

**MAASSTAD  
ZIEKENHUIS**



**LITHIUM NEPHROPATHY: A LONG-TERM COMPLICATION  
OF CHRONIC LITHIUM THERAPY**

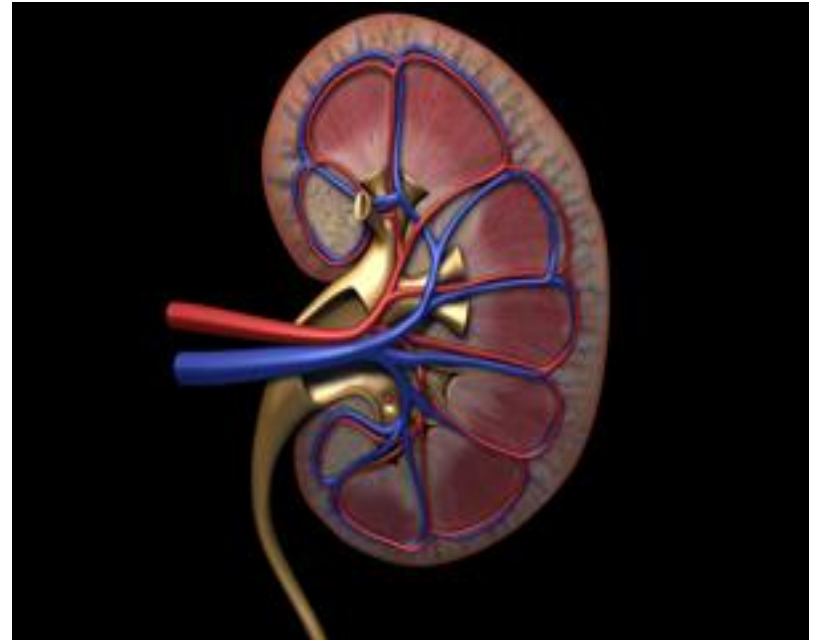
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# Introduction

- Bean-shaped organs serving several regulatory roles:
  - Natural filter of the blood (gfr)
  - Acid-base balance
  - Regulation osmolarity
  - Regulation blood pressure
  - Secretion of hormones



# Lithium-induced nephropathy

- Chronic kidney disease  
prevalence 10 – 35 %  
HR  $\pm$  2
- End stage renal disease  
prevalence 0,5 – 1,5 %

(Shine et al., 2015; Aiff et al., 2015; Bocchetta et al., 2015; Rej et al., 2014; Close et al., 2014; McKnight et al., 2012; Bendz et al., 2010; Tredget et al., 2010; Presne, 2003)

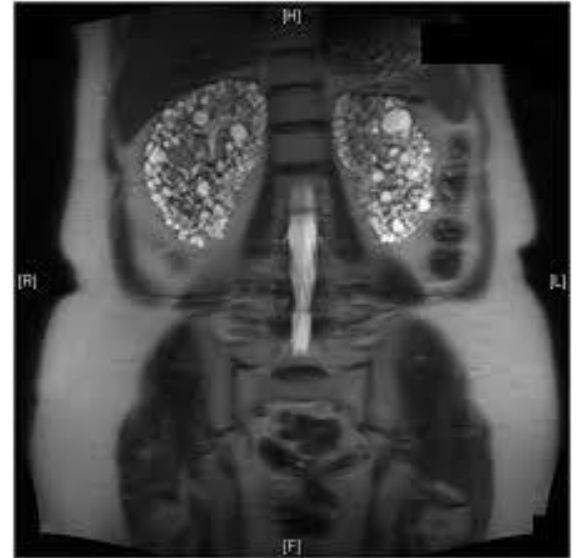
# Risk factors

- Hypertension, diabetes, ischemic heart disease
- Women, age
- >2 yrs lithium use, lithium levels, lithium intoxication



# Lithium-induced nephropathy

- Pathological findings consist of tubulo-interstitial nephritis, focal segmental glomerulosclerosis and renal (micro)cysts
- Asymptomatic



# Aim

- Prevalence
- Role of duration of therapy, serum lithium concentration, lithium intoxication, comorbidity

# Study Design

- Retrospective cohort study
- Study population: 1751 patients on lithium therapy
- Follow-up period 2000-2015



# Definition renal failure:

- Renal insufficiency:  $\geq 2 \times$  MDRD $<60$ , interval  $>6$  weeks in between, last measured MDRD-GFR during follow up  $<60$  ml/min

# Statistics

- Prevalence
- Two subgroups: with and without renal failure
- Logistic regression analysis

# Results

Total study population	All patients
Number of patients (N)	1751
Female/male ratio	1.36 (1010/741)
Age at onset lithium therapy (y)	44.4 ± 13.4
Duration lithium therapy (y)	10.9 ± 9.6
Mean serum lithium concentration (mmol/L)	0.68 ± 0.14
Smoking: number/total group (%)	821/1297 (63.3)
Cardiovascular disease: number/total group (%)	220/1492 (14.7)
Hypertension: number/total group (%)	297/1493 (19.9)
Diabetes Mellitus: number/total group (%)	217/1491 (14.6)

# Results

- Prevalence renal failure in study population 17.4%
- Prevalence ESRD 1.1%

# Results

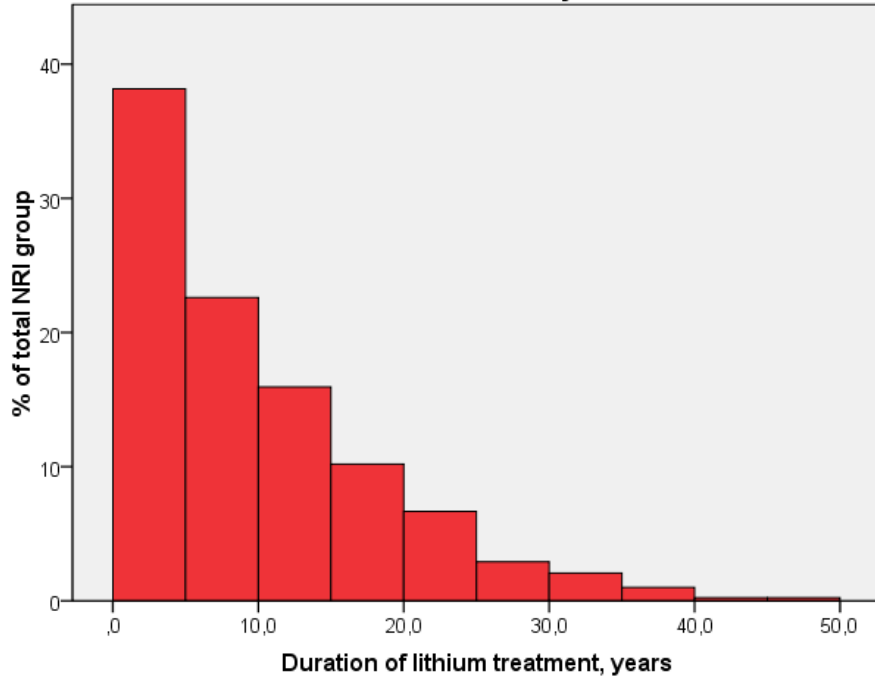
Risk factor	Odds ratio	P-value
Mean serum lithium concentration	7.62	0.004
Duration lithium therapy	1.10	<0.001
Gender	2.16	<0.001
Lithium intoxication	0.93	0.87
Age at onset lithium therapy (y)	1.06	<0.001
Cardiovascular events	1.58	0.02
Hypertension	1.84	0.001
Diabetes mellitus	1.86	0.002

# Lithium intoxication

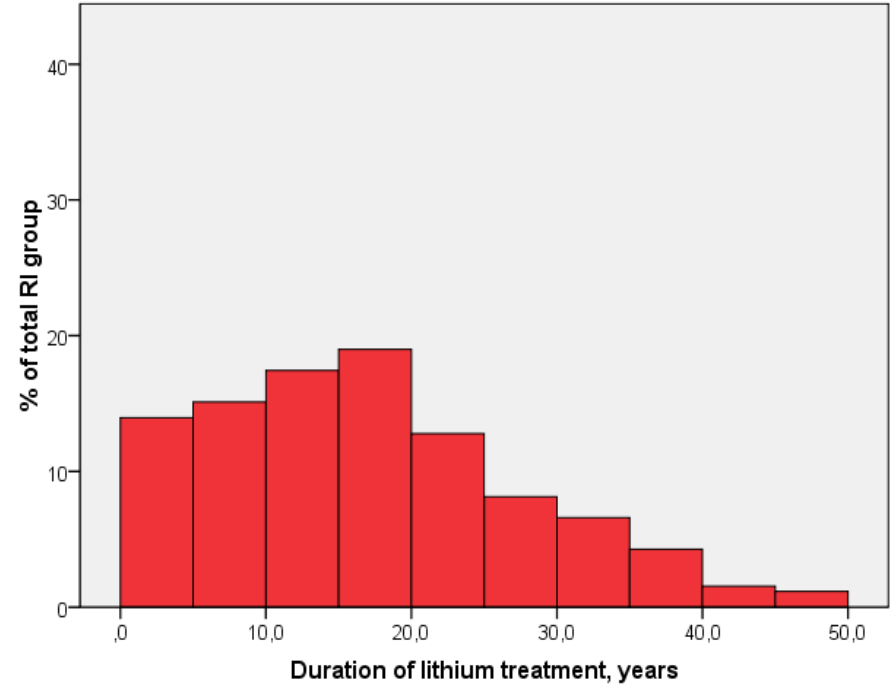
- Patients without renal failure (n=192): 10 intoxications
- Patients with renal failure (n=52): 1 intoxication

# Results

No renal insufficiency



Renal insufficiency



# Discussion

Limitations current study design:

- Retrospective design
- Absence of control group
- Calculation MDRD-GFR
- Incomplete documentation psychiatric medical records with regard to comorbidities



# Conclusions

- Prevalence renal failure comparable to previous reports
- End-stage renal disease very rare
- No association with episodes of lithium intoxication
- Association with female gender, age at onset lithium therapy, duration of lithium therapy and comorbidity

# Conclusions

- Majority of lithium users preserves stable renal function
- Lithium nephropathy = multifactorial disease  
important role classical risk factors renal failure!



# Future plans

- Discontinuation of lithium prevents further deterioration of renal function?
- Can amiloride therapy ameliorate decline in renal function?
- Increasing awareness of classical cardiovascular risk factors in patients receiving lithium treatment

