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Prostatitis and Its Management

Concepts and Recommendations
for Clinical Practice

 Springer

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Foreword

After many years of daily involvement in clinical management of urologic patients, I can surely say that prostatitis is one of the biggest clinical challenges within our discipline. The two main characteristics of the disease are its high frequency while – at the same time – limited knowledge is available to the practitioner about the disease and, secondly, its low prognostic severity yet strong impact on their patients’ quality of life. This is due to the fact that this urological topic still remains poorly understood, inadequately treated and under-researched. Surely much has changed over the last decades. The initial classification system that was based upon the “4-glass test” has been replaced by a more recent classification system introduced by the National Institute of Health (NIH) focusing on clinical symptoms rather than aetiology which still remains largely unknown. For a long time a validated symptom score was not available, and well-conducted clinical trials were completely lacking. Outcome research has improved our understanding of the incidence, quality of life and economic impact of the disease. Finally, we now have a validated symptom score that appears to adequately measure both symptom severity and response to therapy, and numerous randomized placebo-controlled trials using symptoms as an outcome parameter have been conducted over time which has increased our knowledge on how to improve our management of prostatitis patients. The purpose of this book is to review the state of the art in prostatitis combining practical clinical recommendations with cutting-edge clinical research, basic science and questions for the future. The authors are very well-known experts in the field and have surely based their personal contribution on the most updated scientific evidence without forgetting to share the tricks derived from their precious and vast clinical expertise. Chapters cover the epidemiology and classification of the disease, the diagnostic approach – including imaging studies – and the therapeutic approach to different subtypes of prostatitis. Special focus is reserved for the role of phytotherapy, the management of infective complications following prostate biopsy, the contribution of prostate infection and inflammation to BPH and cancer, the role of STD

pathogens in bacterial prostatitis patients and the implications of prostatitis on sexual and reproductive function. It is my sincere hope that the readers will find within this text practical, yet novel, approaches to assist their patients in their clinical practice and come to rely on and refer to it often as a handy reference which enables them to fully recognize, comprehend, diagnose and treat this all-too-common prostate-related pathology.

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Tommaso Cai and Truls E. Bjerklund Johansen

Prostatitis is one of the most common illnesses in young men with different clinical presentation such as pelvic pain, lower urinary tract symptoms, or sexual dysfunction and a high impact on their quality of life. The management of prostatitis patients is still today a challenge for the urologist, andrologist, and the general practitioner. The recent acquisitions in terms of epidemiological data and the latest classification from the National Institutes of Health (NIH) have triggered a better management of the prostatitis patient. However, there are holes in our knowledge about the pathophysiology, pathogenesis, and causative pathogens which can make it difficult to find the best treatment for our patients. The need for an improved knowledge is demonstrated by the high number of patients who drop out from scheduled treatments and are lost to follow-up. At the same time, we see a high number of new drugs and phytotherapeutic compounds being introduced in the pharmacopeia and on the market. The situation calls for a standardization of the management of prostatitis patients. On this background, the idea was born to bring together experts in the field to give an update on current knowledge and share practical advices on the management of prostatitis patients. This book aims to provide a comprehensive description of prostatitis, from diagnosis till therapy. This book will be the first handbook addressing all clinical aspects of the prostatitis syndrome and providing the reader with all necessary information to design a tailored therapy. Furthermore, the editors aim to analyze and discuss all relevant clinical implications of the disease, in particular andrological complications (infertility), the possible link between prostatitis and prostate cancer, and infectious complications of prostate biopsies.

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The final section (questions and answers) is a practical manual for quick consultation in everyday clinical practice. We pay special attention to contemporary aspects of prostatitis related to antibiotic stewardship and elevated PSA: “thoughtless treatment of prostatitis is malpractice, sometimes even a forensic issue.” We believe this book will be the first true practical guide for physicians who are involved in diagnostic work-up and treatment of patients suspected of having the prostatitis syndrome. However, it will also serve as a convenient consultancy guide for all physicians who occasionally see prostatitis patients.

Sandra Mazzoli, Tommaso Cai, Marco Puglisi,
and Riccardo Bartoletti

2.1 Introduction

Human prostate pathologies are one of the most prevalent clinical conditions with a high impact on social, health-related, and individual costs [1]. In particular, the inflammatory pathologies of the prostate are strongly increasing in males between 20 and 40 years old, with important impact on patient's quality of life [2]. In men of all ages and racial origins, prostatitis prevalence has been estimated to be 10–14 % [3, 4], but there are many biases in the epidemiological studies on prostatitis patients due to several reasons: the lack of a standardized diagnostic tool, the heterogeneity of the clinical presentation, the heterogeneity of the etiology, and the lack of comprehension of the pathophysiology. However, the latest classification of the prostatitis syndromes (National Institutes of Health classification) allows a better definition of the diseases, without a complete resolution of the problem [5].

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2.1.1 Epidemiology: International Data

International reports have shown a high heterogeneity that reflects the difficulties in the assessment of the epidemiological data. Roberts et al. estimated that 11 % of Europeans had symptomatic prostatitis [6], while Nickel et al. identified prostatitis in 2.7 % of urological outpatients in Canada with an average age of 50 years [7].

2.1.1.1 European Countries

In Italy, Rizzo et al. performed a national multicenter prospective study on 8503 patients and found a prevalence of prostatitis of 12.8 % (mean age 47.1 years) [4]. Six years later, Bartoletti et al. performed an epidemiological case-control study on prostatitis categories II and III and evaluated the prevalence and estimated the incidence and risk factors of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) in urological outpatients in Italian hospitals [3]. From January to June 2006, they enrolled patients from 28 Italian urological centers aged between 25 and 50 years with symptoms of CP/CPPS [3]. Out of 5540 male urological outpatients, 764 were enrolled with CP/CPPS, including 225 (29.4 %) first-visit patients and 539 (70.6 %) who had undergone previous treatment. It was concluded that the prevalence of the syndrome was 13.8 %, while the estimated incidence was 4.5 % [3].

The same results have been reported by Mehik et al. who found a 14 % lifetime prevalence in a cross-sectional Finnish study, in which 27 % of Finnish men reported symptoms at least once per year and 16 % complained of persistent prostatitis symptoms [8].

Finally, in 2007, Marszalek et al. evaluated the prevalence of symptoms suggestive of chronic pelvic pain syndrome in an urban population (Department of Preventive Health of the City of Vienna) and showed that the prevalence of symptoms suggestive of chronic pelvic pain syndrome was 2.7 % without any particular age dependence [9].

2.1.1.2 USA and North American Countries

Statistical data from the National Kidney and Urologic Disease Advisory Board and the National Center for Health Statistics showed that in the USA, prostatitis was ranked fourth among the 20 principal diagnoses made by physicians on referring patients to urologists, and 25 % of urological outpatient visits were due to chronic prostatitis symptoms [10]. Moreover, of almost 32,000 male health professionals in the USA without prostate cancer, 16 % self-reported a history of prostatitis [11]. Notably, during 1 year prostatitis was diagnosed in 12 million men older than 18 years in the USA, including visits made to general practitioners [12]. Among urological outpatients in Canada with an average age of 50 years, 2.7 % were identified with prostatitis, as demonstrated by Nickel [7]. Moreover, Curtis Nickel in a cohort of 868 patients, enrolled in a survey in Canada and analyzed by self-administration of the National Institutes of Health (NIH) Chronic Prostatitis Symptom Index, showed a prevalence of prostatitis-like symptoms of 11.5 % in men younger than 50 years and 8.5 % in men 50 years or older [13].

2.1.1.3 Asian Countries

Tan et al. in 2002 evaluated the prevalence of prostatitis-like symptoms in Singapore, by using a population-based study. They found that the prevalence of prostatitis-like symptoms in a largely Chinese population was 2.67 % [14].

Moreover, in 2013 Wu et al. showed that the prevalence of asymptomatic prostatitis (NIH-IV class) was 21.1 % among 1868 men aged 19–78 years, highlighting that the prevalence of NIH-IV class prostatitis should be taken into account when estimating the total prevalence of prostatitis in future studies [15]. In a cohort of Japanese patients, Kunishima showed that the prevalence of prostatitis-like symptoms was 4.9 % in randomly selected men [16].

Estimated prevalence of prostatitis-like symptoms

Continent	Country	Prevalence	References
Europe	Austria	2.7	[9]
	Italy	12.8–13.8	[3, 4]
	Finland	14	[8]
America	USA	16	[11]
	Canada	2.7	[7]
	Canada	8.5–11.5	[13]
Asia	China	2.6	[14]
	Japan	4.9	[16]

2.1.2 Microbiology: Bacteria and Causative Pathogens

International data showed that only 5–10 % of prostatitis patients have a microbiologically demonstrated bacterial infection [17]. A correct microbiological analysis should include the use of adequate biological material that has to be homogeneous, quantitatively sufficient, and representative of the site infection organ [18, 19]. Collection and sampling have to be simple, noninvasive, and not bothersome for patients, have a good compliance, and have to be not contaminated by a saprophytic microflora. A correct microbiological analysis should also include identification of a low number of bacteria in expressed prostatic secretion or post-massage urines, as this can be the causative agent in chronic bacterial prostatitis [20]. Critical points of microbiological sampling are immediate/rapid transport to suitable conditions for biological materials, immediate/rapid culture after collection, and the application of bacteriological techniques able to quantify a small number of pathogens [21].

The most common isolated pathogens from prostatitis patients are those involved in urinary tract infections (uropathogens), which include: Gram-negative organisms, most commonly *Escherichia coli*, *Proteus* spp., *Klebsiella* spp. and *Pseudomonas* spp., enterococci, *Staphylococcus aureus*, and rarely anaerobic organisms such as *Bacteroides* spp. [17] (Fig. 2.1).

Fig. 2.1 Bacteria involved in prostatitis [17]

Pathogen
Escherichia coli
Other Enterobacteriaceae
<i>Klebsiella spp.</i>
<i>Enterobacter spp.</i>
<i>Proteus spp.</i>
<i>Serratia spp.</i>
<i>Pseudomonas aeruginosa</i>
Enterococci
<i>Enterococcus faecalis</i>
Staphylococci
<i>Staphylococcus epidermidis</i>
<i>Staphylococcus haemolyticus</i>
Corynebacterium spp
<i>Corynebacterium minutissimum</i>
<i>Corynebacterium group ANF</i>
<i>Corynebacterium scminale</i>
Anaerobic bacteria
Lirogenital Mycoplasmata
<i>Ureaplasma urealyticum</i>
<i>Mycoplasma hominis</i>
Other bacteria
<i>Chlamydia trachomatis</i>
Yeasts
<i>Candida albicans</i>
<i>Candida spp.</i>
<i>Saccaromices spp.</i>
<i>Trichomonas vaginalis.</i>

In a retrospective study Mazzoli S. evaluated 1,686 isolated strains from chronic prostatitis patients [17]. The microbiological findings were as follows: 371 strains of Gram-negatives (22.00 %) and 1,112 Gram-positives (65.9 %), 14 yeast strains (0.83 %), and 189 mycoplasmata (11.2 %) [17]. It is worth considering that Gram-positives represented the majority of isolates with strain *Enterococcus faecalis* being the most common with a prevalence of 42.7 % [17]. Similar results have been confirmed by Cai et al. who enrolled more than 15,000 consecutive outpatients with chronic bacterial prostatitis attending a single sexually transmitted disease center from January 1997 and December 2008 [22]. All patients underwent microbiological cultures of first-void early morning urine, midstream urine, expressed prostatic secretion, and post-prostate massage urine. The prevalence of different bacterial strains was stratified in four different periods: 1997–1999, 2000–2002, 2003–2005,