

The role of erection hardness in determining erectile dysfunction (ED) treatment outcome

John Dean, Bert-Jan de Boer, Alessandra Graziottin, Dimitrios Hatzichristou, Jeremy Heaton, Ann Tailor

Abstract

Whatever the cause of a man's erectile dysfunction (ED), the result is a loss of penile rigidity that impairs or precludes his ability to achieve or maintain vaginal penetration for sexual intercourse. Identification of the degree of impairment of penile rigidity and durability is an important component in the assessment of ED in both clinical practice and in clinical trials of oral drug treatments for ED. This focus on erection hardness is appropriate because men themselves emphasise this quality when they judge the effectiveness of treatment for ED. This attitude is because the ability to achieve a rigid and durable erection is frequently perceived by affected men as central to their sexual satisfaction and self-image as sexually competent; loss of this ability may have important adverse effects on their self-esteem, their sexual confidence, and, directly or indirectly, their relationship with their partner. There is a significant positive correlation between improvement in erection hardness and men's sexual self-confidence, sexual enjoyment, and satisfaction with their sexual relationship. Improvement in the rigidity and durability of erections following successful treatment of ED has the potential to allow men to experience better sex, not only by improving erection hardness, but also by restoring their emotional well-being and their partner's satisfaction.

1. Introduction

We previously proposed three principal factors necessary for men with ED to experience better sex:

- Enhanced hardness of erection
- Enhanced perception of partner sexual satisfaction
- Enhanced self-esteem and sexual confidence of the man

The concept of better sex is important to men; therefore, any successful treatment plan for ED must consider a man's sexual experience in the broader sense including physical, behavioural, relationship, and partner factors.

In this article, we consider the particular importance of erection hardness for men with ED to experience better sex.

2. The mechanism of a hard erection

The penis becomes hard and erect when the flow of blood into the penis exceeds outflow, which is achieved by relaxation of the penile trabecular smooth muscle and its feeder arteries, allowing increased blood flow into the organ and expansion of the sinusoids. In turn, the emissary veins lying between the trabeculae and the tunica albuginea become compressed, resulting in almost total occlusion of venous outflow. In an erect penis, intracavernosal pressure is equivalent to, or above, systolic blood pressure when the penile bulb is compressed following pelvic floor muscle contraction. During sexual intercourse or masturbation, it is this haemodynamic change that causes the penis to become harder [1].

An erection is, essentially, a neurovascular reflex initiated by both the central nervous system and the peripheral stimuli, and modulated by androgens. Psychogenic erections occur in response to afferent signaling (sight, sound, touch, and smell) and to cognitive inputs of memory and fantasy that are integrated within the central nervous system (CNS),

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leading to proerectile signaling and erection. Nocturnal erections, which occur during rapid-eye movement sleep, are thought to be caused by a decrease in sympathetic inhibition, with augmentation of proerectile centres within the CNS. Reflexogenic erections result from direct genital (and sometimes other) tactile stimuli, which are integrated in spinal autonomic centres and within the brain. These pathways function together to influence erection response, but the reflexogenic pathway becomes increasingly important with increasing age: Older men are less likely to attain psychogenic erections in the absence of genital stimulation [1].

As elsewhere within the autonomic nervous system, both sympathetic noradrenergic, and parasympathetic cholinergic fibres innervate the cavernosal tissue. In addition, there is innervation from erectogenic nitrergic nerves from which nitric oxide (NO) is released, activating an intracellular enzyme cascade. NO increases the production of intracellular cyclic guanosine monophosphate (cGMP), ultimately causing cavernosal smooth muscle relaxation. This pathway is regulated by the enzyme phosphodiesterase type 5 (PDE5), which degrades cGMP. Other phosphodiesterases are found in the corpus cavernosum but do not appear to have an important role in the erectile process [1]. As a consequence of this, there is expansion of the cavernosal trabecular walls and lacunar spaces, with a marked increase in intrapenile blood volume. Compression of the plexus of subtunical venules subsequent to this expansion reduces venous outflow. This process, known as the veno-occlusive mechanism, produces an increase in penis size and rigidity, leading to erection.

3. Assessing erection hardness

An erection is a neurovascular event modulated by psychophysiological factors and hormonal status [1], with numerous organic and psychogenic factors [2] disrupting the processes involved, as outlined by the individual components of the International Index of Erectile Function (IIEF), the most commonly used instrument to assess erectile function in research and clinical trials [3] (Table 1). These disruptive factors frequently interact. ED is most commonly of mixed aetiology, involving both organic and psychological factors [1,2]. However, regardless of the interacting causal factors that might contribute to a man's ED, the end result is a loss of hardness.

Loss of hardness impairs a man's ability to achieve, or maintain, vaginal penetration, and may, therefore, also hinder orgasm and ejaculation. It is clear that the ability to attain a hard and sustained erection is central to satisfaction and, to the man himself, acceptable sexual function. Consequently, the degree of impairment of erection hardness and durability is the main component in the assessment of the severity of a man's ED. The 15 components of the IIEF scale are designed to address several domains of male sexual function [4]: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction (Table 1). Questions 1–5 and 15 of the tool are intended to elicit a man's assessment of his ability to achieve and maintain an erection hard enough for penetration and completion of intercourse. This focus on hardness of erection is even more obvious in the IIEF's abbreviated version: IIEF-5 or the Sexual Health Inventory for Men (SHIM) [5]. As shown in Table 2, items 1–5 of the SHIM are taken directly from IIEF items 2, 4, 5, 7, and 15, and as a result, 4 of 5 items focus on the hardness of the erection.

4. Impact of the quality of erectile response in men's lives

The SHIM was designed to be a practical tool for diagnosing the presence and severity of ED in clinical practice, and the focus on erection hardness is probably appropriate because of the emphasis that men place on this quality when they use a treatment for ED. In a recent multicentre study, men's most desired treatment outcomes were, first, to achieve a

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rigid erection (76%) and, second, to be able to engage in sexual activity at any desired time (71%). Furthermore, in this study, these expectations were not influenced by religion, economic status, educational background, or sexual habits [6]. The prevalence of ED increases in a linear fashion with advancing age [7–9] and is the most commonly reported sexual problem for older men [10]. With that in mind, it is also known that sexual activity remains an important part of life for many middle-aged and elderly men. A global survey of sexual attitudes and behaviours in people aged >40 yr reported that 82% of men agreed that “satisfactory sex is essential to maintain a relationship,” whereas 68% were “in favour of the use of medical treatments to help older people enjoy sexual activity” [8].

This survey also indicates that older men are more likely than older women to report continued sexual activity: Whilst 53% of men aged 70–80 yr reported having sexual intercourse in the preceding 12 months, only 21% of women responded positively to this question. It may be that the women were being more honest about their levels of sexual activity, but this difference only serves to emphasise the importance that men of all ages place on their ability to maintain sexual functioning. Men are less likely than women to report lack of interest in sex or that sex is not pleasurable, but they are more likely to report anxiety about their sexual performance [11]. Consequently, feelings of emasculation are the most common initial reaction among men to ED and the loss of their ability to satisfy a sexual partner [12]. This reaction can markedly impair the emotional lives of men, affecting their relationships with their partners and their ability to form new relationships.

The loss of confidence and more negative self-image that result from ED can also have an adverse effect on a man's day-to-day relationships with friends and work colleagues. Men report a sense of isolation because they are no longer “one of the lads” [12], a loss of self-esteem that is often exacerbated by men's unwillingness to discuss their worries. Men are often unable to talk to their male friends about any health concerns and instead rely on their female partners for support [13]. However, some men cannot confide in their sexual partner about their loss of erection hardness, principally because of a desire to avoid the subject or because they feel “belittled” by their condition [12].

The failure of a couple to discuss the man's concerns about his sexual function raises barriers between them that can result in not only loss of emotional intimacy and avoidance of sexual intercourse, but also reduction or cessation of expressions of tenderness, such as hugs, kisses, and cuddles [14]. This withdrawal of affection can only lead to diminished sexual desire for both partners and the compounding of any distance or conflicts that were already present in the relationship. It is not surprising that sexual dysfunction is strongly associated with negative experiences in sexual relationships, with an overall loss of happiness and well-being [11].

5. Impact of ED treatment on erection hardness

Erection hardness was a key criterion for assessing success in studies of non-pharmacologic ED treatments [15], and widespread use of the IIEF in clinical trials has ensured that improvement in grade of erection hardness (Table 3) continues to be an important factor in evaluating outcomes in randomised controlled clinical trials (RCTs) of oral drug treatments for ED. PDE5 inhibitors, which act by inhibiting the activity of the degrading enzyme PDE5 (previously described), are now well established as first-line therapy for the majority of men with ED [16]. Administration of a PDE5 inhibitor, of which there are now three on the market, results in a marked elevation of cGMP levels within the corpora cavernosa, leading in turn to increased smooth muscle relaxation and improved erection hardness [2]. Because of this mode of action, PDE5 inhibitors have no effect on erection hardness when sexual stimulation, either central or peripheral, is absent, as the NO and cGMP pathways are not activated.

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Compared with placebo, all three PDE5 inhibitors – sildenafil, tadalafil, and vardenafil – significantly improve the IIEF-defined grade of erection hardness and increase the likelihood of successful intercourse in men with ED, over a range of aetiologies [16–19]. To date, no large, randomised, controlled methodologically-sound studies have been performed that directly compare all three PDE5 inhibitors. Since the drugs differ in their onset and duration of action, patients and physicians now have a very welcome choice of therapy. The efficacy and tolerability of the PDE5 inhibitors appear to be maintained in long-term use [20–22], although more data have been accumulated for sildenafil as the first drug in the class available in the market [21].

More-recent studies have investigated the association between improvement in erection hardness and men's satisfaction with their sexual relationships. For example, in a 12-week double-blind, placebo-controlled study [23], 532 men with ED graded their erection hardness at baseline and at the end of 12 wk of treatment with placebo or sildenafil 25 mg, 50 mg, or 100 mg. Men receiving active treatment reported an increase in the percentage of grade 3 or grade 4 erections; there was a significant positive correlation between the percentage of men taking sildenafil or placebo who reported grade 3 or 4 erections exclusively at the end of treatment, with the percentage of successful intercourse attempts. This high correlation between greater erection hardness and more successful attempts at intercourse suggests that effective treatment enables men with ED to enjoy better sex, a conclusion that is borne out in a pooled analysis of data from 26 randomised, double-blind, placebo-controlled trials conducted between 1996 and 2003 [24]. Men randomised to sildenafil experienced significantly greater improvement in all measures of assessment of erection hardness and sexual relationship satisfaction, compared with men randomised to placebo. There was also a significant and positive correlation between measures of erection hardness, and enjoyment of sex and sexual confidence.

6. Conclusions

The hardness of a man's erection is often very important to his sense of masculinity. The degree of penile hardness required to allow penetration and intercourse is variable; for satisfactory intercourse, hardness must also be well maintained. Men may tolerate, without significant concern, some degree of loss of hardness and durability; there is considerable variation between men in this respect. Loss of erection hardness may have serious adverse effects on a man's self-esteem, his sexual confidence, and his relationship with his partner. Improvement in the hardness of a man's erections, following successful treatment of ED, has the potential to restore a man's emotional well-being and improve his partner's satisfaction with the relationship—in short, harder erections can lead to better sex.

References

- [1] Lue T. Erectile dysfunction. *N Engl J Med* 2000; 342: 1802-13
- [2] Wespes E, Amar E, Hatzichristou D, et al. EAU guidelines on erectile dysfunction: an update. *Eur Urol* 2006; 49: 806-15
- [3] Rosen R, Shabsigh R, Berber M, et al. Efficacy and tolerability of vardenafil in men with mild depression and erectile dysfunction: The Depression-Related Improvement With Vardenafil For Erectile Response Study. *Am J Psychiatry* 2006; 163: 79-87
- [4] Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Misura A. The International Index of Erectile Function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology* 1997; 49: 822-30

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- [5] Rosen RC, Cappelleri JC, Smith MD, Lipsky J, Ben-[~] a BM. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. *Int J Impot Res* 1999; 11: 319-26
- [6] Gruenwald I, Chen J, Smueli Y, Ravio G, Shenfield O, Vardi Y. What do patients expect from ED treatment? *J Sex Med* 2005; 2: 19 (abstract no. PS-4-8)
- [7] Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. *J Urol* 1994; 151: 54-61
- [8] Nicolosi A, Laumann EO, Glasser DB, Moreira ED, Paik A, Gingell C, for the Global Study of Sexual Attitudes, Behaviours Investigators' Group. Sexual behaviour and sexual dysfunctions after age 40: the Global Study of Sexual Attitudes and Behaviours. *Urology* 2004; 64: 991-7
- [9] Rosen RC, Fisher WA, Eardley I, Niederberger C, Nadel A, Sand M. The multinational Men's Attitudes to Life Events and Sexuality (MALES) study, 1: prevalence of erectile dysfunction and related health concerns in the general population. *Curr Med Res Opin* 2004; 20: 603-17
- [10] Papaharitou S, Athanasiadis L, Nakopoulou E, et al. Erectile dysfunction and premature ejaculation are the most frequently self-reported sexual concerns: profiles of 9,536 men calling a helpline. *Eur Urol* 2006; 49: 557-63
- [11] Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. *JAMA* 1999; 281: 537-44
- [12] Tomlinson JM, Wright D. Impact of erectile dysfunction and its subsequent treatment with sildenafil. *BMJ* 2004; 328: 1037-41
- [13] Tudiver F, Talbot Y. Why don't men seek help? Family physicians' perspectives on help-seeking behaviour in men. *J Fam Pract* 1999; 48: 47-52
- [14] Swierzewski M, Fusia T, Harrington M, Haynie L. Viagra (sildenafil citrate) improves the desire for basic intimacy with increased sexual satisfaction in long-term married relationships. *J Sex Med* 2005; 2 (Suppl 1): 25 (abstract no. PS-6-7)
- [15] Cookson MS, Nadig PW. Long-term results with vacuum constriction device. *J Urol* 1993; 149: 290-4
- [16] Goldstein I, Lue TF, Padma-Nathan H, Rosen RC, Steers WD, Wicker PA, for the Sildenafil Study Group. Oral sildenafil for the treatment of erectile dysfunction. *N Engl J Med* 1998; 338: 1397-404
- [17] Brock GB, McMahon CG, Chen KK, et al. Efficacy and safety of tadalafil for the treatment of erectile dysfunction: results of integrated analyses. *J Urol* 2002; 168: 1332-6
- [18] Donatucci C, Taylor T, Thibonnier M, Bangerter K, Gittelman M, Casey R, for the Vardenafil Study Group. Vardenafil improves patient satisfaction with erection hardness, orgasmic function and overall sexual experience, while improving quality of life in men with erectile function. *J Sex Med* 2004; 1: 185-92
- [19] Sussman DO. Pharmacokinetics, pharmacodynamics, and efficacy of phosphodiesterase type 5 inhibitors. *JAOA* 2004; 104: S11-5
- [20] Montorsi F, Verheyden B, Meuleman E, et al. Long-term safety and tolerability of tadalafil in the treatment of erectile dysfunction. *Eur Urol* 2004; 45: 339-45

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[21] Padma-Nathan H, Eardley I, Kloner RA, Laties AM, Montorsi F. A 4-year update on the safety of sildenafil citrate (Viagra). *Urology* 2002; 60: 67-90

[22] Stief C, Porst H, Saenz de Tejada I, Ulbrich E, Beneke M, for the Vardenafil Study Group. Sustained efficacy and tolerability with vardenafil over 2 years of treatment in men with erectile dysfunction. *Int J Clin Pract* 2004; 58: 239-49

[23] Levinson IP. Improved erectile quality correlates with intercourse success in men treated with Viagra (sildenafil citrate) for erectile dysfunction. *J Sex Med* 2005; 2: 59 (abstract no. P-074)

[24] Levinson IP. Erectile function is associated with sexual relationship satisfaction: a pooled analysis of 26 randomized, double-blind, placebo-controlled trials. *J Sex Med* 2005; 2: 59 (abstract no. P-073)

Table 1 – Components of the IIEF (International Index of Erectile Function)

Item	Designed to assess
1	Erection frequency
2	Erection firmness
3	Ability to penetrate
4	Frequency of maintaining an erection
5	Ability to maintain an erection
6	Intercourse frequency
7	Intercourse satisfaction
8	Intercourse enjoyment
9	Ejaculation frequency
10	Orgasm frequency
11	Desire frequency
12	Level of desire
13	Overall satisfaction
14	Relationship satisfaction
15	Erection confidence

Source: Reference [4].

Table 2 – Sexual Health Inventory for Men

Over the past 6 months:

1. How do you rate your confidence that you could get and keep an erection?
 - Very Low
 - Low
 - Moderate
 - High
 - Very high
2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration (entering your partner)?
 - No sexual activity
 - Almost never or never
 - A few times (much less than half the time)
 - Sometimes (about half the time)
 - Most times (much more than half the time)
 - Almost always or always
3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?
 - Did not attempt intercourse
 - Almost never or never
 - A few times (much less than half the time)
 - Sometimes (about half the time)
 - Most times (much more than half the time)
 - Almost always or always
4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?
 - Did not attempt intercourse
 - Extremely difficult
 - Very difficult
 - Difficult
 - Slightly difficult
 - Not difficult
5. When you attempted sexual intercourse, how often was it satisfactory for you?
 - Did not attempt intercourse
 - Almost never or never
 - A few times (much less than half the time)
 - Sometimes (about half the time)
 - Most times (much more than half the time)
 - Almost always or always

Source: Reference [5].

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Table 3 – Grades of erection hardness

Grade 1	Increase in size, but not hard
Grade 2	Hard, but not hard enough for penetration
Grade 3	Hard enough for penetration, but not completely hard
Grade 4	Completely hard

Source: Reference [16].