

# Hyperuricemia- and gouty arthritis-related medullary gout tophi associate with glomerulosclerosis and interstitial fibrosis in a series of 81,200 kidney biopsies

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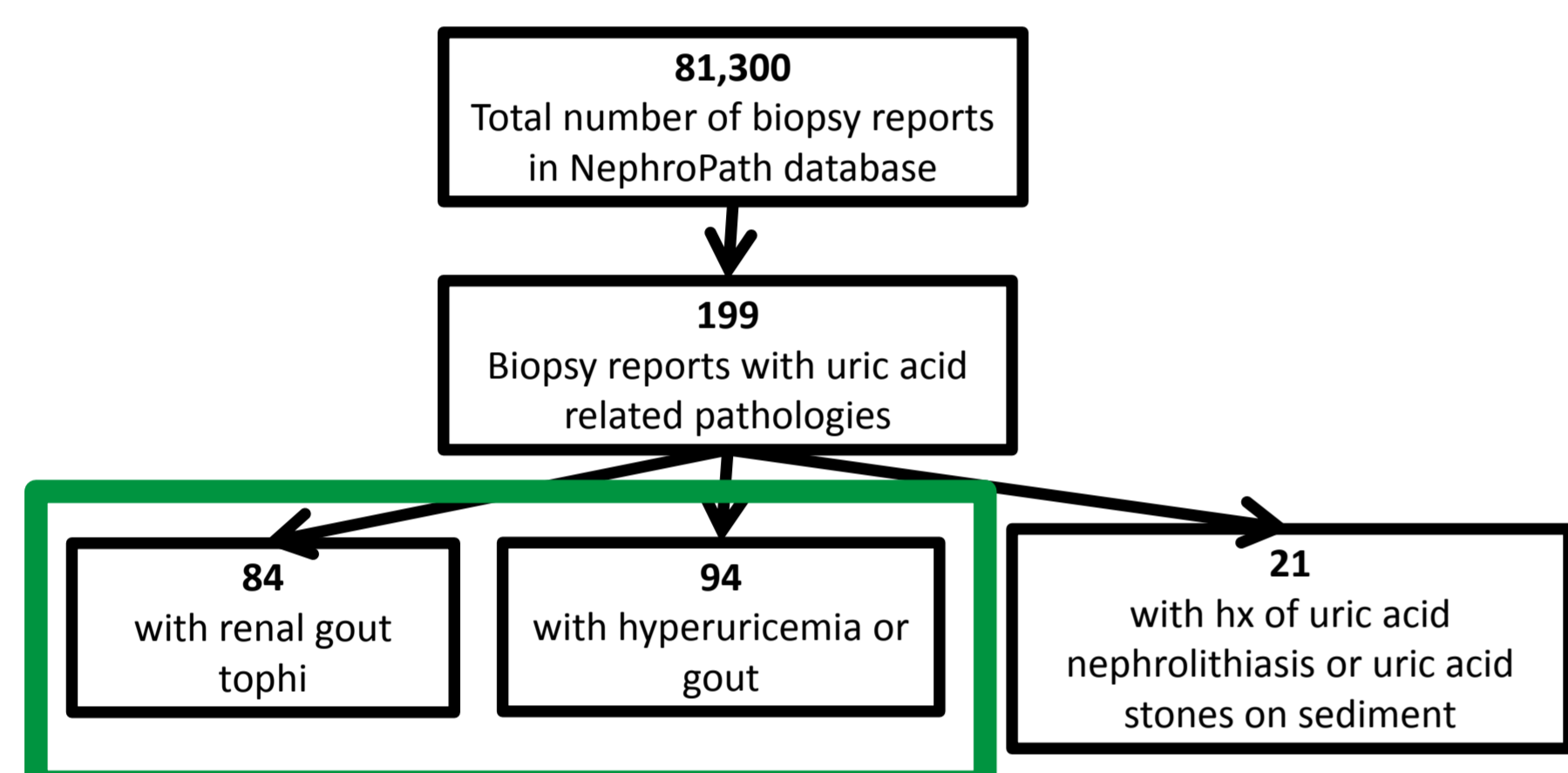
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## Background

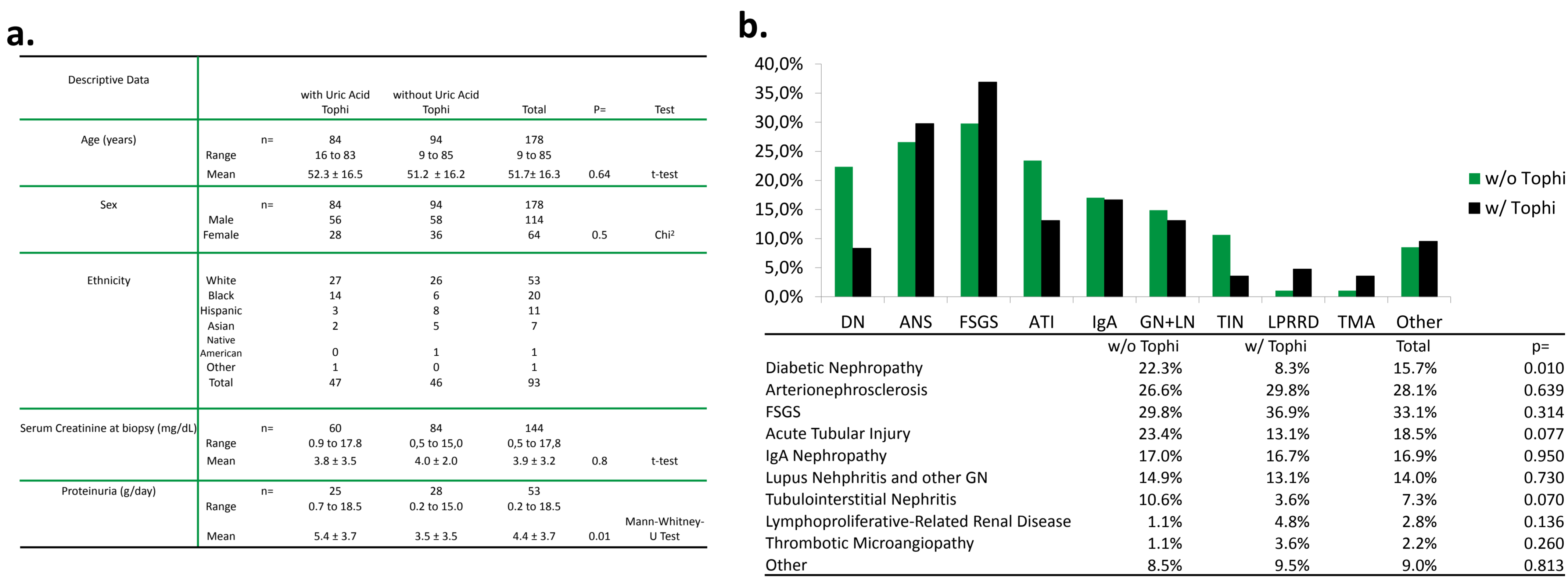
Renal lesions of tophaceous gout are an occasional finding on kidney biopsy. It is unclear whether these are a cause or a complication of CKD<sup>1-3</sup>. We hypothesized that intrarenal uric acid (UA) deposits drive foreign body reactions including giant cell granuloma formation, and is therefore associated with increased kidney fibrosis.

## Methods:

The Arkana Laboratories kidney biopsy bank was searched for patient biopsy reports with uric acid related pathologies. Out of 81,200 kidney biopsies, this search yielded 199 biopsy reports of patients with hyperuricemia, gouty arthritis, renal uric acid tophi, uric acid nephrolithiasis or uric acid stones on sediment. To homogenize the control group and because it is assumed that hyperuricemia or gout are prerequisites for renal gout tophi, the 21 cases with uric acid nephrolithiasis or uric acid stones were ruled out. The remaining two groups with a total of 178 cases were compared using SPSS to determine differences in histological signs of renal damage. Metric and ordinal data was compared using the Mann-Whitney U test; Nominal data was compared using the chi-squared test. Additionally, stained biopsies were analyzed to characterize the different morphologies this pathological finding can take on.

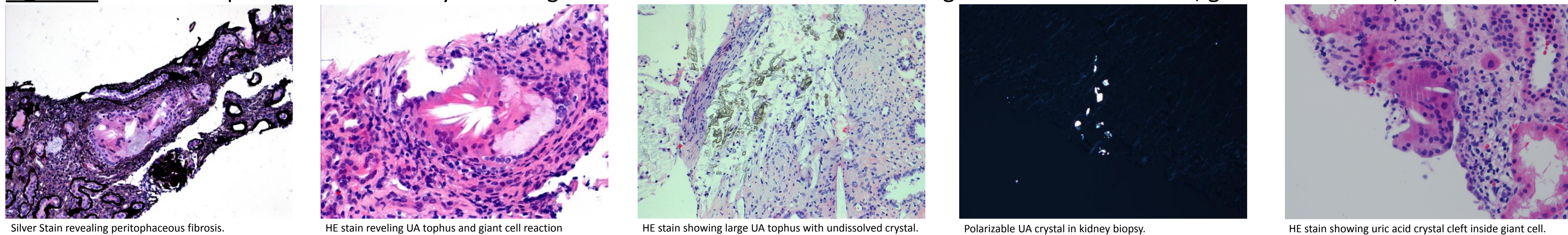


**Figure 1: Descriptive data and main pathological diagnoses**

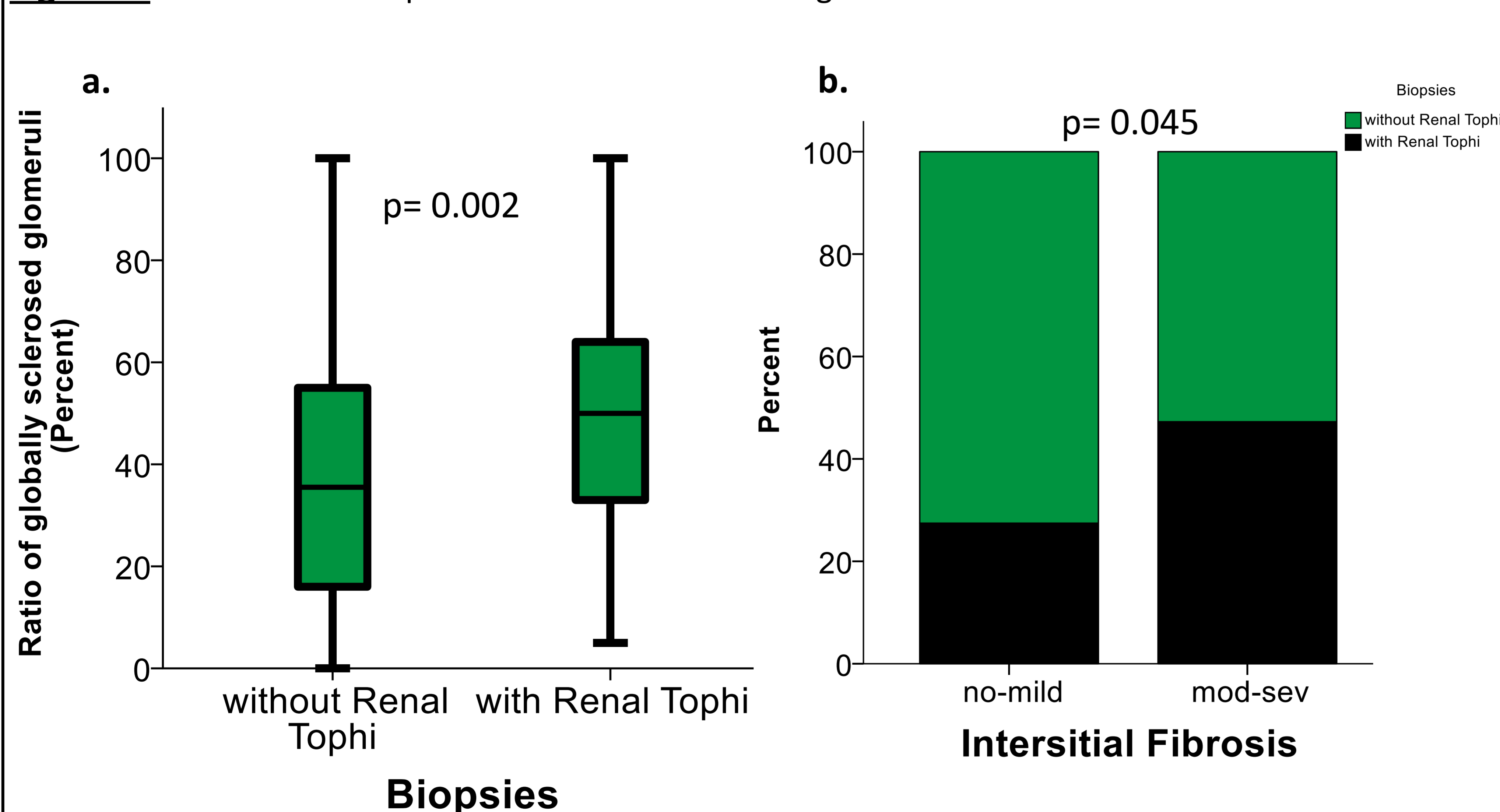


**a. Descriptive data and laboratory values.** There are no significant differences in age, gender, and serum creatinine between the groups. Patients with gouty renal tophi have more proteinuria (5.4 ± 3.7 g/day) compared to the hyperuricemic and gouty control (3.5 ± 3.5 g/day, p=0.01). **b. Main pathological diagnoses.** Both groups show similar pathological diagnoses, however there was a higher rate of diabetic nephropathy in the hyperuricemic and gouty control (p=0.01).

**Figure 2: Uric acid deposition in the kidney leads to granuloma formation with surrounding mononuclear infiltrate, giant cell reaction, and fibrosis**

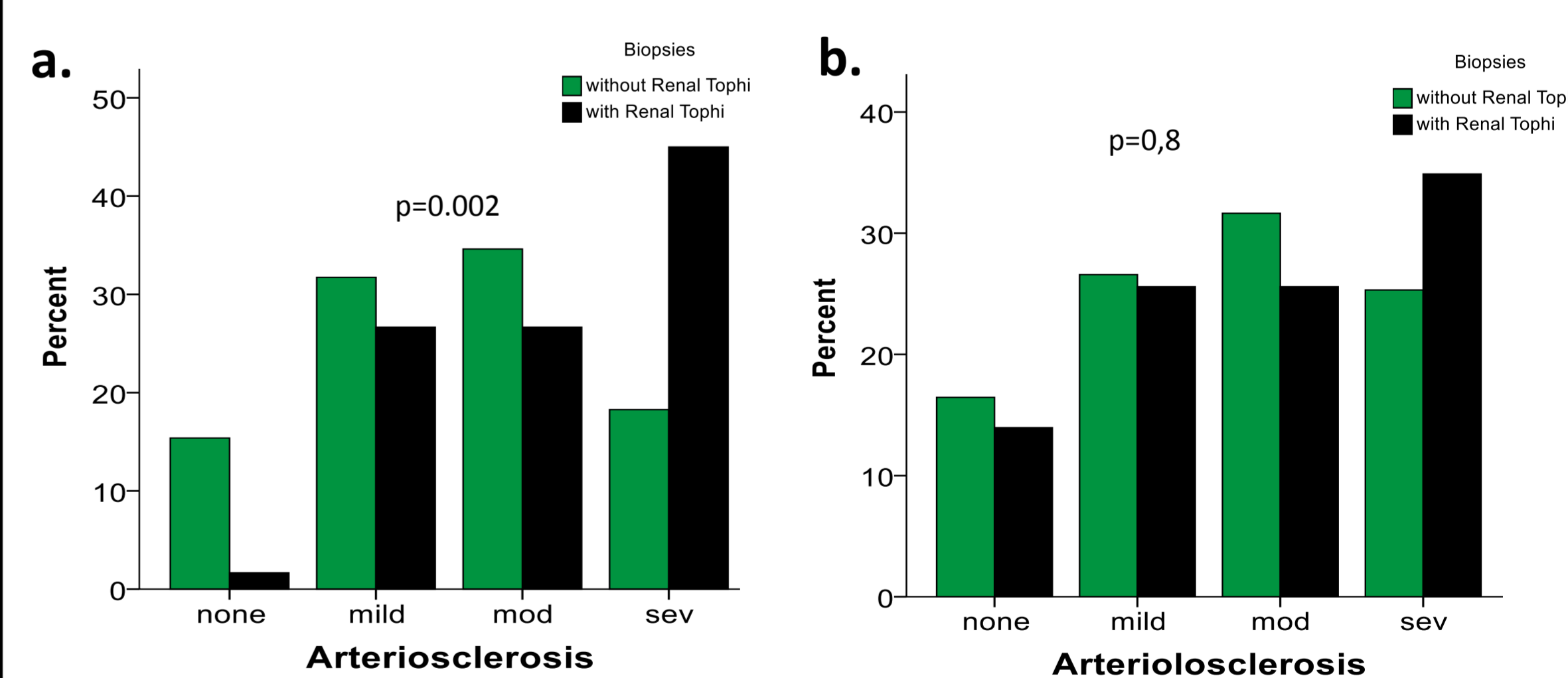


**Figure 3: Renal uric acid tophi associate with increased glomerulosclerosis and interstitial fibrosis**



**a. Renal uric acid tophi associate with increased glomerulosclerosis.** The number of globally sclerosed glomeruli was divided by the total number of glomeruli visualized to for the ratio of global glomerulosclerosis. Biopsies with renal UA tophi (n=81) showed significantly more global glomerulosclerosis (mean=48.1%) than the hyperuricemic and gouty control (mean=36.8%, n=92). **b. Renal UA tophi associated with interstitial fibrosis and tubular atrophy.** Renal pathologist rated interstitial fibrosis and tubular atrophy in biopsies from none to severe. Biopsies with UA tophi (n=74) were significantly more likely to have moderate or severe and significantly less likely to have no or mild interstitial fibrosis and tubular atrophy than the gouty/ hyperuricemic control (n=85).

**Figure 3: Renal uric acid tophi associate with increased renal arteriosclerosis but not with renal arteriolosclerosis**



**a. Renal UA tophi associate with increased arteriosclerosis.** Biopsies with renal UA tophi (n=60) were more likely to have severe and less likely to have no or mild arteriosclerosis than the hyperuricemic/gouty control (n=86). **b. Renal UA tophi are not associated with renal arteriolosclerosis.** Biopsies with renal tophi (n=43) were, however, equally likely to have any severity of arteriolosclerosis as biopsies of hyperuricemic or gouty patients (n=62).

## Conclusion

Medullary gout tophi are foreign body granulomas that form as a manifestation of tophaceous gout and are associated with substantial kidney atrophy. The presence of profound glomerulosclerosis and arteriosclerosis suggests that CKD is a prerequisite for medullary tophus formation. Functional studies in a suitable animal model are needed to prove causality of this concept.

## References:

- Diana I. Jalal (2016): Hyperuricemia, the Kidneys, and the Spectrum of Associated Diseases: A Narrative Review, Current Medical Research and Opinion
- Jing, J. et al. Prevalence and correlates of gout in a large cohort of patients with chronic kidney disease: the German Chronic Kidney Disease (GCKD) study. Nephrology Dialysis Transplantation 30, 613–621 (2014).
- Ayoub, I. et al. Revisiting medullary tophi: a link between uric acid and progressive chronic kidney disease? Clinical Nephrology 85 (2016), 109–113 (2016).