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About Us

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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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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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).

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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.

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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.

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

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

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

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

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-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.

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

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

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7. Manuscript Submission

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

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

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

Submissions must include according to the following sequence:

A-Original Article

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

4) Table(s)

5) Figure(s)

6) Acknowledgements Form

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

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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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Nursing Care in Robotic Radical Cystectomy and Intracorporeal Orthotopic Urinary Diversion Surgeries

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Abstract

In this article, the management of nursing care in robotic cystectomy and urinary diversion surgeries, which are performed for treating bladder cancer, is explained considering the current literature. Bladder cancer is a type of cancer that is highly prevalent worldwide, and it is seen more frequently in men than in women. Radical cystectomy with pelvic lymphadenectomy are the reference treatment for muscle-invasive bladder cancer, and they play a key role in managing high-risk non-muscle-invasive cancer and saving the patient following radiotherapy. While radical cystectomy involves the removal of the bladder, urethra, uterus, Fallopian tubes, ovaries, and anterior vagina in women, it involves the removal of the bladder, urethra, prostate, and seminal glands in men. Urinary diversion performed following robotic cystectomy is a curative surgical method associated with functional and metabolic changes that could affect the patient as well as the quality of life of the patient. Urinary diversions performed following removal of the cancerous bladder aim to divert the urinary flow toward its normal path or form a new path for urine to be released directly or by accumulation. In robotic cystectomy and urinary diversion surgeries, the role of the nurse in the management of the preoperative, perioperative, and postoperative stages is highly important. The optimal management of nursing care and nurse training programs, especially for the postoperative period, aims to increase the quality of life of the patient by preventing complications, shortening their hospital stay, and organizing their activities of daily living.
Keywords: Bladder cancer, urinary diversion, radical cystectomy, nursing care

Introduction

Bladder cancer is a type of cancer that is highly prevalent worldwide, and it is seen more frequently in men (3:1) than in women (1,2). The International Agency for Research on Cancer is an institution of the World Health Organization, and it published the latest Global Cancer Statistics on the global burden of cancer on 5 December 2020. According to the 2020 database of GLOBOCAN, which is the online platform of the Global Cancer Observatory, in men of all ages worldwide, bladder cancer is the sixth most frequently encountered cancer with an incidence of 9.5% (3,4).

In Turkey, according to the 2017 data of Türkiye Unified Database, in the percentage distribution of the most prevalent cancers in men in all age groups, bladder cancer ranks fourth with a prevalence of 7.7% (5).

Radical cystectomy with pelvic lymphadenectomy are the reference treatment for muscle-invasive bladder cancer, and they play a key role in managing high-risk non-muscle-invasive cancer and saving the patient following radiotherapy. While radical cystectomy involves the removal of the bladder, urethra, uterus, fallopian tubes, ovaries, and anterior vagina in women, it involves the removal of the bladder, urethra, prostate, and seminal glands in men.

Radical cystectomy is a comprehensive and major surgery associated with or accompanied by comorbid/chronic diseases, and today, open radical cystectomy is being replaced by robot-assisted radical cystectomy (6,7).

The first robotic radical cystectomy surgery was reported in 2003 by Menon et al. (8), whereas various studies have revealed that robotic cystectomy provides advantages in terms of parameters such as complications, bleeding control, blood transfusion requirement, early mobilization, and the hospital stay duration of the patient (8,9,10,11).

Urinary diversion performed following robotic cystectomy is a curative surgical method associated with functional and metabolic changes that could affect the patient as well as the

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quality of life of the patient. Urinary diversions performed following removal of the cancerous bladder aim to divert the urinary flow toward its normal path or form a new path for the urine to be released directly or by accumulation (1,12,13,14).

The most frequently performed urinary diversions today are conduits, continent cutaneous diversions, and orthotopic neobladders anastomosed to the urethra (15).

This study presents the characteristics of nursing care for the clinically observed intracorporeal orthotopic bladder in the framework of the Enhanced Recovery after Surgery (ERAS) protocol.

The ERAS protocol includes evidence-based practices developed by the ERAS Society that can be described as ERAS or Fast Track Surgery (FTS). The ERAS protocol reduces the rates of complications by 30-50% by recommending evidence-based practices regarding the process of the patient that starts in the pre-operative period and ends at the home of the patient after their discharge, and it shortens the hospital stay of patients by 2 to 3 days (16).

In robotic cystectomy and urinary diversion surgeries, the role of the nurse in the management of the preoperative, perioperative, and postoperative stages is highly important. The optimal management of nursing care and nurse training programs, especially for the postoperative period, aims to increase the quality of life of the patient by preventing complications, shortening their hospital stay, and organizing their activities of daily living. According to Paula Francis, the roles and responsibilities of the nurse in robotic surgeries are examined at three stages: preoperative, perioperative, and postoperative (11,12,17,18). In this review, nursing care is discussed under four categories: preoperative care, perioperative care, postoperative care, and patient education and discharge.

Preoperative Patient Preparation and Nursing Care

Robotic radical cystectomy and urinary diversion surgeries play a significant role in the health and quality of life of individuals. Planning nursing care and education for the patient admitted to the inpatient clinic for robotic surgery in a holistic, humane, and personalized manner is an effective method for the self-care management of the patient, the management of their chronic diseases, and the management of the intraoperative process (1,12,19). Therefore, patient admission, education, and discharge are interrelated processes and should be considered as a whole. The preoperative period starts with the decision of surgery and covers the period until the patient is admitted for surgery (20).

Patient Information

Initiating and maintaining a professional relationship with the patient who is admitted to the urology inpatient clinic for robotic surgery by identification check is highly important for managing the care process with the patient and achieving cooperation. The patient who will undergo this surgery for the first time is probably anxious and concerned. For this reason, at the first encounter, the patient needs to be informed in detail about what they will experience throughout their stay in the hospital in verbal and written form.

It is important to check the informed consent form of each patient who is admitted to the inpatient clinic.

The nursing interventions to be carried out in the patient admission process start with determining the patient's room with suitable characteristics for their surgery, introducing the room and items in the room to the patient, taking the patient's history, checking their vital signs, physical examinations, and planning the necessary screening and diagnostic tests.

Considering a model or theory like the Roper-Logan-Tierney Model for nursing based on activities of daily living, the patient should be systematically followed up, and their needs should be identified. The Roper-Logan-Tierney Model for nursing is based on life expectancy, activities of daily living, factors affecting activities of daily living, the cycle of dependency-independence, and measurable and observable phenomena regarding the fields of nursing care and education. It is also an individual-centered model with its humane and holistic approach (21).

Based on this model, information about the patient's safe spaces, diet, respiration, voiding, communication, personal hygiene and dressing, body temperature, mobility, working and entertainment, sexual expression, sleep, and death at the end of life should be collected. In addition to these items, one should consider their substance and alcohol use, regular medication use, psychosocial factors, and spiritual and religious beliefs. Care should be taken in the collection of data regarding complications that are considered possible to occur in the perioperative period.

In robotic cystectomy and urinary diversion operations that are carried out after the diagnosis of bladder cancer, which is known to emerge especially in elderly male patients, age-specific characteristics, chronic diseases, mental state, and needs changing in relation to reduced functions in areas such as coordination and dexterity should be considered (20).

Before surgery, all test results brought by the patient are received and assessed by all relevant healthcare professionals (e.g., physician, nurse, dietician, physiotherapist) in a multidisciplinary manner.

Generally required tests may include chest radiography, electrocardiogram testing, complete blood count and biochemistry (e.g., Glucose, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, urea, creatinine, sodium, potassium, chloride) tests, coagulation and blood type tests, complete urine analysis, tests on infectious parameters such as HbsAg, anti-hepatitis C virus, and Venereal Disease Research Laboratory, cystoscopy images, respiratory function tests, and bone scan. A copy of the pathology report if the patient underwent a biopsy and CDs and reports of radiological imaging procedures such as BT/MR/IVP must be added to the patient file.

Following the examination of test results, the anesthesiologist who will take part in the surgery of the patient should be informed, and anesthesia consultation should be ensured. Here, nurses are in a key position in the facilitation of communication and interaction among the members of the healthcare team (12,22).

Before the surgical intervention, the patient should be given education about breathing and coughing exercises, a spirometer should be arranged for them, instructions should be provided, and its use should be started. Using a spirometer allows the alveoli to be filled with air by strengthening the weakened respiratory muscles. In this way, it is ensured that the development of diseases such as pneumonia and atelectasis is prevented (20).

Preoperative Bowel Preparation

The bowel preparation before colon surgeries has been a practice for many years. However, recent randomized controlled studies and meta-analyses have reported that mechanical bowel preparation in colorectal surgery does not provide an additional clinical benefit, increases the risk of anastomotic leaks, and causes fluid and electrolyte imbalances, especially in elderly patients. In this context, bowel preparation is contraindicated in major surgeries other than intraoperative colonoscopy and colon surgery.

In the study conducted in 2010 by Tuna (23) on radical cystectomy surgeries, patients in whom preoperative bowel preparation was practiced and those who did not undergo preoperative bowel preparation were compared, and it was reported that there was no significant difference between these groups in terms of patient recovery or complications such as infection.

Therefore, it has been concluded that bowel preparation does not provide the any advantage in radical cystectomy and urinary diversion surgeries (20,22,23).

Antimicrobial Prophylaxis

Based on studies in the literature, while oral antibiotic usage is not recommended before surgery, it has been reported that administering intravenous antibiotics exactly one hour before the incision provides the maximum effect. Thus, the IV antibiotic ordered by the physician should be administered by the nurse after the confirmation of the time of the surgery by communicating with operating room nurses (24,25).

Assessment of Dietary Status and Provision of Nutritional Support If Needed

Malnourishment is a significant risk factor in surgical operations due to the complications it creates in infection and wound healing. It has also been reported to be associated with perioperative survival and mortality. Therefore, to shorten hospital stays and increase the quality of care in radical cystectomy and urinary diversion operations, it is important to manage nutrition (26). In nutrition management, first, nurses should measure the weight and height of the patient who has been admitted to the inpatient clinic and calculate their body mass index. Additionally, serum albumin levels are accepted as a nutritional indicator, and multidisciplinary care should be provided to the inpatient (20). Especially for elderly patients, if malnutrition and protein deficiency are present, total parenteral feeding support should be planned, and appropriate nursing interventions should be included in the care plan (20,22,23).

A few days before surgery, the outpatient clinic nurse should explain the foods that can be consumed by the patient and have the patient repeat back what they say to confirm their comprehension and prevent misunderstandings. It was reported that according to the ERAS protocol, before the operation, the patient admitted to the clinic should fast for 6 h after their intake of solid foods, and they should stop having anything 2 h after their intake of clear fluids (e.g., unsweetened tea, water, juices, soups), whereas consuming 800 mL of fluids containing carbohydrates the night before the operation and 400 mL of fluids containing carbohydrates 2-3 hours before the operation reduces the insulin resistance of the patient, lowers nitrogen loss and loss of muscle strength, and speeds up recovery by reducing postoperative metabolic stress (16,23,27).

Surgical Site Preparation

The night before surgery, the patient should have a shower with a sponge and disinfectant. This is done to minimize bacterial presence without damaging the patient skin (20).

Thromboembolism Prophylaxis

The use of especially anticoagulant and antithrombotic drugs (Aspirin, Coraspin, Ecopirin, Plavix, Coumadin, Dispril) by the patient and when they quit using these drugs should be questioned. If quitting these drugs will be a threat to the patient is, the replacement drug ordered by the physician should be started. In such cases, drugs in the low-molecular-weight heparin class (e.g., clexane-heparin) are usually preferred. For the continuation of the treatment and the reduction of the risk of intraoperative bleeding, nurses should be careful about medication use, follow-up, and changes. Moreover, other factors that are known to affect coagulation should also be kept in mind, and alternative thromboprophylaxis methods such as antiembolic stocking use should be implemented (16,27).

Geriatric Issues

The care requirements of elderly patients are different. Reduced functions with advancing age increase the care needs of the patient. Therefore, nurses should allow patients to have acceptable levels of independence and closely monitor the needs of elderly patients. Fall cases in hospitals are mostly seen in elderly patients. Nurses should accurately assess the fall risk of elderly patients, implement effective fall prevention activities, and inform patient relatives/attendants. The main purpose of care provided to elderly patients is to allow and support their most efficient use of their capacity (28).

Medication Before Anesthesia

- Because opioids prolong hospital stays due to their side effects, unnecessary premedication practices should be avoided. Instead, short-acting anxiolytics can be preferred.

- Preoperative records: Pre-operative preparations should be checked on the surgical safety checklist. The items that are checked in this list are the surgical marking procedure of the patient, their laboratory findings, dental prostheses, appropriate storage of valuables, cleaning nails, removing nail

polish, checking the presence of makeup, checking gowns and antiembolic stockings, directing the family members to waiting and information areas, confirming the preparation of blood products, premedication administration, checking voiding needs, and skin preparation.

- Transfer of the patient to the operating room: The inpatient clinic is called by the operating room staff and informed that the patient will be transferred to the operating room. The operating room staff arrives at the floor with the "patient operating room order chart" and transfers the patient to the unit with the inpatient clinic nurse. Fall prevention measures should be taken if premedication is to be administered (20).

Perioperative Nursing Care

- The perioperative process starts with the arrival of the patient in the operating room and ends with the reanimation of the patient/transfer of the patient to the intensive care unit.

- The patient is received at the operating room by checking their identity, and the surgical safety procedure continues. The surgical consent information of the patient is re-checked at admission, and all information about patient safety is provided by the inpatient clinic nurse.

- All tools and equipment that will be used and are/can be required in robotic surgery are prepared, it is confirmed that they are in working order, and the expiration dates of all consumables and kits are checked.

- The patient is given a position suitable for surgical intervention.

- To prevent the development of pressure injuries, care should be taken to place patient-supporting gel pads appropriately.

- Throughout the entire surgical process, the surgeon and nurse should be in active communication with each other and support each other, and the entire process should be recorded in the patient safety checklist.

- Before the patient is surgically closed, a final count of all equipment and materials is made on the basis of the counting protocol.

- After the surgery is completed and the covers are removed, the patient should be checked thoroughly and transferred safely to the reanimation room (11,29,30).

Postoperative Nursing Care

The postoperative period starts with the transfer of the patient to the reanimation or intensive care unit and ends with their discharge from the hospital (20). It has been reported that with effective nursing care that is planned and implemented well after a surgical intervention, postoperative complications are prevented to a substantial extent. After surgery, based on the Model for Nursing, postoperative nursing care involves the provision and maintenance of the safety of the patient and their environment and regulations of their diet, respiration, voiding, communication, personal hygiene and dressing, body temperature, mobility, working and entertainment, sexual expression, and sleep activity humanely and holistically (31,32).

In addition to basic care principles, nursing care following robotic radical cystectomy and urinary diversion operations should involve information and interventions in a way that includes care practices specific to the preferred type of diversion. Simultaneously provided nursing care and patient education should cover discharge preparation, at-home care, and the support and education of family members.

- When the patient is brought back to their room after they are received from the operating room in verbal and written form with their file, their entire bodily integrity should be checked, their nasogastric tube, Foley catheter, abdominal drains, catheters, and urostomy bag should be emptied by observing and recording the fluids that come out in terms of quantity, color, and consistency.

- As in all surgical interventions, vital signs should be checked throughout 24 h, every 15 min in the first hour and every 30 min in the second hour, followed by 2- and 4-h checks. Based on the institutions policy, nursing care instructions and procedures should be followed. In the follow-up of vital signs, monitoring and alarm systems provide convenience in practice for nurses.

- Skin integrity should be checked and temperature and moisture information should be monitored. Pressure points should be checked for pressure injuries, the pressure injury risk assessment scale preferred by the institution should be applied again, and the results should be recorded. The patient should be given a suitable position, and this position should be changed at appropriate intervals.

- Based on the physician is, oxygen support can be provided to the patient according to their respiratory activity. At the appropriate time, Triflow use with breathing and coughing exercises should be started.

- The fall risk of a patient who has undergone surgical intervention must be assessed again, and preventive nursing measures should be taken (16,20).

Postoperative Analgesia

In each vital sign monitoring step, the pain of the patient should also be assessed, and to the use of analgesics, nurses should also use suitable positioning and relaxation techniques in the management of pain. With pain management, the patient can be mobilized comfortably, and their complication development risk decreases. If pain is not taken under control after the operation, it can lead to limitation in activities, respiratory/circulatory complications, gastrointestinal system problems, and delayed patient recovery (20).

The Stimulation of Gastrointestinal Motility and Postoperative Diet

One of the main purposes of ERAS protocols is to prevent postoperative ileus following abdominal surgery. excess fluids given during and after the operation negatively affect the gastrointestinal system, and thus, these practices should be avoided. Moreover, the use of agents that positively affect motility should be preferred (16).

In the timing of postoperative eating, the main issue is starting oral food intake to an extent tolerable by the patient after the assessment of their gastrointestinal functions. Patients should be encouraged to take fluids orally after the second hour the

following surgery and consume solid foods after the fourth hour. Support can be provided with nutritional solutions until sufficient nutrition is provided. According to recent randomized controlled studies, prolonging the fasting duration of patients after elective gastrointestinal resection does not have any advantage, but in contrast, it leads to several problems. It has been proven that early enteral feeding reduces the risk of infection and the duration of hospital stays, and does not increase the risk of anastomotic leaks or separation. Moreover, by early feeding, appropriate nitrogen compound balance metabolism is preserved and insulin resistance is minimized. However, it has been stated that in patients who start consuming food early, especially in those using opiates, the risk of nausea and vomiting increases, and a set of problems arise, including bloating, pulmonary dysfunction, and delay in mobilization (16,27).

As a nursing intervention, to ensure the oral hygiene of the patient, oral care should be planned for the patient and implemented. Furthermore, IV fluid and electrolyte treatment should be provided, and their fluid intake-output and weight should be monitored to prevent dehydration. When the oral food intake of the patient starts, their sufficient food intake should be monitored.

Monitoring should be performed in terms of nausea, vomiting, and diarrhea that can be seen in patients after surgery (16).

Urinary and Drainage Catheters

To create the neobladder, an approximately 40-45 cm section is taken from small intestinal segments, and the ends of the remaining intestine are sutured together robotically (27).

In robotic radical cystectomy and orthotopic urinary diversion, where a neobladder is created from small intestinal segments, patients usually have three drainage catheters. Two of these catheters are small stents with a diameter of 1 mm each placed into the right and left kidneys that come out of the abdominal wall through the urinary canal and the neobladder. The stents are usually removed on the seventh day of the postoperative period, and the patient is planned to complete their recovery period with only the Foley catheter.

The urine output of the patient should be checked every hour in the first 24 h in terms of color, amount, and consistency, and monitoring should continue at least at 4 h intervals on the following days. The amounts of urine collected from the right-left drainage catheters or Foley catheter should be monitored separately. Increased or decreased urine output as well as changes in urine color should be recorded in the observation chart of the nurse, and the physician should be informed.

The daily laboratory tests of the patient ordered by the physician should be carried out, their results should be followed up, and they should be shared with the members of the healthcare team.

Wound healing: The surgical incision site of the patient should be monitored and appropriate care should be provided. Aseptic techniques should be followed in the monitoring/emptying of drains and wound dressings, and appropriate solutions and methods should be used.

Early Mobilization

With the development of new surgical techniques and technological advancements today, conventional patient care approaches are being replaced by current multifaceted approaches. In one of these multifaceted approaches, called “fast track surgery”, early mobilization has great significance.

The most frequently included practices in nursing interventions about problems of patients in the early postoperative period such as pain, nausea, vomiting, coughing, swallowing difficulties, and constipation include the early mobilization of the patient, giving the patient a suitable position, and administering medication ordered by the physician. Early mobilization speeds up the recovery process and reduces the risk of complications. On the other hand, delayed mobilization or prolonged bed rest may increase insulin resistance, muscle weakening, and muscle atrophy. Increasing mobility in the early period after surgery raises the circulation, prevents venous stasis, and supports optimum respiratory activity. In addition to its physiological effects, early mobilization has significant contributions to the solution of psychosocial problems (20,32,33,34).

Complications and Nursing Interventions for Preventing Complications

After major surgical interventions, the most frequently observed complications are infectious factors such as fever and pyelonephritis, hemorrhage, urinary extravasation, and ileus. These complications are followed by complications such as atelectasises, myocardial infarction, urinary fistulae, and urethral stricture related to the urinary diversion. While postoperative ileus is seen at rates between 2% and 32% in different patient groups, fever and pyelonephritis have been reported in 5% to 40% of patients (35,36,37).

After radical cystectomy and urinary diversion, some electrolyte anomalies arise when intestinal segments are included in the urinary system. These are hypokalemia, hypocalcemia, and hypomagnesemia (38,39).

In the prevention of such complications, the main approach involves the arrangement of sufficient and balanced fluid treatment for the patient, monitoring their fluid intake-output and weight, managing their diet for resolving constipation, and providing laxative treatment when needed (36,38,40).

Geriatric Issues

It is known that with advanced age, neurological symptoms such as delirium and disorientation are seen more frequently in patients. However, studies examining complications following radical cystectomy and urinary diversion have not focused specifically on this issue. These complications after surgery prolong the hospital stay of the patient and substantially increase the costs for the patient and the institution. Large et al. (41) found the postoperative delirium rate in 49 radical cystectomy patients older than 65 as 29%. This rate is similar in cardiovascular surgery and major orthopedic cases (35,41).

Patient Education and Discharge

Patient education starts with the admission of the patient to the institution. Nurses share examination results, examination and diagnosis procedures, routine hospital procedures, and hospital departments with the patient. When the patient is admitted to the inpatient clinic, the nurse introduces himself, the clinic, and the patient's room, informs the patient that different nurses work in different shifts, and provides the working schedule of nurses. The formal education plan should start after the patient has been examined. The education given to the patient should be personalized and focus on the diagnosis/needs of the patient, the treatment their condition requires, and their use of personal care tools and equipment. In cases where the patient is not able to decide/comprehend, their family members should be informed.

The patient and their family should be informed about self-care needs throughout their hospital stay and for discharge, how to meet these needs, pain status and management, the importance of the regular and correct use of medication, perineum care, urine monitoring and its importance, urinary catheter care, drainage monitoring, diabetes and diet, sexual activity, infection signs and symptoms, and cases where the patient would need to contact the physician urgently (15).

In the postoperative period, after the removal of the stents, the patient can shower. There is no problem regarding the exposure of the 5 robotic incision sites on the abdomen and Foley catheter to water. The important point here is drying the incision site after showering and the care of the Foley catheter. In male patients, the penis, the tip of the penis, and the area around the penis should also be cleaned based on the recommendations of the physician.

After cystectomy and subsequent diversions, movements such as cross-legged sitting or crouching, which put excessive tension on the floor muscles, should be avoided. These movements should also be avoided in the presence of catheters and for 2-3 weeks after catheter removal. If the catheter gets detached for various reasons, the physician must be contacted, and the catheter should not be reinserted at different institutions. Depending on the characteristics of the surgery and the patient, catheters are usually removed on the 14th or 21st day in the postoperative period. European-style toilets must be used. The patient should be instructed to urinate every 2 h in the daytime and every 3 h at night. The patient should be informed that they may experience urinary incontinence at first, and this situation will be resolved in time.

Some exercises recommended after catheter removal are as follows:

1. The hands are placed on the abdomen while lying down or sitting.

2. The abdominal muscles should not be contracted but controlled by the hand. Only the area around the rectum and buttock muscles are contracted, and this contraction is held for 4-5 seconds.

3. These muscles are relaxed, followed by a 4-5 s rest.

4. These movements should be followed in three sessions: morning, afternoon, and evening sessions, and each session should include 30 repetitions of contraction and relaxation.

To prevent urinary incontinence, the patient has to perform these exercises while coughing, making sudden movements, and getting up from bed or in a sitting position.

Follow-up and Examination of Results

Blood creatinine and urine culture tests should be conducted 4-5 weeks after the date of surgery. Because culture results cannot be obtained on the same day, the date on which the results will come out should be learned from the laboratory, and follow-up appointments should be planned accordingly.

Based on the pathology results after the operation, routine tests and examination follow-ups are conducted every 3 months for 2 years. Pathology results may affect the times of treatment and follow-up, and the patient should be constantly in contact with the physician. On average, radiological follow-up is performed by CT every 6 months

The checks continue with annual, lifelong follow-ups after the 5th year (27).

Conclusion

With all these nursing care and education processes, it is aimed to meet the self-care requirements of patients regarding their health problems and maximize their quality of life. Moreover, it is aimed for nurses to have increased awareness about robotic radical cystectomy and urinary diversion surgeries, more knowledge about the issue, and more positive outcomes in the success of the treatment with the nursing care they provide.

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Original Article

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Obstructive Uropathy in Advanced Prostate Cancer

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Abstract

Objective: The incidence of advanced prostate cancer increases in proportion to new treatment options and prolonged life expectancy. Especially in advanced disease, prostate cancer is a progressive disease that can cause obstructive uropathy. This study investigated the relationship between the characteristics of advanced prostate cancer and obstructive uropathy.

Materials and Methods: This study retrospectively evaluated the data of prostate adenocarcinoma patients admitted to the Urology Clinic of Manisa Celal Bayar University Hospital between 2017 and 2021. Of them, 48 were advanced prostate cancer patients, and they were all included. All patients in the study received hormonal therapy along with chemotherapy for prostate cancer treatment. The relationship between hydronephrosis and patient age, creatinine and prostate-specific antigen (PSA) values, urinary tract infections, prostate volume, pathological features of cancer, and castration resistance was evaluated.

Results: Parameters that we found to be associated with obstructive uropathy (OU) are as follows: high creatinine level at the time of diagnosis of cancer ($p<0.001$), increase in creatinine at follow-up ($p=0.001$), urinary infection at the time of diagnosis of cancer ($p=0.002$) and at follow-up ($p=0.003$), development of castration resistance during treatment ($p=0.038$) and high PSA values at the time of diagnosis of prostate cancer ($p=0.011$).

Conclusion: Renal functions should be observed very carefully in advanced prostate cancer patients who develop or are at risk of developing OU. High PSA values and/or castration resistance should be approached carefully in terms of the patients prognosis. It should not be forgotten that their significant relationship with OU has been demonstrated.

Keywords: Azotemia, hydronephrosis, prostate cancer

Introduction

The incidence of advanced prostate cancer increases in proportion to new treatment options and prolonged life expectancy (1). Obstructive uropathy (OU) is a condition in which urine flow is restricted in the urinary system by internal or external obstruction. Subsequent aseptic dilatation of the renal pelvis and calyces by filling with urine is called hydronephrosis (2). Especially in advanced stages, prostate cancer is a progressive disease that can cause OU (3). OU requires strict follow-up and intervention, and it has an important place in quality of life (4). Progressive dilation of the upper urinary tract can lead to acute renal failure and, if not treated, nephron loss (5). Castration-resistant and/or metastatic prostate cancer is a patient group whose life expectancy is increasing. Thus, it is clear that OU, one of the most important complications of this patient group, should be studied again. This study investigated the relationship between the characteristics of advanced prostate cancer and OU.

Materials and Methods

This study retrospectively evaluated the data of prostate adenocarcinoma patients admitted to the Urology Clinic of Manisa Celal Bayar University Hospital between 2017 and 2021. Of these, 48 were advanced prostate cancer patients at the time of diagnosis with at least one bony metastasis. They were all included in the study. There was no patient with distant lymph node metastasis at the time of diagnosis. All patients in the study received hormonal therapy with chemotherapy together. Subcutaneous luteinizing hormone-releasing hormone agonist (goserelin acetate) was administered to the patients every 12 weeks. They also received intravenous docetaxel chemotherapy (75 mg/m^2) every 21 days for 6 cycles.

In our study, the relationship between hydronephrosis and the patient's age, creatinine levels, prostate-specific antigen (PSA) values, urinary tract infections, prostate volume, pathological features of cancer, and castration resistance was evaluated. The urinary tract infection (UTI) was diagnosed with a positive urine culture. All biopsies were performed under transrectal

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ultrasound guidance. The expression 'time of diagnosis' in the article refers to the moment when the patient is diagnosed with prostate cancer, not hydronephrosis. This study was accepted by the Ethics Committee of Manisa Celal Bayar University Faculty of Medicine with decision number 20.478.486 (date: 02.12.2020).

Statistical Analysis

SPSS 26.0 (IBM Corporation, Armonk, New York, United States) programs were used in the analysis of variables for statistical calculations. In the comparison of two independent groups according to quantitative data, the independent samples t-test was used together with the bootstrap results, while the Mann-Whitney U test was used together with the Monte Carlo results. Pearson chi-square and Fisher's exact Monte Carlo simulation techniques were used to compare categorical variables with each other. Less than 0.05 for p value was accepted as significant.

Results

Forty-eight patients were included in the study (n=48). Minimum age was 48, maximum was 86, and mean age was 69.2 years. The shortest follow-up period was 22 months, while the longest was 48 months. The median follow-up was 35 months. The minimum prostate volume was 30 cc, and the maximum was 140 cc. The median volume was 54.6 cc. Forty-four patients (91.7%) had a bilateral prostate lobe involvement. Perineural invasion was found in 33 patients (68.8%) on biopsy. The number of patients with extraprostatic involvement in biopsy was 20 (41.7%). The patients were divided into 2 groups: those with (n=19) and without (n=29) hydronephrosis. The detection of hydronephrosis at the time of diagnosis or during follow-up was also studied as two separate subgroups. In 11 (22.9%) of 48 patients, hydronephrosis was present at the time of diagnosis of cancer. Hydronephrosis developed in 8 (21.6%) of 37 patients who were not found to have hydronephrosis at the time of diagnosis. The mean development time of hydronephrosis at follow-up was 22 months.

Bilateral hydronephrosis was in 10 (90.9%) of 11 patients with hydronephrosis at diagnosis. Only 1 patient (9.1%) had isolated left hydronephrosis. In 8 patients who developed hydronephrosis during follow-up, the numbers of those with bilateral, left, and right kidney involvement were 4 (50%), 3 (37.5%), and 1 (12.5%), respectively. Among the patients who had hydronephrosis at the time of diagnosis (n=11), there were 2 patients (18.2%) with grade 1, 6 people with grade 2 (54.5%), 2 people with grade 3 (18.2%), and 1 with grade 4 (9.1%) hydronephrosis. In patients who developed hydronephrosis during the follow-up, there was no patient with grade 1 detected. There were 3 people (37.5%) with grade 2, 4 people (50%) with grade 3, and 1 person (12.5%) with grade 4. Four of 11 patients (36.4%) with hydronephrosis at the time of diagnosis were treated with percutaneous nephrostomy. The treatment of 5 patients (45.5%) was provided by placing a retrograde ureteral stent. Two patients (%18.2) were under active surveillance. Of 8 patients who developed hydronephrosis during follow-up, 6 (80%) were treated with percutaneous nephrostomy and 1 (12.5%) with transurethral resection (TUR). One of them (12.5%) was followed up with no invasive procedure (Table 1).

The mean age was 68.4 years in the group with hydronephrosis, whereas it was 69.7 years in the group without hydronephrosis. Median prostate volume was 50 cc in the hydronephrosis group and 45 cc in the non-hydronephrosis group. At the time of diagnosis, UTI was detected in 13 of 48 patients (27.1%). In follow-up, this rate was 15 (31.3%). There was a significant correlation between the presence of hydronephrosis in the whole patient group and the detection of UTI at the diagnosis (p=0.002). Of the 19 patients who were found to have hydronephrosis, 10 (52.6%) had UTI at the time of diagnosis. There was also a significant relationship between the presence of hydronephrosis in the whole patient group and the detection of UTI in the follow-up (p=0.003). Of the 19 patients who were found to have hydronephrosis, 11 (57.9%) had UTI at follow-up (Table 2).

There is a significant correlation between hydronephrosis and creatinine level at the time of diagnosis (p<0.001). The median creatinine value at the time of diagnosis in 19 patients with hydronephrosis was 1.33 mg/dL. The median creatinine value at the time of diagnosis in 29 patients without hydronephrosis was 0.82 mg/dL. In addition, a significant correlation was found between the increase in creatinine in the follow-up and the diagnosis of hydronephrosis (p=0.001). An increase in creatinine was detected in the follow-up of 8 (42.1%) of 19 patients with hydronephrosis (Table 2).

There was a significant correlation between PSA value at the time of diagnosis and hydronephrosis at diagnosis (p=0.011). The median PSA value at the time of diagnosis was 155 ng/mL in 11 patients with hydronephrosis at the time of diagnosis. The median PSA value of 37 patients without hydronephrosis at diagnosis was 59.6 ng/mL. Therefore, the detection of hydronephrosis at the time of diagnosis and PSA values are significant when

Table 1. Features of hydronephrosis and treatment

		Diagnosis		Follow-up	
		n	%	n	%
Hydronephrosis (HN)					
	Negative	37	77.10%	40	83.30%
	Positive	11	22.90%	8	16.70%
HN side					
	Right	0	0.00%	1	12.50%
	Left	1	9.10%	3	37.50%
	Bilateral	10	90.90%	4	50.00%
HN grade					
	I	2	18.20%	0	0.00%
	II	6	54.50%	3	37.50%
	III	2	18.20%	4	50.00%
	IV	1	9.10%	1	12.50%
HN Treatment					
	Nephrostomy	4	36.40%	6	75.00%
	Retrograde stent	5	45.50%	0	0.00%
	TUR	0	0.00%	1	12.50%
	Active surveillance	2	18.20%	1	12.50%

TUR: Transurethral resection

evaluated as a subgroup. However, no significant correlation was found with PSA values for hydronephrosis patients in the whole group.

The number of people who developed castration resistance during their follow-up was 23 (47.9%). There was a significant correlation between castration resistance and hydronephrosis (p=0.038). Castration resistance was detected in 13 (68.4%) patients with hydronephrosis during follow-up. The median time to develop castration resistance was 22.4 months. The median duration of castration resistance development in the group of patients with hydronephrosis was 21 months and 25 months in patients without hydronephrosis (Table 2). In the subgroup of patients with hydronephrosis at diagnosis, the median time to reach castration resistance was 16 months.

No statistically significant correlation was found between hydronephrosis and patients' age, perineural invasion in biopsy, prostatic apex or extraprostatic involvement in biopsy, time to develop castration resistance, and prostate volume.

Discussion

Oefelein (6) was designed with 260 patients with advanced prostate cancer. The number of patients with OU was 51 (19.6%). This study included patients with one of the following two conditions for the diagnosis of advanced prostate cancer: a newly diagnosed patient with metastasis or a patient with biochemical recurrence after primary local curative therapy. It is seen that the percentage of patients with OU in the study of Oefelein (6) was 19.6%, which is lower than the rate of 39.5%

Table 2. Hydronephrosis and statistical analysis

		Hydronephrosis		p-value
		Negative	Positive	
		(n=29)	(n=19)	
		Mean (SD)	Mean (SD)	
Age (year)		69.7 (8.34)	68.4 (6.13)	0.592[t]
		Median (min/max)	Median (min/max)	
Castration resistance time (month)		25 (7/44)	21 (5/38)	0.317[u]
PSA at diagnosis (ng/mL)		89.9 (10.2/1540)	89 (10.6/1200)	0.928[u]
Creatinine at diagnosis (mg/dL)		0.82 (0.5/1.71)	1.33 (0.6/13.2)	<0.001[u]
Prostate volume at diagnosis (mL)		45 (30/120)	50 (30/140)	0.606[u]
		N (%)	N (%)	
UTI at diagnosis				
	Negative	26 (89.7)[B]	9 (47.4)	0.002[p]
	Positive	3 (10.3)	10 (52.6)[A]	9.6 (2.2-43)[or]
Prostate apex involvement				
	Negative	4 (13.8)	3 (15.8)	0.999[f]
	Positive	25 (86.2)	16 (84.2)	
Perineural invasion				
	Negative	10 (34.5)	5 (26.3)	0.751[f]
	Positive	19 (65.5)	14 (73.7)	
Extraprostatic extension				
	Negative	17 (58.6)	11 (57.9)	0.999[p]
	Positive	12 (41.4)	8 (42.1)	
Creatinine increase at follow-up				
	Negative	28 (96.6)[B]	11 (57.9)	0.001[f]
	Positive	1 (3.4)	8 (42.1)[A]	20.4 (2.3-182.4)[or]
UTI at follow-up				
	Negative	25 (86.2)[B]	8 (42.1)	0.003[p]
	Positive	4 (13.8)	11 (57.9)[A]	8.6 (2.1-34.6)[or]
Castration Resistance				
	Negative	19 (65.5)[B]	6 (31.6)	0.038[p]
	Positive	10 (34.5)	13 (68.4)[A]	4.1 (1.2-14.1)[or]

SD: Standard deviation, UTI: Urinary tract infection, t: Independent Samples t-test (Bootstrap), [u]: Mann-Whitney U test (Monte Carlo), [p]: Pearson chi-square test (Monte Carlo), [f]: Fisher's Exact test (Monte Carlo), [or]: Odds ratio (95% confidence interval), [A]: Significant compared to the non-hydronephrosis group, [B]: Significant compared to the hydronephrosis group

in our study. In our study, there were only patients with bony metastases at the time of diagnosis. We think that the rates are different in this way because we have a more advanced stage patient group that does not include the recurrence group after local treatment.

In the same study (6), 45% transurethral resection of prostate (TUR-P), 15.6% ureteral double J stent, 15.6% percutaneous nephrostomy, 9.8% TUR-P, and ureteral stent were applied together. In our study, 52.6% nephrostomy, 26.3% ureteral stent, and 5.2% TUR-P were applied, while 15.7% of the patients were followed without invasive treatment. This difference is thought to be due to more than one reason. One of them is that the patient needs regional or general anesthesia to perform TUR-P, while this anesthesia is not necessary for percutaneous nephrostomy. Therefore, as mentioned before, we think that the fact that our study was conducted with a more fragile patient group with a more advanced cancer compared to this study was effective in this decision. In addition, TUR passage application in prostate cancer has a higher rate of failure and the need for repeat TUR compared with TUR-P for benign prostate enlargement (7).

In another article by Oefelein et al. (8) with a similar patient group, 254 patients on androgen deprivation therapy were evaluated in terms of survival. Although there are no survival data in our study, the factors that have an effect on survival were investigated in this study and are similar to our data. In this study (8), it was shown that the presence of OU, high nadir PSA values, diagnosis at a later age, lower testosterone levels before treatment, history of tobacco use, and high alkaline phosphatase levels have negative effects on survival. It was shown that both high age at diagnosis and OU had a negative effect on survival. According to these results, it can be said that the patient group, whose age at diagnosis is older and who develops OU in the follow-up, is more disadvantageous in terms of survival. Again, in this study (8), a high nadir PSA was found to have a negative effect on survival. According to our study, OU at diagnosis has a relationship with high PSA levels at the time of diagnosis and castration resistance in treatment. When the results of the two studies are evaluated together, it can be said that the survival of the patient with high nadir PSA will be worse, and if there is high PSA level at diagnosis and/or castration resistance in this patient group, the risk of developing OU, which also has a negative effect on survival, will increase.

Paul et al. (9) was conducted with 820 patients with prostate cancer at different stages. When those with bladder outlet obstruction were excluded, it was observed that 36 (4.3%) patients had bilateral ureteral obstruction and elevated urea levels. There are some reasons why this 4.3% rate is very low compared to our study (19/48 patients, 39.5%). As mentioned earlier, patients with bladder outlet obstruction were excluded in this study; therefore, this patient group was included in our study. In addition, this study was conducted with 820 patients with prostate cancer of all stages. It is seen that the majority of this sample consisted of local disease. Because our group of patients were more advanced-stage patients, there is a difference between the rates. Also, this rate by Paul et al. (9) is for patients with both "bilateral obstruction" and "high urea". In our study, all unilateral or bilateral dilatations were included in the statistics, with or without azotemia.

In the study published by Paul et al. (9), 10 (28%) of 36 patients with bilateral ureteral obstruction and elevated urea were initially referred to hospitals with symptoms of azotemia and were diagnosed with prostate cancer after further investigations (9). In our study, unilateral or bilateral hydronephrosis was present in 11 (22.9%) patients at the time of diagnosis, and creatinine elevation was found in 9 (18.75%) of them. Of the 36 patients in the study by Paul et al. (9) who had bilateral ureteral obstruction and elevated urea, 16 patients received invasive treatment. Of these, 9 were treated with nephrostomy, 5 with stents, and 2 with ureteroneocystostomy. The reason why there is no TUR passage or catheter option among these treatments is that patients with bladder outlet obstruction were excluded from the study, as mentioned before. In our study, 10 nephrostomy, 5 ureteral stents, and 1 TUR-P were performed for treatment, while 3 of the patients were followed without invasive treatment.

Emrich et al. (10) investigated the prognostic factors of 1,020 patients with advanced prostate cancer. According to the results of this study, some parameters that negatively affect the survival time, which were also evaluated in our study, are as follows: inadequate response to hormonal therapy, presence of obstructive symptoms, advanced tumor stage, and advanced patient age at diagnosis. As mentioned before, our study cannon be compared in this way because it does not have survival data. Nevertheless, a comment can be made on similar factors in the studies. Emrich et al. (10) determined that the patients inadequate response to hormonal therapy was a poor prognostic factor. In our study, castration resistance ($p=0.038$) and high PSA level at the time of diagnosis ($p=0.011$) were found to be significantly associated with OU. Emrich et al. (10) also found the presence of obstructive symptoms in the patient as a poor prognostic factor. Emrich et al. (10) determined that a high tumor stage is a poor prognostic factor, and in our study, castration resistance during treatment ($p=0.038$) and high PSA value at the time of diagnosis ($p=0.011$) were significantly associated with OU, and these findings are compatible with each other.

Study Limitation

There are certain natural limitations due to the retrospective nature of the study. Complications related to prostate cancer were either diagnosed when symptomatic or discovered during routine follow-up at wide intervals as a result of the retrospective design. In a prospective study, these complications could have been detected earlier by more frequent monitoring. Additionally, patients could not be evaluated for genetic predisposition, which is believed to lead to faster cancer spread and development of complications, as it is not yet used in routine clinical practice.

Conclusion

Our study examined the parameters affecting the development of OU in patients with advanced prostate cancer. It can be said that advanced prostate cancer is a disease that requires both a multidisciplinary approach and multimodal treatment. Renal

functions should be observed very carefully in patients at risk of developing OU. It is obvious that physicians should be very careful against urinary infections. The development of high PSA values and/or castration resistance should be approached carefully in terms of the patient's prognosis, and it should not be forgotten that their significant relationship with OU has been demonstrated.

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Ethics

Ethics Committee Approval: This study was accepted by the Ethics Committee of Manisa Celal Bayar University Faculty of Medicine with decision number 20.478.486 (date: 02.12.2020).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: O.E., T.M., Concept: O.E., T.M., Design: O.E., T.M., Data Collection or Processing: O.E., Analysis or Interpretation: O.E., Literature Search: O.E., Writing: O.E.

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Original Article

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Treatment of Primary Tumor in Oligometastatic Prostate Cancer: An Observational Study of the Turkish Urooncology Association Prostate Diseases Working Group

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Abstract

Objective: To report the clinical results of patients who had metastatic prostate cancer (PC) at admission and underwent standard androgen deprivation therapy with radiotherapy (RT) and radical prostatectomy (RP) for the primary tumor.

Materials and Methods: This study used the PC database from the Turkish Urooncology Association, to which participating institutions submit online data. The following clinical, radiological, and pathological findings were retrieved from the database: age, total prostate-specific antigen, clinical TNM stage, number of metastases, International Society of Urological Pathology grade group of biopsy, time to castration-resistant disease, type of local treatment, type of staging method, status of survival, type of systemic treatment, and follow-up time.

Results: The median follow-up of the 18 included patients was 59.1 (19.9-180) months. RP and extended lymphadenectomy were performed in 12 patients. RT was performed in 6 patients. The median number of metastases was 2 (1-4) and 3 (1-4) in the RP and RT groups, respectively. In the RP group, 3 of 12 patients developed castration-resistant prostate cancer (CRPC) during the follow-up period. In the RT group, 2 of 6 patients developed CRPC in the follow-up period. The time to CRPC was 48.4 and 43.3 months, respectively.

Conclusion: While primary tumor-directed RT is effective in selected patients, the results of prospective randomized controlled studies are required to demonstrate the effectiveness of RP.

Keywords: Oligometastatic prostate cancer, radical prostatectomy, radiotherapy

Introduction

According to an analysis by the National Prostate Cancer Audit (1), approximately 13% of prostate cancer (PC) cases have distant metastases at the time of diagnosis. Although the incidence of distant metastatic PC has increased over the last decade, the 5-year survival rate has increased from 28.7% to 32.3% due to increased treatment options (2).

Androgen deprivation therapy (ADT) has long been the cornerstone of standard treatment for patients with PC presenting with systemic disease (3). Today, a more aggressive treatment approach is adopted in de novo metastatic disease in terms of both systemic treatment and localized treatment, including radical prostatectomy (RP), radiotherapy (RT) for primary tumors, and metastasis-directed therapy (MDT) for metastatic foci. Many systemic agents, which are used in the castration-resistant stage, have now had their survival advantage proven in hormone-sensitive disease (4-6). Data also suggest that treatments for primary tumors and metastatic foci provide survival advantage in selected patients (7). The term oligometastatic PC (OMPC) has been proposed to identify the patient group that will benefit from this survival advantage.

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Oligometastatic PC was first defined by Hellman and Weichselbaum (8) in 1995. They stated that the biology of oligometastatic disease differs from that of nonmetastatic and widespread metastatic disease, and that local therapies can affect the natural course of the disease and have curative effects. In other words, for a patient to be biologically oligometastatic, both the primary tumor and the metastatic foci must be locally treated with temporary hormonal therapy; thus, the patient can be cured without requiring systemic treatment. In the literature, the terms oligorecurrent disease (metastasis occurring without systemic therapy) and oligoprogressive disease (metastasis occurring under systemic therapy) are also used to describe castration-sensitive oligometastasis and castration-resistant oligometastasis after local treatment, respectively (7). The definition of OMPC, which is the subject of this article, includes de novo hormone-sensitive disease with synchronous metastases. However, one of the most critical shortcomings of OMPC is the lack of consensus in the literature regarding its definition. The definitions currently used are clinical quantitative definitions based on the site and number of metastases, as opposed to a biological definition. Although many definitions exist in the literature, having fewer than 5 metastases, no visceral metastases, and bone lesions in the axial skeleton can be said to be a widely accepted definition (9).

This study aimed to report the clinical results of patients who were metastatic at the time of admission and underwent standard ADT with RT and RP for the primary tumor.

Materials and Methods

Study Design

This study used the PC database from the Turkish Urooncology Association, to which participating institutions submit online data. All patient data were anonymized at the source center before being recorded in the database. For this study to be conducted using the PC database, approval was obtained from the Turkish Urooncology Association Prostate Diseases Working Group. The study was registered with the code TUO-PR-19-05. The study is structured as a database report, and therefore, ethical committee approval was unsought.

A total of 18 patients with PC who had bone or non-regional lymph node metastasis at the time of diagnosis and had undergone RT or RP for the primary tumor between 2005 and 2020 were included in the study. The follow-up data of the patients included in the study were updated by the relevant centers before the analysis.

Data Collection and Definitions

Clinical, radiological, and pathological findings [age, total prostate-specific antigen (PSA), clinical TNM stage, number of metastases, International Society of Urological Pathology (ISUP) grade group] of biopsy, time to castration-resistant disease, type of local treatment, type of staging method, survival status, type of systemic treatment, and follow-up time were retrieved from the PC database. The ISUP grading system revised at the 2014 ISUP consensus conference was used (10). Castration-resistant PC (CRPC) was defined as a biochemical or radiological progression with a serum testosterone level of less than 50 ng/dL or 1.7 nmol/L. Biochemical progression was determined by 3 consecutive rises in PSA at least 1 week apart, resulting in 2 increases of 50% over the nadir and a PSA >2 ng/mL. Furthermore, radiological progression was determined by the presence of 2 or more new bone lesions in a bone scan or of a soft tissue lesion using the Response Evaluation Criteria in Solid Tumors (11).

Statistical Analysis

The normal distribution of continuous variables was evaluated by analytical methods. In the descriptive findings, categorical variables are given as numbers (percentage), and continuous variables are median (minimum-maximum) for normal non-scattering data. Time to CRPC was defined as the time from the date of RP/RT to the date of CRPC. All statistical analyses were performed in R version 4.0.4 through R Studio version 1.4.1106.

Results

The median follow-up of the 18 patients included in the study was 59.1 (19.9-180) months. Their median age was 66 years (48-75) and their median total PSA was 12.3 (4.2-324). Whole-body bone scintigraphy (WBBS) in 10 patients, computed tomography (CT)/magnetic resonance imaging (MRI) in 11 patients, and Gallium-68 prostate-specific membrane antigen positron emission tomography/CT (^{68}Ga-PSMA PET) in 5 patients were used for the systemic staging of PC.

RP was performed along with the extended lymph node dissection in 12 patients. Open RP was performed in 9 patients, and robotic RP was performed in 3 patients. In the RP group, the median operative time was 165 (120-309) minutes and the median time to urethral catheter removal was 14 (8-15) days. Two patients received postoperative adjuvant RT, while 3 patients underwent metastasis-directed stereotactic RT. After diagnosis, all patients were prescribed luteinizing hormone-releasing hormone (LHRH) analog treatment before surgery, which was continued as standard therapy after surgical intervention.

RT was performed in 6 patients. Pelvic RT to the lymph nodes was also applied to all patients. Two patients received conventional external beam RT, while 4 patients received intensity-modulated RT. All patients received a simultaneous LHRH analog therapy, while 1 patient received additional docetaxel chemotherapy. Three patients underwent metastasis-directed stereotactic RT.

The clinical stages and pathological findings are summarized in Table 1. The median number of metastases was 2 (1-4) and 3 (1-4) in the RP and RT groups, respectively. Non-axial skeletal and visceral metastases were not detected in any patient.

In the RP group, 3 of 12 patients developed CRPC during their follow-up, whereas in the RT group, 2 of 6 patients developed CRPC during their follow-up. The time to CRPC was 48.4 and 43.3 months, respectively, while no deaths were observed in the RP group, death due to PC was reported in 2 patients in the RT group who developed CRPC.

Discussion

We report the outcome data of 18 patients who received systemic treatment with ADT with or without docetaxel and underwent RT or RP for the prostatic disease site. There were no restrictions on the number and location of distant metastases in our study. We found that the median number of metastases was 2 (1-4) in the RP group and 3 (1-4) in the RT group. The majority of the patients were in stage M1b. Castration-resistant disease developed in 5 patients during follow-up. The time to castration resistance was 48.4 and 43.3 months in the RP and RT groups, respectively. In the RT group, 2 patients died due to PC during follow-up.

At the time of our patients' initial diagnosis, the standard treatment for hormone-sensitive metastatic PC was ADT. Therefore, the majority of our patients received only LHRH therapy as systemic treatment. However, the current guidelines strongly recommend a combination of ADT with agents such as docetaxel, enzalutamide, and abiraterone acetate, which have been proven to have a survival advantage both in the castration naïve and resistant stages as the first-line treatment for primary metastatic PC (11). In a Cochrane review conducted in 2019, taxane-based chemotherapy given with ADT significantly increases cancer-specific survival (CSS) and overall survival (OS) as well as delays disease progression in the hormone-sensitive stage (12). Furthermore, the STAMPEDE, LATITUDE, ENZAMET, and TITAN studies have demonstrated that abiraterone acetate plus prednisone, enzalutamide, and apalutamide significantly increase OS in metastatic hormone-sensitive PC (mHSPC) with ADT, respectively (13-16). The PEACE-1 study published in 2022 added abiraterone acetate plus prednisone as a third agent to the standard treatments of ADT + docetaxel for de novo mHSPC. It was found that this "triple" treatment significantly increased OS and radiological progression-free survival compared with the standard treatment. Although the study included patients who received and did not receive RT for the primary tumor, no subgroup analysis was performed on this topic (17).

The primary rationale for local treatment in oligometastatic disease is to reduce the volume of cancer cells and interrupt the crosstalk between disseminated tumor cells and primary lesions. As long as this crosstalk continues, the release of inflammatory cytokines can lead to the formation of metastatic foci in disseminated cells as well as aggressive local growth due to increased angiogenesis in primary tumor. The removal of the primary tumor can also result in the regression of distant metastases, similar to the abscopal effect observed in patients treated with RT. In addition, local treatment can eliminate potential lethal cell clones that are responsible for the persistence and progression of the disease after systemic therapy (7). Another benefit of removing as much of the tumor burden as possible in oligometastatic disease is that it may increase the success of targeted therapies (e.g., radionuclide lutetium) that may be given in the future. In a study conducted in 2022 by Gafita et al., (18) which investigated the tumor sink effect, the authors found that GA68 PSMA biodistribution in normal organs was significantly lower in patients with high tumor burden

Table 1. Baseline characteristics

	Radical prostatectomy (n=12)	**Radiotherapy (n=6)**	**Overall (n=18)**
Age [(year) median (range)]	66.0 (48.9-75.0)	68.0 (53.0-73.2)	66.2 (48.9-75.0)
Total PSA [(ng/mL) median (range)]	12.2 (4.2-85.0)	16.0 (4.8-324)	12.3 (4.2-324)
Biopsy ISUP GG n (%)			
1	1 (8.3)	0 (0.0)	1 (5.6)
2	0 (0.0)	2 (33.3)	2 (11.1)
3	4 (33.3)	1 (16.7)	5 (27.8)
4	3 (25.0)	0 (0.0)	3 (16.7)
5	4 (33.3)	3 (50.0)	7 (38.9)
Clinical T stage n (%)			
T2	6 (50.0)	2 (33.3)	8 (44.4)
T3a	3 (25.0)	1 (16.7)	4 (22.2)
T3b	3 (25.0)	2 (33.3)	5 (27.8)
T4	0 (0.0)	1 (16.7)	1 (5.6)
Clinical N stage n (%)			
N0	4 (33.3)	2 (33.3)	6 (33.3)
N1	8 (66.7)	4 (66.7)	12 (66.7)
Clinical M stage n (%)			
M1a	4 (33.3)	1 (16.7)	5 (27.8)
M1b	8 (66.7)	5 (83.3)	13 (72.2)
The number of metastases [(n) median (range)]	2 (1-4)	3 (1-4)	2 (1-4)

ISUP GG: International Society of Urological Pathology grade group

compared with those with low tumor burden. This may be due to the reduction of tumor burden in metastatic disease which allows for higher doses of radionuclides to reach the remaining tumors (18).

The most critical factor to consider when deciding on treatment for primary tumors in mHSPC is disease burden. This concept first appeared in the CHAARTED study, which demonstrated that the administration of ADT along with docetaxel in patients with high-volume mHSPC provided survival advantage. In the study, high-volume disease (HVD) was defined as the presence of visceral metastases or ≥4 bone lesions with ≥1 beyond the vertebral bodies and pelvis. However, these definitions are based on CT and WBBS findings (19). Similarly, definitions of OMPC in the literature are based on the location and number of metastases. In our data, PSMA was used to stage only 5 patients, while 13 patients were staged using BT/MRI and WBBS. Currently, promising studies suggest that Ga-68 PSMA PET, which is now routinely used in staging due to its high sensitivity and specificity, can also be used to accurately determine disease burden. The semiautomatic calculation of tumor burden in bone metastases using PSMA PET CT was first described by Bieth et al. (20) in 2017. Subsequently, in 2019, Gafita et al. (21) developed a software-based "qPSMA" to determine the semiautomatic tumor burden in the whole body, including skeletal, visceral, and lymph node metastases, and stated that its use is feasible. In 2021, Barbato et al. (22) designed a study to determine PSMA PET disease volume criteria in patients with mHSPC compatible with CT-based CHAARTED criteria. According to this study, more lesions were found in 62% of patients with Ga68 PSMA PET/CT, and 40% of patients were upgraded from low-volume disease (LVD) to HVD according to the CHAARTED criteria. When ROC analysis was performed to predict the CT-based CHAARTED HVD criteria, the estimated PSMA PET disease volume was 38.8 cm^3. Therefore, the PSMA disease volume criteria were defined as LVD for unifocal disease or tumor burden <40 cm^3 and as HVD for multifocal disease with a tumor burden ≥40 cm^3 (22).

Although retrospective data exist on primary tumor-directed treatment for metastatic PC, there are limited prospective randomized controlled trials (RCTs). The first RCT designed to evaluate primary tumor-directed treatment for metastatic PC was the HORRAD study by Boevé et al. (23). The control group received only ADT, whereas the experimental group received ADT and RT targeted to the prostate. Pelvic lymph nodes and areas of metastasis were not treated with RT. The study participants were divided into groups based on the number of bone metastases on WBBS as follows: <5, 5-15, and more than 15. At a median follow-up of 47 months, no significant difference existed in OS between the control and experimental groups either in the entire cohort or in the subgroups (23). The STAMPEDE study, another RCT published in 2018, used both WBBS and CT for staging and divided the participants into LVD and HVD groups based on the metastatic burden using the CHAARTED criteria. Unlike the HORRAD study, docetaxel was also given as part of the standard systemic therapy to participants enrolled after 2015. In this study, there was also no significant difference in OS between the control and experimental groups in the general group at a median follow-up of 37 months; however, a statistically significant OS advantage was found in the LVD group of the RT group (p=0.007; 3-year survival 73% with control vs 81% with RT) (24). In our study, time to CRPC in the RT group was 43.3 months; however, in the HORRAD study, the time to PSA progression was 15 months, while the failure-free survival was 26.2 months in the STAMPEDE study. The STOPCAP meta-analysis, which included these 2 studies, demonstrated a 7% 3-year survival advantage in those with fewer than 5 bone metastases (25). The current 2022 EAU guidelines strongly recommend local radiation therapy targeted at the prostate with ADT in low-volume metastatic disease due to survival advantage (11).

Currently, ongoing RCTs (g-RAAMP, TRoMbone, and SWOG S1802) are evaluating the effectiveness of RP in metastatic PC, but all available data in the literature are retrospective (26). Surgical treatment of the primary tumor and local treatment of metastasis are not recommended outside well-designed clinical studies (11). In a meta-analysis published in 2022, Shemshaki et al. (27) included retrospective data and found that in metastatic patients, compared with systemic therapy, cytoreductive RP (cRP) led to statistically significantly higher CSS and OS. However, no difference existed in survival between cRP and RT (27). In a prospective case–control study of 83 patients, Steuber et al. (28) found that although no differences existed in OS and CRPC-free survival, locoregional complications were significantly lower in the cytoreductive RP group (7.0% vs 35%; p<0.01).

In our study, 6 patients from each group were given stereotactic RT as MDT. In a retrospective series, data indicate that MDT along with primary tumor treatment increases CSS and CRPC-free survival in de novo OMPC (7). However, no RCT data are available on MDT for de novo OMPC. In a limited number of RCTs in oligorecurrent disease, MDT statistically significantly increases progression- and ADT-free survival; however, no data indicate that it increases OS (29,30).

Study Limitations

This study had some limitations. First, it was designed as a retrospective database study, and no control group received standard systemic treatment. Second, the number of patients was relatively small because the standard treatment approach for the prostatic disease site is yet to be defined within the context of metastatic disease. Third, staging in most of our patients was performed by conventional methods such as WBBS and BT-MRI. The relatively longer time to castration in patients in our study compared to the literature suggests that there may be false positive results in staging with conventional methods in terms of metastasis in these patients. Fourth, patients were not standardized according to the site and the number of metastases. Furthermore, the techniques and doses used for radiation therapy for primary tumors and metastatic foci are not standardized, and data on complications related to local treatments are incomplete.

Conclusion

It is crucial to objectively determine tumor burden using newer generation imaging methods to achieve satisfactory results in determining treatment approaches for OMPC. This is because tumor burden is critical for determining treatment approaches.

While primary tumor-directed RT is effective in selected patients, our results raise the possibility of similar efficacy with RP. However, the awaited results of ongoing prospective randomized controlled clinical trials will further define the actual role of surgery in this patient population.

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Ethics

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Informed Consent: Database report.

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Original Article

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Our Rates of Concurrent or Differential Development of Urothelial Carcinoma in the Renal Pelvis, Ureter, and Bladder: A Single-center Experience

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Abstract

Objective: This study aimed to compare the age, gender, survival, and etiology of cases diagnosed with urothelial carcinoma (UC) in the genitourinary system simultaneously or later in a different localization (lower tract and/or upper tract).

Materials and Methods: Sixty-four patients diagnosed with concurrent or subsequent lower and/or upper tract UC in the Department of Pathology between 2010 and 2020 were evaluated for age, gender, survival, and etiology. Our study is a retrospective study.

Results: Fifty-eight patients were male and six were female. The ages of the patients ranged between 27 and 87 years. The patients were evaluated for noncoagulable and painless hematuria. While 52 of the patients were smokers, 12 of them were non-smokers. Ten of our patients were initially diagnosed with UC in the renal pelvis and/or ureter and three months to eight years later with UC in the bladder, whereas 14 patients were initially diagnosed with UC in the bladder and four months to 10 years later with UC in the renal pelvis and/or ureter. Of the remaining 40 patients, 14 were diagnosed with UC simultaneously in the bladder and ureter, nine in the renal pelvis and ureter, seven in the renal pelvis and bladder, and 10 in the renal pelvis, ureter, and bladder. The mean duration of symptoms before diagnosis was seven months (range; 7 days to 1.5 years).

Conclusion: Because UC can affect multifocal organs, close surveillance of patients diagnosed with upper or lower urinary tract disease UC and who are smokers is recommended at the time of diagnosis or especially during the first three years after diagnosis to prevent the formation of primary tumors in other regions.

Keywords: Urothelial carcinoma, renal pelvis, ureter, bladder

Introduction

The fourth most prevalent type of tumor is urothelial carcinoma (UC). It may be localized in either the lower (bladder or urethra) or upper (renal pelvis and ureter) urinary tract (1-7). UC is observed at a rate of 90-95% in the bladder and 5-10% in the renal pelvis (1,3).

Tumors developing in different histopathologies, organs, and intervals are referred to as multiple primary cancers. Multiple primary tumors are classified into two groups as synchronous or metachronous tumors (8). However, there is no consensus on the definition of synchronous and metachronous tumors. According to the Surveillance, Epidemiology, and End Results criteria, cancers newly diagnosed within two months of the first tumor diagnosis should be classified as synchronous, whereas cancers identified ≥2 months later should be classified as metachronous (8,9). On the other hand, Moertel (10) classifies it as a synchronous tumor if it occurs within the first six months after the initial tumor diagnosis and as a metachronous tumor if it occurs after six months.

Metachronous tumors are more likely to develop due to previous cancer treatments, whereas synchronous tumors are related to organ-specific carcinogens such as smoking and alcohol. Therefore, synchronous tumors tend to affect the head and neck, lungs, and urinary tract, usually associated with smoking (11). Three theories of the origin of multiple and recurrent urothelial tumors are worth mentioning (8,12,13).

- A piece of the urothelium (patch) is subjected to mutational stress and carcinogenic stimulation by waste accumulated in the urine in the field carcinogenesis model,

- In the intraluminal seeding hypothesis, cancer cells scattered from the primary tumor are reimplanted into the normal mucosa,

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The intraepithelial migration model assumes that tumor cells migrate to the normal mucosa.

Synchronous and metachronous tumors of the genitourinary system are common. In their study, Kilciksiz et al. (14) reported a rate of 30.9% when synchronous and metachronous tumors in the genitourinary system were evaluated together. A characteristic feature of the biological behavior of UCs is that they are multiple and therefore likely to appear synchronously or in a series along the entire urinary tract. The probability of UC in the bladder following UC in the upper urinary system is up to 50% (15). On the contrary, after bladder tumors, UC in the upper urinary tract has been reported at a rate of 2-8% (16,17).

This study aimed to compare the age, gender, survival, and etiology of cases diagnosed with UC in the genitourinary system simultaneously or later in a different localization (lower tract and/or upper tract).

Materials and Methods

Sixty-four patients diagnosed with concurrent or subsequent lower and/or upper tract UC in the Department of Pathology between 2010 and 2020 were evaluated for age, gender, survival and etiology. Our study is a retrospective study. A 10-year electronic diagnostic data search was performed in the hospital medical data management system using the keywords "renal pelvis UC or ureter UC" in the diagnosis line. In the first stage (since the incidence of UC in the renal pelvis and ureter is less), UC originating from the renal pelvis or ureter between the relevant dates were documented. Then, all pathology reports of these patients were retrospectively reviewed one by one. Only cases of UC in the renal pelvis or ureter were excluded from the study. Concomitant cases in the upper or lower tract region at the same time or later were included in the study.

The protocol followed in our hospital to investigate the presence of recurrence or a newly developed tumor in other regions of the cases or to follow-up is as follows:

- When tumors are detected in the renal pelvis and ureter, nephroureterectomy is performed.

Low-risk tumors: cystoscopy performed after three months. If no visible tumor was detected, subsequent cystoscopy was performed nine months later and then yearly for five years.

- High-risk tumors; cystoscopy, and urinary cytology performed after three months. If no visible tumor was detected, subsequent cystoscopy and cytology were performed every three months for a period of two years, and every six months thereafter until five years, and then yearly. The contralateral kidney and ureter were followed with ultrasonography.

- If UC is detected initially in the bladder, the upper tract (renal pelvis/ureter) is followed by computed tomography urography. If creatinine was high, magnetic resonance urography was performed.

This study was approved by the Başkent University Institutional Review Board (project no: KA 22/277, date: 14.06.2022) and supported by the Başkent University Research Fund.

Statistical Analysis

Descriptive statistics for the continuous variables are presented as the mean and standard deviation, while count and percentages for categorical variables.

The SPSS (version 21) statistical program was used for all statistical computations.

Results

A total of 64 patients were evaluated (58 male, 6 female). The mean age of the patients was 65.12 years. There were 15 (23.4%) patients younger than 60 years and 49 (76.6%) patients older than 60 years. Noncoagulable and painless hematuria was the most prevalent complaint, while flank pain was the second most common complaint. While 52 patients (81.25%) were smokers (20-80 packs-years), 12 patients (18.75%) were non-smokers. Furthermore, 13 (20.3%) patients had a history of nephrolithiasis.

Ten of our patients were initially diagnosed with UC in the renal pelvis and/or ureter and three months to eight years later with UC in the bladder (median: 22 months), whereas 14 patients were initially diagnosed with UC in the bladder and four months to 10 years (mean: 57 months) later with UC in the renal pelvis and/or ureter. Of the remaining 40 patients, 14 were diagnosed with UC simultaneously in the bladder and ureter, nine in the renal pelvis and ureter, seven in the renal pelvis and bladder, and 10 in the renal pelvis, ureter, and bladder (Table 1). Three of the cases had bilateral renal pelvic tumors. The mean duration of symptoms before diagnosis was seven months (range; 7 days to 1.5 years). Regarding Pt: Ten cases were pTa, 13 cases were pT1, 23 cases were pT2, 16 cases were pT3, and two was pT4. In eight of the cases, squamous differentiation areas were also present. Of the cases, 52 (81.25%) were alive and 12 (18.75%) were dead. Of our ex-cases, one patient with pTa died of heart failure, one of two cases with pT1 died of heart failure, and one case died of lung and breast carcinoma. Table 2 summarizes the clinical characteristics of our ex-patients.

In addition, three of our patients had gastric carcinoma, four had lung carcinoma (two small-cell, two non-small-cell), two had breast carcinoma, and one patient had lung and breast

Table 1. Clinical features of the cases

Feature	N
Male/female	58/6
Median age	65.2
Follow-up time	3 month - 10 year
Localization	
Diagnosed at different times	24
Renal pelvis and/or ureter + bladder	10
Bladder + renal pelvis and/or ureter	14
Diagnosed at the same time	40
Ureter + bladder	14
Renal pelvis + ureter	9
Renal pelvis + bladder	7
Renal pelvis + ureter + bladder	10

carcinoma, three had prostate carcinoma, one had renal cell carcinoma, and one had hepatocellular carcinoma. Lung metastasis was observed in two cases, bone metastasis was observed in one case, and prostate metastasis was observed in two cases.

Discussion

UC shares histology in the upper and lower tracts and contains similar risk factors. It is more common in men and is very rare in children under 50 years of age (3). In our series, the F/M ratio was 1/9, and 96.9% were more than 50 years old. Smoking, occupational exposure, heavy coffee consumption, high-dose analgesics, HPV, familial diseases (Balkan nephropathy, hereditary non-polyposis colorectal cancer syndrome), loss of chromosome 9, aromatic amines, chronic urinary tract infections, kidney stones, and arsenic exposure have been implicated in etiology (1,3,6,13,18,19). Although smoking is one of the major risk factors, it is associated with a rate of 60-80% (1,3,6). In etiology, stone and infection are observed at a rate of 20-30% (1). In our series, 52 patients (81.25%) were smokers. In 13 cases (20.3%), there was a history of nephrolithiasis, consistent with the literature.

Tumors of the upper urinary tract are rare, and the most common form is UC, with a rate of 90%. The renal pelvis accounts for 5% of all UC and the ureter 1 (1,3,13,19). UC is responsible for approximately 95% of bladder carcinomas (3,13). Hematuria is the most common symptom as well as anemia, flank pain, weight loss, fever, pyelonephritis, and a palpable mass (1). The most common complaint in our series was painless hematuria. Approximately 20-50% of patients with primarily upper tract UC are at risk of developing bladder cancer within two years (particularly between 5 and 15 months) after surgical treatment. The incidence of upper tract UC after primary bladder cancer is about 0.7-4%, and this occurs about 4-6 years after primary bladder cancer (19). Ten of our patients were first diagnosed with UC in the renal pelvis and/or ureter and three months to eight years later with UC in the bladder (median: 22 months), whereas 14 patients were first diagnosed with UC and four months to 10 years (median: 57 months) later with UC in the renal pelvis and/or ureter. Of the remaining 40 patients, 14 were diagnosed with UC simultaneously in the bladder and ureter, nine in the renal pelvis and ureter, seven in the renal pelvis and bladder, and 10 in the renal pelvis, ureter, and bladder. The mean duration of symptoms before diagnosis was seven months (range; 7 days to 1.5 years).

In multifocal UC, cancer cells from the primary lesion may be transplanted to other regions, or in patients with vesicoureteral reflux, reversible transplantation of cells, or smokers, waste products may be excreted by the same systemic route (3).

Radical cystectomy and concurrent nephroureterectomy are considered treatment options for invasive bladder tumors and synchronous UC upper urinary tract (20-22). In our series, cystectomy is performed for muscle invasion in bladder tumors; otherwise, intermittent resections and intravesical chemotherapy are used. Nephroureterectomy is the preferred treatment option for tumors located in the upper urinary tract.

Because the underlying bladder tumor was so close to the orifice, orifice resection was performed in eight of 14 patients in our cohort who initially acquired a bladder tumor and later an upper urinary tract tumor. At the time of diagnosis, three of the eight patients had hydroureteronephrosis on the affected side. Although it has been reported that orifice resection can cause vesicoureteral reflux, which can lead to tumor seeding in the upper urinary system it can be considered as a risk factor, studies reported that orifice resection is not a risk factor for tumor transplantation, and there is no statistical difference in the development of upper urinary system UC after bladder tumor in cases with or without orifice resection (23,24).

Diagnostic ureterorenoscopy for the differential diagnosis of upper urinary tract masses has been identified in the European Association of Urology guidelines as a risk factor for the development of metachronous bladder cancer (25). In our study, six patients who underwent ureterorenoscopy for the differential diagnosis of an upper urinary tract mass had a metachronous bladder tumor.

The prevalence of UC in the ureter, renal pelvis, and bladder in our study was similar to that observed in other studies. UC is mostly observed in men and the 6th decade of life, and smoking is the major risk factor.

Table 2. Clinical features of our expatients

Case	Gender	Localization	Stage	Metastasis	Additional tumor
1	M	Bilateral renal pelvis + ureter + bladder	Pt3	None	Renal cell carcinoma
2	F	The renal pelvis + bladder	Pt1	None	Lung small cell carcinoma + breast carcinoma
3	F	Bladder + ureter	Pt2	None	Breast carcinoma
4	M	The renal pelvis + ureter + bladder	Pt3	None	None
5	M	Renal pelvis + ureter + bladder	Pt2	Lung	None
6	M	The ureter + bladder	Pta	None	None
7	M	The renal pelvis + bladder	Pt3	None	None
8	M	The renal pelvis + bladder	Pt3	Bone	None
9	M	The bilateral renal pelvis + ureter + bladder	Pt2	None	None
10	M	The renal pelvis + ureter + bladder	Pt4	Prostate	None
11	M	Bladder + ureter	Pt1	None	None
12	M	The renal pelvis + ureter + bladder	Pt3	Lung	None

M: Male, F: Female

Study Limitation

The limitation of our study is that it is retrospective and the number of patients is relatively low. Our study should be supported by prospective studies.

Conclusion

As a result, UC can affect multifocal organs; therefore, close surveillance of patients diagnosed with upper or lower urinary tract disease UC and who are smokers is recommended at the time of diagnosis or especially during the first 3 years after diagnosis to prevent the formation of primary tumors in other regions.

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Ethics

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Authorship Contributions

Surgical and Medical Practices: M.R.G., M.V.K., Concept: B.H., Design: B.H., M.R.G., Data Collection or Processing: B.H., M.R.G., M.V.K., Analysis or Interpretation: B.H., M.R.G., Literature Search: B.H., M.V.K., Writing: B.H.

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Original Article

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Treatment Options in Low-risk Prostate Cancer Patients: A Retrospective Database Report

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Abstract

Objective: This report examined the approaches to low-risk patients using the data from the Urologic Cancer Database - Prostate, Urooncology Association.
Materials and Methods: In this study, there were 920 patients with low-risk prostate cancer according to the current guidelines of the European Urology Association. Patient data were obtained from the Urological Cancer Database - Prostate, the Turkish Urooncology Association (UroCaD-P) from records of the years 1995-2021. Ethics committee approval was obtained for this study to publish in the form of a database report.
Results: Our study was conducted with 920 patients with low-risk prostate cancer. Therefore, at the time of diagnosis, all patients in the study were ISUP 1, had a prostate specific antigen (PSA) level lower than 10 ng/mL, and clinically T1-T2a. Surgical treatment was used in 750 (81.5%) of the patients. At the time patients were retrieved from the database for the study, 140 patients (15.2%) were in the active surveillance (AS) process. Thirty patients (3.2%) in the study received their local treatment as radiotherapy (RT). The mean age value at cancer detection in the study was 61.9. The mean ages of the patients who were under AS and who underwent radical prostatectomy (RP) were 61.3 and 61.7 years, respectively. In the RT group, the mean age was 66.7 years. The mean PSA value of the whole group was 5.81 ng/mL. While it was 5.94 in AS patients, it was calculated as 5.89 in patients who underwent radical surgery. The mean PSA value of the RT group was 5.40. The pathological upgrade was detected in 225 patients (30%) after surgery. Surgical margin positivity was in 160 of the patients (21.3%) who underwent surgery. In addition, 100 patients (13.3%) had extracapsular disease. The seminal vesicle invasion was detected in 25 patients (3.3%) after surgery.
Conclusion: We predict that the incidence of low-risk prostate cancer will increase over time due to the aging of the population, the use of PSA, advances in imaging modalities, and increasing biopsy success rates. Therefore, the importance of the existence of multicentric databases containing this patient group is undeniable. More studies are needed with these databases, including both patient demographics and treatment outcomes. Hopefully, this database report will be an important step in this direction.
Keywords: Database, prostate cancer, radical prostatectomy

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Introduction

According to the current literature, prostate cancer is the second most common type of cancer diagnosed in men, and its incidence in developed countries is higher, consistent with increased life expectancy (1). Its relationship with family history and ethnicity has been confirmed (2). The incidence of localized prostate cancer is increasing with the use of prostate specific antigen (PSA) and biopsy techniques with high success rates (3,4). Localized disease is divided into low, intermediate, and high risk (5).

When the life expectancy of the patient is between 10 and 15 years, an active surveillance (AS) approach can be applied to a group of patients from the low-risk group (6). This approach is based on preventing overtreatment and treatment toxicity, and it is designed to make a planned transition to curative treatment options eventually (7). There are two main treatment modalities for localized disease: radical prostatectomy (RP) and radiotherapy (RT) (8). This study was planned to determine the demographic characteristics of patients in the low-risk cancer group and the differences in treatment options.

Materials and Methods

In this study, there were 920 patients with low-risk prostate cancer according to the current guidelines of the European Urology Association (5). Patient data were obtained from the Urological Cancer Database - Prostate, Turkish Urooncology Association (UroCaD-P) from the records of the years 1995-2021. Data were collected by REDCap data collection software developed by Vanderbilt University and licensed by the Urooncology Association in Turkey (9,10). Online and simultaneous data are entered into this database from clinics all over Turkey. These data are stored and used in relevant clinical studies. In addition, the treatment follow-up data of the patients are updated regularly. All data are kept securely in an encrypted and anonymous way in the study, demographic characteristics of our patient group, laboratory results, and differences between the treatment methods, biopsy, pathologies were compared. Ethics committee approval was obtained from Manisa Celal Bayar University Faculty of Medicine Health Sciences Ethics Committee (decision no: 1758, date: 29.03.2023).

Statistical Analysis

SPSS 26.0 (IBM Corporation, Armonk, New York, United States) programs were used in the analysis of variables for statistical calculations. In the comparison of two independent groups according to quantitative data, the Independent-Samples t-test was used together with the Bootstrap results, while the Mann-Whitney U test was used together with the Monte Carlo results. Less than 0.05 for p value was accepted as significant.

Results

Our study was conducted with 920 low-risk prostate cancer patients. Therefore, at the time of diagnosis, all patients were ISUP 1, had a PSA level lower than 10 ng/mL, and clinically T1-T2a. Two hundred of these patients (21.7%) were diagnosed with magnetic resonance imaging (MRI) fusion biopsy, and ultrasound-guided transrectal biopsy was performed in 720 (78.2%) of them.

Surgical treatment was used in 750 (81.5%) patients. Open method was used in 445 patients (59.3%) and laparoscopic method was used in 200 patients (26.6%). Robot-assisted surgery was performed in 105 patients (14%). At the time patients were retrieved from the database for the study, 140 patients (15.2%) were in the AS process. We found that the MR fusion biopsy method was used in 75 patients (%53.5) from the group in AS. Thirty patients (3.2%) in the study received their local treatment as RT, and the MR fusion biopsy method was used in 18 of them (60%).

The mean age value at cancer detection in the study was 61.9. The mean ages of the patients who were under AS and who underwent RP were 61.3 and 61.7 years, respectively. In the RT group, the mean age was 66.7 years. The mean PSA value of the whole group was 5.81 ng/mL. While it was 5.94 in AS patients, it was calculated as 5.89 in patients who underwent radical surgery. The mean PSA value of the RT group was 5.40 (Figure 1).

The pathological upgrade was detected in 225 patients (30%) after surgery. In subgroups, 123 of them (16.4%) was ISUP 2, while 65 of them (8.6%) was ISUP 3. The remaining 37 (4.9%) was ISUP 4 and above. Surgical margin positivity was in 160 patients (21.3%) who underwent surgery. In addition, 100 patients (13.3%) had extracapsular disease. The seminal vesicle invasion (SVI) was detected in 25 patients (3.3%) after surgery. We found that 194 (25.8%) patients underwent lymph node dissection during surgery. While the mean number of lymph nodes removed was 7.7, no lymph node metastasis was detected in the surgery group. According to the pre-operative biopsies, 225 of the patients (30%) had perineural invasion, while this number was 260 (34.6%) according to the postoperative pathologic evaluation (Figure 2).

Discussion

There were 920 low-risk prostate cancer patients in our study. Surgical treatment was used in 750 (81.5%) patients. AS was preferred in 140 (15.2%) patients, and 30 patients (3.2%) received RT. The mean ages of the patients who

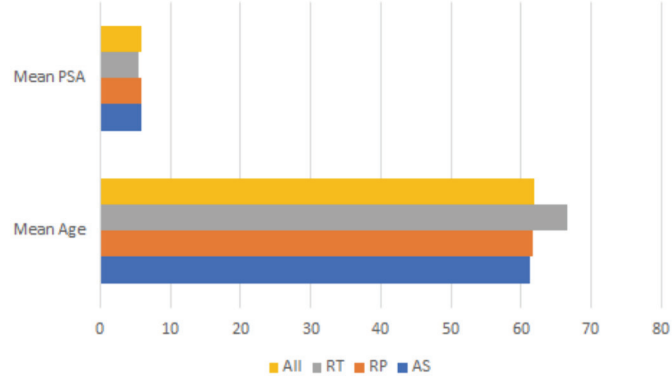

Figure 1. Mean age and PSA values

PSA: Prostate specific antigen, RP: Radical prostatectomy, RT: Radiotherapy, AS: Active surveillance

were under AS and who underwent RP were 61.3 and 61.7 years, respectively. In the RT group, the mean age was 66.7 years. The pathological upgrade was detected in 225 patients (30%). Surgical margin positivity was in 160 of the patients (21.3%) who underwent surgery and 100 patients (13.3%) had extracapsular disease.

Leapman et al. (11) included 895 low-risk patients who received surgical treatment. The mean age was 61 years and the mean PSA level was 5.20 ng/mL. These values are similar to the values of 61.9 and 5.81, respectively, for our study. Of these patients, 642 (71.7%) underwent open retropubic surgery and 197 (22%) underwent open perineal surgery. While 25 (2.7%) patients had laparoscopic approach, 21 (2.3%) patients had robot-assisted surgery. The surgical method of 10 patients is unknown.

In our study, the open method was used in 445 patients (59.3%) and the laparoscopic method was used in 200 patients (26.6) who underwent radical surgery. Robot-assisted surgery was performed in 105 patients (14%). The study by Leapman et al. (11) was multicentric like ours and was conducted with patients are undergoing surgery between 1989 and 2011. The reason why laparoscopic and robot-assisted methods seem to be used less than ours may be that they use patient data from earlier years than ours. However, we see that the most used method is open surgery, which is consistent with the two studies.

In this study (11), the number of pathologic upgrades was found to be 372 (41.5%). In this group, 282 people (31.5%) were ISUP 2, 53 people (5.9%) were ISUP 3, and 37 people (4.1%) had higher ISUP values. In our study, pathological upgrade was detected in 225 patients (30%) after surgery. In subgroups, 123 (16.4%) of them were in ISUP 2, while 65 (8.6%) of them were in ISUP 3 group. The remaining 37 (4.9%) was ISUP 4 and above. It can be seen that the rates of pathological upgrades are lower in the centers in our study. In the pathologic upgrade subgroups, on the other hand, there is a similarity in the scores and the majority is ISUP 2.

In Leapman et al. (11) study, postoperative lymph node metastasis was detected in 1 patient in the entire group. Consistently, there was no lymph node metastasis in our study either. In this study (11), the number of patients with positive surgical margin was given as 323 (36%). In our study, surgical margin positivity was in 160 patients (21.3%). Again, we found

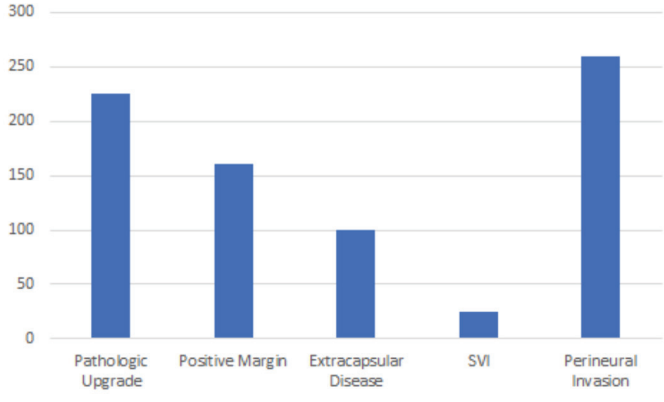

Figure 2. Pathological evaluation
SVI: Seminal vesicle invasion

a lower but consistent rate in our database. The extracapsular extension rate was found to be very similar to our rate of 100 patients (13.3%) with 83 patients (9.27%). Finally, SVI invasion was detected in 24 patients (2.6%), which is almost equal to the 25 patients (3.3%) in our study.

In the study conducted by Stattin et al., (12) there were 6,849 patients who were younger than 70 years with prostate cancer. 2,686 patients were in the low-risk group. Of the 2,686 patients, 1,085 (40.4%) were in the AS group, 1,227 (45.7%) in the RP group, and 374 (13.9%) in the RT group. The mean age of the patients was calculated as 64.7 years for AS, 61.2 years for RP, and 63.4 years for RT. For PSA values, the mean of the AS group was 7.6 ng/mL, while the values for surgery and RT were found to be 8.2 and 9.3, respectively. In our study, surgical treatment was used in 750 (81.5%) patients. In addition, 140 patients (15.2%) were in the AS process. The least group of patients was 30 patients (3.2%) in the study who received their local treatment as RT.

In both studies, the group with the highest number of patients was found to be the radical surgery group. In our database, there is a very high percentage of surgical subgroups. The reason for this may be that patient selection to be entered into the UroCaD-P database is done by prioritizing the surgical group. In our study, the mean age of the surgical group was 61.7, the AS group was 61.3, and RT group was 66.7. The values are very close to each other, especially for the surgical group. However, when the two studies are compared, it is seen that RT is preferred, especially for the older age group in our study. In our study, the mean PSA values were found to be 5.89, 5.94 and 5.40 for the surgery, AS, and RT groups, respectively. When compared with Stattin et al., (12) it is seen that all mean PSA values were calculated lower in ours.

According to the results of two other studies in which pathological upgrade rates were also investigated, there is a 36% upgrade rate for all local prostate cancer risk groups (13,14). For low-risk local disease, this rate was found to be as high as 46% after RP (14). In a study conducted with 10,273 low-risk patients, the pathological upgrade rate was found to be 44% (15). Most of them were upgraded from ISUP 1 to ISUP 2. In our study, all patients were in the low-risk group, and the upgrade rate was 30%, which was consistent with these studies.

In Dinh et al., (15) the extracapsular extension rate was found to be 8.5%. It is seen that this result is compatible with our 13.3% rate. In addition, according to this study, the rate of the SVI was 1.4%. In our article, as stated earlier, this rate was 3.3%. In the mentioned study, the rate of pathological lymph node metastasis was found to be 3.0%. It was not detected in any patient in our group. Although these two situations do not contradict each other, we think that the reason for the difference is that the study by Dinh et al. (15) was conducted with a larger patient group than ours.

Study Limitations

The main limitations of our study are that it is retrospective and multicentric. However, this resulted in many patients compared with the literature. There seems to be a need for prospective studies with this database and patient groups. In addition, a way

such databases can be more inclusive is by coordinating them with radiation oncology.

Conclusion

We predict that the incidence of low-risk prostate cancer will increase over time due to the aging of the population, the use of PSA, advances in imaging modalities, and increasing biopsy success rates. Therefore, the importance of the existence of multicentric databases containing this patient group is undeniable. This study shows that the low-risk prostate cancer patient group is still a heterogeneous group. Multiple treatment and follow-up methods suitable for this patient group are also widely used. It has been seen with the results of postoperative pathological evaluation that the importance of staging before surgery continues. More studies are needed with these databases, including both patient demographics and treatment outcomes. Hopefully, this database report will be an important step in this direction.

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Ethics

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Case Report

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Open Partial Nephrectomy in Giant Papillary Renal Cell Carcinoma: Presentation of 2 Cases

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Abstract

Radical nephrectomy is still considered the standard treatment for clinical T2 (cT2) tumors, but available data mention the potential role of partial nephrectomy in large renal tumors (≥cT2) in selected cases. Because of the increased risk of complications in large masses, the decision for partial nephrectomy should be taken together with an experienced surgeon and a multidisciplinary team. We report two cases with giant renal tumor, that partially resected and final histopathological examination revealed papillary renal cell carcinoma. Considering the risk of developing kidney failure secondary to diabetes and hypertension in both our patients, partial nephrectomy was initially considered and successfully treated with nephron-sparing surgery.

Keywords: Kidney tumors, partial nephrectomy, RCC, urological neoplasms

Introduction

Current guidelines recommend partial nephrectomy for clinical T1a (cT1) renal masses and can be performed for cT1b tumors when technically possible (1). Radical nephrectomy is still considered the standard treatment for cT2 tumors, but available data mention the potential role of partial nephrectomy in large renal tumors (≥cT2) in selected cases (2). The maximum size of a tumor for which partial nephrectomy can be performed is controversial (3). Due to the increased risk of complications in large masses, the decision for partial nephrectomy should be taken together with experienced surgeons and a multidisciplinary team. In this study, we present the case report of 2 patients who underwent open partial nephrectomy for a giant renal mass in our clinic.

Case Reports

Case 1

A 74-year-old female who was being treated for acute pancreatitis had left upper quadrant pain. The patient had an abdominal magnetic resonance imaging (MRI) that showed a large tumor of 185-160-188 mm in the left retroperitoneal area, including the left kidney's upper and middle pole with 64x33 mm solid components at the level of the posterior and superior, and cystic necrotic areas in the central (Figure 1). The patient was referred to our department. Our physical examination showed a large mass in the abdomen. We performed the relevant workup including a thoracoabdominal computed tomography scan and laboratory tests. Laboratory tests were at normal values. She had diabetes and hypertension in her medical history. There was no vascular involvement of the tumor. After the patient gave informed consent, we decided to perform open surgery for exploration and resection. Because of the size of the tumor and the possibility that it could have a fixed contact with gastrointestinal organs, we planned to perform transabdominal surgery and started with the anterior subcostal incision. We successfully performed a nonischemic open left partial nephrectomy. There was a grade 2 intraoperative complication according to the European Association of Urology (EAU) intraoperative adverse incident classification (EAUiaiC), which is 750 cc of blood loss (4). The operative time was 300 min. The pathology report confirmed a papillary renal cell carcinoma (RCC) with a 22-cm tumor size located on the left middle pole. Surgical margins were negative. The tumor had no lymphatic or perineural invasion. Perinephritic fat invasion was detected and the final tumor stage was pT3. Immunohistochemical results showed that CK7, PAX, 8AND and CD68 were positive. During the postoperative follow-up, the patient did not show any complications. Preoperative and

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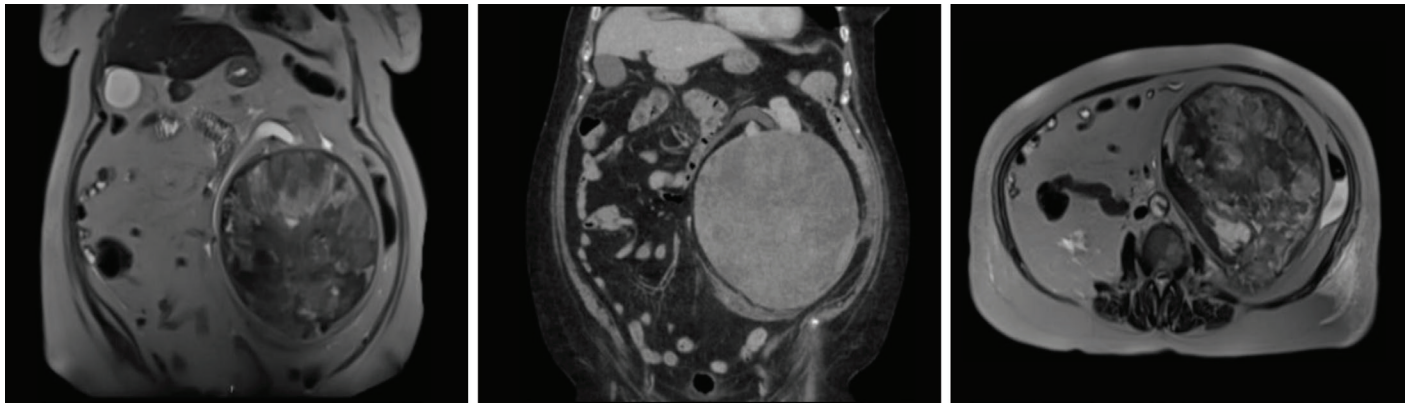

Figure 1. Imaging of the first case

postoperative third-month creatinine values of the patient were observed as 0.65/0.75 mg/dL, respectively. The total follow-up time was 9 months. No recurrence or metastasis was found in the thoracoabdominal CT scans taken during the follow-up.

Case 2

A 63-year-old male patient referred to our clinic with a giant abdominal mass, abdominal distention, and epigastric pain underwent an abdominal computed tomography scan. A 25-cm solid tumor with cystic lesions was found. Physical examination showed a massive palpable solid tumor in the right upper and lower abdominal quadrants. The patient attributed increased abdominal distention to weight gain and did not seek any medical assistance. The patient had no genitourinary symptoms such as hematuria or hydronephrosis. We performed a contrast-enhanced MRI and confirmed a 24-19-25 cm solid and cystic lesion originating from the right kidney (Figure 2). Preoperative laboratory tests were all at normal values. He had diabetes and hypertension in his medical history. We decided to perform an open partial nephrectomy with a high possibility of becoming a radical nephrectomy. As performed in the first case, we decided to perform surgery with the anterior subcostal incision. We successfully performed an open nonischemic partial nephrectomy (Figure 3), and a double J (DJ) stent was placed in the right ureter due to the opening of the renal pelvis. The operation time was 345 min. There was a grade 2 complication according to EAUiaiC, which is 1,300 cc blood loss and DJ stent placement (4). Final histopathological examination revealed papillary RCC with a 22.5 cm diameter. The histological types were 1 and 2, and the histological grade was ISUP 3. There was no vascular or perineural invasion. Surgical margins were negative. The pathological stage was pT2b. Immunohistochemistry has been reported as AMACR, PANKREATN, PAX 8 positive, and CD 10 was focal weak positive. There were no postoperative complications. The DJ stent was removed after six weeks of surgery. Preoperative and postoperative third-month creatinine values of the patient were observed as 1.1/1.2 mg/dL, respectively. The total follow-up time was 7 months. No recurrence or metastasis was found in the thoracoabdominal CT scans taken during the follow-up.

Informed consent was obtained.

Discussion

Papillary renal cell tumors are the second most common malignant renal cell tumors; their incidence ranges from 15-20%. In addition to standard risk factors such as smoking, hypertension, and obesity, papillary RCC is associated with renal dysfunction. It is the most frequently diagnosed RCC in patients with acquired cystic disease associated with chronic kidney disease (5). Preservation of renal functions is necessary for a better quality of life in patients with comorbidities affecting the vascular system and kidney, such as diabetes and hypertension (1).

The major difference between partial and radical nephrectomy is the preservation of kidney functions. This will result in a lower risk of chronic renal failure due to higher GFR and better cardiovascular outcomes and reflect positively on overall survival (2,3). In view of all these long-term benefits and non-oncological compromises, NSS is recommended by current guidelines, if technically possible, for patients with T2 tumors and solitary kidney or chronic kidney disease (1). Especially in large tumors, the minimally invasive approach requires longer operation and ischemia times and can be more technically challenging. In patients whose kidney function needs to be preserved and difficult reconstruction of the kidney is expected, open partial nephrectomy remains popular (6).

In 2022, Huang et al. (5) performed a laparoscopic radical nephrectomy in a 19-year-old patient with an 18-cm RCC which was revealed as papillary RCC type 2. In 2016, Oviedo et al. (7) presented a case of open radical nephrectomy in a 75-year-old patient with a 10,500 cm^3 papillary RCC. In 2020, Takeda et al. (8) performed an open radical nephrectomy in a 59-year-old male patient on a 43 cm tumor, which is the world's largest RCC, and its pathology was reported as papillary RCC type 1. These are the largest RCC that have performed radical nephrectomy published in the literature. Considering the risk of developing renal dysfunction, cardiac comorbidities, and anemia secondary to radical nephrectomy, in both of our patients presented above, partial nephrectomy was initially considered and successfully treated with nephron-sparing surgery.

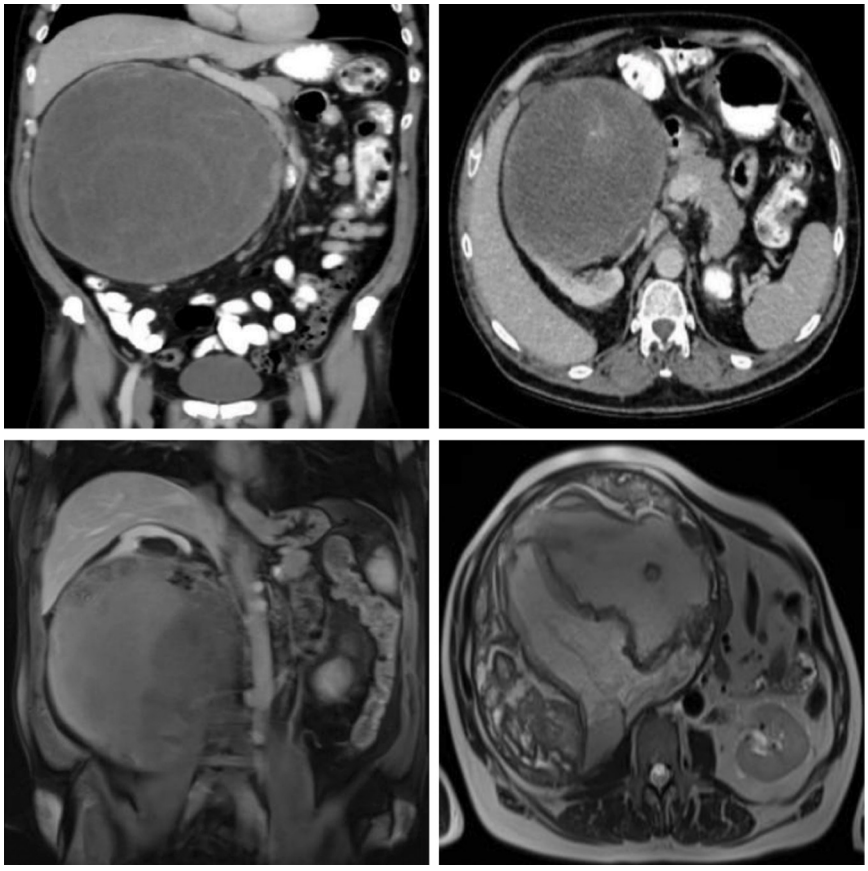

Figure 2. Imaging of the second case

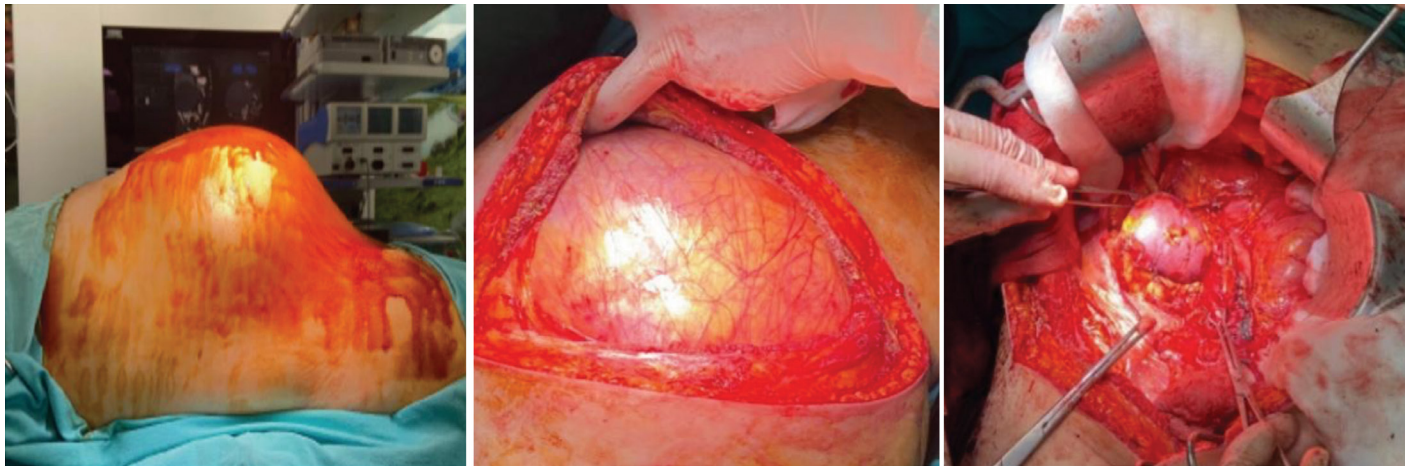

Figure 3. Intraoperative pictures of the second case. The last picture shows the kidney after partial nephrectomy

Conclusion

In addition to its potential benefits, the decision of partial nephrectomy for large tumors should be considered as an alternative to radical surgery in experienced and high-volume centers and selected cases due to its technical complexity and high risk of intra/perioperative complications.

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Ethics

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Authorship Contributions

Surgical and Medical Practices: A.T., M.D.D., M.H.İ., T.A., Concept: A.T., M.D.D., T.A., Design: A.T., M.D.D., T.A., Data Collection or Processing: A.T., M.D.D., M.H.İ., T.A., Analysis or Interpretation: A.T., M.D.D., M.H.İ., T.A., Literature Search: A.T., M.D.D., M.H.İ., T.A., Writing: A.T., M.D.D., M.H.İ., T.A.

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Case Report

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Congenital Adrenal Hyperplasia and Testicular Adrenal Rest Tumors Causing Infertility and Detected by 18F-FDG PET/CT

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Abstract

Testicular adrenal rest tumors (TARTs) are benign tumors often bilaterally located and are mostly diagnosed in adulthood. TARTs are seen in approximately 94% of patients with congenital adrenal hyperplasia (CAH). In this paper, we present a case of TARTs and CAH detected on 18F-fluorodeoxyglucose (FDG) PET/CT, as a rare case described in only one report in the literature. A 42-year-old patient presented to our outpatient clinic due to testicular masses. The patient had azoospermia, and his ultrasound images revealed bilateral solitary masses. In 18F-FDG PET/CT, high activity uptake was observed in both testicles, and bilateral adrenal hyperplasia was detected incidentally. When the patient's anamnesis was questioned, it was determined that pubarche occurred at the age of nine years, his body weight was 82 kg, and his height was 153 cm. Because of the hormonal evaluation, the patient was diagnosed with CAH and TARTs. In conclusion, 18F-FDG PET/CT may play a decisive role in the evaluation of infertile men with testicular masses.

Keywords: Congenital adrenal hyperplasia, infertility, PET/CT, testicular adrenal rest tumor

Introduction

Testicular adrenal rest tumors (TARTs) are most diagnosed in adulthood and are often located bilaterally (1). In patients with congenital adrenal hyperplasia (CAH), elevated adrenal androgen levels suppress the hypophyseal-gonadal axis, resulting in small testicular sizes and infertility. Obstructive azoospermia and oligospermia caused by TARTs are other causes of infertility (2). Positron emission tomography/computed tomography (PET/CT) performed with 18F-fluorodeoxyglucose (FDG) can help diagnose malignancies in the presence of many suspicious lesions, stage diagnose cases, evaluate treatment response, and detect recurrences with high reliability (3). In this paper, we present a case of CAH and TARTs detected on 18F-FDG PET/CT performed due to testicular masses in a patient who presented to our outpatient clinic with infertility.

Case Report

A 42-year-old patient presented to our outpatient clinic due to testicular masses. The patient had azoospermia according to the sperm analysis. In the blood tests, AFP 1.77 (0.89-8.78 ng/mL) and beta HCG 0.82 (0.22-9.75 mıU/mL) were found. His scrotal Doppler ultrasonography (USG) revealed bilateral vascular solitary lesions containing heterogeneous diffuse calcifications, measuring 32x15x14 mm on the left and 35x15x15 mm on the right, as well as a decrease in both testicular volumes (Figure 1). These lesions were evaluated to be malignant, and 18F-FDG PET/CT was planned. The intense involvement of both adrenal glands was visualized, and bilateral adrenal hyperplasia was detected in the tomography images. The metabolic size of the mass was 9x7 mm maximum standardized uptake value (SUV_{max}): 5.9] in the right testis and 13x12 mm (SUV_{max} 4.3) in the left testis, and high levels of metabolic activities were observed, which were interpreted to correspond to the masses defined on USG (Figures 2-4). These findings were considered to be suspicious in terms of primary testicular malignancy and bilateral adrenal metastases, and the patient was referred to the endocrinology department for re-evaluation for other possible underlying conditions. When the anamnesis of the patient was questioned, it was determined that pubarche had started at the

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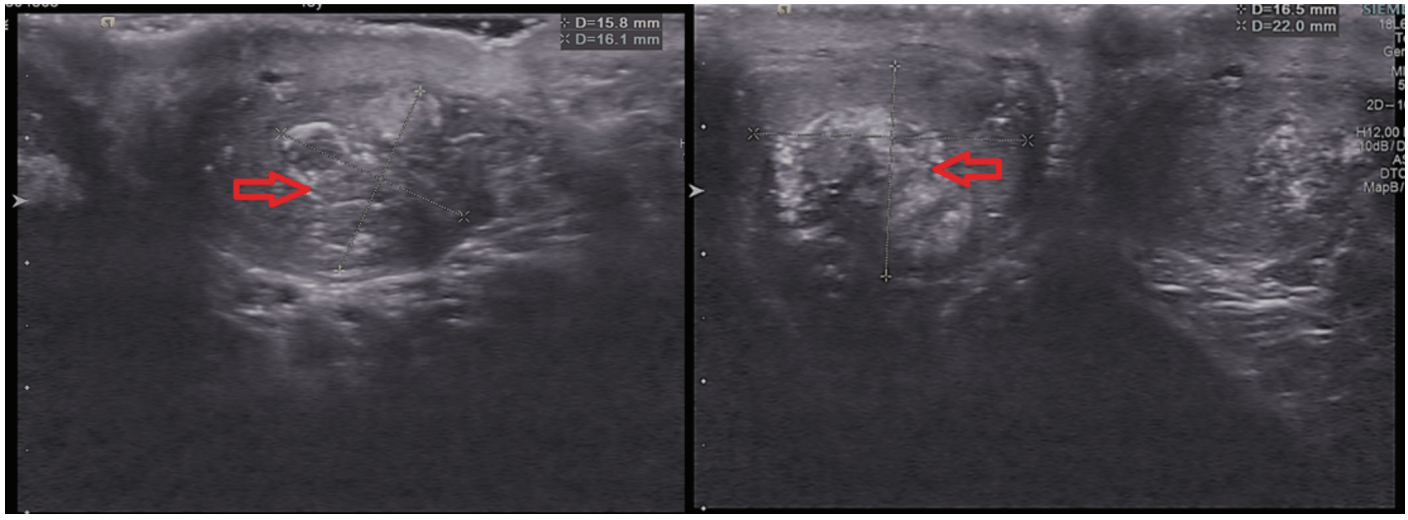

Figure 1. a) Ultrasonography image of the right testicle showing a hypoechoic mass, **b)** Ultrasonography image of the left testicle showing a hypoechoic mass

age of nine years, and his current body weight and height were 82 kg and 153 cm, respectively. System examination findings were normal. The results of the blood tests were as follows: 17-hydroxyprogesterone, >20 ng/mL; androstenedione, >10 ng/mL; ACTH, 306.8 (7.2-63.3) pg/mL; morning basal cortisol, 3.4 (6.2-19.5) mcg/dL; and DHEA-So4, 657 (139-484) mcg/dL. Considering a history of early puberty, short stature, adrenal hyperplasia, bilateral testicular involvement, and elevated androgen levels, a diagnosis of CAH and concomitant TARTs was made, and hydrocortisone treatment was initiated in divided doses of 20 mg/day. Fatigue and erection problems improved after the steroid treatment. In vitro fertilization was planned for infertility treatment. Informed consent was obtained.

Discussion

CAH refers to a group of adrenal steroid synthesis disorders. The disease is autosomal recessive. In these patients, steroid synthesis decreases and consequently the ACTH-level increases. As a result, all cells originating from the adrenal cortex proliferate (1).

TARTs are seen in approximately 94% of patients with CAH (3). These tumors are typically localized in the rete testis and are usually bilateral (4). They are seen in untreated patients and often in young adults (5). One of the most important problems encountered in adult patients with CAH is infertility, as was the case in our patient. In these patients, suppression of the hypophyseal-gonadal axis due to high adrenal androgen levels reduces testicular size and infertility (2).

TARTs are often mistaken for Leydig cell tumors because of their similar features in pathology (6). Microscopic examination of TARTs revealed lobular or nodular cells with extensive eosinophilic granular cytoplasm, separated by fibrous septa. Reinke crystals are characteristic of Leydig cell tumors and seen in 20-40% of cases (4). Leydig cell tumor tends to show a relatively higher metabolic activity on PET/CT (7). However, the diagnosis of TARTs can be made based on a typical history, bilaterality, and characteristic USG and magnetic resonance imaging (MRI) findings. On USG, they are typically seen as bilateral hypoechoic lesions with multifocal acoustic shadowing extending from the hilum to the parenchyma. On MRI, these

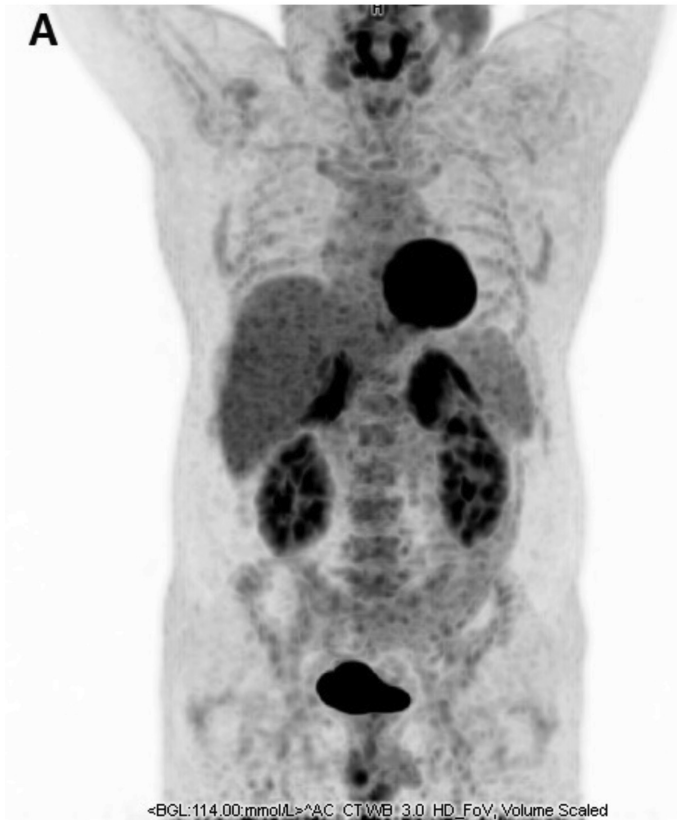

Figure 2. 18F-FDG PET/CT image of congenital adrenal hyperplasia and testicular adrenal rest tumors

FDG: Fluorodeoxyglucose, PET/CT: Positron emission tomography/computed tomography

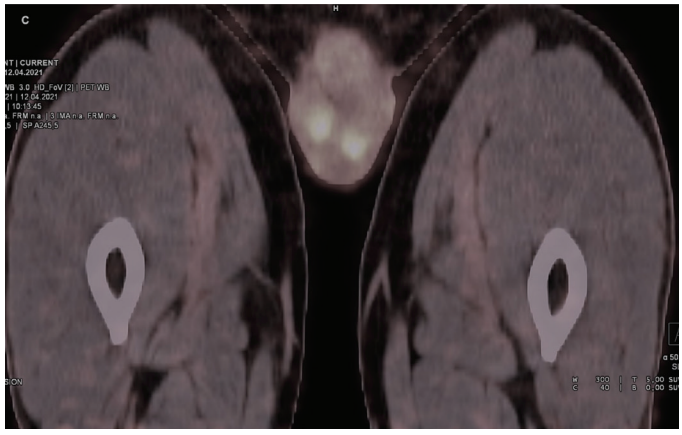

Figure 3. 18F-FDG PET/CT image of testicular adrenal rest tumors

FDG: Fluorodeoxyglucose, PET/CT: Positron emission tomography/computed tomography

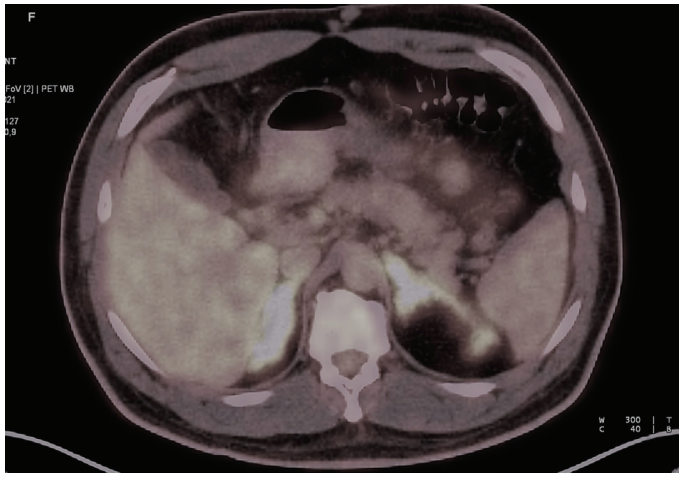

Figure 4. 18F-FDG PET/CT image of congenital adrenal hyperplasia

FDG: Fluorodeoxyglucose, PET/CT: Positron emission tomography/computed tomography

lesions are visualized as bilateral solid masses extending from the hilum to the parenchyma and have contrast enhancement after the contrast agent injection (8). However, it is essential that the endocrine hormone profile supports the diagnosis, and USG and MRI findings alone cannot definitively differentiate TARTs from other testicular malignancies (4).

TARTs may regress in the early period with corticosteroid treatment at a dose that suppresses increased ACTH levels. Response to medical treatment depends on the histological and clinical stage of the tumor (9). In the patient group where medical treatment is not sufficient, if testicular hypofunction has not developed and testicular tissue invasion is not high, testis-sparing surgery can be performed. However, the fertility prognosis in patients with TARTs undergoing testis-sparing surgery remains uncertain. Tumors that cover most of the testicular tissue are considered to be at advanced stages, and orchiectomy is preferred in these patients (10,11).

There is only one case report in which a TART diagnosis was made using 18F-FDG PET/CT in the literature. In this 17-year-old male patient with testicular masses, unilateral orchiectomy was performed, and the pathology result was found to be Leydig cell tumor (12).

Conclusion

CAH and TARTs can be diagnosed following 18F-FDG PET/CT. Our 42-year-old adult patient presented to our outpatient clinic with infertility and was diagnosed with CAH and TARTs based on the 18F-FDG PET/CT findings and endocrine profile before testis loss occurred.

It should be considered that 18F-FDG PET/CT may have a decisive effect in the evaluation of infertile men presenting with a testicular mass.

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Ethics

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

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Case Report

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Bull Urooncol 2023;22(2):84-88

Endovascular Treatment and Follow-up of Retroperitoneal Hemorrhage Caused by Bilateral Giant Renal Angiomyolipoma

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Abstract

Tuberous sclerosis is a multisystem neurocutaneous genetic disease that might be seen in one live birth in 6,000-10,000. Angiomyolipomas (AML) are the most common renal lesions that could be seen in 80% of tuberous sclerosis patients. Nephron-sparing surgery or selective arterial embolization are methods that could be used in the treatment of AML. Here in we present the case who has been admitted to our emergency department with retroperitoneal bleeding due to bilateral giant AML and treated with the endovascular method.

A 55-year-old woman, who has been followed regularly in our hospital since 2016 with the diagnosis of tuberous sclerosis. The patient was admitted to the emergency department of our hospital with complaints of right upper quadrant pain and dizziness. On computed tomography, 4 cm of free fluid was observed at the posterior part of the right kidney posterior, consistent with hemorrhage. On renal angiography, selective arterial angioembolization (SAE) was performed on the inferior segmental artery, which is feeding the AML. Surgical intervention was not considered in the foreground because the patient has bilateral giant AML and would not be anephric. It was decided to begin the patient on everolimus (mTOR inhibitor) treatment. In the patient's first year follow-up, imaging was performed with non-contrast computed tomograpy. Computed tomograpy showed no size change in giant AML in both kidneys. Although the patient's creatinine levels increased to 3.04 mg/dL and urea to 148 mg/dL during the follow-ups, she did not need hemodialysis.

AML, which is seen as a part of tuberous sclerosis, is one of the important causes of mortality in tuberous sclerosis, which causes life-threatening bleeding and requires surgical or endovascular treatments. Nephron-sparing surgery could be difficult in bilateral cases. Therefore, SAE should be considered an important treatment option in emergencies.

Keywords: Angiomyolipoma, MTOR ınhibitors, therapeutic embolization, tuberous sclerosis

Introduction

Tuberous sclerosis (TSC) is a multisystem neurocutaneous genetic disease that might be seen in one live birth in 6,000-10,000 (1,2). TSC is inherited in an autosomal dominant manner and 66% of patients have sporadic mutations (3). It is a multisystem disease which is typically involving the brain, skin, kidneys, heart, eyes, and lungs. The specific features of the disease include glial-neuronal-retinal hamartomas, subependymal giant cell tumors, cardiac rhabdomyoma, renal-extrarenal angiomyolipomas (AML), and pulmonary lymphangioleiomyomatoses (LAM) (4). AML are the most common renal lesions that could be seen in 80% of TSC patients (5). It should be treated in patients with large tumors, fertile women, patients who have difficulty in accessing follow-up or emergency care, and patients with have acute or recurrent bleeding episodes (6). Nephron-sparing surgery or selective arterial embolization are methods that could be used in the treatment of AML (6). Here in we present the case who has been admitted to our emergency department with retroperitoneal bleeding due to bilateral giant AML and treated with the endovascular method.

Case Report

A 55-year-old woman, who has been followed regularly in our hospital since 2016 with the diagnosis of TSC with LAM

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(Figure 1), intracranial tubercles (Figure 1), bilateral renal AML (Figure 2), and who did not come to her follow-up due to the coronavirus disease-2019 pandemic. The patient was admitted to the emergency department of our hospital with complaints of right upper quadrant pain and dizziness in December 2021. Pyschial examination was normal and the patient was conscious, oriented, and cooperative. Arterial blood pressure was 90/60 mmHg and heart rate was 106/min. In the laboratory tests; hemoglobin (Hgb) was 7.4 g/dL, creatinine was 1.78 mg/dL and urea was 95 mg/dL. Ultrasonography (USG) revealed intrabdominal minimal free fluid and a dense collection area in the retroperitoneal area, which was thought to originate from AML. The patient's vitals were stable and the second Hgb value was 7.1 mg/dL. Computed tomography (CT) was performed on the patient. On CT, 4 cm of free fluid was observed at the posterior part of the right kidney posterior, consistent with hemorrhage (Figure 2). The patient was consulted by the interventional radiology clinic and renal angiography (RA) was planned for the patient by interventional radiology clinicians. On RA, selective arterial angioembolization (SAE) was performed on the inferior segmental artery, which is feeding the AML, using 500-700 micron microparticles (Figure 3). After RA, the Hgb value was 6.9 g/dL and 2 units of erythrocyte suspension (ES) were transfused to the patient. The patient's vitals were stable after RA and Hgb was 8.7 g/dL, and creatinine was 3.16 mg/dL after transfusion. On the control CT which was performed four days after the SAE procedure, it was observed that the hematoma area began to resorb (Figure 2). The patient was followed up in nephrology and our clinic for 15 days and she was discharged without any necessary hemodialysis and additional ES replacement. In the controls, which was one month after discharge, Hgb was 10 g/dL and creatinine: 1.89 mg/dL. There were no hematomas or collection areas observed on USG. Surgical intervention was not considered in the foreground because the patient has bilateral giant AML and would not be anephric. The patient was evaluated for initiation of a mammalian target inhibitor of the rapamycin protein complex (mTOR). It was decided to begin the patient on everolimus (mTOR inhibitor) treatment. AFINITOR® preparation was administered at a dose of 10 mg 1*1 for one year. During the period of treatment, the patient did not experience any side effects and the patient was followed up with USG. Six months after the start of the treatment on the USG there was an appearance compatible with bilateral giant angiomyolipoma of 129*60 mm in the right kidney and 128*45 mm in the left kidney. These dimensions were the same as pre-treatment dimensions and did not increase in size. In the patient's first year follow-up, imaging was performed with non-contrast CT due to elevated creatinine and CT showed no size change in giant AML in both kidneys (Figure 4). During the treatment, severe flank pain and hematuria did not occur in the patient. Although the patient's creatinine levels increased to 3.04 mg/dL and urea to 148 mg/dL during the follow-ups, she did not need hemodialysis.

Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Discussion

AML are benign mesenchymal tumors that could occur sporadically or as part of TSC (7). AML belongs to a family called PEComas (perivascular epithelioid cell tumors) which are characterized by the proliferation of perivascular epithelioid cells. Although classical AML are completely benign, the epithelioid type could make a malignant transformation, but this condition is rare. Malignant transformation might manifest as local recurrence or distant metastasis (8-10).

TSC is known to result from a mutation in the *TSC1 (chromosome 9q34)* or *TSC2 (chromosome 16p13)* gene (11). These genes encode the hamartin and tuberin proteins which are inhibiting a serine-threonine kinase known as mTOR (the mammalian target of rapamycin). As a result of removal of inhibition, it causes excessive growth and proliferation in tissues due to the irregular stimulation of cell growth and proliferation (12).

AML could be seen in 80% of all TSC patients. Although AML is benign, it has been proven to be the most common cause of death associated with TSC, because of it causes severe retroperitoneal bleeding that requires dialysis and transplantation as a result of chronic renal failure (11). On the other hand, LAM occurss with the destruction of alveolar tissue in the pulmonary parenchyma

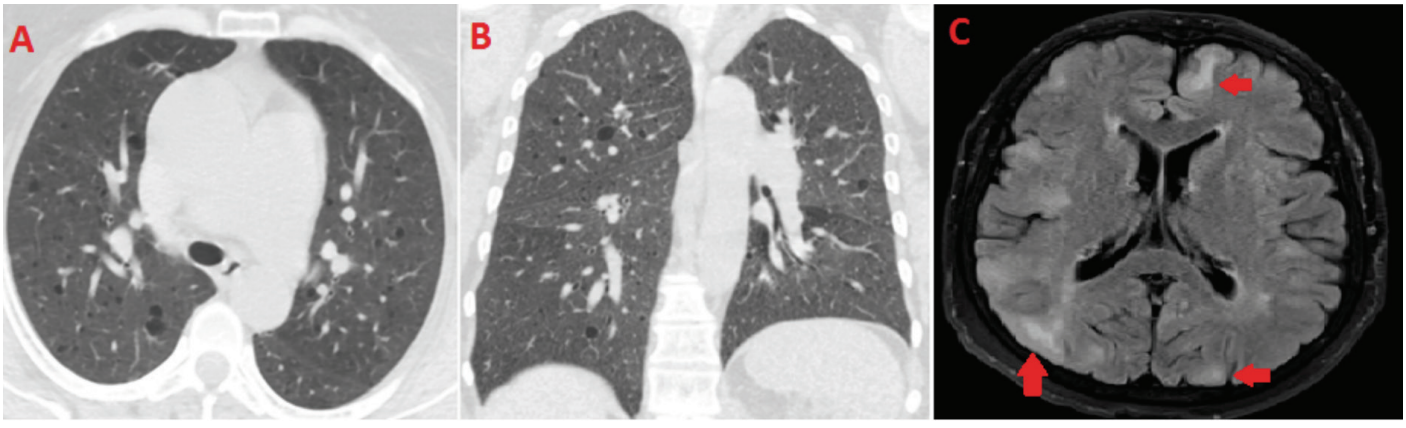

Figure 1. A) In high-resolution CT (HRCT), multiple thin-walled cysts are observed in both lung parenchyma (lymphangioleiomyomatosis). **B)** Lymphangioleiomyomatosis in HRCT (coronally section). **C)** In cranial MRI, cortical tubercles are seen as hyperintense in the T2 FLAIR sequence and shown with red arrows

CT: Computed tomography, MRI: Magnetic resonance imaging

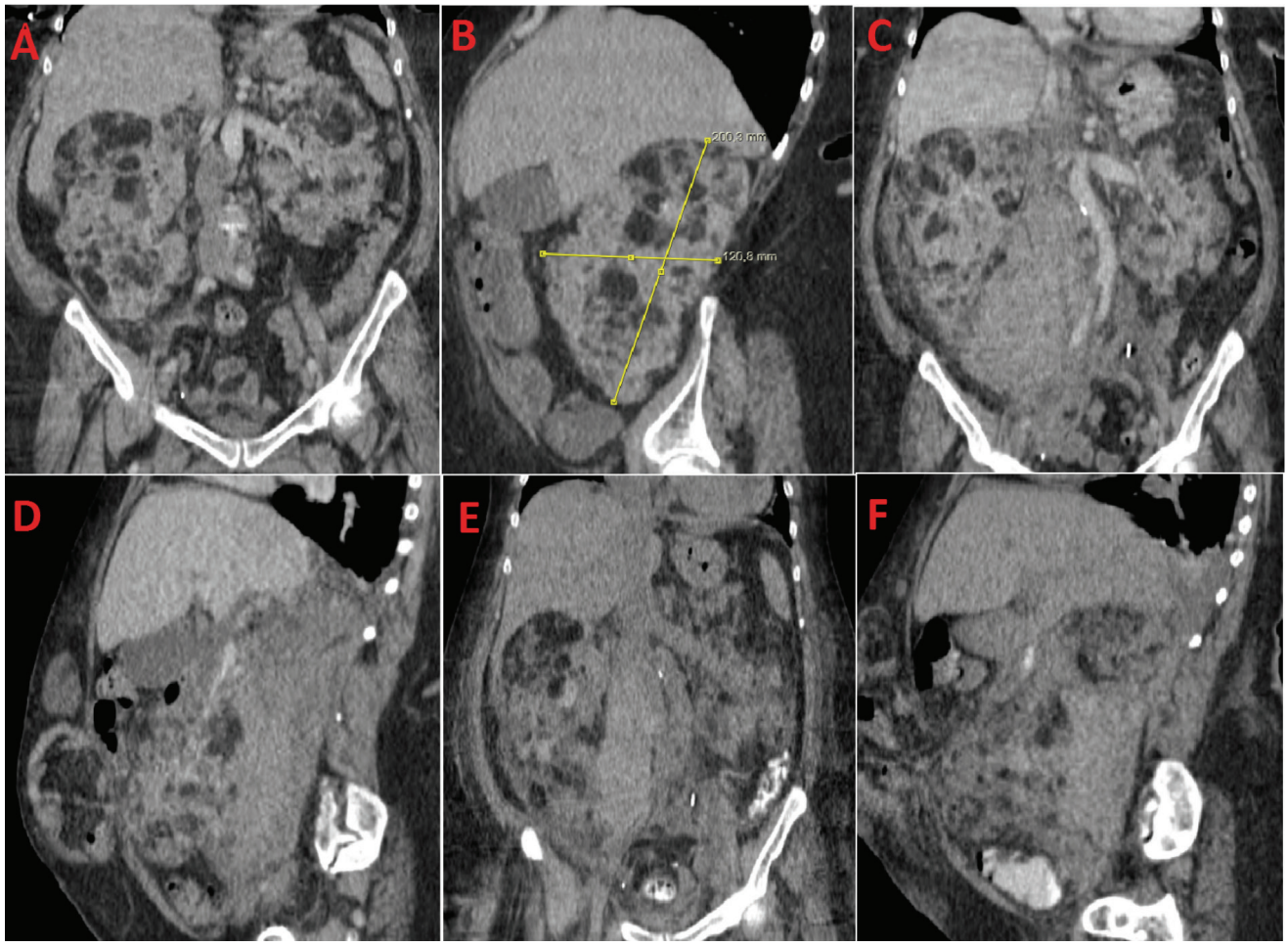

Figure 2. A) Image of bilateral giant angiomyolipomas on computed tomography (CT) of 2019. **B)** Image of right giant angiomyolipoma on CT of 2019. **C)** Retroperitoneal hematoma image due to bleeding thought to originate from right giant angiomyolipoma on the CT performed at the emergency admission of the patient. **D)** Hematoma image in the retroperitoneal area on CT performed at the emergency admission of the patient. **E)** On the CT wich performed on the 4th day after selective arterial angioembolization (SAE), it is observed that the retroperitoneal hematoma size is decreasing (coronal section). **F)** On the CT which performed on the 4th day after SAE, it is observed that the retroperitoneal hematoma size is decreasing (sagittal section)

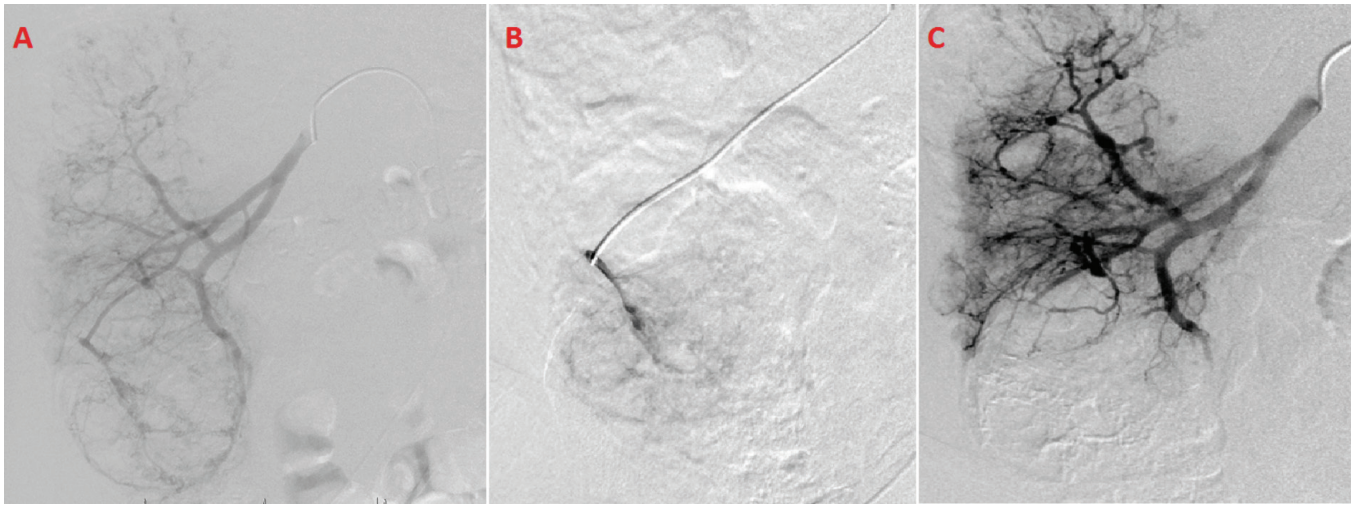

Figure 3. A) Demonstration of arterial branches in the right renal angiography (RA). **B)** Selective embolization with microparticles of the inferior segmental artery which is feeding the giant angiomyolipoma. **C)** RA image after selective embolization

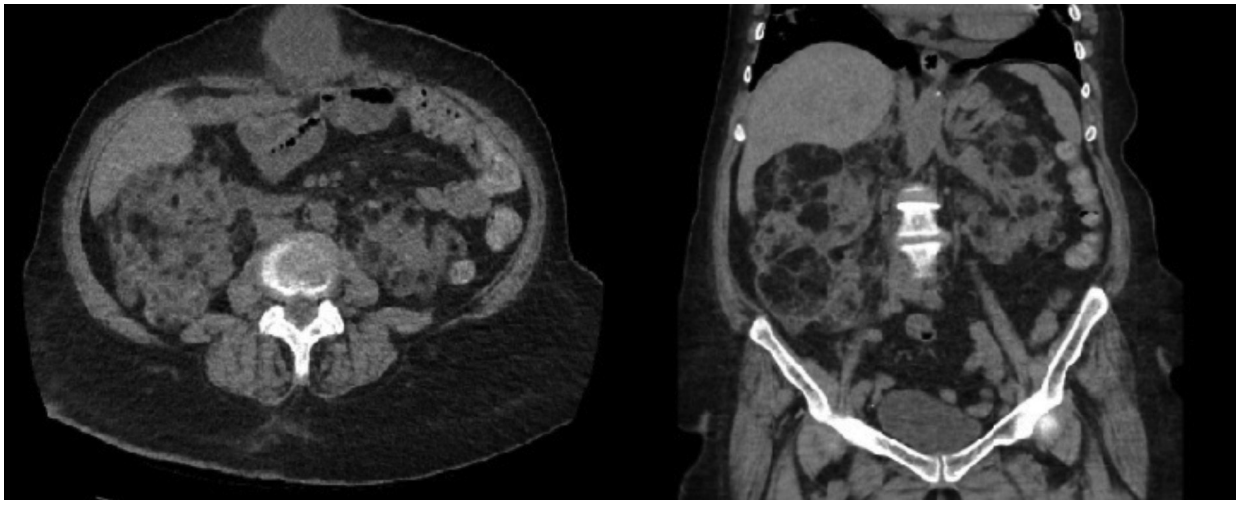

Figure 4. Control CT image at one year after the procedure
CT: Computed tomography

with cystic changes and proliferation of smooth muscle cells and it is third most common cause of TSC morbidity (13).

The main complication of AML is bleeding into the retroperitoneal or collecting system which could be mortal. Bleeding is usually caused by spontaneous rupture of the tumor. Major risk factors for bleeding in AML are; tumor size, grade of angiogenic component, and presence of TSC (14-16).

Usually, USG, CT, and magnetic resonance imaging could diagnose AML by detecting the presence of adipose tissue. However, AML with little adipose tissue content might not be seen clearly. If the lesions could not be identified as benign on initial evaluation, these should be treated as renal cell carcinomas (9-10).

Still, the relationship between the size of AML and the risk of bleeding has not been demonstrated. As conventionally known, a 4 cm tumor size is limited for therapy, and should not be an indication for treatment in patients with AML (14). According to the European Association of Urology guidelines, treating AML is indicated in patients with large tumors (no recommended intervention threshold), fertile women, poor follow-up or access to emergency care, and acute or recurrent bleeding episodes (6). Nephron sparing approach should be preferred as much as possible in the treatment of AML. SAE, which is a minimally invasive treatment, is an alternative to surgery but more recurrences and the need for secondary treatment are the main disadvantages of SAE (14).

An intracellular pathway called the "mammalian target of rapamycin", which plays a role in the regulation of cell proliferation and could be inhibited by rapamycin, is essentially a serine/threonine protein kinase. It consists of two different multi-protein 19 complexes (mTORC1 and mTORC2). The functional process of PI3K/AKT and mTOR protein, which is an important signaling pathway, is closely related to receptor tyrosine kinases (RTK). During malign transformation, various RTK such as vascular endothelial growth factor receptor, platelet-derived growth factor receptor-a, epidermal growth factor, c-Met could be secreted from cancer cells. The PI3K/AKT/mTOR signaling pathway is frequently used to shape the function of cancer cells for these RTKs (17).

Rapamycin acts through mTOR complex 1 and mTOR complex 2. Sirolimus (rapamycin) binds to the cytosolic immunophilin FK506 binding protein (FKBP-12), blocking the FRAP (rapamycin-associated protein - also called mTOR) signaling pathway (17).

Everolimus, produced as a derivative of mTOR inhibitor rapamycin, is used to prevent organ rejection in organ transplants and as an anticancer treatment in oncology (18). Everolimus was approved in 2010 by the US Food and Drug Administration (FDA) for the treatment of TSC-associated subependymal giant cell astrocytoma. Then, in 2012, everolimus was approved by the FDA to treat AML in TSC patients (19). The chemical structure of everolimus differs from sirolimus in that it has 2 hydroxyethyl groups at carbon number 40. Therefore, everolimus is pharmacokinetic and pharmacodynamically different from sirolimus. It has a shorter half-life, 28 hours, and is used twice time daily. The time to reach its constant concentration in the blood is four days and it reaches earlier (six days) compared to sirolimus. Also, unlike sirolimus, no induction dose is required (17).

In randomized controlled studies, it is stated that inhibition of the mTOR pathway using everolimus reduces the size of bilateral AML and surgery could be delayed with this treatment (18). Although it was observed that there was no decrease in AML dimensions during the treatment process in our case, retroperitoneal bleeding did not occur and the patient did not need nephrectomy or hemodialysis. Also, serious adverse effects of everolimus which are anemia and fatigue, as well as hypokalemia, lymphopenia, and vomiting did not observe in our case (20).

Conclusion

AML, which is seen as a part of TSC, is one of the important causes of mortality in TSC, which causes life-threatening

bleeding and requires surgical or endovascular treatments. Nephron-sparing surgery could be difficult in bilateral cases. Therefore, SAE should be considered an important treatment option in emergencies.

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Ethics

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Authorship Contributions

Surgical and Medical Practices: B.Y.E., H.S., O.E., H.Ş., Concept: H.M.D., H.S., A.N.K., Design: H.M.D., B.Y.E., O.E., A.N.K., Data Collection or Processing: H.M.D., H.S., H.Ş., Analysis or Interpretation: H.S., H.Ş., Literature Search: B.Y.E., H.S., H.Ş., A.N.K., Writing: H.M.D., H.S., O.E., A.N.K.

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