

Lower urinary tract symptoms and benign prostatic hyperplasia and their impact on quality of life

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Abstract

LUTS is an acronym that refers to *symptoms* affecting the *lower urinary tract*, which are very common in elderly subjects (between 60 and 70%), and often associated with, but not always caused by, benign prostatic hypertrophy (BPH). BPH is a chronic condition characterized by an increase in the number of cells, particularly in the transition area of the prostate. BPH involves a compression of the surrounding tissues, consequently obstructing vesical voiding. Nycturia and urgency represent the most prevalent symptoms and those with the greatest impact on quality of life measured as *urinary-specific health-related quality*. The prevalence of BPH is directly proportional to age; therefore, the absolute number of subjects affected is growing throughout the world. BPH is one of the most common medical conditions affecting those over 50. The overall cost for the diagnosis and treatment of BPH-related LUTS, in the US, has been estimated at approximately 1.1 billion US\$/year, compared to total annual expenditure for urological conditions of some 9 billion and this cost continues to increase. The *quick prostate test*, which was developed by the Italian Urology Society (SIU), is an easy to use instrument that can be utilized in first-level screening for evaluation of the male population with LUTS. This test can be used both in patients not on pharmacological treatment and as a therapy-monitoring instrument. A positive response to one of the questions is sufficient for requesting a more in-depth investigation, which may provide indications on the therapeutic strategy to be taken.

Definition of lower urinary tract symptoms

LUTS is an acronym that refers to *symptoms* affecting the *lower urinary tract*, which are very common in elderly subjects, and often associated with, but not always caused by, benign prostatic hypertrophy (BPH).^{1,2}

Anatomically speaking, the lower urinary tract consists of the bladder, bladder outlet, prostate, distal sphincter mechanism and urethra. BPH is undoubtedly the most common cause of LUTS, but they can also be caused by: i) overactive bladder; ii) prostatitis; iii) nocturnal polyuria; iv) urinary tract infections; v) prostate cancer; vi) other genital/urinary system tumours; vii) significant comorbidities (for example diabetes, congested heart failure, metabolic disease and obesity, medical nephropathy, vascular disease, *etc.*); viii) concomitant therapies; ix) bladder stones; x) prior pelvic surgery; xi) trauma; xii) individual or combined central/peripheral nervous system abnormalities. These situations must be kept in careful consideration in differential diagnosis, when choosing a treatment option.²

One approach, that is not however universally accepted, is to divide LUTS into obstructive (or pertaining to the voiding phase) and irritative (or pertaining to the filling phase) (Table 1).¹

Definition of benign prostatic hypertrophy

Benign prostatic hypertrophy, also known as prostatic adenoma (*benign prostatic enlargement*), is a chronic condition characterized by an increase in the number of cells, particularly in the transition area of the prostate (the middle part around the prostatic urethra) (Figure 1), unlike prostate cancer, which usually develops in the peripheral area. BPH involves a non-infiltrating compression of the surrounding tissues, consequently obstructing vesical voiding.

Prevalence of lower urinary tract symptoms

Lower urinary tract symptoms affect a high percentage (between 60 and 70%) of the male and female population worldwide.

The EpiLUTS (*epidemiology of lower urinary tract symptoms*) study conducted in 2009 by Coyne *et al.* provides a photograph of the socioeconomic impact of these symptoms in consideration of the prevalence of LUTS in the general population.³

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The study is based on a web-based survey involving approximately 30,000 men and women over 40 years of age. The subjects contacted came from the USA, United Kingdom and Sweden.

The study was conducted on 13,967 male subjects and the main aim of the project was to establish the prevalence of LUTS according to the definition provided by the International Continence Society (ICS). The prevalence of LUTS was defined on the basis of two-symptom frequency *thresholds*: i) *sometimes*, whose prevalence in the male population was 72.3%; ii) *often*, whose prevalence was found to be 47.9%. Nycturia was the most frequent symptom, with a prevalence of 69.4% in the men involved in the study.³

The EPIC (*European prospective investigation into cancer and nutrition*) study, on the other hand, was conducted through a telephone survey in five different countries (Canada, Germany, Italy, Sweden and the United Kingdom). In this study, the researchers contacted 58,139 men and women over 18 years of age, of whom 19,165 were included in the final analysis. In the male population, 62.5% of subjects suffered from at least one LUTS. This percentage rose to 80.7%, when considering subjects over 60 years of age only. A percentage of 48.6 of subjects complained of at least one episode of nycturia, whereas two or more episodes were reported by 20.9% of men.⁴

The prevalence of benign prostatic hypertrophy

The prevalence of BPH is directly proportional to age; therefore, the absolute number of subjects affected is growing throughout the world.

Figure 2 shows the progressive increase in the prevalence of BPH in Italy between 2005 and 2013.⁵

BPH can start as early as 40 years of age; however, prevalence is highest amongst elderly subjects (Figure 3).⁵

BPH is also one of the most common medical conditions affecting those over 50. Longitudinal observational population studies and placebo arms in clinical trials on medicinal products support the hypothesis that BPH is a progressive condition. Its progression is very gradual and worsens with time. Indeed, it has been calculated that the mean reduction in peak urinary stream speed is approximately 0.2 mL/s/year and prostate volume increases on by an average of 1-2 cm³/year.¹

BPH is, fortunately, associated with extremely low mortality and morbidity as severe consequences (for example renal insufficiency) are uncommon.¹

Both dihydrotestosterone and estrogens undoubtedly play a role in the onset of BPH, although this role is still somewhat unclear.¹

Histological alteration (microscopic BPH) is present in 70% of those over seventy-five years of age, whereas 40% of them have LUTS (Figure 4) and half of these have a reduced quality-of-life (QoL), which can also be associated with alterations of the sexual area.^{6,7}

Evaluation of symptoms and discomfort

The semi-quantitative assessment of symptoms and inconveniences (or discomforts) is strongly recommended in order to determine the severity of the LUTS and understand the degree of discomfort, intended also as sexual problems that these symptoms cause the patient. Excellent quantitative evaluation instruments such as the *international prostatic symptoms score* (IPSS) (Table 2) and others have been developed and validated.

It is also possible to ask an eighth question concerning QoL, which may prove very useful also in follow-up as an appropriate comparison for judging, for example, the validity of treatment in terms of QoL (Table 2).⁸

Another questionnaire, borrowed from andrology, is the *international index of erectile function questionnaire* (IIEF-q), which is constituted by a set of 5 dedicated questions (Table 3).⁹

Quick prostate test

The *quick prostate test* (QPT), which was developed by the Italian Urology Society (SIU),

is an easy to use instrument that can be utilized in first-level screening for evaluation of the male population with LUTS; it can be considered a valid instrument for use in particular by those doctors who have the theoretical pos-

sibility of evaluating large cohorts of adult males, such as general practitioners, internal medicine specialists, hospital geriatricians and others.

The QPT investigates and weighs, with 3

Table 1. Distinction between obstructive and irritative lower urinary tract symptoms.

Obstructive LUTS (pertaining to the voiding phase)	Irritative LUTS (pertaining to the filling phase)
Hesitation	Frequency
Hypovalid stream	Urgency
Straining to start urination	Nycturia
Protracted urinary retention	Urge incontinence
Vesicle tenesm	
Acute urinary retention	
Over-filling incontinence	

LUTS, lower urinary tract symptoms.

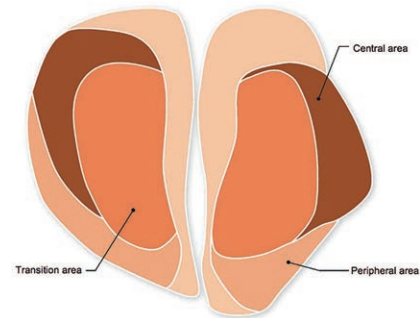


Figure 1. Anatomical areas of a hyperthrophic prostate.

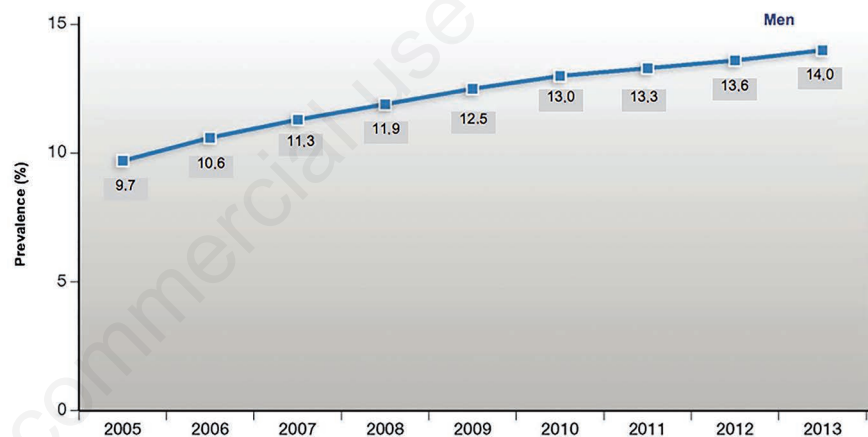


Figure 2. Prevalence of benign prostatic hypertrophy in Italy between 2005 and 2013 (Source: VIII Report Health Search, SIMG 2013/2014).⁵

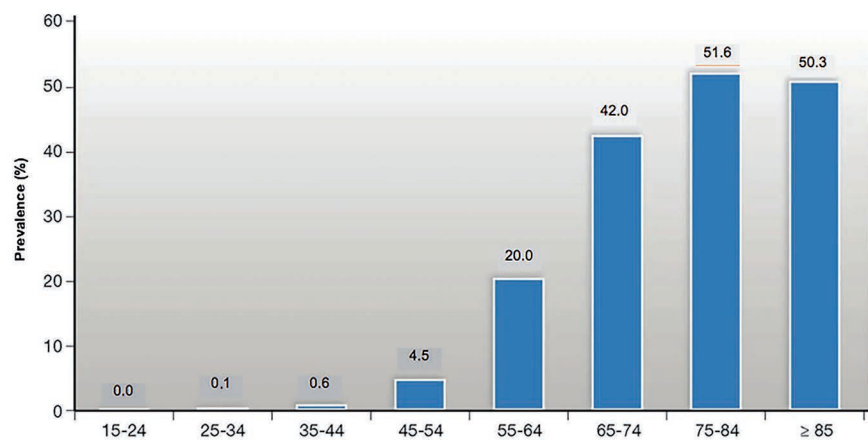


Figure 3. Prevalence of benign prostatic hypertrophy in Italy according to age range for 2005 and 2013 (Source: VIII Report Health Search, SIMG 2013/2014).⁵

simple questions, the symptoms and discomfort experienced by patients with LUTS/BPH, regardless of whether they are being treated.

The questions concern nycturia, urinary urge and tenesm/dysuria (Table 4). The questions concerning nycturia and urgency were chosen because they represent the most prevalent symptoms and those with the greatest impact on QoL, being perceived as *extremely uncomfortable and upsetting*.¹⁰⁻¹³

The question concerning tenesm/dysuria was chosen because these disorders are predictive of acute urinary retention and a clinical risk of surgery.^{14,15}

The QPT can be used both in patients not on pharmacological treatment and as a therapy monitoring instrument.

The QPT is an *opportunistic* test because it makes it possible to suspect the condition during an appointment which the patient may have come to for other reasons, as it immediately makes it possible to evaluate the need for more in-depth diagnostic investigations.

A positive response to one of the questions is sufficient for requesting a more in-depth investigation, which may provide indications on the therapeutic strategy to be taken.

Impact of lower urinary tract symptoms, with or without benign prostatic hypertrophy, on the quality of life

One study conducted in 2009 evaluated the effects of LUTS on quality of life measured as *urinary-specific health-related quality*.¹⁶ It evaluated 30,000 subjects from the United States, United Kingdom and Sweden and found that

35% of subjects met the criteria for a clinical state of anxiety and 29.8% for a clinical state of depression. Nycturia, urgency, incomplete voiding and physical pain were found to be risk factors for anxiety, whereas urination frequency and incomplete voiding were found to be risk factors for depression.

The economic impact of benign prostatic hypertrophy-related lower urinary tract symptoms

As far as the cost of the condition is concerned, in the US, the overall cost for the diagnosis and treatment of BPH has been estimated at approximately 1.1 billion

US\$/year, compared to total annual expenditure for urological conditions of some 9 billion.¹⁷ This cost continues to increase for the reasons mentioned previously. In 2000, it was estimated that for every 100,000 patients, almost 15,000 appointments took place for BPH compared to 10,000 for every 100,000 patients in 1994.¹⁸

In Italy, as already described for the United States, the economic impact of BPH is significant and will continue to increase in the years to come, due to the ageing of the population. In 2050, it is anticipated that there will be a 50% increase in the over-65 population compared to 2000: the Italian National Institute of Statistics (ISTAT) estimates that the over-sixty-fives will increase from 4 million in 2000 to approximately 8 million in 2050.

Expenditure during the first 9 months of

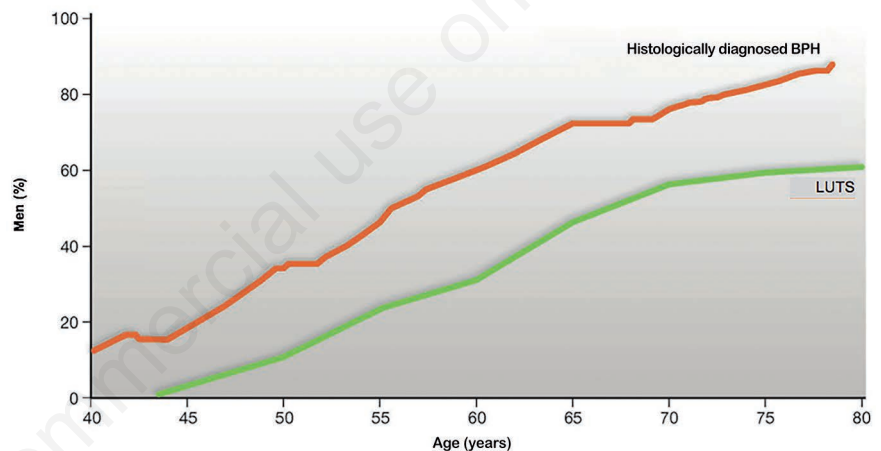


Figure 4. The incidence of histologically diagnosed benign prostatic hypertrophy (BPH) and lower urinary tract symptoms (LUTS) gradually increase with age.

Table 2. International prostatic symptoms score (IPSS) questionnaire and quality of life index.

In the last month:	Score:	Never	<1 in 5 times	<half the time	About half the time	More than half the time	Almost always
		0	1	2	3	4	5
1		How many times have you felt incomplete bladder voiding after urinating?					
2		How many times have you urinated less than 2 h after the previous time?					
3		Have you ever had to split urination?					
4		How often do you have difficulties putting off urination?					
5		How often has the urinary stream seemed weak?					
6		Have you had to strain to start urinating?					
7		How many times have you got up to urinate during the night?					
Total score		0-7 Mild symptoms 3-19 Moderate symptoms 20-36 Severe symptoms					
8		If you had to spend the rest of your life with your current urinary condition how would you feel?					
		Good	Satisfied	Quite satisfied	So-so	Relatively satisfied	Bad
		0	1	2	3	4	5
							Very bad
							6

Table 3. International index of erectile function questionnaire (IIEF-5).

1	How confident are you that you can obtain and maintain an erection?	<input type="checkbox"/> 0 I am not currently sexually active
		<input type="checkbox"/> 1 Very low
		<input type="checkbox"/> 2 Low
		<input type="checkbox"/> 3 Moderate
		<input type="checkbox"/> 4 High
		<input type="checkbox"/> 5 Very high
2	When you have had erections with sexual stimulation, how often were they hard enough to permit penetration?	<input type="checkbox"/> 0 I am not currently sexually active
		<input type="checkbox"/> 1 Never or almost never
		<input type="checkbox"/> 2 A few times (less than half)
		<input type="checkbox"/> 3 Sometimes (about half)
		<input type="checkbox"/> 4 Most times (more than half)
		<input type="checkbox"/> 5 Always or almost always
3	During sexual intercourse, how often are you able to keep an erection after penetration?	<input type="checkbox"/> 0 I am not currently sexually active
		<input type="checkbox"/> 1 Never or almost never
		<input type="checkbox"/> 2 A few times (less than half)
		<input type="checkbox"/> 3 Sometimes (about half)
		<input type="checkbox"/> 4 Most times (more than half)
		<input type="checkbox"/> 5 Always or almost always
4	During sex, how difficult was it to keep the erection until the end of intercourse?	<input type="checkbox"/> 0 I am not currently sexually active
		<input type="checkbox"/> 1 Extremely difficult
		<input type="checkbox"/> 2 Very difficult
		<input type="checkbox"/> 3 Difficult
		<input type="checkbox"/> 4 A little bit difficult
		<input type="checkbox"/> 5 Not at all difficult
5	When you attempted to have sex, how often was it satisfactory for you?	<input type="checkbox"/> 0 I am not currently sexually active
		<input type="checkbox"/> 1 Never or almost never
		<input type="checkbox"/> 2 A few times (less than half)
		<input type="checkbox"/> 3 Sometimes (about half)
		<input type="checkbox"/> 4 Most times (more than half)
		<input type="checkbox"/> 5 Always or almost always
Total score _____		Good sexual potency ≥ 22

Table 4. Quick prostate test.

1	Over the last month have you got up at least twice at night to urinate, between the time you go to bed in the evening and when you get up in the morning? (Nycturia)	Yes No
2	Over the last month have you experienced difficulties holding urine during the day on a number of occasions? (Urgency)	Yes No
3	Over the past month have you ever had the feeling that you were unable to completely empty your bladder? (Dysuria)	Yes No

2010 for class A medicinal products for the genital/urinary system accounted for 3.2% of total spending on all categories of medicines, *i.e.*, 311.5 million euros.

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