

## Serum chloride is a mortality risk predictor in type 2 diabetes mellitus – analysis of 91,159 patients in the West of Scotland

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## Background

- Chloride is the principal extracellular anion in the body
- Chloride functions
  - Maintenance of osmotic pressure
  - Acid-base balance
  - Muscular activity
  - Movement of water between fluid compartments
- >85% of chloride is consumed as sodium chloride (salt)
- Sodium chloride (salt) is known to increase blood pressure and CV risk
- Evidence that the chloride component of NaCl may have a specific role in salt sensitivity



## **Outcome studies**

#### Belgian Inter-university Research on Nutrition and Health (BIRNH)

- General population, 10 year follow up
- 9106 participants,



De Bacquer et al. J Cardiovasc Risk. 1998;5(3):177-184

# CandesartaninHeartfailureAssessmentofReductioninMortality and Morbidity(CHARM)

- Heart failure population
- 2679 participants with bloods, post-hoc analysis
- Each SD increase in chloride associated with reduction in all-cause mortality

	Hazard Ratio*	95% CI	p Value
Laboratory parameters	5		
Chloride	0.78	0.71-0.85	<0.0001
Bilirubin total	1.19	1.11-1.27	<0.0001
Urea nitrogen	1.18	1.10-1.26	<0.0001
Albumin	0.85	0.78-0.93	0.0002
Hemoglobin	0.84	0.76-0.92	0.0002
Sodium	1.14	1.04-1.25	0.004
RDW	1.12	1.03-1.20	0.006
Monocytes	1.11	1.02-1.20	0.0100
Cholesterol	1.10	1.01-1.20	0.03

Felker et al. J Am Coll Cardiol. 2007;50(1):40-47



## **Outcome studies**

#### Glasgow Blood Pressure Clinic (GBPC)

- 12,968 treated hypertensive patients, 35 year follow up
- Serum chloride <100 was associated with 20% higher all cause mortality, CV and non-CV mortality



McCallum et al. Hypertension. 2013;62(5):836-845



## **Outcome studies**

#### **Renal Failure**

■923 pre-dialysis CKD patients, median follow up 33 months

■Increased risk of primary outcome (death or CV event) in Q1 (Cl<sup>-</sup> <103.9mEq/L) and Q4 (Cl<sup>-</sup> >108.1 mEq/L)



Quartile 1 (Cl<sup>-</sup> ≤103.9)
Quartile 2 (Cl<sup>-</sup> 104.0–105.9)
Quartile 3 (Cl<sup>-</sup> 106.0–108.0)
Quartile 4 (Cl<sup>-</sup> ≥108.1)



 To determine if serum chloride is associated with mortality risk in adults with type 2 diabetes mellitus



## **Methods**

#### **Study population**

- Data from NHSGGC SafeHaven
- 91,159 adults with T2DM
- Patients stratified into 2 groups: serum
  - Serum chloride <100 mmol/L and ≥ 100 mmol/L</p>
- 10 years follow up

#### **Survival analysis**

- Cox-PH model used to study the association between serum chloride and mortality
- Adjusted for age, sex, serum sodium



#### **Outcomes**

#### **Primary**

All-cause mortality

#### Secondary cardiovascular outcomes

- Cardiovascular death
- Death from MI
- Death from heart failure
- Death from stroke
- Death from cancer



## **Demographics**

	All N= 91,159	CI- <100 mmol/L N=13,459	CI- ≥100 mmol/L N=77,757	Р
Age, years (SD)	60.0 (15.7)	60.6 (16.9)	59.9 (15.5)	<0.001
Female, N (%)	42774 (47%)	6270 (47%)	36504 (47%)	0.4
Serum chloride, mmol/L (SD)	102.9 (3.6)	96.7 (3.0)	103.9 (2.5)	<0.001
Serum sodium, mmol/L (SD)	138.6 (3.1)	135.3 (3.8)	139.2 (2.5)	<0.001



## **All-cause mortality**





## **CV and MI death**





## Heart failure and stroke death





## **Cancer death**



heart failure. n.events = 5577p = 0.003 HR = 1.12



## Conclusions

- Serum chloride <100 mmol/L was associated with increased risk of death in adults with type 2 diabetes mellitus
- Findings in keeping with studies in other populations
- Mechanism by which low serum chloride is associated with mortality is unknown
- Further study is warranted





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