

Albuminuria in Adults with Congenital Heart Disease

RESULTS FROM THE BOSTON ADULT CONGENITAL HEART BIOBANK

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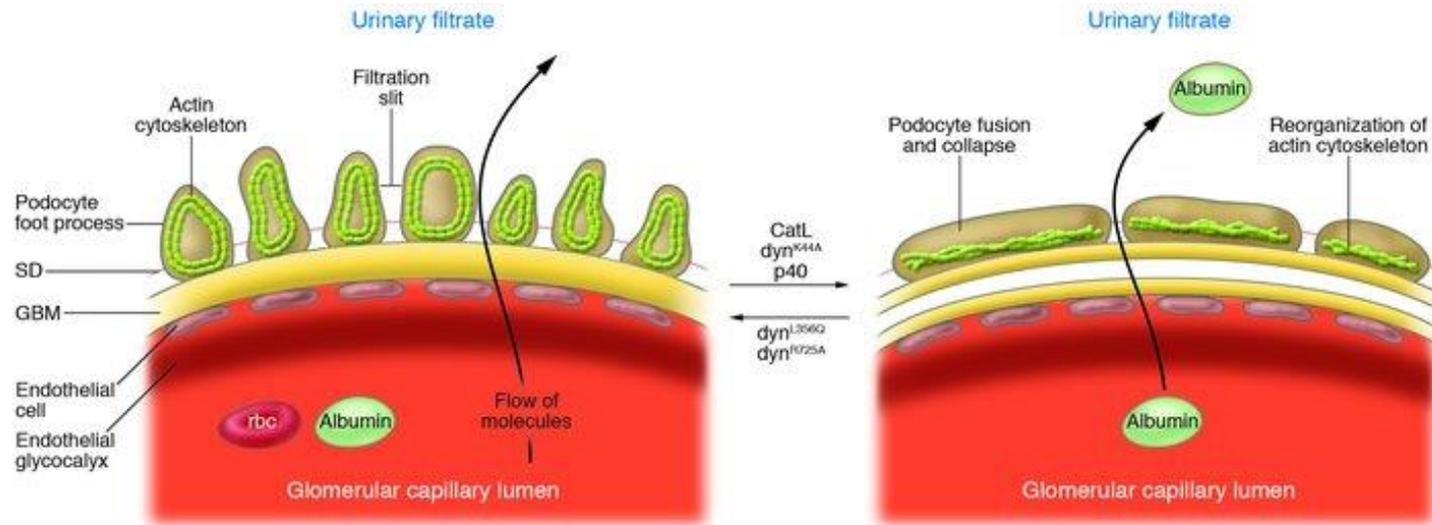
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Background

- Albuminuria is present in ~5-10% of the population with a higher prevalence in diabetes mellitus or HTN
- Albuminuria is associated with increased risk for adverse outcomes in the general population and in specific diseases (e.g. DM, CHF)
- However, few studies have systematically explored the prevalence and implications of albuminuria across the spectrum of adults with CHD

Background - Albuminuria



Albuminuria categories in CKD

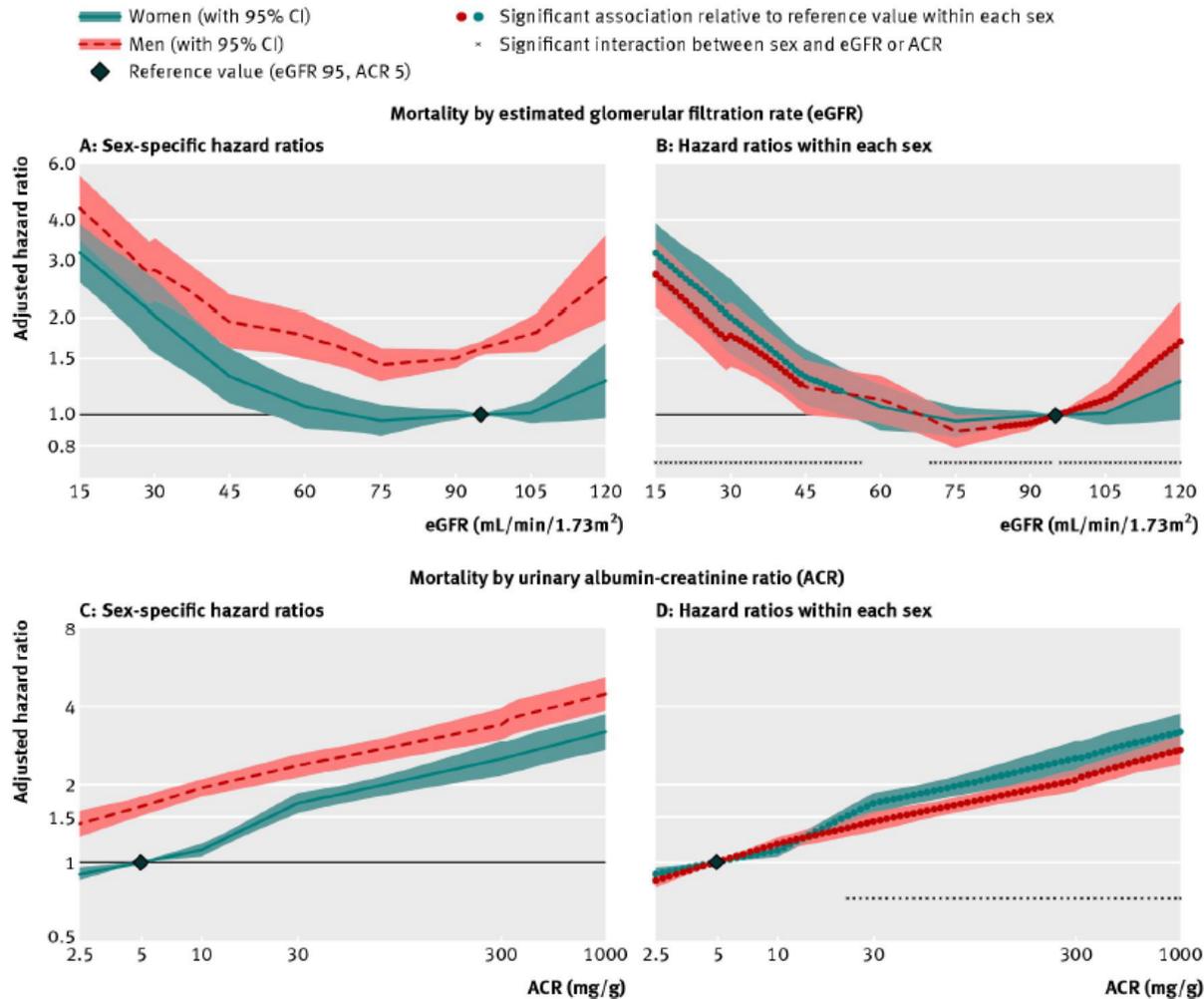
Category	AER (mg/24 hours)	ACR (approximate equivalent)		Terms
		(mg/mmol)	(mg/g)	
A1	< 30	< 3	< 30	Normal to mildly increased
A2	30-300	3-30	30-300	Moderately increased*
A3	> 300	> 30	> 300	Severely increased**

Abbreviations: AER, albumin excretion rate; ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease.

*Relative to young adult level.

**Including nephrotic syndrome (albumin excretion usually > 2200 mg/24 hours [ACR > 2220 mg/g; > 220 mg/mmol]).

Background - Albuminuria



CHD with cyanosis is linked with kidney dysfunction and albuminuria

Congenital Heart Disease with Extreme Secondary Polycythæmia and Orthostatic Albuminuria.

By F. PARKES WEBER, M.D.

Formerly published as Medico-Chirurgical Transactions • 1809–1907

Proceedings of the Royal Society of Medicine

Now published as Journal of the Royal Society of Medicine • 1978–current

Renal function and urate metabolism in late survivors with cyanotic congenital heart disease

EDWARD A. ROSS, M.D., JOSEPH K. PERLOFF, M.D., GABRIEL M. DANOVITCH, M.D.,
JOHN S. CHILD, M.D., AND MARY M. CANOBBIO, R.N., M.N.

Circulation 73, No. 3, 396–400, 1986

Pathogenesis of the Glomerular Abnormality in Cyanotic Congenital Heart Disease

Joseph K. Perloff, MD, Harrison Latta, MD, and Paola Barsotti, PhD

(*Am J Cardiol* 2000;86:1198–1204)

Goals

- To define the prevalence and correlates of albuminuria in adult patients with various types of CHD.
- To understand the prognostic implications of albuminuria in these patients.

Methods – Study Design

- Study Design: Cross-sectional and prospective cohort study
- Study population: Outpatients with CHD ≥ 18 years-old seen between 2012 and 2015 at BCH and BWH
- Exclusion criteria: Patients hospitalized in last 30 days
- Approval: The study was approved by Boston Children's Hospital's Institutional Review Board and informed consent was obtained from all subjects
- Urine creatinine and albumin were measured

Methods - Data Collected

- Patient demographics
- Clinical history and physical exam findings including
 - NYHA functional class
 - Oxygen saturation
 - Underlying CHD diagnosis
 - Prior procedures and interventions
 - Medication use
 - Medical comorbidities
- Electrocardiographic and EP study data
- Exercise testing
- Imaging data (e.g., echo, cMR)

Methods - Definitions

- Albuminuria: ACR > 30 mg/g
 - Normal to mildly increased
 - Moderately increase: >30-300 mg/g
 - Severely increased >300 mg/g
- Cyanosis: O₂ saturation < 91% at rest

Methods - Classification of CHD

- Left sided obstructive lesions
- Tetralogy of Fallot PS/PA or double outlet RV
- Single ventricle Fontan (SVF)
- Simple shunt lesions
- Simple shunt lesion with sequelae (e.g. PH, CHF)
- Simple shunt lesion with Eisenmenger syndrome
- Transposition of the great arteries with a systemic RV
- Transposition of the great arteries with arterial switch
- Valvar pulmonary stenosis
- Ebstein anomaly
- AV septal defect
- Complex or unrepaired single ventricle cyanotic
- Miscellaneous/other

Based on initial analysis complex cyanotic and Eisenmenger groups were combined, AV septal defect group was included in appropriate shunt lesion groups, and the remaining groups with <20 subjects were classified as miscellaneous/other

Primary Outcome

- Non-elective cardiovascular hospitalization
 - Overnight admission for
 - heart failure
 - arrhythmia or symptoms of arrhythmia
 - thrombotic or embolic events
 - cerebral hemorrhage
 - cardiovascular disease specific events (e.g., hyperviscosity symptoms in Eisenmenger syndrome; ascites in Fontan)
- Death
- Cardiac transplant

Results- CHD Diagnosis

- 575 adults with CHD
- Age XXXX, XX% male
- Most common diagnoses were:

TO UPDATE

Diagnosis	% of Cohort	Cumulative %
Left sided obstructive lesions	22.3	22.3
Tetralogy of Fallot/DORV	20.0	42.3
SVF (Fontan)	16.8	59.1
Simple shunt lesions	16.6	75.7
Transposition with systemic RV	9.6	85.3

Results – Albuminuria Prevalence

	ACR	N	%
Increased albuminuria	>30 mg/g	169	29.4
<i>Moderately increased</i>	30-300 mg/g	141	24.5
<i>Severely increased</i>	>300 mg/g	28	4.9

Results- Demographics

Table: Demographic and clinical characteristics of patients by albumin-to-creatinine ratio >30 mg/g

	ACR≤30	ACR>30	P value
Age, years	37.1±13.0	40.7±13.1	<0.01
Sex, male	209 (51.1)	86 (51.0)	0.93
Weight, kg	77.2±18.1	72.9±17.7	0.01
Height, cm	167.9±9.7	167.1±10.1	0.39
BMI >30 kg/m ²	107 (26.6)	31 (18.3)	0.04
Systemic HTN	59 (14.5)	17 (10.1)	0.20
Diabetes mellitus	11 (2.7)	11 (6.5)	0.053
Current tobacco	20 (4.9)	6 (3.6)	0.70
CKD	2 (0.5)	7 (4.1)	0.004
Creatinine, g/dL	0.9±0.2	1.0±0.5	<0.01
Hyperlipidemia	51 (12.6)	23 (13.6)	0.79
Cyanosis, sO ₂ <91%	14 (3.8)	28 (18.2)	<0.001
Mechanical prosthetic valve	19 (4.7)	9 (5.3)	0.83
Fontan	50 (12.3)	45 (26.7)	<0.001
<i>NYHA Functional Class</i>			
I	313 (77.1)	110 (65.1)	<0.01
II	80 (19.7)	46 (27.2)	
III/IV	13 (3.2)	13 (7.7)	
<i>Medications</i>			
Aspirin	126 (31.0)	70 (41.4)	0.02
ACEi/ARB	126 (31.0)	58 (34.3)	0.50
Beta blocker	113 (27.8)	64 (37.9)	0.02
K ⁺ sparing diuretic	28 (6.9)	25 (14.8)	<0.01
Loop diuretic	57 (14.0)	60 (29.4)	<0.001
Statin	39 (9.6)	22 (13.0)	0.24

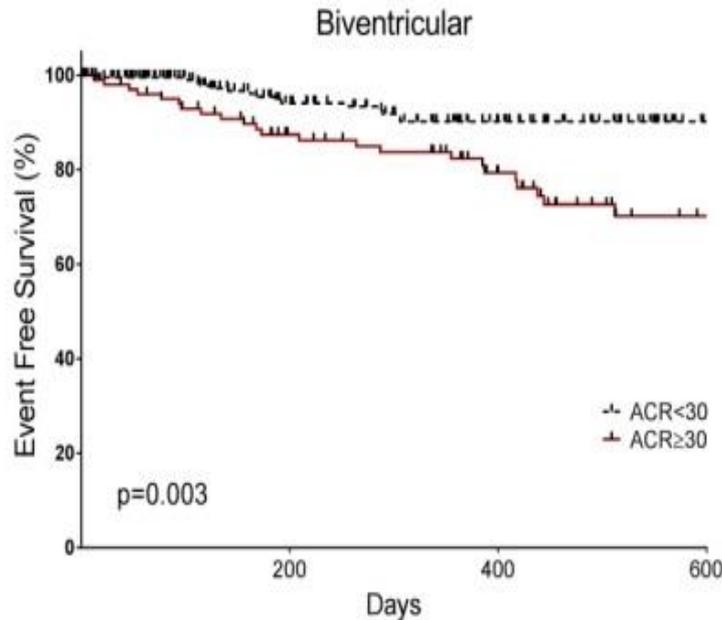
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Data are presented as mean±standard deviation or n (%).
 ACR: Albumin-to-creatinine ratio , BMI: Body mass index,
 ACEi: Angiotensin converting enzyme inhibitor, ARB:
 Angiotensin receptor blocker, CKD: Clinical diagnosis of
 chronic kidney disease, HTN: Hypertension, NYHA: New York
 Heart Association, sO₂: oxygen saturation.

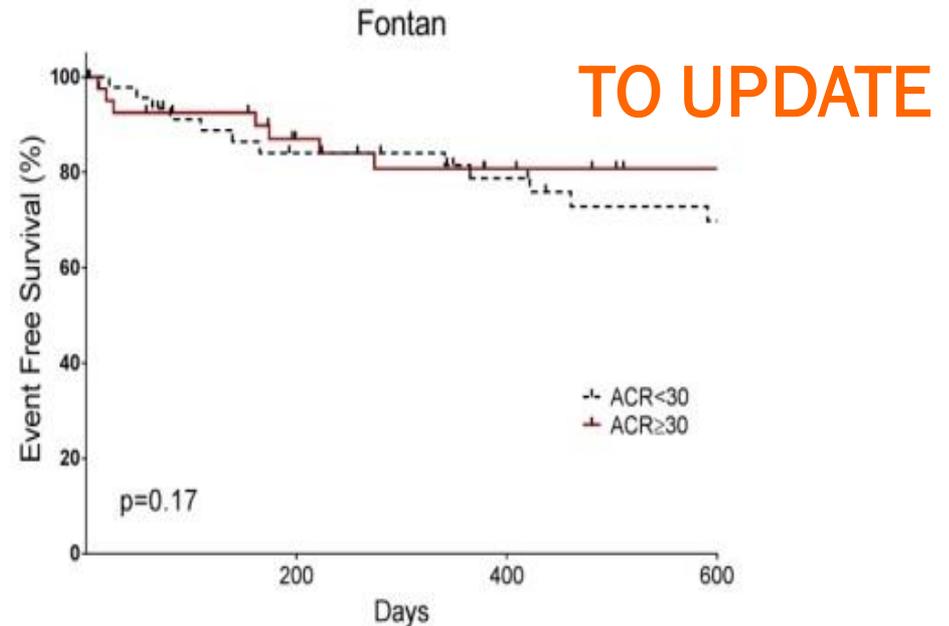
Primary Outcome

- Median Follow-Up: 182 days
- Primary outcome: 12% (n=69/575)
 - Death: 2.7% (n=16/575)
- In the overall cohort, ACR>30 was not a significant predictor of mortality (HR=2.7, 95%CI 0.97-7.4, p=0.06) or the combined outcome (HR=1.5, 95%CI 0.95-2.5, p=0.08)

Outcome – BiV vs SV Fontan



Among patients without SVF, ACR>30 significantly predicted mortality (HR=16.7, 95%CI 2.1-131.7, p=0.007) and the combined outcome (HR=2.5, 95%CI 1.4-4.6, p=0.003)



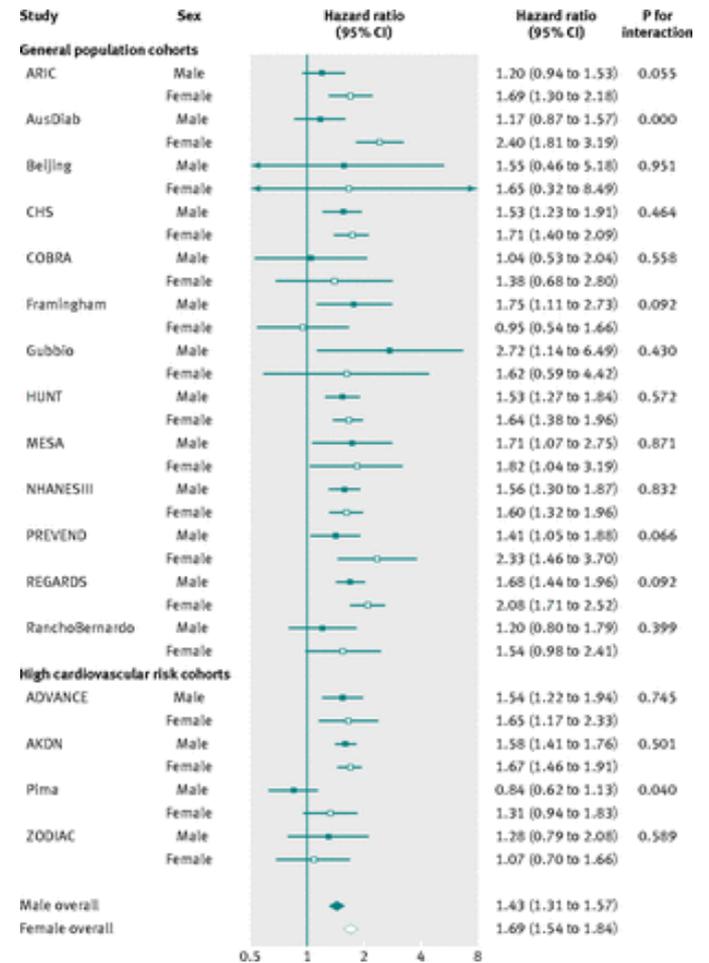
Among patients with SVF, ACR>30 was not a significant predictor of mortality (HR=0.3, 95%CI 0.03-2.2, p=0.21) or the combined outcome (HR=0.6, 95%CI 0.2-1.3, p=0.17)

Summary

- Increased albuminuria is common in ACHD patients.
- Albuminuria is not the result of a high prevalence of diabetes mellitus or hypertension.
- Albuminuria is most frequent among patients with cyanosis or a Fontan circulation.
 - But it is also present in 23% of other patients.
- Albuminuria is associated with older age, lower BMI, and worse NYHA functional class.
 - Use of diuretics or beta-blockers, but not ACEi/ARB, is more common in patients with albuminuria.

Summary

- Albuminuria is associated with increased risk for death or other adverse outcomes in the setting of biventricular CHD but not in the single ventricle Fontan circulation.
- This suggests a distinct mechanism or reason for albuminuria in those with SV Fontan physiology.
- Future research should explore the mechanisms of albuminuria in different types of CHD.



Hazard ratios of all-cause mortality at urinary ACR of 30 (v 5) in women and men per study, adjusted for age, sex, race, smoking status, systolic BP, history of cardiovascular disease, diabetes, serum total cholesterol, BMI, and eGFR splines.