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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.

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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.

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The name of the journal is registered as "Bulletin of Urooncology" in international indices and databases and should be abbreviated as "Bull Urooncol" when referenced.

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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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,

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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.

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

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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)

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B. Case Reports

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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)

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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

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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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Bulletin of Urooncology

Editor in Chief

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Turkey Prostate Cancer Map 2021: Turkish Urooncology Association Prostate Cancer Database Report

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Abstract

Objective: This study aimed to present the data of patients with prostate cancer (PCa) whose detailed information was stored in the Urologic Cancer Database-Prostate, Urooncology Association, Turkey with the title of "Turkey Prostate Cancer Map 2021."
Materials and Methods: Patient data between 1995 and 2020 were retrospectively scanned. The age of the patients, their distribution according to age groups, symptoms during diagnosis, examination findings [digital rectal examination (DRE)], prostate-specific antigen (PSA) values, biopsy methods in the diagnosis, metastatic disease rates, treatment methods, and progression rates at follow-up were examined. These results were compared with the results of the previous report, namely "Prostate Cancer Incidence (Incidence) in Turkey," by the Urooncology Association in Turkey in 2009.
Results: This study analyzed the data of 5040 patients from 19 different centers. The mean patient age was 63.6 (37-97) years. The age distribution examination revealed that most patients (49.8%) were aged 60-69 years. Of the patients, 51.8% were symptomatic at the time of diagnosis. The presence of symptoms was determined in 88.6% in 2009 data. The DRE of patients revealed that 25% of patients had malignancy findings. The PSA distribution examination revealed a >10 ng/mL PSA value in 37.5% of patients. With the increasing use of magnetic imaging resonance (MRI) in PCa diagnosis over the years, increased MR-fusion biopsy rates have been observed. Considering the biopsy data, 91% of patients were diagnosed with a classical transrectal ultrasound-guided biopsy, whereas 9% were diagnosed with MR-Fusion biopsy. Fusion biopsies revealed that 23% of patients with Prostate Imaging-Reporting and Data System (PI-RADS) 4 lesion and 57% with PI-RADS 5 lesion were diagnosed with cancer.
Of the patients, 8.9% of patients had metastases during the initial diagnosis. This rate was 17% in 2009 data. The treatment methods examination after the diagnosis revealed that 73.9% of patients had undergone radical prostatectomy. This rate was 51.8% in 2009. Robotic and laparoscopic approaches, which are among the surgical modalities, have increased over the years. However, the most frequently applied modality in our country was open radical prostatectomy with 62.6%. Considering the follow-up data after treatment, 8.9% of patients had progression, of which 62.6% was biochemical, 30.2% was radiological, and 6.9% was a clinical progression.
Conclusion: Technological advancements for PCa diagnosis (MRI and MR-guided biopsies) are becoming a routine part of daily practice compared to the results of the "Prostate Cancer Incidence in Turkey" project in 2009. The comparative study results revealed that the rate of symptomatic and metastatic disease decreases at the time of diagnosis, and laparoscopic and robotic surgery methods are used at increasing rates for localized disease.
Keywords: Epidemiology, prostate, prostate biopsy, prostate cancer

Introduction

Prostate cancer (PCa) is the most frequently diagnosed male cancer and second leading cancer-related cause of death in males, where overall and cancer-specific survival rates are >90% even at 15 years of localized disease (1). Not many epidemiological studies on PCa in Turkey are reported; however, the Urooncology Association in Turkey conducted and reported "Prostate Cancer Incidence in Turkey" back in 2009 (2).This study aimed to present the data of patients with PCa, whose

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information was stored in the Urologic Cancer Database-Prostate, Urooncology Association in Turkey (UroCaD-P), as well as compare the current results with the previous report (2) and demonstrate the paradigm changes in PCa diagnosis and treatment.

Materials and Methods

The data source for the present study was the nationwide database of UroCaD-P. Data collection revealed 5,040 patients with PCa in UroCaD-P. The study data were collected by REDCap data collection software that was developed by Vanderbilt University and licensed by Urooncology Association in Turkey (3,4). All the data are kept in a secure server, and all personal information of patients was anonymized. Since this study is designed as a database report ethics committee approval was not obtained.

Study Parameters

-Demographic properties (age, place of birth, place of residence, etc.)

-Clinical Features (complaints, concomitant diseases, family history of PCa, etc.)

-Digital rectal examination (DRE) findings

• Prostate-specific antigen (PSA) levels at the time of diagnosis

• Pre-diagnostic magnetic resonance imaging (MRI)

-Biopsy modality

-Histopathologic findings on biopsy

-First-line treatment choices

-Preferred surgical modalities

-Histopathologic findings on surgery

-Pathological stage

-Follow-up data

Statistical Analysis

Statistical analyses were performed with python. The libraries used for analysis include Pandas (5,6), Numpy (7), and Scipy (7). JupyterLab (8) was used as the coding interface. The scaler variables were investigated using visual (Histograms, QQ Plots) and analytical methods (Kolmogorov-Smirnov, Shapiro-Wilk, and D'Agostino's κ^2 tests) to determine the normality of distribution. Descriptive statistics are given as mean and standard deviation if the scalar variable is distributed normally and as median and interquartile range if not. Case numbers and percent were given for statistical analysis of categorical variables. This is a sectional study, thus no hypothesis tests and p-values.

Results

The study consisted of 5,040 patients with PCa who were diagnosed between 1995 and 2021 from 19 different data-providing centers across Turkey. The patient's birthplace and place of the residence revealed that patients were from 80 different cities of Turkey. The mean patient age was 63.6±7.5 years. Most patients were between the ages of 60 and 69 years (Figure 1).

Of the patients, 51.8% had complaints at the time of diagnosis. The most common complaint was lower urinary tract symptoms (Figure 2). Most patients (75.1%) had no pathological finding on their initial DRE. The mean PSA value of patients was 16.2±27.5. Most patients (41.7%) had a PSA value between 4 and 10 (Figure 3).

Our results revealed that MRI before PCa diagnosis has become an increasingly preferred examination over the years (Figure 4). The most common lesion group in patients with PCa was Prostate Imaging-Reporting and Data System (PI-RADS) 4. MRI and MR-guided biopsies increased over the years; however, the ultrasound-guided transrectal biopsy was still the most commonly (90.9%) used technique for PCa diagnosis. The cancer detection ratio was slightly higher in MR-guided biopsies. Of the patients, 57.4% have a (PI-RADS) 5 lesion, thus PCa is diagnosed.

The metastatic disease ratio at the time of diagnosis was 8.9%. The use of Gallium (Ga)-68 prostate-specific membrane antigen (PSMA) positron emission tomography (PET)/computed tomography scintigraphy was determined in 198 patients, of whom 25.3% had metastasis.

The most commonly chosen treatment was radical prostatectomy (RP). Minimally invasive surgical techniques, such

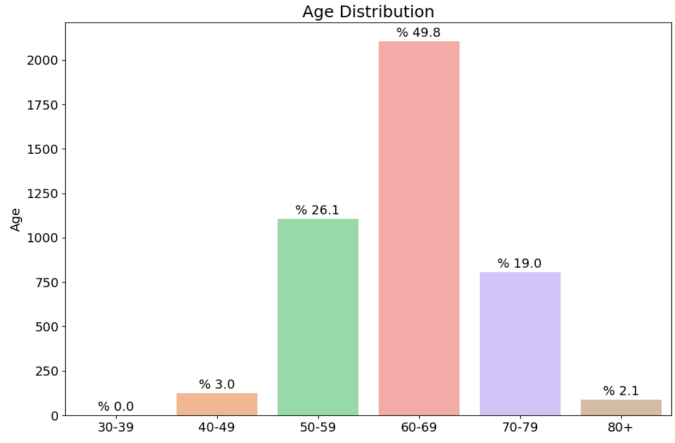

Figure 1. Age distribution of patients

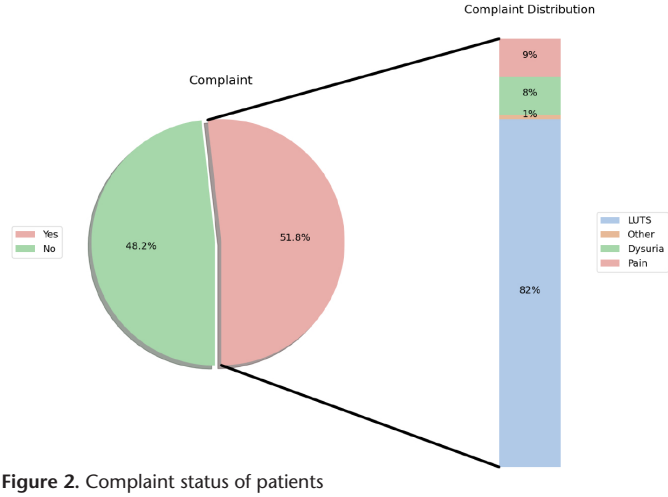

Figure 2. Complaint status of patients

as robotic or laparoscopic RP, have been increasing over the past years; however, open RP was still the most common RP modality (62.6%). The most seen pathological stage was T2, which was observed at the rate of 45.8% in patients after RP.

The follow-up revealed a progression of disease in 8.9% of patients. Biochemical progression was more commonly observed (62.9%) compared to radiological or clinical progression.

Discussion

Turkey had very little reliable data on the epidemiological aspects of PCa. In 2009, Eser et al. (9) published their epidemiological data and demonstrated PCa as the fifth most common cancer in İzmir, and revealed an increased PCa incidence over the years. In the same year, the "Prostate Cancer Incidence in Turkey" project is conducted with the Urooncology Association in Turkey and revealed that 39% of patients were between 60 and 69 years of age (2). Likewise, the most common age group in PCa diagnosis was 60-69 years (49.8%) in this study. Previous studies showed that PCa is rarely observed before the age of 65 years and is more commonly seen between the ages 65 and 70 years, which was in concordance with our study (10,11). Our study revealed that 51. 8% of patients were symptomatic at the time of diagnosis. The presence of symptoms was determined in 88.6% in 2009 data. The presence of complaints was quite different between the two studies; however, DRE positivity was similar (24.9% vs. 25.4%).

In 2009, most patients had a PSA level of <10 ng/dL, which was consistent with our results. The current report revealed that the mean PSA level at the time of diagnosis was similar to 2009 data and two other past studies conducted in Greece and Spain (11,12). Previous data suggests that patients have more advanced PCa with the increasing PSA levels (13,14). Current data also showed that patients with clinically significant PCa were in the higher percentage in the higher PSA level groups. More patients have PSA values of <4 ng/dL in this study compared to previous studies. Some clinics revealed that the threshold for normal PSA value is regarded as 2.5 ng/dL in Turkey and this may be the cause of the increased percentage of patients with lower PSA levels.

Multiparametric prostate MRI has been a promising modality for diagnosing clinically significant PCa (15,16) and is now regarded as one of the first-line imaging modalities before prostate biopsy in the European Association of Urology guidelines with strong recommendations (17). Consistently, data of the current report shows that the use of both MRI and MR-guided biopsies for PCa diagnosis is increasing in recent years.

The treatment methods examination after the diagnosis revealed that 73.9% of patients had undergone RP. This rate was 51.8% in 2009. Robotic and laparoscopic approaches, which are among the surgical modalities, have increased over the years. Similarly, a study in the US demonstrated increased minimally invasive surgical techniques over the years (18).The metastatic disease rate in our study was lower compared to the 2009 study, which may be due to an increased awareness of PCa in the population, increased availability of healthcare services, and increased usage of PSA testing by general practitioners. In recent years, Ga-68 PSMA PET is also used for screening patients with PCa for metastasis. A recent study revealed that the sensitivity and specificity of PSMA PET for lymph node metastasis wave 53.3% and 85.7%, respectively (19). Our study revealed a limited number of patients who had PSMA PET screening before initial treatment and metastasis ratio as 25.3%. A recent study observed the advanced disease in 35.3% of high-risk patients with PCa (20). Our study included not only high-risk patients but also low and intermediate-risk ones, thus our result seems to be in concordance with this recent study.

The progression rate was 8.9% for all the patient groups in our study. Most studies on progression focus on specific patient groups or risk factors (obesity etc.). This study is a population base report, thus further risk factor analysis for progression was not performed; however, our study demonstrates that in most patients, PCa progression is seen as a biochemical progression.

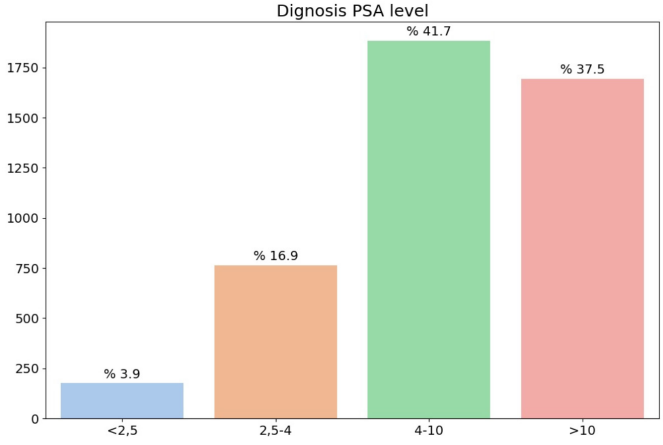

Figure 3. PSA levels at the time of diagnosis

PSA: Prostate-specific antigen

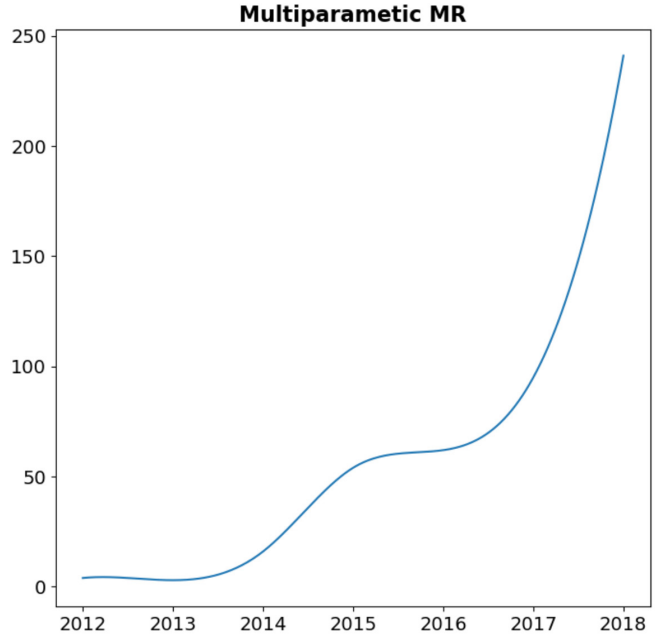

Figure 4. Usage of Multipararmetric MRI with time

MRI: Magnetic resonance imaging

Study Limitations

Our study is not without limitations. It is a population-based study, thus having more participating centers and patients would increase its strength; however, authors feel confident that results of this report could be generalized nationwide since all participating centers were referral centers in their region and all over Turkey.

Conclusion

Therefore, technological advancements for PCa diagnosis (MRI and MR-guided biopsies) are becoming a routine part of daily practice compared to the results of the "Prostate Cancer Incidence in Turkey" project conducted in 2009. The study comparative results revealed that the rate of symptomatic and metastatic disease decreases at the time of diagnosis, and laparoscopic and robotic surgery methods are used at increasing rates for localized disease.

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Publication: The results of the study were not published in full or in part in form of abstracts.

Contribution: There is not any contributors who may not be listed as authors.

Conflict of Interest: No conflict of interest was declared by the authors.

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Ethics

Ethics Committee Approval: Since this study is designed as a database report ethics committee approval was not obtained.

Informed Consent: All the data are kept in a secure server, and all personal information of patients was anonymized.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Supervision: S.E., G.A., S.S., S.A., L.T., Concept: İ.T., S.E., G.A., S.S., S.A., L.T., Design: İ.T., S.E., G.A., S.S., S.A., L.T., Data Collection or Processing: B.Ş., Analysis or Interpretation: B.Ş., Literature Search: B.Ş., Writing: B.Ş., S.Ç., İ.T.

References

1. Howlader N, Noone A, Krapcho M, et al. SEER cancer statistics review, 1975-2017. National Cancer Institute, 2020.
2. Zorlu F, Zorlu R, Divrik RT, et al. Prostate cancer incidence in Turkey: an epidemiological study. 2014;15:9125-9130.
3. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377-381.
4. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform 2019;95:103208.
5. Reback J, McKinney W, Den Van Bossche J, et al. pandas-dev/pandas: Pandas 1.0. 3. Zenodo, 2020.
6. McKinney W. Data structures for statistical computing in python. Proceedings of the 9th Python in Science Conference: Austin: TX; 2010. p. 51-56.
7. Virtanen P, Gommers R, Oliphant TE, et al. SciPy 1.0: fundamental algorithms for scientific computing in Python. Nat Methods 2020;17:261-272.
8. Kluyver T, Ragan-Kelley B, Pérez F, et al. Jupyter Notebooks-a publishing format for reproducible computational workflows. 2016. https://eprints.soton.ac.uk/403913/1/STAL9781614996491-0087.pdf
9. Eser S, Zorlu F, Divtik RT, et al. Incidence and epidemiological features of cancers of the genitourinary tract in Izmir between 1993-2002. Asian Pac J Cancer Prev 2009;10:491-496.
10. Siegel R, Naishadham D, Jemal A. Cancer statistics for hispanics/latinos, 2012. CA Cancer J Clin 2012;62:283-298.
11. Cózar JM, Miñana B, Gómez-Veiga F, et al. Prostate cancer incidence and newly diagnosed patient profile in Spain in 2010. BJU Int 2012;110:701-706.
12. Grivas N, Hastazeris K, Kafarakis V, et al. Prostate cancer epidemiology in a rural area of North Western Greece. Asian Pac J Cancer Prev 2012;13:999-1002.
13. Thompson IM, Ankerst DP, Chi C, et al. Assessing prostate cancer risk: results from the Prostate Cancer Prevention Trial. J Natl Cancer Inst 2006;98:529-534.
14. D'Amico AV, Whittington R, Malkowicz SB, et al. Pretreatment nomogram for prostate-specific antigen recurrence after radical prostatectomy or external-beam radiation therapy for clinically localized prostate cancer. J Clin Oncol 1999;17:168-172.
15. Bratan F, Niaf E, Melodelima C, et al. Influence of imaging and histological factors on prostate cancer detection and localisation on multiparametric MRI: a prospective study. Eur Radiol 2013;23:2019-2029.
16. Le JD, Tan N, Shkolyar E, et al. Multifocality and prostate cancer detection by multiparametric magnetic resonance imaging: correlation with whole-mount histopathology. Eur Urol 2015;67:569-576.
17. Mottet N, van den Bergh RCN, Briers E, et al. EAU - ESTRO - ESUR - SIOG Guidelines on Prostate Cancer 2020. European Association of Urology Guidelines. 2020 Edition. Vol presented at the EAU Annual Congress Amsterdam 2020. Arnhem, The Netherlands: European Association of Urology Guidelines Office; 2020.
18. Lowrance WT, Eastham JA, Savage C, et al. Contemporary open and robotic radical prostatectomy practice patterns among urologists in the United States. J Urol 2012;187:2087-2092.
19. Öbek C, Doğanca T, Demirci E, et al. The accuracy of 68 Ga-PSMA PET/CT in primary lymph node staging in high-risk prostate cancer. Eur J Nucl Med Mol Imaging 2017;44:1806-1812.
20. Klingenberg S, Jochumsen MR, Ulhøi BP, et al. 68Ga-PSMA PET/CT for Primary Lymph Node and Distant Metastasis NM Staging of High-Risk Prostate Cancer. J Nucl Med 2021;62:214-220.

Original Article

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Effects of Androgen Deprivation Therapy on Blood Lipids and Fasting Blood Glucose in Patients with Prostate Cancer

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Abstract

Objective: This study aimed to investigate the changes in the lipid profiles and fasting blood glucose (FBG) values of patients with prostate cancer, who underwent bilateral orchiectomy or started to use luteinizing hormone-releasing hormone (LHRH) agonists and additionally received anti-cyproterone acetate or bicalutamide, and compare these changes between alternative treatments.

Materials and Methods: This retrospective study included 66 patients with complete data. Patients' age, prostate-specific antigen values, prostate volumes, clinical stages, pathology results, type of androgen deprivation therapy, and total cholesterol (TC), low-density cholesterol, high-density cholesterol, triglyceride, and FBG values before and at 6 months after treatment were recorded. Metastatic was determined in 37 patients, whereas 26 had locally advanced and 3 had localized prostate cancer.

Results: The evaluation of all patients revealed an increased FBG (p=0.010) and low-density cholesterol (p=0.012) values was significant. The comparison of patients who underwent orchiectomy and those taking LHRH agonists revealed no difference between the two groups. The difference in the TC values was statistically significant between the cyproterone acetate and bicalutamide groups (p<0.001).

Conclusion: Bicalutamide significantly increases TC compared to cyproterone.

Keywords: Antiandrogens, hormonotherapy, lipid profiles, prostate cancer

Introduction

Prostate cancer is one of the most common cancers among males (1). Androgen deprivation therapy (ADT) has been frequently used to prolong survival and relieve symptoms in patients with prostate cancer. ADT forms the basis of treatment, especially in relapsed and metastatic prostate cancer (2), as well as adjuvant therapy in high-risk localized and locally advanced diseases (3,4). ADT can be surgically (bilateral orchiectomy) and medically [luteinizing hormone-releasing hormone (LHRH) agonist-antagonist and antiandrogens] applied (2). ADT provides significant clinical benefits; however, it is associated with an increased risk of diabetes and cardiovascular diseases and a wide variety of complications, such as hot flashes, anemia, sexual dysfunction, body composition changes, osteoporosis, and fractures (5,6,7). Some complications negatively affect the quality of life, whereas others may induce serious problems, including sudden cardiac death and myocardial infarction (8). Prostate cancer has a favorable prognosis, thus care should be taken when planning ADT due to its complications and patients should be followed up more closely. This study aimed to investigate the changes in the lipid profiles and fasting blood glucose (FBG) values of patients with prostate cancer, who underwent bilateral orchiectomy or started to use LHRH agonists and additionally received anti-cyproterone acetate or bicalutamide and compared these changes between alternative treatments.

Materials and Methods

The files of a total of 98 patients who were diagnosed with prostate cancer in our clinic since the beginning of 2014 and started LHRH agonists or underwent ADT after bilateral orchiectomy were retrospectively reviewed. The hospital patient information system and e-nabız (Personal Health System of Turkey) were screened to record the patients' age, prostate-specific antigen (PSA) values, prostate volumes, clinical stages, pathology results, type of ADT applied, and total cholesterol (TC), low-density cholesterol (LDL), high-density cholesterol (HDL), triglyceride (TG), FBG values before and at 6 months after treatment. This study included 66 patients with complete data, wherein 37 had metastatic, 26 had locally advanced, and 3 had localized prostate cancer. Patients with localized diseases constituted the high-risk group that did not

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accept surgery or radiotherapy. Maximal androgen blockade (MAB) was applied to 61 patients, whereas only LHRH analogs were initiated in 5 patients. Bilateral orchiectomy was performed in 25 patients and LHRH analogs were started in 41 patients. Among the patients receiving MAB, cyproterone acetate was started in 21 and bicalutamide in 40. The general characteristics of patients are presented in Table 1.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences version 17.0 software package. The normal distribution of variables was examined using histogram graphics and the Kolmogorov-Smirnov test. Mean, standard deviation, and median values were used to present descriptive statistics. Changes in measured values were compared between the groups with the repeated-measure analysis and within each group using the Wilcoxon test. Results with a p-value of <0.05 were considered statistically significant.

Approval was obtained from the Ethics Committee of Diyarbakır Gazi Yaşargil Training and Research Hospital with the date and number 772/29.05.2021.

Table 1. Clinical stages of patients and applied treatments

		n	%
Clinical stage	**Localized**	3	4.55
	Localized advanced	26	39.39
	Metastatic	37	56.06
ADT	**OX**	25	37.88
	LHRH	41	62.12
Treatment subgroup	**OX + cyproterone**	12	18.18
	OX + bicalutamide	14	21.21
	LHRH + cyproterone	9	13.64
	LHRH + bicalutamide	26	39.39
	LHRH	5	7.58
Antiandrogen	**Cyproterone**	21	31.82
	Bicalutamide	40	60.61
	None	5	7.58

ADT: Androgen deprivation therapy, LHRH: Luteinizing hormone-releasing hormone, OX: Orchiectomy

Table 2. Comparison of the pre-treatment and sixth-month values of all patients

	Before treatment	Sixth month	p-value
LDL	123.59±33.89	134.53±50.88	**0.012**
HDL	46.82±5.33	52.07±47.45	0.064
TC	190.80±2.37	199.09±47.53	0.301
TG	133.67±57.79	133.85±63.53	0.971
FBG	105.22±37.29	112.25±48.99	**0.010**

Wilcoxon test, LDL: Low-density cholesterol, HDL: High-density cholesterol, TC: Total cholesterol, TG: Triglyceride, FBG: Fasting blood glucose

Results

The mean and standard deviation values of age, PSA, and prostate volume of patients were 72.05±9.91 years, 96.47±133.44, and 55.55±28.03, respectively. The changes in the LDL, HDL, TC, TG, and FBG values were analyzed before and at the sixth month of treatment. Accordingly, the evaluation of all patients revealed a significant increase in the LDL and FBG values. However, no significant changes were observed in the HDL, TC, and TG values (Table 2).

The comparison of patients who underwent orchiectomy (n=25) and those who received LHRH (n=41) for prostate cancer treatment in two separate groups revealed no significant difference. Additionally, changes in the measured values were compared within the orchiectomy and LHRH groups. No significant changes were observed in the LHRH group, whereas the LDL and FBG values significantly increased in the orchiectomy group (Table 3).

Changes in the measured values of patients were also compared between the cyproterone acetate (Androcur®), bicalutamide (Casodex®), and non-antiandrogen (non-ADT) groups, which revealed no significant differences. The examination of changes within the groups revealed increased LDL, HDL, and TC in the bicalutamide group, a decreased TC value, and an increased FBG value in the non-ADT group (Table 4).

Five different subgroups of treatment were applied to the patients, of which statistical comparisons were made; however, their results were excluded in this manuscript due to the small number of patients in each subgroup.

Discussion

ADT benefits have been well accepted for selected patients. Over the last few decades, ADT has substantially increased; however, relatively little attention has been paid to its side effects (9). Males with prostate cancer have higher non-cancer mortality rates than those in the general cancer population, and some of the non-cancer deaths may be associated with treatment (10). Metabolic changes are frequently observed in males undergoing ADT, which may lead to an increased risk of type 2 diabetes, cardiovascular diseases, and metabolic syndrome, and may contribute to increased non-cancer mortality (11). Many studies in the literature discussed ADT without details concerning the drug or treatment methods. Thus, this study investigated the difference between different treatment alternatives in terms of lipid profile or FBG. Differences were determined between the antiandrogen groups (Table 4). Considering the possibility of serious side effects of such drugs, care should be taken in drug treatment selection and our related findings were discussed in detail.

Many publications investigated the effect of ADT on the lipid profile of patients and reported different results. However, the majority of the work suggests that ADT increases TC (12,13,14,15,16,17,18,19). The prospective study of Smith et al. (20) revealed no significant changes in the TC value after 6 months of ADT. Contrarily, a review of 15 studies published by Wolny-Rokicka et al. (21) in 2019 reported that ADT significantly increased TC. The current study evaluated all patients and

revealed no differences in TC changes. Additionally, no significant difference was found between the orchiectomy and LHRH groups in the changes in TC. No increase was observed in TC in the cyproterone group, whereas a significant increase was found in the bicalutamide group, with a statistically significant level. To the best of our knowledge, no literature study had compared the changes in the lipid profile of antiandrogens. Therefore, our findings were compared with the results obtained for bicalutamide and cyproterone in previous studies. Studies that used cyproterone revealed no significant changes (22,23) or a decrease in TC (24). Studies that used bicalutamide have revealed an increased TC (15,25). Our results seem to be consistent with the literature. Studies that examine the effect of ADT on the HDL level offer contradictory results. Studies reported that ADT increases HDL (12,13,14,15,17,19), whereas others indicated no changes in HDL with ADT application (16,18,20). Some studies revealed that ADT decreases HDL (26). A review by Wolny-Rokicka et al. (21) reported no significant changes in HDL. Our study evaluated all patients and revealed no significant changes in HDL. No significant difference was determined between the orchiectomy and LHRH groups in HDL changes. A significant increase was determined in HDL in the bicalutamide group, whereas no increase in the cyproterone group, without statistically significant differences between these two groups. Studies in the literature revealed that cyproterone reduces HDL (22,23,24). However, no significant changes were observed in HDL in studies that use bicalutamide (15,25). Therefore, our findings are not consistent with the literature.

Data obtained from research that examined the effects of ADT on LDL level are also conflicting. Some researchers report that ADT increases LDL (12,13,14,16,19,26), whereas others suggest no changes in LDL (15,20,22). Additionally, other studies revealed that LDL decreases with ADT (22,23,24,25,26). Wolny-Rokicka et al. (21) reported no significant change in LDL in their meta-analysis. The current study evaluated the whole sample and revealed a significantly increased LDL. The treatment group evaluation revealed a significantly increased LDL in the orchiectomy group but revealed no increase in the LHRH group, and the difference between the two groups was not statistically significant. Additionally, LDL significantly increased in the bicalutamide group but did not significantly change in the cyproterone group, without a significant difference between these two groups. Studies in the literature revealed that cyproterone reduces LDL (24) or without significant changes (22,23), whereas an increase in bicalutamide (15,25).

Studies that examine the effect of ADT on the TG level report either an increase (13,15,19,22,26) or no changes (14,16,17,18,20). Wolny-Rokicka et al. (21) reported that the TG value increased with ADT application. Our study revealed no significant changes in TG as evaluated in all patients together or different treatment groups were examined.

The literature review revealed that male hypogonadism is accompanied by an increased risk of insulin resistance and diabetes mellitus (27,28). A meta-analysis of 43 studies involved 6,427 males and revealed significantly lower total testosterone levels in males with type 2 diabetes than those without diabetes (29). Males with prostate cancer who take ADT are excellent examples of hypogonadism; therefore, they may also have insulin resistance and hyperglycemia. Conflicting results were reported in the literature concerning the effect of ADT on FBG. A prospective study of 133 patients by Bo et al. (12) compared patients who received ADT with those who underwent radical prostatectomy and did not receive any other treatment, as well as with a completely healthy group. The group that received ADT revealed no changes in FBG at the third month compared to the other two groups, whereas a significant difference was found at 12 months. A multicenter, prospective study conducted by Morote et al. (13) with 310 patients revealed a significantly increased FBG level at 6 and 12 months. A prospective study by Gagliano-Jucá et al. (14) included 73 patients and compared patients with prostate cancer using ADT to those with localized prostate cancer who had not received hormonal therapy. The authors examined the values of patients at the baseline, 6, 12, and 24 weeks and reported that while insulin resistance significantly increased in the ADT group, FBG did not significantly change. A study by Yannucci et al. (15) reviewed the data of 1,102 patients (obtained from the patient pool of a prospective study), measured the glycosylated hemoglobin (HbA1c) and FBG at the baseline, and 3 and 6 months. HbA1c significantly increased at 3 months, whereas FBG did not significantly change at 3 or 6 months. The current study compared all the patients and revealed a significantly increased FBG. FBG significantly increased in the orchiectomy group, but it did not significantly change in the LHRH group, without significant differences between the two groups. No significant difference was also determined between or within the antiandrogen groups.

Study Limitations

Two important limitations were determined in this study: First is its retrospective nature, and second is the relatively small number of patients.

Table 3. Comparison of the sixth-month values of the orchiectomy and LHRH agonist groups

	OX (n=25)	LHRH (n=41)	p[1]
LDL[1]	121.52±34.15	124.85±34.10	0.595
LDL[2]	136.25±45.58	133.47±54.38	
p[2]	**0.007**	0.267	
HDL[1]	40.46±12.94	50.69±30.03	0.653
HDL[2]	42.71±12.46	57.78±58.97	
p[2]	0.224	0.154	
TC[1]	187.92±39.23	192.55±44.56	0.293
TC[2]	203.72±57.31	196.26±40.98	
p[2]	0.053	0.785	
TG[1]	127.20±58.14	137.62±57.94	0.594
TG[2]	131.92±60.13	135.03±66.22	
p[2]	0.530	0.582	
FBG[1]	101.52±27.60	107.48±42.29	0.088
FBG[2]	119.28±51.85	107.96±47.29	
p[2]	**0.003**	0.399	

[1]Repeated-measures analysis, [2]Wilcoxon test, LHRH: Luteinizing hormone-releasing hormone, OX: Orchiectomy, LDL: Low-density cholesterol, HDL: High-density cholesterol, TC: Total cholesterol, TG: Triglyceride, FBG: Fasting blood glucose

Table 4. Comparison of the antiandrogen groups				
	Cyproterone	**Bicalutamide**	**None**	**p-value**
LDL[1]	121.76±25.70	123.00±36.61	136.00±45.66	0.160
LDL[2]	120.97±30.50	142.36±59.78	128.84±30.84	
p[2]	0.808	**<0.001**	0.892	
HDL[1]	46.01±14.64	47.08±30.84	48.12±8.75	0.330
HDL[2]	40.67±11.44	58.47±9.52	48.74±16.71	
p[2]	0.076	<0.001	0.893	
TC[1]	189.48±29.70	188.96±47.21	211.00±49.84	**<0.001**
TC[2]	179.81±39.09	213.17±46.89	167.42±49.48	
p[2]	0.237	**0.001**	**0.043**	
TG[1]	108.67±4.75	142.41±56.07	168.80±55.22	0.237
TG[2]	94.33±48.51	147.10±62.18	193.84±40.80	
p[2]	0.313	0.757	0.465	
FBG[1]	99.05±23.55	106.15±39.84	123.72±60.92	0.337
FBG[2]	116.52±57.37	107.65±2.88	131.06±62.13	
p[2]	0.135	0.051	**0.043**	

[1]Repeated-measures analysis, [2]Wilcoxon test, LDL: Low-density cholesterol, HDL: High-density cholesterol, TC: Total cholesterol, TG: Triglyceride, FBG: Fasting blood glucose

Conclusion

Many literature studies were reported on the lipid profile of ADT and FBG values of patients with prostate cancer. However, studies that compared different antiandrogen treatments were not determined in the changes in the lipid profile and FBG of these patients. Our results revealed a significantly increased TC value in bicalutamide compared to cyproterone. Statistically significant results would have been probably obtained in the changes in LDL and HDL if a higher number of patients had been evaluated. Prospective studies with a higher number of patients are necessary to clarify this issue.

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References

1. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2007. CA Cancer J Clin 2007;57:43-66.
2. Barry MJ, Delorenzo MA, Walker-Corkery ES, et al. The rising prevalence of androgen deprivation among older American men since the advent of prostate-specific antigen testing: a population-based cohort study. BJU Int 2006;98:973-978.
3. Meng MV, Grossfeld GD, Sadetsky N, et al. Contemporary patterns of androgen deprivation therapy use for newly diagnosed prostate cancer. Urology 2002;60(3 Suppl 1):7-11.
4. Loblaw DA, Virgo KS, Nam R, et al. Initial hormonal management of Androgen-sensitive metastatic, recurrent, or progressive prostate cancer: 2006 Update of an American society of clinical oncology practice guideline. J Clin Oncol 2007;25:1596-1605.
5. Isbarn H, Boccon-Gibod L, Carroll PR, et al. Androgen deprivation therapy for the treatment of prostate cancer: consider both benefits and risks. Eur Urol 2009;55:62-75.
6. Schwandt A, Garcia JA. Complications of androgen deprivation therapy in prostate cancer. Curr Opin Urol 2009;19:322-326.
7. Taylor LG, Canfield SE, Du XL. Review of major adverse effects of androgen-deprivation therapy in men with prostate cancer. Cancer 2009;115:2388-2399.
8. Keating NL, O'Malley AJ, Smith MR. Diabetes and cardiovascular disease during androgen deprivation therapy for prostate cancer. J Clin Oncol 2006;24:4448-4456.
9. Tadros NN, Garzotto M. Androgen deprivation therapy for prostate cancer: not so simple. Asian J Androl 2011;13:187-188.
10. Brown BW, Brauner C, Minnotte MC. Noncancer deaths in white adult cancer patients. J Natl Cancer Inst 1993;85:979-987.
11. Keating NL, O'Malley AJ, Freedland SJ, Smith MR. Diabetes and cardiovascular disease during androgen deprivation therapy: observational study of veterans with prostate cancer. J Natl Cancer Inst 2010;102:39-46.
12. Bo JJ, Zhang C, Zhang LH, et al. Androgen deprivation therapy through bilateral orchiectomy: increased metabolic risks. Asian J Androl 2011;13:833-837.
13. Morote J, Gómez-Caamaño A, Alvarez-Ossorio JL, et al. The metabolic syndrome and its components in patients with prostate cancer on androgen deprivation therapy. J Urol 2015;193:1963-1969.
14. Gagliano-Jucá T, Burak MF, Pencina KM, et al. Metabolic Changes in Androgen-Deprived Nondiabetic Men With Prostate Cancer Are Not Mediated by Cytokines or aP2. J Clin Endocrinol Metab 2018;103:3900-3908.
15. Yannucci J, Manola J, Garnick MB, et al. The effect of androgen deprivation therapy on fasting serum lipid and glucose parameters. J Urol 2006;176:520-525.
16. Braga-Basaria M, Muller DC, Carducci MA, et al. Lipoprotein profile in men with prostate cancer undergoing androgen deprivation therapy. Int J Impot Res 2006;18:494-498.
17. Dockery F, Bulpitt CJ, Agarwal S, et al. Testosterone suppression in men with prostate cancer leads to an increase in arterial stiffness and hyperinsulinaemia. Clin Sci (Lond) 2003;104:195-201.
18. Nishiyama T, Ishizaki F, Anraku T, et al. The influence of androgen deprivation therapy on metabolism in patients with prostate cancer. J Clin Endocrinol Metab 2005;90:657-660.
19. Smith MR, Finkelstein JS, McGovern FJ, et al. Changes in body composition during androgen deprivation therapy for prostate cancer. J Clin Endocrinol Metab 2002;87:599-603.
20. Smith JC, Bennett S, Evans LM, et al. The effects of induced hypogonadism on arterial stiffness, body composition, and metabolic parameters in males with prostate cancer. J Clin Endocrinol Metab 2001;86:4261-4267.
21. Wolny-Rokicka E, Tukiendorf A, Wydmański J, et al. Lipid Status During Combined Treatment in Prostate Cancer Patients. Am J Mens Health 2019;13:1557988319876488.
22. Chen KC, Peng CC, Hsieh HM, et al. Antiandrogenic therapy can cause coronary arterial disease. Int J Urol 2005;12:886-891.

23. Paisey RB, Kadow C, Bolton C, et al. Effects of cyproterone acetate and a long-acting LHRH analogue on serum lipoproteins in patients with carcinoma of the prostate. J R Soc Med 1986;79:210-211.
24. Wallentin L, Varenhorst E. Plasma lipoproteins during treatment with cyproterone acetate in men with prostatic carcinoma. J Clin Endocrinol Metab 1980;51:1118-1122.
25. Salvador C, Planas J, Agreda F, et al. Analysis of the lipid profile and atherogenic risk during androgen deprivation therapy in prostate cancer patients. Urol Int 2013;90:41-44.
26. Sağlam HS, Köse O, Kumsar S, et al. Fasting blood glucose and lipid profile alterations following twelve-month androgen deprivation therapy in men with prostate cancer. ScientificWorldJournal 2012;2012:696329.
27. Stellato RK, Feldman HA, Hamdy O, et al. Testosterone, sex hormone-binding globulin, and the development of type 2 diabetes in middle-aged men: prospective results from the Massachusetts Male Aging Study. Diabetes Care 2000;23:490-494.
28. Simon D, Charles MA, Nahoul K, et al. Association between plasma total testosterone and cardiovascular risk factors in healthy adult men: the Telecom Study. J Clin Endocrinol Metab 1997;82:682-685.
29. Ding EL, Song Y, Malik VS, Liu S. Sex differences of endogenous sex hormones and risk of type 2 diabetes: a systematic review and meta-analysis. JAMA 2006;295:1288-1299.

Original Article

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Risk Factors of Patients with Prostate Cancer Upgrading for International Society of Urological Pathology Grade Group I After Radical Prostatectomy

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Abstract

Objective: This study aimed to determine the predictive factors for patients whose International Society of Urological Pathology (ISUP) score was upgraded in radical prostatectomy (RP) pathologies with a prostate biopsy pathology of ISUP grade group 1.

Materials and Methods: Among patients who underwent RP in our clinic within 10 years, 158 patients with prostate biopsy pathology of ISUP grade group 1 were examined retrospectively. Age, serum prostate-specific antigen (PSA) level, prostate biopsy ISUP grade group, number of cores taken in the prostate biopsy, number of tumor-positive cores, RP pathology ISUP grade group, and pathological stage were evaluated.

Results: The mean age (± standard) of the 158 patients whose prostate biopsy pathology was ISUP grade group 1 were 64.07 (±6.6). ISUP group upgrading was detected in 47 patients (29.7%). The mean PSA value of these patients was 10.6 ng/mL (±6.9). The mean PSA value of the other 111 patients without ISUP group upgrading was 7.98 ng/mL (±4.9). The serum PSA level was significantly higher in patients with upgraded ISUP in the RP pathology (p=0.02). The percentage of tumor-positive cores in the group with ISUP group upgrading (37%) was significantly higher than that in the group without ISUP group upgrading (27%) (p=0.01). The detection rates of surgical margin positivity (42.6% vs. 18%), capsule invasion (55.3% vs. 19.8%), and seminal vesicle invasion (23.6% vs. 3.6%) were also significantly higher in the upgraded ISUP group after RP (p<0.05).

Conclusion: The results of this trial suggest that active surveillance may not be an appropriate option for patients with biopsy ISUP grade group 1 with PSA level >10 ng/mL. Moreover, the presence of a higher number and percentage of tumor-positive cores constituted risks of ISUP group upgrading with concomitant poor pathological outcomes such as surgical margin positivity, capsule invasion, and seminal vesicle invasion.

Keywords: Prostate cancer, international society of urological pathology score, radical prostatectomy

Introduction

Prostate cancer is the second most common cancer among men after lung cancer and the 5th cause of death after lung, liver, stomach, and colorectal cancers (1). With the use of prostate-specific antigen (PSA) as a marker from the late 1980s onwards in prostate cancer screening, an increasing number of prostate cancer cases were detected (2). Mortality decreased due to increased prostate cancer diagnosis; however, it led to overdiagnosis and overtreatment in low-risk cases (3). The widespread use of PSA has led to the diagnosis of many asymptomatic cases as prostate cancer. Prostate cancer does not cause symptoms or death in a certain group of patients and does not affect the overall survival. The guidelines offer active surveillance (AS) as an alternative to curative treatment for low-risk (PSA level <10 ng/mL, stage < T2a, Gleason score <3+3) and very low-risk (PSA level <10 ng/mL, stage <1c, Gleason score <3+3, PSA density <0.15 ng/mL, <3 positive biopsy core count, <50% core positivity) cases with clinically localized prostate cancer and life expectancy of over 10 years (4,5). In intermediate-risk prostate cancer, AS can be recommended

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by discussing the risks with the patient with a low degree of recommendation (4). However, AS in intermediate-risk prostate cancer is controversial (6). Studies have shown that AS may be beneficial in selected patients with favorable intermediate-risk prostate cancer (7,8).

A limited number of prospective randomized controlled studies are comparing AS with standard treatments (4). AS studies are generally cohort studies and have reported that patients demonstrated relatively good average survival and cancer-specific survival rates (4,9). In a cohort study of patients with International Society of Urological Pathology (ISUP) grade group 1 followed up with AS, prostate cancer-specific 5-, 10-, and 15-year cumulative metastasis and mortality rates were at 0.1% (10). However, in one-third of the patients, curative treatment is required depending on the upgrade of the disease, stage progression, or patient's preference (4).

AS aims to avoid unnecessary treatment in men with clinically localized prostate cancer that does not require emergency treatment and to provide cure at the most appropriate time in patients who need treatment during follow-up (11). Knowledge of the disease prognosis in the selection of clinical treatment is important. Since a limited amount of prostate tissue is sampled during biopsy, a risk of upgrading is inevitable after radical prostatectomy (RP). Therefore, it is important to reveal the risk factors for pathological upgrade in patients who received AS. At present, the best prognostic factors include the Gleason score, PSA level, and clinical tumor stage (4,12).In this study, we aimed to determine the predictive factors for patients whose ISUP grade is upgraded in RP pathologies with prostate biopsy pathology of ISUP grade group 1.

Materials and Methods

Data of RP cases within 10 years at our urology department were retrospectively analyzed. Biopsy and RP pathologies were evaluated by the same pathology department. RP cases with a biopsy procedure and/or biopsy pathology evaluation performed at different centers were excluded. Moreover, RP cases with missing data for the PSA value, full biopsy pathology report, and RP pathology findings were excluded. Finally, RP cases with ISUP grade group 1 according to the prostate biopsy constituted the study group. Transrectal ultrasound (TRUS)-guided biopsy was performed for histopathological diagnosis in all patients. ISUP grades were determined from Gleason scores recorded in the pathology report. As a result of staging, all patients have clinically localized prostate cancer. Age, serum PSA level, prostate biopsy ISUP grade group, number of cores taken in prostate biopsy, number of tumor-positive cores, RP pathology ISUP grade group, and pathological stage were evaluated. The patients were divided into two groups: group I with upgrading after RP and group 2 without upgrading based on the final pathology. These groups were compared to determine the risk factors of patients with ISUP group upgrade in RP pathologies. Approval for the study was obtained from Marmara University Clinical Research Ethical Committee (approval no: 09.2021.986, date: 03.09.2021).

Statistical Analysis

Data were analyzed using the independent sample t-test in the IBM Statistical Package for the Social Sciences Statics version 22. All these analyses used a significance level of $p<0.05$.

Results

Within 10 years, 289 patients with RP, whose full data were available, were evaluated. According to prostate biopsy pathologies, 158 patients had ISUP grade group 1, 61 had group 2, 20 had group 3, 28 had group 4, and 22 had group 5. Conclusively, 158 patients with ISUP grade group 1 [mean age, 64.07 years (±6.6)] according to the prostate biopsy were included in this study. Moreover, 47 patients (group 1; 29.7%) with biopsy pathology ISUP grade group 1 were found to have an increase in the ISUP grade group based on the RP pathology. The mean PSA value of these patients was 10.6 ng/mL (±6.9). Within all patients with prostate cancer, the RP pathology of 111 patients was reported as ISUP grade group 1. The mean PSA value of these patients was 7.98 ng/mL (±4.9). In the group comparison, the serum PSA level was

Table 1. Comparison of demographic, biochemical, and pathological findings based on prostate biopsy and radical prostatectomy of the two groups

		Upgrade (+) n=47 (29.7%)	Upgrade (–) n=111 (70.3%)	p
Age [mean years (± std)]		65.7 (±6.4)	63.5 (±7.3)	0.357[1]
Mean PSA (ng/mL) (± std)		10.6 (±6.9)	7.98 (±4.9)	**0.021**[1]
Tumor-positive core count		3.5 (±2.4)	3.2 (±2.5)	0.406[1]
Tumor-positive core percentage		37 (±22.1)	27 (19.6)	**0.011**[1]
Surgical margin positivity	(+)	20 (42.6%)	20 (18%)	**0.01**[1]
	(–)	27 (57.4%)	91 (82%)	
Capsule invasion	(+)	26 (55.3%)	22 (19.8%)	<**0.001**[1]
	(–)	21 (44.7%)	89 (80.2%)	
Seminal vesicle invasion	(+)	11 (23.6%)	4 (3.6%)	<**0.001**[1]
	(–)	36 (76.4%)	107 (96.4%)	

[1]: **Independent sample t-test**, std: Standard, PSA: Prostate-specific antigen

significantly higher in the group with ISUP group upgrading in the RP pathology (p=0.02).

The mean number of TRUS-guided prostate biopsy-positive cores in group 1 was higher than that in group 2 (Table 1). However, no significant difference was noted between the two groups (p=0.46) based on the number of positive cores.

On the contrary, the percentage of tumor-positive cores in group 1 (37%) was significantly higher than that in group 2 (27%) (p=0.01). Similarly, the rates of surgical margin positivity (42.6% vs. 18%), capsule invasion (55.3% vs. 19.8%), and seminal vesicle invasion (23.6% vs. 3.6%) were significantly remarkable in patients with ISUP grade group 1 in the final pathology (p<0.05, Table 1).

Discussion

AS is recommended for localized low-risk prostate cancer cases to protect patients from the side effects of invasive curative treatments, such as radiotherapy and RP, and to maintain their quality of life (13). A study of intermediate-risk prostate cancer cases reported that survival was not different in the 10-year follow-up between AS and RP/RT; however, the incidence of disease progression and metastasis is lower in the RP/RT group (14). AS is controversial in the intermediate-risk group; thus, it is important to identify patients in the low-risk group. Findings in the initial biopsy pathology carry a vital guide in patient selection. However, a study including all ISUP grade groups showed that the discordance rate between prostate biopsy and RP pathologies was 35.7% (15). Another study reported a 36.3% upgrade in ISUP grade group of RP pathologies in patients who had ISUP grade group 1 in the prostate needle biopsy (16). In another study, the rate of Gleason score upgrading was 21.8% in low- and very low-risk cases after the final RP pathology (17). In a study of the AS group, Gleason score upgrading of 32% was observed in initial follow-up biopsies (18). In another study, Gleason score upgrading was observed in 13.8% of patients in the control biopsy (19). In the present study, about one-third of the patients (29.7%) had ISUP group upgrading in the final RP pathology. This upgrading rate in the ISUP grade was comparable with the literature.

Determining the risk factors for possible upgrading in the ISUP evaluation of patients receiving AS is important. Studies have shown that a high PSA level, high PSA density, number of positive cores, percentage of positive cores, high clinical stage, advanced age, and high Gleason score are predictive risk factors for ISUP group upgrading (17,19,20,21). According to our data analysis, the mean age of the group with ISUP group upgrading in the RP pathology was slightly higher without a significant difference (p=0.357). Although 10 ng/mL is taken as the cutoff level for PSA value in AS in many studies, a study accepted higher PSA levels such as 15 ng/mL for AS (22). In our data, the PSA level was 10.6 ng/mL (±6.9) in the group with ISUP group upgrading in RP pathologies and 7.98 (±4.9) in the group without upgrading. The PSA level was significantly higher in the group with ISUP group upgrading (p=0.02). Consistent with the literature, PSA levels <10 ng/mL in patients with prostate cancer of ISUP grade group 1 were more suitable for AS. When the PSA levels are >10 ng/mL, patients have a higher ISUP grade that could not be diagnosed by prostate biopsy. Therefore, these patients with PSA >10 ng/mL should be informed about a higher risk of upgrading. Conclusively, these patients can actually be excluded from the AS program based on the higher change of upgrading after RP according to our results.

As the number and percentage of tumor-positive cores increase, the risk of ISUP group upgrading also increases. According to Akan et al. (23), the maximum percentage of core involvement was significantly higher in the upgraded group in the RP pathology. Our results were similar to the findings of this study. The percentage of tumor-positive cores was 37% (±22.1), and it was significantly higher in the group with ISUP group upgrading (p=0.01). When these data were evaluated, the risk of ISUP group upgrading was higher in patients with ISUP grade group 1 with >3 positive cores.

Although AS aims to avoid unnecessary treatment in men with clinically insignificant localized prostate cancer, it is very important to select the appropriate patient group. Failure to identify the low-risk group properly may cause irreversible problems. A patient with clinically significant prostate cancer will face the risk of disease progression during follow-up with AS. This disease progression will increase the morbidity and mortality of the patients. The rates of surgical margin positivity (42.6% vs. 18%), capsule invasion (55.3% vs. 19.8%), and seminal vesicle invasion (23.6% vs. 3.6%) were significantly higher in patients with ISUP group upgrading in RP pathologies than in patients without ISUP group upgrading (p<0.05). Therefore, our results confirmed that upgraded cases after RP also had unfavorable pathological properties including positive surgical margin, capsule invasion, and seminal vesicle invasion.

Study Limitations

The major limitation of the current trial was the retrospective analysis of data. In addition, the number of patients was relatively limited. Randomized controlled prospective studies with larger number of patients are needed to determine definitive risk factors for ISUP group upgrading in patients with ISUP grade group 1 in the initial prostate biopsy and to identify patients with characteristics appropriate for AS.

Conclusion

Our results suggest that PSA >10 ng/mL constitute a significant risk factor for upgrading after RP in patients with biopsy ISUP grade group I. Therefore, patients with a serum PSA level >10 ng/mL and biopsy ISUP grade group 1 should be monitored very closely if they do not accept definitive treatment. An increased risk of upgrading after RP should be intensively discussed with these patients. Patients with biopsy ISUP grade group 1 with a higher number and/or percentage of tumor-positive cores also carry a remarkable risk of upgrading after RP. In conclusion, AS may not be an appropriate option in patients with PSA >10 ng/mL and a higher number and percentage of tumor-positive cores due to the increased risk of ISUP group upgrading after RP. Moreover, these patients also demonstrated a higher risk of poor pathological outcomes including surgical margin positivity, capsule invasion, and seminal vesicle invasion.

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Ethics

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Authorship Contributions

Supervision: İ.T., H.K.Ç., L.T., Concept: D.F., İ.T., Design: A.Ö., G.Ö., B.Ş., D.F., İ.T., Data Collection or Processing: A.Ö., G.Ö., B.Ş., Analysis or Interpretation: A.Ö., B.Ş., Literature Search: G.Ö., Writing: A.Ö., G.Ö.

References

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
2. Howlader N, Am N, Krapcho M, et al SEER Cancer Statistics Review, 1975-2010. National Cancer Instute, Seer Cancer, 2013.
3. Schröder FH, Hugosson J, Roobol MJ, et al. Prostate-cancer mortality at 11 years of follow-up. N Engl J Med 2012;366:981-990.
4. Mottet N, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer-2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol 2021;79:243-262.
5. NCCN Clinical Practice Guidelines in Oncology Prostate Cancer Version 2, 2021.
6. Loeb S, Folkvaljon Y, Bratt O, et al. Defining Intermediate Risk Prostate Cancer Suitable for Active Surveillance. J Urol 2019;201:292-299.
7. Klotz L. Active surveillance in intermediate-risk prostate cancer. BJU Int 2020;125:346-354.
8. Raldow AC, Zhang D, Chen MH, et al. Risk Group and Death From Prostate Cancer: Implications for Active Surveillance in Men With Favorable Intermediate-Risk Prostate Cancer. JAMA Oncol 2015;1:334-340.
9. Klotz L, Vesprini D, Sethukavalan P, et al. Long-term follow-up of a large active surveillance cohort of patients with prostate cancer. J Clin Oncol 2015;33:272-277.
10. Tosoian JJ, Mamawala M, Epstein JI, et al. Active Surveillance of Grade Group 1 Prostate Cancer: Long-term Outcomes from a Large Prospective Cohort. Eur Urol 2020;77:675-682.
11. Bruinsma SM, Roobol MJ, Carroll PR, et al. Expert consensus document: Semantics in active surveillance for men with localized prostate cancer - results of a modified Delphi consensus procedure. Nat Rev Urol 2017;14:312-322.
12. Lee H, Lee M, Byun SS, et al. Evaluation of Prostate Cancer Stage Groups Updated in the 8th Edition of the American Joint Committee on Cancer Tumor-Node-Metastasis Staging Manual. Clin Genitourin Cancer 2019;17:221-226.
13. Klotz L. Active surveillance for low-risk prostate cancer. Curr Opin Urol 2017;27:225-230.
14. Hamdy FC, Donovan JL, Lane JA, et al. 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer. N Engl J Med 2016;375:1415-1424.
15. Öztürk E, Yıkılmaz TN. Gleason Score Correlation Between Prostate Biopsy and Radical Prostatectomy Specimens. Bull Urooncol 2018;17:1-4.
16. Epstein JI, Feng Z, Trock BJ, Pierorazio PM. Upgrading and downgrading of prostate cancer from biopsy to radical prostatectomy: incidence and predictive factors using the modified Gleason grading system and factoring in tertiary grades. Eur Urol 2012;61:1019-1024.
17. Tosoian JJ, JohnBull E, Trock BJ, et al. Pathological outcomes in men with low risk and very low risk prostate cancer: implications on the practice of active surveillance. J Urol 2013;190:1218-1222.
18. Osses DF, Drost FH, Verbeek JFM, et al. Prostate cancer upgrading with serial prostate magnetic resonance imaging and repeat biopsy in men on active surveillance: are confirmatory biopsies still necessary? BJU Int 2020;126:124-132.
19. Tosoian JJ, Trock BJ, Landis P, et al. Active surveillance program for prostate cancer: an update of the Johns Hopkins experience. J Clin Oncol 2011;29:2185-2190.
20. Cary KC, Cowan JE, Sanford M, et al. Predictors of pathologic progression on biopsy among men on active surveillance for localized prostate cancer: the value of the pattern of surveillance biopsies. Eur Urol 2014;66:337-342.
21. Haberal HB, Artykov M, Hazir B, et al. Predictors of ISUP score upgrade in patients with low-risk prostate cancer. Tumori 2021;107:254-260.
22. Selvadurai ED, Singhera M, Thomas K, et al. Medium-term outcomes of active surveillance for localised prostate cancer. Eur Urol 2013;64:981-987.
23. Akan S, Ediz C, Temel MC, et al. Correlation of the Grade Group of Prostate Cancer according to the International Society of Urological Pathology (Isup) 2014 Classification between Prostate Biopsy and Radical Prostatectomy Specimens. Cancer Invest 2021;39:521-528.

Original Article

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Comparison of the Effect of On-Clamp vs. Off-Clamp Partial Nephrectomy on Renal Function: A Retrospective Analysis

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Abstract

Objective: Partial nephrectomy (PN) suggests a better renal reserve and comparable oncologic results than radical nephrectomy. Zero-ischemia PN is a technique to avoid the deleterious effects of ischemia on renal parenchyma cells. We aimed to determine the factors affecting the postoperative renal function of patients with clinical T_1 tumor who either underwent zero-ischemia or ischemic PN through the open or robotic approach.

Materials and Methods: The medical records of all cases with preoperative normal serum creatinine levels who underwent either on-clamp or off-clamp PN through an open or robot-assisted laparoscopic approach for T_1 tumors between January 2008 and December 2018 at our center were analyzed retrospectively.

Results: In total, 90 patients (i.e., 15 robotic off-clamp, 15 open off-clamp, 30 robotic on-clamp, and 30 open on-clamp PN) were included in the study. Although the decrease in the absolute estimated glomerular filtration rate (eGFR) was significantly higher in the robotic PN procedure, the percentage of decrease in the eGFR was similar between the open and robotic surgeries. According to Spearman's correlation analysis, preoperative eGFR was the only parameter that was significantly associated with a decrease in the eGFR ($r=0.546$, $p<0.001$).

Conclusion: Our findings regarding the results of renal function tests are inadequate to state that either the robotic or open zero-ischemia PN is superior to their ischemic counterpart. Besides the operative time, warm ischemia time, estimated blood loss, and excised healthy renal parenchyma cells must be considered while predicting the long-term renal function after PN.

Keywords: Creatinine, glomerular filtration rate, ischemia, laparoscopy, partial nephrectomy

Introduction

Nephron sparing surgery, also known as a partial nephrectomy (PN), has developed into a standard treatment for clinical T_1 tumors (1). Based on the long-term follow-up data, PN suggests comparable oncologic and better renal function test results when compared with a radical nephrectomy (2). The current PN techniques, whether open or minimally invasive (such as laparoscopy or robotic approach), frequently comprise clamping off the renal artery, which allows a bloodless operative field to view the tumor with an adequate parenchymal margin and to complete the reconstruction precisely. Clamping off the main renal artery leads to ischemia in the injury that can cause postoperative renal dysfunction. Many studies have reported that the deterioration of the renal function after a limited warm ischemia time of under 30 min is temporary and is reversed spontaneously. Gill et al. (3) reported that even this reversible ischemia may lead to damage, especially in elderly patients or those who have chronic kidney disease (CKD) or pre-existing medical comorbidities. Zero-ischemia PN is a technique to eliminate iatrogenic ischemia. The off-clamp technique could be performed without any hilar clamping, whereas the on-clamp technique includes the clamping of the hilum, where the renal artery is clamped with or without the vein, for reducing the blood supply to the renal parenchyma cells. Superficial and small renal masses could be removed without clamping (3). Smith et al. (4) reported the efficacy of the open off-clamped PN and its usefulness for the preservation

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of the renal function in general without specifically looking at tumor complexity.

The adequate long-term renal function after PN is relevant for three factors: preoperative function, the volume of the preserved nephrons, and warm ischemia time (5,6). This study aimed to determine the factors affecting postoperative renal function in patients with clinical T_1 tumor who underwent either zero-ischemia or ischemic PN via the open or robotic approach.

Materials and Methods

The Ethics Committee of University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital approved the study (approval number: 2019/101). The medical records of all patients with preoperative normal serum creatinine levels who underwent either on-clamp or off-clamp PN through an open or robot-assisted laparoscopic approach (The Da Vinci Surgical System, Intuitive Surgical, Inc., Sunnyvale, CA, USA) for T_1 tumors between January 2008 and December 2018 at our center were analyzed retrospectively. All consecutive patients having a follow-up of at least 18 months with complete data available were included in the study. Patients with solitary kidney, CKD, and bilateral or multiple tumors and patients on the learning curve were excluded from the study. The type of the surgery was decided based on the additional cost of robotic surgery, surgical expertise, and patient's preference. All patients were classified into four groups according to the type of surgery: Group 1, robotic off-clamp PN; group 2, open off-clamp PN; group 3, robotic on-clamp PN; and group 4, open on-clamp PN. All patients provided written informed consent.

Most open procedures were performed through a retroperitoneal approach. All robotic procedures and a few difficult open procedures were performed via the transperitoneal approach. In the robotic groups, under general anesthesia, the patient was placed to the full side position at 60°. A Veress needle was used to create a 15 mmHg pneumoperitoneum. An 8 mm camera port was placed at the level of the rectus muscle lateral to the umbilicus level. Under direct vision, 8 mm robotic trocars, one in the subcostal and one in the lower quadrant, were placed at the level of the camera port. Depending on the tumor location, a 12 mm assistant port was placed at least 1 cm below the robotic port location. In both open and robotic on-clamp procedures, after the isolation of the renal artery, the renal artery was controlled using a bulldog clamp. In the off-clamp groups, in case of excessive bleeding during tumor excision, the renal artery was dissected and identified with a vessel loop to ensure rapid hilar control. The tumors were resected with an appropriate parenchymal margin instead of enucleation in all cases. Following tumor resection using cold scissors, the tumor bed was sutured using a 2-0 Vicryl (Ethicon, Somerville, NJ, USA) for hemostasis of the vessels and closure of the collecting system. Thereafter, parenchymal hemostasis was achieved by approximating both edges using continuous 3-0 V-Loc (Covidien, Mansfield, MA, USA) sutures. In the robotic groups, the tumor bed was examined under low insufflation pressure to achieve hemostasis after renal reconstruction. The tumor excision and renal reconstruction were completed without cooling in all cases.

All patients were evaluated with an abdominal multi-slice computed tomography or magnetic resonance imaging before surgery. The studied parameters included patients' demographic data, tumor size and location, renal nephrometry score, operation features, preoperative and postoperative imaging studies, and preoperative and postoperative serum biochemical analysis. The RENAL score was determined by two urologists (EG, NK) as previously described (7). In brief, the RENAL score includes five critical anatomical components of the renal mass: (R)adius (maximal tumor diameter), (E)xophytic/endophytic properties, (N)earness of the deepest portion of the tumor to the collecting system or sinus, (A)nterior/posterior location, and (L)ocation relative to the polar line. The eGFR of patients was measured using the modification of diet in the renal disease formula. The renal function was assessed before the surgery and postoperatively at 3, 6, 12, and 18 months. The percent change in eGFR was calculated as follows:

eGFR=(postoperative eGFR - preoperative eGFR)/preoperative eGFR × 100

The absolute eGFR was calculated as follows:

Absolute eGFR=postoperative eGFR - preoperative eGFR

Statistical Analysis

IBM Statistical Package for the Social Sciences Statistics for Mac v. 21.0 (IBM SPSS Corp., Armonk, NY, USA) was used for the statistical analysis. The mean ± standard deviation has been used to express the quantitative measurements. The numbers and percentages have been provided for quantitative measurements. The normal distribution of the continuous variables was tested using the Shapiro-Wilk test. Mann-Whitney U test was used for comparing the means between the nonnormally distributed groups. Means of more than two normally distributed and non-normally distributed groups were compared using analysis of variance and Kruskal-Wallis tests, respectively. The frequency of the categorical variables was compared using Pearson's chi-square test. $P<0.05$ was considered statistically significant. Logistic regression analysis was used to identify the predictive factors for a decrease of >20 in eGFR.

Results

A total of 90 patients, of whom 45 were males and 45 were females, were included in the study. The distribution of the patients was as follows: 15 robotic off-clamp PN, 15 open off-clamp PN, 30 robotic on-clamp PN, and 30 open on-clamp PN. The average age of the patients was 52.5±12.1 years. Patient characteristics are provided in Table 1. The mean follow-up time of the patients was 40.1±27.7 months. Our cohort was generally healthy, and 87.8% of the patients had an American Society of Anesthesiologists score of 1 or 2. The mean tumor size was 40.7±15.8 mm. The mean preoperative eGFR was 100 mL/min/1.73 m^2. The mean RENAL score of the masses was 7.1±1.9. The mean operative time and the perioperative estimated blood losses were 183±49.2 min and 193.1±134 mL, respectively. The percentage of the patients with minor (Clavien-Dindo grade 1 and 2) complications was 18.8%. Of the 6 minor complications, 2 were postoperative urine leakage that were resolved with a ureteral stent placement, and 4 were postoperative fever that

Table 1. Comparison of the patient demographics, characteristics, and operation features according to the type of surgery					
Variables	Open off-clamp PN group	Robotic off-clamp PN group	Open on-clamp PN group	Robotic on-clamp PN group	p-value
Number of patients (group number)	15 (1)	15 (2)	30 (3)	30 (4)	
Mean age ± SD, years	50.2±14.3	51.4±14.0	56.6±8.7	50.1±12.4	0.162*
Gender, n (%)					0.003**
Male Female	4 (26.7) 11 (73.3)	3 (20) 12 (80)	17 (56.7) 13 (43.3)	21 (70) 9 (30)	1 vs. 4 0.006 2 vs. 3 0.020 2 vs. 4 0.002
ASA score					0.149**
ASA 1	4 (26.7)	3 (20.0)	14 (46.7)	7 (23.3)	
ASA 2	7 (46.7)	10 (66.7)	13 (43.3)	21 (70.0)	
ASA 3	4 (26.7)	2 (13.3)	3 (10.0)	2 (6.7)	
Preoperative GFR	82±19.9	121.6±44.7	92.3±14.8	106±31.5	0.006¥ 1 vs. 2 0.002 1 vs. 4 0.021
Tumor size, (mm)	29.4±5.2	30.6±5.9	57.3±11.6	34.9±12.7	<0.001¥ 1 vs. 3 <0.001 2 vs. 3 <0.001 3 vs. 4 <0.001
RENAL score	6.9±0.7	6.1±0.8	9.2±1.2	5.7±1.6	<0.001¥ 1 vs. 3 <0.001 1 vs. 4 <0.008 2 vs. 3 <0.001 3 vs. 4 <0.001
EBL, (mL)	359.3±140.7	240±90.8	73.6±48.3	206±94.4	<0.001¥ 1 vs. 3 <0.001 1 vs. 4 <0.006 2 vs. 3 <0.001 3 vs. 4 <0.001
OT, (min)	194±29.7	233±24.7	141.1±37.6	194.5±44.6	<0.001* 1 vs. 2 <0.003 1 vs. 3 <0.001 2 vs. 3 <0.001 2 vs. 4 <0.004 3 vs. 4 <0.001
Warm ischemia time, (min)	NA	NA	22.3 ± 5.3	17 ± 3.5	<0.001†
Complications, n (%)	4 (26.7)	2 (13.3)	5 (16.7)	6 (20)	0.798**
Follow-up (months)	92.5±13.2	38±10	26.4±14.7	28.7±16.2	<0.001* 1 vs. 2 <0.001 1 vs. 3 <0.001 1 vs. 4 <0.001 2 vs. 3 0.022
GFR at the 18-month follow-up	63.3±17	82.6±21.1	72.8±11.8	78.7±18.7	0.01*
Absolute GFR change	18.6±10.4	39±30	19.5±5.4	27.3±16.8	0.041¥
Percent GFR change (%)	22.4±10.3	28±15.1	21±4.1	24.7±7.6	0.083

PN: Partial nephrectomy, ASA: American Society of Anesthesiologists, eGFR: Estimated glomerular filtration rate, NA: Not applicable, SD: Standard deviation, *One-Way Analysis of Variance, **Pearson chi-square, ¥Kruskal-Wallis test, †Mann-Whitney U test & to present the post-hoc analysis results, the groups were numbered

were resolved with antipyretics. The mean postoperative nadir eGFR was 80.4±22.2 mL/min/1.73 m^2, which represents an absolute and a percent decrease of 19.6±17.1 mL/min/1.73 m^2 and 18.4%±11.1%, respectively. The longest operative time was observed in the off-clamp robot-assisted laparoscopic PN group (233±24.7 min) (Table 1).

Age and preoperative eGFR were found to be similar between the patients who underwent off-clamp (n=30; p=0.357) and on-clamp PN (n=60; p=0.739). The operative time, estimated blood loss, and percent of eGFR decrease was higher in the off-clamp PN, whereas the RENAL score and tumor size were higher in the on-clamp PN group.

The mean preoperative eGFR and operative time were significantly higher in the robotic PN, whereas the RENAL score and tumor size were significantly higher in the open PN. Although the absolute eGFR decrease was significantly

Table 2. Univariate analysis and logistic regression test to predict perioperative estimated glomerular filtration rate decrease of >20						
	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Age (years)	0.992	0.956-1.028	0.648			
Gender (female)	1.000	0.416-2.403	1.000			
ASA 3	0.583	0.131-2.606	0.480			
Preoperative GFR	1.030	1.007-1.053	0.010	1.051	1.010-1.530	0.006
Tumor size	1.008	0.980-1.037	0.560			
RENAL score	0.951	0.762-1.185	0.653			
EBL	1.001	0.998-1.005	0.430			
OT	1.005	0.996-1.014	0.272			
Warm ischemia time	1.009	0.967-1.054	0.667			
Complications	0.657	0.222-1.944	0.448			
Follow-up	1.003	0.987-1.019	0.742			
GFR at the 18-month follow-up	1.007	0.990-1.024	0.428			
Absolute GFR change	1.476	1.235-1.765	<0.001			
Percent GFR change	1.011	0.998-1.090	0.946			
Operational method (on-clamp OPN and RPN)	1.249	0.498-3.136	0.636			

ASA: American Society of Anesthesiologists, eGFR: Estimated glomerular filtration rate, EBL: Estimated blood loss, OT: Operation time, OPN: Open partial nephrectomy, RPN: Robotic partial nephrectomy, CI: Confidence interval, OR: Odds ratio

higher in the robotic PN, the percent of eGFR decrease was similar between the open and robotic surgeries. No statistically significant difference was observed in percent eGFR decrease between on-clamp and off-clamp robotic PN groups (p=0.43).

Thirty patients had an eGFR decrease of 20%. In a logistic regression analysis, the preoperative eGFR was found to be the sole predictor of eGFR decrease of >20 [p=0.006, Exp (B)=1.051]. However, the operative time, age, ischemia duration, estimated blood loss, RENAL score, and tumor size were not statistically significant (p=0.085, p=0.633, p=0.842, p=0.120, p=0.361, and p=0.141, respectively). According to Spearman's correlation analysis, preoperative eGFR was found as the only parameter that was significantly associated with the percent decrease in eGFR (r=0.546, p<0.001) (Table 2).

Discussion

The extended use of different radiological imaging methods has led to the gain of several small renal masses being detected incidentally in recent years. Further, there is an increased demand for PN for treating the small renal masses. The hilar vascular clamping provides bloodless surgical field results in renal warm ischemic injury. Warm ischemic injury has a deleterious effect on kidney function (8). To overcome this issue, off-clamp PN with zero ischemia has been proposed. PN could be performed with either open or robotic techniques. Although the oncologic outcomes of the two techniques are similar, robotic PN offers faster recovery after surgery, shorter hospital stays, and favorable cosmetic results. Nowadays, robotic PN is considered not only for T_1, but also for T_2 tumors (9).

Gill et al. (10) used the selective vascular dissection technique that was first described as the robotic off-clamp technique. In a study by Kaczmarek et al. (11), the authors introduced the total off-clamp robotic PN technique in 49 patients after at least 12 months of follow-up and reported excellent functional outcomes. In their propensity score-matched analysis, Simone et al. (12) reported that off-clamp PN offers 100% preservation of the preoperative GFR in the postoperative period. They also reported that on-clamp PN is associated with a 7.3-fold higher risk of developing CKD and longer operation time compared with off-clamp PN. In our study, unlike Simone et al. (13), a 21% reduction in eGFR was detected in off-clamp robotic PN at the 18-month follow-up. This may be due to the longer follow-up period. Furthermore, no significant difference was observed in the absolute and percentage eGFR decrease in patients who underwent ischemic or nonchemic robotic PN. The only independent parameter predicting eGFR reduction was preoperative eGFR. Additionally, the operation time was statistically longer in the off-clamp robotic PN group, which may be associated with bleeding at the surgical site or difficulty in parenchymal suturing.

In a study by Smith et al. (4), the functional kidney results of 116 patients who underwent on-clamp open PN and 192 patients who underwent off-clamp open PN were compared. The mean warm ischemia time of patients in the on-clamp PN group was reported to be 23 min. The rate of the percent decrease in eGFR of patients in the off-clamp PN group was statistically lower than the on-clamp PN group (9.8% vs. 12.3%, p=0.037). Furthermore, tumor size, estimated blood loss >200 mL, a Carlson comorbidity index >5, and warm ischemia time longer than 22 min were associated with higher postoperative eGFR decline rate (4). Demirel et al. (14) determined that tumor grade, PADUA score, and C-index were valuable parameters predicting renal dysfunction after partial nephrectomy. In a meta-analysis by Liu et al. (8) comparing the effects of off-clamp and on-clamp PN, the authors concluded that off-clamp PN enables better preservation

of the kidney reserves than on-clamp PN. Additionally, off-clamp PN represents oncologic outcomes that are comparable with superior renal functional outcomes. The complication rate was reported to be significantly lower in patients who underwent off-clamp PN than those who underwent on-clamp PN (12.5% vs. 18%). Each of the five studies constituting the meta-analysis showed better renal functional outcomes based on changes in the eGFR in patients who underwent off-clamp PN (8). In contrast with the aforementioned studies and meta-analysis, in our study, the percentage of eGFR reduction was determined as 22.4%±10.3% in off-clamp open PN and 21%±4.1% in on-clamp open PN, and we could not find evidence of superiority of off-clamp PN over on-clamp PN. In addition to warm ischemia time, the operative time and amount of bleeding may play a role in the decrease in eGFR after PN. Further, preserved renal parenchyma is vital in maintaining renal function after PN. In this study, the largest tumor diameter was observed in open PN with ischemia. This situation could lead to similar percentage of eGFR changes in all four groups.

The robotic off-clamp PN could be performed in many ways, and one of those ways is to excise the tumor without the identification/isolation of the renal hilum, called the purely off-clamp PN. In a study conducted by Simone et al. (13), the purely off-clamp robotic PN was found to be a safe surgical procedure with comparable surgical outcomes and minimal effect on renal function. In our study, we preferred to identify the renal hilum in case of an adverse event. Besides not using the renal hilum isolation, renorrhaphy could be avoided with the use of off-clamp PN. Laparoscopic PN performed without hilar clamping and renorrhaphy has been used effectively, especially in small-peripheral tumors with low nephrometry scores (15). In our study, renorrhaphy was not performed in any case.

The utility of the off-clamp PN is uncertain. We preferred this technique in patients with solitary T_1 tumors, which could be excised in <15 min warm ischemia time. The intraoperative bleeding in off-clamp cases is expected to be higher than in on-clamp ones, which may play an indeterminate role in the alterations in postoperative renal function. To decrease intraoperative blood loss during zero-ischemia PN, manipulations, such as pharmacologically induced hypotension during surgery, have been proposed (6). Our strategy was to keep the blood pressure within the normal limits to avoid renal perfusion injury. A drawback of the zero-ischemia technique could be the possibility of under-visualization during tissue resection because of bleeding, which affects the evaluation of the surgical margin. We suggest using a cold scissor during tumor resection instead of energy to better visualize and avoid tumor violation. The amount of normal parenchyma preserved during PN mainly affects renal function restoration; this should be considered when zero-ischemia robotic PN is planned because similar parenchymal preservation could be performed with <15 min warm ischemia time. Although the impact of short warm ischemia time is reversible, the excised parenchyma is irrecoverable (5).

Study Limitations

Our study also has limitations. Primarily, this study was conducted retrospectively. The study population was relatively small , and data were from a single institution although the follow-up period was sufficient (>18 months). No residual functional volume data were available. Further studies on nuclear imaging modalities, such as scintigraphy, are required to improve the quality and scientific merit of our findings.

Conclusion

Our findings regarding renal functional outcomes were insufficient to propose whether the robotic or open zero-ischemia PN is superior to the ischemic counterpart. Besides warm ischemia time, estimated blood loss, operative time, and excised healthy renal parenchyma must be considered while predicting long-term renal function following PN.

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Ethics

Ethics Committee Approval: The Ethics Committee of University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital approved the study (approval number: 2019/101).

Informed Consent: All patients provided written informed consent.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

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

References

1. Gill IS, Aron M, Gervais DA, Jewett MAS. Clinical practice. Small Renal Mass. N Engl J Med 2010;362:624-634.
2. Touijer K, Jacqmin D, Kavoussi LR, et al. The Expanding Role of Partial Nephrectomy: A Critical Analysis of Indications, Results, and Complications. Eur Urol 2010;57:214-222.
3. Gill IS, Eisenberg MS, Aron M, et al. 'Zero ischemia' partial nephrectomy: Novel laparoscopic and robotic technique. Eur Urol 2011;59:128-134.
4. Smith GL, Kenney PA, Lee Y, Libertino JA. Non-clamped partial nephrectomy: Techniques and surgical outcomes. BJU Int 2011;107:1054-1058.
5. Mir MC, Campbell RA, Sharma N, et al. Parenchymal volume preservation and ischemia during partial nephrectomy: Functional and volumetric analysis. Urology 2013;82:263-268.
6. Thompson RH, Lane BR, Lohse CM, et al. Every minute counts when the renal hilum is clamped during partial nephrectomy. Eur Urol 2010;58:340-345.

7. Kutikov A, Uzzo RG. The R.E.N.A.L. Nephrometry Score: A Comprehensive Standardized System for Quantitating Renal Tumor Size, Location and Depth. J Urol 2009;182:844-853.
8. Liu W, Li Y, Chen M, et al. Off-clamp versus complete hilar control partial nephrectomy for renal cell carcinoma: A systematic review and meta-analysis. J Endourol 2014;28:567-576.
9. Bertolo R, Autorino R, Simone G, et al. Outcomes of Robot-assisted Partial Nephrectomy for Clinical T2 Renal Tumors: A Multicenter Analysis (ROSULA Collaborative Group). Eur Urol 2018;74:226-232.
10. Gill IS, Patil MB, Abreu AL, et al. Zero ischemia anatomical partial nephrectomy: A novel approach. J Urol 2012;187:807-814.
11. Kaczmarek BF, Tanagho YS, Hillyer SP, et al. Off-clamp robot-assisted partial nephrectomy preserves renal function: A multi-institutional propensity score analysis. Eur Urol 2013;64:988-993.
12. Simone G, Capitanio U, Tuderti G, et al. On-clamp versus off-clamp partial nephrectomy: Propensity score-matched comparison of long-term functional outcomes. Int J Urol 2019;26:985-991.
13. Simone G, Misuraca L, Tuderti G, et al. Purely off-clamp robotic partial nephrectomy: Preliminary 3-year oncological and functional outcomes. Int J Urol 2018;25:606-614.
14. Demirel HC, Tokuc E, Turk S, et al. Complication Rates and Postoperative Renal Function in Partial Nephrectomy Which Factors Should be Considered? Grand J Urol 2021;1:101-108.
15. Simone G, Papalia R, Guaglianone S, Gallucci M. 'Zero ischaemia', sutureless laparoscopic partial nephrectomy for renal tumours with a low nephrometry score. BJU Int 2012;110:124-130.

Review

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Testis Sparing Surgery in Pediatric Population

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Abstract

In this review, it is aimed to illuminate the place of testicular sparing surgery in childhood testicular tumors in the light of current literature. The importance of organ-sparing surgery is highlighted because a significant portion of childhood testicular tumors are benign and organ-sparing surgery reduces morbidity without affecting disease-related survival. Testis sparing surgery can be considered as an alternative to radical inguinal orchiectomy in synchronous bilateral testicular tumors, metachronous contralateral tumors, and in the presence of normal solitary testis if preoperative testosterone level is normal and the tumor size is less than 30% of the testicular volume. However, definite recommendations could not be determined due to the lack of literature data.
Keywords: Child, testicular tumor, testis sparing surgery

Introduction

Testicular tumors constitute 1-2% of all childhood solid tumors (1,2,3) and more than 74% of them are benign (4). The incidence of childhood testicular tumors is 0.52/100,000 (5). The incidence of testicular tumors in the postpubertal period is 10 times higher than in children under 12 years of age. The incidence of testicular tumor peaks especially under the age of 3 and during adolescence (15-18 years) (2,6). Undescended testis, testicular atrophy, infertility, contralateral testicular germ cell tumor, familial testicular germ cell tumor and gonadal dysgenesis are among the risk factors for malignant testicular tumor in children. The risk in undescended testis increases 4.8 times (7). It was reported that the risk increases 3.5 times in children who were operated on for undescended testis after the age of 10 (8). In the prospective population-based study conducted by Pettersson et al. (9), it was observed that the least risky group was children who were operated on before the age of 6 (RR=2.02). It was reported that the risk in unilateral undescended testes operated on before the age of 10-12 years was reduced by 2-6 times compared to those operated on later (10). Testicular tumors seen before puberty are generally observed in a single histological type, unlike adult testicular tumors (11) and seminomas are not observed in the prepubertal period (12). 1p deletion, structural defects in 2p and 3p chromosomes, and loss of 6q, which are not common in adults, are common in pediatric germ cell tumors. According to the Prepubertal Testicular Tumor Registry (PTTR), the main testicular tumors are yolk sac tumors and then teratomas. Although extensive database analyzes indicated that teratomas were more common, the results were inconsistent as these data were not limited to prepubertal children (13,14). As a result, yolk sac tumors and teratomas are the most common testicular tumors seen before puberty. According to PTTR data, the age at diagnosis is 16 months for yolk sac tumors and 13 months for teratomas (15,16).

Clinical Findings

The most important clinical finding is painless scrotal mass or stiffness (50-95%) (1,17,18). In addition, testicular mass can be detected after trauma (3%), with detection of hydrocele (10%), with the presence of testicular pain or torsion (21%), or incidentally (10-53%). Early puberty symptoms and gynecomastia can also be counted among the first findings.

Diagnosis

The diagnosis is usually made by scrotal ultrasound (USG) after taking anamnesis and performing physical examination. Physical examination should be done very carefully in terms of differential diagnosis of epididymitis, hydrocele, testicular torsion, orchitis, and inguinal hernia. Testicular tumors may be associated with hydrocele at a rate of 15-20% (15). Although ultrasonography has a high sensitivity in detecting an intra- or extra-testicular

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scrotal mass, its sensitivity is low in the differentiation of malignancy. In intratesticular masses, its sensitivity is over 90% (19), but its specificity is 44.4% (20). It is the imaging method that should be chosen first because it is easily accessible, reliable and non-invasive. In case of malignancy, computer tomography or magnetic resonance imaging of abdomen, pelvis and lungs are performed.

Tumor Markers

Tumor markers can be helpful in distinguishing preoperative histological types and in postoperative follow-up. Alpha-fetoprotein (AFP) is the equivalent of fetal albumin. AFP is produced in fetal yolk sac and later in fetal liver cells. Increased AFP values can be found in pregnancy, hepatocellular cancer, cirrhosis, non-seminatous germ cell tumors and viral hepatitis (21). AFP is also frequently increased (90%) in yolk sac tumors and has a half-life of 5 days. Human chorionic gonadotropin (β-hCG) is found to be elevated in choriocarcinoma and embryonal cell carcinoma, but these tumors are not common in the prepubertal period. Therefore, measurement of β-hCG in childhood testicular tumors does not help the diagnosis much (22). The half-life of β-hCG is 24 hours. AFP is an important tumor marker in the prepubertal period, while β-hCG is a marker in rarer cases (2). AFP is physiologically high in healthy infants up to 8 months of age. It reaches adult levels up to 1 year of age. Therefore, care should be taken in associating AFP levels with tumors (2,23). LH, FSH, testosterone and urinary 17-ketosteroid levels should be examined in testicular tumors seen with early puberty findings.

Classification

Classification is made as primary, secondary and metastatic tumors according to their histopathological features. Benign primary testicular tumors are consisted of epidermoid and dermoid cysts of epithelial origin, Leydig and Sertoli cell tumors of sex cord-stromal origin, and teratomas of germ cell origin. Teratomas are the most common benign tumors. Primary testicular tumors with malignant character are germ cell-derived embryonal carcinoma, yolk sac tumors, choriocarcinoma, gonadoblastoma, and paratesticular rhabdomyosarcoma. Yolk sac tumors are the most common malignant testicular tumors. Secondary tumors include testicular lymphoma and leukemia. Neuroblastoma and Wilms tumor can metastasize to the testis in childhood.

Treatment

The basic approach in the surgical treatment of malignant testicular tumor is radical inguinal orchiectomy. There is no place for scrotal approach and testicular biopsy except in some special cases. In benign tumors, testis sparing surgery (TSS) is the basic approach.

• Radical Inguinal Orchiectomy

Radical inguinal orchiectomy is the basic approach in testicular tumor with clinically malignant character or diagnosed as malignant in frozen examination (24). The fact that the testicles are not a vital organ, sperm bank and hormonal replacement therapy are among the reasons supporting this surgery. However, after inguinal orchiectomy, castration may develop at a young age and sexual functions may decrease. It can cause psychological effects as well as endocrine and fertility related problems.

• Testis Sparing Surgery

Testis-sparing surgery was first performed by Richie (25) in a patient with bilateral seminoma. Pediatric TSS was performed in a patient with cystic teratoma in 1983 (26). The belief that the prevalence of a benign mass originating from the testis was low and that biopsy from a malignant mass would lead to tumor seeding caused the treatment choice to be limited to radical orchiectomy until the 1990s (27). Conservative surgical interventions in testicular tumors have come to the fore, with improvements in oncological outcomes of testicular tumors, long lifespan due to cancer, understanding of the prevalence of benign testicular tumors in childhood, and the increasing number of non-palpable masses with the widespread use of testicular USG (28,29). The high diagnostic value of the frozen examination, the increase in the quality of life, and the preservation of endocrine functions have made the approach that preserves the testis to be preferred. Studies are continuing to strengthen the use of TSS in patients in whom the other testicle is intact, not only in children with bilateral testicular tumors or a single testicle that has lost the other testicle for other reasons. Because there is a risk of losing one of the testicles over time due to trauma, infection or testicular tumor (30,31,32). In addition, in a series of 2.800 patients in whom radical inguinal orchiectomy was performed with the preliminary diagnosis of testicular tumor, it was observed that the cause was benign tumor in 31% of the patients (33). Before this surgery, serum AFP and β-hCG levels should be measured and scrotal ultrasonography should be performed, and peroperative frozen biopsy should be sent (24,34). TSS should be considered teratoma, gonadal stromal tumors and epidermoid cysts in the prepubertal period (24). According to the results of TSS performed in Leydig cell tumors; local recurrence was observed in only one patient during an average follow-up period of 4-8 years, and there was no local or distant recurrence other than that (35,36,37,38). Oncological follow-up is not required in prepubertal patients with Leydig cell tumor, gonadoblastoma, teratoma, epidermoid cyst and juvenile granulosa cell tumor. However, patients with yolk sac tumor and undifferentiated stromal tumor should undergo examination for metastatis and be followed up closely. Although the European Association of Urology (EAU) guidelines do not recommend TSS in patients in whom the contralateral testis is healthy, they recommend that TSS can be performed in patients with synchronous bilateral tumors, metachronous contralateral tumors, or solitary testicles with a tumor volume of less than 30% of the testicular volume and a normal testosterone level before the operation. Since approximately 82% of these testicles have testicular intraepithelial neoplasia (TIN), adjuvant radiotherapy (20 Gy) is recommended after surgery (39). In the "European Consensus Conference on Diagnosis and Treatment of Germ Cell Cancer" 2008 meeting, it was stated that testicular sparing surgery might be an alternative procedure to radical orchiectomy in the presence of synchronous bilateral or metachronous contralateral tumors or in patients with normal

preoperative testosterone levels with solitary testis, as in the EAU guidelines. It was reported that the presence of TIN should be well evaluated and adjuvant radiotherapy should be given in unilateral testicular tumors (40). In a 73-patient study conducted by the German Testicular Cancer group, 18 Gy radiotherapy was given to patients with TIN who underwent TSS, and it was observed that disease-free survival was achieved in 98.6% of the patients in a 91-month follow-up, that 85% of the patients did not need testosterone replacement therapy, and that fertility was preserved in 50% of the patients (41). Local recurrence or distant metastasis was not detected in any patient with pediatric testicular teratoma and epidermoid cyst who underwent TSS with a 22-year follow-up period (34,42). In a comprehensive study by Heidenreich et al. (27), in the 37-year follow-up of 120 patients with testicular epidermoid cyst, no local recurrence or distant metastasis was found in any patient. Apart from epidermoid cyst and Leydig cell tumor, TSS seems to be an appropriate approach in patients with tunica albuginea cysts, intraparenchymal cysts, adenomatoid tumor, dermoid cyst, inflammatory pseudotumor, postinflammatory fibrosis, granulomatous inflammation, hemangioma, and Sertoli cell tumor. The fact that these benign lesions of the testis are masses that can be easily diagnosed without causing confusion in the frozen incision examination facilitates the decision of the surgeon peroperatively (2,3,12,13). In a study conducted with 24 patients with negative serum markers and a mean age of 10.7 years who underwent radical or partial orchiectomy due to unifocal and unilateral intratesticular tumor; while TSS was found sufficient for tumors that were benign in the final pathological examination and did not contain germ cells; lesions containing active germ cell tumor structure were not suitable for TSS (43). In the same study, it was reported that the frozen pathological examination was compatible with the final pathological examination and did not miss patients that were not suitable for TSS. Of the patients who were found to be unsuitable for TSS, it was found that they were statistically older (17.1 vs. 9.3 years; p=0.029). It was stated that 95% (n=19) of the children who had a mass less than 2 cm had the appropriate pathology for TSS (43).

Surgical Technique

For TSS, after passing the layers with an inguinal incision, the external oblique aponeurosis is opened up to the internal ring, and the cord structures are suspended and held with a soft vascular clamp or turned with a tourniquet. The testis is delivered through the inguinal incision, the mass is palpated, and the testis is placed in crushed ice. Routine use of intraoperative USG is another recommended point in order to detect a small mass or a mass focus other than the one previously defined in the testis (44,45). The tunica vaginalis is opened over the mass and an incision is made around the mass. Excisional biopsy is applied to the mass without disturbing the capsule integrity and the tissue is sent for frozen biopsy examination. The edges of the tunica albuginea are then approximated with a thin, absorbable suture. If the frozen result is benign, the clamp is removed and bleeding is controlled, the tunica vaginalis is closed, the testis is placed in the scrotum, the layers are closed and the operation is completed. In case of malignancy, orchiectomy is performed if the patient's other testis is intact. Despite the finding of malignancy in an individual with intact contralateral testis, there is currently insufficient knowledge to perform TSS. In this case, there is a risk of local recurrence, multifocal disease, tumor cell cultivation and progression. In patients in whom there is bilateral masses or a mass in the solitary testis that is malignant as a result of the frozen examination, multiple biopsies are taken from the parenchymal tissue remaining after the mass excision, and another concomitant malignancy focus or TIN is tried to be determined (46,47). Long-term disease-free survival can be achieved with tumor enucleation, biopsy from the tumor bed, frozen examination, peripheral parenchyma biopsy, radiotherapy to the remaining tissue, and close follow-up.

Conclusion

Most prepubertal testicular tumors are benign, but all scrotal masses should be evaluated for malignancy. If a palpable scrotal mass is detected, scrotal USG should be performed and tumor markers should be checked. Today, radical inguinal orchiectomy is the gold standard method in the treatment of testicular tumors. TSS seems to be an alternative method, especially in masses that are thought to be benign in childhood, and the authors recommend that the possible benefits and risks should be discussed with the parents of appropriate patients. If malignancy is detected in the frozen section examination, radical inguinal orchiectomy should be continued.

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References

1. Akiyama S, Ito K, Kim WJ, et al. Prepubertal testicular tumors: a single-center experience of 44 years. J Pediatr Surg 2016;51:1351-1354.
2. Ross JH. Prepubertal testicular tumors. Urology 2009;74:94-99.
3. Brosman SA. Testicular tumors in prepubertal children. Urology 1979;13:581-588.
4. Pohl HG, Shukla AR, Metcalf PD, et al. Prepubertal testis tumors: actual prevalence rate of histological types. J Urol 2004;172:2370-2372.
5. Coppes MJ, Rackley R, Kay R. Primary testicular and paratesticular tumors of childhood. Med Pediatr Oncol 1994;22:329-340.
6. Alanee S, Shukla A. Paediatric testicular cancer: an updated review of incidence and conditional survival from the Surveillance, Epidemiology and End Results database. BJU Int 2009;104:1280-1283.

7. Dieckmann KP, Pichlmeier U. Clinical epidemiology of testicular germ cell tumors. World J Urol 2004;22:2-14.
8. Walsh TJ, Dall'Era MA, Croughan MS, et al. Prepubertal orchiopexy for cryptorchidism may be associated with lower risk of testicular cancer. J Urol 2007;178:1440-1446.
9. Pettersson A, Richiardi L, Nordenskjold A, et al. Age at surgery for undescended testis and risk of testicular cancer. N Engl J Med 2007;356:1835-1841.
10. Wood HM, Elder JS. Cryptorchidism and testicular cancer: separating fact from fiction. J Urol 2009;181:452-461.
11. Ross JH, Kay R. Prepubertal testis tumors. Rev Urol 2004;6:11-18.
12. Mostfi F. Tumors of the male genital system. Atlas of Tumor Pathology 1973:114-119.
13. Sugita Y, Clarnette TD, Cooke-Yarborough C, et al. Testicular and paratesticular tumours in children: 30 years' experience. Aust N Z J Surg 1999;69:505-508.
14. Rushton HG, Belman AB. Testis-sparing surgery for benign lesions of the prepubertal testis. Urol Clin North Am 1993;20:27-37.
15. Javadpour N. Principles and management of testicular cancer: Thieme-Stratton Corp; 1986.
    https://www.sciencedirect.com/science/article/abs/pii/S0022534717457053
16. Ross JH, Rybicki L, Kay R. Clinical behavior and a contemporary management algorithm for prepubertal testis tumors: a summary of the Prepubertal Testis Tumor Registry. J Urol 2002;168:1678-1679.
17. Taskinen S, Fagerholm R, Aronniemi J, et al. Testicular tumors in children and adolescents. J Pediatr Urol 2008;4:134-137.
18. Agarwal PK, Palmer JS. Testicular and paratesticular neoplasms in prepubertal males. J Urol 2006;176:875-881.
19. Benson C. The role of ultrasound in diagnosis and staging of testicular cancer. Semin Urol; 1988.
20. Coret A, Leibovitch I, Heyman Z, et al. Ultrasonographic evaluation and clinical correlation of intratesticular lesions: a series of 39 cases. Br J Urol 1995;76:216-219.
21. Perkins GL, Slater ED, Sanders GK, Prichard JG. Serum tumor markers. Am Fam Physician 2003;68:1075-1088.
22. Palmer J, Morris K, Steinberg G, Kaplan W. Testicular, sacrococcygeal, and other tumors. Comprehensive Textbook of Genitourinary Oncology. Philadelphia: Lippincott Williams & Wilkins, 2000.
23. Grady RW. Current management of prepubertal yolk sac tumors of the testis. Urol Clin North Am 2000;27:503-508.
24. Metcalfe PD, Farivar-Mohseni H, Farhat W, et al. Pediatric testicular tumors: contemporary incidence and efficacy of testicular preserving surgery. J Urol 2003;170:2415-2416.
25. Richie J. Simultaneous bilateral tumors with unorthodox management. World J Urol 1984;2:74.
26. Marshall S, Lyon RP, Scott MP. A conservative approach to testicular tumors in children: 12 cases and their management. J Urol 1983;129:350-351.
27. Heidenreich A, Bonfig R, Derschum W, et al. A conservative approach to bilateral testicular germ cell tumors. J Urol 1995;153:10-13.
28. Oliver T. Conservative management of testicular germ-cell tumors. Nat Rev Urol 2007;4:550-560.
29. Carmignani L, Gadda F, Gazzano G, et al. High incidence of benign testicular neoplasms diagnosed by ultrasound. J Urol 2003;170:1783-1786.
30. Giannarini G, Dieckmann KP, Albers P, et al. Organ-sparing surgery for adult testicular tumours: a systematic review of the literature. Eur Urol 2010;57:780-790.
31. Arık A, Uygur C. Testis koruyucu cerrahi. Bull Urooncol 2004;2:6-8.
32. Kabay Ş. To whom and how to do testis sparing surgery? Bull Urooncol 2011;3:59-62.
33. Haas GP, Shumaker BP, Cerny JC. The high incidence of benign testicular tumors. J Urol 1986;136:1219-1220.
34. Shukla AR, Woodard C, Carr MC, et al. Experience with testis sparing surgery for testicular teratoma. J Urol 2004;171:161-163.
35. Carmignani L, Colombo R, Gadda F, et al. Conservative surgical therapy for Leydig cell tumor. J Urol 2007;178:507-511.
36. Giannarini G, Mogorovich A, Menchini Fabris F, et al. Long-term followup after elective testis sparing surgery for Leydig cell tumors: a single center experience. J Urol 2007;178:872-876.
37. Suardi N, Strada E, Colombo R, et al. Leydig cell tumour of the testis: presentation, therapy, long-term follow-up and the role of organ-sparing surgery in a single-institution experience. BJU Int 2009;103:197-200.
38. Albers P, Albrecht W, Algaba F, et al. Guidelines on testicular cancer: 2015 update. Eur Urol 2015;68:1054-1068.
39. Albers P, Albrecht W, Algaba F, et al. European Association of Urology guidelines on testicular cancer. 2017. https://uroweb org//guideline/testicular-cancer Accessed. 2018;2:2018.
40. Krege S, Beyer J, Souchon R, et al. European consensus conference on diagnosis and treatment of germ cell cancer: a report of the second meeting of the European Germ Cell Cancer Consensus group (EGCCCG): part I. Eur Urol 2008;53:478-496.
41. Passarella M, Usta MF, Bivalacqua TJ, et al. Testicular sparing surgery: a reasonable option in selected patients with testicular lesions. BJU Int 2003;91:337-340.
42. J.S. Valla for the Group D'Etude en Urologie Pédiatrique. Testis-sparing surgery for benign testicular tumors in children. J Urol 2001;165:2280-2283.
43. Caldwell BT, Saltzman AF, Maccini MA, Cost NG. Appropriateness for testis-sparing surgery based on the testicular tumor size in a pediatric and adolescent population. J Pediatr Urol 2019;15:70.
44. Steiner H, Höltl L, Maneschg C, et al. Frozen section analysis-guided organ-sparing approach in testicular tumors: technique, feasibility, and long-term results. Urology 2003;62:508-153.
45. Heidenreich A, Weissbach L, Höltl W, et al. Organ sparing surgery for malignant germ cell tumor of the testis. J Urol 2001;166:2161-2165.
46. Leroy X, Rigot JM, Aubert S, et al. Value of frozen section examination for the management of nonpalpable incidental testicular tumors. Eur Urol 2003;44:458-460.
47. Giannarini G, Mogorovich A, Bardelli I, et al. Testis-sparing surgery for benign and malignant tumors: A critical analysis of the literature. Indian J Urol 2008;24:467-474.

Case Report

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Partial Cystectomy in Patients with Huge Bladder Mass Who are Unfit for Curative Surgery: Case Presentation and Literature Review

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Abstract

Bladder cancer (BC) is a common genitourinary malignancy among the advanced age population. BC with non-metastatic muscle-invasive diseases requires neoadjuvant chemotherapy followed by radical cystectomy or bladder-sparing approach with systemic chemotherapy plus definitive radiation therapy. Patients with advanced age are the fastest-growing segment of the population worldwide. Age itself is not a disease; however, elderly patients with reduced functional organ reserve are more sensitive to any medical stress factor. Therefore, patients may lose their chance of getting chemotherapy, radiotherapy, and surgical treatment. This case series aimed to examine the approach to patients who lost the chance of transurethral bladder mass resection in a single session.
Keywords: Bladder cancer, partial cystectomy, quality of life

Introduction

Bladder cancer (BC) is the second most common genitourinary malignancy, especially in the advanced age population (1). At the initial presentation, 25% of BCs are either invasive or metastatic (2). BC with the non-metastatic muscle-invasive disease requires neoadjuvant chemotherapy followed by radical cystectomy or bladder-sparing approach with systemic chemotherapy plus definitive radiation therapy.

Patients with advanced age are the fastest-growing segment of the population worldwide. Age itself is not a disease; however, elderly patients with reduced functional organ reserve are more sensitive to any medical stress factor (3). Therefore, patients may lose their chance of getting chemotherapy, radiotherapy, and surgical treatment. In this case series after obtaining the written consent of the patients, we tried to examine the approach to patients who lost the chance of transurethral resection of the bladder mass in a single session.

Case Reports

Case 1

An 80-year-old female patient presented with a 2-month history of total incontinence and an incomplete voiding sensation, as well as dysuria, loin, and intermittent flank pain. Physical examination was unremarkable. She had a history of hypertension from a cerebrovascular event. Urine culture detected extended-spectrum beta-lactamase-positive *Escherichia coli*, which was treated with culture-directed antibiotics, and repeat culture was sterile. Blood studies including complete blood count (CBC), urea, and electrolytes showed mild anemia. Urinary ultrasonography (USG) revealed a huge mass within the bladder lumen and bilateral grade two hydroureteronephrosis. Pelvic magnetic resonance imaging (MRI) revealed a giant mass of 11×11×11 cm that filled the bladder lumen with bilateral hydronephrosis (Figure 1a).

At first, cystoscopy was done at which a vegetating mass with right anterolaterally located at the base that fills the bladder lumen was seen. Then the operative management of partial cystectomy (PC) was performed for the quality of life (Figure 1b). Histopathological examination of the mass, which was 20×18 cm, revealed undifferentiated pleomorphic sarcoma (Figure 1c).The patient's voiding complaints improved soon after the operation. The patient was followed up after her discharge, and 3 months later the patient applied to our clinic with a complaint of urinary leakage from her suprapubic incision scar (Figure 1d). A new mass of approximately 10 cm in size in the bladder cavity was seen at the cystoscopic examination.The

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patient died 5 months later because of acute renal failure due to postrenal obstruction secondary to recurrent tumor burden.

Case 2

A 77-year-old male patient presented with unbearable lower urinary tract symptoms and hematuria. Physical examination was unremarkable. He had a history of urothelial cancer without regular follow-up. The urine culture was sterile. CBC, urea, and electrolytes were normal. Urinary USG revealed a huge mass within the bladder lumen. Pelvic MRI revealed a giant heterogeneous mass lesion of 15×16×13 cm that filled the bladder lumen that could not be distinguished from the right iliac artery and the rectus muscles were observed (Figure 2a).

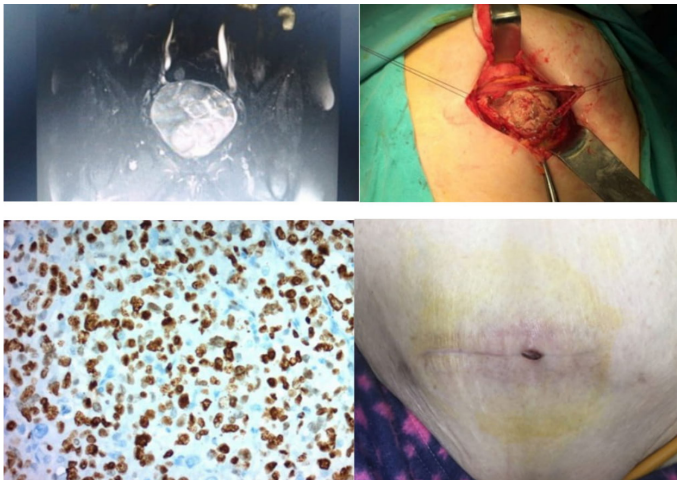

Figure 1a. Magnetic resonance imaging of the mass, **1b.** Mass in the bladder, **1c.** Anti-Ki-67 antibody (30-9, Ventana, USA; ×20) positivity in over 75% of tumor cells, 1d. Fistula to suprapubic incision scar

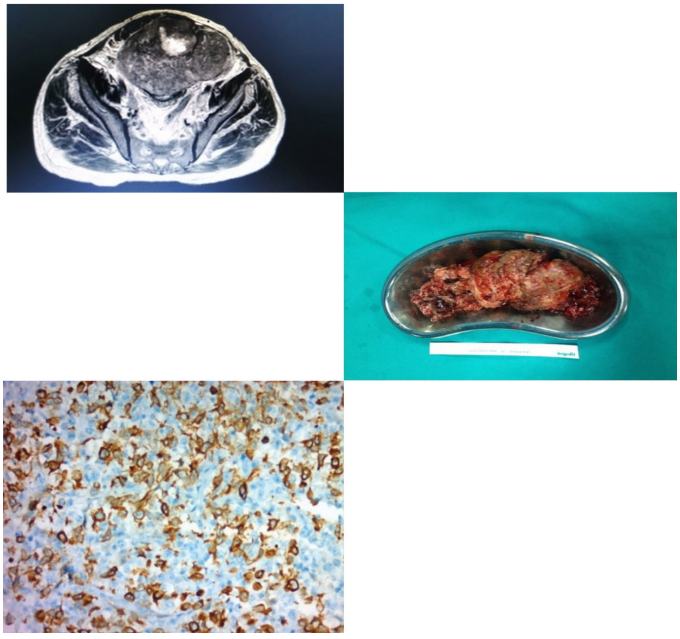

Figure 2a. Magnetic resonance imaging of the mass, **2b.** Removed mass, **2c.** Anti-cytokeratin positivity in atypical cells (AE1/AE3, Genemed, USA; 1/50×20)

The patient's preoperative risk of anesthesia was high because of pulmonary complaints. Thus, cystoscopy was done first, where a vegetating mass with an apically located base that fills the bladder lumen was seen. Then, the operative management of PC was performed for the quality of life (Figure 2b).

Histopathological examination revealed a malign epithelial tumor, which is highly active and observed immunohistochemically and histomorphological epithelial (Figure 2c). The material consists only of tumor tissue. The healthy tissue from the bladder that will clarify the localization was undetected despite numerous samples. However, the primary source of the mass was the bladder wall when the localization of the removed material was considered. Patient complaints were regressed in the early postoperative period; however, after 9 months, the patient died because of respiratory failure due to pneumonia.

Case 3

A 72-year-old male patient presented with lower urinary tract symptoms and hematuria. He had a ruptured urethra from a traffic accident in 1967. Thereafter, several endoscopic procedures were applied due to urethral stricture. The last operation was 3 years ago. Since that date, he had a history

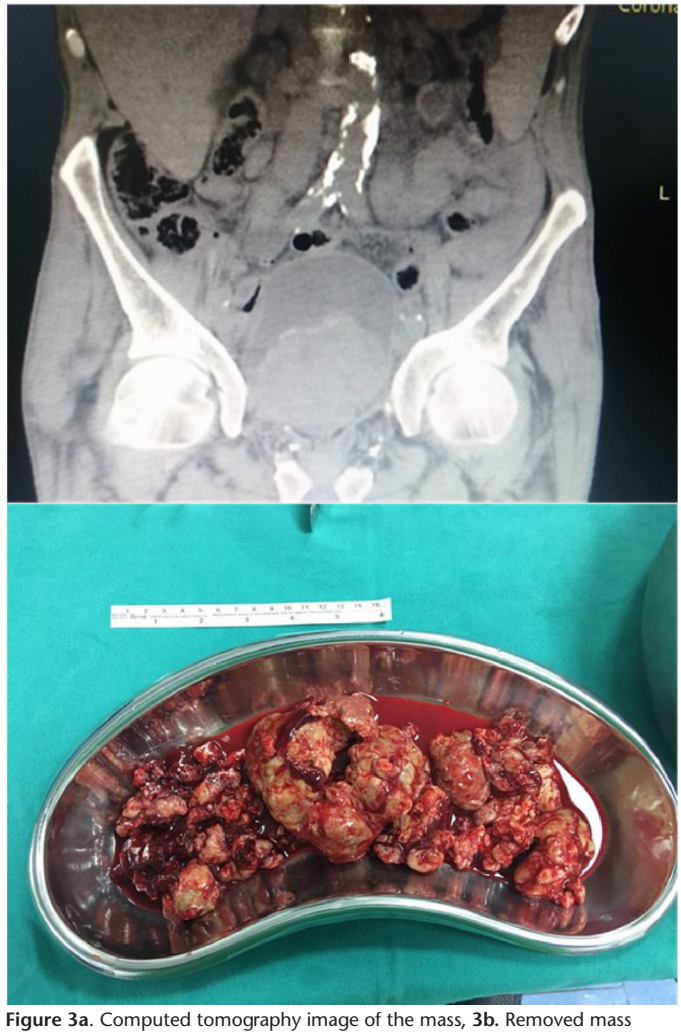

Figure 3a. Computed tomography image of the mass, **3b.** Removed mass

of hematuria without follow-up. He had been undergoing dialysis for 3 days a week for 10 years and was followed up in the endocrinology department due to hypothyroidism for 3 years. His cardiac ejection fraction was 30%, with simultaneous chronic lung disease. Physical examination was unremarkable. The urine culture was sterile. CBC, urea, and electrolytes were normal. Urinary USG revealed a huge mass within the bladder lumen. Abdominal computed tomography revealed a giant heterogeneous mass lesion of 8×8×10 cm that filled the bladder lumen without other pathological findings outside the bladder (Figure 3a).

The patient's preoperative risk of anesthesia was high due to comorbidities. At cystoscopy, a vegetating mass with a left-sided base fills the bladder lumen. Then the operative management of PC was performed for the quality of life (Figure 3b).

Histopathological examination revealed infiltrative urothelial carcinoma. The World Health Organization Quality of Life Brief Version (1998) form was filled by the patient before the operation and at the appropriate postoperative period to evaluate his general health status, physical, psychological health, and social and environmental relations. The answers revealed that general, physical, and psychological health status improved by 50%, 7%, and 16%, respectively. However, changes were not seen among his social and environmental relations. Additionally, after 9 months of follow-up, the patient died because of renal and heart failure. None of the cases had distant organ metastases.

Discussion

Surgical indications for bladder tumors have been well defined nowadays (4,5,6). As emphasized, the overall health status of the patient must be well assessed before the treatment decisions for patients with bladder tumors (7). Miller et al. (7) found an association between comorbidity and adverse pathological and survival outcomes following RC in their study. Similarly, Extermann et al. (8) reported difference in the impact of performance status and comorbidity on treatment outcomes and have suggested independently evaluating these parameters. Our cases revealed that patients were not suitable for chemoradiotherapy and were at high risk for surgery. The urinary tract symptoms were unbearable for these patients, and removing the masses in a single session transurethrally was impossible. The tumor recurred shortly afterward and all patients died after PC. In all cases, comorbidities reduce the tolerance for radical surgery, limiting daily activities that could prevent taking the chemoradiotherapy arm of the organ-preserving treatment strategy and increasing the risks of anesthesia. Therefore, extracting the mass by PC without taking pathological specimens from the existing masses was decided to avoid additional anesthetic burden to the patient. Patients' lower urinary tract complaints had subsided shortly after surgery. However, tumor recurrence was observed 3 months later in the first case and 5 months later in the second and third cases. The first patient died at 5 months, and the second and third patients at the 9-month follow-up. The local recurrences and patient deaths in a short period led us to question our treatment approaches. Hamilton et al. (9) revealed that patients significantly benefited from palliative surgery despite the perioperative complication rates. As the patients' quality of life improved, their future hopes have also increased (9). Therefore, they reported that patients benefited physically and mentally from a palliative surgery although morbidity and mortality were high (9). Our patients also had low morbidity and improved quality of life until death.

The primary goal in cancer surgery is increasing the life span despite its diagnostic, curative, and palliative purpose. The increasing importance of the concept of quality of life has necessitated a change in surgical approaches. Palliative surgical approaches to improve symptom control and improve quality of life have come to light in patients who have missed the chance of curative surgery (10). Cancer surgery completely cleans the tumor cells, and its principles are certain. However, literature on palliative surgery is limited, and knowledge about the indication, purpose, risks, and benefits of palliative surgery is still insufficient. In palliative surgery, the surgeon must use their clinical knowledge and experience to have greater expected treatment benefits than risks and harms. Moreover, the surgeon should inform patients and their relatives in detail about the results of this palliative surgery in improving the quality of life.

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References

1. Maestroni U, Giollo A, Barbieri A, et al. Bladder carcinosarcoma: A case observation. Acta Biomed 2004;75:74-76.
2. Burger M, Catto JW, Dalbagni G, et al. Epidemiology and risk factors of urothelial bladder cancer. Eur Urol 2013;63:234-241.
3. Girgin R, Topaktaş R, Altın S, et al. The Effect of Charlson's Comorbidity Index on Clavien-Dindo Classification of Surgical Complications in Percutaneous Nephrolitotomy. J Urol Surg 2016;3:84-89.
4. Hautmann RE, Gschwend JE, de Petriconi RC, et al. Cystectomy for transitional cell carcinoma of the bladder: results of a surgeryonly series in the neobladder era. J Urol 2006;176:486-492.
5. Witjes JA, Compérat E, Cowan NC, et al. EAU guidelines on muscle-invasive and metastatic bladder cancer: summary of the 2013 guidelines. Eur Urol 2014;65:778-792.
6. Willis D, Kamat AM. Nonurothelial bladder cancer and rare variant histologies. Hematol Oncol Clin North Am 2015;29:237-252.

7. Miller DC, Taub DA, Dunn RL, et al. The impact of co-morbid disease on cancer control and survival following radical cystectomy. J Urol 2003;169:105-109.
8. Extermann M, Overcash J, Lyman GH, et al. Comorbidity and functional status are independent in older cancer patients. J Clin Oncol 1998;16:1582-1587.
9. Hamilton TD, Selby D, Tsang ME, et al. Patients' perceptions of palliative surgical procedures: a qualitative analysis. Ann Palliat Med 2017;6(Suppl 1):77-84.
10. McCahill LE, Krouse RS, Chu DZ, et al. Decision making in palliative surgery. J Am Coll Surg 2002;195:411-422.

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Sertoli Cell Testicular Tumor: A Case Report

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Abstract

Sertoli cell tumors are malignancies that constitute only 1% of all testicular cancers and are frequently observed between the ages of 30 and 40 years. Most Sertoli cell tumors have a benign clinical course. The molecular mechanisms involved in the etiopathogenesis of these tumors are unclear. Herein, presented a 28-years-old male patient with a painless mass in the right testicle and had a diagnosis of Sertoli cell cancer and discussed in the light of the literature.
Keywords: Sertoli cell, testis, tumor, treatment

Introduction

Testicular cancers are rare clinical conditions and account for approximately 1-2% of all male malignancies (1). In 2020, 9.610 new testicular tumors were estimated to be diagnosed in the United States, with 440 deaths due to this malignancy (2). Therefore, the Sertoli cell testicular tumor is a rare malignancy that constitutes approximately 1% of testicular cancers (3) and is observed at all age intervals. However, clinicians encounter patients with Sertoli cell tumors mostly in the third or fourth decades of their lives. Unilateral testicular mass with a slow growth pattern is the most common symptom of patients who present to urology departments (4). Herein, presented a case of Sertoli cell testicular tumor (not otherwise specified) in a patient who presented with complaints of a slowly growing painless mass in the right testicular region for 2 years.

Case Report

A 28-year-old male patient visited our clinic with a painless mass in the right testicle showing a slow growth pattern for 2 years. The genitourinary system examination revealed a mass of approximately 2.5 cm in a hard and fixed character, with clear boundaries. The patient had no history of scrotal trauma, urological surgery, or chronic disease. Additionally, a detailed general examination of the patient did not yield any pathological indication for systemic diseases, such as gynecomastia, lymphadenopathy, or hyperpigmentation. No abnormal values were detected in routine hematologic and biochemical parameters. Further, testicular tumor markers, such as serum lactate dehydrogenase (31 IU/L), α-fetoprotein (4.14 IU/mL), and β-human chorionic gonadotropin (1.02 mIU/mL), were within the normal limits. B-mode ultrasonography revealed a well-bordered, round, and solid mass lesion with echogenic areas inside the right testicle. The mass was observed in Doppler ultrasonography as a heterogeneous hypoechoic solid lesion in 29×21×20 mm dimensions with vascularization in places inside and in its periphery (Figure 1a, b). The patient underwent right high inguinal orchiectomy. Tissue samples were analyzed by two pathologists in the pathology department. Before the pathologic examination, specimens obtained from the patient were first macroscopically evaluated. Then, tissue samples were formalin-fixed, paraffin-embedded, and 4 µ sections were obtained using a tissue microtome. Sections were stained with hematoxylin and eosin and analyzed under an upright light microscope. Immunohistochemical analyses were performed using a Leica Bond Max immunostainer. All sections were then analyzed under light microscopy, which revealed a tumor infiltration in testicular parenchyma. The infiltrative pattern was both solid and tubular. Tumor cells had relatively uniform nuclei with small nucleoli and a large pale eosinophilic cytoplasm with indistinct borders. They lied in different directions and had a solid, trabecular, and insular architecture. The solid

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counterpart was predominant; however, slightly elongated tubular structures were also observed in border areas between the tumor and testicular parenchyma. Tubules were lined in a single layer of cuboidal/columnar cells suggesting Sertoli cells. Mitosis counts were >5 in 10 high power fields. Necrosis was absent (Figure 2a, b, c). The testicular tumor was diagnosed as a "Sertoli cell tumor not otherwise specified" type (Figure 3a, b, c). Thoracic and abdominopelvic computed tomography scan revealed no evidence of lymphatic or distant metastases. The follow-up was uneventful in 30 months. This case report was written after obtaining patient consent.

Discussion

Testicular cancer can be derived from any testicular cell type; however, >95% of testicular cancers are germ cell tumors (5). Seminoma is the most frequent germ cell tumor, constituting approximately 60% of all germ cell neoplasms (6). Sex cord-stromal tumors account for approximately 4%

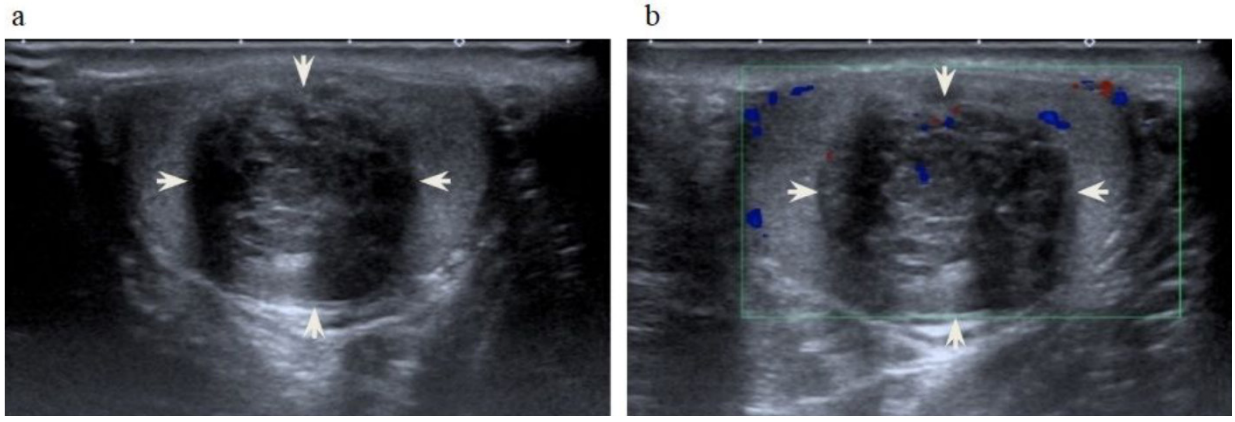

Figure 1a. B-mode USG shows a well-bordered, round, heterogeneous, and solid mass lesion with echogenic areas inside the testicle, **1b.** Doppler USG reveals the vascularization inside the mass and its periphery

USG: Ultrasonography

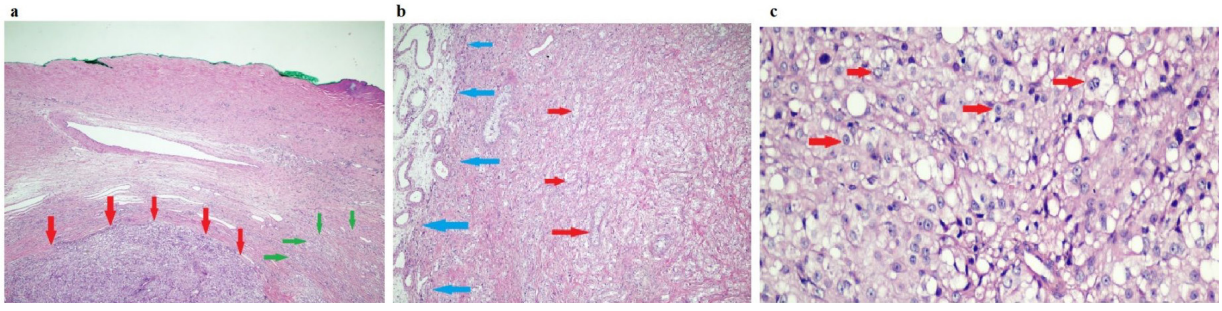

Figure 2a. Expansile solid tumor growing to the tunica albuginea (red arrows). Small tubular pattern tumor infiltration foci are shown (green arrows), **2b.** Tumor is well separated from testicular parenchyma (blue arrows). Weak tubular morphology is observed next to testicular parenchyma (red arrows), **2c.** The tumor is composed of uniform cells. The tumor cells have small and solitary nucleoli and vacuolated cytoplasm (red arrows). Binuclear forms are visible in some foci. Mitoses are rarely observed in tumor areas but necrosis is absent

Figure 3a, b, and c. Results of immunohistochemical analysis: S100 (A), vimentin (B), and WT1 (C) expression are shown

of all testicular cancers. Sex cord-stromal tumors (also known as, "androblastoma") are a spectrum of tumors, which has a differentiation of pure sex cord morphology in one end and pure stromal morphology in the other end, mostly composed of various proportions of both components. Sex cord-stromal tumor includes cells, which show fetal, pubertal, or adult Sertoli cell features (7,8). The pathological analyses categorized them into four groups: Leydig cell tumors, Sertoli cell tumors, granulosa cell tumors, and unclassified. Sertoli cell tumors are rarely observed pathologies and account for 0.4-1.5% of these tumors (9). The most common symptom is a painless and slow-growing testicular mass. Findings may also include gynecomastia and impotence due to hormonal changes (3,9). Studies with large series observed these hormonal changes in an average of 11-25% of cases (10). Concurrently, reports associated these pathologies with genetic syndromes, such as Carney syndrome and Peutz-Jeghers syndrome. This association is more common in bilateral or multiple Sertoli cell tumors (3). Sertoli cell tumors are mostly of benign characters; however, an in-depth literature analysis shows cases with malignant behavior. Generally, the aggressive attitude was estimated to be observed in 10-22% of these tumors (11). Sertoli cell testicular tumors are rarely observed, thus no strict follow-up and treatment protocols are available. The basic treatment approach includes radical inguinal orchiectomy. Currently, many authors report an appropriate evaluation of testicular-sparing surgery among treatment options, as the clinical course is extremely slow in most of these cases. The histopathological tumor features, such as the size of the mass, necrosis, lymphovascular invasion, and pleomorphism, are shown to be very closely related to the clinical course of the disease. Evaluating and analyzing patients who underwent testicular-sparing surgery with testicular ultrasonography is critical in terms of local recurrence and with chest, abdomen, and pelvic imaging to see any distant organ metastases. Grogg et al. (12) reported that 13% of patients underwent testicular-sparing surgery, local recurrence in only 1 patient during the 3-month follow-up, and 1% rate of contralateral recurrence in their meta-analysis of 435 cases. Testicular-sparing surgery was not performed since our patient's social facilities were extremely limited and he lived in a remote location to health centers, which would make his regular follow-ups difficult. However, various aggressive treatment strategies, such as retroperitoneal lymph node dissection, chemotherapy, and radiation therapy combinations, are applied in cases that show remote organ dissemination (13). Survival rates for 1 and 5 years were estimated as 93 and 77% for Stage 1 Sertoli cell tumors, respectively (11). Contrarily, late metastases were reported in some cases at stages up to 10 years (14). The World Health Organization classified this type of cancer in three categories: Sertoli cell tumor not otherwise specified, large cell calcifying Sertoli cell tumors, and sclerosing Sertoli cell tumors (15), of which the most common type is the Sertoli cell tumor not otherwise specified. Young et al. (8) conducted a large series of 60 cases with Sertoli cell tumor not otherwise specified. The average age of patients was 45 years. All tumors were unilateral and with an average size of 3.6 cm (range 0.3-15 cm). The same study reported the presence of metastatic disease by 6.7% at the time of arrival. Sertoli cell tumor not otherwise specified is located in testicular parenchyma, well-circumscribed, and has lobulated contours. The cut surface is solid, yellowish in color, and may contain foci of hemorrhage but necrosis is rare. Tumor cells are arranged in a solid or tubular fashion, and a reticular pattern of growth may be seen. These cells have uniform round or oval nuclei and pale eosinophilic cytoplasm. Atypia and pleomorphism among tumor cells are rare. A fibrous hyalinized stroma-containing dilated vascular structure may be seen between tumor islands. Mitoses are not frequent (<5 mitoses per 10 HPF) (7,8).

Therefore, considering rare pathologies, such as Sertoli cell tumors, among the pre-diagnoses for effective management of follow-up and treatment strategies for patients with painless testicular mass is crucial.

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EthicsE

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References

1. Manecksha RP, Fitzpatrick JM. Epidemiology of testicular cancer. BJU Int 2009;104:1329-1333.
2. Siegel R, Miller K, Jemal A. Cancer Statistics, 2020. Ca Cancer J Clin 2020;70:7-30.
3. Bang S, Lee SD. Testicular Sertoli Cell Tumor in an Adult. Korean J Urol 2009;50:300-302.
4. Cornejo KM, Young RH. Sex cord-stromal tumors of the testis. Diagnostic Histopathology 2019;25:398-407.
5. Cheville JC. Classification and pathology of testicular germ cell and sex cord-stromal tumors. Urol Clin North Am 1999;26:595-609.
6. Özen A, Durankuş NK. Radiotherapy for Germ Cell Testicular Tumors. Turkiye Klinikleri J Urology-Special Topics 2016;9:57-63.
7. Henley JD, Young RH, Ulbright TM. Malignant Sertoli cell tumors of the testis: a study of 13 examples of a neoplasm frequently misinterpreted as seminoma. Am J Surg Pathol 2002;26:541-550.
8. Young RH, Koelliker DD, Scully RE. Sertoli cell tumors of the testis, not otherwise specified: a clinicopathologic analysis of 60 cases. Am J Surg Pathol 1998;22:709-721.
9. Giglio M, Medica M, De Rose AF, et al. Testicular sertoli cell tumours and relative sub-types. Analysis of clinical and prognostic features. Urol Int 2003;70:205-210.

10. Gravas S, Papadimitriou K, Kyriakidis A. Sclerosing sertoli cell tumor of the testis-a case report and review of the literature. Scand J Urol Nephrol 1999;33:197-199.
11. Anglickis M, Stulpinas R, Anglickienė G, et al. Case Report of Misleading Features of a Rare Sertoli Cell Testicular Tumor. Medicina (Kaunas) 2019;55:170.
12. Grogg J, Schneider K, Bode PK, et al. Sertoli Cell Tumors of the Testes: Systematic Literature Review and Meta-Analysis of Outcomes in 435 Patients. Oncologist 2020;25:585-590.
13. Ross JH, Kay R. Prepubertal Testis Tumors. Rev Urol 2004;6:11-18.
14. Compérat E, Tissier F, Vieillefond A. [Late metastasis after a testicular Sertoli cell tumour]. Ann Pathol 2004;24:45-46.
15. Ishida M, Fujiwara R, Tomita K, et al. Sclerosing Sertoli cell tumor of the testis: a case report with review of the literature. Int J Clin Exp Pathol 2013;6:2640-2643.

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An Unusual Solitary Prostate Cancer Metastasis Detected by Gallium-68 Prostate-specific Membrane Antigen-labeled Positron Emission Tomography/Magnetic Resonance Imaging

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Abstract

The two most common sites of prostate cancer metastasis include the lymph nodes and bone. Solid-organ metastases usually occur in the lungs, liver, and brain. Prostate adenocarcinoma metastasis to the skin and subcutaneous cellular tissue occurs in <0.3% and are thus considered exceptional. Herein, we report a unique case of a pectoral subcutaneous metastasis as the first recurrence site after definitive local and systemic therapy for prostate cancer, which was identified by gallium-68 prostate-specific membrane antigen-labeled positron emission tomography/magnetic resonance imaging.
Keywords: Prostate cancer, metastasis, unusual, Ga-68 PSMA PET/MRI

Introduction

Prostate cancer is one of the most important health problems of males today. According to the 2018 GLOBOCAN data, prostate cancer is the second most common cancer in males but is the eighth in cancer-related deaths (1). The most frequent histologic type is adenocarcinoma. The two most common sites of metastasis include the lymph nodes and bone. Solid-organ metastases usually occur in the lungs, liver, and brain (2). Prostate adenocarcinoma metastasis to the skin and subcutaneous cellular tissue occurs in <0.3% and is thus considered exceptional (3). Herein, we report a unique case of a pectoral subcutaneous metastasis as the first recurrence site after definitive local and systemic therapy for prostate cancer, which was identified by Gallium-68 (Ga-68) prostate-specific membrane antigen (PSMA)-labeled positron emission tomography/magnetic resonance imaging (PET/MRI).

Case Report

A 66-year-old male patient had an International Society of Urological Pathology Grade 5 prostate adenocarcinoma with a prostate-specific antigen (PSA) level of 7 ng/mL. Ga-68 PSMA PET/MRI examination at the time of diagnosis did not reveal any systemic metastasis but showed right seminal vesicle invasion. The patient received neoadjuvant chemotherapy (six cycles of docetaxel) along with androgen ablation (after the third cycle of chemotherapy). Then, robot-assisted laparoscopic radical prostatectomy and lymph node dissection were performed. The pathological stage was pT3b N0. Surgical margins were negative, but the seminal vesicle invasion was confirmed. Androgen ablation was postoperatively stopped. Radiotherapy to prostatic bed and pelvis was planned at 6 months after continence was sufficiently achieved. Postoperative nadir PSA was 0 ng/mL at 1 month, which did not change during the follow-up. On postoperative 18 months, PSA recurred as 0.1 and 0.2 ng/mL in two consecutive tests, and immediately, a new Ga-68 PSMA-labeled PET/MRI examination was done. Only a 15×9 mm subcutaneous soft tissue nodule on the right pectoral region with increased Ga-68 PSMA uptake (SUV_{max}: 7.5) was detected on maximum intensity projection (MIP) image, axial T1-w, and fusion PET/MRI images (red arrows, Figure 1a, 1b, and 1c). Axial diffusion-weighted image (DWI, b: 1000) and apparent diffusion coefficient (ADC) map, which was performed

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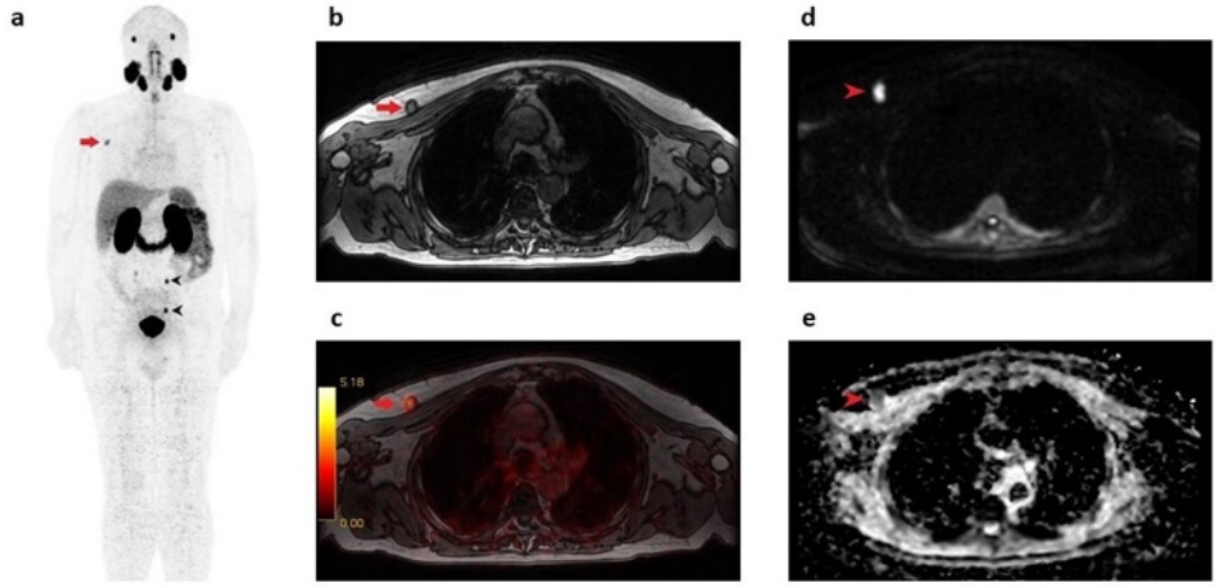

Figure 1a,b,c,d,e. Ga-68 PSMA PET/MRI image

PSMA: Prostate-specific membrane antigen, PET: Positron emission tomography, MRI: Magnetic resonance imaging

in the same imaging session with PET/MRI, also revealed increased signal and diffusion restriction on this lesion (red arrowheads, Figure 1d and 1e). On the MIP image, urinary activities were also seen in the left ureter (black arrowheads, Figure 1a). The nodule was excised, and the pathological examination revealed a well-capsulated adenocarcinoma metastasis with negative surgical margins in the subcutaneous fat tissue. Since then, the patient was followed with a 0-ng/mL PSA level and without disease evidence. This article was written by taking informed consent form from the patient.

Discussion

PSMA ligand PET/computed tomography (CT) or PET/MRI has high sensitivity and specificity for prostate cancer staging (4). Furthermore, Ga-68-labeled PSMA PET imaging demonstrated a higher detection rate of 45% in patients with biochemical recurrence (BR) and PSA values of 0.2-0.49 ng/mL compared with the other conventional imaging methods (5). Previous studies (6,7,8) reported 47% and 57% detection rates for patients with PSA values of ≤0.2 ng/mL and 0.2-0.5 ng/mL after radical prostatectomy. PET/MRI showed higher detection rates in patients with BR compared to the PET/CT due to the additional diagnostic value of MRI with superior soft tissue contrast. A recent study (9) revealed that Ga-68 PSMA PET/MRI showed PSMA-positive lesions in 65% of patients with a PSA level of 0.2-0.5 ng/mL. Recurrent lesions are mostly located in the prostatic bed, lymph nodes, and bones.

Ga-68 PSMA PET/MRI was performed in our reported case with BR after radical prostatectomy. Only a subcutaneous soft tissue nodule on the right pectoral region with increased Ga-68 PSMA uptake on PET, increased signal intensity on DWI, and diffused restriction on ADC map was detected. According to the proposed structured reporting system for PSMA PET imaging, PSMA-RADS Version 1.0 (10), the lesion detected on PSMA PET/MRI was considered as PSMA-RADS-3C because of the intense uptake but highly atypical localization for prostate cancer. Additionally, excisional biopsy to confirm diagnosis histologically was performed, and pathological examination revealed prostatic adenocarcinoma metastasis. The subcutaneous dissemination of prostate cancer is a rare and unusual metastatic site. Previous case reports have reported patients with skin and subcutaneous metastases from small cell carcinoma of the prostate (11,12), but our case did not have neuroendocrine differentiation. Subcutaneous metastasis may be seen in patients in advanced stages and terminal phases (13), but unusual as the first and only site.

Considering its higher sensitivity and specificity, whole-body Ga-68 PSMA-labeled PET/MRI contributes to the diagnostic work-up and restaging of patients with BR during prostatic bed evaluation, as well as in atypically located metastatic lesion detection.

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Supervision: L.Ö.A., Concept: T.S.S., Design: R.T.A., Data Collection or Processing: U.A., S.Ç., Analysis or Interpretation: U.A., S.Ç., Literature Search: U.A., Writing: S.Ç.

References

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
2. Alonso AR, Freire FD, Garcia DP, et al. Metástasis de adenocarcinoma prostático en saco herniario. Actas Urol Esp 1999;23:717-719.
3. Gallego Sánchez JA, Astobieta Odriozola A, Alvarez Martínez J, et al. Skin metastasis as first manifestation of prostatic adenocarcinoma. Actas Urol Esp 1998;22:770-772.
4. Perera M, Papa N, Christidis D, et al. Sensitivity, specificity, and predictors of positive 68Ga–prostate-specific membrane antigen positron emission tomography in advanced prostate cancer: a systematic review and meta-analysis. Eur Urol 2016;70:926-937.
5. Perera M, Papa N, Roberts M, et al. Gallium-68 Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer-Updated Diagnostic Utility, Sensitivity, Specificity, and Distribution of Prostate-specific Membrane Antigen-avid Lesions: A Systematic Review and Meta-analysis. Eur Urol 2020;77:403-417.
6. Afshar-Oromieh A, Avtzi E, Giesel FL, et al. The diagnostic value of PET/CT imaging with the (68)Ga-labelled PSMA ligand HBED-CC in the diagnosis of recurrent prostate cancer. Eur J Nucl Med Mol Imaging 2015;42:197-209.
7. Afshar-Oromieh A, Holland-Letz T, Giesel FL, et al. Diagnostic performance of 68Ga-PSMA-11 (HBED-CC) PET/CT in patients with recurrent prostate cancer: evaluation in 1007 patients. Eur J Nucl Med Mol Imaging 2017;44:1258-1268.
8. Eiber M, Maurer T, Souvatzoglou M, et al. Evaluation of hybrid 68Ga-PSMA ligand PET/CT in 248 patients with biochemical recurrence after radical prostatectomy. J Nucl Med 2015;56:668-674.
9. Kranzbühler B, Müller J, Becker AS, et al. Detection rate and localization of prostate cancer recurrence using 68Ga-PSMA-11 PET/MRI in patients with low PSA values≤ 0.5 ng/ml. J Nucl Med 2020;61:194-201.
10. Rowe SP, Pienta KJ, Pomper MG, Gorin MA. Proposal for a structured reporting system for prostate-specific membrane antigen–targeted PET imaging: PSMA-RADS version 1.0. J Nucl Med 2018;59:479-485.
11. Kaplan M, Atakan IH, Bilgi S, Inci O. Case report: subcutaneous metastasis from small cell carcinoma of the prostate. Int Urol Nephrol 2007;39:157-160.
12. Cecen K, Karadag MA, Demir A, Kocaaslan R. Small cell carcinoma of the prostate presenting with skin metastasis: a case report. J Med Case Rep 2014;8:146.
13. Herrera Puerto J, Pierna Manzano J, Goméz Tejeda LM, Isusquiza Garro I. Subcutaneous supramammary metastasis of prostatic carcinoma. Actas Urol Esp 1999;23:367-369.