Androgen deprivation therapy for prostate cancer, measures of adiposity and strength, and adverse cardiovascular outcomes

Observations from 3500 individuals in 7 countries

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Background

- Androgen deprivation therapy (ADT) is prescribed to nearly half of patients with prostate cancer (PC)¹
- ADT increases adiposity and decreases muscle strength^{2, 3}
 - 1. Shahinian, et al. NEJM 2010; 363: 1822
 - 2. Smith, et al. Cancer 2008; 112: 2188
 - 3. Gonzalez, et al. Support Care Canc 2016; 24: 2201

Body Mass Index and CVD Risk in 1.5M Adults Globally



CVD Risk per 5kg Lower Handgrip Strength

142,861 adults from 17 countries followed for 4 years

Adjusted HR (95% CI)	P-value
1.17 (1.11-1.24)	<0.0001
1.07 (1.02-1.11)	0.0024
1.09 (1.05-1.15)	< 0.0001
	Adjusted HR (95% CI) 1.17 (1.11-1.24) 1.07 (1.02-1.11) 1.09 (1.05-1.15)



ESC Congress 2023 Leong, Teong, Teong

Leong, Teo, Rangarajan, et al. Lancet 2015; 386: 266

Objectives

In patients with PC:

- Evaluate relationship between ADT use and measures of adiposity and muscle strength
- Describe association between baseline measures of adiposity and muscle strength and cardiovascular disease risk



<u>Role of Androgen Deprivation</u> Therapy in <u>Ca</u>rdiovascular Disease – A <u>Longitudinal Prostate Cancer Study</u>

- Ongoing prospective cohort study
- Patients with new PC or being treated with ADT for first time
- 3597 participants from 7 countries
- Characterised thoroughly at baseline and at annual follow-up visits
- Primary outcome Incident CVD: MI, angina, stroke, cerebrovascular disease, PAD, arterial revascularization, VTE, heart failure, AF

Baseline Characteristics

Characteristic	No ADT exposure N=2090	ADT exposure N=1507	P-value
Age, years	66±7	71±8	<0.0001
Education Primary Secondary > Secondary	14% 26% 60%	23% 28% 49%	<0.0001
Tobacco Never Former Current	44% 46% 10%	40% 49% 12%	0.017
Alcohol Never Former Current	14% 11% 75%	17% 18% 65%	<0.0001
Prostate cancer risk Intermediate/ Low High	67% 33%	15% 85%	<0.0001

Baseline Cardiovascular Risk Factors

Characteristic	No ADT exposure N=2090	ADT exposure N=1507	P-value
Diabetes	15%	20%	<0.0001
Hypertension	45%	51%	<0.0001
Blood pressure Rx	51%	59%	<0.0001
Systolic BP	138±18	138±19	1.00
LDL chol, mmol/L	2.6±1.0	2.5±1.1	0.40
Coronary artery Dx	12%	15%	0.005
Cerebrovascular Dx	5%	6%	0.18
Peripheral arterial Dx	2%	2%	0.59

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Baseline Physical Characteristics

Characteristic	No ADT exposure N=2090	ADT exposure N=1507	P-value
Weight, kg	86±15	86±17	0.23
Waist circumference, cm	102±12	104±13	0.0031
Get-up-and-go time, sec	8.6±3.4	10.1±5.2	<0.0001
Handgrip strength, kg	39±11	34±10	<0.0001

Effect of ADT on Physical Measurements at 1 Year





Adjusted for age, education, ethnicity, tobacco & alcohol use, physical activity, baseline CVD, eGFR

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Risk of CVD by Quartile of Baseline Physical Measure

During median 3 years' follow-up, 176 (4.9%) developed CVD





Baseline Physical Measures and Risk of Incident CVD

Physical Measure	HR (95% CI)	P-value
Highest fourth of weight	1.26 (0.87-1.82)	0.23
Highest fourth of waist circumference	1.24 (0.86-1.78)	0.25
Slowest fourth of gait speed	1.12 (0.77-1.64)	0.56
Lowest fourth of handgrip strength	1.78 (1.23-2.57)	0.002

Adjusted for age, education, ethnicity, tobacco & alcohol use, physical activity, baseline CVD, eGFR, ADT exposure

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Conclusions

- **1.** ADT use is associated with accelerated weight gain and central adiposity; slowed gait speed and decreased handgrip strength
- 2. Among baseline physical characteristics, low muscle strength is most closely associated with future CVD

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