Dutasteride vs Finasteride: Assessment of Differences in Acute Urinary Retention Rates and Surgical Risk Outcomes in an Elderly Population Aged ≥65 Years

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Abstract

Objective: To determine comparative differences on rates of acute urinary retention (AUR) and prostate-related surgeries among patients aged ≥65 years treated with dutasteride or finasteride.

Methods: For this retrospective analysis, medical/pharmacy claims data from July 1, 2003, to June 30, 2006, were analyzed for enlarged prostate patients aged ≥65 years treated with 5-alpha reductase inhibitors (5ARIs) regardless of alpha-blocker use. Charlson Comorbidity Index, Thomson Medstat Disease Staging, and propensity score matching techniques were used for comparative analysis.

Results: A total of 5090 patients met selection criteria. After 1 year of 5ARI therapy, the AUR rate was lower for dutasteride (12%) when compared with finasteride (14.7%) (odds ratio [OR], 0.79; $P = .0042$). Risks for prostate-related surgeries were also lower among dutasteride-treated patients (3.9% vs 5.1%, respectively; OR, 0.77; $P = .03$).

Conclusion: Important therapeutic outcome differences exist between dutasteride and finasteride. Patients treated with dutasteride were significantly less likely to experience AUR and prostate-related surgeries than finasteride patients.

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For author information and disclosures, see end of text.

Enlarged prostate (EP) is a progressive disorder that affects more than 50% of men aged ≥50 years and affects close to 90% of men by the time they reach 80 years of age.[1] EP is considered the fourth most commonly diagnosed dysfunction in older men, accounting for 4.5 million outpatient visits and $1.1 billion in total annual direct medical services exclusive of outpatient pharmacotherapy costs.[2] The clinical and economic burden of this disease is expected to become even more dramatic because the population of men aged ≥64 years is projected to expand to approximately 9.3 million by 2020.[3]

Also referred to as benign prostatic hyperplasia (BPH), EP typically manifests itself with nonspecific lower urinary tract symptoms such as urination hesitancy, decreased urination stream, or feelings of inadequate voiding. Over time, this gradual disease progression can result in acute urinary retention (AUR) and lead to other complications requiring invasive surgical interventions. Historically, medical management of this disease has been primarily targeted to symptomatic relief using alpha-blockers.[1,4] With increased awareness and new therapeutic advances, great interest has been placed on the role and use of disease-modifying agents such as the 5-alpha reductase inhibitors (5ARIs) in reducing prostatic growth.

As a class, 5ARIs work by decreasing the size of the prostate and blocking the activity of 5-alpha reductase enzymes in converting testosterone to dihydrotestosterone (DHT), the primary hormone responsible for the development and enlargement of the prostate gland.[5] There are currently only two 5ARI agents available in the US market, dutasteride and finasteride. Unlike alpha-blockers, these agents have been shown to reduce prostate volume by approximately 20% to 26%, with long-term use resulting in symptomatic improvements and risk reductions for AUR and prostate surgery.[6,7] The clinical benefits of 5ARIs are generally apparent after 6 to 12 months of therapy.[7] Pharmacologically, each drug has a distinct mechanism of action. Dutasteride possesses a dual-enzyme inhibition mechanism (type 1 and type 2 isoenzymes) and has been shown to suppress more than 90% of DHT production. In contrast, finasteride is a single-enzyme inhibitor (type 2 isoenzyme) and only produces partial inhibition of the enzyme responsible for DHT production. Additionally, dutasteride has a much

longer half-life when compared with finasteride (5 weeks vs 5-6 hours).[8-11]

The therapeutic differences between dutasteride and finasteride have not been fully explored. However, there is growing evidence to suggest that the advantages of dual inhibition may indeed translate to better clinical outcomes. Dutasteride-treated patients displayed greater improvements in the American Urological Association Symptom Index (AUA-SI) score when compared with finasteride (6.1 vs 3.3) while showing faster clinical improvement (within 3 months) after initiation of therapy.[12] In a large retrospective assessment examining the rates of AUR and prostate-related surgery among men aged ≥50 years, dutasteride-treated patients had significantly less AUR compared with finasteride (5.3% vs 8.3%; $P = .0207$) and were 49.1% less likely to experience an AUR event. Although patients receiving dutasteride exhibited a trend toward fewer prostate surgeries, differences were not significant ($P = .0745$).[13]

Differentiating between the two 5ARIs is important to the medical community in support of optimal outcomes for individual EP patients and cost-effective decision-making for health plans facing rapid growth in their Medicare membership. In fact, elderly men suffer from higher rates of AUR and prostate surgery.[1] As such, the purpose of this study was to examine the rates of AUR and EP-related surgery after treatment initiation of dutasteride or finasteride in men aged ≥65 years.

Table 1. Inclusion and Exclusion *ICD-9-CM* Codes

Inclusion *ICD-9-CM* Codes	
Benign prostatic hypertrophy	222.2, 600
Exclusion *ICD-9-CM* Codes	
Prostate cancer	185, 198.82, 233.4, 236.5, 239.5, V10.46
Bladder cancer	188, 198.1, 223.3, 233.7, 236.7, 239.4, V10.51

ICD-9-CM indicates *International Classification of Diseases, Ninth Revision, Clinical Modification.*

Table 2. *ICD-9-CM* or *CPT-4* Codes for Acute Urinary Retention and Prostate-related Surgeries

Outcomes of Interest	*CPT-4* or *ICD-9-CM* Codes
Transurethral incision of prostate	52450
Transurethral electrosurgical resection of the prostate	52601
Transurethral resection of the prostate	52612, 52614, 52620, 52640
Laser coagulation	52647
Laser vaporization	52648
Prostatectomy	55801, 55821, 55831
Transurethral microwave thermotherapy	53850
Transurethral needle ablation	53852
Transurethral water-induced thermotherapy	53853
Acute urinary retention*	599.6, 788.2 (excluding 788.21)

ICD-9-CM indicates *International Classification of Diseases, Ninth Revision, Clinical Modification; CPT-4, Current Procedural Terminology 4.*
* *ICD-9-CM* codes were used to identify this outcome.

Methods

Medical and pharmacy administrative claims data from patients treated with either dutasteride or finasteride for EP were collected from the Ingenix Lab/Rx database over a 3-year period between July 1, 2003, and June 30, 2006. This database provides de-identified information on medical and pharmacy claims from more than 30 million lives, with up to 10 years of historical data. Analysis of data included inpatient and outpatient diagnoses as determined by *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes[14] and procedures as determined by *Current Procedural Terminology 4 (CPT-4)* formats, as well as prescription records. Dates of service and both paid and charged amounts were available for all services rendered.

Patients were included in the study if they were men, aged ≥65 years, diagnosed with EP, and treated with either dutasteride 0.5 mg/day or finasteride 5 mg/day. Patients were included regardless of previous and/or concurrent alpha-blocker use. Patients were excluded if they were diagnosed with bladder or prostate cancer, receiving nontherapeutic dosages indicative of treatment of male pattern baldness, or used both 5ARIs during the assessment period. Table 1 lists all relevant inclusion and exclusion *ICD-9-CM* codes.

Assessment of AUR and Surgery

The likelihood of experiencing AUR or prostate-related surgery was assessed over a 1-year period among patients identified in the study. Patients with AUR occurring within 15 days of starting therapy were excluded from the analysis to avoid confounding variables related to insufficient treatment duration. Table 2 presents the *ICD-9-CM* and *CPT-4* procedure codes used to identify AUR and prostate-related surgeries.

Table 3. Thomson Medstat Disease Staging Criteria for Enlarged Prostate[17]

Stage	Description	*ICD-9-CM* Codes
1.1	Benign prostatic hypertrophy	222.2, 600.xx
1.2	With urinary tract infection	Stage 1.1 + 599.0
2.1	With bladder outlet obstruction	Stage 1.1 + 593.5, 596.0, 599.6
2.2	With hydronephrosis	Stage 1.1 + 591.xx
3.1	With renal failure	Stage 1.1 + 584.xx, 586.xx
3.2	With sepsis	Stage 1.1 + 038.xx
3.3	With shock	Stage 1.1 + 785.50, 785.59

ICD-9-CM indicates *International Classification of Diseases, Ninth Revision, Clinical Modification.*

Table 4. Baseline Demographics of Study Population

	Finasteride (N = 2545)	Dutasteride (N = 2545)	*P* Value
AB prior, %	46.4	45.7	.63
Pre-AUR,%	20.2	20.9	.51
Age (mean, SD), years	73.3 (6.3)	73.4 (6.4)	.45
CCI (mean, SD)	1.2 (1.9)	1.2 (1.7)	.84
Bladder stones, %	4.6	4.4	.73
Hematuria, %	15.8	15.7	.88
Complicated EP, %	4.6	5.7	.07
Use of urologist care, %	64.3	66.5	.11

AB indicates alpha-blocker; AUR, acute urinary retention; SD, standard deviation; CCI, Charlson Comorbidity Index; EP, enlarged prostate.

Comorbidity Assessment

The Charlson Comorbidity Index (CCI) with the Dartmouth-Manitoba modification was used to assess the comorbidities within the study population.[15,16] The CCI is composed of 19 medical conditions, each assigned with a weight scale ranging from 1 to 6 with a total maximum possible score of 33. Higher scores correlate with greater burdens of comorbidities.[16]

Severity and Sequelae of EP

To determine BPH-related complications before 5ARI therapy, Thomson Medstat Disease Staging coding methods were applied. The Thomson Medstat method is based on electronic screening and identification of a comprehensive map of *ICD-9-CM* diagnosis codes.[17] These proprietary coding criteria have been widely utilized as a classification system for diagnostic categories. It is 1 of 4 systems selected for dissemination with the Healthcare Cost and Utilization Project Nationwide Inpatient Sample (HCUP-NIS).

As defined in the Thomson Medstat system, there are 7 ascending *ICD-9-CM* code criteria used for staging the severity of prostate enlargement (Table 3). Patients initiated on 5ARI treatment in this study were categorized into 1 of the 7 disease severity stages based on these codes. Patients categorized as ≥stage 1.2 were deemed to have complicated EP. Patients with hematuria (*ICD-9-CM* code 599.7) and/or bladder stones (*ICD-9-CM* codes 592.0, 592.1, 592.9, and 594.1) were also identified to capture additional severity risks.

Analysis of Outcomes

To minimize the influence of confounding variables when assessing the correlation between treatment and clinical outcomes, propensity score matching was utilized. The propensity score technique matches patients on the probability of receiving dutasteride or finasteride given the following covariates: age, CCI, use of alpha-blockers, AUR, prior use of urologist care, bladder stones, hematuria, and presence of prostate-related complications. When calculating the probability of receiving dutasteride, patients within each cohort were matched 1:1 within ±0.001 percentage point.

Upon matching, logistic regression analysis was performed to determine the likelihood of AUR and EP-related surgery risks in the study population. The likelihood of AUR/surgery is expressed as an odds ratio. Odds ratios >1 indicate a higher likelihood of occurrence under condition A versus B. Ratios <1 signify a lower likelihood of occurrence under condition A versus B. Lastly, a ratio equal to 1 indicates equivalent likelihood in either condition. All analyses controlled for differences in age, use of urologist care, and the CCI.

All statistical analyses were conducted using SAS version 9.1.3, with an a priori significance level of alpha = 0.05. To characterize the demographics of the study population, univariate analyses of frequencies and means were performed. Chi-square tests were used to compare differences in dichotomous variables, and *t*-tests were used to compare differences in continuous variables as appropriate.

Results

Demographics

A total of 5090 male patients aged ≥65 years met

the inclusion criteria. Baseline demographics between dutasteride- and finasteride-treated patients were comparable (Table 4). Patients had comparatively low levels of morbidity, with a mean CCI score of 1.2. Approximately 95% of the men in this study were classified as stage 1 severity (having EP without bladder outlet obstruction, hydronephrosis, renal failure, sepsis, or shock). The mean age for patients included in the study was approximately 73 years.

Assessment of AUR and Prostate-related Surgery

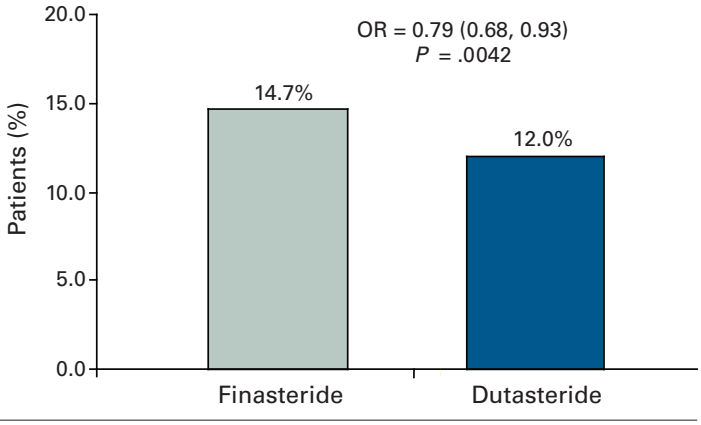
Overall, dutasteride-treated patients experienced lower rates of AUR compared with finasteride-treated patients, at 12% and 14.7% (absolute percentage point reduction, 2.7%), respectively (Figure 1). The risk for prostate-related surgical interventions was also lower for dutasteride compared with finasteride (3.9% vs 5.1%, respectively; absolute percentage point reduction, 1.2%) (Figure 2). After adjusting for background covariates, patients receiving dutasteride were 21% less likely to have AUR (P = .0042) and 23% less likely to have prostate-related surgery (P = .03).

Discussion

Whether dual- or single-isoenzyme mechanistic inhibition or differential half-life among 5ARIs confers different therapeutic outcomes remains the focus of much debate in recent years. It has been postulated that greater DHT suppression would result in greater prostate volume reduction and, hence, a lower risk of disease progression to AUR and EP-related surgery.[18] Although the theoretical clinical advantages of a dual inhibition have not been substantiated, there is a growing body of evidence that indicates better outcomes with dutasteride compared with partial inhibition by finasteride. This study compared the clinical outcomes of these 2 agents within a Medicare-aged population in an attempt to further examine these therapeutic outcome differences.

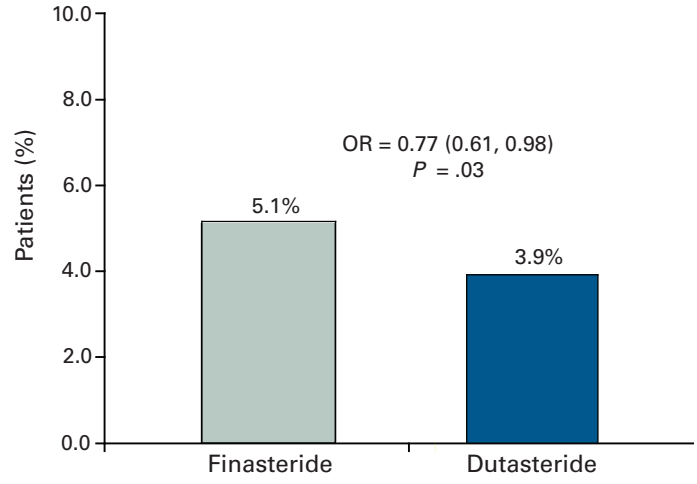
In this study, there was a statistically significant difference in the likelihood of AUR and prostate surgery between dutasteride and finasteride. Dutasteride-treated patients had lower rates of AUR and prostate-related surgeries when compared with finasteride-treated patients. These results support previously published studies demonstrating the clinical benefits of dutasteride in terms of faster symptom relief, greater suppression of DHT, lower risks for AUR, and a trend toward lower prostate-surgery rates.[8,12,13] In a younger population, Issa et al likewise found that dutasteride-treated patients were significantly less likely to experience AUR (P = .027) and showed a trend for lower prostate-related surgeries than finasteride-treated patients.[13] The absolute percentage difference in the Issa analysis resulted in 4.6 (AUR) and 1.0 (surgery) percentage points lower with dutasteride than finasteride, respectively. Compared with our study, the magnitude of difference between dutasteride and finasteride was similar and calculated to be 2.7 (AUR) and 1.2 (surgery) absolute percentage points lower,

Figure 1. Incidence of Acute Urinary Retention Among Enlarged Prostate Patients ≥65 Years of Age (1-Year Adjusted)



OR indicates odds ratio.

Figure 2. Incidence of Enlarged Prostate-related Surgical Events Among Patients Aged ≥65 Years (1-Year Adjusted)



OR indicates odds ratio.

although the overall rates of AUR and surgery varied. These variations in rates are most likely the result of differences in age, geographic distribution, and study methodology (eg, timing, selection criteria). Regardless of these differences, the absolute differences between dutasteride and finasteride in terms of AUR and surgery were consistent across the 2 independent assessments.

The results of this study confer the potential clinical advantages of dutasteride therapy. With the lower rates of disease progression, measured by the presence of AUR and prostate-related surgery, this study underscores the need to consider clinical outcomes as the major driver of value within this therapeutic class. Managed care decision makers, who have a substantial elderly population, may be faced with formulary access considerations regarding the 5ARI class, particularly given that finasteride is generically available. However, with 40% to 70% of the costs of medical care for EP attributable to inpatient hospitalizations arising from AUR and surgery,[19,20] it is incumbent for decision makers to comprehensively evaluate the economic impact of treatment options in light of differences in pharmacy expenditures. As exemplified in this study and several other recently published articles,[13,20,21] the therapeutic difference between dutasteride and finasteride requires a thorough assessment of this class.

This study has several limitations. First, the nonrandom nature of retrospective studies cannot rule out residual confounding although patients were matched on background covariates. This is particularly true with the absence of important clinical parameters, such as prostate-specific antigen (PSA) and prostate volume values. Additionally, patient adherence was not measured and, thus, is reflective of real-world scenarios. This limitation may, in fact, increase the external validity of this study. Since the data were collected from a managed care organization, caution should be taken when generalizing the results to other populations (eg, publicly funded sectors).

Despite this study's limitations, it provides further evidence of the differences in treatment outcomes between dutasteride and finasteride. When combined with previous literature, this study indicates that the reduction in AUR and prostate-related surgery for dutasteride is consistent across specific populations. The potential impact of these differences may not only translate into better clinical outcomes for patients but also into a lessened financial burden for managed care. With 70% of the EP-related medical care costs due to hospitalizations and physician office visits, the use of dutasteride has been shown to consume significantly less in medical resources and costs by lowering AUR and decreasing surgical risks in contrast with finasteride ($P = .0007$).[20] Future studies should explore the economic impact and cost differences between the 2 products, especially within the Medicare-aged population to further assist medical providers and decision makers regarding the cost benefits of dutasteride.

Conclusion

Patients treated with dutasteride were less likely to have AUR and prostate-related surgery than patients receiving finasteride. Overall, patients treated with dutasteride tended to have fewer EP-related progression events compared with patients treated with finasteride.

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