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Do Alpha-Blockers Prevent the Occurrence of Acute Urinary Retention?

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Key Words

Alfuzosin · Postvoid residual urine · Acute urinary retention · BPH

Abstract

Acute urinary retention (AUR) is a common complication of benign prostatic hyperplasia (BPH) and the incidence varies widely from 0.4 to 25% per year in men seen in urology practices. It has been estimated that AUR is the indication for surgery in around 25–30% of patients undergoing transurethral resection of the prostate (TURP) and that emergency TURP for AUR is associated with greater morbidity than elective TURP. Risk factors for AUR include lower urinary tract symptoms (LUTS), depressed peak urinary flow rate, enlarged prostate, high postvoid residual (PVR) urine and old age. Alfuzosin has been shown to significantly increase maximum flow rate and relieve bladder outlet obstruction, resulting in a reduction in PVR urine. A pooled analysis of 11 placebo-controlled studies involving 1,470 patients with LUTS suggestive of BPH indicates that significantly greater improvements were observed in patients treated with alfuzosin than with placebo. A 6-month placebo controlled study of 518 patients reported a 0.4% incidence of AUR in the alfuzosin group compared with a 2.4% incidence with placebo (p = 0.04). These positive effects on PVR could be related to the reduction in incidence of AUR seen in alfuzosin-treated patients.

Introduction

Benign prostatic hyperplasia (BPH) is a common condition among older men [1], resulting in chronic lower urinary tract symptoms (LUTS) that are bothersome, impaired physiological and functional well-being and interference with activities of daily living [2–4]. BPH is rarely life-threatening, but it can contribute to more acute urological complications, particularly acute urinary retention (AUR), often considered to be the most serious complication of BPH. Other complications associated with the disease include: recurrent urinary tract infections, upper tract dilatation, bladder stone formation and recurrent haematuria. AUR is a relatively common complication and refers to the sudden inability to pass urine. It is a painful and distressing condition that is associated with a significant morbidity. Treatment involves emergency hospitalisation, catheterisation and surgery. It has been estimated that AUR is the indication for surgery in around 25–30% of patients undergoing transurethral resection of the prostate (TURP) [3, 5]. Several studies suggest that surgery for BPH carried out as an emergency for

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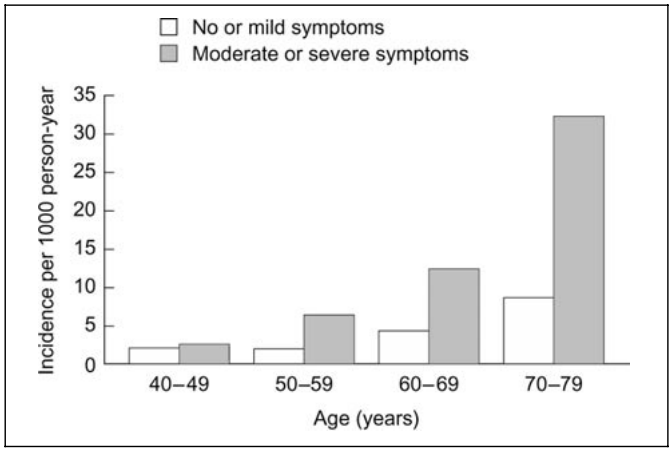

Fig. 1. The incidence of acute urinary retention (AUR) with regard to age and symptom severity [10].

AUR carries greater morbidity than elective TURP [6, 7]. A study of 1,052 men with AUR undergoing TURP showed that overall rate of postoperative complications was 24% compared with 15.7% in 2,833 men without retention [5]. Among patients with and without retention, the postoperative infection rate was 4.3 and 1.5%, respectively, while the failure to void was 11 and 3.6%, respectively, and the incidence of hypotonic bladder was 8.4 and 1.7%, respectively; the difference between each complication and the overall complication rate was significant ($p \leq 0.001$) [5].

The incidence of AUR varies widely, from 0.4 to 25% per year in men seen in urology practices [8, 9]. The community-based Olmsted County Study demonstrated an AUR rate of 0.7% [10].

Risk Factors for AUR

Jacobsen et al. [10] reported on the risk factors associated with AUR in the Olmsted County Study of 2,115 men. A direct relationship was found between the risk of developing retention and LUTS, depressed peak urinary flow rate, enlarged prostate and old age. Among men with moderate to mild symptoms at baseline, the incidence was three-fold higher than in men with no to mild symptoms. For prostate volumes greater than 30 ml, the risk of AUR also increased three-fold. Men with depressed peak urinary flow rate (<12 ml/s) were at four-fold greater risk of AUR than men with urinary flow rates >12 ml/s. In addition, a 10-fold increase in AUR was recorded between men aged 40–49 years and those aged 70–79 years. Indeed, this study predicted that a 60-year-old man has a 23% probability of experiencing an episode of AUR if he survives an additional 20 years (fig. 1). Further reports from the Olmsted Study show that men with high post-void residual (PVR) urine were three times as likely to have a subsequent AUR [11].

Meigs and co-workers [12] reported similar findings in their study of 8,418 men followed for 3 years (1992–95) in the US. They also showed that men with a clinical diagnosis of BPH and a symptom score (American Urological Association [AUA] symptom index) of 8 or greater had the greatest incidence of AUR (age-adjusted incidence 13.7/1,000 person years). However, the sensation of incomplete bladder emptying, having to void again after less than 2 h and a weak urinary stream were the best independent symptom predictors for AUR.

PVR

The International Continence Society defines PVR as the volume of fluid remaining in the bladder immediately following completion of micturition [13]. In most healthy men with normal function, PVR is too small (mean value less then 1 ml) to be measured by conventional techniques [14]. Consistent with these figures, a PVR over 50–100 ml is commonly taken to be abnormally elevated. Very large PVR (> 300 ml) may be associated with upper tract dilation and renal function impairment, particularly if there is elevated detrusor pressure [15–17].

PVR can be measured in a variety of ways, including: (1) by catheter or cystoscope; (2) by nuclear medicine techniques, and (3) by ultrasonography.

Measurement using transabdominal ultrasonography, a simple, non-invasive technique, is recommended by the International Consultation on BPH [18]. This relatively inexpensive technique can provide sufficiently accurate results. The time interval between voiding and the estimation of PVR should be recorded and should be as short as possible to avoid increases due to natural urine production. Another option is to record PVR as a percentage of bladder capacity, so providing an approximation of voiding efficiency [19]. In clinical practice, PVR can be variable regardless of measurement technique [20, 21]. In particular diurnal variation can occur, with volumes in the elderly being 40% larger in the early morning. Due to the large variability of this parameter, an isolated finding of abnormal PVR always needs to be confirmed by additional measurements.

Two forms of incomplete bladder emptying have been described [22, 23]. In the first form, PVR is associated with a high intravesical pressure (>30 cm H_2O), which is commonly observed in bladder outlet obstruction or in the case of uncoordinated detrusor and sphincter mechanism. In this type of PVR, high pressure retention may exert back pressure on the upper urinary tract and is responsible for hydronephrosis and renal function impairment. It is generally considered that the primary cause of elevated PVR in BPH is urethral obstruction, although up to 31% of obstructed patients have a PVR of <50 ml [24, 25]. However, as PVR is often found in both men and women without urethral obstruction or BPH [26], it is likely that urethral obstruction is a contributory factor rather than the primary cause. In the second form, PVR is associated with a low intravesical pressure (<20 cm H_2O), which is related to detrusor underactivity or the failure to sustain an initially adequate detrusor contraction [24, 27].

There is no evidence for a correlation between PVR or its amount and the severity and duration of outlet obstruction [28]. In addition, the absence of PVR does not rule out the severest obstruction. The presence of PVR is associated with a decreased functional bladder capacity, which may be responsible for storage symptoms, although no correlation between LUTS and PVR has been reported. In addition, PVR may predispose the individual to more serious complications of BPH, such as AUR.

Alpha Blockers and PVR

Increased tone of the smooth muscle, the bladder neck and the urethra represent the dynamic component of BPH and also contribute to the pathological state associated with the condition, such as difficulty in urination and incontinence. Sympathetic innervation of the smooth muscle of the prostate, bladder neck and urethra is primarily mediated by α_1 adrenoceptors [29]. By decreasing the tone of the smooth muscle in these areas, α_1 blockers can improve the irritative and obstructive symptoms of BPH [30, 31]. It has also been suggested that α-blockade at the prostatic level may have a direct impact on detrusor activity. Increased tension within the prostate created by contraction of its capsular and stromal muscle triggers afferent (sensory) discharge, which may influence spinal reflexes controlling the activity of vesico-urethral muscularis. There is clinical evidence that this afferent discharge leads to a decreased inhibition (i.e. increased activity) of the detrusor, manifested by storage symptoms (frequency, nocturia and urgency) [28].

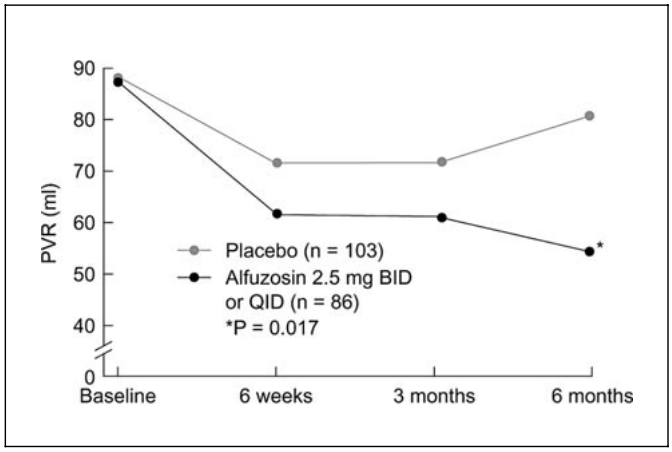

Fig. 2. Changes in postvoid residual (PVR) urine volume in patients treated with alfuzosin or placebo. Reproduced with permission from ref. 33.

Alfuzosin and PVR

Alfuzosin, a selective α_1-adrenoceptor antagonist, has been shown to affect a number of urodynamic parameters. Significant increases in maximum flow (+29%) have been reported as well as a decrease in detrusor pressure at maximum flow (–30.2%), detrusor opening pressure (–39.4%) and maximum detrusor pressure (–28.7%) [32]. It was suggested that alfuzosin did not appear to act directly on the detrusor, but its pharmcological effect on the bladder neck caused lower detrusor pressure to micturition. This decreased detrusor pressure leads to only minor strain to induce and maintain flow and helps to preserve the detrusor muscle.

The relief of bladder outlet obstruction observed with alfuzosin should theoretically be associated with a beneficial effect on PVR. Indeed, this has been demonstrated, despite the large variability in PVR, in patients with LUTS suggestive of BPH. A study by Jardin and co-workers [33] on the effect of alfuzosin on PVR was conducted in patients with BPH. This 6-month, placebo-controlled study indicated that alfuzosin, 7.5–10.0 mg/day, significantly reduced PVR compared with placebo. Mean (SD) PVR in 86 patients treated with alfuzosin decreased from 80.1 (8.34) to 49.3 (6.1) ml at week 26 compared with a mean decrease in the placebo group from 87.8 (7.1) to 79.5 (10.7) ml (p = 0.017) (fig. 2).

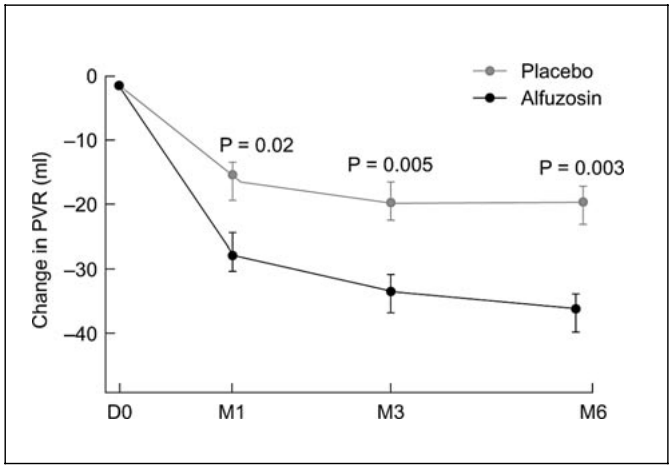

Fig. 3. Effect of alfuzosin on postvoid residual (PVR) urine: pooled analysis of 11 studies [34]. Mean ± SEM values shown.

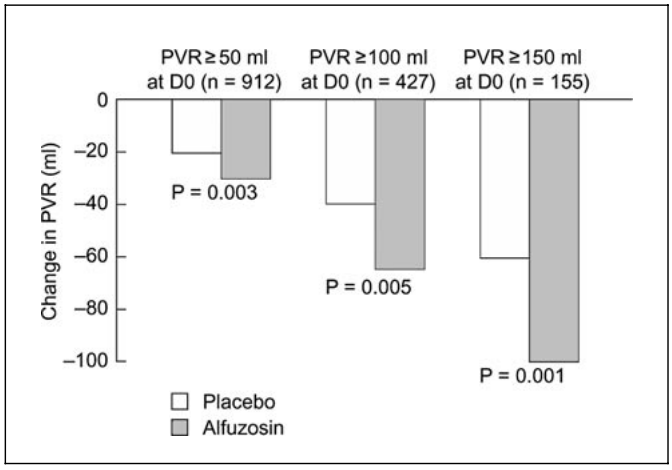

Fig. 4. Mean change in postvoid residual (PVR) urine with 6 months of treatment with alfuzosin according to baseline PVR [34].

Table 1. Baseline patient characteristics from pooled analysis of 11 placebo-controlled trials on alfuzosin (n = 1,470) [34]

Parameter	Value
Mean age, years	64.5 ± 7.4
Mean duration of symptoms, months	39.5 ± 34.0
Mean Boyarsky total score	9.5 ± 2.6
Mean Qmax, ml/s	9.8 ± 4.0
Mean PVR, ml	106.1 ± 54.5
Patients (%) with baseline PVR	
≥ 100 ml	722 (49%)
≥ 150 ml	283 (19%)

PVR = Postvoid residual.

Pooled Analysis

A pooled analysis of 11 double-blind European studies performed with an immediate release formulation of alfuzosin and involving 1,470 patients with LUTS suggestive of BPH and PVR between 50 and 350 ml has been conducted [34]. The analysis aimed to estimate the relationship between PVR and clinical parameters such as age, maximum flow rate, voided volume or prostate-specific antigen (PSA). PVR was measured using transabdominal ultrasound. A total of 607 patients received alfuzosin (2.5 mg t.i.d., n = 267; 5 mg b.i.d., n = 340) and 346 received placebo for 1–6 months. The effect of treatment on PVR was also measured.

In order to take into account various study durations, treatment effect was assessed at three end-points (1, 3 and 6 months) on an intent to treat basis. Treatments were compared at each end-point using a one-way analysis of covariance (treatment) with a fixed-effect model taking as covariate the PVR at D0.

Baseline patient characteristics are shown in table 1. Percentages of patients with a PVR of at least 100 or 150 ml were 49 and 19%, respectively. These percentages were not influenced by patient age, maximum flow rate, voided volume or PSA, although greater percentages were observed in patients likely to be obstructed at baseline (Qmax < 8 ml/s) (table 2).

Regardless of end-point (1, 3 or 6 months), significantly greater improvements in PVR were observed in patients treated with alfuzosin compared with placebo (fig. 3). Changes in PVR with alfuzosin were greater in patients with higher baseline PVRs (fig. 4).

Alfuzosin and AUR

In a 6-month placebo-controlled study involving 518 patients, alfuzosin was associated with a significantly lower incidence of AUR than placebo (0.4 vs. 2.4%, respectively (p = 0.04) [33]. These results were confirmed in a 3-year open study of 3,228 patients in general practice, in which the incidence of AUR in alfuzosin-treated patients was only 0.3% [35] compared with 2.3% in patients managed by watchful waiting [36]. Further evidence comes

Table 2. Relationship between baseline PVR urine and age, maximum flow rate, voided volume and prostate-specific antigen (PSA) [34]

Parameter	Patients	Mean ± SD baseline PVR	Patients with PVR ≥ 100 ml	Patients with PVR ≥ 150 ml
Age, years				
<60	377	104 ± 54	47%	17%
60–65	345	104 ± 58	47%	18%
65–70	377	111 ± 57	51%	23%
≥ 70	370	105 ± 50	52%	19%
Baseline Qmax, ml/s				
<8	406	113 ± 53	60%	22%
8–11	477	106 ± 56	47%	19%
≥ 11	448	98 ± 53	39%	15%
Voided volume, ml				
<200	492	104 ± 52	49%	18%
200–300	476	103 ± 53	45%	17%
≥ 300	368	112 ± 59	50%	23%
PSA, ng/ml				
<1.4	191	110 ± 65	45%	19%
1.4–4.0	353	105 ± 49	49%	16%
≥ 4.0	313	104 ± 51	45%	17%

PVR = Postvoid residual.

from the pooled analysis discussed above, in which fewer patients in the alfuzosin group experienced AUR compared with placebo: 2 (0.3%) vs. 5 (1.4%) [34].

The lower incidence of AUR observed with alfuzosin may be attributed to its positive impact on PVR. Prospective studies are needed to confirm this finding and to examine the use of α_1 blockers in the long-term management of BPH and the prevention of the major complication of the disease – AUR.

Conclusion

Alfuzosin appears to be the first α_1 blocker to have clearly demonstrated a positive impact on PVR measured by transabdominal ultrasonography. The beneficial effect of alfuzosin could be related to the direct relief of bladder outlet obstruction, as demonstrated by pressure-flow studies. This beneficial effect of alfuzosin on PVR could well translate into the positive effects seen in reducing the incidence of AUR and the need for surgery.

References

1 Meigs JB, Barry MJ: The natural history of benign prostatic hyperplasia; in Kirby RS, McConnell JD, Fitzpatrick JM, Roehrborn CG, Boyle P (eds): Textbook of Benign Prostatic Hyperplasia. Oxford, ISIS Medical Media Ltd, 1997, pp 125–135.

2 Girman CJ, Epstein RS, Jacobsen SJ, Guess HA, Pauser LA, Oesterling JE, Lister MM: Natural history of prostatism: Impact of urinary symptoms on quality of life in 2115 randomly-selected community men. Urology 1994;44:825.

3 Fowler FJ, Wennberg JE, Timothy RP, Barry MJ, Mullet AG, Hanley D: Symptom status and quality of life following prostatectomy. JAMA 1988;259:3018–3022.

4 Roberts RO, Jacobsen SJ, Rhodes T, Girman CJ, Guess HA, Lieber MM: Natural history of prostatism: Impaired health states in men with lower urinary tract symptoms. J Urol 1997; 157:1711–1717.

5 Mebust WK, Holtgrewe HL, Cockett ATK, Peters PC, and the Writing Committee: Transurethral prostatectomy: Immediate and postoperative complications. A Cooperative Study of 13 participating institutions evaluating 3,885 patients. J Urol 1989;141:243–247.

6 Higgins PM, French ME, Chadalavada VS: Management of acute retention of urine: A reappraisal. Br J Urol 1991;67:365–368.

7 Malone PR, Cook A, Edmonson R, et al: Prostatectomy: Patients' perception and long-term follow-up. Br J Urol 1988;61:234–238.

8 Ball AJ, Feneley RC, Abrams PH: The natural history of untreated 'prostatism'. Br J Urol 1981;53:613–616.

9 Barry MJ, Fowler FJ, Bin L, Pitts JC, Harris CJ, Mulley AG: The natural history of patients with benign prostatic hyperplasia as diagnosed by North American Urologists. J Urol 1997; 157:10–15.

10 Jacobsen SJ, Jacobsen DJ, Girman CJ, et al: Natural history of prostatism: Risk factors for acute urinary retention. J Urol 1997;158:481–487.
11 Kohlman C, Girman C, Jacobsen SJ, Guess HA, Lieber MM: Post-void residual urine volume in randomly selected community men in Olmsted County. J Urol 1998;159(suppl 5): 139.
12 Meigs JB, Barry MJ, Giovannucci E, Rimm EB, Stampfer MJ, Kawachi I: Incidence rates and risk factors for acute urinary retention: The Health Professionals Followup Study. J Urol 1999;162:376–382.
13 ICS: Standardisation of terminology of lower urinary tract function. Neurourol Urodyn 1988;7:403–426.
14 Rosier PFWM, de Wildt MJAM, de la Rosette JJMCH, Debruyne FMJ, Wijkstra H: Residual urine volume in normal male subjects. J Urol 1995;97:641–645.
15 Abrams PH, Dunn M, George NJR: Urodynamic findings in chronic retention or urine and their relevance to results of surgery. Br Med J 1979;2:1258–1260.
16 George NJR, O'Reilly PH, Barnard RJ, Blacklock NJ: High pressure chronic retention. Br Med J 1983;286:1780–1783.
17 Koch WFRM, El Din KE, de Wildt MJAM, Debruyne FMJ, de la Rosette JJMCH: The outcome of renal ultrasound in the assessment of 556 consecutive patients with benign prostatic hyperplasia. J Urol 1996;155:186–189.
18 Abrams P, Griffiths D, Buzelin JM, et al: The urodynamic assessment of lower urinary tract symptoms; in Denis L, Griffiths K, Khoury S, Cockett ATK, McConnell J, Chatelain C, Murphy G, Yoshida O (eds): 4th International Consultation on Benign Prostatic Hyperplasia (BPH), Paris, July 2–5 1997, pp 325–377.
19 Rosier PFWM, de Wildt MJAM, de la Rosette JJMCH, Debruyne FMJ, Wijkstra H: Analysis of maximum detrusor contraction power in relation to bladder emptying in patients with lower urinary tract symptoms and benign prostatic enlargement. J Urol 1995;154:2137–2142.
20 Bruskewitz RC, Iversen P, Madsen PO: Value of postvoid residual urine determination in evaluation of prostatism. Urology 1982;20: 602–604
21 Birch NC, Hurts G, Doyle PT: Serial residual urine volumes in men with prostatic hypertrophy. Br J Urol 1988;62:571–575.
22 Mitchell JP: Management of chronic urinary retention. Br Med J 1984;289:515–516.
23 Jones DA, George JR: Interactive obstructive uropathy in man. Br J Urol 1992;69:337–345.
24 Turner Warwick RT, Whiteside CG, Arnold EP, et al: A urodynamic view of the prostatic obstruction and the results of prostatectomy. Br J Urol 1973;45:631–645.
25 Griffiths HJ, Castro J: An evaluation of the importance of residual urine. Br J Radiol 1970; 43:409–413.
26 Griffiths DJ, McCracken PN, Harrison GM, Gormley EA: Characteristics of urinary incontinence in elderly patients studied by 24-hour monitoring and urodynamic testing. Age Ageing 1992;21:195–201.
27 Abram P, Griffiths DJ: The assessment of prostatic obstruction from urodynamic measurements and from residual urine. Br J Urol 1979; 51:129–134.
28 Elbadawi A: Voiding dysfunction in benign prostatic hyperplasia: Trends, controversies and recent revelations. Urology 1998;51(suppl 5A):62–82.
29 Cockett ATK, Khoury S, Aso Y, et al: Proceedings of the 3rd International Consultation on Benign Prostatic Hyperplasia. Channel Islands, Scientific Communications International Ltd., 1995, pp 1–651.
30 Caine M, Pfau A, Perlberg S: The use of alpha-adrenergic blockers in benign prostatic obstruction. Urology 1982;20:524–527.
31 Perlberg S, Caine M: Adrenergic response of bladder muscle in prostatic obstruction: Its relation to detrusor instability. Urology 1982;20: 524–527.
32 Martorana G, Giberti C, Di Silverio F, et al: Effects of short-term treatment with the α_1-blocker alfuzosin on urodynamic pressure/flow parameters in patients with benign prostatic hyperplasia. Eur Urol 1997;32:47–53.
33 Jardin A, Bensadoun H, Delauche-Cavallier MC, Attali P, and the BPH-ALF Group: Alfuzosin for treatment of benign prostatic hypertrophy. Lancet 1991;337:1457–1461.
34 McNeill SA, Hargreave TB, Geffriaud-Ricouard C, Santoni J-P, Roehrborn CG: Postvoid residual urine in patients with LUTS suggestive of BPH: Pooled analysis of 11 controlled studies with alfuzosin. Urology 2001 (in press).
35 Lukacs B, Grange JC, Comet D, McCarthy C, and the BPH Group in General Practice: Three-year prospective study of 3228 clinical BPH patients treated with alfuzosin in general practice. Prostate cancer and prostate diseases 1998;5:276–293.
36 Jacobsen SJ, Guess HA, Panser L, et al: A population based study of health care seeking behavior for treatment of urinary syptoms – The Olmsted County Study of Urinary Symptoms and Health Status among Men. Arch Fam Med 1993;2:729–735.