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P142 Androgen Receptor Reduced Sensitivity is Associated with Cardiovascular Mortality in Men with Type 2 Diabetes - A 14-year Follow up Study

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ABSTRACT

Background: Hypogonadism associates with increased cardiovascular morbidity/mortality in type 2 diabetes mellitus (T2DM) [1]. Increasing CAG repeat number within exon 1 of the androgen receptor gene associates with increased androgen receptor resistance/insulin resistance [2]. We here investigated the link between CAG repeat number and metabolic/cardiovascular outcomes in T2DM men.

Methods: We determined in a 14-year follow-up cohort of 274 T2DM Caucasian men in Salford UK, the association between baseline androgen status/CAG repeat number (determined by PCR followed by Sequenom sequencing) and metabolic trajectory plus mortality.

Results: Lower baseline testosterone was associated with higher Body Mass Index (BMI) (kg/m^2) at 14-year follow-up: regression coefficient −0.30 (95% CI: −0.445 to −0.157), $p = 0.0001$ (total testosterone data) and higher HbA1c 2016. Higher baseline CAG repeat number associated with higher follow-up BMI in 2016 - each unit increase in CAG repeat associated with 0.43 increment in BMI 2016. At an average 14 year follow-up 55.8% of hypogonadal men had died vs 36.1% of eugonadal men ($p = 0.001$). 72% of deaths were from cardiovascular causes. There was a 'u' shaped relation between the number of CAG repeats and mortality such that 21–23 CAG repeats was associated with an up to 58% lower mortality rate than <21 CAG repeats and >23 CAG repeats (Figure 1). This was independent of baseline testosterone.

Conclusion: A higher number of CAG repeats at the testosterone receptor gene associates with higher future BMI/increased HbA1c. There was a 'u' shaped relation between CAG repeat number and mortality rate. CAG repeat number may become part of cardiovascular risk assessment in T2DM men.

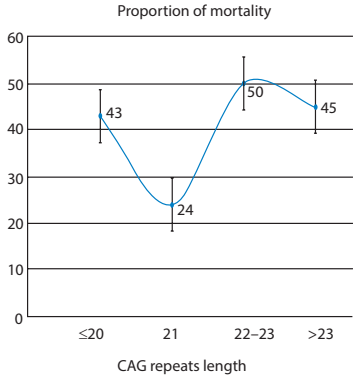

Figure 1

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CAG_cat	Mortality	Proportional mortality rate	Lower bound	Upper bound
≤20	40	43	32	53
21	12	24	13	39
22–23	28	50	36	64
>23	34	45	34	57

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