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The Bulletin of Urooncology is the official journal of the Turkish Urooncology Association. The Bulletin is an independent, peer-reviewed, international journal published quarterly in March, June, September, and December.

The Bulletin accepts research articles in the basic and clinical sciences, reviews of current topics, relevant surgery videos and extraordinary case reports for publication.

The main aim of the journal is to enable all physicians-especially urologists to access research findings from the urooncology field quickly and effectively. It also contributes to physicians' vocational training with specific numbers of reviews, surgery videos and case reports.

The Bulletin accepts manuscripts through an online submission system. Free access to full text versions is provided to members through the website and mobile applications.

SUBMISSION, PROCESSING AND PUBLICATION ARE FREE OF CHARGE. NO FEES ARE REQUESTED FROM THE AUTHORS INCLUDING ALL STEPS FROM SUBMISSION TO PUBLICATION.

After online manuscript submission, leading reviewers from the relevant areas will evaluate the papers and send feedback to the authors within a short time mostly in one month duration.

The Bulletin is included in leading international indices. Currently, the Bulletin of Urooncology is indexed in **Emerging Sources Citation Index (ESCI), TUBITAK/ULAKBIM Turkish Medical Database, Directory of Open Access Journals (DOAJ), EBSCO, Embase, CINAHL Complete Database, Gale/Cengage Learning, ProQuest, Index Copernicus, British Library, Root Indexing, J-Gate, IdealOnline, ROOT INDEXING, Turk Medline, Hinari, GOALI, ARDI, OARE, AGORA, EuroPub and Turkiye Citation Index.**

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Instructions to Authors

1. General Information

The Bulletin of Urooncology is the official scientific publication of the Turkish Society of Urooncology. It is published quarterly (March, June, September, and December). Supplements are also published during the year if necessary. Accepted articles will be published in English online without a hard copy.

The Bulletin publishes basic and clinical research original articles, reviews, editorials, case reports, surgery videos (Video-urooncology) and letters to the editor relevant to urooncology (prostate cancer, urothelial cancers, testis and kidney cancer, benign prostatic hyperplasia, and any aspect of urologic oncology).

The Bulletin of Urooncology is indexed by several well-known international databases including Emerging Sources Citation Index (ESCI), TUBITAK/ULAKBIM Turkish Medical Database, Directory of Open Access Journals (DOAJ), EBSCO, CINAHL Complete Database, Gale/Cengage Learning, ProQuest, Index Copernicus, and British Library.

All submitted manuscripts are committed to rigorous peer review.

THE BULLETIN OF UROONCOLOGY DOES NOT CHARGE ANY ARTICLE SUBMISSION, PROCESSING OR PUBLICATION CHARGES, NOR DO AUTHORS RECEIVE ANY REMUNERATION OR COMPENSATION FOR THEIR MANUSCRIPTS.

Manuscripts must be written in English and must meet the requirements of the Bulletin. Articles are accepted for publication on the condition that they are original, are not under consideration by another journal, and have not been previously published. This requirement does not apply to papers presented in scientific meetings and whose summaries not exceeding 400 words have been published. In this case, however, the name, date, and place of the meeting in which the paper was presented should be stated. Direct quotations, tables, or illustrations taken from copyrighted material must be accompanied by written permission for their use from the copyright owner and authors.

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All manuscripts should comply with the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" produced and updated by the International Committee of Medical Journals Editors (www.icmje.org).

It is the authors' responsibility to ensure their manuscript meets scientific criteria and complies with ethical requirements.

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The Bulletin adheres to the principles set forth in the Declaration of Helsinki 2016 version (http://www.wma.net/en/30publications/10policies/b3/index.html) and holds that all reported research involving human beings is conducted in accordance with such principles. Reports describing data obtained from research conducted in human participants must contain a statement in the "Materials and Methods" section indicating approval by an ethics review committee and affirmation that informed consent was obtained from each participant.

All manuscripts dealing with animal subjects must contain a statement indicating that the study was performed in accordance with "The Guide for the Care and Use of Laboratory Animals" (http://oacu.od.nih.gov/regs/guide/guide.pdf) with the approval (including approval number) of the Institutional Ethic Review Board, in the "Materials and Methods" section.

Prospective clinical trials, surgery videos and case reports should be accompanied by informed consent and the identity of the patient should not be disclosed.

During the evaluation of the manuscript or even after publication, the research data and/or ethics committee approval form and/or patients' informed consent document can be requested from the authors if it is required by the editorial board.

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It is the authors' responsibility to ensure their manuscript meets full ethical criteria detailed at www.uroonkolojibulteni.com/Peer-Review-and-Ethic.

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Manuscripts are submitted online at www.uroonkolojibulteni.com. If you are unable to successfully upload the files, please contact the editorial office by e-mail or through the online submission system. Rejected manuscripts are not sent back to the authors except for art work.

All submissions must include "Copyright Transfer and Author Declaration Statement Form". All authors should sign this form declaring acceptance of full responsibility for the accuracy of all contents in accordance with the order of authors. They should also indicate whether there is a conflict of interest regarding manuscript. The names of the institutions, organizations, or pharmaceutical companies that funded or provided material support for the research work, even in the form of partial support, should be declared and acknowledged in the footnote of the article. Copyright Transfer and Author Declaration Statement Form must also indicate that "Patient Consent Statement" is obtained for human studies particularly prospective clinical trials, surgery videos (Video-urooncology) and case reports. All manuscripts submitted must also be accompanied by an "Acknowledgements Form" which is available at www.uroonkolojibulteni.com.

The ORCID (Open Researcher and Contributor ID) number of the all authors should be provided while sending the manuscript. Free registration can be done at http://orcid.org.

3. Peer-Review Process

The Bulletin of Urooncology is an independent international journal based on double-blind peer-review principles. All articles are subject to review by the editors and peer reviewers. All manuscripts are reviewed by the editor, associate editors, and at least two expert referees. The scientific board guiding the selection of papers to be published in the

Bulletin consists of elected experts of the Bulletin and if necessary, selected from national and international authorities. The editorial board has the right to not publish a manuscript that does not comply with the Instructions for Authors, and to request revisions or re-editing from the authors. The review process will be managed and decisions made by the Editor-in-chief, who will act independently.

The editor and editorial board is the sole authority regarding reviewer selection. The reviewers are mainly selected from a national and international advisory board. The editorial board may decide to send the manuscript to independent national or international reviewers according to the subject.

Authors of accepted manuscripts accept that the editor and associate editors can make corrections without changing the main text of the paper.

THE EDITORS WILL QUICKLY MAKE A SCIENTIFIC EVALUATION OF YOUR ARTICLE AND MOSTLY REACH A FINAL DECISION ABOUT YOUR ARTICLE WITHIN 20 TO 30 DAYS. THUS, WE OFFER A QUICK SYSTEMATIC REVIEW PROCESS TO ALL AUTHORS.

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It is the authors' responsibility to prepare a manuscript that meets scientific criteria. All persons designated as authors should have made substantial contributions to the following:

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(2) drafting the article or revising it critically for intellectual content,

(3) final approval of the version to be submitted.

If the article includes any direct or indirect commercial links or if any institution provided material support to the study, authors must state in the "Copyright Transfer and Author Declaration Statement Form". They must state that they have no relationship with the commercial product, drug, pharmaceutical company, etc. concerned; or specify the type of relationship (consultant, other agreements), if any. This information should also be included in the "Acknowledgements Form".

In case of any suspicion or allegation regarding scientific shortcomings or ethical infringement, the Bulletin reserves the right to submit the manuscript to the supporting institutions or other authorities for investigation. The Bulletin accepts the responsibility of initiating action but does not undertake any responsibility for an actual investigation or any power of decision.

-Abbreviations:

Use only standard abbreviations. Avoid abbreviations in the title and abstract. The full term for an abbreviation should precede its first use in the text, unless it is a standard abbreviation. Abbreviations that are used should be defined in parenthesis where the full word is first mentioned.

-Units of Measurement:

Measurements should be reported using the metric system, according to the International System of Units (SI).

-Statistical Evaluation:

All retrospective, prospective, and experimental research articles must be evaluated in terms of biostatics and should be stated together with an appropriate plan, analysis, and report. P values must be given clearly in the manuscripts (e.g., p=0.033). It is the authors' responsibility to prepare a manuscript that meets biostatistical rules.

-Language:

Accepted articles will be published in English online. It is the authors' responsibility to prepare a manuscript that meets spelling and grammar rules. Authors who feel their English language manuscript may require editing to eliminate possible grammatical or spelling errors and to conform to correct scientific English are encouraged to consult an expert. All spelling and grammar mistakes in the submitted articles are corrected by our redaction committee without changing the data presented.

5. Article Types

The Bulletin of Urooncology publishes articles prepared in compliance with the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals published by International Committee for Medical Journal Editors (ICMJE). Manuscripts that do not meet these requirements will be returned to the author for necessary revision prior to review.

The Bulletin requires that all submissions be submitted according to these guidelines: Manuscripts should be prepared as a word document (*.doc) or rich text format (*.rtf). Text should be double-spaced with 2.5 cm margins on both sides using 12-point type double spaced in Times Roman.

All manuscripts submitted must be accompanied by the "Copyright Transfer and Author Declaration Statement Form" (www.uroonkolojibulteni.com). The corresponding author must also provide a separate "Title Page" including full correspondence address including telephone, fax number, and e-mail address, list of all authors with The ORCID number. Contact information for the corresponding author is published in the Bulletin.

All manuscripts submitted must also be accompanied by an "Acknowledgements Form" (www.uroonkolojibulteni.com). Acknowledgements are given for contributors who may not be listed as authors. Any grants or financial support received for the paper should be stated in the "Acknowledgements Form". If presented as an abstract; the name, date, and place of the meeting should also be stated in this form. A statement of financial, commercial or any other relationships of a declarable nature relevant to the manuscript being submitted, (i.e. a potential conflict of interest) must also be included in "Acknowledgements Form".

Each section of the" Main Text" mentioned below should be started on a new page and be organized according to the following sequence:

1) First page: Title, abstract and keywords (without authors' credentials)

2) Manuscript text structured based on the article type (without authors' credentials)

3) References

4) Figure legends

5) Short Quiz for review articles.

Tables and figures should be uploaded separately.

Also, "Acknowledgements Form" should be uploaded separately.

A. Original Research Articles

Original prospective or retrospective studies of basic or clinical investigations in areas relevant to urologic oncology.

Content (Main text): Each part should start on a new page.

- First page: Title - Abstract (structured abstract limited to 300 words, containing the following sections: Objective, Materials and Methods, Results, Conclusions) - Keywords (List 3-5 keywords using Medical Subjects Headings [MeSH])

-Introduction

- Materials and Methods

- Results

- Discussion

- Study Limitations
- Conclusions
- References
- Figure Legends: These should be included on separate page after the references.

-Tables and figures should be uploaded separately.

- Also, "Acknowledgements Form" should be uploaded separately.

Preparation of research articles, systematic reviews, and meta-analyses must comply with study design guidelines: CONSORT statement for randomized controlled trials (Moher D, Schultz KF, Altman D, for the CONSORT Group. The CONSORT statement revised recommendations for improving the quality of reports of parallel group randomized trials. JAMA 2001; 285: 1987-91) (http://www.consortstatement.org/); PRISMA statement of preferred reporting items for systematic reviews and meta-analyses (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097.) (http://www.prisma-statement.org/); STARD checklist for the reporting of studies of diagnostic accuracy (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al., for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003;138:40-4.)(http://www.stard-statement.org/); STROBE statement, a checklist of items that should be included in reports of observational studies (http://www.strobe-statement.org/); MOOSE guidelines for meta-analysis and systemic reviews of observational studies (Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting Meta-analysis of observational Studies in Epidemiology (MOOSE) group. JAMA 2000; 283: 2008-12).

A word count for the original articles (excluding title page, acknowledgements, references , figure and table legends) should be provided not exceed 3000 words. Number of references should not exceed 30. Number of figure/tables is restricted to five for original articles.

B. Case Reports

Case reports should include cases which are rarely seen and distinctive in diagnosis and treatment. These can include brief descriptions of a previously undocumented disease process, a unique unreported manifestation or treatment of a known disease process, or unique unreported complications of treatment regimens, and should contribute to our present knowledge.

Content (Main text): Each part should start on a new page.

- First page: Title - Abstract (limited to 150 words, unstructured - Keywords (List 3-5 key words using Medical Subjects Headings [MeSH])

-Introduction

-Case Presentation

-Discussion

-References

- Figure Legends: These should be included on separate page after the references.

-Tables and figures should be uploaded separately.

-Also, "Acknowledgements Form" should be uploaded separately.

A word count for the case reports (excluding title page, acknowledgements, references, figure and table legends) should be provided not exceeding 1500 words. Number of references should not exceed 15. Number of figure/tables is restricted to three for case reports.

C. Review Article

These are manuscripts which are prepared on current subjects by experts who have extensive experience and knowledge of a certain subject and who have achieved a high number of publications and citations. Reviews are usually submitted directly or by invitation of the editorial board. Submitted reviews within the scope of the journal will be taken into consideration by the editors. The content of the manuscript should include the latest achievements in an area and information and comments that would lead to future studies in that area. Number of authors should be limited to three.

Content (Main text): Each part should start on a new page.

- First page: Title -Abstract (maximum 250 words; without structural divisions - Keywords (List 3-5 key words using Medical Subjects Headings [MeSH]).

-Introduction

- Text: This part should present detailed information based on current literature about the subject of the review. The author(s) should organize the manuscript into appropriate headings and subheadings to facilitate reading.

-Conclusions

-References

- Figure Legends: These should be included on separate page after the references.

-Short Quiz (a list of 3-5 questions about the context of article for CME credit). The editorial board and Urooncology Association of Turkey executive committee will evaluate the answers and members submitting correct answers may receive education grants).

-Tables and figures should be uploaded separately.

-Also, "Acknowledgements Form" should be uploaded separately.

Number of figure/tables is restricted to five for review articles. Number of references should not exceed 100.

D. Literature Review

These short reviews are solicited by the editor, will go through the peer review process, and will cover recently published selected articles in the field of urologic oncology. It is a mini-review article that highlights the importance of a particular topic and provides recently published supporting data. The guidelines stated above for review articles are applicable. Word count should not exceed 1500 and references are limited to 10.

E. Editorial Commentary

These short comments are solicited by the editor and should not be submitted without prior invitation. An original research article is evaluated by specialists in the area (not including the authors of the research article) and this is published at the end of the related article. Word count should not exceed 500 words and number of references is limited to 5.

F. Letters to the Editor

These are letters that include different views, experiments, and questions from readers about the manuscripts published in the Bulletin within the last year and should be no more that 500 words with maximum of 5 references. There should be no title or abstract. Submitted letters should indicate the article being referenced (with issue number and date) and the name, affiliation, and address of the author(s). If the authors of the original article or the editors respond to the letter, it will also be published in the Bulletin.

G. Surgery Videos on Urooncology (Video-urooncology)

These videos are solicited by the editor. The videos are prepared on urooncological surgeries by experts who have extensive experience and knowledge of certain advanced surgical techniques. This section is also intended to enable urologists to learn, evaluate, and apply new or complex surgical principles in their surgical practice. The videos can describe current sophisticated or new surgical techniques or modification of current techniques. The surgery video must be high quality material.

Videos are only submitted by the invitation of the editorial board. Submitted videos are also evaluated based on double-blind peer-review principles.

The Bulletin of Urooncology publishes original videos containing material that has not been reported elsewhere as a video manuscript, except in the form of an abstract. The authors should describe prior abstract publications in the "Acknowledgements Form". Published videos become the sole property of The Bulletin of Urooncology.

Video-urooncology submission should include:

1) Copyright Transfer and Author Declaration Statement Form: This form must indicate that "Patients' Informed Consent Statement" is obtained.

2) Title Page

3) Summary: Summary should point out critical steps in the surgery up to 500 worlds. This part was published as an abstract to summarize the significance of the video and surgical techniques. The author(s) may add references if it is required.

5) Video: Please upload your video to www.uroonkolojibulteni.com using online submission system. Accepted video formats are Windows Media Video (WMV), AVI, or MPEG (MPG, MPEG, MP4). High-Definition (HD) video is preferred.

6) "Acknowledgements From" should be uploaded separately.

Videos should be up to 30 minutes in duration. The video must include audio narration explaining the procedure. All text and audio in the video must be in English. Audio must include narration in clear, grammatically correct English. Videos must be clear, in focus, and without excessive camera movement. Radiographs and other material must not contain any patient-identifiable information. Limited number of slides incorporated into video may be included to provide details of patient history, clinical and laboratory findings.

6. Manuscript Preparation

Manuscripts should be prepared following sequence according to article type:

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All manuscripts submitted must be accompanied by this form which is available at www.uroonkolojibulteni.com. All of the authors must sign this form. This form must indicate that "Patient Consent Statement" is obtained for prospective trials, surgery videos (Video-oncology) and case reports. By signing this form the authors declare that they obtained the Ethic Committee approval document regarding all experimental, clinical and drug human studies. By signing this form authors also state that the work has not been published nor is under evaluation process for other journals, and they accept the scientific contributions and responsibilities. No author will be added or the order of authors will be changed after this stage. Any funding and/or potential conflict of interest must be declared in this form.

B. Title Page

The title page should include the following:

-Full title

-Running title

-Authors' names and institutions

-The ORCID (Open Researcher and Contributor ID) number of all authors should be provided

-Corresponding author's e-mail and postal address, telephone, and fax numbers

C. Main Text (without authors' credentials)

Each section of the main text should be started on a new page and abide to the following sequence according to article type:

-First page: Title, Abstract and Keywords: Abstracts should be prepared in accordance with the specific instructions for the different article types. Only for original articles, a structured abstract should be provided using the following headings: Objective, Materials and Methods, Results, and Conclusions. Provide 3-5 keywords. English keywords should be provided from Medical Subject Headings (http://www.nlm.nih.gov/mesh).

-Introduction: Introduction should include brief explanation of the topic, the objective of the study, and supporting information from the literature.

-Materials and Methods: This section should describe the study plan, indicating whether the study was randomized or nonrandomized, retrospective or prospective, the number of trials, the characteristics, and statistical methods used. If applicable, it should be indicated that the results should be scrutinized.

-Results: This part should summarize the results of the study, with tables and figures presented in numerical order; results should be indicated in accordance with statistical analysis methods used.

-Discussion: The positive and negative aspects of the study data should be discussed and compared with literature.

-Study Limitations: Limitations of the study should be discussed for only original articles. In addition, an evaluation of the implications of the obtained findings/results for future research should be outlined.

-Conclusions: The conclusion of the manuscript should be highlighted.

- References: The author is responsible for the accuracy of references. Cite references in the text with numbers in parentheses. All authors should be listed if four or fewer, otherwise list the first three authors and add et al. Number references consecutively according to the order in which they first appear in the text. Journal titles should be abbreviated according to the style used in Index Medicus (consult List of Journals Indexed in Index Medicus).

Examples for writing references:

Format for journal articles: initials of author's names and surnames. title of article. journal name date; volume: inclusive pages.

Example:

Journal: Soukup V, Dušková J, Pešl M, et al. The prognostic value of t1 bladder cancer substaging: a single institution retrospective study. Urol Int 2014;92:150-156.

Format for books: initials of author's names and surnames. chapter title. In: editor's name, Eds. Book title. Edition, City: Publisher; Year. p. pages.

Example:

Book Chapters: Lang TF, Duryea J. Peripheral Bone Mineral Assessment of the Axial Skeleton: Technical Aspects. In: Orwoll ES, Bliziotes M, eds. Osteoporosis: Pathophysiology and Clinical Management. New Jersey, Humana Pres Inc, 2003;83-104.Books: Greenspan A. Orthopaedic

Radiology a Practical Approach. 3rd ed. Philadelphia: Lippincott Williams Wilkins; 2000. p. 295-330.

-Figure legends: These should be included in main text on a separate page after the references.

-Short Quiz: A list of 3-5 questions as the last page about the context of article for CME credit only for review articles.

D. Tables and Figures

If you use data from another published or unpublished source, obtain permission and fully acknowledge that source. Number of figure/tables is restricted to five for original article and reviews and three for case reports. Authors should contact the editor prior to submission regarding any manuscript exceeding these figure/table limitations.

Direct quotations, tables, or illustrations taken from copyrighted material must be accompanied by written permission for their use from the copyright owner and authors.

Tables: Supply each table in a separate file. Number tables according to the order in which they appear in the text, and supply a brief caption for each. Give each column a short or abbreviated heading. Write explanatory statistical measures of variation, such as standard deviation or standard error of mean. Be sure that each table is cited in the text.

Figures: Supply each figure in a separate file. Authors should number figures according to the order in which they appear in the text. Figures include graphs, charts, photographs, and illustrations. Each figure should be accompanied by a legend. Figures should be submitted as separate files, not in the text file. Image files must be cropped as close to the actual image as possible. Pictures/photographs must be in color, clear and with appropriate contrast to distinguish details. Figures, pictures/photographs must be uploaded as separate .jpg or .gif files (approximately 500x400 pixels, 8 cm in width and scanned at 300 resolution). Figure legends should be included in main text on a separate page after the references.

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All manuscripts submitted must be accompanied by an "Acknowledgements Form" which is available at www.uroonkolojibulteni.com. The information in this document will be published as a footnote of the article.

If the manuscript presented as an abstract previously; the name, date, and place of the meeting should be mentioned.

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7. Manuscript Submission

As part of the submission process, authors are advised to complete a check-list designed to ensure their submission complies with the instructions for authors, and submissions may be returned to authors who do not adhere to these guidelines.

The Bulletin of Urooncology only accepts electronic manuscript submission at the web site www.uroonkolojibulteni.com.

Manuscripts should be prepared as a word document (*.doc) or rich text format (*.rtf). Text should be double-spaced with 2.5 cm margins on both sides using 12-point type double spaced in Times Roman.

Submissions must include according to the following sequence:

A-Original Article

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3) Main text (without authors' credentials): Each part should start on a new page.

First page (Title- structured abstract – keywords), Introduction, Materials and Methods, Results, Discussion, Study Limitations, Conclusions, References, Figure legends

4) Table(s)

5) Figure(s)

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B. Case Reports

1) Copyright Transfer and Author Declaration Statement Form

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3) Main text (without authors' credentials): Each part should start on a new page.

First page (Title- abstract – keywords), Introduction, Case Presentation, Discussion, References, Figure legends

4) Table(s)

5) Figure(s)

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C-Review Article

1) Copyright Transfer and Author Declaration Statement Form

2) Title Page

3) Main text (without authors' credentials): Each part should start on a new page.

First page (Title- abstract – keywords), Introduction, Text (appropriate headings and subheadings), Conclusions, References, Figure legends, Short Quiz

4) Table(s)

5) Figure(s)

6) Acknowledgements Form

D. Literature Review

1) Copyright Transfer and Author Declaration Statement Form

2) Title Page

3) Main text (without authors' credentials): Each part should start on a new page.

First page (Title- abstract – keywords), Introduction, Text (Appropriate headings and subheadings), Conclusions, References, Figure legends

4) Table(s)

5) Figure(s)

6) Acknowledgements Form

E. Editorial Commentary

1) Copyright Transfer and Author Declaration Statement Form

2) Title Page

3) Main text (Text, References)

4) Acknowledgements Form

F. Letters to the Editor

1) Copyright Transfer and Author Declaration Statement Form

2) Title Page (The title is "Letter to Editor about.....")
3) Main text (Text, References)
4) Acknowledgements Form

G. Surgery Videos (Video-urooncology)

1) Copyright Transfer and Author Declaration Statement Form
2) Title Page
3) Summary (without authors' credentials)
4) Video
5) Acknowledgements Form

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Is Cognitive MR Fusion Biopsy Superior to Standard TRUS Guided Prostate Biopsy? Our Clinical Experience

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Abstract

Objective: To share our clinical experience with cognitive prostate biopsy and compare results of cognitive biopsies with standard biopsies.

Materials and Methods: The data of patients for whom prostate biopsy was performed at Marmara University Faculty of Medicine, Department of Urology in 2020 were retrospectively reviewed. All biopsies, including repeat biopsies are included in the study. Basic clinical characteristics and pathological outcomes were compared between the groups. Clinically significant prostate cancer (PCa) was defined as gleason grade group 2 or more in biopsy pathology.

Results: The mean age of all patients included in the study was 64.9±8.16 years. Median prostate specific antigen (PSA) level was 7.7 (5.0-12.8) ng/dL. There were no statistically significant differences between the two groups with respect to patient age, total and free PSA values, digital rectal examination and radiologic prostate volume. Biopsy pathologies were also similar between the groups. Our data demonstrated that patients with advanced age and higher levels of total PSA value were more likely to have clinically significant PCa. The positive predictive value of digital rectal exam (DRE) was 43.5% for clinically significant cancers and 59.0% for all PCa, which was higher than Prostate Imaging-Reporting and Data System 4 and 5 lesions.

Conclusion: Clinical experience could be the main determining factor in cognitive fusion biopsy results. Our results show that cognitive biopsy is not superior than standard systematic biopsy. So taking standard biopsy core should not be neglected, especially in inexperienced clinics. Our results also support the fact that DRE is still one of the most cost-effective diagnostic tools for clinically significant PCa.

Keywords: Prostate cancer, prostate biopsy, multiparametric prostate MRI, PI-RADS, fusion biopsy, cognitive biopsy

Introduction

Diagnosing clinically significant prostate cancer (PCa) without overdiagnosis is one of the main goals in the diagnostic process PCa. Multiparametric prostate magnetic resonance imaging (mpMRI) has been a promising modality for this purpose (1,2). It is now regarded as one of the first line imaging modalities before prostate biopsy in the European Association of Urology guidelines with a strong recommendation (3). Studies demonstrated that mpMRI with the help of Prostate Imaging-Reporting and Data System (PI-RADS) (v2.1) could improve clinically significant PCa diagnosis rates as well as reduce unnecessary biopsies (4,5). This technological advancements made targeted biopsies a possibility in the diagnosis of PCa diagnosis instead of standard transrectal ultrasound (TRUS) guided biopsies. Targeted prostate biopsy along with standard biopsy is a strong recommendation in The European Association of Urology guidelines for PI-RADS ≥3 lesions in the biopsy naïve patient group (3).

Although targeted biopsies are recommended, there are some technical and economic factors limit their routine use. The need of special instruments and software for fusion biopsies comes with a significant economic burden to the health-care and insurance systems. Although there are some studies demonstrating fusion biopsy as a cost-effective modality for the diagnosis of PCa, economic factors still limit the use of software-enhanced fusion biopsies (6).

Cognitive prostate biopsy, which is defined as taking extra biopsy cores during classical TRUS guided biopsy from the localization of the observed lesions in mpMRI, is an alternative to fusion biopsy. Since cognitive biopsy does not require any additional instruments, it could easily be performed in daily clinical practice. In this study, we shared our clinical experience on cognitive prostate biopsy and compare the results of cognitive biopsies with those of standard biopsies.

Materials and Methods

The data of patients for whom prostate biopsy was performed at Marmara University Faculty of Medicine, Department of Urology in 2020 were reviewed retrospectively. Cognitive biopsies which

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were performed in 63 patients were included as the study group and the most recent consecutive standard biopsies matching the number of cognitive ones were included as the control group. Patients with missing critical data (total PSA, pathology result etc.) were excluded from the study. All biopsies, including repeat biopsies are included. At least 12 cores were taken in each biopsy and in some patients core numbers are adjusted based on the clinical characteristics of the patient. Preoperatively, all patients were informed about the procedure and gave informed consent. Given the retrospective case control nature of this study ethics board approval was not applicable. In standard prostate biopsy, cores were obtained under periprostatic block (10 mL of 1% lidocaine) from the peripheral zone of the prostate at the apex, mid, gland and base (7). For cognitive biopsies, standard TRUS biopsy with at least 12 cores was performed. According to the mpMRI, extra cores were obtained. Core numbers of targeted biopsies are decided per patient, based on factors like lesion size and lesion PI-RADS score. The final patient cohort consisted of 125 patients (59 cognitive vs. 66 standard biopsies). Basic clinical characteristics and pathological outcomes were compared between the groups. Clinically significant PCa was defined as gleason grade group 2 or more in biopsy pathology.

Statistical Analysis

Statistical analyses were performed in the python programming language with the help of pandas, numpy and scipy libraries (8,9,10). JupyterLab was used as the coding interface (11). The scaler variables were investigated using visual (Histograms, QQ Plots) and analytical methods (Kolmogorov-Smirnov, Shapiro-Wilk, D'Agostino's K^2 tests) to determine whether they are normally distributed. Independent samples t-test was used for the comparison of two groups if the variable is normally distributed in each group, otherwise Mann-Whitney U test was used. Categorical variables were compared with the chi-square test if the assumptions of the test were met. When the assumptions of the chi-square do not hold, for two groups Fisher Exact test and for more than two groups likelihood ratio was used to compare categorical variables. Numbers are given as the mean and standard deviation for normally distributed variables and median and interquartile range for non-normally distributed variables. For categorical variables, case number and pe percent were given for each category. For all statistical analyses p values less than 0.05 were statistically significant.

Results

The mean age of all patients included in the study was 64.9±8.16 years. Median PSA level was 7.7 (5.0-12.8) ng/dL. There were no statistically significant differences between the two groups with respect to patient age, total and free PSA values, digital rectal examination and radiologic prostate volume (Table 1). Since it must take more cores from the lesions total core count was higher in the cognitive biopsy group, as expected.

Biopsy pathologies were also similar between the groups. The median-targeted core number was 3 (2-3) cores per lesion. In the cognitive biopsy group, there were 18 (30.5%) patients whose targeted biopsy specimens were diagnosis with adenocarcinoma. This ratio was lower than the general cancer diagnosis ratio of the cognitive biopsy group (40.7%). There was only one (1.7%) patient who was diagnosed with gleason grade group 1 PCa with targeted biopsy while his all-standard biopsy cores resulted benign. Whereas 6 (10.2%) patients had tumor-positive cores in classical biopsy although their targeted biopsy cores were benign and 2 (3.3%) of these patients had clinically significant PCa.

Our data demonstrated that patients with advanced age and higher levels of total PSA value were more likely to have clinically significant PCa. Also, 58.7% of patients with International Society of Urological Pathology (ISUP) grade 2 or more cancer had positive signs on the digital rectal examination (DRE) (Table 2). Positive predictive value (PPV) of DRE was 43.5% for clinically significant cancers and 59.0% for all PCa. DRE had a higher PPV than PI-RADS 4 or 5 lesions for both clinically significant and all PCa groups. (PPV for PI-RADS 4-5 lesions: 31.6% and 50.0%, respectively)

Discussion

The diagnosis of clinically significant PCa without over diagnosing and overeating patients has been the focus of many studies recently. With the technological advancements, mpMRI has been highlighted as the technique of choice for discriminating clinically significant PCa (12). PI-RADS has high PPV for clinically significant PCa (13). Recently the PROstate MRI Imaging Study (PROMIS) trial demonstrated that using mpMRI in the first line evaluation of patients could decrease unnecessary biopsies up to 27% and could reduce the diagnosis of clinically insignificant PCa by 5% (5). The negative predictive value (NPV) of mpMRI was 89% in the PROMIS trial. In our study, NPV of PI-RADS 4 and 5 lesions combined was 69.4% that was lower than that of the PROMIS trial. This difference could be explained by factors like regional variability of PCa and the effect of the experience of both radiologists and urologists on the diagnostic value of mpMRI, as some previous studies demonstrated (14).

The diagnostic value of mpMRI is supported with level 1 evidence and clearly recommended in most guidelines. With the advancement in mpMRI techniques and concatenation of mpMRI images with biopsy procedures made targeted biopsies are a possibility for the prostate. Although some reports on these fusion biopsy procedures combined with standard biopsy demonstrated a possible advantage of these techniques in PCa diagnosis, the need of special enhancements and equipment limit the widespread use of software-enhanced fusion biopsies (15,16). The question of whether or not it is possible to achieve the favorable results with cognitive biopsies without any special instrumentation in biopsy has also been studied by some studies.

Results on the effectiveness of cognitive prostate biopsies are conflicting. Although some studies suggested a clear benefit of cognitive biopsies over routine biopsies in the diagnosis of clinically important PCa, there are also some reports with no clear benefit shown of cognitive biopsy. A recent study showed that cognitive prostate biopsy could increase cancer detection rates in patients with previous cancer negative biopsies (17). Another study with 510 patients showed that no clinically significant difference on biopsy outcomes between cognitive and fusion biopsies whereas both these techniques

were superior than standard biopsy (18). In a meta-analysis conducted by Schoots et al. (19), although cognitive fusion biopsies did not have a statistically significant advantage over standard biopsies, their success rate on the diagnosis of all and significant PCa was comparable with software enhanced fusion biopsies. Furthermore a prospective designed study showed that although pre-biopsy mpMRI increased diagnostic accuracy of prostate biopsy, no difference had been detected between cognitive and software enhanced biopsies (20). Wysock et al. (21) demonstrated that although software enhanced fusion biopsies were more informative histologically than visual targeting there were statistically significant difference in cancer detection rates.

Table 1. General characteristics of patients in two groups

		Standard Bx (n=66) (3rd comment of reviewer 2)	Cognitive Bx (n=59) (3rd comment of reviewer 2)	p-value
Patient age	**Median (IQR)**	64.0 (60.0-70.0)	64.0 (59.0-71.0)	0.538[1]
Total PSA value	**Median (IQR)**	8.72 (4.74-17.98)	7.14 (5.66-11.44)	0.423[1]
Free PSA value	**Median (IQR)**	1.46 (1.02-3.63)	1.36 (1.03-1.98)	0.299[1]
Radiologic prostate diameter	**Median (IQR)**	70.0 (48.25-97.5)	58.5 (41.5-83.0)	0.098[1]
t-PSA/f-PSA ratio	**Median (IQR)**	4.34 (3.85-5.79)	4.8 (3.99-7.41)	0.306[1]
Digital rectal examination n (%)	**Normal**	43 (65.15)	43 (72.88)	0.352[2]
	Abnormal	23 (34.85)	16 (27.12)	
Biopsy pathology n (%)	**Benign**	36 (54.55)	35 (59.32)	0.590[2]
	Malign	30 (45.45)	24 (40.68)	
ISUP grades n (%)	**1**	12 (41.38)	12 (50.0)	0.874[2]
	2	8 (27.59)	4 (16.67)	
	3	2 (6.9)	2 (8.33)	
	4	2 (6.9)	1 (4.17)	
	5	5 (17.24)	5 (20.83)	
Clinically significant cancer n (%)	**No**	49 (74.24)	47 (79.66)	0.474[2]
	Yes	17 (25.76)	12 (20.34)	
Post-op complication n (%)	**0**	59 (89.39)	56 (94.92)	0.332[2]
	1	7 (10.61)	3 (5.08)	

[1]Mann-Whitney U, [2]Chi-square, Bx: Biopsy, IQR: Interquartile range, t-PSA: Total PSA, f-PSA: Free PSA, ISUP: International society of urological pathology, PSA: Prostate specific antigen

Table 2. Comparison of patients who were diagnosed as clinically significant PCa and not

		Clinically significant PCa		
		No	**Yes**	**p-value**
Patient age	**Median (IQR)**	63.0 (58.0-68.0)	72.0 (65.0-75.0)	**<0.001[1]**
Total PSA value	**Median (IQR)**	6.72 (4.76-11.39)	12.71 (9.26-33.24)	**<0.001[1]**
Free PSA value	**Median (IQR)**	1.41 (1.02-2.56)	1.54 (1.04-4.84)	0.553[1]
Radiologic prostate diameter	**Median (IQR)**	68.0 (49.0-94.0)	50.0 (37.0-59.5)	0.018[1]
t-PSA/f-PSA ratio	**Median (IQR)**	4.39 (3.75-5.9)	7.65 (4.23-9.01)	0.051[1]
Lesion diameter (mm)	**Median (IQR)**	10.0 (8.0-15.0)	14.0 (8.0-18.0)	0.269[1]
PI-RADS category n (%)	**≤3**	34 (56.67)	2 (14.29)	0.004[2]
	>3	26 (43.33)	12 (85.71)	
Digital rectal examination n (%)	**Benign**	74 (77.08)	12 (41.38)	**<0.001[2]**
	Malign	22 (22.92)	17 (58.62)	
Biopsy type n (%)	**Standard**	49 (51.04)	17 (58.62)	0.474[2]
	Cognitive	47 (48.96)	12 (41.38)	

[1]Mann-Whitney U, [2]Chi-square, PCa: Prostate Ca, IQR: Interquartile range, t-PSA: Total PSA, f-PSA: Free PSA, PI-RADS: Prostate Imaging-reporting and data system, PSA: Prostate specific antigen

On contrary to these results Yamada et al. (22) showed that software enhanced fusion biopsies can yield higher cancer detection rates compared to cognitive biopsies. Aslan et al. (23) showed that combined mpMRI targeted and systematic biopsy is superior to detect high-grade disease, than either systematic or MPMR-targeted biopsy alone. A recent prospective trial showed that the cancer detection rate by cognitive biopsy alone was lower than the standard biopsy combined with cognitive biopsy (24). Our results did not show the net benefit of cognitive biopsy. In our study, targeted biopsy was detected cancer in only one patient, whose standard biopsy was benign, and this patient had a gleason grade group 1 tumor. No patient was diagnosed with clinically significant PCa only with targeted biopsy in our study; on the other hand, two patients were diagnosed significant PCa with standard biopsy while targeted biopsy cores of these patients were benign.

Although technological advancements have revolutionized the diagnostic process of PCa recently, the importance of DRE has not change. Abnormal DRE is associated with an increased rate of higher ISUP grade PCa (25,26). Gosselaar et al. (25) showed that an abnormal DRE along with elevated PSA value has a PPV of 48.6% for the diagnosis of PCa. Our results were also quite close to these findings. We found that the PPV of DRE 43.5% for clinically significant cancers and 59.0% for all PCa.

Study Limitations

Our study does not without its limitations. As stated before, it is known that operator experience could affect the success rate of cognitive biopsies. Since our clinic is an education clinic, it was impossible to maintain the same standard for the operator experience for all biopsies. Biopsies were not taken by the same physician. This was also the case for standard biopsies, so we believe this factor could have a minimal effect on our results. Also, mpMRI was not performed in every patient who underwent standard biopsy procedure and this was a limiting factor in our study to make comments on the success rate of mpMRI. Furthermore, interobserver variability of mpMRI could affect our results since this study was conducted as a retrospective series, it was impossible to ensure that all mpMRI was evaluated by the same radiologist.

Conclusion

Our study shows that although cognitive biopsy seems as a tempting alternative because no additional funds, education or tools needed to perform it, the net benefit of this procedure is still debatable. Clinical experience could be the main determining factor of cognitive fusion biopsy results and taking a standard biopsy core should not be neglected, especially in inexperienced clinics. Our results also support the fact that DRE is still one of the most cost-effective diagnostic tools for clinically significant PCa.

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Ethics

Ethics Committee Approval: Given the retrospective case control nature of this study ethics board approval was not applicable.

Informed Consent: All patients were informed about the procedure and gave informed consent.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.Ş., H.K.Ç., Design: B.Ş., H.K.Ç., Supervision: İ.T., H.K.Ç., Data Collection or Processing: B.Ş., D.D., İ.T., D.F., Statical Analysis: B.Ş., Literature Review: B.Ş., D.D., Writing: B.Ş., D.D.

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Original Article

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Comparison of Systematic, Targeted and Combined Prostate Biopsy: Our Clinical Outcomes

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Abstract

Objective: Our aim was to compare the diagnostic efficacy of the standard systematic, targeted and combined prostate biopsy methods in prostate cancer.
Materials and Methods: Total of 161 patients who underwent prostate biopsy combined with magnetic resonance imaging-ultrasonography fusion method between August 2018 and March 2021 was evaluated retrospectively. Clinically important and insignificant cancer detection rates of biopsy results between standard, targeted and combined biopsy (CB) methods were compared. Changes in the results were also evaluated in terms of Prostate Imaging-Reporting and Data System (PIRADS) scores.
Results: Prostate cancer was diagnosed in 46 (28.6%) patients by CB. Fourteen (8.7%) patients were interpreted as a clinically insignificant disease. Prostate cancer and clinically significant disease detection rates were statistically significant in favor of CB compared to targeted biopsy (TB). There was no statistically significant difference between systematic biopsy and TB results. Additionally, it was observed that cancer detection rates were higher in PIRADS ≥4 lesions compared to PIRADS 3 lesions in all biopsy methods.
Conclusions: Our results have shown that combined prostate biopsy led to higher detection of prostate cancer and provides increased detection of clinically significant disease. High rates of clinically significant cancer, especially in patients with PIRADS ≥4 lesions, suggest that the PIRADS scoring is a high-level guide in detecting malignancy.
Keywords: Prostate cancer, clinical significance, targeted biopsy, MRI US fusion, combined biopsy

Introduction

Prostate cancer is the first among the most commonly diagnosed cancers in men in the world (1). It also ranks second in cancer-related deaths (2). The diagnosis is based on transrectal ultrasonography (TRUS)-guided biopsy and histopathological examination of biopsy materials is considered the gold standard in diagnosis (3). The TRUS-guided 12-core systematic biopsy is used as the standard method for detecting prostate cancer (4). However, in studies comparative with the autopsy series, prostate biopsy sensitivity was found to be 53% (5).

About a third of cases undergo repeat-biopsy within five years and malignancy is detected in 13-41% of them due to these uncertainties. While the malignancy detection rate is 27-40% with the standard method, 20-25% of clinically significant cancers cannot be detected (6). Saturation biopsy that is recommended to solve these problems, increases the rate of clinically insignificant malignancy detection and therefore may cause overdiagnosis and overtreatment (7). Also, it has also been shown to increase intervention-related morbidity compared with other biopsy methods. It has been stated that the increase in complications is a limiting factor for this method (8).

Suspicious lesions in the prostate gland are more frequently detected with advances in magnetic resonance imaging (MRI) hardware and software and with the widespread use of multiparametric prostate magnetic resonance imaging (mpMRI). With the detection of suspicious malignant lesions with MRI, the targeted prostate biopsies have begun to be performed for these lesions. MpMRI has high sensitivity in detecting clinically significant prostate cancer (9). MRI fusion with ultrasonography (US), a advance in the technology era, enables the imaging of the lesions in the prostate and reduces unnecessary intervention by enhancing to take the biopsy from the right localization (10,11,12).

Fusion imaging provides a safer method for diagnosis by providing a clear correlation between different modalities to show the same anatomy from the same angles. The MRI-US fusion imaging technique by combining the advantages of accurate lesion detection of MRI and real-time imaging of

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the US, has been developed rapidly recently and has been frequently used as an important guiding method in prostate biopsies. The detection of cancer and clinically significant cancer are higher in patients by the use of mpMRI and MRI-US targeted biopsies (13).

Current guidelines recommend a combined biopsy (CB) technique based on the addition of targeted biopsy (TB) to systematic biopsy (SB) (14).

In this retrospective study, patients who underwent MRI-US fusion combined prostate biopsy because of high PSA or abnormal rectal examination findings were evaluated. Standard systematic and targeted prostate biopsies were performed on the patients in the same session. We studied the diagnostic efficacy of the SB, TB, and CB methods.

Materials and Methods

Ethical approval was granted by the local ethics committee of clinical research of Duzce University Ethics Committee (2021/50) on 1 March 2021. Patients who underwent prostate biopsy combined with MRI-US Fusion prostate biopsy were accepted for a retrospective study at the Urology Department of Düzce University Faculty of Medicine Hospital in August 2018 and March 2021. MpMRI was performed in all patients and all lesions were evaluated by radiology Prostate Imaging-Reporting and Data System (PIRADS) version 2 before the biopsy. Suspicious lesions with a PIRADS score of 3 or above were marked and targeted with MRI-US fusion prostate biopsy transrectally.

Siemens AG MagnetomR Skyra (Munich, Germany) 3 Tesla magnet MRI device was used for mpMRI. Based on the mpMRI protocol, T2-weighted imaging was performed in the axial, coronal and sagittal planes with a slice thickness of 3.5 mm. In addition to T1-weighted axial images, diffusion-weighted imaging and dynamic contrast-MRI sequences were used for functional examination. The suspicious lesions were evaluated according to the recommendations in PIRADS version 2.

All biopsies were performed under local anesthesia with appropriate antibiotic prophylaxis by three clinicians in the urology department. All imaging-guided biopsy procedures were performed using an US device (Logiq S8; GE Healthcare, USA) and an 8-10 Mhz endorectal convex probe. Simultaneously, fusion imaging procedures were performed using an US device and an integrated volume navigation system (V Nav; GE Healthcare). The fixed (rigid) method was used as the correlation algorithm of the images.

For volume navigation, an electromagnetic transmitter was placed next to the patient table and electromagnetic sensors were attached to the probe. The transmitter system and sensors were connected to the position sensing unit of the US device (Ascension Technology Corporation, Burlington, USA). The previously obtained MRI images were uploaded to the device. The screen was frozen by selecting one of the transverse MRI images on the right side of the monitor, and the real-time US section passing through this section was determined on the other side of the screen. Plan matching was made to these sections as the first step of matching. As the second step, the patient-specific cyst, calcification, nodule, or other distinctive anatomical points were determined as the reference point. These reference points determined on the real-time US image were matched with the MRI sections on the screen.

After positional matching, MRI images with multiplanar reconstruction, were viewed side-by-side on the screen in synchronization with real-time US images. At least 2 TB cores were obtained from each lesion detected on MRI. After the TB procedure was completed, standard SB of 12 cores of the prostate was performed under the guidance of US only, regardless of the MRI images. The patients whose CB was completed were kept under observation in the daily room for an average of 2 h in terms of pain and spontaneous micturition.

Statistical Analysis

Statistical analysis was performed using SPSS v.21 (IBM Analytics) program. Descriptive statistics were performed to summarize the demographics of the patients. The comparison of qualitative data between dependent groups was performed using the Mc Nemar test, and that of dependent groups was made using Fischer's Exact tests. The odds ratio was calculated for relative risk ratios. Differences were considered statistically significant at $p \leq 0.05$.

Results

In the study, 80 of 161 patients underwent a first biopsy and 81 patients had previous negative biopsy. Because of mpMRI and radiological evaluation of patients, one lesion was detected in 129 (80.1%) of 161 patients and two lesions in 32 (19.8%). Total of 193 lesions, 138 (71.5%) were reported as PIRADS 3 score, 47 (24.3%) as PIRADS 4 and 8 (4.1%) lesions were reported as PIRADS 5 score. The demographic characteristics of the patients are shown in Table 1.

Prostate adenocarcinoma was found in 46 (28.6%) of the patients who underwent prostate biopsy. The histopathological and clinical characteristics of 14 (8.7%) patients were interpreted as clinically insignificant disease according to Epstein's criteria (clinical stage T1c, PSA density <0.15 ng/mL/cc, lack of Gleason 4 or 5, <50% cancer per Cor) (15).

Clinically significant cancer was detected in 26 (16.1%) of 34 (21.1%) patients diagnosed with prostate cancer when using the TB method only, whereas a clinically significant cancer was detected in 28 (17.4%) of 41 (25.5%) patients diagnosed with prostate cancer with SB alone. There was no statistically

Table 1. Demographic characteristics of the patients included in the study

Age	64.19±6.43
PSA (ng/mL)	7.38±5.11
fPSA (ng/mL)	1.47±1.11
Prostate volume (cc)	66.73±39.13
PSA density (ng/mL/cc)	0.13±0.11
Number of biopsy cores	15 (14-20)
Number of cores taken from target lesions per patient	3 (2-8)

PSA: Prostate spesific antigene, fPSA: Free prostate spesific antigene, Data are presented as mean ± SD or mean ± range

significant difference in cancer detection rates between the two methods. (p=0.143, p=0.754)

When the CB results were examined, 32 (19.9%) of 46 (28.6%) patients diagnosed with prostate cancer were found to have clinically significant cancer. Although the rates of diagnosing cancer and clinically-significant cancer in CB method are higher, compared with SB; this difference was not statistically significant (p=0.063, p=0.125). However, prostate cancer and clinically significant cancer detection rates were statistically significant in favor of CB compared with TB (p=0.0001, p=0.031) (Table 2).

There is no significant difference between SB and CB methods applied to patients with only PIRADS 3 lesions in terms of detection of prostate cancer. Both methods were found to be statistically superior to TB in terms of diagnosis of prostate cancer ($p<0.05$). However, no significant difference was found in terms of clinically significant cancer between the 3 groups in patients with PIRADS 3 lesions ($p>0.05$).

There is no significant difference between biopsy methods performed on patients with PIRADS score of ≥4 reported in mpMRI in terms of cancer detection and clinically-important cancer diagnosis ($p>0.05$).

Of the patients with PIRADS ≥4 scored lesions, 55.6% were diagnosed with prostate cancer, and the rate of clinically significant cancer detection in these patients was 48.1%. We observed that the rates of cancer and clinically significant cancer were significantly higher in the PIRADS ≥4 group compared to patients with only PIRADS 3 lesions (p=0.0001) (Table 3).

The odds of diagnosis of prostate cancer [odds ratio (OR): 7.1 95% confidence interval (CI): 3.341-15.130] and clinically significant prostate cancer (OR: 15.6 95% CI: 5.858-41.708) were increased with PIRADS ≥4 lesions compared to PIRADS 3 lesions.

Table 2. Pathology results of SB, TB, CB

	SB[1] n (%)	TB[2] n (%)	CB[3] n (%)
PCa (-)[a]	120 (74.5%)	127 (78.9%)	115 (71.4%)
PCa (+)[a]	41 (25.5%)	34 (21.1%)	46 (28.6%)
Clinically-insignificant PCa[b]	13 (8.1%)	8 (4.9%)	14 (8.7%)
Clinically-significant PCa[b]	28 (17.4%)	26 (16.2%)	32 (19.9%)
Total	161 (100%)	161 (100%)	161 (100%)

SB: Standart biopsy, TB: Targeted biopsy, CB: Combined biopsy, PCa: Prostate cancer, $p_{1a\text{-}2a}$=0.143, $p_{1b\text{-}2b}$=0.754, **$p_{2a\text{-}3a}$=0.0001**, **$p_{2b\text{-}3b}$=0.031**, $p_{1a\text{-}3a}$=0.063, $p_{1b\text{-}3b}$=0.125

Table 3. Combined biopsy; pathology results of patients with only PIRADS 3 and PIRADS ≥4 scored lesions

	PIRADS score	
	3 n (%)[a]	**4 or 5 n (%)[b]**
PCa (-)[1]	91 (85%)	24 (44.4%)
PCa (+)[1]	16 (15%)	30 (55.6%)
Clinically-insignificant PCa[2]	10 (9.3%)	4 (7.4%)
Clinically-significant PCa[2]	6 (5.6%)	26 (48.1%)
Total	107 (100%)	54 (100%)

PIRADS: Prostate imaging-reporting and data system, PCa: Prostate cancer, **$p_{a1\text{-}b1}$= 0.0001, $p_{a2\text{-}b2}$= 0.0001**

The TB is examined based on cores, average number of TB cores taken from lesions per patient was 3 (2,3,4,5,6,7,8). When the pathology results of 138 lesions scored as PIRADS 3 in mpMRI were examined, 8 (5.7%) had cancer and only 2 (1.4%) were compatible with clinically significant prostate cancer. Cancer was detected in 22 (46.8%) of 47 lesions evaluated as PIRADS 4. Eleven (23.4%) of these lesions were clinically-significant. Clinically-significant cancer was detected in all 8 (100%) patients with PIRADS 5. A statistically significant difference was found in cancer detection rates between lesion groups (p=0.0001). It was observed that as the PIRADS score of the lesion increased, the rates of cancer and clinically significant cancer detection increased (Table 4).

Discussion

At present, overdiagnosis and overtreatment of prostate cancer is still discussed and the most effective method for prostate cancer diagnosis remains unclear. It is thought that these uncertainties can be elucidated by the success of MRI in imaging of suspicious lesions, suggesting a clinically significant prostate cancer and the effectiveness of MRI-US fusion-guided biopsy for these lesions (16,17).

In this study, although there was no statistically significant difference in cancer and clinically-significant cancer diagnosis rates of CB and SB, CB had the highest cancer detection rate. We have seen that this success of CB is compatible with the literature (18,19).

Fourcade et al. (20) reported that the prostate cancer detection rate was 55.5% and the clinically significant cancer detection rate was 45%. CB was reported to have the highest rates and no statistically significant difference was found between the results of the TB and SB methods and as in our study. In the same research, patients with a serum PSA value >4 ng/mL were included and the mean serum PSA value was 9 ng/mL. More than half of the patients had PIRADS 5 lesions on the mpMRI. These may have caused the cancer and clinically significant cancer rates to be higher compared to our study. Additionally, unlike the rigid MRI-US fusion biopsy method in our study, performing biopsy with the elastic mpMRI/3D TRUS image fusion method, which was reported by a single experienced radiologist, may have provided more accurate targeting to the lesions (20).

In the literature, studies have reported that the CB and SB methods have statistically similar results as in our study (21). The lack of statistical difference in the results of these two methods can be attributed to the fact that statistical methods are very sensitive to the sample size. Results can be expected to be more meaningful in studies with more patients. Additionally, depending on the fact that biopsy methods are performed by the same physician consecutively, knowing which area is suspicious during standard biopsy may have caused it to be taken like a kind of cognitive biopsy. This may cause the BP and SB results to be similar.

Alternatively, it was observed that there was no statistically significant difference in both cancer detection and clinically-significant cancer diagnosis between TB for which less than 12 cores were taken and the SB methods. This leads to the idea of fewer complications with fewer cores and the same results.

Table 4. Pathology results of cores taken by targeted biopsy from PIRADS 3, 4 and 5 lesions				
PIRADS score	**3 n (%)**	**4 n (%)**	**5 n (%)**	**Total n (%)**
Number of cores	138 (100%)	47 (100%)	8 (100%)	193 (100%)
PCa (-)	130 (94.3%)	25 (53.2%)	0 (0)	155 (80.3%)
PCa (+)	8 (5.7%)	22 (46.8%)	8 (100%)	38 (19.7)
Clinically-significant PCa	2 (1.4%)	11 (23.4%)	8 (100%)	21 (10.8%)
Clinically-insignificant PCa	6 (4.3%)	11 (23.4%)	0 (0)	17 (8.8%)
PIRADS: Prostate imaging-reporting and data system, PCa: Prostate cancer, p=0.0001				

It is thought that the use of MRI-US fusion- TB alone can be discussed.

In a study involving 382 patients, a 15% increase was observed in the diagnosis of clinically-important cancer with the addition of TB, while 62% of tumors missed using this method were found to have clinical-insignificant cancer criteria (22). In our study, TB contributed to a standard method at similar rates in detecting clinically-important cancer. In patients in whom TB could not detect cancer, clinically-insignificant cancer was detected with SB at a similar rate. Additionally, in our study, it was observed that not performing SB would cause cancer to not be detected in 12 (7.4%) patients and clinically significant cancer to be missed in 6 (14.8%) patients.

There are studies reported that TB is superior to SB in the diagnosis of clinically important cancer (23,24,25). Rouvière et al. (26) evaluated CB as a potential improvement in diagnostic methods. Future studies with large numbers of subjects may suggest that only MRI-targeted biopsies may be performed in selected patients.

To determine the treatment options by the actual diagnosis, the true Gleason score, and therefore the actual risk classes; it may be possible by performing a biopsy from the correct lesion. In prostate cancer imaging and the biopsy, the main purpose is to detect clinically-important diseases (27,28).

In the meta-analysis conducted by Gayet et al. (29), considering the studies in which sub-analyzes were performed on the basis of lesions, lesions were grouped as low risk and medium-high risk; PIRADS 3 lesions were considered low risk, and PIRADS 4-5 lesions were considered medium-high risk. Because of this grouping, it was seen that the highest clinically-significant cancer rates were in the medium-high risk group.

Similar to the literature, when we retrospectively examined our biopsy results, cancer and clinically significant cancer levels were significantly increased in patients with a PIRADS ≥4 scored lesion; however, in our study, no difference was found between the biopsy methods applied to patients in this group (20).

However, statistical differences between the methods were found only in patients with PIRADS 3 lesions. In 10 (9.3%) patients, it was observed that CB provided additional benefit in diagnosis compared with the use of SB or TB alone. This statistical superiority makes us think of the CB method as the preferred method, especially for PIRADS 3 lesions.

High rates of cancer and clinically-significant cancer, especially in patients with PIRADS ≥4 lesions, suggest that the PIRADS scoring is a high-level guide in detecting malignancy. In the PROMIS study, it was shown that prostate biopsies can be safely avoided in a quarter of men when mpMRI is used as a triage test. It has also been reported that it gives confidence in the unnecessary diagnosis of clinically-insignificant cancers and the diagnosis rates of clinically-important cancers (23). MpMRI can assist in pre-biopsy risk classification and provide guidance in the decision of biopsy and method selection for detecting high-risk disease considering these findings.

Study Limitation

MRI-US fusion biopsy method, which is a new technology still under development, requires a certain time of learning and experience for optimum results. The limited sample size of the patients in our study, including our first experiences, may have caused the results to be affected by the learning curve process. These two reasons were the limitations of our study.

Conclusions

Among men undergoing biopsy for suspected prostate cancer, combined prostate biopsy, compared with other biopsy methods, was associated with a higher incidence detection of prostate cancer and increased detection of clinically significant disease. High rates of clinically significant cancer, especially in patients with PIRADS ≥4 lesions, suggest that the PIRADS scoring is a high level guide in detecting malignancy. Future studies will be needed to assess the ultimate clinical implications of TB.

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Original Article

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Comparison of DAP Score with RENAL, PADUA and ABC in Prediction of Laparoscopic Partial Nefrectomy Results

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Abstract

Objective: Many nephrometric scoring systems (NSSs) have been published for use in estimating the outcome of laparoscopic partial nephrectomy (LPN). There are conflicting results about the predictive success of these systems. Here, we aimed to determine to what extent radius, exophytic/endophytic properties of the tumor, nearness of tumor to the deepest portion to the collecting system or sinus, anterior/posterior descriptor and the location relative to the polar lines (RENAL), preoperative aspects and dimensions used for an anatomical (PADUA), diameter-axial-polar (DAP), and arterial based complexity (ABC) scoring systems can be included in the treatment plan favoring LPN. We compared these NSSs for their power to predict surgical outcomes.

Materials and Methods: Sixty-two patients who underwent LPN at our clinic were included in this study. Postoperative complication rates, the number of blood transfusions, warm ischemia times (WIT), postoperative hospital stays (PHS), operation times (OT), pathology outcomes, and margin, ischemia, complications (MIC) achievement rates were recorded retrospectively. Total nephrometry scores were calculated from preoperative computed tomography and magnetic resonance imaging images and divided into risk groups. The correlation between nephrometry scores, and surgical outcomes was investigated.

Results: Median age [56.21 (31-80) years] of the patients, and median tumor size (38.89) (11-251) mm was determined. Surgical margin positivity (SMP) developed in 6 (9.7%) cases and major complications (Clavien ≥3) developed in 6 (9.7%) cases. Only DAP scores were statistically correlated with rates of MIC achievement, major complication, is blood transfusion, and PHS (p=0.008, 0.018, 0.011 and 0.006, respectively), while RENAL and PADUA scores with WIT and SMP (p=0.001, 0.002 vs p=0.002, 0.011, respectively), while ABC score with only WIT (p=0.002). None of these scores were correlated with OTs.

Conclusion: DAP score may be used when planning LPN, especially in predicting MIC achievement and major complication rates.

Keywords: DAP score, laparoscopic partial nephrectomy, nephrometry score, RENAL score, PADUA score

Introduction

The rate of incidental diagnosis of kidney masses is increasing with increasing use of imaging methods. These kidney masses usually do not go beyond the renal capsule at the time of diagnosis. The gold standard treatment method for operable T1a (<4 cm) tumors is partial nephrectomy (PN) (1). In non-randomized studies, cancer-specific survival rates of PN equivalent to those of radical nephrectomy (RN) have also been reported for T1b (4-7 cm) tumors (2). Minimally invasive techniques are popular approaches in PN.

Tumor size is not the only factor for PN indication in many kidney masses. The complexity of the tumor anatomy is the main factor in the decision-making process for PN, apart from patient-related factors in clinical practice. Nephrometric scoring systems (NSSs) were, and are being to evaluate this complexity. NSSs such as radius, exophytic/endophytic properties of the tumor, nearness of tumor to the deepest portion to the collecting system or sinus, anterior/posterior descriptor and the location radius, exophytic/endophytic properties of the tumor, nearness of tumor to the deepest portion to the collecting system or sinus, anterior/posterior descriptor and the location relative to the polar lines (RENAL), preoperative aspects and dimensions used for an anatomical (PADUA), Centrality index (C-INDEX), diameter-axial-polar (DAP), arterial based complexity (ABC) are being used in chronological order in clinical practice (3,4,5,6,7). NSSs evaluate the difficulty of surgical management of masses using quantitative parameters.

In many studies conducted, current NSSs have been compared in terms of perioperative and postoperative variables in predicting surgical outcomes. Nevertheless, there is no consensus on which the scoring system is superior and most usable. This study

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aimed to determine which of the RENAL, PADUA, DAP and ABC scoring systems is superior in predicting laparoscopic partial nephrectomy (LPN) outcomes.

Materials and Methods

Patient Selection and DATA Collection

This study was conducted retrospectively, per the Helsinki Declaration and the ethics committee's approval numbered 2019/10-2 and dated 30.10.2019 in the urology clinic of University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital. An informed consent form was obtained from all patients. Patients aged 18-80 years who underwent transperitoneal LPN in a urology clinic for renal masses between January 2016 and November 2019 were investigated. Only patients who had been operated on with the laparoscopic method were included in the study. Patients who had to undergo open nephrectomy and patients who had undergone RN were excluded from the study. Surgical procedures were performed by 4 different experienced surgeons. Two of these surgeons were experienced (minimum experience of 25 NSSs) and the other two were at the beginning of the learning curve (experince level <25 NSSs).

Nephrometry Scores and Surgical Technique

Computed tomography (CT)/magnetic resonance (MR) images of all patients obtained within 3 months preoperatively were examined. The maximum tumor size, depth, location, and laterality of the tumor were recorded. These images were examined in axial and coronal sections to calculate nephrometry scores from one urologist. All nephrometry scores were coded by dividing them into the total score and categorical risk groups according to the complexity level. RENAL scores were calculated based on the maximum tumor size, endophytic/exophytic ratio, distance of the tumor from the collecting system, and its location RENAL. The total RENAL score was assessed in low (4-6), moderate (7-9), and high (10-12) risk groups. The total PADUA score was also assessed in low (6-7), moderate (8-9), and high (10-14) risk groups. The anatomical features examined in this score were the location of the tumor relative to the polar line, exophytic rate, relationship with the renal sinus and collecting system, tumor size, and lateral or medial location of the tumor. The total DAP score was assessed in low (3-5) and high (6-9) risk groups. The DAP score was calculated on the basis of 3 parameters as tumor size, distance of the tumor from the center of the kidney in the axial section, and the distance of the tumor from the center of the kidney in the coronal section. Each parameter was scored between 1 and 3 points, and the DAP sum score ranged between 3 and 9 points.

ABC score was assessed in low (Category 1 and 2) and high (Category 3S and 3H) risk groups. Scores were also assigned to the groups according to the arterial branches to be dissected, including groups 1 (interlobular and arcuate arteries), 2 (interlobar arteries), 3S (segmental arteries), and 3H (renal artery, hilar arteries).

All surgeries were performed laparoscopically through the transperitoneal route. The mass was first exposed after the pneumoperitoneum was created with 4 trocars with the patient in the lateral decubitus position. Then, the pedicle was taken under control. The mass was marked with cautery and cut with scissors. Following renography the mass was removed, and placed in an endobag.

Preoperative and Perioperative Outcome Parameters

Operative demographic data were recorded. Follow-up visits were made at 3 and 6 months postoperatively. At each visit, the evaluation was performed by serum creatinine. Perioperative parameters such as warm ischemia time (WIT), postoperative hospital stay, number of blood transfusions, and operation times (OT) were recorded. WIT was evaluated separately as a numerical value, and the number of patients with WIT <20 min. Postoperative complications were evaluated according to the Clavien-Dindo complication classification system (8). Grade 3 and above group evaluation was recorded as a major complication. Pathological tumor size and histological subtypes were evaluated according to the World Health Organization (9), and tumor extent and stage were assessed according to tumor-node-metastasis classification (10). The surgical margin positivity (SMP) was also evaluated as a tumor extending beyond the parenchymal margin marked with ink. Besides, the margin, ischemia, complication (MIC) score was used to evaluate the optimal outcome success in PN (11), which takes negative surgical margin, WIT <20 min and absence of major complications into consideration. We assessed only patients whose pathology was reported as malignant according to the MIC achievement criteria.

Statistical Analysis

SPSS (Statistical Package for the Social Sciences) version 22.0 program and the Shapiro-Wilk test were used for the analysis of data. The Mann-Whitney U test was used for pairwise comparisons and the Kruskal-Wallis test to compare more than two groups. Pearson's chi-square test and Fisher's chi-square test were used for the comparison of categorical variables. Relationships between the variables were calculated by Spearman correlation analysis. The significance level of outcomes was set at $p<0.05$.

Results

Ninety-three patients who met the inclusion criteria were included in the study. From this retrospective study, 10 patients who did not come to their postoperative controls, 9 patients with missing data, and 12 patients who switched to open surgery during LPN were not included. The remaining 62 patients who underwent LPN were included in the study.

The median age of the 62 patients was 56.21 (31-80), and the female/male ratio was 22/40. The median tumor size measured by CT was 38.89 (11-251) mm. The median tumor size in the pathology specimen was 38.57 (11-242) mm. SMP developed in 6 (9.7%) patients.

Table 1: Median scores and pathological characteristics.

The median postoperative hospital (PHS) was 4 (2-16) days. Median WIT was recorded as 20 (11-35) min. Two patients were operated using non-clamp technique. Median OT was recorded

Table 1. Demographic, pathological and radiological data of the patients	
n=62	
Age (year) (median) (min-max)	56.21 (31-80)
Gender (n%)	
Female	22 (35.5)
Male	40 (64.5)
Side (n%)	
Right kidney	33 (53.2)
Left kidney	29 (46.8)
Tumor size (mm) (median) (min-max)	38.89 (11-251)
Renal score (median) (min-max)	6 (4-10)
Padua score (median) (min-max)	8 (6-13)
Dap score (median) (min-max)	5 (3-9)
Malign tumors (n%)	49 (79)
Pathology (n%)	
Angiomyolipoma	5 (8.1)
Oncocytoma	3 (4.8)
Cyst	1 (1.6)
Chronic pyelonephritis	4 (6.5)
RCC clear cell	43 (69.4)
RCC papillary	5 (8.1)
RCC chromophobe	1 (1.6)
STAGE (n%)	
STAGE 1a	35 (71.4)
STAGE 1b	12 (24.5)
STAGE 2a	2 (4.1)
Tumor size (In the pathology specimen) (mm) (median) (min-max)	38.57 (11-242)
Surgical margin positivity (n%)	6 (9.7)

Table 2. Perioperative variables	
Operation time (minutes) (median) (min-max)	200 (110-255)
Warm ischemia time (minutes) (median) (min-max)	20 (11-35)
Warm ischemia time (minutes)	
<20 minutes	39 (63)
>20 DK minutes	21 (33)
Non clamp	2 (4)
Postoperative hospital stay (day) (median) (min-max)	4 (2-16)
For malign tumors	
MIC success (n%)	27 (55.1)
MIC failure (n%)	22 (44.9)
MIC: Margin, ischemia, complications	

as 200 (110-255) min. MIC achievement criteria for malign tumors were met in 27 (27/49: 55.1%) patients (Table 2).

According to the Clavien classification of surgical complications complications were observed in 22 (35.4%) patients within the first month postoperatively. Complications were grade 1 (8%) in 5, grade 2 (17.7%) in 11, grade 3a (6.5%) in 4, and grade 3b (3.2%) in 2 patients. Double J stent was required due to opening of the collecting system in 3 patients with grade 3a complications. In one patient, the hematoma was evacuated from the bladder by performing cystoscopy. Postoperative angioembolization was required in 2 patients with grade 3b complications. No patient developed grade 4 or 5 complications.

Table 3: The distribution of patients' nephrometry scores according to risk groups and total scores.

All nephrometry scores were correlated with each other and continuously variable surgical outcomes (WIT, OT, PHS). DAP score was statistically significantly correlated with WIT and PHS ($p<0.001$, $p=0.021$). While the RENAL score was statistically significantly correlated with WIT ($p<0.001$), no statistically significant correlation was found with PHS ($p=0.157$). PADUA score was statistically significantly correlated with WIT ($p<0.001$). ABC score was statistically significantly correlated with WIT ($p<0.001$), no correlation was found with PHS ($p=0.155$). None of the scores were statistically significantly correlated with OT (Table 4).

Table 3. Patient-based distribution of scoring systems		
	Risk Group	**n (%)**
RENAL	**Low** **Intermediate** **High**	36 (58) 18 (29) 8 (13)
PADUA	**Low** **Intermediate** **High**	27 (4.6) 23 (37.1) 12 (19.3)
DAP	**Low** **High**	38 (61.3) 24 (38.7)
ABC	**Low** **High**	38 (61.3) 24 (38.7)
RENAL: Radius, exophytic/endophytic properties of the tumor, nearness of tumor to the deepest portion to the collecting system or sinus, anterior/posterior descriptor and the location relative to the polar lines, PADUA: Preoperative aspects and dimensions used for an anatomical, DAP: Diameter-axial-polar, ABC: Arterial based complexity		

Table 4. Correlation between continuously variable surgical outcomes and nephrometry scores			
	WIT	**PHS**	**OT**
RENAL score	r=0.482*	r=0.182	r=0.236
PADUA score	r=0.490*	r=0.225	r=0.212
DAP score	r=0.542*	r=0.292*	r=0.195
ABC score	r=0.446*	r=0.183	r=0.147
RENAL: Radius, exophytic/endophytic properties of the tumor, nearness of tumor to the deepest portion to the collecting system or sinus, anterior/posterior descriptor and the location relative to the polar lines, PADUA: Preoperative aspects and dimensions used for an anatomical, DAP: Diameter-axial-polar, ABC: Arterial based complexity, WIT: Warm ischemia times, OT: Operation times, PHS: Postoperative hospital stays, *p<0.05 (Spearman correlation test was used)			

Table 5. Mean scores and p values according to SMP, MIC success, general complication, major complication and presence of transfusion								
	RENAL	**p**	**PADUA**	**p**	**DAP**	**p**	**ABC**	**p**
SMP								
+	8.17±1.72	**0.007**	9.83±1.72	0.02	6.17±0.41	0.069	2.33±0.52	0.950
-	6.02±1.53		8.07±1.53		5.26±1.59		2.28±0.73	
MIC success								
+	6.00±1.66	0.187	7.96±1.76	0.089	5.00±1.71	0.014	2.15±0.77	0.167
-	6.64±1.70		8.68±1.43		5.8±1.14		2.45±0.59	
General complication								
+	6.59±2.06	0.386	8.18±1.59	0.822	6.00±1.90	0.073	2.29±0.69	0.485
-	6.07±1.79		8.13±1.83		5.04±1.55		2.13±0.84	
Major complication								
+	7.50±1.76	0.076	9.00±1.41	0.146	7.00±1.41	0.009	2.5±0.84	0.297
-	6.07±1.84		8.05±1.77		5.13±1.63		2.14±0.79	
Presence of transfusion								
+	6.91±2.21	0.234	8.55±1.75	0.373	6.73±1.79	0.005	2.36±0.81	0.346
-	6.06±1.77		8.06±1.76		5.0±1.52		2.14±0.8	

RENAL: Radius, exophytic/endophytic properties of the tumor, nearness of tumor to the deepest portion to the collecting system or sinus, anterior/posterior descriptor and the location relative to the polar lines, PADUA: Preoperative aspects and dimensions used for an anatomical, DAP: Diameter-axial-polar, ABC: Arterial based complexity, MIC: Margin, ischemia, complications, SMP: Surgical margin positivity, Mann-Whitney U test was used

In terms of the correlation between nephrometric scores and categorical outcomes (MIC achievement, complication, SMP), only the DAP score was statistically significantly correlated with MIC achievement, major complications, and transfusion rates (p=0.014; 0.009; 0.005). Only RENAL and PADUA scores were statistically significantly correlated with SMP (p=0.007; p:0.02, respectively). None of the scores were statistically significantly correlated with the presence of general complications (Table 5).

When the scores were divided into risk groups, WIT and all nephrometry scores were found to be statistically significantly correlated (p values for RENAL, PADUA, DAP, ABC scores were 0.001, 0.002, <0.001, 0.002, respectively). The presence of major complications, PHS and MIC achievement were statistically significantly correlated with only the DAP score (p=0.018, p=0.006, p=0.008). RENAL, PADUA and DAP scores were significantly correlated with SMP (p=0.002; p=0.011; p=0.003). Only the DAP score was statistically significantly correlated with perioperative blood transfusion (p=0.011). The presence of general complications and OT did not significantly correlate with any nephrometry score (Table 6).

Discussion

NSSs help surgeons who are hesitant to make decisions favoring nephron-sparing surgery for renal masses. The most successful system for predicting perioperative outcomes has not yet been determined. Many authors have compared scoring systems in dual, triple, or quad combinations and obtained different results (12,13). We conducted an analysis comparing four NSSs. According to the results of our study, the DAP score was superior to RENAL and PADUA scores, which are the best known and most used scores in predicting MIC achievement and complications.

In the literature, there are different definitions for the term trifecta (14,15). We used the MIC score defined by Buffi et al. (11). Twenty-seven (55.1%) of 49 patients with malignant pathology in our study met the MIC achievement criteria. Among these criteria, the rates of surgical margin negativity, WIT of <20 min, and lack of major complications were recorded as 90.3%, 63%, and 90.3%, respectively. The rates obtained from our study were slightly lower than the reference study consisting of 99 patients who had undergone robot-assisted PN (surgical margin: 93%, ischemiea: 83%, complication: 90%, MIC: 76%) (11). Since the cases in our series were performed using the laparoscopic method, the achievement rate of MIC was lower. The difficulties in the suturing and reconstruction stages in the laparoscopic technique reduce the MIC achievement rates compared to the robotic technique (16). Only the DAP score was correlated with MIC achievement rates in our study. The study by Borgmann et al. (13) is the only study evaluating the MIC achievement rate of the DAP score. In this study, DAP score was not found to be a predictor of MIC achievement in univariate or multivariate logistic regression analysis. A study was published showing that DAP score is a predictor of the trifecta, although the authors used a different definition for trifecta (14,17). For the first time, our study has demonstrated the correlation between MIC achievement, which is the criterion showing the optimal surgical success of DAP score and provides information to the literature.

In our study, consistent with the literature, the overall, and major complication rates were 35.4% and 9.7%, respectively, while none of the nephrometry scores were correlated with overall complication rates. Only the DAP score was significantly correlated with major complications and blood transfusion rates. A limited number of external validation studies of the DAP scoring system have been performed for predicting complications both in the index study and other studies, especially the decrease in GFR and its correlations with WIT have been demonstrated (5,18). Only in one study of robotic series, DAP was shown to be a predictor of major complications (19). As far as we know,

firstly our study has shown that DAP score is a predictor of major complications seen in laparoscopic series.

During PN, the risk of SMP remains a matter of concern. In the literature, its incidence ranges from 0% to 7% (20). Although its effect on cancer recurrence and mortality is controversial, it is imperative to avoid SMP as much as possible. The rate of SMP was determined as 9.7% in our study. Besides, RENAL, PADUA, and DAP scores could predict SMP in our study. The RENAL score showed the best correlation with SMP. According to our estimation, the reason for the success of the RENAL score in this regard may be its assessment of parameters such as the depth of the tumor, its relationship with the collecting system, or renal sinus, which are strongly correlated with SMP.

A high nephrometry score almost always directly affects WIT, which reflects tumor complexity. Although the cut-off value of WIT in terms of long and short-term maintenance of renal function varies between 20 and 25 minutes, it has also been reported that WIT even up to 40 min does not cause loss of renal function (21). In our study, when 2 patients in whom arterial clamping was not performed were excluded, the mean WIT was found to be 20 (11-35) min. Besides, all four NSSs were correlated with increased WIT. Nevertheless, the DAP score showed the best correlation. WIT essentially reflects the difficulty of surgical resection. The DAP score showed the best correlation with WIT in our series because of the influence of the C-INDEX score in creating the DAP score. The C-INDEX score was revealed in a laparoscopic series, which was also significantly correlated with WIT in this study (p=0.004) (6).

A shorter PHS is a benefit of the minimally invasive approaches. The median PHS of the patients in our series was 4 (2-16) days. PHS is essentially correlated with the presence of some postoperative complications. Although major complications are more frequent, the development of any complication is expected to prolong PHS. The DAP score, which is the only predictor of the major complication rate, was the score that correlated with PHS in our study. Since patient-related factors other than tumor characteristics may affect the PHS, conflicting results have been reported in the literature.

OT affect the surgical outcomes and reducing this time helps decrease the rates of perioperative complications. The correlation between nephrometry scores and OT has been investigated and a significant correlation between OT and nephrometry scores has been demonstrated (13,22). Contrary to the literature findings, in our study none of the nephrometry scores were significantly correlated with OT. To our knowledge, factors such as patient characteristics, surgical history, difficulty of hilar dissection affect OT more than tumor size and location. In particular, the thickness of perinephric fatty tissue and adherent perirenal adipose tissue significantly and adversely affects the dissection process and thus OT. Khene et al. (23) reported that patients with adherent perirenal adipose tissue had a more significant blood loss, prolonged OT, and conversion to RN. Macleod et al. (24), as for that, showed that the thickness of the perinephritic fatty tissue, especially in the medial and posterior, increased OT. The Mayo Adhesive Probability score predicts the presence of adherent perinephritic fatty tissue based on radiological and clinical data (25). Therefore, it would be more logical to use a

Table 6. Correlation of nephrometric risk groups with surgical outcomes

	RENAL				PADUA				DAP			ABC		
	Low (n=36)	Intermediate (n=18)	High (n=8)		Low n=27	Intermediate n=23	High n=12		Low n=38	High n=24		Low n=38	High n=24	
WIT (mean ± SD)	19±5	23±5	26±7	**p=0.001**	18±5	23±6	23±6	**p=0.002**	19±5	25±6	**p<0.001**	19±5	24±6	**p=0.002**
OT (mean ± SD)	181±38	204±18	188±37	p=0.066	178±41	196±24	198±30	p=0.13	186±38	193±29	p=0.556	184±39	195±26	p=0.302
Complication clavien >0 (n%)	9 (25)	8 (44)	5 (62.5)	p=0.545	7 (25)	11 (47)	4 (33)	p=0.266	10 (26)	12 (50)	p=0.157	10 (26)	12 (50)	p=0.506
Complication major (n/%)	1 (2.7)	4 (22)	1 (12.5)	p=0.072	1 (3.7)	3 (13)	2 (16.6)	p=0.355	1 (2.6)	5 (20.8)	**p=0.018**	1 (2.6)	5 (20.8)	p=0.068
Blood transfusion (n%)	4 (11.1)	4 (22.2)	3 (37.5)	p=0.176	3 (11.1)	6 (26)	2 (16.6)	p=0.383	3 (7.8)	8 (33.3)	**p=0.011**	4 (10.5)	7 (29.1)	p=0.162
PHS (mean ± SD)	4±2	5±4	5±2	p=0.286	4±2	5±3	5±2	p=0.221	4±1	6±4	**p=0.006**	4±2	5±3	p=0.322
MIC success (n%)	17 (47.2)	8 (44.4)	2 (25)	p=0.454	13 (48.1)	9 (39.1)	5 (41.6)	p=0.173	20 (52.6)	7 (29.1)	**p=0.008**	16 (42.1)	11 (45.8)	p=0.517
SMP (n%)	1 (2.7)	2 (11.1)	3 (37.5)	**p=0.002**	1 (3.7)	1 (4.3)	4 (33)	**p=0.011**	0 (0)	6 (25)	**p=0.003**	4 (10.5)	2 (8.3)	p=0.543

RENAL: Radius, exophytic/endophytic properties of the tumor, nearness of tumor to the deepest portion to the collecting system or sinus, anterior/posterior descriptor and the location relative to the polar lines, PADUA: Preoperative aspects and dimensions used for an anatomical, DAP: Diam-eter-axial-polar, ABC: Arterial based complexity, WIT: Warm ischemia times, OT: Operation times, PHS: Postoperative hospital stays, MIC: Margin, ischemia, complications, SMP: Surgical margin positivity, SD: Standard deviation, Mann-Whitney U, Kruskal-Wallis, chi-square and Fisher's Exact tests were used

nephrometry score that also considers perinephric fatty tissue thickness to predict OS.

RENAL and PADUA scores have been used most prevalently. In a meta-analysis of 51 published studies conducted on nephrometry scores in 2019, the ability of all nephrometry scores to predict surgical outcomes was examined (26). Due to this meta-analysis, RENAL and PADUA scores, which are the first-generation scores, were found to be more successful than other scoring systems. Despite that, some results in our study contradict the results of this meta-analysis. In our study, as supported by some publications, DAP score was superior to RENAL and PADUA scores in general and especially in estimating MIC achievement rates. Yoshida et al. (27) stated that the DAP score was more predictive of WIT and median blood loss than the RENAL score, while Naya et al. (28) stated that the DAP score showed a better correlation with the choice of surgical method (laparoscopic/open) than the RENAL score. Indeed, DAP score is "simply the enriched" version of the RENAL score. Namely, in the index study in which the DAP score was defined, by removing parameters with low predictivity such as "position relative the polar lines" and "anterior/posterior location" in the RENAL score from the system and integrating it with the C-INDEX score, DAP score has been optimized and made easier to calculate (5). Besides, the cut-off values in the tumor size parameter were changed as they were thought to be too stringent. These moves explain why the DAP score is superior to the RENAL score.

In our study, ABC and PADUA scoring systems had partially lower predictivity relative to DAP and RENAL systems in foreseeing perioperative outcomes. In line with our results, the study of Antonelli et al. (22), the ABC NSS has not been shown to be superior to the RENAL and PADUA systems in terms of predicting perioperative outcomes. The ABC scoring system may include tumors of different complexity in the same category. This system needs to be better defined, in terms of other anatomical characteristics (for example; such as tumor size, distance from the collecting system, and renal sinus). We think that some parameters of the PADUA NSS, such as polar location and renal contours, reduce the predictive feature of this score. Our opinion was also supported by Minervini et al. (29) They investigated the predictive values of the parameters of the score separately and the PADUA score evaluated and showed that only endophytic/exophytic ratio, renal sinus invasion, collecting system invasion, and tumor size had significant predictive values. Ficarra et al. (30) who defined the PADUA system in 2009, tried simplifying this scoring system, and 10 years later, in 2019, they developed a new scoring system called Simplified Padua Renal. In this publication, parameters as the polar location and collecting system invasion were excluded from the system, and their novel 4-parameter system was found to be similar to the original PADUA system in predicting complication(s). Therefore, parameters with low predictivity should not be included in the criteria of the PADUA scoring system.

Study Limitations

Predominant strength of our study is the demonstration of the higher predictive value of DAP scoring system in foreseeing the MIC achievement rate relative to the first-generation NSSs. However, retrospective design of the study, and small number of patients were the limitations of our study. Nevertheless, in the literature, series with a larger number of patients have compared nephrometry scores in cases undergoing open, laparoscopic or robotic methods in various combinations. Since we believe that surgical technique may affect the results independently of nephrometry scores, only laparoscopic surgery patients were included in our study. Hence, we think that although our study group consisted of a small number of patients, it was more homogeneous. As another study limitation, the surgeries were performed by different surgeons. We conceive that the experience of the surgeon seriously affects the results. Accordingly, performing all operations by a single experienced surgeon may provide a more objective evaluation of the predictive value of nephrometry scores.

Conclusions

In conclusion, DAP score is a strong predictor of pre-LPN MIC achievement and complications.

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Ethics

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Original Article

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The Evaluation of Goal-Directed Antibiotics Prophylaxis Applied Via Rectal Swab Before Transrectal Ultrasound-Guided Prostate Biopsy

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Abstract

Objective: This study examined bacterial resistance to antibiotics administered for prophylaxis in rectal swaps taken before biopsy in patients who underwent transrectal ultrasound-guided prostate biopsy (TRUS).

Materials and Methods: This prospective study evaluated 251 patients who underwent TRUS in the clinic between January 2015 and December 2016. The patients were administered ciprofloxacin one day before the biopsy, the day of the biopsy, and five days after the biopsy. Urinalysis of patients was performed before biopsy and those with active infection were excluded from the study. Swap samples of patients were taken from the rectal mucosa before the biopsy. These samples were cultivated in blood agar and EMB growth medium. *E. coli* and *Klebsiella* reproductions were assessed. Antibiogram tests were studied in terms of resistance/sensitivity after identifying these bacterial subgroups.

Results: In the comparison of resistance and sensitivity of microorganism-independent antibiotics, the highest resistance was detected in amoxicillin (70%). The resistance to ciprofloxacin was 41.8%. The highest sensitivity was detected for fosfomycin (97.6%) and ceftazidime (91.6%). Extended spectrum beta-lactamase (ESBL) positivity was detected based on the bacterial species (p=0.001). The study found that ESBL positivity did not affect prostatitis development (p=0.447). The study also found that prostatitis development was not based on ciprofloxacin sensitivity/resistance in the rectal swap (p=0.803). A total of 105 patients showed resistance to ciprofloxacin. Prostatitis development was observed in 5 (4.8%) of these patients. Prostatitis development was observed in 11 (4.3%) of 251 patients.

Conclusion: According to the results of this study, antibiotic prophylaxis for rectal swab culture taken before TRUS does not affect prostatitis development after the biopsy. Although rectal swap guided goal-oriented prophylaxis does not reduce infective complications, it may be beneficial so as not to administer additional antibiotics to patients.

Keywords: Antibiotherapy, benign prostatic obstruction, prostate needle biopsy, prostatitis

Introduction

Prostate cancer is one of the most common types of cancer among men and is ranked the second among deaths due to cancer after lung cancer (1). The main diagnostic methods for prostate cancer are digital rectal examination (DRE) and the measurement of prostate-specific antigen (PSA) in blood. However, the definitive diagnosis of prostate cancer is made by histopathological examination. Transrectal ultrasound guided prostate biopsy (TRUS) is the standard technique used in the histopathological examination for the diagnosis of prostate cancer (2). Despite generally being a safe and well-tolerated process, different complications are reported in 50% of patients after the biopsy. These complications are pain, hematuria, urinary retention and infection (3). The incidence of urinary tract infection reported after TRUS changes between 2% and 6%. The incidence of severe sepsis settings accompanied by bacteremia is between 0.1-2.2% (4). It is recommended to use antimicrobials before the biopsy to prevent infectious complications after the surgery (5). Thus, fluoroquinolones are usually preferred as the first option in prophylaxis choice (6). However, increasing

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resistance to fluoroquinolone use has been associated with increased infection rates after biopsy in many countries (7,8). The new recommendation is screening of patients for resistant pathogens before biopsy instead of the classical approach (9). Some approaches recommend rectal swap culture-oriented antibiotic treatment in patients with risk factors to minimize serious infections induced by resistant rectal flora (10).

This study was conducted to examine bacterial resistance to antibiotics administered before biopsy in patients who underwent TRUS, and to investigate the effectiveness of taking rectal swap as prophylactic agent choice and which antibiotics group should be selected in the patients who underwent TRUS with the data obtained.

Materials and Methods

This prospective study was approved by the Local Ethical Committee (KAEK 2015/61). The sample size was calculated as 181 patients with the power analysis. This prospective study evaluated 351 male patients who underwent TRUS-guided TRUS in the Urology Clinic of our hospital between January 2015 and December 2016. Written informed consent was obtained from all patients who agreed to participate in this study. Each patient was administered antibiotic prophylaxis with ciprofloxacin for seven days, including one day before the biopsy, the day of the biopsy, and five days after the biopsy. Complete urinalysis was conducted on all patients, and the patients with active infection were excluded from the study. The patients underwent TRUS guided 12 core prostate biopsy. Abnormal DRE findings, serum total PSA value of more than 4 ng/mL, and/or the presence of abnormal PSA derivatives were determined as criteria for biopsy decision. Treatments of patients who received antiaggregant therapy were discontinued seven days before the biopsy after consultations with relevant clinics. Biopsy procedure was performed in the lateral decubitus position, using a standard gray-scale ultrasonography and 7.5 MHz rectal probe (Mindray M5, Shenzhen, P.R. China) guided 18 Gauge biopsy needle and an automatic biopsy gun (GEOTEK Estacore, Daventry, UK). Twelve aliquots were resected from each patient, and all aliquots were sent for pathological examination in individually numbered tubes. Patients with colorectal pathology, urinary infection due to resistant microorganisms that may increase the risk of developing infective complications after TRUS, with urethral catheter, heart valve prosthesis, and non-pathogenic bacterial reproduction in their rectal swabs were excluded from the study. After considering all exclusion criteria, 251 patients were evaluated. Swap samples of each patient were taken from the rectal mucosa before the biopsy and these samples were cultivated in blood agar and EMB growth medium. *E. coli* and *Klebsiella* species reproductions was examined in these growth mediums and the subgroups of these bacteria with reproduction were identified. Antibiogram tests in terms of resistance/sensitivity. The antibiotics to be studied in the antibiogram were determined as amoxicillin, ciprofloxacin, gentamicin, ceftriaxone, fosfomycin, trimethoprim sulfamethoxazole (TMP-SMX), ceftazidime, cefoxitin and cefazolin. Patients with a fever above 38.5, polyuria, urgency, dysuria, and reproduction in the urine culture were acute prostatitis in this study.

Statistical Analysis

The results of the study were analyzed using IBM SPSS V23. Chi-square test was used to compare the qualitative variables. Sensitivity rates were compared with the Marascuillo technique using the R Project package program. The results are presented as frequency (percentage). The significance level was $p<0.05$.

Power analysis was performed to determine the minimum number of patients to be included in the study considering previous studies. The number of patients to be included in the study was determined using the "simple random sampling" method based on the criteria of the number of patients who applied to the hospital in the last six months, and it was concluded that at least 181 patients should be studied at a 95% confidence level and 5% margin of error to obtain clinically significant results.

Results

Mean age was 66 (44-93), mean total PSA was 7 (0.6-704) ng/dL, mean free PSA was 1.8 (0.2-90) ng/dL and the mean prostate volume was 45 (18-220) cc (Table 1).

In the comparison of resistance and sensitivities of microorganism independent antibiotics, the lowest sensitivity was detected in amoxicillin. Ciprofloxacin was determined to be the antimicrobial agent with the second lowest sensitivity rate. The highest sensitivity rates were obtained for fosfomycin and ceftazidime (Table 2).

Considering the examination of ESBL positivity according to bacterial species, the positivity rate was 3.8% in *E. coli* while it was 25% in *Klebsiella* (p=0.001) (Table 3).

Table 1. Patient's demografic data

	Mean	Minimum	Maximum
Age (Year)	66.0	44.0	93.0
Total PSA (ng/dL)	7.0	0.6	704.0
Free PSA (ng/dL)	1.8	0.2	90.0
Prostate volume (cc)	45.0	18.0	220.0

PSA: Prostate-specific antigen

Table 2. Comparison of the sensitivity rates of antibiotics

	Sensitive	Resistant
Amoxicillin	75 (29.9%)	176 (70.1%)
Ciprofloxacin	146 (58.2%)	105 (41.8%)
Ceftriaxone	192 (76.5%)	59 (23.5%)
TMP-SMX	149 (59.4%)	102 (40.6%)
Ceftazidime	230 (91.6%)	21 (8.4%)
Phosphomycine	245 (97.6%)	6 (2.4%)
Cefoxitin	218 (86.9%)	33 (13.1%)
Cefazolin	202 (80.5%)	49 (19.5%)
Gentamicin	208 (82.9%)	43 (17.1%)

TMP-SMX: Trimethoprim sulfamethoxazole

A total of 105 patients showed resistance to ciprofloxacin. Prostatitis development was observed in 5 (4.8%) of 105 patients with ciprofloxacin resistance. Prostatitis development was observed in 6 (4.1%) of 146 patients without ciprofloxacin resistance. While the rate of sensitivity to ciprofloxacin was 54.5% in patients who developed prostatitis, it was 58.3% in patients who did not develop prostatitis. There was no difference between the results. The study determined that prostatitis development is not based on sensitivity/resistance to ciprofloxacin in rectal swab (p=0.803) (Table 4).

Considering the relationship between ESBL positivity and the development of prostatitis development, the ESBL positivity rate was 5% in those who did not develop prostatitis while ESBL was found to be negative in those who developed prostatitis. The study found that ESBL positivity was not effective in prostatitis development (p=0.447) (Table 5).

This study found the ciprofloxacin resistance was 72.7% in urine culture antibiograms of patients who developed prostatitis (Table 6).

Discussion

Histopathological examination and TRUS-guided TRUS are needed for the definitive diagnosis of prostate cancer in today's world (11). Although different complications may occur after TRUS, most serious complications are due to infectious causes (12). The lack of standard definitions of infectious complications, and differences in the biopsy technique and patient preparation before biopsy make it difficult to objectively determine the incidence of these complications (12,13). Therefore, antibiotic prophylaxis is often administered peroperatively to protect the patient from infectious complications and is also recommended as guidelines. Ciprofloxacin, recommended in many clinical practices and guidelines, is routinely used without goal-oriented examination. Studies conducted because of an increase in the frequency of urinary tract infections that develop due to ciprofloxacin-resistant bacteria after TRUS reveal the *E. coli* colonization resistant to fluoroquinolone in the rectum (14). Despite the different prophylaxis regimens performed, the rates of development of acute prostatitis after biopsy in the literature changes from 0% to 37% (15,16,17). This rate was detected as 4.3% in this group of patients considering the evaluation of *Klebsiella* and *E. coli*. The most common factor in the patients who developed an infection after the prostate biopsy was *E. coli* (*E. coli* in 10 patients, *Klebsiella* in 1 patient). Considering all the patients with infection, ciprofloxacin resistance was detected as 72.7% in urine culture antibiograms. Considering that 10-20% fluoroquinolone resistance rates were reported in patients with *E. coli* in urine culture after TRUS in various studies, it can be said that the ciprofloxacin resistance rate in our patient group with prostatitis is quite high (18,19).

The literature reported the discontinuation of the use of ciprofloxacin in prophylaxis or new prophylaxis administrations with different combinations in which Ciprofloxacin is included (20,21,22,23). Although positive results and recommendations regarding individual-specific and goal-oriented prophylaxis administrations by taking rectal swabs and studying antibiotics in addition to a general prophylaxis application are reported, some studies show otherwise. Singh et al. (24) focused on the concept of targeted prophylaxis and applied prophylaxis by performing rectal swabs and antibiogram evaluations in all 247 patients whom they prospectively applied biopsy. It has been reported that only two patients (0.9%) developed a fever and no patients developed sepsis. This rate is quite low compared to the rate found in this study as 4.3%. The same study determined a fluoroquinolone resistance of 41.7% in rectal swabs. A new study by Dai et al. (25) conducted with 487 patients showed that prostate biopsy prophylaxis based on rectal swab results taken before biopsy reduced infective complications from 2.9% to 1.9% compared with empirical prophylactic antibiotic therapy. A recent study conducted in North America reported a significant decrease in hospitalization from 1.19% to 0.47% compared to the historical practice of empirical antibiotic prophylaxis after the addition of antibiotic prophylaxis according to culture results (26). Taylor et al. (27) found ciprofloxacin resistance in 20% of patients in their study conducted to detect fluoroquinolone resistance in rectal swabs. In their study conducted with 457 men, they found that goal-oriented antimicrobial prophylaxis reduces infective complications, while 38 rectal swabs taken before biopsy can prevent one infective complication. Considering this rate, although it suggests that rectal swab sampling before biopsy may cause a serious cost, Qi et al. (28) demonstrated that targeted antibiotic prophylaxis with rectal swab culture can be a cost-effective way to reduce increased fluoroquinolone resistance.

Table 3. Comparison of EBSL positivity based on the type of bacteria

		ESBL			
		Negative	Positive	Test statistic	p
Bacteria	*E. coli*	230 (96.2%)	9 (3.8%)	$\chi2$ =11.317	0.001
	Klebsiella	9 (75%)	3 (25%)		

Frequency (percentage), χ^2: Chi-square test statistic, ESBL: Extended spectrum beta-lactamase

Table 4. Comparison of prostatitis development and ciprofloxacin resistance/sensitivity

		Ciprofloxacin			
		Sensitive	Resistant	Test statistic	p
Prostatitis	Negative	140 (58.3%)	100 (41.7%)	$\chi2$ =0.062	0.803
	Positive	6 (54.5%)	5 (45.5%)		

Frequency (percentage), χ^2: Chi-square test statistic

Table 5. Examination of the relation between prostatitis development and ESBL

	ESBL			
Prostatitis	Negative	Positive	Test statistic	p
No prostatitis development	228 (95%)	12 (5%)	$\chi2$ =0.578	0.447
Prostatitis development	11 (100%)	0 (0%)		

Frequency (percentage), χ^2: Chi-square test statistic, ESBL: Extended spectrum beta-lactamase

But some authors expressed the opinion that targeted prophylaxis with rectal swab culture before TRUS does not affect the development of prostatitis after TRUS (29,30,31). Farrell et al. (30) conducted a study with 268 in 2017 and administered antibiotic prophylaxis for rectal swab culture to 152 patients and empirical antibiotic prophylaxis to 116 patients. Considering the analysis results of the study, they found the incidence of prostatitis development after TRUS as 4.3% and 0.66%, respectively, and found no statistical difference between the groups (p=0.08). A multicenter study by Liss et al. (29) in 2015 retrospectively examined the data of 5.355 patients and grouped them into 1803 patients in the prophylactic antibiotic group and 3.553 patients in the empirical prophylactic antibiotic group according to the rectal swab result. The development of prostatitis was detected in eight patients (0.4%) in the prophylaxis group according to the results of the rectal swab. In the group administered empirical antibiotic prophylaxis, the development of prostatitis was observed in 20 patients (0.6%). It was found that prophylaxis administered based on the rectal swab results did not statistically affect the development of sepsis compared with normal prophylaxis (p=0.568). It was observed that ciprofloxacin was sensitive in patients who developed prostatitis in the group administered prophylactic antibiotic prophylaxis based on the rectal swab results, while no prostatitis development was observed in five patients (60%) although ciprofloxacin prophylaxis was given. Ciprofloxacin resistance was observed in 105 patients in this study. Prostatitis development was observed in five (4.8%) of 105 patients with ciprofloxacin resistance while prostatitis development was observed in six (4.1%) of 146 patients without ciprofloxacin resistance. Ciprofloxacin sensitivity was detected in the rectal swabs of six (54.5%) of 11 patients who developed prostatitis while ciprofloxacin resistance was detected in the rectal swabs of five other patients (45.5%). There was no statistical difference in prostatitis development between two groups of patients with and without ciprofloxacin resistance in rectal swabs (p=0.803). Although there are different findings and opinions on this issue in the literature, the data of this study suggest that the development of prostatitis after TRUS is independent of possible ciprofloxacin resistance that will be detected because of the rectal swab, and that rectal swab culture is insufficient to predict the development of prostatitis.

An important issue examined in this study was whether ESBL positivity was effective in predicting the development of prostatitis. A study conducted in Korea reported the incidence of ESBL-secreting *E. coli* and *Klebsiella* as 3.8% and 1%, respectively (32). This study determined the rates of ESBL-secreting *E. coli* and *Klebsiella* as 3% and 25%. The rate of ESBL-positive *E. coli* in rectal swabs was found as 19% in another prospective study conducted with 400 patients in 2014 (33). However, no statistically significant difference was found between the development of prostatitis after biopsy and ESBL positivity in rectal swabs. This study detected ESBL-positive bacteria in rectal swabs of 12 (4.7%) of 251 patients (9 *E. coli*, 3 *Klebsiella*). ESBL positivity rate was 5% in the group of patients who did not develop prostatitis after biopsy, while all patients who developed prostatitis were found to be ESBL negative (p=0.447). The results of the study that ESBL positivity detected in rectal swab did not affect the development of prostatitis were consistent with the literature.

Although the findings discussed so far in this study show that the antibiogram study with rectal swabs and goal-oriented antibiotic prophylaxis is not effective, it is a fact that we are

Table 6. Comparison of prostatitis development and antibiotics resistance/sensitivity in rectal swab and urine cultures

		Urine	Rectal	Test statistic	p
Amoxicillin	Sensitive	3 (27.3%)	4 (36.4%)	Z=-0.46	0.646
	Resistant	8 (72.7%)	7 (63.6%)		
Ciprofloxacin	Sensitive	3 (27.3%)	6 (54.5%)	Z=-1.35	0.176
	Resistant	**8 (72.7%)**	5 (45.5%)		
Ceftriaxone	Sensitive	7 (63.6%)	9 (81.8%)	Z=-0.98	0.328
	Resistant	4 (36.4%)	2 (18.2%)		
TMP-SMX	Sensitive	5 (45.5%)	10 (90.9%)	Z=-2.62	0.009
	Resistant	6 (54.5%)	1 (9.1%)		
Ceftazidime	Sensitive	7 (63.6%)	10 (90.9%)	Z=-1.61	0.107
	Resistant	4 (36.4%)	1 (9.1%)		
Phosphomycine	Sensitive	10 (90.9%)	11 (100%)	Z=-1.05	0.294
	Resistant	**1 (9.1%)**	0 (0%)		
Cefoxitin	Sensitive	7 (63.6%)	11 (100%)	Z=-2.51	0.012
	Resistant	4 (36.4%)	0 (0%)		
Cefazolin	Sensitive	4 (36.4%)	10 (90.9%)	Z=-3.23	0.001
	Resistant	7 (63.6%)	1 (9.1%)		
Gentamicin	Sensitive	9 (81.8%)	11 (100%)	Z=-1.56	0.118
	Resistant	2 (18.2%)	0 (0%)		

Frequency (percentage), χ^2: Chi-square test statistic, TMP-SMX: Trimethoprim sulfamethoxazole

faced with a serious resistance to ciprofloxacin. It was found that the resistance rates to fosfomycin (9.1%), ceftazidime (36.4%) and ciprofloxacin (72.7%) in urine cultures in the group of patients who develop prostatitis are similar to the resistance rates found in rectal swabs taken in general. Considering the rectal swab culture resistance rates of the patients evaluated in this study, it was found that resistance rates to fosfomycin, ceftriaxone, ceftazidime and gentamicin were significantly lower than quinolone resistance in accordance with the literature. Thus, the use of non-quinolone antibiotics is necessary to pre-TRUS prophylaxis. However, studies evaluating this subject in a prospective randomized controlled manner are needed to determine the correct prophylaxis.

Study Limitations

The limitation of our study is all the patients with serum PSA below 4 ng/mL were not subjected to TRUS-Bx. Hence the sensitivity, specificity, positive and negative predictive values for PSA cut off of 4 ng/mL is not accurate in this study. The other limitation of our study, the antibiotic taken 1 day before the rectal swab culture may affect the results.

Conclusion

In the selection of prophylactic antibiotics for prostate biopsy result, which is the gold standard in the diagnosis of prostate cancer, antibiotic resistance via rectal swab culture taken before the procedure and/or goal-oriented antibiotic prophylaxis applied with ESBL do not affect the development of prostatitis after biopsy in patients. Although the contribution of goal-oriented prophylaxis administration has not been determined, the detection of high ciprofloxacin resistance found in the swab culture results in this study and the similarly high ciprofloxacin-resistant microorganism in patients with prostatitis revealed that the use of ciprofloxacin in prophylaxis should be seriously questioned. Although resistance to fosfomycin, ceftriaxone, ceftazidime, and gentamicin is been significantly lower than quinolone resistance, prospective randomized controlled trials on this issue are needed to determine the correct pre-TRIB prophylaxis.

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Ethics

Ethics Committee Approval: Approval for the study was obtained from Ondokuz Mayıs University Clinical Research Ethical Committee (approval no: 2015/16, date: 12.02.2015).

Informed Consent: Written informed consent was obtained from all patients who agreed to participate in this study.

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Authorship Contributions

Concept: E.A., Design: E.A., M.K., Supervision: M.A., Ö.G., M.K.A., L.I., Data Collection or Processing: A.B., Analysis-Interpretation: S.G., Writing: E.A.

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Case Report
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Paratesticular Liposarcoma: A Case Report

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Abstract

Paratesticular masses represent 2-3% of all scrotal masses and are usually benign tumors, most of them being adenomatoid tumors. Liposarcomas are rare malignant tumors originating from mesodermal tissue. About 200 cases have been reported in the literature. We encountered a case of paratesticular liposarcoma.
Keywords: Paratesticular liposarcoma, case report, scrotal masses

Introduction

Scrotal masses may be testicular or paratesticular in origin. Paratesticular masses are usually benign, and most of them are adenomatoid tumors. The paratesticular masses represent 2-3% of all scrotal masses (1). The anatomy of the paratesticular region includes the epididymis, spermatic cord, testicular tunica, epididymal and testicular appendix and traces of the residue. For this reason, the neoplasm arising from this region forms a heterogeneous tumor group (2). Scrotal ultrasonography is primarily used in the diagnosis of scrotal masses (3). We present a case with paratesticular liposarcoma.

Case Report

A 29-year-old man complained of mass in the scrotum was referred to our clinic. Two separate masses (the largest one is 3 cm in diameter) were detected independently of the left testicle on physical examination. Two adjacent sharply marginated lesions (partially echogenic and heterogeneous appearance) approximately 16x25 mm and 25x30 mm in size were reported in the left testis inferior in the ultrasonographic examination. No abnormality was detected in the tumor markers. Surgical removal of both the lesions was performed with scrotal incision. The lesions were found to be separate from the testis during the surgery. As the tumor markers are normal and the masses are separate from the testis, we considered it as a benign lesion and we performed mass excision in the first place. The pathological examination report was "compatible with atypical lipomatous tumor/well-differentiated (WDLPS) liposarcoma." Mouse double minute 2 homolog (MDM2) (-), S-100 and CDK4 (+) and Ki-67 positive staining stromal cells were detected in the immunohistochemical staining (Figure 1). The nearest surgical margin of the lesion was reported to be 1 mm. Magnetic resonance imaging (MRI) of the patient revealed left ectopic kidney and agenesis of the left seminal vesicle (Figure 2). Then, left orchiectomy and extended fat tissue excision from the paratesticular area to the perineum was performed with scrotal incision. The pathological examination revealed that the neoplasm was observed in a limited area within the mature fat tissues, and the surgical margin was reported to be intact. The patient was referred to the oncology council. The council decided that the patient to be transferred to the radiation oncology clinic for radiation therapy. No recurrence was detected at the 1-year follow-up. This case report was written after obtaining patient consent.

Discussion

Primary paratesticular neoplasms are very uncommon, mostly present in the spermatic cord (4). Liposarcomas are rare malignant tumors originating from mesodermal tissue (5). Paratesticular liposarcomas account for about 3-7% of paratesticular sarcomas (6). About 265 cases have been reported in the English literature (7). Paratesticular liposarcomas are usually seen in 50-60 years of age, but cases between 16 and 90 years of age have been reported in the literature (8).

Liposarcomas are often studied in four different groups. These are WDLPS or atypical lipomatous tumor, myxoid/round cell type, de-differentiated and pleomorphic type (9). WDLPS

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liposarcoma is a locally aggressive neoplasm and its recurrence rate is high (10,11).

Ultrasonography has a sensitivity of 95-100% in distinguishing extratesticular masses from intratesticular masses (10). However, ultrasonography provides little information on paratesticular sarcomas (5). Computed tomography and MRI can be more specific, fat components may be more easily distinguishable (3).

MDM2 and CDK4 are the most commonly used immunosensory agents in the diagnosis of liposarcoma (8,10). S-100 protein is positive in 90% of liposarcoma cases (10).

Radical orchiectomy and extensive excision of the surrounding tissues are recommended in the treatment (3,9,12). Inguinal orchiectomy cases with negative surgical margins, decreased morbidity and leads to ga goodprognosis (13). There is no additional benefit of routine lymphadenectomy (4,14). Liposarcomas are locally aggressive lesions and up to 50% recurrence rates have been reported (5). Even after orchiectomy, recurrence rates are reported as 25-37% (2). Some studies recommend radiotherapy for local control with the disease, but its effectiveness is uncertain (7,14). In cases with lymphatic invasion, high-grade tumors and positive surgical margins, cases

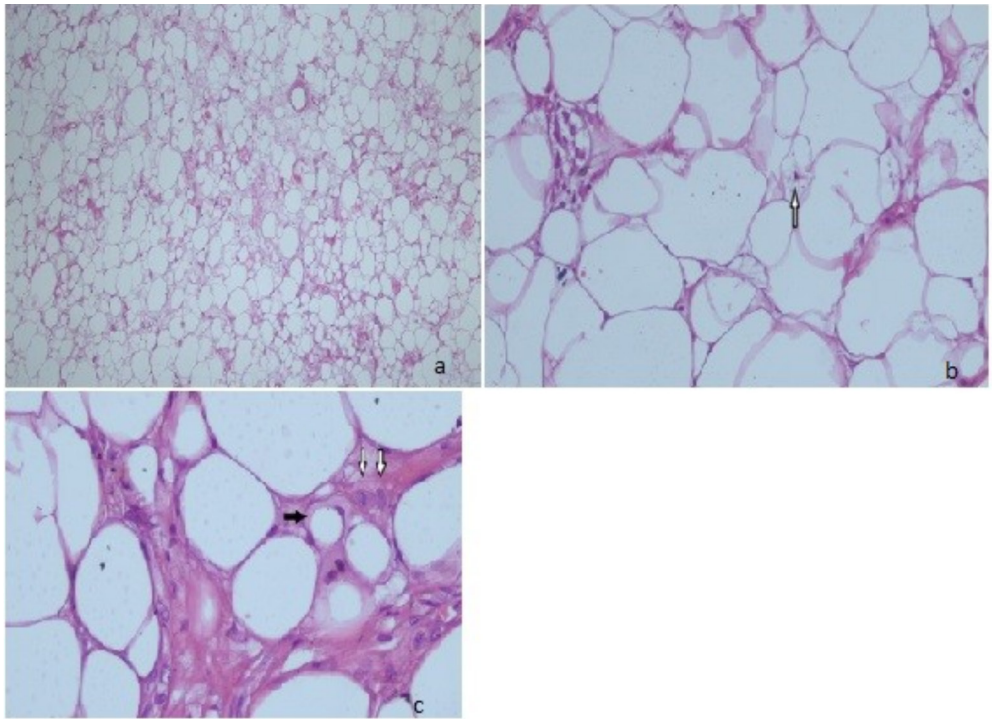

Figure 1. a. There are size and shape differences between adipocytes, fibrous areas (HE x40), b. Lipoblasts (arrow) (HE x200), c. Atypical stromal cells and lipoblasts

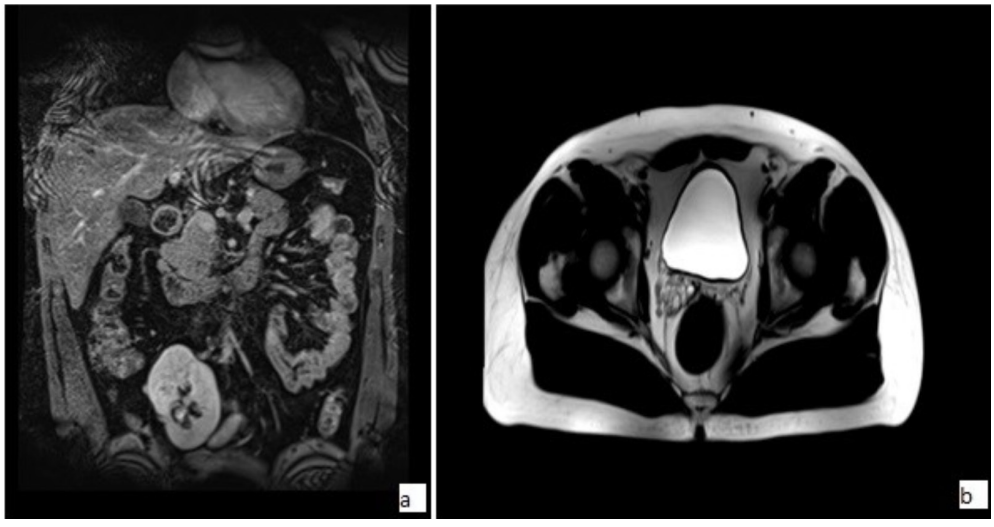

Figure 2. a. Ectopic left kidney in magnetic resonance imaging, b. Left seminal vesicle agenesis in magnetic resonance imaging

where radiotherapy and surgery were used together have been reported (15).

Responses to chemotherapy are generally low and gemcitabine and docetaxel are given in the first line chemotherapy. Eribulin is effective in advanced liposarcomas (11).

Some studies have reported that recurrence-free survival in paratesticular liposarcoma is 76% for 3 years and 67% for 5 years. In another study, 5-year survival was reported as 75% and recurrence was 50-70% (8). The 3-year recurrence-free survival rate was 79.8% in patients who underwent high inguinal orchiectomy, whereas it was 54.1% in patients who underwent tumor excision alone (7).

Conclusion

In conclusion, paratesticular liposarcomas should be kept in mind in the differential diagnosis of scrotal masses. After surgical excision, the possibility of recurrence should be considered.

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Ethics

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Case Report

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Case Report: Very Rarely Synovial Sarcoma with an Intrapelvic Location

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Abstract

Computed lower abdomen tomography and pelvic magnetic resonance imaging were performed in a 59-year-old male patient who presented with complaints of urinary retention and pelvic pain. It was observed that there was a mass lesion with a heterogeneous internal structure, located in the midline in the pelvic region, with a lobulated contour, approximately 14x13 cm in size, pushing the bladder forward and the rectum backward, containing cystic and contrasting solid areas. The patient underwent pelvic exploration and mass excision. These recent pathological findings were consistent with the diagnosis of synovial sarcoma (SS). SSs are tumors that occur mostly in the para-articular soft tissue of the extremities in young adults and are extremely rare in the primary pelvic region.
Keywords: Intrapelvic mass, synovial sarcoma, acute urinary retention

Introduction

Synovial sarcoma (SS) constitutes approximately 5 to 10% of all soft tissue sarcomas. It is a high-grade spindle cell tumor with t (X; 18) (p11;q11) chromosomal translocation detected in more than 95% of cases (1,2). SS is frequently detected in the extremities, especially in the periarticular region, and rarely shows intra-articular localization (3,4). Clinically, they appear as a palpable and painful soft tissue mass. It can also occur in other body parts such as the neck, tongue, larynx, mediastinum, the esophagus, heart, lung, abdominal wall, small bowel mesentery, vessels, and retroperitoneum. The intrapelvic location of the SS has been reported very rarely in the literature. Our aim in this case; to contribute to the literature by examining intrapelvic SS, which is a place where SS is very rare, clinically, radiologically, and histopathologically.

Case Report

A 59-year-old male patient was admitted with complaints of acute urinary retention and pain in the pelvic region. On digital rectal examination; fairly large, soft mass was palpated. The serum prostate-specific antigen level was measured at 1.31 ng/mL. In the complete urinalysis, eight erythrocytes were seen in each field and the urine culture was sterile.

A giant solid mass lesion in the pelvic region and bilateral hydroureteronephrosis due to possible mass compression were detected the abdominopelvic computed tomography (CT). In the pelvic magnetic resonance imaging (MRI) examination performed with an intravenous contrast material for the localization and characterization of the mass; a giant mass lesion with a heterogeneous internal structure was observed, located in the midline in the pelvic region, with a lobulated contour, approximately 14x13 cm in size, pushing the bladder anteriorly and the rectum posteriorly, containing cystic and contrasting solid areas. At the level of the pelvic floor, it was observed that the mass pushed the prostate of normal size forward, resulting in the displacement of the prostate toward the symphysis pubis. It was noted that the mass was separate from the prostate but closely adjacent to the posterior prostate capsule. Extraprostatic pelvic mesenchymal tumor or tumor originating from the prostate capsule was considered in the radiological differential diagnosis (Figure 1).

After the examination of the patient, his preoperative preparations were completed, his informed and informed

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consent was obtained, and he was hospitalized with a pelvic exploration planned. Under general anesthesia, in the supine position, after providing appropriate sterility conditions, a suprapubic transverse skin incision was made. The bladder was deperitonized. The bladder was opened with the help of a scalpel. In intraoperative observation; in the prostatic lodge after opening the bladder; the prostate was of normal size on inspection. However, upon the observation of giant cystic mass that pushed the bladder anteriorly, originating between the prostate and rectum and extending superiorly to the level of the umbilicus, the incision area was enlarged median below the umbilicus. A 5 cm long incision was made on the wall of the cystic mass. Approximately one liter of hemorrhagic cyst content and necrotic soft tissue pieces were removed from the cystic mass. Frozen tissue samples were sent for the diagnosis of pathological tissue. The frozen report; the tumor that is very rich in small cells, came as a mass that required examination of paraffin sections for malignancy exclusion. After the bleeding control was achieved, the layers were closed in the appropriate plan and the operation was terminated.

The tissues taken intraoperatively were sent to the pathology laboratory for pathological examination (Figure 2). It was decided to differentiate between benign and malignant tumors paraffin sections, as the diagnosis of frozen tissue was reported as a tumor rich in small cells by microscopic examination of irregular tissue pieces, which were macroscopically observed as 6 cm in diameter, and were sent for frozen examination. In the macroscopic examination of the material, which was completely sent after the operation, 14x13x1 cm, yellow-white colored, soft consistency, mostly necrotic tissue pieces were observed, which were considered irregular tissue pieces. On microscopic examination, monotonous tumor cells with small and spindle morphology, hyperchromatic nuclei, narrow cytoplasm, and a spindle pattern distribution within areas of intense necrosis and fresh bleeding were noted (1,5). No prostate and rectal tissue were observed in the histopathological examination of the tumoral mass, which was clinically expressed as originating between the prostate and rectum. In the immunohistochemical examination; while no staining was observed with pan-cytokeratin, desmin, smooth muscle actin, CD34, CD31, c-kit, and DOG-1, diffuse, strong, cytoplasmic staining was observed with vimentin. Approximately 50% proliferative activity was observe with Ki-67, and the case was reported as SS due to extensive, strong, cytoplasmic staining with TLE and BCL-2 (Figure 3) (1,2,5).

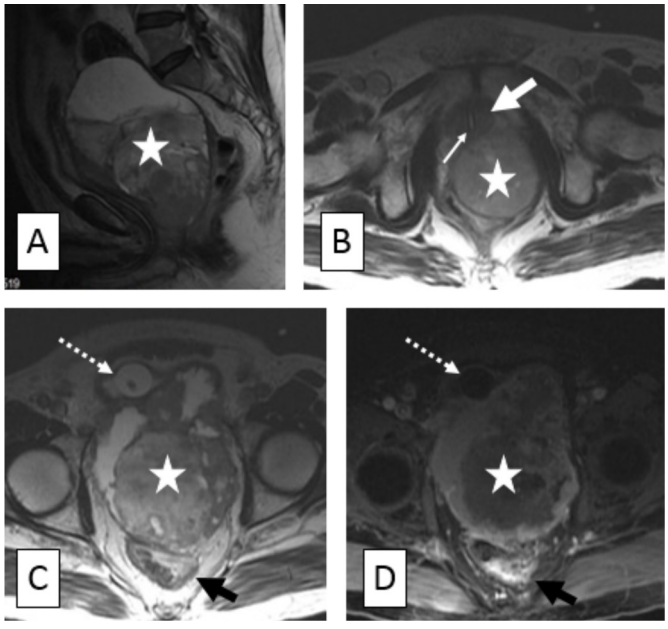

Figure 1. MRI examination; A. Sagittal T2 weighted image, B. Transverse T2 weighted image at the the pelvic floor, C. Transvers T2 weighted image, D. Transverse contrast-enhanced T1 weighted image.

A giant pelvic mass with cystic and solid areas (star) located between the bladder (dashed white arrow: urethral catheter balloon in the bladder lumen) and rectum (black arrow). The mass is adjacent to the prostate and pushes the prostate (white arrow) forward (thin white arrow: catheter in the prostatic urethra lumen)

MRI: Magnetic resonance imaging

Discussion

A SSs is are tumors originating from undifferentiated mesenchymal tissue and constitutes 5-10% of all malignant mesenchymal tumors. It shows slow growth in an expansile character. Usually 3-5. occurs between decades (2). The male/female ratio has been reported as 2/3. Although the most common locations are the extremities, it should be kept in mind that it can occur in any part of the body (3,4). Patients with extremely rare intrapelvic SS; may present with acute urinary retention, pain in the pelvic region, constipation, and lower urinary tract symptoms. In the presented case; benign prostatic hyperplasia was considered in the preliminary diagnosis of the patient who developed acute urinary retention and presented with lower urinary tract symptoms; SS was determined by imaging and histopathological examination of the mass removed after pelvic exploration.

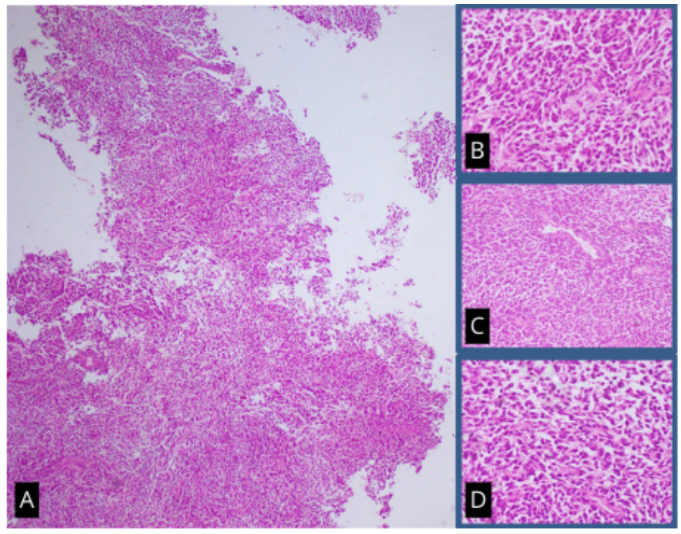

Figure 2. A. At small magnification; tumor cells with a spindle-like distribution, monotonous, hyperchromatic nuclei and narrow cytoplasm are observed (H&E X40). B. Among the tumor cells with spindle, hyperchromatic nuclei and narrow cytoplasm, an area where mitotic active cells can be selected is observed (H&E X400). C. Tumor cells with spindle-like patterns lined up around the vascular structure are seen (H&E X200). D. There is an area where the spindle structures of the tumor cells can be clearly observed (H&E X400)

Histologically, the tumor may be monophasic or biphasic, with varying proportions of epithelial and spindle cells. Specific immunohistochemical markers; may indicate vimentin and cytokeratin. In 90% of cases, there is a specific fixed translocation, usually a balanced reciprocal translocation in the form of t (X; 18) (p11.2;q11.2) (1,2). However, the presence of the said translocation was not investigated in the case examined. On CT examination, it typically presents as a soft tissue mass with slightly higher attenuation than muscle tissue, and there may be infiltration into adjacent tissues. While a heterogeneous density structure is observed, cystic density lesions containing fluid-fluid levels corresponding to bleeding areas can be rarely detected. The tumor usually shows a heterogeneous enhancement.

T1 and T2-weighted MRI usually show the heterogeneous signal intensity and may contain varying amounts of septation. Hyperintensity detected on T1 and T2-weighted images corresponds to bleeding areas. Fluid-liquid levels can be detected in 10-25% of cases (6,7,8). Mixed-signal appearance is detected in MRI examination in approximately one-third of the cases. In this case; in pelvic MRI examination; a giant mass lesion with a heterogeneous internal structure was observed, located in the midline in the pelvic region, with a lobulated contour, approximately 14x13 cm in size, pushing the bladder anteriorly and the rectum posteriorly, containing cystic and contrasting solid areas. At the level of the pelvic floor, it was observed that the mass pushed the prostate of normal size forward, resulting in the displacement of the prostate toward the symphysis pubis. It was noted that the mass was separate from the prostate but closely adjacent to the posterior prostate capsule. An extraprostatic pelvic mesenchymal tumor or tumor originating from the prostate capsule was considered in the radiological differential diagnosis.

Soft tissue sarcomas such as fibrosarcoma, malignant fibrous histiocytoma, rhabdomyosarcoma, malignant schwannoma, which may contain calcification, and malignancies such as hemangiopericytoma and lymphoma, which are observed as lesions in soft tissue density or attenuation on CT and MRI, often in which low-density or attenuated areas of necrosis are observed; it shows radiological features similar to SS. Although the radiological findings described in this study can be detected in other malignant tumoral lesions, which are more common, in the presence of the defined imaging findings, SS must be considered in the differential diagnosis.

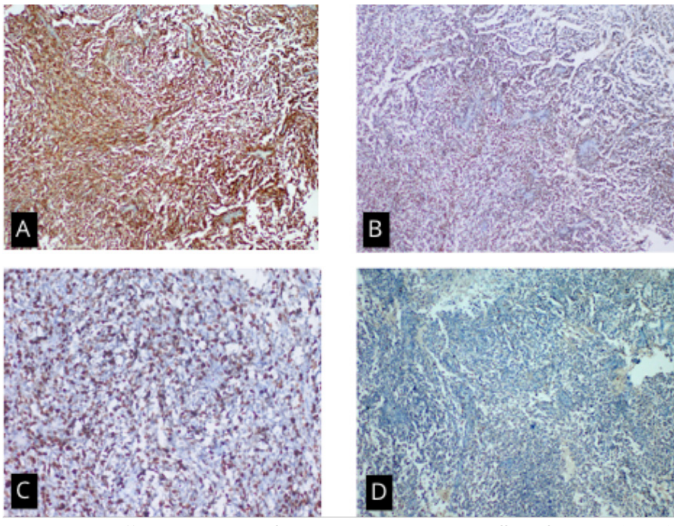

Figure 3. A. Diffuse strong cytoplasmic staining in tumor cells with BCL-2 (x100) B. Diffuse strong cytoplasmic staining in tumor cells with TLE (x100) C. 50% proliferative activity was observed in tumor cells with Ki-67 (X200) D. Diffuse pale cytoplasmic staining (x100) in tumor cells with EMA

EMA: Epithelial membrane antigen

The preferred treatment method in SSs; wide radical excision alone or along with radiotherapy. Healing is closely related to how radical the excision is. Tumor size, mitotic rate, and extensive tumor necrosis are considered as the most important prognostic determinants. Recurrence can be seen.

The incidence of SS was increasing day by day. We present a very rare case of intrapelvic SS causing acute urinary retention. This soft tissue tumor has a poor prognosis and may be confused with benign prostatic hyperplasia in the preliminary diagnosis, as it causes lower urinary tract symptoms (decreased urinary flow, incomplete emptying of the bladder, acute urinary retention, etc.). It is of great importance to report such cases for a better understanding of their pathophysiology and treatment options.

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Ethics

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Authorship Contributions

Concept: H.E.D., Design: Y.Y.K., Supervision: H.E.D., Data Collection or Processing: F.E.G.S., Analysis or Interpretation: F.D.A., Literature Review: A.N., Critical Review: Y.Y.K., Writing: A.N.

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Case Report

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A Giant Paratesticular Liposarcoma

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Abstract

Liposarcoma is a tumour originating from the mesoderm, which captures nearly twenty percent of all sarcomas. It first described by Lesauvage in 1845. Seventy percent of cases are extremity and retroperitoneum masses. Paratesticular liposarcoma is a rare entity. For treatment, a tumour-free margin radical orchiectomy with wide local excision and high ligation of the spermatic cord should be performed. If needed radiotherapy should be applied. An eighty-six-year-old male patient with paratesticular liposarcoma is reported in this article.

Keywords: Orchiectomy, sarcoma, testicular tumor, urologic oncology

Introduction

Liposarcoma is a tumor originating from the mesoderm, which captures nearly twenty percent of all sarcomas. It was first described by Lesauvage in 1845 (1). There are four known histological subtypes; well differentiated, dedifferentiated, myxoid and pleomorphic (1,2). As a soft tissue malignancy, liposarcomas are largely found in areas like head and neck, extremities, gastrointestinal tract and retroperitoneum (3). Seventy percent of cases are extremity and retroperitoneum masses (4). Paratesticular liposarcoma is a rare entity, with about two hundred case reports. Additionally, few these tumors are larger than ten centimeters, referred to as giant liposarcoma (1). It is mostly seen in the elderly population (4). We will present a paratesticular liposarcoma case. Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Case Report

Eighty-six-year-old male patient presented with a swelling in his left scrotum, which had been growing slowly for two years and recently caused pain. On physical examination, it was found that the left scrotum reached a size of at least fifteen centimeters and the ipsilateral testicle inside was not palpable. The patient underwent scrotal Doppler ultrasonography and blood tests were performed. The patient's full blood count values and testicular tumor marker test results were within normal limits. On ultrasonography, a solid mass lesion with an extra testicular location in the left scrotum, associated with the spermatic cord, reaching a diameter of fifteen centimeters, containing locally fatty tissue echoes was observed. To the proximal of this mass, there was a second mass lesion with a similar feature reaching eight centimeters in diameter in the inguinal canal. The total dimension of the two masses reached twenty-five centimeters. To confirm the diagnosis and check for abdominal and thoracic metastases, contrast-enhanced computed tomography (CT) was performed. No other mass was found. The features of the mass were also were consistent with liposarcoma on CT.

In the surgery, the mass was reached by inguinal incision. The adhesions around it have been removed. It was observed that the mass extended to the spermatic cord. Invasion was detected macroscopically with the ipsilateral testis. During orchiectomy, mass removal was performed from the highest level of the spermatic cord that could be detected. After removal, a second specimen was removed from the residual spermatic cord with a new resection to determine the surgical margin. The surgery was completed without complications. The patient was discharged after one day of follow-up.

By the pathological evaluation, the gross examination of the well circumscribed lobulated paratesticular mass, the longest diameter was twenty-one centimeter (Figure 1). Hypo-spermatogenetic testis was entirely rounded by a tumor diagnosed as liposarcoma. Histopathologically, in most areas the liposarcoma was well-differentiated type without necrosis (Figure 2). Nevertheless, there were some areas containing

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prominent myxoid stroma in about 20% of the tumor (Figure 3). However, classical pattern of myxoid liposarcoma was detected in only one slide. Since fluorescence *in situ* hybridization examination for the *MDM2* gene applied for differential diagnosis between myxoid and well-differentiated liposarcoma types showed prominent amplification, the diagnosis of well-differentiated liposarcoma was made. Additionally, in one side tumor was characterized by increased cellularity and minimal atypia, which was interpreted as a possible early dedifferentiation area. The surgical margins were clear.

Discussion

Paratesticular liposarcoma is usually found in men over the age of forty with slowly developing scrotal swelling and stiffness (1,4). Pain is not essential, even if there is, it may develop slowly. They are difficult to distinguish from testicular masses, especially when the mass originates from the spermatic cord and extends to the lower part of the scrotum. It should also be distinguished from diseases such as inguinal hernia, epididymitis, or cord lipoma. Especially, cross-sectional imaging including the abdomen is valuable because it shows the inguinal canal level of the mass, the condition of the retroperitoneal lymph nodes and distant metastases. Biopsy was not recommended for diagnosis. Performing CT or magnetic resonance imaging (MRI) can lead to a more definitive diagnosis. CT and MRI are successful in diagnosing liposarcomas and detecting compression or invasion of nearby organs. Some imaging studies, especially with retroperitoneal liposarcomas, found MRI more successful than CT in diagnosis and follow-up (5). Additionally, they provide high success in determining the histological type and stage of the tumour, with again MRI being better (5,6). Although there is no strong recommendation for the diagnosis, combined positron emission tomography (PET)/CT has been found to be particularly useful in detecting and staging recurrence in the follow-up after surgery or radiotherapy. Combined PET/CT is also superior to using these two methods alone (7).

For treatment, a tumour-free margin radical orchiectomy with wide local excision and high ligation of the spermatic cord is determined as the gold standard (1,4,8,9,10). Recurrence is strongly associated with incomplete excision, and care should be taken to prevent tumor spilling during the procedure (1,4). If margin status is positive or suspicious, radiotherapy should be applied to the inguinal area and to the scrotum depending on the situation (8,9,10). Studies reported that with adjuvant radiotherapy there was no recurrence in median eighteen months of follow-up (11). It should be known that radiation treatment is effective for local control and for positive margin cases. Recurrence was associated with a poor prognosis. The effects of radiotherapy on the other testicle and the adjacent organs should be closely monitored. Data on the efficacy of adjuvant chemotherapy in paratesticular liposarcoma are limited. This is mostly because these masses are rare for sufficient studies and practice. Vincristine, cyclophosphamide and doxorubicin are known suitable agents for metastatic or positive margin paratesticular liposarcomas (12). For the follow-up, particularly cross-sectional imaging is recommended, starting at three months, then at six months, and annually thereafter. It is argued that the total follow-up time should be a minimum of ten years (4).

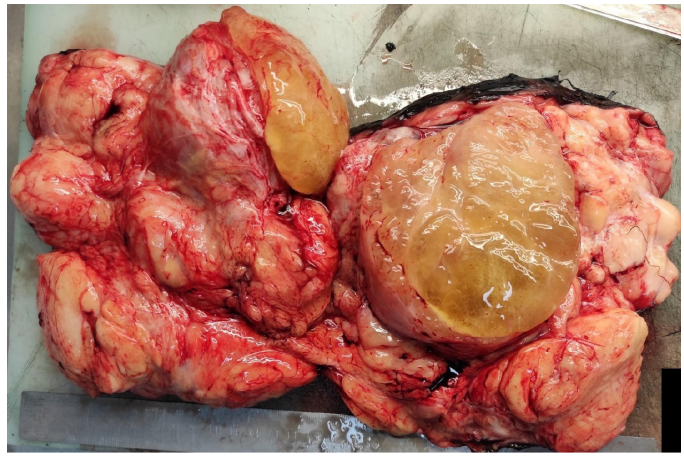

Figure 1. Macroscopically, the paratesticular tumor was lobulated and the cut surface was yellow and fatty

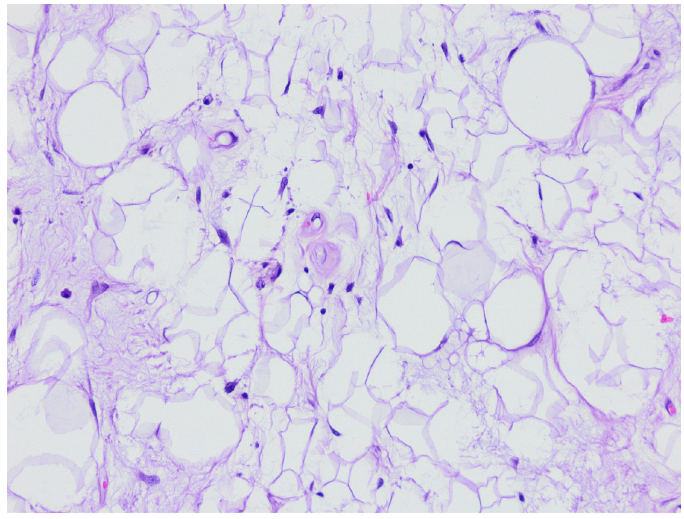

Figure 2. The well-differentiated areas of the tumor (HE, x200)

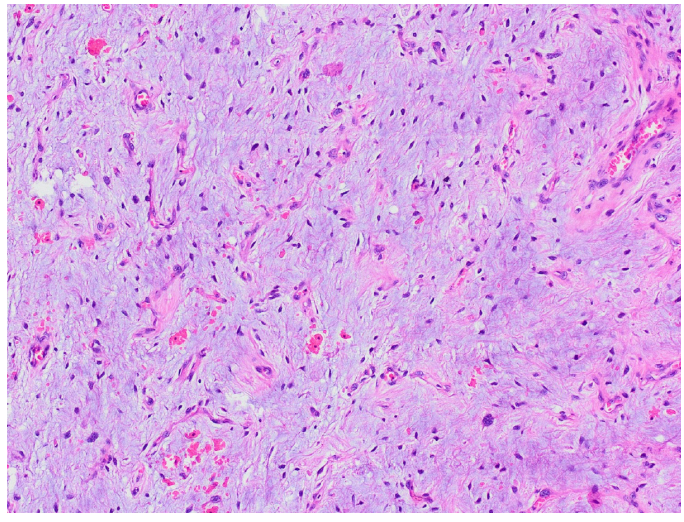

Figure 3. The areas reminiscent myxoid liposarcoma (HE, x200)

In a study of primary retroperitoneal well-differentiated liposarcoma cases that treated surgically, concomitant organ resection was observed in nearly half of the cases. However, the invasion was found to be approximately 15% in the pathology reports (13). Again, in this study, it was argued that routine concomitant organ resection did not have a positive effect on overall survival and disease-free survival, but in contrast, it increased the complication rate and hospital stay. In a similar study investigating the characteristics of salvage surgery in patients with recurrent retroperitoneal well-differentiated liposarcoma, it was observed that routine concomitant organ resection was applied to more than 50% of the patients, but the actual invasion was still about 15% (14). It has also been shown that concomitant organ resection increases the complication rate and hospital stay in these patients too. Both of these single-centre studies with retroperitoneal masses suggest the preservation of uninvolved organs if surgically possible. But as in our case, organ resection with the mass is inevitable in surgically detected invasions. Additionally, it should be remembered that these two studies were conducted with patients with retroperitoneal masses, not paratesticular masses, and because of anatomical features, it is riskier to intervene with nearby structures in the abdomen. In conclusion, it should not be forgotten that high ligation of the spermatic cord with tumour-free margins is the main treatment for paratesticular liposarcoma, as in this study.

Liposarcomas are tumors originating from the mesoderm, which are relatively rare and require a multidisciplinary approach. It should be kept in mind that diagnosis may be delayed due to anatomical features or patient's habits. Providing tumour-free surgical margin and applying suitable radiotherapy if necessary are key points in the treatment. Long-term cross-sectional imaging at regular intervals, including screening for distant metastases are necessary to follow-up.

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Case Report

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Giant Bladder due to Chronic Urinary Retension: A Rarely Case Seen in the Emergency Department a Case Report

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Abstract

The giant bladder (GB) is a very rare condition in the elderly population in which the bladder volume increases progressively, usually painlessly. It often develops due to chronic urinary obstruction caused by benign prostatic hyperplasia or neurogenic disorders. Here, we present a case of a GB with a volume of 5,500 mL developed due to chronic urinary retention in a 63-year-old male patient. Only 5 GB cases with a volume of 5 L or more have been reported in the literature. It can lead to a condition that disrupts the quality of life of the patient, such as kidney failure. Rarely, it can cause life-threatening conditions (such as pulmonary embolism) by compressing the large vessels in the abdomen. The GB should be considered in the differential diagnosis of patients admitted to the emergency department with complaints of voiding symptoms and progressive abdominal distension.

Keywords: Giant, obstruction, bladder, urinary retention

Introduction

The giant bladder (GB) is an extremely rare condition in aging men, and is characterized by a generally painless increase in bladder volume (1). It often develops due to chronic urinary obstruction caused by benign prostatic hyperplasia (BPH) or neurogenic disorders. It is a clinical entity that progresses slowly and possibly asymptomatically for a long time (2). Only five cases of GB with a volume of 5 L or more have been reported in the literature. In this study, we present a case of a GB with a volume of 5,500 milliliters in a 63-year-old male patient who was admitted to the emergency department with the complaint of abdominal pain and distension.

Case Report

A 63-year-old male patient without a history of systemic disease was admitted to the emergency department with complaints of abdominal pain, abdominal distension and mild difficulty in urinating. Vital signs of the patient were stable and no problems were detected. He did not have any systemic diseases, such as diabetes or neurogenic disorders. Although he previously stated that he was diagnosed with BPH at another center, he did not use any medication for his BPH. There was sensitivity in the abdominal examination. Digital rectal examination revealed growth that was compatible with the adenoma. Results of urinalysis and prostate specific antigen tests were within normal limits. Bacterial growth was not detected in the urine culture. On ultrasonography, a cystic lesion that filled the entire abdomen and compatible with the globe vesicale was described. Prostate volume was determined as 190 grams. On the whole abdominal tomography of the patient, a large bladder measuring 189x163x252 mm extending to the epigastric region was observed [Figure 1A (Sagittal section: red arrow)/1B (Coronal section)/1C (Transverse section: red arrow)]. Additionally, pelvic sagging of approximately 5 cm was observed at the bladder floor (Figure 1A: blue arrow). In transverse sections, it was observed that the bladder dome reached the level of the renal pelvis Figure 1C: bladder dome (red arrow), renal pelvis (blue arrow). Detrusor atony was found in the urodynamic study of the patient (Figure 2). Neurological examination was evaluated as normal by the neurology consultation. No abnormal findings were found on cranial and lumbar magnetic resonance imaging. Approximately 5.500 mL of residual urine was evacuated with a urethral catheter. The catheter of the patient was removed after a week of follow-up. Clean intermittent catheterization (TAC) was initiated by providing the patient with the necessary training. This article was written after obtaining informed consent form from the patient.

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Discussion

GB is a condition characterized by a progressive increase in bladder volume without pain due to chronic urinary retention (CUR). Unlike acute urinary retention, which is a sudden and painful condition, CUR is usually painless and can be palpated even after urinating. To diagnose CUR, post-void residual urine volume (PVRV) is measured in patients who can urinate, and bladder volume in men who cannot urinate. Neurological disorders such as insufficient detrusor activity, diabetic neuropathy, and causes such as BPH leading to prolonged bladder outlet obstruction may lead to CUR (3). In the cystometry of our case, decreased bladder filling pressure, atonic detrusor and high PVRV were detected. There was no dilatation in the upper urinary system. In the literature, a case of GB with a volume of 6 liters has been reported, which is called idiopathic because the etiological cause could not be determined (4). However, in this study, there is no data showing that a urodynamic study was conducted on the patient to detect bladder outlet obstruction or detrusor atony. The fact that all five cases with a bladder volume of 5 liters or more reported in the literature are male, is important in terms of showing the additional contribution of BPH to the development of GB, even if diabetic neuropathy is shown as an etiological factor in some (5).

Patients may present with complaints such as difficulty in urination in cases where the etiology is bladder outlet obstruction such as BPH. Additionally, GB may cause symptoms such as abdominal pain, distension and constipation by compressing the surrounding organs. Similarly, compression of the vena cava inferior may cause edema in the lower extremities due to vena cava inferior syndrome (VCIS) (2). However, BPH-related GB has been reported in 30 cases with VCIS with smaller PVRVs (1). Another case with pulmonary artery embolism due to VCIS caused by a 5 liters GB has also been reported (6). Although ultrasonography is the gold standard diagnostic tool, neighboring organs cannot be evaluated clearly due to the GB. Computed tomography can be performed to reveal the problems that may occur in adjacent organs due to external compression. Urodynamic tests should be performed to reveal bladder outlet obstruction or detrusor atony.

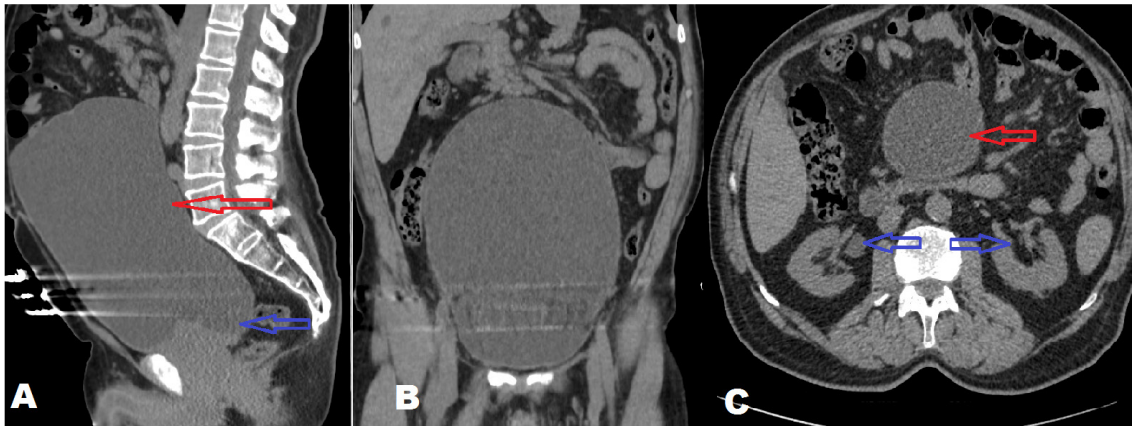

Figure 1. A. Sagittal view of the bladder on abdominal CT (red arrow). Approximately 5 cm of pelvic saging is observed at the bladder floor (blue arrow). B. Coronal view of the bladder on abdominal CT. C. Transverse sections of the abdominal CT show the bladder dome (red arrow) reaching the renal pelvis (blue arrow) level
CT: Computed tomography

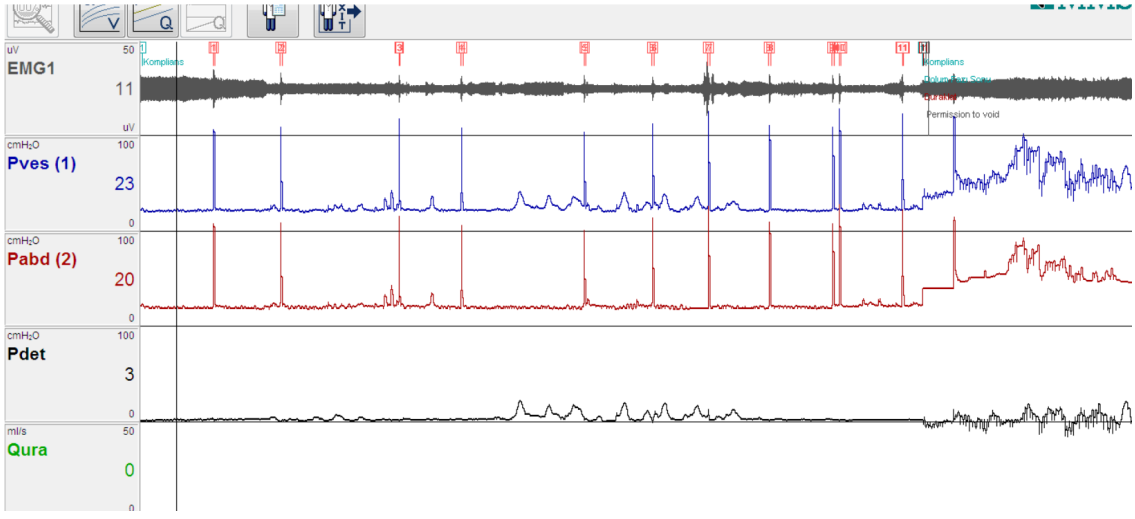

Figure 2. Image of the patient's urodynamic study

In the treatment, first, the patient should be catheterized and bladder decompression should be achieved. Etiological factors such as BPH or stones that lead to obstruction should be treated. Reduction cystoplasty can be performed in suitable cases. As in our case, the evacuation of the bladder and protection of the upper urinary system should be aimed by recommending a clean intermittent catheterization to patients with detrusor atony.

GB should be considered in the differential diagnosis of patients admitted to the emergency department with complaints of voiding symptoms and progressive abdominal distension. In addition to impairing the quality of life by causing renal failure, GB may cause life-threatening conditions such as pulmonary embolism because of compression on neighboring organs.

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Authorship Contributions

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