

Women with diabetes at increased relative risk of heart failure compared to men with diabetes

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Background

- ❖ Diabetes growing issue worldwide with increasing associated costs for treatment, with the complications of diabetes often more devastating and costly.^{1,2}
- ❖ Heart failure is the most common cardiac complication for people with diabetes and can occur independent of commonly known risk factors.^{3,4}
- ❖ Sex differences have been observed in the risk of heart failure within people with diabetes in a meta-analysis of 12million people.⁵
- ❖ We explore the findings in the UK Biobank population for further clarification on the effect of confounders on the risk of heart failure.

Methods

493, 167 participants aged 40 – 69 recruited included (recruited 2006 – 2010 as part of UK Biobank prospective study)

22, 685 (4.6%) participants had prevalent diabetes (9,339 excluded for incident diabetes)

Survival analysis

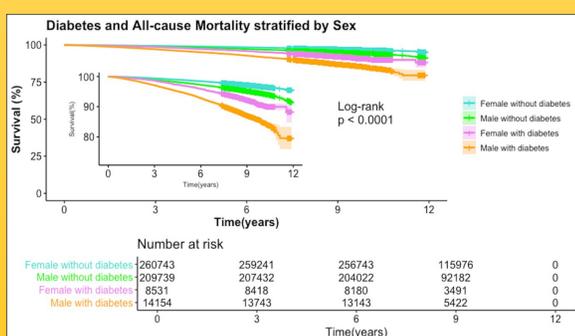
Mortality 9 year follow up

Heart failure 8 year follow up

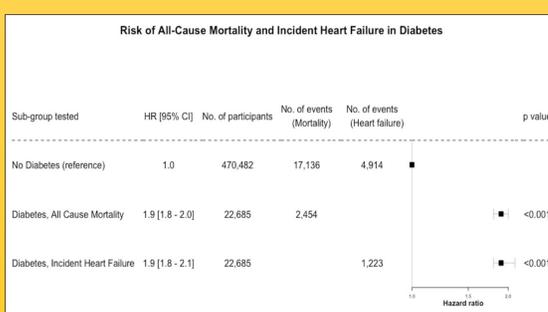
	Control	Participants with Diabetes	Type 1 DM	Type 2 DM
Total, n	470,482	22, 685	2,626	20,059
Demographics				
Age at enrolment (years), mean	56	60	57	60
Female sex, n (%)	260,743 (55%)	8,531 (38%)	1,123 (43%)	7,408 (37%)
Ethnicity, n (%)				
Caucasian	444,873 (94.5%)	19,638 (86.6%)	2,395 (91.2%)	17,243 (85.9%)
Other	25,609 (5.5%)	3,047(13.4%)	231 (8.8%)	2816 (14.1%)
Lifestyle factors				
Smoking n (%)	49,462 (10.5%)	2,506 (11%)	343 (13%)	2,163 (10.8%)
Physical activity – meeting or above WHO recommendation (%)	279,296 (59%)	10767 (47%)	1,409 (54%)	9,444 (47%)
BMI, median, kg/m ² , (IQR)	26.5 (24.0- 29.6)	30.6 (27.3 – 34.7)	27.4 (24.4 – 31.1)	31.0 (27.8 – 35.0)
Medical background				
Duration of diabetes mellitus, median years, y, (IQR)	0 (0 – 0)	14 (11 – 19)	Male: 28 (18 – 41) Female: 27 (17 – 40)	Male: 14 (11 – 18) Female: 13 (10 – 17)
Hba1c (mmol/mol), median (IQR)	35 (33-37)	Male: 51 (44 - 60) Female: 51 (44 - 61)	Male: 59 (50 - 68) Female: 61 (54 - 70)	Male: 51 (44 - 59) Female: 50 (44 - 58)
Diagnosed/ treated for coronary artery disease	18,324 (3.9%)	3,947 (17.4%)	400 (15.2%)	3,547 (17.7%)
Diagnosed/ treated for hypertension	121,005 (25.7%)	15,709 (69.2%)	1,496 (57%)	14,213 (70.9%)
Diagnosed/ treated for hyperlipidaemia	70,100 (14.9%)	14,789 (65.2%)	1,469 (55.9%)	13,320 (66.4%)

*WHO – World Health Organisation, *BMI – Body Mass Index, *IQR – Interquartile range, *Hba1c – Glycated haemoglobin

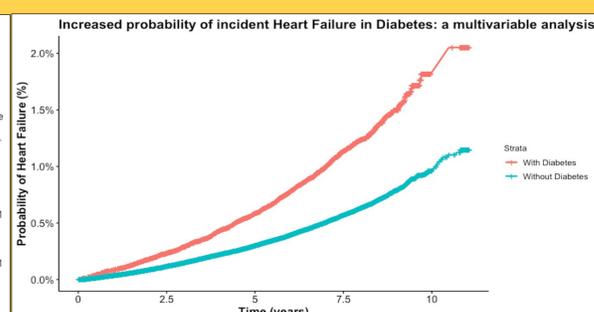
Results & Conclusions



Men have a lower survival probability compared to women, which is also true in those with diabetes.⁶



A multivariate analysis was performed for outcomes of all cause mortality and heart failure. The analysis stratified for age, ethnicity, hypertension, hypercholesterolaemia, smoking, BMI, alcohol status with coronary artery disease. In those with diabetes, the risk of mortality and heart failure are almost doubled.⁶



Association between Diabetes, Gender and Incident of Heart Failure – multivariate, competitive risk and sensitivity analysis					
Men			Women		
Sub-group tested	HR[95%CI]	sHR[95%CI]	No. of participants	No. of events	p value
Without Diabetes	1.0		209,739	3130	
With Diabetes (both types)	1.8 [1.7-2.0]		14,154	893	<math>p < 0.001</math>
Competing risk analysis	1.7 [1.6-1.8]				<math>p < 0.0001</math>
Sensitivity analysis	1.6 [1.3 - 1.8]		9,811	206	<math>p < 0.001</math>
With T1DM	2.5 [2.0-3.0]		1,503	105	<math>p < 0.001</math>
Competing risk analysis	2.3 [1.9-2.6]				<math>p < 0.0001</math>
Sensitivity analysis	2.4 [1.5 - 3.8]		1,068	22	<math>p < 0.001</math>
With T2DM	1.7 [1.6-1.9]		12,651	788	<math>p < 0.001</math>
Competing risk analysis	1.6 [1.4-1.7]				<math>p < 0.0001</math>
Sensitivity analysis	1.5 [1.2 - 1.7]		8,743	184	<math>p < 0.001</math>

Forest plot demonstrating risk of HF between men and women for each subset of participants with diabetes. The multivariate cox models were adjusted for age, ethnicity, hypertension, hypercholesterolaemia, smoking, BMI, alcohol status with coronary artery disease stratified. Interaction term between sex and heart failure is significant in the T1DM group ($p = 0.0001$) and for the overall diabetes group ($p = 0.007$). Interaction term for sex and heart failure in T2DM is $p = 0.1$. Competing risk confirms the trend seen in the multivariate analysis, and indicates that the increased risk in women especially with T1DM is significant enough to be above all-cause mortality. T1DM: type 1 diabetes. T2DM: type 2 diabetes. HR: Hazard ratio. sHR: sub-distribution hazard ratio. ⁶

Conclusions

- ❖ Diabetes increases the risk of heart failure for both men and women, but the increase in risk is relatively higher for women with diabetes than men.
- ❖ This study shows that the excess risk in women persists despite stratification for risk factors including coronary disease, previously unknown.
- ❖ Diabetic cardiomyopathy may be a contributor to this excess risk of heart failure and may affect women with diabetes more than men.
- ❖ Further research investigating the structural and functional cardiovascular differences in those with diabetes according to sex is underway

References

- KAISER AMYB, ZHANG N, DER PLUIJM WVAN (2018) Global Prevalence of Type 2 Diabetes over the Next Ten Years (2018-2028). Diabetes 67(Supplement 1):202-LB. <https://doi.org/10.2337/db18-202-LB>
- Hex N, Bartlett C, Wright D, Taylor M, Varley D (2012) Estimating the current and future costs of Type1 and Type2 diabetes in the UK, including direct health costs and indirect societal and productivity costs. Diabet Med 29(7):855–862. <https://doi.org/10.1111/j.1464-5491.2012.03698>.
- Packer M (2018) Heart Failure: The Most Important, Preventable, and Treatable Cardiovascular Complication of Type 2 Diabetes. Diabetes Care 41(1):11–13. <https://doi.org/10.2337/DC17-0052>
- From AM, Scott CG, Chen HH (2010) The Development of Heart Failure in Patients With Diabetes Mellitus and Pre-Clinical Diastolic Dysfunction: A Population-Based Study. J Am Coll Cardiol 55(4):300–305. <https://doi.org/10.1016/j.jacc.2009.12.003>
- Ohkuma T, Komorita Y, Peters SAE, Woodward M (2019) Diabetes as a risk factor for heart failure in women and men: a systematic review and meta-analysis of 47 cohorts including 12 million individuals. Diabetologia 62(9):1550–1560. <https://doi.org/10.1007/s00125-019-4926-x>
- Chadalavada S, Jensen MT, Aung N, Cooper J, Lekadir K, Munroe PB and Petersen SE (2021) Women With Diabetes Are at Increased Relative Risk of Heart Failure Compared to Men: Insights From UK Biobank. Front. Cardiovasc. Med. 8:658726. doi: 10.3389/fcvm.2021.658726