ANDROLOGY

ISSN: 2047-2919

ANDROLOGY

ORIGINAL ARTICLE

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Keywords:
clinical characteristics, concomitant occurrence, differences, erectile dysfunction, premature ejaculation, similarities

Received: 5-Sep-2018
Revised: 9-Nov-2018
Accepted: 1-Dec-2018

doi: 10.1111/andr.12579

Clinical characteristics of men complaining of premature ejaculation together with erectile dysfunction: a cross-sectional study

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ABSTRACT

Background: Premature ejaculation (PE) is present in up to 30% of men with erectile dysfunction (ED).

Objectives: To assess the clinical features of men complaining of both ED and PE (ED-PE) as compared to men reporting only ED or PE.

Materials and methods: A consecutive series of 4024 men (mean age 51.2 ± 13.2 years) consulting for sexual dysfunction was studied. The population was categorized into ED-only (n = 2767; 68.8%), PE-only (n = 475; 1.8%), and ED-PE (n = 782; 19.4%). Sexual symptoms were evaluated using the structured interviews SIEDY and ANDROTEST. Penile color Doppler ultrasound (PDCU) parameters were also assessed.

Results: When compared to PE alone, ED-PE reported more sexual complaints, including impaired morning erections [OR = 5.8 (4.1; 8.3)], decreased sexual desire [OR = 2.6 (1.8; 3.7)], decreased ejaculate volume [OR = 2.7 (1.8; 4.0)], and reduced frequency of sexual intercourse [OR = 1.4 (1.0; 2.0)]. Conversely, ED-PE and ED-only men had a similar prevalence of sexual symptoms. In ED-PE men, the characteristics of ED were similar to ED-only men, whereas the characteristics of PE were milder than in PE-only men. ED-PE men had a significantly higher prevalence of hypertension, diabetes, and cardiovascular (CV) diseases [OR = 1.8 (1.1; 3.0), 2.7 (1.3; 5.6) and 2.7 (1.1; 6.5), respectively] than PE-only subjects. Moreover, ED-PE men showed worse dynamic peak systolic velocity at PDCU [B = −12.0 (−17.7; −6.2)] and a greater 10-year estimated CV risk [B = 3.8 (2.5; 5.1)] than PE-only patients. Conversely, comorbidities and PDCU parameters were similar in ED-PE and ED-only men.

Discussion: The present results suggest that men reporting ED and PE should be considered as patients with ED-only, at least at first glance. Consequently, the diagnosis—including the CV risk stratification—and treatment should be primarily focused on the erectile problem.

Conclusions: Erectile dysfunction-PE patients present several similarities with those consulting only for ED, whereas their characteristics are different from PE-only men. In agreement with the guidelines, our results confirm that ED-PE men might be considered (and managed) primarily as patients with ED.

INTRODUCTION

Erectile dysfunction (ED) and premature ejaculation (PE) are the most common sexual complaints worldwide. It can be estimated that their prevalence, although presenting a great deal of variation according to the geographic area and the age of the population studied (McCabe *et al.*, 2016), ranges from 15 to 20% for ED (Corona *et al.*, 2010a; McCabe *et al.*, 2016) and 20 to 30% for PE in the general population (Laumann *et al.*, 2005; Porst *et al.*, 2007). As expected, their frequency is similar, or even higher, when considering specific settings, such as a sexual medicine outpatient clinic, where PE was reported by about 25% of men and ED was the most common symptom, reported by almost 90% of men (Corona *et al.*, 2011a). This indicates that the extent of bother derived by these conditions—which frequently leads men to seek medical care—is different from their prevalence in the general population. Due to the frequency of ED and

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PE and their negative consequences on quality of life, much work has been done to understand their physiopathology in order to identify useful targets for therapy. Indeed, at present, empirical therapies for both ED and PE are limited to second- or third-line options, while medications specifically acting on the mechanisms involved in the pathogenesis of these disorders—that is phosphodiesterase inhibitors or selective serotonin reuptake inhibitors (SSRI)—represent the highest standard of therapy due to their great efficacy and few adverse events (Hatzimouratidis *et al.*, 2016). ED and PE are commonly regarded as two separate entities, with different risk factors, pathogenesis and treatments. However, in clinical practice, their concomitant occurrence is a frequent finding. In a large study involving almost 5000 heterosexual men from the general population of nine Asia-Pacific countries, aged 18–65 years and involved in a stable couple relationship, ED was present in more than 30% of men with PE (McMahon *et al.*, 2012). An even higher prevalence has been recently found in a cross-sectional study on 1104 men aged 18–80 years from the general Italian population (Verze *et al.*, 2018). In this survey, ED prevalence among PE men ranged from 28.6 to 86.9% with an age-dependent increase and it was higher than in non-PE men irrespectively of age (Verze *et al.*, 2018). This is in line with a recent meta-analysis from our group (Corona *et al.*, 2015), including data from 18 studies on overall 57,229 patients, of which 21.2% reported PE, which has shown that men with PE have an almost 3-fold higher probability of reporting ED than men without PE. On the other hand, the Global Study of Sexual Attitudes and Behaviors, which evaluated sexual disorders in 13,618 middle-aged/older men from 29 countries worldwide, found that having ED increases the probability of PE from 4 to 11 times depending on the country (Laumann *et al.*, 2005).

The close epidemiological relationship between ED and PE raises questions on whether these two entities could represent two different manifestations of the same clinical condition, rather than two separate disorders. In line with this hypothesis, the use of phosphodiesterase type five inhibitors (PDE5i) in PE patients with or without ED has been proposed (Jannini *et al.*, 2011, 2013). In addition, current guidelines suggest that, in men with both ED and PE, treatment should start from the improvement of erectile function because this could extend per se the ejaculatory latency time (ELT) (Jannini *et al.*, 2013; McMahon *et al.*, 2013).

In the hypothesis that the concomitant presence of ED and PE is a different clinical manifestation of an erectile disorder, it could be expected that men with ED and PE have similar phenotypical characteristics of men with ED. Conversely, if the concomitant presence of ED and PE is the expression of two different conditions occurring together, men with ED and PE may share clinical characteristics with either men reporting only ED or only PE.

The aim of the present study is to evaluate the clinical characteristics of men who attend an Outpatients Clinic of Sexual Medicine for complaints of ED and PE in order to assess whether they share clinical features with those who report only one of the two disorders. This would help in evaluating if the concomitant presence of ED and PE represents a distinct entity, a different clinical expression of ED or PE or simply the presence of two conditions in the same patient.

MATERIALS AND METHODS

A consecutive series of 4024 patients consulting between 2000 and 2015 the Sexual Medicine and Andrology Unit of the University of Florence for sexual dysfunction were studied. According to our routine clinical practice, each patient underwent a standard diagnostic protocol. An informed consent for collecting these data was obtained from each patient. Before starting any diagnostic or therapeutic procedure, all patients were interviewed using the Structured Interview on Erectile Dysfunction (SIEDY) and ANDROTEST. SIEDY is a validated 13-item structured interview evaluating the pathogenic components of ED (Petrone *et al.*, 2003), whereas ANDROTEST is a validated 12-item structured interview for the screening of hypogonadism in patients with sexual dysfunction (Corona *et al.*, 2011b). For both interviews, answers to each question are arranged on a Likert scale. The algebraic sum of all the questions in the ANDROTEST provides the total score and the probability of having hypogonadism is higher as the score increases (Corona *et al.*, 2011b). The sum of answers to questions #4, #13, and #15 of SIEDY provides Scale 1, the score of which is higher as the organic risk factors for sexual dysfunction increase; the sum of answers to questions #7, #8, #9, and #10 of SIEDY provides Scale 2 whereas that the sum for questions #2, #3, #6, #11, #12, and #14 provides Scale 3, the scoring of which is higher as the relational or the psychological component of sexual dysfunction increases, respectively. ED was evaluated by question #1A (Do you have a full erection sufficient for penetration? rating 0 = always, 1 = often, 2 = quite often, and 3 = sometimes) and question #2 (Does it happen to you to have a normal erection which you are not able to maintain? rating 0 = sometimes, 1 = quite often, 2 = often, and 3 = always) of Appendix A of SIEDY. The score derived by the sum of these two questions has been previously validated vs. the International Index of Erectile Function (IIEF-5): a score >2 has a sensitivity and a specificity of 90 and 79%, respectively, for IIEF-5 score <21 (Corona *et al.*, 2012) and it was used for defining ED in the present study. The characteristics of ED have been evaluated as follows: ED severity: score to question #1A of Appendix A of SIEDY (see before); ED duration: score to question #3 of Appendix A of SIEDY (Since when have you had erectile problems? rating 0 < 1 month, 1 < 6 months, 2 < 2 years, and 3 > 2 years); ED worsening: score to question #4 of Appendix A of SIEDY (Since when has it gotten worse? rating 0 < 1 month, 1 < 6 months, 2 < 2 years, and 3 > 2 years); ED onset: question #5 of Appendix A of SIEDY (Did the problem start suddenly or gradually? rating 0 = suddenly and 1 = gradually).

Premature ejaculation was defined using a standard question (During the last three months, has it happened that you ejaculated too quickly? rating 0 = no PE, if self-assessed ELTs were >60 s or 1 = PE, if self-assessed ELTs were <60 s). PE severity was further categorized as follows: mild PE, self-assessed ELTs of 30–60 s; moderate PE, self-assessed ELTs of 15–30 s; severe PE, self-assessed ELTs <15 or occurring before penetration. PE frequency was assessed by a standard question (During the last three months, how frequently has it happened that you ejaculated too quickly? rating 0 = sometimes, 1 = quite often, 2 = often, 3 = always). PE onset was defined as lifelong if the patient reported that it had occurred since the first sexual intercourse or acquired if it started later on during sexual life.

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Patients were defined as (i) ED-only when meeting the criteria for ED but not PE, (ii) PE-only when meeting the criteria for PE but not ED, and (iii) ED-PE when meeting both the criteria for ED and PE.

Impairment in morning erections, decreased sexual desire, decreased ejaculate volume, stability of couple relationship, conflicts within the couple, and presence of an extramarital sexual relationship have been assessed by questions #13, #14, #15, #5, #6, and #12 of SIEDY (Petrone *et al.*, 2003) and used as dummy variables. Frequency of sexual intercourse and perception of privacy during intercourse have been evaluated by two standard questions and treated as dummy variables, as previously reported (Corona *et al.*, 2011c; Boddi *et al.*, 2014).

All patients were also asked to report all their comorbidities and drugs used. All patients underwent a complete physical examination, with measurement of blood pressure (mean of three measurements 5 min apart, in a sitting position, with a standard sphygmomanometer), height, weight, and testis volume (using Prader orchidometer). Blood samples were drawn in the morning, after an overnight fast, for determination of high-density lipoprotein (HDL) cholesterol and total testosterone (TT). Blood sample analyses were performed in the central laboratory of the Careggi Teaching Hospital (University of Florence, Italy). TT was measured by immunoassay.

The 10-year CV risk was estimated by the Progetto Cuore algorithm (Palmieri *et al.*, 2004), validated on the general Italian population, and previously demonstrated as a proper algorithm also for men with sexual dysfunction (Rastrelli *et al.*, 2012). Penile blood flows were measured by penile color Doppler ultrasound (PCDU) after an intracavernosal injection of 10 μg of prostaglandin E_1 (dynamic evaluation). PCDU assessment was available for 2265 men (56.3%). Before May 2014, according to our clinical practice, PCDU was performed in men complaining of ED. On May 7, 2014, our Hospital provided the approval for a protocol (ID# L99-A08 292/2014) aimed to homogenize the diagnostic work-up for each patient referred to our Unit for sexual dysfunction. Hence, after May 2014 PDCU parameters were also collected for men complaining only for PE (n = 86; 18.1% of PE-only subjects).

The Middlesex Hospital Questionnaire (MHQ) (Crown & Crisp, 1966) was administered to each patient in order to quantify the psychological symptoms. The MHQ is a brief self-reported questionnaire for the screening of the symptoms of mental disorders in non-psychiatric settings, which provides scores for free-floating anxiety (MHQ-A), phobic anxiety (MHQ-P), obsessive–compulsive traits and symptoms (MHQ-O), somatization (MHQ-S), depressive symptoms (MHQ-D), and histrionic/hysterical symptoms (MHQ-H).

Statistical analysis

Data are reported as mean ± standard deviation when normally distributed and as median [interquartile range] when non-normally distributed. Unadjusted differences between ED-only, PE-only, and ED-PE groups have been assessed with chi-squared or ANOVA tests for categorical or continuous variables, respectively. Multivariable analyses have been conducted using binary logistic or linear regressions for categorical or continuous dependent variables, respectively, using ED-PE as the category of interest compared with ED-only or PE-only groups, which have been used alternatively as the referents in all the analyses. Results from binary logistic or linear regressions were reported as odds ratio (OR) or unstandardized B coefficients, respectively, along with their 95% confidence interval (CI). All statistical analyses were conducted using STATA MP 13.1 for Windows (StataCorp, College Station, TX, USA) and p values <0.05 were considered statistically significant. All figures were produced using GRAPHPAD PRISM 5.02 (GraphPad Software, Inc., San Diego, CA, USA).

RESULTS

Among the patients studied (n = 4024), 2767 (68.8%) complained of only ED, 475 (11.8%) only PE, whereas 782 (19.4%) reported both ED and PE (ED-PE group). Hence, among men complaining of ED (n = 3549), 22.0% have comorbid PE, whereas, among those reporting PE (n = 1257), 62.2% had concomitant ED. The characteristics of the three groups are reported in Table 1. Since the three groups had significantly different ages, body mass index (BMI), education level (all $p < 0.0001$), and alcohol intake habits ($p = 0.005$), all the following analyses were adjusted for these confounders along with smoking habits, unless otherwise specified.

Sexual characteristics

Men with ED-PE were compared with those complaining of only ED or only PE. Figure 1 shows results having ED-only (closed diamonds) or PE-only (closed boxes) as the referents. ED-PE men reported more frequently than PE-only patients a decrease in morning erections, sexual desire, ejaculate volume, and frequency of sexual activity (Fig. 1A). Conversely, there were few differences in sexual complaints between ED-PE and ED-only men, with only the perception of decreased ejaculate volume being less frequent in ED-PE than ED alone (Fig. 1A). Consistently, the characteristics of ED, such as its severity, duration, time since it worsened, and onset modality, were similar in ED-PE and ED-only patients (Fig. 1B). In contrast, PE occurring together with ED had milder characteristics than PE alone: They were less severe, more often acquired and characterized by an occasional occurrence (Fig. 1C).

Figure 2 shows the scores from the structured interviews SIEDY and ANDROTEST represented as continuous variables, having ED-only (closed diamonds) and PE-only (closed boxes) as referents. ED-PE was characterized by an almost 3-point higher ANDROTEST score than PE alone, whereas the scoring was slightly (less than 1 point) lower than ED-only patients. Similar, although smaller, differences were found for SIEDY scale 1 (organic domain) between the three ED/PE phenotypes. Scale 3 (psychological domain) scoring was slightly but significantly higher in ED-PE than PE alone, whereas no differences were found in comparison with ED alone. The three phenotypes did not differ with respect to SIEDY scale 2 (relational domain) score.

Characteristics of ED-PE patients: organic parameters

History of hypertension, diabetes, or CVD was more frequent in ED-PE than PE alone, whereas only a trend toward a significantly lower frequency of diabetes was observed between ED-PE and ED alone (Fig. 3A). When considering accepted thresholds of TT for the definition of hypogonadism, we found that only TT below 8 nmol/L was able to discriminate ED-PE and ED-only men, as hypogonadism was less frequent in the former than in the latter group. The prevalence of hypogonadism—any

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Table 1 Characteristics of the patients in the three study groups

	ED-only *n* = 2767 (0)	ED-PE *n* = 782 (1)	PE-only *n* = 475 (2)	*p* 1 vs. 0	*p* 1 vs. 2
Age (years)	53.2 ± 12.9	50.0 ± 12.6	41.4 ± 11.5	<0.0001	<0.0001
Education (%)					
Primary	13.1	17.0	4.5	0.215	<0.0001
Secondary	32.9	31.3	29.5		
Higher	34.5	33.3	40.5		
University	19.4	18.6	25.5		
Current smoker (%)	30.0	30.9	32.4	0.615	0.585
Alcohol intake>4 drinks daily (%)	3.8	4.5	1.1	0.005	0.001
Hypertension (%)	30.3	23.7	9.7	<0.0001	<0.0001
Diabetes mellitus (%)	25.6	19.3	5.4	<0.0001	<0.0001
Cardiovascular diseases (%)	13.7	9.2	3.6	0.001	<0.0001
Stable couple relationship (%)	89.3	88.6	90.3	0.554	0.351
Limited privacy during intercourse (%)	14.4	20.2	16.6	<0.0001	0.864
Extramarital relationship (%)	17.8	11.2	10.0	<0.0001	0.587
Conflictual couple relationship (%)	33.1	33.9	28.8	0.715	0.082
Impaired morning erections (%)	73.8	65.7	27.6	<0.0001	<0.0001
Decreased sexual desire (%)	40.8	35.5	19.2	0.009	<0.0001
Decreased ejaculate volume (%)	42.2	31.0	15.0	<0.0001	<0.0001
Decreased frequency of intercourse (%)	53.9	48.7	37.6	0.013	<0.0001
Body mass index (kg/m^2)	26.9 ± 4.4	26.3 ± 4.0	25.2 ± 3.5	0.003	<0.0001
Systolic blood pressure (mmHg)	135 [125–145]	135 [120–145]	130 [120–140]	0.189[a]	<0.0001[a]
Diastolic blood pressure (mmHg)	80 [80–90]	80 [80–90]	80 [75–85]	0.850[a]	<0.0001[a]
Total testosterone (nmol/L)	15.4 ± 6.3	16.1 ± 6.0	16.7 ± 6.3	0.025	0.257
SHBG (nmol/L)	37.1 ± 18.6	36.9 ± 19.6	31.8 ± 13.2	0.979	0.003
Total Testosterone <12 nmol/L	31.5	25.2	24.7	0.001	0.852
Total Testosterone <10.4 nmol/L	21.2	16.2	10.3	0.003	0.008
Total Testosterone <8 nmol/L	8.9	4.5	3.3	<0.0001	0.368
Penile color Doppler ultrasound					
Flaccid peak systolic velocity (cm/s)	16.6 ± 5.8	16.9 ± 6.1	18.5 ± 6.0	0.580	0.045
Flaccid acceleration (m/s^2)	2.8 ± 1.4	2.8 ± 1.3	3.5 ± 1.4	0.806	<0.0001
Dynamic peak systolic velocity (cm/s)	50.0 ± 19.3	51.4 ± 19.0	64.5 ± 27.3	0.381	<0.0001
MHQ subscales					
Free floating anxiety	5.2 ± 3.6	5.4 ± 3.8	5.0 ± 3.5	0.593	0.222
Phobic anxiety	4.2 ± 2.7	4.0 ± 2.8	4.3 ± 2.6	0.106	0.211
Obsessive symptoms	5.5 ± 3.8	5.4 ± 4.0	5.6 ± 3.8	0.782	0.764
Somatized anxiety	3.5 ± 2.8	3.6 ± 3.1	2.8 ± 2.6	0.976	<0.0001
Depressive symptoms	4.5 ± 3.2	4.3 ± 3.4	4.1 ± 3.2	0.452	0.484
Hysterical traits	4.6 ± 3.1	4.5 ± 3.2	5.2 ± 3.1	0.720	0.002
Total score	27.6 ± 15.0	27.1 ± 16.7	27.0 ± 14.3	0.752	0.998

ED, erectile dysfunction; MHQ= Middlesex Hospital Questionnaire; PE, premature ejaculation; SHBG, sex hormone binding globulin. Data are reported as mean ± standard deviation if normally distributed or median [interquartile range] when non-normally distributed. *p* values derive from analysis of variance (ANOVA) with Tukey post hoc comparisons for continuous values and from chi-squared test for categorical values. [a]For these variables, not normally distributed in our sample, a log transformation was performed and the values thus obtained were analyzed by the ANOVA.

definition—was not different between ED-PE and PE-only subjects. ED-PE men were characterized by significantly worse penile blood flows as compared with PE-only men, with D-PSV resulting as more than 10 cm/s lower on average in the former than in the latter group (Fig. 3B). In contrast, ED-PE did not differ from ED alone in terms of penile blood flows (Fig. 3B). Concerning the Progetto Cuore risk score, ED-PE men showed a risk of developing CV events during the following 10 years, which was intermediate between those reporting only one of the symptoms. In particular, ED-PE men had a predicted CV risk of 3.8% (2.5–5.2) higher than PE alone and 2.1% (0.9–3.3) lower than ED alone (Fig. 3B).

Characteristics of ED-PE patients: relational parameters

Figure 4 shows results from relational parameters, reported as dummy variables, using ED-only (closed diamonds) or PE-only (closed boxes) as the referents. When compared with PE-only, ED-PE was more often characterized by an unstable couple relationship. When compared with ED-only, extramarital affairs were less frequent in ED-PE (Fig. 4). Complaints of limited privacy during sexual intercourse characterized ED-PE men, with a fully significant association observed in comparison with ED alone and a trend toward significance in comparison with PE alone (Fig. 4).

Characteristics of ED-PE patients: psychological parameters

Figure 5 shows the MHQ questionnaire subscale scores represented as continuous variables, having ED-only (closed diamonds) and PE-only (closed boxes) as referents. ED-PE men, as compared with those complaining of only PE, were characterized by more severe somatized anxiety symptoms. No differences in psychological symptoms were found between ED-PE and ED alone (Fig. 5).

DISCUSSION

Erectile dysfunction and PE are often comorbid. However, the specific phenotype of ED-PE men has never been systematically

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Figure 1 Sexual complaints reported by men with concomitant ED and PE. (A) Shows the prevalence of several sexual symptoms in ED-PE men as compared with ED-only subjects (referent; closed diamonds) or PE-only subjects (referent; closed boxes). (B) Reports the comparison between ED-PE and ED-only patients concerning the characteristics of ED. (C) Reports the comparison between ED-PE and PE-only patients concerning the characteristics of PE. Results are derived from multivariable binary logistic regressions adjusted for age, body mass index, education, smoking habits, and alcohol intake. Data are expressed as OR and 95% CI. ED, erectile dysfunction; PE, premature ejaculation; OR, odds ratio; CI, confidence interval.

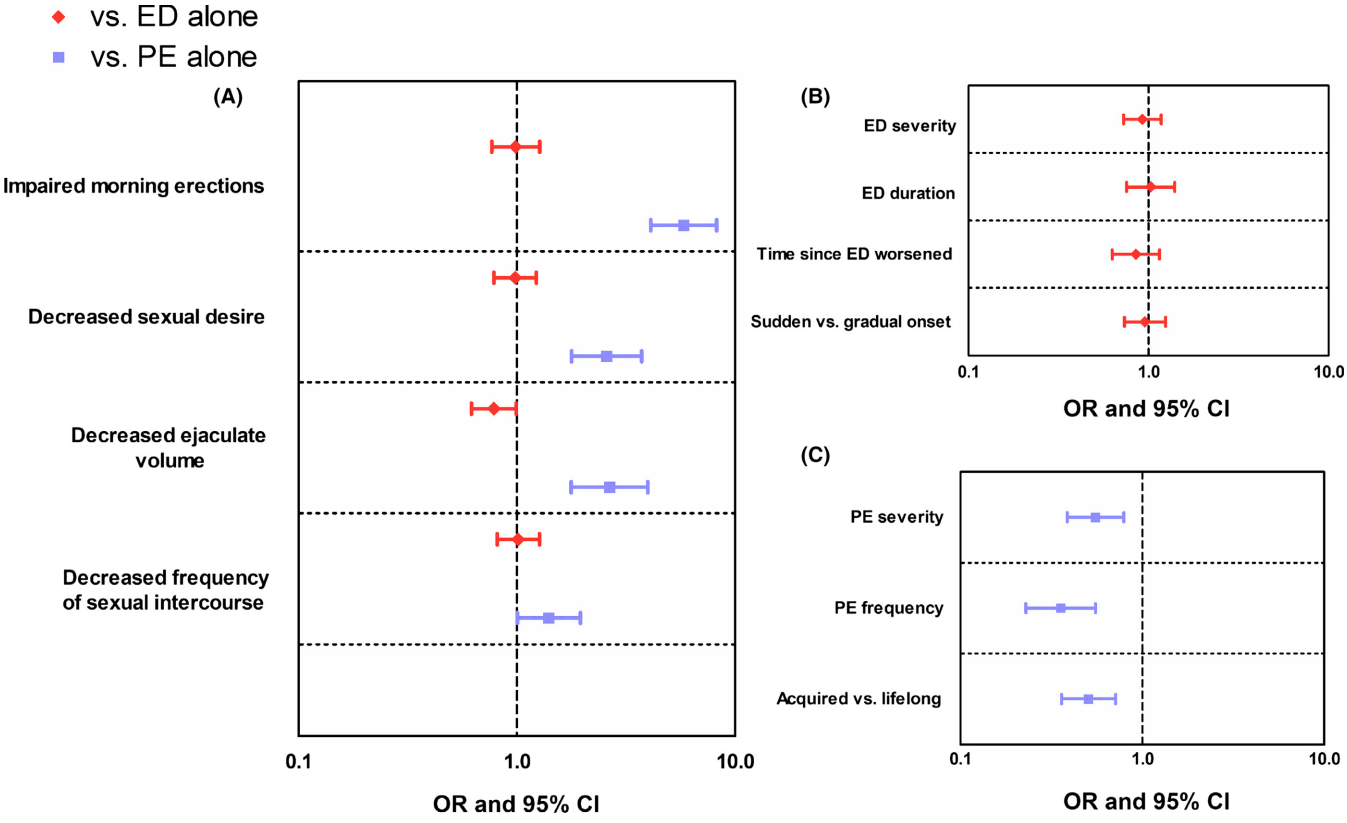
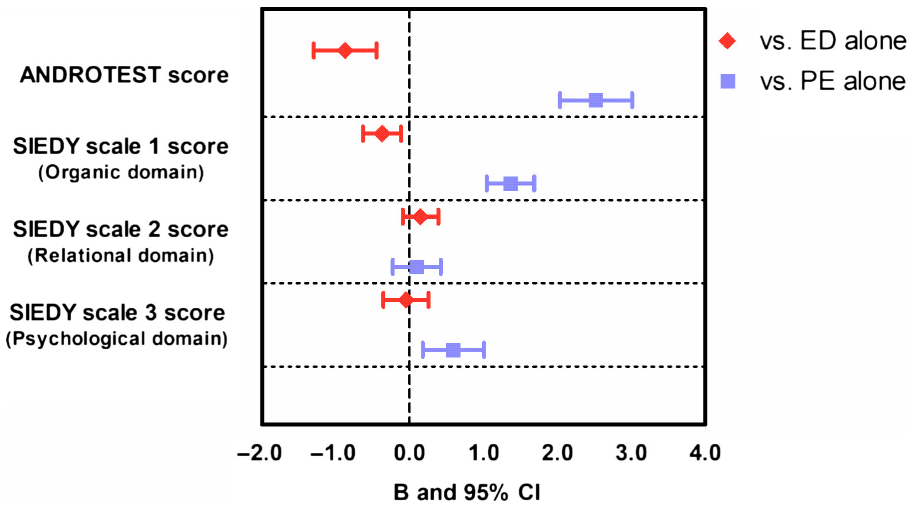


Figure 2 ANDROTEST and SIEDY scale scores in men with concomitant ED and PE as compared with ED-only subjects (referent; closed diamonds) or PE-only subjects (referent; closed boxes). Results are derived from multivariable linear regressions adjusted for age, body mass index, education, smoking habits, and alcohol intake, except for the analysis of the ANDROTEST score, as it includes age and body mass index within the score; thus, these covariates were omitted. Data are expressed as unstandardized B coefficient and 95% CI. Abbreviations: CI, confidence interval; ED, erectile dysfunction; PE, premature ejaculation; SIEDY, Structured Interview on Erectile Dysfunction.



investigated. Our results confirm a consistent (almost 20%) association between the two conditions, as envisaged by epidemiological studies (McMahon *et al.*, 2012; Corona *et al.*, 2015; Verze *et al.*, 2018). We here describe the clinical phenotype of men having both ED and PE, underlining differences and similarities in comparison with those having only ED or only PE. We essentially found that ED-PE men present several similarities with ED-only men in terms of characteristics of erectile difficulties, associated sexual complaints, metabolic disorders, and psychological symptoms. On the other hand, ED-PE men are substantially different from PE-only men, having milder characteristics of PE, a more adverse cardio-metabolic profile, and more severe psychological symptoms. This suggests that the concomitant presence of ED and PE represents an expression of the erectile disorder, rather than a separate sexual dysfunction.

The present results are in line with the suggestions from the International Society of Sexual Medicine (Jannini *et al.*, 2013; McMahon *et al.*, 2013) and the European Association of

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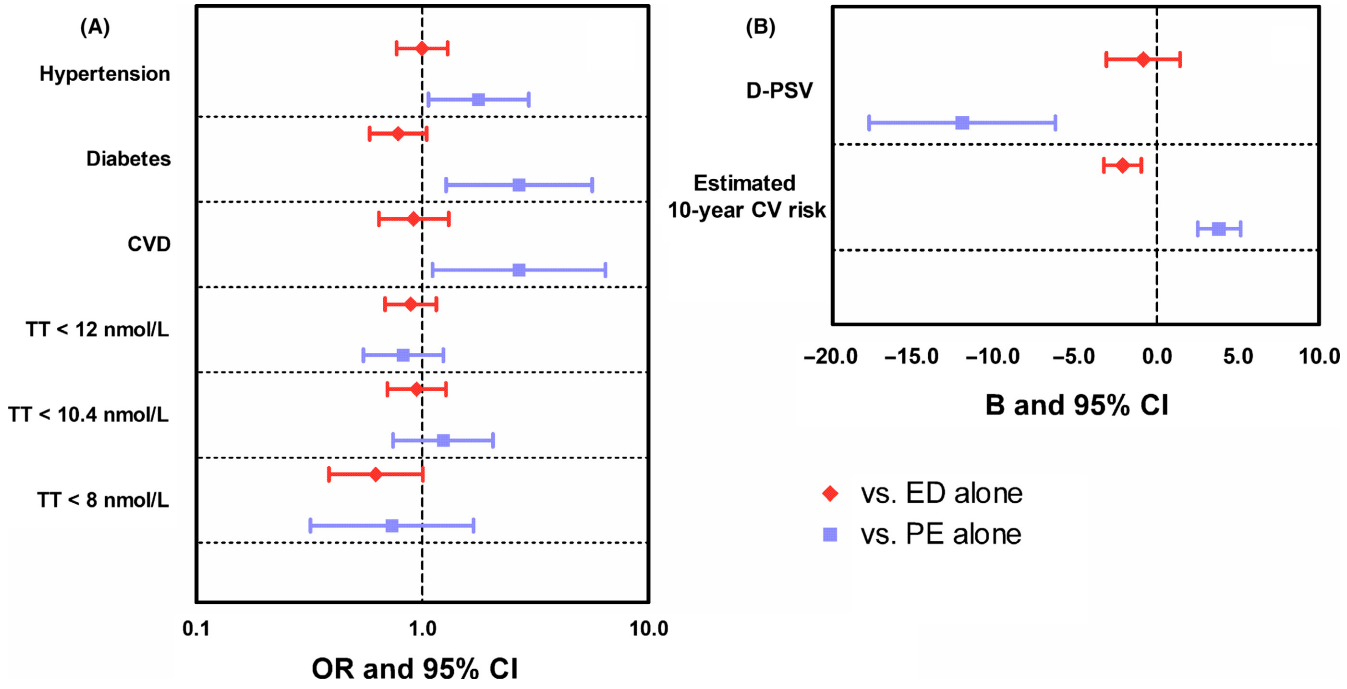
Figure 3 Metabolic diseases and cardiovascular parameters in men with concomitant ED and PE as compared with ED-only subjects (referent; closed diamonds) or PE-only subjects (referent; closed boxes). Results are derived from multivariable binary logistic regressions (A) and linear regressions (B) adjusted for age, body mass index, education, smoking habits, and alcohol intake, except for the analysis of the Progetto Cuore CV risk score (estimated 10-year CV risk), as it includes age and smoking habits; thus, these covariates were omitted. Data are expressed as OR and 95% CI or unstandardized B coefficient and 95% CI in (A) and (B), respectively. CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; D-PSV, dynamic peak systolic velocity; ED, erectile dysfunction; OR, odds ratio; PE, premature ejaculation; TT, total testosterone.



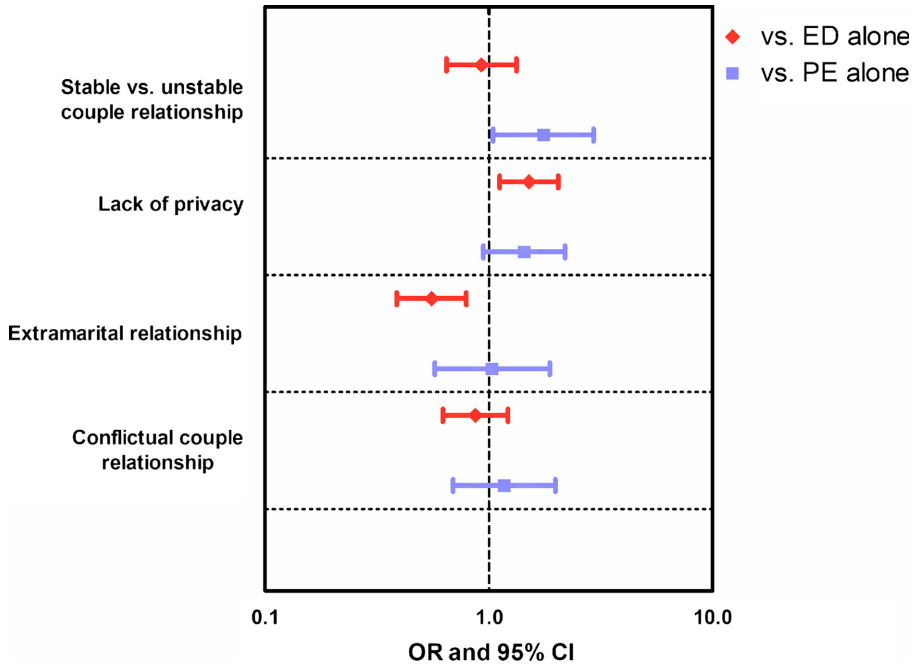


Figure 4 Relational issues reported by men with concomitant ED and PE as compared with ED-only subjects (referent; closed diamonds) or PE-only subjects (referent; closed boxes). Results are derived from multivariable binary logistic regressions adjusted for age, body mass index, education, smoking habits, and alcohol intake. Data are expressed as OR and 95% CI. CI, confidence interval; ED, erectile dysfunction; OR, odds ratio; PE, premature ejaculation.

Urology (Hatzimouratidis *et al.*, 2015) that every man with PE should be adequately screened for ED and, whenever present, this should be treated first. In fact, men with erectile difficulties can experience performance anxiety, which may also favor PE (Jannini *et al.*, 2011), or can be inclined to increase their arousal and/or rush the intercourse in order to obtain and/or maintaining erection, thus possibly resulting in shorter ELTs. Accordingly, treating ED-PE men with ED medications improves both erection and ELTs (Chia, 2002; Li *et al.*, 2003; Xu *et al.*, 2005; McMahon *et al.*, 2006). Conversely, there is no robust evidence for the use of PDE5i in men with only PE (Castiglione *et al.*, 2016; Martyn-St James *et al.*, 2017), thus

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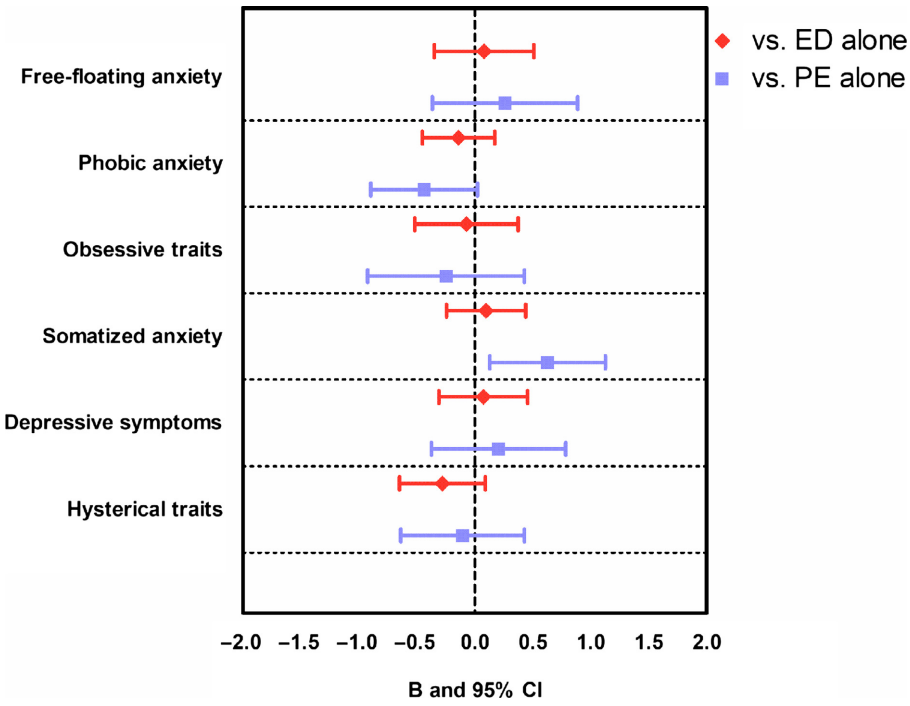

Figure 5 Psychological symptoms reported by men with concomitant ED and PE. Psychological symptoms, as assessed by the MHQ domains, in ED-PE men as compared with ED-only subjects (referent; closed diamonds) or PE-only subjects (referent; closed boxes). Results are derived from multivariable linear regressions adjusted for age, body mass index, education, smoking habits, and alcohol intake. Data are expressed as unstandardized B coefficient and 95% CI. CI, confidence interval; ED, erectile dysfunction; PE, premature ejaculation.

supporting the view that ED-PE men represent a phenotype different from 'pure' PE. In addition, there is no evidence that SSRI could improve ED, which is even negatively affected by their chronic use (Corona *et al.*, 2009).

In our study, men with both the disorders more often had acquired PE, which occurred occasionally and with less severity in terms of self-perceived ELTs, as compared with men who consulted only for PE. This is in agreement with the results of our previous meta-analysis, which showed that ED in men with PE was increasingly more prevalent in studies enrolling a greater percentage of men with acquired PE (Corona *et al.*, 2015). The lower severity of PE observed in ED-PE men is consistent with an acquired PE, which has been previously reported to be characterized by longer ELTs than lifelong PE (Porst *et al.*, 2010; Gao *et al.*, 2013). However, it should be noted that, in men with ED and PE, a lack of significant association between erectile function and ELTs (Porst *et al.*, 2010) or even worse ELTs than PE-only men (Brody & Weiss, 2015) have been described. The reasons for this inconsistency with our study could depend on the different populations evaluated. We here report an observation in a setting of a Sexual Medicine Outpatients Clinic where the most prevalent complaint was ED, whereas other studies were conducted in general populations (Brody & Weiss, 2015) or in men with diagnosed PE (Porst *et al.*, 2010). It is conceivable that men who consult for ED as the primary concern—as opposed to those consulting for PE or those from the general population—are more inclined to underestimate the severity of the ancillary problem. In addition, it has been reported that up to 30% of men with PE who do not complain of ED have pathological scores on the questionnaires for the assessment of their erectile function (McMahon, 2009), most likely because they confuse their short ELTs with difficulties in maintaining erection, particularly when PE is more severe (McMahon, 2009). The use of a structured interview, conducted with a trained physician who can provide explanations and assist the patients in the replies, minimizes the risk of this bias.

Erectile dysfunction-PE men and ED-only men have comparable CV risk (as assessed by the Progetto Cuore risk score) and prevalence of metabolic diseases, such as hypertension, diabetes, and previous cardiovascular (CV) events. Accordingly, D-PSV, a marker of penile vascular integrity and cardiovascular health (Corona *et al.*, 2008, 2010b), was similar in ED-PE and ED-only men. When compared with PE-only patients, those with ED and PE have a higher prevalence of hypertension, diabetes, and heart diseases, more organic risk factors for sexual dysfunction (as denoted by a higher SIEDY scale 1 score), worse penile blood flows and, accordingly, a greater estimated 10-year CV risk. This suggests that ED-PE men should be regarded as patients at higher CV risk and not considered similar to PE-only men, who are not usually characterized by cardio-metabolic risk factors (Corona *et al.*, 2006; Lotti *et al.*, 2013; Gao *et al.*, 2017). Hence, in PE patients, clinicians should carefully investigate the concomitant presence of ED not only for choosing the most proper treatment, but also for identifying overall unhealthier subjects.

Erectile dysfunction-PE patients report more symptoms suggestive of hypogonadism than PE-only men, as denoted by a higher ANDROTEST score; conversely, they score slightly lower than ED-only men. Indeed, PE *per se* is not a typical symptom of hypogonadism and it has been previously associated with even higher T levels (Rastrelli *et al.*, 2015); hence, it is not surprising that PE-only patients have less clinical features of hypogonadism and that, among subjects with severely reduced total testosterone (<8 nmol/L), ED-PE is less prevalent than ED alone.

Consistent with our previous meta-analysis (Corona *et al.*, 2015), we found that patients reporting ED and PE are more often involved in unstable relationships than those with only PE. A possible explanation is that an unstable relationship induces a greater burden of performance anxiety, which is a common favoring factor for both PE and ED. Limited privacy for sexual intercourse, more commonly reported in the present study in men with concomitant ED and PE, is another factor which can

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generate anxiety. Accordingly, we found that symptoms of somatized anxiety and psychological risk factors for sexual dysfunction, as assessed by SIEDY scale 3 score, distinguished ED-PE men from those with only PE. This is consistent with the findings of our previous meta-analysis showing that the prevalence of ED in men with PE increases according to the prevalence of anxiety or depressive disorders (Corona *et al.*, 2015). It is interesting to note that, in men consulting for sexual dysfunction, we previously found that somatization is associated with a broad spectrum of sexual complaints, rather than a single symptom (Fanni *et al.*, 2016). This is in keeping with the present results, obtained in a larger population, which show that the combination of ED and PE, significantly associated with several other sexual complaints (see before), is reported by subjects with more symptoms of somatization.

A strength of this study is the very large sample size along with the systematic assessment of a relevant number of sexual symptoms, which allowed a detailed characterization of the clinical phenotype of men with concomitant ED and PE. This represents the originality of the study; in fact, so far, the characteristics of men with ED and PE, who are commonly encountered in clinical practice, have not been systematically assessed and most information derives from studies with different objectives. This study has also a number of limitations. Firstly, the data derive from a cohort of men seeking medical care for sexual dysfunction at a Sexual Medicine Clinic and they could be different from men in the general population. However, our results are intended for supporting physicians in their clinical practice rather than for providing a general description of ED-PE. For this reason, a population of men consulting for sexual dysfunction provides the clinical context that sexual medicine practitioners actually deal with. The cross-sectional design is a further limitation, since it is not possible to infer a cause–effect relationship for the associations found. In addition, in men with both ED and PE, it is not possible to assess whether ED, PE, or both were the primary reasons for consulting. Finally, the definition of PE is based on self-reported ELTs <60 s for both lifelong and acquired PE. This is because the diagnostic protocol, including the standard question on PE, was introduced in our practice before the publication of the updated ISSM guidelines (Althof *et al.*, 2014). However, it should be recognized that the timing criteria for acquired PE are still not precisely defined and the use of the same criterion of lifelong PE might be appropriate (Althof *et al.*, 2010).

CONCLUSIONS

Among men seeking medical care for sexual dysfunction, the concomitant presence of ED and PE is frequent, with a prevalence of almost 20%. This category of patients is different from those consulting only for PE, since the characteristics of the ejaculatory problem are milder and they report a broader spectrum of concomitant sexual complaints. Conversely, ED-PE patients present several similarities with those consulting only for ED who share the sexual impairments as well as the footprints of CV risk. Recognizing these differences/similarities is important for sexual medicine practitioners because it could help them in deciding the diagnostic and therapeutic work-up. In line with the suggestions of the guidelines (Jannini *et al.*, 2013; McMahon *et al.*, 2013), our study infers that men reporting ED and PE should be primarily considered as patients with an erectile impairment. Consequently, the diagnosis—including the CV risk stratification—and treatment should be primarily focused on the erectile problem and only later on the ELT problem, if not appropriately treated by ED medications.

FUNDING

This research did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

DISCLOSURE

The authors declare that there are no conflicts of interest in connection with this article.

AUTHORS' CONTRIBUTIONS

Giulia Rastrelli and Mario Maggi conceived and designed the study. Giulia Rastrelli, Giovanni Corona, and Sarah Cipriani acquired the data. Giulia Rastrelli and Mario Maggi analyzed and interpreted the data. Giulia Rastrelli and Mario Maggi drafted the article. Giulia Rastrelli, Giovanni Corona, Linda Vignozzi, and Mario Maggi revised the article for intellectual contents. Giulia Rastrelli, Giovanni Corona, Sarah Cipriani, Linda Vignozzi, and Mario Maggi provided the final approval of the completed article.

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