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Benign Prostatic Obstruction

Management of Lower Urinary Tract Symptoms Related to Benign Prostatic Hyperplasia in Real-life Practice in France: A Comprehensive Population Study

Bertrand Lukacs[a,*,†], *Jean-Nicolas Cornu*[a,b,†], *Mounir Aout*[c], *Natacha Tessier*[c], *Christophe Hodée*[d], *François Haab*[a], *Olivier Cussenot*[a], *Yvon Merlière*[e,f], *Véronique Moysan*[f,g], *Eric Vicaut*[c]

[a] *Department of Urology, Tenon Hospital, Assistance Publique – Hôpitaux de Paris, University Pierre et Marie Curie (UPMC), Paris, France;* [b] *Laboratory of Translational Genomics Division of Cancer, Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA;* [c] *Clinical Research Unit, Lariboisière Fernand Widal Hospital, Assistance Publique – Hôpitaux de Paris, University Denis Diderot, Paris, France;* [d] *Department of Informatics, Assistance Publique – Hôpitaux de Paris, Paris, France;* [e] *Centre de recherche pour l'étude et l'observation des conditions de vie (CREDOC), Paris, France;* [f] *Caisse Nationale de l'Assurance Maladie des Travailleurs Salariés (CNAMTS), Paris, France;* [g] *Caisse Nationale de l'Assurance Maladie des Travailleurs Salariés (CNAMTS), Bordeaux, France*

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Abstract

Background: Male lower urinary tract symptoms (LUTS) are one of the most treated diseases, but little is known about patient trajectories in current clinical practice.
Objective: To describe the dynamic treatment patterns of LUTS presumably due to benign prostatic obstruction (BPO).
Design, settings, and participants: All prescriptions of α_1-adrenergic receptor blocking agents (α_1-blockers), 5α-reductase inhibitors (5-ARIs), and phytotherapy, and all surgeries related to BPO performed in France from 2004 to 2008 were identified using two distinct administrative claim databases maintained by the National Health Insurance system that covers the entire population. After linking the two data sets, all consecutive treatment events were analyzed for each patient.
Outcome measurements and statistical analysis: Drug prescription details were assessed for each year, region, and prescriber qualification. Medical treatment initiation, interruption, evolution, and events after surgical management (hospital stay, reoperation, complication rates, and subsequent medical prescriptions) were also investigated.
Results and limitations: Overall, 2 620 269 patients were treated within 5 yr, with important geographic variations. Medical treatment was interrupted for approximately 16% of patients. The α_1-blockers were prescribed most frequently, but phytotherapy surprisingly accounted for 27% of all monotherapies and 54% of all combination therapies. General practitioners and urologists (92% and 3.7% of overall prescribers, respectively) exhibited a similar prescription profile. Treatment initiation was medical in 95.4% of cases, consisting primarily of monotherapy using α_1-blockers (60.3%), phytotherapy (31.8%), or 5-ARIs (7.9%). Treatment was modified at extremely high rates within 12 mo of initiation (8.7%, 14.6%, and 12.9%, respectively). The median hospital stay for surgical management was far higher than in clinical trials. Long-term surgical complications and reoperation rates favored open prostatectomy. Incidence of pharmacologic treatment after surgery was as high as 13.8% at 12 mo.
Conclusions: This unique dynamic evaluation of clinical practice revealed unexpected results that contrast with previously published evidence from clinical trials. This approach may merit monitored and targeted measures to improve the level of care in the field.

† These authors contributed equally to this work.
* Corresponding author. Department of Urology, Tenon Hospital, 4 rue de la Chine, 75020 Paris, France. Tel. +33 156016495; Fax: +33 156017306.
E-mail addresses: bertrand.lukacs@tnn.aphp.fr (B. Lukacs), jncornu@hotmail.fr (J.-N. Cornu).

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1. Introduction

Benign prostatic hyperplasia (BPH) can result in benign prostatic obstruction (BPO), regarded as a major etiology of lower urinary tract symptoms (LUTS) in men >40 yr of age [1,2]. Pharmacologic treatment of LUTS presumably due to BPO (LUTS/BPO) is mainly based on α_1-adrenergic receptor blocking agents (α_1-blockers) and 5α-reductase inhibitors (5-ARIs), alone or in combination [2–4]. Antimuscarinics and phosphodiesterase-5 inhibitors were recently suggested as add-ons or alternatives [3,4]. When medical treatment fails or results in complications, surgical treatment is required for relief from BPO [2–4].

LUTS/BPO management represents an incredibly high economic burden [1,5,6]. However, current knowledge about effective LUTS/BPO management in clinical practice is limited. Descriptive population studies [1,7–9] have focused on records rather than individuals and have been unable to provide follow-up data. Treatment patterns (including combinations), prescription modalities, and patients' trajectories are only indirectly estimated by partial surveys, polls, or bulky evaluations from population samples [10–16]. Clinical trials, based on stringent selection criteria and focused on one primary objective with a limited follow-up period, fail to reflect current clinical practice [16,17].

A putative solution to this lack of information may be an exhaustive and dynamic patient-centered data set collected at a population level. To our knowledge, such a project has not been conducted. We present a unique comprehensive prospective nationwide database including all men who have been medically or surgically treated for LUTS/BPO in France over a 5-yr period. Our goal was to use individual data to describe the patterns and outcomes of medical and surgical treatments.

2. Materials and methods

2.1. Database construction

Information was extracted from two comprehensive claim databases covering all the population (Supplementary methods and Supplementary Fig. 1), compiling hospital stays and medical procedures (Programme de Médicalisation des Systèmes d'Information [PMSI]) and medication deliveries (Système National Inter Régimes de l'Assurance Maladie [SNIIR-AM]).

Extractions from the PMSI database concerning any hospital stay where the main diagnosis was BPH and the intervention was transurethral resection of the prostate (TURP), transurethral incision of the prostate, open prostatectomy (OP), hyperthermia by transurethral microwave therapy (TUMT), or transurethral needle ablation of the prostate (TUNA) were analyzed (Supplementary Table 1). Alternative endoscopic procedures were not individually identified because no specific code was available; they were encoded as a TURP.

Extractions from the SNIIR-AM database included all prescriptions containing α_1-blockers, 5-ARIs, and/or phytotherapy with *Serenoa repens* or *Pygeum africanum*, the only two plant extracts marketed in France (Supplementary Table 1). These drugs are all partially reimbursed and only available with a medical prescription. Over-the-counter medications are rare in France, so almost every prescription could be tracked. These three classes of drugs were considered specific to LUTS/BPO management because they were rarely administered for other indications at the time of the study. Antimuscarinics were not included in the main analysis because they were not indicated for male LUTS management before 2008 [18–20], but they were studied in the population that had undergone surgery.

Medical and surgical data were extracted yearly and merged via anonymous patient identification numbers to track all consecutive treatment events for each individual. After the first extraction in 2004, the data set was updated yearly. A patient was designated as *treated* if he was already included in the data set, *new* if he had never been treated before, *untreated* if he was present in previous records but absent in the update, or *retreated* if he was untreated the year before but was present in the update. Data about death were recorded by a national registry and automatically included in the SNIIR-AM database. Less than 5% of the extraction samples were excluded because of identification number inconsistencies.

2.2. Data analysis

A descriptive analysis was conducted to estimate the overall prevalence of each LUTS/BPO treatment modality. Drug prescription data were stratified by the patient's age, drug class and combination types, and prescriber specialty. Standardized treatment rates adjusted for the number of men >50 yr of age (obtained from the national demographic agency [21]) were estimated for each region in France.

Treatment initiation was specifically studied in the new patient subgroup. Subsequent modifications to the initial medical treatment were assessed by the cumulative incidence of the following events: a *class switch*, where patients remain on monotherapy but change their medication class; a *type switch*, where patients switched to combination therapy; and a *global switch*, for overall changes.

Surgical treatment outcomes were assessed based on the rate of reintervention for BPO, the rate of subsequent surgery to correct potential complications from BPO surgery (clot retention, incontinence, and urethral stenosis), and the number of medical prescriptions after surgery including antimuscarinics (Supplementary Table 1). Results are presented as the cumulative incidence rates for surgical complications and medical prescriptions and as survival without recurrence curves for reoperation for BPO relief. The incidence of the studied events was calculated using Kaplan-Meier estimates, and patients were censored at the time of their last data collection. All analyses were performed using SAS software v.9.3. The legal authorization to analyze and publish these data was obtained from the national authorities in 2011.

3. Results

3.1. Overall treatment patterns

Between 2004 and 2008, 2 620 269 men were treated for LUTS/BPO. The yearly amounts of medical prescriptions continuously increased, whereas the number of surgeries slightly decreased over the study period (Fig. 1). The mean treated population age decreased between 2004 and 2008, from 69.7 $\pm$ 11.4 yr to 68.03 $\pm$ 11.12 yr for medical prescriptions and from 71.5 $\pm$ 9.3 yr to 69.0 $\pm$ 9.8 yr for surgical procedures. Overall, 91% of patients were >50 yr of age. Important geographic variations, up to 1.5-fold, were noted from one region to another for medical- and surgical-adjusted treatment rates (Fig. 2).

Only 1 503 733 patients were treated continuously without interruption (Fig. 3). The yearly global rate of treatment interruption ranged from 21% to 26%; 3–5% of