Muscle Mitochondrial Function in Klinefelter Syndrome

Stephanie Cung[1], Melanie Cree-Green[1], Kristin Nadeau[1], Dana Dabelea[2], Shanlee Davis[1]
[1]Children's Hospital Colorado, Aurora, CO; [2]Department of Epidemiology, University of Colorado SOM, Aurora, CO

BACKGROUND

- Klinefelter Syndrome (XXY), or 47,XXY, occurs in 1/600 males and is associated with testosterone deficiency
- XXY adults have lower exercise capacity and higher risk of type 2 diabetes and cardiovascular disease
- Testosterone deficiency is associated with insulin resistance through impaired mitochondrial function, but this has not been studied in XXY
- Aim: to investigate differences in post-exercise muscle mitochondrial function in XXY

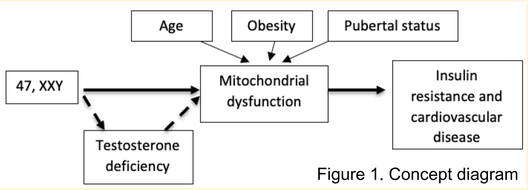

Figure 1. Concept diagram

METHODS

- Case-control cross sectional study in males 12-18
  - Cases: 47,XXY (XXY) (n=27)
  - Controls: two cohort studies (EPOCH and SEARCH) with available data (n=75)
- Outcome: in vivo soleus muscle mitochondrial function using phosphorus MRS -- ADP time constant, oxidative phosphorylation, PCr time constant, Q_{max}
  - VO_2 analyzed via bike ergometry for XXY

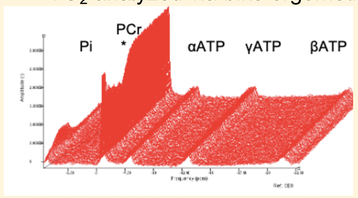

Figure 2. ^{31}P-MRS during 70% exercise. Each line represents two seconds of data, and * indicates recovery post-exercise.

- Analysis: Multiple linear regression to adjust for age in XXY vs. controls. Within XXY, analysis by testosterone treatment status; p<0.05 is statistically significant

RESULTS

Table 1. Descriptive Characteristics of Study Participants

	XXY (n=27)	Controls (n=75)	P value
Age (years)	14.7 ± 1.8	16.7 ± 1.3	<0.01*
BMI (kg/m²)	19.6 (18.6, 24.2)	21.8 (19.5, 26.4)	0.07
BMI-Z	0.19 ± 1.53	0.26 ± 1.22	0.83
Waist (cm)	74.0 (70.6, 88.8)	78.2 (72.4, 89.5)	0.41
Race, n(%)			0.05*
Non-Hispanic white	21 (77.8)	40 (53.3)	
Hispanic	3 (11.1)	25 (33.3)	
Non-Hispanic black	3 (11.1)	5 (6.7)	
Non-Hispanic other	0	5 (6.7)	
Tanner stage, n(%)			0.17
2	2 (7.4)	3 (4.0)	
3	0	1 (1.3)	
4	15 (55.6)	29 (38.7)	
5	10 (37.0)	42 (56.0)	
Treatment with Exogenous Testosterone, n(%)	13 (48.1%)		

Data presented as mean ± standard deviation or median (25%, 75%).
***Statistically significant difference**

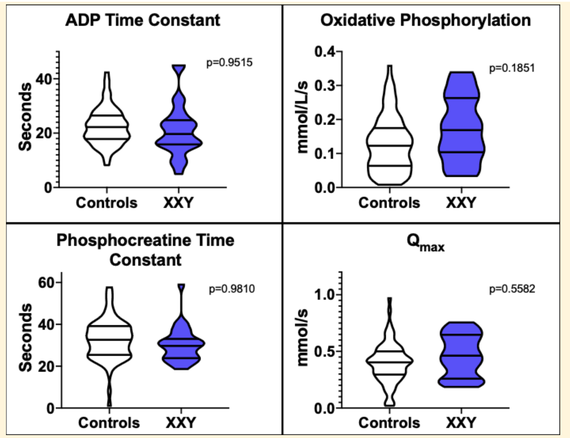

Figure 3. ^{31}P-MRS outcomes in XXY males were not statistically significant compared to controls after controlling for differences in age.

Subanalysis of XXY Group

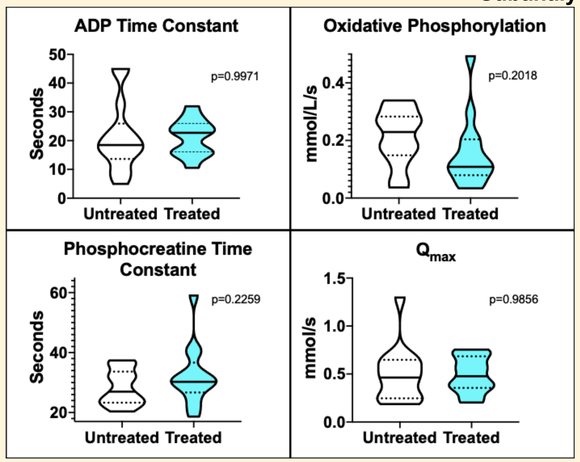

Figure 4. ^{31}P-MRS outcomes in XXY males based on treatment status with exogenous testosterone.

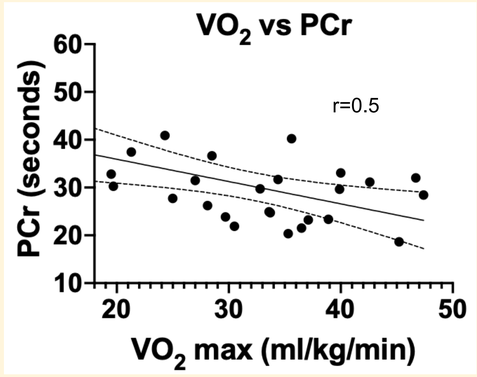

Figure 5. Exercise capacity (VO_2 max) correlates with faster recovery of PCr, as expected.

CONCLUSION

In vivo post-exercise muscle mitochondrial function is not impaired in adolescents with XXY compared to controls.

DISCUSSION

- No significant difference in muscle mitochondrial function with exercise between XXY and controls
- Relationship between VO_2 max and PCr time constant suggests mitochondrial function may be contributing to lower exercise capacity
- Exercise intolerance seen in XXY cannot be explained by muscle mitochondrial dysfunction

NEXT STEPS

- Resting energy expenditure for a measure of systemic mitochondrial function and other measures of tissue-specific mitochondrial function
- Evaluate other mechanisms for exercise intolerance and cardiovascular disease

FUNDING

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