

Effect of body mass and physical activity at younger age on the risk of prostatic enlargement and erectile dysfunction: Results from the 2018 #Controllati survey

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Summary

Objective: Overweight and low physical activity (PA) increase the risk of prostatic enlargement and erectile dysfunction (ED). Less clear is the role of these factors at young age on the lifelong risk.

Materials and methods: During June 2018 the Italian Society of Urologists organized the month of Male Urologic Prevention "#Controllati". Men aged 18 years or more were invited to attend urologic centers for a visit and counselling about urologic/androgenic conditions. Each participating man underwent a physical examination and was asked about urologic symptoms, sexual activity and possible related problems.

Results: We analyzed data from 2786 men, aged 55.1 years (SD 10.9, range 19-97). A total of 710 (25.5%) subjects had a diagnosis of prostatic enlargement and 632 (22.7%) of DE. Overweight/obese men were at increased risk of prostatic enlargement and ED with corresponding odds ratio (OR) in comparison with normal or underweight men, being respectively 1.18 (95% Confidence Interval (CI) 1.00-1.44) and 1.69 (95% CI 1.39-2.05). The OR of prostatic enlargement in comparison with men reporting at age 25 a BMI < 25.0 was 1.22 (95% CI 1.01-1.51) for men with a BMI at 25 years of age ≥ 25; the corresponding OR value for ED was 1.17 (0.92-1.48). Considering total PA at diagnosis, the OR of prostatic enlargement in comparison with no or low PA, was 0.69 (95%CI 0.55-0.86) for men reporting moderate PA and 0.75 (95%CI 0.58-0.98) for those reporting intense PA. When we considered PA at 25 years of age, the OR of subsequent diagnosis of prostatic enlargement, in comparison with men reporting no/low PA at 25 years of age was 0.81 (95%CI 0.63-1.04) for men reporting moderate PA and 0.70 (95%CI 0.52-0.99) for those reporting intense PA.

Conclusions: These findings underline the utility of encouraging healthy lifestyle habits among young men in order to reduce the subsequent risk of prostatic enlargement and ED.

KEY WORDS: Benign prostatic enlargement; Hypertension; Diabetes; Heart disease; Body mass index; Physical activity.

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INTRODUCTION

Benign prostatic enlargement (BPE) and erectile dysfunction (ED) are the two most common urologic diseases in men, the estimated prevalence of PE being about 10% in

the fourth decades increasing up to 50% thereafter and that of ED being 12% (1, 2).

Among the risk factors for these two conditions, lifestyles play a major role.

It is well recognized, for example, that overweight, low physical activity (PA), hypertension, hypercholesterolemia and hypertriglyceridemia increase the risk of these conditions at advanced age (3-6).

Less clear is the role of these factors on the lifelong risk when they were present at younger age (7).

Since 2016 the Italian Urologic Society (SIU, Società Italiana di Urologia) coordinates a huge preventive initiative: the month of Male Urologic Prevention "#Controllati" (8, 9).

In the framework of this preventive campaign data have been collected on determinants of the risk of prostatic enlargement and ED.

In this paper we present the results of the 2018 initiative with a special focus on risk factors for prostatic enlargement and ED and on lifelong risk for these condition in relation to lifestyle at younger age.

METHODS

During June 2018, men aged 18 year or more were invited to attend the participating urologic centers for a free of charge visit and counselling about urologic or androgenic conditions.

A pamphlet inviting men for check-up was distributed in chemists and general practitioners' waiting rooms. An advertising campaign was also set on media.

At visit, general data were recorded using a simple questionnaire. The first section of the questionnaire, including data on age, life habits height and weight, was completed by the patient. The section on PA included questions on self-reported intensity of PA ('none', 'low', 'moderate', 'intense') at work and in leisure time separately. History of hypertension, diabetes, cardiopathy, hypertriglyceridemia and hypercholesterolemia were checked by the urologist. Information was also collected on *body mass index* (BMI) and total PA at age 25 year among men aged 30 year or more.

Each participating man underwent a physical examination, including *digital rectal examination* (DRE), and was asked by the urologist about urologic symptoms, sexual activity and possible related problems. Diagnosis of prostatic enlargement was made by the urologist by DRE.

Erectile function was assessed by asking men about their sexual performance: ED was diagnosed, according to the definition of the *NIH Consensus Development Panel* (10), when a man was consistently unable to attain or maintain a penile erection sufficient for satisfactory sexual performance.

The 2002 ICS definitions were used for frequency, nocturia, urgency, dysuria (intermittency, slow stream, straining, terminal dribble, postmicturition dribble) incomplete emptying (11).

A man was considered a smoker if he had smoked more than one cigarette/day for at least one year; ex-smoker if he had smoked more than one cigarette/day for at least one year, but had stopped more than one year before the interview, and non-smoker if he had never smoked more than one cigarette/day.

Total PA was evaluated combining occupational and leisure time PA. Frequencies (%) were computed as appropriate. *Odds ratios* (OR), and the corresponding 95% *confidence intervals* (CI), adjusted for age were derived using unconditional multiple logistic regression, fitted by the method of maximum likelihood, in which the dependent variable was the presence (case) or absence (control) of the condition and the independent ones were the exposures considered in the analysis. We included in the model age considered as categorical variable (12).

RESULTS

During the 2018 campaign a total of 3092 men entered the study. After exclusion of men who underwent previous surgery for partial or complete prostatectomy and those who did not answer at least one of two questions

about PA, we analyzed data from 2786 men, aged 55.1 years (SD 10.9, range 19-97). The reason for visit was urinary symptoms in 504 (18.1%), sexual problems in 270 (9.7%), renal disease in 68 (2.4%) and prostatic problems in 429 (15.4%) (more than one reason was allowed). Prevention was the only reason for consultation in 1776 subjects (63.8%). A total of 710 (25.5%) subjects had a diagnosis of prostatic enlargement and 632 (22.7%) of DE. Table 1 shows the distribution, and the corresponding OR, of study subjects according to the diagnosis of prostatic enlargement, ED and age, smoking habits and BMI.

The risk of prostatic enlargement and ED increased with age: in comparison with men aged <=40 years or less, the risk of prostatic enlargement was 2.57, 7.22, 17.97 and 39.1 in the age classes 41-50, 51-60, 61-70 and >=71, respectively. The corresponding values for ED were 1.15, 1.63, 3.06 and 4.87.

Smoking increased the risk of ED: in comparison with never smokers, ex-smokers had an increased risk of ED of 1.38 (95%CI 1.11-1.69) and current smokers of 1.92 (95%CI 1.49-2.48).

Overweight/obese men were at increased risk of prostatic enlargement and ED the corresponding OR, in comparison with normal or underweight men, being respectively 1.18 (95%CI 1.00-1.44) and 1.69 (95%CI 1.39-2.05).

We have also considered (among men aged 30 years or more) the role of overweight/obesity at 25 years of age on the subsequent risk of prostatic enlargement and ED.

In comparison with men reporting at age 25 a BMI < 25.0, the OR of prostatic enlargement was for men with a BMI at 25 years of age >= 25, 1.22 (95%CI 1.01-1.51); the corresponding value for ED was 1.17 (95%CI 0.92-1.48).

Table 2 considers the relation between prostatic enlargement and DE and urinary symptoms, hypertension, diabetes, cardiopathy, hypertriglyceridemia and hypercholesterolemia.

Table 1. Odds ratios (and corresponding 95% confidence intervals) of BPE and erectile dysfunction according to selected factors.

	Benign prostatic enlargement		Age adj OR (95%CI)		Erectile dysfunction		Age adj OR (95%CI)			
	No No.* (%)	Yes No.* (%)			No No.* (%)	Yes No.* (%)				
Age (years)										
≤ 40	166	7.8	7	0.9	1°	150	6.8	23	3.5	1°
41-50	782	36.8	87	11.5	2.57 (1.17-5.66)	736	33.2	133	20.0	1.15 (0.71-1.85)
51-60	718	33.8	225	29.6	7.22 (3.34-15.63)	752	33.9	191	28.7	1.63 (1.02-2.60)
61-70	339	16.0	269	35.4	17.97 (8.29-38.96)	413	18.6	195	29.3	3.06 (1.91-4.90)
≥ 71	118	5.6	171	22.5	35.10 (15.83-77.86)	165	7.4	124	18.6	4.87 (2.94-8.06)
Smoking habits										
Never	1131	53.3	342	45.1	1°	1198	54.1	275	41.3	1°
Ex smokers	624	29.4	303	39.9	1.2 (0.98-1.47)	668	30.1	259	38.9	1.38 (1.12-1.69)
Current smokers	343	16.2	103	13.6	1.1 (0.84-1.47)	317	14.3	129	19.4	1.92 (1.49-2.48)
< 10 cig/day	127	8.5	34	7.5	0.94 (0.58-1.53)	130	8.5	31	7.6	1.49 (0.96-2.29)
≥ 10 cig/day	192	12.9	67	14.8	1.27 (0.90-1.78)	174	11.3	85	21.0	2.25 (1.66-3.06)
BMI (kg/m ²)										
< 25.0	891	43.2	253	35.8	1°	949	44.1	195	30.8	1°
≥ 25.0	1172	56.8	453	64.2	1.18 (1.00-1.44)	1189	55.2	436	69.0	1.69 (1.39-2.05)
BMI at 25 years of age										
< 25.0	1293	62.3	443	62.4	1°	1335	62.0	401	63.4	1°
≥ 25.0	384	18.5	123	17.3	1.22 (1.01-1.51)	381	17.7	126	19.9	1.17 (0.92-1.48)

*Sometimes, the sums do not add up the total due to missing values; °reference category OR: odds ratio; CI: confidence interval.

Table 2. Odds ratios (and corresponding 95% confidence intervals) of BPE and erectile dysfunction according to medical history.

	Benign prostatic enlargement		adj OR (95%CI)		Erectile dysfunction		adj OR (95%CI)			
	No No.* (%)	Yes No.* (%)	No No.* (%)	Yes No.* (%)	No No.* (%)	Yes No.* (%)	No No.* (%)	Yes No.* (%)		
Urinary symptoms**										
No	987	46.5	101	13.3	1°	924	41.7	164	24.6	1°
Yes	1136	53.5	658	86.7	5.14 (3.97-6.67)	1292	58.3	502	75.4	1.82 (1.47-2.25)
Erectile dysfunction										
No	1698	80.0	518	68.2	1°	-	-	-	-	-
Yes	425	20.0	241	31.8	1.27 (1.03-1.57)	-	-	-	-	-
Benign prostatic enlargement										
No	-	-	-	-	-	1698	76.6	425	63.8	1°
Yes	-	-	-	-	-	518	23.4	241	36.2	1.27 (1.03-1.57)
Hypertension										
No	1492	70.3	369	48.6	1°	1524	68.8	337	50.6	1°
Yes	407	19.2	275	36.2	1.6 (1.30-2.619)	457	20.6	225	33.8	1.60 (1.29-1.99)
Missing	224	10.6	115	15.2		235	10.6	104	15.6	--
Diabetes										
No	1884	88.7	599	78.9	1°	1964	88.6	519	77.9	1°
Yes	78	3.7	80	10.5	1.57 (1.08-1.85)	82	3.7	76	11.4	2.43 (1.70-3.47)
Missing	161	7.6	80	10.5		170	7.7	71	10.7	-
Cardiopathy										
No	1857	87.5	577	76.0	1°	1925	86.9	509	76.4	1°
Yes	76	3.6	74	9.7	1.30 (1.02-1.67)	80	3.6	70	10.5	2.12 (1.47-3.06)
Missing	190	8.9	108	14.2		211	9.5	87	13.1	-
Hypertriglyceridemia										
No	1753	82.6	586	77.2	1°	1830	82.6	509	76.4	1°
Yes	130	6.1	62	8.2	1.31 (0.92-1.85)	130	5.9	62	9.3	1.59 (1.13-2.22)
Missing	240	11.3	111	14.6		256	11.6	95	14.3	-
Hypercholesterolemia										
No	1548	72.9	492	64.8	1°	1613	72.8	427	64.1	1°
Yes	301	14.2	143	18.8	1.30 (1.02-1.67)	315	14.2	129	19.4	1.42 (1.11-1.81)
Missing	274	12.9	124	16.3		288	13.0	110	16.5	-

*Sometimes, the sums do not add up the total due to missing values; **one or more of the followings: nocturia, urgency, dysuria (intermittency, slow stream, straining, terminal dribble, postmicturition dribble) incomplete emptying; °reference category; adjOR: adjusted odds ratio; CI: confidence interval.

Table 3. Odds ratios (and corresponding 95% confidence intervals) of premature ejaculation and erectile dysfunction according to physical activity.

	Benign prostatic enlargement		adj OR (95%CI)		Erectile dysfunction		adj OR (95%CI)			
	No No.* (%)	Yes No.* (%)	No No.* (%)	Yes No.* (%)	No No.* (%)	Yes No.* (%)	No No.* (%)	Yes No.* (%)		
Occupational PA										
None/Low	1002	48.3	354	49.9	1°	1035	48.1	321	50.8	1°
Moderate (0,7-1,1)	631	30.4	198	27.9	0.89 0.86 (0.69-1.08)					
Intense	657	30.5	172	27.2	0.97 (0.72-1.31)	286	13.3	77	12.2	0.98 (0.73-1.30)
Missing	283	13.6	80	11.3		176	8.2	62	9.8	-
Leisure PA										
Low	160	7.7	78	11.0	1°	785	36.4	299	47.3	1°
Moderate	767	36.9	317	44.6	0.67 (0.55-0.83)	926	43.0	239	37.8	0.66 (0.54-0.80)
Intense	893	43.0	272	38.3	0.64 (0.51-0.91)	342	15.9	61	9.7	0.48 (0.36-0.66)
Missing	319	15.4	84	11.8		101	4.7	33	5.2	-
Total PA										
Low	97	4.7	37	5.2	1°	544	25.3	221	35.0	1°
Moderate	537	25.9	228	32.1	0.69 (0.55-0.86)	995	46.2	273	43.2	0.65 (0.53-0.80)
Intense	960	46.2	308	43.4	0.75 (0.58-0.98)	545	25.3	114	18.0	0.56 (0.43-0.72)
Missing	515	24.8	144	20.3		70	3.2	24	3.8	-
PA at 25 years of age										
Low	64	3.1	30	4.2	1°	415	19.3	146	23.1	1°
Moderate	401	19.3	160	22.5	0.81 (0.63-1.04)	858	39.8	235	37.2	0.78 (0.61-0.99)
Intense	820	39.5	273	38.5	0.70 (0.52-0.99)	785	36.4	232	36.7	0.74 (0.58-1.10)
Missing	773	37.2	244	34.4		96	4.5	19	3.0	-

*Sometimes, the sums do not add up the total due to missing values; °reference category; adjOR: adjusted odds ratio; CI: confidence interval.

A history of hypertension, diabetes, cardiopathy, high cholesterol levels were significantly associated to an increased risk of prostatic enlargement in the total series.

Likewise, hypertension, diabetes, cardiopathy, high triglyceride and cholesterol levels were significantly associated to an increased risk of ED.

PA was significantly associated with a decreased risk of prostatic enlargement: considering the total PA at diagnosis, the OR of prostatic enlargement, in comparison with men reporting no or low PA, was 0.69 (95%CI 0.55-0.86) among men reporting moderate PA and 0.75 (95%CI 0.58-0.98) among those reporting intense PA. The OR of subsequent diagnosis of prostatic enlargement were, in comparison with men reporting no/low PA at 25 years of age 0.81 (95%CI 0.63-1.04) for men reporting moderate PA and 0.70 (95%CI 0.52-0.99) for those reporting intense PA at 25 years of age. Similar findings emerged when we considered ED risk.

DISCUSSION

The general results of this analysis show that low PA, high BMI and a history of hypertension, diabetes, hypercholesterolemia, cardiopathy increase the risk of prostatic enlargement. High BMI and low PA at 25 year of age increase the risk of prostatic enlargement at older ages. Similar results emerged also for the risk profile of ED.

Limitations

As already discussed in the papers presenting the results of 2016 and 2017 initiative (8, 9), the major flaw of this study is that the study population were men voluntarily presenting to the participating centers. The participating centers were not randomly identified among all Italian urologic centers, so they cannot be considered representative of all Italian centers. However, they were well distributed over the main areas of the country. In any case, any inference from the present analysis must be made in strictly comparative terms and strictly referred to men attending urologic services.

The diagnosis of PE was based on DRE that tends to underestimate the prostatic volume (2). Any misclassification of men with or without BPE or should lower the observed associations. With regard to the diagnosis of DE, it was reported by the men and checked for standard criteria by the physician.

The results of this study confirm data from different populations that have reported that high BMI, low PA and a history of hypertension, diabetes, hypercholesterolemia, increase the risk of BPE at all ages (13, 14). All these findings underline that benign BPE shares similar risk factors with metabolic syndrome and cardiovascular diseases.

The etiological mechanisms that links these risk factors and prostatic growth are not completely understood. However, it has been shown that lipids (oxidized low-density lipoproteins) increase in vitro the secretion of growth and pro-inflammatory factors by human stromal BPE cells in culture (15). Along this line, in a clinical perspective, the addition of statins to standard therapy for benign PE lowered prostate volume (16). Further, alteration of sex steroid hormone metabolism caused by both obesity and diabetes could lead to 'pro-inflammatory' conditions, causing release of chemokines potentially associated with prostate enlargement (17).

Regular PA has been consistently reported to decrease the risk of BPE. A meta-analysis has shown that moderate-to-vigorous physical activity was associated with up

to a 25% decreased risk of benign prostatic enlargement, with the magnitude of the protective effect increasing with the higher levels of activity (18).

An interesting finding from the present study is the observation that the OR of BPE and ED associated with none/low PA and high BMI at 25 years were higher than unity.

Few data have been published on the role of PA at younger ages on the lifetime risk of BPE.

A previous Italian case control study have reported that moderate/intense recreational physical activity (> 2 hours week) at age 30-39 decrease the risk of benign BPE of about 30%. The Authors concluded that avoidance of sedentary lifestyle through a moderate recreational PA at any age may help preventing a sizeable number (e.g., approximately 20%) of BPE cases (7).

With regard to erectile dysfunction, the risk profile of ED was largely similar with that observed for prostatic enlargement. In particular, the present analysis confirms that smoking, overweight, low PA and history of diabetes, hypertension, cardiopathy, hypercholesterolemia, hypertriglyceridemia, all increased the risk of ED.

All these findings underline the role of encouraging healthy lifestyle habits among young men in order to reduce the subsequent risk of prostatic enlargement and ED.

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