Prevalence and predictors of unrecognized low sexual desire/interest in men with new onset erectile dysfunction: findings from a cross-sectional, real-life study

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Abstract

The interrelationship between male sexual desire and erectile dysfunction (ED) has been scantly investigated. Thus, we aimed at investigating the prevalence of and the predictors of unrecognized low sexual desire/interest (uLSD/I) in a cohort of men with new onset ED. Complete data from 1509 men seeking for first medical help for ED between 2010 and 2021 were analysed. Comorbidities were scored with the Charlson Comorbidity Index (CCI). At entrance, all patients were asked to self-report LSD/I and completed the International Index of Erectile Function (IIEF) and the Beck Depression Inventory (BDI) (depressive symptoms scored as BDI ≥ 11). The IIEF-erectile function (IIEF-EF) domain was categorized according to Cappelleri's criteria. The median value of the IIEF-sexual desire domain (IIEF-SD) was used to dichotomize men with uLSD/I along with ED (IIEF-SD < 7) vs. ED-only (IIEF-SD ≥ 7). Circulating hormones were measured in every patient. Hypogonadism was defined as total testosterone (tT) < 3.0 ng/mL. Descriptive statistics and logistic regression models tested the association between clinical variables and uLSD/I. Of 1197 patients not self-reporting LSD/I, 369 (30.8%) had IIEF-SD < 7. Patients with ED + uLSD/I were older [median (IQR) 54(41–63) vs. 49(36–59) years], had lower IIEF-EF [10.5(5-21.8) vs. 22(11–28)] but higher BDI [6(3–12) vs. 4(1–8)] and lower tT [4.3(3.2–5.7) vs. 4.8(3.2–6.8) ng/mL] compared to ED-only men (all $p < 0.05$). Overall, ED + uLSD/I men had higher rate of severe ED (49.9% vs. 23.1%), and of BDI ≥ 11 (30.6% vs. 18.2%) (all $p < 0.05$). At multivariable logistic regression analysis, lower tT (OR: 0.82), lower IIEF-EF scores (OR:0.95) and BDI ≥ 11 (OR:2.51) were independently associated with ED + uLSD/I, after accounting for age (all $p < 0.05$). Almost 30% of men seeking first medical help for ED-only had also uLSD/I. Men with both conditions were older, had higher rates of severe ED and more depressive symptoms. A detailed investigation of sexual desire should be always included in men self-complaining only of ED.

Introduction

Male sexual dysfunctions (SD) are defined as personal or couple's difficulty during any stage of a normal sexual activity, thus including physical pleasure, desire, preference, arousal or orgasm (1, 2). Men presenting at outpatient clinics because of SD mostly complain of erectile dysfunction (ED), premature ejaculation (PE), Peyronie's disease (PD) and low sexual desire/interest (LSD/I) (3). ED is the most prevalent male SD, affecting more than 40% of men presenting with any SD in the real-life setting (4), with age at first presentation significantly decreasing over the past decades (5). However, in clinical practice, it is more and more common to deal with patients complaining of more than one SD at a time (6–10).

In this context, also due to the specific difficulty in investigating such a delicate and complex problem in the male, the interrelationship between ED and LSD/I has been scantly investigated (11). The contemporary experience of both ED and LSD/I indeed has been mostly related to aging, hormonal changes and psychological factors (12, 13). Historically, it has been postulated that ED and LSD/I are affected by various endocrinological factors such as the balance between circulating testosterone (T) and oestradiol (E_2) (14), prolactin levels (15), and thyroid hormonal levels (16). As a whole, on the one hand the impact of serum T on sexual functioning in men may be direct (17). On the other, circulating T

may have indirect effects. In this context, as reported by Shigehara et al., T levels, which play an important role in maintaining both normal libido and erectile function, generally decrease with ageing, thus triggering age-related mental and physical changes with consequent decline of sexual arousal (18). Furthermore, low T levels could also impact sexual activity due to an overall decreased energy, thus leading to mood deflection and depressive symptoms (19). Accordingly, depressive symptoms, which may be associated with decreased sexual desire, are commonly and even independently associated with hypogonadism (20, 21).

Since LSD/I is often unreported during office visits for SD, but may have a detrimental impact toward male sexual health, we aimed to i) investigate the prevalence of unreported LSD/I (uLSD/I) in a homogenous cohort of heterosexual men seeking first medical help for ED as their primary compliant; ii) explore and compare the baseline sociodemographic and clinical characteristics of men with only ED versus men presenting with uLSD/I and ED; and, iii) investigate the predictors of uLSD/I among men presenting for new-onset ED only at a single tertiary-referral centre for sexual medicine over the last 11 years.

Materials And Methods

Data from 1587 heterosexual men seeking first medical help for new-onset ED as their primary complaint between 2010 and 2021 were analysed. To this aim, ED was defined as the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance (3).

For the specific purpose of this exploratory study, only data from patients complaining of ED and naïve for phosphodiesterase type 5 inhibitor (PDE5i) therapy were considered. Likewise, low sexual desire/interest was defined according to the Standard Operational Procedures (SOPs) of the International Society for Sexual Medicine (ISSM) 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 (22), for which hypoactive sexual desire disorder (HSDD) would represent only a subtype. All subjects were assessed via a detailed medical history including data on health-significant comorbidities as scored using the Charlson comorbidity index (CCI) (23). Body mass index (BMI) was measured for each patient. Patients were invited to complete the International Index of Erectile Function (IIEF) at first clinical assessment; ED severity was classified according to Cappelleri's criteria (24, 25). Furthermore, all patients compiled the Beck's Inventory for Depression (BDI), with clinical depression defined as BDI score $\geq$11 (26, 27). Literacy problems as well as other reading and writing problems were excluded in all patients.

Venous blood samples were drawn from each patient between 7 a.m. and 11 a.m. after an overnight fast. Follicle-stimulating hormone (FSH), luteinizing hormone (LH), total testosterone (tT), prolactin, E_2, thyroid-stimulating hormone (TSH), sex hormone binding globulin (SHBG), and albumin levels were measured for every individual. Hypogonadism was defined as tT $\leq$ 3 ng/ml (28). Calculated free T was obtained in each patient (21).

Exclusion criteria were patients self-reporting LSD/I at first assessment (n = 312); patients with a known history of depression or depressive symptoms, or those taking any antidepressant therapy (n = 21); known conditions that may contribute to SD, such as history of major pelvic surgery (n = 61); hyperprolactinemia and/or thyroid function disturbances (n = 23). None of the patients had been receiving recent or current testosterone therapy (TTh), androgen deprivation therapy, or any other hormonal treatment, either during the study or in their history. Thereof, a convenient sample of 1197 patients was included in the final analysis.

Data collection followed the principles outlined in the Declaration of Helsinki; all patients had signed an informed consent agreeing to deliver their own anonymous information for future studies. The study was approved by the IRCCS San Raffaele Hospital Ethical Committee (Prot. 2014—Pazienti Ambulatoriali).

Statistical analysis

For the specific purpose of this study, the median value of the IIEF-Sexual Desire (IIEF-SD) domain score was used to arbitrary defined uLSD/I, and to categorize the entire cohort into: i) patients complaining of ED but with an IIEF-SD score ≥ 7 (ED-only); and, ii) patients complaining of ED and with an IIEF-SD score < 7 (ED + uLSD/I).

Statistical analyses consisted of three steps. First, medians and interquartile ranges (IQR) or frequencies and proportions were reported for continuous or categorical variables, respectively. Mann-Whitney and Chi-square tests were used to compare the statistical significance of differences in the distribution of continuous or categorical variables among the two groups (ED-only vs. ED + uLSD/I), respectively. Second, univariable and multivariable logistic regression models were fitted to assess the presence of potential predictors of unreported LSD/I at baseline in men self-seeking for first medical help solely for ED.

Statistical analyses were performed using SPSS v.26 (IBM Corp., Armonk, NY, USA). All tests were two sided, and statistical significance level was determined at $p < 0.05$.

Results

Table 1 details descriptive statistics for the whole cohort of 1197 patients and after further segregation according to IIEF-SD median score ≥ 7 (ED-only) vs. IIEF-SD < 7 (ED + uLSD/I), respectively. Of all, 828 (69.2%) men were ED-only and 369 (30.8%) were subsequently categorized as ED + uLSD/I. At first clinical assessment, ED + uLSD/I patients were older ($p < 0.001$), with a higher rate of health significant comorbidities ($p = 0.01$) and presented higher serum levels of TSH ($p = 0.04$) and FSH ($p = 0.03$), but lower levels of tT ($p = 0.02$) as compared with ED-only patients. Groups did not differ for other variables (Table 1).

Table 1
Descriptive statistics of the whole cohort of patients as segregated according to IIEF-SD domain scores (i.e., IIEF-SD score ≥ 7 vs. IIEF-SD score < 7)

Variable	Whole Cohort	IIEF-SD ≥ 7	IIEF-SD < 7	p-value
Number of patients [No. (%)]	1197	828 (69.2)	369 (30.8)	
Age (years)	50 (37–61)	49 (36–59)	54 (41.2–63)	< 0.001
BMI (Kg/m^2)	24.9 (23-27.2)	24.9 (22.9–27.3)	25.1 (23.3–27.1)	0.46
CCI ≥ 1 [No. (%)]	245 (20.5)	159 (19.2)	86 (23.4)	0.01
TSH (mUI/L)	1.6 (1.3–2.3)	1.6 (1.1–2.2)	1.7 (1.2–2.6)	0.04
PRL (ng/mL)	8.9 (6.5-13-2)	9.2 (6.7–13.3)	8.1 (6-12.9)	0.2
LH (mUI/L)	4.2 (2.8–5.8)	4.2 (2.8–5.8)	4.8 (2.7–5.9)	0.91
FSH (mUI/L)	4.2 (2.7–8.2)	3.9 (2.5–7.4)	5.2 (3.1–8.8)	0.03
E_2 (ng/ml)	0.03 (0.02–0.04)	0.03 (0.02–0.03)	0.02 (0.02–0.03)	0.28
SHBG (nmol/L)	35 (26-45.1)	33 (26–45)	37 (26–48)	0.12
tT (ng/mL)	4.6 (3.2–6.1)	4.8 (3.2–6.3)	4.3 (3.2–5.7)	0.02
tT (ng/mL) ≤ 3 [No. (%)]	230 (19.2)	159 (19.2)	71 (19.3)	1.0
cfT (ng/mL)	2 (1.7–2.3)	2 (1.7–2.3)	1.9 (1.6–2.3)	0.16
T/E_2 ratio	162.7 (112.5-230.5)	158.2 (107.5-241.9)	163.6 (116.2-228.5)	0.84
Albumin (g/dL)	44.6 (42.3–46.7)	44.7 (42.5–47)	43.9 (41.5–46.2)	0.03
Data are expressed in median (IQR), except where otherwise noted				
Keys: IIEF: International Index of Erectile Function; SD: Sexual Desire domain; BMI: Body Mass Index; CCI: Charlson Comorbidity Index; TSH: Thyroid-stimulating hormone; PRL: Prolactin; LH: Luteinizing hormone; FSH: Follicle-stimulating hormone; E_2: Oestradiol; SHBG: Sex Hormone Binding Globulin; tT: total testosterone; cfT: calculated free testosterone. T/E_2 ratio = total testosterone / oestradiol ratio; IQR: interquartile range.				

Likewise, ED + uLSD/I patients showed higher median BDI scores and a greater rate of BDI ≥ 11 suggestive for clinical depression (all $p < 0.001$). Both total-IIEF and IIEF-sub-domains scores were lower in ED + uLSD/I compared to ED-only patients. Severe ED was more frequently observed in in ED + uLSD/I as compared with ED-only patients (all $p < 0.001$) (Table 2).

Table 2
Questionnaires scores of the whole cohort of patients as segregated according to IIEF-SD domain scores (i.e., IIEF-SD score ≥ 7 vs. IIEF-SD score < 7)

Variable	Whole Cohort	IIEF-SD ≥ 7	IIEF-SD < 7	p-value
BDI	5 (2-9.3)	4 (1–8)	6 (3–12)	< 0.001
BDI ≥ 11 [No. (%)]	264 (22.1)	151 (18.2)	113 (30.6)	< 0.001
IIEF-Total	47 (28–61)	53 (36–64)	31 (14.5-47-5)	< 0.001
IIEF-EF	19 (8–26)	22 (11–28)	10.5 (5-21.8)	< 0.001
IIEF-OS	6 (3–8)	7 (4–8)	4 (2–6)	< 0.001
IIEF-OF	9 (6–10)	10 (6–10)	6 (2–10)	< 0.001
IIEF-IS	8 (3–11)	9 (5–12)	5 (0–8)	< 0.001
Erectile dysfunction severity † [No. (%)]				< 0.001
Normal erectile function	329 (27.6)	284 (34.2)	45 (12.2)	
Mild ED	187 (15.7)	140 (16.9)	47 (12.7)	
Mild-to-moderate ED	132 (11.1)	93 (11.2)	39 (10.6)	
Moderate ED	162 (13.6)	108 (13.0)	53 (14.4)	
Severe ED	382 (32.0)	198 (23.9)	184 (49.9)	
Data are expressed in median (IQR), except where otherwise noted				
Keys: IIEF: International Index of Erectile Function; SD: Sexual Desire domain; IQR: interquartile range; BDI: Beck's Depression Inventory; EF: Erectile Function domain; IS: Intercourse Satisfaction domain; OF: Orgasmic Function domain; OS: Overall Satisfaction domain.				
† Erectile dysfunction (ED) severity according to Cappelleri's criteria (defining; normal erectile function as an IIEF-EF > 26; mild ED as an IIEF-EF of 26 – 22; mild-to-moderate ED as an IIEF-EF of 21 – 17; moderate ED as an IIEF-EF of 16 – 11; and severe ED as an IIEF-EF < 11)				

Table 3 reports univariable and multivariable logistic regression analysis showing variables potentially associated with uLSD/I status. At univariable logistic regression analysis, patients with older age (OR: 1.02), lower tT levels (OR: 0.9) and higher FSH levels (OR: 1.01) were more likely to have uLSD/I at baseline (all p < 0.001). Similarly, lower IIEF-EF scores (OR: 0.93) and BDI ≥ 11 (OR: 1.96) were univariably associated with uLSD/I status at presentation (all p < 0.001) (Table 3). At multivariable logistic regression analysis, lower serum tT levels (OR: 0.82), higher rates of depressive symptoms (OR: 2.51) and lower IIEF-EF scores (OR: 0.95) emerged as independently associated with uLSD/I (all p < 0.05, Table 3).

Table 3
Univariable (UVA) and multivariable (MVA) logistic regression analysis showing potential predictors of uLSD/I at baseline.

	UVA		MVA	
Variable	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.02 (1.01–1.03)	< 0.001	1.01 (0.98–1.04)	0.38
BMI (Kg/m^2)	1.02 (0.98–1.05)	0.3	/	/
CCI ≥ 1	1.28 (0.95–1.73)	0.1	/	/
FSH (mUI/L)	1.01 (0.99–1.03)	< 0.001	0.98 (0.95–1.01)	0.17
tT (ng/mL)	0.9 (0.83–0.97)	0.007	0.82 (0.67–0.99)	0.04
BDI ≥ 11	1.96 (1.4–2.76)	< 0.001	2.51 (0.11–5.33)	0.03
IIEF-EF	0.93 (0.92–0.94)	< 0.001	0.95 (0.91–0.98)	0.005

Keys: uLSD/I: unreported Low Sexual Desire/Interest; BMI: Body Mass Index; CCI: Charlson Comorbidity Index; FSH: Follicle-stimulating hormone; tT: total testosterone; BDI: Beck's Depression Inventory; IIEF-EF: International Index of Erectile Function - Erectile Function domain.

Discussion

Current retrospective analysis of real-life data from a cohort of consecutive white-European heterosexual sexually-active men at a single outpatient centre over the last 11 years depicted that one out of three patients (30.8%) seeking first medical help for new-onset ED as their primary and only self-complaint also suffered from concomitant uLSD/I. Patients with ED and uLSD/I were older, had more comorbid conditions, showed a worse hormonal profile and had more severe ED than those with only ED. As such, lower levels of tT, lower IIEF-EF scores and BDI scores ≥ 11 at baseline emerged to be independently associated with uLSD/I in men self-presenting for ED only. As a whole, these observations emerged to be clinically relevant since they should lead to a significant rethinking of any tailored management work-up of ED patients, especially of those who could conceal other concomitant SDs (thus making patient management significantly more complex in the everyday clinical practice). This emerges to be of particular importance since the combination of embarrassment also linked to desire makes men even more fragile, with different expectations and probably less prone to follow physicians' suggestions (29, 30).

The prevalence of ED in the general population has been largely explored in several studies with a steep age-related increase from 2.3–53.4% (3). Conversely, only few data exist concerning the actual prevalence of a broader concept and even more delicate concept such as LSD/I in men. Meissner et al. reported a 4.7% prevalence of LSD/I in the general population by using an online survey directed to 12,646 German middle-aged men (31). Similarly, an Italian cross-sectional study with data from 2,013 at

a single tertiary academic centre reported a prevalence of LSD/I of approximately 10% (4). Moreover, previous studies showed that the coexistence of ED and LSD/I varies between 4 and 40% (11, 13, 32). Noteworthy, data from existing literature investigated LSD/I presence in men as self-reporting with online survey or as primary reason for office evaluation; on the contrary, we deliberately excluded men who have declared LSD/I at entrance to specifically capture uLSD/I (as defined by using IIEF-SD sub domain). In this context, our results depicted that almost 30% of men seeking first medical investigation for new onset ED had concomitant uLSD/I. Therefore, our results depicted the lack of awareness of a common disorder in patients seeking first medical help only for ED and warn sexual medicine experts to more comprehensively investigate other SD in every patient.

Older patients have higher risk of ED (33) and age is commonly used to guide treatment decision making in men with poor erectile function (29). Moreover, data from the European Male Ageing Study (EMAS), showed that aging impact directly on sexual desire (34). Furthermore, many comorbidities are listed in the pathogenic pathways of both ED and LSD/I (3, 35–37). Accordingly, Laumann et al., in the Global Study of Sexual Attitudes and Behaviours, showed that in a cohort of 13.618 men aged 40–80 years from 29 countries a decreased sexual interest was associated with older age and an overall poor health (2). Considering the impact of both age and comorbidities on the coexistence of ED and LSD/I, Salonia et al. conducted a cross-sectional study involving 790 patients and showed that severe CCI scores were independently associated with the coexistence of both self-reported ED and LSD/I (11). Conversely, Corona et al. found that in men presenting for new-onset ED, a decreased sexual desire was more frequently associated with a healthier status (32). Here we confirm that the prevalence of uLSD/I in men seeking medical for new onset ED only was higher in older men and in those with more comorbidities at the time of first investigation.

The coexistence of low sexual desire, decreased morning erections and ED has been recognized as the strongest predictor of testosterone deficiency, with circulating T being the most clinically relevant factor influencing men's sexual desire (38, 39). Of clinical importance, current findings depicted that men with ED + uLSD/I have significantly lower values of tT than men with ED-only and lower tT values emerged to be associated with uLSD/I, although groups were comparable in terms of prevalence of T deficiency (as for tT $\leq$ 3 ng/mL (28)). To this regard, data from existing literature declares that in men with ED the loss of sexual interest was not associated to a defined hypogonadism status, although patients with decreased libido had lower levels of tT with respect to men complaining of ED without LSD/I (13). Furthermore, Corona et al. reported that the hormonal balance orchestrates an important role in defining sexual health, and endocrine abnormalities are common in men with the impairment of both sexual desire and erectile function (40). In this context, our results revealed that men with ED and uLSD/I had higher serum levels of TSH and FSH, even if both were within the range of normality. Noteworthy, in the consideration of the open debate on the actual importance of T/E_2 ratio in determining the coexistence of both ED and LSD/I (12), our analysis did not depict any significant difference between groups.

Lastly, the loss of sexual desire could be considered as an acquired and psychological consequence of ED status (13). Decreased sexual function may have detrimental impact toward both partners quality of

life (41), and men with ED are at higher risk of depressive moods (42). Our findings substantiate this previous observation; indeed, ED + uLSD/I patients had worse scores for depression than ED-only patients.

A first strength of our study is that all patients were enrolled at a same outpatient clinic thus representing a typical real-life scenario. Second, our analyses were limited to a large cohort of same-race, sexually active patients thus eliminating potential ethnic difference. Third, we have assessed only patients not self-reporting LSD/I by means of validated questionnaires (i.e., IIEF-SD domain score, with the median value as an instrument to highlight the presence of uLSD/I).

Our study is certainly not devoid of limitations. First, it is a cross-sectional retrospective analysis at a single, tertiary referral academic centre thus raising the possibility of selection biases. Second, our data may not reflect an actual change of disease incidence, defined as the number of cases observed over one year, but rather a change in the prevalence of each condition among patients seeking help for ED. Thereof, larger cohort studies across different centres and populations are needed to validate our findings. Yet, all patients have been consistently analysed over time by a single expert physician, thus limiting at least potential heterogeneity associated with differences in diagnostic work-up methodology. Third, although every patient has been comprehensively and homogeneously investigated we have arbitrarily considered the median value of the IIEF-SD domain as a valid threshold below which patients had been defined as having uLSD/I. In contrast, more adequate validated questionnaires to assess LSD/I (e.g., Male Sexual Health Questionnaire (MSHQ) (43)) are actually available. Therefore, the methodology we adopted for this specific analysis is probably not the best available in terms of psychometric tools and questionnaires, and it may only indicate to physicians the need to better investigate patients' needs and sexual satisfaction with a more appropriate multimodal approach. However, despite this may be a major bias of the analysis, we consider that it could even be eventually considered a major strength, as IIEF-SD can be easily used in daily clinical practice, and even more useful for better tailoring the management work-up.

In conclusion, one out of three men seeking first medical help for ED only had criteria for an unreported LSD/I, according to the IIEF-SD domain score. Compared to those with normal sexual desire, men with both conditions were older, had higher rates of severe ED, more prevalent depressive symptoms, and lower serum tT levels, even if not suggestive for hypogonadism. A detailed investigation of sexual desire should be always included in the diagnostic work-up of men with ED, in order to better tailoring patient therapeutic management.

Declarations

AUTHORS' CONTRIBUTIONS

Conception and design of the study: SC, LB, PC, AS.

Data acquisition: FB, AD, EP.

Analysis and interpretation of data: SC, LB, GF, AS.

Drafting the manuscript: SC, LB, CC.

Style revision: CI, VM, AP, FM.

All authors revised the manuscript and read and approved the version submitted.

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Availability of data and material

Data and materials are available whenever requested.

Code availability

Code is available whenever requested.

Conflict of interest

None of the authors have conflicts of interest to disclose.

Statement of Ethics

Data collection followed the principles outlined in the Declaration of Helsinki; all patients had signed an informed consent agreeing to deliver their own anonymous information for future studies. The study was approved by our local ethics committee.

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