

Gender differences in cardiac organ damage in hypertension: Assessing the role of drug nonadherence

Arleen Aune^{a,b}, Annabel Ohldieck^{a,b}, Lene V. Halvorsen^{c,d,e}, Karl Marius Brobak^{f,g}, Eirik Olsen^h, Stine Rognstad^{c,i}, Anne Cecilie K. Larstorp^{c,e,j}, Camilla L. Sørås^{c,e,k}, Anne B. Rossebø^l, Assami Rösner^m, Marianne Aa. Grytaasⁿ, Eva Gerds^{a,b}

^a Department of Clinical Science, University of Bergen, Bergen, Norway; ^b Department of Heart Disease, Haukeland University Hospital, Bergen, Norway; ^c Section for Cardiovascular and Renal Research, Oslo University Hospital Ullevål, Oslo, Norway; ^d Department of Nephrology, Oslo University Hospital Ullevål, Oslo, Norway; ^e Institute of Clinical Medicine, University of Oslo, Norway; ^f Section of Nephrology, The Arctic University of Norway, Tromsø, Norway; ^g Renal Research Group, UiT The Arctic University of Norway, Tromsø, Norway; ^h Department of Emergency Medicine, St. Olavs University Hospital, Trondheim, Norway; ⁱ Department of Pharmacology, Oslo University Hospital Ullevål, Oslo, Norway; ^j Department of Medical Biochemistry, Oslo University Hospital Ullevål, Oslo, Norway; ^k Section for Environmental and Occupational Medicine, Oslo University Hospital Ullevål; ^l Department of Cardiology, Oslo University Hospital Ullevål, Oslo, Norway; ^m Department of Clinical Medicine, UiT, The Arctic University, Tromsø, Norway ⁿ Department of Medicine, Haukeland University Hospital, Bergen, Norway;

Table S1. Covariables of LV hypertrophy in women and men with uncontrolled hypertension, uni- and multivariable logistic regression analysis. Secondary models.

Variable	All, n=523		Women, n=186		Men, n=337	
	Univariable OR (95% CI)	Multivariable OR (95% CI)	Univariable OR (95% CI)	Multivariable OR (95% CI)	Univariable OR (95% CI)	Multivariable OR (95% CI)
Female sex	1.66(1.15-2.41)*	2.01(1.30-3.10)*	n.a.	n.a.	n.a.	n.a.
Nonadherence	1.33(0.71-12.49)	1.96 (0.91-4.22)	1.72(0.57-5.18)	3.10 (0.81-11.94)	1.21(0.56-2.66)	1.54 (0.60-3.94)
Age (years)	1.02(1.00-1.04)*	1.04 (1.01-1.06)*	1.00(0.97-1.03)	1.02 (0.98-1.06)	1.03(1.00-1.06)*	1.04 (1.01-1.07)*
Body mass index (kg/m ²)	1.13(1.09-1.17)*	1.15 (1.10-1.20)*	1.13(1.07-1.20)*	1.16 (1.09-1.24)*	1.13(1.08-1.19)*	1.13 (1.06-1.20)*
24-h systolic BP (mmHg)	1.05(1.03-1.07)*	1.03 (1.01-1.06)*	1.05(1.01-1.08)*	1.03 (1.00-1.07)	1.06(1.03-1.09)*	1.04 (1.01-1.07)*
Duration of hypertension (years)	1.02(1.02-1.03)*	1.00 (0.98-1.02)	1.03(1.00-1.06)*	1.02 (1.00-1.05)	1.00(0.98-1.03)	
ACR ≥ 3 mg/mmol	1.91 (1.27-2.87)*	1.70 (1.03-2.82)*	2.38 (1.09-5.19)*	1.66 (0.68-4.06)	2.01 (1.22-3.92)*	1.58 (0.89-2.78)
Type 2 diabetes mellitus	1.44(0.94-2.22)*	1.02 (0.61-1.73)	2.17(1.01-4.69)*	1.25 (0.50-3.12)	1.25(0.73-2.14)	
Hypercholesterolemia	1.44(0.94-2.22)*	1.22 (0.80-1.87)	1.08(0.60-1.92)		1.71(1.08-2.71)*	1.32 (0.78-2.33)
Cardiovascular disease	1.64(1.05-2.55)*	1.41 (0.85-2.33)	1.21(0.60-2.46)		1.94(1.10-3.43)*	1.66 (0.89-3.12)

*p<0.05

BP, blood pressure; ACR, albumin-creatinine ratio; OR, odds ratio; CI, confidence interval; n.a., not applicable

Table S2. Covariables of LV hypertrophy in women and men with uncontrolled hypertension, uni- and multivariable logistic regression analysis including elevated ARR.

Variable	All, n=523		Women, n=186		Men, n=337	
	Univariable OR (95% CI)	Multivariable OR (95% CI)	Univariable OR (95% CI)	Multivariable OR (95% CI)	Univariable OR (95% CI)	Multivariable OR (95% CI)
Female sex	1.66 (1.15-2.41)*	2.00(1.28-3.10)*	n.a.	n.a.	n.a.	n.a.
Nonadherence	1.33 (0.71-12.49)	1.86 (0.84-4.12)	1.72(0.57-5.18)	3.90 (0.80-18.90)	1.21(0.56-2.66)	1.39 (0.52-3.73)
Age (years)	1.02 (1.00-1.04)*	1.03 (1.01-1.06)*	1.00(0.97-1.03)	1.02 (0.98-1.06)	1.03(1.00-1.06)*	1.05 (1.01-1.08)*
Body mass index (kg/m ²)	1.13 (1.09-1.17)*	1.15 (1.10-1.20)*	1.13(1.07-1.20)*	1.16 (1.08-1.25)*	1.13(1.08-1.19)*	1.12 (1.05-1.20)*
24-h systolic BP (mmHg)	1.05 (1.03-1.07)*	1.02 (1.00-1.05)	1.05(1.01-1.08)*	1.02 (0.98-1.06)	1.06(1.03-1.09)*	1.03 (1.00-1.06)
Duration of hypertension (years)	1.02 (1.02-1.03)*	1.00 (0.98-1.02)	1.03(1.00-1.06)*	1.03 (0.99-1.06)	1.00(0.98-1.03)	0.98 (0.96-1.01)
ACR ≥ 3 mg/mmol	1.91 (1.27-2.87)*	1.72 (1.04-2.87)*	2.38 (1.09-5.19)*	1.84 (0.70-4.79)	2.01 (1.22-3.92)*	1.69 (0.91-3.15)
Type 2 diabetes mellitus	1.44 (0.94-2.22)*	1.03 (0.61-1.77)	2.17(1.01-4.69)*	1.16 (0.44-3.09)	1.25(0.73-2.14)	0.99 (0.51-1.92)
Hypercholesterolemia	1.44 (0.94-2.22)*	1.31 (0.85-2.01)	1.08(0.60-1.92)	1.13 (0.56-2.31)	1.71(1.08-2.71)*	1.47 (0.84-2.58)
Cardiovascular disease	1.64 (1.05-2.55)*	1.40 (0.83-2.35)	1.21(0.60-2.46)	1.18 (0.48-2.92)	1.94(1.10-3.43)*	1.39 (0.72-2.71)
Elevated ARR	2.08 (1.38-3.13)*	1.78 (1.10-2.89)*	1.39 (0.72-2.67)	1.48 (0.67-3.28)	2.62 (1.55-4.44)*	2.12 (1.12-4.00)*

*p<0.05

BP, blood pressure; ACR, albumin-creatinine ratio; ARR, aldosterone-to-renin; OR, odds ratio; CI, confidence interval n.a., not applicable

Table S3. Covariables of left atrium enlargement in women and men with uncontrolled hypertension, uni- and multivariable logistic regression analysis. Secondary models.

Variable	All, n=523		Women, n= 186		Men, n= 337	
	Univariable OR (95% CI)	Multivariable OR (95% CI)	Univariable OR (95% CI)	Multivariable OR (95% CI)	Univariable OR (95% CI)	Multivariable OR (95% CI)
Female sex	2.07(1.35-3.17)*	1.90 (1.17-3.10)*	n.a.	n.a.	n.a.	n.a.
Drug nonadherence	0.50(0.27-0.94)*	0.48 (0.23-1.00)*	0.44(0.14-1.39)	0.38(0.07-1.96)	0.55(0.26-1.15)	0.49(0.21-1.10)
Age (years)	1.04(1.02-1.06)*	1.03 (1.01-1.06)*	1.01(0.98-1.04)	1.01(0.96-1.04)	1.05(1.02-1.07)*	1.04 (1.01-1.07)*
Body mass index (kg/m ²)	1.09(1.05-1.13)*	1.10 (1.04-1.15)*	1.13(1.05-1.22)*	1.11(1.01-1.22)*	1.09(1.03-1.15)*	1.07 (1.01-1.14)*
24-h systolic BP (mmHg)	1.05(1.02-1.07)*	1.03 (1.00-1.06)*	1.07(1.02-1.13)*	1.05(0.99-1.10)	1.04(1.01-1.07)*	1.02 (0.99-1.06)
Duration of hypertension (years)	1.02(1.00-1.04)*	1.00 (0.98-1.02)	1.02(0.98-1.05)		1.02(0.10-1.04)	
ACR ≥ 3 mg/mmol	1.60(1.99-2.55)	1.20 (0.70-2.04)	1.19(0.45-3.14)		1.97(1.15-3.38)*	1.26 (0.70-2.27)
LV hypertrophy	4.77(2.92-7.79)*	3.09 (1.84-5.27)*	12.88(3.78-43.88)*	6.50(1.96-21.54)*	3.28(1.13-3.66)*	2.50 (1.38-4.55)*
Mitral valve regurgitation	2.19(1.46-3.29)*	2.22 (1.41-3.50)*	4.36(1.86-10.20)*	5.62(2.15-14.70)*	1.61(1.00-2.60)	
Atrial fibrillation	1.39(0.75-2.58)		0.51(0.18-1.44)		2.26(1.04-4.89)*	1.77(0.76-4.15)

*p<0.05

BP, blood pressure; ACR, albumin-creatinine ratio; LV, left ventricular; OR, odds ratio; CI, confidence interval n.a., not applicable