ISSN: 2047-2919

ORIGINAL ARTICLE

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Keywords:
clinical practice, comorbidities, erectile dysfunction, health status, International Index of Erectile Function, libido, sexual desire

Received: 20-Jan-2014
Revised: 9-May-2014
Accepted: 12-May-2014

doi: 10.1111/j.2047-2927.2014.00236.x

Prevalence and predictors of concomitant low sexual desire/interest and new-onset erectile dysfunction – a picture from the everyday clinical practice

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SUMMARY

Prevalence and risk factors of concomitant primary low sexual desire/interest (LSD/I) and subsequent new-onset erectile dysfunction (ED) in men have been only partially investigated. We looked at the sociodemographic and clinical predictors of the concomitant condition of primary LSD/I – defined as the reduction in the usual level of SD/I which precedes ED or another sexual dysfunction – and new-onset ED (LSD/I + ED) in a cohort of consecutive Caucasian-European patients seeking their first medical help for sexual dysfunction at a single outpatient clinic in the everyday clinical practice setting. Data from 439 sexually active patients were analysed. Health-significant comorbidities were scored with the Charlson Comorbidity Index (CCI). Patients' LSD/I were evaluated according to the findings of a comprehensive sexual history. Moreover, patients completed the International Index of Erectile Function (IIEF). Descriptive statistics and logistic regression models tested the prevalence and predictors of LSD/I + ED as compared with ED only. Of the 439 men, LSD/I + ED was observed in 33 (4.2%) individuals. One of three men with LSD/I + ED was younger than 40 years. Patients complaining of LSD/I + ED or ED alone did not differ in terms of hormonal milieu. No significant differences emerged between groups in terms of sexual orientation, rates of stable sexual relationships, educational status, recreational habits and comorbid sexual dysfunctions. Patients with LSD/I + ED had significantly lower IIEF-sexual desire and IIEF-overall satisfaction scores than ED-only individuals (all $p \leq 0.003$). At multivariable analysis younger age and severe CCI scores emerged as independent predictors of LSD/I + ED (all $p \leq 0.04$). These findings showed that primary LSD/I is concomitant with new-onset ED in less than 5% of men seeking first medical help. Younger age and severe CCI emerged as independent predictors of LSD/I + ED. Patients with both conditions reported an impaired overall sexual satisfaction.

INTRODUCTION

Disorders of male sexual desire have been only partially investigated (Derogatis *et al.*, 2012; Corona *et al.*, 2013a), and done so mostly in relation to conditions of aging and hypogonadism (Corona *et al.*, 2010, 2013b; Rubio-Aurioles & Bivalacqua, 2013). In this context, data from the European Male Ageing Study (EMAS) showed that thinking/fantasizing about sex presents a clear age dependency in middle-aged and older men (Corona *et al.*, 2010). Likewise, in the same cohort of men, frequency of sexual thinking was not affected by overall general health and quality of life or by organic comorbidities [including LUTS, metabolic and cardiovascular diseases (CVD)], but was significantly decreased by psychological disturbances, such as depression (Corona *et al.*, 2010).

The Diagnostic and Statistical Manual for Mental Disorders text revision (DSM-IV-TR) American Psychiatric Association, (2000) used the diagnostic concept of hypoactive sexual desire disorder (HSDD) in men to define a disorder of male desire with persistently or recurrently deficient (or absent) sexual fantasies and desire for sexual activity, necessarily causing/being associated with marked distress or interpersonal difficulty. In addition, the DSM-IV-TR definition of HSDD also clarifies that the dysfunction should not be accounted for by another psychiatric disorder (except another sexual dysfunction) and must not be exclusively owing to the physiological effects of a substance or a general medical condition. Overall, research on HSDD in men is scarce (Derogatis *et al.*, 2012) and rates of low desire with accompanying distress in men have yet to be comprehensively

studied (Brotto, 2010). Based on the finding in women that less than half of those reporting low desire also experienced distress, Brotto suggested that one might speculate that the approximate rate of HSDD in men ranges between 1 and 20%, depending on age, country and method of assessment (Brotto, 2010).

The Standard Operational Procedures (SOPs) of the International Society for Sexual Medicine (ISSM) (Rubio-Aurioles & Bivalacqua, 2013) proposed the concept of low sexual desire/interest (LSD/I) in men as a convenient umbrella term to refer to the clinical condition where the male individual complains of a modification in his usual level of sexual interest or desire, for which HSDD would represent only a subtype; in this context, LSD/I is frequent in the general male population, although still scantly reported (Laumann *et al.*, 1999, 2005; Brotto, 2010; Derogatis *et al.*, 2012). Of major relevance, during daily practice LSD/I may often be observed in men who, from the onset, have suffered from erectile dysfunction (ED), thus suggesting either a possible causal relationship between ED and impaired SD, or the existence of common pathogenetic factors for the two sexual complaints. In this specific situation, LSD/I is considered an acquired and psycho-pathogenetic consequence of ED (Corona *et al.*, 2004); SOPs thus suggest to use 'LSD/I' as a general term for the symptom/syndrome which might be linked to different medical conditions, relationship factors, medications or abuse of recreational substances. Therefore, taking into account the fact that male sexual dysfunction is a complex cluster of interrelated biological, psychological and contextual factors (Althof & Needle, 2011), many conditions have been proposed as potential underlying factors of LSD/I (Rochira *et al.*, 2003).

Corona *et al.* (2013a) recently investigated the risk factors for the condition conceptualized as 'reduced libido', which was considered a symptom referring more to a person's drive for sexual activity rather than a specific clinical entity. These authors distinguished a number of different risk factors and clinical characteristics for the condition of either primary (i.e. not associated with conditions causing loss of libido such as hypogonadism, hyperprolactinaemia, psychopathology and/or psychoactive medications) or secondary reduced libido (i.e. with aforementioned conditions) in men with sexual dysfunction (Corona *et al.*, 2013a).

The aim of our exploratory, retrospective analysis was to investigate a number of sociodemographic and clinical predictors of the condition of primary LSD/I – defined as a reduced level of sexual interest or desire before, and regardless of, either ED or another sexual dysfunction – combined with acquired ED (LSD/I + ED) in a cohort of consecutive Caucasian-European patients seeking their first medical attention for sexual dysfunction at a single outpatient clinic in the everyday clinical practice setting.

MATERIALS AND METHODS

Population

The analyses were based on a cohort of 790 consecutive Caucasian-European sexually active patients seeking first-medical attention for new-onset sexual dysfunction between January 2010 and June 2012 at a single academic outpatient clinic. For the specific purpose of this exploratory study, only data from patients complaining of either primary LSD/I or new-onset ED were considered. Likewise, patients were asked to self-report the delay between ED onset (namely, failure of at least 50% of four consecutive attempts at sexual intercourse) and the first time they sought medical attention (DSH, number of months). Patients were comprehensively assessed with a detailed medical and sexual history, including sociodemographic data. Health-significant comorbidities were scored with the Charlson Comorbidity Index (CCI) (Charlson *et al.*, 1987) as both continuous and categorized variables (i.e. 0 vs. 1 vs. ≥2). We used the *International Classification of Diseases*, 9th revision, Clinical Modification (ICD-9-CM). Body mass index (BMI), defined as weight in kilograms by height in square meters, was considered for each patient. For BMI, we used the cut-offs proposed by the National Institutes of Health (1998): normal weight (18.5–24.9), overweight (25.0–29.9), class ≥1 obesity (≥30.0). Hypertension was defined when antihypertensive medication was taken and/or for high blood pressure (≥140 mmHg systolic or ≥90 mmHg diastolic). Hypercholesterolaemia was defined when lipid-lowering therapy was taken and/or HDL cholesterol was <40 mg/dL. Similarly, hypertriglyceridaemia was defined when plasma triglycerides were ≥150 mg/dL (Grundy *et al.*, 2005). National Cholesterol Education Program–Adult Treatment Panel III (NCEP–ATPIII) criteria were retrospectively used to define metabolic syndrome (MeTs) prevalence in the entire cohort of ED men (Grundy *et al.*, 2005).

For the specific purpose of this study and to reflect the common practice of a clinical biochemistry laboratory, we elected to measure levels of circulating total testosterone (tT), prolactin and thyroid stimulating hormone (TSH) using commercially available analytical methods. Hypogonadism was defined as tT < 3 ng/mL (Bhasin *et al.*, 2010).

Patients were then stratified according to their relationship status (defined as 'stable sexual relationship' if the individual had the same sexual partner for six or more consecutive months; otherwise "no stable sexual relationship"). Likewise, patients were segregated according to their educational status into a low educational level group (LL), which included patients with an elementary or secondary school education, and a high educational level (HL), which consisted of men with either a high school degree and/or a university/post-graduate degree.

Patients' LSD/I was evaluated according to the findings of sexual history, along with the results of the general assessment question: 'Did you have a low frequency of sexual thoughts throughout the last 3 months?'. Likewise, to provide a frame of reference for objectively interpreting psychometric data on sexual functioning, patients were invited to complete the International Index of Erectile Function (IIEF) domains [thus considering erectile function (EF), SD, orgasmic function (OF), intercourse satisfaction (IS) and overall satisfaction (OS)] (Rosen *et al.*, 1997). To interpret ED severity, we used the IIEF-EF domain classification as proposed by Cappelleri *et al.* (1999). Conversely, normality for the other IIEF domains was arbitrarily defined for values greater than equal to the median for each domain.

Prevalence and characteristics of the combined condition of LSD/I + ED were also assessed in young men seeking their first medical attention in the everyday clinical setting, according to the widely used arbitrary cut-off of 40 years of age (Capogrosso *et al.*, 2013). Literacy problems as well as other reading and writing problems were excluded in all patients.

Statistical analyses

Data are presented as means (median; range). The statistical significance of differences in means and proportions was tested with the two-tailed *t*-test and the Pearson χ^2 test respectively. Univariable (UVA) and multivariable (MVA) logistic regression models tested potential predictors associated with LSD/I + ED. Statistical analyses were performed using SPSS statistical software, v 13.0 (IBM Corp., Armonk, NY, USA). All tests were two sided, with a significance level set at 0.05.

Data collection was done following the principles outlined in the Declaration of Helsinki; all patients signed an informed consent agreeing to provide their anonymous information for future studies.

RESULTS

New-onset ED and primary LSD/I were found in 439 (55.6%) and 49 (6.2%) of the 790 patients respectively; conversely, the concomitant condition of LSD/I+ED was observed in 33 (4.2%) men. Therefore, 33 (7.5%) of the 439 patients with ED complained of primary LSD/I in addition to new-onset ED.

Of the 439 patients with new-onset ED, 114 (26.0%) were ≤40 years of age at the time they first seeked medical help for ED; of these patients, 10 (8.8%) had LSD/I+ED. Therefore, 10 (30.3%) of the 33 patients complaining of both primary LSD/I and new-onset ED were ≤40 years of age.

Table 1 details patients' clinical characteristics and descriptive statistics according to the condition of ED-only compared with LSD/I+ED in the whole cohort of men.

Patients complaining of ED only or LSD/I + ED did not differ in terms of age, BMI and general health, as scored with the CCI. Similarly, comparable rates of patients with hypertension, hypercholesterolaemia, hypertriglyceridaemia, MeTs and hypogonadism were observed in the two groups.

Table 1 Descriptive statistics and clinical characteristics in ED only and LSD/I + ED patients (No. = 439)

	ED only	LSD/I + ED	*p*-value*
No. of patients (%)	406 (92.5)	33 (7.5)	
Age [years; mean (SD)]	51.0 (14.0)	47.4 (13.7)	0.17
Range	18–87	19–82	
CCI [No. (%)]			
0	267 (65.8)	25 (75.8)	0.41 (χ^2, 1.77)
1	63 (15.5)	5 (15.2)	
2+	76 (18.7)	3 (9.0)	
BMI [kg/m^2; mean (SD)]	26.1 (3.8)	25.6 (4.2)	0.45
BMI (NIH classification) [No. (%)]			
<18.5	1 (0.2)	0 (0.0)	0.91 (χ^2, 0.54)
18.5–24.9	175 (43.1)	15 (45.5)	
25–29.9	177 (43.6)	14 (42.4)	
≥30	53 (13.1)	4 (12.1)	
Hypertension [No. (%)]	123 (30.3)	5 (15.2)	0.07 (χ^2, 3.35)
Hypercholesterolaemia [No. (%)]	39 (9.6)	3 (9.1)	0.92 (χ^2, 0.01)
Hypertriglyceridaemia [No. (%)]	8 (0.0)	0 (0.0)	0.42 (χ^2, 0.66)
MeTs [No. (%)]	8 (0.0)	0 (0.0)	0.32 (χ^2, 1.01)
tT [ng/mL; mean (SD)]	4.8 (1.8)	4.6 (2.1)	0.71
Hypogonadism (tT < 3 ng/mL) [No. (%)]	59 (14.5)	6 (18.2)	0.81 (χ^2, 0.06)
Prolactin [ng/mL; mean (SD)]	4.3 (6.5)	4.4 (5.3)	0.97
TSH [microUI/mL; mean (SD)]	0.9 (2.6)	0.9 (1.1)	0.76

SD, standard deviation; CCI, Charlson Comorbidity Index; BMI, body mass index; NIH, National Institutes of Health; MeTs, metabolic syndrome; tT, total testosterone; TSH, thyroid stimulating hormone. *p value according to χ^2 test or two-tailed independent *t*-test, as indicated.

Similarly, no differences were found between groups for circulating levels of tT, prolactin and TSH. Likewise, when segregated according to the arbitrary age cut-off of 40 years, no differences were observed between ED-only and LSD/I + ED patients in terms of CCI, BMI, rates of patients with MeTs or hypogonadism, or circulating values of tT, prolactin and TSH (data not shown).

Table 2 lists the drugs taken by the patients of the two groups, segregated by family of drugs. Similarly, Table 2 also details the recreational products reported by patients. No differences were observed for any family of drugs between groups, except for antiplatelet drugs which were more frequently reported in men with LSD/I + ED (Table 2). Furthermore, no significant differences emerged between groups in terms of recreational habits, including chronic cigarette smoking, alcohol intake and addiction to illicit drugs (Table 2).

Table 3 depicts sociodemographic and psychometric characteristics and descriptive statistics in patients with ED only as compared with LSD/I + ED individuals. Groups did not differ in terms of sexual orientation, rates of stable sexual relationships, educational status and comorbid sexual dysfunction (thus including either pre-mature ejaculation or Peyronie's disease). Conversely, DSH was significantly shorter in men with LSD/I+ED as compared with those complaining of only ED. Mean IIEF-EF values were similar between groups; in this context, a comparable proportion of severe ED patients was retrieved in both groups. Similarly, IIEF–IS and IIEF–OF values were comparable between groups. Conversely, IIEF–SD and IIEF–OS were significantly lower for men with LSD/I + ED than in those with ED only ($p \leq 0.003$) (Table 3). When the arbitrary criterion of normality was applied to the IIEF domains (namely, normal values were defined for scores ≥ the median for each domain other than IIEF-EF), patients in both groups did not differ for rates of normal IS and OF. Conversely, significantly higher rates of abnormal IIEF-SD and IIEF-OS were observed in men with LSD/I + ED compared with ED only patients (all $p \leq 0.008$) (Table 3).

Table 4 reports UVA and MVA logistic regression models predicting LSD/I + ED in the entire cohort of patients. At UVA, no significant associations were observed between predictors and LSD/I + ED. At MVA patient age and severe health status (defined as CCI ≥ 2) reached independent predictor status for LSD/I + ED (all $p \leq 0.04$). No other clinical or psychometric variable was associated with the comorbid condition of LSD/I + ED.

DISCUSSION

We retrospectively evaluated prevalence and predictors of the comorbid condition of primary LSD/I and new-onset ED in a cohort of consecutive sexually active Caucasian-European men seeking medical attention for the first time for sexual dysfunction in the everyday clinical practice setting over a 30-month period. To this specific aim, we arbitrarily used the umbrella concept of LSD/I suggested by the ISSM (Rubio-Aurioles & Bivalacqua, 2013), considering that the more appropriate DSM-IV-TR definition of male HSDD could not be applied to our cohort because we lacked data regarding the distress linked to the loss of interest in sex (Derogatis *et al.*, 2012; Rubio-Aurioles & Bivalacqua, 2013). Our findings confirm that ED is the main male sexual complaint in the daily practice; overall, roughly 6% of patients seek medical help for a condition of primary LSD/I, and approximately 4% for a combined condition of LSD/I + ED.

Table 2 Therapeutic drugs and recreational habits in ED only and LSD/I + ED patients (No. = 439)

	ED only	LSD/I + ED	*p*-value*
No. of patients (%)	406 (92.5)	33 (7.5)	
Antihypertensive drugs			
ACE-i	45 (11.1)	3 (9.1)	0.95 (χ^2, 0.004)
Angiotensin-II receptor antagonist	41 (10.1)	2 (6.1)	0.66 (χ^2, 0.19)
Beta-1 blockers	45 (11.1)	1 (3.0)	0.24 (χ^2, 1.36)
Calcium antagonists	37 (9.1)	2 (6.1)	0.79 (χ^2, 0.07)
Diuretics			
Loop diuretics	6 (1.5)	0 (0.0)	0.95 (χ^2, 0.004)
Thiazide diuretics	18 (4.4)	0 (0.0)	0.44 (χ^2, 0.60)
Other cardiovascular drugs			
Digoxin	2 (0.5)	0 (0.0)	0.35 (χ^2, 0.86)
Antiarrhythmic drugs	6 (1.5)	1 (3.0)	0.95 (χ^2, 0.004)
Anticoagulant drugs	6 (1.5)	1 (3.0)	0.95 (χ^2, 0.004)
Antiplatelet drugs	6 (1.5)	5 (15.2)	<0.001 (χ^2, 18.06)
Lipid-lowering drugs (statins and/or fibrates)	38 (9.4)	5 (15.2)	0.44 (χ^2, 0.60)
Central nervous system drugs			
Anticonvulsant drugs	5 (1.2)	2 (6.1)	0.15 (χ^2, 2.10)
Barbiturates	2 (0.5)	0 (0.0)	0.35 (χ^2, 0.86)
Benzodiazepine	17 (4.2)	0 (0.0)	0.47 (χ^2, 0.54)
Neuroleptics	5 (1.2)	0 (0.0)	0.82 (χ^2, 0.05)
Opioid drugs	1 (0.2)	1 (3.0)	0.32 (χ^2, 1.00)
SNRIs	2 (0.5)	0 (0.0)	0.35 (χ^2, 0.86)
SSRIs	15 (3.7)	1 (3.0)	0.78 (χ^2, 0.08)
Endocrinological drugs			
Antithyroid drugs	1 (0.2)	1 (3.0)	0.32 (χ^2, 1.00)
Thyroxin	18 (4.4)	1 (3.0)	0.95 (χ^2, 0.004)
Corticosteroids	15 (3.7)	0 (0.0)	0.53 (χ^2, 0.39)
Darbepoetin	1 (0.2)	0 (0.0)	0.06 (χ^2, 3.42)
Desmopressin	2 (0.5)	0 (0.0)	0.35 (χ^2, 0.86)
Dopamine agonists	5 (1.2)	1 (3.0)	0.94 (χ^2, 0.006)
Dopamine antagonists	6 (1.5)	1 (3.0)	0.95 (χ^2, 0.004)
Hypoglycemic drugs			
Antidiabetic drugs	33 (8.1)	2 (0.5)	0.21 (χ^2, 1.56)
Insulin	21 (5.2)	5 (1.2)	0.55 (χ^2, 0.37)
Respiratory system drugs			
Antihistamines	14 (3.4)	2 (0.5)	0.69 (χ^2, 0.16)
Beta2-agonist	4 (1.0)	0 (0.0)	0.71 (χ^2, 0.14)
BPH/LUTS-related drugs			
5-alpha reductase inhibitors	7 (1.7)	0 (0.0)	0.98 (χ^2, 0.000)
Alfa-blockers	41 (10.1)	1 (3.0)	0.31 (χ^2, 1.10)
Other drugs			
Anticholinergic drugs	2 (0.5)	0 (0.0)	0.35 (χ^2, 0.86)
Immunomodulators/ immunosuppressors	15 (3.7)	0 (0.0)	0.53 (χ^2, 0.40)
Proton pump inhibitors	33 (8.1)	2 (0.5)	0.21 (χ^2, 1.56)
Non-steroidal anti-inflammatory drugs	20 (4.9)	1 (3.0)	0.95 (χ^2, 0.005)
Triptans	1 (0.2)	0 (0.0)	0.06 (χ^2, 3.42)
Vitamins	13 (3.2)	0 (0.0)	0.61 (χ^2, 0.26)
Uricosuric drugs	17 (4.2)	0 (0.0)	0.46 (χ^2, 0.54)
Cigarette smoking [No. (%)]			
Current smokers	112 (27.6)	11 (33.3)	0.58 (χ^2, 1.09)
Previous smokers	8 (2.0)	0 (0.0)	
Never smoked	286 (70.4)	22 (66.7)	
Alcohol intake (volume/week) [No. (%)]			
<1 litre/week	224 (55.2)	23 (69.7)	0.15 (χ^2, 2.05)
1–2 L/week	23 (5.7)	2 (6.1)	
>2 L/week	159 (39.1)	8 (24.2)	
Chronic illicit drugs (any type) [No. (%)]	33 (8.1)	3 (9.1)	0.79 (χ^2, 0.07)
Cannabis/marijuana	30 (7.4)	3 (9.1)	0.70 (χ^2, 0.14)
Cocaine	3 (0.7)	0 (0.0)	0.19 (χ^2, 1.76)

ACE-i, angiotensin-converting enzyme inhibitors; SNRIs, serotonin and noradrenail reuptake inhibitors; SSRIs, selective serotonin reuptake inhibitors; BPH, benign prostatic hyperplasia; LUTS, lower urinary tract symptoms. *p value according to χ^2 test or two-tailed independent t-test, as indicated.

Table 3 Sociodemographic and psychometric characteristics in ED only and LSD/I + ED patients (No. = 439)

	ED only	LSD/I+ED	*p*-value*
No. of patients (%)	406 (92.5)	33 (7.5)	
Sexual orientation [No. (%)]			
Heterosexual	398 (98.0)	33 (100.0)	0.42 (χ^2, 0.66)
Homosexual	8 (2.0)	0 (0.0)	
Relationship status [No. (%)]			
Stable sexual relationship ≥ 6 months	353 (87.0)	32 (96.7)	0.17 (χ^2, 1.84)
No stable sexual relationship	53 (13.0)	1 (3.3)	
Educational status [No. (%)]			
Elementary school	20 (4.9)	1 (3.0)	0.54 (χ^2, 3.14)
Secondary school	75 (18.5)	7 (21.2)	
High school	186 (45.8)	11 (33.3)	
University degree	125 (30.8)	14 (42.4)	
DSH (months)			
Mean (SD)	40.7 (45.3)	28.6 (24.7)	0.04
Range	0–360	1–96	
IIEF-domains [Mean (SD)]			
IIEF-EF	13.9 (8.6)	16.0 (7.7)	0.2
IIEF severity* [No (%)]			
Normal EF	46 (11.3)	3 (9.2)	0.57 (χ^2, 2.92)
Mild ED	65 (16.0)	6 (18.2)	
Mild to moderate ED	52 (12.8)	8 (24.2)	
Moderate ED	62 (15.3)	8 (24.2)	
Severe ED	181 (44.6)	8 (24.2)	
IIEF-IS	6.5 (4.1)	6.3 (4.2)	0.88
Pathological IIEF-IS [No (%)]	186 (45.8)	16 (48.5)	0.79 (χ^2, 0.07)
IIEF-OF	7.2 (3.4)	7.0 (3.6)	0.97
Pathological IIEF-OF [No (%)]	201 (49.5)	14 (42.4)	0.6 (χ^2, 0.27)
IIEF-SD	6.9 (2.2)	4.9 (1.8)	0.003
Pathological IIEF-SD [No (%)]	175 (43.1)	27 (81.8)	0.008 (χ^2, 7.02)
IIEF-OS	5.1 (2.5)	4.1 (2.4)	0.03
Pathological IIEF-OS [No (%)]	171 (42.1)	26 (78.8)	<0.001 (χ^2, 15.17)
Concomitant sexual complaints [No. (%)]			
PE	33 (8.1)	1 (3.0)	0.31 (χ^2, 1.04)
Peyronie's disease	40 (9.9)	2 (6.1)	0.48 (χ^2, 0.51)

DSH, delay of time between ED onset and seeking medical help; IIEF, International Index of Erectile Function; EF, erectile function domain; ED, erectile dysfunction; IS, intercourse satisfaction domain; OF, orgasmic function domain; SD, sexual desire domain; OS, overall satisfaction domain; PE, pre-mature ejaculation. *p value according to χ^2 test or two-tailed independent t-test, as indicated.

Moreover, we found that one of three men with LSD/I + ED was younger than 40 years. Therefore, this observation as a whole appeared to be a worrisome picture from the everyday clinical practice.

Patients reporting both sexual disorders showed a significant lower overall sexual satisfaction than those with ED only. The current findings seem to confirm the 5.1% rate of isolated reduced libido reported in a recently published retrospective analysis on a large non-selected series of men attending an outpatient clinic for sexual dysfunction (Corona *et al.*, 2013a).

Younger age at survey and a high CCI – which may be considered a reliable proxy of lower male general health status – emerged as the only independent predictors of the combination of the two sexual complaints, after adjusting for several clinical and sociodemographic variables. From the everyday clinical practice standpoint, these three findings are of major importance because they first demonstrate that the prevalence of

Table 4 Logistic regression models predicting ED and concomitant primary LSD/I in the entire cohort of patients (No. = 439)

	UVA OR (*p*-value)	MVA OR (*p*-value)
Age	0.98 (0.17)	0.80 (0.02)
CCI 0 (ref)	– (0.43)	– (0.13)
CCI 1	2.26 (0.19)	0.0 (1.00)
CCI 2+	2.07 (0.35)	3.0 (0.04)
BMI		
BMI <24.9 (ref)	– (0.57)	– (0.22)
BMI 25.0–29.9	1.56 (0.13)	2.19 (0.09)
BMI ≥30	1.80 (0.84)	1.40 (0.86)
MeTs (yes vs. no)	0.00 (1.00)	0.00 (1.00)
Hypogonadism (yes vs. no)	0.85 (0.81)	0.11 (0.15)
Prolactin	1.00 (0.98)	1.14 (0.35)
TSH	1.01 (0.87)	1.62 (0.34)
IIEF severity (cat)	0.89 (0.58)	1.02 (0.84)
Stable relationship (no vs. yes)	4.08 (0.17)	5.00 (1.00)

UVA, univariate logistic regression analysis; MVA, multivariate logistic regression analysis; OR, odds ratio; CCI, Charlson Comorbidity Index; BMI, body mass index; MeTs, metabolic syndrome; tT, total testosterone; TSH, thyroid stimulating hormone; IIEF-EF, International Index of Erectile Function-Erectile Function domain.

primary LSD/I (a condition not secondary to the onset of ED) is relatively low in men seeking their first medical help in the daily practice. However, when LSD/I and ED result as combined sexual dysfunctions, patients may suffer from reduced overall sexual satisfaction and they will require a visit by a specialist for their problem significantly earlier than those complaining of only ED (Salonia *et al.*, 2012). As a whole, this could make any therapeutic approach even tougher for non-experts in the field of sexual health, thus suggesting that these patients especially should be sent to a professional psychological therapist for a combined approach. Finally, the current findings also demonstrated that one of three men with LSD/I + ED was younger than 40 years. Because patients age was associated with the combined condition of LSD/I + ED (i.e. the older the patients, the lower the risk of having a comorbid sexual impairment), younger men should be even more comprehensively and sensibly evaluated by non psychologically related physicians. This would eventually stress the importance of a multimodal therapeutic approach, primarily in younger individuals complaining of any type of sexual dysfunction.

Although it is not easy to make direct comparative evaluations of our results with those previously published – mainly because the type of LSD/I and the cohort of individuals which we have studied were different from those previously assessed – our findings would seem to emphasize previous observations in young individuals, where one of four men with ED was younger than 40 years (Capogrosso *et al.*, 2013) and also the current figure of the young age for LSD/I + ED, whereas previously this combination had been widely described in ageing men. Corona *et al.* (2004), for instance, observed that over 40% of their patients suffered from both ED and hypoactive sexual desire. Furthermore, findings from the Global Study of Sexual Attitudes and Behaviors among adults across Europe aged 40–80 years showed that lack of sexual interest in men ranged between 12.5 and 17.6% (Laumann *et al.*, 2005) with lack of interest in sex being associated with older age, overall poor health and comorbid depression (Laumann *et al.*, 2005). Similarly, data from the National Health and Social Life Survey (NHSLS) in the US showed that increasing age for men was positively associated with a reduction in desire for sex (Laumann *et al.*, 1999); in this context, the oldest cohort of examined men (aged 50–59 years) was more than three times as likely to report low SD (95% CI, 1.6–5.4) as compared with men aged 18–29 years. Comparable pictures have been also reported by Lindau *et al.* (2007) who observed a 28% prevalence of lack of interest in sex (and the concomitant rate of 68% of bothered men owing to reduced libido) in a national probability sample of 3005 US adults (1455 men) aged 57–85 years. In contrast, in a relatively small cohort of men without concomitant ED, Derogatis *et al.* (2012) recently showed that there were no clinically relevant differences in age between men with or without HSDD.

A strength of our analysis emerges from the fact that we assessed prevalence and characteristics of LSD/I + ED in men extrapolated from a cohort of same-race, sexually active patients who consecutively attended a single outpatient clinic seeking medical assistance for the first time for sexual dysfunction, and who were assessed with a consistent method. The analyses of same-race (i.e. Caucasian-European) individuals may emerge as of particular importance, taking into account the potential ethnic differences in terms of aspects of sexuality and sexual disorders – also including LSD/I – previously described in the literature (Laumann *et al.*, 2005).

Moreover, we examined the effect of several sociodemographic, lifestyle and clinical variables upon the condition of LSD/I + ED compared with the condition of ED only. Given the well-known correlations between medical comorbidities and ED – including obesity (Kolotkin *et al.*, 2012), diabetes mellitus (Phé & Rouprêt, 2012), hypertension and antihypertensive treatment (Nunes *et al.*, 2012), CVD (Nehra *et al.*, 2012), MeTs (Corona *et al.*, 2009; Lee *et al.*, 2012), and a number of recreational habits (Christensen *et al.*, 2011) – the findings of this exploratory analysis corroborate the validity of this cohort of patients seeking medical help for sexual dysfunction as representative of the real life scenario. The current findings showed that LSD/I + ED was independently associated with the highest CCI scores. In this context, while comorbid conditions and unhealthy lifestyle factors are certainly widely present in new-onset ED patients, primary reduced libido was conversely reported to be associated with an overall healthier status by Corona *et al.* (2013a). Similarly, Derogatis *et al.* (2012) also showed that no clinically relevant differences in concomitant illness, or medication use, were detectable between men with HSDD and men without HSDD.

Overall, current observations would suggest that it is probably not possible to ascribe the whole pathogenetic responsibility of a sensitive issue such as LSD/I to sociodemographic or clinical variables, no or to the hormonal milieu either. Therefore, in daily clinical practice, even the most-experienced Sexual Medicine physicians need a multidisciplinary approach when dealing with 'multi-dysfunctional' patients.

A potential further strength of our study comes from the fact that all enrolled patients were sexually active, regardless of their relationship status. In this context, the correlation between ED and the lack of a regular partner has been described (Lewis *et al.*, 2010). In addition, Koskimäki *et al.* (2008) also demonstrated that regular intercourse may eventually protect against the development of ED in men aged 55–75 years. Interestingly, Laumann *et al.* (1999) showed that married men reported significantly lower rates of lacking interest in sex than never-married

men (OR 2.75) or divorced/separated or widowed (OR 1.69) individuals. Similarly, previous data suggested that low SD, along with erection problems and performance anxiety, emerged as the most prevalent self-reported symptom of sexual dysfunction among men who have sex with men (MSM) extrapolated from an Internet sample of US MSM aged 18 or older (Hirshfield *et al.*, 2010). Overall, our findings in sexually active men did not support these latter results; indeed, rates of LSD/I were different neither in men with unstable sexual relationship nor in MSM.

Our study is not devoid of limitations. First, the study reports the results of an exploratory analysis in a relatively small cohort of individuals that would deserve external validation with an independent larger sample and, possibly, with men from different countries or ethnic backgrounds. In this context, we highlighted that the homogeneity of the cohort and consistency of the method of evaluation should be considered as strengths of the analyses. It is certainly true, however, that sexologists may see many more patients with libido disorders, especially young ones, so as to limit the statistical power of our findings. Conversely, this is the actual strength of our analysis; indeed, even urologists with specific interests in Sexual Medicine may be routinely exposed to the evaluation of young men with complex and multiple sexual problems in the daily clinical practice. Likewise, it is certainly true that these findings cannot be simply translated to the general population or, and this is even more clinically significant, to the average patient seeking medical help from an urological clinic.

Second, we defined LSD/I using the 'umbrella' criteria taken from the SOPs of ISSM (Rubio-Aurioles & Bivalacqua, 2013). Conversely, we lacked a validated patient-reported outcome measure for evaluating low desire and related psychological distress. Therefore, we were not able to precisely define HSDD rates in our cohort of men (Brotto, 2010; Derogatis *et al.*, 2012). Third, we did not assess rates of depression or anxiety using validated psychometric tools. In this context, the causal relationship between ED and either depression or anxiety, or both, is probably bidirectional (Shabsigh *et al.*, 1998; Shiri *et al.*, 2007). Indeed, ED may be acquired after either depression or anxiety which, in turn, may be consequences of any sexual dysfunction, including ED and LSD/I. Shabsigh *et al.* (1998) demonstrated that ED per se is associated with high incidence of depressive symptoms, regardless of age, marital status or comorbidities. Patients with ED have an acquired decreased libido compared with controls, and individuals with depressive symptoms have a lower libido than patients without depressive symptoms (Shabsigh *et al.*, 1998). Interestingly, Derogatis *et al.* (2012) recently reported that depressive symptomatology in their cohort was no different between men with and without HSDD.

Lastly, the finding of a higher prevalence of use of antiplatelet drugs in men with LSD/I + ED would deserve greater discussion. However, because of the lack of significant data in the literature and the specific clinically oriented aim of this analysis, we cannot derive general conclusions or further speculation on this potential correlation; additional studies in larger population-based samples are certainly needed to confirm these results.

CONCLUSIONS

Our findings show new evidence that primary LSD/I is comorbid in less than 5% of sexually active men seeking their first medical help for new-onset ED. However, one of three men with LSD/I + ED is younger than 40 years. As a whole, younger age and an overall lower health status emerged as independent predictors of the combination of LSD/I and ED, after adjusting for several sociodemographic and clinical variables. The delay between ED onset and first seeking medical help was significantly shorter in men with LSD/I + ED as compared with those complaining of only ED. Because the current sample size is limited, we probably cannot derive general conclusions; therefore, additional studies in larger population-based samples are needed to confirm these results and to further characterize the potential role of ED severity as a harbinger of acquired LSD/I, even, and above all, in young individuals.

ACKNOWLEDGEMENTS

The authors thank Ms. Chiara Molteni and Dana Kuefner PhD for reviewing the language in this manuscript.

FUNDING

None.

CONFLICT OF INTEREST

All the authors declare that they have no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

A.S., N.S., R.D., F.M.: substantial contributions to research design. A.S., M.C.C., E.V., M.C., P.C., G.C., L.B.: substantial contributions to the acquisition of data. A.S., E.V., M.C., F.C., N.S., F.C.: substantial contributions to the analysis or interpretation of data. A.Salonia, M.C.C., F.C., R.D., F.M.: drafting the paper or revising it critically. A.S., M.C.C., E.V., M.C., P.C., G.C., L.B., F.C., N.S., F.C., R.D., F.M.: approval of the submitted and final versions.

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