher rates of IgA nephropathy than other glomerular lesions [Hall et al. 2004] and among people living in Australia, IgA nephropathy is more often reported as the cause of ESRD in East and Southeast Asian-born patients compared to those born in the Middle East or in Southern Europe [Stewart et al. 2004].

Despite apparent geographic and ethnic variations in the prevalence of IgA nephropathy, few studies have described international differences in disease characteristics and practice patterns. Geddes et al. [2003] reported differences in outcomes among IgA nephropathy patients of primarily Caucasian background in Canada, Finland, Scotland and Australia. Differences in the indications for kidney biopsy between Finland and Canada partly accounted for lower glomerular filtration rates, greater proteinuria and higher mean arterial pressures (MAP) at presentation in Canada compared to Finland.

Few studies have examined the regional variations in Asian patients with IgA nephropathy between countries. The purpose of this study was to describe baseline features and rates of renal function decline in two groups of Asian patients with IgA nephropathy at two centers, one from Bangkok, Thailand, and the second from Toronto, Canada.

Subjects and methods

Study design, data sources and patient selection

We retrospectively studied patients with biopsy-proven IgA nephropathy from The King Chulalongkorn Memorial Hospital (KCMH) in Bangkok, Thailand (1994 – 2005) and The Metropolitan Toronto Glomerulonephritis registry in Toronto, Canada (1975 – 2006), respectively. We included all registry patients of Asian race who had at least three estimated glomerular filtration rate (eGFR) measurements and excluded those with eGFR values < 15 ml/min/1.73 m² or those with biopsy tissue reported as inadequate (< 10 glomeruli and 3 arterioles). Patients were also excluded if there were coexisting conditions suggestive of a secondary cause for the IgA deposition (such as systemic lupus erythematosus (SLE), or Henoch-Schoenlein purpura (HSP)), or systemic conditions that are associated with renal disease (e.g. diabetes mellitus, hepatitis B or C virus infection).

Demographic and clinical characteristics

Both the Thai and Canadian registries collected clinical and demographic information including age, sex and time-updated information on body mass index (BMI), systolic (SBP) and diastolic blood pressures (DBP) and urine protein-to-creatinine ratio or a 24-hour urine protein and serum creatinine values. The protein-to-creatinine ratio was utilized to estimate to the 24-hour urine protein when a 24-hour urine collection was not available for a patient [Ginsberg et al. 1983]. Body surface area (BSA) was recorded in the Canadian registry and was calculated for the Thai data, using the height and weight measurements. BMI was present in the Thai registry but calculated for the Canadian patients using height and weight values. For both groups of patients, the mean arterial pressure (MAP) was calculated using the equation: $MAP = 2/3(DBP) + 1/3(SBP)$. Estimated glomerular filtration rates (eGFR) were calculated using the abbreviated Modification of Diet in Renal Disease (MDRD) formula

[Wetzels et al. 2007]. Medications were listed in a dichotomous yes/no fashion at each visit for each patient. These were aggregated into the following 4 groups: (1) angiotensin converting enzyme inhibitors (ACE-I) or angiotensin receptor blockers (ARB), (2) other antihypertensive agents (non-ACE-I/ARB), (3) prednisone and (4) other immunosuppressive agents, which included azathioprine or cyclophosphamide.

Renal biopsy evaluation

Renal biopsies were interpreted and reported by local pathologists in the two countries. All biopsy reports were reviewed by one nephrologist and assigned a Haas class and chronicity score [Haas 1997, To et al. 2000]. Glomerular sclerosis was graded on a scale of 1 – 3 as follows: 1) 0 – 25% of the glomeruli had sclerosis, 2) 25 – 50% sclerosis, and 3) > 50% sclerosed. The amount of tubular atrophy was graded as follows: 0: absent or < 5%, 1) 5 – < 25% atrophy, 2) 25 – 50%, and 3) > 50% atrophy. Interstitial fibrosis was graded on the same scale as tubular atrophy. Hyaline arteriosclerosis was defined as the presence of arteriolar hyaline or protein-aceous exudation with or without smooth muscle hyperplasia or luminal reduction and was scored as present (1) or absent (0) [To et al. 2000]. The chronicity score was calculated as the sum of the glomerular, tubular, interstitial and arterial scores.

Statistical analysis

Baseline characteristics were defined as the proportion, mean and median values for dichotomous, normal and non-normal continuous variables, respectively, for data collected within the first 3 months of entry into the registry. Standard deviations and inter-quartile ranges follow mean and median values, respectively. Dichotomous variables were compared between the Thai and Canadian groups using χ^2 -tests. Normal and non-normal continuous variables were compared between the two groups using two-sample t-tests and Wilcoxon rank-sum tests, respectively.

The slopes of the estimated glomerular filtration rates (eGFR) over time were calculated for the Canadian and Thai patients in two separate models. Longitudinal trends in eGFR were modeled using generalized estimating equation (GEE) methods to account for repeated measures on each subject. These models were adjusted for age, sex, MAP, proteinuria, body mass index, Haas histological grade, chronicity scores and baseline medications. All analyses were conducted using SAS version 9.1 (SAS Institute Inc., Cary, NC, USA).

Comparison of medication use

Given that the beginning of the Canadian registry predates the introduction of angiotensin-converting enzyme inhibitors (ACE-I) or angiotensin receptor blockers (ARB) to Canada, an analysis comparing the use of ACE-I/ARB between Canadian and Thai patients after 1994 (the year the Thai registry began) was performed. We also examined use of ACE-I/ARB and prednisone over the total follow up period, rather than only at baseline in the Thai and Canadian groups. These differences were compared with χ^2 -tests. Since prednisone therapy may be an indicator of disease severity and many Thai patients received prednisone, we performed stratified analyses in the Thai group to determine if there were significant differences in patient characteristics or demographics in patients who received vs. did not receive baseline prednisone. In the Thai group, we determined the number of patients with positive vs. negative eGFR slopes and compared the proportion of baseline prednisone use between these groups.

Ethics

Ethics approval was obtained from the Institutional Review Board of University Health Network in Toronto, Canada, and King Chulalongkorn Memorial Hospital in Bangkok, Thailand.

Results

Patients

There were initially 121 and 177 patients in the Thai and the Canadian registries, respectively. We excluded 45 Thai and 25 Canadian patients of Asian origin due to missing baseline data or because less than 3 serum creatinine values were recorded. The final study sample consisted of 76 Thai and 152 Canadian patients of Asian ethnic origin. The mean times of follow-up in the Thai and Canadian patients ($\pm$ standard deviations) were 1.5 ± 1.2 and 3.3 ± 2.4 years, respectively ($p < 0.01$).

Baseline characteristics and estimated GFR

Among Thai patients the mean baseline age was 35.3 ± 11.4 years, 63.2% were female. Most patients had relatively well controlled hypertension (mean systolic and diastolic blood pressures of 128.7 ± 16.0 mmHg and 81.9 ± 8.5 mmHg, respectively), mild proteinuria (median value 1.2 ($0.7 - 2.3$) g/d), and renal dysfunction (median eGFR value 57.2 ($34.4 - 84.0$) ml/min/ 1.73 m^2) (Table 1). At baseline, 64% of patients were on ACE-I and 41% were on prednisone. The unadjusted and adjusted slopes of eGFR with 95% confidence intervals for the Thai group were -0.92 ($-2.4, 0.5$) ml/min/ 1.73 m^2 /year and -0.82 ($-3.3, 1.7$) ml/min/ 1.73 m^2 /year, respectively. In the Thai group, baseline chronicity score had a significant effect on slope of eGFR, with each one point increase in the chronicity score associated with an 8 ml/min/ 1.73 m^2 /year decrease in GFR ($p < 0.01$). Increasing baseline age was associated with more rapid decline in eGFR but this did not reach statistical significance ($p = 0.06$) (Table 2).

In the group from Canada, the mean baseline age was 39.0 ± 13.0 years and 44.1% were female. There was also relatively well controlled hypertension among the Canadians who had systolic and diastolic blood pressures of 130.6 ± 19.8 mmHg and 82.9 ± 11.9 mmHg, respectively. Median baseline urine protein excretion was 1.7 ($0.9, 2.7$) g/d, and eGFR was 64.9 ($47.6, 81.4$) ml/min/ 1.73 m^2 . At baseline, 15% of patients were on ACE-I and 5% were on prednisone (Table 1). The unadjusted and adjusted slopes of eGFRs with 95% confidence intervals for the Canadian group were -2.42 ($-3.29, -1.54$) ml/min/ 1.73 m^2 /year and -3.35 ($-4.6, -2.1$) ml/min/ 1.73 m^2 /year, respectively. Baseline ACE-I/ARB ($p < 0.01$) and prednisone ($p < 0.01$) utilization had a significant impact on slope of eGFR in the Canadian group with temporal changes in eGFR being more rapid in those that had baseline use of ACE-I/ARB and less rapid in those that had baseline use of prednisone (Table 3).

Comparisons of baseline features and medication use

Several significant differences between the countries were noted. Thai patients were more likely to be female and were more likely to have been prescribed angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACE-I/ARB), prednisone and other immunosuppressive agents (mainly azathioprine) at baseline, while Canadian patients were more likely to have been prescribed non ACE-I/ARB antihypertensive medication at baseline. Canadian patients had greater 24-hour urine protein excretion, however, this difference did not reach statistical significance with a p value of 0.08 (Table 1).

The post-1994 Canadian group had 30.0% of their patients on ACE-I/ARB at baseline compared to 64.0% of the Thai group ($p < 0.01$). Over the course of the follow-up period, 70.9% of Canadian patients and 90.7% of Thai patients received ACE-I/ARB therapy ($p < 0.01$). Although significantly more Thai patients received ACE-I/ARB over the follow-up period, there was a 57% increase in ACE-I/ARB utilization in the Canadian group between baseline and overall time. 60.0% of Thai patients and 21.2% of Canadian patients were on prednisone at some point during the overall follow-up period ($p < 0.01$).

Thai patients who received prednisone at baseline were younger, 32.1 vs. 38.9 years ($p = 0.008$), and had a higher baseline eGFR, 71.8 ml/min/1.73 m²/year vs. 56.9 ml/min/1.73 m²/year ($p = 0.04$), than Thai patients who did not receive prednisone at baseline. There were no other significant between group differences including baseline proteinuria. There were 48 and 28 patients, respectively, who had eGFR slopes that decreased and increased over time. Prednisone was used equally between these groups at baseline (42.1 and 39.3%, $p = 0.83$, in the negative and positive eGFR slope groups, respectively).

Discussion

We report several differences in the clinical characteristics and management of Asian IgA nephropathy patients in Thailand and Canada. In the Thai group, IgA nephropathy patients were more likely to be female and treated with ACE-I/ARB, steroids and immunosuppressants, despite similar disease severity at presentation to the Canadian patients. The adjusted annual rate of eGFR decline was also lower in the Thai group: -0.82 ($-3.3, 1.7$) ml/min/1.73 m²/year vs. -3.35 ($-4.6, -2.1$) ml/min/1.73 m²/year. This suggests that earlier therapy with these medications may be beneficial in slowing progression of chronic kidney disease (CKD) in IgA nephropathy. The role of gender differences and the timing and duration of therapy in the management in of IgA nephropathy need to be confirmed and prospectively evaluated in future studies.

In a previous study, Riansuwan et al. [2006] reported baseline characteristics on a larger group of patients with IgA nephropathy from the same Thai registry used in this study and found that the average age was 36 years, male: female ratio was 1 : 1.2; 30% of patients had hypertension and 34% had serum creatinine value higher than 132.6 μ mol/l (1.5 mg/dl) and urine protein values of more than 3 g/d. We build on this work by determining the slope of eGFR over time in this group and the Canadian group and comparing the baseline features between the Thai and Canadian groups. The Thai group had a slope of eGFR consistent with minimal change over time whereas the Canadian group experienced a significant decline in eGFR. Proteinuria is associated with worse prognosis and faster decline in renal function [Bartosik et al. 2001, Milovanceva-Popovska et al. 2006]. The Thai patients received more aggressive initial therapy for IgA nephropathy despite similar or less severe disease at baseline than the Canadian group. This may help account for the smaller magnitude of the decrement in eGFR over time in the Thai group.

Interestingly in the Canadian group, ACE-I/ARB use was correlated with a more rapid decline in eGFR. One plausible explanation is that we examined the role of baseline features and on eGFR. ACE-I/ARB therapy can cause a physiologic but reversible fall in the eGFR and cause a rise in serum creatinine levels. This may have caused some patients to have lower eGFR initially. It would be interesting to determine effects of ACE-I/ARB on eGFR over time in the Thai group once this data is accrued. It is possible that the differences in baseline medication utilization might have contributed to the differences in slopes over time between the two groups, however, this finding needs further confirmation in future studies. A second potential explanation for the unusual finding of the negative correlation between ACE-I/ARB utilization and eGFR in the Canadian group in this study may be that patients who had more severe disease received these medications; however, this study was conducted retrospectively and, therefore, not designed to answer this specific question.

Prednisone is commonly used in treatment of IgA nephropathy for patients with prognostic indicators for worse renal outcome such as at least 1 gram per day of proteinuria or abnormal renal function. It is not as frequently used at baseline without having these features. Even though the Thai and Canadian groups had similar baseline 24-hour urine protein excretion and eGFR values, the Thai group received significantly more prednisone and ACE-I/ARB therapy

than the Canadian group at baseline and over the follow-up period as well. Previous studies of patients with IgA nephropathy have shown that angiotensin-converting enzyme inhibitors significantly reduce proteinuria and prevented decline in renal function over time [Praga et al. 2003]. Corticosteroids decrease proteinuria [Horita et al. 2007, Kobayashi et al. 1996] and slow the reduction in renal function in those with proteinuria [Horita et al. 2007, Pozzi et al. 1999]. It might be suggested that the magnitude of eGFR decline was smaller in the Thai vs. Canadian group because of increased treatment with prednisone among Thai patients; however, it is not possible for us to demonstrate this, given the retrospective nature of this study. The possibility that prednisone may improve prognosis in earlier stages of IgA nephropathy warrants investigation in future prospective studies.

There are a few potential explanations for the baseline differences in medication use observed between the two groups in this study. The Canadian registry was initiated much earlier than the Thai registry. The Metropolitan Toronto registry began in 1975, at which point ACE-I and ARB medications were not commercially available and not standard of care for renal disease. Several of the Canadian patients (> 50%) entered the registry prior to the start of the Thai registry (1994). It is, therefore, not surprising that there is a large baseline difference in ACE-I/ARB utilization between the two groups. Over time, however, many more of the Canadian patients were started on ACE-I/ARB therapy. This is reflected in the fact that when one examines the entire follow-up period, 70.9 and 90.7% of Canadian and Thai patients were initiated on this class of medications. Chronological time difference is the most likely explanation for the baseline difference in ACE-I/ARB utilization.

With regard to the differences in baseline prednisone use, a potential reason may be the differences in access to specialist care between the two countries. In Thailand, the number of hemodialysis centers in the country increased dramatically from 26 to 201 between 1990 and 2003, however, even in 2003, 73% of the country's nephrologists worked in Bangkok and the remaining 27% were spread over the rest of the provinces [The Nephrology Society of Thailand 2007]. Therefore, it was not uncommon that if a patient needed to either see a nephrologist or receive a kidney biopsy they would have had to travel fair distances at their own expense. Also most people did not have health coverage in Thailand until recently whereas in Canada, healthcare is government funded so patients would not incur an expense for seeing a nephrologist in Canada. Consequently in Thailand, many patients were started on ACE-I/ARB and prednisone therapy at baseline by their referring primary care doctor or internist prior to seeing a nephrologist.

Some of the other nonmedication predictors of eGFR and baseline features are discussed in more detail and compared to previous literature. In the Thai group, increased baseline chronicity score was a negative predictor of eGFR. Higher chronicity score on renal biopsy was determined to be an independent predictor of progression of renal disease in IgA nephropathy patients [Nieuwhof et al. 1998]. The female predominance in the Thai group in our study is similar to other Asian studies of IgA nephropathy [Li et al. 2002] and the male predominance in the Canadian-Asian group is in keeping with studies from North America [Hall et al. 2004]. Neugarten et al. [2000] found a positive correlation between male gender and worse renal outcome and with aging, men exhibit greater decrements in renal function and increased glomerular sclerosis than do women [Gandolfo et al. 2004]. Other studies have found no differences between sexes with regards to progression of chronic kidney disease in IgA nephropathy over time [Cattran et al. 2008]. Other factors that have been associated with progression of CKD in IgA nephropathy are genetics and social/cultural factors such as smoking. Six single nucleotide polymorphisms located in a polymeric immunoglobulin receptor gene were noted to predispose Japanese patients to developing IgA nephropathy [Hsu et al. 2000, Obara et al. 2003]. Reports of familial aggregation of primary IgA nephropathy provide evidence of a genetic role in the development and progression of this condition [Hsu

et al. 2000, Chow et al. 2005]. In a Chinese sample of patients with IgA nephropathy, the polymorphism of megalin A23167G was associated with susceptibility to and progression of IgA nephropathy [Xia et al. 2006]. In a retrospective analysis, Stengel et al. [2000] determined that there was a strong dose effect between smoking and the risk of end-stage renal disease in men with IgA nephropathy.

Our analyses had several limitations. Conclusions need to be confirmed in other cohorts because of the retrospective nature of this study. In the Canadian registry, nativity was not recorded and, therefore, subgroups of Asian ethnicity could not be compared. Genetic determinants of IgA nephropathy among Asians may differ by country of origin. We also excluded many patients because of the limited availability of renal biopsy reports and creatinine data. In addition, the renal biopsy slides were not available for many patients, given that the patients in each registry were referred over a wide range of time and from multiple different centers. We, therefore, had a single nephrologist review biopsy reports and rate the chronicity and Haas scores on all patients from both countries. Finally, comparisons were restricted because of the chronological time gap the starting dates between the two registries, shorter duration of follow-up and smaller number of patients in the Thai group.

In spite of its limitations, our study may be hypothesis generating and serve as a basis for future studies. Possible future directions include prospectively examining the change in eGFR over time in Asians with and without early prednisone utilization by gender. Studying two groups simultaneously and prospectively, one in Asia and the other in North America, might allow for the role of environmental influences on IgA nephropathy progression to be delineated. Further research exploring these international differences in demographic and environmental factors and disease management is needed to determine how these variables may impact long-term outcomes in Asian patients with IgA nephropathy.

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Table 1
Baseline characteristics by country.

Baseline characteristic	Thailand	Canada	p value
Patient			
Age (years)	35.3 (11.4)	39.0 (13.0)	0.04
Sex (% female)	63.2	44.1	0.01
Systolic blood pressure (mmHg)	128.7 (16.0)	130.6 (19.8)	0.50
Diastolic blood pressure (mmHg)	81.9 (8.5)	82.9 (11.9)	0.49
Mean arterial pressure (mmHg)	97.5 (10.6)	98.8 (13.7)	0.46
Urine protein (g/day)	1.2 (0.7 – 2.4)	1.7 (0.9 – 2.7)	0.08
Height (cm)	160.0 (6.7)	163.3 (9.4)	0.02
Weight (kg)	61.0 (54.3 – 70.3)	62.0 (52.0 – 73.0)	0.92
Body mass index (kg/m ²)	23.7 (21.2 – 26.5)	23.4 (20.5 – 25.2)	0.18
Body surface area (m ²)	1.6 (0.2)	1.7 (0.2)	0.60
Serum creatinine (μmol/l)	110.5 (81.0 – 174.6)	108.0 (85.0 – 143.5)	0.63
Estimated GFR (ml/min/1.73 m ²)	53.8 (29.2 – 70.7)	50.8 (41.3 – 65.6)	0.35
Renal biopsy			
Haas classification	3.0 (2.0 – 5.0)	3.0 (2.0 – 5.0)	0.35
Chronicity score	3.0 (2.0 – 6.0)	3.0 (2.0 – 5.0)	0.31
Medications			
ACE-I inhibitor use (%)	64.0	15.2	< 0.01
Other antihypertensive agent use (%)	16.0	29.8	0.02
Prednisone use (%)	41.3	4.6	< 0.01
Immunosuppression use (%)	6.7	0.0	0.01

Normally distributed values are recorded as mean (standard deviations) and were compared using two-sample t-tests. Non-normal continuous variables are shown as median (25th – 75th percentile) and were compared using Wilcoxon rank-sum tests. Dichotomous variables were compared using χ^2 -tests. GFR = glomerular filtration rate.

Table 2

Effect of variables on estimated GFR slope in ml/min per 1.73 m² in Thailand.

Predictor	Thailand	p value
Age (per year)	-0.84 (-1.69, 0.02)	0.06
Mean arterial pressure (per mmHg)	-0.29 (-0.87, 0.29)	0.33
Male sex (reference is female)	-8.70 (23.52, 6.11)	0.25
Urine protein (per g/d)	-3.27 (-9.12, 2.58)	0.27
Body mass index (per kg/m ²)	0.33 (-2.27, 2.92)	0.81
ACE-I/ARB use	0.90 (-16.18, 17.98)	0.92
Other antihypertensive use	-9.82 (-25.87, 6.23)	0.23
Prednisone use	7.51 (-8.24, 23.25)	0.13
Other immunosuppressive use	-20.56 (-48.06, 6.15)	0.35
Haas class	-0.89 (-9.20, 7.41)	0.83
Chronicity score	-8.48 (-13.23, -3.73)	< 0.01

Baseline predictor values were used in the regression analyses. The eGFR decline in the Thai group was not significantly different than 0. In the Thai group, the estimates for chronicity was significant ($p < 0.01$) and age had borderline significance ($p = 0.06$) with respect to impact on eGFR. 95% confidence intervals for the estimates are shown in parentheses.

Table 3

Effect of variables on estimated GFR slope in ml/min per 1.73 m² in Canada.

Predictor	Estimate	p value
Age (per year)	-0.04 (-0.57, 0.49)	0.89
Mean arterial pressure (per mmHg)	0.38 (-0.36, 1.12)	0.31
Male sex (reference is female)	-2.01 (-14.85, 10.83)	0.78
Urine protein (per g/d)	-3.29 (-8.21, 1.63)	0.19
Body mass index (per kg/m ²)	-0.52 (-2.15, 1.15)	0.54
ACE-I/ARB use	-27.87 (-43.66, -12.08)	< 0.01
Other antihypertensive use	-9.28 (-27.4, 8.96)	0.32
Prednisone use	74.01 (41.75, 106.26)	< 0.01
Other immunosuppressive use	0.00	N/A
Haas class	0.24 (-7.45, 7.92)	0.95
Chronicity score	-0.18 (-4.46, 4.11)	0.94

Baseline predictor values were used in the regression analyses. The eGFR decline in the Canadian group was significantly greater than 0. In the Canadian group, the estimates for ACE-I/ARB and prednisone use were significant (both p values < 0.01) with respect to effect on eGFR. 95% confidence intervals for the estimates are shown in parentheses.